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Carbohydrate-based 1,3-oxazoline-2-thiones as original bioactive structures. Synthesis and reactivity.

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Wonder is the beginning of all science

Aristotle

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To my parents

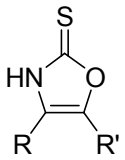
To my sister

To my grandparents

Abstract

The resistance of microorganisms to antibiotics is, in our days, one of the biggest problems in terms of public health. The research for new artificial and natural families of compounds throws us towards innovative methodologies leading to novel antibiotics.

In the present work, we are invited to dive in the "new world" of 1,3-oxazoline-2-thiones (OXTs, structure-type **i**) regarding their synthesis, reactivity and biological activity. In fact, this heterocycle is a simple synthon readily obtained by condensation of thiocyanic acid with an α-hydroxycarbonyl species. When compared to their non-aromatic counterpart 1,3-oxazolidine-2-thiones (OZTs, structure-type **ii**), this family of compounds is still unexplored.



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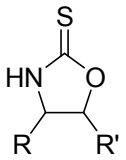
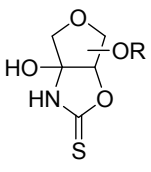


ii

When the heterocycle is anchored on a carbohydrate template (i.e. a more complex chiral α-hydroxycarbonyl moiety), original structures are expected such as OZTs fused to five- or six-membered rings (structures-type **iii**, **iv**, **v** and **vi)** and OXTs C-C linked to sugars (structure-type **vii)**, with a broad potential in organic chemistry and bioorganic applications.



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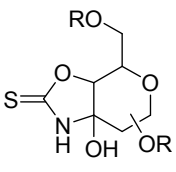

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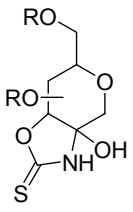

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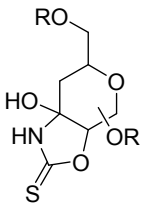

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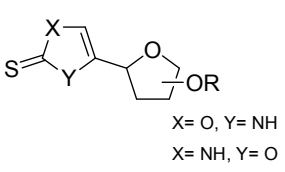


vii

The work developed in this PhD is presented in five chapters. In the first one, the formation and reactivity of sulfur and nitrogen centres of a simple OXT were investigated.

In the second one, we have developed the synthesis of thionocarbamates fused to carbohydrate templates, as well as the study of the reactivity of the sulfur center in such bicyclic systems, leading to the formation of new carbohydrate-fused oxazolidinones (OZOs).

The third chapter is dedicated to the synthesis and reactivity of C-C linked OXTs to a sugar moiety. Moreover, from the exploitation of the sulfur and nitrogen centers, different families of compounds were raised, such as pseudo-C-iminosugars and oxazoles.

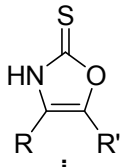
In the fourth chapter, we have explored the use of thioxo compounds as electrophiles in Pd-assisted cross-coupling methods, such as Suzuki and Stille reactions. A new modified Sonogashira cross-coupling reaction, in which copper (I) is used in catalytic amount, was developed and its feasibility was proven for a variety of substrates.

In the last chapter, we focused on the biological potential of the new molecules. We have targeted a broad spectrum of antimicrobial activity for some OXTs and OZTs, to which was added a screening of glycosidases inhibition for the pseudo-C-iminosugars.

Resumo

A resistência dos microorganismos aos antibióticos é um dos maiores problemas nos dias de hoje, em termos de saúde pública. É pois urgente desenvolver novas formas de combate a este problema, que nos orientem para a investigação de novos antibióticos naturais e artificiais.

No âmbito deste projecto de investigação somos convidados a mergulhar no "novo mundo" das 1,3-oxazolina-2-tionas (OXTs), estudando a sua síntese, reactividade e actividade biológica. Este heterociclo aromático, de estrutura **i**, é um composto facilmente obtido através da condensação do ácido tiociânico com uma unidade estrutural α-hidroxicarbonilo e, ao contrário dos compostos com o anel não aromático 1,3-oxazolidina-2-tiona (OZT, estrutura **ii)**, não está bem estudado, sendo a literatura bastante escassa no que respeita a esta família de heterociclos.



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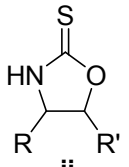
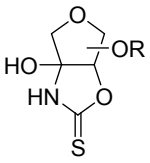


ii

A ligação de OXTs a hidratos de carbono modelo, que possuem a unidade α-hidroxicarbonilo, conduz à formação de estruturas originais, como por exemplo derivados de OZT fusionada a açúcares de cinco e seis membros (estruturas de tipo **iii**, **iv**, **v** e **vi)**, bem como pseudo-*C*-nucleósidos de tipo **vii**, com enorme potencial em química orgânica e em aplicações bioorgânicas.



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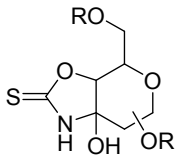

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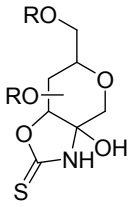

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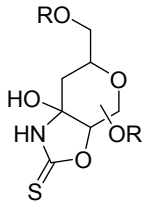

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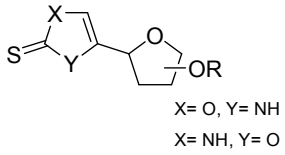

vii

O projecto desenvolvido neste doutoramento é apresentado em cinco capítulos.

Numa primeira parte do projecto, foram investigadas as condições ideais para a síntese de OXTs, tendo sido demonstrado que a sua formação é possível com uma vasta gama de solventes e ácidos, sendo o aspecto mais importante a escolha do par solvente/ácido para efectuar a reacção. Esta primeira parte foi também dirigida para o estudo de reactividade padrão do enxofre e do azoto, envolvendo processos de alquilação, acilação, sulfonilação e adições de tipo Michael. Durante todos estes processos, verificou-se que a aromaticidade do anel assume um papel muito importante na reactividade do enxofre e, em especial, na do azoto, ficando demonstrado que a reactividade de OXTs é completamente diferente da descrita na literatura referente às OZTs.

Numa segunda parte do trabalho, os nossos esforços concentraram-se na síntese de tionocarbamatos fusionados a hidratos de carbono modelo, com estruturas de tipo **iii**, **iv**, **v** e **vi**. Assim, envolvendo reacções de protecção, desprotecção e oxidação, foi introduzida a unidade α-hidroxicarbonilo em açúcares a partir dos compostos 1,2-isopropilideno-α-D-xylofuranose, α-D-glucopiranósido de metilo e β-D-glucopiranósido de metilo. Estas α-hidroxicetonas complexas foram utilizadas como precursores das moléculas-alvo, as OXTs fusionadas aos acúcares. No entanto, a condensação com o ácido tiociânico conduziu à formação de OXTs fusionadas hidratadas, que revelaram uma maior estabilidade em relação às correspondentes OXTs fusionadas.

Muito importante é também o facto de a estereoquímica destas OXTs fusionadas hidratadas depender absolutamente da posição e da orientação do grupo hidroxilo envolvido na reacção – uma relação *cis* foi sempre verificada.

Quando a condensação com o ácido tiociânico é realizada entre as posições 2 e 3 do hidrato de carbono, a configuração da posição anomérica mostra ter influência decisiva na formação das OXTs hidratadas – para os α-glicósidos, em que se observa a relação 1,2-*cis*, a reacção de condensação mostra-se ineficaz. No entanto, quando a condensação é efectuada nos β-glicósidos, a mesma decorre sem problemas e com bons rendimentos.

Após protecção do enxofre através de uma reacção de *S*-benzilação e tratamento com ácido tríflico foi possível a desidratação dos compostos de tipo **iii,** conduzindo à formação das correspondentes OXTs fusionadas. Os compostos *S*-benzilados foram também transformados em 1,3-oxazolidina-2-onas, recorrendo ao uso de *m*-CPBA, com bons rendimentos.

A terceira parte deste projecto foi dedicada à elaboração de OXTs ancoradas a hidratos de carbono modelo, com estrutura geral **vii**. Se, por um lado, a condensação de α-hidroxicetonas com o ácido tiociânico foi efectuada com bons rendimentos, por outro lado, recorrendo ao rearranjo de Pummerer, foi possível sintetizar α-hidroxaldeídos que, após condensação com o ácido tiociânico, conduziram à formação de OXTs ancoradas a açúcares, que se distinguem das primeiramente sintetizadas através da permuta entre as posições dos átomos de oxigénio e azoto no heterociclo.

A partir do estudo de reactividade de alguns dos pseudo-*C*-nucleósidos sintetizados, foi possível explorar diversas metodologias que conduziram à formação de diferentes famílias de compostos. Assim, quando as estruturas de tipo **vii** são submetidas directamente à acção de *m*-CPBA, foi verificada a extrusão do enxofre, levando à formação dos oxazoles correspondentes. Este estudo levou ao desenvolvimento de uma nova metodologia que permite o acesso à formação de oxazoles, a partir de OXTs.

Uma outra família de moléculas "nasceu" aquando da exploração do carácter nucleófilo do azoto nas OXTs ancoradas a açúcares, em reacções de adição intramolecular ao grupo aldeído, originando pseudo-*C*-iminoaçúcares a partir de hexoses. Assim, alguns compostos análogos à castanospermina foram facilmente preparados, com rendimentos globais entre os 52% e os 67%, a partir de 1,2:5,6-di-*O*-isopropilideno-α-D-glucofuranose.

No decurso da quarta parte deste projecto, o nosso interesse foi dirigido à exploração do uso de tioamidas como electrófilos em reacções de acoplamento assistidas por paládio, sob a irradiação micro-ondas.

Assim, no caso dos acoplamentos de Suzuki e Stille modificados a partir de OZTs fusionadas, foi comparada a reactividade para uma sequência a dois passos (*S*-benzilação selectiva + condições de acoplamento de Suzuki ou Stille) e a um passo (condições de acoplamento de Suzuki ou Stille), tendo-se verificado um aumento significativo do rendimento das reacções de acoplamento quando foi utilizada a sequência com dois passos.

Contrariamente ao observado para as OZTs fusionadas, quando os protocolos de Suzuki e Stille foram aplicados a OXTs, estes foram bastante eficazes, sendo assim dispensável a reacção de protecção do enxofre antes da reacção de acoplamento. Mostrou-se, assim, que tanto para a reacção de acoplamento de Suzuki como para a de Stille, o sucesso do acoplamento directo assistido por Pd e mediado por Cu(I) depende da natureza aromática/não aromática do anel.

Como extensão às reacções de acoplamento anteriormente mencionadas, a reacção de Sonogashira foi então explorada. Esta investigação levou ao desenvolvimento de uma nova metodologia no que respeita ao acoplamento directo duma função tiocarbamato com um alcino terminal. Neste processo modificado da reacção de Sonogashira, o efeito cooperativo de duas espécies diferentes de cobre (I) – CuI e CuTC –, sob irradiação microondas, foi estratégico para o sucesso desta nova reacção de acoplamento C-C catalisada por cobre.

Os compostos sintetizados foram totalmente caracterizados recorrendo a diversas técnicas, como a ressonância magnética nuclear mono- e bidimensional, espectrometria de massa, espectrometria de massa de alta resolução, infra-vermelhos e, para compostos cristalinos, recorreu-se também à cristalografia por raios-X.

Na quinta e última parte do projecto, o nosso interesse foi dedicado ao potencial biológico de alguns dos compostos sintetizados. Assim, alguns dos compostos foram submetidos a testes de actividade antimicrobiana, bem como de inibição de glicosidases. Embora alguns compostos apresentem actividade biológica promissora, não nos foi possível estabelecer uma relação estrutura/actividade.

Assim, o projecto aqui apresentado descreve a síntese, a exploração química e biológica de OXTs simples, OXTs ancoradas e OZTs fusionadas a hidratos de carbono modelo. A exploração da química do enxofre nestes sistemas bicíclicos originou novas famílias de compostos, como as OZO (no caso das OZT hidratadas fusionadas) ou oxazoles (no caso das OXTs ancoradas). A electrofilia da ligação C=S permitiu também a exploração de reacções de acoplamento dos tipos Suzuki e Stille, verificando-se que, ao aplicar directamente o protocolo das reacções de Suzuki e Stille às OXTs aromáticas, o processo revelou ser muito eficiente, enquanto que duas etapas são necessárias quando as OZTs não aromáticas fusionadas são usadas como electrófilos. A electrofilia desta ligação permitiu também o desenvolvimento e a generalização de uma nova metodologia, em que o cobre (I) é usado em quantidades catalíticas, que levou ao acoplamento de tiocarbamatos com alcinos terminais – reacção de Sonogashira modificada.

Já a exploração do carácter nucleófilo do azoto para as OXTs ancoradas aos hidratos de carbono, levou à rápida formação de pseudo-*C*-iminoaçúcares, com geometrias originais e potenciais inibidores de glicosidases.

Keywords / Palavras Chave

1,3-oxazoline-2-thione	1,3-oxazolina-2-tiona
1,3-oxazolidine-2-thione	1,3-oxazolidina-2-tiona
Oxazoles	Oxazoles
Condensation	Condensação
α-hydroxycarbonyl	α-hidroxicarbonilo
Carbohydrates	Hidratos de carbono
Pseudo-*C*-nucleosides	Pseudo-*C*-nucleósidos
Pseudo-iminosugars	Pseudo-iminoaçucares
Coupling reactions	Reacções de acoplamento
Aromatic ring	Anel aromático

List of abbreviations

BPSE	1,2-bis-(phenylsulfonyl)ethylene
ca	*circa*, approximately
CSA	camphorsulfonic acid
Cy	cyclo-hexane
DAG	diacetoneglucose
DCM	dichloromethane
DIEA	Diisopropylamine
DMF	dimethylformamide
DMP	dimethoxypropane
DMSO	dimethylsulfoxide
eq	equivalent
h	hour
Hz	Hertz
IR	Infra Red
m-CPBA	*m*-Chloroperbenzoic acid
min	minute
mL	milliliter
mmol	millimole
MS	mass spectometry
NBS	*N*-bromosuccinimide
NMR	Nuclear Magnetic Ressonance
NOESY	Nucleor Overhauser Effect Spectroscopy
OXT	1,3-oxazoline-2-thione
OZO	1,3-oxazolidinone
OZT	1,3-oxazolidine-2-thione
PDC	pyridinium dichromate
PE	petroleum ether
ppm	parts per million
r.t.	room temperature
S.M.	starting material
TBDMSCl	*tert*-butyldimethylsilyl chloride
TEMPO	2,2,6,6-tetramethylpiperidioxyl
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
THF	tetrahydrofuran
TsOH	toluenesulfonic acid

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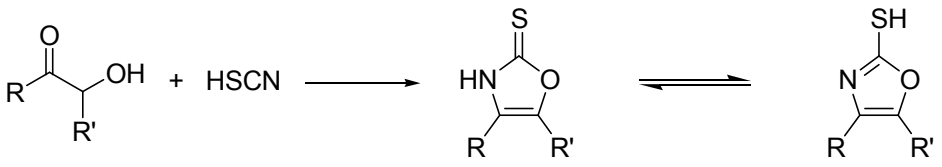
CHAPTER I

Simple 1,3-oxazoline-2-thiones

1. Introduction – General methods for the synthesis of 1,3-oxazoline-2-thiones

Despite their simple structure, 1,3-oxazoline-2-thiones have scarcely been studied, in comparison with their non-aromatic counterparts 1,3-oxazolidine-2-thiones or heteroaromatic analogues such as imidazolinethiones. Considering our main goal – i.e. conjugation of OXTs onto carbohydrate scaffolds – it was pertinent to start with the investigation of the preparation and reactivity of simple OXTs.

Surprisingly, only a few representatives of this simple heterocyclic family are reported in the literature. Until the 80s, the only known methodology to synthesize OXTs was the procedure described by Willems and Vandenberghe[1,2,3]: condensation of an α-hydroxycarbonyl entity with thiocyanic acid. A possible thione-thiol tautomeric equilibrium could be written between an OXT and a 2-mercapto-1,3-oxazole (Scheme 1).



R= Me, R'= H **1**

R= Me, R'= Me **2**

R= Ph, R'= Ph **3**

Scheme 1

The above method allows the preparation of OXTs bearing substituents at C-4 and C-5 positions. A limited group of molecules has been prepared: 4-methyl-1,3-oxazoline-2-thione (**1**), 4,5-dimethyl-1,3-oxazoline-2-thione (**2**) and 4-phenyl-1,3-oxazoline-2-thione **(3)**.[4,5,6,7]

[1] Willems, J.F.; Vandenberghe, A. *Bull. Soc. Chim. Belg*. **1961**, *70*, 745-748.
[2] Lacasse, G.; Mucowki, J. M. *Can. J. Chem.* **1972**, *50*, 3082-3083.
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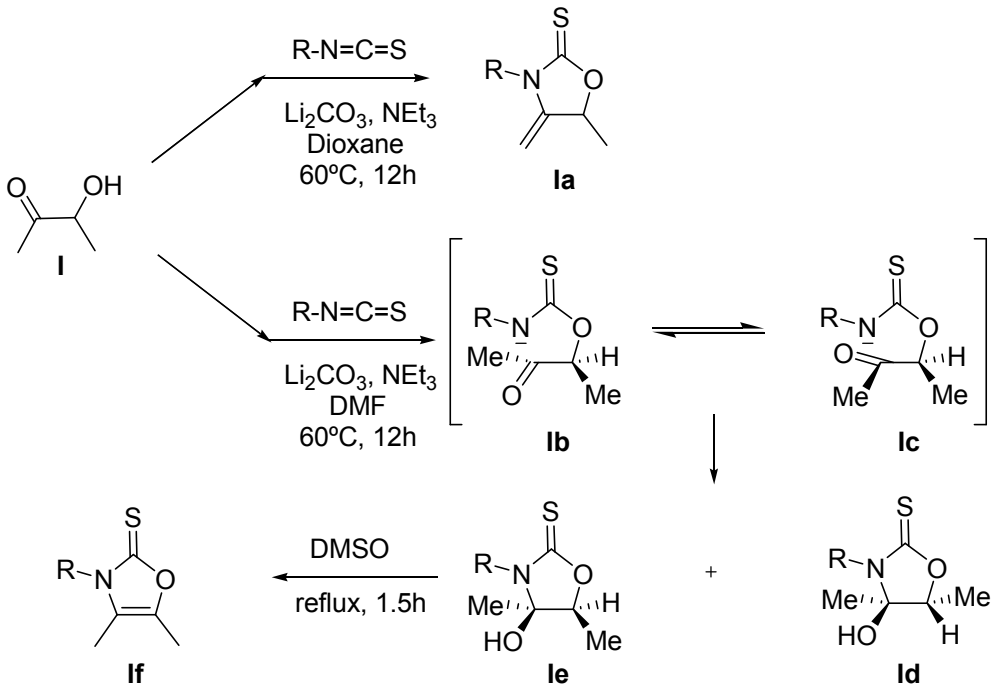
[6] Kapsomenos, G. S.; Akrivos, P. D. *Can. J. Chem.* **1988**, *66*, 2835-2838.

More recently, and following a similar synthetic approach, Tamariz[8] made use of a regioselective tandem condensation between α-hydroxyketones and isothiocyanates (Scheme 2).



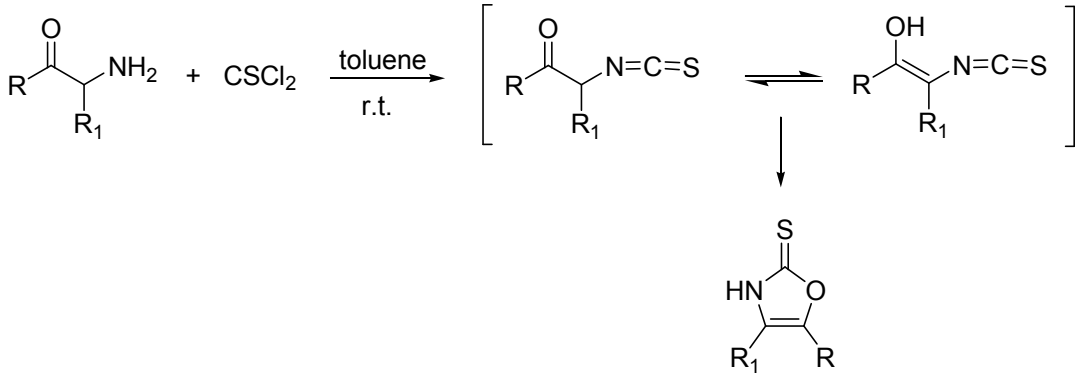
Scheme 2

Tamariz and coll. observed that when the reaction between the α-ketol **I** and isothiocyanates is performed in dioxane, the OZT **Ia** was formed while DMF appeared to be a solvent of choice to efficiently obtain the hemiaminals **Id** and **Ie**. In refluxing DMSO, the hemiaminals undergo dehydration to afford the *endo* heterocyclic N-substituted OXTs **If** in good yields (66-89%). The regioselectivity observed in the dehydration step resulted from a thermodynamic control to the more stable aromatic structure.[9] The authors have explored a one-pot process to obtain

[7] Shafer, C. M.; Molinski, T. F. *J. Org. Chem.* **1998**, *63*, 551-555.
[8] Gonzalez-Romero, C.; Martinez-Palou, R.; Jimenez-Vazquez, H. A.; Fuentes, A.; Jimenez, F.; Tamariz, J. *Heterocycles* **2007**, *71*, 305-321.
[9] Traynelis, V. J.; Hergenrother, W. L.; Livingston, J. R. *J. Org. Chem.* **1962**, *27*, 2377-2383.

compounds **If** through a cascade sequence involving condensation between **I** and the isothiocyanate, followed by cyclization and dehydration.

In 1983, Maretvon and coll. have demonstrated that the condensation of thiophosgene with an aminoketone is also an efficient method to obtain OXTs in good yields.[10] When thiophosgene reacts with the aminoketone, the isothiocyanate is first formed. The keto-enol equilibrium allows cyclization at room temperature. The authors noticed that the presence of base not surprisingly increased the rate of cyclization (Scheme 3).



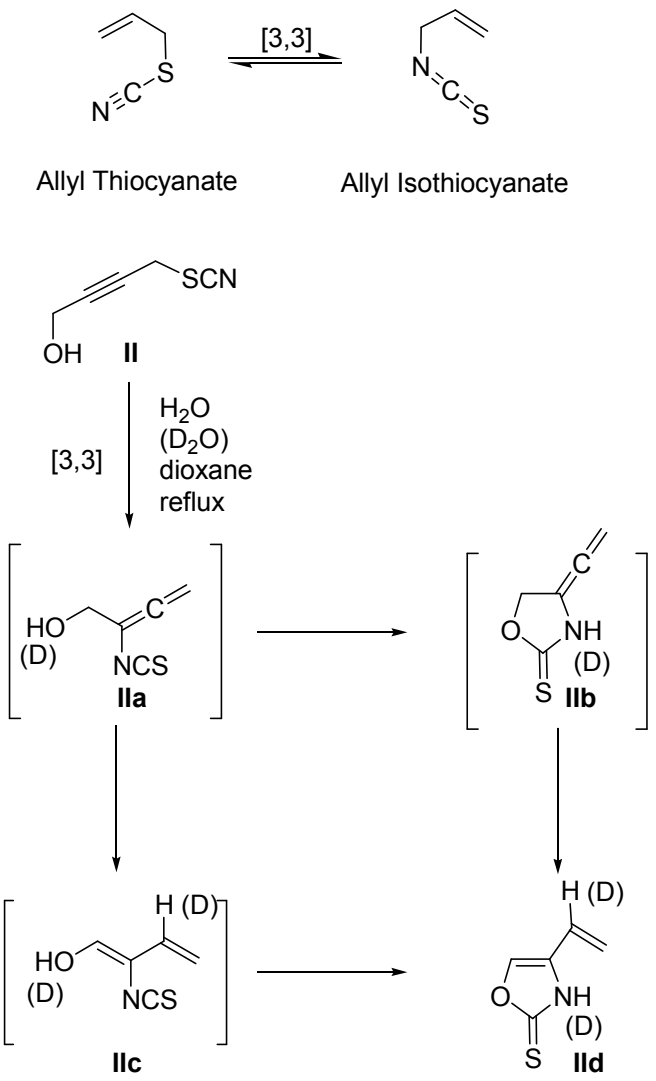
Scheme 3

In recent years, Banert and coll.[11] have disclosed an original way to prepare an OXT, with the synthesis of 4-ethenyl-3H-oxazole-2-thione (**IId**). The authors applied a [3,3] sigmatropic rearrangement of propargyl thiocyanates (Scheme 4), a very old reaction discovered independently by Billeter[12] and by Gerlich.[13] Those showed that by heating the propargyl thiocyanate (**II**) in a protic solvent, an intramolecular reaction occurred to give rise to the OXT **IId** in 56% yield. It was postulated that the dienyl isothiocyanates **IIa** and **IIc** underwent an intramolecular nucleophilic addition of the alcohol to form the OXT **IId**. When performed in D_2O instead of H_2O, the

[10] Bobosik, V.; Piklerova, A.; Maretvon, A. *Coll. Czech. Chem. Commun*. **1983**, *48*, 3421-3425.
[11] Banert, K., Groth, S.; Hückstädt, H.; Lehmann, J.; Scholtt, J.; Vrobel, K. *Synthesis* **2002**, 1423-1433.
[12] Billeter, O. *Ber. Dtsch. Chem. Ges.* **1875**, *8*, 462-466.
[13] Gerlich, G. *Justus Liebigs Ann. Chem.* **1875**, *178*, 80-91.

reaction displayed deuterium incorporation, not only onto the nitrogen atom, but also in the α position of the side chain.

An intramolecular hydrogen shift was therefore excluded, the protic solvent thus appearing crucial in the C=C bond migration step.

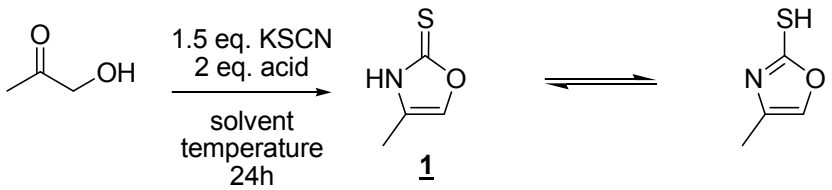


Scheme 4

2. OXT Formation

2.1. Optimization of the conditions

Considering those previous approaches for the synthesis of OXTs and with a view to understanding more about this interesting heterocycle, we decided to reconsider and optimize the conditions for the formation of OXTs from a α-hydroxycarbonyl precursor. With that in mind, we turned back to Willems and Vandenberghe's report[1], describing the simplest method for the synthesis of non N-functionalised OXTs and allowing us to study the different reactivity centers of an OXT. The initial paper, reported the use of acetol (1-hydroxypropan-2-one) as starting material, which underwent condensation with thiocyanic acid in refluxing ethanol over 24h to produce 4-methyl-1,3-oxazoline-2-thione **1** in 77% yield (Scheme 5).



Scheme 5

We have reconsidered the condensation and modified some of its parameters - namely the solvent and the acid presented in solution - in order to try and optimize the reaction conditions for the synthesis of OXTs. The results are shown in Table 1.[14]

[14] Leconte, N.; Silva, S.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301-305.

entry	solvent	acid	Δ	yield (%)
1	EtOH	HCl	78	74
2	H_2O	$TsOH.H_2O$	65	70
3	H_2O	H_2SO_4	65	17
4	H_2O	HCl	65	52
5	THF	HCl	65	75
6	THF	H_2SO_4	65	75
7	THF	$TsOH.H_2O$	65	37
8	H_2O	AcOH	65	---
9	AcOH	-	65	---

Table 1

From the previous table, it clearly emerged that under diverse acidic conditions, both protic and aprotic solvents could be used to prepare OXT **1**. The reaction seemed to depend mostly on the choice of a proper solvent-acid couple, with 70-75% yields in optimal cases. For entry 7, (THF/$TsOH.H_2O$) the yield obtained was moderate due to purification problems. For entries 8 and 9, no reaction was observed: the lower acid strength of acetic acid might be the reason for the non-formation of OXT.

2.2. Formation of miscellaneous OXTs

With the purpose of extending the protocol, we have modulated the α-hydroxyketone structures by using commercially available starting materials: α-hydroxyacetophenone, glycolaldehyde dimer, 2,2-dimethoxyethanol and 1,3-dihydroxyacetone. The method of Willems and Vandenberghe was applied with some variations of the reaction conditions (Table 2).

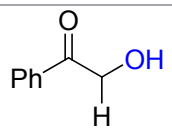
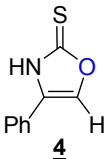
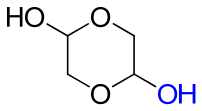
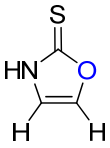
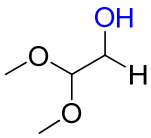
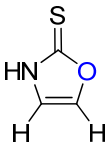
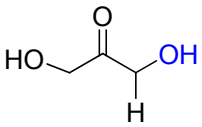
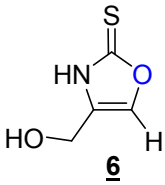
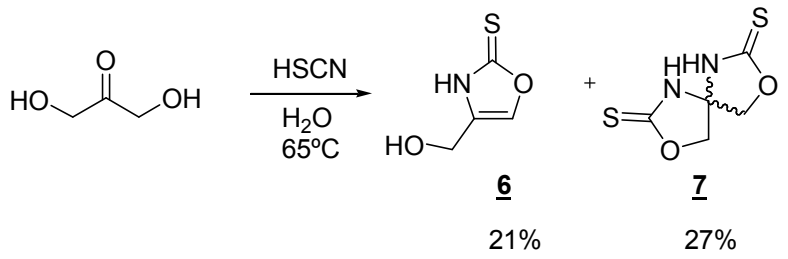
starting material	solvent	acid	Δ	KSCN (eq)	yield %	product
 α-hydroxyacetophenone	EtOH	HCl	Reflux	1.5	83	 **4**
	EtOH/H_2O	HCl	65	1.5	Deg.	
	H_2O	HCl	65	1.5	Deg.	
 glycolaldehyde dimer	EtOH	HCl	reflux	1.5	95	 **5**
	H_2O	HCl	80	1.5	41	
	THF	HCl	60	1.5	54	
 dimethoxyethanol	EtOH	HCl	Reflux	1.5	91	 **5**
	H_2O	HCl	80	1.5	62	
 1,3-dihydroxyacetone	EtOH	HCl	65	1.5	5	 **6**
	EtOH/H_2O(5%)	HCl	65	1.5	16	
	EtOH/H_2O(5%)	HCl	65	1	18	
	H_2O	HCl	65	1	21	

Table 2

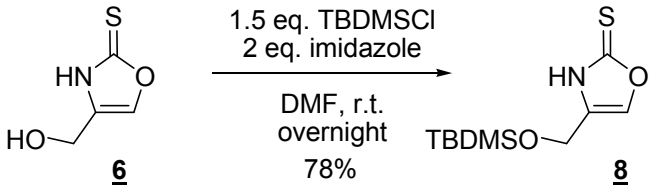
The above results demonstrate that for the three top substrates, the best results were obtained by applying the EtOH/HCl system. In presence of water, the yields dropped significantly and even degradation occurred in the case of α-hydroxyacetophenone. In contrast, the formation of OXT **6** from 1,3-dihydroxyacetone seemed to be favored in presence of water. Nevertheless, the above starting material proved more tricky, mainly due to a competitive reaction leading to the formation of a spiro-bis-OZT (Scheme 6) previously reported by Köll et al.[15]

[15] Saul, R.; Kern, T.; Kopf, J.; Pinter, I.; Köll, P. *Eur. J. Org. Chem*. **2000**, 205-209.



Scheme 6

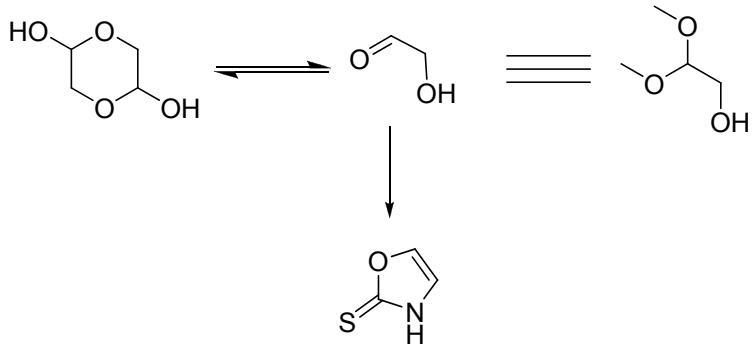
The OXT **6** showed limited stability: in order to overcome this problem, the primary alcohol was protected, for a better characterization. In doing so, we have chosen the *tert*-butyldimethylsilyl ether (TBDMS) as protective group for its neutral conditions of introduction.[16,17] Under standard conditions, the *O*-silylated compound **8** was prepared in good yield (Scheme 7).



Scheme 7

From a general point of view, it can be concluded that the couple EtOH/HCl allows the synthesis of OXTs in good yields. Moreover, the presence of a free carbonyl group is not an essential requisite for the reaction: the assays with 2,2-dimethoxyethanol and glycolaldehyde dimer are indicative that protected aldehydes can be used as substrates. In fact, when applying acidic conditions, deprotection regenerates the electrophilic center able to condense with thiocyanic acid (Scheme 8). This fact is significant for the synthesis of OXTs, considering that (i) a limited range of α-hydroxyketones is commercially available and (ii) most of them pose stability problems. In opposite way, protected ketones are quite easily prepared and generally stable.

[16] Corey E. J., Venkateswarlu A. *J. Am. Chem. Soc.* **1972**, *94*, 6190-6191.
[17] Greene T. W.; Wuts P. G. M. *Protective Groups in Organic Synthesis* 4th Edition, John Wiley&Sons Ed., **1999**.



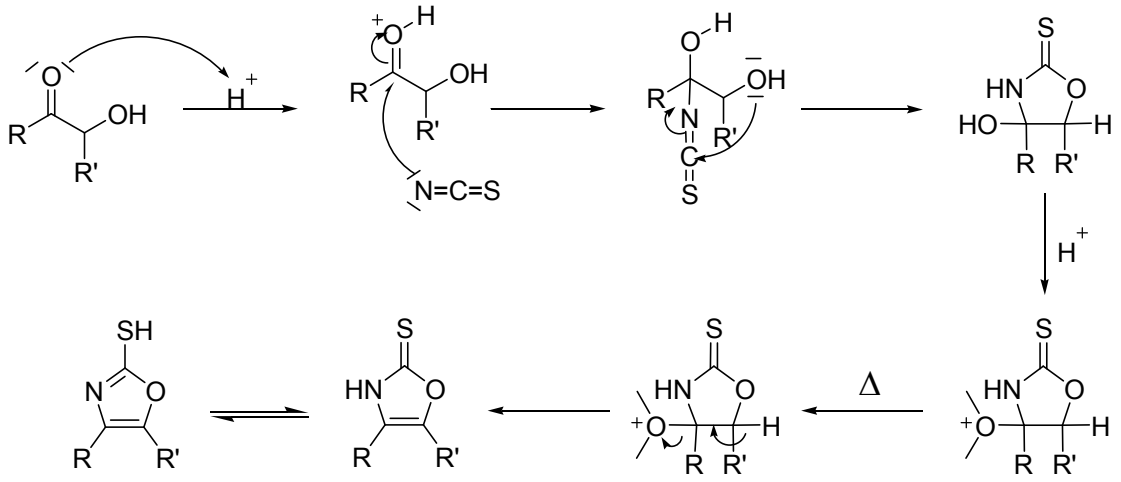
Scheme 8

In terms of UV absorption, OXTs are far superior to the starting materials, which makes their detection easier (λ_{max} in the 280-300 nm range) and subsequent purification by column chromatography.[18]

2.3. What about the mechanism?

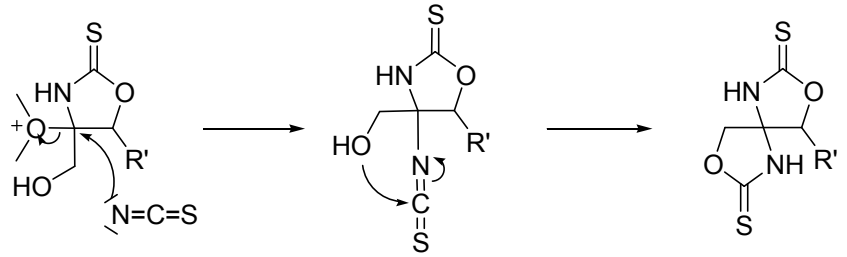
In fact, different mechanisms could be postulated for OXT formation. However, it can be assumed that, after ketone activation in acidic medium, the thiocyanate ion reacts by nucleophilic addition forming a transient isothiocyanate, which cyclize with the α-alcohol. The cyclization product – an 1,3-oxazolidine-2-thione – undergoes (under acidic and thermal condition) water elimination to consequently form the aromatic OXT (Scheme 9).

[18] Gompper, R.; Herlinger, H. *Chem. Ber*. **1956**, *89*, 2816-2824.



Scheme 9

In the case of spiro-bis-OZT **7**, a second nucleophilic attack on the C-4 position of the hydroxyl-OZT can be postulated and the second cyclisation then follows a similar mechanism (Scheme 10).

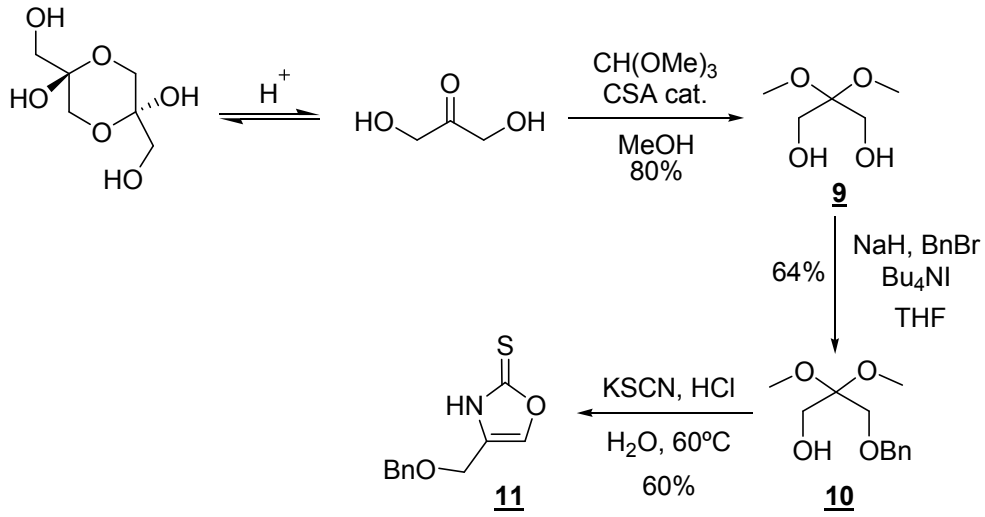


Scheme 10

2.4. In order to prevent spiro-bis-OZT formation – the importance of monobenzylation

In order to preclude the competitive formation of a bis-OZT and considering that protected ketones can be efficiently transformed into an OXT, we have considered the selective protection of 1,3-dihydroxyacetone. Protection of the keto group followed by hydroxyl monoprotection was envisaged. This pathway was applied to the dihydroxyacetone dimer, which equilibrates in solution with the monomer. The dimethyl acetal **9** was prepared in good yield, according to a slight

modification of a previously reported method.[19,20] The acetal **9** was selectively mono *O*-benzylated[21] to give the monoalcohol **10** in 64% yield. The best result was obtained after reaction optimization, using direct alkylation with sodium hydride in THF (Scheme 11). OXT formation was applied on precursor **10** using water as solvent (the best conditions used for OXT formation when starting from 1,3-dihydroxyacetone) and condensation with thiocyanic acid occurred in 60% yield. Thus, a new 4-substituted OXT **11** was obtained in 31% overall yield.



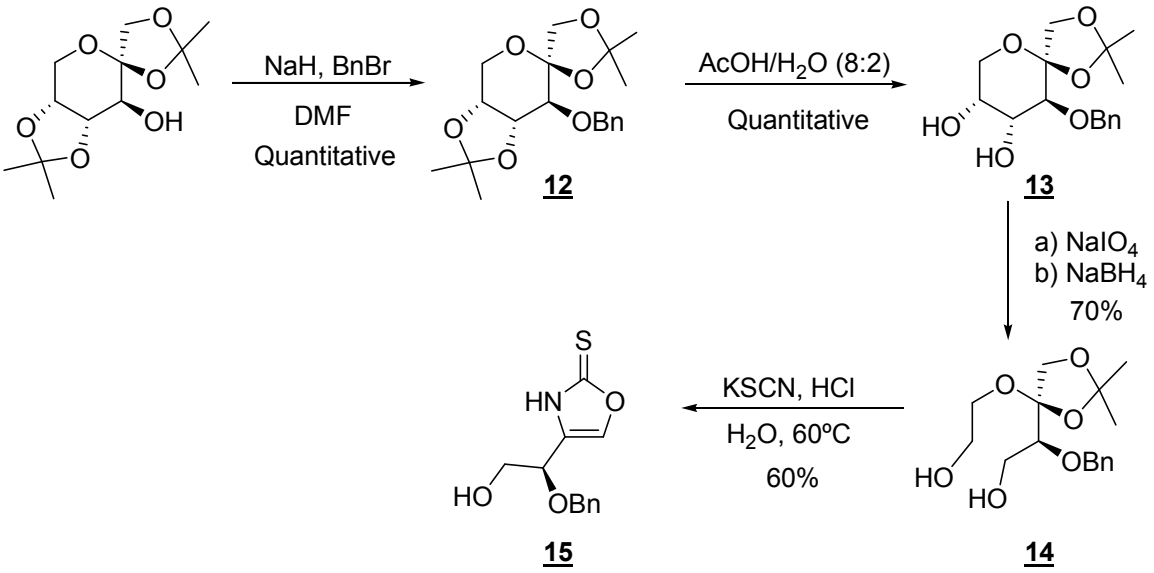
optimization of the monobenzylation reaction	
reaction conditions	**yield of 10 (%)**
Bu_2SnO/BnBr/toluene	34
BnBr/NaH/DMF	18
BnBr/NaH/THF	64

Scheme 11

[19] Cesarotti, E.; Antognazza, P.; Pallavicini, M.; Villa, L. *Helv. Chim. Acta* **1993**, *76*, 2344-2349.
[20] Ferroni, E. L.; DiTella, V.; Ghanayem, N.; Jeske, R.; Jodlowski, C.; O'Connell, M.; Styrsky, J.; Svoboda, R.; Venkataraman, A.; Winkler, B. M. *J. Org. Chem.* **1999**, *64*, 4943-4945.
[21] Gennari, C.; Cozzi, P. G. *J. Org. Chem* **1988**, *53*, 4015-4021

2.5. Formation of more complex OXT: carbohydrates – source of chirality

The study was further extended to OXT formation on a more complex structure involving a carbohydrate backbone. Starting with 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose, benzylation of the free 3-OH was realized under standard conditions.[22,23] The benzyl ether **12** underwent selective 4,5-hydrolysis[24] and the *cis* vicinal diol **13** was submitted to oxidative cleavage followed by reduction.[24] The acyclic diol **14** was obtained in 70% overall yield. Direct condensation of **14** with thiocyanic acid leads to the OXT **15** in a reasonable 60% yield. This OXT bearing a well-defined chirality center at 6-position has thus been prepared through a short reaction sequence involving simple and efficient steps (Scheme 12).

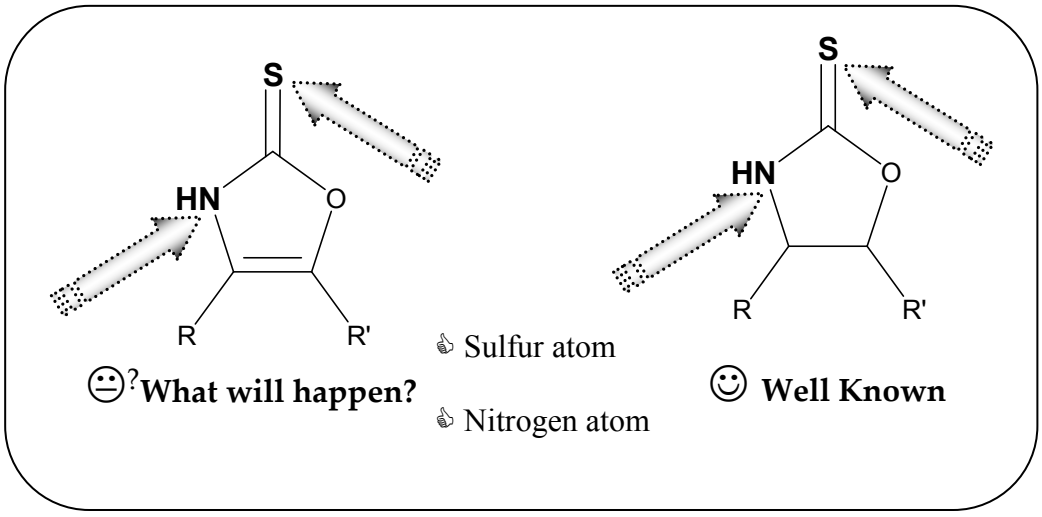


Scheme 12

[22] Tatibouet, A.; Lefoix, M.; Nadolny, J.; Martin, O. R.; Rollin, P.; Yang, J.; Holman, G. D. *Carbohydr. Res.* **2001**, *333*, 327-334.
[23] Tatibouet, A.; Lawrence, S.; Rollin, P.; Holman, G. D. *Synlett* **2004**, 1945-1948.
[24] Milecki, J.; Zamaratski, E.; Maltseva, T. V.; Foldesi, A.; Adamiak, R. W.; Chattopadhyaya, J. *Tetrahedron* **1999**, *55*, 6603-6622.

3. Reactivity of OXTs

The study of the conditions for the formation of OXTs gave us the opportunity to prepare a panel of molecules using different conditions and various starting materials. To develop our knowledge on this aromatic heterocycle, it is logical to compare its reactivity to that of a closely-related structure, the non aromatic 1,3-oxazolidine-2-thione (OZT), which has been extensively studied in our laboratory. On both heterocycles, two major reactive centers could be targeted: the nitrogen and sulfur atoms.



3.1. Pearson theory

The two nucleophilic characters of a thionocarbamate function open two possibilities depending, from one side, on the reaction conditions and from another side, on the properties of both atoms. The difference of reactivity between sulfur and nitrogen atoms, two electron-rich centers, can be rationalized according to the Hard/Soft Acid Base principle (HSAB), introduced by Ralph Pearson in 1963.[25,26,27]

[25] Pearson, R. G. *J. Am. Chem. Soc*. **1963**, *85*, 3533-3539.
[26] Ho, T.-L. *Chem. Rev.* **1975**, *75*, 1-20.
[27] Woodward, S. *Tetrahedron* **2002**, *58*, 1017-1050.

Trying to give an explanation for the chemical reactivity, selectivity and stability of compounds, Pearson has classified the chemical entities, including atoms, molecules, ions and free radicals as:

- ☑ Hard bases – donor atoms:
  - Have low polarizability;
  - Have high electronegativity (low HOMO);
  - Are not easily oxidizable;
  - Are associated with empty orbitals of high energy.
- ☑ Hard acids – acceptor atoms:
  - Have small size,
  - Have low polarizibility;
  - Have high positive charge;
  - Have high electronegativity (high LUMO);
  - Do not contain unshared electron pairs in their valence shells.
- ☑ Soft bases – donor atoms:
  - Have high polarizibility;
  - Have low electonegativity (high HOMO);
  - Are easily oxidizable;
  - Are associated with empty orbitals of low energy.
- ☑ Soft acids – acceptor atoms:
  - Have large size;
  - Have high polarizibility;
  - Have low positive charge or no charge;
  - Have low electronegativity (low LUMO);
  - Contain unshared electron pairs in their valence shells.

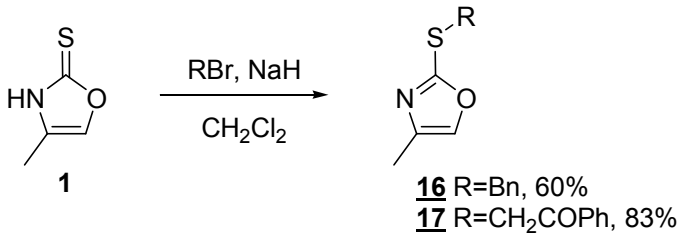
Pearson's principle states that hard acids (high LUMO) prefer to coordinate to hard bases (low HOMO) – ionic interaction –, while soft acids (low LUMO) prefer to coordinate to soft bases (high HOMO) – covalent bonding.

Accordingly to the HSAB theory, for a thionocarbamate structure, the sulfur atom should be a softer base compared to the nitrogen atom which would be a harder base.[28]

To investigate the parallel S and N reactivities, we have selected OXT **1** as key synthon and compared the results with those previously reported on OZTs.

3.1.1. Sulfur alkylation

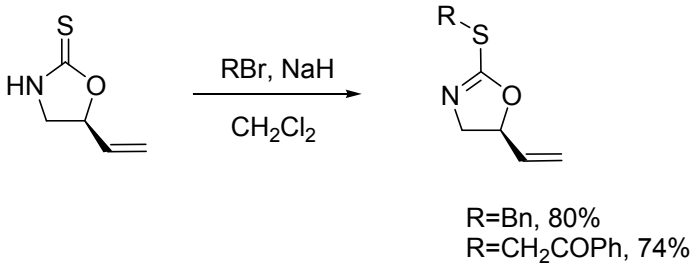
Application to our reference OXT **1** of standard alkylation conditions - treatment of OXT with sodium hydride in the presence of benzyl bromide or bromoacetophenone – leads to the formation of 2-alkylsulfanyloxazoles **16** and **17** in good yields (Scheme 13).



Scheme 13

These results are in agreement with those reported by Rollin and coll.[29,30] in the case of simple OZTs, namely a thio-selective reaction with halides R-X, leading to the formation of alkylsulfanyloxazolines (Scheme 14).[31,32,33]

[28] Fujita, E.; Nagao, Y.; Seno, K.; Takao, S.; Miyasaka, T.; Kimura, M.; Watson, W. H. *J. Chem. Soc., Perkin Trans. I* **1981**, 914-919.
[29] Leoni, O.; Bernardi, R.; Gueyrard, D.; Rollin, P.; Palmieri, S. *Tetrahedron: Asymm.* **1999**, *10*, 4775-4780.
[30] Gueyrard D.; Grumel V.; Leoni O.; Palmieri S.; Rollin P. *Heterocycle*s **2000**, *52*, 827-843.
[31] Pridgen, L. N.; Killmer, L. B.; Webb, L. *J. Org. Chem*. **1982**, *47*, 1985-1989.
[32] Davidson R. M.; Byrd G. D.; White E.; Margolis S.; A.; Coxon B. *Magn. Res. Chem.* **1986**, *24*, 929-937.
[33] Meszaros, P.; Pinter, I.; Kovacs, J.; Toth, G. *Carbohydr. Res.* **1994**, *258*, 287-291.



Scheme 14

☝ Taking into consideration that both R-Br used are soft electrophiles, the above results express that sulfur center in OXTs behaves as a soft nucleophilic center as in OZTs, in conformity with Pearson's theory.

3.1.2. *N*-Acylation

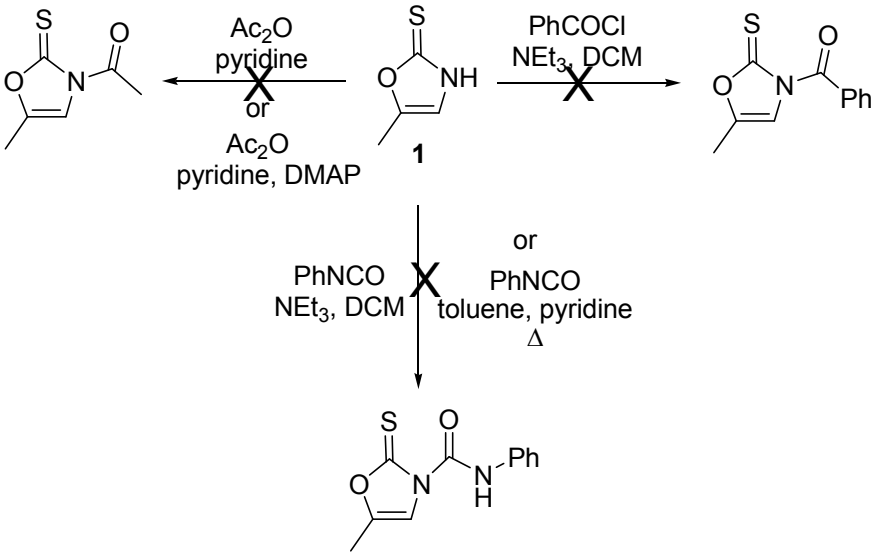
Further reactivity study of OXTs should take the nitrogen center into consideration: an acylation reaction would constitute a simple test.

Based on literature, we scrutinized that acylating reagents such as acyl chlorides or carboxylic anhydrides generally behave as hard electrophiles species, leading to regiospecific *N*-acylation.[34,35]

From previous reports, OZTs or thiazolidinethiones are best *N*-acylated with acyl chlorides in the presence of NEt_3 at room temperature.[36]

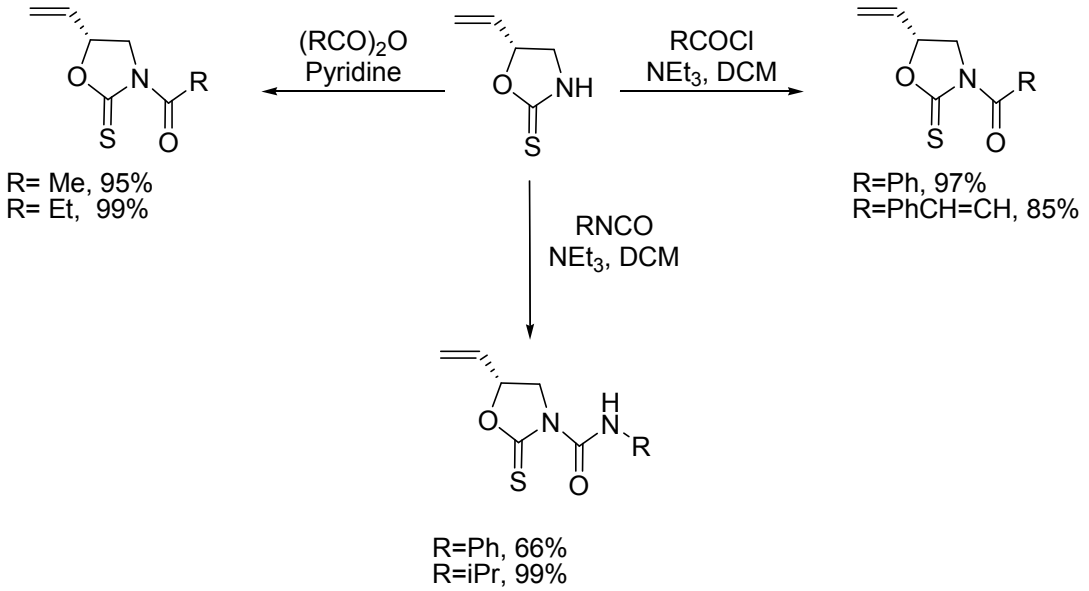
When standard *N*-acetylation conditions (acetic anhydride in pyridine) were applied to OXT **1,** no reactivity was observed. Trying to force the reaction conditions by the use of DMAP, no improvement was noticed. Benzoyl chloride in the presence of NEt_3 was then tested, but again without results. Following a similar approach, treatment of OXT **1** with phenyl isocyanate did not produce the desired urea (Scheme 15). In all cases, the starting material was totally recovered.

[34] Brown E.; Joyeu R.; Paterne M. *Tetrahedron Lett.* **1977**, 2575-2578.
[35] Crimmins T.; King B. W.; Tabet E. A.; Chaudhary K. *J. Org. Chem.* **2001**, *66*, 894-902.
[36] Plusquellec D.; Roulleau F.; Bertho F.; Lefeuvre M.; Brown E. *Tetrahedron* **1986**, *42*, 2457-2467.



Scheme 15

These results contrast strongly with those reported by Gueyrard et al, which demonstrated that simple OZTs smoothly react with acyl chlorides, carboxylic anhydrides and isocyanates to afford the corresponding *N*-acylated products in good yields (Scheme 16).[30]



Scheme 16

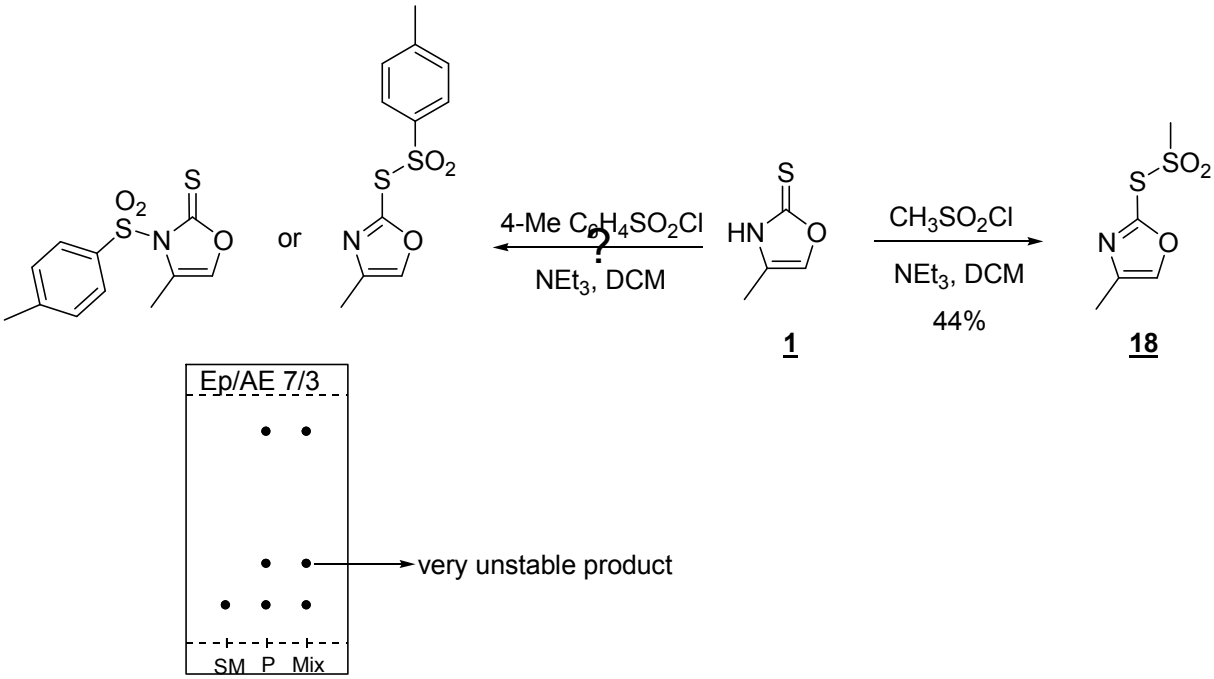
☝ Analyzing the above results, it becomes clear that the nitrogen atom behaves differently when incorporated into an OXT or into an OZT heterocycle. At this stage of our study, a simple conclusion could be that the nucleophilicity in the OXT is much smaller than in OZT, and thus hampers the acylation reaction.

3.1.3. Sulfonylation

In order to understand more about the reactivity of the N-center, the sulfonylation reaction was also attempted on OXT **1**, expecting, by use of sulfonyl chlorides, a N-functionalisation.

Under standard conditions, *p*-toluenesulfonyl chloride converted OXT **1** into a faster-moving product (TLC), whose isolation proved very tricky. A crude sample allowed ^{1}H NMR analysis of this very unstable tosylated product; however, a clear ^{13}C spectrum could not be measured and consequently, the site of sulfonylation remained uncertain.

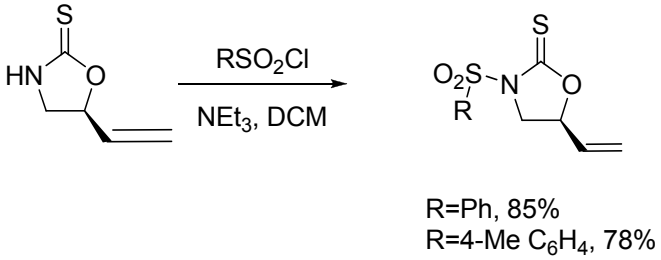
Moving from *p*-toluenesulfonyl chloride to methanesulfonyl chloride, a less unstable product was formed, which could be purified by column chromatography (44% isolated yield) and identified as a methanethiosulfonate **18**. This product resulted from a thiophilic attack (Scheme 17).



Scheme 17

The structure of **18** was ascertained by ^{13}C NMR analysis: the chemical shift of C-2 was detected at 150.9 ppm and not around 180 ppm, value expected for a thionocarbonyl group. The low stability of such thiosulfonates might account for the moderate reaction yields and for the difficulties met in purifying the *p*-toluenethiosulfonate.

Once again, the above results did not match our previous laboratory reports about the sulfonylation of simple OZTs, which underwent *N*-sulfonylation to produce sulfonamides (Scheme 18).



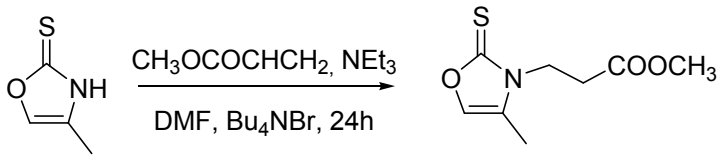
Scheme 18

☝ A huge difference of reactivity has to be considered between an OXT and an OZT with regard to the reactivity of the nitrogen center. For both acylation and sulfonylation reactions, a dramatically reduced nucleophilicity of the N atom was observed. These results are to some extent in contradiction with Pearson's theory, which claims acyl chlorides, carboxylic anhydrides, isocyanates and sulfonyl chlorides to be hard electrophiles, expected to interact preferentially with the N atom.

3.1.4. Michael additions

Puzzled by this unanticipated reactivity of the OXT, we were keen to investigate another *N*-regioselective reactivity, the *N*-alkylation using a Michael acceptor.

In a first approach, we have used methyl acrylate as Michael acceptor and after 24 h we were able to isolate the N-alkylated derivative **19** in only 14% yield (Scheme 19). This poor result might be attributed to the instability of the product: in order to limit the degradation observed, the reaction time was decreased for 2 h but the conversion was not complete and degradation could still be detected.

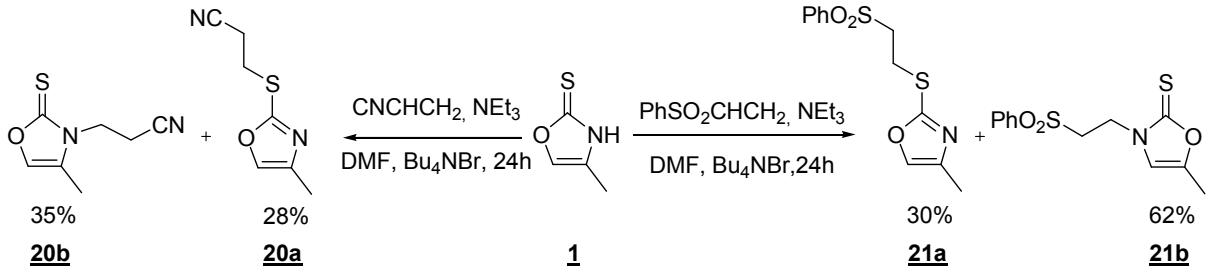


1 **19**

Scheme 19

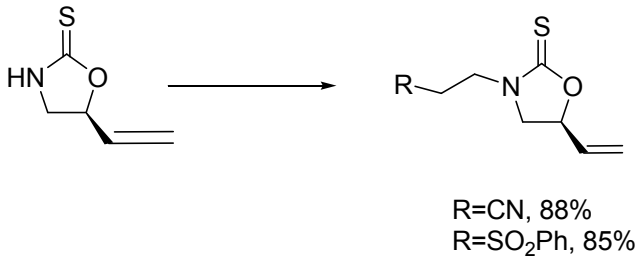
Although this result is in accordance with Pearson's theory, the yield is much too low to put forward a conclusion about the reactivity of OXTs in Michael additions.

We have considered appropriate apply identical reaction conditions on two more Michael acceptors – acrylonitrile and phenyl vinyl sulfone. In both cases, the reaction occurred in good yield but the OXT was converted into a mixture of *N*- and *S*-alkylated regioisomers. In the case of acrylonitrile, the *S*- and *N*- alkylated derivatives **20a** and **20b** were obtained in 28% and 35% yields respectively. With phenyl vinyl sulfone, the *S*-alkylated product **21a** was obtained in 30% yield, while the *N*-alkylated product **21b** was obtained in 62% yield (Scheme 20).



Scheme 20

Once again, our results appeared strongly divergent when compared with those reported by Gueyrard et al. on a simple OZT (Scheme 21), which displaying marked *N*-nucleophilicity and high chemo/regioselectivity.



Scheme 21

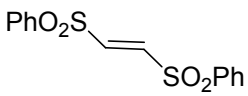
☝ In the case of the OXT, even though not complete, some *N*-alkylation chemoselectivity was observed. The *N*-alkylated product was more predominant with phenyl vinyl sulfone than with acrylonitrile, which might be attributed to the better electron-withdrawing capacity of a sulfonyl group when compared with a nitrile group, thus resulting in a better *N*-selectivity.

Regarding the results obtained for Michael additions with OXT, a stronger electron- withdrawing (and thus harder) electrophile might induce improved *N*-selectivity. Can we reach a complete N-selectivity as in the case of simple OZTs[30]?

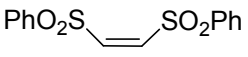
3.1.4.1. Michael additions; BPSE – a harder electrophile

3.1.4.1.1. Considerations about BPSE

In recent years, our group has made huge efforts to develop a broad study of 1,2-bis-(phenylsulfonyl)ethylene (BPSE, Scheme 22)[37,38] and promote it as a useful reagent in organic synthesis.[39] The doubly electron-withdrawing bis-sulfonyl system induces strong activation of the insaturation, which makes it suitable for Dields-Alder reactions[40] as well as a good Michael acceptor with an extension for asymmetric reactions.[41,42]



E-1,2-bis-phenylsulfonylethylene



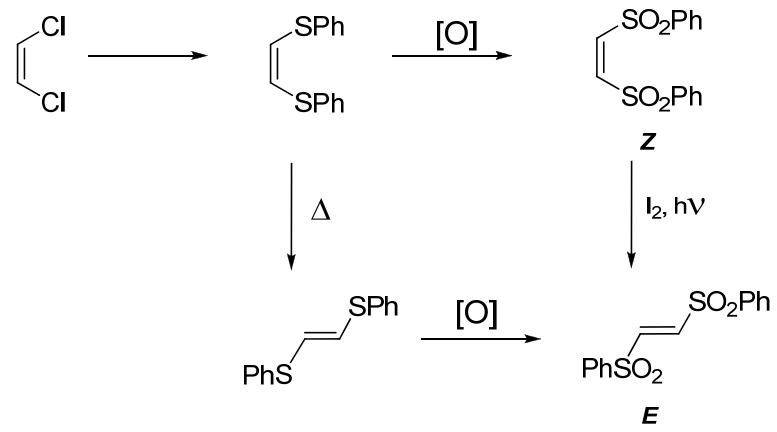
Z-1,2-bis-phenylsulfonylethylene

Scheme 22

This reagent, commercially accessible albeit costly, can be readily prepared in the laboratory. The bis-sulfone *Z* is prepared by oxidation of the corresponding thioether[40] obtained from (*Z*) – 1,2-dichloroethylene or 1,1-dichloroethylene.[43] A mixture of (*Z*) and (*E*) –dichloroethylenes can be used but the *E*-isomer is not reactive in the reaction conditions (Scheme 23).[43] The (*E*)-isomer is prepared by iodine-

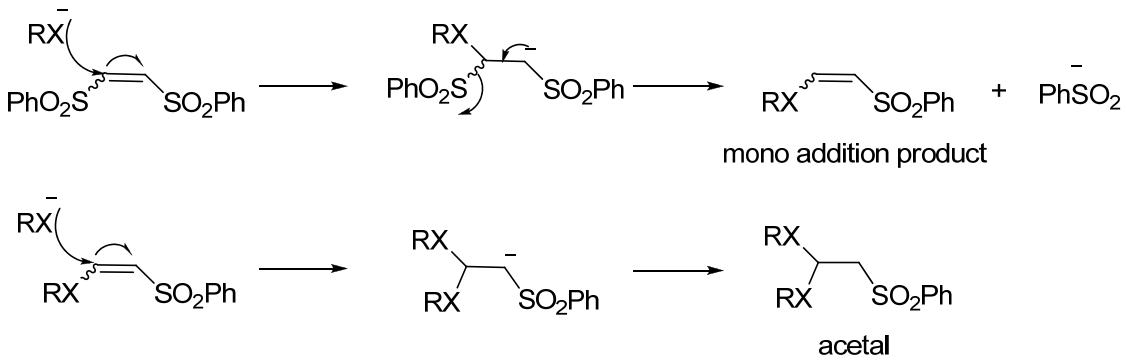
[37] Cossu S.; De Lucchi O.; Fabbri D.; Licini G.; Pasquato L. *Org. Prep. Proc. Int.* **1991**, *23*, 573-592.
[38] De Lucchi, O.; Pasquato, L.; Rollin, P.; Tatibouët, A. In e-EROS *Enyclopedia of Reagents for Organic Synthesis*; John Wiley & Sons, Ltd, **2005**. doi:10.1002/047084289X.rb183
[39] Meek, J. S.; Fowler, J. S. *J. Org. Chem.* **1968**, *33*, 985-991.
[40] De Lucchi O.; Lucchini V.; Pasquato L.; Modena G. *J. Org. Chem.* **1984**, *49*, 596-604.
[41] Cossu S.; De Lucchi O.; Pasetto P. *Angew. Chem. Int. Ed.* **1997**, *36*, 1504-1505
[42] Cossu S.; De Lucchi O.; Peluso P.; Volpicelli R. *Tetrahedron Lett.* **1999**, *40*, 8705-8709.
[43] Truce, W. E.; Boudakian, M. M.; Heine, R. F.; McManimie, R. J. *J. Am. Chem. Soc.* **1956**, *78*, 2743-2748.

catalyzed photochemical isomerisation. Both isomers, crystalline and stable, can be handled without difficulty.



Scheme 23

BPSE can undergo two successive nucleophilic additions (Scheme 24). The first one leads to a mono-substituted derivative, which can in turn undergo another attack to finally afford an acetal. The valorization of this type of acetal will be discussed in the next chapter. For now, we are interested in the mono-substituted product.



Scheme 24

In our laboratory, Dr. Florence Chery and Dr. E. Cabianca[44,45] have successively studied the reaction of BPSE with alcohols, thiols and amines. It was

[44] Cabianca, E.; Chéry, F.; Rollin, P.; Cossu, S.; De Lucchi, O. *Synlett* **2001**, 1962-1964.

observed that the nature of the nucleophile correlates the base that should be used in the reaction. The next table shows the best conditions used for the mono-substitution with nucleophiles.

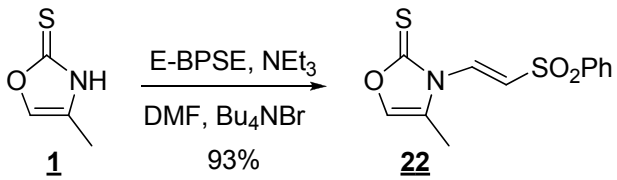
R	best conditions
R-OH	LiHMDS THF
R-SH	NEt_3 DCM
$R-NH_2$	$R-NH_2$ CH_3CN

Table 3

In fact, the acidity of the reagent is the conditioning factor to choose the strength of the base, in order to form the nucleophile.

3.1.4.1.2. Results and discussion

Using *E*-BPSE, Michael type *N*-alkylation conditions were applied to OXT **1**, resulting in a complete *N*-selectivity, with a high 93% yield of the *E*-vinylogous sulfonamide **22** (Scheme 25).

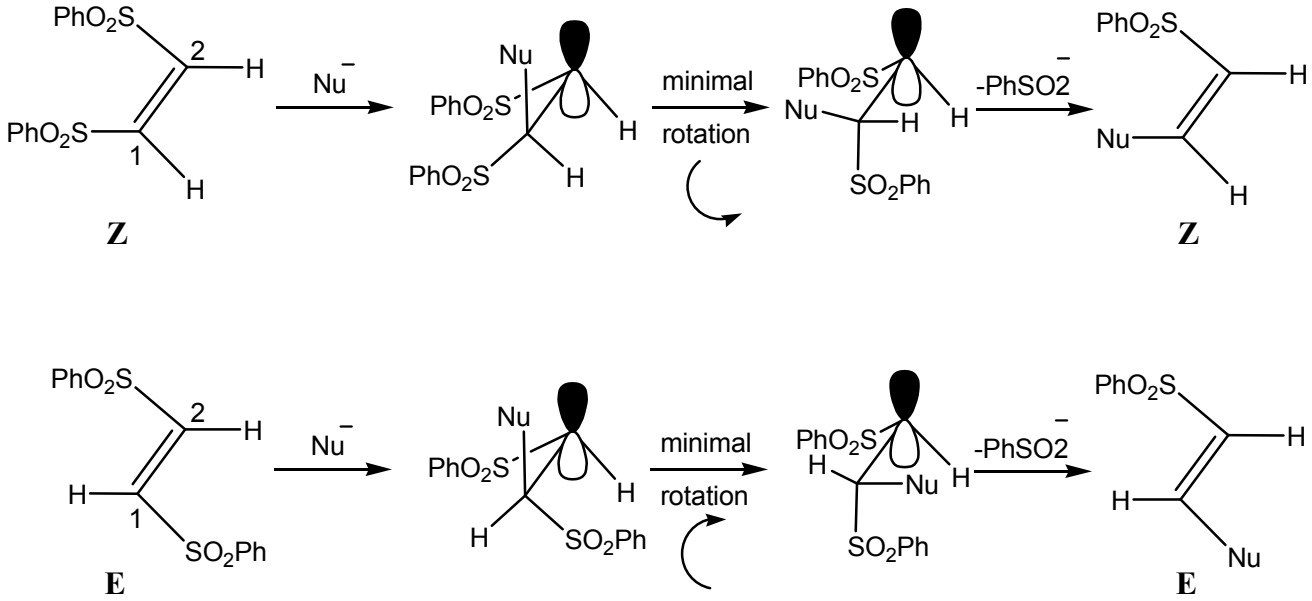


1 **22**

Scheme 25

[45] Chéry, F.; Desroses, M.; Tatibouët, A.; De Lucchi, O.; Rollin, P. *Tetrahedron* **2003**, *59*, 4563-4572.

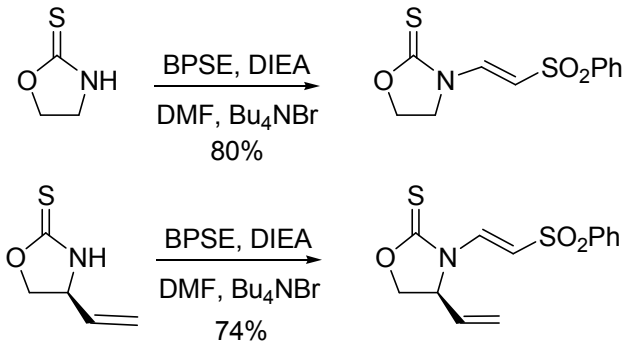
☝ The Michael addition reaction with BPSE is totally N-regioselective (no trace of *S*-alkylated derivative detected) and also stereoselective with a retention of the *E* configuration (^3J = 13.8 Hz). One explanation for this phenomenon was proposed by Meek and Fowler.[39] Those authors postulated that a nucleophilic attack on the double bond of BPSE leads to a negatively-charged intermediate which, after minimal rotation of carbon 1, adopts the favorable conformation in which orbital p of carbon 2 is coplanar to the leaving group. Phenylsulfinate ion elimination produced the mono-substituted derivative with preservation of the configuration (Scheme 26).



Scheme 26

A complete *N*-selectivity in the reaction of BPSE with OXTs was also observed by Girniene et al.[46] (Scheme 27).

[46] Girniene, J.; Tardy, S.; Tatibouët, A.; Sackus, A.; Rollin, P. *Tetrahedron Lett.* **2004**, *45*, 6443-6446.



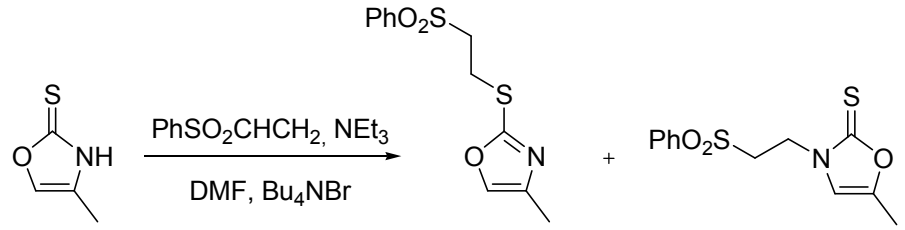
Scheme 27

Clearly, it is possible to reach a complete N-selectivity for OXT in reactions with strong and hard electrophiles: in such situation, the N atom in OXT behaves accordingly to Pearson's theory.

3.1.4.2. Mechanism of Michael additions

All the results obtained for Michael additions reactions - with at times display a mixture of *N*- and *S*-substituted products – brought some questions about the mechanism of OXT alkylation. One of these questions was "Does the results reflect the direct nucleophilic attack of both S- and N-centers or is it a more subtle mechanism?"

Taking account the high yield obtained, phenyl vinyl sulfone was the choosed reagent for the study of the reaction evolution – related yields of *N*- and *S*-alkylated derivatives in function of time (Scheme 28). After 2 h of reaction, the Michael addition was complete with almost 90% overall yield, the major product (48% yield) being the *S*-alkylated adduct. When the reaction time was increased to 24 h, the *N*-alkylated derivative became prevalent with 62% yield. No significant yield changes for *N*- and *S*-alkylated derivatives were observed over 48 h.

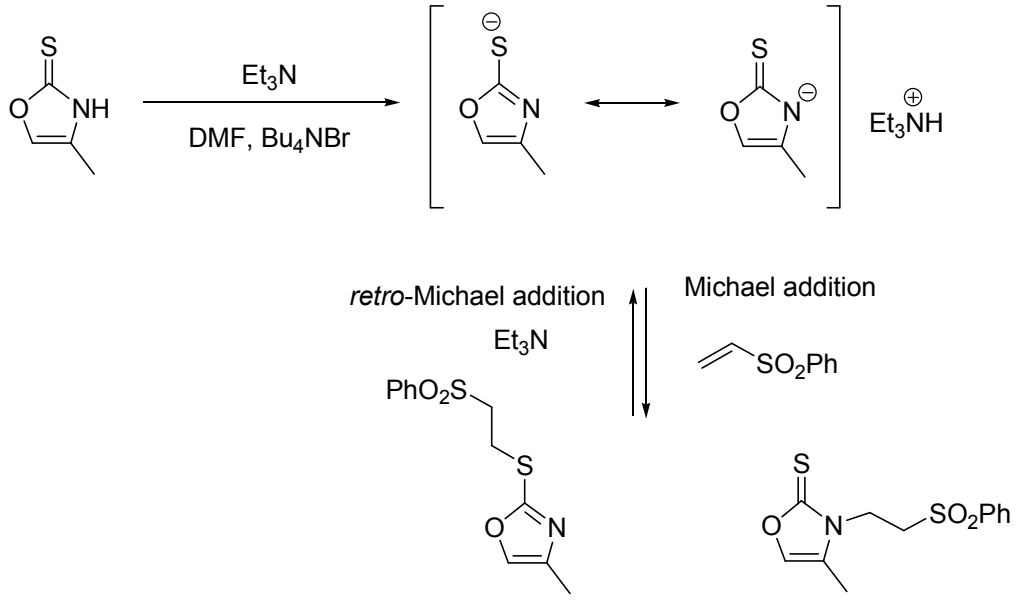


1 **21a** **21b**

time (h)	yield of 21a (%)	yield of 21b (%)
2	48	40
24	30	62
48	32	64

Scheme 28

The above results suggest that equilibrium takes place to reach a thermodynamic stability after 24 h, but also that a thiophilic attack occurs in the first stage of the reaction. Thus, we might propose a mechanism in which a kinetic Michael sulfur addition first takes place. The *S*-alkylated species then undergoes a retro-Michael elimination which returns the electrophile and the OXT, able to repeat the addition with both nitrogen- or sulfur-site (Scheme 29).



Scheme 29

4. Structures confirmation

All those results are supported by ^{13}C NMR analysis. As described before, the chemical shifts for thionocarbonyl compounds present values around 180 ppm for C-2 whereas the observed reduced values are in agreement with aryl alkyl thioethers. Table 4 shows C-2 chemical shifts for some of the compounds of this chapter, namely for Michael additions products.

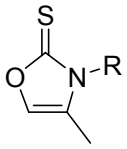
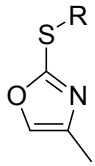
structure	R=	^{13}C (ppm)
	H	180.6
	CH_2CH_2COOMe	178.7
	CH_2CH_2CN	178.9
	$CH_2CH_2SO_2Ph$	178.5
	$CHCHSO_2Ph$	177.1
	Bn	159.3
	CH_2COPh	158.7
	CH_2CH_2CN	158.8
	$CH_2CH_2SO_2Ph$	157.7

Table 4

The strong UV-absorbing character for all OXTs is one of their amazing characteristics: the sulfur atom and the aromaticity of the ring make their structure easily identifiable. We have measured the UV-Vis spectra for OXT **1**: applying the Lambert-Beer law, the maximum absorbance was determined at 268 nm with a ε_{max} of 1.35 10^4 $mol^{-1}.cm^{-1}.l^{-1}$, a value in concordance with those reported by Gompper and Herlinger.[3,18,47,48]

[47] Gompper, R.; Herlinger, H. *Chem. Ber* **1956**, 89, 1748-1762.
[48] Gompper, R.; Herlinger, H. *Chem. Ber* **1956**, 89, 2825-2833.

5. Conclusion

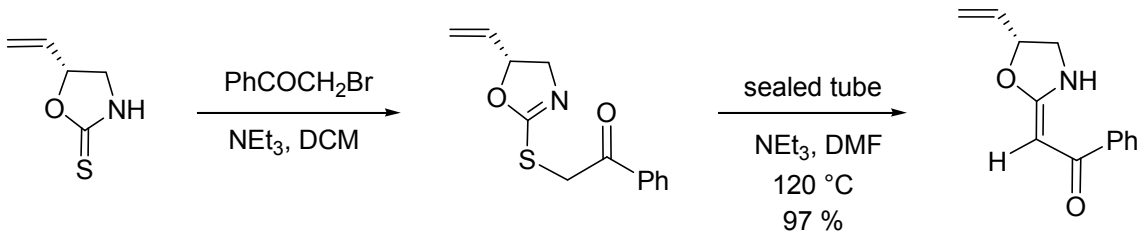
In this chapter we have focused on the synthesis and representative reactivity of some simple OXTs. In the light of the results obtained, some preliminary statements can be put forward:

- ☑ OXTs were prepared by condensation of an α-hydroxyketone with thiocyanic acid. After optimization of the reaction, it can be concluded that their preparation mostly depends on the proper choice of the solvent-acid couple.
- ☑ New structures of this family were synthesized in good yields, mostly using the EtOH/HCl system.
- ☑ Glycolaldehyde dimer and 2,2-dimethoxyethanol proved that masked ketones can be used for the synthesis of OXT.
- ☑ In terms of reactivity, *S*-functionalization was performed selectively (sulfur alkylation) using a soft electrophile (alkyl bromide), in agreement with Pearson's theory.
- ☑ *N*-functionalization revealed more complex. Reactions expected to be *N*-selective (acylation, sulfonylation, Michael additions) according to Pearson's theory either failed or showed poor chemoselectivity. Only a strong and hard electrophile like BPSE showed complete *N*-selectivity in the reaction with OXT.
- ☑ The observed reduced nucleophilicity of the nitrogen atom in OXT (as compared to an OZT) might be explained by the electron lone pair delocalization of the N atom into the aromatic system of OXT. One example of the ring aromaticity importance was demonstrated by Eschenmoser reaction.[49] This coupling reaction represents a versatile procedure to prepare vinylogous amides and urethanes by *S*-alkylation of a thiolactam with an appropriated

[49] Roth, M.; Dubs, P.; Götschi, E.; Eschenmoser A. *Helv. Chim. Acta*, **1971**, *54*, 710-734

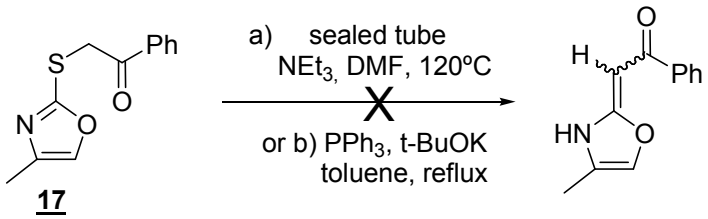
electrophilic partner, followed by sulfur extrusion, in the presence of base or a thiophilic entity[50].

The reaction of sulfur extrusion, particularly developed with thiolactams, proved to be very efficient with (5*R*)-5-vinyl-1,3-oxazolidine-2-thione, as it was reported by Gueyrard et al. (Scheme 30). [30]



Scheme 30

We have explored the Eschenmoser reaction on the *S*-alkylated precursor **17,** the alkylthiooxazole derived from α-bromoacetophenone. Two methods have been applied: the first used the basic conditions in sealed tube and the second used a thiophile species (triphenylphosphine).[51] Unfortunately, neither of those methods led to the expected transformation (Scheme 31).

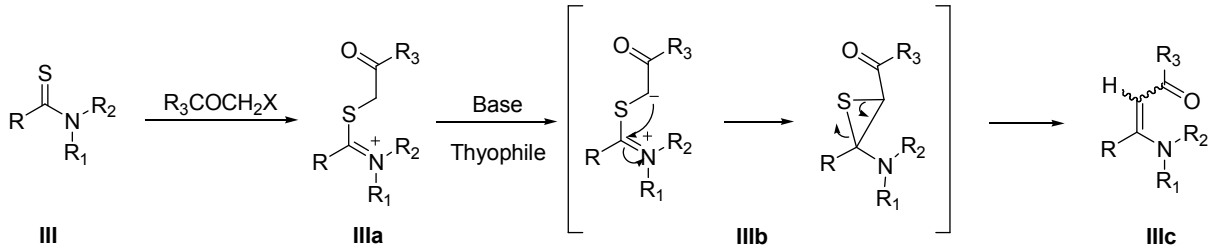


17

Scheme 31

[50] Michael, J. P.; Koning, C. B.; Van der Westhuyzen, C. W.; Fernandes, M. A. *J. Chem. Soc Perkin Trans. I*, **2001**, 2055-2062.
[51] Girniene, J. PhD*, Université d'Orléans*, **2000**.

When taking a look at the Eschenmoser reaction mechanism[52,53] (Scheme 32), a reasonable interpretation can be proposed for this result. In the reaction, thioamides or thiolactams **III** are treated with enolisable α-halocarbonyl compounds to form α-thioiminium salts **IIIa**, from which sulfur is expelled upon deprotonation in the presence of a suitable sulfur scavenger (usually triphenylphosphine) (**IIIb**), to give β-acylated enamines, in the two possible configurations (*E* and *Z*) (**IIIc**).



Scheme 32

The main difference between Gueyrard's OZT used by and the OXT studied by us lies in the aromaticity of the OXT ring, that doesn't exist in the OZT ring. In the case of the alkylsulfanyl oxazole, the formation of the transient thiirane is strongly hampered for two main reasons. The first one is that to form the thiirane system, the carbanion should attack an aromatic ring! The second one is straightforward, because of the huge tension generated in the ring when the thiirane **IIIb** is formed when compared to an OZT derived analogue. In order to "validate" this presupposition, the values of heat of formation for intermediates **IIIb** derived from the simplest OZT and OXT (Figure 1) were calculated using a semi-empirical modelling process (MOPAC, AM1). While in the case of OZT, the intermediate **IIIb** is calculated to have a 27.8 kcal/mol, in the case of OXT, **IIIb** was calculated with a 68.07 kcal/mol heat of formation. This huge difference between the two heats of formation, strongly supports our hypothesis; in our case, **IIIb** is not formed and the starting material is recovered (Figure 1).

[52] Shiosaki K. *Comprehensive Organic Synthesis*, Vol. 2, Pergamon Press: Oxford, **1991**, 865-892 and cited references.
[53] Li, J. J. *Name Reactions*, 2nd edition, Springer Press: Heidelberg, **2003**, 127 and cited references.

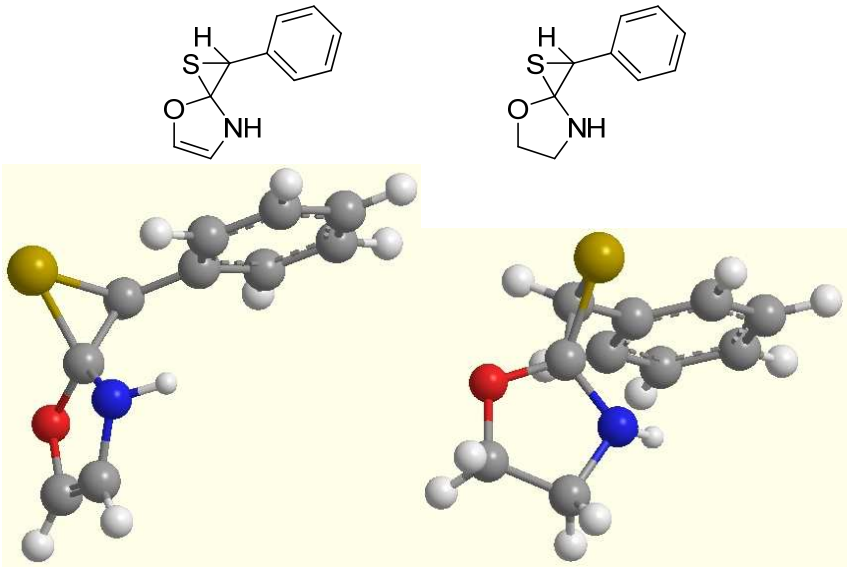


Figure 1

CHAPTER II

1,3-oxazoline-2-thiones fused on carbohydrate templates

1. Introduction – Synthesis of thionocarbamates fused on carbohydrate templates

In the previous chapter, we have studied the synthesis of simple 1,3-oxazoline-2-thiones (OXT), through condensation of thiocyanic acid with native (or precursors of) α-hydroxycarbonyl acyclic chains. The association of the OXT heterocycle with carbohydrate scaffolds could generate original structures – fused or antennary systems –, giving us opportunities to develop new methodologies.

To our knowledge, the association of an OXT with a carbohydrate frame has never been reported before. However, we can support our studies using the scarce literature related to carbohydrate-based 1,3-oxazolidine-2-thiones (OZT), since those heterocycles are structurally closely related.

Our interest in combining 2-thio-N,O-heterocycles and glyco-skeletons was not only stirred up because of the attractive aspect of original chemistry involved but also because of the broad variety of applications.

In fact, such structural arrangements have given birth to analogues of natural compounds such as pseudo *C*- and *N*-nucleosides,[54,55,56] spironucleosides[57,58] or spiro-C-glycosides.[59]

The present chapter is dedicated to the methodologies developed by us to prepare fused bicycles containing an OXT moiety. Of course, we cannot explore this synthesis without taking into account the numerous synthetic methods for the formation of fused-OZTs.

Among the different applications, the fused OZT sugar derivatives could potentially be exploited as chiral auxiliaries,[29] glycosidase inhibitors[60] or precursors of nucleosides.[61,62,63,64,65,66,67]

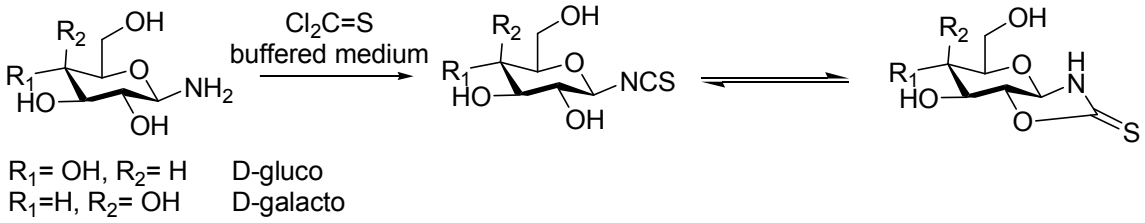
[54] Garcia Fernández, J. M.; Ortiz Mellet C.; Fuentes J. *J. Org. Chem.* **1993**, *58*, 5192-5199.
[55] Bolaños J. G. F.; Zafra E.; Lopez O.; Robina I.; Fuentes J. *Tetrahedron: Asymm.* **1999**, *10*, 3011-3023.
[56] Gasch C.; Pradera A.; Salameh B. A. B.; Molina J. L.; Fuentes J. *Tetrahedron: Asymm.* **2000**, *11*, 435-452.
[57] Bolaños, J. G. F.; López, A. B.; Mota J. F. *Carbohydr. Res.* **1990**, *199*, 239-242.
[58] Mota J. F.; Blanco J. L. J.; Ortiz Mellet C.; Garcia Fernández, J. M.; *Carbohydr. Res.* **1994**, *257*, 127-135.
[59] Gasch C.; Pradera A.; Salameh B. A. B.; Molina J. L.; Fuentes J. *Tetrahedron: Asymm.* **2001**, *12*, 1267-1277.
[60] Blanco, J. L. J.; Pérez, V. M. D.; Mellet, C.O.; Fuentes, J.; Fernandez, J. M.G.; Arribas, J. C. D.; Canada F. J. *J. Chem. Soc., Chem. Commun.* **1997**, 1960-1970.
[61] Ranganathan, R. *Tetrahedron Lett.* **1975**, *13*, 1185-1188.

1.1. Starting with glycosylamines

In the case of OZTs, the main synthetic pathway is the reaction of a β-aminoalcohol with thiophosgene, under basic conditions.

Isothiocyanates are attractive synthons in organic chemistry due to their availability and their tendency to undergo nucleophilic additions and cycloadditions.[68,69] In particular, sugar-based isothiocyanates have been used for the synthesis of a wide spectrum of carbohydrate derivatives of synthetic, biological and pharmaceutical interests.[55,59]

With the objective to synthesise unprotected glycosylthioureas from anomeric isothiocyanates in aldohexose series (D-Glc, D-Gal and D-Man), Fuentes et al have reported a crucial result:[70] in β-D-Glc and β-D-Gal series, when the glycosylpyranosylamines condensed with thiophosgene in buffered medium, an equilibrium between the anomeric isothiocyanate and the corresponding OZT occurred, showing the possibility of a *trans*-fused system between an OZT and a pyrano ring (Scheme 33).

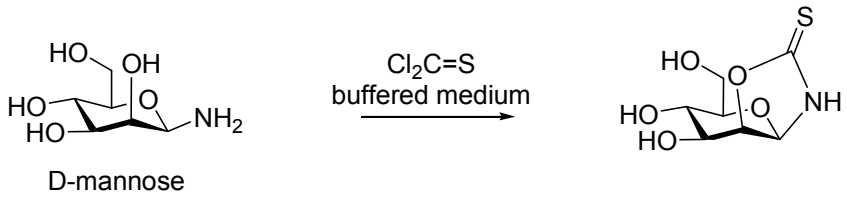


Scheme 33

In contrast, when reacting β-D-mannopyranosylamine with thiophosgene, only the *cis* bicyclic thionocarbamate was formed and the transient isothiocyanate could not be detected (Scheme 34). The different behaviour of the *cis* and *trans*

[62] Ranganathan, R. *Tetrahedron Lett.* **1977**, *15*, 1291-1294.
[63] Rayner, B.; Tapiero, C., Imbach J.L. *J. Heterocycl. Chem.* **1982,** *19*, 593-596.
[64] Gosselin, G.; Bergogne, M. C.; Rudder, J.; Clerq, E.; Imbach, J.L. *J. Med. Chem.* **1986**, *29*, 203-213.
[65] Grouiller, A.; Mackenzie, G.; Najib, B.; Shaw, G.; Ewig, D. *J. Chem. Soc., Chem. Commun.* **1988**, 671-672.
[66] Buchanan, J. G.; McGaig, A. E.; Wightman, R.H. *J. Chem. Soc. Perkin Trans. 1* **1990**, 955-963.
[67] Girniene, J.; Gueyrard, D.; Tatibouët, A.; Sackus, A.; Rollin, P. *Tetrahedron Lett.* **2001**, *42*, 2977-2980
[68] Mukerjee, A.K; Ashare, R. *Chem. Rev*. **1991**, *91*, 1-24.
[69] Al-Masoudi, N.; Hassan, N. A.; Al-Soud, Y. A.; Schmidt, P.; Gaafar, A. E. D. M.; Amer, A.; Jochins, J. C. J. *Chem. Soc., Perkin Trans. 1* **1998**, 947-953.
[70] Maya I.; Lopez O.; Bolanos J. G. F.; Robina I.; Fuentes J. *Tetrahedron Lett.* **2001**, *42*, 5413-5416.

hydrindane-type systems could be explained by the strain in the ring fusion for a *trans* species.



Scheme 34

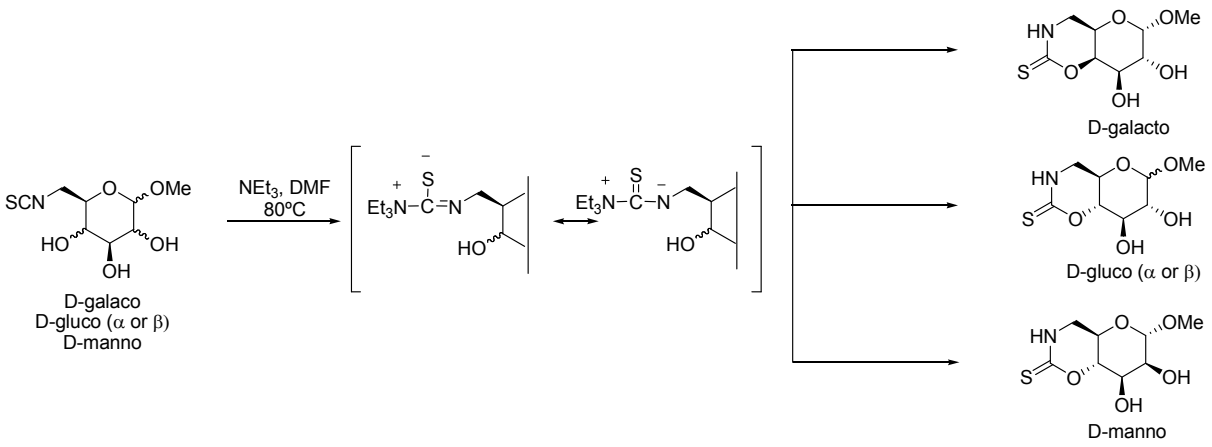
The above results agreed with the fact that the bicyclic compounds can be formed either in a 5 + 5 or 6 + 5 ring fusion but in both cases the *cis* isomers are more stable than the *trans* isomers.[71]

1.2. 6-amino-6-deoxy aldoses

Following the same process, in D-Glc, D-Gal and D-Man series, Ortiz Mellet and coll. have made an extensive study of the utilization of 6-deoxy-6-isothiocyanates as precursors to prepare fused tetrahydro-1,3-oxazine-2-thiones,[54,72] an heterocycle that is closed to our OXTs.

Reaction of methyl 6-amino-6-deoxyaldopyranosides with thiophosgene leads to the corresponding 6-isothiocyanates which, in the presence of a catalytic amount of Et_3N, produce the corresponding oxazinethiones through intramolecular cyclisation. The nucleophilic attack by the 4-OH of the pyranoside may be activated by formation of a complex between the isothiocyanate and Et_3N (Scheme 35).[73]

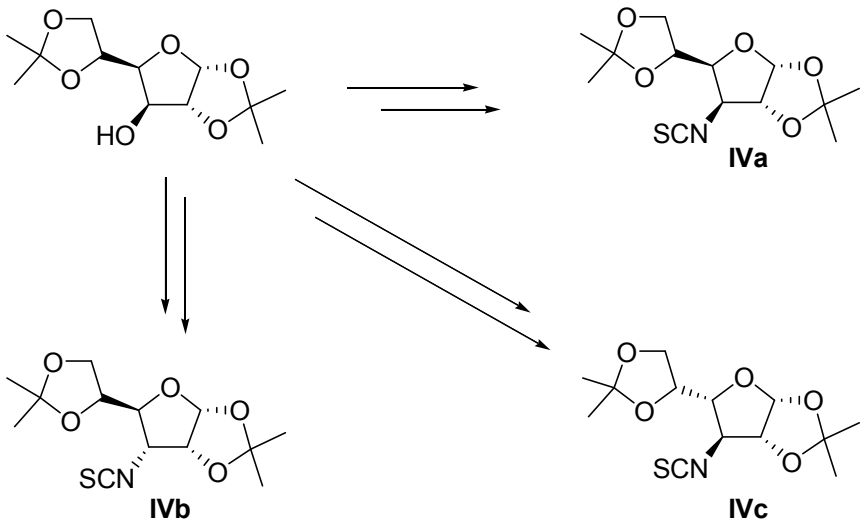
[71] Paizs B.; Pinter I.; Csizmadia I.G. *Theochem* **1998**, *455*, 267-274.
[72] Garcia Fernandéz J. M.; Ortiz Mellet C.; Fuentes J. *Tetrahedron Lett.* **1992**, *33*, 3931-3934.
[73] Avalos M.; Babiano R.; Garcia-Verdugo C.; Jimenez J. L.; Palacios J. C. *Tetrahedron Lett.* **1990**, *17*, 2467-2470.



Scheme 35

1.3. 3-amino-3-deoxy aldoses

Another central study has been carried out by Fuentes et al[74] on the introduction in position 3 of an isothiocyanate and its reactivity with secondary hydroxyls in aldohexoses. For this purpose, they have synthesized from commercial DAG 3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-isothiocyanato-α-D-hexofuranoses in D-gluco (**IVa**), D-allo (**IVb**) and D-galacto (**IVc**) series (Scheme 36). In theory, on totally unprotected 3-deoxy-3-isothiocyanato-hexoses, the intramolecular cyclization might induce the carbohydrate to adopt a furano, pyrano or open-chain structure.



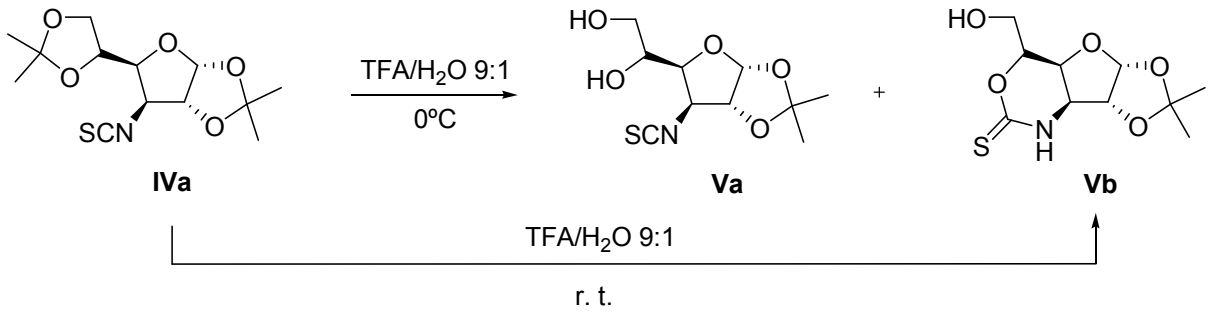
Scheme 36

[74] Garcia Fernandéz J. M.; Ortiz Mellet C.; Blanco J. L. J.; Fuentes J. *J. Org. Chem.* **1994**, *59*, 5565-5572.

As the isothiocyanate function is compatible with the acidic conditions used for acetal deprotection, Fuentes et al have studied the reactivity of 3-deoxy-3-isothiocyanates both in the case of 5,6-deprotected and in the case of totally deprotected species.

☑ Selective deprotection of a 5,6-isopropylidene ketal

The treatment of 1,2:5,6-di-*O*-isopropylidene-3-isothiocyanato-α-D-glucopyranose **IVa** with 90% aqueous TFA at low temperature resulted in the formation of a mixture of the isothiocyanate **Va** and the tetrahydro-oxazinethione **Vb**. At room temperature, **Vb** was produced quantitatively (Scheme 37).

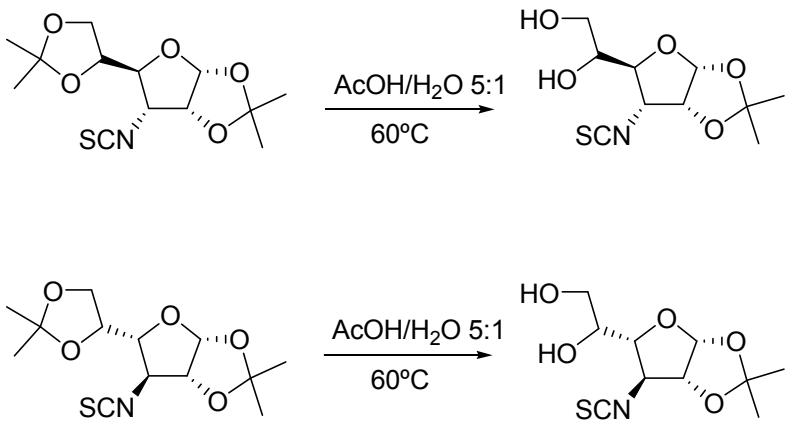


Scheme 37

Previously, we have seen that in the case of 6-deoxy-6-isothiocyanato aldoses in pyrano form, cyclization to the corresponding 4,6-cyclic thionocarbamates occurred only under base catalysis, for both *cis* and *trans*-type systems. Here, the behaviour is different and the spontaneous cyclization is illustrative of a lower activation energy for the furanoid isothiocyanate when compared to pyranoid derivatives.

Furthermore, no intramolecular cyclization occurred when D-allofurano (**IVb**) and D-galactofurano (**IVc**) isothiocyanates were selectively deprotected. The hydrolysis produced the corresponding isothiocyanates devoid of 5,6-protection,

which remained reluctant to cyclisation, even in the presence of Et_3N in DMF (Scheme 38).



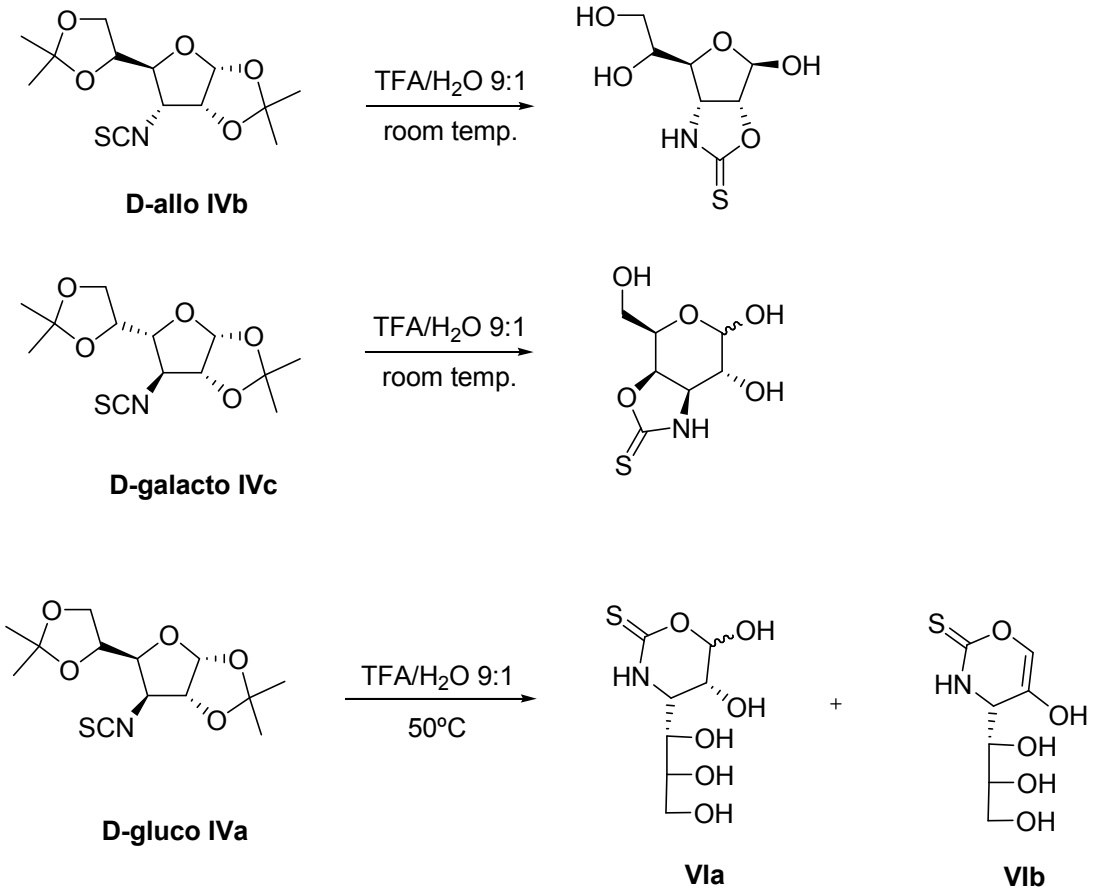
Scheme 38

The difference of reactivity is linked to configuration parameters: in the gluco series, the isothiocyanate and the appendage are in a *cis* relation while in the other two cases, the relation is *trans*. On contrary to a pyrano entity, the furano ring prevented the formation of an oxazine ring when both reactive ends are *trans*.

☑ Deprotection of both ketals

The complete deprotection of the aldohexoses lead to three types of compounds, depending on the stereochemical relationship in α to the isothiocyanate group.

The deprotection of D-allo **IVb** and D-galacto **IVc** derivatives are a good illustration of the influence of a *cis*-relation between the isothiocyanate and a hydroxyl on the geometry of the molecule. The 2,3-*cis* relation in D-allo **IVb** led to the formation of a 2,3-OZT imposing a furanose ring, while the 3,4-*cis* relation in D-galacto **IVc** led to a 3,4-OZT which forced the carbohydrate into a pyrano ring. On the contrary, D-gluco **IVa** did not possess any *cis* relation, thus forcing the molecule to generate an oxazinethione-type moiety – **VIa** and **VIb** being the most stable (Scheme 39).



Scheme 39

1.4. Condensation of aldoses and ketoses with thiocyanic acid

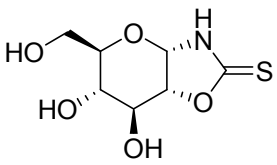
For the synthesis of fused thionocarbamates, a more subtle approach consists of using an α-hydroxyaldehyde or ketone possessing an extra γ- or δ-hydroxyl group, able to promote intramolecular cyclization during the condensation process with thiocyanic acid, and thus leading to fused or spiranic furano- or pyrano-structures.

The first preparation of bicyclic structures on carbohydrate scaffolds was reported by Zemplen and coll.,[75] who condensed the thiocyanic acid generated *in situ* with unprotected sugars. In the D-gluco[75] and the D-fructo[76] series, the products were described as oxazolidine-2-thiones fused to pyrano skeletons of D-glucose and D-fructose. This work was re-examined and developed by Bromund et al[77], who have

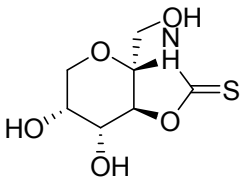
[75] Zemplen G.; Gerecs A.; Rados M. *Ber*. **1936**, *39*, 748-754.
[76] Zemplen G.; Gerecs A.; Illés E. *Ber*. **1938**, *71*, 590-596.
[77] Bromund W. H.; Herbst R. M. *J. Org. Chem*. **1945**, *10*, 267-276.

explored the same reaction in diverse aldose series (D-galacto, D-xylo, L-arabino). Similar bicyclic fused structures (OZT-pyrano backbone) were proposed (Scheme 40).

ZEMPLEN

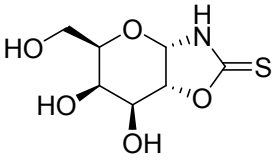


D-gluco

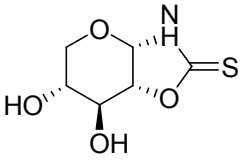


D-fructo

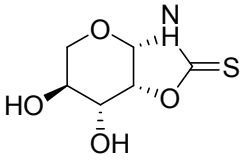
BROMUND



D-galacto



D-xylo

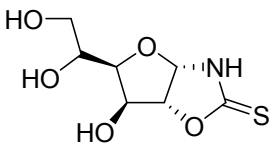


L-arabino

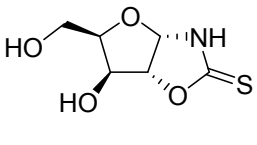
Scheme 40

The structural determination of those bicyclic compounds remained under discussion for some time, until Wickstrom and Wold[78] (1) confirm the formation of fused bicyclic OZT-sugars and, more important (2) demonstrate the furano form for aldoses and the pyrano form for ketoses (Scheme 41). These results were later confirmed by Jochims and his team,[79] who performed the first NMR analysis for the OZTs.

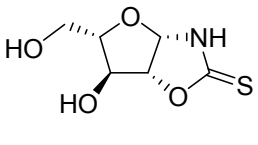
WICKSTROM / WOLD



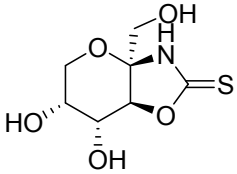
D-gluco



D-xylo



L-arabino



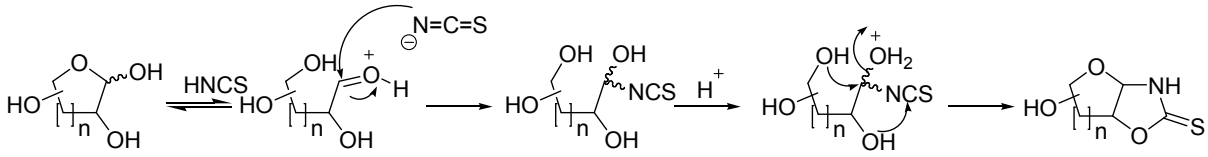
D-fructo

Scheme 41

[78] Wickstrom A.; Wold J. K. *Acta Chem. Scand.* **1959**, *13*, 1129-1136.
[79] Jochims J. C.; Seeliger A.; Taigel G. *Chem. Ber.* **1967**, *100*, 845-854.

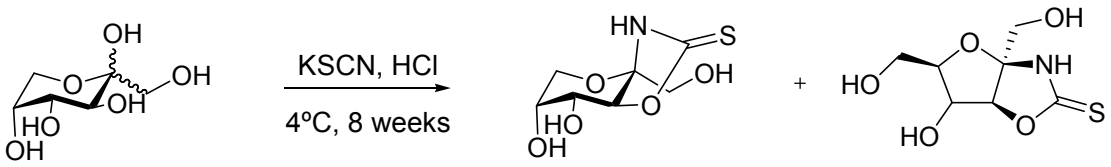
In 1975, Ranganathan[61] has used the OZT derived from D-arabinofuranose as a precursor to purine nucleosides. The fusion between OZT and D-xylofuranose was later reported in 1986 by Imbach[64] for the same purpose, and for the synthesis of α- and β- D-xylofuranosyl nucleosides.

All these observations have shown the possibilities to condense aldoses with thiocyanic acid and produce, in good yields, bicyclic furano compounds. Little has been proposed about the reaction mechanism but one can about an equilibrium between the hemiacetal and its free aldehyde form, which undergoes nucleophilic addition by HSCN followed by intramolecular addition of a hydroxyl to the transient isothiocyanate, in order to generate the thermodynamically more stable product (Scheme 42).



Scheme 42

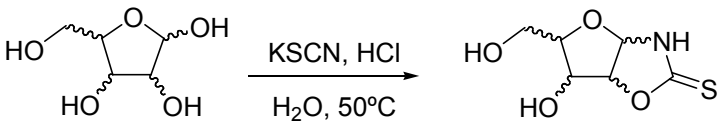
Ketoses should react under a similar scheme but with more complexity. Indeed, an important problem in the chemistry of ketoses lies in the lack of selectivity due (1) to the complexity of their tautomeric equilibria and (2) to their tendency to form tertiary oxocarbenium ions under acidic conditions. Thus, mixtures of open-chain, cyclic and dehydrated products are frequently obtained.[58] The discussion about OZT structures obtained from D-fructose as proposed by Zemplen, Wickstrom and Wold and more recently by Grouiller, still continues today. In fact, the first authors consider the fusion of OZT on a pyrano form of fructose, while Grouiller suggests the formation of a mixture of fused OZTs with β-pyrano and β-furano forms (Scheme 43).[65]



Scheme 43

In order to learn more about how aldoses and ketohexoses behave when confronted with thiocyanic acid, our laboratory has developed the synthesis and reactivity of that class of bicyclic OZT-sugar systems. Notably, Dr. Girniene has selected this method - the only one leading directly to fused OZTs from naked carbohydrates.

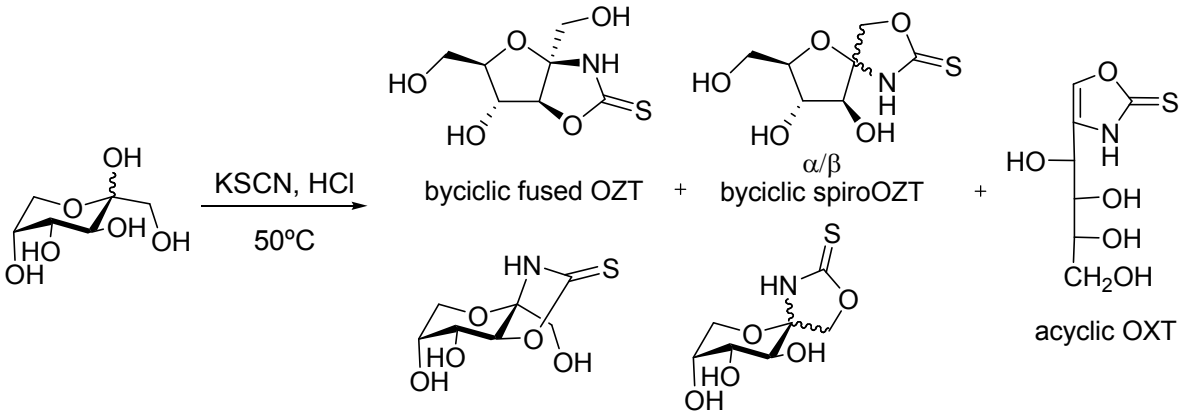
Slightly modifying the Bromund and Herbst conditions with non protected aldoses (D- and L-arabinoses, D-xylose, D-ribose), bicyclic OZT-sugar systems were prepared and the geometries of the sugar ring were completely defined. A furano-form was obtained, as confirmed by ^{1}H and ^{13}C NMR spectra, and the anomeric configuration was controlled by the location of the hydroxyl group in C-2 position. Girniene's results[14] are presented in Scheme 44.



series	yield (%)
L-arabino	97
D-arabino	90
D-xylo	80
D-ribo	70

Scheme 44

In the case of ketohexoses, condensations are not so simple. In fact, by reacting those with HSCN, one can expect the formation of up to 10 different thionocarbamates: fused and spiro bicycles on pyranose or furanose skeletons, as well as acyclic OXTs (Scheme 45).[79]

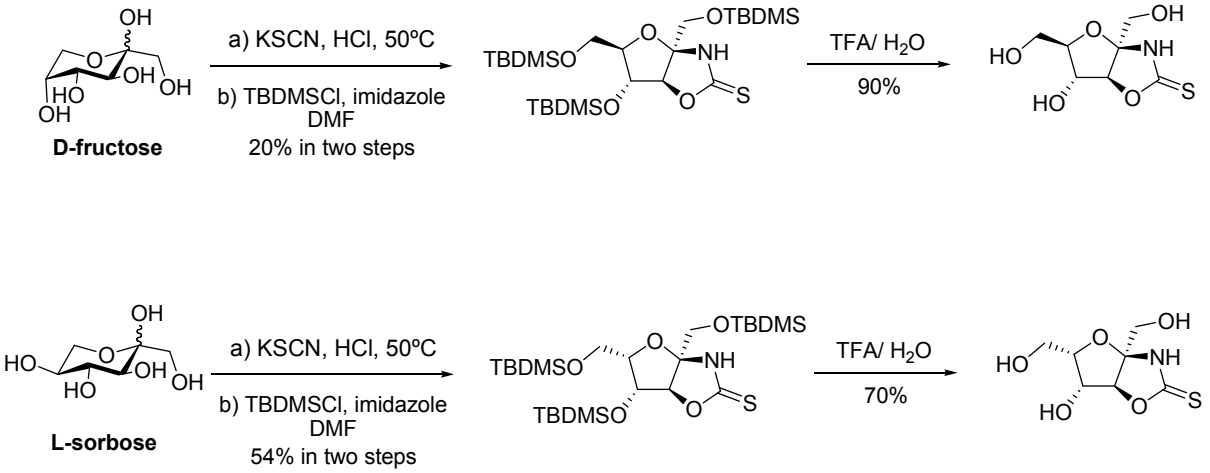


Scheme 45

The above structures have been postulated from the synthesis of 1,3-oxazolidin-2-ones (OZO) (OZT analogues) studied by Lichtenthaler et al.[80] who demonstrated that reacting D-fructose with potassium cyanate, four OZOs (one fused furano-structure and three spiro-structures) can be delivered.

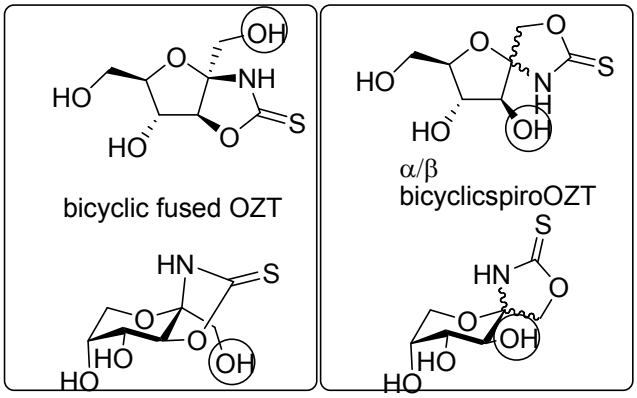
The reaction of D-fructose and L-sorbose with thiocyanic acid in aqueous solution was examined by Dr. Girniene: as expected, the complex mixture of products obtained did not allow easy separation by column chromatography. According to Grouiller, the crude material was per-*O*-silylated (TBDMS), in order to facilitate isolation of the fused bicyclic thionocarbamates. For both ketose series, the same type of fused-furano thionocarbamate was isolated. Acid-catalyzed deprotection returned naked OZTs in good yield (Scheme 46).[81]

[80] Lichtenthaler F W.; Klotz J.; Flath F.-J. *Liebigs Ann.* **1995**, 2069-2080.
[81] Girniene J.; Tatibouët A.; Sackus A.; Yang J.; Holman G. D.; Rollin P. *Carbohydrate Res.* **2003**, *338*, 711-719.



Scheme 46

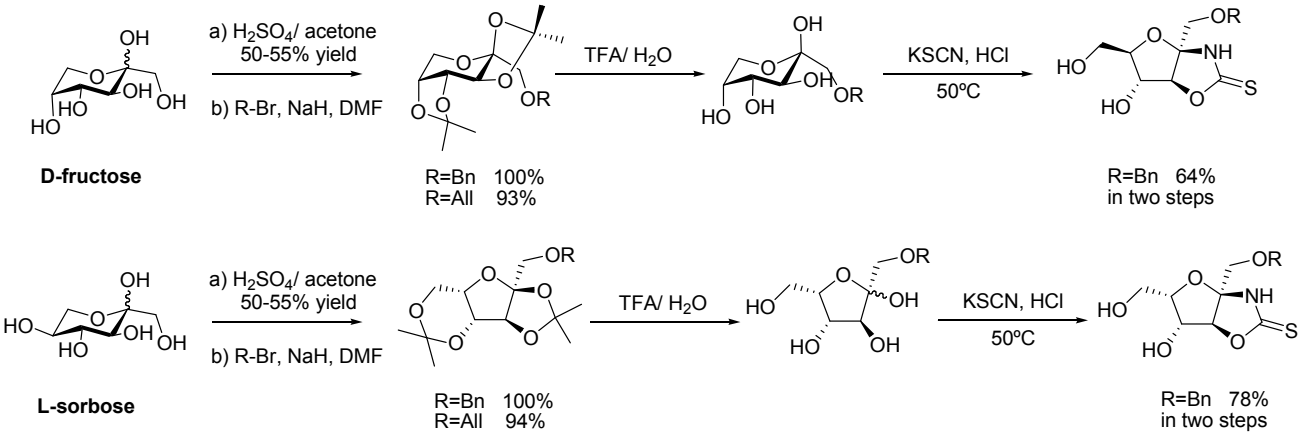
With a view to increasing the selectivity in OZT formation (i.e. reducing the number of products shown in Scheme 45), selective hydroxyl protections were performed. Protection of the alcohol in C-1 would induce limitation to fused structures, whereas 3-*O*-protection would only allow formation of *spiro*-derivatives (Scheme 47).



Scheme 47

The O-1 protection of D-fructose and L-sorbose was developed by Dr. Girniene. The free ketoses were first protected in the form of isopropylidene acetals, then the remaining primary alcohol underwent etherification (benzylation or allylation) in excellent yields. Acid-catalyzed hydrolysis of the isopropylidene groups, followed by condensation with HSCN produced efficiently the fused bicyclic

OZTs. In all cases, a unique OZT isomer was isolated. The synthesis of these bicyclic systems was achieved in reasonable overall yields (30-35% in D-fructo series and 34-43% in L-sorbo series) (Scheme 48).



Scheme 48

In the continuation of this work, Tatibouët et al have prepared diverse selectively protected derivatives from D-fructose and L-sorbose.[82] Applying classical methods of glycochemistry, they have synthesized and isolated a number of stereo-defined bicyclic products, thus validating some of the possibilities showed in Scheme 45.

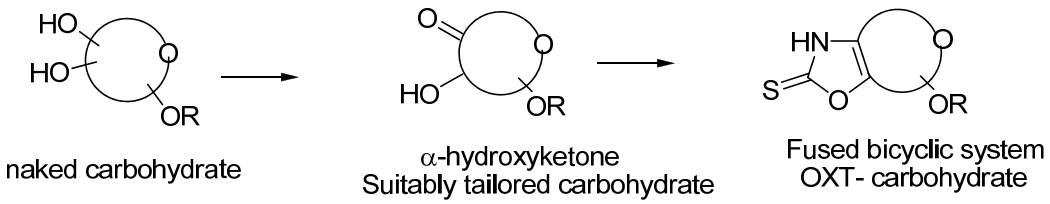
[82] Tatibouët, A.; Lawrence, S.; Rollin, P.; Holman, G. D. *Synlett* **2004**, 1945-1948.

2. Synthesis of fused OXTs on carbohydrate templates

The main similitude between OZTs and OXTs resides in the fact that both structural types can be attained in a single process of condensation with thiocyanic acid, starting from an α-hydroxylated aldehyde or –ketone moiety.

As previously seen in the above examples, condensation with HSCN not only requires a free anomeric position, but also one free hydroxyl in position γ- or δ, in order to accomplish the intramolecular cyclization during the condensation process (Scheme 42). Whenever an OXT is targeted, no other intramolecular cyclization should interfere during the reaction with HSCN.

In the previous chapter, we have reinvestigated the preparation of simple OXTs using α-hydroxyketones. Hence, if we wish to synthesise carbohydrate-based fused bicyclic OXTs, it is clear that the carbohydrate templates should be suitably tailored in order to build the desired α-hydroxyketones to be submitted to the condensation with HSCN (Scheme 49).



Scheme 49

Several factors should be then considered before attempting the formation of these OXTs:

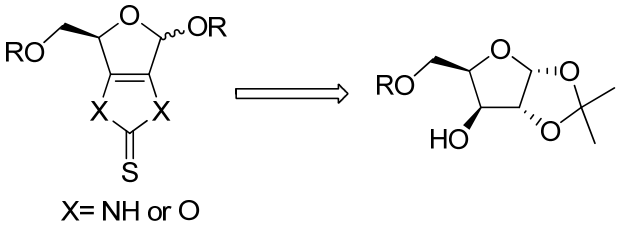
- ☑ Selection of best-adapted carbohydrate series
- ☑ Protecting groups compatibility
- ☑ Oxidation ability
- ☑ Anomeric protection stability for OXT formation.

We have explored both furano- and pyrano-carbohydrate templates.

2.1. OXTs fused on carbohydrate templates in pentose series

2.1.1. Simple assays with a keto-group in position 3

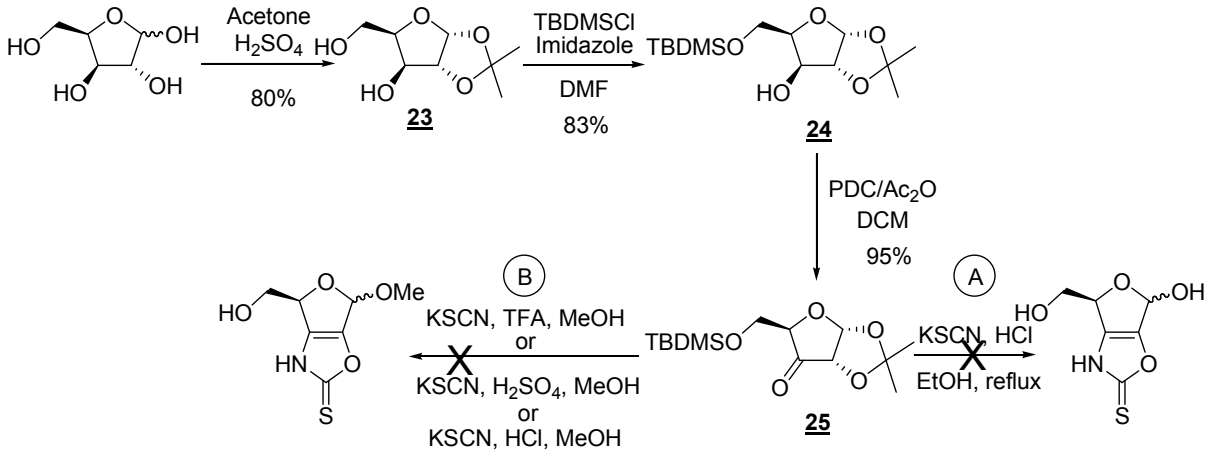
First to be considered was the case of an α-hydroxycarbonyl segment inserted in a furanoid structure. Indeed, a pentofuranose-based approach seemed to be the most appropriate to establish such functional relationship between positions 2 and 3 and therefore D-xylose was firstly targeted (Scheme 50).



Scheme 50

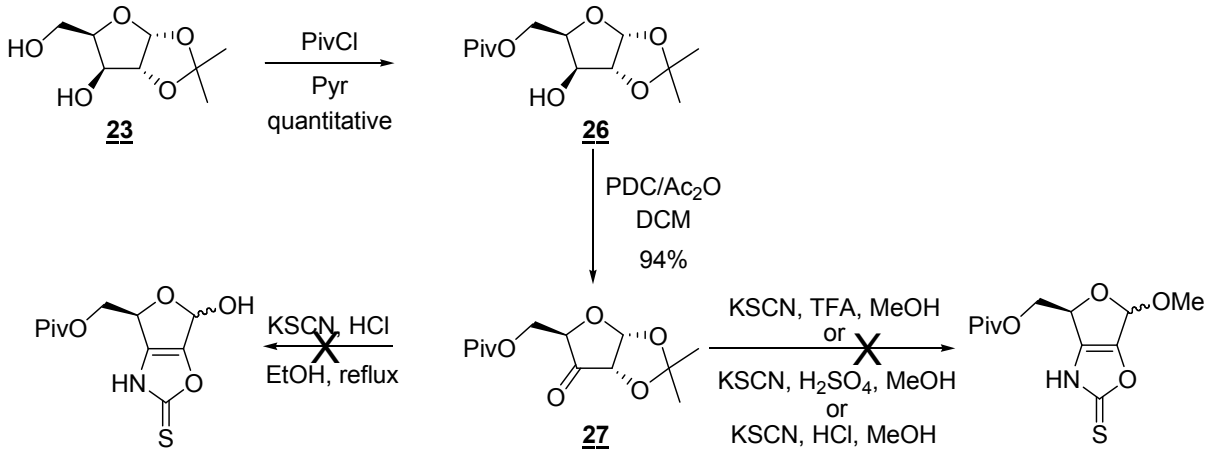
One dominant idea was to readily access synthetic precursors via a limited number of steps. Therefore, we have started with 1,2-*O*-isopropylidene-α-D-xylofuranose **23**, easily prepared from D-xylose,[83] which was selectively 5-*O*-protected with a TBDMS group in 83% yield.[84,85] The resulting silyl ether **24** was then oxidized to the 3-ulose **25** in 95% yield.[86] Taking into account that an isopropylidene acetal cleaves in acidic medium, we have applied standard conditions for direct OXT formation, but only degradation occurred (A). In order to overcome the problems associated with anomeric instability, we have changed the solvent and the acid catalyst (B) in order to provoke methyl glycosidation together with HSCN condensation: however none of our attempts proved successful (Scheme 51).

[83] Moravcovà, J.; Capkovà, J.; Stanek, J. *Carbohydr. Res*. **1994**, *263*, 61-66.
[84] Lu, Y.; Just, G. *Tetrahedron* **2001**, *57*, 1677-1687.
[85] Parr. I. B.; Horenstein, B. A. *J. Org. Chem*. **1997**, *62*, 7489-7494.
[86] Xavier, N. M.; Rauter, A. P. *Org. Lett*. **2007**, *9*, 3339-3341.



Scheme 51

As the problem might be a consequence of the acid-sensitivity of the silyl ether, *O*-5 protecting group was changed for a more acid-resistant one. The primary alcohol of 1,2-*O*-isopropylidene-α-D-xylofuranose was then selectively and quantitatively pivaloylated.[87,88] Subsequently oxidation of **26** was achieved with PDC/Ac2O in 94% yield. Unfortunately, when submitted to the reaction sequence previously described, the ulose **27** underwent degradation (Scheme 52).



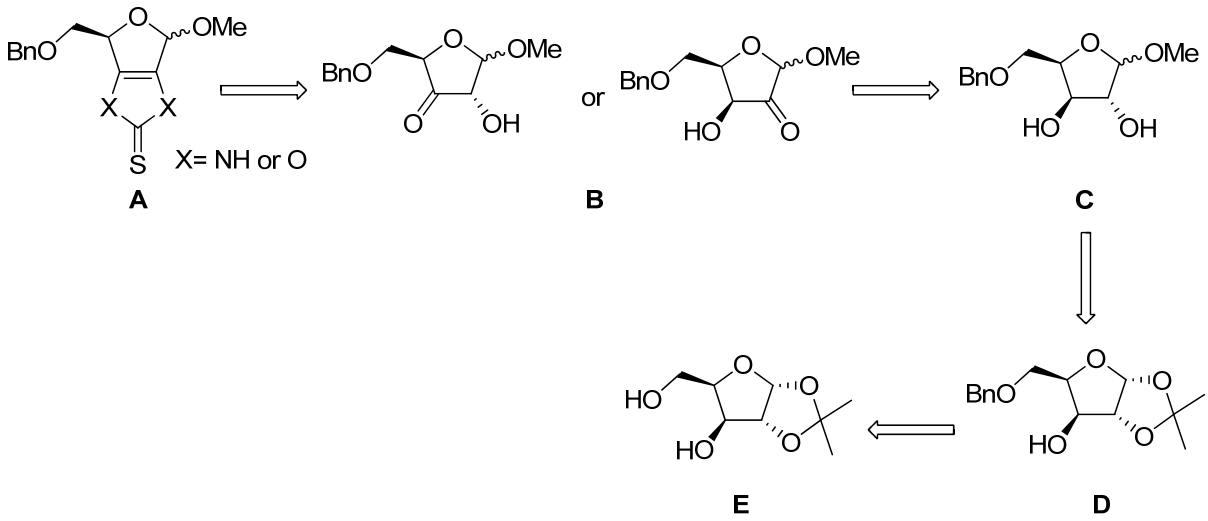
Scheme 52

[87] Francisco, C. G.; Martín, C. G.; Suárez, E. *J. Org. Chem*. **1998**, *63*, 2099-2109.
[88] Suhara, Y.; Nihei, K.; Kurihara, M.; Kittaka, A.; Yamaguchi, K.; Fujishima, T.; Konno, K.; Miyata, N.; Takayama, H. *J. Org. Chem*. **2001**, *66*, 8760-8771.

With those results, we were convinced that protection of the anomeric position by an isopropylidene ketal was not suitable under the used conditions. Following *O*-5 blocking by a "permanent" group, the introduction of a glycoside should be accomplished before the HSCN condensation process.

2.1.2. A new retrosynthetic analysis

With those considerations in mind, our new retrosynthetic analysis towards fused OXTs **A** was devised as depicted in Scheme 53.



Scheme 53

The fused furano-OXT **A** might be obtained from the α-hydroxy keto sugars **B** which could be prepared by a key-reaction - selective oxidation of the diols **C**. The anomeric mixture **C** would result from methanolysis of a 5-*O*-benzyl protected D-xylose **D**, easily available from 1,2-*O*-isopropylidene-α-D-xylofuranose **A**.

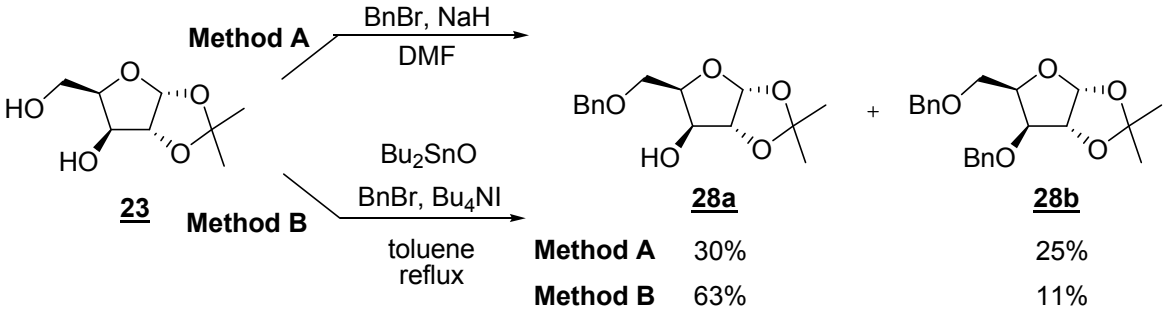
Subsequently, all optimizations, difficulties and surprises discovered on each step of this synthesis will be described.

2.1.3. Starting from 1,2-*O*-isopropylidene-α-D-xylofuranose

2.1.3.1. First step: selective mono-benzylation

Among the arsenal of hydroxyl protecting groups, benzyl ether was selected as permanent protection throughout the synthesis.

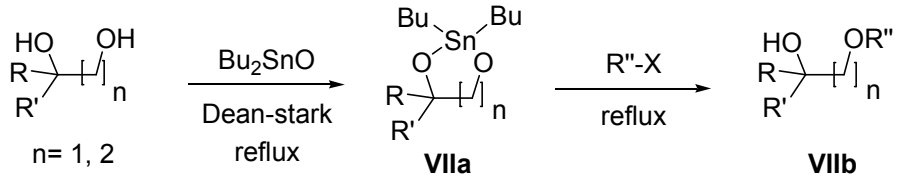
Hence, two trials were performed in order to produce the desired mono-ether **28a** (Scheme 54). In the first attempt (method A), standard benzylation conditions were applied to **23**:[89] compound **28a** was obtained in 30% yield only and a large amount of 3,5-diether **28b** was formed.



Scheme 54

In 1985, David has reported the utility of organotin derivatives of alcohols in regioselective reactions, leading to indirect acylation, oxidation and alkylations.[90] The introduction of dibutylstannylene acetals derived from diol moieties, provided a major leap in carbohydrate chemistry[91,92] (Scheme 55). Produced by reaction of a diol with dibutyltin oxide, a stannylene ketal **VIIa** can undergo substitution to afford a monosubstituted species **VIIb** under essentially neutral conditions. A notable feature of these reactions is the regiochemical control: in the case of stannylene ketals involving a primary and a secondary O-center, alkylation at the primary oxygen group prevails.

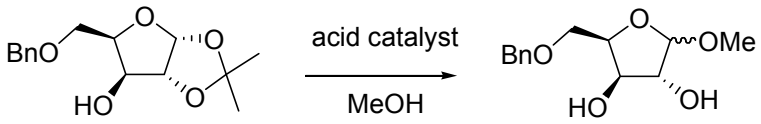
[89] Enholm, E. J.; Bhardawaj, A. *Tetrahedron Lett.* **2003**, *44*, 3763-3765.
[90] David, S.; Hanessian, S. *Tetrahedron* **1985**, *41*, 643-663.
[91] Alper, P. B.; Hendrix, M.; Sears, P.; Wong, C.H. *J. Am. Chem. Soc.* **1998**, *120*, 1965-1978.
[92] Simas, A. B. C.; País, K. C.; Silva, A. A. T. *J. Org. Chem*. **2003**, *68*, 5426-5428.



Scheme 55

Applying David's approach to **23** (method B), we have obtained the 5-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranose **28a** in 63% yield, in accordance to literature.[91] However, the di-*O*-benzyl derivative **28b** was still obtained as a side product.

2.1.3.2. Second step: methyl glycosylation



28 **29** (α, β)

solvent	acid catalyst	yield (%)	α/β ratio
MeOH	H_2SO_4	44	55/45
MeOH	HCl	58	62/38
MeOH	CH_3SO_2Cl	70	44/56

Scheme 56

The methyl glycosylation was carried out using three different acid catalysts (Scheme 56). Treatment of **28a** with H_2SO_4 in methanol was attempted[93] affording the anomeric mixture **29** in only 44 % yield. This disappointing result might be due to a fast degradation of the products in the reaction medium. Slight improvement of the

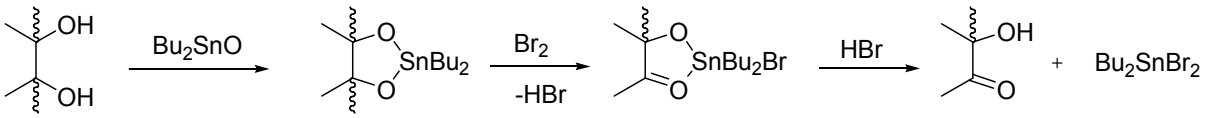
[93] Chu, C. K.; Cheng, Y.; Pai, B. S.; Yao, G. PCT Int. Appl. WO 9520595, 1995; *Chem. Abstr*. **1995**, *124*, 56575.

yield was obtained by using HCl,[94] but the best result (70% yield) was attained by applying mesyl chloride to promote the glycosylation.[95] In spite of many efforts made to separate α and β anomers, no success was reached.

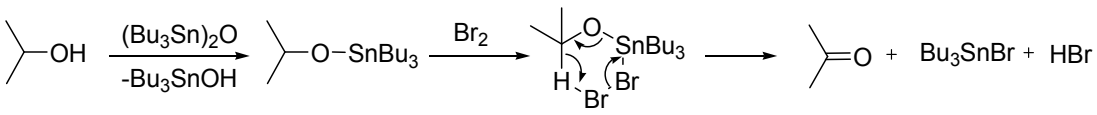
2.1.3.3. Third step: selective oxidation

It is known that the O-Sn linkages in tributyltin ethers or stannylene ketals are very sensitive to brominolysis and can give rise to carbonyl compounds at the speed of titration[37] (Scheme 57).

Bromolysis of a dibutylstannylene derivative:

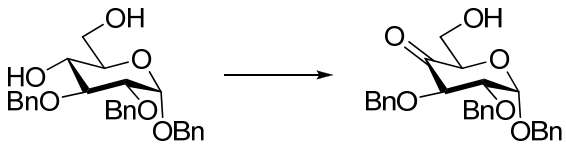


Bromolysis of a tributylstannylene derivative:



Scheme 57

Accordingly, David and Thieffry[96] succeeded in mono-oxidation of partially protected carbohydrate diols on treatment with Bu_2SnO followed by brominolysis, through which oxidation occurred at the secondary hydroxyl group in good yield (Scheme 58).

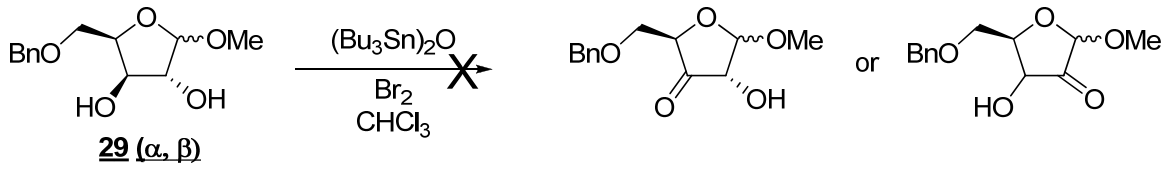


Scheme 58

[94] Cuzzupe, A. N.; Florio, R.; Rizzacasa, M. A. *J. Org. Chem*. **2002**, *67*, 4392-4398.
[95] Leroux, J.; Perlin, A. S. *Carbohydr. Res*. **1978**, *67*, 163-178.
[96] Serge, D.; Thieffry, A. *J. Chem. Soc. Perkin Trans. 1* **1979**, 1568-1572.

Four years later, Tsuda and coll.[97] reported the mono-oxidation of non protected glycosides, comparing Bu_2SnO-Br_2 and $(Bu_3Sn)_2O$-Br_2 systems. Surprisingly, the latter method was sometimes superior to the former in terms of both yields and selectivity. After several fruitless attempts, the authors found that stannylation of the glycosides in refluxing chloroform with an excess of $(Bu_3Sn)_2O$ in the presence of 3Å molecular sieves followed by *in situ* bromolysis of the cooled mixture, is the suitable procedure for a smooth oxidation of glycosides.

However, in our case, when submitting the mixture **29** to the above conditions, no oxidation was observed and the starting material was recovered unchanged (Scheme 59).



29 (α, β)

Scheme 59

This lack of reactivity might be attributed to a non-stannylation process so that no brominolysis could take place. As the direct formation of an α-hydroxyketone through regioselective oxidation could not be performed, a standard approach involving protection-deprotection steps was required.

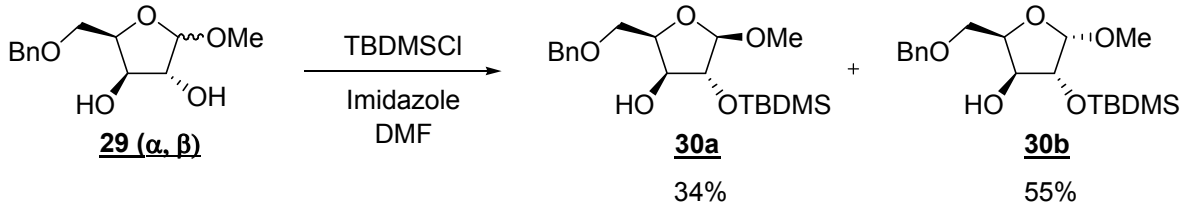
The choice of the protecting group is not straightforward. Indeed, some considerations should be taken into account before carrying out the process:

- ☑ The protection should be easily introduced.
- ☑ It should be rather large-sized to favour monoprotection.
- ☑ It should be sensitive to acidic conditions: after oxidation, the deprotection and condensation with thiocyanic acid can thus be achieved in a one step process.

[97] Tsuda, Y.; Hanajima, M.; Naohisa, M.; Okund, Y.; Kanemitsu, K. *Chem. Pharm. Bull*. **1989**, *37*, 2344-2350.

Tert-butyldimethylsilyl ether (TBDMS) – one of the most common silyl protecting groups used in organic synthesis – meets all those requirements.

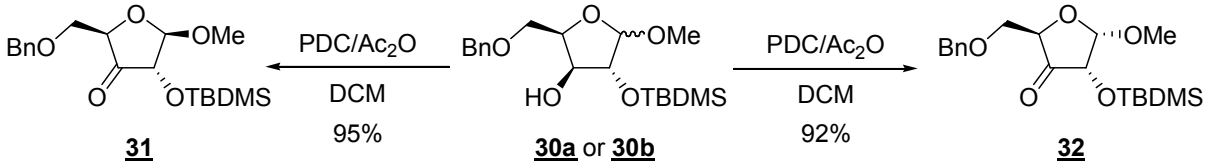
Thus, the mixture **29** was submitted to standard silylation conditions (Scheme 60) and a regioselective protection of the less hindered hydroxyl group was attained in 89% overall yield.[98]



Scheme 60

Furthermore, at this stage, the separation of β and α epimers was monitored without difficulty by column chromatography (α/β diastereomeric ratio 1.6:1).

Further PDC oxidation of the free hydroxyl gave β- and α-ulosides **31** and **32** in 95% and 92% yield, respectively (Scheme 61).

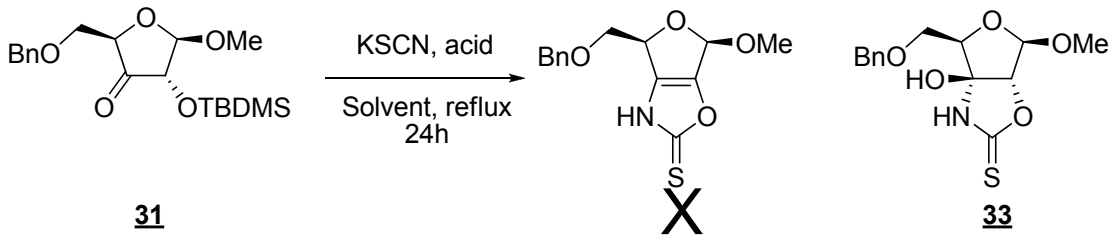


Scheme 61

2.1.3.4. Fourth step: condensation with thiocyanic acid

Knowing that *tert*-butyldimethysilyl group is acid-sensitive, its deprotection can occur during condensation of **31** and **32** with thiocyanic acid; therefore just one more step should be enough to achieve the desired OXT A. First, the uloside **31** was submitted to different conditions for the OXT formation (Scheme 62).

[98] Cuzzupe, A. N.; Florio, R.; White, J. M.; Rizzacasa, M. A. *Org. Biomol. Chem*. **2003**, *1*, 3572-3577.



31 **33**

solvent	acid	yield (%)
EtOH	HCl	81
THF	HCl	61
THF	TsOH.H_2O	92

Scheme 62

Interestingly, we first observed that the condensation product obtained was not the expected OXT, but a hydrated form displaying a hemi-aminal type function at C-3.[99] In fact, no water elimination was observed and a *cis* relationship was postulated for OZT **33** from the control of the configuration by OH-2.

When applying our optimal conditions for OXT formation (KSCN, EtOH, HCl), the condensation yield remained good, but some degradation also took place. With the purpose of preventing partial anomeric hydrolysis or transacetalation, EtOH was replaced by THF but the THF/ HCl combination was not as efficient. Changing the acid to TsOH.H_2O helped to optimize the chemical yield: HSCN efficiently condensed (92% yield) on the β-uloside.

The relative configuration was determined by crystallographic analysis, (Figure 2), and confirmed our hypothesis. In the crystal lattice, two molecules were detected in the unit. The results related to this study are grouped in Table 5.

[99] Silva, S.; Simão, A. C.; Tatibouët, A.; Rollin, P.; Rauter, A. P. *Tetrahedron Lett*. **2008**, *49*, 682-686.

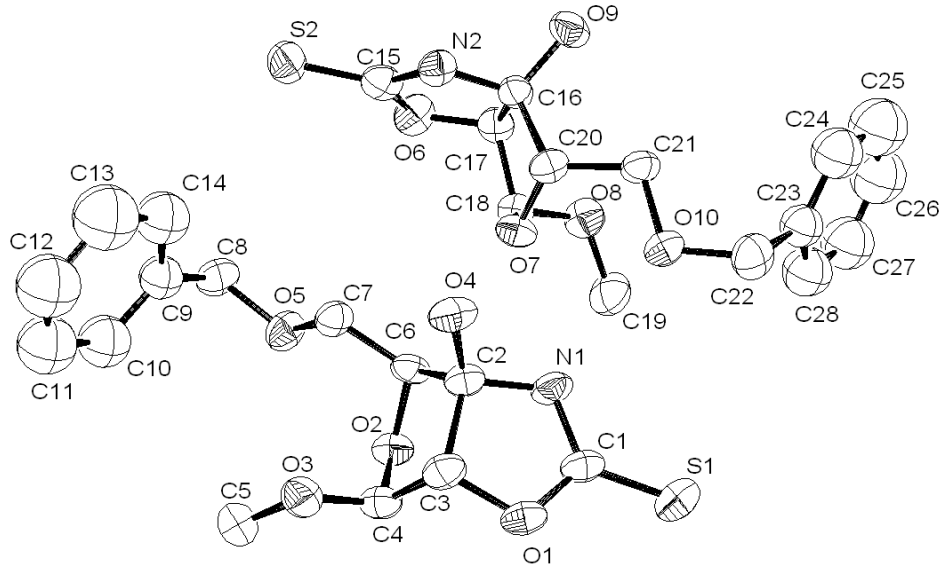


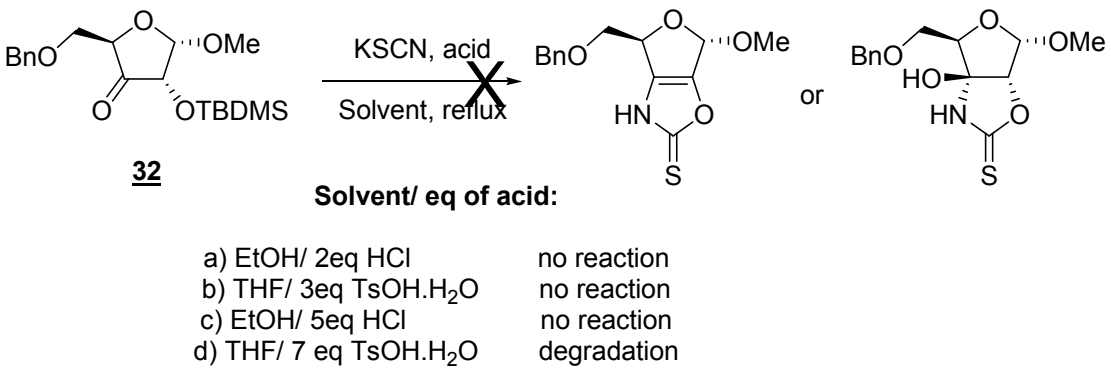
Figure 2

crystal data	results
Identification code	SS 33
Empirical formula	$C_{14}H_{17}NO_5$
Masse molaire (g.mol^{-1})	622.69
Temperature (K)	293 (2)
Wavelength (Å)	0.71
Recristalization solvent	DCM
Z, Calculated density (g.cm^{-3})	1.374
Absorption coefficient (mm^{-1})	0.235
Crystal size (mm)	0,2 × 0,3 × 0,3
Crystal system, space group	Triclinic, P1
Unit cell dimensions	a = 7.080(5) Å, b = 8.552(5) Å, c = 13.195(5) Å α = 101.85°, γ = 90.00°, β = 105.47°
Volume (Å^3)	752.3 (7)

Table 5

The α-uloside **32** was then submitted to HSCN condensation under the conditions previously established for **31** but no conversion into OXT or OZT was

observed. Even by increasing the number of HSCN equivalents in solution (up to 7 equivalents), only degradation was observed (Scheme 63).

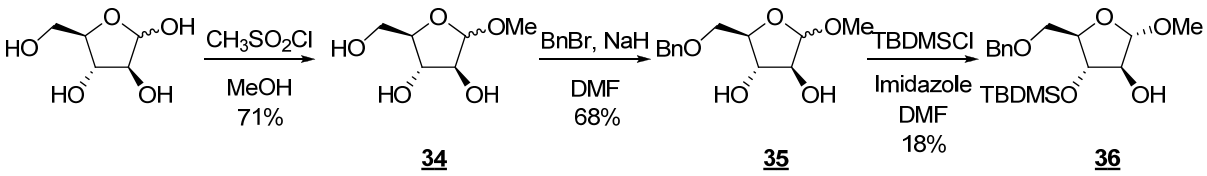


Scheme 63

The dramatic difference of reactivity between α and β anomers could be attributed to some steric hindrance or electronic repulsion induced by the *cis*-relationship between α-OMe and OH-2. This point will be further discussed at the end of the chapter.

2.1.4. Assays with D-arabino pentofuranose

We have also explored a permutation between the oxygen and nitrogen atoms in 2- and 3- positions of the carbohydrate ring. D-Arabinose was chosen as starting material for the synthesis presented in Scheme 64.



Scheme 64

In the first step we used the optimized conditions previously described. The methyl arabinofuranoside **34** was prepared in 71% yield as an anomeric mixture. Both anomers were engaged in standard benzylation to afford regioselectively the mono-benzylated products **35** in 68% yield. The silylation step proved quite disappointing because of its non-selectivity. In fact, contrary to D-xylo series, in which the silylation was oriented to O-2 because of the steric hindrance on the access to O-3, in the D-arabino series, spatial differentiation between OH-2 and OH-3 is not so strong, what makes possible the formation of both 2- and 3- *O*-silyl ethers, together with the 2,3-di-*O*-silyl ether.

By column chromatography we were able to separate the *O*-silylated α-arabinoside **36** in 18% yield. The structure of this compound could be ascertained by the typical *trans* H-1,H-2 coupling constant ($J_{1\text{-}2}$ < 2 Hz) (figure 3).[100]

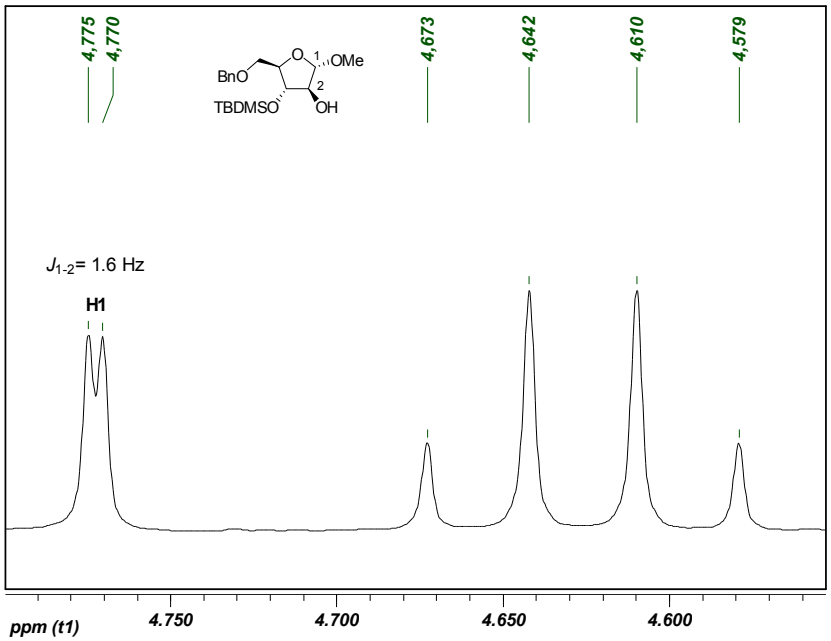
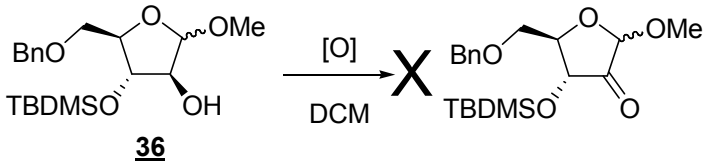


Figure 3

Other silylated products of this reaction were detected by NMR analysis but in our hands, their separation by column chromathography revealed not possible.

[100] Ferrières, V.; Bertho, J. N.; Plusquellec, D. *Tetrahedron Lett.* **1995**, *36*, 2749-2752.

Despite the mediocre selectivity and the low yield of the silylation reaction, several assays were carried out in order to achieve oxidation of the free 2-OH of compound **36** but despite all our attempts, no oxidation occurred. The reaction conditions used to oxidize are shown below (Scheme 65).



36

oxidizing agent	yield
PDC/Ac_2O	S.M.
TFAA/DMSO/NEt_3[101]	S.M.
Dess Martin[102]	S.M.
TEMPO[103]	S.M.

Scheme 65

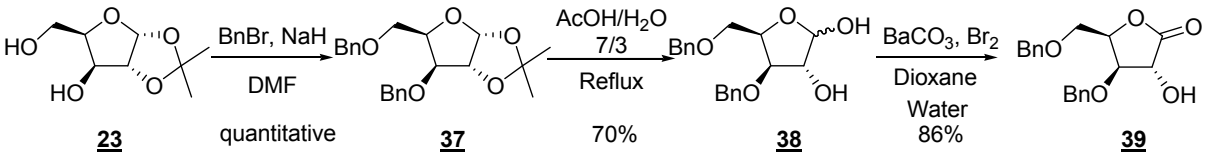
The low selectivities, moderate yields and the difficulty to oxidize the second position in the sequence when addressing the D-arabino series, didn't allow the synthesis of the desired fused bicyclic OXT systems.

2.1.5. Assays with a lactone

Following with the study of OXTs fused on pentofuranoses, we were interested to know whether the carbonyl group in a lactone would react with thiocyanic acid in a similar way as in aldehydes or ketones.

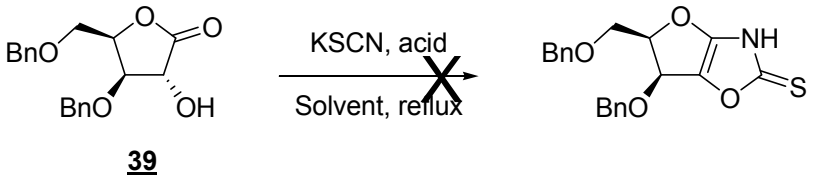
[101] Mancuso, A. J.; Huang, S. L.; Swern, D. *J. Org. Chem*. **1978**, *43*, 2480-2482.
[102] Ye, J. D.; Liao, X.; Piccirilli, J. A. *J. Org. Chem*. **2005**, *70*, 7902-7910.
[103] Anelli, P. L.; Banfi, S.; Montanari, F.; Quici, S. *J. Org. Chem*. **1989**, *54*, 2970-2972.

In order to explore this question, a simple route was designed to build up an α-hydroxylactone derivative, which could be exposed to thiocyanic acid. 1,2-*O*-isopropylidene-α-D-xylofuranose **23** was quantitatively converted into the dibenzyl ether **37**.[104] Removal of the isopropylidene group under acidic conditions[105] followed by selective anomeric oxidation with bromine[106] provided the lactone **39** in 60% yield over two steps (Scheme 66).



Scheme 66

The di-*O*-benzyl lactone **39** was then submitted to condensation with thiocyanic acid. However, despite the variety of reaction conditions attempted, the expected fused OXT could not be synthesised (Scheme 67).



solvent	acid	KSCN (eqs)	time	results
EtOH	HCl	2	24h	S.M.
EtOH	HCl	4	24h	S.M.
THF/DMF (8:1)	HCl	4	24h	S.M.
THF/DMF (8:1)	TsOH.H_2O	4	24h	S.M.
Dioxane	H_2SO_4	4	24h	S.M.
DMF	TsOH.H_2O	4	24h	S.M.
CH_3CN	HCl	4	48h	deg.

Scheme 67

[104] Matsuda, F.; Terashima, S. *Tetrahedron* **1998**, *44*, 4721-4736.
[105] Ning, J.; Kong, F. *Carbohydr. Res*. **1997**, *300*, 355-360.
[106] Witty, D. R,; Fleet, G. W. J.; Vogt, K,; Wilson, F. X.; Wang, Y.; Storer, R.; Myers, P. L.; Wallis, C. J. *Tetrahedron. Lett*. **1990**, *31*, 4787-4790.

These results confirmed the lower reactivity of the carbonyl group in a lactone when compared to that of a ketone or an aldehyde. This observation was somehow expected, since the esters are far less reactive against electrophiles.

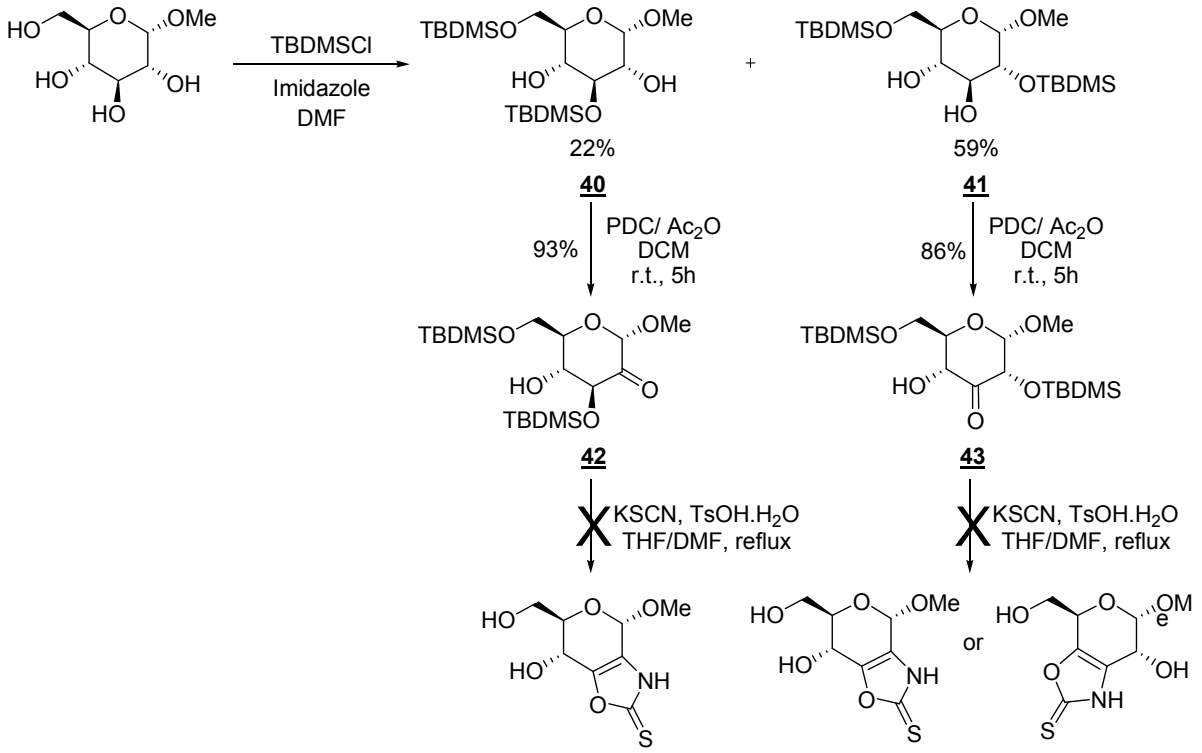
2.2. OXTs fused on pyrano carbohydrate templates

2.2.1. Starting from methyl α-D-glucopyranoside: ketone in position 2 or in position 3

To extend our knowledge about the formation of OXTs or hydroxyl-OZTs, we have developed α-hydroxyketo segments inserted in pyrano-type structures derived from methyl D-glucopyranosides.

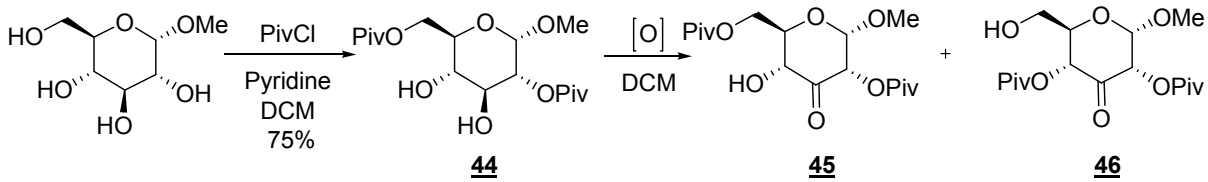
We first turned our attention to methyl α-D-glucopyranoside as starting material. With the aim to obtain fused OXTs in positions 2-3 or 3-4 of the selected template, a simple route was traced. Recurring again to versatile silyl ethers, the glucopyranoside was reacted with 2.1 eq. of TBDMSCl in the presence of imidazole - good regioselectivity was attained, with two major products isolated: the 3,6-di-*O*-silylated derivative **40** (22% yield) and the 2,6-di-*O*-silylated compound **41** (59% yield).[107] The silylated regioisomers were then subjected to PDC oxidation to selectively afford the respective keto-derivatives **42** and **43** in very good yields, with no trace of oxidation at O-4. The standard conditions of HSCN condensation were applied to those uloses and in both cases, no cyclic thionocarbamate could be isolated and only degradations occurred (Scheme 68).

[107] Chung, M.Y.; Orlova, G.; Goddard, J. D.; Schlaf, M.; Harris, R.; Beveridge, T. J.; White, G.; Hallett, F. R. *J. Am. Chem. Soc.* **2002**, *124*, 10508-10518.



Scheme 68

The observed behaviour of **42/43** could be connected with the acid-sensitivity of the TBDMS protecting group. During condensation with thiocyanic acid, partial TBDMS deprotection could occurs, leading to a complex mixture of products. To overcome this problem, we have designed a new approach using a more acid-stable protecting group, a pivaloyl ester. Hence, a new α-hydroxyketone suitable for HSCN condensation was readily prepared from methyl α-D-glucopyranoside using a chemoselective sequence of two reactions (Scheme 69).



Scheme 69

The regioselective 2,6-bis-*O*-pivaloate **44** was obtained following a method described in literature.[108] Pivaloyl chloride reacted regioselectively with the glucoside at -20ºC to afford the *trans* diol **44** in 75% yield, which was regioselectively oxidized[109] at O-3, to furnish the ketol **45**. The high yields reported in the literature when using PCC adsorbed on alumina could not be reproduced in our hands. Therefore, we have optimized the oxidative system using PDC-Ac_2O and found that the reaction was extremely sensitive to the PDC:Ac_2O ratio. As a matter of fact, when large amounts of Ac_2O are used, formation of the regioisomer **46** can be detected. This product might be the result of a O-6 to O-4 pivaloyl migration.[110] By changing parameters (Table 6), optimal conditions (87% yield) involving a large excess of PDC could be fixed.

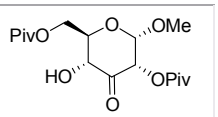
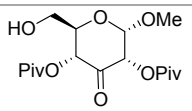
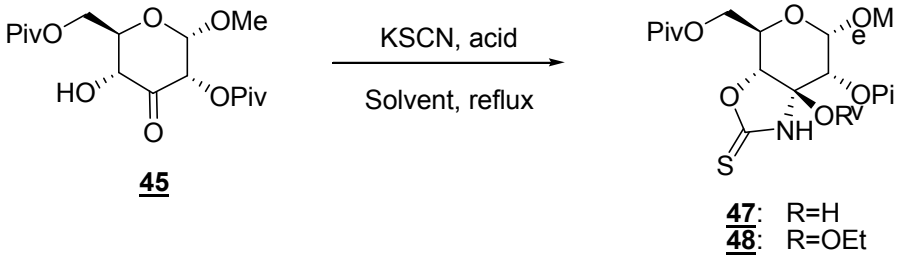
oxidizing system	**[O] (eq.)**	**Ac_2O (eq.)**	**time**	**Δ**	**yield (%)**	
					 **45**	 **46**
PCC/Al_2O_3	1.5	---	48h	reflux	33	---
PCC/Al_2O_3	2	---	48h	reflux	26	---
PDC	0.6	4	24h	rt	23	27
PDC	0.6	4	8h	reflux	33	27
PDC	0.6	---	1 week	rt	50	---
PDC	0.6	1	8h	rt	53	**---**
PDC	3	1	2.5	rt	87	**---**

Table 6

[108] Jing, L.; Chan, T. H. *J. Org. Chem*. **1998**, *63*, 6035-6038.
[109] Rauter, A. P.; Fernandes, A. C.; Czernecki, S.; Valery, J. M. *J. Org. Chem*. **1996**, *61*, 3594-3598.
[110] Tomic, S.; Petrovic, V.; Matanovic, M. *Carbohydr. Res*. **2003**, *338*, 491-494.

The α-hydroxyketone **45** was ready for condensation with HSCN and various conditions were tested to investigate the formation of the OZTs **47** and **48** (Scheme 70). Under the conditions used, the hemiaminal was formed as previously observed on furano templates. No OXT formation was detected and only very minor degradation could be observed. When performing the reaction in EtOH, both OZTs **47** and **48** were formed in 22% yield and 61% yield, respectively. In that particular case, the major alkoxy-OZT **48** is supposed to result from further transacetalation of **47** with the solvent.



45

47: R=H
48: R=OEt

solvent	acid	time (h)	yield of 47 (%)	yield of 48 (%)
EtOH	HCl	30	22	61
H_2O	HCl	48	33	---
DMF	HCl	25	23	---
DMF/THF (1:1)	HCl	64	79	---
DMF/THF (1:1)	TsOH.H_2O	64	62	---

Scheme 70

Changing the solvent to water allowed selective formation of **47**, albeit in poor low yield. Finally, optimal synthesis of **47** was performed in 79% yield by running the experiment for more than 2.5 days with HCl in a mixture of aprotic solvents.

The stereochemistry of compounds **47** and **48** was expected to follow the same results obtained with the D-xylo derivatives, being controlled by the 4-OH group. These considerations were assessed by a NOESY experiment on compound **48**, in

which a clear effect was observed between H-4 and CH_2 in the ethoxy group, which means that both entities should be positioned on the same face of the carbohydrate ring (Figure 4).

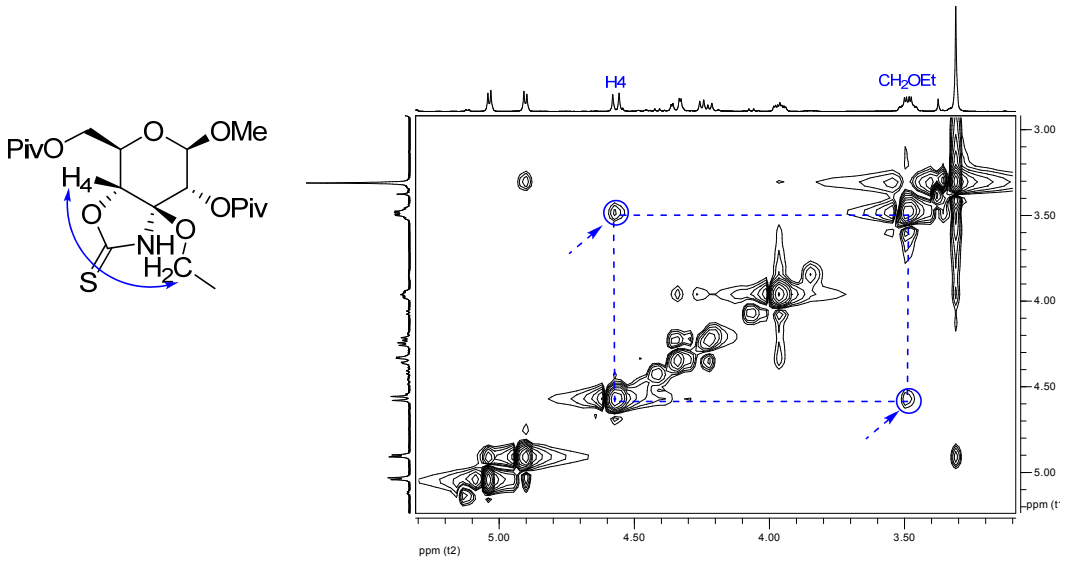


Figure 4

At this point, we were able to synthesize fused OZTs in position 3-4 of the pyrano template, with a well-defined stereochemistry.

As part of our ongoing research, the construction of α-hydroxyketones in position 2-3 of the glucopyranoside was planned.

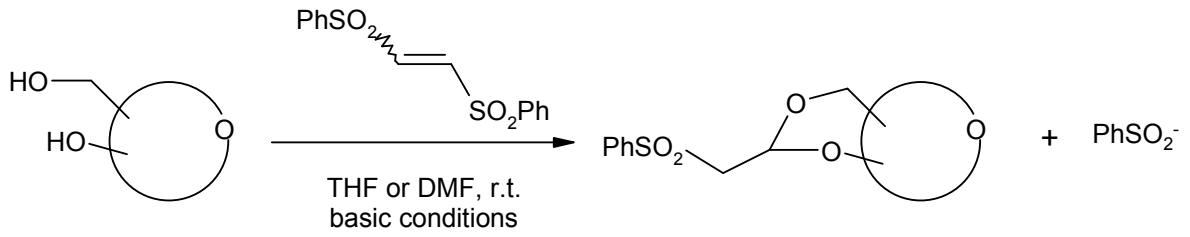
Taking into consideration the problems met when using TBDMS protection, non acid-labile groups are thus required for O-6 and O-4.

An impressive part of carbohydrate chemistry has dealt with cyclic acetals. Besides being useful for selective protection of monosacharides, cyclic acetals can display a large number of interesting reactions. This is particularly true for benzylidene acetals which can undergo regiospecific oxidative[111] and reductive[112] openings. The problem with such acetals is that they easily undergo hydrolytic ring-cleavage under mild acidic conditions[113] and thus appear inappropriate for our synthetic plan.

[111] Hanessian, S. *Methods Carbohydr. Chem*. **1972,** *6*, 183-189.
[112] Garegg, P. J.; Hultberg, H. *Carbohydr. Res*. **1981**, *93*, C10-C-12.
[113] Söderman, P.; Widmalm, G. *J. Org. Chem*. **1999**, *64*, 4199-4200.

In chapter I, we have introduced the BPSE as a useful Michael acceptor that can undergo two successive nucleophilic additions, leading to the formation of phenylsulfonylethylidene (PSE) acetals.

It was demonstrated in our group that PSE acetals can be readily prepared from unprotected glycosides under basic conditions (Scheme 71).[114,115]



Scheme 71

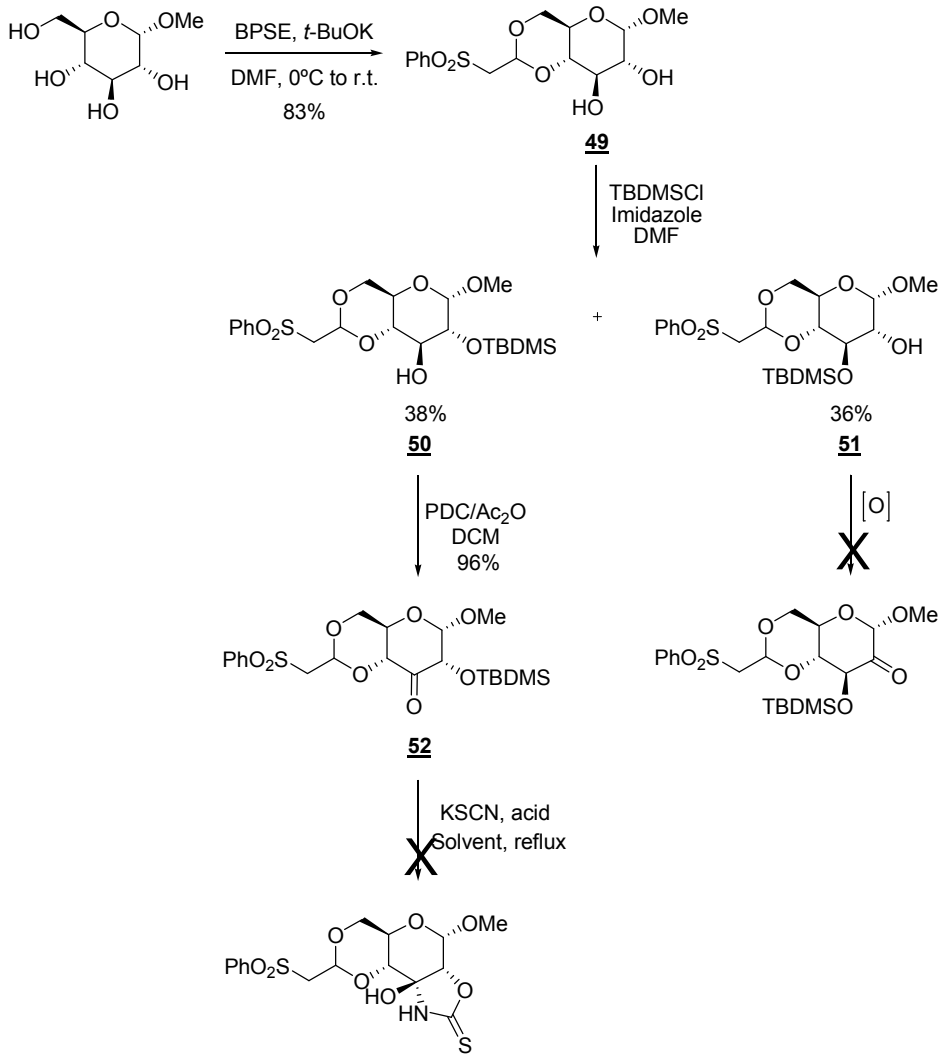
PSE acetals display a high resistance to hydrolytic conditions in acidic media, a property that makes them suitable for our synthesis.

By reaction with *Z*-1,2-bis(phenylsulfonyl)-ethylene under basic conditions, methyl α-D-glucopyranoside was converted into the PSE acetal **49** in 83% yield.[115]

Following a similar approach used in D-xylofurano series, a silylation step was required. However in this case, no regioselectivity was attained,[116] the 2-and 3-*O*-silyl ethers **50** and **51** being obtained in 38% and 36% yields, respectively. Each of the previous silylated compounds was subjected to oxidation. While derivative **50** was readily oxidized (PDC/Ac_2O) to the ulopyranoside **52** in 96% yield, the regioisomer **51** showed complete reluctance to oxidation, whatever the oxidant system applied [PDC/Ac_2O, $(COCl)_2$/ DMSO/ NEt_3 or $(CF_3CO)_2O$/ DMSO/ NEt_3].

The silylated uloside **52** was finally submitted to HSCN condensation but, despite all the different conditions tested, no formation of the expected hydrated-OXT was observed (Scheme 72).

[114] Chéry, F.; Rollin, P.; De Lucchi, O.; Cossu, S. *Tetrahedron Lett*. **2000**, *41*, 2357-2360.
[115] Chéry, F.; Rollin, P.; De Lucchi, O.; Cossu, S. *Synthesis* **2001**, *2*, 286-292.
[116] Tulshian, D. B.; Tsang, R.; Frase-Reid, B. *J. Org. Chem*. **1984**, *49*, 2337-2355.



Conditions used for HSCN condensation		
solvent	**acid**	**yield**
EtOH	HCl	S.M.
THF	HCl	S.M.
THF	TsOH.H_2O	S.M.

Scheme 72

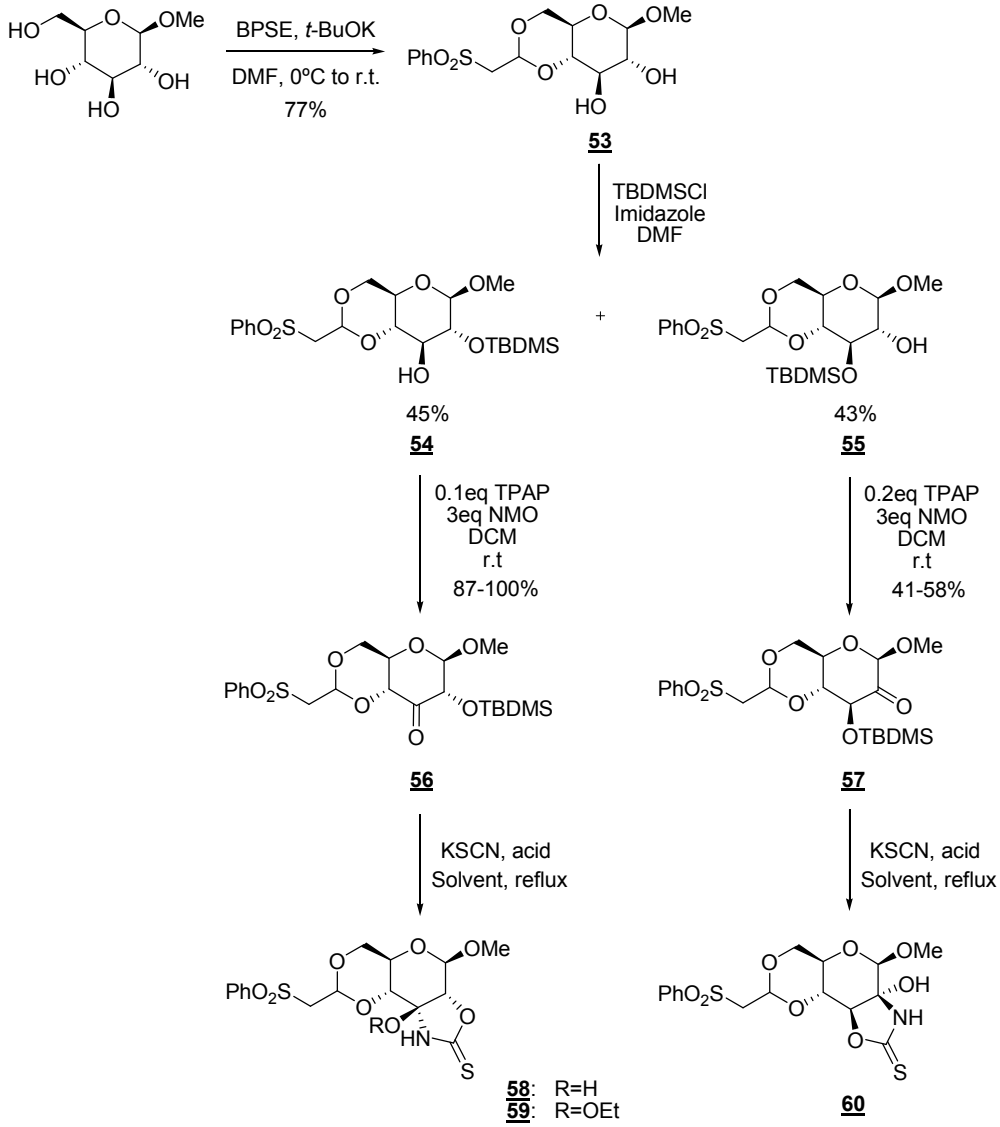
These results were compared with those obtained for the α-furanoside **32** (Scheme 63). On the contrary, the β-furanoside **31** nicely condensed with HSCN to

afford the hydroxy-OZT **33** in good yield. A similar influence of the anomeric configuration in ulopyranosides could be hypothesized. For that reason, the same sequence was repeated in the β-series.

2.2.2. Starting from methyl β-D-glucopyranoside: ketone in position 2 or in position 3

Methyl β-D-glucopyranoside was first converted into the PSE acetal **53** in 77% yield. Masking hydroxyl groups on either position 2 or 3 was therefore undertaken. Non-regioselective *O*-silylation of **53** led to a separable mixture of isomers **54** and **55** in 45% and 43% yields respectively. Subsequent oxidation of both compounds was performed with TPAP-NMO system,[117] which proved to be more efficient than PDC/Ac_2O in this case. In that way, oxidation on position 3 was achieved in 87-100% yields instead of 73%. Interestingly, oxidation in position 2 was achieved in 41-58% yield instead of 37%. Ulopyranosides **56** and **57** reacted with thiocyanic acid under standard conditions (KSCN, EtOH/ HCl) to provide, as expected for both cases, the OZTs **58**-**60**. The ulopyranoside **56** gave a mixture of the hemi-aminal **58** in 44% yield and the alkoxy-OZT **59** in 49% yield. In contrast, the uloside **57** afforded the hemiaminal **60** as the sole product (69% yield). Changing to aprotic solvents (THF/DMF) under $TsOH.H_2O$ catalysis only yielded the hemiaminals **58** (83% yield) and **60** (88% yield) (Scheme 73).

[117] Bloch, R.; Brillet, C. *Synlett*, **1991**, *11*, 829-830.

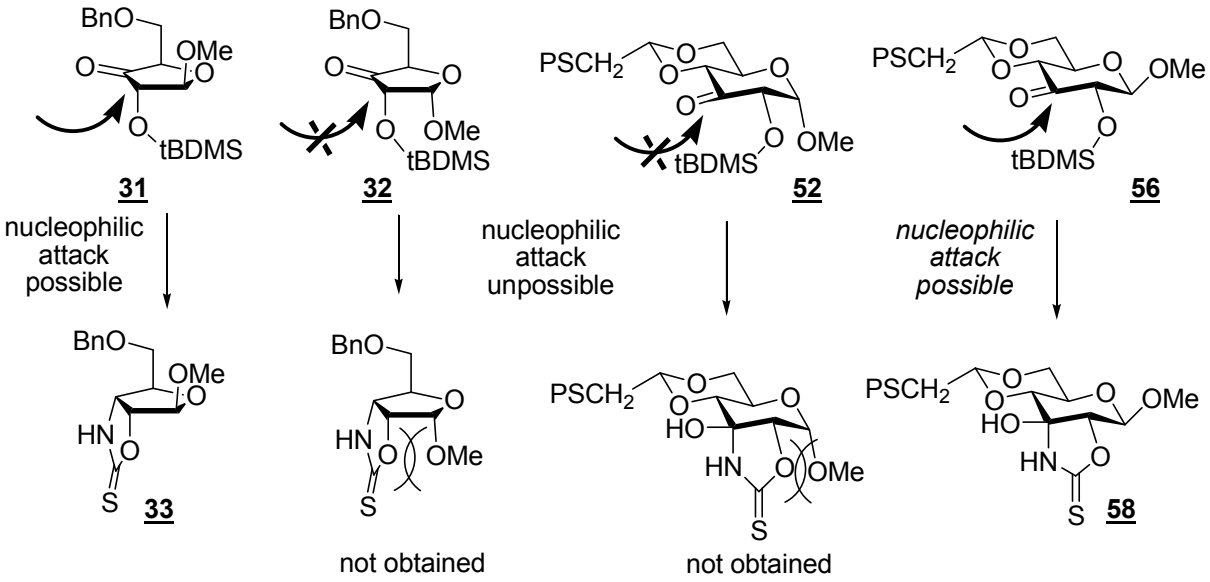


Scheme 73

Once more, we can observe that no water elimination has occurred and that the configuration of the OZT formed depends on the orientation of the hydroxyl group involved in the condensation. The configuration of the quaternary stereogenic centers in hemiaminals **58** and **60** was assigned by NOESY experiments; all OZTs showed a strict *cis* relationship.

It appears that the anomeric configuration has a decisive influence on the formation of 2-3 positioned fused OZTs: with both α-glycosides **32** and **43** which share the same 1,2-*cis* relationship, no reaction took place while on both β anomers, HSCN condensation occurred in good yields. Such behaviour might appear as a consequence of two possible phenomena (Scheme 74):

- firstly, the approach of HSCN, which is supposed to take place on the ring face congested by the masked α-hydroxyl, might be blocked because of steric or electronic effects
- secondly, unfavourable repulsive effects in the case of a 1,2-*cis* relationship to the anomeric oxygen might bring additional limitation to the construction of a fused OZT.
-



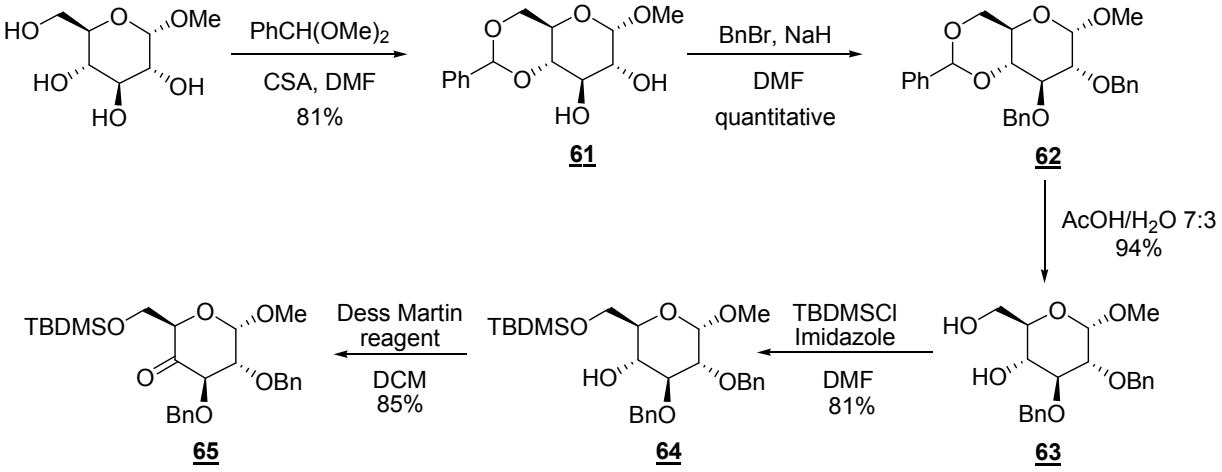
Scheme 74

At this stage of our study, we have clarified the behaviour of thiocyanic acid when opposed to a carbohydrate-based α-hydroxyketones. In all cases, the reaction leads to bicyclic OZT-sugar systems except when the 2-OH is *cis* in relation to the

anomeric position. We have also explored the reactivity of an α-hydroxylactone, which shows a strong reluctance to condensate with HSCN.

A further interesting issue was to investigate the condensation of a β-hydroxyketone with thiocyanic acid.

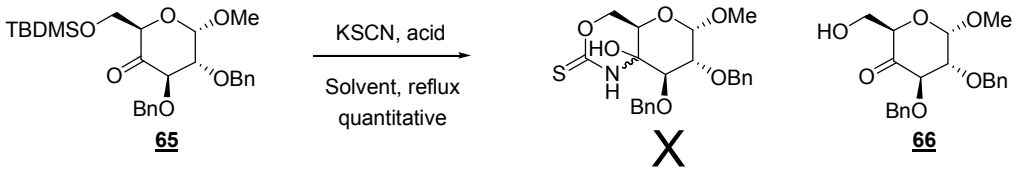
In order to bring a preliminary answer, a simple approach was devised. Following a classical method, the protected glucopyranoside **61** was synthetised in 81% yield from methyl-α-D-glucopyranoside.[118] After quantitative conversion of **61** into the di-*O*-benzyl derivative **62**, selective hydrolysis of the benzylidene ring[119] afforded compound **63** in 94% yield. This diol was regioselectively silylated at O-6 to produce **64** in 81% yield. Oxidation at position 4 was performed with Dess-Martin reagent, furnishing in 85% yield the ulopyranoside **65**, ready to condensate with thiocyanic acid (Scheme 75).



Scheme 75

However, despite all efforts, no condensation with HSCN took place and no formation of the desired 1,3-oxazine-2-thione occurred. The sole reaction observed was complete de-*O*-silylation, affording quantitatively the uloside **66** (Scheme 76).

[118] Cervi, G.; Peri, F.; Battistini, C.; Gennari, C.; Nicotra, F. *Bioorg. Med. Chem*. **2006**, *14*, 3349-3367.
[119] Boulineau, F. P.; Wei, A. *J. Org. Chem*. **2004**, *69*, 3391-3399.



Scheme 76

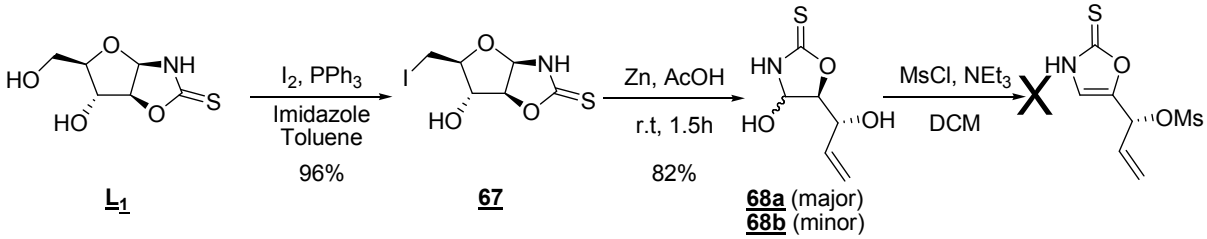
As no presence of isothiocyanate could be detected, we reasoned that the carbonyl group in position 4 has a low electrophilicity, which severely hampers nucleophilic attacks. As a consequence, we didn't investigate further HSCN condensation between positions 3 and 4 on a 4-uloside.

3. An approach to acyclic hydroxy-OXTs: fragmentation-route for elimination

The assumed standard reactivity of a carbohydrate-based α-hydroxyketone when condensed with HSCN, results in the formation of bicyclic fused systems, generating OXTs in hydrated form. Dehydration has never been detected during the reaction process.

When an α-hydroxyketone react with HSCN in acyclic systems (cf. chapter I), OXTs were readily synthesized without traces of their hydrated forms. Thus, is it possible to control the formation of an OXT in hydrated form? If so, what would be a good model to study the conditions to eliminate water?

Combining the possibility to synthesize OZT on the anomeric position and the known fragmentation reactions on carbohydrate structures, a possible access to a hydrated OXT could be hypothesized. Starting with the pre-formed OZT fused on a D-arabino scaffold **L1**, the mono-iodide **67** was prepared in 96% yield, applying Garegg conditions.[120] The epimeric hydrated OXTs **68a** and **68b** (diastereoisomeric ratio 86:14) were obtained in 82% yield through reductive fragmentation[121,122] of **67**.



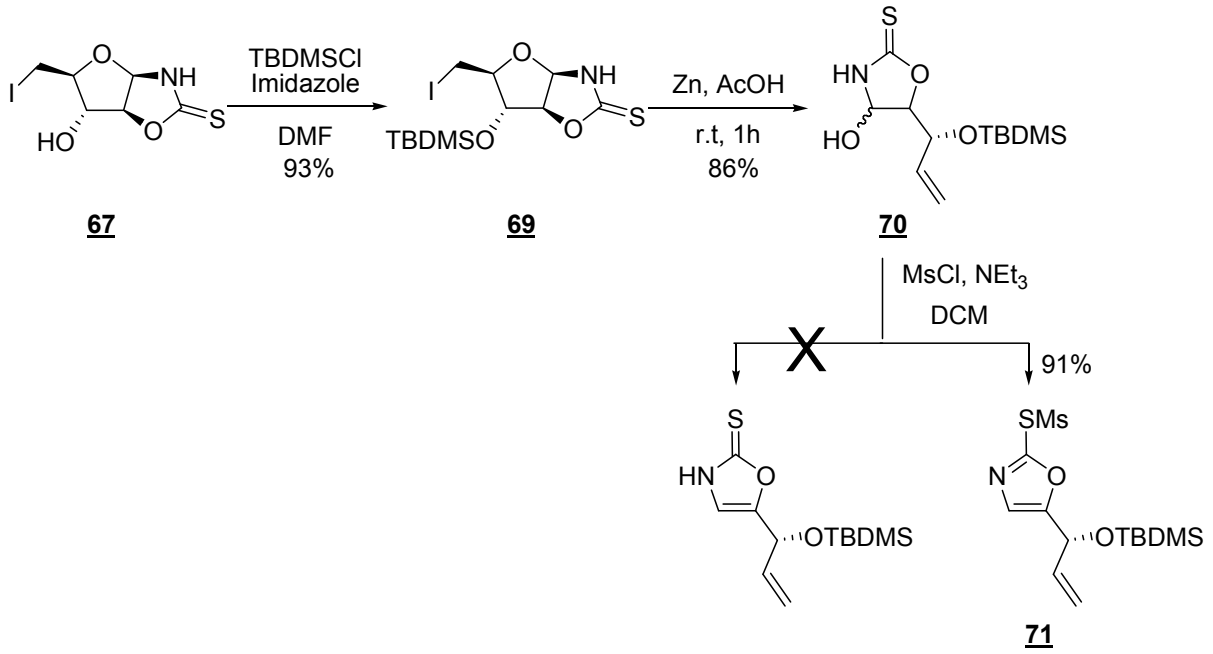
Scheme 77

3.1. Mesylation

The model **68ab** was used to test the dehydration step. Mesylation of the 4-OH was firstly experienced[123,124] but only full degradation was observed (Scheme 77). It

[120] Garegg, J.; Samuelsson, B. *J. Chem. Soc., Chem. Comm.*; **1979**, 979-980.
[121] Bernet, B.; Vasella, A. *Helv. Chim. Act*. **1979**, 62, 1990-2016.
[122] Henon, E.; Bercier, A.; Plantier-Royon, R.; Harakat, D.; Portella, C. *J. Org. Chem*. **2007**, *72*, 2271-2278.
[123] Padwa, A.; Zhang, H. *J. Org. Chem*. **2007**, *72*, 2570-2582.

was hypothesized that preliminary protection of the allylic OH would help in order to prevent degradation. In that way, iodide derivative **67** was *O*-silylated (93% yield) in standard conditions to furnish **69**, which underwent reductive fragmentation in 86% yield to produce the hydrated OXT **70**. Curiously, at this stage, only one diastereoisomer was detected by NMR, which might indicate that no isomerisation had occurred. The dehydration process was then tested on compound **70** in a single step. However - and in connection with previous observations (cf. chapter I, Scheme 17) - the sulfur atom displayed high reactivity towards mesyl chloride, and the finally product obtained in 91% yield was the oxazole-derived methanethiosulfonate **71** (Scheme 78).



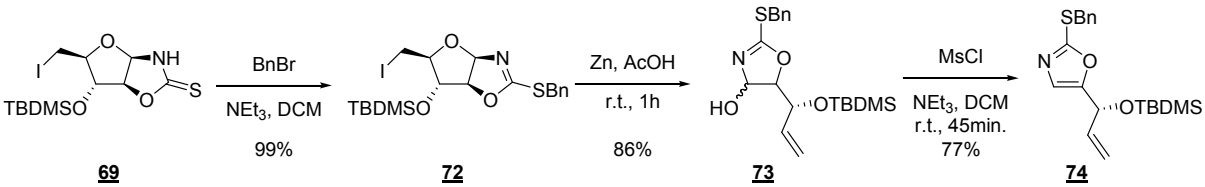
Scheme 78

The structure of **71** was ascertained by NMR: a chemical shift of 151.0 ppm was measured for C-2, which appears strongly shielded when compared to C=S in a thionocarbamate (ca 180 ppm). As previously described **18**, compound **71** is quite unstable and undergoes easy degradation. Therefore, trying to improve stability of

[124] Reeves, J. *Org. Lett*. **2007**, *9*, 1879-1881.

the end-product requires, not only the protection of the allylic hydroxyl, but also the selective introduction of a stabilizing group on the S-atom.

S-benzylation of OZT **69** was quantitatively achieved using benzyl bromide/Et_3N system. Following the previous sequence, the fragmentation was then accomplished to achieve 2-benzylsulfanyl-1,3-oxazolidine **73** in 86% yield. Once again, the fragmentation produced only one diastereoisomer. When submitted to mesylation conditions, dehydration of **73** took place to produce 2-benzylsulfanyl-1,3-oxazole **74,** which was isolated in 77% yield (Scheme 79).



69 **72** **73** **74**

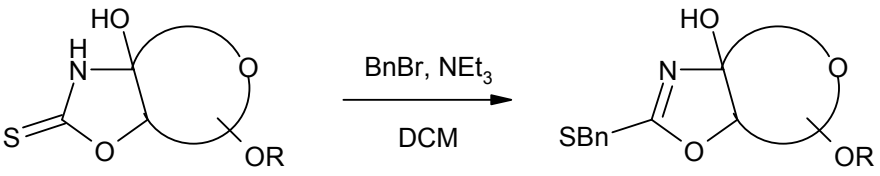
Scheme 79

☝ We have thus demonstrated the possibility to dehydrate the heterocycle to attain the oxazole aromatic structure. However, to obtain a stable molecule, the C=S group should be masked by an *S*-alkyl derivative.

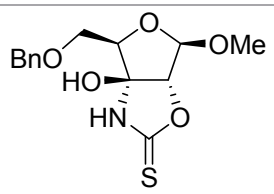
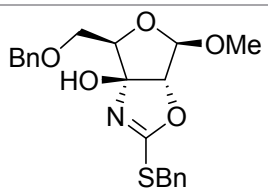
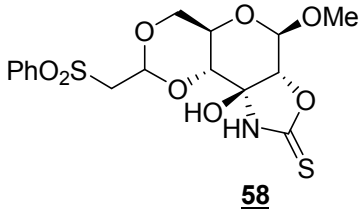
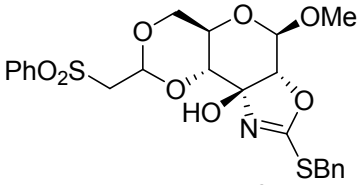
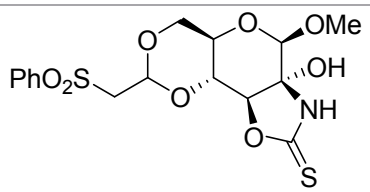
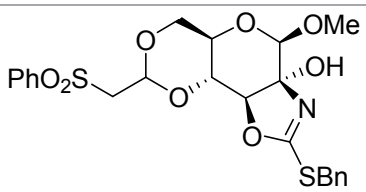
3.2. Mesyl chloride vs. *triflic anhydride*

We have then envisaged the application of the above approach, in order to explore dehydration on other hydrated OXT templates.

Preliminary benzylation at sulfur on OZTs **33**, **58** and **60** was afforded, in order to produce 2-benzylsulfanyl derivatives **75**, **76** and **77**, respectively (Scheme **80**).



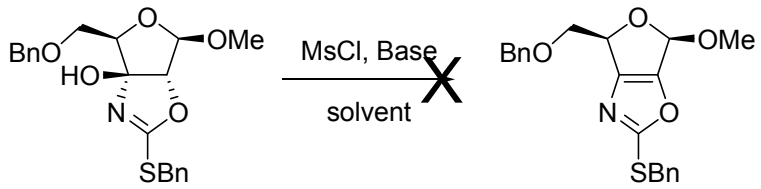
Fused hydrated OXT

starting material	yield (%)	product
 **33**	86%	 **75**
 **58**	56%	 **76**
 **60**	79%	 **77**

Scheme 80

Some variability in *S*-benzylation yields can be observed and no apparent motif justifies this difference of reactivity.

The dehydration process was then applied to compound **75**; however, whatever the conditions used, the reaction with mesyl chloride failed, and the starting material was recovered (Scheme 81). Could this lack of reactivity be attributed to steric hindrance?



75

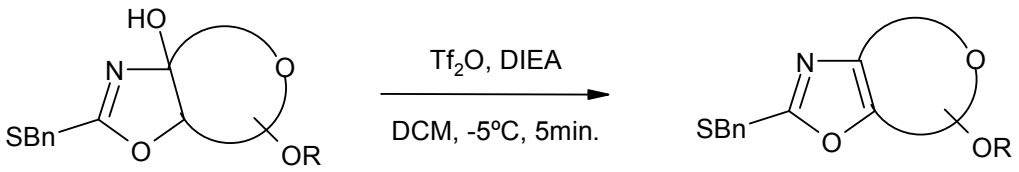
conditions used for mesylation			
base	**solvent**	**temp.**	**yield**
NEt_3	DCM	r.t.	S.M.
NEt_3	DCM	reflux	S.M.
NaH	THF	r.t.	S.M.

Scheme 81

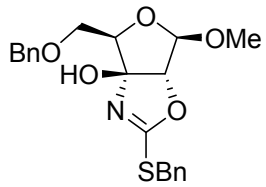
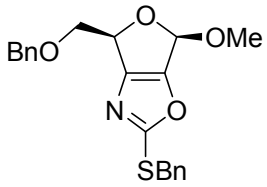
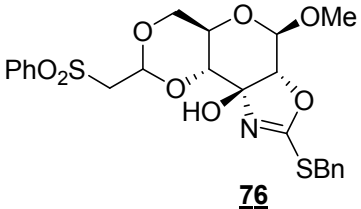
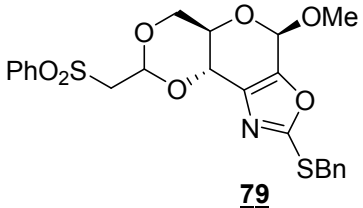
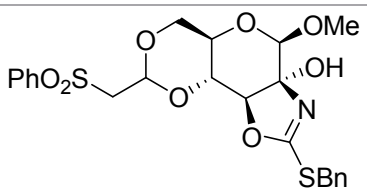
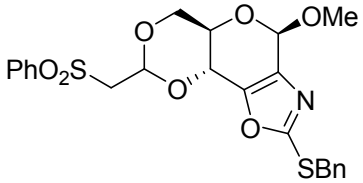
With a view to forcing the conditions, a more powerful electrophile was used: triflic anhydride.[125,126]

The *S*-alkylated hydrated oxazolines **75**, **76** and **77** were submitted to triflic anhydride in the presence of DIEA, at low temperature. Under these conditions, dehydration occurred within 5 min for all compounds and oxazoles **78**, **79** and **80** were obtained in good yields (Scheme 82).

[125] Justribo, V.; Pellegrinet, S. C.; Colombo, M, I. *J. Org. Chem*. **2007**, *72*, 3702-3712.
[126] Baraznenok, I. L.; Nenajdenko,V. G.; Balenkova, E. S. *Tetrahedron* **2000**, *56*, 3077-3119.



Hydrated fused OXT — Fused OXT

starting material	yield (%)	product
 **75**	98	 **78**
 **76**	74	 **79**
 **77**	72	 **80**

Scheme 82

The time of reaction was critical: after no more than 15 min, complete degradation was observed.

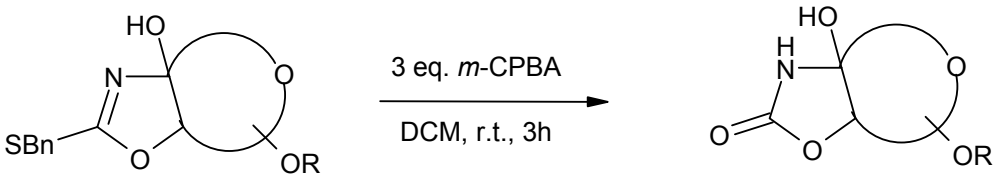
In the selected examples, hydroxyl-OZTs showed some reluctance to undergo water elimination so that, after sulfur masking, a strong electrophile was needed to force dehydration. Those carbohydrate-fused oxazoles proved to be quite stable after 1 month at -20°C – with the exception of the benzylsulfanyloxazole **78**.

4. Reactivity of fused OZTs: oxidation of the C=S bond

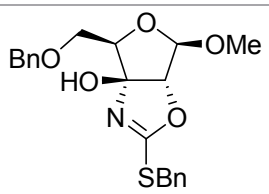
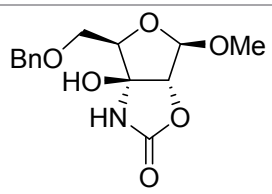
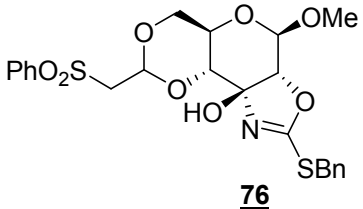
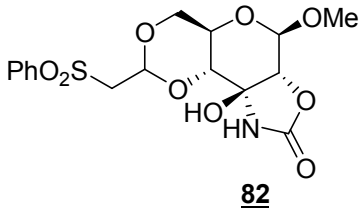
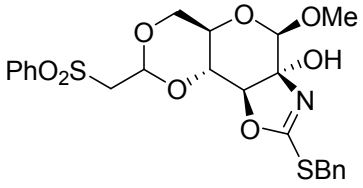
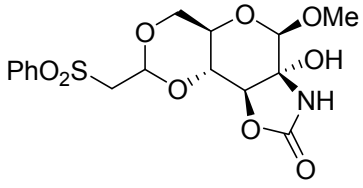
Considering the importance of oxazolidinones (OZOs) described in the literature, it appeared essential to explore the oxidative desulfurization of some OZTs synthesized in this chapter. Among various organic and inorganic reagents, *m*-CPBA demonstrated to be a good candidate to smoothly convert OZTs into OZOs.[30,81]

Whereas the previous known approach was to oxidize the *N*-acylated thionocarbamate, we have turned to try oxidation of the above studied *S*-benzylated forms. With an excess of *m*-CPBA, the sulfur function would be oxidized to an unstable sulfone derivative. This intermediate should be sensitive to a nucleophilic attack of the remaining water in the medium, leading to formation of an OZO through expulsion of a sulfinyl moiety.

The benzylsulfanyloxazolidines **75**, **76** and **77** were submitted to oxidation in DCM and the corresponding 1,3-oxazolidin-2-ones **81**, **82** and **83** were obtained in good yields (Scheme 83).



Hydrated fused OXT — Hydrated fused OXO

starting material	yield (%)	product
 **75**	92%	 **81**
 **76**	84%	 **82**
 **77**	92%	 **83**

Scheme 83

The structure of the oxo compounds were ascertained by ^{13}C NMR experiments. The chemical shifts for the C=O groups were close to 160 ppm while the related C-SBn of the starting materials were close to 170 ppm (Table 7).

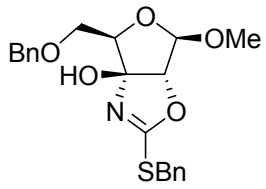
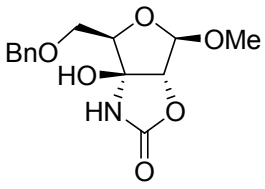
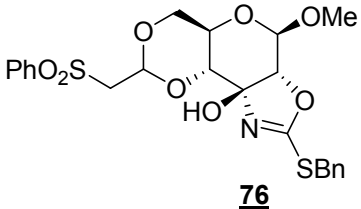
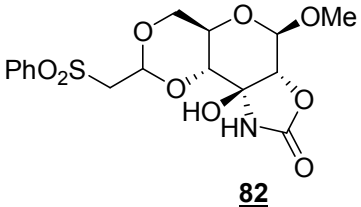
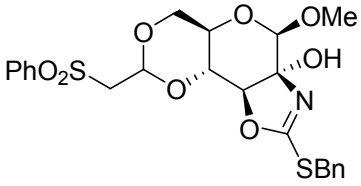
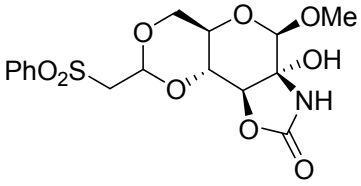
compound	C–SBn (ppm)	compound	C=O (ppm)
 **75**	168.1	 **81**	159.1
 **76**	170.0	 **82**	157.4
 **77**	171.0	 **83**	157.9

Table 7

This oxidation process generated some representatives of a novel family of molecules, hemiaminals of 1,3-oxazolidin-2-ones, which had not appeared in the literature so far. Those compounds are closely related to enantiomerically pure 1,3-oxazolidin-2-ones, which have been extensively studied either in therapeutic chemistry[127,128,129] or in asymmetric synthesis.[130,131]

[127] Ellestad G. A.; Cosulich D. B.; Broschard R.W.; Martin J. H.; Kunstmann M. P.; Morton G. O.; Lancaster J. E.; Fulmor W.; Lovell F. M. *J. Am. Chem. Soc.* **1978**, *100*, 2515-2524.
[128] Shimada J.; Suzuki F.; Nonaka H.; Karasawa A.; Mizumoto H.; Ohno T.; Kubo K.; Ishii A. *J. Med. Chem.* **1991**, *34*, 469-471.
[129] Park C.-H.; Brittelli D. R.; Wang C. L.-J.; Marsh F. D.; Gregory W. A.; Wuonola M. A.; McRipley R. J.; Eberly V. S.; Slee A. M.; Forbes M. *J. Med. Chem*. **1992**, *35*, 1156-1165.
[130] Evans D. A.; Bartroli J.; Shih T. L. *J. Am. Chem. Soc.* ***1981****, 103*, 2127-2129.
[131] Evans D. A.; Weber A. E. *J. Am. Chem. Soc.* ***1986****, 108*, 6757-6761.

- When compared to their thiono analogues, the oxo compounds showed a stronger polarity and a much weaker U.V. absorption, which was at the origin of some difficulties of purification.

The UV spectra of the hydrated OXT **33** and the hydrated OXO **81** were compared: applying the Lambert–Beer law, we found for **33** a maximum of absorbance ($\log\varepsilon = 4.42$) at 243 nm and for **81**, a maximum of absorbance ($\log\varepsilon = 3.27$) at 262 nm. These values characterize the difference of U.V. behaviour for the two compounds.

5. Conclusion

In this chapter we have focused on the reactivity of carbohydrate-based α-hydroxycarbonyl scaffolds and the formation of bicyclic systems, towards the synthesis of fused OXTs on carbohydrate backbones In the light of the results obtained, some preliminary statements can be put forward:

- ☑ Condensation of carbohydrate-based α-hydroxyketones with thiocyanic acid favours the formation of fused hydroxy-OZTs over the expected OXTs.
- ☑ The position and orientation of the hydroxyl group involved is critical with regard to the stereochemistry of the hydrated OXT formed; a strict *cis* relationship was always observed.
- ☑ The anomeric configuration has a decisive influence on the formation of a hydrated OXT between positions 2 and 3 on the carbohydrate backbone.
- ☑ The hydrated form of an OXT could also be introduced on an acyclic structure, when the pre-formed heterocycle OZT was subjected to a reductive fragmentation.
- ☑ The direct elimination of the free hydroxyl was not possible. Before elimination step, thiono group should be masked (*S*-benzylation). On the acyclic structure, the elimination was easily effected while on cyclic carbohydrate structures, precise conditions were needed.
- ☑ Furthermore, oxidation of benzylsulfanyl derivatives revealed very efficient to produce a novel family of oxazolidinones.

CHAPTER III

1,3-oxazoline-2-thiones anchored on carbohydrate templates

1. Introduction – Synthesis of antennary OZTs on carbohydrate templates

In the previous chapter, we have investigated the synthesis of 1,3-oxazoline- and 1,3-oxazolidine- 2-thiones fused on carbohydrate templates, as well as the reactivity at the sulfur center of those bicyclic systems, for which some interesting conclusions have been discussed.

In the literature, we can found some sugar-bound antennary heterocycles with a broad biological potential, such as antiviral and antitumor weapons.[132,133,134] In the present section, we turned our attention to the synthesis and reactivity of OXTs anchored on carbohydrate skeletons, giving birth to original structures such as pseudo-*C*-nucleosides.[54,55,56,135]

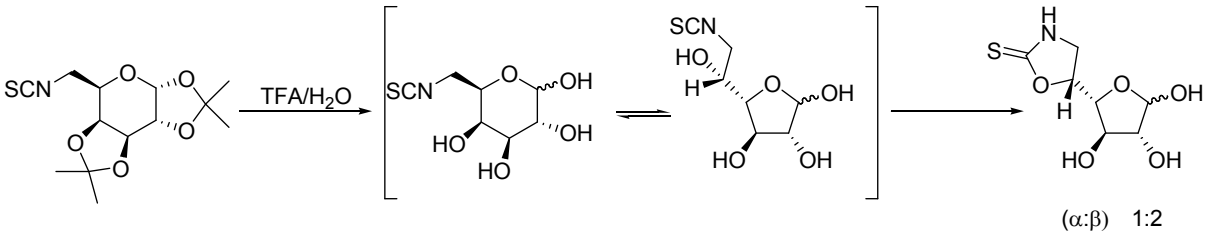
To our knowledge, there exist no references of antennary OXTs linked to carbohydrate scaffolds. However, the present study could be supported by the literature relating antennary connections between sugar and OZT moieties.

1.1. 6-amino-6-deoxy aldoses

We have mentioned in chapter II that Ortiz Mellet and coll. have reported the reaction of 6-amino-6-deoxyaldopyranosides with thiophosgene to afford stable 6-deoxy-6-isothiocyanatoaldopyranosides and subsequent base-induced intramolecular cyclization can provide bicyclic 2-thioxo-tetrahydro-1,3-oxazines (Scheme 35). However, the Sevilla group has also reported that the reactivity of the sugar hemiacetal is different. For the preparation of chiral sugar-derived OZTs, two types of reactions were used: (i) deprotection of 6-deoxy-di-*O*-isopropylidene-6-isothiocyanatoaldoses and (ii) reaction of 6-amino-6-deoxy sugars with thiophosgene.[54,72] In this manner, the deprotection of 6-deoxy-1,2:3,4-di-*O*-

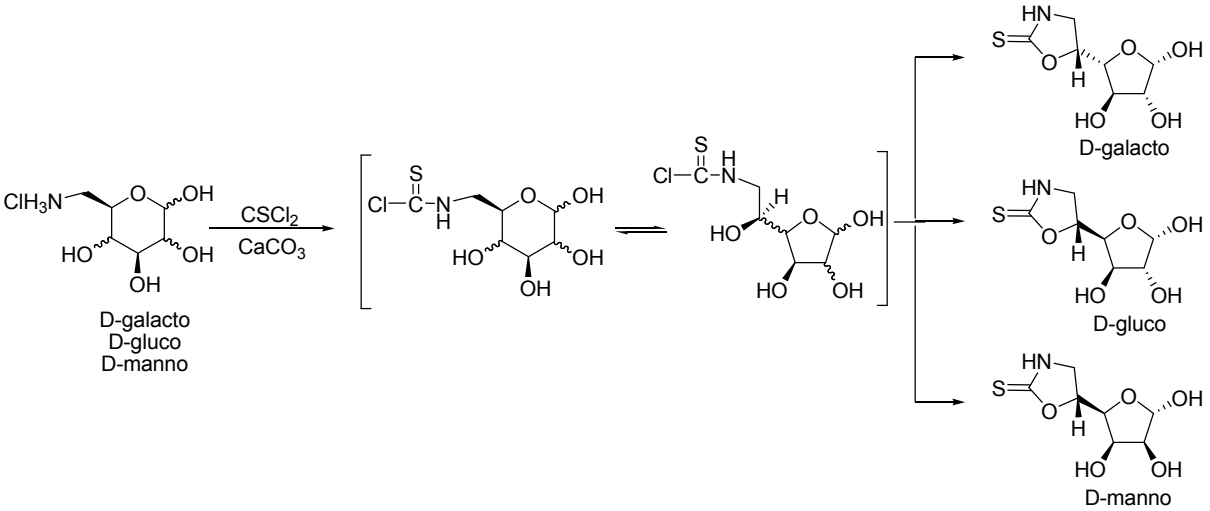
[132] Srivastava, P. C.; Pickering, M. V.; Allen, L. B.; Streeter, D. G.; Campbell, M. T.; Witkowski, J. T.; Sidwell, R. W.; Robins, R. K. *J. Med. Chem*. **1977**, *20*, 256-262.
[133] Melink, T. J.; von Hoff, D. D.; Kuhn, J. G.; Hersh, M. R.; Sterson, L. A.; Patton, T. F.; Siegler, R.; Boldt, D. H.; Clark, G. M. *Cancer Res*. **1985**, *45*, 2859-2865.
[134] Carney, D. N.; Ahluwalia, G. S.; Jayaram, H. N.; Cooney, D. A.; Johns, D. G. *J. Clin. Invest*. **1985**, *75*, 175-182.
[135] Tronchet, J. M. *J. Biol. Med*. **1975**, *4*, 83-87.

isopropylidene-6-isothiocyanate-α-D-galactopyranose (Scheme 84) in acidic medium, generates the hemiacetal which leads to spontaneous cyclization through the furano form, affording an D-galacto antennary OZT.



Scheme 84

Similar results were obtained with unprotected 6-amino-6-deoxyhexoses. When treated directly with thiophosgene, those conduct selectively to antennary OZTs anchored on hexofurano rings. The reaction mechanism likely involves chlorothioformamide intermediates, which undergo subsequent and very fast nucleophilic displacement of the chlorine atom by the β-OH group located at C-5 of the furano form of the sugar (Scheme 85).

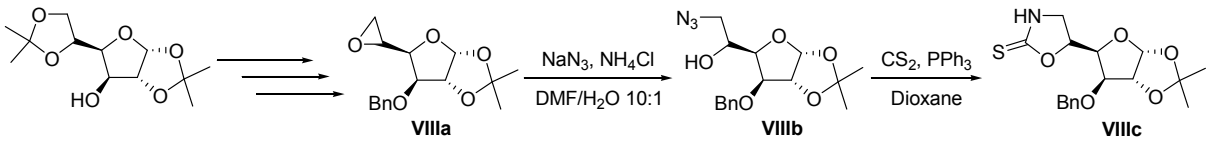


Scheme 85

The same kind of branched OZTs were also explored in our laboratory using a different methodology. While Ortiz Mellet accessed antennary OZTs from

isothiocyanates resulting from the reaction of thiophosgene with a C-6 primary amine, Dr. Tardy synthesized isothiocyanates by reacting carbon disulfide with an azido group, following the Staudinger-aza-Wittig process developed by several authors.[136,137]

In that way, starting from 1,2-*O*-isopropylidene-α-D-glucopyranose and following standard procedures, the epoxide[138,139] **VIIIa** was successfully obtained. Under ammonium chloride activation, the epoxide was opened by azide anion;[140] in the presence of triphenylphosphine and carbon disulfide, the β-azidoalcohol **VIIIb** was transformed into isothiocyanate which was spontaneously converted into the OZT **VIIIc** (Scheme 86).

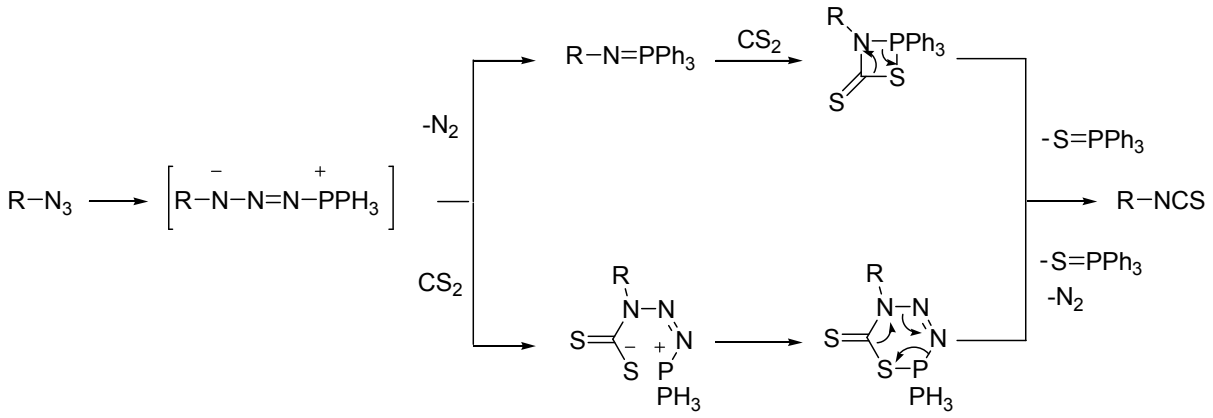


Scheme 86

The formation of isothiocyanates by Staudinger-aza-Wittig reaction[136,137] takes away the manipulation of a primary amine, known to be difficult to purify by column chromatography.

The mechanism suggested by the authors for this reaction can be double, overtaking either the formation of phosphazide or the formation of iminophosphorane. In both cases, the thiophilic character of the phosphorane is crucial (Scheme 87).

[136] Garcia-Moreno, M. I.; Diaz-Perez, P.; Benito, J. M.; Ortiz-Mellet, C.; Defaye, J.; Garcia-Fernandez, J. M. *Carbohydr. Res.* **2002**, *337*, 2329-2334.
[137] Isoda, T.; Hayashi, K.; Tamai, S.; Kumagai, T.; Nagao, Y. *Chem.Pharm. Bull.* **2006**, *54*, 1616-1619.
[138] Liang, D.; DeCamp Schuda, A.; Fraser-Reid, B. *Carbohydr. Res.* **1987**, *164*, 229-240.
[139] Morillo, M.; Lequart, V.; Grand, E.; Goethals, G.; Usubillaga, A.; Villa, P.; Martin, P. *Carbohydr. Res.* **2001**, *334*, 281-287.
[140] Ogawa, S.; Maruyama, A.; Odagiri, T.; Yuasa, H.; Hashimoto, H. *Eur. J. Org. Chem.* **2001**, 967-974.

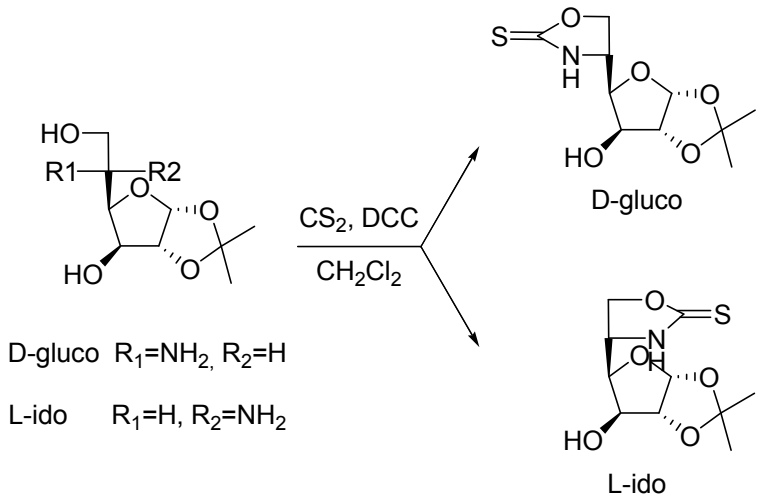


Scheme 87

The antennary OZT **VIIIc** was obtained as a result of two key reactions: epoxide opening by azido group and isothiocyanate formation.

1.2. 5-amino-5-deoxy aldoses

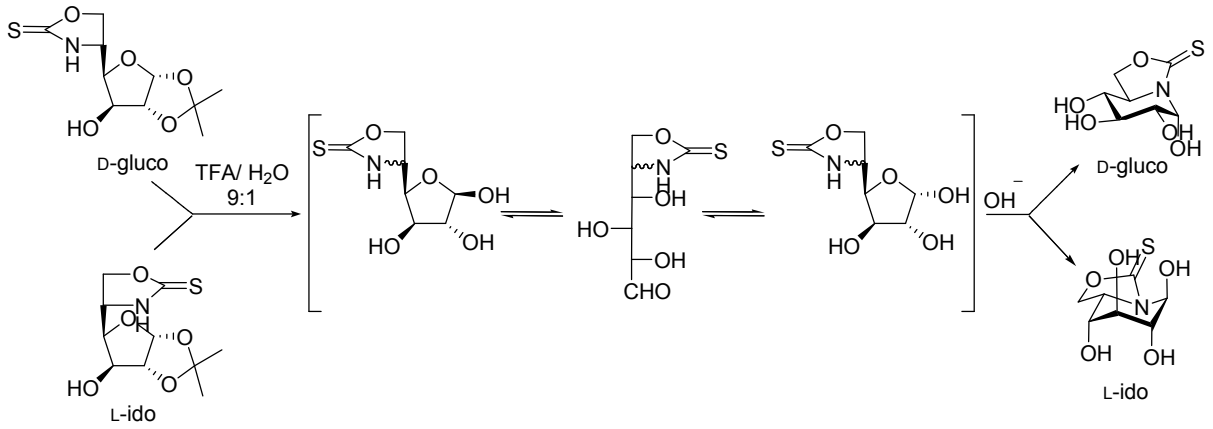
Ortiz Mellet has also developed antennary OZTs derived from 5-amino-5-deoxy-hexofuranose intermediates.[141] Thiocarbonylation using carbon disulfide/DCC afforded regioselectively the five-membered cyclic thionocarbamates, giving birth to the respective antennary OZT (Scheme 5).[60]



Scheme 88

[141] Dax, K.; Gaigg, B.; Grassberger, V.; Köblinger, B.; Stütz, A.E. *J. Carbohydr. Chem*. **1990**, *9*, 479-499.

Acid-catalyzed hydrolysis of the anomeric ketal afforded a mixture of the protonated α- and β- furanoses, which after neutralization, rearranged to the fused bicyclic azasugars by intramolecular nucleophilic addition of the thiocarbamate *N*-atom onto the masked aldehydo group[142] (Scheme 89).



Scheme 89

NMR analysis revealed for each sugar a single stereoisomeric form at the pseudoanomeric centers, with a *R* configuration for D-glucopyranose and *S* for L-idose. No traces of furano isomers were detected.

In conclusion, the formation of those pseudo iminosugars occurred with complete stereoselectivity, a finding which will further prove very useful in the synthesis of pseudo-iminosugars carried out in our laboratory.

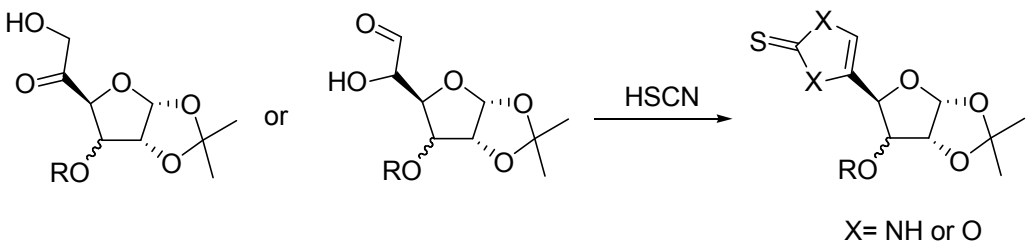
[142] Diaz Perez V. M.; Garcia Moreno I.; Ortiz Mellet C.; Fuentes J.; Diaz Arribas J. C.; Canada F. J.; Garcia Fernandez J. M. *J. Org. Chem*. **2000**, *65*, 136-143.

2. Synthesis of antennary OXTs on carbohydrate templates

In the precedent chapter, we have defended that the major common point between OZT and OXT resides in the fact that both structures can be obtained via thiocyanic acid condensation. Although this is formally true, it has to be pointed out that antennary OZTs cannot be prepared that way. As seen before, the only methods to build up that kind of structure always involve either thiophosgene or carbon disulfide: both reagents (as reported in chapter I) could also be useful for the preparation of OXTs through condensation with an aminoketone (Scheme 3).

However, our general approach over this whole work has been to perform the synthesis of antennary OXTs with using the simplest way of condensation of an α-hydroxyketone or an α-hydroxyaldehyde with thiocyanic acid. This strategy has reduced the number of synthetic steps and avoided the amine manipulation.

With that in mind, starting with 1,2:5,6–di-*O*-isopropylidene-α-D-glucofuranose, our aim was to synthesize α-ketols (Scheme 90) in order to use them as precursors for our target antennary OXTs.



Scheme 90

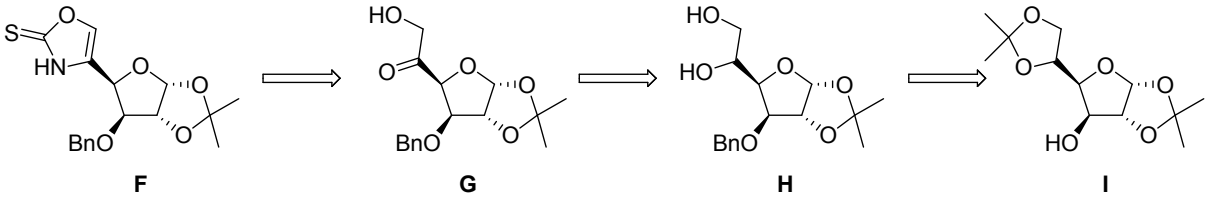
2.1. Antennary OXTs from α-hydroxyketones and study of their reactivity

2.1.1. Synthesis of antennary OXTs using α-hydroxyketones as precursors

The choice of diacetoneglucose as starting material comes from the availability and accessibility of this commercial compound. Moreover, in order to guide the

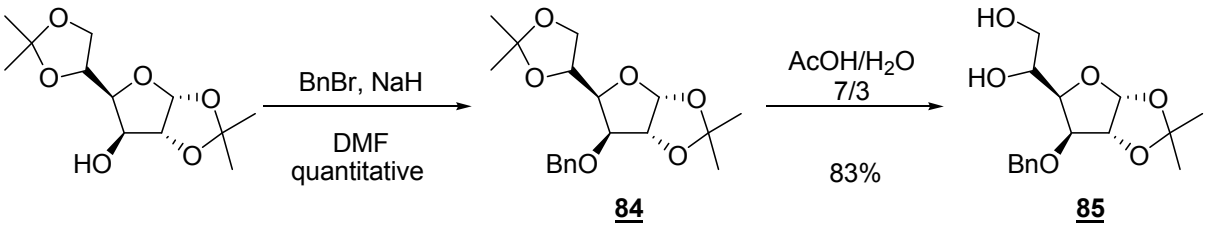
formation of an antennary OXT, it was necessary to block the configuration of D-glucose in a furano form and this intention could be easily guaranteed by a thermodynamically stable 1,2-isopropylidene acetal. In our first assay, the 3-hydroxyl will be protected by a benzyl group, our initial target being the OXT structure **F**.

Retrosynthetic analysis indicate that OXT might be obtained via thiocyanic acid condensation with the ulose **G**, prepared by selective oxidation of diol **H**, derived from starting material **I** through 2 standard steps (Scheme 91).



Scheme 91

Starting from 1,2:5,6–di-*O*-isopropylidene-α-D-glucofuranose and following standard procedures,[143,144] benzylation of the 3-hydroxyl and regioselective 5,6 isopropylidene cleavage in acidic medium led to diol **85** in 83% overall yield (Scheme 92).



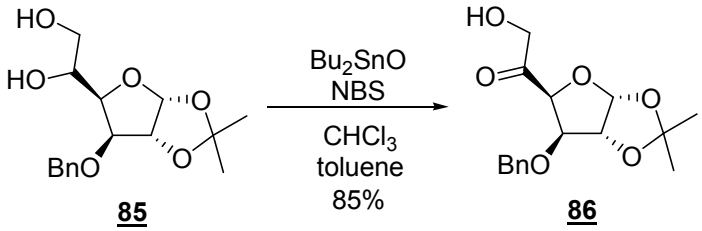
Scheme 92

Regioselective oxidation of position 5 was less straightforward. It was reported in chapter II that David and coll[96] have developed regioselective bromine oxidations of carbohydrate-derived dialkylstannylene acetals to effectively produce α- hydroxyketones at the speed of a titration (Schemes 57 and 58). Later, Kong and

[143] Wang, J.; Tuttle, D.; Takemoto, J. Y.; Tom-Chang, C. W. *Org. Lett.* **2002**, *4*, 23, 3997-4000.
[144] Takahashi, S.; Kuzuhara, H.; Nakajima, M. *Tetrahedron* **2001**, *57*, 6915-6926.

Grindley[145] have shown that dibutylstannylene acetals – particularly those derived from terminal diols – could be regiospecifically oxidized by NBS with good to excellent yields, a method that improved yields of conversion of carbohydrate diols into α-hydroxyketones.

Synthesis of the 5-keto sugar **86**[145,146] was achieved by regioselective oxidation of the secondary hydroxyl group of **85** with Bu_2SnO/NBS system in 85% yield (Scheme 93). The kinetic rate of the reaction was very high, as confirmed by the hasty discolouration.



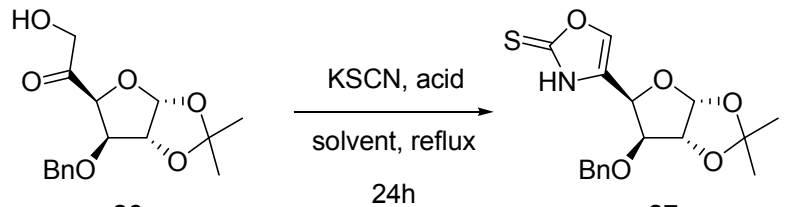
85 **86**

Scheme 93

The ^{1}H-NMR spectra of the α-hydroxyketone **86** displayed an AB system pattern for H-6a, H-6b, with a geminal coupling constant of *ca* 20 Hz. The presence of the carbonyl group was confirmed by its ^{13}C-NMR signal at δ 208.2, as well as its I.R. spectrum with the signal 1725 cm^{-1}.

Finally, our standard conditions (KSCN, EtOH, HCl) for OXT formation were applied to reach the target compound **87** in 89% yield. Performing the reaction with $TsOH.H_2O$ in an aprotic solvent increased the yield of this first synthesized pseudo-*C*-nucleoside to 94% (Scheme 94).

[145] Kong, X.; Grindley, T. B. *J. Carbohydr. Chem.* **1993**, *12*, 557-571.
[146] Söderman, P.; Widmalm, G. *Carbohydr. Res*. **1999**, *316*, 184-186.



86 **87**

solvent	acid	yield of 87(%)
EtOH	HCl	89
THF	$TsOH.H_2O$	94

Scheme 94

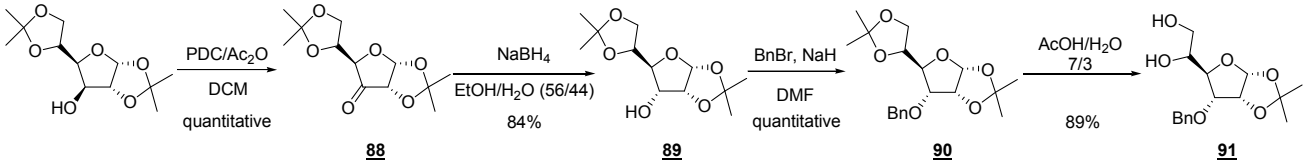
The D-xylo-type structure for OXT **87** was confirmed at first by ^{13}C-NMR. The chemical shift for the C=S bond was present at 179.0 ppm, a normal value for thiocarbonyl groups in OXTs. In the ^{1}H NMR spectrum, the chemical shift for H-5 appears downfield, between 7.18 and 7.23 ppm – a standard for aromatic-type protons.

👍 By this way, the formation in four steps of the antennary OXT **87** was very efficient and our first pseudo-*C*-nucleoside was obtained in 63% overall yield.

With a view to developing more pseudo-*C*-nucleosides bearing an OXT unit, the synthesis of the C-3 epimer was envisaged. In order to invert the configuration at C-3, the ketone **88**, obtained by DAG oxidation[147,148,149] using PDC/Ac_2O, was stereoselectively reduced with $NaBH_4$[150] to give the known 1,2:5,6–di-*O*-isopropylidene-α-D-allofuranose **89** in good yield. Standard benzylation of the 3-OH

[147] Saito, Y.; Zevaco, T. A.; Agrofoglio, L. A. *Tetrahedron* **2002**, *58*, 9593-9603.
[148] Nacro, K.; Lee, J.; Barchi, J. J.; Lewin, N. E.; Blumberg, P. M.; Marquez, V. E. *Tetrahedron* **2002**, *58*, 5335-5345.
[149] Loiseleur, O.; Ritson, D.; Nina, M.; Crowley, P.; Wagner, T.; Hanessian, S. *J. Org. Chem*. **2007**, *72*, 6353-6363.
[150] Lee, J. C.; Chang, S. W.; Liao, C. C.; Chi, F. C.; Wen, Y. S.; Wang, C. C.; Kulkarni, S. S.; Ramachandra, P.; Liu, Y. H.; Hung, S. C. *Chem. Eur. J*. **2004**, *10*, 399-415.

was performed[151] and the diacetonide **90** underwent selective hydrolysis under acidic conditions[148] to provide the precursor diol **91** in 75% overall yield (Scheme 95).



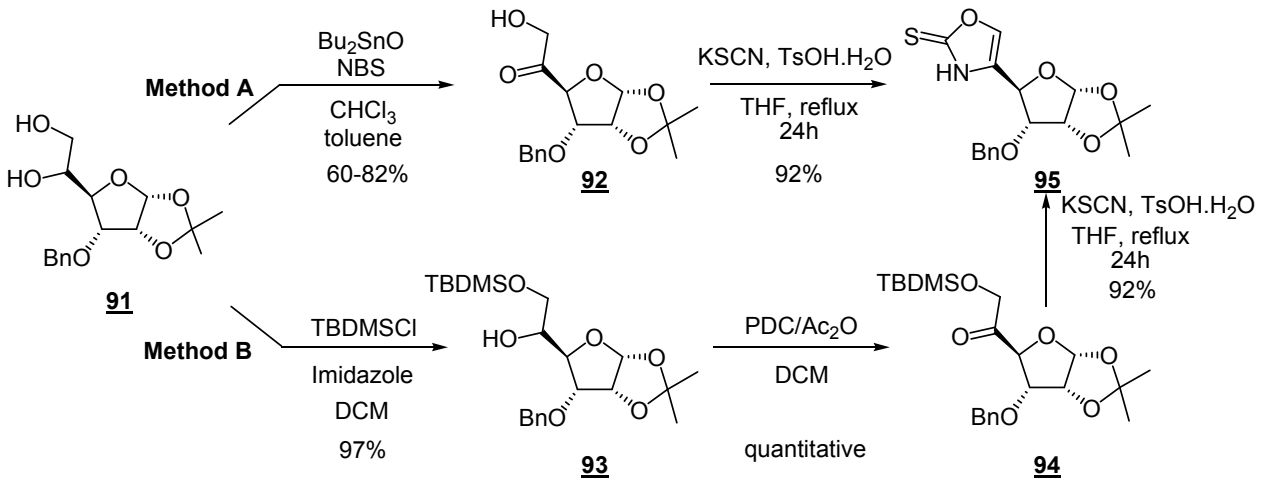
Scheme 95

The oxidation in position 5 was carried out following two methods.

In method A, the Bu_2SnO/NBS system allowed the selective oxidation to 5-keto-sugar **92** in 60-82% yield. The disparity of the results obtained for this ribo-type derivative may result from dimerization of the α-hydroxyketone, which must depend on the stereochemistry at C-3, as suggested in literature.[145] Hence, dimerization occurs in a larger extent for the ribo-type than for the xylo-type compound, in which the orientation of the C-3 substituent results in a higher steric hindrance to the formation of dimers.

In order to prevent dimerization, the synthesis of **92** was planned following a two-step strategy (method B). The primary hydroxyl was first regioselectively protected as an acid-sensitive silyl ether[152], affording derivative **93** in 97% yield, which was subsequently oxidized to furnish the 5-keto sugar **94** in quantitative yield. When submitted to thiocyanic acid condensation, both ketones **92** and **94** gave birth to the antennary OXT **95** in 92% yield (Scheme 96).

[151] Augustyns, K.; Rozenski, J.; Aerschot, A. V.; Janssen, G.; Herdewijn, P. *J. Org. Chem*. **1993**, *58*, 2977-2982.
[152] Roy, A.; Achari, B.; Mandal, B. *Synthesis* **2006**, *6*, 1035-1039.

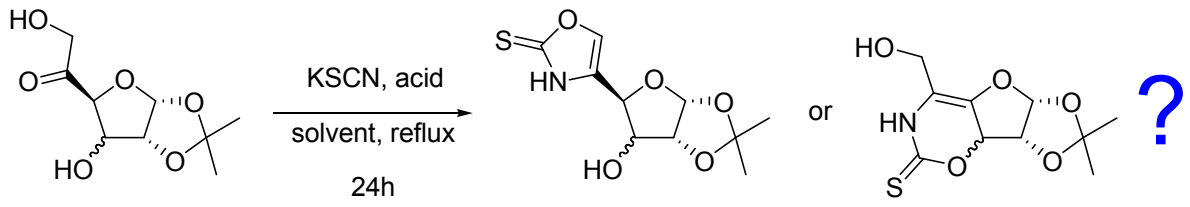


Scheme 96

The presence of the OXT thiocarbonyl group was confirmed by the signal at δ 179.0 in its ^{13}C spectra.

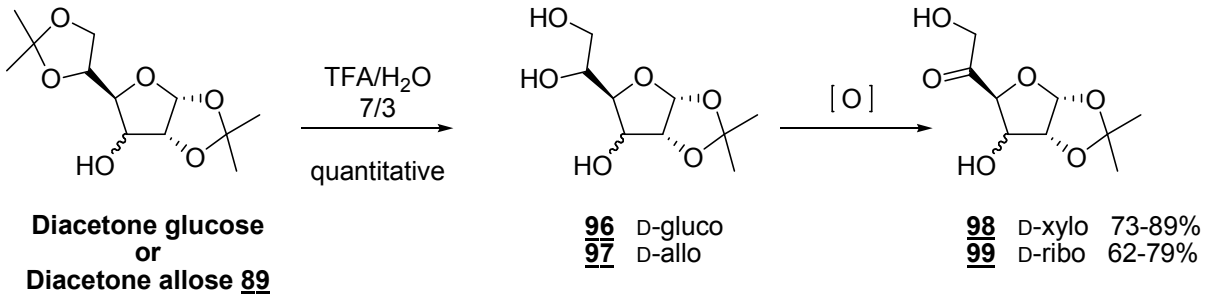
☝ The overall yields (41 – 67%) for the multi-step processes leading to the target ribo-type pseudo-*C*-nucleoside **95** are satisfactory and the synthesis showed to be as efficient as for the xylo-type derivative. Although the second process is longer and more costly, this allowed ketone formation in higher yield and good reproducibility – parameters to be taken into consideration when scaling up the reaction.

At this stage, knowing that antennary OXTs can readily be synthesized, two questions arouse: how condensation with thiocyanic acid either with xylo- or ribo-derivatives would run without ether protection in position 3? Would antennary OXTs be selectively formed or would the free 3-OH participate via nucleophilic attack on the transient isothiocyanate to produce hydroxylated oxazinethiones (Scheme 97)?



Scheme 97

In order to answer this question, D-ribo and D-xylo precursors were prepared starting from diacetoneglucose or diacetoneallose. Selective isopropylidene hydrolysis was performed with AcOH/ H_2O 7/3[153,154] to deliver triols **96** and **97** in quantitative yield. Subsequent selective oxidation in position 5 required optimization of the reaction conditions. Making use of the Bu_2SnO/NBS system allowed formation of 5-keto xylo-derivative **98** and 5-keto ribo-derivative **99** in 73% and 62% yield, respectively. Replacing NBS by Br_2 as oxidant[155,156,157] allowed a yield increase to 89% and 79% correspondingly (Scheme 98).



Selective oxidation reaction		
oxidizing system	**yield of 98 (%)**	**yield of 99 (%)**
Bu_2SnO/NBS	73	62
Bu_2SnO/Br_2	89	79

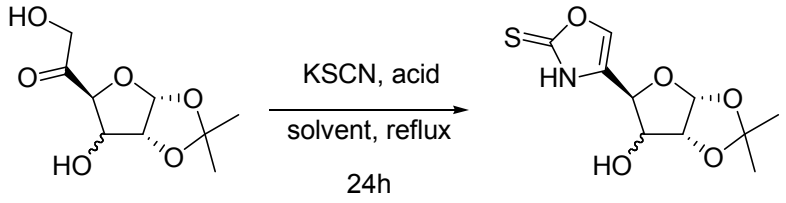
Scheme 98

[153] Sato, K. S.; Akai, S.; Sakuma, M.; Kojima, M.; Suzuki, K. *Tetrahedron Lett*. **2003**, *44*, 4903-4907.
[154] Gallier, F.; Peyrottes, S.; Périgaud, C. *Eur. J. Org. Chem*. **2007**, 925-933.
[155] Robins, M. J.; Guo, Z.; Wnuk, F. *J. Am. Chem. Soc*. **1997,** *119*, 3637-3638.
[156] Ionita, M.; Krishna, S.; Léo, P. M.; Morin, C.; Patel, A. P. *Bioorg. Med. Chem*. Lett. **2007**, *17*, 4934-4937.
[157] Baxter, E.; Reitz, A. *J. Org. Chem*. **1994**, *59*, 3175-3185.

It can be observed once again that the results obtained in D-gluco series are better than those in D-allo series, for the reasons explained before. However, and contrary to the literature,[146] we have shown that bromine was more efficient than NBS for the oxidation of carbohydrate-based dialkylstannylene acetals.

The α-hydroxyketones **98** and **99** were then condensed with thiocyanic acid under standard conditions, affording antennary OXTs **100** and **101** in *ca* 70% yield. Perform the reaction with $TsOH.H_2O$ in a 1:1 THF/DMF mixture, allowed the increase of the yields to 86% and 89% respectively (Scheme 99).

The use of DMF as co-solvent was very important, in order to ensure dissolution of the starting materials.



98 D-xylo
99 D-ribo

100 D-xylo 71-86%
101 D-ribo 72-89%

solvent	acid	yield of 100	yield of 101 (%)
EtOH	HCl	71	72
THF/DMF (1/1)	$TsOH.H_2O$	86	89

Scheme 99

A TLC and NMR follow-up of the condensation indicated that in both series, only the five membered ring OXT connected to the carbohydrate backbone was formed and no traces of oxazinethiones were detected. First, the absence of signals related to CH_2 (H-6A, H-6B and C-6) in ^1H and ^{13}C NMR spectra of **100** and **101**, revealed participation of the 6-position of precursors **98** and **99**. Secondly, the ^1H NMR signals at δ 7.55 ppm and 7.64 ppm in compounds **100** and **101,** respectively, as well as the ^{13}C NMR signals for C-4 and C-2 (128.4 and 180.9 ppm (in **100**) and 130.2 and 181.9 ppm (in **101**)) are indicative of OXT structures.

Besides, after several attempts, compound **100** could be recrystallized and its stereostructure was confirmed by crystallographic analysis (Figure 5), showing only one steroisomer in the unit. The results of the crystallographic study are grouped in Table 8.

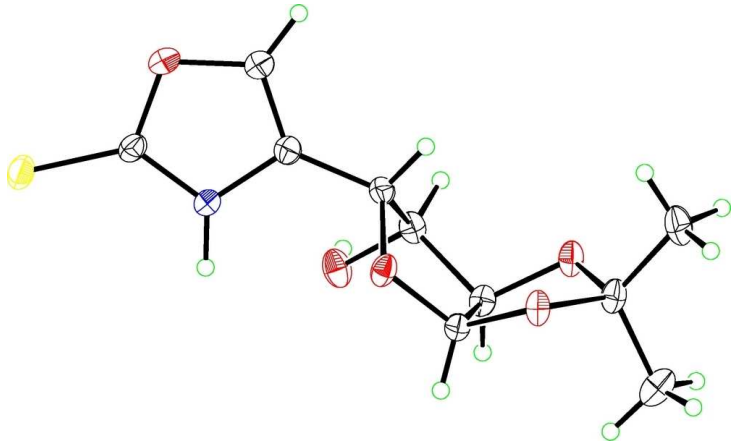


Figure 5

crystal data	**results**
Identification code	SS 100
Empirical formula	$C_{10}H_{13}NO_5S$
Molar mass ($g.mol^{-1}$)	259.28
Temperature (K)	293.0
Wavelength (Å)	0.71
Recrystalization solvent	AE/ EP/DCM
Z, Calculated density ($g.cm^{-3}$)	1.407
Absorption coefficient (mm^{-1})	0.273
Crystal size (mm)	0,4 × 0,15 × 0,1
Unit cell dimensions	a = 6.2271 (4) Å, b = 11.9331 (7) Å, c =16.466 (2) Å α = 90.00º, γ = 90.00°, β = 90.00°
Volume ($Å^3$)	1223.6 (2)

Table 8

From all above considerations, we can conclude that the formation of antennary OXTs was selective and efficient, being pseudo-*C*-nucleosides **100** and **101** synthesised in good overall yields.

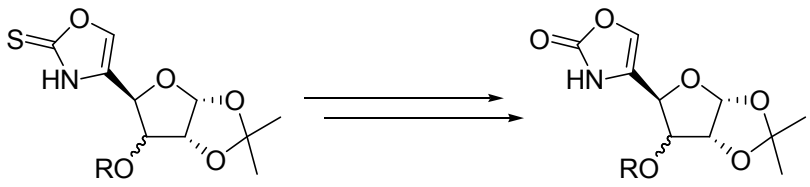
One important characteristic of all antennary OXTs synthesized by us is their stability at room temperature, which contrasts with the low stability observed for the fused OXTs synthesized previously.

2.1.2. Reactivity of antennary OXTs

After the synthesis of these four pseudo-*C*-nucleosides and as part of our ongoing research, we were interested in the study of the reactivity of the OXT motif in antennary position on carbohydrate templates, in order to explore the chemical potential of this new class of compounds.

2.1.2.1. Sulfur oxidation

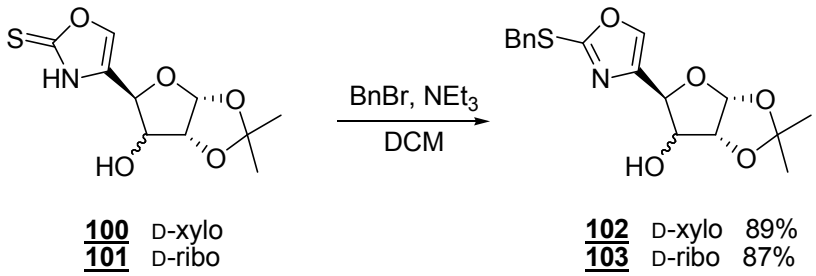
Looking to the chemical reactivity of the hydrated OZO investigated in the last chapter, we had to test the oxidative desulfurization of these new OXTs in order to explore the formation of the corresponding oxazolinones (OXO) (Scheme 100).



Scheme 100

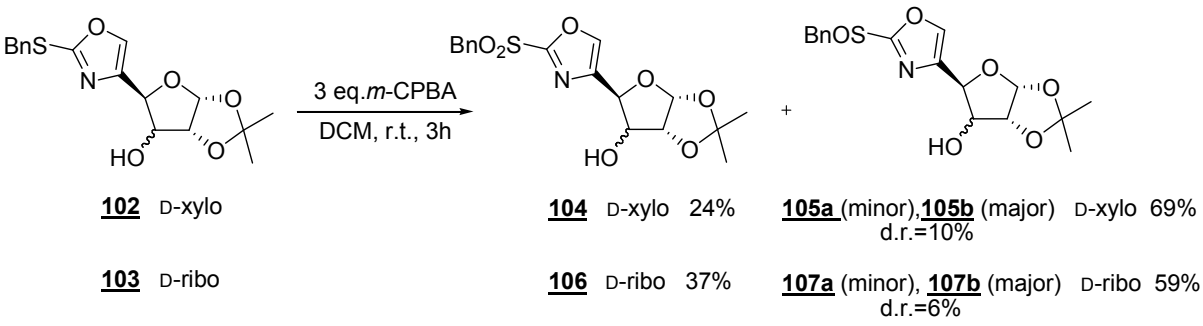
In a fist attempt, antennary OXTs **100** and **101** were used as starting materials, since their preparation is faster than that of the corresponding 3-*O*-benzylated derivatives. The methodology envisaged was identical to that applied for the synthesis of OZOs in the previous chapter. Hence, preliminary *S*-benzylation was

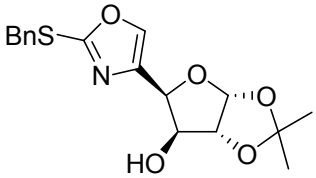
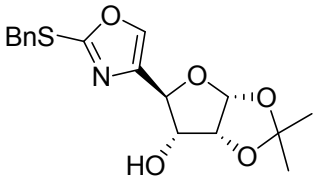
efficiently performed to deliver alkylsulfonyls **102** and **103** in 89% and 87% yields, respectively (Scheme 101).



Scheme 101

As previously reported by us, compounds **102** and **103** were submitted to per-acid oxidation conditions. In the presence of *m*-CPBA (3 eq.) in DCM during 3h, only the corresponding sulfones and sulfoxides were formed. Surprisingly, the major products obtained for this reaction time were the sulfoxides **105ab** (69% yield) and **107ab** (59% yield) while sulfones **104** and **106** were formed in 24% and 37% yield, respectively. Increase of either reaction time or *m*-CPBA equivalents, or both, allowed complete conversion of sulfoxides into the respective sulfones, as shown in table below (Scheme 102).

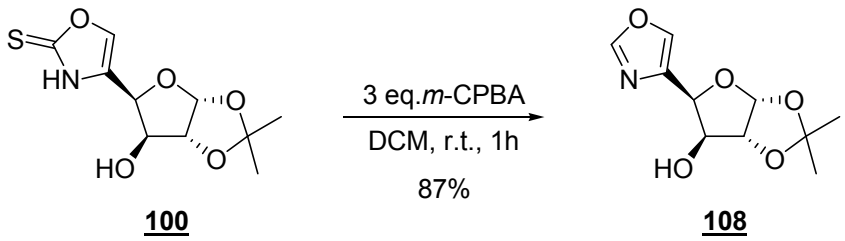


starting material	*m*-CPBA (eq.)	time (h)	yield of sulfone (%)	Compound	yield of sulfoxides (%)	Compound
 **102**	3	3	24	**104**	69	**105a/ 105b**
	3	10	92		---	
	6	3	88		---	
	6	10	90		---	
 **103**	3	3	37	**106**	59	**107a/ 107b**
	3	10	84		---	
	6	3	87		---	
	6	10	89		---	

Scheme 102

Accordingly to preceding results in chapter II (scheme 83), we expected an oxy-attack with expulsion of benzylsulfinate to achieve the formation of OXO. Unfortunately, even when forcing the reaction conditions, the sulfone group in compounds **104** and **106** revealed to be highly stable and averse to any hydrolytic process. The most probable reason for this difference of behaviour between OZTs and OXTs would be the aromaticity of the second. Electron delocalization into the oxazoline cycle decreases the electrophilicity of C-2 (C-SO_2Bn), which hampers nucleophilic attacks.

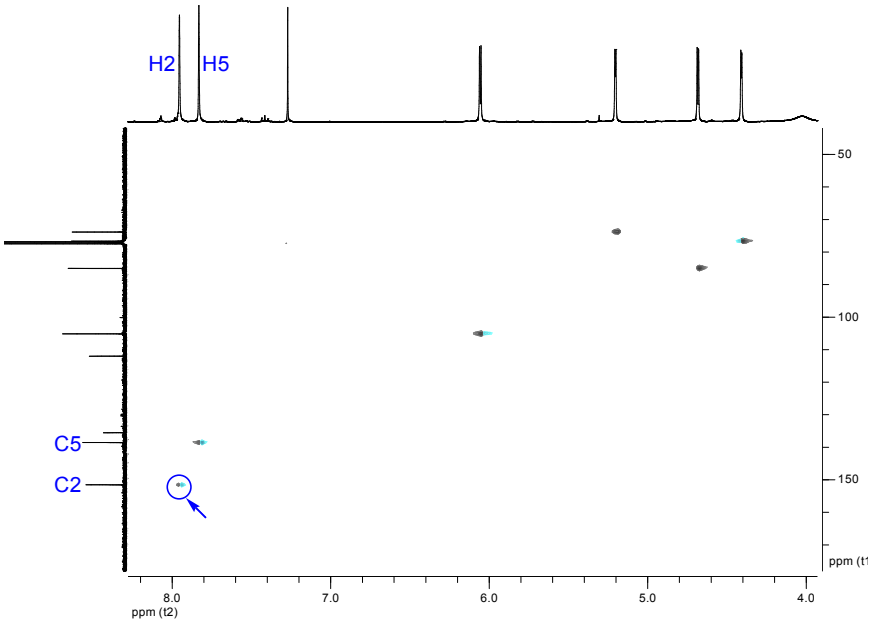
Viewing the high stability of the formed sulfones, another approach was considered in order to achieve the desired OXOs. Thus, thionocarbamate **100** was directly subjected to the action of *m*-CPBA (3 eq.) in DCM but surprisingly, after 1h reaction, sulfur extrusion was observed and oxazole **108** was formed in 87% yield (Scheme 103).



100 **108**

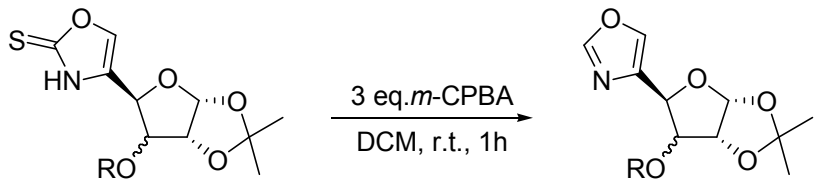
Scheme 103

The oxazolic structure of compound **108** was ascertained by NMR: ^{13}C spectrum showed a signal at δ 151.5 ppm and ^{1}H spectrum a signal at δ 7.95 ppm, both characteristic shifts for a C-2 and H-2 in oxazole. The signal assignments were confirmed by correlation ^{1}H - ^{13}C spectra (Scheme 104).



Scheme 104

With a view to exploring the scope of this reaction, the same conditions were applied to OXTs **87**, **95** and **101**, leading efficiently to the corresponding oxazoles **109**, **110** and **111** in 85%, 84% and 83% yields, respectively (Scheme 105).



87 R=Bn, D-xylo
95 R=Bn, D-ribo
101 R=H, D-ribo

109 R=Bn, D-xylo, 85%
110 R=Bn, D-ribo, 83%
111 R=H, D-ribo, 84%

Scheme 105

The oxazole moiety of compounds **109-111** was ascertained by their C-2 NMR signals at δ 150.8, 151.6 and 151.8, respectively, as well as by their H-2 signals at δ 7.88, 7.85 and 7.90 ppm, respectively.

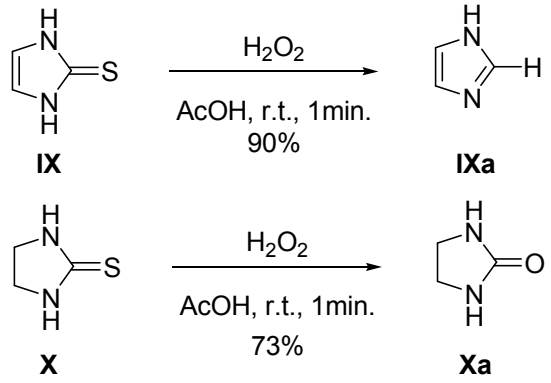
☝ Although the above methodology does not give access to OXOs, we have disclosed a general and useful tool for the synthesis of oxazoles, never explored before.

In order to explain this puzzling reaction, a detailed literature search was made, which revealed that desulfurization of sulfur-containing compounds had been achieved by the use of different reagents, being Raney nickel the most often employed.[158] Other methods involve the use of nickel-sodium hydride complexes[159] and other transition metal compounds,[160] alkali bromates and iodates[161] and dimethyldioxirane.[162] However, only a few isolated papers dealing with the desulfurization of sulfur-containing compounds has been published using per-acid

[158] Belen'kii, L. I. In: Belen'kii, L. I., Ed.; *Chemistry of Organosulfur* Compounds: General Problems, Ellis Horwood, Chichester **1990**, Chap. 9.
[159] Becker, S.; Fort, Y.; Vanderesse, R.; Caubère, P. *J. Org. Chem*, **1989**, *54*, 4848-4853.
[160] Luh, T. Y.; Ni, Z. T. *Synthesis* **1990**, *2*, 89-103.
[161] Capps, H. H.; Dehn, W. M. *J. Am. Chem. Soc*. *1932*, *54*, 4301-4305.
[162] Frachey, G.; Crestini, C.; Bernini, R.; Saladino, R.; Mincione, E. *Heterocycles* **1994,** *38*, 2621-2630.

conditions: to our knowledge, no results related to *m*-CPBA as desulfurizing agent of reactions have been reported so far.

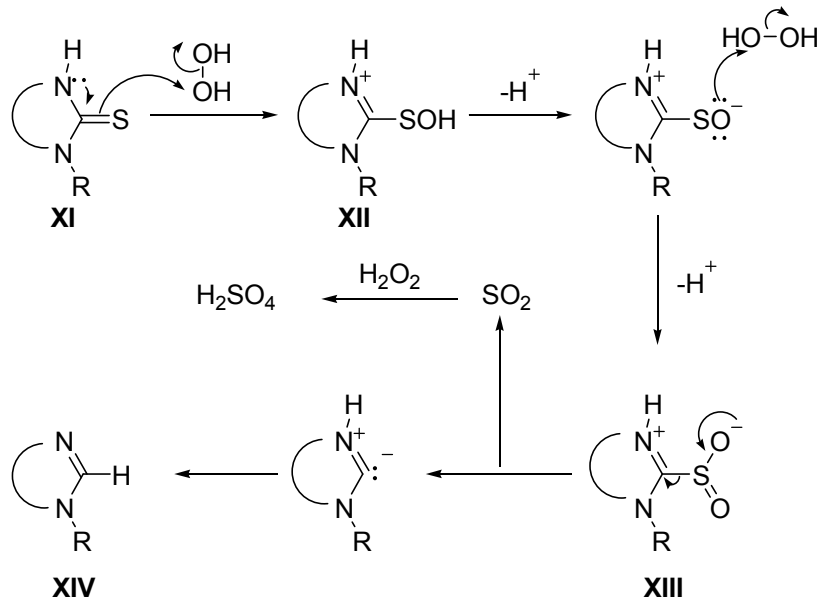
In 1995, Grivas and Ronne[163] described the desulfurization of cyclic thioureas by hydrogen peroxide in acetic acid, in order to establish a possible mechanism for this transformation. In that way, they have shown that: (i) H_2O_2 oxidation of 2-mercaptoimidazole **IX** gave imidazole **IXa** in 90% yield and (ii) the same conditions applied to 2-mercaptoimidazolidine **X** afforded the corresponding 2-imidazolidinone **Xa** in 73% yield (Scheme 106).



Scheme 106

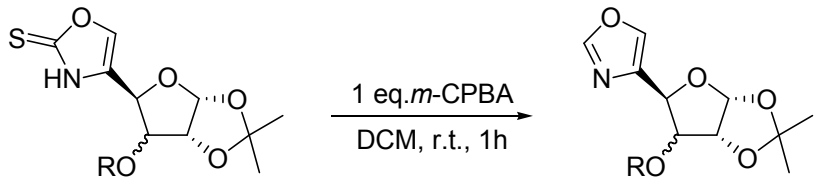
For insaturated thioureas, one possible mechanism can first involve formation from **XI** of the thioamide *S*-oxide which can tautomerise into the sulfenic acid **XII.** This transient species - not detected in the reaction mixture – can react with another molecule of peroxide to produce the sulfinic acid **XIII**. Next, sulfur dioxide is expelled and an intermediate ylide is formed. The desulfurized product **XIV** is finally formed by proton migration. One more equivalent of hydrogen peroxide is consumed to convert sulfur dioxide into sulfuric acid (Scheme 107). For saturated thioureas (**X**), it was postulated that the formation of **Xa** is due to hydrolysis of the corresponding *S*-oxide derivative.

[163] Grivas, S.; Ronne, E. *Acta Chemica Scandinavica* **1995**, *49*, 225-229.



Scheme 107

In Grivas and Ronne's experiments, the use of a 3:1 molar ratio of hydrogen peroxide was clearly necessary for complete desulfurization. In order to check the above mechanism, thioamides **87**, **95**, **100** and **101** were treated with 1eq. of *m*-CPBA in DCM during 1h: much to our surprise, the corresponding oxazoles were produced in very good yields, similarly to the experiment with 3 eq of *m*-CPBA (Scheme 108).



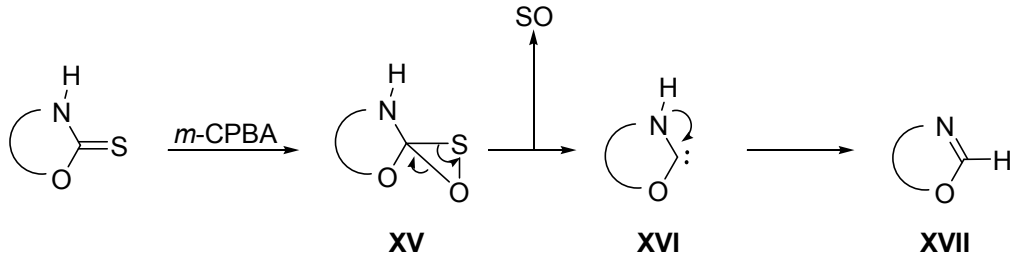
87 R=Bn, D-xylo
95 R=Bn, D-ribo
100 R=H, D-xylo
101 R=H, D-ribo

109 R=Bn, D-xylo, 87%
110 R=Bn, D-ribo, 82%
108 R=H, D-xylo, 86%
111 R=H, D-ribo, 84%

Scheme 108

This puzzling result is questioning the mechanism described in Scheme 107: indeed, 3 eq. of peracid are not required for complete desulfurization of OXTs and only one is necessary. We believe that one plausible mechanism for this type of

transformation would involve an intermediate oxathiirane[164,165] **XV** which can generate the carbene **XVI** through extrusion of sulfur monoxide. The oxazole derivative **XVII** finally results from hydrogen migration (Scheme 109).



Scheme 109

We can conclude that *m*-CPBA is an excellent oxidant for the desulfurization of OXTs, leading to the corresponding oxazoles in high yield. Altogether, this method is mild, highly efficient and inexpensive, with a stoichiometric quantity of peracid.

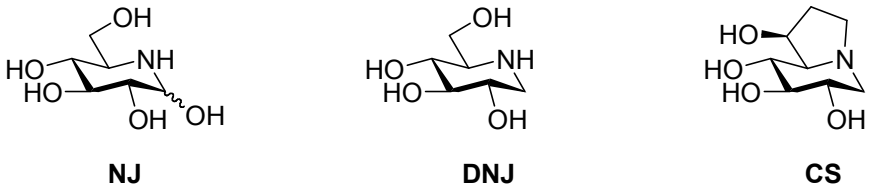
2.1.2.2. Nitrogen nucleophilicity: synthesis of pseudo-iminosugars

After studying the sulfur reactivity potential, in which a new route for oxazole formation was developed, our efforts were focused on the nucleophilicity of the nitrogen atom, aiming at synthesizing original pseudo-iminosugars.

Why would the synthesis of this family of compounds appear important? In fact, natural and synthetic polyhydroxylated alkaloids with glycosidase inhibitory properties, have been receiving a great deal of attention both as useful biological tools for studies on glycoconjugate function, targeting and turnover[166,167] and as potential chemotherapeutic agents for the treatment of viral infections,[168] cancer[169]

[164] Marrière, E.; Chevrie, D.; Metzner, P. *J. Chem. Soc. Perkin Trans. I* **1997**, 2019-2020.
[165] Chevrie, D.; Metzner, P. *Tetrahedron Lett*. **1998**, *39*, 8983-8986.
[166] Dwek, R. A. *Chem. Rev*. **1996**, *96*, 683-720.
[167] Sinnot, M. L. *Chem. Rev*. **1990**, *90*, 1171-1202.
[168] Karlson, G. B.; Butters, T. D.; Dwek, R.A.; Platt, F. M. *J. Biol. Chem*. **1993**, *268*, 570-576.
[169] Gross, P. E.; Backer, M. A.; Carver, J. P.; Dennis, J. W. *Clin. Cancer Res*. **1995**, *1*, 935-944.

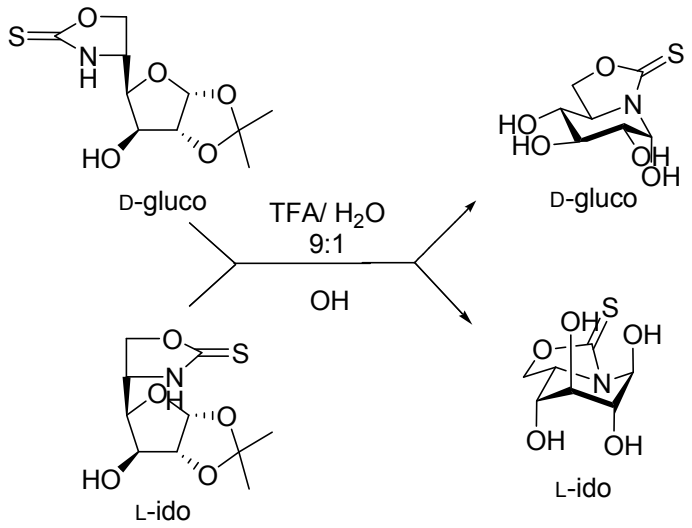
and metabolic disorders such as diabetes.[170] Most of the biologically interesting members of this class of compounds, termed generically as iminosugars ("azasugars") are related to nojirimycin (**NJ**), 1-deoxynojirimicin (**DNJ**)[171], nitrogenous-ringed stereochemical mimics of D-glucose, or to castanospermine (**CS**)[172,173] (Scheme 110).



Scheme 110

The feasibility of the intramolecular nucleophilic addition of the nitrogen atom in pseudo-*C*-nucleosidic thiocarbamates to the masked carbonyl in aldose precursors, was reported by Ortiz Mellet and coll., as illustrated on Scheme 111.[142,174] As mentioned previously, the isopropylidene hydrolysis using TFA affords an anomeric mixture of α- and β-furanoses which, under neutralisation conditions, are converted into the target pseudo iminosugars.

[170] Platt, F. M.; Neises, G. R.; Reinkensmeier, G.; Townsend, M. J.; Perry, V. H.; Proia, R. L.; Winchester, B.; Dwek, R. A.; Butters, T. D. *Science* **1997**, *276*, 428-431.
[171] Gijsen, H. J.; Qiao, L.; Fitz, W.; Wong, C. H. *Chem. Rev*. **1996**, *96*, 443-474.
[172] Burgess, K.; Henderson, I. *Tetrahedron* **1992**, *48*, 4045-4066.
[173] Overkleeft, H. S.; Pandit, U. K. *Tetrahedron Lett*. **1996**, *37*, 547-550.
[174] Pérez, P. D.; Moreno, M. I. G.; Mellet, C. O.; Fernández, J. M. *Eur. J. Org. Chem*. **2005**, 2903-2913.

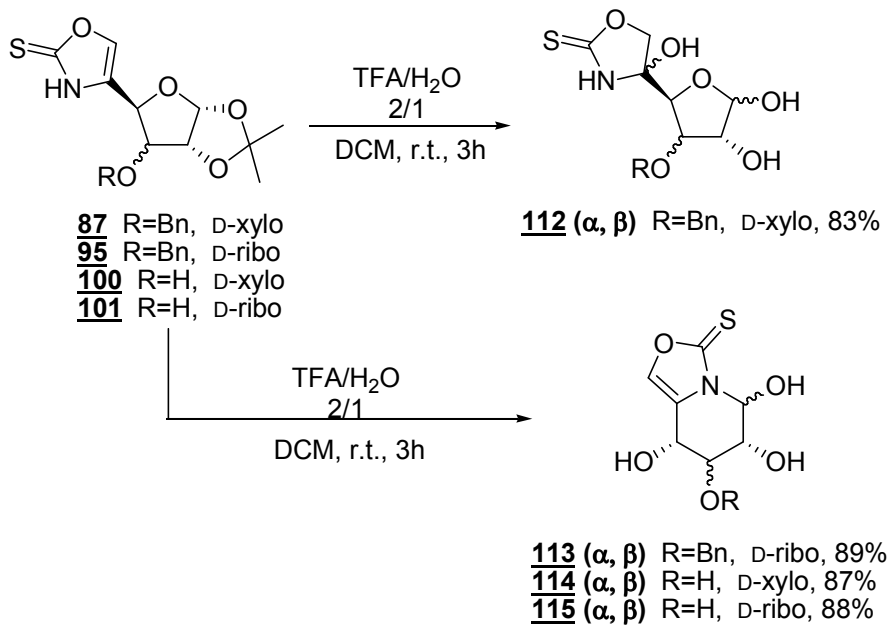


Scheme 111

We have used the same synthetic strategy, based on the ability of the ambident thionocarbamate to act as a N-nucleophile in coupling reactions with carbonyl compounds and applied this to the previously synthesised anchored OXTs. In our case, TFA/ H_2O hydrolysis of the anomeric acetal protecting group led to contrasted results. The 3-*O*-benzyl xylo-type derivative **87** was converted in 83% yield into the trihydroxylated OZT **112,** as a mixture of stereoisomers. Quite differently, when submitted to the same hydrolysis conditions, the 3-*O*-benzyl ribo-type epimer **95** as well as pseudo-*C*-nucleosides **100** and **101** afforded anomeric mixtures of the corresponding oxaindolizidines **113**, **114** and **115** in 89%, 87 % and 88% yield, respectively (Scheme 112). Changing the acidic medium to 6M HCl led to very similar results. The reluctance to intramolecular cyclization of compound **87** can be ascribed to the high steric hindrance caused by the benzyl group in position 3: the spatial rearrangement of the latter hampers the N-nucleophilic attack on the masked aldehyde, impeding the formation of the corresponding pseudo-iminosugar.

In contrast with the reports of Ortiz Mellet and coll., the formation of our castanospermine analogues **113-115** did not require preliminary neutralisation of the acidic medium – which is an additional evidence of nitrogen's nucleophilicity. One more difference resides in stereochemistry: Ortiz Mellet reports total stereoselectivity

in the synthesis of pseudo-iminosugars (Scheme 111) whereas in our experiments anomerization was observed. NMR was used to estimate the α/β ratios for **113-115**, for which the aminoketalic bicyclic structure was confirmed by chemical shift values of the pseudo-anomeric carbon (Scheme 112).



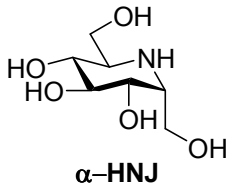
iminosugars	α/β ratio (%)	$^{13}C_1$ ppm	
		α	β
113	84/16	80.7	78.1
114	57/43	79.5	83.9
115	77/23	82.8	78.3

Scheme 112

We can conclude that, by exploiting the ability of the nitrogen atom of oxazoline-2-thiones to act as a nucleophile in intramolecular addition to the masked aldehyde in hexose precursors, a series of castanospermine analogues were readily prepared. From DAG, pseudo iminosugars **113**, **114** and **115** were obtained in 59%, 67% and 52 % overall respective yields, thus showing that the strategy used for the assembly of the oxaindolizidine skeleton is quite efficient.

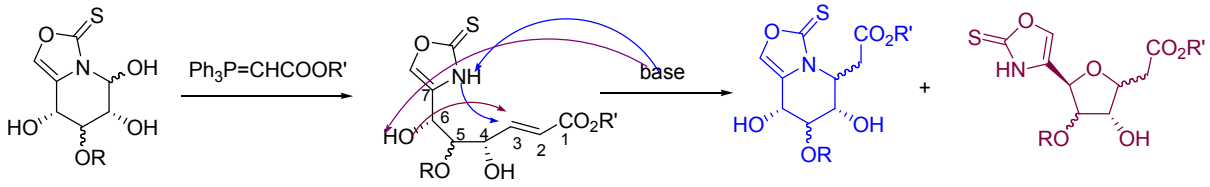
2.1.3. Wittig reactions with pseudo-iminosugars

The design and synthesis of iminosugar *C*-glycosides[175,176,177] has attracted attention since α-homonojirimycin (Scheme 113), firstly synthesised by Liu[178] and thereafter isolated from a natural source,[179] has proven to be a potent and, more significantly, selective inhibitor of α-glycosidases from the mouse gut and human intestine. In addition, properly functionalized iminosugar *C*-glycosides could be useful building blocks for the synthesis of more complex iminosugar conjugates.



Scheme 113

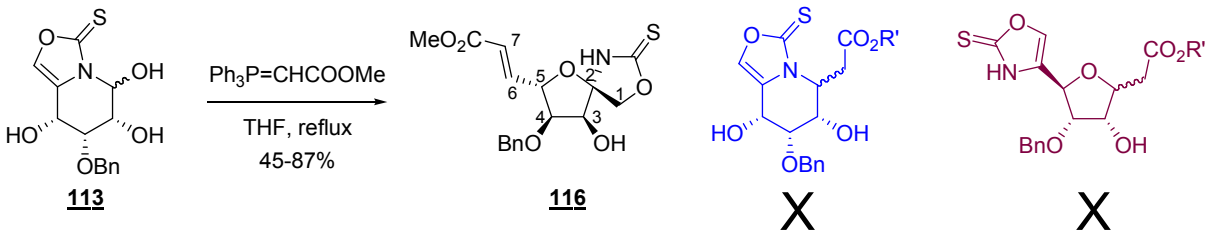
Considering the structure of the above mentioned pseudo-iminosugars, we have imagined the formation of α-HNJ analogues, in order to develop some new imino-*C*-glycosides. With that in mind, we wanted to investigate the opening of the iminosugar by a stabilized Wittig reagent[180,181,182] with consequent olefination of the aldehyde, followed, under base-catalysis, by intramolecular re-cyclization to form an imino-*C*-glycoside. One could also expect a competitive reaction, with possible attack of the 6-OH, to afford an antennary OXT *C*-glycoside (Scheme 114).



Scheme 114

[175] Johns, B. A.; Pan, Y. T.; Elbein, A. D.; Johnson, C. R. *J. Am. Chem. Soc*. **1997**, *119*, 4856-4865.
[176] Godin, G.; Compain, P.; Martin, O. R. *Org Lett*. **2003**, *5*, 3269-3272.
[177] Ferla, B.; Bugada, P.; Cipolla, L.; Peri, F.; Nicotra, F. *Eur. J. Org. Chem*. **2004**, 2451-2470.
[178] Liu, P. S.; *J. Org. Chem*. **1987**, *52*, 4717-4721.
[179] Kite, G. C.; Fellows, L. E.; Fleet, G. W. J.; Liu, P. S.; Scofield, A. M.; Smith, N. G. *Tetrahedron Lett*. **1988**, *29*, 6483-6486.
[180] Dawe, R. D.; Reid, F. *J. Org. Chem*. **1984**, 49, 522-528.
[181] Keck, G. E.; Boden, E. P.; Wiley, M. R. *J. Org. Chem*. **1989**, *54*, 896-906.
[182] Maryanoff, B. E.; Reitz, A. B. *Chem. Rev*. **1989**, *89*, 863-927.

Putting that into practice, compound **113** was engaged in the Wittig reaction using (carbomethoxymethylene)triphenylphosphorane in refluxing THF in the presence of a catalytic amount of benzoic acid, known to increase significantly the selectivity of E/Z isomers.[183] Surprisingly, the product obtained after 1h reaction was none of the expected, but a psicofurano-configurated spiranic OZT **116**. Extending the reaction time from 1h to 8h allowed the improvement of the yield of **116** from 45 to 87% (Scheme 115).



113 **116**

Scheme 115

This new structure – particularly the configuration of the newly formed stereocenters – was ascertained by NMR analysis. The signal at δ 189.8 ppm in the ^{13}C NMR spectra of **116** was characteristic for C=S in an OZT, while C=S in an OXT usually resonates ca 179 ppm. The presence of OZT was corroborated by the ^{1}H NMR spectrum, which displays for H-1a and H-1b an AB pattern at 4.54 and 4.95 ppm, correlated to a secondary carbon with a 76.9 ppm signal in ^{13}C NMR. Furthermore, the presence of a C-2 quaternary carbon is confirmed (98.9 ppm in ^{13}C NMR) and consequently accounts for a spiro OZT. The configuration of the chiral centers C-2 and C-5 was established through bidimensional NOESY. A strong NOE was observed between NH and H-3 and H-4. As the configuration of C-3 and C-4 does not change with the reaction and H-3 and H-4 are in *cis* relation, we can infer that NH is on the same side of the furano plan and C-2 is (*S*)- configurated. On the other

[183] Harcke, C.; Martin, S. F. *Org. Lett*. **2001**, *3*, 3591-3593.

hand, the absence of NOE between H-5 and H-4 or H-3 indicates that H-5 is up in relation to the furano plan, and therefore C-5 is also (*S*)- configurated (Figure 6).

Last, but not least, in ^{1}H NMR spectrum, the 15.6 Hz value for $J_{6\text{-}7}$ coupling constant reveals the presence of a *E*-stereoisomer.

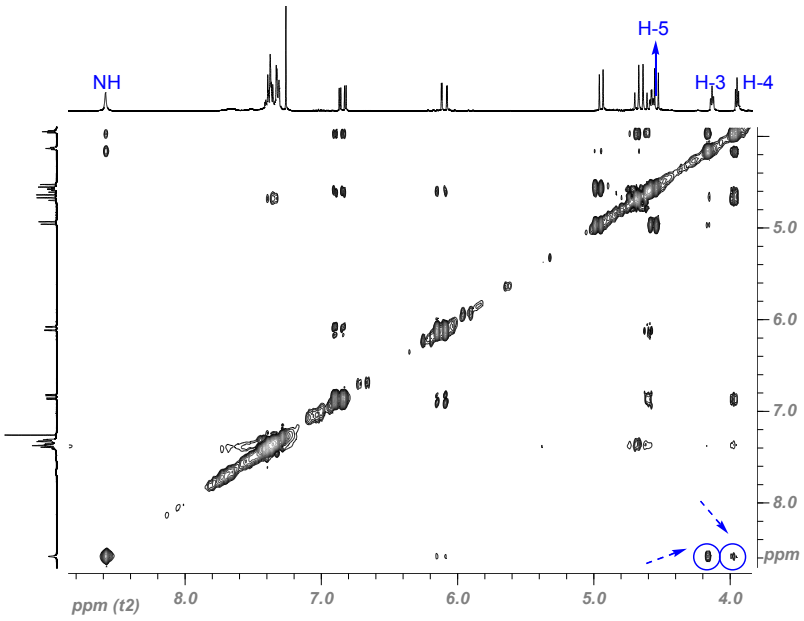


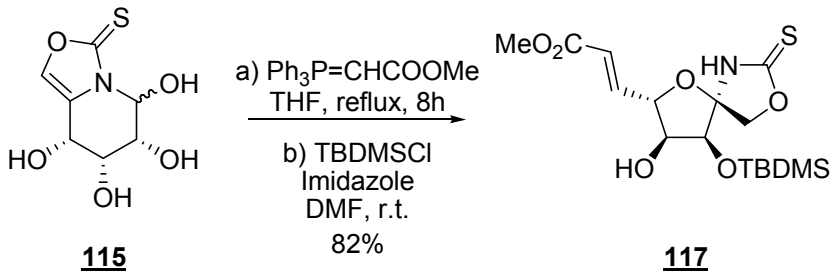
Figure 6

☝ From the above observations, we can conclude that the Wittig reaction is achieved with total control on the stereoselectivity. This transformation is particularly interesting because an enantiomerically pure spiro-OZT is easily formed, which – as mentioned earlier – would not be possible by condensing a ketose with thiocyanic acid. Besides, this compound **116** displays a rich chemical potential, notably with the Michael acceptor segment introduced at C-5.

Applying the same Wittig conditions to compound **114** proved disappointing: the iminosugar revealed very stable and only starting material was recovered after 8h reaction.

Treatment of compound **115** under Wittig conditions afforded a new product detected by TLC, which was directly silylated without isolation: in that way, the α-spiro-psicofurano derivative **117** was formed in 82% yield over the two steps. Once

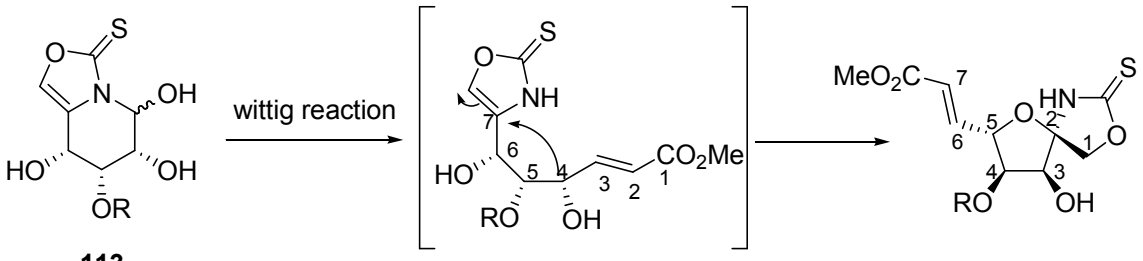
again, the compound was obtained in enantiopure form and the configuration of all stereogenic centers was determined in the same way that for compound **116** (Scheme 116).



115 **117**

Scheme 116

The mechanism for the Wittig reaction with compounds **113** and **115** can be sketched out as follows: attack of the Wittig reagent onto the masked aldehyde leads to the formation of intermediate **XVIII,** which cannot be isolated and undergoes internal cyclization through attack of OH-4 on the OXT double bond, to finally form *E*-α-spiro-psicofurano derivatives **XIX** (Scheme 117).



113
115 **XVIII** **XIX**

Scheme 117

Those experiments led us to question the aromaticity of the OXT ring. Indeed, having another look at intermediate **XVIII,** the supposed aromaticity of its OXT part no longer exists after addition of 4-OH. Knowing that, we can hypothesize that the OXT system probably does not possess a pronounced aromaticity.

This was further confirmed by theoretical calculations related to the electronic density in the OXT ring (Figure 7).

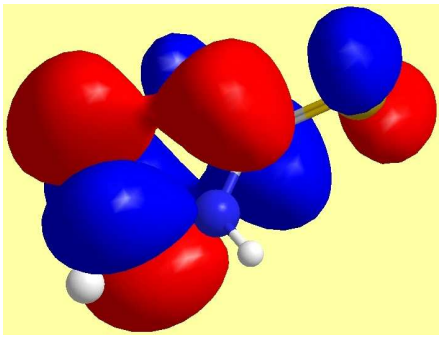


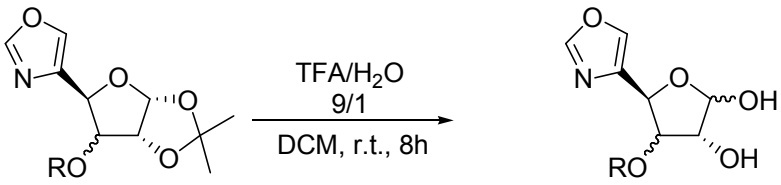
Figure 7

After minimization with GAMESS, LUMO, using force field type HF, 6G-21, it was clear that carbons C-4 and C-5 in OXT are relatively poor in electrons, which could explain the nucleophilic attack on these carbons.

2.1.4. Wittig reactions with oxazoles

Having now a clearer idea about the aromaticity of an OXT cycle, we thought interesting to test and compare the aromatic character of an oxazole ring, when submitted to the same Wittig conditions.

With that purpose, oxazoles **108-111** were first submitted to isopropylidene hydrolysis to produce the related anomeric mixtures **118-121** in 83%, 72%, 82% and 85% yields, respectively (Scheme 118).



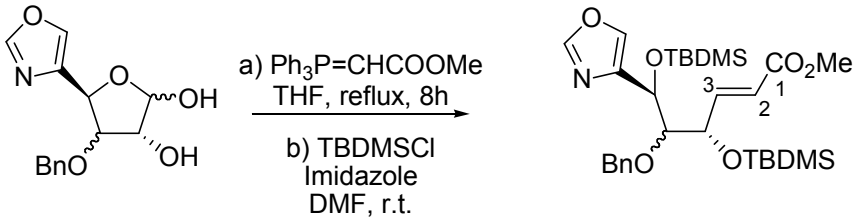
108 R=H, D-xylo
109 R=Bn, D-xylo
110 R=Bn, D-ribo
111 R=H, D-ribo

118 (α, β) R=H, D-xylo, 83%
119 (α, β) R=Bn, D-xylo, 72%
120 (α, β) R=Bn, D-ribo, 82%
121 (α, β) R=H, D-ribo, 85%

oxazoles	α/β ratio (%)
118	60/40
119	63/37
120	67/33
121	47/53

Scheme 118

Applying the same Wittig conditions to anomeric mixtures **119** and **120**, with subsequent silylation of the intermediate products, led to the expected decyclized derivatives **122** and **123** in 66% and 78% yields, respectively (Scheme 119).



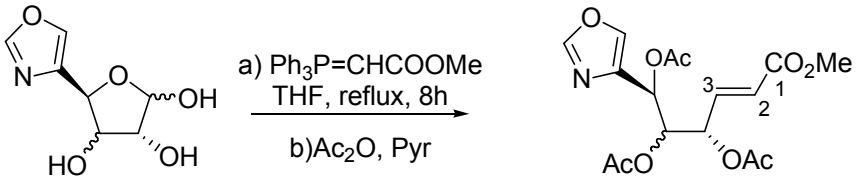
119 R=Bn, D-xylo
120 R=Bn, D-ribo

122 R=Bn, D-xylo, 66%
123 R=Bn, D-ribo, 78%

Scheme 119

The transformation is completely stereoselective: the 15.6 and 15.7 Hz values measured for the $J_{2\text{-}3}$ coupling constant in the ^{1}H-NMR spectrum of **122** and **123** is revealing of *E*-stereoisomers.

On the other hand, when submitted to Wittig reaction conditions followed by peracetylation, the compounds **118** and **121** are converted into the corresponding 4,5,6-tri-*O*-acetylated decyclized products **124** and **125** in 71% and 64% yield, respectively (Scheme 120). Again, the *E*-stereoselectivity of the transformation is complete, as corroborated by a $J_{2\text{-}3}$ = 15.6 Hz for both products.



118 R=H, D-xylo
121 R=H, D-ribo

124 R=Ac, D-xylo, 71%
125 R=Ac, D-ribo, 64%

Scheme 120

None of the oxazole derivatives **122-125** undergoes further transformation via subsequent internal nucleophilic attack. Such behaviour is indicative of a more pronounced aromatic character for oxazoles than for OXTs.

This was further confirmed by theoretical calculations related to the electronic density in the oxazole ring (Figure 8).

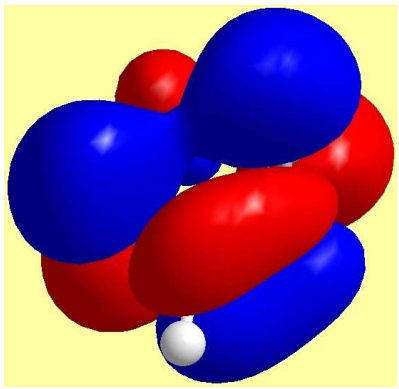


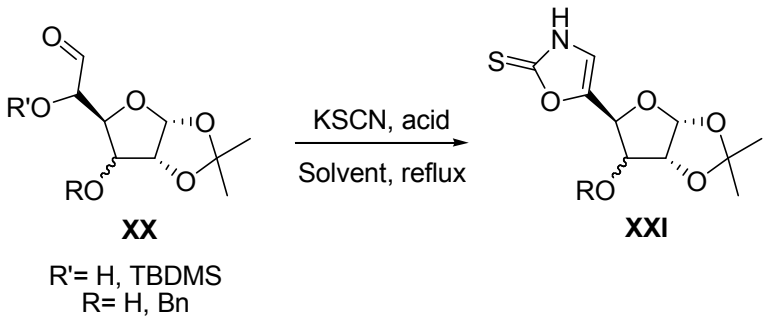
Figure 8

After minimization with GAMESS, LUMO, using force field type HF, 6G-21, it appeared that there are no differences between the electronic distributions in oxazole atoms, hence no preferential attack onto one of those atoms.

With this observation, we can conclude that oxazoles possess a "real" aromatic character, revealing to be very reluctant towards a possible nucleophilic attack. Going back to the hydrolysis of compound **87** (Scheme 112), a nucleophilic addition onto the double bond of OXT was shown to afford the hydrated OZT **112**. Such a nucleophilic water addition was never observed in the course of hydrolysis for oxazoles **108-111**.

2.2. Antennary OXTs from α-hydroxyaldehyde precursors

After having studied the synthesis and reactivity of antennary OXTs derived from α-hydroxyketones, our challenge was the permutation between the oxygen and the nitrogen atoms in order to provide regioisomeric OXTs. This requires the formation of α-hydroxyaldehydes **XX** which would condense with thiocyanic acid to deliver antennary OXTs **XXI** (Scheme 121).



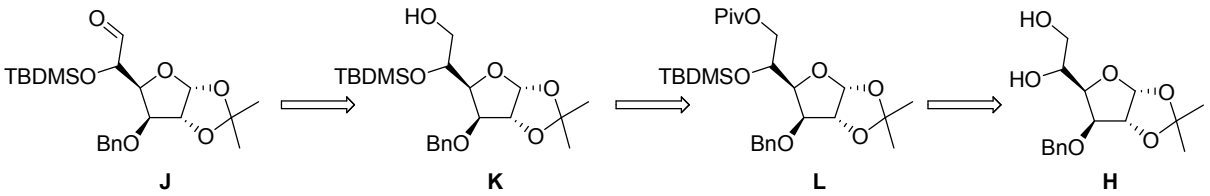
XX

R'= H, TBDMS
R= H, Bn

XXI

Scheme 121

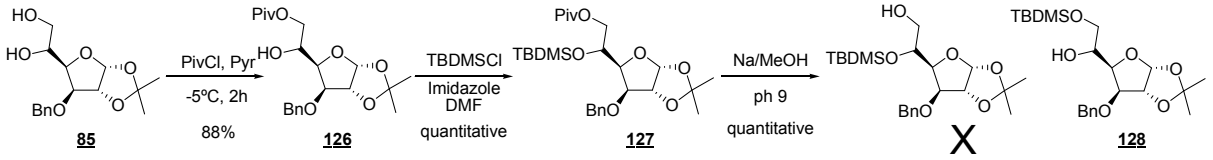
Introduction of an aldehyde function in position 6 revealed much more difficult than what we expected. Our first attempt to build up α-hydroxyaldehydes of type **XX** is summarized in the retrosynthetic Scheme 122:



Scheme 122

The aldehyde **J** might be obtained via oxidation of the monoalcohol **K**, resulting from transesterification of pivaloate **L**. The previous ester would be prepared by regioselective pivaloylation and subsequent O-5 silylation of the diol **H**.

Consequently, the 3-*O*-protected diol **85** was selectively pivaloylated under standard conditions,[88] affording the ester **126** in 88% yield. Silylation at O-5 was then performed to give compound **127** in quantitative yield. Removal of the pivaloyl group was effected using sodium in methanol:[87] however the reaction was followed by migration of the silyl group to O-6 and compound **128** was obtained quantitatively (Scheme 123).

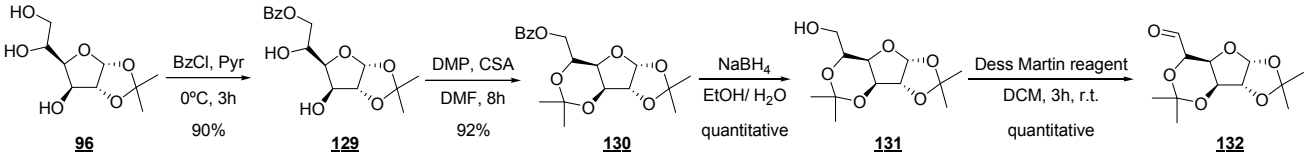


Scheme 123

Silyl groups are known to undergo migration under basic conditions,[184] and therefore isomerisation of our TBDMS ether is not a surprising result. Nevertheless, this first synthetic sequence to access the aldehyde had to be forgotten.

[184] Hamdach, A.; Bentama, A.; Gil, S.; Garcá, E. Z.; Arques, J. S.; Zaragozá, R. J. *Lett. Org. Chem*. **2006**, *3*, 477-483.

Hence, a new route was scrutinized for introducing the aldehyde in correct position. Selective 6-*O*-benzoylation of 1,2-*O*-isopropylidene-D-glucofuranose under standard conditions[185] afforded the monoester **129** in 90% yield. Subsequently, simultaneous protection of positions 3 and 5 was achieved by isopropylidene acetal formation[186,187] producing the bis-acetal **130** in 92% yield. Quantitative de-*O*-benzoylation was achieved under reductive conditions[188] and – after testing several oxidants – the resulting alcohol **131** was quantitatively oxidized into aldehyde **132** using Dess-Martin reagent [102](Scheme 124).



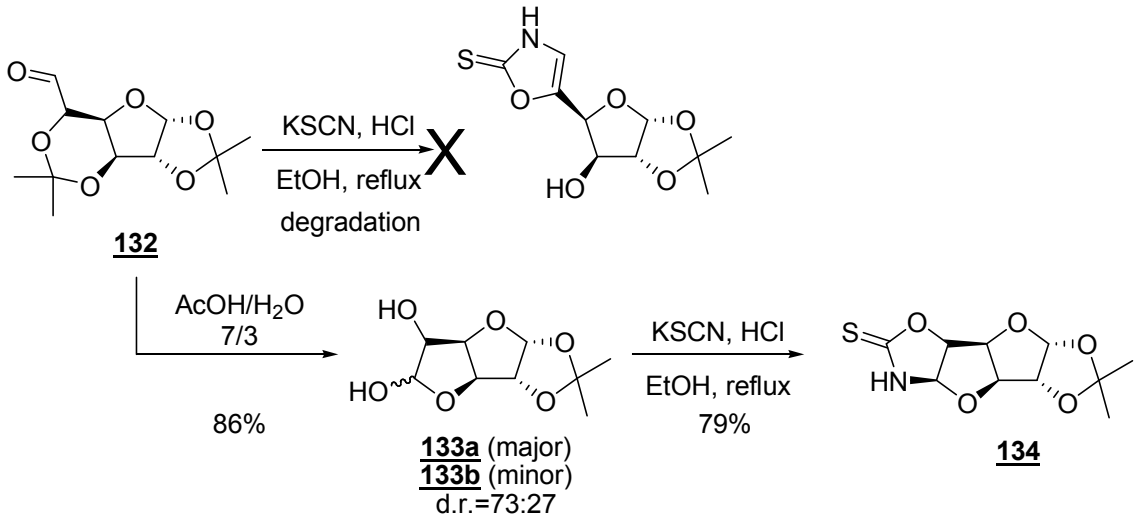
96 **129** **130** **131** **132**

Optimization of conditions for aldehyde formation					
oxidizing agents	**number of eqs**	**solvent**	**Δ**	**time (h)**	**yield**
PCC	1.5	DCM	r.t.	24	-
PCC	4	DCM	r.t.	8	-
PCC/mol.sieves	2	DCM	r.t.	24	-
PCC/mol.sieves	9	DCM	r.t.	8	-
PDC/Ac_2O(1/0.2)	1	DCM	r.t.	8	-
PDC/Ac_2O(1/0.2)	2	DCM	reflux	8	-
$(COCl)_2/NEt_3$	1.2	DMSO	-77 to r.t.	4	-
Dess-Martin reagent	1.5	DCM	r.t.	3	quantitative

Scheme 124

[185] Mort, C. J. W.; Migaud, M. E.; Galione, A.; Potter, B. V. L. *Bioorg. Med. Chem*. **2004**, *12*, 475-487.
[186] Nicolaou, K. C.; Li, J.; Zenke, G. *Helv. Chim. Acta* **2000**, *83*, 1977-2006.
[187] Bartalucci, G.; Bianchini, R.; catelani, G.; D'Andrea, F.; Guazzelli, L. *Eur. J. Org. Chem*. **2007**, 588-595.
[188] Just, G.; Wang, Z. Y.; Chan, L. *J. Org. Chem*. **1988**, *53*, 1030-1033.

As the dioxano-isopropylidene acetal in positions 3 and 5 is supposed to hydrolyze must faster than the dioxolano-isopropylidene acetal in positions 1 and 2, we applied to aldehyde **132** the optimal conditions for OXT formation, expecting 3,5-*O*-isopropylidene cleavage and condensation with thiocyanic acid in one step, with formation of the corresponding antennary OXT. Unfortunately, only degradation was observed, and this result compel us to perform 3,5-*O*-isopropylidene cleavage and condensation with thiocyanic acid in two separate steps. However, when submitted to selective hydrolysis conditions (AcOH/H_2O system), the dialdose **132** underwent rearrangement[189,190,191] to the hemiacetalic mixture **133** in 86% yield. The hemiacetal **133** underwent condensation with thiocyanic acid and OZT **134** was obtained regioselectively in 79% yield (Scheme 125).



Scheme 125

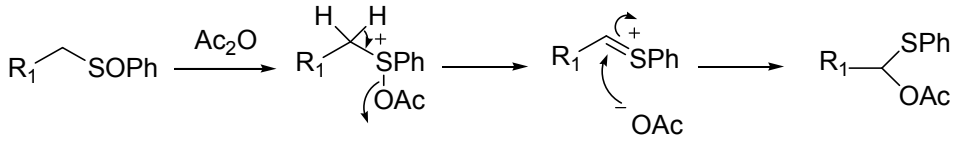
The configuration of the newly formed chiral centers in compound **134** was determined thanks to bidimensional NOESY. A strong NOE was observed between H-5 and H-6. As H-5 is down in relation to the molecule plan, we can conclude that H-6 is also down in relation to molecule plan: therefore, C-6 should be *R*-configurated. The strong NOE observed between H-5 and H-3 corroborate also with this conclusion.

[189] Morgenlie, S. *Carbohydr. Res*. **1977**, *59*, 73-80.
[190] Morris, M. K.; Bondo, P. B. *Carbohydr. Res*. **1988**, *175*, 49-58.
[191] Drijver, L. *Carbohydr. Res*. **1987**, *161*, 65-73.

Even though OZT derivative **134** is a very interesting compound because of its geometry, we were still interested in the synthesis of the antennary OXTs, as displayed in Scheme 121. Another pathway was therefore imagined to introduce the aldehyde function in position 6, based the Pummerer rearrangement.[192,193]

2.2.1. Pummerer rearrangement – Some considerations

The Pummerer reaction of sulfoxides[194,195,196] is a well known rearrangement which gives sulfides with concomitant oxidation of the α-carbon. It may also can be regarded as a transfer of the oxidative state of sulfur to the α-carbon. This reaction begins with an electrophilic activation (Ac_2O or TFAA) at the oxygen of the sulfoxide. In that way, the α-hydrogens becoming more acidic and one proton can be eliminated to form a sulfenium ion, which undergoes counter attack of the carboxylate ion present in the medium (Scheme 126).



Scheme 126

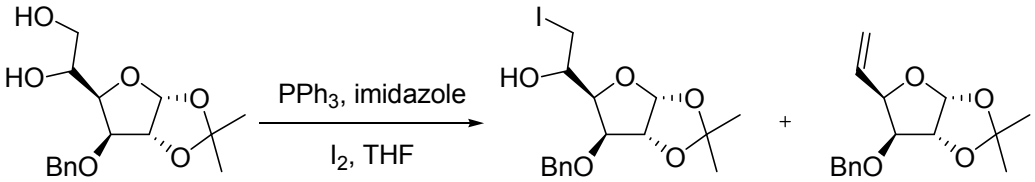
The thioacetal formed can be hydrolyzed, producing the aldehyde function,[197] or the α-carbon can be used as a target for the attack of various nucleophiles. In the work we develop here, these two approaches for dealing with the thioacetal function will be considered.

[192] Pummerer, R. *Chem. Ber.* **1909**, *42*, 2282-2284.
[193] Craig, D.; Daniels,K. *Tetrahedron* **1993**, *49* (48), 11263-11304.
[194] Iriuchijima, S.; Maniwa, K.; Tsuchihashi, G. *J. Am. Chem. Soc*. **1794**, *96*, 4280-4283.
[195] Tai, C. H.; Wu, H. C.; Li, W. R. *Org. Lett*. **2004**, *6*, 2905-2908.
[196] Veerapen N.; Taylor, A.; Walsby, C. J.; Pinto, B. M. *J. Am. Chem. Soc*. **2006**, *128*, 227-239.
[197] Mandai, T.; Takeshita, M.; Kawada, M.; Otera, J. *Chem. Lett*. **1984**, 1259-1260.

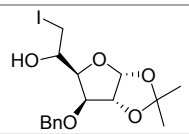
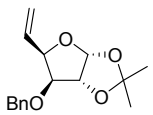
2.2.1.1. Pummerer rearrangement using Ac_2O

Making use of Ac_2O to perform the Pummerer rearrangement, we have exploited the eletrophilic character of the α-acetoxylated carbon when opposed to a thiocyanate ion. Our efforts were first focused on the synthesis of the sulfoxide in position 6 – the precursor to the Pummerer reaction.

Having this goal in mind, selective iodination in position 6 of diol **85** was achieved under Garegg's conditions.[120] In a first attempt, the desired iodinated derivative **135** was obtained only in 35% yield, because of the formation (50% yield) of a side-product **136**, resulting from the elimination reaction.[198,199,200] In order to limit this side-reaction, the iodination conditions were optimized to finally reach compound **135** in 95% yield (Scheme 127).



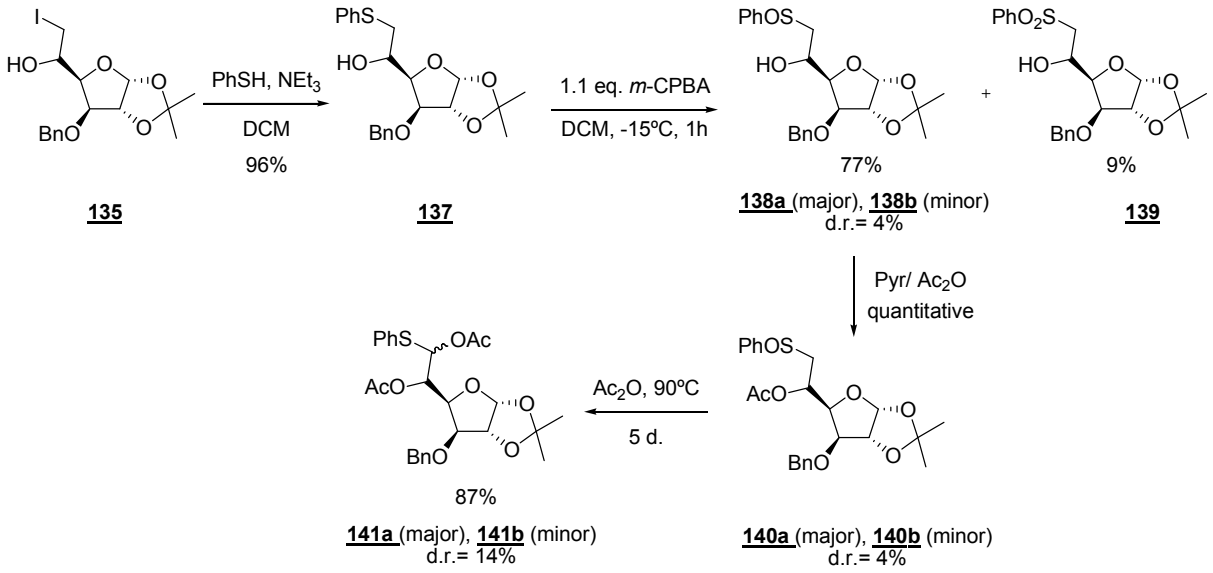
85 **135** **136**

Optimization of conditions for iodination				
iodine (eq)	time	Δ (ºC)	yield (%)	
				
1.2	8h	0-r.t.	35	50
1.2	1h	0-r.t.	62	30
1.2	25 min	0	95	---

Scheme 127

[198] Bessodes, M.; Abushanab, E.;Panzica, R. P. *J. Chem. Soc., Chem. Comm.*; **1981**, 26-29.
[199] Liu, Z.; Classon, B. *J. Org. Chem*. **1990**, *55*, 4273-4275.
[200] Luzzio, F.; Menes, M. E. *J. Org. Chem*. **1994**, *59*, 7267-7272.

Therefore, compound **135** was subjected to nucleophilic substitution with thiophenol, producing the phenylsulfanyl derivative **137** in 96% yield. The latter was then oxidized using *m*-CPBA[201,202,203] and the mixture of diastereoisomeric sulfoxides **138** was obtained in 77% yield. The oxidation also afforded in 9% yield the corresponding sulfone **139**. Standard *O*-acetylation of **138** led, quantitatively, to the protected sulfoxides **140**. Pummerer rearrangement was then accomplished with acetic anhydride at 90ºC during five days, and the mixture of stereoisomers **141** was obtained in 87% yield (Scheme 128).

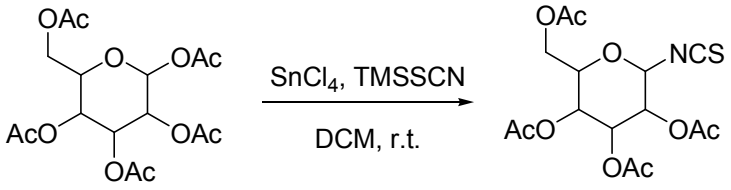


Scheme 128

With these Pummerer precursors in hand, we wanted first to exploit the electrophilic character at C-6, in order to introduce an isothiocyanate moiety in the structure. Then via *O*-5 deacetylation, one could expect intramolecular cyclization to an antennary OXT.

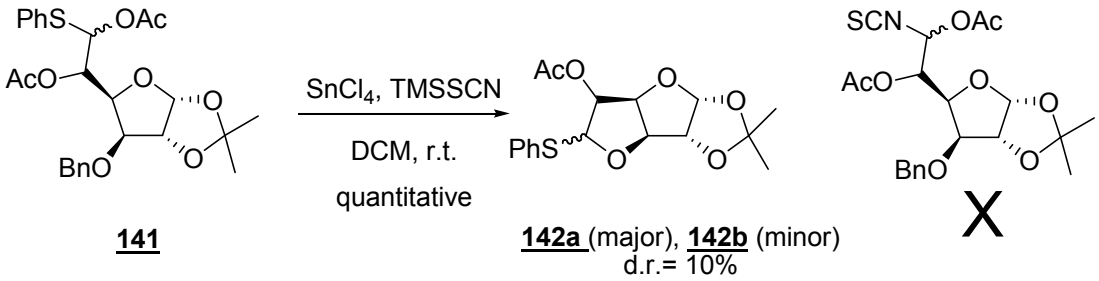
[201] Fur, N.; Mojovic, L.; Plé, N.; Quéguiner, G.; Reboul, V.; Perrio, S.; Metzner, P. *Tetrahedron* **2004**, *60*, 7983-7994.
[202] Betson, M. S.; Clayden, J.; Helliwell, M.; Mitjans, D. *Org. Biomol. Chem*. **2005**, *3*, 3898-3904.
[203] Hok, S.; Schore, N. E. *J. Org. Chem*. **2006**, *71*, 1736-1738.

In 2002, Lindhorst and coll. disclosed a simple method for the preparation of glycosyl isothiocyanates by using trimethylsilyl isothiocyanate (TMSNCS) under tin tetrachloride catalysis, from 1-*O*-acetylated precursors (Scheme 129).[204]



Scheme 129

When applying this methodology to our Pummerer precursors **141**, the expected nucleophilic substitution at C-6 did not take place. Instead of that, concomitant de-*O*-benzylation/transacetalation was observed and thioglycosides **142** were obtained quantitatively. By NOESY experiments, it was possible to estimate a 55/45 R/S ratio at C-6 (Scheme 130).



141

142a (major), **142b** (minor)
d.r.= 10%

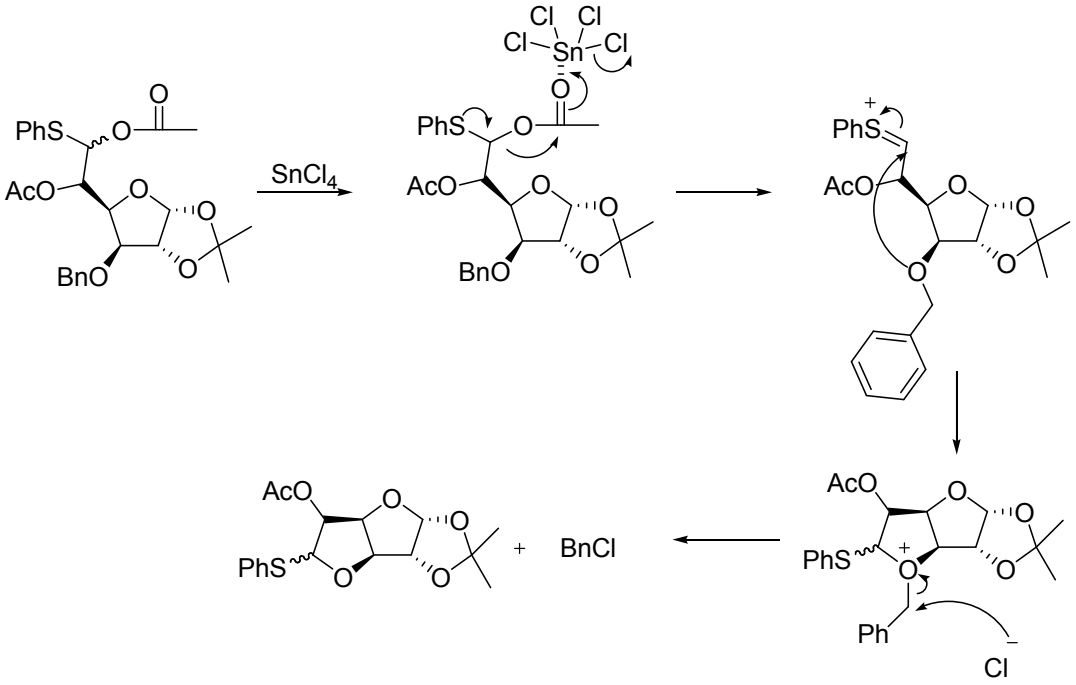
Scheme 130

This result can be explained by the ability of benzyloxy groups to participate in ring formation reactions, as recognized and described by several teams.[205,206,207,208,209]

The reaction mechanism can be rationalized by claiming preliminary tin tetrachloride activation of the C-6 acetyl group, thus producing a transient sulfenium cation which can undergo intramolecular attack of the pendant benzyloxy group.

[204] Kühne, M.; Györgydeák, Z.; Lindhorst, T. K. *Synthesis* **2006**, *6*, 949-951.
[205] Gray, G. R.; Hartman, F. C.; Barker, R. *J. Org. Chem*. **1965**, *30*, 2020-2024.
[206] Hori, H.; Nishida, Y.; Ohrui, H.; Meguro, H. *J. Org. Chem*. **1989**, *54*, 1346-1353.
[207] Yang, B. H.; Jiang, J. Q.; Wu, H. M. *Tetrahedron Lett*. **1995**, *36*, 2831-2834.
[208] Martin, O. R.; Yang, F.; Xie, F. *Tetrahedron Lett*. **1995**, *36*, 47-50.
[209] Zemribo, R.; Champ, M. S.; Romo, D. *Synlett* **1996**, 278-280.

Debenzylation of the benzyloxonium ion was affected by transfer of the benzyl group to the nucleophile present in the medium, leading to the thioacetalic structure (Scheme 131).



Scheme 131

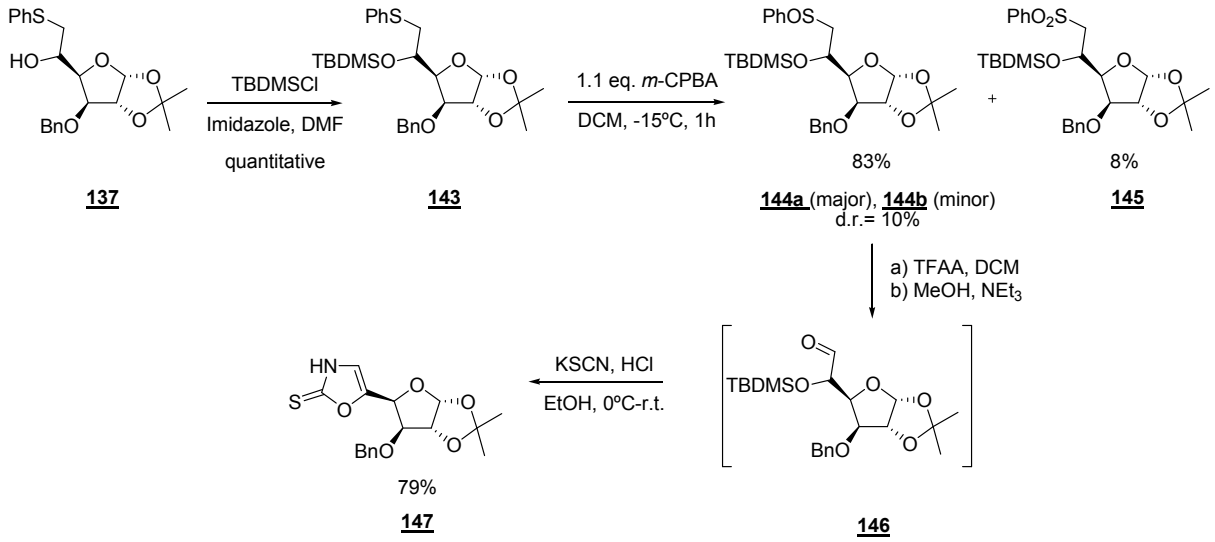
This result, although interesting, was not opening a way to the long time desired antennary OXTs. Consequently, we stopped our exploration of the electrophilic character of acetylated Pummerer precursors.

2.2.1.2. Pummerer rearrangement using TFAA

It was then decided to investigate the aldehyde formation using TFAA.[210,211] The previously prepared thio-derivative **137** was quantitatively *O*-silylated on position 5. The resulting product **143** underwent *m*-CPBA oxidation to provide the sulfoxides mixture **144** in 83% yield, together with 8% of the corresponding sulfone

[210] Omura, K.; Sharma, A. K.; Swern, D. *J. Org. Chem*, **1976**, *41*, 957-962.
[211] Sugihara, H.; Tanikaga, Sugihara, H.; Tanikaga, R.; Kaji, A. *Synthesis* **1978**, 881-886.

145. Sulfoxides **144** were then submitted to a Pummerer reaction with TFAA, which was completed after 2h. Treatment of the reaction mixture with MeOH/NEt_3 effected mild transformation of the thioacetal into the unstable aldehyde **146**, which could not be isolated, but directly engaged in the condensation with thiocyanic acid. We were pleased to find that the antennary OXT **147** was formed in 79% yield (Scheme 132).



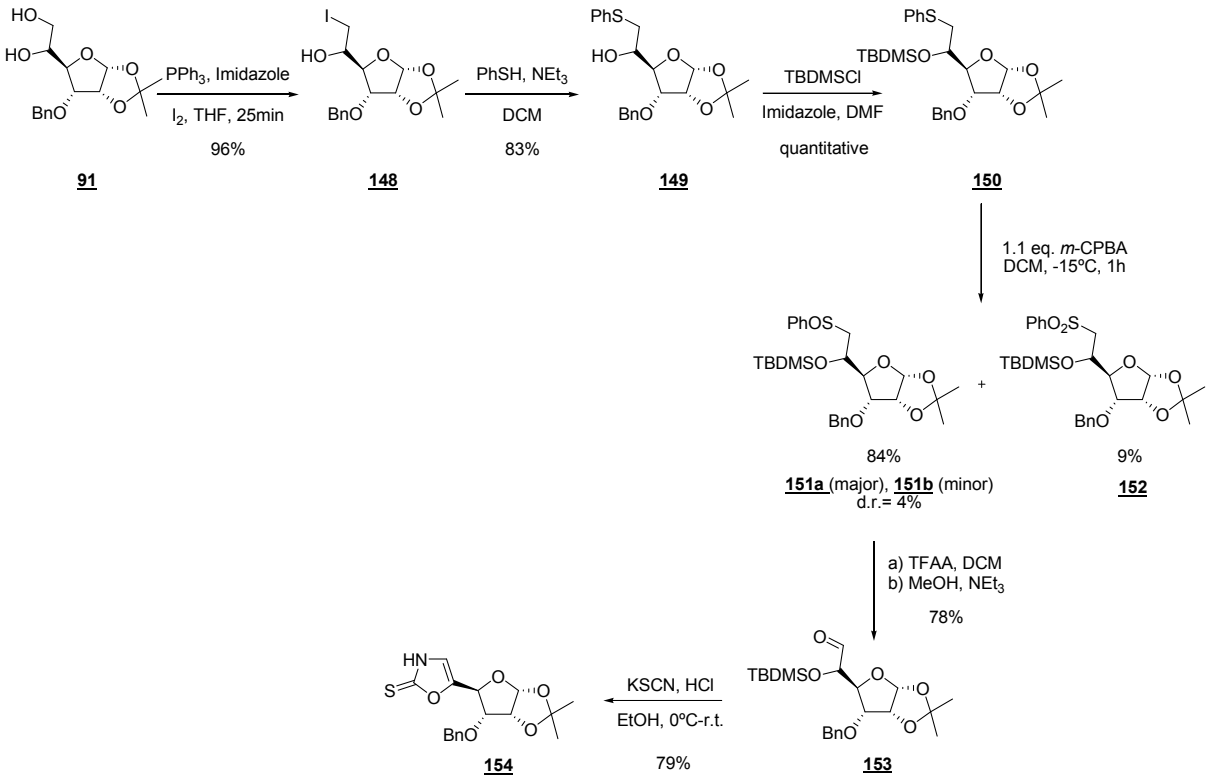
Scheme 132

Confirmation of the antennary OXT structure was obtained from analysis of its NMR spectra, which are very close to those of its regioisomer **87**. The chemical shift for the C=S bond was present at 178.1 ppm, a normal value for an OXT cycle. In the ^1H NMR spectrum, strong deshielding of H-4 was observed at 7.61 ppm.

Motivated – after arduous efforts – by this good result, we envisaged the synthesis of the ribo-type epimer of OXT **147**, following the same reaction scheme.

In so doing, optimal conditions for selective iodination were applied on diol **91** and the expected 6-iodo derivative **148** was produced in 96% yield. Thiophenol nucleophilic substitution delivers in 83% yield the sulfide **149**, which was quantitatively converted into the *O*-5 silylated derivative **150**. This silyl ether underwent *m*-CPBA oxidation to provide the sulfoxides mixture **151** in 84% yield, together with 9% of the corresponding sulfone **152**. Sulfoxides **151** were then

submitted to the Pummerer reaction with TFAA, which was completed after 2h. Treatment of the reaction mixture with MeOH/NEt_3 effected mild transformation of the thioacetal into the aldehyde **153**, which could be isolated in 78% yield through quick purification. The aldehyde was then condensed with thiocyanic acid to afford the desired OXT **154** in 79% yield (Scheme 133).



Scheme 133

☝ Our objective of permutation between O- and N- atoms in relation to antennary OXTs **87** and **95** has proven tricky to attain: however, thanks to TFAA-induced Pummerer rearrangement, the reaction sequence was efficient enough with a conversion of diols **85** and **91** into OXTs **147** and **154** in 60% and 41% overall yield, respectively.

3. Conclusion

In this chapter, we have put our efforts in the synthesis of OXTs anchored onto carbohydrate scaffolds and also in the study of their reactivity. From the results obtained, some statements can be put into light:

- ☑ The formation of antennary OXTs derived from α-hydroxyketones was easily achieved.
- ☑ In presence of *m*-CPBA, antennary OXTs underwent sulfur extrusion leading to oxazoles. This reaction can be used as a new method for oxazole formation.
- ☑ The nitrogen atom in antennary OXTs is able to act as a nucleophile in intramolecular addition to the masked aldehyde group in carbohydrate precursors.
- ☑ Comparing the aromaticity of the oxazolinethione and oxazole rings, we observe that the aromatic character of oxazole is much more pronounced than the one demonstrated for the OXT system.
- ☑ TFAA-induced Pummerer rearrangement is the key-step in the conversion of α-hydroxyaldehydes into antennary OXTs.

CHAPTER IV

Palladium catalysed reactions

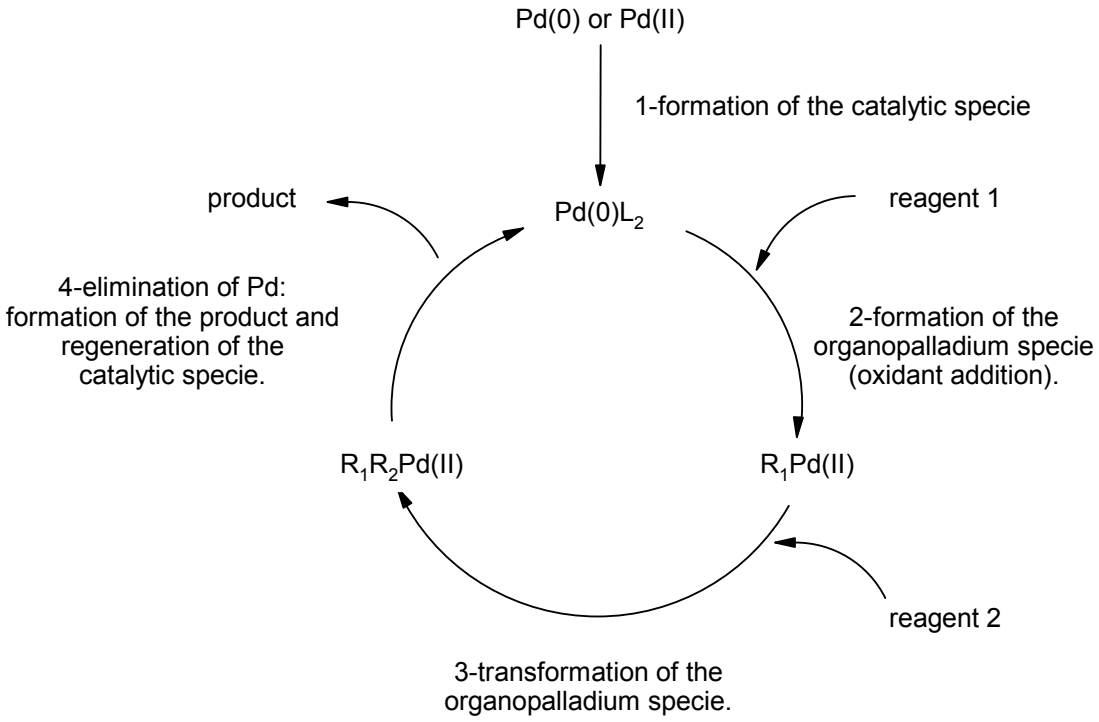
1. Introduction

Palladium was discovered by W. H. Wollaston in 1803. This metal is known for its ability to absorb large amounts of hydrogen gas (up to 900 times its own volume of H_2 at room temperature), which led to one of its earliest chemical uses, as a hydrogenation catalyst. In the last few decades, palladium compounds have been used as catalysts to develop new synthetic transformations, mainly for carbon-carbon and carbon-heteroatom coupling reactions (as Suzuki, Stille, Sonogashira, etc…) in generally mild reaction conditions. The high functional group tolerance and broad availability of starting materials, have contributed to the growing success of many palladium cross-coupling reactions as one of the major tools for the construction of complex molecules[212,213,214,215,216,217,218].

The mechanism of the Pd (0) catalysed reactions can be summarized in four successive operations[219] (Scheme 134):

- ☑ The first operation is the beginning of the catalytic cycle, involving formation of the catalytic species $Pd(0)L_2$ from the stable salts of Pd(0) or Pd (II) (pre-catalysts).
- ☑ The second step consists of an oxidation step between the reagent 1 and the catalytic specie $Pd(0)L_2$ to form the organopalladium species $R_1Pd(II)$.
- ☑ The third step is the insertion of reagent 2 through a ligand exchange.
- ☑ The final step corresponds to the elimination of palladium (regeneration of the catalytic species) which generates the final coupling product.

[212] Heck, R. F. *Palladium Reagents in Organic Synthesis;* Academic Press: New York, **1985**.
[213] Tsuji, J. *Palladium Reagents and Catalysts: Innovations in Organic Synthesis*; Wiley & Sons: New York, **1995**.
[214] Stille, J. K. *Angew. Chem., Int. Ed.* **1986**, *25*, 508-524.
[215] Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457-2483.
[216] Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176-4211.
[217] Dubbaka, S. R.; Vogel, *Angew. Chem., Int. Ed.* **2005**, *44*, 7674-7684.
[218] Yang, H.; Liebskind, S. L. *Org. Lett*. **2007**, *9*, 2993-2995.
[219] Campagne, J. M.; Prim, D. *Les complexes de palladium en synthèse organique*; CNRS Editions, Paris, **2001**.



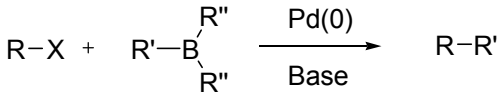
Scheme 134

This chapter is dedicated to the use of thioamides as electrophiles in Suzuki, Stille and Sonogashira cross coupling reactions.

2. Suzuki cross-coupling reaction

2.1. Small introduction

The Suzuki coupling - a palladium-catalyzed cross-coupling reaction of organoboranes with organic halides, triflates, etc. in the presence of a base - is one of the most efficient methods for the generation of a carbon-carbon bond. Further advantages associated with the reaction are the non toxicity of organoboranes and their high stability when compared to other organometallic reagents (Scheme 135).[220]

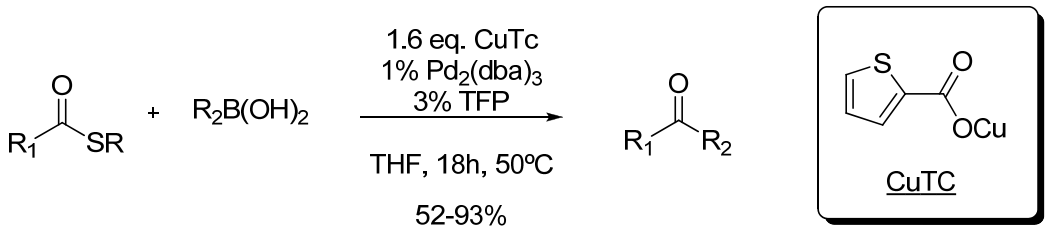


Scheme 135

In addition to aryl or alkenyl halides, the use of organosulfur compounds as electrophilic reaction partners has recently been reported,[221] involving for instance sulfonyl chlorides,[222] sulfones[223] and sulfonium salts.[224]

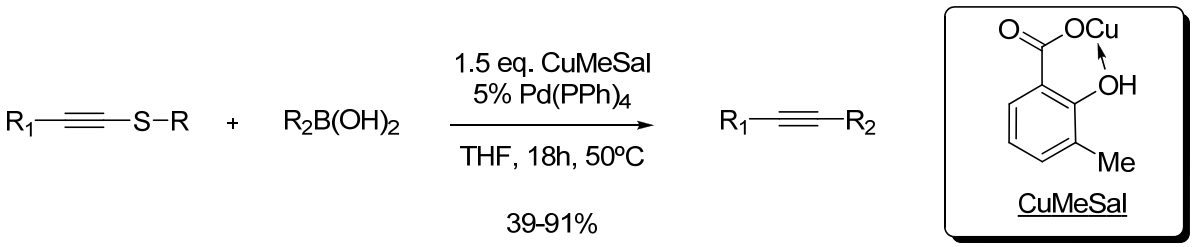
In 2000, Liebeskind et al[225] disclosed a mild and general method for the coupling reactions of thiol esters and boronic acids under "baseless" conditions, in presence of 1 % of $Pd_2(dba)_3$, 3 % of TFP and in over-stoechiometric ratio (1.6 equiv.) the copper(I) thiophene-2-carboxylate cofactor (CuTc), indispensable for the occurrence of this reaction (Scheme 136).

[220] Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359-1469.
[221] Dubbaka, S. R.; Vogel, P. *Angew. Chem.* **2005**, *117*, 7848-7859.
[222] Dubbaka, S. R.; Vogel, P. *Org. Lett.* **2004**, *6*, 95-98.
[223] Liu, J.; Robins, M. J. *Org. Lett.* **2005**, *7*, 1149-1151.
[224] Srogl, J.; Allred, G. D.; Liebskind, L. S. *J. Am. Chem. Soc.* **1997**, *119*, 12376-12377.
[225] Liebeskind, L. S.; Srogl, J. *J. Am. Chem. Soc.* **2000**, *122*, 11260-11261.



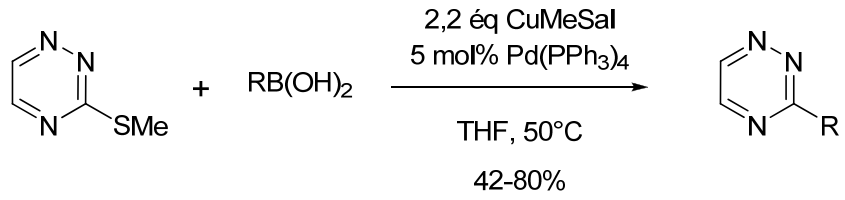
Scheme 136

In 2001, the same team[226] reported a new and mild method for the synthesis of substituted alkynes, involving the coupling of boronic acids and thioalkynes, in the presence of a catalytic amount of $Pd(PPh_3)_4$ and either cofactor CuTc or Cu (I) 3-methylsalicylate (CuMeSal) (Scheme 137).



Scheme 137

In 2002, Guillaumet and coll. (ICOA, Orléans) have demonstrated, for the first time, that this methodology could be applied to π electron-deficient heteroaromatic rings, namely 3-methylsulfanyl-1,2,4-triazine (Scheme 138).[227]



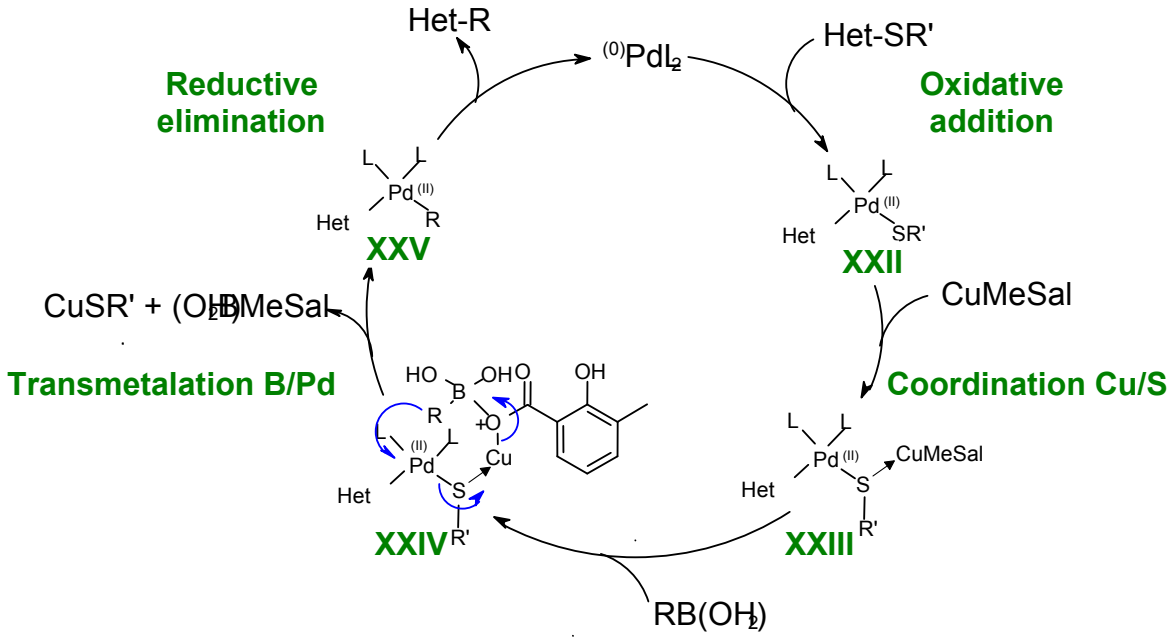
Scheme 138

[226] Savarin, C.; Srogl, J.; Liebeskind, L. S. *Org Lett.* **2001**, *3*, 91-93.
[227] Alphonse, F. A.; Suzenet, F.; Keromnes, A.; Lebret, B.; Guillaumet, G. *Synlett* **2002**, 447-450.

The above reaction was then generalized by Liebeskind to other π electron-deficient heteroaromatic thioethers,[228] thiamidines,[229] alkyl or aryl thiocyanates,[230] oximes[231] and thioesters.[232,233,234,235]

From a mechanistic point of view (Scheme 139), Liebeskind has proposed that the oxidative addition involving palladium in the heteroaryl-SR' bond, produces the intermediate $HetPdL_2$-SR' **XXII**. The copper(I) cofactor (CuMeSal) then coordinates with the sulfur atom to form the organopalladium species **XXIII**. In the transmetallation process, the Cu(I) carboxylate plays the dual role of simultaneously polarizing the Pd-S bond through Cu(I) coordination to S while activating the trivalent boron through coordination of carboxylate to B ("complex ate" **XXIV**). In a concerted mechanism, the copper atom assists the departure of the thioether group, and the aryl transfer to form the organo-palladium species **XXV**. Reductive elimination then affords the expected product Het-R and regenerates a catalytically active Pd(0).

[228] Liebeskind, L.S.; Srogl, J. *Org. Lett.* **2002**, *4*, 979-981.
[229] Kusturin, C.L.; Liebeskind, L.S.; Neumann, W.L. *Org. Lett.* **2002**, *4*, 983-985.
[230] Zhang, Z.; Liebeskind, L.S. *Org. Lett.* **2006**, *8*, 4331-4333.
[231] Liu, S.; Yu, Y.; Liebeskind, L. S. *Org. Lett.* **2007**, *9*, 1947-1950.
[232] Yang, H.; Li, H.; Wittenberg, R.; Egi, M.; Huang, W.; Liebeskind, L. S. *J. Am. Chem. Soc.* **2007**, *129*, 1132-1140.
[233] Yang, H.; Liebeskind, L. S. *Org. Lett.* **2007**, *9*, 2993-2995.
[234] Aguilar, A. A.; Liebeskind, L. S.; Cabrera, E. P. *J. Org. Chem*. **2007**, *72*, 8539-8542.
[235] Yu, Y.; Liebeskind, L. S. *J. Org. Chem*. **2004**, *69*, 3554-3557.

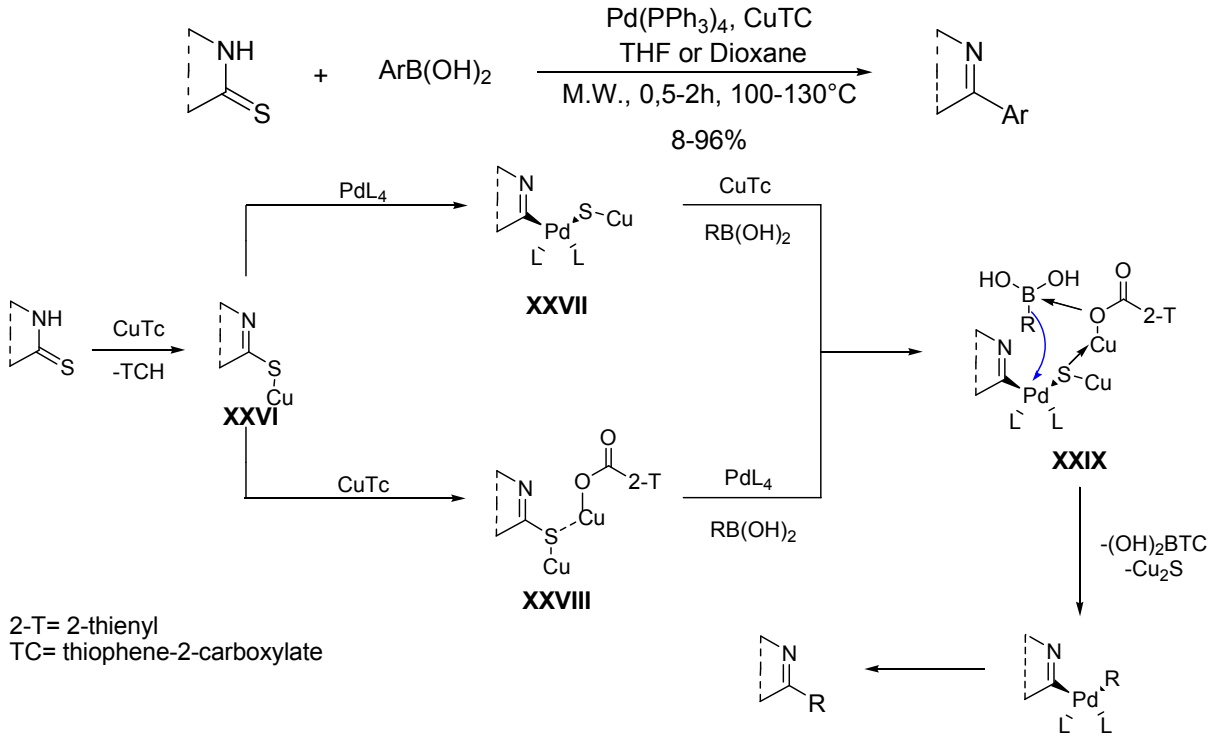


Scheme 139

In the group of Guillaumet (ICOA, Orléans), direct application of this methodology has allowed the synthesis of new families of polyfunctionalized heterocycles such as triazines,[236] tetrazines[237] and oxazolidines.[238]

Kappe has recently published a modified desulfurative cross-coupling method, using a direct reaction on thioamides under microwave assistance.[239,240] It was shown that, in contrast to cross-coupling between alkylsufanyl-N-heteroaromatics and boronic acids, 2 to 3 equivalents of CuTc cofactor were needed to achieve high yielding conversions. Kappe suggested the initial formation of a Cu(I) thiolate species (**XXVI)**, which could undergo either oxidative addition to the Pd(0) catalyst (**XXVII**) or further complexation with an additional equivalent of CuTc cofactor (**XXVIII**). Both pathways would ultimately lead to the key intermediate **XXIX**, which subsequently undergoes base-free transmetallation with extrusion of Cu_2S followed by reductive elimination to provide the carbon-carbon cross-coupled products (Scheme 140).

[236] Alphonse, F. A.; Suzenet, F.; Keromnes, A.; Lebret, B.; Guillaumet, G. *Synthesis* **2004**, 2893-2899.
[237] Leconte, N.; Keromnes-Wuillaume, A.; Suzenet, F.; Guillaumet, G. *Synlett* **2007**, 204-210.
[238] Leconte, N.; Pellegatti, L.; Tatibouët, A.; Suzenet, F.; Rollin, P.; Guillaumet, G. *Synthesis* **2007**, 857-864.
[239] Prokopcová, H.; Kappe, C. O. *J. Org. Chem.* **2007**, *72*, 4440-4448.
[240] Prokopcová, H.; Kappe, C. O. *Adv. Synth. Catal.* **2007**, *349*, 448-452.



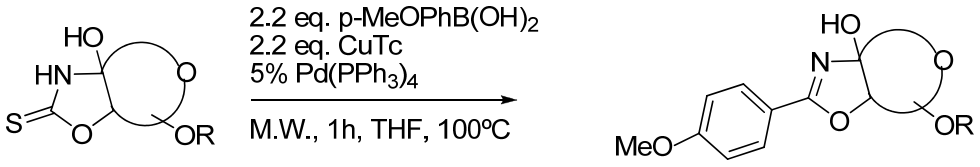
Scheme 140

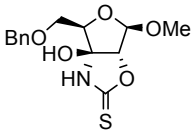
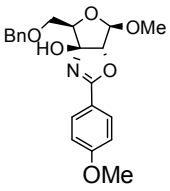
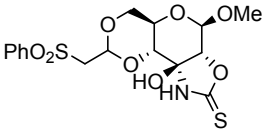
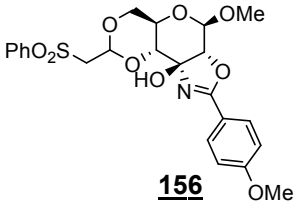
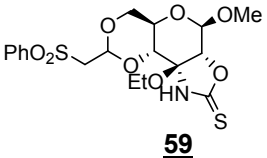
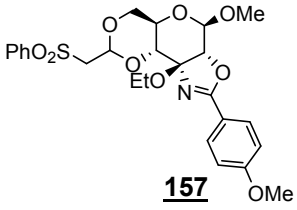
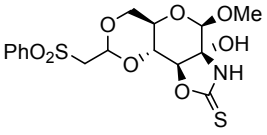
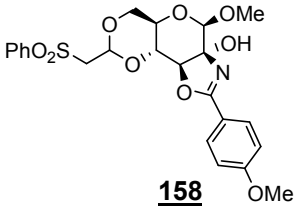
2.2. Modified Suzuki cross-coupling with non aromatic carbohydrate based OZTs

Those observations prompted us to disclose our own results.[241] We had indeed investigated in the same period of time an extension of our own procedure to the direct coupling protocol on some complex thionocarbamate molecules.

Our first approach targeted the study of some carbohydrate–based OZTs synthesized during this PhD work, as substrates for this modified Suzuki protocol. Fused hydrated OXTs **33**, **58**, **59** and **60** were engaged in the reaction with *p*-methoxyphenylboronic acid, in the presence of an excess of CuTc and a catalytic amount of $Pd(PPh_3)_4$, in order to synthesize oxazoles **155**, **156**, **157** and **158** albeit in moderate yields (42%, 47%, 44% and 51%, respectively). Starting OZTs were recovered in 43%, 39%, 44% and 32% yield, correspondingly. The results obtained are detailed in Scheme 141.

[241] Silva, S.; Tardy, S.; Routier, S.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Tetrahedron Lett.* **2008**, *49*, 5583-5586.

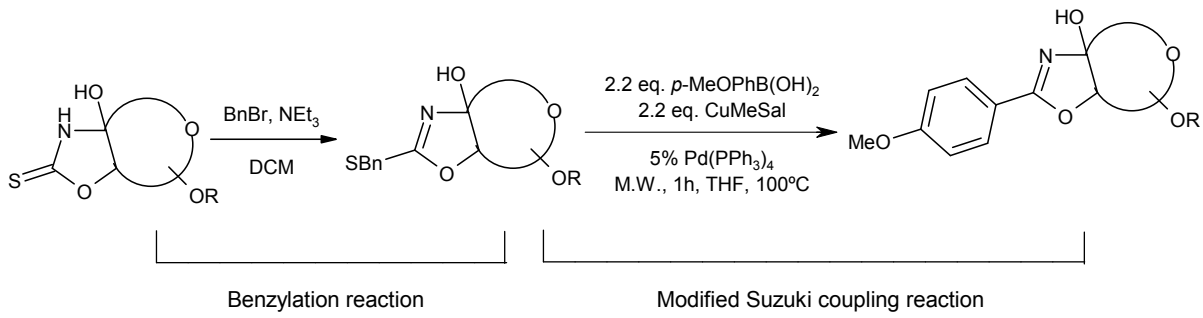


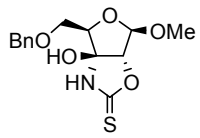
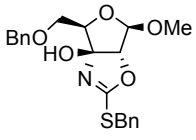
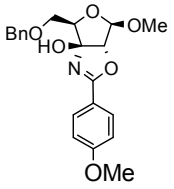
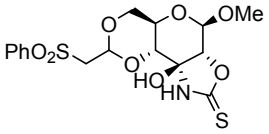
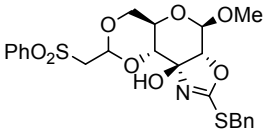
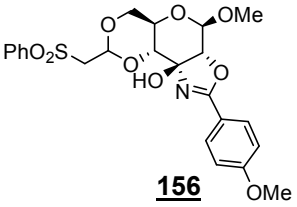
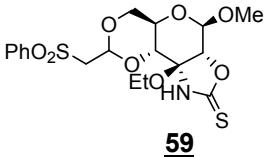
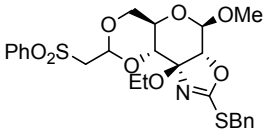
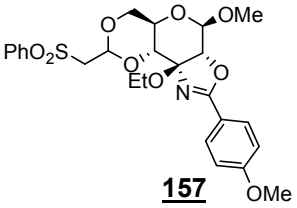
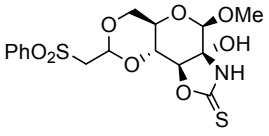
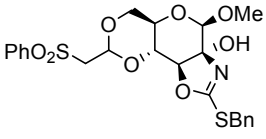
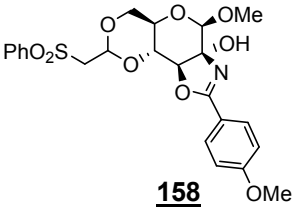
entry	starting material	yield (%)	product
1	 **33**	42	 **155**
2	 **58**	47	 **156**
3	 **59**	44	 **157**
4	 **60**	51	 **158**

Scheme 141

It clearly emerged from the above results that the "direct" cross-coupling procedure was obviously not efficient enough. We therefore applied the two-step procedure developed in our laboratory,[238] with a view to compare the sequences. All four carbohydrate-based OZTs were readily converted into the corresponding 2-benzylsulfanyloxazolines (three of them being already mentioned in chapter II,

Scheme 80), which were then submitted to the modified Suzuki cross-coupling reaction. The results obtained are expressed in Scheme 142.



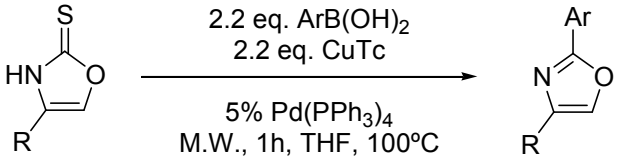
	S-benzylation reaction		modified Suzuki coupling reaction			
entry	**starting material**	**yield (%)**	***S*-benzylation product**	**yield (%)**	**coupling product**	**ov. yield (%)**
1	 **33**	86	 **75**	80	 **155**	69
2	 **58**	56	 **76**	87	 **156**	49
3	 **59**	89	 **159**	89	 **157**	79
4	 **60**	79	 **77**	86	 **158**	68

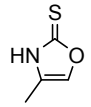
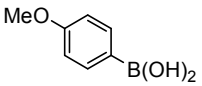
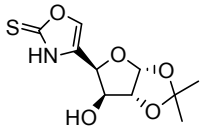
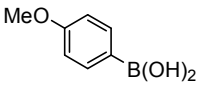
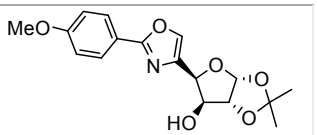
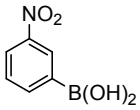
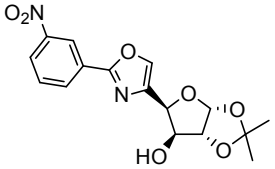
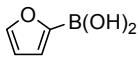
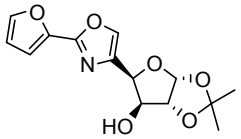
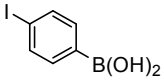
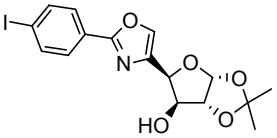
Scheme 142

☝ Through analyzing those results, it clearly emerged that the two-step procedure proved to be much more efficient for all substrates. It is worth noticing that the overall yields were not limitated by the modified Suzuki cross-coupling reaction but rather by the *S*-benzylation process (OZT **58**). This aspect of an efficient two-step procedure over the direct coupling correlates well with other examples investigated in our laboratory.[241]

2.3. Modified Suzuki cross-coupling with aromatic OZTs

The aromatic parent OXT structure was also explored in modified Suzuki coupling. Two representative substrates were selected from the panel synthesized during this PhD work: the simple 4-methyl-1,3-oxazoline-2-thione **1** and the D-xylo-based OXT **100**. When in presence of *p*-methoxyphenylboronic acid, under the known conditions for direct modified Suzuki cross-coupling, OXT **1** underwent complete degradation. In contrast, the carbohydrate-based OXT **100** reacted with four different boronic acids to afford oxazoles **160**, **161**, **162** in good yields and **163** in moderate yield (entry 5). The results are shown in Scheme 143.



starting material	coupling agent	yield (%)	coupling product	entry
 **1**		---	---	1
 **100**		86	 **160**	2
		66	 **161**	3
		61	 **162**	4
		38	 **163**	5

Scheme 143

In the case of *p*-iodophenylboronic acid, the disappointing result obtained could be ascribed to a side reaction: boronic acid homo-coupling.

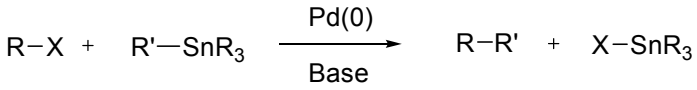
☝ We have observed that, when submitted to modified Suzuki cross- coupling conditions, the non aromatic OZTs show better results when a two-step procedure involving *S*-benzylated intermediates is used rather than a microwave-assisted direct coupling. In the case of aromatic OXTs, good results are obtained in a direct coupling process, avoiding preliminary *S*-benzylation.

As a conclusion, the Suzuki coupling greatly depends on the aromaticity or non-aromaticity of heterocycle involved: on an OXT (aromatic) a direct MW-coupling could be performed while on an OZT (non-aromatic) a two step sequence should be preferred.

3. Stille cross-coupling reaction

3.1. Small introduction

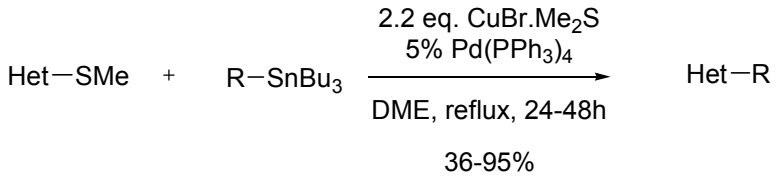
The above interesting results led us to explore other coupling reactions.[241] The Stille coupling – palladium catalyzed cross-coupling reaction between an organostannane and organic halides, triflates, etc – is another versatile and useful method to form new C-C single bonds(Scheme 144).[242,243,244,245,246] In fact, two reasons can be pointed for that: first, the organostannanes can readily be prepared, purified and stored; second, the non basic conditions of the reaction are compatible with a wide variety of functional groups. The pitfall of the Stille reaction is the toxicity of stannanes, making it not suitable for large scale synthesis or the synthesis of pharmaceutical products.



Scheme 144

In addition to halides and triflates, Guillaumet[247] and Liebeskind[248] have introduced heteroaromatic thioethers as substrates for the Stille cross-coupling reaction – modified Stille reaction. The strong difference between the above two papers is that, contrary to Liebeskind's proposal, Guillaumet et al have demonstrated that the use of copper carboxylate is not required. In fact, copper bromide–dimethyl sulfide complex ($CuBr.Me_2S$) is efficient enough to run the reaction (Scheme 145).

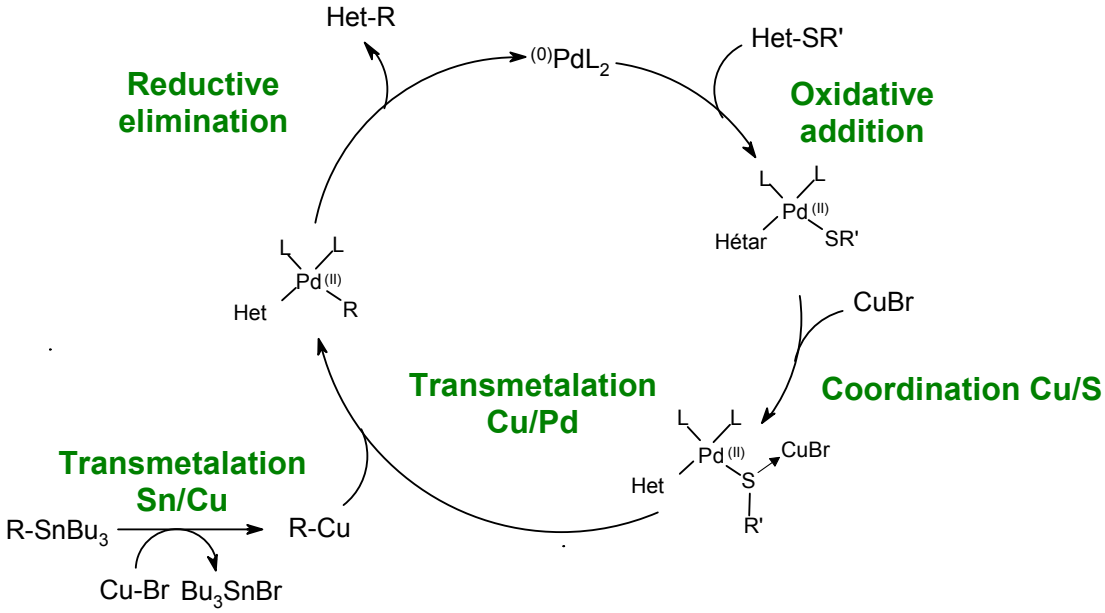
[242] Milstein, D.; Stille, J. K. *J. Am. Chem. Soc*. **1978**, *100*, 3636-3638.
[243] Milstein, D.; Stille, J. K. *J. Am. Chem. Soc*. **1979**, *101*, 4992-4998.
[244] Stille, J. K. *Angew. Chem. Int. Ed*. **1986**, *25*, 508-524.
[245] Farina, V.; Krishnamurphy, V.; Scott, W. *Organic Reactions* **1997**, *50*, 1-652.
[246] Duncton, M. J.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1*, **1999**, 1235-1246.
[247] Alphonse, F.A.; Suzenet, F.; Keromnes, A.; Lebret, B.; Guillaumet, G. *Org. Lett.* **2003**, *5*, 803-805.
[248] Egi, M.; Liebeskind, L.S. *Org. Lett.* **2003**, *5*, 801-802.



Scheme 145

This result can be explained because in the case of the coupling with boronic acids, the presence of the carboxylate counterion of the copper is clearly important to form the "ate" boronic complex. In the Stille mechanism, the pentacoordinate tin intermediate is not essential for the transmetallation step.[249]

In the mechanism proposed by Guillaumet, copper is not implicated in the oxidative addition of the arylthioether to palladium but rather plays a role at two stages: transmetallation from tin to copper and (most probably) activation of the Pd-S bond to ease the transmetallation step in the palladium catalytic coupling cycle (Scheme 146).[250,251,252,253]



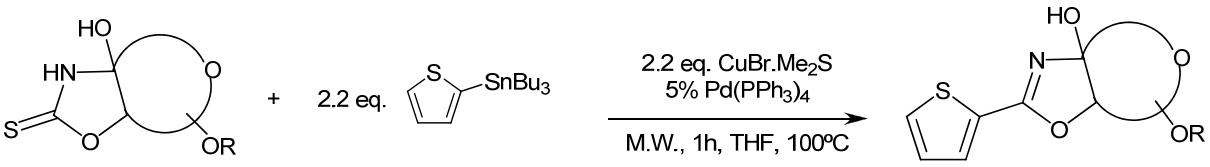
Scheme 146

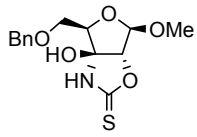
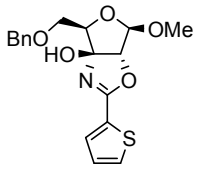
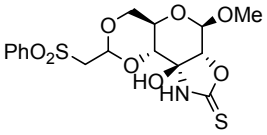
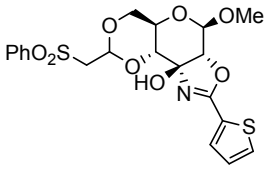
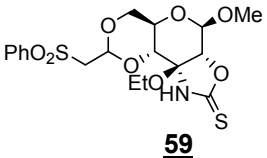
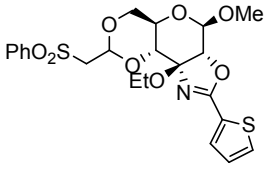
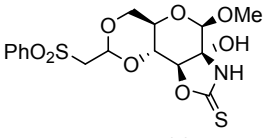
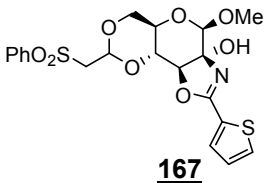
[249] Casado, A. L.; Espinet, P. *J. Am. Chem. Soc.* **1998**, *120*, 8978-8985.
[250] Piers, E.; Yee, J. G. K.; Gladstone, P. L. *Org. Lett.* **2000**, *2*, 481-484.
[251] Piers, E.; McEachern, E. J.; Romero, M. A. *J. Org. Chem.* **1997**, *62*, 6034-6040.
[252] Piers, E.; Romero, M. A. *J. Am. Chem. Soc.* **1996**, *118*, 1215-1216.
[253] Piers, E.; Wong, T. *J. Org. Chem.* **1993**, *58*, 3609-3610.

3.2. Modified Stille cross-coupling with non aromatic carbohydrate based OZTs

We were keen to know the outcome of applying, for the first time on a thioxo function, the direct coupling process in modified Stille conditions.

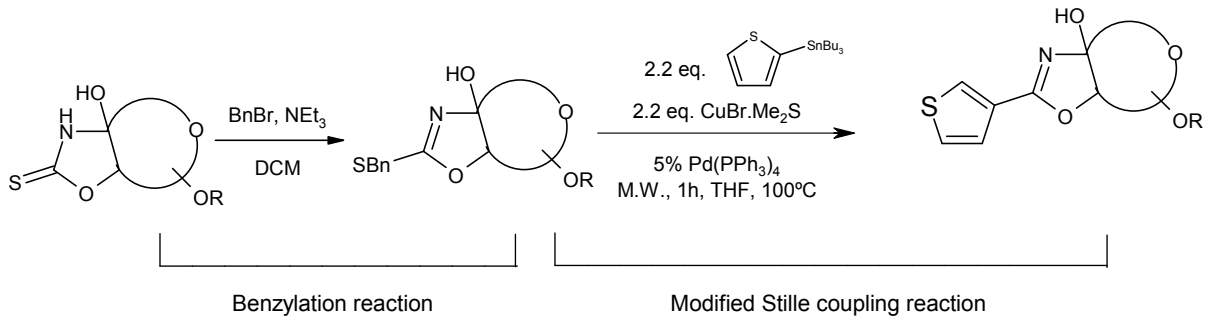
Carbohydrate-based OZTs **33**, **58**, **59** and **60** reacted with 2-tributylstannylthiophene, in the presence of CuBr.Me_2S and a catalytic amount of $Pd(PPh_3)_4$ to furnish oxazoles **164**, **165**, **166** and **167** albeit in only 27%, 25%, 33% and 37% yields respectively.Starting OZTs were recovered in 44%, 46%, 41% and 40% correspondingly (Scheme 147).

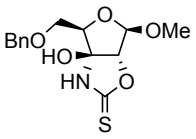
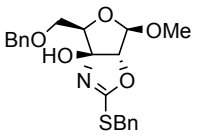
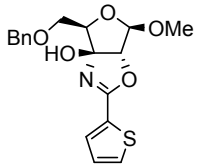
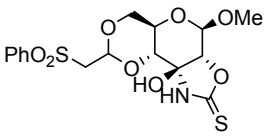
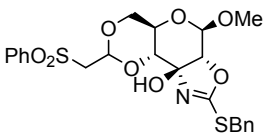
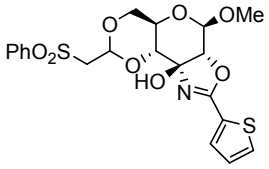
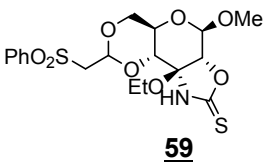
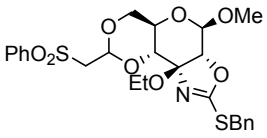
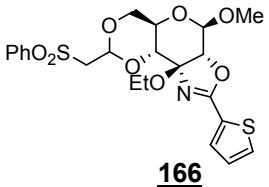
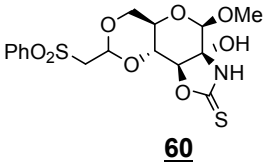
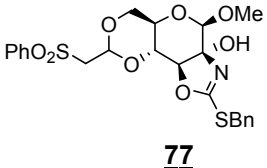
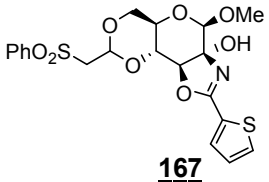


entry	starting material	yield (%)	product
1	 **33**	27	 **164**
2	 **58**	25	 **165**
3	 **59**	33	 **166**
4	 **60**	37	 **167**

Scheme 147

Following a similar behaviour as in the direct Suzuki coupling, the direct modified Stille cross-coupling under microwave activation revealed to be poorly efficient. We have thus explored the two-step procedure in order to compare reactivities. Again, the carbohydrate-based OZTs were converted into the corresponding 2-benzylsulfanyloxazolines, which were subsequently submitted to the modified Stille cross-coupling reaction. The results obtained are shown in Scheme 148.



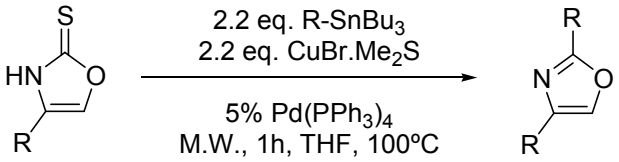
	S-benzylation reaction		Modified Suzuki coupling reaction			
entry	**starting material**	**yield (%)**	***S*-benzylation product**	**yield (%)**	**coupling product**	**Ov. yield (%)**
1	 **33**	86	 **75**	78	 **164**	67
2	 **58**	56	 **76**	86	 **165**	48
3	 **59**	89	 **159**	95	 **166**	85
4	 **60**	79	 **77**	89	 **167**	70

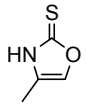
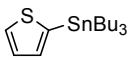
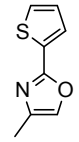
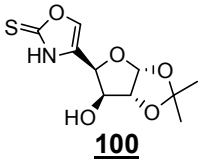
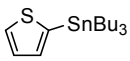
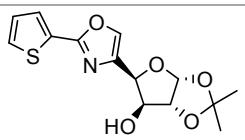
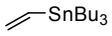
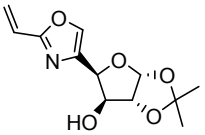
Scheme 148

☝ The results obtained for the coupling reaction were very good and similar to those of the "pseudo-Suzuki" reaction. The complete conversion of thioethers **75**, **76**, **159** and **77** and the great increase in overall yields for the formation of oxazoles **164**, **165**, **166** and **167** is indicative of the superiority of the two-step procedure over the direct coupling on the thioxo derivatives.

3.3. Modified Stille cross-coupling with aromatic OZTs

Following the tracks we have set for the Suzuki coupling, we then studied the reactivity of the aromatic OXTs **1** and **100** in a direct modified Stille cross-coupling reaction. Under microwave activation, 2-tributylstannylthiophene reacted with OXT **1** in fair yield (59%) to give the corresponding 2-substituted oxazole **168**. The antennary D-xylofurano-OXT **100** was reacted with two tributylstannyl reagents and gave the respective oxazoles **169** and **170** in better yields, 86% and 72 % respectively. The results are shown in Scheme 149.



starting material	coupling agent	yield (%)	coupling product	entry
 **1**		59	 **168**	1
 **100**		86	 **169**	2
		72	 **170**	3

Scheme 149

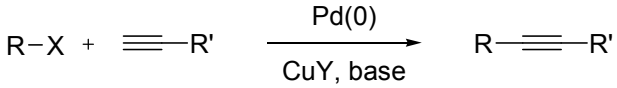
As for the Suzuki coupling, we have observed that, when submitted to modified Stille conditions, the non aromatic OZTs show better results when a two-step procedure involving *S*-benzylated intermediates is applied, while good results are obtained in a direct coupling process with aromatic OXTs.

Once more, it seems that the success of direct Pd-catalysed, Cu(I)-mediated carbon-carbon cross-coupling depends on the aromatic/non aromatic nature of the ring.

4. Sonogashira cross-coupling reaction

4.1. Small introduction

Considering its impressive impact on modern chemistry, the Sonogashira coupling was the next reaction to be investigated.[254] This Pd-catalyzed cross-coupling reaction between terminal alkynes and organohalides or triflates, in the presence of an aliphatic amine (Scheme 150), has become the most important method to prepare arylalkynes[255,256,257] and conjugated enynes,[258] crucial precursors for natural products, pharmaceuticals and molecular organic materials.



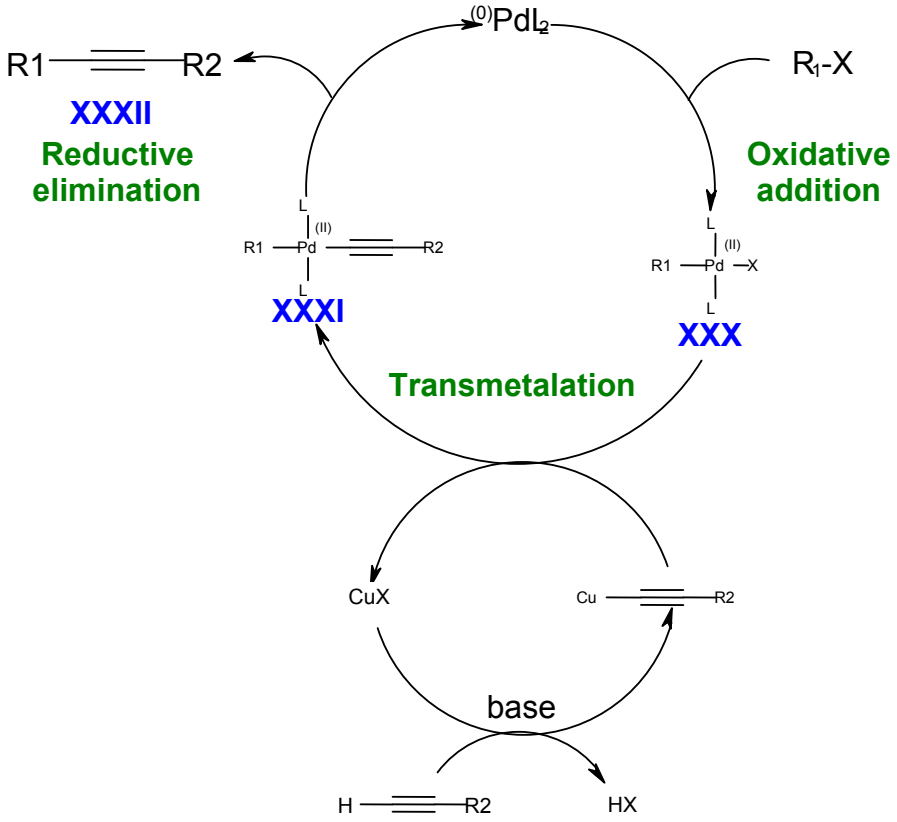
Scheme 150

In the copper co-catalysed Sonogashira reaction, two independent catalytic cycles are believed to take place (Scheme 151). The accepted cycle for Pd catalysis is based on a usually oxidative addition to the R_1-X bond by palladium, leading to the intermediate **XXX**. The characteristics of the R_1-X substrate are critical, with this step being facilitated if X=I or OTf and if the electronic density of the C-X bond is reduced by the presence of electron-withdrawing groups. The next step would be the connection with the copper cycle (Cu-cycle). A transmetallation from the copper acetylide (formed in the Cu-cycle) would generate the intermediate **XXXI**, which, after reductive elimination, would give the coupled alkyne **XXXII** while regenerating the catalyst.

In the Cu-cycle, the base is supposed to abstract the acetylenic proton of the terminal alkyne, which react with the Cu(I) salt to form the copper acetylide. These copper acetylides could also be involved in the formation of the initial $Pd(0)L_2$

[254] Chinchilla, R.; Nájera, C. *Chem. Rev*. **2007**, *107*, 874-922.
[255] Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett*. **1975**, *50*, 4467-4470.
[256] Hundertmark, T.; Littke, A. F.; Buchwald, S. L.; Fu, G. C. *Org. Lett*. **2000**, *2*, 1729-1731.
[257] Batey, R. A.; Shen, M.; Lough, A. J. *Org. Lett*. **2002**, *4*, 1411-1414.
[258] Alami, M.; Crousse, B.; Ferri, F. *J. Organomet. Chem*. **2001**, *624*, 114-123.

catalytic species by reaction with the starting palladium (II) complexes, thus forming Pd-(-C≡CR$_2$)$_2$L$_2$, which after reductive elimination, would regenerate Pd(0)L$_2$ and some amounts of a diacetylene side-product (Scheme 151).



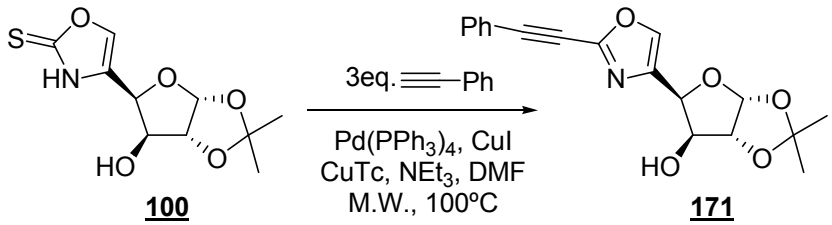
Scheme 151

4.2. Sonogashira optimization and proposed mechanism for the catalytic process

Extending the Sonogashira coupling to OXTs and OZTs would open new attractive synthetic ways to alkynyloxazoles and alkynyloxazolines – quite useful synthons in total synthesis and medicinal chemistry.[259,260,261,262]

Our starting point for these investigations was to examine the coupling abilities of phenylacetylene with the D-xylose-OXT **100**, readily accessible from D-glucose.[263] Our selected Sonogashira conditions required a source of Pd(0), CuI and Et_3N in DMF, in order to obtain a homogeneous medium. Microwave irradiation was applied in the process, according to the beneficial activation previously observed in Suzuki and Stille reactions. The different conditions explored are reported in Scheme 152. Using the sole standard Sonogashira copper additive (CuI) in catalytic amount, no results were obtained (entry 1). Likewise (entry 2) replacing CuI by CuTC (effective copper additive for Suzuki coupling), no coupling reaction was observed. The implication of Cu(I) in the reaction mechanism was taken into account on two distinct steps: the transmetallation of CuI with the alkyne and the copper-assisted activation of the thioxo derivatives. Consequently, we postulated that a conjunction of both species (CuI and CuTC) in the medium would react at their proper place without interfering one with the other and this approach revealed fruitful.

[259] Su, Q.; Dakin, L.A.; Panek, J. S. *J. Org. Chem.* **2007**, *72*, 2-24.
[260] Cook, G. R., Manivannan, E.; Underdhal, T.; Lukacova, V.; Zhang, Y.; Balaz, S. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 4935-4939.
[261] Paterson, I.; Tudge, M. *Tetrahedron* **2003**, *59*, 6833-6849.
[262] Talley, J. J.; Bertenshaw, S. R.; Brown, D. L.; Carter, J. S.; Graneto, M. J.; Koboldt, C. M.; Masferrer, J. L.; Norman, B. H.; Rogier, D. J.; Zweifel, B. S.; Seibert, K. *Med. Res. Rev.* **1999**, *19*, 199-208.
[263] Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett.*, **2008**, *10*, 853-856.



entry	NEt_3 (ml)	DMF (ml)	$Pd(PPh_3)_4$	CuI (eqs.)	CuTc (eqs.)	time (h)	yield
1	5	2	0.1	0.5	---	1	---
2	5	2	0.1	---	2.2	1	---
3	5	2	0.1	0.5	2.2	1	63
4	5	2	0.1	0.5	1.1	1	85
5	5	2	0.05	0.5	1.1	1	83
6	5	2	0.05	0.5	0.5	1	85
7	5	2	0.05	0.5	0.1	1	79
8	5	2	0.05	0.5	0.1	1	73 [a]
9	---	2	0.05	0.5	0.1	1	---
10	5	---	0.05	0.5	0.1	1	33
11	5	2	---	0.5	0.1	1	---
12	5	2	0.05	0.5	0.1	0.25	77
13	5	2	0.05	0.1	0.1	0.25	56
14	5	2	0.05	0.1 [b]	0.1	0.25	33
15	5	2	0.05	0.5	0.1 [c]	0.25	53
16	5	2	0.05	0.5	0.1 [d]	0.25	75

[a] 1.5 eq. of phenylacetylene.

[b] Cu_2S was used instead of CuI.

[c] CuBr.Me_2S was used instead of CuTC.

[d] CuMeSal was used instead of of CuTC.

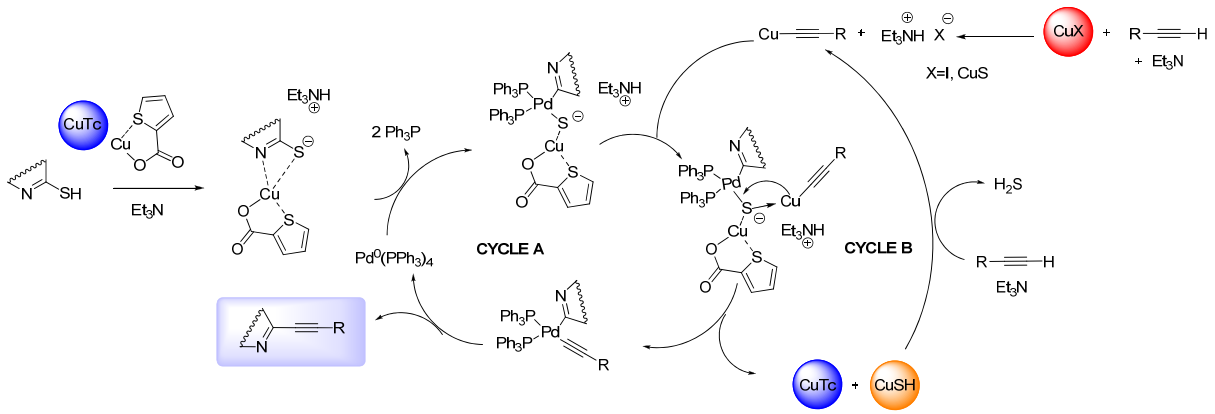
Scheme 152

By mixing CuI and CuTC (entry 3), the 2-phenylacetynyloxazole **171** was obtained with a reasonable 63% yield. We then engaged a search for reducing the amount of copper additive. First by modifying CuTC to 1.1 equivalent (entry 4), a net improvement was detected with 85% yield. Further reducing Pd(0) to 0.05 equivalent did not lower the yield (entry 5). We went on to explore the catalytic application of copper by using 0.5 equivalent of CuTC (entry 6), again resulting in no yield lowering. Encouraged by this major breakthrough, we went down to 0.1 equivalent of CuTC and the yield was only slighlty decreased to 79% yield (entry 7).

Some additional modifications of the conditions were investigated: reducing the amount of phenylacetylene to 1.5 equivalent (entry 8), still afforded the coupling product **171** with a fair yield; removing one solvent led to a drop of yield to no reaction without Et_3N (entry 9) and a low 33% in neat Et_3N (entry 10). In this last case, the poor solubility of antennary OXT **100** was to blame. No coupling reaction occurred when $Pd(PPh_3)_4$ was removed from the reaction mixture (entry 11), but reducing the time of the reaction to 15 min (entry 12) did not appreciably hamper the cross-coupling process (77% yield) and these conditions were therefore adopted as a standard onto different OXT and OZT structures. Bringing the catalytic quantity of CuI down to 10 mol% (entry 13) still kept the catalytic process efficient but gave a much lower yield (56%).

The most surprising aspect of this original copper-catalyzed desulfurative Sonogashira cross-coupling is the catalytic amount of both palladium and CuTC used in the procedure. From the first experiments performed, both types of copper (CuI and CuTC) were needed for the chemical coupling which might mean that both copper complexes are implicated in the catalytic process (Scheme 153). Based on the catalytic cycle proposed by Kappe,[239] the copper(I) sulfide formed *in situ* might play a central role in the catalytic process. Indeed, by replacing CuI by Cu_2S (entry 14) the catalytic process still operates but with a lower yield of 33%. Our proposed mechanism (Scheme 153) highlights the important role of the alkynylcopper in the regeneration of CuTC and in the formation of CuSH which could then be a source of

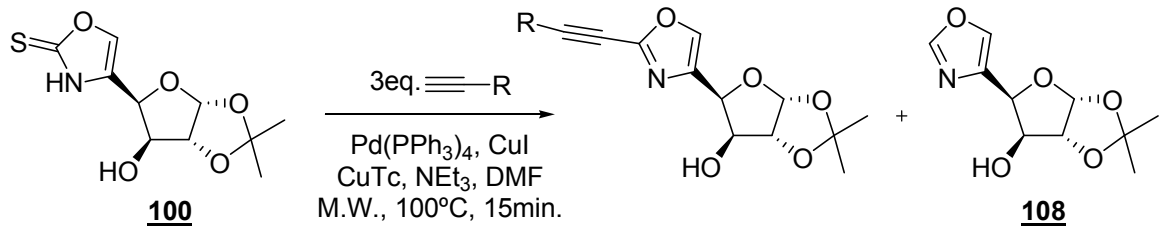
Cu(I) (cycle B) able to regenerate the alkynylcopper species. Under the same conditions, CuBr.Me_2S (entry 15) as well as CuMeSal (entry 16) could be used but a clear preference for the Suzuki Cu(I) additives was observed.

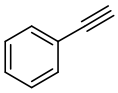
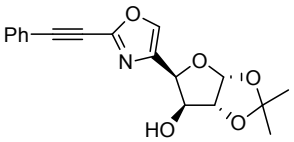
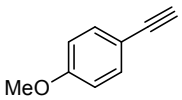
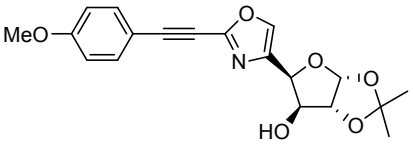
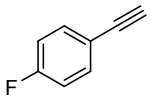
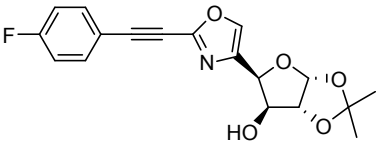
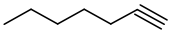
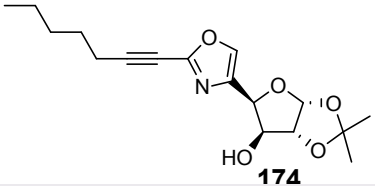
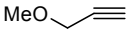
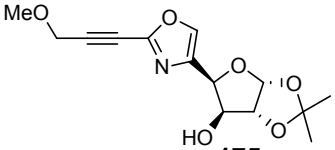
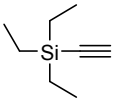
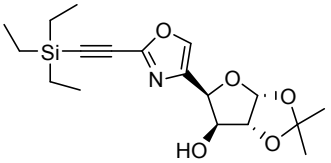


Scheme 153

4.3. Generalization of Sonogashira modified reaction for different alkynes and different carbohydrate-based thioamides

One of the main stream of our research is the structural-modulation potential of OXTs and OZTs connected to carbohydrate templates to mimick C-linked nucleosides. We have thus applied the optimal conditions with different alkynes to react on OXT **100** (Scheme 154). A careful analysis of the reaction has shown the formation in various proportions of a side product, the oxazole **108** (Scheme 154).

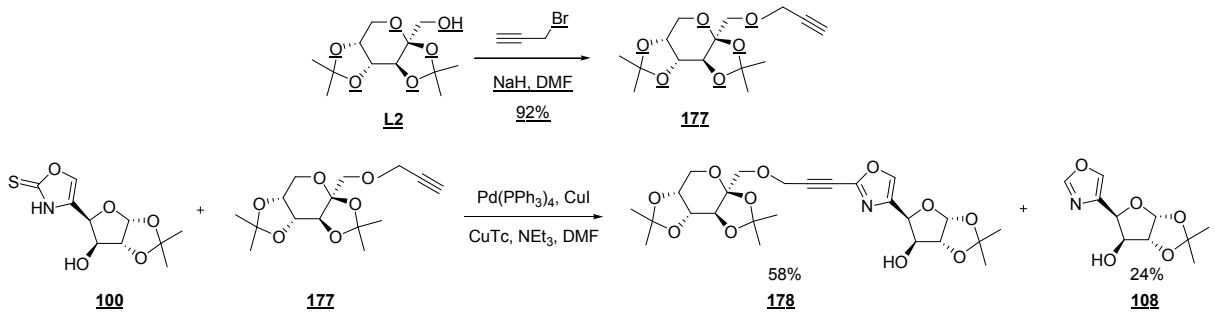


entry	coupling agent	coupling product	yield (%)	yield of 108 (%)
1		 **171**	77	7
2		 **172**	63	11
3		 **173**	42	21
4		 **174**	78	12
5		 **175**	66	23
6		 **176**	67	21

Scheme 154

Aromatic substitution on phenylacetylene (entries 2 and 3) showed important yield fluctuations especially with the fluoro derivative **173**, which undergoes coupling with a moderate yield and produces a significant amount of the oxazole **108**: the reactivity of alkyne **173** was clearly perturbed by the electron-withdrawing effect of the fluorine atom. The heptyne reagent (entry 4) did show the same reactivity as phenylacetylene with a good 78% yield of compound **174**; however, slightly reduced efficiency was observed in the formation of derivatives **175** and **176** with enhanced production of oxazole **108**.

Finally, the process was also tested in a complex carbohydrate derived alkyne, the 1-*O*-propargyl-2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose **177,** prepared in 92% yield by propargylation[264,265] of the readily available 2,3:4,5-di-*O*-isopropylidene β-D-fructopyranose **L2**. The Sonogashira coupling product **178** was obtained in a reasonable 58% yield and the oxazole **108** was formed in 24% yield (Scheme 155).



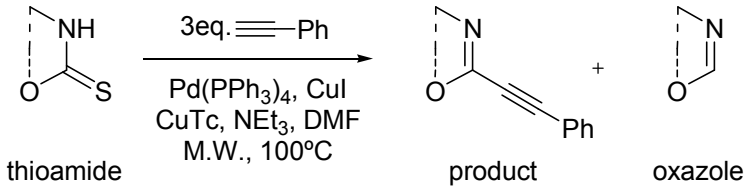
Scheme 155

Taking into account those experiments, we can conclude that the coupling reaction occurs with various alkynes in fair to good yields. In all cases, the oxazole formation (7-24%) is indicative of a competing reaction during the transmetallation process.

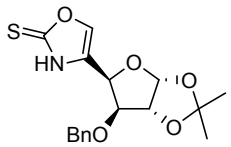
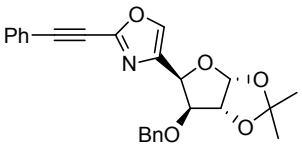
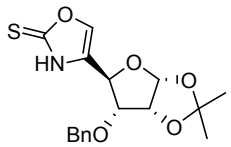
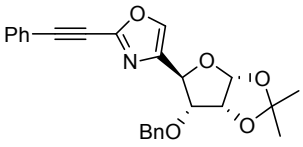
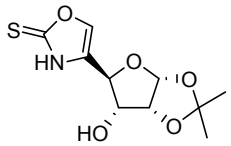
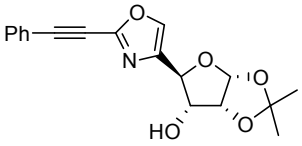
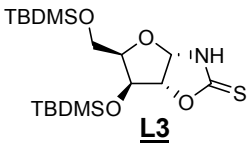
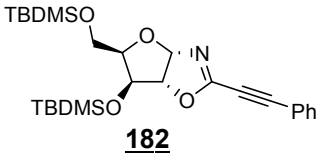
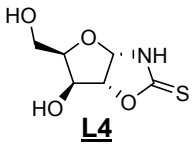
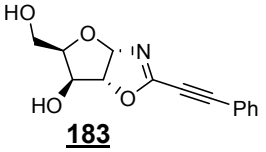
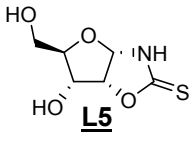
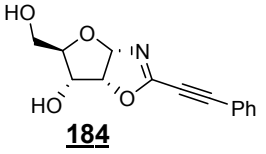
The scope of the reaction was then explored in two different directions (Scheme 156): one consisted in changing the carbohydrate scaffold bearing the OXT

[264] Mereyala, H. B.; Gurrala, S. R. *Carbohydr. Res*. **1998,** *307*, 351-354.
[265] Roy, B.; Mukhopadhyay, B. *Tetrahedron Lett*. **2008**, *48*, 3783-3787.

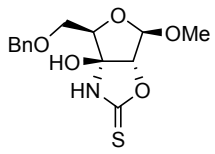
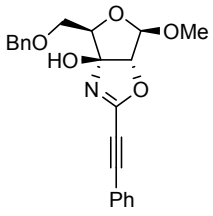
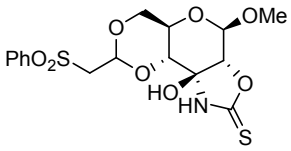
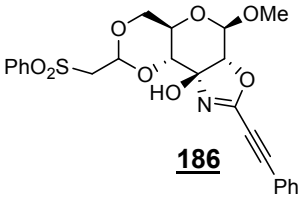
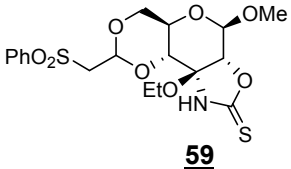
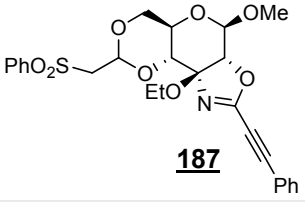
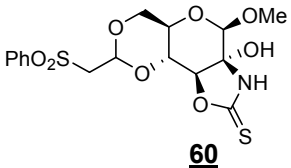
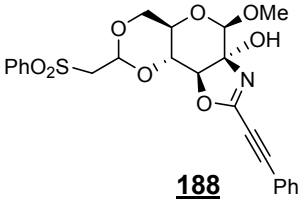
heterocycles (entries 1-3), and the other focused on the parent OZTs connected with miscellaneous templates (entries 4-10). Some of those carbohydrate-based OZTs were not synthesized during this PhD work, because already available in the laboratory (entries 4-6).



thioamide product oxazole

entry	starting material	product	yield (%)	oxazole yield (%)
1	 **87**	 **179**	80	**109** 5%
2	 **95**	 **180**	76	**110** 8
3	 **101**	 **181**	73	**111** 6
4	 **L3**	 **182**	82	---
5	 **L4**	 **183**	57	---
6	 **L5**	 **184**	61	---

(Scheme continues on next page)

entry	starting material	product	yield (%)	oxazole yield (%)
7	 **33**	 **185**	71	---
8	 **58**	 **186**	86	---
9	 **59**	 **187**	89	---
10	 **60**	 **188**	82	---

Scheme 156

An overview of the reactions showed the ability of the method for C-C bond formation on either the aromatic OXTs or non aromatic OZTs. Phenylacetylene coupling process with the α-D-xylo **87** and the α-D-ribo **95** and **101** respectively afforded the alkynes **179**, **180** and **181** in good yields (73-80%). In all OXT cases, the reductive process gave small (5-8%) yields of oxazoles. On the contrary, no oxazole side-products were detected when the modified Sonogashira protocol was applied on fused OZT derivatives. In the D-xylo and D-ribo series, in which OZT is anchored in anomeric position, a good efficiency of coupling was observed with the silyl protected D-xylose **L3**, yielding in 82% the alkynyl derivative **182** whereas a drop of reactivity was detected in the case of unprotected OZTs **L4** and **L5** with the formation

of compounds **183** and **184** in 57% and 61% yield, respectively. Nevertheless, the above experiments clearly indicate that unprotected hydroxyls are compatible with our coupling process; such complex alkynyl derivatives could be produced in only two steps from the corresponding pentoses. When the standard conditions were applied to the fused D-xylo derivative **33** and D-gluco derivatives **58**, **59** and **60**, the respective coupling alkyne products **185**, **186**, **187** and **188** were obtained in good to very good yields (71-89%). An overall analysis of the various experiments performed demonstrates the versatility of our coupling process protocol, in which diverse sensitive carbohydrate derivatives, either *O*-protected with benzyl/silyl ethers or acetal groups, or even unprotected ones, can be used under microwave heating conditions at 100ºC. Moreover and in contrast to what was observed for Suzuki and Stille cross-coupling reactions with fused OZTs, a thioether group is not needed for the coupling process, which has proven very efficient either with OXTs or OZTs.

- This study on Sonogashira coupling gave us the opportunity not only to disclose the first alkynyl C-C bond formation using thionocarbamates but moreover, to discover the possibility to use copper(I) in catalytic amount and to suggest a mechanism in which CuSH might play the key role.

5. Conclusion

In this chapter we have focused our efforts on the reactivities of OXTs and fused OZTs in Suzuki, Stille and Sonogashira cross-coupling processes. Considering the results obtained, some statements could be put into light:

- ☑ For both Suzuki and Stille modified reactions, the success of the direct Pd-catalysed, Cu(I)-mediated carbon-carbon cross-coupling depends on the aromatic/non aromatic nature of the ring.
- ☑ Direct Suzuki and Stille modified reactions were very efficient when aromatic OXTs were used as electrophiles, while a two-step procedure was preferable when non aromatic electrophiles were uszed.
- ☑ For the first time, the Stille modified reaction was applied directly with a thioxo function.
- ☑ For the first time, microwave activation was applied for the Stille reaction.
- ☑ The development and generalization of a new modified Sonogashira cross-coupling reaction, in which copper (I) is used in catalytic amount, allowed the formation of alkynyl C-C bonds, using thionocarbamates as electrophiles.

CHAPTER V

Biological screening

1. Brief introduction

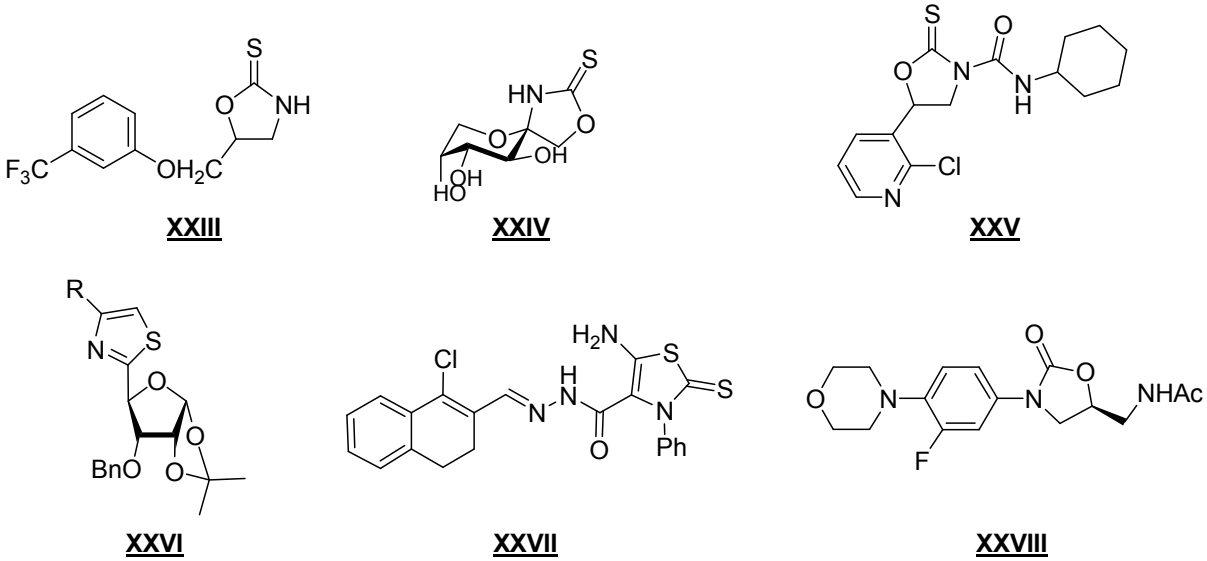
In this PhD project, we focused on the synthesis of simple and complex OXTs and OZTs, as well as on the exploitation of their chemistry, opening a way to the formation of various classes of new compounds, new methodologies and unexpected results.

Part of our interest was also dedicated to explore the biological potential of those new molecules. We were convinced that inside those OXTs and OZTs families, many compounds also possess a significant biological profile. Despite of the fact that, to the best of our knowledge, the literature is scarce on the bio-activity of OXTs, our conviction was based on what can be found about OZTs and some related compounds in terms of biological properties. We have thus targeted a broad spectrum of antimicrobial activities for some OXTs and OZTs, to which a screening of glycosidases inhibition for the iminosugar analogues **113-115** was added.

2. Antimicrobial screening

Among others, some OZTs exhibited biological properties such as effective antifertility action in rats (**XXXIII**)[266], D-fructose transport inhibition (GLUT-5 inhibitors) (**XXXIV**)[23] and herbicidal activity[267] (**XXXV**). Examples of bioactive molecules that hold in their structure a heterocycle related to OXT or OZTs are given below:

- ☑ Compound **XXXVI** has a thiazole ring and is powerful insecticide against *Musca domestica*;[268]
- ☑ Compound **XXXVII** has a thiazoline moiety and exhibits high antifungal and antimicrobial activities; [269]
- ☑ Linezolida (**XXXVIII**)[270,271] (Zyvox™), which opened the 1,3-oxazolidin-2-one class of antibacterial agents, is approved for the treatment of Gram-positive pathogens such as *Staphylococcus aureus* (MRSA) and *Staphylococcus epidermis* (MRSE), and has been used in humans since 2000 (Scheme 157).



XXIII **XXIV** **XXV**

XXVI **XXVII** **XXVIII**

Scheme 157

[266] Youngdale, G. A.; Duncan, G. W.; Emmert, D. E. Lednicer, D. *J. Med. Chem.* **1966**, *9*, 155-157.
[267] Li, G.; Qian, X.; Cui, J.; Huang, Q.; Zhang, R.; Guan, H. *J. Agric. Food Chem.* **2006**, *54*, 125-129.
[268] Rauter, A. P.; Padilha, M.; Figueiredo, J. A.; Ismael, M. I.; Justino, J.; Ferreira, H.; Ferreira, M. J.; Rajendran, C.; Wikkins, R.; Vaz, P.; Calhorda, M. J. *J. Carbohydr. Chem.* **2005**, *24*, 275-296.
[269] Bondock, S.; Khalifa, W.;Fadda, A. A. *Eur. J. Med. Chem.* **2007**, *42*, 948-954.
[270] Chien, J. W.; Kucia, M. L.; Salata, R. A. *Clinical Infectious Diseases* **2000**, *30*, 146-151.
[271] Diekema, D. J.; Jones, R. N. *Drugs* **2000**, *59*, 7-16.

2.1. Methodology for susceptibility testing

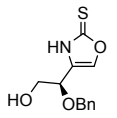
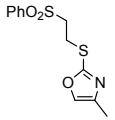
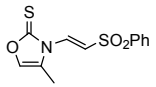
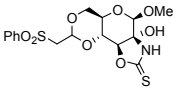
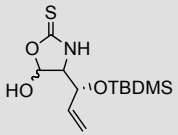
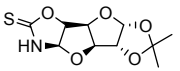
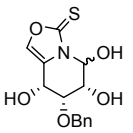
The antimicrobial activities of 20 compounds were screened using the paper disk diffusion method: OXTs **1**, **5**, **15**, **16**, **20b**, **21a**, **21b**, **22**, **74**, **87**, **95** and **74**, OZTs **47**, **58**, **59**, **60**, **70**, **73** and **134** and iminosugars **113** and **115** [272,273]. These compounds were evaluated for their *in vitro* antibacterial and antifungal activities. The microorganisms used in the tests belong to the American Type Culture Collection (ATCC) and Centraalbureau voor Schimmelcultures (CBS) collections, from United States and The Netherlands, respectively. Regarding bacteria, tests were carried out with *Bacillus cereus (ATCC 11778), Bacillus subtilis (ATCC 6633), Enterococcus faecalis (ATCC 29212), Escherichia coli (ATCC 8739), Listeria monocytogenes (ATCC 7644), Pseudomonas aeruginosa (ATCC 27853), Salmonella enteritidis (ATCC 13076)* and *Staphylococcus aureus (ATCC 25923).* With respect to fungi, the yeast *Candida albicans (ATCC 10231)* and the following filamentous fungi were used: *Alternaria alternata (CBS 108.41), Biscogniauxia mediterranea (CBS 101016), Botrytis* spp., *Byssochlamys fulva (CBS 146.48), Colletotrichum coffeanum (CBS 396.67), Fusarium culmorum (CBS 129.73), Pyricularia oryzae (CBS 433.70* and *Rhizopus* spp The culture medium, incubation temperature and time used for bacteria growth was nutrient agar incubated at 37 ºC for 24 h, whereas for fungi potato dextrose agar was used, at 25 ºC for 48 h. Paper disks of 6.4 mm were placed on the agar and the solution of each substance (300 μg) in DMSO (15 μL) was applied on each disk. Chloramphenicol and actidione were used as antimicrobial controls for bacteria and fungi, respectively. After incubation, the nearest diameter of the inhibition zone was measured. At least two replicates were made.

[272] Bauer, A. W.; Kirby, W. M. M.; Sherris, J. C.; Turck, M. *Am. J. Clinic. Pathol.* **1966**, 493-496.
[273] Methods for antimicrobial susceptibility tests for bacteria that grow aerobically: approved standard, 2 nd ed. National Committee for Clinical Laboratory Standards, document M7-A3, **1993**, Villanova, PA.

2.2. Antimicrobial activity results

The results of the compounds exhibiting moderate and strong antimicrobial activity are presented in Tables 9 and 10, and are expressed in terms of the average diameter of inhibition (∅) in mm for the active compounds (300 μg). For comparison purposes, the inhibition diameter for control substances (chloramphenicol or actidione) ∅ are also shown for doses of 30 μg and 300 μg. Zones less than 10 mm in diameter and uniform growth in the dish were considered indicative of weak antimicrobial activity; 10-15mm, moderate activity, more than 15 mm, strong activity.

Table 9. Antibacterial compounds: diameter of inhibition in mm caused by 300 μg of compound[a].

	5 	**15** 	**21a** 	**22** 	**60** 	**70** 	**134** 	**113** 	Control[b]	
									I	II
Bacillus cereus	12	12	13	11	9	19	9	9	24	45
Bacillus subtilis	12	<6.4	20	11	16	28	14	16	30	46
Enterococcus faecalis	12	11	<6.4	<6.4	<6.4	16	<6.4	<6.4	26	43
Escherichia coli	<6.4	<6.4	<6.4	<6.4	<6.4	10	<6.4	<6.4	28	41
Listeria monocytogenes	nt	nt	<6.4	<6.4	nt	nt	nt	nt	31	45
Pseudomonas aeruginosa	<6.4	<6.4	<6.4	<6.4	<6.4	8	9	<6.4	<6.4	23
Salmonella enteritidis	nt	nt	nt	nt	<6.4	<6.4	<6.4	<6.4	36	46
Staphylococcus aureus	11	11	<6.4	<6.4	11	21	12	9	27	41

nt- means not tested.

[a] Compounds **16**, **58**, **59**, **87**, **95** and **115** presented traces of antibacterial activity (diameter of inhibition ranging from 8 to 10 mm) over some of the bacteria tested, and results are not shown in the Table. Compounds **1**, **20b**, **21b**, **47**, **73** and **74** showed no antibacterial activity at all.

[b]The antibiotic chloramphenicol was used as control for all bacteria and was tested in the quantities of I=30 and II=300 μg

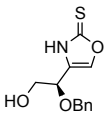
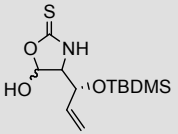
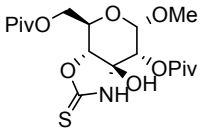
2.2.1 Antibacterial activity results

OXTs **5**, **15**, **21a** and **22** displayed moderate antibacterial activity against *Bacillus cereus* while OZT **70** showed a strong activity. For the others compounds tested, only OZTs **60** and **134** showed weak activity against this pathogen. Most of the tested compounds exhibited antibacterial activity against *Bacillus subtilis* and the highest activities were exhibited by compounds **21a**, **60**, **70** and **113** (strong activity), **f**ollowed by derivatives **134**, **5** and **22** with moderate activity.

Against *Enterococcus faecalis*, only compounds **70**, **5** and **15** proved to be efficient, showing the first one a strong activity and the others a moderate activity. For the pathogens *Escherichia coli*, *Listeria monocytogenes*, *Pseudomonas aeruginosa* and *Salmonella enteritidis*, all the tested compounds showed a weak or negligible antibacterial activity. Regarding *Staphylococcus aureus*, compound **70** proved once again to be efficient promoting a a strong antibacterial effect, while compounds **5**, **15**, **60** and **134** exhibited a moderate action against it. Derivative **113** was also ineffective against *Staphylococcus aureus* and demonstrated a weak antibacterial effect.

When considering the antibacterial results obtained, it clearly emerges that it is difficult to correlate the structure of the tested molecules with the detected antibacterial activity. However, the best antibacterial effect was obtained with OZT **70**, which possesses a strong effect against four of the studied bacteria.

Table 10. Antifungal compounds inhibition diameter in mm caused by 300 μg of compound.[a]

	15 	**70** 	**47** 	Control[b]	
				I	II
Alternaria alternata	<6.4	10	<6.4	<6.4	<6.4
Biscogniauxia mediterranea	nt	12	<6.4	52	70
Botrytis spp.	<6.4	15	<6.4	<6.4	20
Byssochlamys fulva	<6.4	19	<6.4	18	45
Candida albicans	12	20	11	<6.4	15
Colletotrichum coffeanum	12	15	11	16	24
Fusarium culmorum	nt	11	<6.4	12	18
Pyricularia oryzae	<6.4	18	<6.4	40	70
Rhizopus spp.	<6.4	15	nt	11	19

nt- means not tested.

[a] Compounds **16**, **95**, **58**, **59**, **60**, **134** and **113** presented traces of antifungal activity (inhibition diameter ranging from 8 to 10 mm) over some of the fungi tested, and results are not shown in the Table. Compounds **1**, **5**, **20b**, **21a**, **22**, **74**, **87**, **73** and **115** showed no antifungal activity at all.

[b] Actidione was used as positive control for all the filamentous fungi whereas chloramphenicol was the control substance tested for *C. albicans*. Inhibitions caused by I=30 μg and II=300 μg of control were assessed.

2.2.2 Fungicidal activity results

Considering all the compounds tested, only a few presented an interesting antifungal activity. Derivatives **15** and **47** presented moderate antifungal activity against *Candida albicans* and *Colletotrichum coffeanum* but, as already observed for the antimicrobial activity, it is OZT **70** that proved to be the most interesting compound.

In fact, it demonstrated a broad and strong antifungal activity against *Botrytis spp*, *Byssochlamys fulva*, *Candida albicans*, *Colletotrichum coffeanum*, *Pyricularia oryzae*, *Rhizopus spp* and a moderate activity against *Alternaria alternate*, *Biscogniauxia mediterranea* and *Fusarium culmorum*. From these results it clearly emerged that, as for antibacterial activity, it is not possible to establish a correlation between the structure of the tested molecules and the antifungal activity exhibited by them. However and remarkably, OZT **70**, which has a strong effect over six of the studied fungi, its activity over *Candida albicans* is higher than that of chloramphenicol, the positive control.

2.3. Antimicrobial activities conclusion

Of the various compounds tested OZT **70** emerged as one compound with a broad range of either antibacterial or antifungal activities. We might speculate from its structure that this "hydrated"-OXT, its acyclic moiety and/or the allylic function might be responsible for this strong activity thus encouraging the further study of the family of hydroxy-OZTs regarding their antimicrobial activity.

3. Glycosidases inhibitors

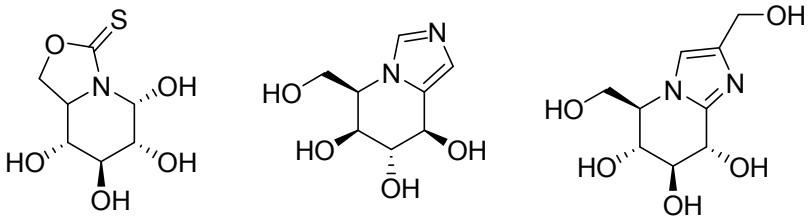
Glycosidases are very important enzymes for their implication in numerous key-biological processes.[274] Compounds that can modify or inhibit such enzymes, the glycosidase inhibitors, bear strong biological potential in different therapies.

Carbohydrates mimics with nitrogen replacing the endocyclic oxygen have attracted an impressive amount of interest as inhibitors of glycosidases.[275,276,277,278]

As reported in chapter III, Ortiz Mellet and her team have developed a new family of highly selective glycosidase inhibitors, analogues to castanospermine (**CS**), in which the sp^3 amine-type nitrogen typical of iminosugars is replaced by a (thio) carbamic type nitrogen atom, with a substantial sp^2-character.[142,174] One compound of this family is the α-D-gluco-thionocarbamate derivative **XXXIX**, which demonstrated to be a powerful inhibitor of isomaltase (K_i =30 μM) and yeast α-glucosidase (K_i= 40 μM).

For their part, Weinberg and coll[279] have replaced the thionocarbamate moiety by an imidazole system: the imidazolo derivative **XL** demonstrated selective inhibitions against α-D-galactosidase (from green coffee beans) and β-D-galactosidase (from *Escherichia coli*) with K_i values of 90 μM and 100 μM, respectively. Changing the carbohydrate series, as well as the nitrogen position in the imidazole system, Vasella and co-workers [280] have demonstrated that derivative **XLI** showed selective and high inhibitory properties against β-glucosidase (from almonds), β-glucosidase (from *Caldocellum s*.) and α-glucosidase (from brewer's yeast) with K_i values of 11 nM, 5 nM and 69 μM, respectively (Scheme 158).

[274] Lillelund, V. H.; Jensen, H. H.; Liang, X.; Bols, M. *Chem. Rev.* **2002**, *102*, 515-553.
[275] Moreno, M. I. G.; Ortiz Mellet, C.; Garcia Fernández, J. M. *Tetrahedron* **2007**, *63*, 7879-7884.
[276] Dubost, E.; Tshamber, T.; Streith, J. *Tetrahedron Lett.* **2003**, *44*, 3667-3670.
[277] Joseph, C. C.; Regeling, H.; Zwanenburg, B.; Chittenden, G. J. F. *Carbohydr. Res.* **2002**, *337*, 1083-1087.
[278] Benltifa, M.; Moreno, M. I. G.; Mellet, C. O.; Fernández, J. M. G.; Wadouachi, A. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 2805-2808.
[279] Frankowski, A.; Deredas, D.; Dubost, E.; Gessier, F.; Jankowski, S.; Neuburger, M.; Seliga, C.; Tschamber, T.; Weinberg, K. *Tetrahedron* **2003**, *59*, 6503-6520.
[280] Pandy, N.; Canac, Y.; Vasella, A. *Helv. Chim. Acta* **2000**, *83*, 58-79.



XXXIX **XL** **XLI**

Scheme 158

We have considered compound **XXXIX** as a reference, as its structure is closely related to the structures of the OXT iminosugars synthesized in this work. Therefore, in collaboration with Prof. Ortiz Mellet, we were able to test the anomeric mixtures of iminosugars **113**, **114** and **115** as glycosidase inhibitors and compare the results with α-D-gluco-thionocarbamate derivative **XXXIX**.

3.1. Methodology for inhibition assays

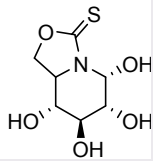
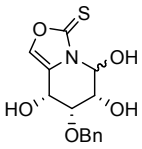
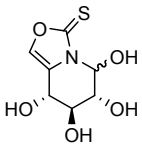
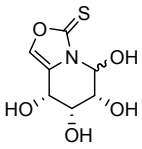
Inhibitory potencies of the iminosugars **113-115** were determined by spectrophotometric measurement of the residual hydrolytic activities of glycosidases against the corresponding *p*- or *o*- nitrophenyl α- or β- D-glycopyranosides (substrates). The glycosidases used were β-galactosidase (from bovine liver), β-galactosidase (from *Escherichia coli*), β-glucosidase (from almonds), α-glucosidase (from yeast), α-galactosidase (from green coffee), isomaltase, trehalase (from pork kidney), α-mannosidase (from jack bean), β-mannosidase (from *Helix pomatia*) and amyloglucosidase (from *Aspergillus níger*). All enzymes, as well as the corresponding substrates, were purchased from Sigma Chemical Co.

Each assay was performed in a phosphate buffer at the optimal pH for each enzyme. The reactions were initiated by the addition of the enzyme to a solution of the substrate in the presence or absence of various concentrations of inhibitor. After incubation of the mixture for 10-30 min at 37 ºC, the reaction was quenched by adding 1M Na_2CO_3. The absorbance of the resulting mixture was determined at 405 nm.

The K_i value and enzyme inhibition mode were determined from the slope Lineweaver-Burk plots and double reciprocal analysis. The results of inhibition assay are expressed in Table 11.

3.2. Results of inhibition assays

Table 11. Results of inhibition assays

	XXXIX 	**113** 	**114** 	**115** 
β-galactosidase (bovine liver)	ni	ni	274 μM	ni
β-galactosidase (*E. coli*, 7.3 KPi)	nt	nt	ni	nt
β-glucosidase (almonds pH 7.3)	ni	ni	ni	ni
α-glucosidase (yeast)	40 μM	688 μM	ni	319 μM
α-galactosidase (green coffee)	ni	ni	ni	ni
Isomaltase	30 μM	ni	74.7 μM	52 μM
Trehalase (pig kidney)	ni	505 μM	87 μM	416 μM
α-mannosidase (jack bean)	ni	ni	ni	ni
β-mannosidase (*Helix pomatia*)	nt	ni	ni	ni
Amiloglucosidase (*Aspergillus níger*)	ni	ni	ni	ni

nt means not tested
ni means no inhibition at [I] 2mM

As previously discussed in chapter III, the main difference between the derivative **XXXIX** and iminosugars **113**, **114** and **115** is that for the first compound, only the α–anomer was identified and tested as glycosidase inhibitor and for compounds **113-115**, although the α–anomer predominated, both α– and β–anomers were present in solution. From the three anomeric mixtures of iminosugars tested, only the D-*xylo*-anomers **114** expressed K_i values against β-galactosidase from bovine liver (K_i = 274 μM). This can be explained by the presence of a large proportion of the β-anomer in **114** in solution (α/β ratio =57/43). However, none of the tested compounds inhibits the β-galactosidase from *E. coli* or β-glucosidase from sweet almonds. D-*ribo* derivatives **113** and **115** also demonstrated inhibition power against α-glucosidase from yeast (K_i = 688 μM, 319μM, respectively), although with a less pronounced effect as compared to the D-*gluco* derivative **XXXIX**. The non-effect of **114** can derive from the reason postulated earlier. For isomaltase, both unsubstituted in O-3 D-*xylo*- and D-*ribo*-derivatives gave high values of inhibition in the order of magnitude of the value exhibited by compound **XXXIX** (K_i = 74.7 (M, 72μM, respectively). The 3-*O*-benzylated D-*ribo*-derivatives **113** did not show inhibitory activity for this enzyme, maybe due to the presence of the bulky benzyl group. In fact, for the isomaltase inhibition, it seemed important the presence of a free hydroxyl in position 3. In contradiction with derivative **XXXIX**, trehalase from pig kidney was inhibited by all the free anomeric mixtures tested, revealing high inhibitory activity for mixture **114** (K_i = 87 μM). Once again, this value can be explained by the β-anomers present in solution for all compounds tested, with high incidence for derivatives **114**. The C=C double bond present in derivatives **113**, **114** and **115** and non present in compound **XXXIX** can be, also, a plausible explanation for the inhibition of trehalase from pig kidney. No inhibitory activity was detected for α-galactosidase from green coffee, α-mannosidase from jackbean, β-mannosidase from *Helix pomatia* and amyloglucosidase from *Aspergillus niger*.

3.3. Glycosidases inhibition conclusion

The 3-*O*-benzyl-D-*ribo*-derivatives **113** did not lead to a remarkable inhibitory activity against the tested enzymes. However, the OH-3 free analogues **114** and **115** revealed high inhibitory activities against isomaltase and trehalase for the first anomeric mixtrure and isomaltase for the second one. For the inhibition of isomaltase, it seemed important to have a free hydroxyl in position 3. In relation to trehalase, the presence of C=C double bond in derivatives **113**, **114** and **115,** seemed too be crucial for its inhibition. In the last, but not the least, the inhibition of β-galactosidase and trehalase appear to be directly correlated with the presence of the β-anomers in solution of the tested iminosugars.

4. Conclusion

In this chapter we focused our efforts on the examination of biological properties for some of the compounds synthesized during this PhD work. Considering the results obtained, some statements can be put into light:

- ☑ The number and structure of the compounds tested does not allow an obvious correlation between structure and activity;
- ☑ The OZT **70** is a powerful antibacterial and antifungal compound;
- ☑ Inhibition of glycosidases by the tested iminosugars depends on the stereochemistry of the sugar moiety, in particular on the anomeric configuration. The presence of an aromatic/non aromatic moiety fused to carbohydrate template and the existance of a free hydroxyl group in position 3, seemed to be conditionate factors for some glycosidases inhibition.

Broad conclusion

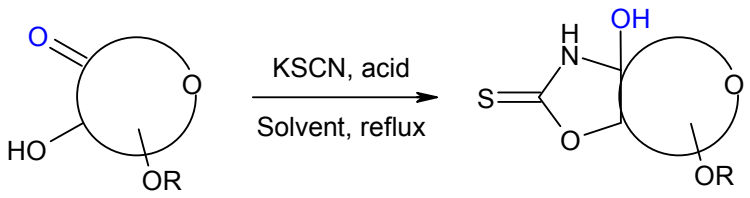
During this work, we have investigated the synthesis and reactivity of simple and complex OXTs and OZTs for which a preliminary biological screening was performed.

In a first part, we have developed optimal reaction conditions for the synthesis of simple OXTs from α–hydroxycarbonyl compounds: it can be concluded that the preparation of OXTs depends on the appropriate choice of a solvent-acid couple. Dimeric glycolaldehyde and 2,2-dimethoxyethanol brought examples that masked carbonyl compounds can be used for the synthesis of OXT **5** in 95% and 91% yield, respectively.

In other respects, starting from 1,2:4,5-di-*O*-isopropylidene-D-fructopyranose, the first synthesis of a simple chiral OXT (**15**) was achieved over 5 steps in 42% overall yield.

In terms of reactivity centers in OXTs, *S*-functionalization was performed selectively using soft electrophiles, giving derivatives **16** and **17** in 60% and 83% yields, respectively. In contrast, reactions expected to be N-selective (acylation, sulfonylation, Michael additions) either failed or showed poor chemoselectivity. Only a strong and hard nucleophile (BPSE) showed complete N-selectivity in the reaction with OXT. This lack of nucleophilicity might be explained by the electron lone pair delocalization of the N atom into the aromatic system of OXT.

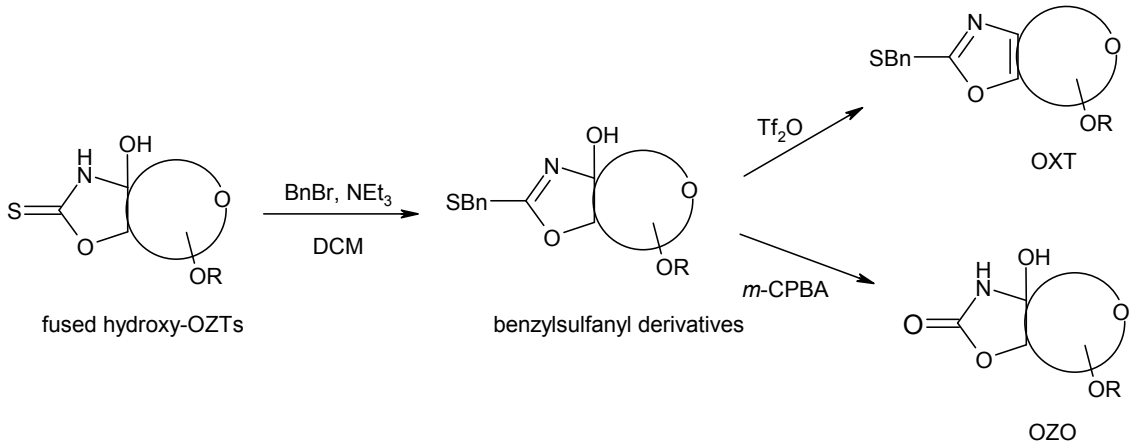
In the second chapter, our efforts focused in the preparation of fused bicyclic systems assembling a carbohydrate backbone and an OXT moiety. We have tailored some carbohydrate frames (1,2-isopropylidene-α-D-xylofurano, methyl-α-D-glucopyrano and methyl-β-D-glucopyrano) with the aim to build the desired α-hydroxyketones. However, condensation of carbohydrate-based α-hydroxyketones with thiocyanic acid favours the formation of fused hydroxy-OZTs (**33**, **47**, **58** and **60**) over the expected OXTs (Scheme 159).



Scheme 159

Moreover, the stereochemistry of the hydrated OXT formed depends on the position and orientation of the hydroxyl involved in the reaction: a strict *cis* relationship was always observed. We can also conclude that the anomeric configuration exerts a decisive influence on the formation of a hydrated OXT between positions 2 and 3 on the carbohydrate backbone. For this reason, for both α-glycosides **32**, **43** and **52**, which share the same 1,2-*cis* relationship, no reaction occurred when the condensation with HSCN took place, while on both β-isomers (**31** and **56**), the same condensation occurred in good yields. This difference of behavior is very likely due to steric and electronic effects.

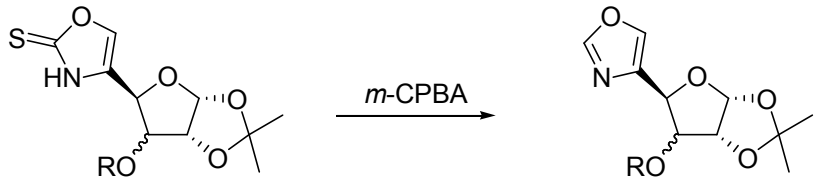
The direct elimination of the free hydroxyl was not possible. However, protecting the thiono group via *S*-benzylation and reacting benzylsulfanyl derivatives **75**, **76** and **77** with triflic anhydride, dehydration took place and OXTs **78**, **79** and **80** were obtained in good yields. Additionally, on *m*-CPBA oxidation, benzylsulfanyl derivatives **75**, **76** and **77** easily led to the formation of OZO derivatives **81**, **82** and **83** in very good yields (Scheme 160).



Scheme 160

In other respects, the synthesis of antennary OXTs **87**, **95**, **100** and **101** was achieved by high-yielding condensation of HSCN with the corresponding α-hydroxyketones. TFAA-induced Pummerer rearrangement revealed to be the key-step for the conversion of α-hydroxyaldehydes into antennary OXTs **147** and **154**.

Contrary to what occurs with fused benzylsulfanyl derivatives, reacting antennary benzylsulfanyl derivatives **102** and **103** with *m*-CPBA furnished the corresponding sulfoxides and sulfones and no formation of OXO derivatives were detected. However, when thionocarbamates **87**, **95**, **100** and **101** were directly subjected to the action of *m*-CPBA, sulfur extrusion took place and formation in high yield of the corresponding oxazoles **109**, **110**, **108** and **111** was observed. In that way, a new methodology for oxazole formation, starting from an OXT, was disclosed (Scheme 161).

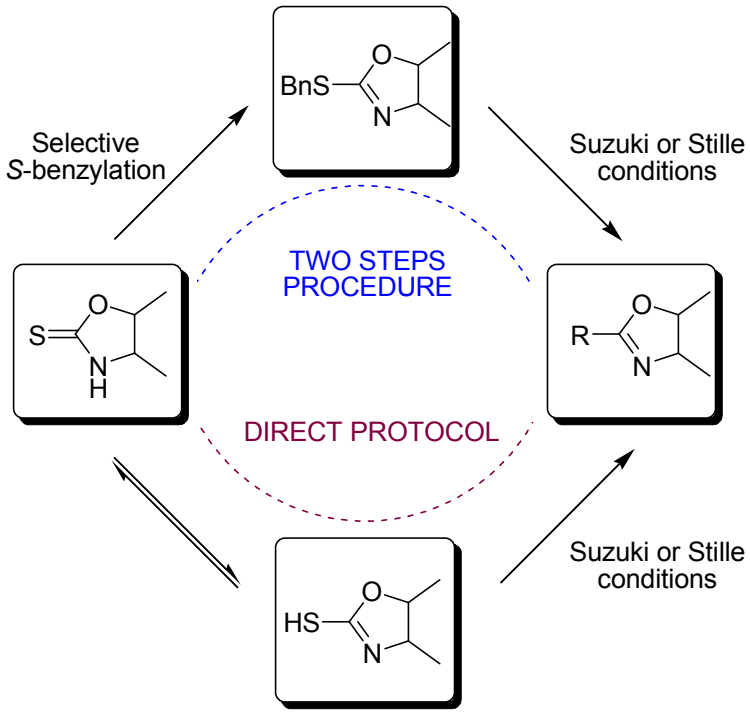


Scheme 161

Another interesting observation was that, by exploiting the ability of nitrogen to act as a nucleophile in intramolecular addition to the masked aldehyde group of hexose precursors, some castanospermine analogues could readily be prepared. From diacetone glucose, pseudo iminosugars **113**, **114** and **115** were obtained in good overall yields, showing the strategy used for the assembly of the oxaindolizidine skeleton to be quite efficient.

In the fourth chapter, the use of thioxo derivatives as electrophiles in Suzuki, Stille and Sonogashira cross-coupling reactions was studied.

In the case of the fused OZTs **33**, **58**, **59** and **60**, for Suzuki and Stille cross-coupling reactions, we have compared the reactivities between a two-step and one-step sequence and we had to admit that the two-step procedure was more efficient in this case (Scheme 162).



Scheme 162

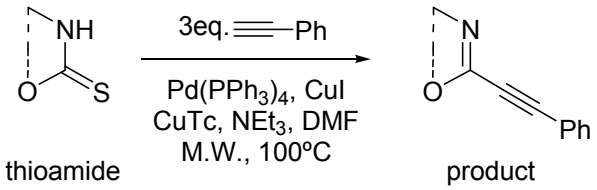
Contrary to the case of fused OZTs, the application of the protocol for Suzuki or Stille cross-coupling reactions to OXTs **1** and **100** resulted in increased efficiency.

In short, we can conclude that for both Suzuki and Stille modified reactions, the success of direct Pd-catalysed, Cu(I)-mediated carbon-carbon cross-coupling, depends on the aromatic/non aromatic nature of the ring.

It was also the first time that thionocarbamates were used as electrophiles in Stille cross-coupling reactions.

Following, Sonogashira cross-coupling reaction was considered: the standard Sonogashira conditions (CuI, Pd (II), NEt_3) were unfortunately unsuccessful in our

hands. In consequence, we have developed a new methodology for the direct cross-coupling reaction between a thionocarbamate and a terminal alkyne. In this modified Sonogashira protocol, a cooperative effect of two different copper(I) species – CuI and CuTC – under micro-wave irradiation accounts for this new copper-catalysed carbon-carbon cross-coupling reaction (Scheme 163).



Scheme 163

Taking advantage of this new methodology, we have prepared up to 17 new compounds, mostly in good yields.

The antimicrobial activities of 20 compounds were screened using the paper disk diffusion method: among all the tested compounds, only OZT **70** appeared as one compound with a broad range of activities, either bacterial or fungicidal. Unfortunately, no obvious structure-activity correlation could be brought to light.

Anomeric mixtures of pseudo-iminosugars **113**, **114** and **115** were tested as glycosidase inhibitors and the mixture of compounds **114** and **115** revealed inhibitory activities against some enzymes (isomaltase and trehalase for the first and isomaltase for the second). We have verified also that the inhibition of some glycosidases depends, not only on the structure of the tested iminosugars, but also on the ratio between α- and β-anomers. The presence of an aromatic/non aromatic moiety fused to a carbohydrate template and the existance of a free hydroxyl group in position 3, seemed to conditionate the inhibition of some glycosidases.

In summary, the present work describes the synthesis, chemical and preliminary biological exploitation of simple OXTs and fused or antennary bicyclic

carbohydrate-based scaffolds. The exploitation of the sulfur chemistry of those bicyclic systems has led to new families of compounds such as OZO derivatives (in the case of fused hydrated OXTs) or oxazoles (in the case of antennary OXTs). The eletrophilicity of the thiocarbonyl bond also permitted exploitation of Suzuki and Stille cross-coupling reactions, and the efficiency of direct Suzuki and Stille modified procedures was ascertained when aromatic OXTs were used as electrophiles, wheras a more standard two-step procedure was needed when non aromatic OZTs were involved. In addition, we have developed and generalized a new modified Sonogashira cross-coupling reaction, in which copper (I) is used in catalytic amount, allowing creation of alkynyl C-C bonds from electrophilic thionocarbamates.

In other respects, exploiting the nucleophilicity of the nitrogen site in anchored OXTs, led to the quick acquirement of pseudo-iminosugars, bearing original geometries.

The antimicrobial properties of some of the compounds prepared were evaluated: OXTs and OZTs do not display as strong antimicrobial activities as the reference and only hydroxy-OZT **70** has shown notable antibacterial and antifungal activity.

Inhibitory potencies of the iminosugars **113-115** were determined against 10 glycosidases, showing for anomeric mixtures **114** and **115** high inhibition against isomaltase and trehalase for the first (K_i= 74.7 μM and 87 μM respectively) and isomaltase for the second (K_i= 52 μM).

Experimental part

General methods

BPSE, $Pd(PPh_3)_4$[281] and CuTC[282] were prepared following the procedures described in literature.

Solvents and reagents were bought from Fluka, Merck, Aldrich or Acros Organics.

Solvents were distilled following the procedures described by D. D. Perrin, W. L. F. Armarego and D. R. Perrin, *Purification of Laboratory Chemicals*, Pergamon, Oxford, 1986. The quality of the used solvents is the subsequent:

- ☑ DCM was distilled in the presence of P_2O_5.
- ☑ Toluene was distilled in the presence of CaH_2.
- ☑ THF was distilled in the presence of sodium/benzophenone.
- ☑ MeOH (HPLC) was dried over molecular sieves 3 Å.
- ☑ DMF (HPLC) was dried over molecular sieves 4 Å.
- ☑ Chloroform (HPLC) and cyclohehane (HPLC) were used without further purification.

Thin layer chromatography (TLC) was carried out on Silica Gel 60F-254 precoated plates (Merck). The visualization of the compounds was made by UV light (254 nm) and spraying with a 10% solution of conc. sulfuric acid in methanol or with a mixture EtOH/ molibdenic acid (5%), followed by heating. Column chromatography was carried out using Silica gel 60N (spherical, neutral, 40-63μm).

[281] Coulson, D. *Inorg. Synth*. **1972**, *13*, 121-124.
[282] Zhang, S.; Zhang, D.; Liebeskind, L. S. *J. Org. Chem*. **1997**, *62*, 2312-2313.

Microwaves-assisted reactions were carried out in a Biotage Initiator microwave synthesis instrument and temperatures were measured by IR-sensor.

Melting points were obtained using a Büchi 510 capillary apparatus and are uncorrected.

Optical rotation was measured at 20°C with a perkin Elmer 341 polarimeter with a path length of 1 dm.

NMR spectra were recorded on a spectrometer (400MHz Brucker Avance2) or (250 MHz Brucker Avance DPX250) using tetramethylsilane as the internal standard. Chemical shifts were reported in parts per million (ppm, δ units). Coupling constants are reported and expressed in Hz, splitting patterns are designated as br (broad), s (singlet), d (doublet), dd (double doublet), q (quartet), dt (double triplet), td (triple doublet), ddd (double double doublet), m (multiplet) and t (triplet).

IR spectra were reported on Thermo-Nicolet AVATAR 320 AEK0200713.

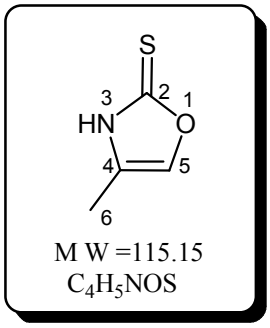
Mass spectra were recorded on Perkin Elmer Sciex API 300 for negative (ISN) and positive (ISP) electrospray ionization. High resolution mass spectra (HRMS) were recorded with a TOF spectrometer in the electrospray ionisation (ESI) mode or in chemical ionisation (CI) mode.

4-Methyloxazole-2(3*H*)-thione (1)

PROCEDURE

1-Hydroxypropan-2-one (2.00 g, 27.00 mmol) and KSCN (3.94 g, 40.50 mmol) were dissolved in EtOH (85 mL). After cooling at –5°C, 12M aqueous HCl (4.05 mL, 48.60 mmol) was carefully added and the mixture was stirred under reflux for 24 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 50 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **1** (2.31 g, **74% yield**) as a yellow solid.

CAS [13016-17-6]



M W =115.15
C_4H_5NOS

Rf = 0.5 (PE/EtOAc 1:1); **mp**: 148-149 °C; **I.R.** (NaCl) ν (cm^{-1}) 3300 (NH), 3140, 3044, 2889 (CH), 1660 (C=C), 1488, 1384, 1353, 1063 (N-CS-O); **^{1}H NMR** (250 MHz, DMSO) δ 1.99 (s, 3H, Me), 7.45 (s, 1H, H-5), 12.99 (brs, 1H, NH); **^{13}C NMR** (62.89 MHz, DMSO) δ 8.1 (C-6), 128.1 (C-4), 134.3 (C-5), 180.6 (C=S), **HRMS**: calcd. for C_4H_6NOS $[M+H]^+$ 116.0110, found 116.0113.

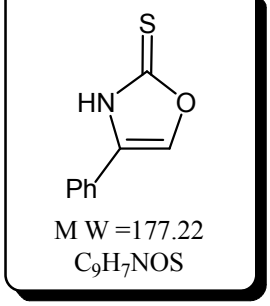
[1] Willems, J.F.; Vandenberghe, A. *Bull. Soc. Chim. Bel*g. **1961**, *70*, 745-748.

4-Phenyloxazole-2(3*H*)-thione (4)

PROCEDURE

α-Hydroxyacetophenone (1.00 g, 7.34 mmol) and KSCN (1.07 g, 11.01 mmol) were dissolved in EtOH (30ml). After cooling at –5°C, 12M aqueous HCl (1.10 mL, 13.21 mmol) was carefully added and the mixture was stirred under reflux for 24 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAct 9:1) to afford compound **4** (1.09 g, **84%yield**) as a red oil.

CAS [17371-97-0]



M W =177.22
C_9H_7NOS

Rf = 0.5 (PE/ EtOAc 7:3); **MS** (IS): m/z = 178.0 $[M+H]^+$, 195.5 $[M+NH_4]^+$; **I.R.** (NaCl) ν (cm^{-1}) 3280 (NH), 1635 (C=C), 1495, 1054 (N-CS-O), 1455, 1451 (Ph), 3041, 2876, 1726, 1602, 1497; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 7.37-7.43 (m, 2H, Ph), 7.44-7.45 (m, 1H, Ph) 7.48-7.52 (m, 2H, Ph), 7.54 (s, 1H, H-5), 12.50 (brs, 1H, N-H); **^{13}C**

NMR (62.89 MHz, $CDCl_3$) δ 124.7 (Cq-Ph), 125.3 (CH-Ph), 128.7 (C-4), 129.4, 129.7 (CH-Ph), 131.9 (C-5), 179.3 (C=S).

[48] Gompper, R.; Herlinger, H. *Chem. Ber*. **1956**, *89*, 2825-2833.

Oxazole-2(3*H*)-thione (5)

PROCEDURE

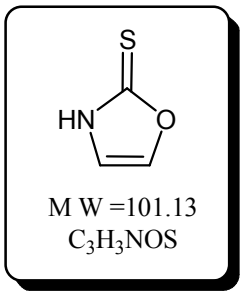
Method A

Glycoaldehyde dimer (1.00 g, 8.33 mmol) and KSCN (1.21 g, 12.49 mmol) were dissolved in EtOH (30 mL). After cooling at –5°C, 12M aqueous HCl (1.25 mL, 14.99 mmol) was carefully added and the mixture was stirred under reflux for 24 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **5** (0.80 g, **95% yield**) as white crystals.

Method B

2,2-Dimethoxyethanol (0.80 g, 7.55 mmol) and KSCN (1.10 g, 11.32 mmol) were dissolved in EtOH (30 mL). After cooling at –5°C, 12M aqueous HCl (1.13 mL, 13.59 mmol) was carefully added and the mixture was stirred under reflux for 24 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **5** (0.70 g, **91% yield**) as white crystals.

CAS [32091-51-3]



M W =101.13
C_3H_3NOS

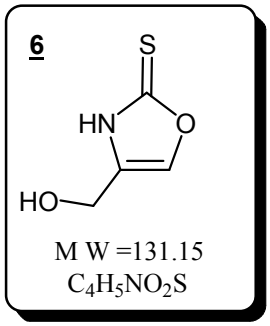
Rf = 0.3 (PE/EtOAc 1:1); **mp**: 147-148 °C; **I.R.** (NaCl) ν (cm^{-1}) 3380 (NH), 3165, 3105, 2755 (CH), 1657 (C=C), 1595, 1490, 1463, 1064 (N-CS-O); **^{1}H NMR** (250 MHz, MeOH) δ 7.14 (s, 1H, H-4), 7.54 (s, 1H, H-5); **^{13}C NMR** (62.89 MHz, MeOH) δ 116.9 (C-4), 137.7 (C-5), 181.1 (C=S); **HRMS**: calcd. for C_3H_4NOS $[M+H]^+$ 102.0115, found 102.0117.

[2] Lacasse, G.; Mucowki, J. M. *Can. J. Chem.* **1972**, *50*, 3082-3083.

4-(Hydroxymethyl)oxazole-2(3*H*)-thione (6) and 1,6-Dioxa-3,8-diazaspiro[4.4]nonane-2,7-dithione (7)

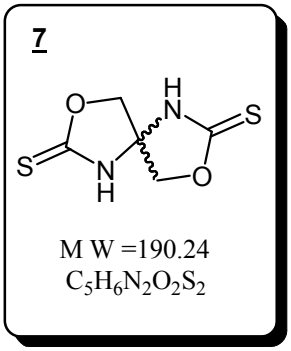
PROCEDURE

1,3-Dihydroxyacetone (1.00 g, 5.55 mmol) and KSCN (0.54 g, 5.55 mmol) were dissolved in H_2O (30 mL). After cooling at –5°C, 12M aqueous HCl (0.83 mL, 9.99 mmol) was carefully added and the mixture was stirred at 65 ºC for 24 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compounds **6** (0.15 g, **21% yield**) as yellow oil and **7** (0.28 g, **27% yield**) as a yellow solid.



CAS [260051-77-2]

Rf = 0.3 (PE/EtOAc 3:7); **MS** (IS): m/z = 132.5 $[M+H]^+$, 149.0 $[M+NH_4]^+$; **I.R.** (NaCl) ν (cm^{-1}) 3500 (OH), 3276 (NH), 3142, 2926, 2889, 2853 (CH), 1659 (C=C), 1502, 1463, 1414, 1061 (N-CS-O); **^{1}H NMR** (250 MHz, DMSO) δ 4.24 (s, 2H, H-6), 5.35 (brs, 1H, OH), 7.60 (s, 1H, H-5), 12.87 (brs, 1H, NH); **^{13}C NMR** (62.89 MHz, DMSO) δ 52.1 (C-6), 131.5 (C-4), 133.7 (C-5), 178.6 (C=S).



Rf = 0.6 (PE/EtOAc 3:7); **mp**: 203-204 °C; **^{1}H NMR** (250 MHz, DMSO) δ 4.61 (d, 2H, 2J= 10.4 Hz, CH2), 4.68 (d, 2H, 2J= 10.4 Hz, CH2), 11.84 (brs, 2H, NH); **^{13}C NMR** (62.89 MHz, DMSO) δ 76.4 (CH2), 80.3 (Cq), 188.0 (C=S).

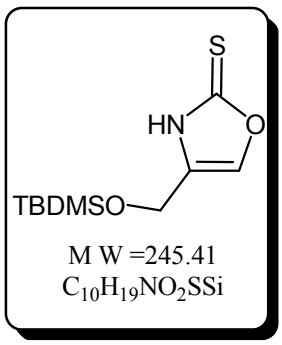
[14] Leconte, N.; Silva, S.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301-305.
[15] Saul, R; Kern, T.; Kopf, J.; Pinter, I.; Köll, P. *Eur. J. Org. Chem*. **2000**, 205-209.

4-(*tert*-Butyldimethylsilyloxymethyl)oxazole-2(3*H*)-thione (8)

PROCEDURE

To OXT **6** (50.0 mg, 0.38 mmol) in dry DMF (5 ml) at 0ºC, were added imidazole (51.7 mg, 0.76 mmol) and TBDMSCl (85.8 mg, 0.57 mmol). The reaction was stirred at room temperature during one night, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 20 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum,

the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **8** (73 mg, **78% yield**) as a yellow solid**.**



M W =245.41
$C_{10}H_{19}NO_2SSi$

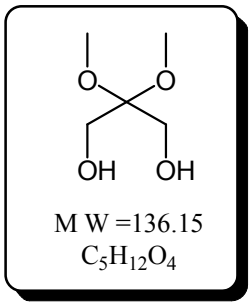
Rf = 0.2 (PE/EtOAc 8:2); **mp**: 122-124 °C; **I.R.** (NaCl) ν (cm^{-1}) 3250 (NH), 2926, 2889 (CH), 1658 (C=C), 1224 ($Si(CH_3)_2$), 1520, 1352, 1049 (N-CS-O); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 0.12 (s, 6H, $Si(CH_3)_2$), 0.91 (s, 9H, *t*-Bu), 4.53 (s, 2H, H-6A, H-6B), 7.16 (s, 1H, H-5), 11.31 (brs, 1H, NH); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -5.4 (Si ($CH_3)_2$), 18.3 (Cq, t-Bu), 25.8 ($(CH_3)_3C$), 54.5 (C-6), 126.0 (C-5), 130.6 (C-4), 179.4 (C=S); **HRMS**: calcd. for $C_{10}H_{20}NO2SSi$ $[M+H]^+$ 246.1211, found 246.1215.

2,2-Dimethoxy-1,3-propanediol (9)

PROCEDURE

In dry conditions, the dihydroxyacetone (10.0 g, 55.51 mmol) was dissolved in MeOH (100ml). The trimethyl orthoformate (8.50 mL, 77.71 mmol) and CSA (64.47 mg, 0.28mmol) were added and the mixture was stirred at room temperature during 20h. The reaction was quenched with triethylamine and then evaporated under vacuum. The residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **9** (12.20 g, **80%yield**) as a white solid.

CAS [153214-82-5]



M W =136.15
$C_5H_{12}O_4$

Rf = 0.4 (EtOAc); **mp**: 43-45 °C; **MS** (IS): m/z = 137.5 $[M+H]^+$, 159.0 $[M+Na]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 3.12 (brs, 2H, OH), 3.27 (s, 6H, OMe), 3.65 (d, 4H, $J_{1\text{-}OH}$= 4.0 Hz, CH_2OH); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 49.1 (O*Me*), 61.1 (CH_2OH), 100.0 (C-1).

[19] Cesarotti, E.; Antognazza, P.; Pallavicini, M.; Villa, L. *Helv. Chim. Acta* **1993**, *76*, 2344-2349.

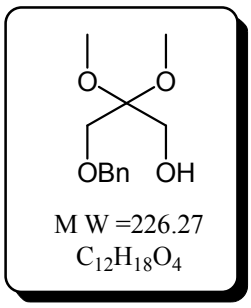
3-Benzyloxy-2,2-dimethoxypropan-1-ol (10)

PROCEDURE

A suspension of NaH 60% dispersion in oil (146.9 mg, 3.67 mmol) in THF (15 mL) was treated at 0ºC with a solution of the diol **9** (500 mg, 3.67 mmol) in THF (15 mL). After 30 min, a catalytic amount of Bu_4NI (42 mg, 0.11 mmol) and BnBr (3.95 mL, 3.30 mmol) were added and the mixture stirred during 8 h and then quenched by treating with crushed ice. After extraction with ethyl acetate (3x 20 mL), the combined organic phases were washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum,

the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **10** (480.0 mg, **64% yield**) as a colourless oil.

CAS [40166-30-1]



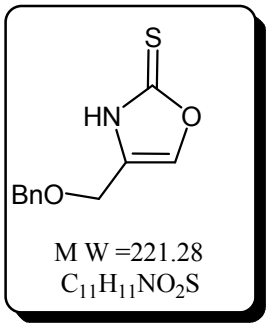
M W =226.27
$C_{12}H_{18}O_4$

Rf = 0.2 (PE/EtOAc 6:4); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 2.39 (t, 1H, $J_{OH\text{-}2A}$= $J_{O\text{-}H\text{-}2B}$= 5.5 Hz, OH), 3.24 (s, 6H, OMe), 3.53 (s, 2H, CH_2OBn), 3.68 (d, 2H, H-2A, H-2B), 4.56 (s, 2H, CH_2Ph), 7.27-7.34 (m, 5H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 48.2 (O*Me*), 60.2 (CH_2OH), 67.9 (CH_2OBn), 76.4 (CH_2Ph), 99.8 (C-1), 127.2, 127.7, 128.2 (CH-Ph), 137.4 (Cq-Ph); **HRMS**: calcd. for $C_{12}H_{18}O_4Na$ $[M+Na]^+$ 249.1099, found 249.1103.

4-(Benzyloxymethyl)oxazole-2(3*H*)-thione (11)

PROCEDURE

The alcohol **10** (80.0 mg, 0.35 mmol) and KSCN (34.0 mg, 0.35 mmol) were dissolved in H_2O (10 mL). After cooling at –5°C, 12M aqueous HCl (0.05 mL, 0.63 mmol) was carefully added and the mixture was stirred at 60 ºC for 24 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 15 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **11** (47 mg, **60% yield**) as an orange oil.



M W =221.28
$C_{11}H_{11}NO_2S$

Rf = 0.6 (PE/EtOAc 6:4); **MS** (IS): m/z = 222.5 $[M+H]^+$, 239.0 $[M+NH_4]^+$; **I.R.** (NaCl) ν (cm^{-1}) 3239 (NH), 2926, 2902 (CH), 1650 (C=C), 1518, 1350, 1049 (N-CS-O), 1466, 1464 (Ph); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 4.33 (s, 2H, CH_2OBn), 4.56 (s, 2H, CH_2Ph), 7.20 (s, 1H, H-5), 7.26-7.36 (m, 5H, Ph), 11.38 (brs, 1H, NH); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 59.8 (CH_2OBn), 72.9 (CH_2Ph), 127.8 (C-4), 128.2, 128.5, 128.8 (CH-Ph), 134.2 (C-5), 136.6 (Cq-Ph), 179.6 (C=S).

[14] Leconte, N.; Silva, S.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301-305.

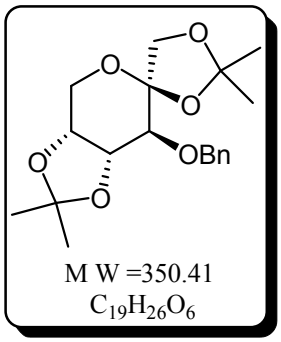
3-*O*-Benzyl-1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose (12)

PROCEDURE

1,2:4,5-di-*O*-isopropylidene-fructopyranose (2.00 g, 7.68 mmol) was dissolved in dry DMF (20 mL) and after cooling at -5ºC, NaH 60% dispersion in oil (460.8 mg, 11.52 mmol) was added . After stirring the reaction until release of H_2 stopped, BnBr (1.10 mL, 9.21 mmol) was added dropwise. The reaction was stirred during one night at room temperature, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 50 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After

filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compound **12** quantitatively, as a yellow oil.

CAS [85458-76-0]



Rf = 0.8 (PE/EtOAc 7:3); $[\alpha]_D$ = - 79 (C=1.3, MeOH); **MS** (IS): m/z = 351.5 $[M+H]^+$, 368.0 $[M+NH_4]^+$; 373.0 $[M+Na]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 1.38 (s, 3H, Me), 1.41 (s, 3H, Me), 1.49 (s, 3H, Me), 1.53 (s, 3H, Me), 3.49 (d, 1H, $J_{3\text{-}4}$= 7.3 Hz, H-3), 3.87 (d, 1H, $J_{A\text{-}B}$=7.3 Hz, H-1B), 3.98 (d, 1H, $J_{A\text{-}B}$=13.3 Hz, H-6B), 4.08 (d, 1H, $J_{A\text{-}B}$=7.3 Hz, H-1A), 4.14 (dd, 1H, $J_{6\text{-}5}$= 2.3 Hz, $J_{A\text{-}B}$=13.3 Hz, H-6A), 4.21 (dd, 1H, $J_{5\text{-}4}$=5.6 Hz, $J_{5\text{-}6}$=2.3 Hz, H-5), 4.38 (dd, 1H, $J_{4\text{-}3}$=7.3 Hz, $J_{4\text{-}5}$=5.6 Hz, H-4), 4.66 (d, 1H, $J_{A\text{-}B}$=12.0 Hz, O*C*H_2Ph), 4.96 (d, 1H, $J_{A\text{-}B}$=12.0 Hz, O*C*H_2Ph), 7.31-7.36 (m, 5H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 26.7, 26.8, 27.5, 28.8 (Me), 78.2 (C-3), 72.5 (C-1), 60.8 (C-6), 74.4 (C-5), 78.4 (C-4), 73.6 (O*C*H_2Ph), 105.0 (C-2), 109.6, 112.7 (Cq-isop), 128.2, 128.3, 128.9 (CH-Ph), 138.8 (Cq-Ph).

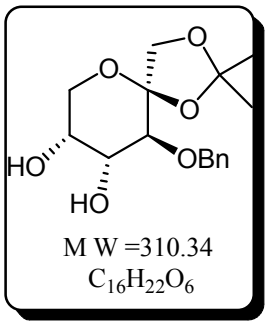
[14] Leconte, N.; Silva, S.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301-305.

3-*O*-Benzyl-1,2-*O*-isopropylidene-β-D-fructopyranose (13)

PROCEDURE

Compound **12** (260.0 mg, 0.74 mmol) was dissolved in an aqueous solution of AcOH (80%) and the reaction was stirred during one night at room temperature. The residue was co-evaporated with toluene (3x) and after concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **13** quantitatively, as a white solid.

CAS [70551-32-5]



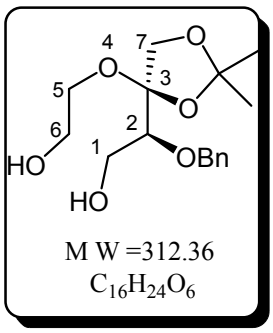
Rf = 0.4 (PE/EtOAc 1:1); $[\alpha]_D$ = - 90 (C=1.1, $CHCl_3$); **mp**: 95-96 °C; **MS** (IS): m/z = 311.5 $[M+H]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 1.43 (s, 3H, Me), 1.49 (s, 3H, Me), 2.43 (brs, 1H, OH), 2.51 (brs, 1H, OH), 3.68 (d, 1H, $J_{A\text{-}B}$= 9.3 Hz, H-1B), 3.77 (dd, 1H, $J_{A\text{-}B}$=13.0 Hz, $J_{5\text{-}6}$=13.0 Hz, H-6B), 3.94-.07 (m, 5H, H-1A, H-6A, H-3, H-4, H-5), 4.75 (d, 1H, $J_{A\text{-}B}$=11.5 Hz, O*C*H_2Ph), 4.81 (d, 1H, $J_{A\text{-}B}$=11.5 Hz, O*C*H_2Ph), 7.28-7.38 (m, 5H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 26.3, 27.0 (Me), 63.7 (C-6), 69.8 (C-3), 71.5 (C-4), 72.0 (C-5), 77.1 (C-1), 75.5 (O*C*H_2Ph), 105.7 (C-2), 112.1 (Cq-isop), 128.1, 128.2, 128.8 (CH-Ph), 138.0 (Cq-Ph).

[14] Leconte, N.; Silva, S.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301-305.

(*S*)-2-(Benzyloxy)-2-((*S*)-4-(2-hydroxyethoxy)-2,2-dimethyl-1,3-dioxalan-4-yl)ethanol (14)

PROCEDURE

Diol **13** (0.23 g, 0.74 mmol) was dissolved in 0.1M aqueous solution of $NaIO_4$ (0.79 g, 3.70 mmol). Protected from the light, the solution was stirred during 30 min at room temperature and then evaporated under vacuum. The resulting dialdehyde was dissolved in 8 ml of water and was treated with sodium borohydride (0.17 g, 4.44 mmol). After stirring at room temperature during 30min, the excess of $NaBH_4$ was decomposed by addition of CO_2. The solution was co-evaporated with toluene (3x), then filtered with Celite®, and concentrated under vacuum. The residue was purified by column chromatography (PE/EtOAc 3:7) to afford compound **14** (0.162 g, **70% yield**) as a white solid.



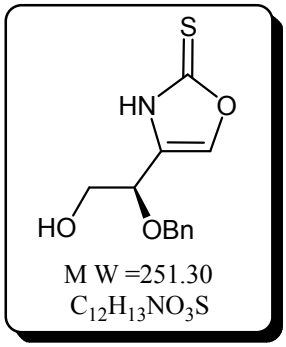
Rf = 0.4 (PE/EtOAc 3:7); $[\alpha]_D$ = - 25 (C=1.8, $CHCl_3$); **mp**: 39-40°C; **mp**: 43-45 °C;; **I.R.** (NaCl) ν (cm^{-1}) 3480 (OH), 2968, 2956, 2904 (CH), 1465, 1462, 1455 (Ph) **^{1}H NMR** (250 MHz, DMSO) δ 1.30 (s, 3H, Me), 1.43 (s, 3H, Me), 3.44-3.58 (m, 5H, H-1B, H-5A, H-5B, H-6A, H-6B), 3.64-3.67 (m, 2H, H-2, H-1A), 3.85 (d, 1H, $J_{A\text{-}B}$= 9.2 Hz, H-7B), 4.03 (d, 1H, $J_{A\text{-}B}$= 9.2 Hz, H-7A), 4.56 (t, 1H, $J_{OH\text{-}6A}$= $J_{OH\text{-}6B}$= 5.5 Hz, OH), 4.63 (t, 1H, $J_{OH\text{-}1A}$= $J_{OH\text{-}1B}$ = 5.5 Hz, OH), 4.70 (d, 1H, $J_{A\text{-}B}$=11.7 Hz, O*C*H_2Ph), 4.75 (d, 1H, $J_{A\text{-}B}$=11.7 Hz, O*C*H_2Ph), 7.22-7.41 (m, 5H, Ph); **^{13}C NMR** (62.89 MHz, DMSO) δ 25.8, 26.2 (Me), 60.3 (C-6), 61.4 (C-1), 63.3 (C-5), 70.9 (C-7), 73.0 (O*C*H_2Ph), 80.8 (C-2), 106.3 (C-3), 110.3 (Cq-isop), 127.2, 127.5, 128.0 (CH-Ph), 138.9 (Cq-Ph); **HRMS**: calcd. for $C_{16}H_{24}O_6Na$ $[M+Na]^+$ 335.1566, found 335.1567.

[14] Leconte, N.; Silva, S.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301-305.

4-[(1*R*)-1-(Benzyloxy)-2-hydroxyethyl]oxazole-2(3*H*)-thione (15)

PROCEDURE

Diol **14** (0.17 g, 0.54 mmol) and KSCN (0.05 g, 0.54 mmol) were dissolved in H_2O (15 mL). After cooling at –5°C, 12M aqueous HCl (0.08 mL, 0.97 mmol) was carefully added and the mixture was stirred at 60 ºC for 24 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 20 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **15** (81 mg, **60% yield**) as a yellow oil.



M W =251.30
$C_{12}H_{13}NO_3S$

Rf = 0.3 (PE/EtOAc 6:4); $[\alpha]_D$ = - 60 (C=1.0, MeOH); **I.R.** (NaCl) ν (cm^{-1}) 3520 (OH), 3246 (NH), 2927, 2877, 2849 (CH), 1654 (C=C), 1502, 1414, 1061 (N-CS-O); 1466, 1462, 1460 (Ph); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 1.79 (brs, 1H, OH), 3.77 (dd, 1H, J_{7B-7A}= 11.8 Hz; J_{6-7B}= 3.8Hz, H-7B), 3.95 (dd, 1H, J_{7A-7B}= 11.8 Hz; J_{6-7A}= 3.8 Hz, H-7A), 4.32 (t, 1H, J_{6-7A}= J_{6-7B}= 3.8Hz, H-6), 4.37 (d, 1H, J_{A-B}= 11.7 Hz, OCH_2Ph), 4.63 (d, 1H, J_{A-B}= 11.7 Hz, OCH_2Ph), 7.26 (s, 1H, H-5), 7.30-7.43 (m, 5H, Ph), 10.72 (brs, 1H, NH); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 64.5 (C-7), 70.3 (C-6), 71.4 (OCH_2Ph), 128.1 (C-4), 128.2, 128.5, 128.8 (CH-Ph), 134.5 (C-5), 136.5 (Cq-Ph), 179.7 (C=S); **HRMS**: calcd. for $C_{12}H_{14}NO_3S$ $[M+H]^+$ 252.0113, found 252.0116.

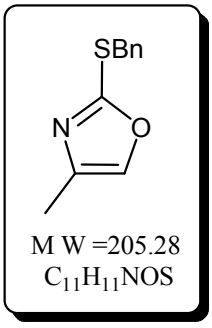
[14] Leconte, N.; Silva, S.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301-305.

2-(Benzylsulfanyl)-4-methyloxazole (16)

PROCEDURE

OXT **1** (0.50 g, 4.34 mmol) was dissolved in dry DMF (20ml). After cooling at -5ºC, NaH 60% dispersion in oil (0.26 g, 6.51 mmol) was carefully added. After 15 min, benzyl bromide (0.57 mL, 4.77 mmol) was added and the reaction stirred during 2.5 h at room temperature, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 20 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 95:5) to afford compound **16** (0.53 g, **60% yield**) as a colourless oil.

CAS [62124-50-9]



M W =205.28
$C_{11}H_{11}NOS$

Rf = 0.2 (PE/EtOAc 95:5); **I.R.** (NaCl) ν (cm^{-1}) 3180, 2976, 2885 (CH), 1649 (C=C), 1616, 1021 (N=CS-O), 1463, 1459, 1454 (Ph); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 2.14 (s, 3H, Me), 4.37 (s, 2H, SCH_2Ph), 7.24-7.38 (m, 6H, H-5, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 11.7 (C-6), 37.0 (SCH_2Ph), 129.0, 127.8, 128.7 (CH-Ph), 135.8 (C-5), 136.4 (Cq-Ph), 137.9 (C-4), 159.3 (C-2); **HRMS**: calcd. for $C_{11}H_{12}NOS$ $[M+H]^+$ 206.0648, found 206.0645.

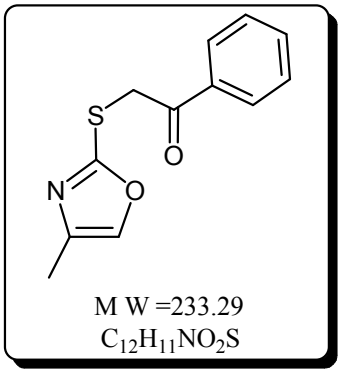
[14] Leconte, N.; Silva, S.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301-305.

2-(Benzoylmethylsulfanyl)-4-methyloxazole (17)

PROCEDURE

A solution of OXT **1** (100.0 mg, 0.87 mmol) in dry DMF (4 mL) was cooled at -5ºC and a NaH 60% dispersion in oil (38.4 mg, 0.96 mmol) was added. After 15 min stirring, bromoacetophenone (190.9 mg, 0.96 mmol) was added and the reaction stirred 1 h more at

room temperature. The mixture was quenched by treating with crushed ice, then extracted with ethyl acetate (3 x 15 mL). The combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **17** (168 mg, **83% yield**) as a yellow oil.



M W =233.29
$C_{12}H_{11}NO_2S$

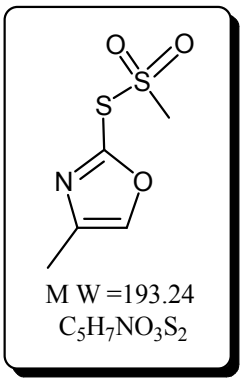
Rf = 0.8 (PE/EtOAc 1:1); **I.R.** (NaCl) ν (cm^{-1}) 3020, 2966, 2884 (CH), 1675, 1630, 1080 (N=CS-O), 1696 (C=O), 1625 (C=C), 1424, 1449, 1398 (Ph), 1050, 929; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 2.13 (s, 3H, Me), 4.76 (s, 2H, S*CH*$_2$CO), 7.36 (s, 1H, H-5), 7.47-7.53 (m, 2H, Ph), 7.59-7.65 (m, 1H, Ph), 8.01-8.04 (m, 2H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 11.6 (C-6), 40.9 (SCH_2CO), 128.6, 128.9, 133.9 (CH-Ph), 135.3 (Cq-Ph), 136.1 (C-5), 137.9 (C-4), 158.7 (C-2), 192.9 (CO); **HRMS**: calcd. for $C_{12}H_{12}NO_2S$ $[M+H]^+$ 234.0581, found 234.0589.

[14] Leconte, N.; Silva, S.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301-305.

2-(Methanothiosulfonate)-4-methyloxazole (18)

PROCEDURE

OXT **1** (O.20 g, 1.74 mmol) was dissolved in dry DCM (5 mL). Triethylamine (0.38 mL, 2.61 mmol) and methanesulfonyl chloride (0.20 mL, 2.61 mmol) were successively added and the reaction stirred during 2h at room temperature. The reaction mixture was quenched by treating with crushed ice. After extraction with DCM (3 x 20 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **18** (144 mg, **44% yield**) as a yellow oil.



M W =193.24
$C_5H_7NO_3S_2$

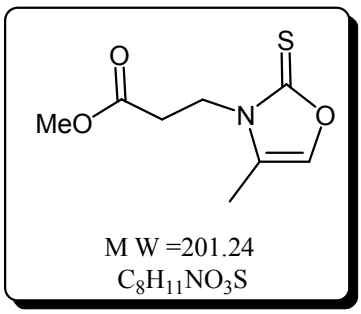
Rf = 0.2 (PE/EtOAc 8:2); **MS** (IS): m/z = 194.5 $[M+H]^+$, 216.0 $[M+Na]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 2.27 (s, 3H, Me), 3.56 (s, 3H, $MeSO_2$), 7.67 (s, 1H, H-5); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 11.8 (C-6), 49.9 (*CH*$_3$SO$_2$), 140.5 (C-5), 140.8 (C-4), 150.7 (C-2).

[14] Leconte, N.; Silva, S.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301-305.

3-(2-Methoxycarbonyl)ethyl-4-methyloxazole-2(3*H*)-thione (19)

PROCEDURE

OXT **1** (100.0 mg, 0.87 mmol) was dissolved in dry DMF (3 mL).Triethylamine (3.14 mL, 21.75 mmol) and methyl acrylate (0.12 mL, 1.31 mmol) were added and the reaction stirred during 24 h at room temperature. The mixture was quenched by treating with crushed ice. After extraction with ethyl acetate (3 x 15 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **19** (24.1 mg, **14% yield**) as a yellow oil.



M W =201.24
$C_8H_{11}NO_3S$

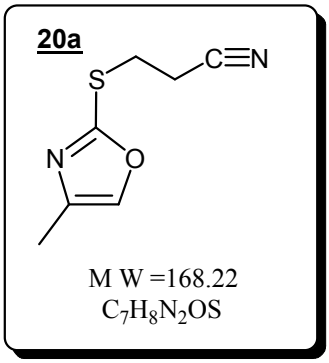
Rf = 0.4 (PE/EtOAc 6:4); **I.R.** (NaCl) ν (cm^{-1}) 3020, 2977 2930 (CH), 1742 (C=O), 1626 (C=C), 1516, 1055 (N-CS-O); **MS** (IS): m/z = 202.5 $[M+H]^+$, 219.0 $[M+NH_4]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 2.20 (s, 3H, Me), 3.00 (t, 2H, J_{vic}= 6.8 Hz, CH_2CO), 3.70 (s, 3H, OMe), 4.15 (t, 2H, J_{vic}= 6.8 Hz, CH_2N), 7.05 (s, 1H, H-5); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 8.6 (C-6), 31.0 (CH_2CO), 40.9 (CH_2N), 52.1 (OMe), 127.9 (C-4), 131.6 (C-5), 171.4 (CO), 178.7 (C=S).

[14] Leconte, N.; Silva, S.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301-305.

2-(2-Cyano)ethylsulfanyl-4-methyloxazole (20a) and 3-(2-Cyano)ethyl-4-methyloxazole-2(3*H*)-thione (20b)

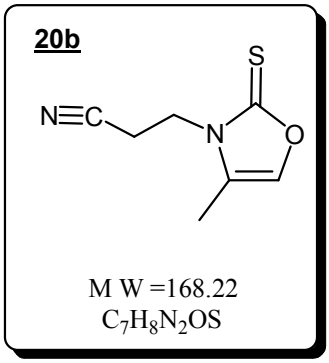
PROCEDURE

OXT **1** (100.0 mg, 0.87 mmol) was dissolved in dry DMF (3 mL).Triethylamine (3.14 mL, 21.75 mmol) and acrylonitrile (86.1 μL, 1.31 mmol) were added and the reaction stirred during 24 h at room temperature. The mixture was quenched by treating with crushed ice. After extraction with ethyl acetate (3 x 15 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compounds **20a** (40.3 mg, **28% yield**) as a yellow oil and **20b** (50.4 mg, **35% yield**) as a yellow solid.



M W =168.22
$C_7H_8N_2OS$

Rf = 0.6 (PE/EtOAc 1:1); **I.R.** (NaCl) ν (cm^{-1}) 3150, 3020, 2982 (CH), 2255 (CN), 1625 (C=C), 1640 (-N=CS-O); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 2.15 (s, 3H, Me), 2.95 (t, 2H, J_{vic}= 7.0 Hz, CH_2CN), 3.37 (t, 2H, J_{vic}= 7.0 Hz, CH_2S), 7.40 (s, 1H, H-5); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 11.7 (C-6), 18.8 (CH_2CN), 28.0 (CH_2S), 117.9 (C≡N), 136.4 (C-5), 138.1 (C-4), 158.8 (C-2); **HRMS**: calcd. for $C_7H_9N_2OS$ $[M+H]^+$ 169.0685, found 169.0689.



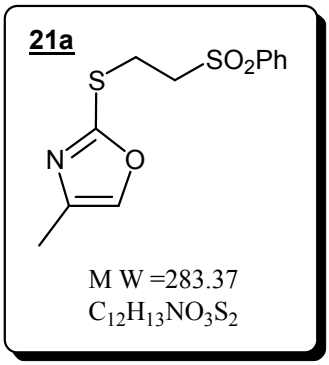
Rf = 0.3 (PE/EtOAc 1:1); **mp**: 43-45 °C; **I.R.** (NaCl) ν (cm^{-1}) 3140, 3020, 2977 (CH), 2255 (CN), 1627 (C=C), 1050 (N-CS-O); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 2.25 (s, 3H, Me), 3.06 (t, 2H, J_{vic}= 6.0 Hz, CH_2CN), 4.17 (t, 2H, J_{vic}= 6.0 Hz, CH_2N), 7.11 (s, 1H, H-5); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 8.7 (C-6), 15.7 (CH_2CN), 41.2 (CH_2N), 117.2 (C≡N), 127.3 (C-4), 132.0 (C-5), 178.9 (C=S); **HRMS**: calcd. for $C_7H_9N_2OS$ $[M+H]^+$ 169.0166, found 169.0169.

[14] Leconte, N.; Silva, S.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301-305.

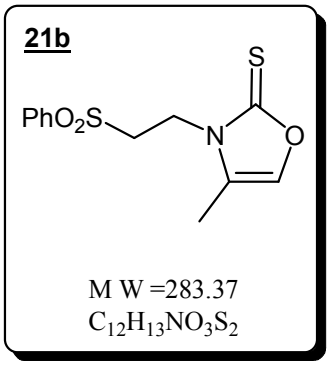
2-(2-Phenylsulfonyl)ethylsulfanyl-4-methyloxazole (21a) and 3-(2-Phenylsulfonyl)ethyl-4-methyloxazole-2(3*H*)-thione (21b)

PROCEDURE

OXT **1** (100.0 mg, 0.87 mmol) was dissolved in dry DMF (3 mL).Triethylamine (3.14 mL, 21.75 mmol) and phenylvinylsulfone (220.0 mg, 1.31 mmol) were successively added and the mixture stirred during 24 h at room temperature. The reaction mixture was quenched by treating with crushed ice. After extraction with ethyl acetate (3 x 15 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compounds **21a** (74 mg, **30% yield**) as a colorless oil and **21b** (153 mg, **62% yield**) as a white solid.



Rf = 0.6 (PE/EtOAc 1:1); **I.R.** (NaCl) ν (cm^{-1}) 3145, 3020, 2982 (CH), 1630 (C=C), 1640, 1511 (-N=CS-O), 1419, 1481 (Ph), 1370 (SO_2), 1040, 933; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 2.08 (s, 3H, Me), 3.32-3.39 (m, 2H, CH_2S), 3.60-3.66 (m, 2H, CH_2SO_2), 7.34 (s, 1H, H-5), 7.57-7.63 (m, 2H, Ph), 7.67-7.70 (m, 1H, Ph), 7.93-7.96 (m, 2H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 11.6 (C-6), 25.1 (CH_2S), 55.9 (CH_2SO_2), 128.3, 129.5, 134.1 (CH-Ph), 136.3 (C-5), 138.1, 138.7 (C-4, Cq-Ph), 157.7 (C-2); **HRMS**: calcd. for $C_{12}H_{14}NO_3S_2$ $[M+H]^+$ 284.0425, found 284.0423.



Rf = 0.3 (PE/EtOAc 1:1); **mp**: 128-129 °C; **I.R.** (NaCl) ν (cm^{-1}) 3140, 3020, 2977 (CH), 1625 (C=C), 1511, 1143 (N-CS-O), 1420, 1481 (Ph), 1390 (SO_2) 1045, 917; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 2.24 (s, 3H, Me), 3.76 (t, 2H, J_{vic}= 6.4 Hz, CH_2SO_2), 4.30 (t, 2H, J_{vic}= 6.4 Hz, CH_2N), 7.02 (s, 1H, H-5), 7.56-7.62 (m, 2H, Ph), 7.66-7.72 (m, 1H, Ph), 7.88-7.91 (m, 2H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 8.6 (C-6), 38.8 (CH_2N), 51.7 (CH_2SO_2), 127.8 (CH-Ph), 127.9 (C-4), 129.6, 131.7 (CH-Ph),

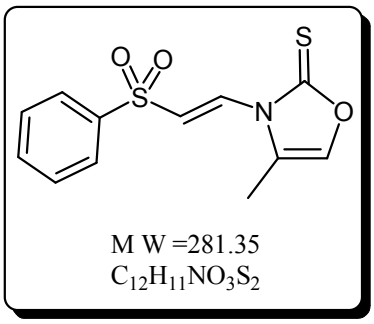
134.4 (C-5), 138.7 (Cq-Ph), 178.5 (C=S); **HRMS**: calcd. for $C_{12}H_{14}NO_3S_2$ $[M+H]^+$ 284.0418, found 284.0415.

[14] Leconte, N.; Silva, S.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301-305.

4-Methyl-3-((*E*)-2-phenylsulfonyl)vinyl)oxazole-2(3*H*)-thione (22)

PROCEDURE

OXT **1** (100.0 mg, 0.87 mmol) was dissolved in dry DMF (3ml). After stirring at 0ºC during 15 min, triethylamine (0.25 mL, 1.80 mmol), *E*-BPSE (274.0 mg, 0.88 mmol) and a few crystals of Bu_4NBr were added and the reaction stirred during 24h at room temperature. The mixture was quenched by treating with crushed ice. After extraction with ethyl acetate (3 x 15 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **22** (228 mg, **90% yield**) as a yellow solid.



Rf = 0.5 (PE/EtOAc 1:1); **mp**: 124-126 °C; **I.R.** (NaCl) ν (cm^{-1}) 3172, 3074, 3020 (CH), 1675 (N-C=C), 1625 (C=C), 1481, 1449, 1398 (Ph), 1375 (SO_2), 1143 (N-CS-O); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 2.24 (s, 3H, Me), 7.08 (s, 1H, H-5), 7.53-7.59 (m, 2H, Ph), 7.62-7.64 (m, 1H, Ph), 7.70 (d, 1H, J_{vic}= 13.8 Hz, *CH*SO_2), 7.91-7.94 (m, 2H, Ph), 8.38 (d, 1H, J_{vic}= 13.8 Hz, *CH*N); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 8.9 (C-6), 120.2 (*CH*SO_2), 126.4 (C-4), 127.5, 129.5, 131.7 (*C*H-Ph), 132.3 (C-5), 133.7 (*CH*N), 140.4 (Cq-Ph), 177.1 (C=S); **HRMS**: calcd. for $C_{12}H_{12}NO_3S_2$ $[M+H]^+$ 282.0267, found 282.0259.

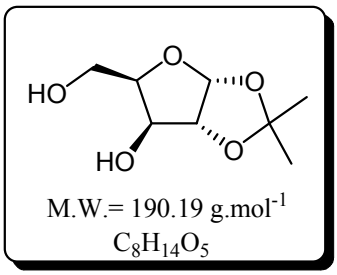
[14] Leconte, N.; Silva, S.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301-305.

1,2-*O*-Isopropylidene-α-D-xylofuranose (23)

PROCEDURE

D-Xylose (10.0 g, 67 mmol) was dissolved in acetone (260 mL) containing 0.66 M H_2SO_4 (10 mL, 96%) by stirring for 30 min. A solution of Na_2CO_3 (13.0 g, 123 mmol) in water (112 mL) was carefully added under external cooling so as to keep the temperature of the mixture at 20ºC, and the mixture was stirred for a further 2.5 h. Then, solid Na_2CO_3 (7.0 g, 66 mmol), Na_2SO_4 was filtered off and washed with acetone, and the combined filtrates were evaporated. The crude was purified by column chromatography (PE/EtOAc 3:7) to afford compound **23** (11.0 g, **80% yield**) as a white solid.

CAS [20031-21-4]



M.W.= 190.19 g.mol^{-1}
$C_8H_{14}O_5$

^{1}H NMR (250 MHz, DMSO) δ 1.22 (s, 3H, Me), 1.37 (s, 3H, Me), 3.44-3.65 (m, 2H, H-5A, H-5B), 3.95-3.99 (m, 2H, OH), 4.37 (d, 1H, $J_{1\text{-}2}$= 3.5 Hz, H-2), 4.59-4.63 (m, 1H, H-4), 5.13 (d, 1H, $J_{3\text{-}4}$= 3.8 Hz, H-3), 5.80 (d, 1H, $J_{1\text{-}2}$= 3.5 Hz, H-1).

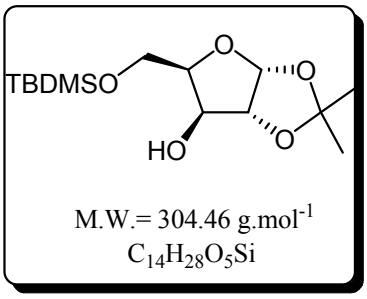
[83] Moravcovà, J.; Capkovà, J.; Stanek, J. *Carbohydr. Res*. **1994**, *263*, 61-66.

1,2-*O*-Isopropylidene-5-*O*-(*tert*-butyldimethylsilyl)-α-D-xylofuranose (24)

PROCEDURE

To 1,2-*O*-isopropylidene-α-D-xylofuranose **23** (1.00 g, 5.26 mmol) in dry DMF (10 ml) at 0ºC, were added imidazole (0.72 g, 10.52 mmol) and TBDMSCl (1.19 g, 7.89 mmol). The reaction was stirred at room temperature during one night, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 30 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 95:5) to afford compound **24** (1.33 g, **83% yield**) as a colorless oil**.**

CAS [85951-12-8]



M.W.= 304.46 g.mol^{-1}
$C_{14}H_{28}O_5Si$

Rf = 0.3 (PE/EtOAc 95:5); $[\alpha]_D$ = - 9 (C=1.1, $CHCl_3$); **MS** (IS): m/z = 305.5 $[M+H]^+$, 322.5 $[M+NH_4]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ -0.08 (s, 6H, $Si(CH_3)_2$), 0.71 (s, 9H, *t*-Bu), 1.10 (s, 3H, Me), 1.27 (s, 3H, Me), 3.83-3.86 (m, 2H, H-5A, H-5B), 3.89-3.95 (m, 1H, H-4), 4.07 (brs, 1H, H-3), 4.13 (brs, 1H, OH), 4.28 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-2), 5.72 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-1); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -5.8 ($Si(CH_3)_2$), 17.9 (Cq, *t*-Bu), 25.5 ($(CH_3)_3C$), 25.9, 26.5 (Me), 61.4 (C-5), 75.4 (C-3), 78.9 (C-4), 85.1 (C-2), 104.6 (C-1), 111.1 (Cq-isop).

[85] Parr. I. B.; Horenstein, B. A. *J. Org. Chem*. **1997**, *62*, 7489-7494.

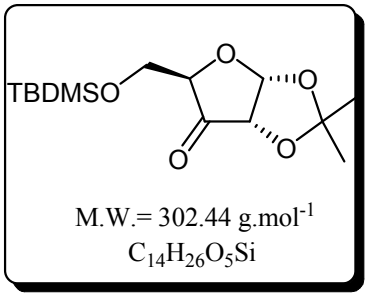
1,2-*O*-Isopropylidene-5-*O*-(*tert*-butyldimethylsilyl)-α-D-*erythro*-pentofuranos-3-ulose (25)

PROCEDURE

Compound **24** (460.0 mg, 1.51 mmol) was dissolved in dry DCM (10 ml). PDC (341.0 mg, 0.91 mmol) and Ac_2O (0.57 mL, 6 mmol) were added and the reaction was stirred under reflux

during 2h. After evaporation of the mixture, the residue was submitted to a small column chromatography (EtOAc) and the filtrated was co-evaporated with toluene (3x). Compound **25** (437.0 mg, **95% yield**) was obtained as a colourless oil.

CAS [103931-45-9]



Rf = 0.4 (PE/EtOAc 95:5); $[\alpha]_D$ = + 36 (C=1.0, $CHCl_3$); **MS** (IS): m/z = 303.5 $[M+H]^+$, 325.5 $[M+Na]^+$; **I.R.** (NaCl) ν (cm^{-1}) 1730 (C=O); **^{1}H NMR** (250 MHz, $CDCl_3$) δ -0.06 (s, 6H, $Si(CH_3)_2$), 0.80 (s, 9H, *t*-Bu), 1.33 (s, 6H, Me), 3.69-3.81 (m, 2H, H-5A, H-5B), 4.17 (d, 1H, $J_{1\text{-}2}$= 4.5 Hz, H-2), 4.26 (s, 1H, H-4), 6.03 (d, 1H, $J_{1\text{-}2}$= 4.5 Hz, H-1); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -5.7 (Si $(CH_3)_2$), 18.1 (Cq, *t*-Bu), 25.7 ($(CH_3)_3C$), 27.1, 27.6 (Me), 63.9 (C-5), 77.1 (C-4), 81.6 (C-2), 103.7 (C-1), 113.9 (Cq-isop), 210.8 (C=O).

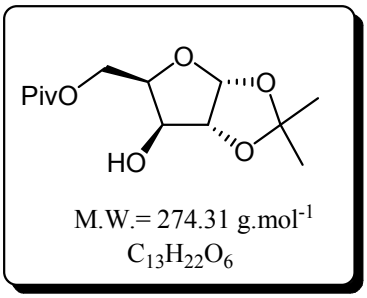
[86] Xavier, N. M.; Rauter, A.P. *Org. Lett*. **2007**, *9*, 3339-3341.

1,2-*O*-Isopropylidene-5-*O*-pivaloyl-α-D-xylofuranose (26)

PROCEDURE

To a cold (0 ºC) and stirred solution of 1,2-*O*-isopropylidene-α-D-xylofuranose **23** (500.0 mg, 2.63 mmol) in pyridine (10 mL), PivCl (0.32 mL, 2.63 mmol) was added dropwise. The reaction was stirred at room temperature during 2h, then co-evaporated with toluene (3x). After concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compounds **26** quantitatively as a colourless oil**.**

CAS [55174-91-9]



Rf = 0.2 (PE/EtOAc 8:2); $[\alpha]_D$ = + 28 (C=1.0, $CHCl_3$); **MS** (IS): m/z = 275.5 $[M+H]^+$; **I.R.** (NaCl) ν (cm^{-1}) 1724 (C=O); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 1.17 (s, 9H, *t*-Bu), 1.27 (s, 3H, Me), 1.45 (s, 3H, Me), 3.31 (brs, 1H, OH), 4.03 (d, 1H, $J_{3\text{-}4}$= 2.2 Hz, H-3), 4.10 (dd, 1H, $J_{4\text{-}5B}$= 5.0 Hz, $J_{5B\text{-}5A}$= 10.8 Hz, H-5B), 4.18 (ddd, 1H, $J_{3\text{-}4}$= 2.2 Hz, $J_{4\text{-}5A}$= 6.7 Hz, $J_{4\text{-}5B}$= 5.0 Hz, H-4), 4.46 (dd, 1H, $J_{5A\text{-}5B}$= 10.8 Hz, $J_{4\text{-}5A}$= 6.7 Hz, H-5A), 4.51 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-2), 5.74 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-1); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 25.9, 26.5 (Me), 26.8 ($(CH_3)_3C$), 38.5 (Cq, *t*-Bu), 61.7 (C-5), 74.1 (C-3), 78.3 (C-4), 84.8 (C-2), 104.6 (C-1), 111.4 (Cq-isop), 178.8 (*C*O*C*$(CH_3)_3$).

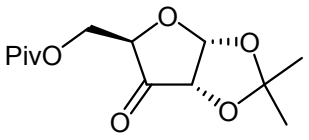
[88] Suhara, Y.; Nihei, K.; Kurihara, M.; Kittaka, A.; Yamaguchi, K.; Fujishima, T.; Konno, K.; Miyata, N.; Takayama, H. *J. Org. Chem*. **2001**, *66*, 8760-8771.

1,2-*O*-Isopropylidene-5-*O*-pivaloyl-α-D-*erythro*-pentofuranos-3-ulose (27)

PROCEDURE

Compound **26** (470.0 mg, 1.71 mmol) was dissolved in dry DCM (10 ml). PDC (385.9 mg, 1.02 mmol) and Ac_2O (0.64 mL, 6.84 mmol) were added and the reaction was stirred under reflux during 2h. After evaporation of the mixture, the residue was submitted to a small column chromatography (EtOAc) and the filtrated was co-evaporated with toluene (3x). Compound **27** (435 mg, **94% yield**) was obtained as a colourless oil.

CAS [55174-92-0]



M.W.= 272.29 g.mol^{-1}
$C_{13}H_{20}O_6$

Rf = 0.3 (PE/EtOAc 8:2); $[\alpha]_D$ = + 22 (C=1.0, $CHCl_3$); **MS** (IS): m/z = 273.5 $[M+H]^+$, 290.5 $[M+NH_4]^+$; **I.R.** (NaCl) ν (cm^{-1}) 1722 (*CO*C(CH_3)$_3$), 1734 (C=O); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 1.04 (s, 9H, *t*-Bu), 1.33 (s, 3H, Me), 1.35 (s, 3H, Me), 4.07-4.12 (m, 1H, H-5B), 4.24-4.27 (m, 2H, H-4, H-5A), 4.47 (d, 1H, $J_{1\text{-}2}$= 3.1 Hz, H-2), 5.99 (d, 1H, $J_{1\text{-}2}$= 3.1 Hz, H-1); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 26.9 ((CH_3)$_3$C), 27.3, 27.5 (Me), 38.4 (Cq, *t*-Bu), 63.1 (C-5), 76.0 (C-4), 77.1 (C-2), 103.0 (C-1), 114.1 (Cq-isop), 177.4 (*CO*C(CH_3)$_3$), 208.0 (C=O).

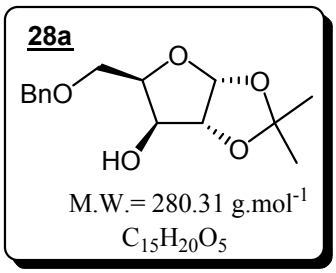
[88] Suhara, Y.; Nihei, K.; Kurihara, M.; Kittaka, A.; Yamaguchi, K.; Fujishima, T.; Konno, K.; Miyata, N.; Takayama, H. *J. Org. Chem*. **2001**, *66*, 8760-8771.

5-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-xylofuranose (28a) and 3,5-di-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-xylofuranose (28b)

PROCEDURE

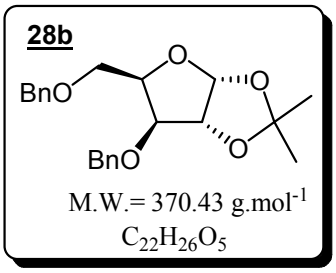
1,2-*O*-isopropylidene-α-D-xylofuranose **23** (4.20 g, 22.08 mmol) was dissolved in toluene (120 mL) and treated with Bu_2SnO (6.05 g, 24.29 mmol). The reaction was then refluxed overnight with azeotropic removal of water. The Dean-Stark trap was then removed and replaced by a standard reflux condenser. The reaction was treated with BnBr (3.96 mL, 33.12 mmol) and kept at 110ºC for 7h. The mixture was cooled at room temperature and the reaction was quenched by treating with crushed ice. After extraction with ethyl acetate (3 x 150 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compounds **28a** (3.90 g, **63% yield**) as a colourless oil and **28b** (0.9 g, **11% yield**) as a colourless oil.

CAS [2592-42-9]



Rf = 0.6 (PE/EtOAc 6:4); $[\alpha]_D$ = + 8 (C=1.0, $CHCl_3$); **MS** (IS): m/z = 281.5 $[M+H]^+$, 298.5 $[M+NH_4]^+$, 303.0 $[M+Na]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 1.28 (s, 3H, Me), 1.46 (s, 3H, Me), 3.76 (d, 1H, J_{OH-3}= 3.8 Hz, OH), 3.82-3.86 (m, 2H, H-5A, H-5B), 4.21-4.24 (m, 1H, H-4), 4.46 (d, J_{1-2}= 3.7 Hz, H-2), 4.56 (s, 2H, O*C*H_2Ph), 5.93 (d, J_{1-2}= 3.7 Hz, H-1), 7.26-7.32 (m, 5H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 26.1, 26.6 (Me), 68.0 (C-5), 73.7, (O*C*H_2Ph), 78.5 (C-4), 85.2 (C-2), 104.7 (C-1), 111.4 (Cq-isop), 127.7, 127.8, 128.4 (CH-Ph), 137.3 (Cq-Ph).

CAS [41341-99-5]



Rf = 0.8 (PE/EtOAc 8:2); **MS** (IS): m/z = 371.5 $[M+H]^+$, 388.2 $[M+NH_4]^+$, 393.2 $[M+Na]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 1.31 (s, 3H, Me), 1.48 (s, 3H, Me), 3.73 (d, 1H, J_{A-B}= 6.1 Hz, H-5B), 3.78 (d, 1H, J_{A-B}= 6.1 Hz, H-5B), 3.97 (d, 1H, J_{3-4}= 6.1 Hz, H-3), 4.29-4.37 (m, 1H, H-4), 4.59 (d, 1H, J_{A-B}= 12.2 Hz, O*C*H_2Ph), 4.61 (d, 1H, J_{A-B}= 12.2 Hz, O*C*H_2Ph), 4.63 (d, 1H, J_{A-B}= 11.8 Hz, O*C*H_2Ph), 4.65 (d, 1H J_{A-B}= 11.8 Hz, O*C*H_2Ph), 4.67 (d, 1H, J_{1-2}= 3.0 Hz, H-2), 5.93 (d, 1H, J_{1-2}= 3.0 Hz, H-1), 7.26-7.36 (m, 10H, Ph).

[91] Alper, P. B.; Hendrix, M.; Sears, P.; Wong, C.H. *J. Am. Chem. Soc.* **1998**, *120*, 1965-1978.

Methyl 3-*O*-benzyl-α-D-xylofuranoside (29α) and Methyl 3-*O*-benzyl-β-D-xylofuranoside (29β)

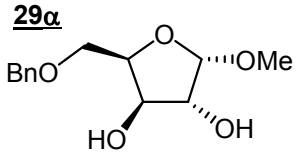
PROCEDURE

Mono benzylated compound **28a** (600.0 mg, 2.14 mmol) was dissolved in dry MeOH and methanesulfonyl chloride (16.4 µL, 0.214 mmol) was carefully added. The reaction was stirred during 5h at room temperature, then quenched by treating with Et_3N. After co-evaporation with toluene under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford the anomeric mixture **29** (380.9 mg, **70% yield**), as a colourless oil, in a proportion α/β: 44/56.

For both anomers:

Rf = 0.2 (PE/EtOAc 1:1); **HRMS**: calcd. for $C_{13}H_{18}O_5Na$ $[M+Na]^+$ 277.1052, found 277.1054.

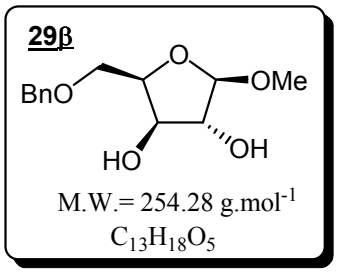
CAS [79083-35-5]



M.W.= 254.28 g.mol^{-1}
$C_{13}H_{18}O_5$

^{1}H NMR (250 MHz, $CDCl_3$) δ 3.46 (s, 3H, OMe), 3.79-3.82 (m, 2H, $J_{4\text{-}5A}$= 4.6 Hz, $J_{5A\text{-}5B}$= 10.5 Hz, H-5A, H-5B), 4.07-4.08 (m, 1H, H-3), 4.10-4.11 (m, 1H, H-2), 4.46 (q, 1H, $J_{4\text{-}5B}$= 6.1 Hz, $J_{4\text{-}5A}$= 4.6 Hz =$J_{3\text{-}4}$= 4.6 Hz, H-4), 4.57 (s, 2H, O*C*H_2Ph), 4.94 (d, 1H, $J_{1\text{-}2}$= 4.3 Hz, H-1), 3.16-3.20 (m, 2H, OH), 7.30-7.34 (m, 5H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 55.1 (OMe), 69.7 (C-5), 73.8, (O*C*H_2Ph), 78.5 (C-3), 79.9 (C-2), 81.4 (C-4), 101.8 (C-1), 127.8, 128.4, 128.5 (CH-Ph), 138.0 (Cq-Ph).

CAS [79083-36-6]



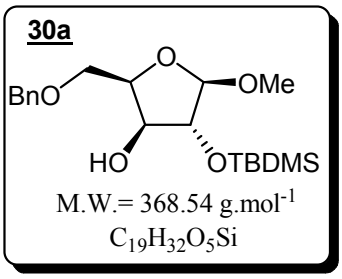
M.W.= 254.28 g.mol^{-1}
$C_{13}H_{18}O_5$

^{1}H NMR (250 MHz, $CDCl_3$) δ 3.34 (s, 3H, OMe), 3.63-3.70 (m, 2H, OH), 3.73-3.74 (m, 2H, H-5A, H-5B), 4.03-4.05 (m, 1H, H-3), 4.23-4.28 (m, 1H, H-4), 4.59 (brs, 3H, H-2, O*C*H_2Ph), 4.82 (s, 1H, H-1), 7.30-7.34 (m, 5H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 55.7 (OMe), 69.3 (C-5), 73.5, (O*C*H_2Ph), 73.8 (C-2), 76.7 (C-3), 76.9 (C-4), 108.1 (C-1), 127.8, 128.4, 128.5 (CH-Ph), 137.5 (Cq-Ph).

Methyl 5-*O*-benzyl-2-*O*-(*tert*-butyldimethylsilyl)-β-D-xylofuranoside (30a) and Methyl 5-*O*-benzyl-2-*O*-(*tert*-butyldimethylsilyl)-α-D-xylofuranoside (30b)

PROCEDURE

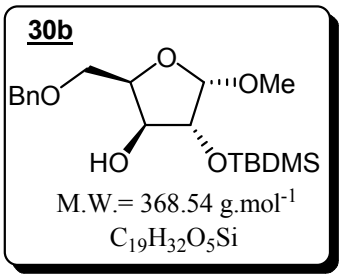
To anomeric mixture **29** (250.0 mg, 0.98 mmol) in dry DMF (5 ml) at 0ºC, were added imidazole (133.4 mg, 1.96 mmol) and TBDMSCl (162.6 mg, 1.08 mmol). The reaction was stirred at room temperature during one night, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 95:5) to afford compounds **30a** (122 mg, **34% yield**) and **30b** (199 mg, **55% yield**) as colourless oils**.**



M.W.= 368.54 g.mol^{-1}
$C_{19}H_{32}O_5Si$

Rf = 0.4 (PE/EtOAc 8:2); $[\alpha]_D$ = - 29 (C=1.0, $CHCl_3$); **^{1}H NMR** (250 MHz, $CDCl_3$) δ -0.06 (s, 6H, Si(CH_3)$_2$), 0.78 (s, 9H, *t*-Bu), 2.84 (brs, 1H, OH), 3.25 (s, 3H, OMe), 3.56 (dd, 1H, $J_{4\text{-}5A}$= 4.4 Hz, $J_{5A\text{-}5B}$= 10.3 Hz, H-5B), 3.74 (dd, 1H, $J_{4\text{-}5B}$= 4.4 Hz, $J_{5A\text{-}5B}$= 10.3 Hz, H-5A), 3.83 (dd, 1H, $J_{3\text{-}4}$= 4.3 Hz, $J_{OH\text{-}3}$= 10.5 Hz, H-3), 4.00 (s, 1H, H-2), 4.35 (dt, 1H, $J_{4\text{-}5A}$= $J_{4\text{-}5B}$= 4.4 Hz, $J_{3\text{-}4}$= 4.3 Hz, H-4), 4.52 (s, 2H, O*C*H_2Ph), 4.65 (s, 1H, H-1), 7.14-7.28 (m, 5H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -4.8 (Si (CH_3)$_2$), 18.1 (Cq, *t*-Bu), 25.8 ((CH_3)$_3$C), 53.1 (OMe), 69.8 (C-5), 73.6, (O*C*H_2Ph), 77.1 (C-3), 80.4 (C-2), 82.0

(C-4), 109.2 (C-1), 127.7, 127.9, 128.5 (CH-Ph), 138.2 (Cq-Ph); **HRMS**: calcd. for $C_{19}H_{32}O_5SiNa$ $[M+Na]^+$ 391.1917, found 391.1921.

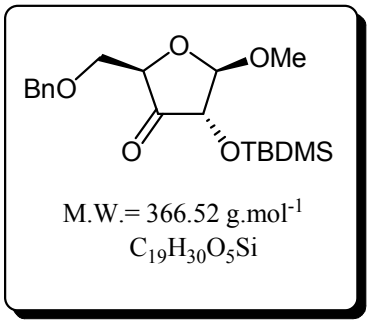


Rf = 0.2 (PE/EtOAc 8:4); $[\alpha]_D$ = + 79 (C=1.0, $CHCl_3$); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 0.09 (s, 6H, $Si(CH_3)_2$), 0.90 (s, 9H, *t*-Bu), 2.98 (d, 1H, J_{OH-3}= 6.8 Hz, OH), 3.42 (s, 3H, OMe), 3.75 (d, 1H, J_{4-5B}= 2.5 Hz, H-5B), 3.77 (d, 1H, J_{4-5A}= 2.5 Hz, H-5A), 4.08 (t, 1H, J_{1-2}= J_{2-3}= 5.0 Hz, H-2), 4.26-4.32 (m, 2H, H-3, H-4), 4.54 (d, 1H, J_{A-B}= 11.6 Hz, O*C*H_2Ph), 4.63 (d, 1H, J_{A-B}= 11.6 Hz, O*C*H_2Ph), 4.79 (d, 1H, J_{1-2}= 5.0 Hz, H-1), 7.28-7.37 (m, 5H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -4.9 (Si $(CH_3)_2$), 18.5 (Cq, *t*-Bu), 26.0 $(CH_3)_3C$), 55.7 (OMe), 69.7 (C-5), 74.1, (O*C*H_2Ph), 75.9 (C-4), 79.9 (C-3), 86.5 (C-2), 102.3 (C-1), 127.9, 128.1, 128.6 (CH-Ph), 137.5 (Cq-Ph); **HRMS**: calcd. for $C_{19}H_{32}O_5SiNa$ $[M+Na]^+$ 391.1917, found 391.1920.

Methyl 5-*O*-benzyl-2-*O*-(*tert*-butyldimethylsilyl)-β-D-*erythro* pentofuranos-3-uloside (31)

PROCEDURE

Compound **30a** (290.0 mg, 0.79 mmol) was dissolved in dry DCM (20 ml). PDC (176.8 mg, 0.47 mmol) and Ac_2O (0.30 mL, 3.16 mmol) were added and the reaction was stirred under reflux during 2h. After evaporation of the mixture, the residue was submitted to a small column chromatography (EtOAc) and the filtrated was co-evaporated with toluene (3x). Compound **31** (275 mg, **95% yield**) was obtained as colourless oil.

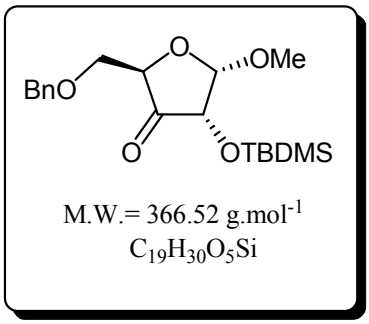


Rf = 0.3 (PE/EtOAc 9:1); $[\alpha]_D$ = - 37 (C=1.0, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 1220 ($Si(CH_3)_2$), 1500, 1459, 1456 (Ph), 1740 (C=O);; **^{1}H NMR** (250 MHz, $CDCl_3$) δ -0.02 (s, 6H, $Si(CH_3)_2$), 0.76 (s, 9H, *t*-Bu), 3.42 (s, 3H, OMe), 3.53 (dd, 1H, J_{4-5B}= 4.6 Hz, J_{5A-5B}= 10.8 Hz, H-5B), 3.60 (dd, 1H, J_{4-5A}= 2.8 Hz, J_{5A-5B}= 10.8 Hz, H-5A), 3.93 (d, 1H, J_{1-2}= 5.2 Hz, H-2), 4.10 (m, 1H, H-4), 4.35 (d, 1H, J_{A-B}= 12.1 Hz, O*C*H_2Ph), 4.44 (d, 1H, J_{A-B}= 12.1 Hz, O*C*H_2Ph), 4.76 (d, 1H, J_{1-2}= 5.2 Hz, H-1), 7.10-7.23 (m, 5H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -4.9, -4.6 (Si $(CH_3)_2$), 18.4 (Cq, *t*-Bu), 25.8 ($(CH_3)_3C$), 56.6 (OMe), 69.6 (C-5), 73.6, (O*C*H_2Ph), 77.7 (C-4), 79.9 (C-2), 106.5 (C-1), 127.7, 127.8, 128.5 (CH-Ph), 137.8 (Cq-Ph), 210.1 (C=O); **HRMS**: calcd. for $C_{19}H_{30}O_5SiNa$ $[M+Na]^+$ 389.1760, found 389.1760.

Methyl 5-*O*-benzyl-2-*O*-(*tert*-butyldimethylsilyl)-α-D-*erythro*-pentofuranos-3-uloside (32)

PROCEDURE

Compound **30b** (290.0 mg, 0.79 mmol) was dissolved in dry DCM (20 ml). PDC (178.8 mg, 0.47 mmol) and Ac_2O (0.30 mL, 3.16 mmol) were added and the reaction was stirred under reflux during 2h. After evaporation of the mixture, the residue was submitted to a small column chromatography (EtOAc) and the filtrated was co-evaporated with toluene (3x). Compound **31** (266 mg, **92% yield**) was obtained as a yellow oil.



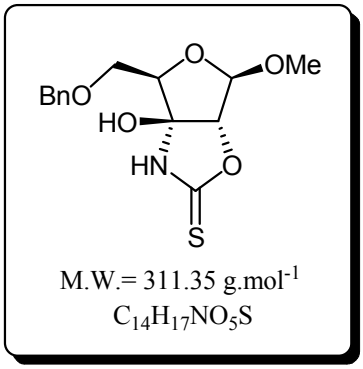
M.W.= 366.52 g.mol^{-1}
$C_{19}H_{30}O_5Si$

Rf = 0.3 (PE/EtOAc 9:1); $[\alpha]_D$ = + 49 (C=1.0, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 1224 ($Si(CH_3)_2$), 1501, 1466, 1464 (Ph), 1744 (C=O); **^{1}H NMR** (250 MHz, $CDCl_3$) δ -0.06 (s, 6H, $Si(CH_3)_2$), 0.76 (s, 9H, *t*-Bu), 3.32 (s, 3H, OMe), 3.56 (d, 1H, $J_{4\text{-}5B}$= 2.6 Hz, H-5B), 3.58 (d, 1H, $J_{4\text{-}5A}$= 2.6 Hz, H-5A), 3.91-3.94 (m, 1H, H-4), 4.28 (d, 1H, $J_{1\text{-}2}$= 5.0 Hz, H-2), 4.31 (d, 1H, $J_{A\text{-}B}$= 12.1 Hz, O*CH*$_2$Ph), 4.44 (d, 1H, $J_{A\text{-}B}$= 12.1 Hz, O*CH*$_2$Ph), 4.95 (d, $J_{1\text{-}2}$= 5.0 Hz, H-1), 7.09-7.19 (m 5H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -4.8 (Si (CH_3)$_2$), 18.5 (Cq, *t*-Bu), 25.8 ((CH_3)$_3$C), 55.4 (OMe), 68.5 (C-5), 73.7, (O*CH*$_2$Ph), 76.2 (C-4), 76.7 (C-2), 100.8 (C-1), 127.8, 128.4, 128.5 (CH-Ph), 137.6 (Cq-Ph), 209.5 (C=O); **HRMS**: calcd. for $C_{19}H_{30}O_5SiNa$ $[M+Na]^+$ 389.1760, found 389.1764.

4,5-Dihydro[methyl (2-deoxy-5-*O*-benzyl-β-D-xylofuranosid)][3,2-d]-1,3-oxazolin-2-thione (33)

PROCEDURE

Uloside **31** (100.0 mg, 0.27 mmol) and KSCN (39.8 mg, 0.41 mmol) were dissolved in THF (10 mL). After cooling at –5°C, $TsOH.H_2O$ (102.7 mg, 0.54 mmol) was carefully added and the mixture was stirred overnight under reflux, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **33** (77.0 mg, **92% yield**) as a white solid. Crystallisation was performed in DCM.



M.W.= 311.35 g.mol^{-1}
$C_{14}H_{17}NO_5S$

Rf = 0.4 (PE/EtOAc 7:3); $[\alpha]_D$ = - 4 (C=0.3, MeOH); **mp**: 157-158 °C; **I.R.** (NaCl) ν (cm^{-1}) 3500 (OH), 3225 (NH), 2977, 2956 (CH), 1508, 1030 (N-CS-O), 1464, 1466 (Ph); **^{1}H NMR** (400 MHz, MeOH) δ 3.36 (s, 3H, OMe), 3.64-3.79 (m, 2H, J_{5A-5B}= 10.6 Hz, H-5A, H-5B), 4.31 (dd, 1H, J_{4-5A}=5.0 Hz, J_{4-5B}=8.4 Hz, H-4), 4.52 (d, 1H, J_{A-B}= 12.0 Hz, O*C*H_2Ph), 4.59 (d, 1H, J_{A-B}= 12.1 Hz, O*C*H_2Ph), 4.72 (s, 1H, H-2), 4.99 (s, 1H, H-1), 7.28-7.36 (m, 5H, H-Ph); **^{13}C NMR** (100 MHz, MeOH) δ 55.5 (OMe), 71.8 (C-5), 74.4 (O*C*H_2Ph), 86.1 (C-4), 95.5 (C-2), 108.0 (C-3), 109.3 (C-1), 128.8, 129.1, 129.4 (CH-Ph), 139.3 (Cq-Ph), 189.3 (C=S); **HRMS**: calcd. for $C_{14}H_{18}NO_5S$ $[M+H]^+$ 312.0906, found 312.0901.

[99] Silva, S.; Simão, A. C.; Tatibouët, A.; Rollin, P.; Rauter, A. P. *Tetrahedron Lett*. **2008**, *49*, 682-686.

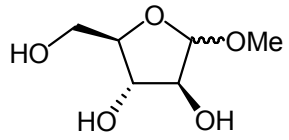
Methyl D-arabinofuranosides (34)

PROCEDURE

Arabinose (1.00 g, 6.7 mmol) was dissolved in dry MeOH and methanesulfonyl chloride (51.6 μL, 0.67 mmol) was carefully added. The reaction was stirred overnight at room temperature, then quenched by treating with Et_3N. After co-evaporation with toluene under vacuum, the anomeric mixture **34** was directly engaged in the next reaction.

For both anomers:
MS (IS): m/z = 165.5 $[M+H]^+$, 182.5 $[M+NH_4]^+$, 187.0 $[M+Na]^+$

34α and 34β



M.W.= 164.16 g.mol^{-1}
$C_6H_{12}O_5$

Methyl 5-*O*-benzyl-α-D-arabinofuranoside (35α) and methyl 5-*O*-benzyl-β-D-arabinofuranoside (35β)

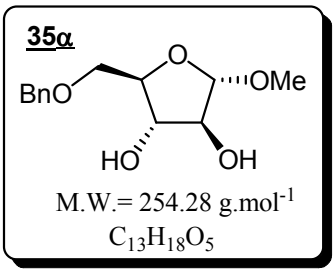
PROCEDURE

Anomeric mixture **34** (1.10 g, 6.70 mmol) was dissolved in THF/DMF (10:1 mL) and after cooling at -5ºC, NaH 60% dispersion in oil (0.27 g, 6.76 mmol) was added . After stirring the reaction until release of H_2 stopped, BnBr (0.81 mL, 6.76 mmol) was added dropwise. The reaction was stirred during one night at room temperature, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was

washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 3:7) to afford the anomeric mixture **35** (373 mg, 68% yield), as colourless oil, in a proportion α/β: 54/46.

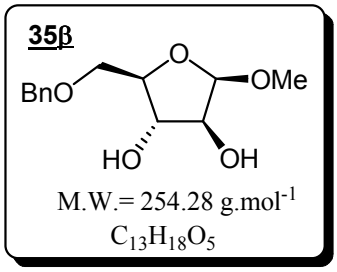
For both anomers:
Rf = 0.5 (PE/EtOAc 3:7); **MS** (IS): m/z = 255.5 $[M+H]^+$, 277.0 $[M+Na]^+$

CAS [237410-28-5]



^{1}H NMR (250 MHz, $CDCl_3$) δ 3.37 (s, 3H, OMe), 3.63 (dd, 1H, $J_{4\text{-}5B}$= 5.2 Hz, $J_{5A\text{-}5B}$= 11.9 Hz, H-5B), 3.75 (dd, 1H, $J_{4\text{-}5A}$= 3.2 Hz, $J_{5A\text{-}5B}$= 11.9 Hz, H-5A), 3.83 (dd, 1H, $J_{2\text{-}3}$= 3.5 Hz, $J_{3\text{-}4}$= 6.2 Hz, H-3), 3.88-3.93 (m, 1H, H-4), 3.93-3.95 (m, 1H, H-2), 4.57 (s, 2H, O*CH*$_2$Ph), 4.76 (s, 1H, H-1), 4.88 (brs, 2H, OH), 7.31-7.36 (m, 5H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 55.2 (OMe), 69.8 (C-5), 73.9, (O*CH*$_2$Ph), 78.7 (C-3), 83.3 (C-2), 85.4 (C-4), 110.5 (C-1), 127.8, 128.4, 128.5 (CH-Ph), 137.4 (Cq-Ph).

CAS [75774-54-6]

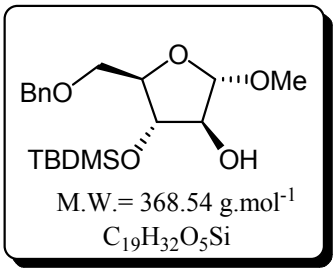


^{1}H NMR (250 MHz, $CDCl_3$) δ 3.34 (s, 3H, OMe), 3.63-3.70 (brs, 2H, OH), 3.73-3.74 (m, 2H, H-5A, H-5B), 4.02-4.09 (m, 1H, H-3), 4.15-4.23 (m, 1H, H-4), 4.51 (s, 1H, H-2), 4.54 (brs, 2H, O*CH*$_2$Ph), 4.86 (s, 1H, H-1), 7.30-7.34 (m, 5H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 55.7 (OMe), 73.3 (C-5), 73.9, (O*CH*$_2$Ph), 79.7 (C-3), 80.8 (C-2), 81.2 (C-4), 101.6 (C-1), 127.9, 128.2, 128.8 (CH-Ph), 138.7 (Cq-Ph).

Methyl 5-*O*-benzyl-3-*O*-(*tert*-butyldimethylsilyl)-α-D-arabinofuranoside (36)

PROCEDURE

To the anomeric mixture **35** (250.0 mg, 0.98 mmol) in dry DMF (5 ml) at 0ºC, were added imidazole (133.4 mg, 1.96 mmol) and TBDMSCl (162.6 mg, 1.08 mmol). The reaction was stirred at room temperature during one night, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 95:5). Among different compounds, the only purified was **36** (65 mg, 18%) as a colourless oil**.**



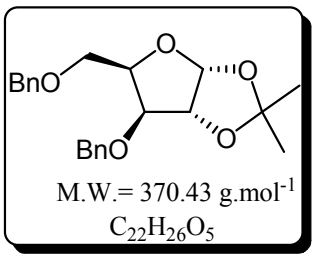
Rf = 0.4 (PE/EtOAc 8:2); $[\alpha]_D$ = + 55 (C=1, MeOH); **MS** (IS): m/z = 369.5 $[M+H]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ -0.07 (s, 6H, Si(CH_3)$_2$), 0.91 (s, 9H, *t*-Bu), 2.52 (d, 1H, J_{OH-2}= 0.8 Hz, OH), 3.40 (s, 3H, OMe), 3.79 (dd, 1H, J_{4-5B}= 6.7 Hz, J_{5A-5B}= 10.5 Hz, H-5B), 3.90-3.94 (m, 2H, H-3, H-5A), 4.19 (ddd, 1H, J_{OH-2}= 0.8 Hz, J_{1-2}= 1.6 Hz, J_{2-3}= 2.6 Hz, H-2), 4.27-4.30 (m, 1H, H-4), 4.60 (d, 1H, J_{A-B}= 12.3 Hz, O*C*H_2Ph), 4.65 (d, 1H, J_{A-B}= 12.3 Hz, O*C*H_2Ph), 4.77 (d, 1H, J_{1-2}= 1.6 Hz, H-1), 7.28-7.34 (m, 5H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -5.2 (Si (CH_3)$_2$), 18.5 (Cq, *t*-Bu), 26.0 ((CH_3)$_3$C), 55.9 (OMe), 62.7 (C-5), 72.5, (O*C*H_2Ph), 79.7 (C-2), 82.0 (C-4), 83.0 (C-3), 109.5 (C-1), 127.8, 128.4, 128.5 (CH-Ph), 138.1 (Cq-Ph).

3,5-di-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-xylofuranose (37)

PROCEDURE

1,2-*O*-isopropylidene-α-D-xylofuranose **23** (3.00 g, 15.77 mmol) was dissolved in dry DMF (25 mL) and after cooling at -5ºC, NaH 60% dispersion in oil (2.52 g, 63.08 mmol) was added . After stirring the reaction until release of H_2 stopped, BnBr (6.60 mL, 55.3 mmol) was added dropwise. The reaction was stirred during one night at room temperature, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 50 mL), the combined organic phases were washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **37** quantitatively, as a yellow oil.

CAS [41341-99-5]



See compound 28b.

[104] Matsuda, F.; Terashima, S. *Tetrahedron* **1998**, *44*, 4721-4736.

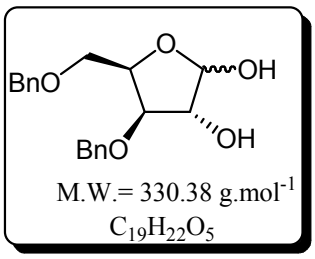
3,5-di-*O*-Benzyl-1,2-*O*-dihydroxy-D-xylofuranose (38)

PROCEDURE

Dibenzyl ether **37** (1.00 g, 2.69 mmol) was dissolved in an aqueous solution of AcOH (70%) and the reaction stirred under reflux during 3 h. The mixture was co-evaporated with toluene (3x) and after concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 4:6) to afford the anomeric mixture **38** (0.62 g, 70% yield) as a yellow solid, in a proportion α/β: 4/1.

For both anomers:

CAS (α) [120693-82-5]
CAS (β) [120693-83-6]
Rf = 0.3 (PE/EtOAc 4:6); **MS** (IS): m/z = 331.0 $[M+H]^+$, 348.5 $[M+NH_4]^+$



^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (d, 0.25H, $J_{2\beta\text{-}OH\text{-}2\beta}$= 6.0 Hz, OH-2β), 2.80 (d, 1H, $J_{2\alpha\text{-}OH\text{-}2\alpha}$= 6.0 Hz, OH-2α), 3.63 (d, 1H, OH-1α), 3.67 (d, 0.25H, $J_{4\beta\text{-}5B\beta}$= 3.8 Hz, H-5Bβ), 3.68 (d, 0.25H, $J_{4\beta\text{-}5A\beta}$ = 5.5 Hz, $J_{5a\beta\text{-}5B\beta}$ = 7.0 Hz, H-5Aβ), 3.73 (d, 1H, $J_{4\alpha\text{-}5B\alpha}$ = 4.8 Hz, H-5Bα), 3.78 (d, 1H, $J_{4\alpha\text{-}5A\alpha}$ = 5.0 Hz, $J_{5A\alpha\text{-}5B\alpha}$ = 9.8 Hz, H-5Aα), 3.86 (d, 0.25H, OH-1β), 4.00 (dd, 1H, $J_{2\alpha\text{-}3\alpha}$ = 2.4 Hz, $J_{3\alpha,4\alpha}$ = 5.0 Hz, H-3α), 4.02 (dd, 0.25H, $J_{2\beta\text{-}3\beta}$= 2.4 Hz, $J_{3\beta\text{-}4\beta}$ = 5.0 Hz, H-3β), 4.22 (m, 1H, H-2α), 4.26 (dd, 0.25H, $J_{2\beta\text{-}3\beta}$ = 2.4 Hz, $J_{3\beta\text{-}4\beta}$ = 5.0 Hz, H-2β), 4.42 (q, 1H, $J_{4\alpha\text{-}5B\alpha}$ = 4.8 Hz, $J_{4\alpha\text{-}5A\alpha}$ = 5.0 Hz, $J_{3\alpha,4\alpha}$ = 5.0 Hz, H-4α), 4.71-4.47 (m, 5.25H, 2OCH_2Ph (α+β), H-4β), 5.10 (d, 0.25H, $J_{1\beta\text{-}OH1\beta}$ =11.5 Hz, H-1β), 5.50 (t, 1H, $J_{1\alpha\text{-}2\alpha}$= $J_{1\alpha\text{-}OH}$= 4.8 Hz, H-1α), 7.38-7.26 (m, 12.5H, 2Ph (α+β)).

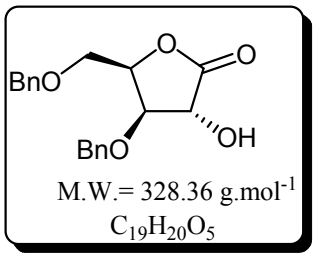
[105] Ning, J.; Kong, F. *Carbohydr. Res*. **1997**, *300*, 355-360.

3,5-di-*O*-Benzyl-D-xylono-1,4-lactone (39)

PROCEDURE

To a 0.03 M solution of the free diol **38** (2.0 g, 6.1 mmol) in dioxane/water (1:2) was added barium carbonate (1.6 g, 8.5 mmol). After cooling the solution to 0 ºC, bromine (2.5 mL, 48.8 mmol) was added dropwise. The reaction mixture was stirred in the dark during 4h. The reaction mixture was then cooled to +10 °C, and sodium carbonate was added until neutralization. In order to destroy the bromine residues, sodium thiosulfate was added until a white precipitate appeared, and the reaction mixture was filtered over Celite. The solvents were evaporated under vacuum, and after the addition of water the product was extracted with EtOAc (3 x 50 mL). The organic phases were washed with brine, dried with MgSO4, filtered and concentrated. The product was crystalised from a mixture of ether and n-hexane to afford derivative **39** (1.7 g, **86% yield**) as colourless crystals.

CAS [131139-04-3]



Rf = 0.2 (PE/EtOAc 7:3); $[\alpha]_D$ = + 40 (C=1.0, $CHCl_3$); **mp**: 68-70 °C; **MS** (IS): m/z = 329.0 $[M+H]^+$, 346.5 $[M+NH_4]^+$, 351.5 $[M+Na]^+$; **I.R.** (NaCl) ν (cm^{-1}) 3480 (OH), 3023, 2977, 2956 (CH), 1780 (C=O), 1464, 1466, 1461 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.71 (d, 1H, $J_{4,5B}$ = 2.8 Hz, H-5B), 3.79 (d, 1H, $J_{5A\text{-}5B}$ = 11.0 Hz, H-5A), 4.37 (t, 1H, $J_{2\text{-}3}$ = 8.0 Hz, $J_{3\text{-}4}$ = 8.0 Hz, H-3), 4.52 (d, 1H, $J_{A\text{-}B}$= 12.0 Hz, OCH_2Ph), 4.58 (d, 1H, $J_{A\text{-}B}$= 12.0 Hz,

OCH_2Ph), 4.58 (m, 1H, H-4), 4.81 (d, 1H, $J_{2\text{-}3}$ = 8.0 Hz, H-2), 4.83 (d, 1H, $J_{A\text{-}B}$= 12.0 Hz, OCH_2Ph), 4.66 (d, 1H, $J_{A\text{-}B}$= 12.0 Hz, OCH_2Ph), 7.39-7.29 (m, 10H, 2xPh).

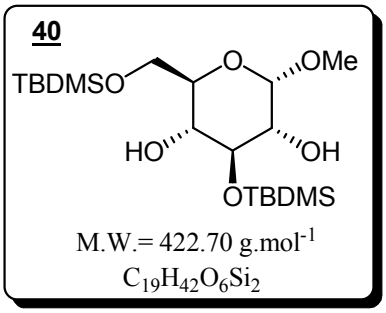
[106] Witty, D. R,; Fleet, G. W. J.; Vogt, K,; Wilson, F. X.; Wang, Y.; Storer, R.; Myers, P. L.; Wallis, C. J. *Tetrahedron. Lett*. **1990**, *31*, 4787-4790.

Methyl 3,6-bis-*O*-(*tert*-butyldimethylsilyl)-α-D-glucopyranoside (40) and Methyl 2,6-bis-*O*-(*tert*-butyldimethylsilyl)-α-D-glucopyranoside (41)

PROCEDURE

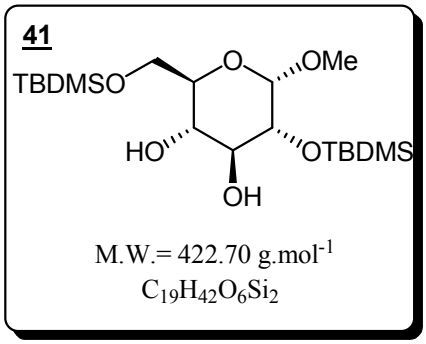
To methyl-α-D-glucopyranoside (3.00 g, 15.45 mmol) in dry DMF (30 ml) at 0ºC, were added imidazole (2.63 g, 38.63 mmol) and TBDMSCl (4.89 mg, 32.45 mmol). The reaction was stirred at room temperature during one night, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 50 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compounds **40** (1.44 g, **22% yield**) as white solid and **41** (3.85 g, **59% yield**) as a colourless oil.

CAS [68102-62-5]



Rf = 0.6 (PE/EtOAc 8:2); $[\alpha]_D$ = + 72 (C=0.4, $CHCl_3$); **mp**: 63-64 °C; **MS** (IS): m/z = 423.5 $[M+H]^+$; **^{1}H NMR** (400 MHz, DMSO) δ 0.03 (s, 6H, $Si(CH_3)_2$), 0.04 (s, 6H, $Si(CH_3)_2$), 0.85 (s, 18H, 2 x *t*-Bu), 2.95 (dd, 1H, $J_{3\text{-}4}$= 8.8 Hz, $J_{4\text{-}5}$= 10.1 Hz, H-4), 3.14 (m, 1H, H-2), 3.25 (s, 3H, OMe), 3.33 (m, 1H, H-5), 3.50 (t, 1H, $J_{2\text{-}3}$= $J_{3\text{-}4}$= 8.8 Hz, H-3), 3.58 (dd, 1H, $J_{5\text{-}6B}$= 6.4 Hz, $J_{6A\text{-}6B}$= 11.2 Hz, H-6B), 3.85 (d, 1H, $J_{6A\text{-}6B}$= 11.2 Hz, H-6A), 4.49 (d, 1H, $J_{1\text{-}2}$ = 3.2 Hz, H-1), 4.64 (d, 1H, $J_{OH\text{-}2}$= 7.6 Hz, OH-2), 4.79 (d, 1H, $J_{OH\text{-}4}$= 8.0 Hz, OH-4); **^{13}C NMR** (100 MHz, DMSO) δ -5.2, -4.2 (Si $(CH_3)_2$), 18.0, 18.3 (Cq, *t*-Bu), 25.8, 26.1 ($(CH_3)_3C$), 54.0 (OMe), 63.0 (C-6), 70.6 (C-4), 72.1 (C-2), 72.7 (C-5), 75.7 (C-3), 99.8 (C-1).

CAS [68102-59-0]



Rf = 0.4 (PE/EtOAc 8:2); $[\alpha]_D$ = + 38 (C=0.4, $CHCl_3$); **MS** (IS): m/z = 423.5 $[M+H]^+$; **^{1}H NMR** (400 MHz, DMSO) δ 0.02 (s, 6H, $Si(CH_3)_2$), 0.03 (s, 6H, $Si(CH_3)_2$), 0.85 (s, 18H, 2 x *t*-Bu), 3.00 (m, 1H, H-4), 3.25 (s, 3H, OMe), 3.31-3.39 (m, 3H, H-2, H-3, H-5), 3.60 (dd, 1H, $J_{5\text{-}6B}$= 6.0 Hz, $J_{6A\text{-}6B}$= 11.2 Hz, H-6B), 3.82 (d, 1H, $J_{6A\text{-}6B}$= 11.2 Hz, H-6A), 4.48 (d, 1H, $J_{1\text{-}2}$ = 3.6 Hz, H-1), 4.84 (d, 1H, $J_{OH\text{-}3}$= 4.8 Hz, OH-3), 4.93 (d, 1H, $J_{OH\text{-}4}$= 5.6 Hz, OH-4); **^{13}C NMR** (100 MHz, DMSO) δ -5.3, -5.0 (Si

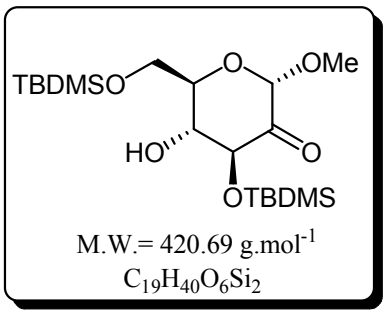
(CH_3)$_2$), 17.9 (2 x Cq, *t*-Bu), 25.7 (2 x (CH_3)$_3$C), 54.3 (OMe), 62.8 (C-6), 70.2 (C-4), 72.6 (C-3), 73.1 (C-5), 73.6 (C-2), 99.6 (C-1).

[107] Chung, M.Y.; Orlova, G.; Goddard, J. D.; Schlaf, M.; Harris, R.; Beveridge, T. J.; White, G.; Hallett, F. R. *J. Am. Chem. Soc.* **2002**, *124*, 10508-10518.

Methyl 3,6-bis-*O*-(*tert*-butyldimethylsilyl)-α-D-*arabino*-hexopyranos-2-uloside (42)

PROCEDURE

Compound **40** (220.0 mg, 0.52 mmol) was dissolved in dry DCM (10 ml). PDC (116.6 mg, 0.31 mmol) and Ac_2O (0.20 mL, 2.08 mmol) were added and the reaction was stirred under reflux during 2h. After evaporation of the mixture, the residue was submitted to a small column chromatography (EtOAc) and the filtrated was co-evaporated with toluene (3x). Compound **42** (203 mg, **93% yield**) was obtained as a colourless oil.



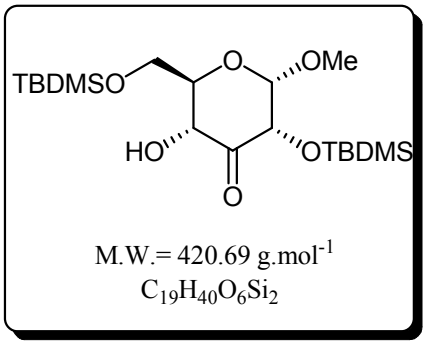
M.W.= 420.69 g.mol^{-1}
$C_{19}H_{40}O_6Si_2$

Rf = 0.8 (PE/EtOAc 8:2); $[\alpha]_D$ = + 45 (C=0.3, MeOH); **MS** (IS): m/z = 421.5 $[M+H]^+$; 444.0 $[M+Na]^+$; **I.R.** (NaCl) ν (cm^{-1}) 3480 (OH), 2988, 2954 (CH), 1730 (C=O), 1215, 1220 (Si(CH_3)$_2$; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.07 (s, 6H, Si(CH_3)$_2$), 0.08 (s, 6H, Si(CH_3)$_2$), 0.93 (s, 18H, 2 x *t*-Bu), 3.44 (s, 3H, OMe), 3.73 (t, 1H, $J_{3\text{-}4}$= $J_{4\text{-}5}$= 9.2 Hz, H-4), 3.91-3.97 (m, 3H, H-5, H-6A, H-6B), 4.54 (d, 1H, $J_{3\text{-}4}$= 9.2 Hz, H-3), 4.66 (s, 1H, H-1); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -5.2, -4.5 (Si (CH_3)$_2$), 18.6, 18.9 (Cq, *t*-Bu), 25.9, 26.0 ((CH_3)$_3$C), 55.4 (OMe), 63.2 (C-6), 71.8 (C-5), 75.2 (C-4), 78.7 (C-3), 101.1 (C-1), 198.6 (C=O).

Methyl 2,6-bis-O-(*tert*-butyldimethylsilyl)-α-D-*ribo*-hexopyranos-3 uloside (43)

PROCEDURE

Compound **41** (220 mg, 0.52 mmol) was dissolved in dry DCM (10 ml). PDC (116.6 mg, 0.31 mmol) and Ac_2O (0.20 mL, 2.08 mmol) were added and the reaction was stirred under reflux during 2h. After evaporation of the mixture, the residue was submitted to a small column chromatography (EtOAc) and the filtrated was co-evaporated with toluene (3x). Compound **43** (188 mg, **86% yield**) was obtained as a colourless oil.



M.W.= 420.69 g.mol^{-1}
$C_{19}H_{40}O_6Si_2$

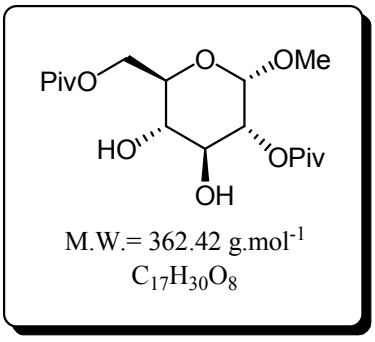
Rf = 0.7 (PE/EtOAc 8:2); $[\alpha]_D$ = + 29 (C=0.3, MeOH); **MS** (IS): m/z = 421.5 $[M+H]^+$; 444.5 $[M+Na]^+$; **I.R.** (NaCl) ν (cm^{-1}) 3480 (OH), 3110, 2981, 2956 (CH), 1725 (C=O), 1210, 1217 ($Si(CH_3)_2$; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.07 (s, 6H, $Si(CH_3)_2$), 0.11 (s, 6H, $Si(CH_3)_2$), 0.91 (s, 18H, 2 x *t*-Bu), 3.40 (s, 3H, OMe), 3.63 (d, 1H, $J_{4\text{-}5}$= 9.2 Hz, H-5), 3.89-3.98 (m, 2H, H-6A, H-6B), 4.16 (d, 1H, $J_{4\text{-}5}$= 9.2 Hz, H-4), 4.46 (d, 1H, $J_{1\text{-}2}$ = 4.0 Hz, H-2), 4.46 (d, 1H, $J_{1\text{-}2}$ = 4.0 Hz, H-1); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -5.2, -4.2 ($Si(CH_3)_2$), 18.6, 18.7 (Cq, *t*-Bu), 25.8, 26.1 ($(CH_3)_3C$), 55.7 (OMe), 62.8 (C-6), 72.1 (C-4), 75.6 (C-5), 76.1 (C-2), 102.9 (C-1), 205.1 (C=O).

Methyl 2,6-di-*O*-pivaloyl-α-D-glucopyranoside (44)

PROCEDURE

To a cold (-20ºC) and stirred solution of methyl-α-D-glucopyranose (3.00 g, 15.45 mmol) in pyridine (30 mL), a solution of PivCl (4.19 mL, 33.99 mmol) in DCM (10 mL) was added dropwise. The reaction was stirred at -20 ºC during 3h, then co-evaporated with toluene (3x). After concentration under vacuum, the reaction mixture was diluted with DCM (200 mL), then washed, first with 10% aqueous solution of H_2SO_4, then with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **44** (4.20 g, **75% yield**) as a white solid.

CAS [76520-84-8]



M.W.= 362.42 g.mol^{-1}
$C_{17}H_{30}O_8$

Rf = 0.3 (PE/EtOAc 7:3); $[\alpha]_D$ = + 70 (C=1.4, $CHCl_3$); **mp**: 92-93 °C; **I.R.** (NaCl) ν (cm^{-1}) 3488 (OH), 1729, 1725 (C=O), 1481, 1445, 1333, 1292; **^{1}H NMR** (400 MHz, DMSO) δ 1.15 (s, 9H, *t*Bu), 1.16 (s, 9H, *t*-Bu), 3.16-3.22 (m, 1H, H-4), 3.27 (s, 3H, OMe), 3.56-3.65 (m, 2H, H-3, H-5), 4.04 (dd, 1H, $J_{5\text{-}6A}$= 6.8 Hz, $J_{6A\text{-}6B}$= 11.5 Hz, H-6A), 4.34 (dd, 1H, $J_{5\text{-}6B}$= 1.5 Hz, $J_{6A\text{-}6B}$= 11.5 Hz, H-6B), 4.41 (dd, 1H, $J_{1\text{-}2}$= 3.8 Hz, $J_{2\text{-}3}$= 10.0 Hz, H-2), 4.70 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-1), 5.22 (d, 1H, $J_{3\text{-}OH}$= 6.1 Hz, OH), 5.39 (d, 1H, $J_{4\text{-}OH}$= 6.0 Hz, OH); **^{13}C NMR** (100 MHz, DMSO) δ 26.7, 26.8 (*t*-Bu), 39.7, 39.9 (Cq, *t*-Bu), 54.4 (OMe), 63.3 (C-6), 69.7 (C-5), 70.2 (C-3), 70.3 (C-4), 72.9 (C-2), 96.3 (C-1), 177.1, 177.2 (*C*O*C*$(CH_3)_3$); **HRMS**: calcd. for $C_{17}H_{30}O_8Na$ $[M+Na]^+$ 385.1838, found 385.1825.

[109] Rauter, A. P.; Fernandes, A. C.; Czernecki, S.; Valery, J. M. *J. Org. Chem.* **1996**, *61*, 3594-3598.

Methyl 2,6-di-*O*-pivaloyl-α-D-*ribo*-hexopyranos-3-uloside (45) and Methyl 2,4-di-*O*-pivaloyl-α-D-*ribo*-hexopyranos-3-uloside (46)

PROCEDURE

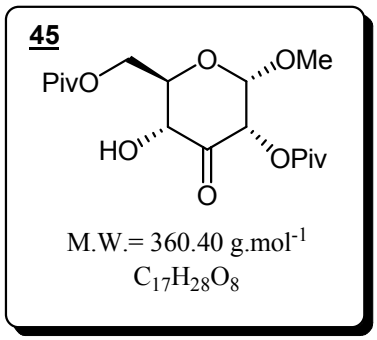
Method A

2,6-bis-*O*-pivaloylate **44** (300.0 mg, 0.83 mmol) was dissolved in dry DCM (15 ml). PDC (188.1 mg, 0.50 mmol) and Ac_2O (0.31 mL, 3.32 mmol) were added and the reaction was stirred under reflux during 8h. After evaporation of the mixture, the reaction mixture was submitted to a small column chromatography (EtOAc) and the filtrated was co-evaporated with toluene (3x). The residue was purified by column chromatography (PE/EtOAc 9:1) to afford compounds **45** (98.0 mg, **33% yield**) and **46** (80.0 mg, **27% yield**) as colourless oils.

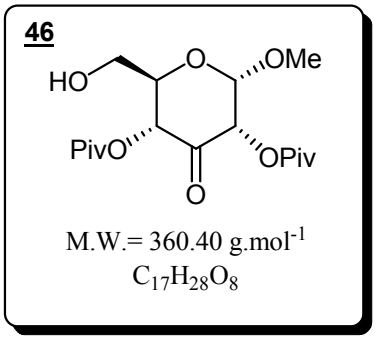
Method B- In order to achieve only derivative 45

2,6-bis-*O*-pivaloylate **44** (300.0 mg, 0.83 mmol) was dissolved in dry DCM (15 ml). PDC (936.7 mg, 2.49 mmol) and Ac_2O (78.3 μL, 0.83 mmol) were added and the reaction was stirred at room temperature during 2.5 h. After evaporation of the mixture, the residue was submitted to a small column chromatography (EtOAc) and the filtrated was co-evaporated with toluene (3x). Compound **45** (260.0 mg, **87% yield**) was obtained as colourless oil.

CAS [90213-79-9]



Rf = 0.4 (PE/EtOAc 7:3); $[\alpha]_D$ = + 41 (C=0.6, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3490 (OH), 1730, 1727, 1725 (C=O), 1481, 1445, 1333, 1292; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.23 (s, 9H, *t*-Bu), 1.28 (s, 9H, *t*-Bu), 3.42 (s, 3H, OMe), 3.88 (ddd, 1H, $J_{4\text{-}5}$= 9.3 Hz, $J_{5\text{-}6A}$= 1.8 Hz, $J_{5\text{-}6B}$= 5.6 Hz, H-5), 4.22 (d, 1H, $J_{5\text{-}4}$= 9.3 Hz, H-4), 4.35 (dd, 1H, $J_{5\text{-}6B}$= 5.6 Hz, $J_{6A\text{-}6B}$= 12.1 Hz, H-6B), 4.52 (dd, 1H, $J_{5\text{-}6A}$= 1.8 Hz, $J_{6A\text{-}6B}$= 12.1 Hz, H-6A), 5.16 (d, 1H, $J_{1\text{-}2}$= 4.3 Hz, H-1), 5.34 (d, 1H, $J_{1\text{-}2}$= 4.3 Hz, H-2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.5, 27.7 (*t*-Bu), 39.7, 39.9 (Cq, *t*-Bu), 55.5 (OMe), 62.9 (C-6), 72.0 (C-4), 73.4 (C-5), 74.8 (C-2), 100.9 (C-1), 177.3, 178.0 (C=O, Piv), 199.7 (C=O); **HRMS**: calcd. for $C_{17}H_{28}O_8Na$ $[M+Na]^+$ 383.1682, found 383.1672.



Rf = 0.6 (PE/EtOAc 7:3); $[\alpha]_D$ = + 53 (C=0.3, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3500 (OH), 1730, 1728, 1723 (C=O), 1480, 1445, 1348, 1287; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.21 (s, 9H, *t*-Bu), 1.24 (s, 9H, *t*-Bu), 3.43 (s, 3H, OMe), 4.19 (ddd, 1H, $J_{4\text{-}5}$= 10.2 Hz, $J_{5\text{-}6A}$= 1.8 Hz, $J_{5\text{-}6B}$= 4.3 Hz, H-5), 4.26 (dd, 1H, $J_{5\text{-}6B}$= 4.3 Hz, $J_{6A\text{-}6B}$= 12.1 Hz, H-6B), 4.32 (dd, 1H, $J_{5\text{-}6A}$= 1.8 Hz, $J_{6A\text{-}6B}$= 12.1 Hz, H-6A), 5.14 (d, 1H, $J_{1\text{-}2}$= 4.0 Hz, H-1), 5.28 (d, 1H, $J_{4\text{-}5}$= 10.2 Hz, H-4), 5.35 (d, 1H, $J_{1\text{-}2}$= 4.0 Hz, H-2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.6, 27.8 (*t*-Bu), 38.9, 39.1 (Cq, *t*-Bu), 55.8 (OMe),

62.3 (C-6), 69.0 (C-5), 72.3 (C-4), 74.4 (C-2), 99.1 (C-1), 177.1, 178.1 (C=O, Piv), 193.3 (C=O); **HRMS**: calcd. for $C_{17}H_{28}O_8Na$ $[M+Na]^+$ 383.1682, found 383.1671.

[99] Silva, S.; Simão, A. C.; Tatibouët, A.; Rollin, P.; Rauter, A. P. *Tetrahedron Lett.* **2008**, *49*, 682-686.

4,5-dihydro[methyl (4-deoxy-2,6-di-*O*-pivaloyl)-α-D-glucopyranosid][3,4-d]-1,3-oxazoline-2-thione (47) and 4,5-dihydro[methyl (4-deoxy-3-*O*-ethyl-2,6-di-*O*-pivaloyl)-α-D-glucopyranosid][3,4-d]-1,3-oxazoline-2-thione (48)

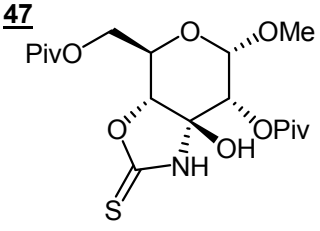
PROCEDURE

Method A

Ketone **45** (1.00 g, 2.77 mmol) and KSCN (0.40 g, 4.16 mmol) were dissolved in EtOH (20 mL). After cooling at –5°C, 12M aqueous HCl (0.42 mL, 4.99 mmol) was carefully added and the mixture was stirred under reflux for 30 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 20 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compounds **47** (0.26 g, **22% yield**) as a white solid and **48** (0.76 g, **61% yield**) as a yellow oil.

Method B- in order to synthesize only OZT 47

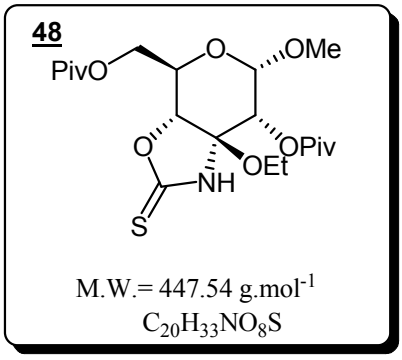
Ketone **45** (1.00 g, 2.77 mmol) and KSCN (0.40 g, 4.16 mmol) were dissolved in DMF/THF (10 mL/ 10 mL). After cooling at –5°C, 12M aqueous HCl (0.42 mL, 4.99 mmol) was carefully added and the mixture was stirred under reflux for 64 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 20 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compound **47** (0.93 g, **79% yield**) as a white solid.



M.W.= 419.49 g.mol^{-1}
$C_{18}H_{29}NO_8S$

Rf = 0.3 (PE/EtOAc 8:2); $[\alpha]_D$ = + 15 (C=1.0, $CHCl_3$); **mp**: 164-165 °C; **I.R.** (NaCl) ν (cm^{-1}) 3403 (OH), 3019 (NH), 2977, 2956 (CH), 1729, 1724 (C=O), 1516, 1038 (N-CS-O), 759, 669; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.24 (s, 9H, *t*-Bu), 1.26 (s, 9H, *t*-Bu), 3.39 (s, 3H, OMe), 4.03 (ddd, 1H, $J_{4\text{-}5}$= 9.5 Hz, $J_{5\text{-}6A}$= 2.8 Hz, $J_{5\text{-}6B}$= 6.0 Hz, H-5), 4.30 (dd, 1H, $J_{5\text{-}6B}$= 6.0 Hz, $J_{6A\text{-}6B}$= 12.1 Hz, H-6B), 4.40 (dd, 1H, $J_{5\text{-}6A}$= 2.8 Hz, $J_{6A\text{-}6B}$= 12.1 Hz, H-6A), 4.61 (d, 1H, $J_{4\text{-}5}$= 9.5 Hz, H-4), 4.98 (d, 1H, $J_{1\text{-}2}$= 4.5 Hz, H-1), 5.12 (d, 1H, $J_{1\text{-}2}$= 4.5 Hz, H-2), 8.10 (brs, 1H, NH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 27.2, 27.3 (*t*-Bu), 39.0, 39.2 (Cq, *t*-Bu), 56.1 (OMe), 63.2 (C-6), 67.5 (C-5), 70.1 (C-2), 84.2 (C-4), 87.5 (C-3), 95.9 (C-

1), 178.0, 178.3 (C=O, Piv), 188.3 (C=S); **HRMS**: calcd. for $C_{18}H_{29}NO_8SNa$ $[M+Na]^+$ 442.1512, found 442.1511.



Rf = 0.4 (PE/EtOAc 8:2); $[\alpha]_D$ = + 50 (C=1.0, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3019 (NH), 2977, 2956 (CH), 1733 (C=O), 1518, 1045 (N-CS-O), 1215, 928; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.12 (t, 3H, $J_{CH2-CH3}$= 7.0 Hz, $OCH_2\mathit{CH_3}$), 1.16 (s, 9H, *t*-Bu), 1.18 (s, 9H, *t*-Bu), 3.30 (s, 3H, OMe), 3.42-3.52 (m, 2H, $O\mathit{CH_2}CH_3$), 3.95 (ddd, 1H, $J_{4\text{-}5}$= 9.3 Hz, $J_{5\text{-}6A}$= 2.8 Hz, $J_{5\text{-}6B}$= 5.9 Hz, H-5), 4.22 (dd, 1H, $J_{5\text{-}6B}$= 5.9 Hz, $J_{6A\text{-}6B}$= 11.9 Hz, H-6B), 4.34 (dd, 1H, $J_{5\text{-}6A}$= 2.8 Hz, $J_{6A\text{-}6B}$= 11.9 Hz, H-6A), 4.55 (d, 1H, $J_{4\text{-}5}$= 9.3 Hz, H-4), 4.89 (d, 1H, $J_{1\text{-}2}$= 4.5 Hz, H-1), 5.02 (d, 1H, $J_{1\text{-}2}$= 4.5 Hz, H-2), 7.89 (brs, 1H, NH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 15.2 ($OCH_2\mathit{CH_3}$), 27.0, 27.2 (*t*-Bu), 38.9, 39.2 (Cq, *t*-Bu), 56.0 (OMe), 58.7 ($OCH_2\mathit{CH_3}$), 63.0 (C-6), 67.3 (C-5), 69.7 (C-2), 80.7 (C-4), 90.6 (C-3), 95.7 (C-1), 177.2, 177.9 (C=O, Piv), 188.4 (C=S); **HRMS**: calcd. for $C_{20}H_{33}NO_8SNa$ $[M+Na]^+$ 470.1825, found 470.1828.

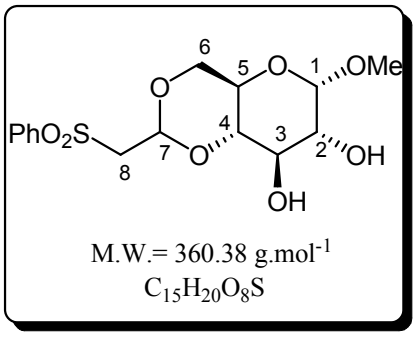
[99] Silva, S.; Simão, A. C.; Tatibouët, A.; Rollin, P.; Rauter, A. P. *Tetrahedron Lett.* **2008**, *49*, 682-686.

Methyl 4,6-*O*-(2-phenylsulfonyl)ethylidene-α-D-glucopyranoside (49)

PROCEDURE

To a solution of methyl α-D-glucopyranoside (4.00 g, 20.61 mmol) in DMF (30 mL) was added *t*-BuOK (4.62 g, 41.22 mmol) at 0ºC. After 15 min at room temperature, BPSE (6.99 g, 22.67 mmol) and a few crystals of Bu_4NBr were added. After stirring for 12 h at room temperature, the mixture was treated with brine and extracted with EtOAc (3 x 100 mL). The combined organic phase was dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (EtOAc) to afford compound **49** (6.16 g, **83% yield**) as a colourless oil.

CAS [280557-41-7]



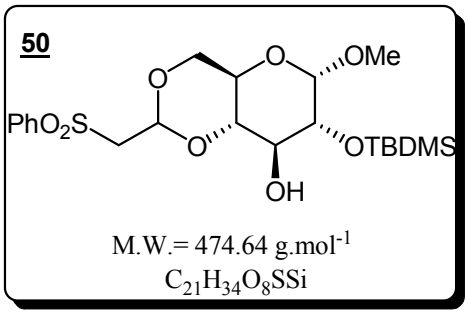
Rf = 0.6 (EtOAc/MeOH 9:1); $[\alpha]_D$ = + 76 (C=1.0, $CHCl_3$); **MS** (IS): m/z = 361.5 $[M+H]^+$, 378.0 $[M+NH_4]^+$, 383.0 $[M+Na]^+$; **I.R.** (NaCl) ν (cm^{-1}) 3480 (OH), 2986, 2957 (CH), 1465, 1467 (Ph), 1370, 1312 (SO_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.22 (t, 1H, $J_{3\text{-}4}$= $J_{4\text{-}5}$= 9.2 Hz, H-4), 3.36 (s, 3H, OMe), 3.42-3.59 (m, 6H, H-2, H-3, H-5, H-6B, H-8A, H-8B), 4.02 (dd, 1H, $J_{5\text{-}6A}$= 3.6 Hz, $J_{6A\text{-}6B}$= 8.9 Hz, H-6A), 4.71 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-1), 4.99 (t, 1H, $J_{7\text{-}8A}$= $J_{7\text{-}8B}$= 4.9 Hz, H-7), 7.52-7.68 (m, 3H, Ph), 7.89-7.93 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 55.6 (OMe), 60.1 (C-8), 62.1 (C-5), 68.9 (C-6), 71.6 (C-3), 73.2 (C-2), 81.0 (C-4), 97.2 (C-7), 100.1 (C-1), 128.7, 129.5, 134.3 (CH-Ph), 140.1 (Cq-Ph).

[115] Chéry, F.; Rollin, P.; Luchi, O.; Cossu, S. *Synthesis* **2001**, *2*, 286-292.

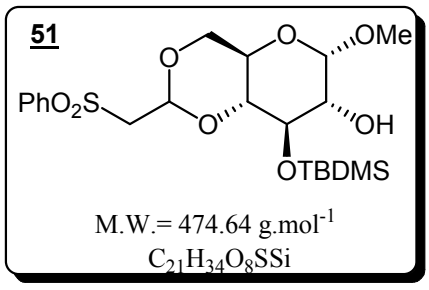
Methyl 4,6-*O*-(2-phenylsulfonyl)ethylidene-2-*O*-*tert*-butyldimethylsilyl-α-D-glucopyranoside (50) and Methyl 4,6-*O*-(2-phenylsulfonyl) ethylidene-3-*O*-*tert*-butyldimethylsilyl-α-D-glucopyranoside (51)

PROCEDURE

To the acetal **49** (630.0 mg, 1.75 mmol) in dry DMF (10 ml) at 0ºC, were added imidazole (238.3 mg, 3.50 mmol) and TBDMSCl (290.6 mg, 1.93 mmol). The reaction was stirred at room temperature during one night, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compounds **50** (316 mg, **38% yield**) and **51** (299.0 mg, **36% yield**) as white solids.



Rf = 0.2 (PE/EtOAc 8:2); $[\alpha]_D$ = + 68 (C=0.6, $CHCl_3$); **mp**: 135-136 °C; **I.R.** (NaCl) ν (cm^{-1}) 3480 (OH), 2930, 2874 (CH), 1461, 1420 (Ph), 1379, 1304 (SO_2), 1256 ($Si(CH_3)_2$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.05 (s, 6H, $Si(CH_3)_2$), 0.82 (s, 9H, *t*-Bu), 2.43 (brs, 1H, OH), 3.18 (t, 1H, $J_{3\text{-}4}$= $J_{4\text{-}5}$= 9.1 Hz, H-4), 3.29 (s, 3H, OMe), 3.38-3.56 (m, 5H, H-2, H-5, H-6B, H-8A, H-8B), 3.70 (t, 1H, $J_{2\text{-}3}$= $J_{3\text{-}4}$= 9.1 Hz, H-3), 3.96 (dd, 1H, $J_{5\text{-}6A}$= 3.9 Hz, $J_{6A\text{-}6B}$= 9.3 Hz, H-6A), 4.51 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-1), 4.96 (t, 1H, $J_{7\text{-}8A}$= $J_{7\text{-}8B}$= 5.1 Hz, H-7), 7.46-7.58 (m, 3H, Ph), 7.59-7.62 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.7, -4.5 ($Si(CH_3)_2$), 18.2 (Cq, *t*-Bu), 25.8 ($(CH_3)_3C$), 55.5 (OMe), 59.7 (C-8), 61.6 (C-5), 68.6 (C-6), 70.4 (C-3), 73.9 (C-2), 80.9 (C-4), 96.8 (C-7), 100.6 (C-1), 128.3, 128.9, 133.8 (CH-Ph), 139.7 (Cq-Ph); **HRMS**: calcd. for $C_{21}H_{34}O_8SSiNa$ $[M+Na]^+$ 497.1641, found 497.1645.



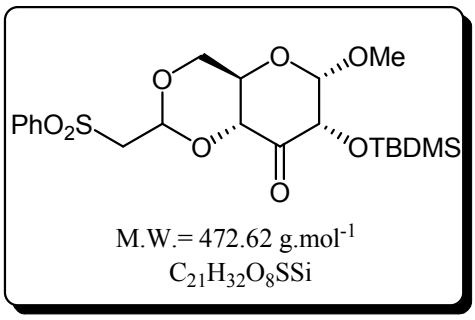
Rf = 0.1 (PE/EtOAc 8:2); $[\alpha]_D$ = + 67 (C=1.3, $CHCl_3$); **mp**: 137-138 °C; **I.R.** (NaCl) ν (cm^{-1}) 3420 (OH), 2997, 2925 (CH), 1456, 1425 (Ph), 1374, 1305 (SO_2), 1246 ($Si(CH_3)_2$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.04 (s, 6H, $Si(CH_3)_2$), 0.84 (s, 9H, *t*-Bu), 2.18 (brs, 1H, OH), 3.22 (t, 1H, $J_{3\text{-}4}$= $J_{4\text{-}5}$= 8.5 Hz, H-4), 3.27 (s, 3H, OMe), 3.33-3.53 (m, 4H, H-5, H-6A, H-6B, H-8A, H-8B), 3.88-3.97 (m, 3H, H-2, H-3, CH_2SO_2), 4.80 (d, 1H, $J_{1\text{-}2}$= 3.2 Hz, H-1), 4.97 (t, 1H, $J_{7\text{-}8A}$= $J_{7\text{-}8B}$= 4.6 Hz, H-7), 7.49-7.59 (m, 3H, Ph), 7.63-7.68 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.7, -4.2 ($Si(CH_3)_2$), 18.2 (Cq, *t*-Bu), 25.7 ($(CH_3)_3C$),55.3 (OMe), 60.1 (C-8), 61.6 (C-5), 68.4 (C-

6), 70.9 (C-3), 73.7 (C-2), 80.8 (C-4), 96.8 (C-7), 97.7 (C-1), 128.3, 129.2, 133.9 (CH-Ph), 139.7 (Cq-Ph); **HRMS**: calcd. for $C_{21}H_{35}O_8SSi$ $[M+H]^+$ 475.1822, found 475.1812.

Methyl 2-*O*-*tert*-butyldimethylsilyl-4,6-*O*-(2-phenylsulfonyl)ethylidene-α-D-*ribo*-hexopyranos-3-uloside (52)

PROCEDURE

Compound **50** (246.0 mg, 0.52 mmol) was dissolved in dry DCM (10 ml). PDC (116.6 mg, 0.31 mmol) and Ac_2O (0.20 mL, 2.08 mmol) were added and the reaction was stirred under reflux during 2h. After evaporation of the mixture, the residue was submitted to a small column chromatography (EtOAc) and the filtrated was co-evaporated with toluene (3x). Compound **52** (235 mg, **96% yield**) was obtained as colourless oil.



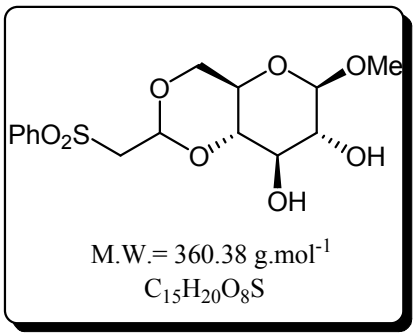
M.W.= 472.62 g.mol^{-1}
$C_{21}H_{32}O_8SSi$

Rf = 0.4 (PE/EtOAc 8:2); $[\alpha]_D$ = + 41 (C=0.8, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2950, 2894 (CH), 1732 (C=O), 1464, 1456 (Ph), 1374, 1312 (SO_2), 1227 ($Si(CH_3)_2$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.08 (s, 6H, $Si(CH_3)_2$), 0.76 (s, 9H, *t*-Bu), 3.23 (s, 3H, OMe), 3.33 (d, 1H, $J_{A\text{-}B}$= 15.0 Hz, H-8B), 3.48 (d, 1H, $J_{A\text{-}B}$= 15.0 Hz, H-8A), 3.55 (t, 1H, $J_{5\text{-}6B}$= $J_{6A\text{-}6B}$= 10.0 Hz, H-6B), 3.67 (ddd, 1H, $J_{4\text{-}5}$= 9.5 Hz, $J_{5\text{-}6A}$= 4.3 Hz, $J_{5\text{-}6B}$= 10.0 Hz, H-5), 3.94 (dd, 1H, $J_{4\text{-}5}$= 9.5 Hz, $J_{2\text{-}4}$= 1.3 Hz, H-4), 4.00 (dd, 1H, $J_{6A\text{-}6B}$= 10.0 Hz, $J_{5\text{-}6A}$= 4.3 Hz, H-6A), 4.25 (dd, 1H, $J_{1\text{-}2}$= 4.3 Hz, $J_{2\text{-}4}$= 1.3 Hz, H-2), 4.82 (d, 1H, $J_{1\text{-}2}$= 4.3 Hz, H-1), 4.97 (t, 1H, $J_{7\text{-}8A}$= $J_{7\text{-}8B}$= 4.0 Hz, H-7), 7.41-7.52 (m, 2H, Ph), 7.56-7.59 (m, 1H, Ph), 7.82-7.85 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -5.3, -4.5 (Si $(CH_3)_2$), 18.4 (Cq, *t*-Bu), 25.6 ($(CH_3)_3C$), 55.5 (OMe), 59.6 (C-8), 64.5 (C-5), 68.9 (C-6), 76.3 (C-2), 81.4 (C-4), 96.8 (C-7), 103.8 (C-1), 128.1, 129.1, 133.9 (CH-Ph), 139.5 (Cq-Ph), 196.3 (C=O); **HRMS**: calcd. for $C_{21}H_{32}O_8SSiNa$ $[M+Na]^+$ 495.1485, found 495.1488.

Methyl 4,6-*O*-(2-phenylsulfonyl)ethylidene-β-D-glucopyranoside (53)

PROCEDURE

To a solution of methyl β-D-glucopyranoside (4.00 g, 20.61 mmol) in DMF (30 mL) was added *t*-BuOK (4.62 g, 41.22 mmol) at 0ºC. After 15 min at room temperature, BPSE (6.99 g, 22.67 mmol) and a few crystals of Bu_4NBr were added. After stirring for 12 h at room temperature, the mixture was treated with brine and extracted with EtOAc (3 x 100 mL). The combined organic phase was dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (EtOAc) to afford compound **53** (5.72 g, **77% yield**) as a white solid.



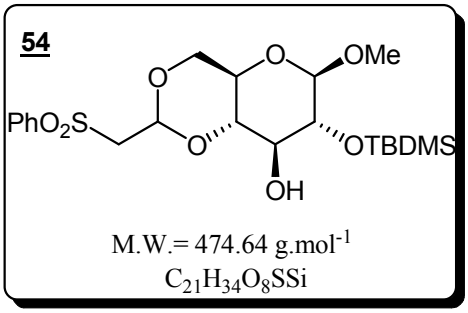
M.W.= 360.38 g.mol^{-1}
$C_{15}H_{20}O_8S$

Rf = 0.3 (EtOAc); $[\alpha]_D$ = - 25 (C=0.9, $CHCl_3$); **mp**: 134-135 °C; **I.R.** (NaCl) ν (cm^{-1}) 3400 (OH), 2997, 2969 (CH), 1461, 1425 (Ph), 1372, 1306 (SO_2); **^{1}H NMR** (400 MHz, DMSO) δ 3.00 (dt, 1H, $J_{1\text{-}2}$=$J_{2\text{-}3}$= 7.9 Hz, $J_{2\text{-}OH}$= 5.1 Hz, H-2), 3.11-3.16 (m, 1H, H-5), 3.20 (t, 1H, $J_{3\text{-}4}$=$J_{4\text{-}5}$= 8.4 Hz, H-4), 3.22-3.29 (m, 1H, H-3), 3.35 (s, 3H, OMe), 3.47 (t, 1H, $J_{5\text{-}6A}$= $J_{6A\text{-}6B}$= 10.0 Hz, H-6A), 3.62 (dd, 1H, $J_{7\text{-}8A}$= 4.3 Hz, $J_{8A\text{-}8B}$= 14.8 Hz, H-8A), 3.68 (dd, 1H, $J_{7\text{-}8B}$= 4.3 Hz, $J_{8A\text{-}8B}$= 14.8 Hz, H-8B), 3.93 (dd, 1H, $J_{5\text{-}6B}$= 4.9 Hz, $J_{6A\text{-}6B}$= 10.0 Hz, H-6B), 4.15 (d, 1H, $J_{1\text{-}2}$= 7.9 Hz, H-1), 4.96 (t, 1H, $J_{7\text{-}8A}$=$J_{7\text{-}8B}$= 4.3 Hz, H-7), 5.16 (d, 1H, $J_{2\text{-}OH}$= 5.1 Hz, OH), 5.35 (d, 1H, $J_{3\text{-}OH}$= 5.2 Hz, OH), 7.61-7.65 (m, 2H, Ph), 7.71-7.75 (m, 1H, Ph), 7.91-7.94 (m, 2H, Ph); **^{13}C NMR** (100 MHz, DMSO) δ 56.3 (OMe), 58.8 (C-8), 65.1 (C-5), 67.4 (C-6), 72.4 (C-3), 74.3 (C-2), 80.2 (C-4), 96.2 (C-7), 104.3 (C-1), 128.1, 129.0, 133.7 (CH-Ph), 139.6 (Cq-Ph); **HRMS**: calcd. for $C_{15}H_{20}O_8SNa$ $[M+Na]^+$ 383.0777, found 383.0782.

Methyl 4,6-*O*-(2-phenylsulfonyl)ethylidene-2-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranoside (54) and Methyl 4,6-*O*-(2-phenylsulfonyl) ethylidene-3-*O*-*tert* -butyldimethylsilyl-β-D-glucopyranoside (55)

PROCEDURE

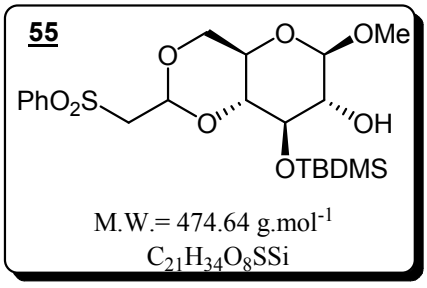
To the acetal **53** (630.0 mg, 1.75 mmol) in dry DMF (10 ml) at 0ºC, were added imidazole (238.3 mg, 3.50 mmol) and TBDMSCl (290.6 mg, 1.93 mmol). The reaction was stirred at room temperature during one night, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compounds **54** (373.8 mg, **45% yield**) as colourless oil and **55** (357.2 mg, **43% yield**) as a white solid.



M.W.= 474.64 g.mol^{-1}
$C_{21}H_{34}O_8SSi$

Rf = 0.5 (PE/EtOAc 7:3); $[\alpha]_D$ = - 31 (C=0.5, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3505 (OH), 2925, 2877 (CH), 1466, 1445 (Ph), 1323, 1305 (SO_2), 1251 ($Si(CH_3)_2$); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 0.08 (s, 3H, $Si(CH_3)_2$), 0.10 (s, 3H, $Si(CH_3)_2$), 0.88 (s, 9H, *t*-Bu), 2.09 (d, 1H, $J_{3\text{-}OH}$= 2.0 Hz, OH), 3.11-3.19 (m, 1H, H-5), 3.20-3.24 (m, 1H, H-4), 3.32-3.35 (m, 1H, H-2), 3.46 (s, 3H, OMe), 3.47-3.56 (m, 4H, H-3, H-6A, H-8A, H-8B), 4.11 (dd, 1H, $J_{5\text{-}6B}$= 4.5 Hz, $J_{6A\text{-}6B}$= 10.5 Hz, H-6B), 4.12 (d, 1H, $J_{1\text{-}2}$= 7.4 Hz, H-1), 5.00 (t, 1H, $J_{7\text{-}8A}$=$J_{7\text{-}8B}$= 5.0 Hz, H-7), 7.53-7.69 (m, 3H, Ph), 7.90-7.94 (m, 2H, Ph);

^{13}C NMR (62.89 MHz, $CDCl_3$) δ -4.8, -4.3 ($Si(CH_3)_2$), 18.4 (Cq, *t*-Bu), 26.0 ($(CH_3)_3C$), 57.5 (OMe), 59.9 (C-8), 65.6 (C-5), 68.5 (C-6), 74.2 (C-3), 75.9 (C-2), 80.2 (C-4), 96.9 (C-7), 105.1 (C-1), 128.5, 129.2, 133.9 (CH-Ph), 139.9 (Cq-Ph); **HRMS**: calcd. for $C_{21}H_{34}O_8SSiNa$ $[M+Na]^+$ 497.1641, found 497.1651.

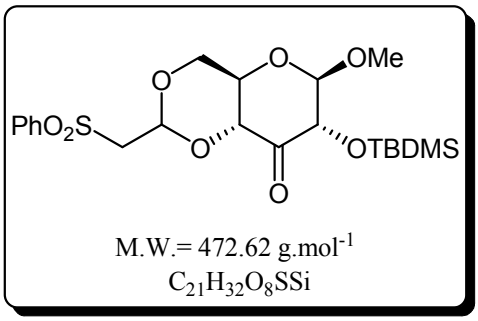


Rf = 0.3 (PE/EtOAc 7:3); $[\alpha]_D$= - 23 (C=0.5, $CHCl_3$); **mp**: 143-144 °C; **I.R.** (NaCl) ν (cm^{-1}) 3470 (OH), 2944, 2926 (CH), 1466, 1444 (Ph), 1374, 1302 (SO_2), 1246 ($Si(CH_3)_2$); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 0.03 (s, 3H, $Si(CH_3)_2$), 0.07 (s, 3H, $Si(CH_3)_2$), 0.87 (s, 9H, *t*-Bu), 2.33 (d, 1H, $J_{2\text{-}OH}$= 2.7 Hz, OH), 3.10- 3.18 (m, 1H, H-5), 3.24 (t, 1H, $J_{3\text{-}4}$=$J_{4\text{-}5}$= 8.6 Hz, H-4), 3.31-3.36 (m, 1H, H-2), 3.41-3.53 (m, 6H, H-6A, H-8A, H-8B, OMe), 3.55-3.59 (m, 1H, H-3), 4.05 (dd, 1H, $J_{5\text{-}6B}$= 4.7 Hz, $J_{6A\text{-}6B}$= 10.5 Hz, H-6B), 4.18 (d, 1H, $J_{1\text{-}2}$= 7.6 Hz, H-1), 4.99 (dd, 1H, $J_{7\text{-}8A}$= 2.5 Hz, $J_{7\text{-}8B}$= 7.1 Hz, H-7), 7.52-7.66 (m, 3H, Ph), 7.88-7.94 (m, 2H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -4.6, -4.2 ($Si(CH_3)_2$), 18.4 (Cq, *t*-Bu), 25.9 ($(CH_3)_3C$), 57.6 (OMe), 60.1 (C-8), 65.9 (C-5), 68.2 (C-6), 74.3 (C-3), 75.4 (C-2), 81.2 (C-4), 96.8 (C-7), 104.4 (C-1), 128.3, 129.2, 134.0 (CH-Ph), 139.8 (Cq-Ph); **HRMS**: calcd. for $C_{21}H_{34}O_8SSiNa$ $[M+Na]^+$ 497.1641, found 497.1650.

Methyl 2-*O*-*tert*-butyldimethylsilyl-4,6-*O*-(2-phenylsulfonyl)ethylidene-β-D-*ribo*-hexopyranos-3-uloside (56)

PROCEDURE

Solid tetrapropylammonium perruthenate (TPAP) (14.8 mg, 0.042 mmol) was added in one portion to a stirred mixture of compound **54** (200.0 mg, 0.42 mmol) and 4-methyl-morpholine *N*-oxide (NMO) (147.6 mg, 1.26 mmol) in DCM (10 mL). The reaction was stirred during 6 h at room temperature, then filtered through a pad of silica. The filtrate was evaporated under vacuum and the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **56** quantitatively, as a colourless oil.



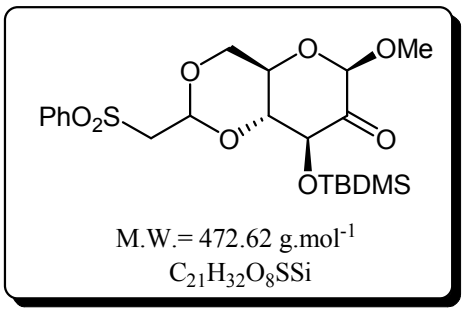
Rf = 0.6 (PE/EtOAc 9:1); $[\alpha]_D$ = - 30 (C=1.5, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2935, 2853 (CH), 1747 (C=O), 1464, 1445 (Ph), 1394, 1309 (SO_2), 1249 ($Si(CH_3)_2$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.01 (s, 3H, $Si(CH_3)_2$), 0.08 (s, 3H, $Si(CH_3)_2$), 0.86 (s, 9H, *t*-Bu), 3.26-3.33 (m, 1H, H-5), 3.49-3.56 (m, 5H, H-8A, H-8B, OMe), 3.62 (t, 1H, $J_{5\text{-}6A}$=$J_{6A\text{-}6B}$= 10.4 Hz, H-6A), 4.01-4.05 (m, 2H, H-2, H-4), 4.20 (dd, 1H, $J_{5\text{-}6B}$=5.0 Hz, $J_{6A\text{-}6B}$= 10.4 Hz, H-6B), 4.29 (d, 1H, $J_{1\text{-}2}$= 7.4 Hz, H-1), 5.07 (dd, 1H, $J_{7\text{-}8A}$= 3.9 Hz, $J_{7\text{-}8B}$= 5.9 Hz, H-7), 7.49-7.63 (m, 3H, Ph), 7.83-7.88 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -5.3, -4.9 ($Si(CH_3)_2$), 18.5 (Cq, *t*-Bu), 25.6 ($(CH_3)_3C$), 57.9 (OMe), 59.7

(C-8), 65.7 (C-5), 68.7 (C-6), 78.7 (C-2), 81.3 (C-4), 96.9 (C-7), 106.9 (C-1), 128.2, 129.1, 134.0 (CH-Ph), 139.6 (Cq-Ph), 196.5 (C=O); **HRMS**: calcd. for $C_{21}H_{32}O_8SSiNa$ $[M+Na]^+$ 495.1485, found 495.1504.

Methyl 3-*O*-*tert*-butyldimethylsilyl-4,6-*O*-(2-phenylsulfonyl)ethylidene-β-D-*arabino*-hexopyranos-2-uloside (57)

PROCEDURE

Solid tetrapropylammonium perruthenate (TPAP) (29.5 mg, 0.084 mmol) was added in one portion to a stirred mixture of compound **55** (200.0 mg, 0.42 mmol) and 4-methyl-morpholine *N*-oxide (NMO) (147.6 mg, 1.26 mmol) in DCM (10 mL). The reaction was stirred during 6 h at room temperature, then filtered through a pad of silica. The filtrate was evaporated under vacuum and the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **57** (115.1 mg, **58% yield**) as an colourless oil.



M.W.= 472.62 g.mol^{-1}
$C_{21}H_{32}O_8SSi$

Rf = 0.1 (PE/EtOAc 7:3); $[\alpha]_D$ = - 13 (C=0.7, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2978, 2874 (CH), 1742 (C=O), 1464, 1451 (Ph), 1370, 1304 (SO_2), 1229 ($Si(CH_3)_2$); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 0.01 (s, 3H, $Si(CH_3)_2$), 0.10 (s, 3H, $Si(CH_3)_2$), 0.88 (s, 9H, *t*-Bu), 3.44-3.49 (m, 2H, H-8A, H-8B), 3.52 (s, 3H, OMe), 3.54-3.60 (m, 3H, H-4, H-5, H-6A), 4.17-4.24 (m, 2H, H-3, H-6B), 4.73 (s, 1H, H-1), 4.99 (dd, 1H, $J_{7\text{-}8A}$= 3.0 Hz, $J_{7\text{-}8B}$= 6.4 Hz, H-7), 7.52-7.67 (m, 3H, Ph), 7.89-7.92 (m, 2H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -5.1, -4.7 ($Si(CH_3)_2$), 18.7 (Cq, *t*-Bu), 25.7 ($(CH_3)_3C$), 57.1 (OMe), 59.9 (C-8), 65.7 (C-5), 68.1 (C-6), 77.9 (C-3), 82.9 (C-4), 96.6 (C-7), 101.6 (C-1), 128.3, 129.3, 134.0 (CH-Ph), 139.7 (Cq-Ph), 196.7 (C=O); **HRMS**: calcd. for $C_{21}H_{33}O_8SSi$ $[M+Na]^+$ 473.1665, found 473.1684.

4,5-dihydro{methyl [2-deoxy-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[3,2-d]-1,3-oxazoline-2-thione (58) and 4,5-dihydro{methyl [2-deoxy-3-*O*-ethyl-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[3,2-d]-1,3-oxazoline-2-thione (59)

PROCEDURE

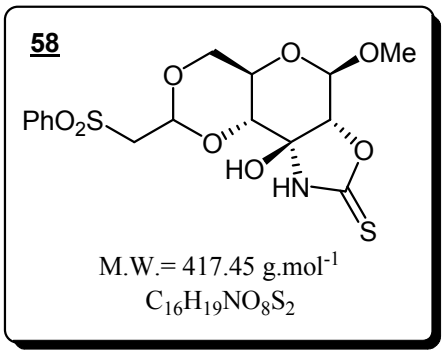
Method A

Ketone **56** (1.31 g, 2.77 mmol) and KSCN (0.40 g, 4.16 mmol) were dissolved in EtOH (20 mL). After cooling at –5°C, 12M aqueous HCl (0.42 mL, 4.99 mmol) was carefully added and

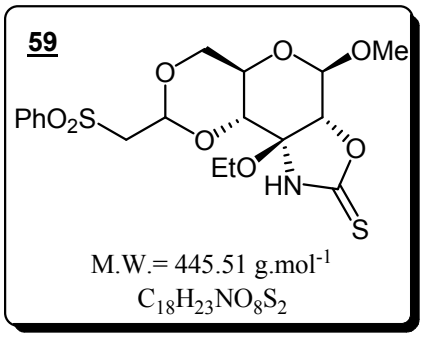
the mixture was stirred under reflux for 30 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 50 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compounds **58** (0.51 g, **44% yield**) and **59** (0.60 g, **49% yield**) as white solids.

Method B- in order to synthesize only OZT 58

Ketone **56** (1.31 g, 2.77 mmol) and KSCN (0.40 g, 4.16 mmol) were dissolved in DMF/THF (4 mL/ 16 mL). After cooling at –5°C, $TsOH.H_2O$ (1.05 g, 5.54 mmol) was carefully added and the mixture was stirred overnight under reflux, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 30 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **58** (0.96 g, **83% yield**) as a white solid.



Rf = 0.2 (PE/EtOAc 7:3); $[\alpha]_D$ = - 11 (C=0.8, $CHCl_3$); **mp**: 73-74 °C; **I.R.** (NaCl) ν (cm^{-1}) 3480 (OH), 3200 (NH), 2986, 2925 (CH), 1476, 1440 (Ph), 1516, 1077 (N-CS-O), 1383, 1305 (SO_2), 836, 785, 749; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.44 (s, 3H, OMe), 3.46-3.55 (m, 3H, H-5, H-6A, H-8A), 3.63 (dd, 1H, $J_{7\text{-}8B}$= 5.1 Hz, $J_{8A\text{-}8B}$= 14.6 Hz, H-8B), 4.08-4.14 (m, 2H, H-4, H-6B), 4.59 (d, 1H, $J_{1\text{-}2}$= 4.0 Hz, H-2), 4.62 (d, 1H, $J_{1\text{-}2}$= 4.0 Hz, H-1), 5.16 (dd, 1H, $J_{7\text{-}8A}$= 4.1 Hz, $J_{7\text{-}8B}$= 5.1 Hz, H-7), 5.61 (brs, 1H, OH), 7.56-7.60 (m, 2H, Ph), 7.66-7.70 (m, 1H, Ph), 7.92-7.94 (m, 2H, Ph), 8.72 (brs, 1H, NH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 56.7 (OMe), 59.6 (C-8), 64.3 (C-5), 68.7 (C-6), 78.3 (C-4), 87.3 (C-2), 88.1 (C-3), 96.9 (C-7), 100.5 (C-1), 128.4, 129.5, 134.4 (CH-Ph), 139.2 (Cq-Ph), 188.9 (C=S); **HRMS**: calcd. for $C_{16}H_{20}NO_8S_2$ $[M+H]^+$ 418.0630, found 418.0630.



Rf = 0.3 (PE/EtOAc 7:3); $[\alpha]_D$ = - 25 (C=1.0, $CHCl_3$); **mp**: 79-80 °C; **I.R.** (NaCl) ν (cm^{-1}) 3020 (NH), 2978, 2959 (CH), 1477, 1458 (Ph), 1516, 1051 (N-CS-O), 1370, 1304 (SO_2), 928, 854, 778; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.23 (t, 3H, $J_{CH2\text{-}CH3}$= 7.0 Hz, $OCH_2\mathit{CH_3}$), 3.39 (dt, 1H, $J_{5\text{-}6B}$= 4.8 Hz, $J_{5\text{-}4}$=$J_{5\text{-}6A}$= 10.3 Hz, H-5), 3.44 (s, 3H, OMe), 3.46-3.56 (m, 5H, $O\mathit{CH_2}CH_3$, H-6A, H-8A, H-8B), 4.01 (d, 1H, $J_{4\text{-}5}$= 10.3 Hz, H-4), 4.08 (dd, 1H, $J_{5\text{-}6B}$=4.8 Hz, $J_{6A\text{-}6B}$= 10.3 Hz, H-6B), 4.08 (d, 1H, $J_{1\text{-}2}$= 4.0 Hz, H-2), 4.56 (d, 1H, $J_{1\text{-}2}$= 4.0 Hz, H-1), 5.11 (t, 1H, $J_{7\text{-}8A}$=$J_{7\text{-}8B}$= 4.8 Hz, H-7), 7.52-7.56 (m, 2H, Ph), 7.64-7.69 (m, 1H, Ph), 7.90-7.92 (m, 2H, Ph), 7.98 (brs, 1H, NH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 15.3 ($OCH_2\mathit{CH_3}$), 56.8 (OMe), 59.4 ($O\mathit{CH_2}CH_3$), 59.5 (C-8), 64.3 (C-5), 68.6 (C-6), 78.1 (C-4), 85.3 (C-2), 90.5 (C-3), 97.3 (C-7), 100.9 (C-1), 128.4, 129.2,

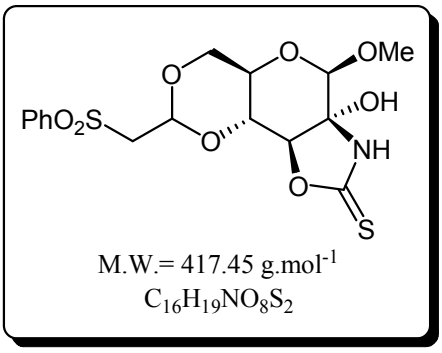
134.1 (CH-Ph), 139.9 (Cq-Ph), 188.9 (C=S); **HRMS**: calcd. for $C_{18}H_{23}NO_8S_2Na$ $[M+Na]^+$ 468.0763, found 468.0765.

[99] Silva, S.; Simão, A. C.; Tatibouët, A.; Rollin, P.; Rauter, A. P. *Tetrahedron Lett*. **2008**, *49*, 682-686.

4,5-dihydro{methyl [3-deoxy-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[2,3-d]-1,3-oxazoline-2-thione (60)

PROCEDURE

Ketone **57** (1.31 g, 2.77 mmol) and KSCN (0.40 g, 4.16 mmol) were dissolved in DMF/THF (4 mL/ 16 mL). After cooling at –5°C, $TsOH.H_2O$ (1.05 g, 5.54 mmol) was carefully added and the mixture was stirred overnight under reflux, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 50 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (Cy/EtOAc 6:4) to afford compound **60** (1.02 g, **88% yield**) as a white solid.



M.W.= 417.45 g.mol^{-1}
$C_{16}H_{19}NO_8S_2$

Rf = 0.1 (Cy/EtOAc 6:4); $[\alpha]_D$ = - 118 (C= 1.0, $CHCl_3$); **mp**: 74-75 °C; **I.R.** (NaCl) ν (cm^{-1}) 3500 (OH), 3194 (NH), 2989, 2945 (CH), 1477, 1456 (Ph), 1508, 1073 (N-CS-O), 1370, 1305 (SO_2), 789, 723; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.36 (dt, 1H, $J_{5\text{-}6A}$= 5.1 Hz, $J_{5\text{-}6B}$= 9.9 Hz, $J_{5\text{-}4}$= 10.0 Hz, H-5), 3.47-3.51 (m, 2H, H-8), 3.54 (s, 1H, Me), 3.55-3.57 (m, 2H, H-6B, H-4), 4.20 (dd, 1H, $J_{6A\text{-}6B}$= 10.7 Hz, $J_{5\text{-}6A}$= 5.1 Hz, H-6A), 4.52 (d, 1H, $J_{3\text{-}4}$= 7.5 Hz, H-3), 4.62 (s, 1H, H-1), 4.86 (brs, 1H, O-H), 5.00 (t, 1H, $J_{7\text{-}8A}$= $J_{7\text{-}8B}$= 5.0 Hz, H-7), 7.60-7.63 (m, 2H, Ph), 7.66-7.70 (m, 1H, Ph), 7.91-7.93 (m, 2H, Ph), 8.11 (brs, 1H, N-H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 57.9 (OMe), 59.7 (C-8), 63.3 (C-5), 68.4. (C-6), 78.8 (C-4), 87.3 (C-3), 88.1 (C-2), 97.1 (C-7), 101.9 (C-1), 128.6, 129.5, 134.3 (CH-Ph), 139.2 (Cq-Ph), 189.0 (C=S); **HRMS**: calcd. for $C_{16}H_{20}NO_8S_2$ $[M+H]^+$ 418.0630, found 418.0636.

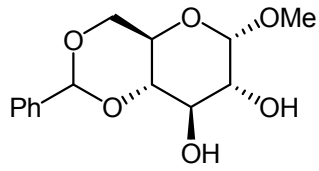
[99] Silva, S.; Simão, A. C.; Tatibouët, A.; Rollin, P.; Rauter, A. P. *Tetrahedron Lett*. **2008**, *49*, 682-686.

Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (61)

PROCEDURE

Methyl α-D-glucopyranoside (15.00 g, 77.24 mmol) was dissolved in DMF (120 mL). $PhCH(OMe)_2$ (13.4 mL, 88.8 mmol) and CSA (360 mg, 1.50 mmol) were added and the reaction was stirred at room temperature during 24 h. After extraction with ethyl acetate (3 x 250 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, compound **61** (22.54 g, **81% yield**)) as white solid.

CAS [3162-96-7]



M.W.= 282.30 g.mol^{-1}
$C_{14}H_{18}O_6$

Rf = 0.5 (DCM/PE 9:1); $[\alpha]_D$ = + 108 (C=1.2, $CHCl_3$); **mp**: 157-158 °C; **MS** (IS): m/z = 283.0 $[M+H]^+$; 305.0 $[M+Na]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 2.84 (brs, 1H, OH-3), 3.36-3.48 (m, 5H, H-5, H-6A, OMe), 3.57 (brs, 1H, OH-2), 3.70 (ft, 1H, $J_{4\text{-}5}$= 10.3 Hz, $J_{4\text{-}3}$= 9.2 Hz, H-4), 3.75 (dd, 1H, $J_{2\text{-}3}$ = 9.4 Hz, $J_{2\text{-}1}$= 4.0 Hz, H-2), 3.89 (ft, 1H, $J_{3\text{-}2}$ = 9.4 Hz, $J_{3\text{-}4}$= 9.2 Hz, H-3), 4.25 (dd, 1H, $J_{6A\text{-}6B}$= 9.4 Hz, $J_{5\text{-}6B}$= 3.8 Hz, H-6B), 4.72 (d, 1H, $J_{1\text{-}2}$ =4.0 Hz, H-1), 5.49 (s, 1H, H-7), 7.30-7.40 (m, 3H, Ph), 7.40-7.55 (m, 2H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 55.6 (OMe), 62.5 (C-5), 69.0 (C-6), 71.7 (C-3), 72.9 (C-2), 81.0 (C-4), 99.9 (C-1), 102.0 (C-7), 126.4, 128.3, 129.3 (CH-Ph), 137.2 (Cq-Ph).

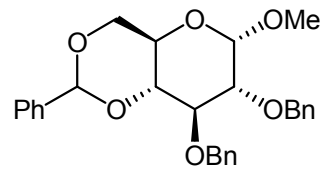
[119] Boulineau, F. P.; Wei, A. *J. Org. Chem*. **2004**, *69*, 3391-3399.

Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (62)

PROCEDURE

Compound **61** (4.45 g, 15.77 mmol) was dissolved in dry DMF (50 mL) and after cooling at -5ºC, NaH 60% dispersion in oil (2.52 g, 63.08 mmol) was added. After stirring the reaction until release of H_2 stopped, BnBr (6.60 mL, 55.3 mmol) was added dropwise. The reaction was stirred during one night at room temperature, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 75 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **62** quantitatively, as a white solid.

CAS [78738-75-7]



M.W.= 462.53 g.mol^{-1}
$C_{28}H_{30}O_6$

Rf = 0.4 (PE/EtOAc 8:2); $[\alpha]_D$ = - 18 (C=1.2, $CHCl_3$); **mp**: 82-83 °C; **MS** (IS): m/z = 463.0 $[M+H]^+$; 485.5 $[M+Na]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 3.38 (s, 3H, OMe), 3.55 (dd, 1H, $J_{2\text{-}3}$= 9.4 Hz, $J_{1\text{-}2}$= 3.8 Hz, H-2), 3.59 (ft, 1H, $J_{2\text{-}3}$= 9.4 Hz, $J_{3\text{-}4}$= 9.2 Hz, H-3), 3.68 (ft, 1H, $J_{6A\text{-}6B}$= 10.0 Hz, $J_{5\text{-}6A}$= 9.8 Hz, H-6A), 3,82 (ftd, 1H, $J_{5\text{-}6A}$ =9.8 Hz, $J_{4\text{-}5}$= 9.5 Hz, $J_{5\text{-}6B}$ = 4.5 Hz), 4.05 (ft, 1H, $J_{4\text{-}5}$= 9.5 Hz, $J_{3\text{-}4}$ = 9.2 Hz, H-4), 4.25 (dd, 1H, $J_{6A\text{-}6B}$= 10.0 Hz, $J_{5\text{-}6B}$= 4.5 Hz, H-6B), 4.59 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-1), 4.68 (d, 1H, $J_{A\text{-}B}$= 12.1 Hz, O*C*H_2Ph), 4.83 (d, 1H,$J_{A\text{-}B}$= 11.3 Hz, OCH_2Ph), 4,84 (d, 1H, $J_{A\text{-}B}$= 12.1 Hz, O*C*H_2Ph), 4,92 (d, 1H,$J_{A\text{-}B}$= 11.3 Hz, OCH_2Ph), 5.53 (s, 1H, H-7), 7.20-7.40 (m, 13H, Ph), 7.45-7.55 (m, 2H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 55.4 (OMe), 62.4 (C-5), 69.1 (C-6), 73.8, 75.4 (O*C*H_2Ph), 78.6 (C-3), 79.2 (C-2), 82.2 (C-4), 99.3 (C-1), 101.3 (C-7), 125.9, 126.1, 127.6, 127.8, 128.0, 128.2, 128.3, 128.4, 128.5, (CH-Ph), 137.5, 138.2, 138.8 (Cq-Ph).

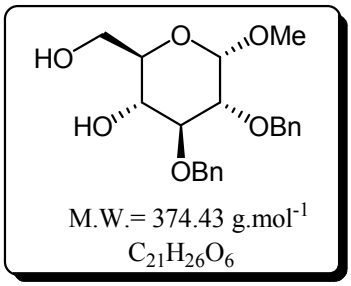
[119] Boulineau, F. P.; Wei, A. *J. Org. Chem*. **2004**, *69*, 3391-3399.

Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside (63)

PROCEDURE

Dibenzyl ether **62** (3.00 g, 6.49 mmol) was dissolved in an aqueous solution of AcOH (70%) and the reaction stirred at room temperature during 10 h. The mixture was co-evaporated with toluene (3x) and after concentration under vacuum, the residue was purified by column chromatography (Cy/EtOAc 7:3) to afford compound **63** (2.28 g, **94% yield**) as white solid.

CAS [17791-36-5]



M.W.= 374.43 g.mol^{-1}

$C_{21}H_{26}O_6$

Rf = 0.5 (Cy/EtOAc 1:1); $[\alpha]_D$ = + 22 (C=1.0, $CHCl_3$); **mp**: 73-74 °C; **MS** (IS): m/z = 375.0 $[M+H]^+$; 397.0 $[M+Na]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 2.28 (brs, 1H, OH), 2.72 (brs, 1H, OH), 3.36 (s, 3H, OMe), 3.52 (dd, 1H, $J_{2\text{-}3}$ = 9.5 Hz, $J_{1\text{-}2}$= 3.7 Hz, H-2), 3.55-3.97 (m, 5H, H-3, H-6A, H-5, H-4, H-6B), 4.63 (d, 1H, $J_{A\text{-}B}$= 11,9 Hz, O*C*H_2Ph), 4.66 (d, 1H, $J_{1\text{-}2}$ = 3.7 Hz, H-1), 4.72 (d, 1H, $J_{A\text{-}B}$ = 11.9 Hz, O*C*H_2Ph), 4.85 (d, 1H, $J_{A\text{-}B}$ = 11.3 Hz, O*C*H_2Ph), 5.01 (d, 1H, $J_{A\text{-}B}$ = 11.3 Hz, O*C*H_2Ph), 7.27-7.47 (m, 10H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 55.3 (OMe), 62.3 (C-6), 70.3 (C-5), 70.8 (C-4), 73.2, 75.5 (O*C*H_2Ph), 79.9 (C-3), 81.4 (C-2), 98.2 (C-1), 127.9, 128.0, 128.2, 128.6, 128.7, 128.9 (CH-Ph), 138.1, 138.8 (Cq-Ph).

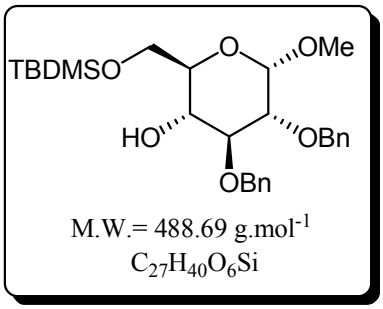
[119] Boulineau, F. P.; Wei, A. *J. Org. Chem*. **2004**, *69*, 3391-3399.

Methyl 2,3-di-*O*-benzyl-6-*O*-*tert*-butyldimethylsilyl-α-D-glucopyranoside (64)

PROCEDURE

To compound **63** (655.3 mg, 1.75 mmol) in dry DMF (10 ml) at 0ºC, were added imidazole (238.3 mg, 3.50 mmol) and TBDMSCl (290.6 mg, 1.93 mmol). The reaction was stirred at room temperature during 4 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **64** (692.7 mg, **81% yield**) as a colourless oil.

CAS [111727-15-2]



M.W.= 488.69 g.mol^{-1}
$C_{27}H_{40}O_6Si$

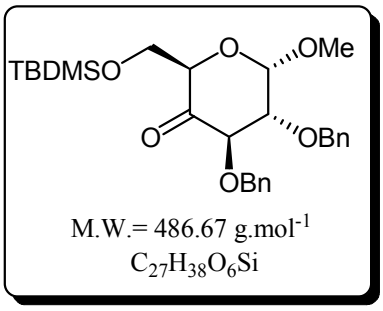
Rf = 0.7 (PE/EtOAc 7:3); $[\alpha]_D$ = - 14 (C=1.0, $CHCl_3$); **MS** (IS): m/z = 489.5 $[M+H]^+$; 511.5 $[M+Na]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 0.06 (s, 6H, $Si(CH_3)_2$), 0.88 (s, 9H, *t*-Bu), 2.62 (d, 1H, $J_{4\text{-}OH}$= 1.8 Hz, OH), 3.37 (s, 3H, OMe), 3.48 (dd, 1H, $J_{1\text{-}2}$= 3.5 Hz, $J_{2\text{-}3}$= 9.8 Hz, H-2), 3.49-3.54 (m, 2H, H-3, H-4), 3.76-3.83 (m, 3H, H-5, H-6A, H-6B), 4.61 (d, 1H, $J_{1\text{-}2}$= 3.5 Hz, H-1), 4.64 (d, 1H, $J_{A\text{-}B}$ = 11.5 Hz, OCH_2Ph), 4.76 (d, 2H, $J_{A\text{-}B}$ = 11.1 Hz, OCH_2Ph), 5.01 (d, 1H, $J_{A\text{-}B}$ = 11.5 Hz, OCH_2Ph), 7.25-7.39 (m, 10H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -4.9, -4.5 (Si $(CH_3)_2$), 21.5 (Cq, *t*-Bu), 26.3 ($(CH_3)_3C$), 55.5 (OMe), 60.8 (C-6), 71.2 (C-5), 71.9 (C-4), 73.2, 75.5 (OCH_2Ph), 80.0 (C-3), 81.9 (C-2), 98.4 (C-1), 127.7, 128.2, 128.4, 128.6, 128.8, 128.9 (CH-Ph), 138.4, 138.7 (Cq-Ph).

[118] Cervi, G.; Peri, F.; Battistini, C.; Gennari, C.; Nicotra, F. *Bioorg. Med. Chem*. **2006**, *14*, 3349-3367.

Methyl 2,3-di-*O*-benzyl-6-*O*-*tert*-butyldimethylsilyl-α-D-*xylo* hexopyranos-4-uloside (65)

PROCEDURE

Compound **64** (220.0 mg, 0.45 mmol) was dissolved in dry DCM. Dess-Martin periodinane (1.43 mL, 0.68 mmol) was added and the reaction was stirred at room temperature during 6 h, then treated by addition of 10 mL of saturated aqueous solutions of $NaHCO_3$ and $Na_2S_2O_3$. After extraction with diethyl ether (3 x 20 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 95:5) to afford compound **65** (186.2 mg, **85% yield**) as a colourless oil.



M.W.= 486.67 g.mol^{-1}
$C_{27}H_{38}O_6Si$

Rf = 0.4 (PE/EtOAc 9:1); $[\alpha]_D$= - 24 (C=0.5, $CHCl_3$); **MS** (IS): m/z = 487.5 $[M+H]^+$; 509.5 $[M+Na]^+$; **I.R.** (NaCl) ν (cm^{-1}) 2987, 2869 (CH), 1730 (C=O), 1477, 1464, 1456 (Ph), 1215 ($Si(CH_3)_2$); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 0.03 (s, 6H, $Si(CH_3)_2$), 0.79 (s, 9H, *t*-Bu), 3.40 (s, 3H, OMe), 3.69-3.76 (m, 2H, H-2, H-6B), 3.99 (dd, 1H, $J_{5\text{-}6A}$= 2.9 Hz, $J_{6A\text{-}6B}$= 11.5 Hz, H-6A), 4.06 (dd, 1H, $J_{5\text{-}6A}$= 2.9 Hz, $J_{5\text{-}6B}$= 6.5 Hz, H-5), 4.34 (d, 1H, $J_{2\text{-}3}$= 9.7 Hz, H-3), 4.58 (d, 1H, $J_{A\text{-}B}$ = 11.9 Hz, OCH_2Ph), 4.67 (d, 1H, $J_{A\text{-}B}$ = 11.9 Hz, OCH_2Ph), 4.72 (d, 1H, $J_{1\text{-}2}$= 3.5 Hz, H-1), 4.79 (d, 1H, $J_{A\text{-}B}$ = 11.5 Hz, OCH_2Ph), 4.89 (d, 1H, $J_{A\text{-}B}$ = 11.5 Hz, OCH_2Ph), 7.18-7.37 (m, 10H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -4.9, -4.5 (Si $(CH_3)_2$), 18.3 (Cq, *t*-Bu), 25.9 ($(CH_3)_3C$), 55.8 (OMe), 61.4 (C-6), 73.9 (OCH_2Ph), 74.2 (C-5), 74.3 (OCH_2Ph), 80.2 (C-2),

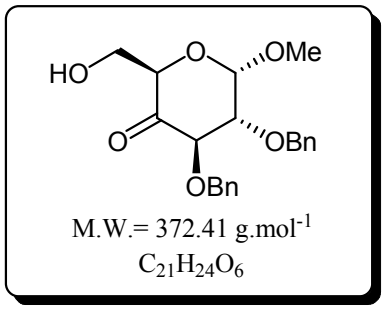
82.6 (C-3), 98.2 (C-1), 127.8, 128.1, 128.4, 128.6, 128.8, 128.9 (CH-Ph), 137.8, 137.9 (Cq-Ph), 202.6 (C=O).

Methyl 2,3-di-*O*-benzyl-α-D-*xylo*-hexopyranos-4-uloside (66)

PROCEDURE

Ketone **65** (1.34 g, 2.77 mmol) and KSCN (0.40 g, 4.16 mmol) were dissolved in EtOH (20 mL). After cooling at –5°C, 12M aqueous HCl (0.42 mL, 4.99 mmol) was carefully added and the mixture was stirred under reflux for 30 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 20 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **66** quantitatively, as a colourless oil.

CAS [223590-83-8]



M.W.= 372.41 g.mol^{-1}
$C_{21}H_{24}O_6$

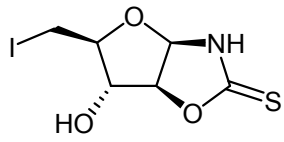
Rf = 0.3 (PE/EtOAc 1:1); $[\alpha]_D$ = + 75 (C=1.5, $CHCl_3$); **MS** (IS): m/z = 373.5 $[M+H]^+$; 395.5 $[M+Na]^+$; **I.R.** (NaCl) ν (cm^{-1}) 2985, 2861 (CH), 1732 (C=O), 1466, 1459 (Ph); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 2.38 (brs, 1H, OH), 3.47 (s, 3H, OMe), 3.79 (dd, 1H, $J_{1\text{-}2}$= 3.5 Hz, $J_{2\text{-}3}$= 10.0 Hz, H-2), 3.87-3.89 (m, 2H, H-6A, H-6B), 4.13 (ft, 1H, $J_{5\text{-}6A}$= 4.9 Hz, $J_{5\text{-}6B}$= 4.7 Hz, H-5), 4.46 (d, 1H, $J_{2\text{-}3}$= 10.0 Hz, H-3), 4.66 (d, 1H, $J_{A\text{-}B}$ = 11.5 Hz, OCH_2Ph), 4.68 (d, 1H, $J_{A\text{-}B}$ = 11.3 Hz, OCH_2Ph), 4.78 (d, 1H, $J_{1\text{-}2}$= 3.5 Hz, H-1), 4.86 (d, 1H, $J_{A\text{-}B}$ = 11.5 Hz, OCH_2Ph), 4.96 (d, 1H, $J_{A\text{-}B}$ = 11.3 Hz, OCH_2Ph), 7.29-7.45 (m, 10H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 56.2 (OMe), 60.6 (C-6), 72.9 (C-5), 74.0, 74.5 (OCH_2Ph), 80.1 (C-2), 82.6 (C-3), 98.5 (C-1), 127.8, 127.9, 128.0, 128.1, 128.4, 128.5 (CH-Ph), 137.7, 137.8 (Cq-Ph), 203.9 (C=O).

[283] Söderman, P.; Widmalm, G. J. Org. Chem. 1999, 64, 4199-4200.

4,5-dihydro-(1,2,5-trideoxy-5-iodo-β-D-arabinofuranoso) [1,2-d]-1,3-oxazoline-2-thione (67)

PROCEDURE

The arabino OZT derivative **L$_1$** (2.18 g, 11.40 mmol), triphenylphosphine (5.97 g, 22.80 mmol) and imidazole (1.55 g, 22.80 mmol) were dissolved in dry THF (30 mL). The solution was cooled at 0ºC and after 15 min, iodine (3.47 g, 13.68 mmol) was added gradually. After disappearance of the solution coloration, the mixture was stirred at room temperature overnight. The solvent was evaporated under vacuum and the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **67** (3.30 g, **96% yield**) as a white solid.



M.W.= 301.10 g.mol^{-1}
$C_6H_8INO_3S$

Rf = 0.3 (PE/EtOAc 1:1); $[\alpha]_D$ = - 24 (C=0.5, $CHCl_3$); **mp**: 168-170 °C; **I.R.** (NaCl) ν (cm^{-1}) 3500 (OH), 3155 (NH), 2950, 2925, 2858 (CH), 1480, 1311, 1027 (N-CS-O), 609 (C-I); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.09-3.22 (m, 2H, H-5A, H-5B), 4.04 (td, 1H, $J_{3\text{-}4}$= 1.7 Hz, $J_{4\text{-}5A}$= $J_{4\text{-}5B}$= 7.1 Hz, H-4), 4.25 (brs, 1H, H-3), 5.11 (d, 1H, $J_{1\text{-}2}$= 5.6 Hz, H-2), 5.88 (d, 1H, $J_{1\text{-}2}$= 5.6 Hz, H-1), 5.97 (d, 1H, $J_{3\text{-}OH}$= 4.2 Hz, OH), 11.00 (brs, 1H, NH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 6.2 (C-5), 76.3 (C-3), 85.4 (C-4), 89.5 (C-1), 91.1 (C-2), 188.0 (C=S); **HRMS**: calcd. for $C_6H_9INO_3S$ $[M+H]^+$ 302.9348, found 302.9349.

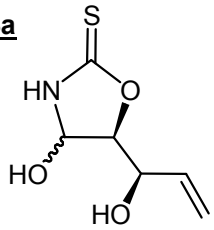
4,5-dihydro-4-hydroxy-5-[(1*R*)-1-hydroxy-prop-2-en-1-yl]-1,3-oxazoline-2-thione (68a) and (68b)

PROCEDURE

To a solution of compound **67** (110.0 mg, 0.37 mmol) in acetic acid (5 mL), was added activated zinc dust (169.4 mg, 2.59 mmol). The reaction was stirred during 1.5 h at room temperature, then filtered through cotton to discard zinc. The residue was co-evaporated with toluene (3x) and after concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford the epimeric hydrated OXTs **68a** and **68b** (53.16 mg, **82% yield**) as colourless oils, in a proportion **68a**/**68b**: 86/14.

For both isomers:
Rf = 0.2 (PE/EtOAc 1:1); **HRMS**: calcd. for $C_6H_{10}NO_3S$ $[M+H]^+$ 176.0381, found 176.0383.

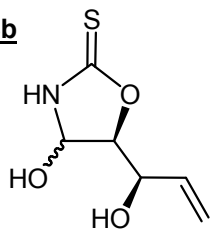
68a



M.W.= 175.21 g.mol^{-1}
$C_6H_9NO_3S$

^{1}H NMR (400 MHz, DMSO) δ 4.20-4.26 (m, 1H, H-6), 4.39 (dd, 1H, $J_{4\text{-}5}$= 2.6 Hz, $J_{5\text{-}6}$= 4.6 Hz, H-5), 4.60 (d, 1H, $J_{4\text{-}5}$= 2.6 Hz, H-4), 5.12 (dt, 1H, $J_{8Z\text{-}8E}$= 1.6 Hz, $J_{7\text{-}8Z}$= 10.7 Hz, H-8Z), 5.33 (dt, 1H, $J_{8Z\text{-}8E}$= $J_{6\text{-}8E}$= 1.6 Hz, $J_{7\text{-}8E}$= 17.2 Hz, H-8E), 5.73 (brs, 2H, OH), 5.78 (ddd, 1H, $J_{6\text{-}7}$= 5.5 Hz, $J_{7\text{-}8Z}$= 10.7. Hz, $J_{7\text{-}8E}$= 17.2. Hz, H-7), 9.19 (brs, 1H, NH); **^{13}C NMR** (100 MHz, DMSO) δ 81.2 (C-6), 91.2 (C-4), 102.1 (C-5), 127.3 (C-8), 146.0 (C-7), 199.7 (C=S).

68b



M.W.= 175.21 g.mol^{-1}
$C_6H_9NO_3S$

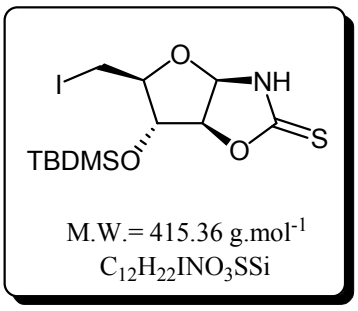
^{1}H NMR (400 MHz, DMSO) δ 4.16-4.20 (m, 1H, H-6), 4.42 (dd, 1H, $J_{4\text{-}5}$= 3.1 Hz, $J_{5\text{-}6}$= 4.7 Hz, H-5), 4.53-4.55 (m, 1H, H-4), 5.15 (dt, 1H, $J_{8Z\text{-}8E}$= 1.9 Hz, $J_{7\text{-}8Z}$= 10.7 Hz, H-8Z), 5.39 (dt, 1H, $J_{8Z\text{-}8E}$= $J_{6\text{-}8E}$= 1.9 Hz, $J_{7\text{-}8E}$= 17.2 Hz, H-8E), 5.95 (ddd, 1H, $J_{6\text{-}7}$= 4.6 Hz, $J_{7\text{-}8Z}$= 10.7. Hz, $J_{7\text{-}8E}$= 17.2. Hz, H-7), 9.21 (brs, 1H, NH); **^{13}C**

NMR (100 MHz, DMSO) δ 79.7 (C-6), 90.4 (C-4), 98.4 (C-5), 126.7 (C-8), 146.7 (C-7), 200.0 (C=S).

4,5-dihydro-(1,2,5-trideoxy-5-iodo-3-*tert*-butyldimethylsilyl-β-D-arabinofuranoso) [1,2-d]-1,3-oxazoline-2-thione (69)

PROCEDURE

To the iodo derivative **67** (114.4 mg, 0.38 mmol) in dry DMF (10 ml) at 0ºC, were added imidazole (51.7 mg, 0.76 mmol) and TBDMSCl (85.8 mg, 0.57 mmol). The reaction was stirred at room temperature during 5 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 20 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compound **69** (146.8 mg, **93% yield**) as a white solid**.**



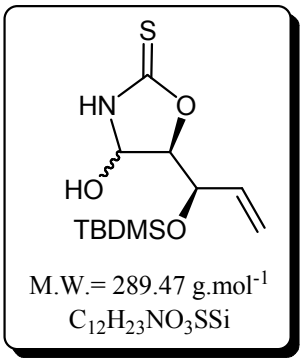
M.W.= 415.36 g.mol^{-1}
$C_{12}H_{22}INO_3SSi$

Rf = 0.3 (PE/EtOAc 8:2); $[\alpha]_D$ = - 53 (C=0.7, $CHCl_3$); **mp**: 112-113 °C; **I.R.** (NaCl) ν (cm^{-1}) 3224 (NH), 2980, 2956, 2920 (CH), 1479, 1319, 1024 (N-CS-O), 1220 ($Si(CH_3)_2$), 609 (C-I); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.17 (s, 6H, $Si(CH_3)_2$), 0.89 (s, 9H, *t*-Bu), 3.09 (t, 1H, J_{5A-5B}= J_{4-5B}= 10.0 Hz, H-5B), 3.22 (dd, 1H, J_{4-5A}= 5.6 Hz, J_{5A-5B}= 10.0 Hz, H-5A), 4.24 (dd, 1H, J_{4-5A}= 5.6 Hz, J_{4-5B}= 10.0 Hz, H-4), 4.58 (s, 1H, H-3), 5.03 (d, 1H, J_{1-2}= 5.3 Hz, H-2), 5.93 (d, 1H, J_{1-2}= 5.3 Hz, H-1), 8.10 (brs, 1H, NH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.6, -4.4 (Si $(CH_3)_2$), 4.1 (C-5), 18.0 (Cq, *t*-Bu), 25.7 ($(CH_3)_3C$), 77.7 (C-3), 87.6 (C-4), 89.8 (C-1), 92.6 (C-2), 188.7 (C=S); **HRMS**: calcd. for $C_{12}H_{23}INO_3SSi$ $[M+H]^+$ 416.0213, found 416.0213.

4,5-dihydro-4-hydroxy-5-[(1*R*)-1-*tert*-butyldimethylsilyloxy-prop-2-en-1-yl]-1,3-oxazoline-2-thione (70)

PROCEDURE

To a solution of compound **69** (153.7 mg, 0.37 mmol) in acetic acid (5 mL), was added activated zinc dust (169.4 mg, 2.59 mmol). The reaction was stirred during 1 h at room temperature, then filtered through cotton to discard zinc. The residue was co-evaporated with toluene (3x) and after concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compound **70** (92.1 mg, **86% yield**) as a yellow oil.



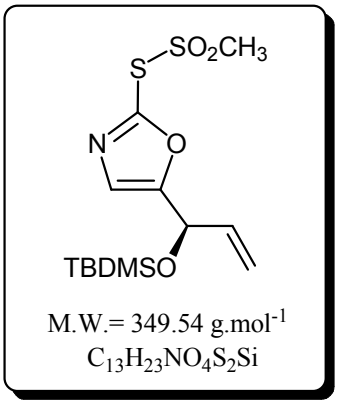
M.W.= 289.47 g.mol^{-1}
$C_{12}H_{23}NO_3SSi$

Rf = 0.3 (PE/EtOAc 8:2); $[\alpha]_D$= - 30 (C=1.0, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3488 (OH), 3224 (NH), 2950, 2925, 2853 (CH), 1640 (C=C), 1480, 1345, 1030 (N-CS-O), 1220 ($Si(CH_3)_2$); **^{1}H NMR** (400 MHz, DMSO) δ 0.10 (s, 6H, $Si(CH_3)_2$), 0.90 (s, 9H, *t*-Bu), 3.49 (brs, 1H, OH), 4.42-4.44 (m, 1H, H-6), 4.59 (dd, 1H, $J_{4\text{-}5}$= 2.3 Hz, $J_{5\text{-}6}$= 4.6 Hz, H-5), 5.30 (dt, 1H, $J_{8Z\text{-}8E}$= 1.3 Hz, $J_{7\text{-}8Z}$= 10.7 Hz, H-8Z), 5.34 (d, 1H, $J_{4\text{-}5}$= 2.3 Hz, H-4), 5.42 (dt, 1H, $J_{8Z\text{-}8E}$= $J_{6\text{-}8E}$= 1.3 Hz, $J_{7\text{-}8E}$= 17.2 Hz, H-8E), 5.82 (ddd, 1H, $J_{6\text{-}7}$= 5.6 Hz, $J_{7\text{-}8Z}$= 10.7. Hz, $J_{7\text{-}8E}$= 17.2. Hz, H-7), 7.75 (brs, 1H, NH); **^{13}C NMR** (100 MHz, DMSO) δ -4.9, -4.3 (Si $(CH_3)_2$), 18.2 (Cq, *t*-Bu), 25.8 ($(CH_3)_3C$), 71.7 (C-6), 80.9 (C-4), 92.1 (C-5), 119.0 (C-8), 134.1 (C-7), 189.4 (C=S); **HRMS**: calcd. for $C_{12}H_{24}NO_3SSi$ $[M+H]^+$ 290.1246, found 290.1255.

2-methanothiosulfonate-5-[(1*R*)-1-*tert*-butyldimethylsilyloxy-prop-2-en-1-yl]-1,3-oxazole (71)

PROCEDURE

Compound **70** (503.7 mg, 1.74 mmol) was dissolved in dry DCM (5 mL). Triethylamine (0.99 mL, 6.96 mmol) and methanesulfonyl chloride (0.40 mL, 5.22 mmol) were successively added and the reaction stirred during 45 min. at room temperature. The reaction mixture was quenched by treating with crushed ice. After extraction with DCM (3 x 25 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **71** (553.5 mg, **91% yield**) as a yellow oil.



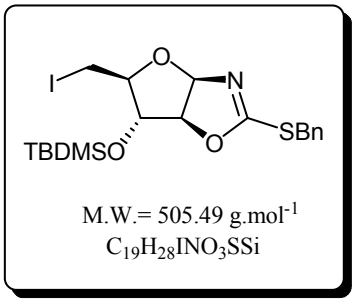
M.W.= 349.54 g.mol^{-1}
$C_{13}H_{23}NO_4S_2Si$

Rf = 0.3 (PE/EtOAc 8:2); **MS** (IS): m/z = 350.5 $[M+H]^+$, 367.5 $[M+NH_4]^+$, 372.5 $[M+Na]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 0.10 (s, 6H, $Si(CH_3)_2$), 0.92 (s, 9H, *t*-Bu), 3.54 (s, 3H, $MeSO_2$), 5.29 (d, 1H, $J_{6\text{-}7}$= 5.6 Hz, H-6), 5.31 (dt, 1H, $J_{8Z\text{-}8E}$= 1.4 Hz, $J_{7\text{-}8Z}$= 9.6 Hz, H-8Z), 5.45 (dt, 1H, $J_{8Z\text{-}8E}$= $J_{6\text{-}8E}$= 1.4 Hz, $J_{7\text{-}8E}$= 16.8 Hz, H-8E), 5.98 (ddd, 1H, $J_{6\text{-}7}$= 5.6 Hz, $J_{7\text{-}8Z}$= 9.6 Hz, $J_{7\text{-}8E}$= 16.8. Hz, H-7), 7.16 (brs, 1H, H-4); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -4.9, -4.3 (Si $(CH_3)_2$), 18.4 (Cq, *t*-Bu), 25.8 ($(CH_3)_3C$), 49.8 (CH_3SO_2), 62.2 (C-6), 117.4 (C-8), 127.2 (C-4), 136.1 (C-7), 151.0 (C-2), 159.2 (C-5).

2-Benzylsulfanyl-4,5-dihydro-(1,2,5-trideoxy-5-iodo-3-*tert*-butyldimethylsilyl-β-D-arabinofuranoso)[1,2-d]-1,3-oxazole (72)

PROCEDURE

To the iodo derivative **69** (300.0 mg, 0.72 mmol) in dry DCM (10 ml), were added Et_3N (0.12 mL, 0.86 mmol) and BnBr (0.13 mL, 1.08 mmol). The reaction was stirred during 3 h at room temperature, then cooled by treating with crushed ice. After extraction with DCM (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 95:5) to afford compound 72 (360.3 mg, **99% yield**) as a colourless oil**.**



M.W.= 505.49 g.mol^{-1}
$C_{19}H_{28}INO_3SSi$

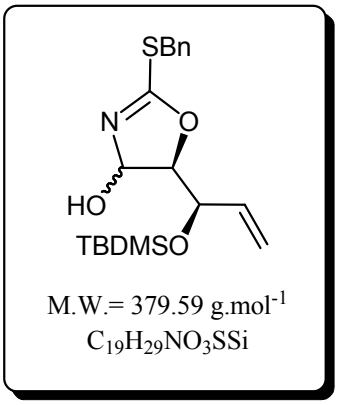
Rf = 0.4 (PE/EtOAc 9:1); $[\alpha]_D$ = - 59 (C=0.9, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2961, 2925, 2848 (CH), 1594, 1037 (-N=CS-O), 1461, 1458 (Ph), 1251 ($Si(CH_3)_2$), 698 (C-I); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 0.10 (s, 6H, $Si(CH_3)_2$), 0.74 (s, 9H, *t*-Bu), 2.73 (dd, 1H, $J_{4\text{-}5B}$= 9.4 Hz, $J_{5A\text{-}5B}$= 10.3 Hz, H-5B), 2.91 (dd, 1H, $J_{4\text{-}5A}$= 4.9 Hz, $J_{5A\text{-}5B}$= 10.3 Hz, H-5A), 3.88 (ddd, 1H, $J_{3\text{-}4}$= 2.6 Hz, $J_{4\text{-}5A}$= 4.9. Hz, $J_{5\text{-}5B}$= 9.4 Hz, H-4), 4.01 (d, 1H, $J_{A\text{-}B}$= 13.3 Hz, SCH_2Ph), 4.14 (d, 1H, $J_{A\text{-}B}$= 13.3 Hz, SCH_2Ph), 4.17 (brs, 1H, H-3), 4.60 (dd, 1H, $J_{1\text{-}2}$= 5.9 Hz, $J_{2\text{-}3}$= 1.1 Hz, H-2), 5.96 (d, 1H, $J_{1\text{-}2}$= 5.9 Hz, H-1), 7.10-7.23 (m, 5H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -4.6, -4.5 (Si $(CH_3)_2$), 5.2 (C-5), 18.0 (Cq, *t*-Bu), 25.8 ($(CH_3)_3C$), 36.6 (SCH_2Ph), 79.4 (C-3), 85.7 (C-4), 90.8 (C-2), 101.1 (C-1), 127.9, 128.8, 129.2 (CH-Ph), 136.4 (Cq-Ph), 169.9 (C-SBn); **HRMS**: calcd. for $C_{19}H_{29}INO_3SSi$ $[M+H]^+$ 506.0682, found 506.0695.

2-Benzylsulfanyl-4,5-dihydro-4-hydroxy-5-[(1*R*)-1-*tert*-butyldimethylsilyloxy-prop-2-en-1-yl]-1,3-oxazole (73)

(73)

PROCEDURE

To a solution of compound 72 (187.0 mg, 0.37 mmol) in acetic acid (5 mL), was added activated zinc dust (169.4 mg, 2.59 mmol). The reaction was stirred during 1 h at room temperature, then filtered through cotton to discard zinc. The residue was co-evaporated with toluene (3x) and after concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compound 73 (120.8 mg, **86% yield**) as a yellow oil.



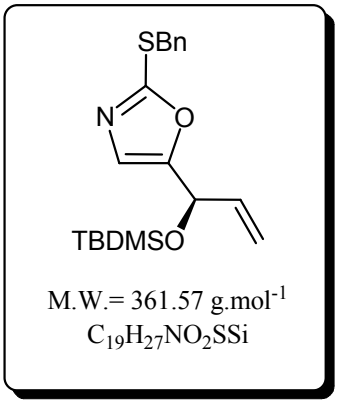
M.W.= 379.59 g.mol^{-1}
$C_{19}H_{29}NO_3SSi$

Rf = 0.4 (PE/EtOAc 8:2); $[\alpha]_D$ = - 52 (C=0.5 $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3488 (OH), 2950, 2925, 2853 (CH), 1635 (C=C), 1584, 1030, 697 (-N=CS-O), 1468, 1466 (Ph), 1220 ($Si(CH_3)_2$); **^{1}H NMR** (400 MHz, DMSO) δ 0.08 (s, 6H, $Si(CH_3)_2$), 0.89 (s, 9H, *t*-Bu), 4.23 (s, 2H, SCH_2Ph), 4.25-4.28 (m, 1H, H-6), 4.33 (dd, 1H, $J_{4\text{-}5}$= 3.5 Hz, $J_{5\text{-}6}$= 4.6 Hz, H-5), 5.20 (dt, 1H, $J_{8Z\text{-}8E}$= 1.4 Hz, $J_{7\text{-}8Z}$= 10.4 Hz, H-8Z), 5.31 (dt, 1H, $J_{8Z\text{-}8E}$= $J_{6\text{-}8E}$= 1.4 Hz, $J_{7\text{-}8E}$= 17.2 Hz, H-8E), 5.53 (d, 1H, $J_{4\text{-}5}$= 3.5 Hz, H-4), 5.76 (ddd, 1H, $J_{6\text{-}7}$= 6.3 Hz, $J_{7\text{-}8Z}$= 10.4 Hz, $J_{7\text{-}8E}$= 17.2 Hz, H-7), 7.26-7.37 (m, 5H, Ph); **^{13}C NMR** (100 MHz, DMSO) δ -4.9, -4.3 (Si $(CH_3)_2$), 18.3 (Cq, *t*-Bu), 25.8 ($(CH_3)_3C$), 36.3 (SCH_2Ph), 73.1 (C-6), 90.2 (C-5), 91.0 (C-4), 117.8 (C-8), 127.8, 128.8, 129.2 (CH-Ph), 135.7 (C-7), 135.9 (Cq-Ph), 170.0 (C-2); **HRMS**: calcd. for $C_{19}H_{30}NO_3SSi$ $[M+H]^+$ 380.1716, found 380.1719.

2-Benzylsulfanyl-5-[(1*R*)-1-*tert*-butyldimethylsilyloxy-prop-2-en-1-yl]-1,3-oxazole (74)

PROCEDURE

Compound **73** (660.5 mg, 1.74 mmol) was dissolved in dry DCM (8 mL). Triethylamine (0.99 mL, 6.96 mmol) and methanesulfonyl chloride (0.40 mL, 5.22 mmol) were successively added and the reaction stirred during 45 min at room temperature. The reaction mixture was quenched by treating with crushed ice. After extraction with DCM (3 x 25 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 95:5) to afford compound **74** (484.4 mg, **77% yield**) as a yellow oil.



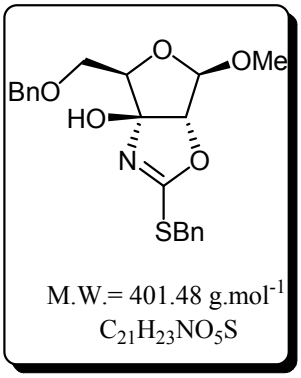
M.W.= 361.57 g.mol^{-1}
$C_{19}H_{27}NO_2SSi$

Rf = 0.3 (PE/EtOAc 9:1); $[\alpha]_D$ = - 67 (C=1.1 $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}), 2950, 2930, 2884 (CH), 1671, 1638 (C=C), 1580, 1027, 696 (-N=CS-O), 1456, 1454 (Ph), 1230 ($Si(CH_3)_2$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.10 (s, 6H, $Si(CH_3)_2$), 0.84 (s, 9H, t-Bu), 4.29 (s, 2H, SCH_2Ph), 5.12-5.14 (m, 1H, $J_{6\text{-}7}$= 5.4 Hz, $J_{6\text{-}8E}$= 1.4 Hz, H-6), 5.17 (dt, 1H, $J_{8Z\text{-}8E}$= 1.4 Hz, $J_{7\text{-}8Z}$= 10.3 Hz, H-8Z), 5.35 (dt, 1H, $J_{8Z\text{-}8E}$= $J_{6\text{-}8E}$= 1.4 Hz, $J_{7\text{-}8E}$= 17.1 Hz, H-8E), 5.90 (ddd, 1H, $J_{6\text{-}7}$= 5.4 Hz, $J_{7\text{-}8Z}$= 10.3 Hz, $J_{7\text{-}8E}$= 17.1 Hz, H-7), 6.79 (d, 1H, $J_{4\text{-}6}$= 0.6 Hz, H-4), 7.18-7.31 (m, 5H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.8, -4.7 (Si $(CH_3)_2$), 18.4 (Cq, *t*-Bu), 25.8 ($(CH_3)_3C$), 37.0 (sCH_2Ph), 67.8 (C-6), 116.4 (C-8), 124.7 (C-7), 127.8, 128.7, 129.0 (CH-Ph), 136.6 (Cq-Ph), 136.7 (C-7), 154.5 (C-5), 159.6 (C-2); **HRMS**: calcd. for $C_{19}H_{28}NO_2SSi$ $[M+H]^+$ 362.1610, found 362.1611.

2-Benzylsulfanyl-4,5-dihydro[methyl (2-deoxy-5-*O*-benzyl-β-D-xylofuranosid}[3,2-d]-1,3-oxazole (75)

PROCEDURE

To OZT **33** (224.2 mg, 0.72 mmol) in dry DCM (10 ml), were added Et_3N (0.12 mL, 0.86 mmol) and BnBr (0.13 mL, 1.08 mmol). The reaction stirred during 3 h at room temperature, then cooled by treating with crushed ice. After extraction with DCM (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compound **75** (248.6 mg, **86% yield**) as a yellow solid**.**

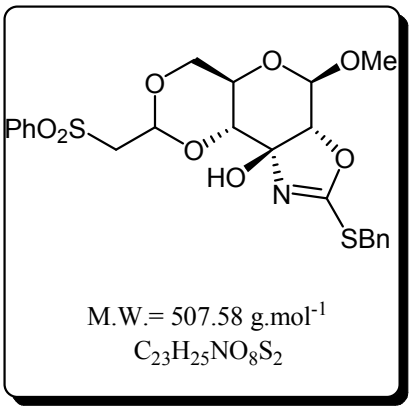


Rf = 0.3 (PE/EtOAc 9:1); $[\alpha]_D$ = - 58 (C=1.5, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3489 (OH), 3022, 2935 (CH), 1578, 1092, 691 (-N=CS-O), 1492, 1456 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.32 (s, 3H, OMe), 3.69 (dd, 1H, $J_{4\text{-}5A}$= 6.1 Hz, $J_{5A\text{-}5B}$= 9.7 Hz, H-5A), 3.93 (dd, 1H, $J_{4\text{-}5B}$= 8.2 Hz, $J_{5A\text{-}5B}$= 9.7 Hz, H-5B), 4.22-4.27 (m, 2H, S*CH*$_2$Ph), 4.32 (dd, 1H, $J_{4\text{-}5A}$= 6.1 Hz, $J_{4\text{-}5B}$= 8.2 Hz, H-4), 4.54 (d, 1H, $J_{A\text{-}B}$= 11.9 Hz, O*CH*$_2$Ph), 4.60 (d, 1H, $J_{A\text{-}B}$= 11.9 Hz, O*CH*$_2$Ph), 4.66 (s, 1H, H-2), 4.87 (s, 1H, H-1), 5.16 (brs, 1H, OH), 7.24-7.33 (m, 10H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 36.5 (S*CH*$_2$Ph), 55.0 (OMe), 70.5 (C-5), 73.6 (O*CH*$_2$Ph), 84.3 (C-4), 92.5 (C-2), 107.8 (C-1), 108.0 (C-3), 127.8, 127.8, 127.9, 128.5, 128.7, 129.0 (CH-Ph), 135.8, 137.5 (Cq-Ph), 168.1 (C-SBn); **HRMS**: calcd. for $C_{21}H_{24}NO_5S$ $[M+H]^+$ 402.1375, found 402.1372.

2-Benzylsulfanyl-4,5-dihydro{methyl [2-deoxy-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[3,2-d]-1,3-oxazole(76)

PROCEDURE

To OZT **58** (300.5 mg, 0.72 mmol) in dry DCM (10 ml), were added Et_3N (0.12 mL, 0.86 mmol) and BnBr (0.13 mL, 1.08 mmol). The reaction was stirred during 3 h at room temperature, then cooled by treating with crushed ice. After extraction with DCM (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **76** (204.7 mg, **56% yield**) as a yellow oil.



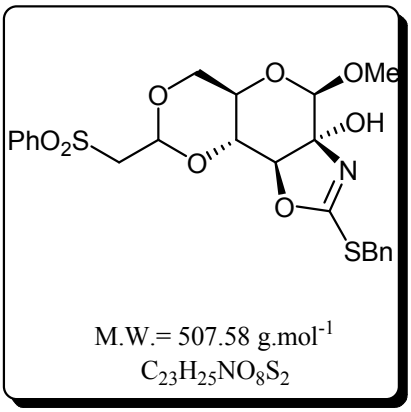
M.W.= 507.58 g.mol^{-1}
$C_{23}H_{25}NO_8S_2$

Rf = 0.6 (Cy/EtOAc 4:6); $[\alpha]_D$ = - 18 (C=0.4, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3485 (OH), 2996, 2935 (CH), 1574, 1074, 696 (-N=CS-O), 1476, 1458 (Ph), 1367, 1309 (SO_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.12 (brs, 1H, OH), 3.27 (dt, 1H, $J_{4\text{-}5}$=$J_{5\text{-}6A}$= 10.2 Hz, $J_{5\text{-}6B}$= 4.9 Hz, H-5), 3.40 (s, 3H, OMe), 3.45 (t, 1H, $J_{5\text{-}6A}$=$J_{6A\text{-}6B}$= 10.2 Hz, H-6A), 3.53 (dd, 1H, $J_{7\text{-}8A}$= 4.8 Hz, $J_{8A\text{-}8B}$= 14.8 Hz, H-8A), 3.65 (dd, 1H, $J_{7\text{-}8B}$= 4.8 Hz, $J_{8A\text{-}8B}$=14.8 Hz, H-8B), 4.04 (dd, 1H, $J_{5\text{-}6B}$= 4.9 Hz, $J_{6A\text{-}6B}$= 10.2 Hz, H-6B), 4.16-4.19 (m, 2H, H-4, SCH_2Ph), 4.26 (d, 1H, $J_{A\text{-}B}$= 13.6 Hz, SCH_2Ph), 4.39 (d, 1H, $J_{1\text{-}2}$= 3.0 Hz, H-2), 4.49 (d, 1H, $J_{1\text{-}2}$= 3.0 Hz, H-1), 5.11 (t, 1H, $J_{7\text{-}8A}$= $J_{7\text{-}8B}$= 4.8 Hz, H-7), 7.25-7.66 (m, 8H, Ph), 7.93-7.95 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 36.3 (SCH_2Ph), 56.2 (OMe), 59.8 (C-8), 64.5 (C-5), 69.5 (C-6), 78.8 (C-4), 86.4 (C-2), 95.5 (C-3), 97.6 (C-7), 100.1 (C-1), 127.8, 128.3, 128.7, 129.0, 129.1, 133.9 (CH-Ph), 136.5, 139.9 (Cq-Ph), 170.0 (C-SBn); **HRMS**: calcd. for $C_{23}H_{26}NO_8S_2$ $[M+H]^+$ 508.1100, found 508.1081.

2-Benzylsulfanyl-4,5-dihydro{methyl [3-deoxy-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[2,3-d]-1,3-oxazole(77)

PROCEDURE

To OZT **60** (300.5 mg, 0.72 mmol) in dry DCM (10 ml), were added Et_3N (0.12 mL, 0.86 mmol) and BnBr (0.13 mL, 1.08 mmol). The reaction was stirred during 3 h at room temperature, then cooled by treating with crushed ice. After extraction with DCM (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **77** (288.7 mg, **79% yield**) as a yellow oil.



M.W.= 507.58 g.mol^{-1}
$C_{23}H_{25}NO_8S_2$

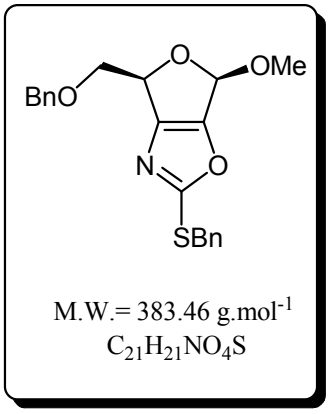
Rf = 0.6 (PE/EtOAc 4:6); $[\alpha]_D$ = - 90 (C=1.0, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3485 (OH), 3023, 2987, 2976 (CH), 1577, 1032, 691 (-N=CS-O), 1466, 1458 (Ph), 1369, 1309 (SO_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.36 (s, 3H, OMe), 3.43-3.56 (m, 4H, H-5, H-6A, H-8A, H-8B), 3.98 (dd, 1H, $J_{3\text{-}4}$= 7.9 Hz, $J_{4\text{-}5}$= 9.8 Hz, H-4), 4.11-4.16 (m, 2H, H-3, H-6B), 4.21 (d, 1H, $J_{A\text{-}B}$= 13.0 Hz, SCH_2Ph), 4.30 (d, 1H, $J_{A\text{-}B}$= 13.0 Hz, SCH_2Ph), 4.59 (s, 1H H-1), 4.88 (brs, 1H, OH), 5.03 (t, 1H, $J_{7\text{-}8A}$= $J_{7\text{-}8B}$= 4.9 Hz, H-7), 7.29-7.63 (m, 8H, Ph), 7.86-7.90 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 36.2 (SCH_2Ph), 56.1 (OMe), 59.7 (C-8), 63.0 (C-5), 69.4 (C-6), 77.4 (C-4), 85.6 (C-3), 96.8 (C-7), 97.5 (C-2), 102.0 (C-1), 127.8, 128.3, 128.7, 129.0, 129.1, 133.9 (CH-

Ph), 135.7, 139.6 (Cq-Ph), 171.0 (C-SBn); **HRMS**: calcd. for $C_{23}H_{26}NO_8S_2$ $[M+H]^+$ 508.1100, found 508.1101.

2-Benzylsulfanyl[methyl (2,3-dideoxy-5-*O*-benzyl)-β-D-*glycero*-furanosid][3,2-d]-1,3-oxazole (78)

PROCEDURE

The S-alkylated oxazoline **75** (150.0 mg, 0.37 mmol) was dissolved in dry DCM (10 ml). After cooling at -5ºC, DIEA (0.26 mL, 1.48 mmol) was added and after stirring 30 min at -5ºC, Tf_2O (0.12 mL, 0.74 mmol) was added. The reaction was stirred during 5 min then treated with crushed ice. After extraction with DCM (3 x 20 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **78** (139.0 mg, **98% yield**) as a yellow oil**.**



M.W.= 383.46 g.mol^{-1}
$C_{21}H_{21}NO_4S$

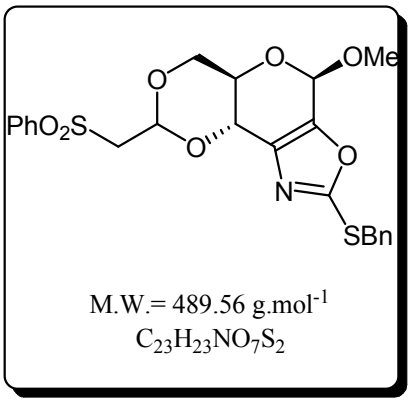
Rf = 0.4 (PE/EtOAc 7:3); $[\alpha]_D$ = - 12 (C=0.4, $CHCl_3$); **MS** (IS): m/z = 384.5 $[M+H]^+$, 406.5 $[M+Na]^+$; **I.R.** (NaCl) ν (cm^{-1}) 3011, 2944, 2895 (CH), 1633 (C=C), 1572, 1070, 694 (-N=CS-O), 1495, 1466, 1457 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.40 (s, 3H, OMe), 3.69 (dd, 1H, $J_{4\text{-}5A}$= 5.1 Hz, $J_{5A\text{-}5B}$= 11.6 Hz, H-5A), 3.93 (dd, 1H, $J_{4\text{-}5B}$= 5.1 Hz, $J_{5A\text{-}5B}$= 11.6 Hz, H-5B), 4.41 (d, 1H, $J_{A\text{-}B}$= 13.1 Hz, SCH_2Ph), 4.46 (d, 1H, $J_{A\text{-}B}$= 13.1 Hz, SCH_2Ph), 4.59 (d, 1H, $J_{A\text{-}B}$= 12.4 Hz, OCH_2Ph), 4.64 (d, 1H, $J_{A\text{-}B}$= 12.4Hz, OCH_2Ph), 4.91 (t, 1H, $J_{4\text{-}5A}$= $J_{4\text{-}5B}$= 5.1 Hz, H-4), 5.86 (s, 1H, H-1), 7.30-7.44 (m, 10H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 37.9 (SCH_2Ph), 55.5 (OMe), 70.1 (C-5), 73.8 (OCH_2Ph), 76.8 (C-4), 101.3 (C-1), 127.8, 128.0, 128.6, 128.9, 129.3, 129.4 (CH-Ph), 135.6, 137.6 (Cq-Ph), 132.6 (C-3), 134.6 (C-2), 175.1 (C-SBn)

2-Benzylsulfanyl{methyl [2,3-dideoxy-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-*erythro*-pyranosid}[3,2-d]-1,3-oxazole (79)

PROCEDURE

The S-alkylated oxazoline **76** (200.0 mg, 0.39 mmol) was dissolved in dry DCM (10 ml). After cooling at -5ºC, DIEA (0.28 mL, 1.58 mmol) was added and after stirring 30 min at -5ºC, Tf_2O (0.13 mL, 0.78 mmol) was added. The reaction was stirred during 5 min then treated with crushed ice. After extraction with DCM (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and

concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **79** (141.3 mg, **74% yield**) as a yellow oil**.**



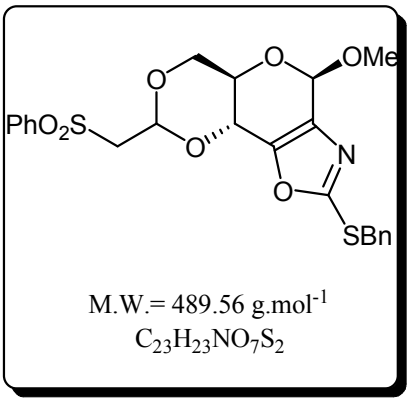
M.W.= 489.56 g.mol^{-1}
$C_{23}H_{23}NO_7S_2$

Rf = 0.4 (PE/EtOAc 4:6); $[\alpha]_D$ = - 46 (C=1.2, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3026, 2944, 2876 (CH), 1645 (C=C), 1579, 1024, 662 (-N=CS-O), 1479, 1451 (Ph) 1367, 1306 (SO_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.45 (s, 3H, OMe), 3.53 (dd, 1H, $J_{7\text{-}8A}$= 6.1, $J_{8A\text{-}8B}$= 14.6 Hz, H-8A), 3.59-3.65 (m, 2H, H-5, H-8B), 3.82 (t, 1H, $J_{5\text{-}6A}$=$J_{6A\text{-}6B}$= 10.5 Hz, H-6A), 4.14 (dd, 1H, $J_{5\text{-}6B}$= 4.5 Hz, $J_{6A\text{-}6B}$= 10.5 Hz, H-6B), 4.42 (d, 1H, $J_{A\text{-}B}$= 12.7 Hz, S*CH*$_2$Ph), 4.46 (d, 1H, $J_{A\text{-}B}$= 12.7 Hz, S*CH*$_2$Ph), 4.63 (dd, 1H, $J_{1\text{-}4}$= 1.9 Hz, $J_{4\text{-}5}$= 8.4 Hz, H-4), 5.27 (dd, 1H, $J_{7\text{-}8B}$= 3.7 Hz, $J_{7\text{-}8A}$= 6.1 Hz, H-7), 5.77 (d, 1H, $J_{1\text{-}4}$= 1.9 Hz, H-1), 7.29-7.39 (m, 5H, Ph), 7.54-7.64 (m, 3H, Ph), 7.93-7.96 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 37.1 (S*CH*$_2$Ph), 55.3 (OMe), 59.9 (C-8), 68.4 (C-6), 71.3 (C-5), 74.2 (C-4), 96.8 (C-1), 97.4 (C-7), 128.1, 128.5, 128.9, 129.2, 129.4, 134.0 (CH-Ph), 136.5, 139.8 (Cq-Ph), 135.6 (C-3), 144.9 (C-2), 162.9 (C-SBn); **HRMS**: calcd. for $C_{23}H_{24}NO_7S_2$ $[M+H]^+$ 490.0994, found 490.0998.

2-Benzylsulfanyl{methyl [2,3-dideoxy-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-*erythro*-pyranosid}[2,3-d]-1,3-oxazole (80)

PROCEDURE

The S-alkylated oxazoline **77** (200.0 mg, 0.39 mmol) was dissolved in dry DCM (10 ml). After cooling at -5ºC, DIEA (0.28 mL, 1.58 mmol) was added and after stirring 30 min at -5ºC, Tf_2O (0.13 mL, 0.78 mmol) was added. The reaction was stirred during 5 min then treated with crushed ice. After extraction with DCM (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **80** (137.5 mg, **72% yield**) as a yellow oil**.**



M.W.= 489.56 g.mol^{-1}
$C_{23}H_{23}NO_7S_2$

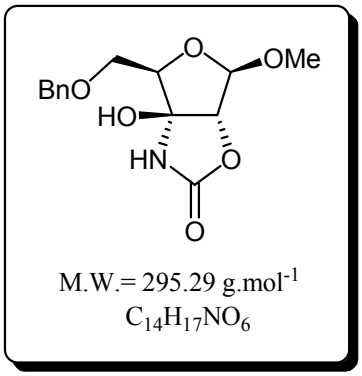
Rf = 0.4 (PE/EtOAc 4:6); $[\alpha]_D$= - 4.8 (C= 0.6, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2998, 2987 (CH), 1638 (C=C), 1567, 1036, 689 (-N=CS-O), 1466, 1462, 1458 (Ph) 1371, 1309 (SO_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.28 (dd, 1H, $J_{7\text{-}8A}$= 4.1 Hz, $J_{8A\text{-}8B}$= 14.6 Hz, H-8A), 3.36 (dd, 1H, $J_{7\text{-}8B}$= 5.6 Hz, $J_{8A\text{-}8B}$= 14.6 Hz, H-8B), 3.47 (s, 3H, OMe), 3.61-3.65 (m, 2H, H-5, H-6A), 4.14 (dd, 1H, $J_{5\text{-}6B}$= 4.3 Hz, $J_{6A\text{-}6B}$= 10.1 Hz, H-6B), 4.43 (d, 1H, $J_{A\text{-}B}$= 12.5Hz, S*CH*$_2$Ph),

4.47-4.51 (m, 2H, H-4, SCH_2Ph), 4.87 (dd, IH, $J_{7\text{-}8A}$= 4.1, $J_{7\text{-}8B}$= 5.6 Hz, H-7), 5.43 (d, 1H, $J_{1\text{-}4}$= 1.8Hz, H-1), 7.33-7.61 (m, 8H, Ph), 7.90-7.92 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 37.7 (SCH_2Ph), 55.5 (OMe), 59.4 (C-8), 67.9 (C-6), 69.3 (C-5), 72.4 (C-4), 96.9 (C-1), 97.1 (C-7), 128.2, 128.8, 129.2, 129.5, 129.6, 134.3 (CH-Ph), 136.7, 139.6 (Cq-Ph), 134.3 (C-2), 140.9 (C-3), 175. 9 (C-SBn); **HRMS**: calcd. for $C_{23}H_{24}NO_7S_2$ $[M+H]^+$ 490.0994, found 490.0997.

4,5-Dihydro[methyl (2-deoxy-5-*O*-benzyl-β-D-xylofuranosid)][3,2-d]-1,3-oxazolin-2-one (81)

PROCEDURE

The S-alkylated oxazoline **75** (110.0 mg, 0.27 mmol) was dissolved in dry DCM (10 ml) and *m*-CPBA 77% (184.2 mg, 0.82 mmol) was added. The reaction was stirred during 3 h at room temperature, then hydrolysed with a saturated solution of NaS_2O_3. After extraction with DCM (3 x 25 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **81** (73.4 mg, **92% yield**) as a white solid.



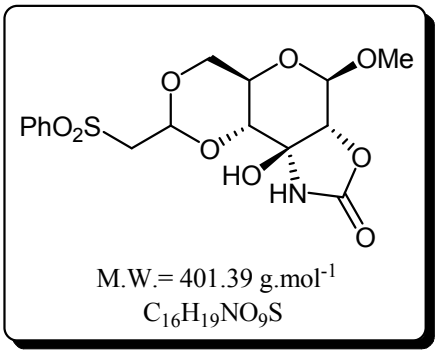
M.W.= 295.29 g.mol^{-1}
$C_{14}H_{17}NO_6$

Rf = 0.7 (PE/EtOAc 6:4); $[\alpha]_D$ = - 15 (C=0.5, $CHCl_3$); **mp**: 175-176 °C; **I.R.** (NaCl) ν (cm^{-1}) 3200 (NH), 2935, 2766 (CH), 1768 (C=O), 1577 (-N-CO-O), 1498, 1466, 1451 (Ph); **^{1}H NMR** (400 MHz, MeOH) δ 3.05 (s, 3H, OMe), 3.69 (dd, 1H, $J_{4\text{-}5A}$= 8.6 Hz, $J_{5A\text{-}5B}$= 10.5 Hz, H-5A), 3.73 (dd, 1H, $J_{4\text{-}5B}$= 4.6 Hz, $J_{5A\text{-}5B}$= 10.5 Hz, H-5B), 4.26 (dd, 1H, $J_{4\text{-}5A}$= 8.6 Hz, $J_{4\text{-}5B}$= 4.6 Hz, H-4), 4.49 (s, 1H, H-2), 4.54 (d, 1H, $J_{A\text{-}B}$= 11.8 Hz, OCH_2Ph), 4.58 (d, 1H, $J_{A\text{-}B}$= 11.8 Hz, OCH_2Ph), 4.93 (s, 1H, H-1), 7.31-7.37 (m, 5H, Ph); **^{13}C NMR** (100 MHz, MeOH) δ 55.5 (OMe), 71.9 (C-5), 74.3 (OCH_2Ph), 86.4 (C-4), 91.4 (C-2), 94.7 (C-3), 109.6 (C-1), 128.8, 129.2, 129.4 (CH-Ph), 139.4 (Cq-Ph), 159.1 (C=O); **HRMS**: calcd. for $C_{14}H_{18}NO_6$ $[M+H]^+$ 296.1134, found 296.1126.

4,5-dihydro{methyl [2-deoxy-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[3,2-d]-1,3-oxazoline-2-one (82)

PROCEDURE

The S-alkylated oxazoline **76** (150.0 mg, 0.30 mmol) was dissolved in dry DCM (10 ml) and *m*-CPBA 77% (201.7 mg, 0.90 mmol) was added. The reaction was stirred during 3 h at room temperature, then hydrolysed with a saturated solution of NaS_2O_3. After extraction with DCM (3 x 25 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **82** (101.2 mg, **84% yield**) as a white solid.



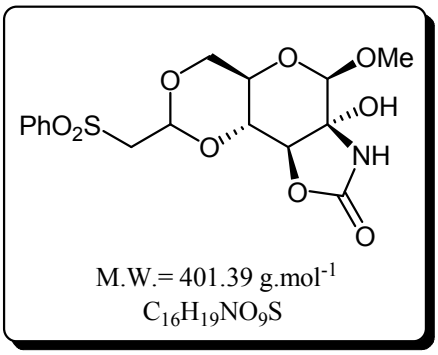
M.W.= 401.39 g.mol^{-1}
$C_{16}H_{19}NO_9S$

Rf = 0.3 (PE/EtOAc 1:1); $[\alpha]_D$ = - 23 (C=0.5, $CHCl_3$); **mp**: 72-73 °C; **I.R.** (NaCl) ν (cm^{-1}) 3250 (NH), 2945, 2878 (CH), 1761 (C=O), 1540 (-N-CO-O), 1466, 1455 (Ph) 1370, 1308 (SO_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.45 (s, 3H, OMe), 3.47-3.62 (m, 4H, H-5, H-6A, H-8A, H-8B), 3.96 (d, 1H, $J_{4\text{-}5}$= 9.1 Hz, H-4), 4.09 (dd, 1H, $J_{5\text{-}6B}$= 3.8 Hz, $J_{6A\text{-}6B}$= 9.3 Hz, 1H, H-6B), 4.32 (d, 1H, $J_{1\text{-}2}$= 4.0 Hz, H-2), 4.50 (d, 1H, $J_{1\text{-}2}$= 4.0 Hz, H-1), 5.10 (t, 1H, $J_{7\text{-}8A}$= $J_{7\text{-}8B}$= 4.8 Hz, H-7), 5.21 (brs, 1H, OH), 6.85 (s, 1H, NH), 7.54-7.58 (m, 2H, Ph), 7.64-7.68 (m, 1H, Ph), 7.90-7.92 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 56.8 (OMe), 59.6 (C-8), 64.3 (C-5), 68.6 (C-6), 78.8 (C-4), 83.6 (C-2), 84.2 (C-3), 97.1 (C-7), 101.6 (C-1), 128.4, 129.4, 134.3 (CH-Ph), 139.5 (Cq-Ph), 157.4 (C=O); **HRMS**: calcd. for $C_{16}H_{19}NO_9SNa$ $[M+Na]^+$ 424.0678, found 424.0692.

4,5-dihydro{methyl [3-deoxy-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[2,3-d]-1,3-oxazoline-2-one (83)

PROCEDURE

The S-alkylated oxazoline **77** (150.0 mg, 0.30 mmol) was dissolved in dry DCM (10 ml) and *m*-CPBA 77% (201.7 mg, 0.90 mmol) was added. The reaction was stirred during 3 h at room temperature, then hydrolysed with a saturated solution of NaS_2O_3. After extraction with DCM (3 x 25 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 3:7) to afford compound **83** (110.7 mg, **92% yield**) as a white solid.



M.W.= 401.39 g.mol^{-1}
$C_{16}H_{19}NO_9S$

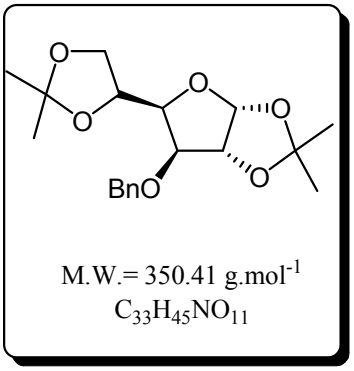
Rf = 0.1 (PE/EtOAc 4:6); $[\alpha]_D$ = - 74 (C=0.8, $CHCl_3$); **mp**: 82-83 °C; **I.R.** (NaCl) ν (cm^{-1}) 3230 (NH), 2950, 2884 (CH), 1769 (C=O), 1545 (-N-CO-O), 1478, 1469 (Ph) 1368, 1305 (SO_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.33 (dt, 1H, $J_{5\text{-}4}$=$J_{5\text{-}6A}$= 9.9 Hz, $J_{5\text{-}6B}$= 5.1 Hz, H-5), 3.45-3.46 (m, 2H, H-8A, H-8B), 3.48 (s, 3H, OMe), 3.51-3.59 (m, 2H, H-4, H-6A), 4.14 (dd, 1H, $J_{5\text{-}6B}$= 5.1 Hz, $J_{6A\text{-}6B}$= 10.5 Hz, H-6B), 4.22 (d, 1H, $J_{3\text{-}4}$= 7.5 Hz, H-3), 4.54 (s, 1H H-1), 4.98 (t, 1H, $J_{7\text{-}8A}$= $J_{7\text{-}8B}$= 5.1 Hz, H-7), 5.27 (brs, 1H, OH), 6.77 (brs, 1H, NH), 7.52-7.56 (m, 2H, Ph), 7.60-7.64 (m, 1H, Ph), 7.86-7.88 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 57.4 (OMe), 59.6 (C-8), 63.1 (C-5), 68.4 (C-6), 79.4 (C-4), 82.7 (C-3), 85.6 (C-2), 97.0 (C-7), 102.2 (C-1), 128.5, 129.2, 134.1 (CH-Ph), 139.4 (Cq-Ph), 157.9 (C=O); **HRMS**: calcd. for $C_{16}H_{20}NO_9S$ $[M+H]^+$ 402.0859, found 402.0863.

3-*O*-Benzyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (84)

PROCEDURE

1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (7.80 g, 29.97 mmol) was dissolved in dry DMF (65 mL) and after cooling at -5ºC, NaH 60% dispersion in oil (1.80 g, 44.96 mmol) was added . After stirring the reaction until release of H_2 stopped, BnBr (5.38 mL, 44.96 mmol) was added dropwise. The reaction was stirred during one night at room temperature, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 100 mL), the combined organic phases were washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, compound **84** was obtained quantitatively, as a colourless oil.

CAS [18685-18-2]



M.W.= 350.41 g.mol^{-1}
$C_{33}H_{45}NO_{11}$

Rf = 0.7 (PE/EtOAc 7:3); $[\alpha]_D$ = -16 (C=0.7, MeOH); **MS** (IS): m/z = 351.5 $[M+H]^+$, 368.0 $[M+NH_4]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 1.29 (s, 3H, Me), 1.36 (s, 3H, Me), 1.42 (s, 3H, Me), 1.48 (s, 3H, Me), 3.99 (dd, 1H, $J_{6A\text{-}6B}$= 8.6 Hz, $J_{5\text{-}6B}$= 6.0 Hz, H-6B), 4.01 (d, 1H, $J_{3\text{-}4}$= 3.1 Hz, H-3), 4.10 (dd, 1H, $J_{6A\text{-}6B}$= 8.6 Hz, $J_{5\text{-}6B}$= 6.0 Hz, H-6A), 4.15 (dd, 1H, $J_{4\text{-}5}$= 7.7 Hz, $J_{3\text{-}4}$= 3.1 Hz, H-4), 4.37 (dt, 1H, $J_{4\text{-}5}$= 7.7 Hz, $J_{5\text{-}6A}$= $J_{5\text{-}6B}$= 6.0 Hz, H-5), 4.57 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-2), 4.60 (d, 1H, $J_{A\text{-}B}$= 11.8 Hz, O*C*H_2Ph), 4.67 (d, 1H, $J_{A\text{-}B}$= 11.8 Hz, O*C*H_2Ph), 5.88 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-1), 7.23-7.38 (m, 5H, Ph).

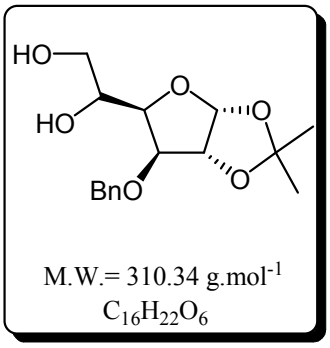
[144] Takahashi, S. ; Kuzuhara, H. ; Nakajima, M. *Tetrahedron* **2001**, *57*, 6915-6926.

3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (85)

PROCEDURE

Compound **84** (260.0 mg, 0.74 mmol) was dissolved in an aqueous solution of AcOH (70%) and the reaction was stirred during one night at room temperature. The residue was co-evaporated with toluene (3x) and after concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 3:7) to afford compound **85** (190.6 mg, **83% yield**) as a colourless oil.

CAS [22529-61-9]



M.W.= 310.34 g.mol^{-1}
$C_{16}H_{22}O_6$

Rf = 0.1 (PE/EtOAc 8:2); $[\alpha]_D$ = - 22 (C=0.8, MeOH); **MS** (IS): m/z = 311.5 $[M+H]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 1.37 (s, 3H, Me), 1.55 (s, 3H, Me), 3.36 (brs, 2H, OH), 3.75 (dd, 1H, J_{6A-6B}= 11.6 Hz, J_{5-6B}= 6.0 Hz, H-6B), 3.88 (dd, 1H, J_{6A-6B}= 11.6 Hz, J_{5-6A}= 3.2 Hz, H-6A), 4.11 (m, 1H, H-5), 4.18-4.28 (m, 2H, H-3, H-4), 4.66 (d, 1H, J_{A-B}= 11.8 Hz, O*C*H_2Ph), 4.68 (d, 1H, J_{1-2}= 3.8 Hz, H-2), 4.75 (d, 1H, J_{A-B}= 11.8 Hz, O*C*H_2Ph), 5.98 (d, 1H, J_{1-2} = 3.8 Hz, H-1), 7.30-7.50 (m, 5H, Ph).

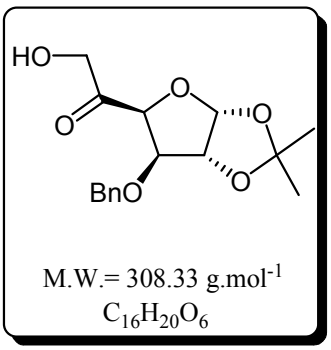
[144] Takahashi, S. ; Kuzuhara, H. ; Nakajima, M. *Tetrahedron* **2001**, *57*, 6915-6926.

3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (86)

PROCEDURE

Diol **85** (250.0 mg, 0.81 mmol) was dissolved in toluene (6 mL) and dibutyltin oxide (221.5 mg, 0.89 mmol) was added to the solution. The mixture was stirred under reflux during 14 h with a Dean-Stark apparatus. The solvent was evaporated and the residue was dried in vacuum for 30 min. The crude was then taken and up in dry $CHCl_3$ (6 mL) and NBS (158.4 mg, 0.89 mmol) was added. The resulting solution was stirred for 5 min. The solvent was evaporated and the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **86** (212.2 mg, **85% yield**) as a white solid.

CAS [17231-20-8]



M.W.= 308.33 g.mol^{-1}
$C_{16}H_{20}O_6$

Rf = 0.6 (PE/EtOAc 1:1); $[\alpha]_D$ = - 116 (C=1.0, $CHCl_3$); **mp**: 115-116 °C; **MS** (IS): m/z = 309.5 $[M+H]^+$, 331.5 $[M+Na]^+$; **I.R.** (NaCl) ν (cm^{-1}) 1725 (C=O); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.32 (s, 3H, Me), 1.47 (s, 3H, Me), 2.87 (brs, 1H, OH), 4.31 (d, 1H, J_{3-4}= 3.6 Hz, H-3), 4.47 (d, 1H, J_{A-B}= 11.7 Hz, O*C*H_2Ph), 4.48 (d, 1H, J_{6A-6B}= 20.4 Hz, H-6B), 4.52 (d, 1H, J_{6A-6B}= 20.4 Hz, H-6A), 4.57 (d, 1H, J_{A-B}= 11.7 Hz, O*C*H_2Ph), 4.60 (d, 1H, J_{1-2}= 3.5 Hz, H-2), 4.82 (d, 1H, J_{3-4}= 3.6 Hz, H-4), 6.05 (d, 1H, J_{1-2} = 3.5 Hz, H-1), 7.18-7.34 (m, 5H, Ph); **^{13}C NMR** (100 MHz,

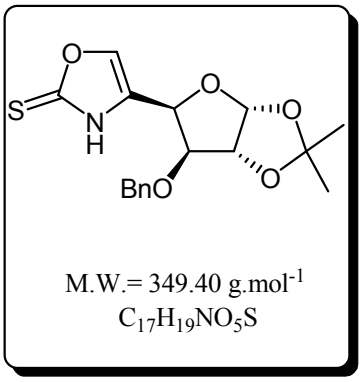
$CDCl_3$) δ 26.3, 26.9 (Me), 68.3 (C-6), 72.6 (O*C*H_2Ph), 81.7 (C-2), 83.4 (C-3), 84.5 (C-4), 106.0 (C-1), 112.7 (Cq-isop), 127.7, 128.2, 128.6 (CH-Ph), 136.6 (Cq-Ph), 208.2 (C=O).

[145] Kong, X.; Grindley, T. B. *J. Carbohydr. Chem.* **1993**, *12*, 557-571.

4-[(4*R*)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-threofuranos-4-*C*-yl]-1,3-oxazoline-2-thione (87)

PROCEDURE

The ulose **86** (83.3 mg, 0.27 mmol) and KSCN (39.8 mg, 0.41 mmol) were dissolved in THF (10 mL). After cooling at –5°C, TsOH.H_2O (102.7 mg, 0.54 mmol) was carefully added and the mixture was stirred during 24 h under reflux, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **87** (88.7 mg, **94% yield**) as a yellow oil.



M.W.= 349.40 g.mol^{-1}
$C_{17}H_{19}NO_5S$

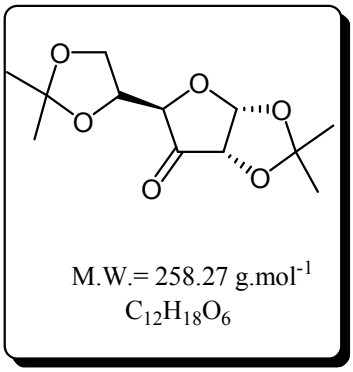
Rf = 0.4 (PE/EtOAc 7:3); $[\alpha]_D$ = - 16 (C=1.0, MeOH); **I.R.** (NaCl) ν (cm^{-1}) 3230 (NH), 2986, 2909 (CH), 1636 (C=C), 1492, 1130 (N-CS-O), 1469, 1464 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.32 (s, 3H, Me), 1.50 (s, 3H, Me), 4.02 (d, 1H, $J_{3'-4'}$= 3.1 Hz, H-3'), 4.45 (d, 1H, J_{A-B}= 11.7 Hz, O*C*H_2Ph), 4.65 (d, 1H, J_{A-B}= 11.7 Hz, O*C*H_2Ph), 4.69 (d, 1H, $J_{1'-2'}$= 3.3 Hz, H-2'), 5.04 (d, 1H, $J_{3'-4'}$= 3.1 Hz, H-4'), 5.99 (d, 1H, $J_{1'-2'}$= 3.3 Hz, H-1'), 7.18-7.23 (m, 3H, H-5, Ph), 7.24-7.37 (m, 3H, Ph), 11.0 (brs, 1H, NH); **^{13}C NMR** (100 MHz, MeOH) δ 26.0, 26.7 (Me), 72.0 (C-4'), 72.4 (O*C*H_2Ph), 82.0 (C-2'), 82.4 (C-3'), 104.8 (C-1'), 112.4 (Cq-isop), 125.9 (C-4), 128.1, 128.4, 128.7 (CH-Ph), 138.8 (C-5), 136.2 (Cq-Ph), 179.0 (C=S); **HRMS**: calcd. for $C_{17}H_{20}NO_5S$ $[M+H]^+$ 350.1062, found 350.1054.

1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose (88)

PROCEDURE

1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (10.0 g, 38.42 mmol) was dissolved in dry DCM (60 ml). PDC (8.67 g, 23.05 mmol) and Ac_2O (14.5 mL, 0.15 mol) were added and the reaction was stirred under reflux during 2h. After evaporation of the mixture, the residue was submitted to a small column chromatography (EtOAc) and the filtrated was co-evaporated with toluene (3x). Compound **88** was obtained quantitatively as a colourless oil.

CAS [2847-00-9]



M.W.= 258.27 g.mol^{-1}
$C_{12}H_{18}O_6$

Rf = 0.2 (PE/EtOAc 8:2); $[\alpha]_D$ = + 76 (C=1.0, $CHCl_3$); **MS** (IS): m/z = 259.5 $[M+H]^+$, 281.5 $[M+Na]^+$; **I.R.** (NaCl) ν (cm^{-1}) 1745 (C=O); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 1.34 (s, 6H, Me), 1.43 (s, 3H, Me), 1.46 (s, 3H, Me), 3.97-4.11 (m, 2H, H-6A, H-6B), 4.31-4.43 (m, 3H, H-2, H-4, H-5), 6.14 (d, 1H, J_{1-2}= 4.3 Hz, H-1); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 25.2, 25.9, 27.1, 27.5 (Me), 64.2 (C-6), 76.3 (C-5), 77.2 (C-4), 78.9 (C-2), 103.0 (C-1), 110.2, 114.1 (Cq-isop), 208.9 (C=O).

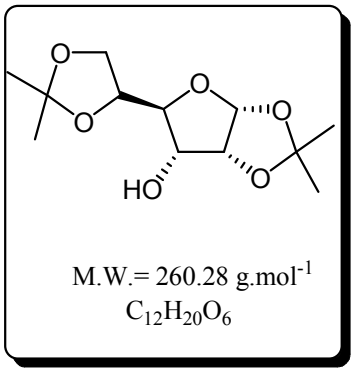
[147] Saito, Y. ; Zevaco, T. A. ; Agrofoglio, L. A. *Tetrahedron* **2002**, *58*, 9593-9603.

1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (89)

PROCEDURE

A solution of sodium borohydride (1.76 g, 47.0 mmol) in water (50 mL) was added at room temperature to a solution of **88** (10 g, 39.2 mmol) in 56% aqueous EtOH (43 mL). After stirring for 3h, the mixture was extracted with DCM (3 x 100 mL) and the combined organic phase was dried over MgSO4. After filtration and concentration under vacuum, compound **89** (8.57 g, **84% yield**) was obtained as a colourless solid.

CAS [2595-05-3]



M.W.= 260.28 g.mol^{-1}
$C_{12}H_{20}O_6$

Rf = 0.7 (Cy/EtOAc 1:1); $[\alpha]_D$ = + 40 (C=0.5, $CHCl_3$); **mp**: 72-73 °C; **MS** (IS): m/z = 261.5 $[M+H]^+$; **^{1}H NMR** (250 MHz, $CDCl_3$) δ 1.40 (s, 6H, Me), 1.49 (s, 3H, Me), 1.61 (s, 3H, Me), 2.57 (s, 1H, OH), 3.85 (dd, 1H, J_{2-3}= 4.7 Hz, J_{3-4}= 8.5 Hz, H-3), 4.07 (m, 3H, H-4, H-5, H-6B), 4.33 (dd, 1H, J_{5-6A}= 6.4 Hz, J_{6A-6B}= 11.2 Hz, H-6A), 4.64 (m, 1H, H-2), 5.83 (d, 1H, J_{1-2}= 3.8 Hz, H-1).

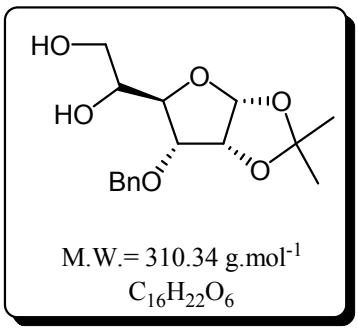
[149] Loiseleur, O.; Ritson, D.; Nina, M.; Crowley, P.; Wagner, T.; Hanessian, S. *J. Org. Chem*. **2007**, *72*, 6353-6363.

3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-allofuranose (91)

PROCEDURE

1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose **89** (7.80 g, 29.97 mmol) was dissolved in dry DMF (65 mL) and after cooling at -5ºC, NaH 60% dispersion in oil (1.80 g, 44.96 mmol) was added . After stirring the reaction until release of H_2 stopped, BnBr (5.38 mL, 44.96 mmol) was added dropwise. The reaction was stirred during one night at room temperature, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 100 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, compound **90** was dissolved in an aqueous solution of AcOH (70%) and the reaction was stirred during one night at room temperature. The residue was co-evaporated with toluene (3x) and after concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 4:6) to afford compound **91** (8.28 g, **89% yield**) as a yellow solid.

CAS [57099-04-4]



M.W.= 310.34 g.mol^{-1}
$C_{16}H_{22}O_6$

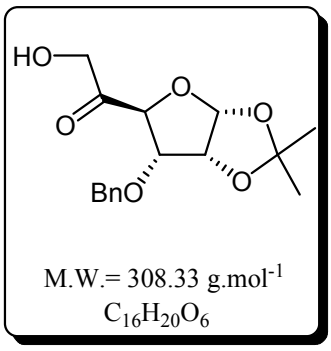
Rf = 0.4 (PE/EtOAc 3:7); $[\alpha]_D$ = + 105 (C=1.0, $CHCl_3$); **^{1}H NMR** (400 MHz, DMSO) δ 1.29 (s, 3H, Me), 1.45 (s, 3H, Me), 3.39-3.49 (m, 2H, H-6A, H-6B), 3.67-3.73 (m, 1H, H-5), 3.94-4.01 (m, 2H, H-3, H-4), 4.47 (m, 2H, OH, O*CH*$_2$Ph), 4.63 (d, 1H, $J_{A\text{-}B}$= 11.9 Hz, O*CH*$_2$Ph), 4.68-4.70 (m, 1H, H-2), 4.85 (d, 1H, $J_{5\text{-}OH}$= 4.8 Hz, OH), 5.71 (d, 1H, $J_{1\text{-}2}$= 3.7 Hz, H-1), 7.30-7.36 (m, 5H, Ph); **^{13}C NMR** (100 MHz, DMSO) δ 25.6, 26.7 (Me), 62.1 (C-6), 70.7 (C-5), 70.8 (O*CH*$_2$Ph), 76.9 (C-3), 77.2 (C-2), 79.0 (C-4), 103.7 (C-1), 111.5 (Cq-isop), 127.3, 127.7, 128.1 (CH-Ph), 138.0 (Cq-Ph); **HRMS**: calcd. for $C_{16}H_{22}O_6Na$ $[M+Na]^+$ 333.1314, found 333.1312.

[148]Nacro, K.; Lee, J.; Barchi, J. J.; Lewin, N. E.; Blumberg, P. M.; Marquez, V. E. *Tetrahedron* **2002**, *58*, 5335-5345.

3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranos-5-ulose (92)

PROCEDURE

Diol **91** (250.0 mg, 0.81 mmol) was dissolved in toluene (6 mL) and dibutyltin oxide (221.5 mg, 0.89 mmol) was added to the solution. The mixture was stirred under reflux during 14 h with a Dean-Stark apparatus. The solvent was evaporated and the residue was dried in vacuum for 30 min. The crude was then taken and up in dry $CHCl_3$ (6 mL) and N-bromosuccinimide (158.4 mg, 0.89 mmol) was added. The resulting solution was stirred for 5 min. The solvent was evaporated and the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **92** (204.7 mg, **82% yield**) as a yellow oil.



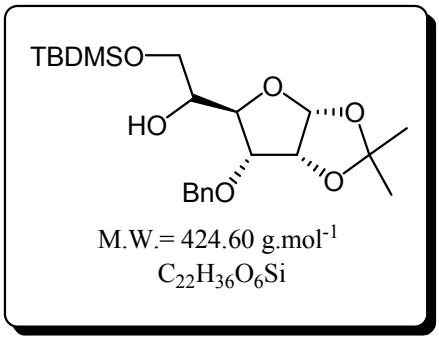
M.W.= 308.33 g.mol^{-1}
$C_{16}H_{20}O_6$

Rf = 0.3 (PE/EtOAc 1:1); $[\alpha]_D$ = + 43 (C=1.0, $CHCl_3$); **mp**: 115-116 °C; **MS** (IS): m/z = 309.5 $[M+H]^+$, 331.5 $[M+Na]^+$; **I.R.** (NaCl) ν (cm^{-1}) 1730 (C=O), 1477, 1456 1455 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.33 (s, 3H, Me), 1.47 (s, 3H, Me), 3.81 (dd, 1H, $J_{2\text{-}3}$= 4.4 Hz, $J_{3\text{-}4}$= 9.3 Hz, H-3), 4.35 (d, 1H, $J_{6A\text{-}6B}$= 20.2 Hz, H-6B), 4.43 (d, 1H, $J_{6A\text{-}6B}$= 20.2 Hz, H-6A), 4.57 (dd, 1H, $J_{1\text{-}2}$= 3.4 Hz, $J_{2\text{-}3}$= 4.4 Hz, H-2), 4.59-4.64 (m, 2H, H-4, OCH_2Ph), 4.75 (d, 1H, $J_{A\text{-}B}$= 11.9 Hz, OCH_2Ph), 5.81 (d, 1H, $J_{1\text{-}2}$= 3.4 Hz, H-1), 7.27-7.37 (m, 5H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.3, 26.9 (Me), 66.5 (C-6), 72.5 (OCH_2Ph), 77.6 (C-2), 79.4 (C-3), 80.4 (C-4), 104.6 (C-1), 113.8 (Cq-isop), 128.1, 128.3, 128.6 (CH-Ph), 136.7 (Cq-Ph), 207.1 (C=O).

3-*O*-Benzy-6-*tert*-butyldimethylsilyl-α-D-allofuranose (93)

PROCEDURE

To diol **91** (117.9 mg, 0.38 mmol) in dry DMF (10 ml) at 0ºC were added imidazole (51.7 mg, 0.76 mmol) and TBDMSCl (85.8 mg, 0.57 mmol). The reaction was stirred at room temperature during 5 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 20 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **93** (156.5 mg, **97% yield**) as a white solid**.**



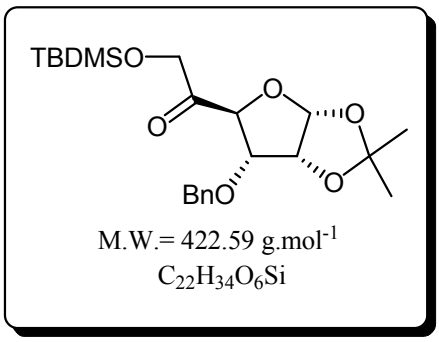
M.W.= 424.60 g.mol^{-1}
$C_{22}H_{36}O_6Si$

Rf = 0.5 (PE/EtOAc 1:1); $[\alpha]_D$ = + 43 (C=0.5, $CHCl_3$); **mp**: 115-116 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.06 (s, 6H, Si(CH_3)$_2$), 0.89 (s, 9H, *t*-Bu), 1.58 (s, 3H, Me), 1.59 (s, 3H, Me), 2.53 (d, 1H, J5-OH= 3.1 Hz, OH), 3.63-3.74 (m, 2H, H-6A, H-6B), 3.88-3.93 (m, 1H, H-5), 3.96 (dd, 1H, $J_{2\text{-}3}$= 4.5 Hz, $J_{3\text{-}4}$= 8.7 Hz, H-3), 4.06 (dd, 1H, $J_{3\text{-}4}$= 8.7 Hz, $J_{4\text{-}5}$= 4.2 Hz, H-4), 4.55 (t, 1H, $J_{1\text{-}2}$= $J_{2\text{-}3}$= 4.5 Hz, H-2), 4.60 (d, 1H, $J_{A\text{-}B}$= 11.7 Hz, OCH_2Ph), 4.76 (d, 1H, $J_{A\text{-}B}$= 11.7 Hz, OCH_2Ph), 5.74 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-1), 7.28-7.41 (m, 5H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.8, -4.7 (Si (CH_3)$_2$), 18.5 (Cq, *t*-Bu), 26.0 ((CH_3)$_3$C), 26.7, 26.9 (Me), 63.9 (C-6), 72.1 (C-5), 72.3 (OCH_2Ph), 77.9 (C-2), 78.0 (C-3), 78.1 (C-4), 104.2 (C-1), 113.1 (Cq-isop), 128.1, 128.2, 128.6 (CH-Ph), 137.7 (Cq-Ph); **HRMS**: calcd. for $C_{22}H_{36}O_6SiNa$ $[M+Na]^+$ 447.2179, found 447.2183.

3-*O*-Benzy-6-*tert*-butyldimethylsilyl-α-D-*ribo*-hexofuranos-5-ulose (94)

PROCEDURE

Compound **93** (150.0 mg, 0.35 mmol) was dissolved in dry DCM (10 ml). PDC (79.0 mg, 0.21 mmol) and Ac_2O (0.13 mL, 1.40 mmol) were added and the reaction was stirred under reflux during 2h. After evaporation of the mixture, the residue was submitted to a small column chromatography (EtOAc) and the filtrated was co-evaporated with toluene (3x). Compound **94** was obtained quantitatively as a yellow oil.



M.W.= 422.59 g.mol^{-1}
$C_{22}H_{34}O_6Si$

Rf = 0.6 (PE/EtOAc 8:2); $[\alpha]_D$ = + 16 (C=1.0, $CHCl_3$); **MS** (IS): m/z = 423.5 $[M+H]^+$; **I.R.** (NaCl) ν (cm^{-1}) 1727 (C=O), 1461 (Ph), 1215 ($Si(CH_3)_2$); **^{1}H NMR** (400 MHz, $CDCl_3$) 0.08 (s, 6H, $Si(CH_3)_2$), 0.91 (s, 9H, t-Bu), 1.36 (s, 3H, Me), 1.60 (s, 3H, Me), 3.87 (dd, 1H, $J_{2\text{-}3}$= 4.0 Hz, $J_{3\text{-}4}$= 9.1 Hz, H-3) 4.49 (s, 2H, H-6A, H-6B), 4.54 (t, 1H, $J_{1\text{-}2}$= $J_{2\text{-}3}$= 4.5 Hz, H-2), 4.60 (d, 1H, $J_{3\text{-}4}$= 9.1 Hz, H-4), 4.63 (d, 1H, $J_{A\text{-}B}$= 11.9 Hz, OCH_2Ph), 4.75 (d, 1H, $J_{A\text{-}B}$= 11.9 Hz, OCH_2Ph), 5.81 (d, 1H, $J_{1\text{-}2}$= 4.5 Hz, H-1), 7.31-7.39 (m, 5H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.8, -4.7 (Si $(CH_3)_2$), 18.6 (Cq, *t*-Bu), 25.9 ($(CH_3)_3C$), 26.6, 27.0 (Me), 68.0 (C-6), 72.5 (OCH_2Ph), 77.9 (C-2), 79.6 (C-3), 80.0 (C-4), 104.7 (C-1), 113.7 (Cq-isop), 128.2, 128.6, 129.1 (CH-Ph), 137.1 (Cq-Ph), 205.0 (C=O).

4-[(4*R*)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-*C*-yl]-1,3-oxazoline-2-thione (95)

PROCEDURE

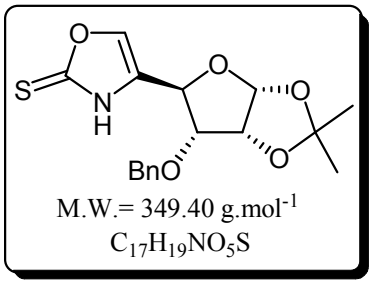
Method A

The ulose **94** (114.1 mg, 0.27 mmol) and KSCN (39.8 mg, 0.41 mmol) were dissolved in THF (15 mL). After cooling at –5°C, $TsOH.H_2O$ (102.7 mg, 0.54 mmol) was carefully added and the mixture was stirred during 24 h under reflux, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (Cy/EtOAc 6:4) to afford compound **95** (86.7 mg, **92% yield**) as a white solid.

Method B

The ulose **92** (100.0 mg, 0.32 mmol) and KSCN (46.6 mg, 0.48 mmol) were dissolved in THF (15 mL). After cooling at –5°C, $TsOH.H_2O$ (121.7 mg, 0.64 mmol) was carefully added and the mixture was stirred during 24 h under reflux, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first

with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (Cy/EtOAc 6:4) to afford compound **95** (102.8 mg, **92% yield**) as a white solid.



M.W.= 349.40 g.mol^{-1}
$C_{17}H_{19}NO_5S$

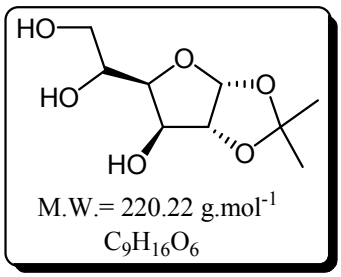
Rf = 0.3 (Cy/EtOAc 1:1); $[\alpha]_D$ = - 50 (C=1.0, MeOH); **mp**: 174-175 °C; **I.R.** (NaCl) ν (cm^{-1}) 3223 (NH), 2987, 2910 (CH), 1650 (C=C), 1497, 1112 (N-CS-O), 1465, 1454 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.37 (s, 3H, Me), 1.61 (s, 3H, Me), 3.89 (dd, 1H, $J_{2'-3'}$= 4.0 Hz, $J_{3'-4'}$= 9.0 Hz, H-3'), 4.52 (d, 1H, J_{A-B}= 11.8 Hz, O*CH*$_2$Ph), 4.68 (brt, 1H, $J_{1'-2'}$= 3.4 Hz, $J_{2'-3'}$= 4.0 Hz, H-2'), 4.75 (d, 1H, J_{A-B}= 11.8 Hz, O*CH*$_2$Ph), 4.87 (d, 1H, $J_{3'-4'}$= 9.0 Hz, H-4'), 5.83 (d, 1H, $J_{1'-2'}$= 3.4 Hz, H-1'), 7.20 (s, 1H, H-5), 7.25-7.36 (m, 5H, Ph), 11.8 (brs, 1H, NH); **^{13}C NMR** (100 MHz, MeOH) δ 26.4, 26.8 (Me), 70.5 (C-4'), 72.6 (O*CH*$_2$Ph), 77.0 (C-2'), 80.7 (C-3'), 104.3 (C-1'), 113.8 (Cq-isop), 128.3 (CH-Ph), 128.4 (C-4), 128.5, 128.6 (CH-Ph), 134.8 (C-5), 136.6 (Cq-Ph), 179.0 (C=S); **HRMS**: calcd. for $C_{17}H_{20}NO_5S$ $[M+H]^+$ 350.1062, found 350.1056.

1,2-*O*-Isopropylidene-α-D-glucofuranose (96)

PROCEDURE

1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (5.00 g, 19.21 mmol) was dissolved in an aqueous solution of AcOH (70%) and the reaction was stirred during overnight at room temperature. The solvent was co-evaporated with toluene (3x) and the residue was dried under vacuum for one night to afford quantitatively compound **96** as a white solid.

CAS [18549-40-1]



M.W.= 220.22 g.mol^{-1}
$C_9H_{16}O_6$

$[\alpha]_D$ = - 24 (C=0.6, MeOH); **mp**: 159-160 °C; **MS** (IS): m/z = 221.5 $[M+H]^+$; **^{1}H NMR** (400 MHz, MeOH) δ 1.29 (s, 3H, Me), 1.45 (s, 3H, Me), 3.59 (dd, 1H, J_{6A-6B}= 11.5 Hz, J_{5-6B}= 5.8 Hz, H-6B), 3.76 (dd, 1H, J_{6A-6B}= 11.5 Hz, J_{5-6A}= 3.2 Hz, H-6A), 3.88 (ddd, 1H, J_{5-6A}= 3.2 Hz, J_{5-6B}= 5.8 Hz, J_{4-5}= 8.9 Hz, H-5), 4.01 (dd, 1H, J_{3-4}= 2.4 Hz, J_{4-5}= 8.9 Hz, H-4), 4.20 (d, 1H, J_{3-4}= 2.4 Hz, H-3), 4.47 (d, 1H, J_{1-2}= 3.5 Hz, H-2), 5.86 (d, 1H, J_{1-2}= 3.5 Hz, H-1).

[154] Gallier, F.; Peyrottes, S.; Périgaud, C. *Eur. J. Org. Chem*. **2007**, 925-933.

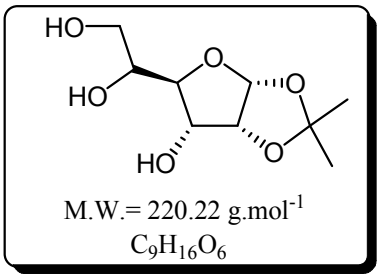
1,2-*O*-Isopropylidene-α-D-allofuranose (97)

PROCEDURE

1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose **89** (5.00 g, 19.21 mmol) was dissolved in an aqueous solution of AcOH (70%) and the reaction was stirred overnight at room

temperature. The solvent was co-evaporated with toluene (3x) and the residue was dried under vacuum for one night to afford quantitatively compound **97** as a white solid.

CAS [4495-04-9]



$[\alpha]_D$ = + 35 (C=0.9, MeOH); **mp**: 140-141 °C**; MS** (IS): m/z = 221.5 $[M+H]^+$; **^{1}H NMR** (400 MHz, MeOH) δ 1.33 (s, 3H, Me), 1.53 (s, 3H, Me), 3.62 (dd, 1H, J_{6A-6B}= 11.4 Hz, J_{5-6B}= 6.1 Hz, H-6B), 3.69 (dd, 1H, J_{6A-6B}= 11.4 Hz, J_{5-6A}= 4.3 Hz, H-6A), 3.87-3.92 (m, 2H, H-4, H-5), 4.10 (dd, 1H, J_{2-3}= 4.6 Hz, J_{3-4}= 8.5 Hz, H-3), 4.56 (brt, 1H, J_{1-2}= 3.8 Hz, J_{2-3}= 4.6 Hz, H-2), 5.73 (d, 1H, J_{1-2}= 3.8 Hz, H-1).

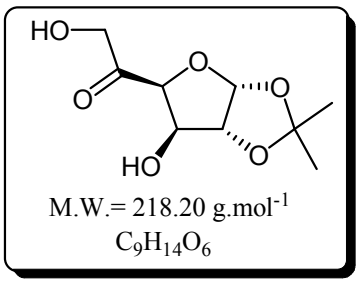
[154] Gallier, F.; Peyrottes, S.; Périgaud, C. *Eur. J. Org. Chem*. **2007**, 925-933.

1,2-*O*-Isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (98)

PROCEDURE

Triol **96** (178.4 mg, 0.81 mmol) was dissolved in dry MeOH (10 mL) and dibutyltin oxide (403.3 mg, 1.62 mmol) was added to the solution. The mixture was stirred under reflux during 2 h. The solvent was evaporated and the residue was dried in vacuum for 30 min. The crude was then taken and up in dry DCM (10 mL) and Br_2 (41.5 µL, 0.89 mmol) was added. The resulting solution was stirred for 20 min. The solvent was evaporated and the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **98** (157.3 mg, **89% yield**) as a colourless oil.

CAS [19684-32-3]



Rf = 0.3 (PE/EtOAc 1:1); $[\alpha]_D$ = - 50 (C=1.1, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 1727 (C=O); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.32 (s, 3H, Me), 1.48 (s, 3H, Me), 3.83 (brs, 1H, OH), 4.12 (brs, 1H, OH), 4.48 (d, 1H, J_{6A-6B}= 20.4 Hz, H-6B), 4.53 (d, 1H, J_{6A-6B}= 20.4 Hz, H-6A), 4.55 (d, 1H, J_{1-2}= 3.5 Hz, H-2), 4.56 (d, 1H, J_{3-4}= 3.3 Hz, H-3), 4.75 (d, 1H, J_{3-4}= 3.3 Hz, H-4), 6.06 (d, 1H, J_{1-2}= 3.5 Hz, H-1); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.3, 26.9 (Me), 62.1 (C-6), 68.0 (C-6), 76.3 (C-3), 84.6 (C-2), 85.3 (C-4), 105.8 (C-1), 112.5 (Cq-isop), 209.1 (C=O); **HRMS**: calcd. for $C_9H_{14}O_6Na$ $[M+Na]^+$ 241.0688, found 241.0686.

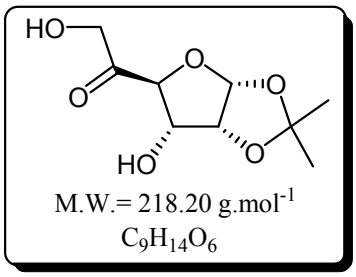
[155] Robins, M. J.; Guo, Z.; Wnuk, F. *J. Am. Chem. Soc*. **1997,** *119*, 3637-3638.

1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranos-5-ulose (99)

PROCEDURE

Triol **97** (178.4 mg, 0.81 mmol) was dissolved in dry MeOH (10 mL) and dibutyltin oxide (403.3 mg, 1.62 mmol) was added to the solution. The mixture was stirred under reflux

during 2 h. The solvent was evaporated and the residue was dried in vacuum for 30 min. The crude was then taken and up in dry CH_2Cl_2 (10 mL) and Br_2 (41.5 µL, 0.89 mmol) was added. The resulting solution was stirred for 20 min. The solvent was evaporated and the residue was purified by column chromatography (PE/EtOAc 2:8) to afford compound **99** (139.6 mg, **79% yield**) as a colourless oil.



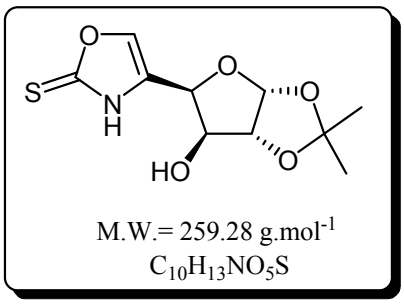
M.W.= 218.20 g.mol^{-1}
$C_9H_{14}O_6$

Rf = 0.2 (PE/EtOAc 2:8); $[\alpha]_D$ = + 63 (C=1.2, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 1730 (C=O); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.36 (s, 3H, Me), 1.58 (s, 3H, Me), 4.09-4.14 (m, 3H, H-3, H-6A, H-6B), 4.40 (d, 1H, $J_{3\text{-}4}$= 9.2 Hz, H-4), 4.50 (brs, 2H, OH), 4.64 (brt, 1H, $J_{1\text{-}2}$= 3.8 Hz, $J_{2\text{-}3}$= 4.1 Hz, H-2) 5.89 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-1); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.4, 26.5 (Me), 66.1 (C-6), 73.9 (C-3), 78.8 (C-2), 81.7 (C-4), 104.2 (C-1), 113.4 (Cq-isop), 207.8 (C=O); **HRMS**: calcd. for $C_9H_{14}O_6Na$ $[M+Na]^+$ 241.0688, found 241.0676.

4-[(4*R*)-1,2-*O*-isopropylidene-α-D-threofuranos-4-*C*-yl)]-1,3-oxazoline-2-thione (100)

PROCEDURE

Ulose **98** (150.0 mg, 0.69 mmol) and KSCN (100.6 mg, 1.04 mmol) were dissolved in 15 mL of a mixture of THF/DMF (1:1). After cooling at –5°C, $TsOH.H_2O$ (262.5 mg, 1.38 mmol) was carefully added and the mixture was stirred during 24 h under reflux, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (Cy/EtOAc 1:2) to afford compound **100** (153.9 mg, **86% yield**) as a yellow solid.



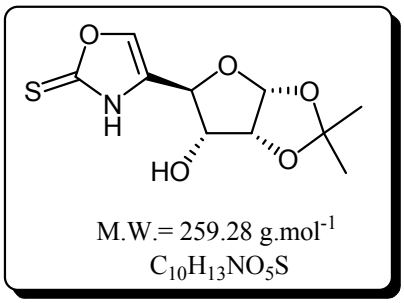
M.W.= 259.28 g.mol^{-1}
$C_{10}H_{13}NO_5S$

Rf = 0.3 (PE/EtOAc 1:2); $[\alpha]_D$ = - 58 (C=0.6, $CHCl_3$); **mp**: 148-149 °C; **I.R.** (NaCl) ν (cm^{-1}) 3480 (OH), 3240 (NH), 2974, 2954 (CH), 1655 (C=C), 1503, 1375 1108 (N-CS-O); **^{1}H NMR** (400 MHz, $(CD_3)_2CO$) δ 1.28 (s, 3H, Me), 1.44 (s, 3H, Me), 3.41 (brs, 1H, OH), 4.32 (d, 1H, $J_{3'\text{-}4'}$= 2.8 Hz, H-3'), 4.63 (d, 1H, $J_{1'\text{-}2'}$= 3.5 Hz, H-2'), 5.12 (d, 1H, $J_{3'\text{-}4'}$= 2.8 Hz, H-4'), 5.98 (d, 1H, $J_{1'\text{-}2'}$= 3.5 Hz, H-1'), 7.55 (s, 1H, H-5), 11.60 (brs, 1H, NH); **^{13}C NMR** (100 MHz, $(CD_3)_2CO$) δ 27.6, 28.0 (Me), 75.1 (C-4'), 77.4 (C-3'), 86.8 (C-2'), 106.4 (C-1'), 113.3 (Cq-isop), 128.4 (C-4), 136.4 (C-5), 180.9 (C=S); **HRMS**: calcd. for $C_{10}H_{14}NO_5S$ $[M+H]^+$ 260.0593, found 260.0600.

4-[(4*R*)-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-*C*-yl]-1,3-oxazoline-2-thione (101)

PROCEDURE

Ulose **99** (150.0 mg, 0.69 mmol) and KSCN (100.6 mg, 1.04 mmol) were dissolved in 15 mL of a mixture of THF/DMF (1:1). After cooling at –5°C, $TsOH.H_2O$ (262.5 mg, 1.38 mmol) was carefully added and the mixture was stirred during 24 h under reflux, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 4:6) to afford compound **101** (159.2 mg, **89% yield**) as a white solid.



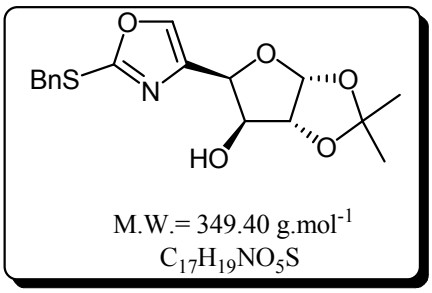
M.W.= 259.28 g.mol^{-1}
$C_{10}H_{13}NO_5S$

Rf = 0.4 (PE/EtOAc 2:8); $[\alpha]_D$ = + 57 (C=1.5, $CHCl_3$); **mp**: 145-146 °C; **I.R.** (NaCl) ν (cm^{-1}) 3479 (OH), 3200 (NH), 2986, 2940 (CH), 1655 (C=C), 1474, 1374 1140 (N-CS-O); **^{1}H NMR** (400 MHz, $(CD_3)_2CO$) δ 1.31 (s, 3H, Me), 1.49 (s, 3H, Me), 4.18-4.19 (m, 1H, H-3'), 4.45 (brs, 1H, OH), 4.69 (brt, 1H, $J_{1'-2'}$= 3.6 Hz, $J_{2'-3'}$= 4.2 Hz, H-2'), 4.73 (d, 1H, $J_{3'-4'}$= 9.0 Hz, H-4'), 5.82 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-1'), 7.64 (s, 1H, H-5), 11.90 (brs, 1H, NH); **^{13}C NMR** (100 MHz, $(CD_3)_2CO$) δ 27.6, 27.9 (Me), 73.5 (C-4'), 76.4 (C-3'), 80.8 (C-2'), 105.48 (C-1'), 114.3 (Cq-isop), 130.2 (C-4), 136.7 (C-5), 181.9 (C=S); **HRMS**: calcd. for $C_{10}H_{14}NO_5S$ $[M+H]^+$ 260.0593, found 260.0586.

4-[(4*R*)-1,2-*O*-isopropylidene-α-D-threofuranos-4-*C*-yl]-2-(benzylsulfanyl)-1,3-oxazole (102)

PROCEDURE

To OZT **100** (186.7 mg, 0.72 mmol) in dry DCM (10 ml), were added Et_3N (0.12 mL, 0.86 mmol) and BnBr (0.13 mL, 1.08 mmol). The reaction stirred during 3 h at room temperature, then cooled by treating with crushed ice. After extraction with DCM (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **102** (223.9 mg, **89% yield**) as a white solid**.**



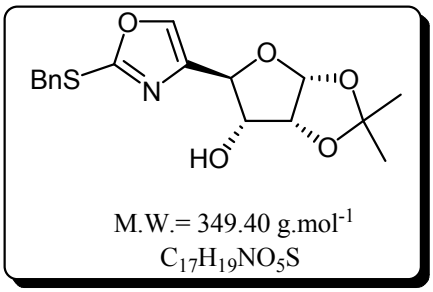
M.W.= 349.40 g.mol^{-1}
$C_{17}H_{19}NO_5S$

Rf = 0.4 (PE/EtOAc 7:3); $[\alpha]_D$= - 19 (C=0.9, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3480 (OH), 3110, 2976, 2843 (CH), 1610, 1098, 668 (-N=CS-O), 1466, 1453 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.32 (s, 3H, Me) 1.52 (s, 3H, Me), 4.11 (brs, 1H, OH), 4.30-4.37 (m, 3H, H-3', S*CH*$_2$Ph), 4.62 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-2'), 5.09 (d, 1H, $J_{3'-4'}$= 2.5 Hz, H-4'), 6.01 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-1'), 7.24-7.34 (m, 5H, Ph), 7.72 (s, 1H, H-5); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.0, 26.7 (Me), 36.7 (S*CH*$_2$Ph), 74.1 (C-4'), 76.2 (C-3'), 84.8 (C-2'), 104.8 (C-1'), 111.7 (Cq-isop), 127.8, 128.6, 128.8 (CH-Ph), 135.7 (Cq-Ph), 136.8 (C-4), 139.3 (C-5), 161.0 (C-SBn); **HRMS**: calcd. for $C_{17}H_{20}NO_5S$ $[M+H]^+$ 350.1062, found 350.1058.

4-[(4*R*)-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-*C*-yl]-2-(benzylsulfanyl)-1,3-oxazole (103)

PROCEDURE

To OZT **101** (186.7 mg, 0.72 mmol) in dry DCM (10 ml), were added Et_3N (0.12 mL, 0.86 mmol) and BnBr (0.13 mL, 1.08 mmol). The reaction stirred during 3 h at room temperature, then cooled by treating with crushed ice. After extraction with DCM (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **103** (218.9 mg, **87% yield**) as a yellow solid**.**



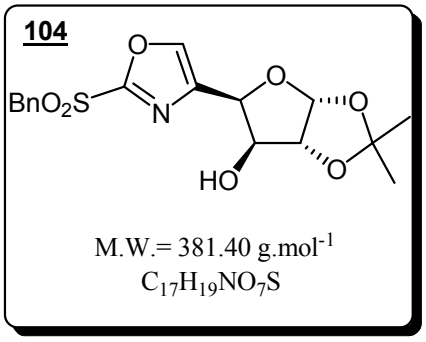
M.W.= 349.40 g.mol^{-1}
$C_{17}H_{19}NO_5S$

Rf = 0.5 (PE/EtOAc 6:4); $[\alpha]_D$ = + 24 (C=0.5, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3544 (OH), 3140, 2981, 2835 (CH), 1604, 1102, 667 (-N=CS-O), 1461, 1458 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.32 (s, 3H, Me) 1.54 (s, 3H, Me), 2.61 (d, 1H, $J_{3'-OH}$= 9.3 Hz, OH), 4.17-4.22 (m, 1H, H-3'), 4.30 (d, 1H, J_{A-B}= 12.9 Hz, S*CH*$_2$Ph), 4.34 (d, 1H, J_{A-B}= 12.9 Hz, S*CH*$_2$Ph), 4.58-4.62 (m, 2H, H-2', H-4'), 5.86 (d, 1H, $J_{1'-2'}$= 3.7 Hz, H-1'), 7.19-7.30 (m, 5H, Ph), 7.61 (s, 1H, H-5); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.6, 26.9 (Me), 37.0 (S*CH*$_2$Ph), 74.5 (C-4'), 75.0 (C-3'), 78.5 (C-2'), 104.2 (C-1'), 112.9 (Cq-isop), 127.9, 128.8, 129.1 (CH-Ph), 136.1 (Cq-Ph), 138.5 (C-4), 138.6 (C-5), 161.1 (C-SBn); **HRMS**: calcd. for $C_{17}H_{20}NO_5S$ $[M+H]^+$ 350.1062, found 350.1049.

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(benzylsulfonyl)-1,3-oxazole (104) and 4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(benzylsulfinyl)-1,3-oxazole (105)

PROCEDURE

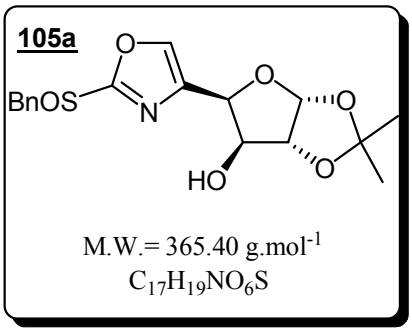
The *S*-alkylated oxazoline **102** (150.0 mg, 0.43 mmol) was dissolved in dry DCM (10 ml) and *m*-CPBA 77% (292.1 mg, 1.29 mmol) was added. The reaction was stirred during 3 h at room temperature, then hydrolysed with a saturated solution of NaS_2O_3. After extraction with DCM (3 x 25 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compounds **104** (39.4 mg, **24% yield**) as a yellow oil and the mixture of *S*-epimers **105a** and **105b** (108.4 mg, **69% yield**) as a yellow solid, in a proportion **105a**/**105b**: 45/55.



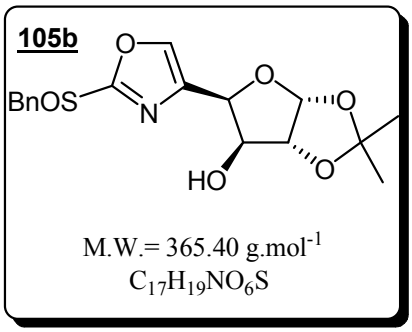
Rf = 0.6 (PE/EtOAc 1:1); $[\alpha]_D$ = - 38 (C=0.7, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3455 (OH), 2981, 2925 (CH), 1746 (-N=CS-O), 1696 (C=C), 1492, 1451 (Ph), 1374, 1162 (SO_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.35 (s, 3H, Me) 1.53 (s, 3H, Me), 2.33 (brs, 1H, OH), 4.42 (d, 1H, $J_{3'-4'}$= 2.5 Hz, H-3'), 4.61 (s, 2H, S*CH*$_2$Ph), 4.63 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-2'), 5.21 (d, 1H, $J_{3'-4'}$= 2.5 Hz, H-4'), 6.02 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-1'), 7.20-7.35 (m, 5H, Ph), 7.83 (s, 1H, H-5); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.3, 26.9 (Me), 61.8 (S*CH*$_2$Ph), 75.7 (C-3'), 76.3 (C-4'), 85.0 (C-2'), 105.1 (C-1'), 112.4 (Cq-isop), 125.6 (Cq-Ph), 129.3, 129.7, 131.0 (CH-Ph), 138.7 (C-4), 141.5 (C-5), 157.4 (C-2); **HRMS**: calcd. for $C_{17}H_{19}NO_7SNa$ $[M+Na]^+$ 404.0780, found 404.0776.

For both sulfoxides:

Rf = 0.1 (PE/EtOAc 1:1); **HRMS**: calcd. for $C_{17}H_{20}NO_6S$ $[M+H]^+$ 366.1011, found 366.1012.



^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 3H, Me) 1.54 (s, 3H, Me), 3.07 (brs, 1H, OH), 4.37-4.39 (m, 1H, H-3'), 4.48 (d, 1H, J_{A-B}=12.8 Hz, S*CH*$_2$Ph), 4.53 (d, 1H, J_{A-B}=12.8 Hz, S*CH*$_2$Ph), 4.62 (d, 1H, $J_{1'-2'}$= 3.7 Hz, H-2'), 5.19 (d, 1H, $J_{3'-4'}$= 2.0 Hz, H-4'), 6.06 (d, 1H, $J_{1'-2'}$= 3.7 Hz, H-1'), 7.15-7.18 (m, 5H, Ph), 7.90 (s, 1H, H-5); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.2, 26.9 (Me), 60.4 (S*CH*$_2$Ph), 75.7 (C-3'), 76.2 (C-4'), 84.9 (C-2'), 105.0 (C-1'), 112.2 (Cq-isop), 128.2 (Cq-Ph), 129.1, 130.1, 130.9 (CH-Ph), 138.5 (C-4), 141.4 (C-5), 161.4 (C-2).

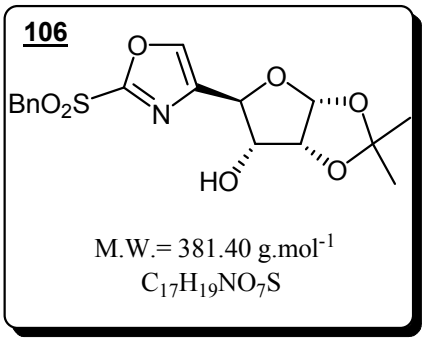


^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 3H, Me) 1.54 (s, 3H, Me), 3.07 (brs, 1H, OH), 4.37-4.39 (m, 1H, H-3'), 4.45 (d, 1H, $J_{A\text{-}B}$=13.0 Hz, SCH_2Ph), 4.51 (d, 1H, $J_{A\text{-}B}$=13.0 Hz, SCH_2Ph), 4.65 (d, 1H, $J_{1'\text{-}2'}$= 3.7 Hz, H-2'), 5.22 (d, 1H, $J_{3'\text{-}4'}$= 3.0 Hz, H-4'), 6.06 (d, 1H, $J_{1'\text{-}2'}$= 3.7 Hz, H-1'), 7.15-7.18 (m, 5H, Ph), 7.90 (s, 1H, H-5); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.2, 26.9 (Me), 60.6 (SCH_2Ph), 75.8 (C-3'), 76.1 (C-4'), 84.9 (C-2'), 105.1 (C-1'), 112.2 (Cq-isop), 128.2 (Cq-Ph), 129.1, 130.3, 131.0 (CH-Ph), 138.4 (C-4), 141.4 (C-5), 161.7 (C-2).

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-erythrofuranos-4-*C*-yl]-2-(benzylsulfonyl)-1,3-oxazole (106) and 4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-erythrofuranos-4-*C*-yl]-2-(benzylsulfinyl)-1,3-oxazole (107)

PROCEDURE

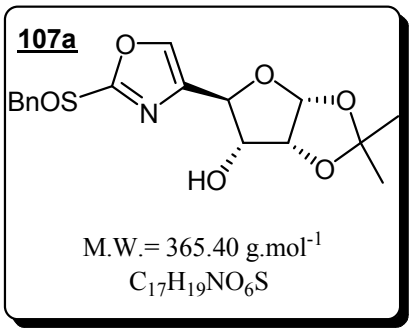
The *S*-alkylated oxazoline **103** (150.0 mg, 0.43 mmol) was dissolved in dry DCM (10 ml) and *m*-CPBA 77% (292.1 mg, 1.29 mmol) was added. The reaction was stirred during 3 h at room temperature, then hydrolysed with a saturated solution of NaS_2O_3. After extraction with DCM (3 x 25 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compounds **106** (60.7 mg, **37% yield**) as a white solid and the mixture of *S*-epimers **107a** and **107b** (92.7 mg, **59%yield**) as a colourless, in a proportion **107a**/**107b**: 47/53.



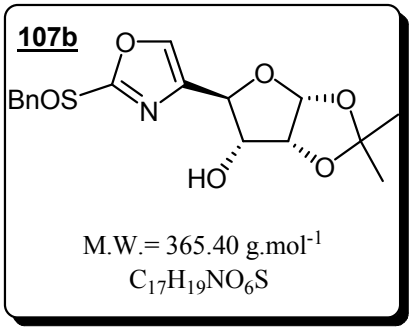
Rf = 0.6 (PE/EtOAc 4:6); $[\alpha]_D$ = + 33 (C=0.5, $CHCl_3$); **mp**: 106-107 °C; **I.R.** (NaCl) ν (cm^{-1}) 3450 (OH), 2976, 2934 (CH), 1745 (-N=CS-O), 1694 (C=C), 1456, 1443 (Ph), 1372, 1159 (SO_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.35 (s, 3H, Me) 1.56 (s, 3H, Me), 2.49 (d, 1H, $J_{3'\text{-}OH}$= 9.4 Hz, OH), 4.12-4.17 (m, 1H, H-3'), 4.56 (s, 2H, SCH_2Ph), 4.62 (dd, 1H, $J_{1'\text{-}2'}$= 3.9 Hz, $J_{2'\text{-}3'}$= 5.0 Hz, H-2'), 4.68 (d, 1H, $J_{3'\text{-}4'}$= 8.7 Hz, H-4'), 5.87 (d, 1H, $J_{1'\text{-}2'}$= 3.9 Hz, H-1'), 7.15-7.29 (m, 5H, Ph), 7.69 (s, 1H, H-5); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.6, 26.7 (Me), 61.7 (SCH_2Ph), 74.4 (C-4'), 75.7 (C-3'), 78.5 (C-2'), 104.4 (C-1'), 113.3 (Cq-isop), 125.5 (Cq-Ph), 129.2, 129.7, 131.1 (CH-Ph), 140.0 (C-4), 140.5 (C-5), 157.4 (C-2); **HRMS**: calcd. for $C_{17}H_{19}NO_7SNa$ $[M+Na]^+$ 404.0780, found 404.0778.

For both sulfoxides:

Rf = 0.3 (PE/EtOAc 6:4); **HRMS**: calcd. for $C_{17}H_{20}NO_6S$ $[M+H]^+$ 366.1011, found 366.1021.



^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 3H, Me) 1.41 (s, 3H, Me) 1.64 (s, 3H, Me), 4.21 (dd, 1H, $J_{2'-3'}$= 5.0 Hz, $J_{3-4'}$= 8.7 Hz, H-3'), 4.49 (d, 1H, J_{A-B}=12.9 Hz, SCH_2Ph), 4.51 (d, 1H, J_{A-B}=12.9 Hz, SCH_2Ph), 4.68-4.69 (m, 1H, H-2'), 4.75 (d, 1H, $J_{3'-4'}$= 8.7 Hz, H-4'), 5.94 (d, 1H, $J_{1'-2'}$= 3.8 Hz, H-1'), 7.18-7.33 (m, 5H, Ph), 7.85 (s, 1H, H-5); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.6, 26.7 (Me), 60.8 (SCH_2Ph), 74.4 (C-4'), 75.5 (C-3'), 78.5 (C-2'), 104.3 (C-1'), 113.1 (Cq-isop), 128.3 (Cq-Ph), 129.1, 129.3, 130.3 (CH-Ph), 139.8 (C-4), 140.5 (C-5), 162.2 (C-2).

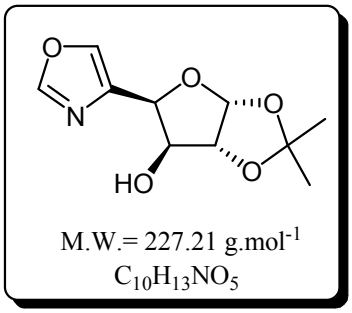


^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (s, 3H, Me) 1.63 (s, 3H, Me), 4.18 (dd, 1H, $J_{2'-3'}$= 5.1 Hz, $J_{3-4'}$= 8.6 Hz, H-3'), 4.47 (d, 1H, J_{A-B}=12.9 Hz, SCH_2Ph), 4.51 (d, 1H, J_{A-B}=12.9 Hz, SCH_2Ph), 4.67-4.69 (m, 1H, H-2'), 4.75 (d, 1H, $J_{3'-4'}$= 8.6 Hz, H-4'), 5.93 (d, 1H, $J_{1'-2'}$= 3.5 Hz, H-1'), 7.18-7.33 (m, 5H, Ph), 7.84 (s, 1H, H-5); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.6, 26.7 (Me), 60.9 (SCH_2Ph), 74.5 (C-4'), 75.6 (C-3'), 78.5 (C-2'), 104.3 (C-1'), 113.1 (Cq-isop), 128.4 (Cq-Ph), 129.1, 129.2, 130.3 (CH-Ph), 139.7 (C-4), 140.6 (C-5), 162.2 (C-2).

4-[(4*R*)-1,2-*O*-isopropylidene-α-D-threofuranos-4-*C*-yl)]-1,3-oxazole (108)

PROCEDURE

OXT **100** (100.0 mg, 0.39 mmol) was dissolved in dry DCM (10 ml) and *m*-CPBA 77% (86.3 mg, 0.39 mmol) was added. The reaction was stirred during 1 h at room temperature, then hydrolysed with a saturated solution of NaS_2O_3. After extraction with DCM (3 x 15 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **108** (76.2 mg, **86% yield**) as a yellow solid.



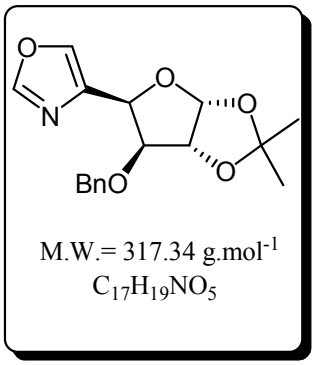
M.W.= 227.21 g.mol^{-1}
$C_{10}H_{13}NO_5$

Rf = 0.3 (PE/EtOAc 4:6); $[\alpha]_D$ = - 69 (C=0.5, $CHCl_3$); **mp**: 99-100 °C; **I.R.** (NaCl) ν (cm^{-1}) 3480 (OH), 2972, 2930 (CH), 1730 (-N=C-O), 1645 (C=C); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.36 (s, 3H, Me), 1.56 (s, 3H, Me), 4.02 (brs, 1H, OH), 4.41 (d, 1H, $J_{3'-4'}$=2.5 Hz, H-3'), 4.68 (d, 1H, $J_{1'-2'}$=3.7 Hz, H-2'), 5.20 (d, 1H, $J_{3'-4'}$=2.4 Hz, H-4'), 6.06 (d, 1H, $J_{1'-2'}$= 3.7 Hz, H-1'), 7.83 (s. 1H, H-5), 7.95 (s, 1H, H-2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.2, 26.9 (Me), 73.9 (C-4'), 76.7 (C-3'), 85.0 (C-2'), 105.1 (C-1'), 112.0 (Cq-isop), 135.5 (C-4), 138.6 (C-5), 151.5 (C-2); **HRMS**: calcd. for $C_{10}H_{14}NO_5$ $[M+H]^+$ 228.0872, found 228.0866.

4-[(4*R*)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-threofuranos-4-*C*-yl]-1,3-oxazole (109)

PROCEDURE

The OXT **87** (100.0 mg, 0.29 mmol) was dissolved in dry DCM (10 ml) and *m*-CPBA 77% (64.9 mg, 0.29 mmol) was added. The reaction was stirred during 1 h at room temperature, then hydrolysed with a saturated solution of NaS_2O_3. After extraction with DCM (3 x 15 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **109** (80.0 mg, **87% yield**) as a yellow oil.



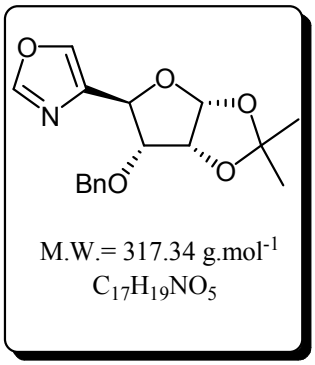
M.W.= 317.34 g.mol^{-1}
$C_{17}H_{19}NO_5$

Rf = 0.4 (PE/EtOAc 7:3); $[\alpha]_D$ = - 34 (C=0.5, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2976, 2930 (CH), 1725 (-N=C-O), 1650 (C=C), 1456, 1451 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.34 (s, 3H, Me), 1.53 (s, 3H, Me), 4.19 (d, 1H, $J_{3'-4'}$= 3.2 Hz, H-3'), 4.37 (d, 1H, J_{A-B}= 12.2 Hz, OCH_2Ph), 4.49 (d, 1H, J_{A-B}= 12.2 Hz, OCH_2Ph), 4.69 (d, 1H, $J_{1'-2'}$ = 3.6 Hz, H-2'), 5.31 (d, 1H, $J_{3'-4'}$= 2.9 Hz, H-4'), 6.03 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-1'), 7.11-7.13 (m, 2H, Ph), 7.25-7.29 (m, 3H, Ph), 7.75 (s. 1H, H-5), 7.88 (s, 1H, H-2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.4, 26.9 (Me), 72.7 (OCH_2Ph), 77.2 (C-4'), 82.4 (C-3'), 83.2 (C-2'), 104.9 (C-1'), 112.1 (Cq-isop), 127.7, 127.9, 128.5 (CH-Ph), 136.0 (C-4), 137.4 (C-5), 137.7 (Cq-Ph), 150.8 (C-2); **HRMS**: calcd. for $C_{17}H_{20}NO_5$ $[M+H]^+$ 318.1341, found 318.1347.

4-[(4*R*)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-*C*-yl]-1,3-oxazole (110)

PROCEDURE

The OXT **95** (100.0 mg, 0.29 mmol) was dissolved in dry DCM (10 ml) and *m*-CPBA 77% (64.9 mg, 0.29 mmol) was added. The reaction was stirred during 1 h at room temperature, then hydrolysed with a saturated solution of NaS_2O_3. After extraction with DCM (3 x 15 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **110** (75.5 mg, **82% yield**) as a yellow oil.



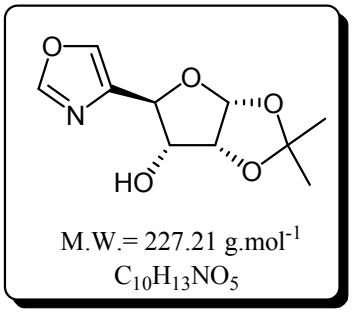
M.W.= 317.34 g.mol^{-1}
$C_{17}H_{19}NO_5$

Rf = 0.3 (PE/EtOAc 6:4); $[\alpha]_D$ = + 58 (C=0.8, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2984, 2927 (CH), 1725 (-N=C-O), 1648 (C=C), 1465, 1459 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.38 (s, 3H, Me), 1.66 (s, 3H, Me), 4.18 (dd, 1H, $J_{2'-3'}$= 4.3 Hz, $J_{3'-4'}$= 8.9 Hz, H-3'), 4.53 (d, 1H, J_{A-B}= 11.9 Hz, O*CH*$_2$Ph), 4.61-4.65 (m, 2H, H-2', O*CH*$_2$Ph), 5.02 (d, 1H, $J_{3'-4'}$= 8.9 Hz, H-4'), 5.86 (d, 1H, $J_{1'-2'}$= 3.8 Hz, H-1'), 7.23-7.29 (m, 5H, Ph), 7.67 (s, 1H, H-5), 7.85 (s, 1H, H-2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.5, 26.9 (Me), 72.3 (C-4'), 72.6 (O*CH*$_2$Ph), 77.8 (C-2'), 80.9 (C-3'), 104.1 (C-1'), 113.2 (Cq-isop), 128.0, 128.1, 128.4 (CH-Ph), 137.0 (C-4), 137.5 (C-5), 138.1 (Cq-Ph), 151.6 (C-2); **HRMS**: calcd. for $C_{17}H_{19}NO_5Na$ $[M+Na]^+$ 340.1161, found 340.1167.

4-[(4*R*)-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-*C*-yl]-1,3-oxazole (111)

PROCEDURE

OXT **101** (100.0 mg, 0.39 mmol) was dissolved in dry DCM (10 ml) and *m*-CPBA 77% (86.3 mg, 0.39 mmol) was added. The reaction was stirred during 1 h at room temperature, then hydrolysed with a saturated solution of NaS_2O_3. After extraction with DCM (3 x 15 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 4:6) to afford compound **111** (74.4 mg, **84% yield**) as a yellow solid.



M.W.= 227.21 g.mol^{-1}
$C_{10}H_{13}NO_5$

Rf = 0.2 (PE/EtOAc 4:6); $[\alpha]_D$ = + 77 (C=0.5, $CHCl_3$); **mp**: 107-108 °C; **I.R.** (NaCl) ν (cm^{-1}) 3488 (OH), 2972, 2930 (CH), 1725 (-N=C-O), 1651 (C=C); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.41 (s, 3H, Me), 1.63 (s, 3H, Me), 4.27 (ddd, 1H, $J_{3'-4'}$= 8.7 Hz, $J_{2'-3'}$= 4.9 Hz, $J_{3'-OH}$= 1.3 Hz, H-3'), 4.70 (dd, 1H, $J_{1'-2'}$= 3.8 Hz, $J_{2'-3'}$= 4.9 Hz, H-2'), 4.75 (d, 1H, $J_{3'-4'}$= 8.7 Hz, H-4'), 5.96 (d, 1H, $J_{1'-2'}$= 3.8 Hz, H-1'), 7.74 (s. 1H, H-5), 7.90 (s, 1H, H-2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.7 (Me), 75.4 (C-4'), 76.8 (C-3'), 78.5 (C-2'), 104.3 (C-1'), 113.0 (Cq-isop), 137.1 (C-4), 137.4 (C-5), 151.8 (C-2); **HRMS**: calcd. for $C_{10}H_{13}NO_5Na$ $[M+Na]^+$ 250.0691, found 250.0682.

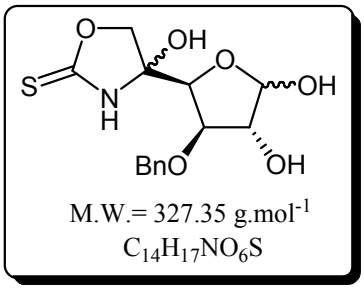
4-[(4*S*)-4-hydroxy-3-*O*-benzyl-α-D-threofuranos-4-*C*-yl)]-1,3-oxazolidine-2-thione (112)

PROCEDURE

A solution of OXT **87** (100.0 mg, 0.29 mmol) in 10 mL of DCM/TFA/H_2O (2:2:1) was stirred at room temperature during 3 h. The solvent was eliminated under reduced pressure and the residue was co-evaporated several times with water and after concentration under vacuum, purified by column chromatography (PE/EtOAc 7:3) to afford the anomeric mixture **112** (78.8 mg, **83% yield**) as a yellow oil, in a proportion α/β: 31/69.

For both anomers:

Rf = 0.5 (PE/EtOAc 1:1); **HRMS**: calcd. for $C_{14}H_{18}NO_6S$ $[M+H]^+$ 328.0855, found 328.0845.



M.W.= 327.35 g.mol^{-1}
$C_{14}H_{17}NO_6S$

^{1}H NMR (250 MHz, $CDCl_3$) δ 4.02 (d, $J_{3'\alpha-4'\alpha}$= 3.2 Hz, H-4'α), 4.15-4.17 (m, H-3'β), 4.35-4.37 (m, H-2'β), 4.63-4.70 (m, H-2'α, H-4'β, OCH_2Phα, OCH_2Phβ, H-5Aα, H-5Aβ, H-5Bα, H-5Bβ), 4.99 (d, $J_{3'\alpha-4'\alpha}$= 3.2 Hz, H-3'α), 5.68 (brs, H-4'β), 5.99 (d, $J_{1'\alpha-2'\alpha}$= 3.8 Hz, H-1'α), 7.28-7.35 (m, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 73.4, 73.6 (OCH_2Ph), 74.9, 75.0 (C-4'α, C-4'β), 77.4, 77.5 (C-5), 78.1, 79.8 (C-2'α, C-2'β), 83.6, 83.8 (C-3'α, C-3'β), 97.0 (C-1'α), 105.0 (C-1'β), 112.6, 112.7 (C-4), 127.5, 128.1, 128.7, 128.9, 129.0, 129.4 (CH-Ph), 135.3, 135.6 (Cq, Ph), 187.6, 188.3 (C=S).

6*R*, 7*R*, 8*R*-7-benzyloxy-5,6,8-trihydroxy-5,6,7,8-tetrahydro-3-thioxo (3H)-oxazolo[3,4-a]pyridine (113)

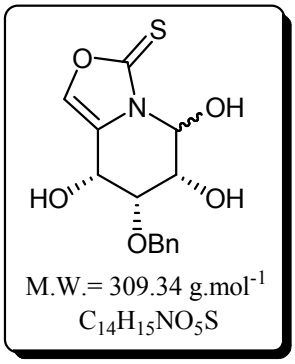
PROCEDURE

A solution of OXT **95** (100.0 mg, 0.29 mmol) in 10 mL of DCM/TFA/H_2O (2:2:1) was stirred at room temperature during 3 h. The solvent was eliminated under reduced pressure and the

residue was co-evaporated several times with water and after concentration under vacuum, purified by column chromatography (PE/EtOAc 1:1) to afford the anomeric mixture **113** (79.8 mg, **89% yield**) as a yellow oil, in a proportion α/β: 84/16.

For both anomers:

Rf = 0.2 (PE/EtOAc 4:6); **HRMS**: calcd. for $C_{14}H_{15}NO_5SNa$ $[M+Na]^+$ 332.0569, found 332.0586.



M.W.= 309.34 g.mol^{-1}
$C_{14}H_{15}NO_5S$

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.67 (brs, OH), 3.82 (dd, $J_{3\beta\text{-}4\beta}$= 1.5 Hz, $J_{2\beta\text{-}3\beta}$= 4.0 Hz, H-3β), 3.98 (dd, $J_{3\alpha\text{-}4\alpha}$= 1.6 Hz, $J_{2\alpha\text{-}3\alpha}$= 3.9 Hz, H-3α), 4.06 (brs, OH), 4.18-4.23 (m, H-2α H-2β), 4.73 (d, $J_{A\text{-}B}$= 11.3 Hz, O*C*H_2Ph), 4.80 (d, $J_{A\text{-}B}$= 11.3 Hz, O*C*H_2Ph), 4.84 (brs, H-4α, H-4β), 5.47 (brs, OH), 5.54 (brt, $J_{1\beta\text{-}2\beta}$= 4.3 Hz, $J_{1\beta\text{-}OH}$= 4.5 Hz, H-1β), 5.69 (d, $J_{1\alpha\text{-}2\alpha}$= 3.5 Hz, H-1α), 5.98 (d, $J_{1\beta\text{-}OH}$= 4.5 Hz, OH), 7.30-7.36 (m, Ph, H-6α, H-6β); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 61.6 (C-4α), 62.0 (C-4β), 68.9 (C-2β), 71.8 (C-2α), 72.9 (O*C*H_2Phα), 73.5 (O*C*H_2Phβ), 74.0 (C-3α), 75.5 (C-3β), 78.1 (C-1β), 80.7 (C-1α), 128.3, 128.7, 128.9 (CH-Phβ), 128.4, 128.6, 128.9 (CH-Phα), 128.9 (Cq, Phβ), 129.6 (Cq, Phα), 134.4 (C-6α), 134.6 (C-6β), 136.6 (C-5β), 136.9 (C-5α), 178.1, 178.2 (C=S).

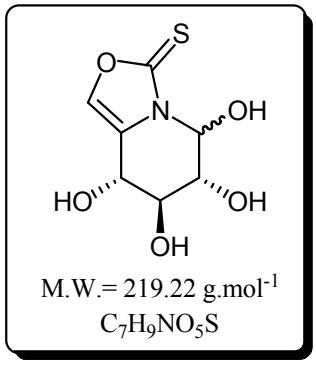
6*R*, 7*S*, 8*R*-5,6,7,8-tetrahydroxy-5,6,7,8-tetrahydro-3-thioxo-(3H)-oxazolo[3,4-a]pyridine (114)

PROCEDURE

A solution of OXT **100** (100.0 mg, 0.39 mmol) in 10 mL of DCM/TFA/H_2O (2:2:1) was stirred at room temperature during 3 h. The solvent was eliminated under reduced pressure and the residue was co-evaporated several times with water and after concentration under vacuum, purified by column chromatography (EtOAc) to afford the anomeric mixture **114** (74.4 mg, **87% yield**) as a colourless oil, in a proportion α/β: 57/43.

For both anomers:

Rf = 0.2 (EtOAc); **HRMS**: calcd. for $C_7H_{10}NO_5S$ $[M+H]^+$ 220.0280, found 220.0271.



M.W.= 219.22 g.mol^{-1}
$C_7H_9NO_5S$

^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 3.78-3.89 (m, H-2α, H-2β), 4.01-4.02 (m, H-4α, H-4β), 4.38 (brs, OH), 4.57 (d, $J_{2\beta\text{-}3\beta}$= 7.5 Hz, H-3β), 4.72 (d, $J_{2\alpha\text{-}3\alpha}$= 6.6 Hz, H-3α), 5.06 (brs, OH), 5.52 (t, $J_{1\beta\text{-}2\beta}$= $J_{1\beta\text{-}OH}$= 4.9 Hz, H-1β), 5.80 (t, $J_{1\alpha\text{-}2\alpha}$= $J_{1\alpha\text{-}OH}$= 3.4 Hz, H-1α), 5.96 (d, $J_{1\beta\text{-}OH}$= 4.9 Hz, OH), 6.12 (d, $J_{1\alpha\text{-}OH}$= 3.4 Hz, OH), 7.50 (d, $J_{4\alpha\text{-}6\alpha}$= 1.8 Hz, H-6α), 7.53 (d, $J_{4\beta\text{-}6\beta}$= 1.7 Hz, H-6β); **^{13}C NMR** (100 MHz, $(CD_3)_2CO$) δ 67.5 (C-3α), 68.6 (C-3β), 72.0 (C-2α), 72.7 (C-2β), 75.3, 75.3 (C-4), 79.5 (C-1α), 83.9 (C-1β), 132.6, 132.6 (C-5), 134.5 (C-6β), 136.6 (C-6α), 180.4 (C=S).

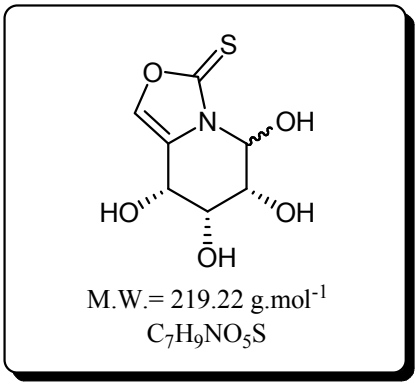
6*R*, 7*R*, 8*R*-5,6,7,8-tetrahydroxy-5,6,7,8-tetrahydro-3-thioxo-(3H)-oxazolo[3,4-a]pyridine (115)

PROCEDURE

A solution of OXT **101** (100.0 mg, 0.39 mmol) in 10 mL of DCM/TFA/H_2O (2:2:1) was stirred at room temperature during 3 h. The solvent was eliminated under reduced pressure and the residue was co-evaporated several times with water and after concentration under vacuum, purified by column chromatography (EtOAc) to afford the anomeric mixture **115** (75.2 mg, **88% yield**) as a colourless oil, in a proportion α/β: 77/23.

For both anomers:

Rf = 0.3 (EtOAc); **HRMS**: calcd. for $C_7H_{10}NO_5S$ $[M+H]^+$ 220.0280, found 220.0271.



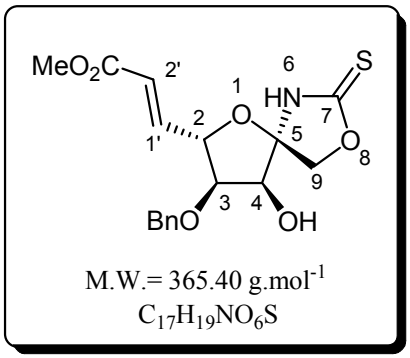
M.W.= 219.22 g.mol^{-1}
$C_7H_9NO_5S$

^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 3.90-3.91 (m, H-2β), 3.98–3.99(m, H-2α), 4.05-4.06 (m, H-3α), 4.17 (brs, H-3β), 4.70-4.71 (m, H-4β), 4.77 (brs, H-4α), 5.50 (d, $J_{1\alpha\text{-}2\alpha}$= 3.9 Hz, H-1α), 5.53 (d, $J_{1\beta\text{-}2\beta}$= 4.9 Hz, H-1β), 7.41 (s, H-6β), 7.48 (s, H-6α); **^{13}C NMR** (100 MHz, $(CD_3)_2CO$) δ 64.7 (C-4α), 65.8 (C-4β), 68.9 (C-2β), 70.6 (C-3α), 74.3 (C-3β), 75.0 (C-2α), 80.7 (C-1β), 82.8 (C-1α), 132.9 (C-5), 135.6 (C-6), 180.2 (C=S).

2*S*,3*R*,4*S*,5*S*,*E*-2-(2-methoxycarbonyl)vinyl-3-benzyloxy-4-hydroxy-6-aza-1,8-dioxaspiro[4.4]nonane-7-thione (116)

PROCEDURE

The iminosugar **113** (92.1 mg, 0.42 mmol) was dissolved in dry THF (10 mL). (Carbomethoxymethylene)triphenylphosphorane (0.42 g ,1.26 mmol) and benzoic acid (2.56 mg, 0.021 mmol) were added and the reaction was stirred under reflux during 8 h. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **116** (133.5 mg, **87% yield**) as a yellow oil.



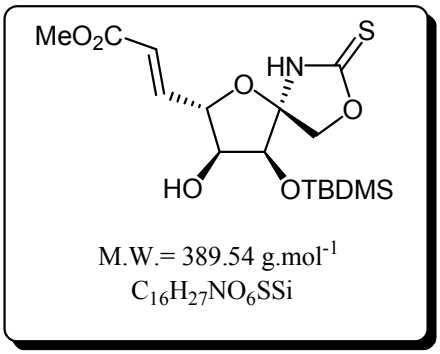
M.W.= 365.40 g.mol^{-1}
$C_{17}H_{19}NO_6S$

Rf = 0.4 (PE/EtOAc 4:6); $[\alpha]_D$ = + 33 (C=0.6, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3480 (OH), 3250 (NH), 3032, 2922, 2852 (CH), 1715 (C=O), 1648 (C=C), 1484, 1170 (N-CS-O), 1456, 1453 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.04 (d, 1H, $J_{4\text{-}OH}$= 4.8 Hz, OH), 3.75 (s, 3H, OMe), 3.95 (t, 1H, $J_{3\text{-}4}$= $J_{2\text{-}3}$= 4.6 Hz, H-3), 4.13 (brt, 1H, $J_{4\text{-}OH}$= 4.8 Hz, $J_{3\text{-}4}$= 4.6 Hz, H-4), 4.54 (d, 1H, $J_{9A\text{-}9B}$= 11.0 Hz, H-9B), 4.58 (dt, 1H, $J_{2\text{-}2'}$= 1.7 Hz, $J_{2\text{-}3}$= $J_{2\text{-}1'}$= 4.6 Hz, H-2), 4.63 (d, 1H, $J_{A\text{-}B}$= 11.5 Hz, OCH_2Ph), 4.69 (d, 1H, $J_{A\text{-}B}$= 11.5 Hz, OCH_2Ph), 4.95 (d, 1H, $J_{9A\text{-}9B}$= 11.0 Hz, H-9A), 6.10 (dd, 1H, $J_{2\text{-}1'}$= 1.7 Hz, $J_{1'\text{-}2'}$= 15.6 Hz, H-2'), 6.84 (dd, 1H, $J_{2\text{-}1'}$= 4.6 Hz, $J_{1'\text{-}2'}$= 15.6 Hz, H-1'), 7.31-7.39 (m, 5H, Ph), 8.54 (brs, 1H, NH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 52.1 (OMe), 72.8 (C-4), 73.6 (OCH_2Ph), 76.9 (C-9), 79.7 (C-2), 81.1 (C-3), 98.9 (C-5), 122.4 (C-2'), 128.3, 128.9, 129.0 (CH-Ph), 136.3 (Cq-Ph), 143.8 (C-1'), 166.5 (C=O), 189.8 (C=S); **HRMS**: calcd. for $C_{17}H_{20}NO_6S$ $[M+H]^+$ 366.1011, found 366.1000.

2*S*,3*R*,4*S*,5*S*,*E*-2-(2-methoxycarbonyl)vinyl-3-hydroxy-4-(*tert*-butyldimethylsilyloxy)-6-aza-1,8-dioxaspiro[4.4]nonane-7-thione (117)

PROCEDURE

The iminosugar **115** (130.0 mg, 0.42 mmol) was dissolved in dry THF (10 mL). (Carbomethoxymethylene)triphenylphosphorane (0.42 g ,1.26 mmol) and benzoic acid (2.56 mg, 0.021 mmol) were added and the reaction was stirred at reflux during 8 h. The solvent was evaporated and the residue was dissolved in dry DMF (10 mL). Imidazole (114.4 mg, 1.68 mmol) and TBDMSCl (189.9 mg, 1.26 mmol) were added and the reaction was stirred at room temperature overnight, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 20 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **117** (134.2 mg, **82% yield**) as a yellow oil**.**



M.W.= 389.54 g.mol^{-1}
$C_{16}H_{27}NO_6SSi$

Rf = 0.5 (PE/EtOAc 1:1); $[\alpha]_D$ = + 47 (C=0.9, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3498 (OH), 3230 (NH), 2920, 2850 (CH), 1717 (C=O), 1647 (C=C), 1502, 1173 (N-CS-O), 1215 ($Si(CH_3)_2$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.07 (s, 3H, $Si(CH_3)_2$), 0.15 (s, 3H, $Si(CH_3)_2$), 0.92 (s, 9H, t-Bu), 3.74 (d, 1H, $J_{3\text{-}OH}$= 3.8 Hz, OH), 3.77 (s, 3H, OMe), 3.95 (d, 1H, $J_{3\text{-}4}$= 4.6 Hz, H-4), 4.11-4.12 (m, 1H, H-3), 4.54 (d, 1H, $J_{9A\text{-}9B}$= 11.0 Hz, H-9B), 4.45

(dt, 1H, $J_{2\text{-}2'}$= 1.7 Hz, $J_{2\text{-}3}$= $J_{2\text{-}1'}$= 5.0 Hz, H-2), 4.95 (d, 1H, $J_{9A\text{-}9B}$= 11.0 Hz, H-9A), 6.16 (dd, 1H, $J_{2\text{-}2'}$= 2.0 Hz, $J_{1'\text{-}2'}$= 15.3 Hz, H-2'), 6.88 (dd, 1H, $J_{2\text{-}1'}$= 5.0 Hz, $J_{1'\text{-}2'}$= 15.3 Hz, H-1'), 8.57 (brs, 1H, NH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.7, -4.5 (Si $(CH_3)_2$), 18.1 (Cq, *t*-Bu), 25.8 ($(CH_3)_3C$), 52.1 (OMe), 73.9 (C-4), 75.6 (C-3), 76.9 (C-9), 81.9 (C-2), 98.6 (C-5), 122.6 (C-2'), 143.5 (C-1'), 166.4 (C=O), 189.9 (C=S); **HRMS**: calcd. for $C_{16}H_{28}NO_6SSi$ $[M+H]^+$ 390.1014, found 390.1021.

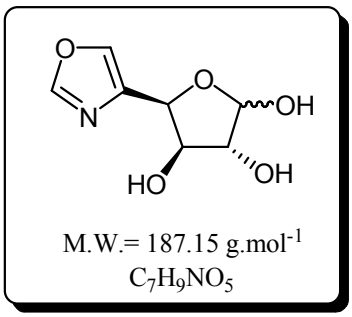
4-[(4*R*)-α-D-threofuranos-4-*C*-yl)]-1,3-oxazole (118)

PROCEDURE

A solution of oxazole **108** (100.0 mg, 0.44 mmol) in 20 mL of DCM/TFA/H_2O (10:9:1) was stirred at room temperature during 8 h. The solvent was eliminated under reduced pressure and the residue was co-evaporated several times with water and after concentration under vacuum, purified by column chromatography (EtOAc/ MeOH 9:1) to afford the anomeric mixture **118** (68.3 mg, **83% yield**) as a yellow oil, in a proportion α/β: 60/40.

For both anomers:

Rf = 0.1 (EtOAc); **HRMS**: calcd. for $C_7H_9NO_5Na$ $[M+Na]^+$ 210.0378, found 210.0379.



M.W.= 187.15 g.mol^{-1}
$C_7H_9NO_5$

^{1}H NMR (400 MHz, MeOD) δ 3.44-3.47 (m, H-3'α, H-3'β), 4.15-4.17 (m, H-2'α, H-2'β), 4.60 (d, $J_{3'\alpha\text{-}4'\alpha}$= 2.0 Hz, H-4'α), 4.62 (d, $J_{3'\beta\text{-}4'\beta}$= 1.6 Hz, H-4'β), 5.25 (s, H-1β), 5.54 (d, $J_{1'\alpha\text{-}2'\alpha}$= 3.9 Hz, H-1'α), 7.86 (s, H-5β), 7.88 (s, H-5α), 8.18 (s, H-2α), 8.20 (s, H-2β); **^{13}C NMR** (100 MHz, MeOD) δ 74.6, 74.8 (C-3'α,C-3'β), 78.1 (C-4'α), 78.6 (C-4'β), 82.1, 82.2 (C-2'α, C-2'β), 97.9 (C-1'α), 104.1 (C-1'β), 138.1, 138.3 (C-4α, C-4β), 138.9 (C-5α), 139.1 (C-5β), 153.2 (C-2α), 153.6 (C-2β).

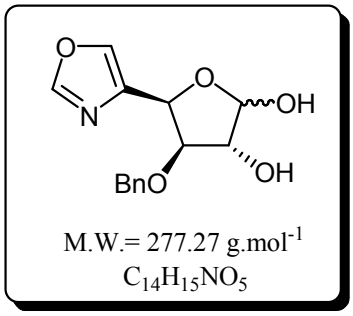
4-[(4*R*)-3-*O*-benzyl-α-D-threofuranos-4-*C*-yl)]-1,3-oxazole (119)

PROCEDURE

A solution of oxazole **109** (150.0 mg, 0.47 mmol) in 20 mL of DCM/TFA/H_2O (10:9:1) was stirred at room temperature during 8 h. The solvent was eliminated under reduced pressure and the residue was co-evaporated several times with water and after concentration under vacuum, purified by column chromatography (PE/ EtOAc 2:8) to afford the anomeric mixture **119** (93.8 mg, **72% yield**) as a yellow oil, in a proportion α/β: 63/37.

For the both anomers:

Rf = 0.1 (PE/EtOAc 3:7); **HRMS**: calcd. for $C_{14}H_{15}NO_5Na$ $[M+Na]^+$ 300.0848, found 300.0844.



M.W.= 277.27 g.mol^{-1}
$C_{14}H_{15}NO_5$

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.17-4.21 (m, H-3'α, H-3'β), 4.33-4.34 (m, H-2'α), 4.37-4.41 (m, H-2'β, OCH_2Phβ), 4.49 (d, $J_{A\text{-}B}$= 11.8 Hz, OCH_2Phα), 4.52 (d, $J_{A\text{-}B}$= 11.8 Hz, OCH_2Phα), 4.85 (brs, OH), 5.25 (s, H-1'β), 5.29-5.34 (m, H-4'α, H-4'β), 5.59 (d, $J_{1'\alpha\text{-}2'\alpha}$= 4.1 Hz, H-1'α), 7.22-7.36 (m, Ph), 7.65 (s, H-5α), 7.67 (s, H-5β), 7.85 (s, H-2α), 7.89 (s, H-2β); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 73.1, 73.5 (OCH_2Ph), 74.9 (C-4'α), 75.8 (C-4'β), 77.1 (C-2'α), 80.0 (C-2'β), 83.9 (C-3'α), 84.5 (C-3'β), 97.0 (C-1'α), 104.0 (C-1'β), 128.3, 128.4, 128.5, 128.8, 129.1, 129.2 (CH-Ph), 133.9 (Cq-Ph), 137.0 (C-4α), 137.8 (C-4β), 138.2 (C-5α), 138.3 (C-5β), 151.8 (C-2α), 151.9 (C-2β).

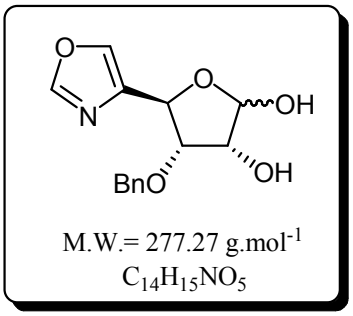
4-[(4*R*)-3-*O*-benzyl-α-D- erythrofuranos-4-*C*-yl)-1,3-oxazole (120)

PROCEDURE

A solution of oxazole **110** (150.0 mg, 0.47 mmol) in 20 mL of DCM/TFA/H_2O (10:9:1) was stirred at room temperature during 8 h. The solvent was eliminated under reduced pressure and the residue was co-evaporated several times with water and after concentration under vacuum, purified by column chromatography (PE/ EtOAc 2:8) to afford the anomeric mixture **120** (106.9 mg, **82% yield**) as a yellow oil, in a proportion α/β: 67/33.

For both anomers:

Rf = 0.2 (PE/EtOAc 3:7); **HRMS**: calcd. for $C_{14}H_{15}NO_5Na$ $[M+Na]^+$ 300.0848, found 300.0834.



M.W.= 277.27 g.mol^{-1}
$C_{14}H_{15}NO_5$

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.11-4.19 (m, H-3'α, H-3'β), 4.32-4.41 (m, H-2'α, H-2'β), 4.55 (d, $J_{A\text{-}B}$= 11.8 Hz, OCH_2Phβ), 4.59 (d, $J_{A\text{-}B}$= 11.8 Hz, OCH_2Phβ), 4.65 (d, $J_{A\text{-}B}$= 11.9 Hz, OCH_2Phα), 4.71 (d, $J_{A\text{-}B}$= 11.9 Hz, OCH_2Phα), 5.02 (d, $J_{3'\beta\text{-}4'\beta}$= 6.0 Hz, H-4'β), 5.10 (d, $J_{3'\alpha\text{-}4'\alpha}$= 5.8 Hz, H-4'α), 5.37 (s H-1'β), 5.45 (d, $J_{1'\alpha\text{-}2'\alpha}$= 3.8 Hz, H-1'α), 5.52 (brs, OH), 7.25-7.31 (m, Ph), 7.46 (s, H-5α), 7.56 (s, H-5β), 7.85 (s, H-2α), 7.89 (s, H-2β); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 70.5 (C-2'α), 73.2, 73.4 (OCH_2Ph), 74.9 (C-3'α), 75.0 (C-3'β) 75.5 (C-4'α), 75.6 (C-4'β), 80.5 (C-3'β), 82.1 (C-2'β), 96.8 (C-1'α), 102.7 (C-1'β), 128.1, 128.3, 128.4, 128.7, 129.8, 130.2 (CH-Ph), 131.7, 133.5 (Cq-Ph), 136.6 (C-4α), 136.9 (C-4β), 138.2 (C-5α), 138.3 (C-5β), 151.9 (C-2α), 152.1, (C-2β).

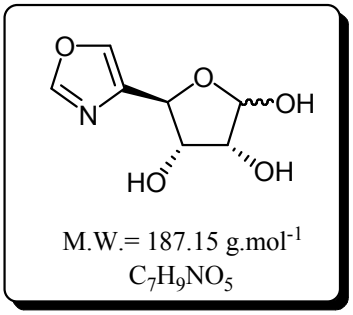
4-[(4*R*)-α-D-erythrofuranos-4-*C*-yl)]-1,3-oxazole (121)

PROCEDURE

A solution of oxazole **111** (100.0 mg, 0.44 mmol) in 20 mL of DCM/TFA/H_2O (10:9:1) was stirred at room temperature during 8 h. The solvent was eliminated under reduced pressure and the residue was co-evaporated several times with water and after concentration under vacuum, purified by column chromatography (EtOAc/ MeOH 9:1) to afford the anomeric mixture **121** (70.0 mg, **85% yield**) as a yellow oil, in a proportion α/β: 47/52.

For both anomers:

Rf = 0.1 (EtOAc); **HRMS**: calcd. for $C_7H_9NO_5Na$ $[M+Na]^+$ 210.0378, found 210.0363.



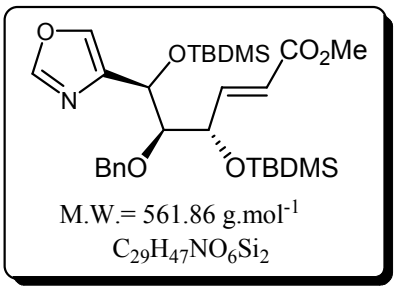
M.W.= 187.15 g.mol^{-1}
$C_7H_9NO_5$

^{1}H NMR (400 MHz, MeOD) δ 3.97 (dd, 1H, $J_{1'\beta\text{-}2'\beta}$=, 1.6 Hz, $J_{2'\beta\text{-}3'\beta}$= 4.8 Hz, H-2'β), 4.21 (dd, $J_{2'\alpha\text{-}3'\alpha}$= 3.5 Hz, $J_{3'\alpha\text{-}4'\alpha}$= 5.5 Hz, H-3'α), 4.27-4.30 (m, H-2'α), 4.40 (dd, $J_{2'\beta\text{-}3'\beta}$= 4.8 Hz, $J_{3'\beta\text{-}4'\beta}$= 6.6 Hz, H-3'β), 4.83 (d, $J_{3'\beta\text{-}4'\beta}$= 6.6 Hz, H-4'β), 5.04 (d, $J_{3'\alpha\text{-}4'\alpha}$= 5.5 Hz, H-4'α), 5.23 (d, $J_{1'\beta\text{-}2'\beta}$=, 1.6 Hz, H-1'β), 5.42 (d, $J_{1'\alpha\text{-}2'\alpha}$= 4.3 Hz, H-1'α), 7.89 (s, H-5α), 7.91 (s, H-5β), 8.18 (s, H-2α, H-2β); **^{13}C NMR** (100 MHz, MeOD) δ 72.2 (C-2'α), 75.0 (C-3'α), 75.8 (C-3'β), 77.3 (C-2'β), 77.9 (C-4'β), 79.2 (C-4'α), 97.8 (C-1'α), 103.5 (C-1'β), 138.0 (C-4α), 138.3 (C-4β), 140.2 (C-5α), 141.2 (C-5β), 153.8 (C-2α) 154.1 (C-2β).

Methyl (4*S*,5*R*,6*R*,*E*)-5-(benzyloxy)-4,6-bis-(*tert*-butyldimethylsilyloxy)-6-(oxazol-4-yl)hex-2-enoate (122)

PROCEDURE

The anomeric mixture **119** (125.0 mg, 0.45 mmol) was dissolved in dry THF (10 mL). (Carbomethoxymethylene)triphenylphosphorane (0.45 g, 1.35 mmol) and benzoic acid (2.81 mg, 0.023 mmol) were added and the reaction was stirred under reflux during 8 h. The solvent was evaporated and the residue was dissolved in dry DMF (10 mL). Imidazole (122.5 mg, 1.80 mmol) and TBDMSCl (203.4 mg, 1.35 mmol) were added and the reaction was stirred at room temperature overnight, then cooled by treating with crushed ice. After extraction with DCM (3 x 20 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 95:5) to afford compound **122** (166.9 mg, **66% yield**) as a colourless oil**.**

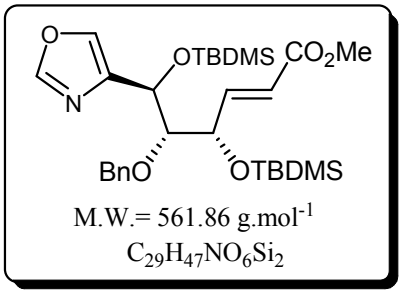


Rf = 0.2 (PE/EtOAc 9:1); $[\alpha]_D$ = + 47 (C=0.9, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2940, 2867 (CH), 1723 (-N=C-O), 1715 (C=O), 1647, 1650 (C=C), 1467, 1452 (Ph), 1210, 1212 ($Si(CH_3)_2$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.01 (s, 3H, $Si(CH_3)_3$), 0.05 (s, 3H, $Si(CH_3)_3$), 0.07 (s, 3H, $Si(CH_3)_3$), 0.08 (s, 3H, $Si(CH_3)_3$), 0.92 (s, 9H, *t*-Bu), 0.93 (s, 9H, *t*-Bu), 3.64 (dd, 1H, $J_{5'-6'}$= 4.7 Hz, $J_{4'-5'}$= 6.1 Hz, H-5'), 3.81 (s, 3H, OMe), 4.43 (ddd, 1H, $J_{4'-5'}$= 6.1 Hz, $J_{3'-4'}$= 4.5 Hz, $J_{2'-4'}$= 1.8 Hz, H-4'), 4.68 (s, 2H, OCH_2Ph), 4.92 (d, 1H, $J_{5'-6'}$= 4.7 Hz, H-6'), 6.05 (dd, 1H, $J_{2'-3'}$= 15.6 Hz, J_{2-4}= 1.8 Hz, H-2'), 7.20 (dd, 1H, $J_{2'-3'}$= 15.6 Hz, $J_{3'-4'}$= 4.5 Hz, H-3'), 7.28-7.32 (m, 5H, Ph), 7.68 (s, 1H, H-5), 7.79 (s, 1H, H-2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.9, -4.7, -4.8, -4.6 ($Si(CH3)_2$), 18.1, 18.2 (Cq, *t*-Bu), 25.8, 25.9 (*t*-Bu), 51.5 (OMe), 68.5 (C-6'), 72.3 (C-4'), 74.7 (OCH_2Ph), 83.6 (C-5'), 120.5 (C-2'), 127.6, 128.4, 128.6 (CH-Ph), 136.7 (C-5), 138.4 (Cq-Ph), 141.1 (C-4), 148.9 (C-3'), 151.2 (C-2), 166.9 (C=O); **HRMS**: calcd. for $C_{29}H_{48}NO_6Si_2$ $[M+H]^+$ 562.3020, found 562.3017.

Methyl (4*S*,5*S*,6*R*,*E*)-5-(benzyloxy)-4,6-bis-(*t*-butyldimethylsilyloxy)-6-(oxazol-4-yl)hex-2-enoate (123)

PROCEDURE

The anomeric mixture **120** (125.0 mg, 0.45 mmol) was dissolved in dry THF (10 mL). (Carbomethoxymethylene)triphenylphosphorane (0.45 g, 1.35 mmol) and benzoic acid (2.81 mg, 0.023 mmol) were added and the reaction was stirred under reflux during 8 h. The solvent was evaporated and the residue was dissolved in dry DMF (10 mL). Imidazole (122.5 mg, 1.80 mmol) and TBDMSCl (203.4 mg, 1.35 mmol) were added and the reaction was stirred at room temperature overnight, then cooled by treating with crushed ice. After extraction with DCM (3 x 20 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 95:5) to afford compound **123** (197.2 mg, **78% yield**) as a colourless oil**.**



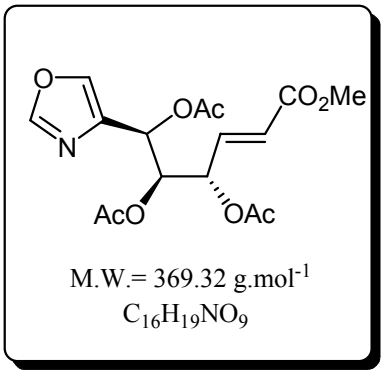
Rf = 0.2 (PE/EtOAc 9:1); $[\alpha]_D$ = - 42 (C=0.7, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2923, 2859 (CH), 1725 (-N=C-O), 1715 (C=O), 1649, 1650 (C=C), 1458, 1453 (Ph), 1215, 1217 ($Si(CH_3)_2$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.01 (s, 3H, $Si(CH_3)_3$), 0.09 (s, 3H, $Si(CH_3)_3$), 0.11 (s, 3H, $Si(CH_3)_3$), 0.16 (s, 3H, $Si(CH_3)_3$), 0.97 (s, 9H, *t*-Bu), 0.99 (s, 9H, *t*-Bu), 3.82 (s, 3H, OMe), 4.01 (dd, 1H, $J_{5'-6'}$= 5.8 Hz, $J_{4'-5'}$= 3.6 Hz, H-5'), 4.59 (d, 1H, J_{A-B}= 11.4 Hz, OCH_2Ph), 4.78 (ddd, 1H, $J_{4'-5'}$= 3.6 Hz, $J_{3'-4'}$= 5.1 Hz, $J_{2'-4'}$= 1.5 Hz, H-4'), 4.82 (d, 1H, J_{A-B}= 11.4 Hz, OCH_2Ph), 4.92 (d, 1H, $J_{5'-6'}$= 5.8 Hz, H-6'), 6.16 (dd, 1H, $J_{2'-3'}$= 15.7 Hz, $J_{2'-4'}$= 1.5 Hz, H-

2'), 7.19-7.34 (m, 6H, H-3', Ph), 7.68 (s, 1H, H-5), 7.90 (s, 1H, H-2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.9, -4.7, -4.6, -4.5 ($Si(CH3)_2$), 18.1, 18.2 (Cq, *t*-Bu), 25.9, 26.0 (*t*-Bu), 51.6 (OMe), 68.8 (C-6'), 72.6 (C-4'), 74.6 (OCH_2Ph), 85.8 (C-5'), 121.5 (C-2'), 127.5, 127.9, 128.2 (CH-Ph), 136.9 (C-5), 138.5 (Cq-Ph), 141.0 (C-4), 148.9 (C-3'), 151.0 (C-2), 166.9 (C=O); **HRMS**: calcd. for $C_{29}H_{48}NO_6Si_2$ $[M+H]^+$ 562.3020, found 562.3008.

Methyl (4*S*,5*R*,6*R*,*E*)-4,5,6-tri-*O*-acetoxy-6-(oxazol-4-yl)hex-2-enoate (124)

PROCEDURE

The anomeric mixture **118** (150.0 mg, 0.80 mmol) was dissolved in dry THF (10 mL). (Carbomethoxymethylene)triphenylphosphorane (0.80 g, 2.40 mmol) and benzoic acid (4.88 mg, 0.040 mmol) were added and the reaction was stirred under reflux during 8 h. The solvent was evaporated and the residue was dissolved in 9 mL of Pyr/ Ac_2O (2:1). The reaction was stirred at room temperature during 1 h. The residue was co-evaporated with toluene (3x) and after concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **124** (209.8 mg, **71% yield**) as a yellow oil.



M.W.= 369.32 g.mol^{-1}
$C_{16}H_{19}NO_9$

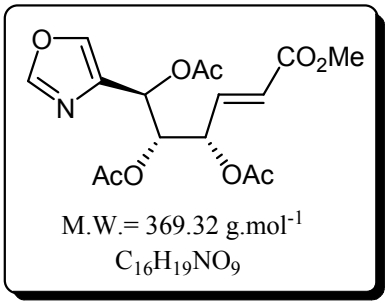
Rf = 0.2 (PE/EtOAc 1:1); $[\alpha]_D$ = + 25 (C=0.9, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2932, 2876 (CH), 1725 (-N=C-O), 1718, 1717 (C=O), 1647, 1651 (C=C); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.98 (s, 3H, OAc), 2.04 (s, 3H, OAc), 2.07 (s, 3H, OAc), 3.78 (s, 3H, OMe), 5.67 (dd, 1H, $J_{5'-6'}$= 4.8 Hz, $J_{4'-5'}$= 6.2 Hz, H-5'), 5.83 (ddd, 1H, $J_{4'-5'}$= 6.2 Hz, $J_{3'-4'}$= 4.6 Hz, $J_{2'-4'}$= 1.6 Hz, H-4'), 6.03 (dd, 1H, $J_{2'-3'}$= 15.6 Hz, $J_{2'-4'}$= 1.6 Hz, H-2'), 6.09 (d, 1H, $J_{5'-6'}$= 4.8 Hz, H-6'), 6.95 (dd, 1H, $J_{2'-3'}$= 15.6 Hz, $J_{3'-4'}$= 4.6 Hz, H-3'), 7.68 (s, 1H, H-5), 7.82 (s, 1H, H-2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 20.7, 20.8, 21.0 (OAc), 51.5 (OMe), 66.4 (C-6'), 70.2 (C-4'), 71.7 (C-5'), 121.6 (C-2'), 135.6 (C-4), 137.6 (C-5), 141.1 (C-3'), 151.0 (C-2), 166.9 (C=O, COOMe), 169.6, 169.8, 170.2 (C=O, Ac); **HRMS**: calcd. for $C_{16}H_{19}NO_9Na$ $[M+Na]^+$ 392.0958, found 392.0964.

Methyl (4*S*,5*S*,6*R*,*E*)-4,5,6-tri-*O*-acetoxy-6-(oxazol-4-yl)hex-2-enoate (125)

PROCEDURE

The anomeric mixture **121** (150.0 mg, 0.80 mmol) was dissolved in dry THF (10 mL). (Carbomethoxymethylene)triphenylphosphorane (0.80 g, 2.40 mmol) and benzoic acid (4.88 mg, 0.04 mmol) were added and the reaction was stirred under reflux during 8 h. The solvent was evaporated and the residue was dissolved in 9 mL of Pyr/ AcOH (2:1). The

reaction was stirred at room temperature during 1 h. The residue was co-evaporated with toluene (3x) and after concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **125** (189.1 mg, **64% yield**) as a yellow oil**.**



M.W.= 369.32 g.mol^{-1}
$C_{16}H_{19}NO_9$

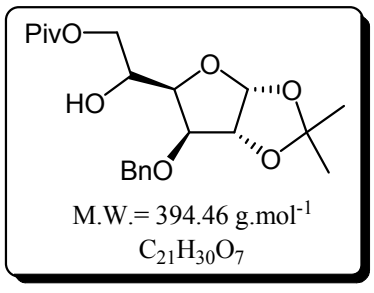
Rf = 0.3 (PE/EtOAc 1:1); $[\alpha]_D$ = - 18 (C=0.8, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2950, 2915 (CH), 1723 (-N=C-O), 1715, 1717 (C=O), 1650 (C=C); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.99 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.09 (s, 3H, OAc), 3.75 (s, 3H, OMe), 5.65 (dd, 1H, $J_{5'-6'}$= 6.9 Hz, $J_{4'-5'}$= 3.9 Hz, H-5'), 5.76 (ddd, 1H, $J_{4'-5'}$= 3.9 Hz, $J_{3'-4'}$= 5.6 Hz, $J_{2'-4'}$= 1.6 Hz, H-4'), 5.99 (dd, 1H, $J_{2'-3'}$= 15.6 Hz, $J_{2'-4'}$= 1.6 Hz, H-2'), 6.03 (d, 1H, $J_{5'-6'}$= 6.9 Hz, H-6'), 6.95 (dd, 1H, $J_{2'-3'}$= 15.6 Hz, $J_{3'-4'}$= 5.6 Hz, H-3'), 7.70 (s, 1H, H-5), 7.85 (s, 1H, H-2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 20.8, 20.9, 21.0 (OAc), 51.9 (OMe), 66.0 (C-6'), 70.8 (C-4'), 72.3 (C-5'), 123.2 (C-2'), 135.8 (C-4), 137.9 (C-5), 141.1 (C-3'), 151.4 (C-2), 166.1 (C=O, COOMe), 169.4, 169.5, 169.6 (C=O, Ac); **HRMS**: calcd. for $C_{16}H_{19}NO_9Na$ $[M+Na]^+$ 392.0958, found 392.0959.

3-*O*-Benzyl-1,2-*O*-isopropylidene-6-*O*-pivaloyl-α-D-glucofuranose (126)

PROCEDURE

To a cold (0 ºC) and stirred solution of diol **85** (500.0 mg, 1.61 mmol) in pyridine (10 mL), PivCl (0.20 mL, 1.61 mmol) was added dropwise. The reaction was stirred at room temperature during 2h, then co-evaporated with toluene (3x). After concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **126** (559.9 mg, **88% yield**) as a white solid**.**

CAS [321380-09-0]



M.W.= 394.46 g.mol^{-1}
$C_{21}H_{30}O_7$

Rf = 0.3 (PE/EtOAc 8:2); $[\alpha]_D$ = - 49 (C=1.2, $CHCl_3$); **mp**: 101-102 °C; **I.R.** (NaCl) ν (cm^{-1}) 3450 (OH), 2926, 2855 (CH), 1729 (C=O), 1475, 1460 (Ph), 1373 ($C(CH_3)_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.22 (s, 9H, t-Bu), 1.32 (s, 3H, Me), 1.47 (s, 3H, Me), 2.55 (d, 1H, $J_{5\text{-}OH}$= 5.6 Hz, OH), 4.10-4.22 (m, 4H, H-3, H-4, H-5, H-6B), 4.36 (dd, 1H, $J_{5\text{-}6A}$= 5.2 Hz, $J_{6A\text{-}6B}$= 13.7 Hz, H-6A), 4.59 (d, 1H, $J_{A\text{-}B}$= 11.7 Hz, O*C*H_2Ph), 4.62 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-2), 4.73 (d, 1H, $J_{A\text{-}B}$= 11.7 Hz, O*C*H_2Ph), 5.94 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-1), 7.30-7.39 (m, 5H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 25.6, 26.9 (Me), 27.3 ($(CH_3)_3C$), 39.2 (Cq, *t*-Bu), 66.8 (C-6), 68.1 (C-3), 72.4 (O*C*H_2Ph), 79.4 (C-4), 81.9 (C-5), 82.3 (C-2), 105.4 (C-1), 111.3 (Cq-isop), 128.0, 128.4, 128.8 (CH-Ph), 137.3

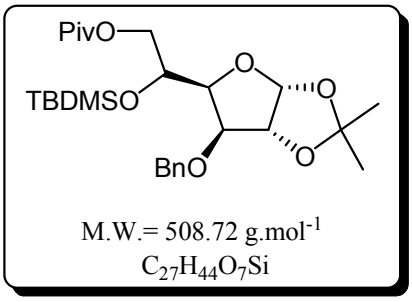
(Cq-Ph), 178.8 (*CO*C(CH$_3$)$_3$); **HRMS**: calcd. for $C_{21}H_{30}O_7Na$ [M+Na]$^+$ 417.1889, found 417.1891.

[284]Tiwari, P.; Misra, A. K. *Carbohydr. Res*. **2006**, *341*, 339-350.

3-*O*-Benzyl-1,2-*O*-isopropylidene-6-*O*-pivaloyl-5-*O*-*tert*-butyldimethylsilyl-α-D-glucofuranose (127)

PROCEDURE

To compound **126** (386.7 mg, 0.98 mmol) in dry DMF (5 ml) at 0ºC, were added imidazole (133.4 mg, 1.96 mmol) and TBDMSCl (162.6 mg, 1.08 mmol). The reaction was stirred at room temperature overnight, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compound **127** in quantitative yield, as a white solid**.**



Rf = 0.7 (PE/EtOAc 7:3); $[\alpha]_D$ = - 50 (C=1.0, $CHCl_3$); **mp**: 93-94 °C; **I.R.** (NaCl) ν (cm^{-1}) 2987, 2927 (CH), 1727 (C=O), 1456, 1452 (Ph), 1373 (C(CH$_3$)$_3$), 1207 (Si(CH$_3$)$_2$) ; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.01 (s, 6H, Si(CH$_3$)$_3$), 0.86 (s, 9H, *t*-Bu), 1.22 (s, 9H, *t*-Bu), 1.31 (s, 3H, Me), 1.50 (s, 3H, Me), 4.04 (d, 1H, $J_{4\text{-}5}$= 2.0 Hz, H-5), 4.10 (dd, 1H, $J_{5\text{-}6B}$= 2.0 Hz, $J_{6A\text{-}6B}$= 11.6 Hz, H-6B), 4.34-4.30 (m, 2H, H-3, H-4), 4.36 (dd, 1H, $J_{5\text{-}6A}$= 1.5 Hz, $J_{6A\text{-}6B}$= 11.6 Hz, H-6A), 4.58 (d, 1H, $J_{A\text{-}B}$= 11.6 Hz, O*CH*$_2$Ph), 4.60 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-2), 4.67 (d, 1H, $J_{A\text{-}B}$= 11.6 Hz, O*CH*$_2$Ph), 5.86 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-1), 7.29-7.37 (m, 5H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.9, -4.7, (Si(CH3)$_2$), 18.1 (Cq, *t*-Bu), 25.4 (*t*-Bu), 26.6, 26.7 (Me), 28.0 ((CH$_3$)$_3$C), 40.8 (Cq, *t*-Bu), 66.8 (C-6), 68.1 (C-3), 72.0 (O*CH*$_2$Ph), 79.7 (C-4), 81.0 (C-2), 82.3 (C-5), 105.6 (C-1), 111.9 (Cq-isop), 127.3, 127.9, 128.6 (CH-Ph), 133.8 (Cq-Ph), 175.5 (*CO*C(CH$_3$)$_3$); **HRMS**: calcd. for $C_{27}H_{44}O_7SiNa$ [M+Na]$^+$ 531.2754, found 531.2770.

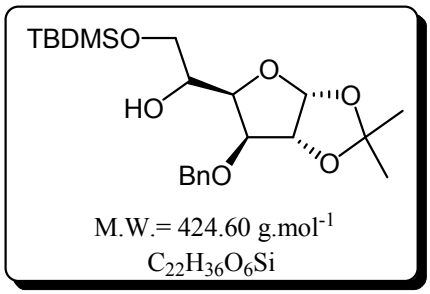
3-*O*-Benzyl-1,2-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-α-D-glucofuranose (128)

PROCEDURE

To a cold (0 ºC) and stirred solution of compound **127** (100.0 mg, 0.20 mmol) in MeOH (10 mL), Na was added until pH ≈ 9. The reaction was stirred at room temperature overnight and the solution was then neutralized with Amberlite. After filtration and concentration

under vacuum, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **128** in quantitative yield as a colourless oil**.**

CAS [106445-04-9]



M.W.= 424.60 g.mol^{-1}
$C_{22}H_{36}O_6Si$

Rf = 0.5 (PE/EtOAc 6:4); $[\alpha]_D$ = + 43 (C=0.8, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.10 (s, 6H, $Si(CH_3)_3$), 0.92 (s, 9H, *t*-Bu), 1.37 (s, 3H, Me), 1.49 (s, 3H, Me), 2.72 (d, 1H, $J_{6\text{-}OH}$= 6.6 Hz, OH), 3.77 (dd, 1H, $J_{5\text{-}6B}$= 4.8 Hz, $J_{6A\text{-}6B}$= 10.1 Hz, H-6B), 3.83 (dd, 1H, $J_{5\text{-}6A}$= 3.8 Hz, $J_{6A\text{-}6B}$= 10.1 Hz, H-6A), 3.98-4.06 (m, 1H, H-5), 4.11-4.17 (m, 2H, H-3, H-4), 4.62 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-2), 4.69 (d, 1H, $J_{A\text{-}B}$= 11.6 Hz, O*C*H_2Ph), 4.73 (d, 1H, $J_{A\text{-}B}$= 11.6 Hz, O*C*H_2Ph), 5.93 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-1), 7.36-7.50 (m, 5H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.9, -4.8, ($Si(CH3)_2$), 18.2 (Cq, *t*-Bu), 25.9 (*t*-Bu), 26.6, 26.9 (Me), 64.5 (C-6), 72.2 (C-5), 72.5 (O*C*H_2Ph), 78.0 (C-2), 79.9 (C-3), 80.3 (C-4), 104.7 (C-1), 111.9 (Cq-isop), 128.2, 128.4, 128.9 (CH-Ph), 137.7 (Cq-Ph); **HRMS**: calcd. for $C_{22}H_{36}O_6SiNa$ $[M+Na]^+$ 447.2179, found 447.2181.

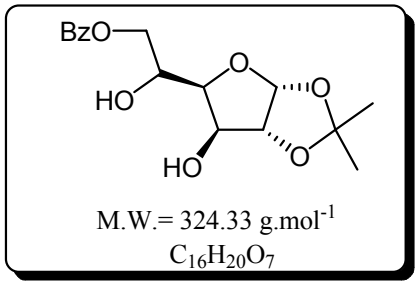
[285]Roy, A.; Achari, B.; Mandal, S. B. *Synthesis* **2006**, *6*, 1035-1039.

6-*O*-Benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (129)

PROCEDURE

To a cold (0 ºC) and stirred solution of triol **96** (500.0 mg, 2.27 mmol) in pyridine (10 mL), BzCl (0.29 mL, 2.50 mmol) was added dropwise. The reaction was stirred at low temperature during 3 h, then co-evaporated with toluene (3x). After concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **129** (662.6 mg, **90% yield**) as a white solid**.**

CAS [3254-32-8]



M.W.= 324.33 g.mol^{-1}
$C_{16}H_{20}O_7$

Rf = 0.2 (PE/EtOAc 1:1); $[\alpha]_D$ = -38 (C=0.8, $CHCl_3$); **mp**: 192-193 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.33 (s, 3H, Me), 1.49 (s, 3H, Me), 4.18 (dd, 1H, $J_{3\text{-}4}$= 2.3 Hz, $J_{4\text{-}5}$= 6.0 Hz, H-4), 4.37-4.39 (m,1H, H-5), 4.44 (d, 1H, $J_{3\text{-}4}$= 2.3 Hz, H-3), 4.51 (dd, 1H, $J_{5\text{-}6B}$= 6.1 Hz, $J_{6A\text{-}6B}$= 12.1 Hz, H-6B), 4.57 (d, 1H, $J_{1\text{-}2}$= 3.3 Hz, H-2), 4.70 (dd, 1H, $J_{5\text{-}6A}$= 2.5 Hz, $J_{6A\text{-}6B}$= 12.1 Hz, H-6A), 6.00 (d, 1H, $J_{1\text{-}2}$= 3.3 Hz, H-1), 7.46 (t, 2H, $J_{m\text{-}o}$= $J_{m\text{-}p}$= 7.6 Hz, H_m-Ph), 7.59 (t, 1H, $J_{p\text{-}o}$= $J_{p\text{-}m}$= 7.6 Hz, H_p-Ph), 8.02 (d, 2H, $J_{o\text{-}m}$= 7.6 Hz, H_o-Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.3, 27.0 (Me), 66.8 (C-6), 69.9 (C-5), 75.9 (C-3), 79.5 (C-4), 85.3 (C-2), 105.1 (C-1), 112.0 (Cq-isop), 128.7 (CH_m-Ph), 129.6 (CH_o-Ph), 129.9 (CH_p-Ph), 133.6 (Cq-Ph), 167.4 (*C*OPh); **HRMS**: calcd. for $C_{16}H_{20}O_7Na$ $[M+Na]^+$ 347.1107, found 347.1101.

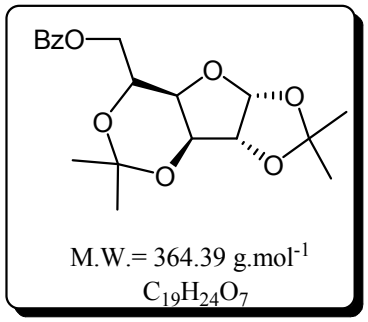
[185] Mort, C. J. W.; Migaud, M. E.; Galione, A.; Potter, B. V. L. *Bioorg. Med. Chem*. **2004**, *12*, 475-487.

6-*O*-Benzoyl-1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose (130)

PROCEDURE

Compound **129** (150.0 mg, 0.46 mmol) was dissolved in dry DMF (5 mL). DMP (0.11 mL, 0.92 mmol) and CSA (10.7 mg, 0.046 mmol) were added and the reaction was stirred at room temperature during 8 h, then quenched by addition of Et_3N until pH ≈ 7. After concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **130** (154.2 mg, **92% yield**) as a white solid**.**

CAS [76491-06-0]



Rf = 0.2 (PE/EtOAc 1:1); $[\alpha]_D$ = + 6 (C=0.4, $CHCl_3$); **mp**: 58-59 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.34 (s, 3H, Me), 1.39 (s, 6H, Me), 1.50 (s, 3H, Me), 3.94 (td, 1H, $J_{4\text{-}5}$= $J_{5\text{-}6B}$= 7.6 Hz, $J_{5\text{-}6A}$= 3.3 Hz, H-5), 4.28 (d, 1H, $J_{3\text{-}4}$= 3.8 Hz, H-3), 4.38-4.45 (m, 2H, H-4, H-6B), 4.54 (dd, 1H, $J_{5\text{-}6A}$= 3.3 Hz, $J_{6A\text{-}6B}$= 11.8 Hz, H-6A), 4.61 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-2), 6.04 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-1), 7.44 (brt, 2H, $J_{m\text{-}o}$= 7.6 Hz, $J_{m\text{-}p}$= 7.9 Hz, H_m-Ph), 7.57 (brt, 1H, $J_{p\text{-}o}$= 7.3 Hz, $J_{p\text{-}m}$= 7.6 Hz, H_p-Ph), 8.02 (dd, 2H, $J_{o\text{-}m}$= 7.6 Hz, $J_{o\text{-}p}$= 7.3 Hz, H_o-Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 24.0, 26.7, 27.3 (Me), 65.1 (C-6), 70.5 (C-5), 75.2 (C-3), 79.7 (C-4), 84.0 (C-2), 101.2 (Cq-isop), 106.6 (C-1), 112.4 (Cq-isop), 128.5 (CH_m-Ph), 129.8 (CH_o-Ph), 130.1 (Cq-Ph), 133.2 (CH_p-Ph), 166.4 (*CO*Ph); **HRMS**: calcd. for $C_{19}H_{24}O_7Na$ $[M+Na]^+$ 387.1420, found 387.1411.

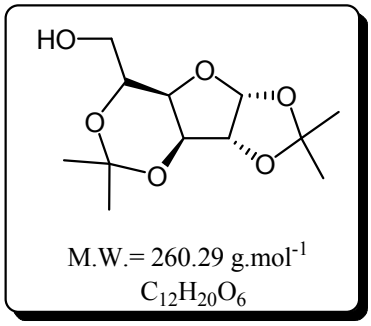
[187] Bartalucci, G.; Bianchini, R.; catelani, G.; D'Andrea, F.; Guazzelli, L. *Eur. J. Org. Chem*. **2007**, 588-595.

1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose (131)

PROCEDURE

A solution of sodium borohydride (17.1 mg, 0.45 mmol) in water (10 mL) was added at room temperature to a solution of **130** (150.0 mg, 0.41 mmol) in 56% aqueous EtOH (4.3 mL). After stirring for 3h, the mixture was extracted with DCM (3 x 25 mL) and the combined organic phase was dried over MgSO4. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **131** quantitatively, as a colourless oil.

CAS [28528-94-1]



M.W.= 260.29 g.mol^{-1}
$C_{12}H_{20}O_6$

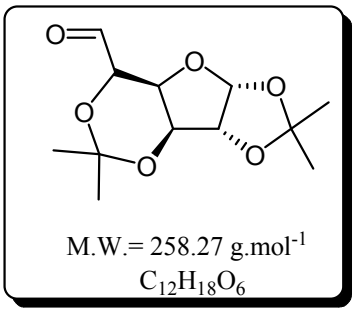
Rf = 0.4 (PE/EtOAc 6:4); $[\alpha]_D$ = + 20 (C=1.0, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.33 (s, 3H, Me), 1.37 (s, 6H, Me), 1.49 (s, 3H, Me), 3.62-3.75 (m, 2H, H-5, H-6B), 3.85 (d, 1H, J_{6A-6B}= 11.0 Hz, H-6A), 4.19 (d, 1H, J_{3-4}= 3.8 Hz, H-3), 4.30 (dd, 1H, J_{3-4}= 3.8 Hz, J_{4-5}= 6.6 Hz, H-4), 4.59 (d, 1H, J_{1-2}= 3.8 Hz, H-2), 6.00 (d, 1H, J_{1-2}= 3.8 Hz, H-1); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 24.1, 24.2, 26.6, 27.2 (Me), 63.6 (C-6), 72.6 (C-5), 75.2 (C-3), 79.1 (C-4), 84.1 (C-2), 101.1 (Cq-isop), 106.5 (C-1), 112.3 (Cq-isop); **HRMS**: calcd. for $C_{12}H_{20}O_6Na$ $[M+Na]^+$ 283.1158, found 283.1152.

[188] Just, G.; Wang, Z. Y.; Chan, L. *J. Org. Chem*. **1988**, *53*, 1030-1033.

1,2:3,5-di-*O*-isopropylidene-α-D-gluco-hexodialdo-1,4-furanose (132)

PROCEDURE

Compound **131** (117.1 mg, 0.45 mmol) was dissolved in dry DCM. Dess-Martin periodinane (1.43 mL, 0.68 mmol) was added and the reaction was stirred at room temperature during 3h, then treated by addition of 10 mL of saturated aqueous solutions of $NaHCO_3$ and $Na_2S_2O_3$. After extraction with diethyl ether (3 x 20 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (Cy/EtOAc 6:4) to afford compound **132** quantitatively, as a colourless oil.



M.W.= 258.27 g.mol^{-1}
$C_{12}H_{18}O_6$

Rf = 0.3 (Cy/EtOAc 6:4); $[\alpha]_D$ = + 2.2 (C=1.0, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 1707 (C=O); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.33 (s, 3H, Me), 1.40 (s, 6H, Me), 1.50 (s, 3H, Me), 4.23-4.25 (m, 2H, H-3, H-4), 4.55-4.58 (m, 2H, H-2, H-5), 6.02 (d, 1H, J_{1-2}= 3.6 Hz, H-1), 9.77 (s, 1H, CO*H*); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 23.0, 25.7, 26.4, 26.9 (Me), 73.8 (C-3), 74.7 (C-5), 76.8 (C-4), 83.8 (C-2), 100.2 (Cq-isop), 105.8 (C-1), 112.2 (Cq-isop), 199.1 (*C*OH); **HRMS**: calcd. for $C_{12}H_{19}O_6$ $[M+H]^+$ 259.1182, found 259.1165.

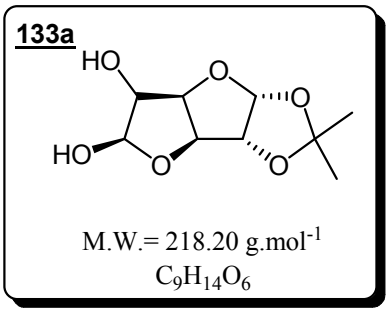
1,2-*O*-Isopropylidene-α-D-gluco-hexodialdo-1,4:6,3-difuranose (133a) and (133b)

PROCEDURE

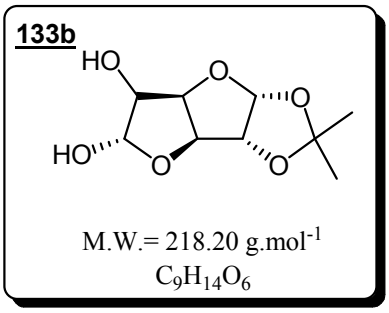
Compound **132** (191.1 mg, 0.74 mmol) was dissolved in an aqueous solution of AcOH (70%) and the reaction was stirred overnight at room temperature. The residue was co-evaporated with toluene (3x) and after concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford the mixture of isomers **133a** and **133b** (138.9 mg, **86% yield**) as a colourless oil, in a proportion **133a**/**133b**: 73/27.

For both isomers:

Rf = 0.4 (PE/EtOAc 4:6); **HRMS**: calcd. for $C_9H_{14}O_6Na$ $[M+Na]^+$ 241.0688, found 241.0681.



^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 3H, Me), 1.49 (s, 3H, Me), 3.14 (brs, 1H, OH), 3.51 (brs, 1H, OH), 4.03 (t, 1H, $J_{4\text{-}5}$= $J_{5\text{-}6}$= 4.7 Hz, H-5), 4.59 (d, 1H, $J_{3\text{-}4}$= 4.7 Hz, H-3), 4.72 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-2), 4.80 (t, 1H, $J_{3\text{-}4}$= $J_{4\text{-}5}$= 4.7 Hz, H-4), 5.24 (d, 1H, $J_{5\text{-}6}$= 4.7 Hz, H-6), 6.04 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-1); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 27.1, 27.7 (Me), 73.0 (C-5), 80.6 (C-4), 84.1 (C-3), 86.5 (C-2), 96.5 (C-6), 107.3 (C-1), 113.3 (Cq-isop).



^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 3H, Me), 1.50 (s, 3H, Me), 2.91 (brs, 2H, OH), 4.08-4.11 (m, 1H, H-5), 4.68 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-2), 4.76 (d, 1H, $J_{3\text{-}4}$= 5.0 Hz, H-3), 4.91 (t, 1H, $J_{3\text{-}4}$= $J_{4\text{-}5}$= 5.0 Hz, H-4), 5.24 (d, 1H, $J_{5\text{-}6}$= 2.2 Hz, H-6), 5.96 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-1); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.9, 27.5 (Me), 77.3 (C-5), 82.2 (C-4), 84.5 (C-3), 84.6 (C-2), 104.1 (C-6), 107.3 (C-1), 113.3 (Cq-isop).

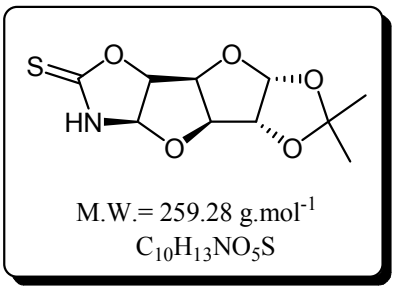
[189] Morgenlie, S. *Carbohydr. Res*. **1977**, *59*, 73-80.

4,5-dihydro (5,6-dideoxy-1,2-*O*-isopropylidene-α-D-gluco-hexodialdo-1,4,:6,3-difuranose) [6,5-d]-1,3-oxazoline-2-thione (134)

PROCEDURE

Compound **133** (120.0 mg, 0.55 mmol) and KSCN (80.6 mg, 0.83 mmol) were dissolved in EtOH (15 mL). After cooling at –5°C, 12M aqueous HCl (82.5 μL, 0.99 mmol) was carefully added and the mixture was stirred under reflux for 24 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 20 mL), the combined organic phase was

washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **134** (112.7 mg, **79% yield**) as a colourless oil.



M.W.= 259.28 g.mol^{-1}
$C_{10}H_{13}NO_5S$

Rf = 0.4 (PE/EtOAc 3:7); $[\alpha]_D$ = + 55 (C=1.4, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3237 (NH), 2991, 2950, (CH), 1491, 1160 (N-CS-O); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.34 (s, 3H, Me), 1.48 (s, 3H, Me), 4.63 (d, 1H, J_{3-4}= 3.8 Hz, H-3), 4.71 (d, 1H, J_{1-2}= 3.5 Hz, H-2), 5.01 (dd, 1H, J_{3-4}= 3.8 Hz, J_{4-5}= 5.6 Hz, H-4), 5.32 (t, 1H, J_{4-5}=J_{5-6}= 5.6 Hz, H-5), 5.82 (d, 1H, J_{5-6}= 5.6, H-6), 6.01 (d, 1H, J_{1-2}= 3.5 Hz, H-1), 8.02 (brs, 1H, NH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.9, 27.5 (Me), 80.9 (C-4), 84.2 (C-2), 85.4 (C-5), 86.9 (C-3), 90.6 (C-6), 107.4 (C-1), 113.4 (Cq-isop), 189.8 (C=S); **HRMS**: calcd. for $C_{10}H_{14}NO_5S$ $[M+H]^+$ 260.0593, found 260.0578.

3-*O*-Benzyl-6-deoxy-6-iodo-1,2-*O*-isopropylidene-α-D-glucofuranose (135) and 3-*O*-Benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-xylo-hex-5-enofuranose (136)

PROCEDURE

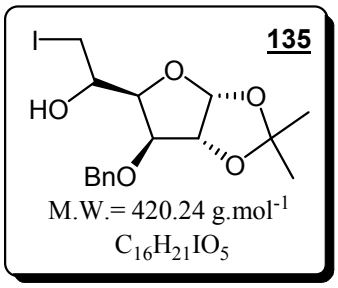
Method A

The diol **85** (3.53 g, 11.40 mmol), triphenylphosphine (5.97 g, 22.80 mmol) and imidazole (1.55 g, 22.80 mmol) were dissolved in dry THF (30 mL). The solution was cooled at 0ºC and after 15 min, iodine (3.47 g, 13.68 mmol) was added gradually. After discolouration of the solution, the mixture was stirred at room temperature during 8 h. The solvent was evaporated under vacuum and the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compounds **135** (1.68 g, **35% yield**) and **136** (1.57 g, **50% yield**) as colourless oils.

Method B-in order to synthesize only compound 135

The diol **85** (3.53 g, 11.40 mmol), triphenylphosphine (5.97 g, 22.80 mmol) and imidazole (1.55 g, 22.80 mmol) were dissolved in dry THF (30 mL). The solution was cooled at 0ºC and after 15 min, iodine (3.47 g, 13.68 mmol) was added gradually. After discolouration of the solution, the mixture was stirred during 25 min. The solvent was evaporated under vacuum and the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compound **135** (4.55 g, **95% yield**) as colourless oil.

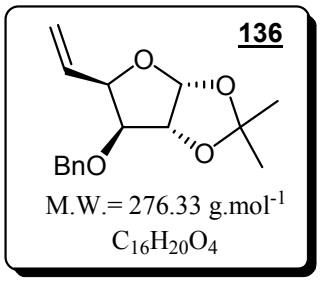
CAS [88776-76-5]



M.W.= 420.24 g.mol^{-1}
$C_{16}H_{21}IO_5$

Rf = 0.3 (PE/EtOAc 8:2); $[\alpha]_D$ = - 37 (C=1.0, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3479 (OH), 2991, 2930, (CH), 1459, 1456 (Ph), 565 (C-I); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.32 (s, 3H, Me), 1.50 (s, 3H, Me), 2.29 (d, 1H, $J_{5\text{-}OH}$= 6.3 Hz, OH), 3.38 (dd, 1H, $J_{5\text{-}6B}$= 6.8 Hz, $J_{6A\text{-}6B}$= 10.8Hz, H-6B), 3.53 (dd, 1H, $J_{5\text{-}6A}$= 3.5 Hz, $J_{6A\text{-}6B}$= 10.8Hz, H-6A), 3.75-3.81 (m, 1H, H-5), 4.06-4.11 (m, 2H, H-3, H-4), 4.56 (d, 1H, $J_{A\text{-}B}$= 11.9Hz, O*C*H_2Ph), 4.62 (d, 1H, $J_{1\text{-}2}$= 4.0 Hz, H-2), 4.72 (d, 1H, $J_{A\text{-}B}$= 11.9Hz, O*C*H_2Ph), 5.92 (d, 1H, $J_{1\text{-}2}$= 4.0Hz, H-1), 7.32-7.39 (m, 5H, Ph) ; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 13.7 (C-6), 26.5, 27.0 (Me), 68.0 (C-5), 72.4 (O*C*H_2Ph), 81.5 (C-3), 82.1 (C-2), 82.4 (C-4), 105.3 (C-1), 112.2 (Cq-isop), 128.0, 128.4, 128.8 (CH-Ph), 137.2 (Cq-Ph) ; **HRMS**: calcd. for $C_{16}H_{21}IO_5Na$ $[M+Na]^+$ 443.0331, found 443.0333.

CAS [19877-13-5]



M.W.= 276.33 g.mol^{-1}
$C_{16}H_{20}O_4$

Rf = 0.6 (PE/EtOAc 8:2); $[\alpha]_D$ = - 38 (C=1.2, $CHCl_3$); **MS** (IS): m/z = 277.5 $[M+H]^+$, 294.0 $[M+NH_4]^+$; 299.0 $[M+Na]^+$; **I.R.** (NaCl) ν (cm^{-1}) 2950, 2925, 2858 (CH), 1674 (C=C), 1456 (Ph), 1258, 1213, 1163; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.31 (s, 3H, Me), 1.49 (s, 3H, Me), 3.87 (d, 1H, $J_{3\text{-}4}$= 3.9 Hz, H-3), 4.53 (d, 1H, $J_{A\text{-}B}$= 12.4 Hz, O*C*H_2Ph), 4.61-4.66 (m, 3H, O*C*H_2Ph, H-2, H-4), 5.30 (dt, 1H, $J_{6Z\text{-}6E}$= 1.7 Hz, $J_{5\text{-}6Z}$= 10.5 Hz, H-6Z), 5.42 (dt, 1H, $J_{6E\text{-}6Z}$= $J_{4\text{-}6E}$= 1.7 Hz, $J_{5\text{-}6E}$= 17.4 Hz, H-6E), 5.95 (d, 1H, $J_{1\text{-}2}$= 4.1 Hz, H-1), 6.01 (ddd, 1H, $J_{5\text{-}4}$= 7.1 Hz, $J_{5\text{-}6Z}$= 10.5 Hz, $J_{5\text{-}6E}$= 17.4 Hz, H-5), 7.29-7.33 (m, 5H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.2, 26.8 (Me), 72.0 (O*C*H_2Ph), 81.5 (C-2), 82.9 (C-4), 83.4 (C-3), 104.8 (C-1), 111.4 (Cq-isop), 118.9 (C-6), 127.5, 127.7, 128.4 (CH-Ph), 132.3 (C-5), 137.6 (Cq-Ph).

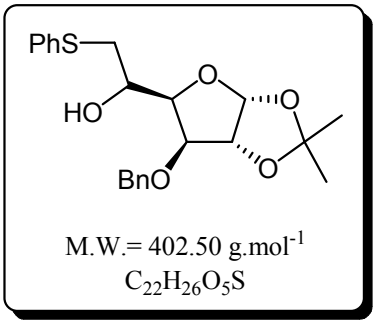
[199] Liu, Z.; Classon, B. *J. Org. Chem*. **1990**, *55*, 4273-4275.
[286] Seo, K. Carbohydr. Res. 1983, 123, 201-207.

3-*O*-Benzyl-1,2-*O*-isopropylidene-6-phenylsulfanyl-α-D-glucofuranose (137)

PROCEDURE

The iodo derivative **135** (1.05 g, 2.50 mmol) was dissolved in dry DCM (30 mL). Triethylamine (2.14 mL, 15.0 mmol) and thiophenol (0.27 mL, 2.63 mmol) were successively added and the reaction was stirred under reflux during 3 h. The reaction mixture was quenched by treating with crushed ice. After extraction with DCM (3 x 30 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compound **137** (0.97 g, **96% yield**) as a yellow oil.

CAS [118149-34-1]



Rf = 0.3 (PE/EtOAc 8:2); **MS** (IS): m/z = 403.5 $[M+H]^+$; $[\alpha]_D$= - 12 (C=0.6, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.31 (s, 3H, Me), 1.46 (s, 3H, Me), 2.67 (d, 1H, $J_{5\text{-}OH}$= 4.5 Hz, OH), 3.01 (dd, 1H, $J_{5\text{-}6B}$= 7.8 Hz, $J_{6A\text{-}6B}$= 13.9 Hz, H-6B), 3.38 (dd, 1H, $J_{5\text{-}6a}$= 3.4 Hz, $J_{6A\text{-}6B}$= 13.9 Hz, H-6A), 4.04-4.13 (m, 3H, H-3, H-4, H-5), 4.54 (d, 1H, $J_{A\text{-}B}$= 11.5 Hz, O*C*H_2Ph), 4.60 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-2), 4.69 (d, 1H, $J_{A\text{-}B}$= 11.5 Hz, O*C*H_2Ph), 5.92 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-1), 7.24-7.39 (m, 10H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.4, 26.9 (Me), 39.2 (C-6), 67.5 (C-5), 72.3 (O*C*H_2Ph), 81.8 (C-3), 81.9 (C-4), 82.4 (C-2), 105.3 (C-1), 111.9 (Cq-isop), 126.5, 128.0, 128.3, 128.8, 129.1, 129.7 (CH-Ph), 135.6, 137.2 (Cq-Ph).

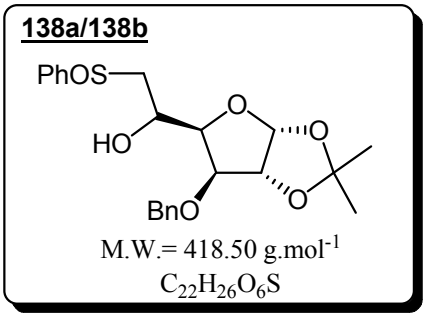
3-*O*-Benzyl-1,2-*O*-isopropylidene-6-phenylsulfinyl-α-D-glucofuranose (138a/138b) and 3-*O*-Benzyl-1,2-*O*-isopropylidene-6-phenylsulfonyl-α-D-glucofuranose (139)

PROCEDURE

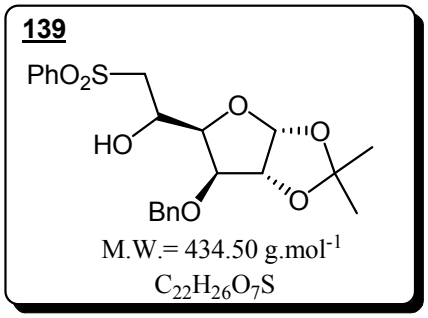
The thio-derivative **137** (3.00 g, 7.45 mmol) was dissolved in dry DCM (50 ml) and, after cooling at -15 ºC, *m*-CPBA 77% (1.84 g, 8.20 mmol) was added. The reaction was stirred during 1 h at low temperature, then hydrolysed with a saturated solution of NaS_2O_3. After extraction with DCM (3 x 50 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford the mixture of *S*-epimers **138a** and **138b** (2.40 g, **77% yield**) as a colourless oil (proportion **138a**/**138b**: 52/48) and compound **139** (0.29 g, **9% yield**) as a colourless oil.

For both sulfoxides:

Rf = 0.3 (PE/EtOAc 1:1); **MS** (IS): m/z = 419.5 $[M+H]^+$



^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (s, Me), 1.29 (s, Me), 2.96-3.15 (m, H-6Ba, H-6Ab, H-6Bb), 3.22 (d, $J_{5a\text{-}6Aa}$= 1.7 Hz, $J_{6Aa\text{-}6Ba}$= 13.3 Hz, H-6Aa), 4.00-4.05 (m, H-4a), 4.08-4.10 (m, H-4b), 4.14-4.18 (m, H-3), 4.49-4.56 (m, H-2), 4.63-4.75 (m, H-5, O*C*H_2Ph), 5.82 (d, $J_{1b\text{-}2b}$= 3.6 Hz, H-1b), 5.88 (d, $J_{1a\text{-}2a}$= 3.6 Hz, H-1a), 7.32-7.65 (m, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.4, 26.5, 26.9, 27.0 (Me), 60.5 (C-6), 66.8, 67.2 (C-5), 72.6, 72.9 (O*C*H_2Ph), 81.2, 81.3 (C-3), 82.1, 82.3 (C-4), 82.6, 82.8 (C-2), 105.1, 105.3 (C-1), 112.0, 112.1 (Cq-isop), 123.9, 124.2, 128.0, 128.1, 128.2, 128.7, 128.5, 129.5, 131.3, 131.6 (CH-Ph), 137.5, 137.6, 139.3, 139.4 (Cq-Ph).



Rf = 0.5 (PE/EtOAc 1:1); **I.R.** (NaCl) ν (cm^{-1}) 3483 (OH), 2976, 2920 (CH), 1459, 1451 (Ph), 1369, 1142 (SO_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.27 (s, 3H, Me), 1.43 (s, 3H, Me), 3.31 (dd, 1H, $J_{5\text{-}6B}$= 10.0 Hz, $J_{6A\text{-}6B}$= 14.4Hz, H-6B), 3.49 (brs, 1H, OH), 3.60 (dd, 1H, $J_{5\text{-}6A}$= 1.5 Hz, $J_{6A\text{-}6B}$= 14.4Hz, H-6A), 4.04-4.14 (m, 2H, H-3, H-4), 4.47-4.55 (m, 2H, O*CH*$_2$Ph, H-5), 4.56 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-2), , 4.65 (d, 1H, $J_{A\text{-}B}$= 11.6 Hz, O*CH*$_2$Ph), 5.80 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-1), 7.27-7.38 (m, 5H, Ph), 7.47-7.52 (m, 3H, Ph), 7.86-7.90 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.2, 26.7 (Me), 59.8 (C-6), 64.0 (C-5), 72.4 (O*CH*$_2$Ph), 81.1 (C-3), 81.5 (C-4), 82.3 (C-2), 105.0 (C-1), 111.9 (Cq-isop), 127.7, 127.8, 128.0, 128.5, 129.3, 133.9 (CH-Ph), 137.2, 139.3 (Cq-Ph); **HRMS**: calcd. for $C_{22}H_{27}O_7S$ $[M+H]^+$ 435.1478, found 435.1487.

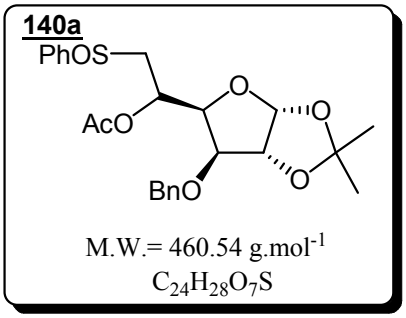
5-*O*-acetyl-3-*O*-benzyl-1,2-*O*-isopropylidene-6-phenylsulfinyl-α-D-glucofuranose (140a and 140b)

PROCEDURE

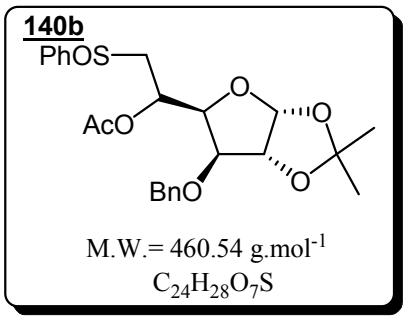
The mixture of *S*-epimers **138** (1.20 g, 2.87 mmol) was dissolved in 15 mL of Pyr/ Ac_2O (2:1). The reaction was stirred at room temperature during 1 h. The residue was co-evaporated with toluene (3x) and after concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford the mixture of *S*-epimers **140a** and **140b** quantitatively, as a colourless oil (proportion **140a**/**140b**: 52/48). We were able to separate a little amount of **140a**, which allowed its total characterization.

For both sulfoxides:

Rf = 0.4 (PE/EtOAc 1:1); **HRMS**: calcd. for $C_{24}H_{29}O_7S$ $[M+H]^+$ 461.1634, found 461.1638.



$[\alpha]_D$ = + 80 (C=1, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2981, 2935 (CH), 1455 (Ph), 1020 (SO); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.30 (s, 3H, Me), 1.47 (s, 3H, Me), 2.02 (s, 3H, OAc), 3.09 (dd, 1H, $J_{5\text{-}6B}$= 7.9Hz, $J_{6A\text{-}6B}$= 14.0 Hz, H-6B), 3.40 (dd, 1H, $J_{5\text{-}6A}$= 2.9 Hz, $J_{6A\text{-}6B}$= 14.0 Hz, H-6b), 4.05 (d, 1H, $J_{3\text{-}4}$= 3.4 Hz, H-3), 4.48 (dd, $J_{3\text{-}4}$= 3.4 Hz, $J_{4\text{-}5}$= 5.4 Hz, H-4), 4.52-4.62 (m, 3H, O*CH*$_2$Ph, H-2), 5.60 (ddd, 1H, $J_{5\text{-}6A}$= 2.9 Hz, $J_{4\text{-}5}$= 5.4 Hz, $J_{5\text{-}6B}$= 7.9 Hz, H-5), 5.85 (d, 1H, $J_{1\text{-}2}$= 3.7 Hz, H-1), 7.29-7.36 (m, 5H, Ph), 7.43-7.59 (m, 5H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 21.0 (OAc), 26.3, 26.9 (Me), 59.8 (C-6), 66.9 (C-5), 72.3 (OCH_2Ph), 80.3 (C-4), 81.3 (C-3), 81.9 (C-2), 105.1 (C-1), 112.1 (Cq-isop), 124.0, 128.2, 128.3, 128.6, 129.3, 131.0 (CH-Ph), 136.8 (Cq-Ph), 144.6 (Cq-SOPh), 169.9 (C=O).



^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (s, 3H, Me), 1.48 (s, 3H, Me), 1.91 (s, 3H, OAc), 3.21 (dd, 1H, $J_{5\text{-}6B}$= 8.3 Hz, $J_{6A\text{-}6B}$= 14.1 Hz, H-6B), 3.35 (dd, 1H, $J_{5\text{-}6A}$= 2.8 Hz, $J_{6A\text{-}6B}$= 14.1 Hz, H-6A), 3.98 (d, 1H, $J_{3\text{-}4}$= 3.3 Hz, H-3), 4.34 (dd, $J_{3\text{-}4}$= 3.3 Hz, $J_{4\text{-}5}$= 6.3 Hz, H-4), 4.48-4.64 (m, 3H, O*C*H_2Ph, H-2), 5.60 (ddd, 1H, $J_{5\text{-}6A}$= 2.8 Hz, $J_{4\text{-}5}$= 6.3 Hz, $J_{5\text{-}6B}$= 8.3 Hz, H-5), 5.86 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-1), 7.28-7.36 (m, 5H, Ph), 7.43-7.60 (m, 5H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 21.1 (OAc), 26.4, 27.0 (Me), 59.3 (C-6), 66.7 (C-5), 72.4 (O*C*H_2Ph), 80.8 (C-4), 81.1 (C-3), 81.7 (C-2), 105.2 (C-1), 112.3 (Cq-isop), 124.3, 128.3, 128.7, 129.2, 129.3, 130.9 (CH-Ph), 136.9 (Cq-Ph), 144.3 (Cq-SOPh), 170.0 (C=O).

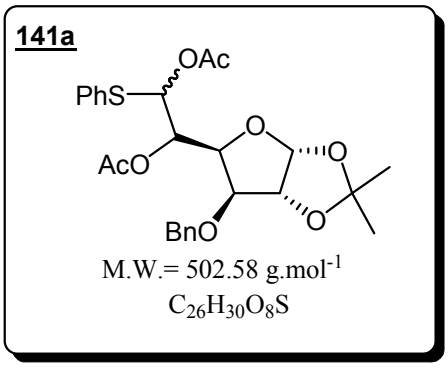
5,6-di-*O*-acetyl-3-*O*-benzyl-1,2-*O*-isopropylidene-6-*C*-phenylsulfanyl)-α-D-glucofuranose (141a and 141b)

PROCEDURE

Sulfoxides **140** (500.0 mg, 1.09 mmol) were dissolved in Ac_2O (20 mL) and the reaction was stirred under reflux during 5 days. The residue was co-evaporated with toluene (3x) and after concentration under vacuum, purified by column chromatography (PE/EtOAc 9:1) to afford the mixture of stereoisomers **141a** and **141b** (476.6 mg, **87% yield**) as colourless oils (proportion **141a**/**141b**: 57/43). We were able to separate a little amount of **141a** and **141b**, which allowed characterization of both isomers.

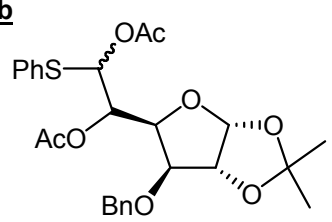
For both stereoisomers:

Rf = 0.2 (PE/EtOAc 7:3); **MS** (IS): m/z = 503.5 $[M+H]^+$



$[\alpha]_D$ = + 86 (C=0.4, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.34 (s, 3H, Me), 1.52 (s, 3H, Me), 1.88 (s, 3H, OAc), 2.02 (s, 3H, OAc), 3.95 (d, 1H, $J_{3\text{-}4}$ = 3.2 Hz, H-3), 4.42 (d, 1H, $J_{A\text{-}B}$= 11.8 Hz, O*C*H_2Ph), 4.57-4.62 (m, 3H, H-2, H-4, O*C*H_2Ph), 5.66 (dd, 1H, $J_{4\text{-}5}$ = 9.7 Hz, $J_{5\text{-}6}$= 2.1 Hz, H-5), 5.97 (d, 1H, $J_{1\text{-}2}$ = 3.5 Hz, H-1), 6.43 (d, 1H, $J_{5\text{-}6}$ = 2.1 Hz, H-6), 7.26-7.34 (m, 8H, Ph), 7.51-7.53 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 20.8, 21.1 (OAc), 26.7, 27.2 (Me), 70.6 (C-5), 72.0 (O*C*H_2Ph), 78.5 (C-4), 80.4 (C-3), 81.6 (C-2), 83.8 (C-6), 105.6 (C-1), 112.4 (Cq-isop), 128.1, 128.2, 128.6, 128.7, 129.2, 133.1 (CH-Ph), 133.2 (Cq-Ph), 136.9 (Cq-SOPh), 169.0, 169.6 (C=O).

141b



M.W.= 502.58 g.mol^{-1}
$C_{26}H_{30}O_8S$

$[\alpha]_D$ = - 17 (C= 0.3, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.29 (s, 3H, Me), 144 (s, 3H, Me), 2.04 (s, 3H, OAc), 2.06 (s, 3H, OAc), 3.88 (d, 1H, $J_{3\text{-}4}$ = 3.0 Hz, H-3), 4.24 (dd, 1H, $J_{3\text{-}4}$= 3.0 Hz, $J_{4\text{-}5}$= 8.3 Hz, H-4), 4.48 (d, 1H, $J_{A\text{-}B}$= 11.4 Hz, O*CH*$_2$Ph), 4.53-4.56 (m, 2H, H-2, O*CH*$_2$Ph), 5.71 (dd, 1H, $J_{4\text{-}5}$ = 8.3 Hz, $J_{5\text{-}6}$= 2.5 Hz, H-5), 5.82 (d, 1H, $J_{1\text{-}2}$ = 3.7 Hz, H-1), 6.39 (d, 1H, $J_{5\text{-}6}$ = 2.5 Hz, H-6), 7.26-7.56 (m, 10H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 20.8, 20.9 (OAc), 26.5, 26.9 (Me), 70.8 (C-5), 72.3 (O*CH*$_2$Ph), 78.4 (C-4), 80.7 (C-6), 81.0 (C-3), 81.6 (C-2), 105.2 (C-1), 112.0 (Cq-isop), 128.2, 128.5, 128.6, 128.7, 129.1, 132.4 (CH-Ph), 133.2 (Cq-Ph), 137.0 (Cq-SOPh), 168.8, 169.4 (C=O).

6-Phenylsulfanyl-5-O-acetyl-1,2-O-isopropylidene-α-D-gluco-hexodialdo-1,4:6,3-difuranose (142a and 142b)

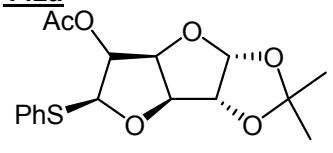
PROCEDURE

Stereoisomers **141** (77.0 mg, 0.15 mmol) and $SnCl_4$ (0.15 mL, 1 M soln in dry DCM) were dissolved in dry DCM (5 mL). After 5 min, TMSSCN (23.3 µL, 0.165mmol) was added and the reaction mixture was stirred at room temperature during 2 h. Saturated aqueous $NaHCO_3$ was then added and the aqueous phase was extracted with DCM (3 x 15 mL). The combined organic phase was washed with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 95:5) to afford the mixture of isomers **142a** and **142b** quantitatively, as a yellow oil, in a proportion **142a**/**142b**: 55/45.

For both isomers:

Rf = 0.5 (PE/EtOAc 8:2); **HRMS**: calcd. for $C_{17}H_{20}O_6SNa$ $[M+Na]^+$ 375.0878, found 375.0873.

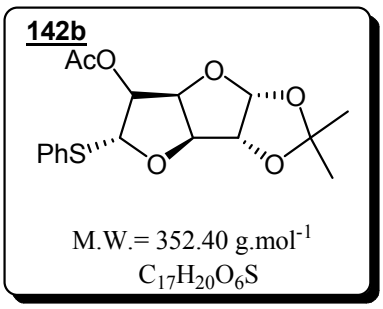
142a



M.W.= 352.40 g.mol^{-1}
$C_{17}H_{20}O_6S$

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (s, 3H, Me), 1.46 (s, 3H, Me), 2.15 (s, 3H, OAc), 4.66 (d, 1H, $J_{1\text{-}2}$ = 3.5 Hz, H-2), 4.65 (d, 1H, $J_{3\text{-}4}$= 4.1 Hz, H-3), 4.92 (t, 1H, $J_{3\text{-}4}$= $J_{4\text{-}5}$= 4.1 Hz, H-4), 5.00 (dd, 1H, $J_{4\text{-}5}$ = 4.1 Hz, $J_{5\text{-}6}$= 6.9 Hz, H-5), 5.36 (d, 1H, $J_{5\text{-}6}$ = 6.9 Hz, H-6), 5.96 (d, 1H, $J_{1\text{-}2}$ = 3.5 Hz, H-1), 7.31-7.39 (m, 5H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 20.8 (OAc), 26.8, 26.9 (Me), 76.4 (C-5), 80.4 (C-4), 84.3 (C-2), 85.1 (C-3), 88.3 (C-6), 107.3 (C-1), 113.1 (Cq-isop), 128.4,

128.5, 129.2 (CH-Ph), 133.4 (Cq-Ph), 169.9 (C=O).

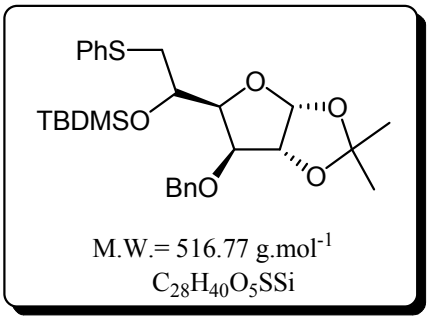


^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 3H, Me), 1.48 (s, 3H, Me), 2.16 (s, 3H, OAc), 4.67 (d, 1H, $J_{1\text{-}2}$ = 3.6 Hz, H-2), 4.81 (d, 1H, $J_{3\text{-}4}$= 4.1 Hz, H-3), 5.04 (t, 1H, $J_{3\text{-}4}$= $J_{4\text{-}5}$= 4.1 Hz, H-4), 5.10 (t, 1H, $J_{4\text{-}5}$ = $J_{5\text{-}6}$= 4.1 Hz, H-5), 5.48 (d, 1H, $J_{5\text{-}6}$ = 4.1 Hz, H-6), 5.92 (d, 1H, $J_{1\text{-}2}$ = 3.6 Hz, H-1), 7.28-7.39 (m, 5H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 20.7 (OAc), 27.4, 27.5 (Me), 78.5 (C-5), 80.1 (C-4), 83.9 (C-2), 85.9 (C-3), 89.0 (C-6), 107.4 (C-1), 113.5 (Cq-isop), 128.6, 128.9, 129.5 (CH-Ph), 133.5 (Cq-Ph), 169.6 (C=O).

3-*O*-Benzyl-1,2-*O*-isopropylidene-6-phenylsulfanyl-5-*O*-*tert*-butyldimethylsilyl-α-D-glucofuranose (143)

PROCEDURE

To a solution of the phenylsulfanyl derivative **137** (2.11 g, 5.26 mmol) in dry DMF (30 ml) at 0ºC, were added imidazole (0.72 g, 10.52 mmol) and TBDMSCl (1.19 g, 7.89 mmol). The reaction was stirred at room temperature overnight, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 35 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 95:5) to afford compound **143** quantitatively, as a colourless oil**.**



Rf = 0.8 (PE/EtOAc 9:1); $[\alpha]_D$ = - 40 (C=0.5, $CHCl_3$); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 0.20 (s, 3H, $Si(CH_3)_2$), 0.28 (s, 3H, $Si(CH_3)_2$), 1.10 (s, 9H, *t*-Bu), 1.52 (s, 3H, Me), 1.71 (s, 3H, Me), 3.36 (dd, 1H, $J_{5\text{-}6B}$= 6.1 Hz, $J_{6A\text{-}6B}$= 13.5 Hz, H-6B), 3.70 (dd, 1H, $J_{5\text{-}6A}$= 2.7 Hz, $J_{6A\text{-}6B}$= 13.5 Hz, H-6A), 4.23 (dd, 1H, $J_{3\text{-}4}$= 2.3 Hz, $J_{4\text{-}5}$= 4.3 Hz, H-4), 4.55-4.58 (m, 2H, H-3, H-5), 4.77 (d, 1H, $J_{A\text{-}B}$= 11.8 Hz, OCH_2Ph), 4.82 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-2), 4.89 (d, 1H, $J_{A\text{-}B}$= 11.8 Hz, OCH_2Ph), 6.10 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-1), 7.33-7.61 (m, 10H, Ph); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ -4.6, -3.9 ($Si(CH_3)_2$), 18.3 (Cq, *t*-Bu), 26.1 (*t*-Bu), 26.6, 27.0 (Me), 39.5 (C-6), 68.3 (C-5), 71.3 (OCH_2Ph), 81.4 (C-3), 81.8 (C-4), 81.9 (C-2), 102.9 (C-1), 112.0 (Cq-isop), 125.5, 127.1, 128.8, 128.9, 129.3, 129.8 (CH-Ph), 137.8, 137.9 (Cq-Ph); **HRMS**: calcd. for $C_{28}H_{40}O_5SSiNa$ $[M+Na]^+$ 539.2263, found 539.2274.

3-*O*-Benzyl-1,2-*O*-isopropylidene-6-phenylsulfinyl-5-O-*tert*-butyldimethylsilyl-α-D-glucofuranose (144a/144b) and 3-*O*-Benzyl-1,2-*O*-isopropylidene-6-phenylsulfonyl-5-*O*-*tert*-butyldimethylsilyl-α-D-glucofuranose (145)

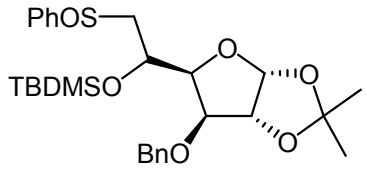
PROCEDURE

The phenylsulfanyl derivative **143** (3.00 g, 5.81 mmol) was dissolved in dry DCM (50 ml) and, after cooling at -15 ºC, m-CPBA 77% (1.43 g, 6.38 mmol) was added. The reaction was stirred during 1 h at low temperature, then hydrolysed with a saturated solution of NaS_2O_3. After extraction with DCM (3 x 50 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford the mixture of *S*-epimers **144a** and **144b** (2.57 g, **83% yield**) as a colourless oil (proportion **144a**/**144b**: 55/45) and compound **145** (0.26 g, **8% yield**) as a white solid.

For both sulfoxides:

Rf = 0.2 (PE/EtOAc 8:2); **HRMS**: calcd. for $C_{28}H_{41}O_6SSi$ $[M+H]^+$ 533.2393, found 533.2387.

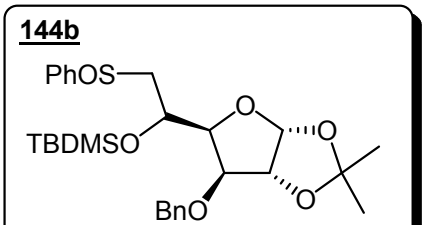
144a



M.W.= 532.76 g.mol^{-1}
$C_{28}H_{40}O_6SSi$

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.24 (s, 3H, $Si(CH_3)_3$), 0.35 (s, 3H, $Si(CH_3)_3$), 1.09 (s, 9H, *t*-Bu), 1.45 (s, 3H, Me), 1.63 (s, 3H, Me), 3.08 (dd, 1H, $J_{5\text{-}6B}$= 9.2 Hz, $J_{6A\text{-}6B}$= 13.5 Hz, H-6B), 3.48 (dd, 1H, $J_{5\text{-}6A}$= 2.5 Hz, $J_{6A\text{-}6B}$= 13.5 Hz, H-6A), 4.16 (d, 1H, $J_{3\text{-}4}$= 3.2 Hz, H-3), 4.40 (dd, 1H, $J_{3\text{-}4}$= 3.2 Hz, $J_{4\text{-}5}$= 5.7 Hz, H-4), 4.64-4.66 (m, 1H, H-5), 4.69-4.74 (m, 2H, H-2, O*CH*$_2$Ph), 4.80 (d, 1H, $J_{A\text{-}B}$= 11.7 Hz, O*CH*$_2$Ph), 5.97 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-1), 7.43-7.81 (m, 10H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.4, -4.3 ($Si(CH_3)_2$), 18.3 (Cq, *t*-Bu), 25.9 (*t*-Bu), 26.4, 26.9 (Me), 64.4 (C-6), 65.2 (C-5), 71.7 (O*CH*$_2$Ph), 81.4 (C-2), 81.9 (C-3), 83.4 (C-4), 104.8 (C-1), 111.8 (Cq-isop), 123.9, 124.4, 127.7, 127.9, 128.6, 130.6 (CH-Ph), 137.2 (Cq-Ph), 145.3 (Cq-SOPh).

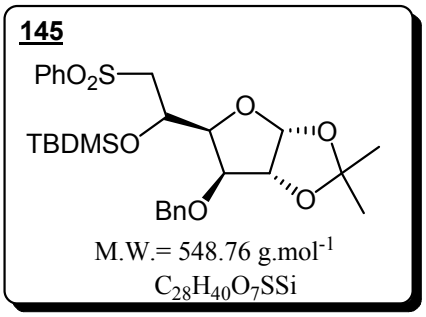
144b



M.W.= 532.76 g.mol^{-1}
$C_{28}H_{40}O_6SSi$

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.20 (s, 3H, $Si(CH_3)_3$), 0.25 (s, 3H, $Si(CH_3)_3$), 1.06 (s, 9H, *t*-Bu), 1.46 (s, 3H, Me), 1.70 (s, 3H, Me), 3.26 (dd, 1H, $J_{5\text{-}6B}$= 5.3 Hz, $J_{6A\text{-}6B}$= 13.5 Hz, H-6B), 3.43 (dd, 1H, $J_{5\text{-}6A}$= 3.6 Hz, $J_{6A\text{-}6B}$= 13.5 Hz, H-6A), 4.18 (d, 1H, $J_{3\text{-}4}$= 2.8 Hz, H-3), 4.56-4.65 (m, 2H, H-4, H-5), 4.71 (d, 1H, $J_{A\text{-}B}$= 12.3 Hz, O*CH*$_2$Ph), 4.73 (d, 1H, $J_{1\text{-}2}$= 3.9 Hz, H-2), 4.80 (d, 1H, $J_{A\text{-}B}$= 12.3 Hz, O*CH*$_2$Ph), 6.02 (d, 1H, $J_{1\text{-}2}$= 3.9 Hz, H-1), 7.40-7.83 (m, 10H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.5, -3.8 ($Si(CH_3)_2$), 18.2 (Cq, *t*-Bu), 26.0 (*t*-Bu), 26.7, 27.0 (Me), 64.0 (C-6), 65.8 (C-5), 71.4 (O*CH*$_2$Ph), 81.5 (C-2), 81.7

(C-3), 82.8 (C-4), 105.0 (C-1), 112.2 (Cq-isop), 124.4, 124.5, 127.3, 127.9, 128.5, 130.9 (CH-Ph), 137.6 (Cq-Ph), 145.2 (Cq-SOPh).

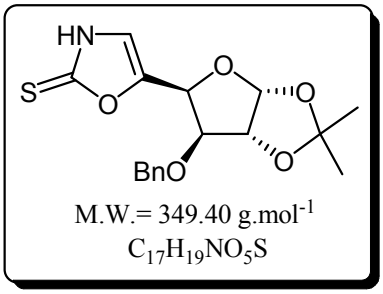


Rf = 0.7 (PE/EtOAc 8:2); $[\alpha]_D$ = + 43 (C=1.7, $CHCl_3$); **mp**: 111-112 °C; **I.R.** (NaCl) ν (cm^{-1}) 2953, 2925 (CH), 1467, 1455 (Ph), 1370, 1134 (SO_2), 1224 ($Si(CH_3)_2$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.07 (s, 3H, $Si(CH_3)_3$), 0.16 (s, 3H, $Si(CH_3)_3$), 0.88 (s, 9H, *t*-Bu), 1.28 (s, 3H, Me), 1.46 (s, 3H, Me), 3.40 (dd, 1H, $J_{5\text{-}6B}$= 6.9 Hz, $J_{6A\text{-}6B}$= 14.7 Hz, H-6B), 3.70 (dd, 1H, $J_{5\text{-}6A}$= 2.6 Hz, $J_{6A\text{-}6B}$= 14.7 Hz, H-6A), 3.97 (d, 1H, $J_{3\text{-}4}$= 3.3 Hz, H-3), 4.20 (dd, 1H, $J_{3\text{-}4}$= 3.3 Hz, $J_{4\text{-}5}$= 4.4 Hz, H-4), 4.48-4.53 (m, 2H, O*CH*$_2$Ph, H-2), 4.63 (d, 1H, $J_{A\text{-}B}$= 11.6 Hz, O*CH*$_2$Ph), 4.75 (ddd, 1H, $J_{5\text{-}6A}$= 2.6 Hz, $J_{4\text{-}5}$= 4.4 Hz, $J_{5\text{-}6B}$= 6.9 Hz, H-5), 5.65 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-1), 7.31-7.46 (m, 8H, Ph), 7.76-7.80 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.6, -4.2 ($Si(CH3)_2$), 18.2 (Cq, *t*-Bu), 26.0 (*t*-Bu), 26.4, 26.9 (Me), 60.6 (C-6), 65.4 (C-5), 71.7 (O*CH*$_2$Ph), 81.5 (C-2), 81.8 (C-3), 83.3 (C-4), 104.7 (C-1), 111.9 (Cq-isop), 127.8, 127.9, 128.1, 128.6, 129.0, 133.2 (CH-Ph), 137.2 (Cq-Ph), 141.1 (Cq-SO_2Ph); **HRMS**: calcd. for $C_{28}H_{41}O_7SSi$ $[M+H]^+$ 549.2342, found 549.2347.

5-[(4*R*)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-threofuranos-4-*C*-yl]-1,3-oxazoline-2-thione (147)

PROCEDURE

The sulfoxide **144** (170.0 mg, 0.32 mmol) was dissolved in DCM (10 mL) and $(CF_3CO)_2O$ (0.18 mL, 1.28 mmol) was added. The reaction was stirred at room temperature during 1 h then, saturated aqueous $NaHCO_3$ was added. The aqueous phase was extracted with EtOAc (3 x 15 mL) and the combined organic phase was dried over $MgSO_4$. The residue was dissolved in DCM (10 mL) then, MeOH (28.3 µL, 0.70 mmol) and Et_3N (0.032 mmol) were added at 0ºC and the reaction stirred during 30 min at low temperature. After extraction with DCM (3 x 15 mL), the combined organic phase was washed with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was directly submitted to the OXT formation step. Therefore, the crude of the reaction and KSCN (46.6 mg, 0.48 mmol) were dissolved in EtOH (15 mL). After cooling at –5°C, 12M aqueous HCl (48.3 µL, 0.58 mmol) was carefully added and the mixture was stirred at room temperature for 5 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 20 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **147** (88.3 mg, **79% yield**) as a colourless oil.



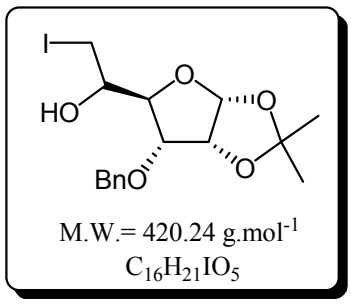
M.W.= 349.40 g.mol^{-1}
$C_{17}H_{19}NO_5S$

Rf = 0.3 (PE/EtOAc 7:3); $[\alpha]_D$ = - 23 (C=1.0, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3225 (NH), 2987, 2934 (CH), 1635 (C=C), 1490, 1127 (N-CS-O), 1456, 1452 (Ph); **^{1}H NMR** (400 MHz, DMSO) δ 1.29 (s, 3H, Me), 1.43 (s, 3H, Me), 4.09 (d, 1H, $J_{3'-4'}$= 3.4 Hz, H-3'), 4.45 (d, 1H, J_{A-B}= 11.8 Hz, OCH_2Ph), 4.64 (d, 1H, J_{A-B}= 11.8 Hz, OCH_2Ph), 4.82 (d, 1H, $J_{1'-2'}$= 3.8 Hz, H-2'), 5.07 (d, 1H, $J_{3'-4'}$= 3.4 Hz, H-4'), 5.96 (d, 1H, $J_{1'-2'}$= 3.8 Hz, H-1'), 7.20-7.34 (m, 5H, Ph), 7.61 (s, 1H, H-5), 13.2 (brs, 1H, NH); **^{13}C NMR** (100 MHz, DMSO) δ 26.9, 26.6 (Me), 71.1 (OCH_2Ph), 72.8 (C-4'), 81.6 (C-2'), 81.8 (C-3'), 104.4 (C-1'), 111.3 (Cq-isop), 126.4 (C-4), 127.5, 127.6, 128.2 (CH-Ph), 134.8 (C-5), 137.3 (Cq-Ph), 178.1 (C=S); **HRMS**: calcd. for $C_{17}H_{20}NO_5S$ $[M+H]^+$ 350.1062, found 350.1061.

3-*O*-Benzyl-6-deoxy-6-iodo-1,2-*O*-isopropylidene-α-D-allofuranose (148)

PROCEDURE

Diol **91** (3.53 g, 11.40 mmol), triphenylphosphine (5.97 g, 22.80 mmol) and imidazole (1.55 g, 22.80 mmol) were dissolved in dry THF (30 mL). The solution was cooled at 0ºC and after 15 min, iodine (3.47 g, 13.68 mmol) was added gradually. After discolouration of the solution, the mixture was stirred during 25 min. The solvent was evaporated under vacuum and the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compound **148** (4.60 g, **96% yield**) as a colourless oil.



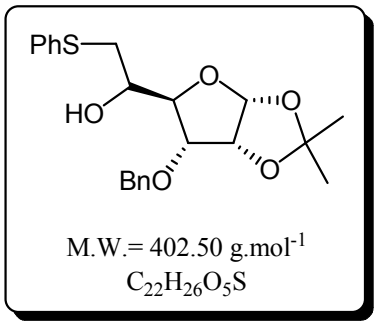
M.W.= 420.24 g.mol^{-1}
$C_{16}H_{21}IO_5$

Rf = 0.3 (PE/EtOAc 7:3); $[\alpha]_D$ = + 74 (C=0.5, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3487 (OH), 2972, 2958, (CH), 1463, 1453 (Ph), 571 (C-I); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.36 (s, 3H, Me), 1.60 (s, 3H, Me), 2.54 (d, 1H, J_{5-OH}= 3.3 Hz, OH), 3.23 (dd, 1H, J_{5-6B}= 8.2 Hz, J_{6A-6B}= 10.4 Hz, H-6B), 3.36 (dd, 1H, J_{5-6A}= 3.3 Hz, J_{6A-6B}= 10.4 Hz, H-6A), 3.82-3.86 (m, 1H, H-5), 3.88 (dd, 1H, J_{2-3}= 4.4 Hz, J_{3-4}= 8.8 Hz, H-3), 4.11 (dd, 1H, J_{4-5}= 4.8 Hz, J_{3-4}= 8.8 Hz, H-4), 4.55-4.59 (m, 2H, OCH_2Ph, H-2), 4.78 (d, 1H, J_{A-B}= 11.7 Hz, OCH_2Ph), 5.72 (d, 1H, J_{1-2}= 3.6 Hz, H-1), 7.31-7.38 (m, 5H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 8.63 (C-6), 26.8, 27.0 (Me), 72.1 (C-5), 72.3 (OCH_2Ph), 77.6 (C-2), 78.3 (C-3), 79.1 (C-4), 104.3 (C-1), 113.6 (Cq-isop), 128.2, 128.4, 128.7 (CH-Ph), 137.1 (Cq-Ph); **HRMS**: calcd. for $C_{16}H_{21}IO_5Na$ $[M+Na]^+$ 443.0331, found 443.0335.

3-*O*-Benzyl-1,2-*O*-isopropylidene-6-phenylsulfanyl-α-D-allofuranose (149)

PROCEDURE

The iodo derivative **148** (1.05 g, 2.50 mmol) was dissolved in dry DCM (30 mL). Triethylamine (2.14 mL, 15.0 mmol) and thiophenol (0.27 mL, 2.63 mmol) were successively added and the reaction stirred under reflux during 3 h. The reaction mixture was quenched by treating with crushed ice. After extraction with DCM (3 x 30 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **149** (0.84 g, **83% yield**) as a colourless oil.



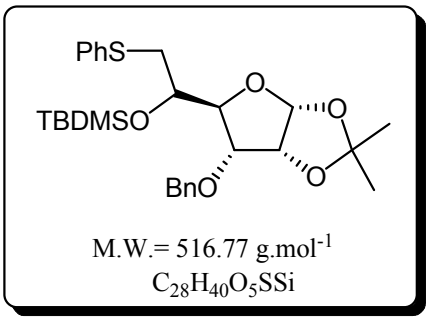
M.W.= 402.50 g.mol^{-1}
$C_{22}H_{26}O_5S$

Rf = 0.2 (PE/EtOAc 8:2); **MS** (IS): m/z = 403.5 $[M+H]^+$; $[\alpha]_D$ = + 73 (C=0.4, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.36 (s, 3H, Me), 1.58 (s, 3H, Me), 2.54 (d, 1H, $J_{5\text{-}OH}$= 2.4 Hz, OH), 2.99 (dd, 1H, $J_{5\text{-}6B}$= 9.3 Hz, $J_{6A\text{-}6B}$= 13.9Hz, H-6B), 3.19 (dd, 1H, $J_{5\text{-}6A}$= 3.5 Hz, $J_{6A\text{-}6B}$= 13.9Hz, H-6A), 3.96-3.99 (m, 2H, H-3, H-5), 4.12 (dd, 1H, $J_{3\text{-}4}$= 8.8 Hz, $J_{4\text{-}5}$= 3.5 Hz, H-4), 4.55-4.60 (m, 2H, H-2, O*CH*$_2$Ph), 4.77 (d, 1H, $J_{A\text{-}B}$= 11.6Hz, O*CH*$_2$Ph), 5.73 (d, 1H, $J_{1\text{-}2}$= 3.8 Hz, H-1), 7.25-7.37 (m, 10H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.7, 27.0 (Me), 37.2 (C-6), 69.2 (C-5), 72.2 (O*CH*$_2$Ph), 77.3 (C-3), 77.8 (C-2), 79.9 (C-4), 104.3 (C-1), 113.3 (Cq-isop), 126.6, 128.2, 128.3, 128.7, 129.1, 130.0 (CH-Ph), 135.4, 137.4 (Cq-Ph)

3-*O*-Benzyl-1,2-*O*-isopropylidene-6-phenylsulfanyl-5-*O*-*tert*-butyldimethylsilyl-α-D-allofuranose (150)

PROCEDURE

To the phenylsulfanyl derivative **149** (2.11 g, 5.26 mmol) in dry DMF (30 ml) at 0ºC, were added imidazole (0.72 g, 10.52 mmol) and TBDMSCl (1.19 g, 7.89 mmol). The reaction was stirred at room temperature overnight, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 35 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 95:5) to afford compound **150** quantitatively, as a colourless oil**.**



M.W.= 516.77 g.mol^{-1}
$C_{28}H_{40}O_5SSi$

Rf = 0.8 (PE/EtOAc 9:1); $[\alpha]_D$ = + 32 (C=0.8, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.15 (s, 3H, $Si(CH_3)_2$), 0.22 (s, 3H, $Si(CH_3)_2$), 1.05 (s, 9H, *t*-Bu), 1.58 (s, 3H, Me), 1.83 (s, 3H, Me), 3.19 (dd, 1H, $J_{5\text{-}6B}$= 7.0 Hz, $J_{6A\text{-}6B}$= 13.7 Hz, H-6B), 3.36 (dd, 1H, $J_{5\text{-}6A}$= 4.8 Hz, $J_{6A\text{-}6B}$= 13.7 Hz, H-6A), 4.29-4.33 (m, 2H, H-3, H-5), 4.53 (dd, 1H, $J_{4\text{-}5}$= 1.1 Hz, $J_{3\text{-}4}$= 8.7 Hz, H-4), 4.75-4.81 (m, 2H, H-2, OCH_2Ph), 5.00 (d, 1H, $J_{A\text{-}B}$= 11.8Hz, OCH_2Ph), 5.88 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-1), 7.38-7.59 (m, 10H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.8, -3.8 ($Si(CH_3)_2$), 18.3 (Cq, *t*-Bu), 26.1 (*t*-Bu), 26.7, 27.0 (Me), 37.9 (C-6), 69.5 (C-5), 72.5 (OCH_2Ph), 76.3 (C-3), 77.8 (C-2), 79.2 (C-4), 103.9 (C-1), 112.4 (Cq-isop), 125.6, 127.3, 127.8, 128.2, 128.8, 129.0 (CH-Ph), 136.8, 137.4 (Cq-Ph); **HRMS**: calcd. for $C_{28}H_{40}O_5SSiNa$ $[M+Na]^+$ 539.2263, found 539.2250.

3-*O*-benzyl-1,2-*O*-isopropylidene-6-phenylsulfinyl-5-*O*-*tert*-butyldimethylsilyl-α-D-allofuranose (151a/151b) and 3-*O*-benzyl-1,2-*O*-isopropylidene-6-phenylsulfonyl-5-*O*-*tert*-butyldimethylsilyl-α-D-allofuranose (152)

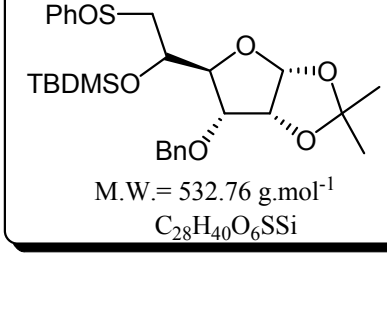
PROCEDURE

The phenylsulfanyl derivative **150** (3.00 g, 5.81 mmol) was dissolved in dry DCM (50 ml) and after cooling at -15 ºC, m-CPBA 77% (1.43 g, 6.38 mmol) was added. The reaction was stirred during 1 h at low temperature, then hydrolysed with a saturated solution of NaS_2O_3. After extraction with DCM (3 x 50 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 9:1) to afford the mixture of *S*-epimers **151a** and **151b** (2.60 g, **84% yield**) as a colourless oil (proportion **151a**/**151b**: 52/48) and compound **152** (0.29 g, **9% yield**) as a yellow oil.

For both sulfoxides:

Rf = 0.2 (PE/EtOAc 8:2); **HRMS**: calcd. for $C_{28}H_{41}O_6SSi$ $[M+H]^+$ 533.2393, found 533.2396.

151a

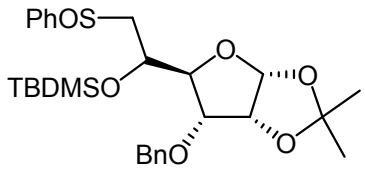


M.W.= 532.76 g.mol^{-1}
$C_{28}H_{40}O_6SSi$

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.10 (s, 3H, $Si(CH_3)_3$), 0.27 (s, 3H, $Si(CH_3)_3$), 0.90 (s, 9H, *t*-Bu), 1.34 (s, 3H, Me), 1.53 (s, 3H, Me), 2.79 (dd, 1H, $J_{5\text{-}6B}$= 2.6 Hz, $J_{6A\text{-}6B}$= 13.5 Hz, H-6B), 2.87 (dd, 1H, $J_{5\text{-}6A}$= 5.9 Hz, $J_{6A\text{-}6B}$= 13.5 Hz, H-6A), 3.92-3.99 (m, 2H, H-3, H-4), 4.48 (d, 1H, $J_{A\text{-}B}$= 11.4 Hz, OCH_2Ph), 4.57-4.62 (m, 2H, H-2, H-5), 4.72 (d, 1H, $J_{A\text{-}B}$= 11.4 Hz, OCH_2Ph), 5.67 (d, 1H, $J_{1\text{-}2}$= 3.5 Hz, H-1), 7.23-7.54 (m, 10H, Ph); **^{13}C NMR** (100 MHz,

$CDCl_3$) δ -4.9, -3.8 ($Si(CH3)_2$), 18.4 (Cq, *t*-Bu), 26.1 (*t*-Bu), 26.8, 27.0 (Me), 63.2 (C-6), 65.5 (C-5), 72.0 (OCH_2Ph), 76.1 (C-3), 77.6 (C-2), 81.0 (C-4), 104.0 (C-1), 113.2 (Cq-isop), 123.8, 128.1, 128.3, 128.5, 129.3, 130.9 (CH-Ph), 137.2 (Cq-Ph), 144.8 (Cq-SOPh)

151b

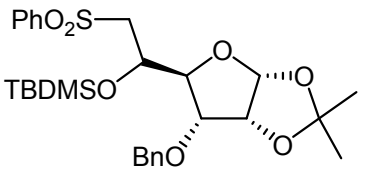


M.W.= 532.76 g.mol^{-1}

$C_{28}H_{40}O_6SSi$

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 3H, $Si(CH_3)_3$), 0.26 (s, 3H, $Si(CH_3)_3$), 0.82 (s, 9H, *t*-Bu), 1.37 (s, 3H, Me), 1.61 (s, 3H, Me), 2.88 (dd, 1H, $J_{5\text{-}6B}$= 5.3 Hz, $J_{6A\text{-}6B}$= 13.0 Hz, H-6B), 3.16 (dd, 1H, $J_{5\text{-}6A}$= 8.9 Hz, $J_{6A\text{-}6B}$= 13.0 Hz, H-6A), 4.06 (dd, 1H, $J_{2\text{-}3}$= 3.9 Hz, $J_{3\text{-}4}$= 8.5 Hz, H-3), 4.34-4.42 (m, 2H, H-4, H-5), 4.50 (d, 1H, $J_{A\text{-}B}$= 11.3 Hz, OCH_2Ph), 4.60 (t, 1H, $J_{1\text{-}2}$= $J_{2\text{-}3}$= 3.9 Hz, H-2), 4.79 (d, 1H, $J_{A\text{-}B}$= 11.3 Hz, OCH_2Ph), 5.69 (d, 1H, $J_{1\text{-}2}$= 3.9 Hz, H-1), 7.27-7.50 (m, 10H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.8, -4.2 ($Si(CH3)_2$), 18.2 (Cq, *t*-Bu), 25.9 (*t*-Bu), 26.8, 27.1 (Me), 62.3 (C-6), 66.2 (C-5), 72.2 (OCH_2Ph), 76.1 (C-3), 77.3 (C-2), 79.8 (C-4), 104.1 (C-1), 113.3 (Cq-isop), 124.1, 128.3, 128.5, 128.7, 129.3, 131.0 (CH-Ph), 137.3 (Cq-Ph), 144.5 (Cq-SOPh)

152



M.W.= 548.76 g.mol^{-1}

$C_{28}H_{40}O_7SSi$

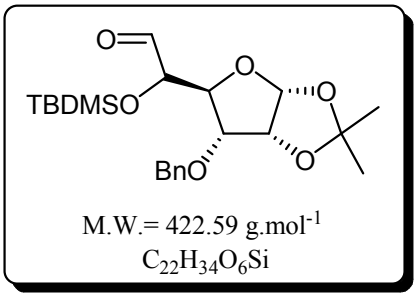
Rf = 0.4 (PE/EtOAc 8:2); $[\alpha]_D$ = + 39 (C=1.5, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2987, 2946 (CH), 1461, 1456 (Ph), 1365, 1130 (SO_2), 1220 ($Si(CH_3)_2$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.07 (s, 3H, $Si(CH_3)_3$), 0.10 (s, 3H, $Si(CH_3)_3$), 0.89 (s, 9H, *t*-Bu), 1.45 (s, 3H, Me), 1.64 (s, 3H, Me), 3.18 (dd, 1H, $J_{5\text{-}6B}$= 4.0 Hz, $J_{6A\text{-}6B}$= 14.8 Hz, H-6B), 3.81 (dd, 1H, $J_{5\text{-}6A}$= 6.9 Hz, $J_{6A\text{-}6B}$= 14.8 Hz, H-6A), 4.07 (dd, 1H, $J_{2\text{-}3}$= 3.6 Hz, $J_{3\text{-}4}$= 8.8 Hz, H-3), 4.16 (dd, 1H, $J_{4\text{-}5}$= 1.3 Hz, $J_{3\text{-}4}$= 8.8 Hz, H-4), 4.59-4.62 (m, 2H, OCH_2Ph, H-5), 4.64 (t, 1H, $J_{1\text{-}2}$= $J_{2\text{-}3}$= 3.6 Hz, H-2), 4.86 (d, 1H, $J_{A\text{-}B}$= 11.9 Hz, OCH_2Ph), 5.73 (d, 1H, $J_{1\text{-}2}$= 3.6 Hz, H-1), 7.42-7.44 (m, 5H, Ph), 7.62-7.76 (m, 3H, Ph), 7.96-7.98 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -5.2, -4.4 ($Si(CH3)_2$), 18.1 (Cq, *t*-Bu), 25.9 (*t*-Bu), 26.8, 27.0 (Me), 59.4 (C-6), 65.4 (C-5), 72.0 (OCH_2Ph), 75.7 (C-3), 77.5 (C-2), 80.6 (C-4), 103.9 (C-1), 113.3 (Cq-isop), 128.0, 128.2, 128.6, 129.0, 129.4, 133.7 (CH-Ph), 137.3 (Cq-Ph), 139.9 (Cq-SO_2Ph); **HRMS**: calcd. for $C_{28}H_{40}O_7SSiNa$ $[M+Na]^+$ 571.2162, found 571.2179.

3-*O*-benzyl-1,2-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-α-D-allo-hexodialdo-1,4-furanose (153)

PROCEDURE

The sulfoxide **151** (170.0 mg, 0.32 mmol) was dissolved in DCM (10 mL) and $(CF_3CO)_2O$ (0.18 mL, 1.28 mmol) was added. The reaction was stirred at room temperature during 1 h then, saturated aqueous $NaHCO_3$ was added. The aqueous phase was extracted with EtOAc (3 x 15 mL) and the combined organic phase was dried over $MgSO_4$. The residue was dissolved in

DCM (10 mL) then MeOH (28.3 µL, 0.70 mmol) and Et_3N (0.032 mmol) were added at 0ºC and the reaction was stirred during 30 min. After extraction with DCM (3 x 15 mL), the combined organic phase was washed with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 95:5) to afford compound **153** (105.5 mg, **78% yield**), as a colourless oil**.**

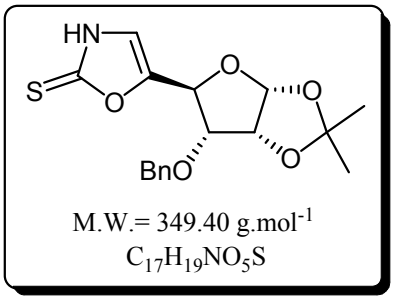


Rf = 0.2 (PE/EtOAc 7:3); **MS** (IS): m/z = 423.5 $[M+H]^+$, 445.5 $[M+Na]^+$; $[\alpha]_D$ = - 51 (C=0.5, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) **I.R.** (NaCl) ν (cm^{-1}) 2954, 2921 (CH), 1710 (C=O), 1461, 1452 (Ph), 1220 ($Si(CH_3)_2$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.01 (s, 3H, $Si(CH_3)_3$), 0.07 (s, 3H, $Si(CH_3)_3$), 0.87 (s, 9H, *t*-Bu), 1.35 (s, 3H, Me), 1.60 (s, 3H, Me), 3.98 (dd, 1H, $J_{2\text{-}3}$= 3.9 Hz, $J_{3\text{-}4}$= 8.8 Hz, H-3), 4.36 (brs, 1H, H-5), 4.41 (dd, 1H, $J_{4\text{-}5}$= 1.8 Hz, $J_{3\text{-}4}$= 8.8 Hz, H-4), 4.48 (t, 1H, $J_{1\text{-}2}$= $J_{2\text{-}3}$= 3.9 Hz, H-2), 4.52 (d, 1H, $J_{A\text{-}B}$= 12.0 Hz, OCH_2Ph), 4.67 (d, 1H, $J_{A\text{-}B}$= 12.0 Hz, OCH_2Ph), 5.66 (d, 1H, $J_{1\text{-}2}$= 3.9 Hz, H-1), 7.29-7.37 (m, 5H, Ph), 9.56 (d, 1H, $J_{5\text{-}6}$= 0.8Hz, H-6); **^{13}C NMR** (100 MHz, $CDCl_3$) δ -4.9, -4.8 ($Si(CH3)_2$), 18.4 (Cq, *t*-Bu), 25.8 (*t*Bu), 26.6, 27.1 (Me), 72.3 (OCH_2Ph), 75.4 (C-3), 76.9 (C-5), 77.5 (C-2), 79.7 (C-4), 104.4 (C-1), 113.5 (Cq-isop), 128.2, 128.3, 128.6 (CH-Ph), 137.3 (Cq-Ph), 201.2 (C=O).

5-[(4*R*)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-*C*-yl]-1,3-oxazoline-2-thione (154)

PROCEDURE

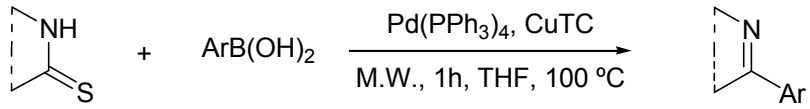
The aldehyde **153** (100.0 mg, 0.24 mmol) and KSCN (34.5 mg, 0.35 mmol) were dissolved in EtOH (15 mL). After cooling at –5°C, 12M aqueous HCl (35.08 µL, 0.43 mmol) was carefully added and the mixture was stirred at room temperature for 5 h, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 20 mL), the combined organic phase was washed, first with saturated aqueous $NaHCO_3$, then water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **154** (66.2 mg, **79% yield**) as a colourless oil.



M.W.= 349.40 g.mol^{-1}
$C_{17}H_{19}NO_5S$

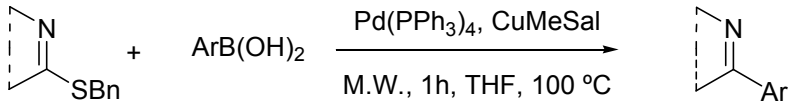
Rf = 0.4 (PE/EtOAc 6:4);); $[\alpha]_D$ = - 39 (C=0.9, MeOH); **I.R.** (NaCl) ν (cm^{-1}) 3234 (NH), 2945, 2934 (CH), 1647 (C=C), 1503, 1117 (N-CS-O), 1462, 1455 (Ph); **^{1}H NMR** (400 MHz, DMSO) δ 1.33 (s, 3H, Me), 1.50 (s, 3H, Me), 4.02 (dd, 1H, $J_{2'-3'}$= 4.0 Hz, $J_{3'-4'}$= 9.0 Hz, H-3'), 4.50 (d, 1H, J_{A-B}= 11.9 Hz, O*CH*$_2$Ph), 4.63 (d, 1H, J_{A-B}= 11.9 Hz, O*CH*$_2$Ph), 4.74 (d, 1H, $J_{3'-4'}$= 9.0 Hz, H-4'), 4.83 (t, 1H, $J_{1'-2'}$= $J_{2'-3'}$= 4.0 Hz, H-2'), 5.78 (d, 1H, $J_{1'-2'}$= 4.0 Hz, H-1'), 7.24-7.33 (m, 5H, Ph), 7.86 (s, 1H, H-5), 13.3 (brs, 1H, NH); **^{13}C NMR** (100 MHz, DMSO) δ 26.3, 26.6 (Me), 69.8 (C-4'), 70.9 (O*CH*$_2$Ph), 76.5 (C-2'), 79.6 (C-3'), 103.8 (C-1'), 112.3 (Cq-isop), 126.4 (C-4), 127.3, 127.7, 128.1 (CH-Ph), 136.2 (C-5), 137.4 (Cq-Ph), 178.8 (C-2); **HRMS**: calcd. for $C_{17}H_{20}NO_5S$ $[M+H]^+$ 350.1062, found 350.1054.

General procedure for modified Suzuki cross-coupling reaction (one step sequence) G.P.1



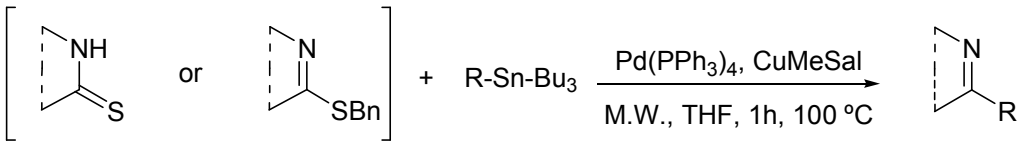
In a microwave vial tube, a solution of OXT or OZT (0.10 g) in THF (5 mL) with a stirring bar was prepared under argon. Following the order, CuTc (2.2 eq.), the boronic acid (2.2 eq.) and $(PPh_3)_4Pd$ (0.05 eq.) were added under argon. The tube was sealed with a silicon septum and subjected to microwave irradiation at 100°C for 60 min with stirring. The reaction vessel was allowed to cool down to room temperature, the solvent was evaporated under vacuum and residue was purified by column chromatography on silica gel (PE/ EtOAc) to afford the corresponding oxazole.

General procedure for modified Suzuki cross-coupling reaction (two-step sequence) G.P.2



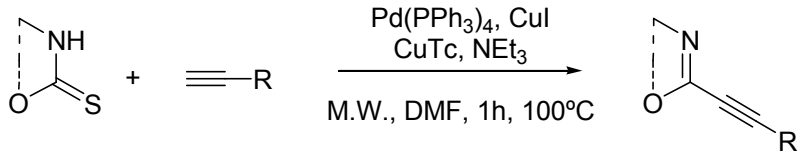
In a microwave vial tube, a solution of *S*-benzylsulfanyloxazole/oxazoline (0.10 g) in THF (5 mL) with a stirring bar was prepared under argon. Following the order, CuMeSal (2.2 eq.), boronic acid (2.2 eq.) and $(PPh_3)_4Pd$ were added under argon. The tube was sealed with a silicon septum and subjected to microwave irradiation at 100°C for 60 min with stirring. The reaction vessel was allowed to cool down to room temperature, the solvent was evaporated under vacuum and residue was purified by column chromatography on silica gel (PE/ EtOAc) to afford the corresponding oxazole/oxazoline.

General procedure for modified Stille cross-coupling reaction (one- or two-step sequence) G.P.3



In a microwave vial tube, a solution of OXT or OZT or *S*-benzylsulfanyl derivative (0.10 g) in THF (5 mL) with a stirring bar was prepared under argon. Following the order, $CuBr.Me_2S$ (2.2 eq.), the stannane (2.2 eq.) and $(PPh_3)_4Pd$ (0.05 eq.) were added under argon. The tube was sealed with a silicon septum and subjected to microwave irradiation at 100°C for 60 min with stirring. The reaction vessel was allowed to cool down to room temperature, the solvent was evaporated under vacuum and the residue was purified by column chromatography on silica gel (PE/ EtOAc) to afford the corresponding oxazole or oxazoline.

General procedure for Sonogashira cross-coupling reaction G.P.4



In a microwave vial tube, a solution of OXT or OZT (0.10 g) in DMF (2mL) with a stirring bar was prepared. Following the order, CuTc (0.1eq), the alkyne (3 equiv), triethylamine (5ml), CuI (0.5eq), and $(Ph_3P)_4Pd$ (0.05 equiv) were added under argon. The tube was sealed with a silicon septum and subjected to microwave irradiation at 100°C for 15 min with stirring. The reaction vessel was allowed to cool down to room temperature, the solvent were evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (EtOAc/PE).

2-(4-methoxyphenyl)-4,5-dihydro[methyl (2-deoxy-5-*O*-benzyl-β-D-xylofuranosid)][3,2-d]-1,3-oxazole (155)

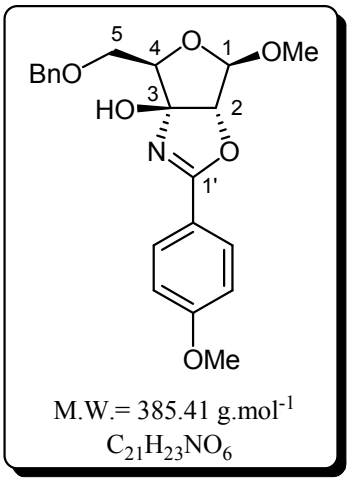
PROCEDURE

Method A

From OZT **33** and *p*-methoxyphenylboronic acid using G.P.1; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **155** (51.9 mg, **42% yield**) as a yellow oil.

Method B

From benzysulfanyl derivative **75** and *p*- methoxyphenylboronic acid using G.P.2; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **155** (76.8 mg, **80% yield**) as a yellow oil.



Rf = 0.3 (PE/EtOAc 6:4); $[\alpha]_D$ = - 29 (C=0.3, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3480 (OH), 2977, 2981, 2927 (CH), 1680 (N=C-O), 1465, 1457 (Ph); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 3.38 (s, 3H, OMe), 3.75 (dd, 1H, $J_{4\text{-}5B}$= 5.6 Hz, $J_{5A\text{-}5B}$= 9.2 Hz H-5B), 3.85 (s, 3H, PhOMe), 4.02 (t, 1H, $J_{4\text{-}5A}$= $J_{5A\text{-}5B}$= 9.2 Hz, H-5A), 4.39 (dd, 1H, $J_{4\text{-}5A}$=9.2 Hz, $J_{4\text{-}5B}$=5.6 Hz, H-4), 4.59 (d, 1H, $J_{A\text{-}B}$= 11.7 Hz, O*CH*$_2$Ph), 4.64 (d, 1H, $J_{A\text{-}B}$= 11.7 Hz, O*CH*$_2$Ph), 4.73 (s, 1H, H-2), 4.99 (s, 1H, H-1), 6.91 (d, 2H, $J_{o\text{-}m}$= 9.0 Hz, H$_o$-*Ph*OMe), 7.28-7.36 (m, 5H, Ph), 7.90 (d, 2H, $J_{o\text{-}m}$= 9.0 Hz, H$_m$-*Ph*OMe); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 55.0, 55.4 (OMe), 70.4 (C-5), 73.5 (O*CH*$_2$Ph), 84.1 (C-4), 90.8 (C-2), 108.3 (C-3), 108.4 (C-1), 113.8 (CH$_o$-*Ph*OMe), 118.9

(Cq-PhOMe), 127.8, 127.9, 128.5, (CH-Ph), 130.6 (CH_m-*Ph*OMe), 133.7, 137.4 (Cq-Ph), 162.7 (C-1'); **HRMS**: calcd. for $C_{21}H_{24}NO_6$ $[M+H]^+$ 386.1604, found 386.1614.

[241]Silva, S.; Tardy, S.; Routier, S.; Suzenet, F.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Tetrahedron Lett* **2008**, *49*, 5583-5586.

2-(4-methoxyphenyl)-4,5-dihydro{methyl [2-deoxy-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[3,2-d]-1,3-oxazole (156)

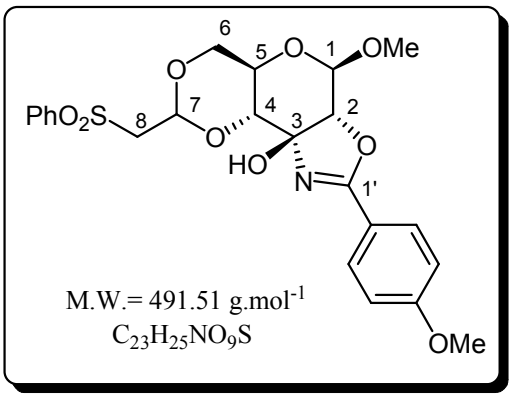
PROCEDURE

Method A

From OZT **58** and *p*-methoxyphenylboronic acid using G.P.1; the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **156** (55.3 mg, **47% yield**) as a colourless oil.

Method B

From benzysulfanyl derivative **76** and *p*- methoxyphenylboronic acid using G.P.2; the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **156** (84.2 mg, **87% yield**) as a colourless oil.



Rf = 0.5 (PE/EtOAc 1:1); $[\alpha]_D$ = - 17 (C=1.0, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3498 (OH), 1684 (N=C-O), 1456, 1451 (Ph), 1370, 1310 (SO_2); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 3.33-3.39 (m, 1H, H-5), 3.44 (s, 3H, OMe), 3.46-3.51 (m, 2H, H-8B, H-6B), 3.65-3.68 (m, 1H, H-8A), 3.82 (m, 3H, PhOMe), 4.02 (dd, 1H, $J_{5\text{-}6A}$= 4.6 Hz, $J_{6A\text{-}6B}$= 10.2 Hz, H-6A), 4.26 (d, 1H, $J_{4\text{-}5}$= 10.0 Hz, H-4), 4.48 (s, 1H, H-2), 4.63 (s, 1H, H-1), 5.13-5.14 (m, 1H, H-7), 6.86 (d, 2H, $J_{o\text{-}m}$= 8.2 Hz, H_o-*Ph*OMe), 7.53-7.66 (m, 5H, Ph), 7.92 (d, 2H, $J_{o\text{-}m}$= 8.2 Hz, H_m-*Ph*OMe); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 55.5, 55.3 (OMe), 56.6 (C-8), 64.7 (C-5), 69.4 (C-6), 78.9 (C-4), 84.5 (C-2), 95.8 (C-3), 96.8 (C-7), 100.5 (C-1), 113.9 (CH_o-*Ph*OMe), 118.4 (Cq-PhOMe), 128.8, 128.9, 129.2 (CH- Ph), 133.9 (CH_m-*Ph*OMe), 133.7, 139.8 (Cq-Ph), 163.2 (C-1'); **HRMS**: calcd. for $C_{23}H_{26}NO_9S$ $[M+H]^+$ 492.1328, found 492.1320.

2-(4-methoxyphenyl)-4,5-dihydro{methyl [2-deoxy-3-*O*-ethyl-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[3,2-d]-1,3-oxazole (157)

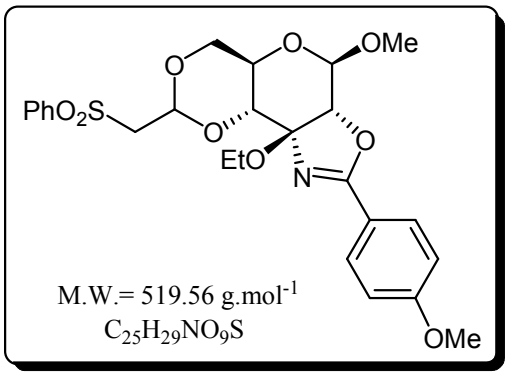
PROCEDURE

Method A

From OZT **59** and *p*-methoxyphenylboronic acid using G.P.1; the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **157** (51.2 mg, **44% yield**) as a colourless oil.

Method B

From benzysulfanyl derivative **159** and *p*-methoxyphenylboronic acid using G.P.2; the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **157** (86.5 mg, **89% yield**) as a colourless oil.



Rf = 0.4 (PE/EtOAc 7:3); $[\alpha]_D$ = - 13 (C=1.2, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2986, 2978 (CH), 1680 (N=C-O), 1463, 1456 (Ph), 1367, 1303 (SO_2); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 1.18 (t, 3H, $J_{CH2-CH3}$= 7.1 Hz, OCH_2CH_3), 3.43 (s, 3H, OMe), 3.47-3.63 (m, 6H, OCH_2CH_3, H-5, H-6B, H-8A, H-8B), 3.82 (s, 3H, PhOMe), 4.02 (dd, 1H, J_{5-6A}=5.1 Hz, J_{6A-6B}= 10.4 Hz, H-6A), 4.39 (d, 1H, J_{4-5}= 9.8 Hz, H-4), 4.49 (d, 1H, J_{1-2}= 2.5 Hz, H-2), 4.68 (d, 1H, J_{1-2}= 2.5 Hz, H-1), 5.16 (dd, 1H, J_{7-8A}= 3.1 Hz, J_{7-8B}= 6.8 Hz, H-7), 6.87 (d, 2H, J_{o-m}= 9.0 Hz, H_o-*Ph*OMe), 7.49-7.62 (m, 3H, Ph), 7.87-7.98 (m, 4H, Ph); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 15.4 (OCH_2CH_3), 55.5, 55.1 (OMe), 58.3 (OCH_2CH_3), 60.0 (C-8), 64.6 (C-5), 69.4 (C-6), 78.7 (C-4), 81.8 (C-2), 97.5 (C-7), 99.9 (C-3), 100.3 (C-1), 113.9 (CH_o-*Ph*OMe), 118.5 (Cq-PhOMe), 128.2, 129.1, 131.1 (CH- Ph), 133.8 (CH_m-*Ph*OMe), 134.7, 139.9 (Cq-Ph), 163.1 (C-1'); **HRMS**: calcd. for $C_{25}H_{30}NO_9S$ $[M+H]^+$ 520.1641, found 520.1653.

2-(4-methoxyphenyl)-4,5-dihydro{methyl [3-deoxy-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[2,3-d]-1,3-oxazole (158)

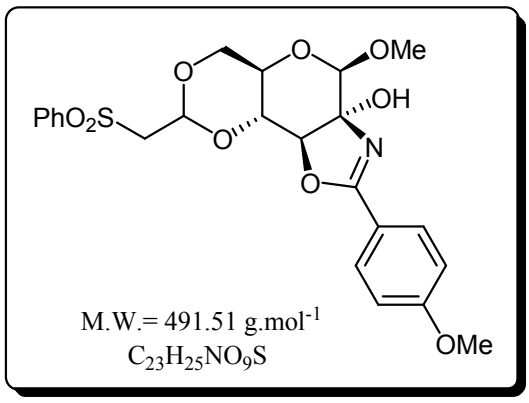
PROCEDURE

Method A

From OZT **60** and *p*-methoxyphenylboronic acid using G.P.1; the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **158** (60.2 mg, **51% yield**) as a colourless oil.

Method B

From benzysulfanyl derivative **77** and *p*-methoxyphenylboronic acid using G.P.2; the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **158** (83.3 mg, **86% yield**) as a colourless oil.

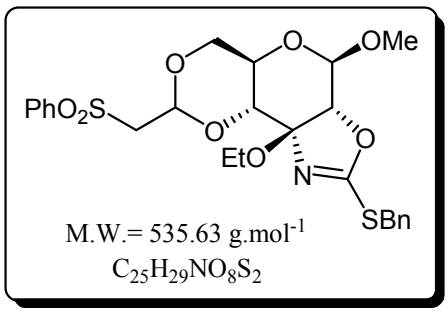


Rf = 0.5 (PE/EtOAc 1:1); $[\alpha]_D$ = - 104 (C=1.0, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3494 (OH), 1680 (N=C-O), 1461, 1455 (Ph), 1369, 1307 (SO_2); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 3.33 (s, 3H, OMe), 3.44-3.52 (m, 3H, H-8A, H-8B, H-6B), 3.61-3.67 (m, 1H, H-5), 3.8 (s, 3H, PhOMe), 4.09-4.23 (m, 3H, H-3, H-4, H-6A), 4.72 (s, 1H, H-1), 5.09 (t, 1H, $J_{7\text{-}8A}$= $J_{7\text{-}8B}$= 4.9 Hz, H-7), 5.82 (brs, 1H, OH), 6.90 (d, 2H, $J_{o\text{-}m}$= 8.7 Hz, H_o-*Ph*OMe), 7.53-7.57 (m, 3H, Ph), 7.90-7.95 (m, 4H, Ph); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 55.6, 55.9 (OMe), 59.8 (C-8), 63.2 (C-5), 69.6 (C-6), 77.1 (C-4), 84.2 (C-3), 96.5 (C-7), 98.1 (C-2), 102.2 (C-1), 114.0 (CH_o-*Ph*OMe), 118.7 (Cq-PhOMe), 128.6, 129.0, 130.9 (CH- Ph), 133.9 (CH_m-*Ph*OMe), 134.8, 139.9 (Cq-Ph), 163.2 (C-1'); **HRMS**: calcd. for $C_{23}H_{26}NO_9S$ $[M+H]^+$ 492.1328, found 492.1317.

2-Benzylsulfanyl-4,5-dihydro{methyl [2-deoxy-3-*O*-ethyl-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[3,2-d]-1,3-oxazole(159)

PROCEDURE

To the OZT **59** (320.7 mg, 0.72 mmol) in dry DCM (10 ml), were added Et_3N (0.12 mL, 0.86 mmol) and BnBr (0.13 mL, 1.08 mmol). The mixture was stirred during 3 h at room temperature, then cooled by treating with crushed ice. After extraction with DCM (3 x 25 mL), the combined organic phase was washed, first with water, then with brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **159** (343.2 mg, **89% yield**) as a yellow oil.



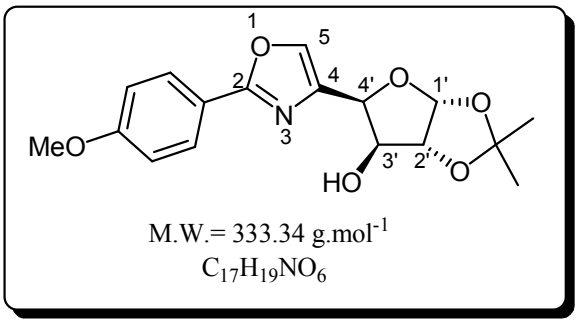
Rf = 0.5 (Cy/EtOAc 7:3); $[\alpha]_D$ = - 29 (C=0.7, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2976, 2953 (CH), 1578, 1069, 687 (-N=CS-O), 1466, 1458 (Ph), 1370, 1304 (SO_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.20 (t, 3H, $J_{CH2\text{-}CH3}$= 6.9 Hz, OCH_2CH_3), 3.32 (dt, 1H, $J_{5\text{-}6B}$= 4.8 Hz, $J_{4\text{-}5}$=$J_{5\text{-}6A}$= 10.3 Hz, H-5), 3.39 (s, 3H, OMe), 3.42-3.50 (m, 3H, OCH_2CH_3, H-6A), 3.57 (dd, 1H, $J_{7\text{-}8A}$= 6.4 Hz, $J_{8A\text{-}8B}$=, 14.6 Hz, H-8A), 3.63 (dd, 1H, $J_{7\text{-}8B}$= 3.5 Hz, $J_{8A\text{-}8B}$=

14.6 Hz, H-8B), 4.02 (dd, 1H, $J_{5\text{-}6B}$=4.8 Hz, $J_{6A\text{-}6B}$= 9.9 Hz, H-6B), 4.20 (d, 1H, $J_{A\text{-}B}$= 13.3 Hz, S*CH*$_2$Ph), 4.30-4.36 (m, 2H, H-4, S*CH*$_2$Ph), 4.42 (d, 1H, $J_{1\text{-}2}$= 2.5 Hz, H-2), 4.55 (d, 1H, $J_{1\text{-}2}$= 2.5 Hz, H-1), 5.16 (dd, 1H, $J_{7\text{-}8A}$= 6.4 Hz, $J_{7\text{-}8B}$= 3.5 Hz, H-7), 7.24-7.38 (m, 5H, Ph), 7.51-7.67 (m, 3H, Ph), 7.91-7.94 (m, 2H, Ph); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 15.4 (OCH$_2$*CH*$_3$), 36.2 (S*CH*$_2$Ph), 56.0 (OMe), 58.6 (OCH$_2$*CH*$_3$), 60.0 (C-8), 64.3 (C-5), 69.3 (C-6), 78.7 (C-4), 83.6 (C-2), 97.3 (C-7), 99.4 (C-3), 99.6 (C-1), 127.7, 128.2, 128.6, 128.8, 129.1, 133.8 (CH-Ph), 136.6, 140.0 (Cq-Ph), 169.2 (C-SBn); **HRMS**: calcd. for $C_{25}H_{30}NO_8S_2$ $[M+H]^+$ 536.1413, found 536.1410.

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(4-methoxyphenyl)-1,3-oxazole (160)

PROCEDURE

From OXT **100** and *p*-methoxyphenylboronic acid using G.P.1; the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **160** (110.7 mg, **86% yield**) as a yellow solid.



M.W.= 333.34 g.mol^{-1}
$C_{17}H_{19}NO_6$

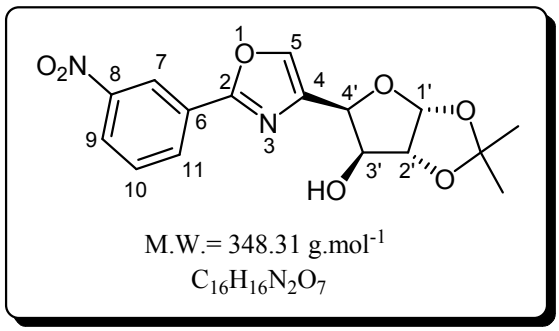
Rf = 0.6 (PE/EtOAc 1:1); $[\alpha]_D$ = - 34 (C=1.0, MeOH); **mp**: 113-114 °C; **I.R.** (NaCl) ν (cm^{-1}) 3489 (OH), 2998, 2967 (CH), 1684 (N=C-O), 1654 (C=C); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 1.36 (s, 3H, Me), 1.56 (s, 3H, Me), 3.84 (s, 3H, OMe), 4.41 (s, 1H, H-3'), 4.69 (d, 1H, $J_{1'\text{-}2'}$=3.6, H-2'), 4.75 (sl, 1H, O-H), 5.18 (d, 1H, $J_{3'\text{-}4'}$= 2.1 Hz,H-4'), 6.08 (d, 1H, $J_{1'\text{-}2'}$= 3.5 Hz, H-1'), 6.95 (d, 2H, $J_{o\text{-}m}$=8.8 Hz, H-o), 7.77 (s. 1H, H-5), 7.94 (d, 2H, $J_{o\text{-}m}$= 8.8 Hz, H-m); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 26.2, 26.9 (Me), 55.5 (O-Me), 73.5 (C-4'), 76.9 (C-3'), 85.1 (C-2'), 105.2 (C-1'), 111.9 (Cq-isop), 114.4 (CH$_o$-Ph), 119.4 (Cq-Ph), 128.5 (CHm-Ph), 129.5 (Cq-Ph), 136.6 (C-4), 137.6 (C-5), 161.9 (C-2); **HRMS**: calcd. for $C_{17}H_{20}NO_6$ $[M+H]^+$ 334.1291, found 334.1286.

[241]Silva, S.; Tardy, S.; Routier, S.; Suzenet, F.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Tetrahedron Lett*. **2008**, *49*, 5583-5586.

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(3-nitrophenyl)-1,3-oxazole (161)

PROCEDURE

From OXT **100** and *p*-methoxyphenylboronic acid using G.P.1; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **161** (88.7 mg, **66% yield**) as a white solid.



M.W.= 348.31 g.mol^{-1}
$C_{16}H_{16}N_2O_7$

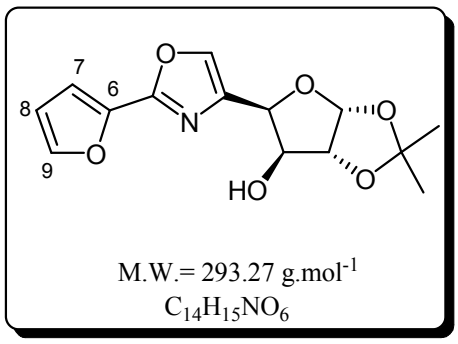
Rf = 0.3 (PE/EtOAc 1:1); $[\alpha]_D$ = - 28 (C=1.0, MeOH); **mp**: 129-130 °C; **I.R.** (NaCl) ν (cm^{-1}) 3493 (OH), 2976, 2952 (CH), 1682 (N=C-O), 1650 (C=C), 1584 (NO_2); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 1.38 (s, 3H, Me), 1.58 (s, 3H, Me), 3.95 (d, 1H, $J_{OH-3'}$= 2.5 Hz, O-H), 4.46 (s, 1H, H-3'), 4.72 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-2'), 5.25 (d, 1H, $J_{3'-4'}$= 2.4 Hz, H-4'), 6.09 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-1'), 7.68 (t, 1H, J_{9-10}= J_{10-11}= 8.2 Hz, H-10), 7.92 (s, 1H, H-5), 8.31-8.34 (m, 2H, H-9, H-11), 8.85 (t, 1H, J_{7-9}= J_{7-11}= 2.0 Hz, H-7); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 26.2, 26.9 (Me), 74.1 (C-4'), 76.7 (C-3'), 85.1 (C-2'), 105.2 (C-1'), 112.1 (Cq-isop), 121.6 (C-7), 125.4 (C-11), 128.3 (C-6), 130.3 (C-10), 132.2 (C-9), 137.7 (C-4), 139.1 (C-5), 148.8 (C-8), 160.1 (C-2); **HRMS**: calcd. for $C_{16}H_{16}N_2O_7Na$ $[M+Na]^+$ 371.0855, found 371.0875.

[241]Silva, S.; Tardy, S.; Routier, S.; Suzenet, F.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Tetrahedron Lett.* **2008**, *49*, 5583-5586.

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(furyl)-1,3-oxazole (162)

PROCEDURE

From OXT **100** and furyl-2-boronic acid using G.P.1; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **162** (69.1 mg, **61% yield**) as a yellow solid.



M.W.= 293.27 g.mol^{-1}
$C_{14}H_{15}NO_6$

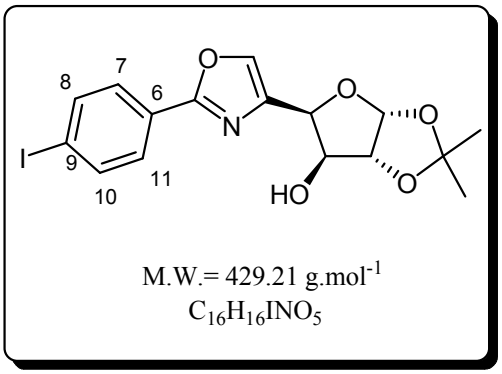
Rf = 0.4 (PE/EtOAc 1:1); $[\alpha]_D$ = - 27 (C=1.0, MeOH); **mp**: 88-89 °C; **I.R.** (NaCl) ν (cm^{-1}) 3503 (OH), 2989, 2945 (CH), 1680 (N=C-O), 1653 (C=C), 1555 (furyl); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 1.37 (s, 3H, Me), 1.56 (s, 3H, Me), 3.83 (s, 1H, O-H), 4.45 (s, 1H, H-3'), 4.69 (d, 1H, $J_{1'-2'}$= 3.5 Hz, H-2'), 5.22 (d, 1H, $J_{3'-4'}$= 2.3 Hz, H-4'), 6.07 (d, 1H, $J_{1'-2'}$= 3.5 Hz, H-1'), 6.55 (dd, 1H, J_{7-8}= 3.5 Hz, J_{8-9}= 1.8 Hz, H-8), 7.06 (d, 1H, J_{7-8}= 3.5 Hz, H-7), 7.57 (d, 1H, J_{8-9}= 1.8 Hz, H-9), 7.77 (s, 1H, H-5); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 26.3, 26.9 (Me), 74.5 (C-4'), 76.6 (C-3'), 85.0 (C-2'), 105.2 (C-1'), 112.0 (Cq-isop), 112.1 (C-8), 112.7 (C-7), 137.0 (C-4), 137.4 (C-5), 142.4 (C-6), 145.0 (C-9), 155.0 (C-2); **HRMS**: calcd. for $C_{14}H_{15}NO_6Na[M+Na]^+$ 316.0797, found 316.0803.

[241]Silva, S.; Tardy, S.; Routier, S.; Suzenet, F.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Tetrahedron Lett.* **2008**, *49*, 5583-5586.

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(4-iodophenyl)-1,3-oxazole (163)

PROCEDURE

From OXT **100** and *p*-iodophenylboronic acid using G.P.1; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **163** (63.0 mg, **38% yield**) as a white solid.



Rf = 0.4 (PE/EtOAc 1:1); $[\alpha]_D$ = - 7 (C=1.0, MeOH); **mp**: 95-97 °C; **I.R.** (NaCl) ν (cm^{-1}) 3459 (OH), 2994, 2965 (CH), 1680 (N=C-O), 1653 (C=C), 584 (CI); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 1.37 (s, 3H, Me), 1.57 (s, 3H, Me), 4.34 (d, 1H, $J_{OH-3'}$=1.8 O-H), 4.43 (s, 1H, H-3'), 4.71 (d, 1H, $J_{1'-2'}$=3.8, H-2'), 5.20 (d, 1H, $J_{3'-4'}$=2.4, H-4'), 6.09 (d, 1H, $J_{1'-2'}$= 3.7, H-1'), 7.73-7.75 (m, 2H, H-7, H-11), 7.80-7.83 (m, 2H, H-8, H-10), 7.84 (s, 1H, H-5); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 26.2, 26.9 (Me), 73.7 (C-4'), 77.4 (C-3'), 85.1 (C-2'), 97.9 (C-9), 105.2 (C-1'), 112.0 (Cq-isop), 126.1 (C-6), 128.2 (C-8, C-10), 138.3 (C-7, C-11), 138.4 (C-5), 139.6 (C-4), 161.8 (C-2); **HRMS**: calcd. for $C_{16}H_{17}INO_5$ $[M+H]^+$ 430.0151, found 430.0156.

[241]Silva, S.; Tardy, S.; Routier, S.; Suzenet, F.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Tetrahedron Lett*. **2008**, *49*, 5583-5586.

2-(2-thienyl)-4,5-dihydro[methyl (2-deoxy-5-*O*-benzyl)-β-D-xylofuranosid][3,2-d]-1,3-oxazole (164)

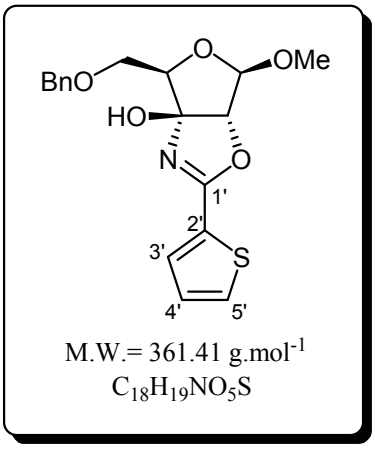
PROCEDURE

Method A

From OZT **33** and 2-tributylstannylthiophene using G.P.3; the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **164** (31.3 mg, **27% yield**) as a colourless oil.

Method B

From benzysulfanyl derivative **75** and 2-tributylstannylthiophene using G.P.3; the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **164** (70.2 mg, **78% yield**) as a colourless oil.



M.W.= 361.41 g.mol^{-1}
$C_{18}H_{19}NO_5S$

Rf = 0.5 (PE/EtOAc 7:3); $[\alpha]_D$ = - 32 (C=0.6, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3495 (OH), 2989, 2957, 2937 (CH), 1678 (N=C-O), 1535 (thienyl), 1456, 1450 (Ph); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 3.38 (s, 3H, OMe), 3.74 (dd, 1H, $J_{4\text{-}5B}$= 5.6 Hz, $J_{5A\text{-}5B}$= 9.4 Hz H-5B), 4.01 (t, 1H, $J_{4\text{-}5A}$= $J_{5A\text{-}5B}$= 9.4 Hz, H-5A), 4.43 (dd, 1H, $J_{4\text{-}5A}$=9.4 Hz, $J_{4\text{-}5B}$=5.6 Hz, H-4), 4.58 (d, 1H, $J_{A\text{-}B}$= 11.9 Hz, O*C*H_2Ph), 4.63 (d, 1H, $J_{A\text{-}B}$= 11.9 Hz, O*C*H_2Ph), 4.77 (s, 1H, H-2), 4.92 (s, 1H, OH), 5.01 (s, 1H, H-1), 7.09 (dd, 1H, $J_{3'\text{-}4'}$= 5.0 Hz, $J_{4'\text{-}5'}$= 3.8 Hz, H-4'), 7.28-7.38 (m, 5H, Ph), 7.51 (dd, 1H, $J_{3'\text{-}4'}$= 5.0 Hz, $J_{3'\text{-}5'}$= 1.3 Hz, H-3'), 7.69 (dd, 1H, $J_{3'\text{-}5'}$= 1.3 Hz, $J_{4'\text{-}5'}$= 3.8 Hz, H-5'); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 55.2, (OMe), 70.5 (C-5), 73.7 (O*C*H_2Ph), 84.1 (C-4), 91.4 (C-2), 108.2 (C-3), 108.7 (C-1), 127.9 (C-4'), 128.0, 128.1, 128.3 (CH-Ph), 128.6 (C-5'), 130.2 (C-2'), 131.6 (C-3'), 137.4 (Cq-Ph), 160.6 (C-1'); **HRMS**: calcd. for $C_{18}H_{20}NO_5S$ $[M+H]^+$ 362.1062, found 362.1057.

[241]Silva, S.; Tardy, S.; Routier, S.; Suzenet, F.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Tetrahedron Lett.* **2008**, *49*, 5583-5586.

2-(2-thienyl)-4,5-dihydro{methyl [2-deoxy-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[3,2-d]-1,3-oxazole (165)

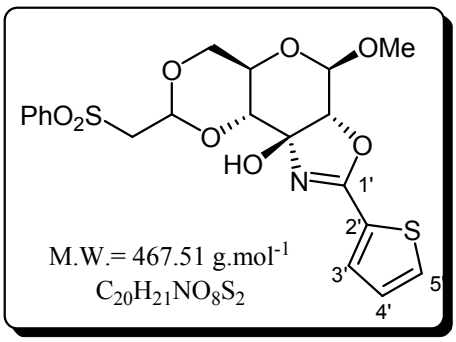
PROCEDURE

Method A

From OZT **58** and *2*-tributylstannylthiophene using G.P.3; the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **165** (28.1 mg, **25% yield**) as a yellow solid.

Method B

From benzysulfanyl derivative **76** and *2*-tributylstannylthiophene using G.P.3; the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **165** (79.2 mg, **86% yield**) as a yellow solid.



M.W.= 467.51 g.mol^{-1}
$C_{20}H_{21}NO_8S_2$

Rf = 0.3 (PE/EtOAc 1:1); $[\alpha]_D$ = - 27 (C=1.0, $CHCl_3$); **mp**: 96-97 °C; **I.R.** (NaCl) ν (cm^{-1}) 3507 (OH), 2984, 2965 (CH), 1681 (N=C-O), 1517 (thienyl), 1467, 1454 (Ph), 1379, 1307 (SO_2); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 3.42-3.57 (m, 6H, OMe, H-5, H-6B, H-8B), 3.89 (dd, 1H, $J_{7\text{-}8A}$= 4.1 Hz, $J_{8A\text{-}8B}$= 14.6 Hz, H-8A), 4.07 (dd, 1H, $J_{5\text{-}6A}$= 4.0 Hz, $J_{6A\text{-}6B}$= 10.6 Hz, H-6A), 4.28 (d, 1H, $J_{4\text{-}5}$= 9.6 Hz, H-4), 4.62 (d, 1H, $J_{1\text{-}2}$= 2.5 Hz, H-2), 4.66 (d, 1H, $J_{1\text{-}2}$= 2.5 Hz, H-1), 4.74 (brs, 1H, OH), 5.21 (t, 1H, $J_{7\text{-}8A}$= $J_{7\text{-}8B}$= 4.1 Hz, H-7), 7.11 (brt, 1H, $J_{3'\text{-}4'}$= 4.1 Hz, $J_{4'\text{-}5'}$= 4.5 Hz, H-

4'), 7.53-7.64 (m, 5H, Ph), 7.93-7.95 (m, 2H, H-3', H-5'); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 56.4, (OMe), 59.7 (C-8), 64.7 (C-5), 69.2 (C-6), 78.2 (C-4), 85.9 (C-2), 95.3 (C-3), 97.6 (C-7), 100.3 (C-1), 127.0 (C-4'), 128.2, 128.4, 128.5 (CH- Ph), 129.3 (C-5'), 132.2 (C-2'), 133.7 (C-3'), 139.6 (Cq-Ph), 163.9 (C-1'); **HRMS**: calcd. for $C_{20}H_{22}NO_8S_2$ $[M+H]^+$ 468.0787, found 468.0790.

2-(2-thienyl)-4,5-dihydro{methyl [2-deoxy-3-*O*-ethyl-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[3,2-d]-1,3-oxazole (166)

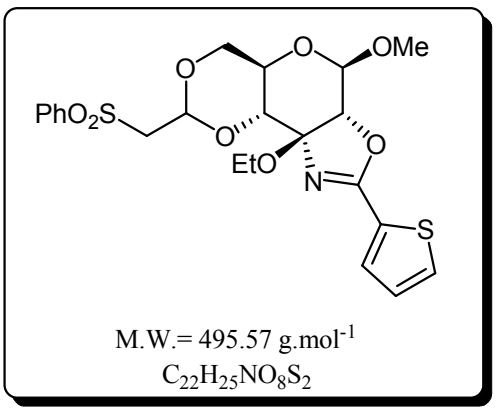
PROCEDURE

Method A

From OZT **59** and 2-tributylstannylthiophene using G.P.3; the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **166** (36.6 mg, **33% yield**) as a yellow oil.

Method B

From benzysulfanyl derivative **159** and 2-tributylstannylthiophene using G.P.3; the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **166** (88.0 mg, **95% yield**) as a yellow oil.



Rf = 0.3 (PE/EtOAc 7:3); $[\alpha]_D$ = - 23 (C=0.7, $CHCl_3$); **mp**: 79-84 °C; **I.R.** (NaCl) ν (cm^{-1}) 2995, 2876 (CH), 1687 (N=C-O), 1509 (thienyl), 1467, 1456 (Ph), 1373, 1307 (SO_2); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 1.19 (t, 3H, $J_{CH2-CH3}$= 6.9 Hz, $OCH_2\mathit{CH_3}$), 3.44 (s, 3H, OMe), 3.46-3.58 (m, 5H, OCH_2CH_3, H-6A, H-6B, H-8B), 3.65 (dd, 1H, J_{7-8A}= 3.1 Hz, J_{8A-8B}= 14.7 Hz, H-8A), 3.96-4.06 (m, 1H, H-5), 4.40 (d, 1H, J_{4-5}= 9.4 Hz, H-4), 4.50 (d, 1H, J_{1-2}= 2.5 Hz, H-2), 4.70 (d, 1H, J_{1-2}= 2.5 Hz, H-1), 5.17 (dd, 1H, J_{7-8A}= 3.1 Hz, J_{7-8B}= 6.9 Hz, H-7), 7.09 (dd, 1H, $J_{3'-4'}$= 4.9 Hz, $J_{4'-5'}$= 3.7 Hz, H-4'), 7.50-7.66 (m, 5H, Ph), 7.76 (dd, 1H, $J_{3'-4'}$= 4.9 Hz, $J_{3'-5'}$= 1.3 Hz, H-3'), 7.89 (dd, 1H, $J_{3'-5'}$= 1.3 Hz, $J_{4'-5'}$= 3.7 Hz, H-5'); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 15.4 ($OCH_2\mathit{CH_3}$), 55.1 (OMe), 58.6 (OCH_2CH_3), 60.0 (C-8), 64.6 (C-5), 69.5 (C-6), 78.6 (C-4), 82.2 (C-2), 97.6 (C-7), 100.0 (C-3), 100.2 (C-1), 127.9 (C-4'), 128.2, 128.6, 129.1 (CH- Ph), 131.8 (C-5'), 132.6 (C-2'), 133.8 (C-3'), 140.0 (Cq-Ph), 161.8 (C-1'); **HRMS**: calcd. for $C_{22}H_{26}NO_8S_2$ $[M+H]^+$ 496.1100, found 496.1111.

2-(2-thienyl)-4,5-dihydro{methyl [3-deoxy-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[2,3-d]-1,3-oxazole (167)

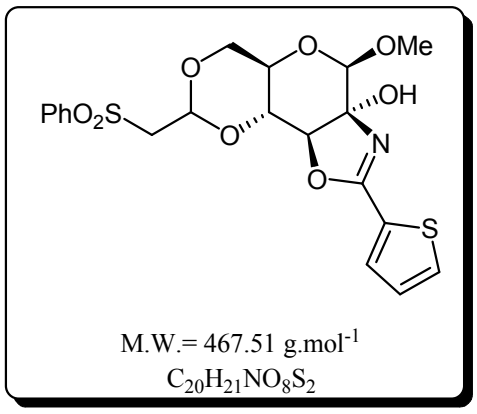
PROCEDURE

Method A

From OZT **60** and 2-tributylstannylthiophene using G.P.3; the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **167** (41.5 mg, **37% yield**) as a yellow solid.

Method B

From benzysulfanyl derivative **77** and 2-tributylstannylthiophene using G.P.3; the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **167** (82.0 mg, **89% yield**) as a yellow solid.



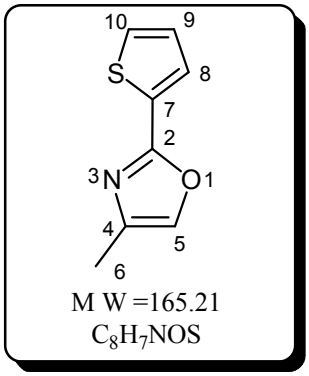
M.W.= 467.51 g.mol^{-1}
$C_{20}H_{21}NO_8S_2$

Rf = 0.5 (PE/EtOAc 6:4); $[\alpha]_D$ = - 27 (C= 0.6, $CHCl_3$); **mp**: 96-97 °C; **I.R.** (NaCl) ν (cm^{-1}) 3499 (OH), 2998, 2972 (CH), 1680 (N=C-O), 1512 (thienyl), 1458, 1450 (Ph), 1370, 1304 (SO_2); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 3.35 (s, 3H, OMe), 3.43-3.50 (m, 3H, H-8A, H-8B, H-6B), 3.52-3.57 (m, 1H, H-5), 4.16-4.42 (m, 3H, H-3, H-4, H-6A), 4.75 (s, 1H, H-1), 5.14 (t, 1H, $J_{7\text{-}8A}$= $J_{7\text{-}8B}$= 5.1 Hz, H-7), 6.05 (brs, 1H, OH), 7.12 (brt, 1H, $J_{3'\text{-}4'}$= 5.1 Hz, $J_{4'\text{-}5'}$= 4.8 Hz, H-4'), 7.53-7.66 (m, 5H, Ph), 7.79 (dd, 1H, $J_{3'\text{-}4'}$= 5.1 Hz, $J_{3'\text{-}5'}$= 1.2 Hz, H-3'), 7.85 (dd, 1H, $J_{3'\text{-}5'}$= 1.2 Hz, $J_{4'\text{-}5'}$= 4.8 Hz, H-5'); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 55.1 (OMe), 60.1 (C-8), 63.5 (C-5), 70.2 (C-6), 77.1 (C-4), 84.5 (C-3), 96.9 (C-7), 99.1 (C-2), 101.9 (C-1), 127.5 (C-4'), 128.3, 128.5, 129.7 (CH- Ph), 131.0 (C-5'), 132.7 (C-2'), 134.1 (C-3'), 139.7 (Cq-Ph), 161.3 (C-1'); **HRMS**: calcd. for $C_{20}H_{22}NO_8S_2$ $[M+H]^+$ 468.0787, found 468.0791.

4-Methyl-2-(2-thienyl)-oxazole (168)

PROCEDURE

From 4-methyloxazole-2(3*H*)-thione **1** and 2-tributylstannylthiophene using G.P.3; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **168** (84.6 mg, **59% yield**) as a yellow oil.



M W =165.21
C_8H_7NOS

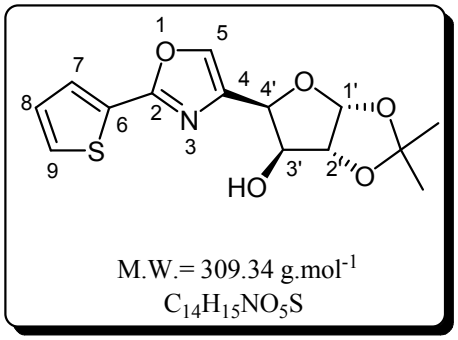
Rf = 0.4 (PE/EtOAc 6:4); **MS** (IS): m/z = 166.5 $[M+H]^+$; **I.R.** (NaCl) ν (cm^{-1}) 3036, 2943 (CH), 1679 (N=C-O),1519 (thienyl), 1658 (C=C), 1488, 1384, 1353, 1063 (N-CS-O); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 2,22 (d, 3H, $J_{5\text{-}6B}$ = 1.3 Hz, Me), 7.09 (dd, 1H, $J_{9\text{-}10}$= 3.6 Hz, $J_{8\text{-}9}$= 5.0 Hz, H-9), 7.34 (dd, 1H, $J_{5\text{-}6A}$= 1.3 Hz, $J_{5\text{-}6B}$= 2.5 Hz, H-5), 7.38 (dd, 1H, $J_{8\text{-}9}$= 5.0 Hz, $J_{8\text{-}10}$= 1.1 Hz, H-8), 7.64 (dd, 1H, $J_{8\text{-}10}$= 1.1 Hz, $J_{9\text{-}10}$= 3.6 Hz, H-10); **^{13}C NMR** (62.89 MHz, $CDCl_3$) δ 11.7 (C-6), 127.5 (C-10), 128.0 (C-9), 128.1 (C-8), 129.2 (C-7), 133.8 (C-5), 137.8 (C-4), 157.7 (C-2).

[241]Silva, S.; Tardy, S.; Routier, S.; Suzenet, F.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Tetrahedron Lett*. **2008**, *49*, 5583-5586.

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(2-thienyl)-1,3-oxazole (169)

PROCEDURE

From OXT **100** and 2-tributylstannylthiophene using G.P.3; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **169** (102.7 mg, **86% yield**) as a yellow oil.



M.W.= 309.34 $g.mol^{-1}$
$C_{14}H_{15}NO_5S$

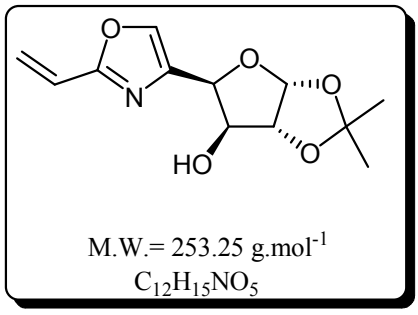
Rf = 0.5 (PE/EtOAc 1:1); $[\alpha]_D$ = - 29 (C=1.0, MeOH); **I.R.** (NaCl) ν (cm^{-1}) 3498 (OH), 2975, 2923 (CH), 1683 (N=C-O), 1648 (C=C), 1557 (thienyl); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 1.36 (s, 3H, Me), 1.56 (s, 3H, Me), 4.25 (d, 1H, $J_{OH\text{-}3'}$= 1.8 Hz, O-H), 4.43 (s, 1H, H-3'), 4.69 (d, 1H, $J_{1'\text{-}2'}$= 3.6 Hz, H-2'), 5.19 (d, 1H, $J_{3'\text{-}4'}$= 2.5 Hz, H-4'), 6.07 (d, 1H, $J_{1'\text{-}2'}$= 3.6 Hz, H-1'), 7.11 (dd, 1H, $J_{7\text{-}8}$= 5.1 Hz, $J_{8\text{-}9}$= 3.8 Hz, H-8), 7.45 (dd, 1H, $J_{7\text{-}8}$= 5.1 Hz, $J_{7\text{-}9}$= 1.1 Hz, H-7), 7.68 (dd, 1H, $J_{7\text{-}9}$= 1.1 Hz, $J_{8\text{-}9}$= 3.8 Hz, H-9), 7.75 (s, 1H, H-5); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 26.2, 26.9 (Me), 74.1 (C-4'), 76.6 (C-3'), 85.1 (C-2'), 105.1 (C-1'), 111.9 (Cq-isop), 128.1 (C-8), 128.8 (C-9), 129.0 (C-6), 129.3 (C-7), 136.9 (C-4), 137.5 (C-5), 158.5 (C-2); **HRMS**: calcd. for $C_{14}H_{15}NO_5SNa$ $[M+Na]^+$ 332.0569, found 332.0577.

[241] Silva, S.; Tardy, S.; Routier, S.; Suzenet, F.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Tetrahedron Lett*. **2008**, *49*, 5583-5586.

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(vinyl)-1,3-oxazole (170)

PROCEDURE

From OXT **100** and tributylvinyltin using G.P.3; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **170** (70.4 mg, **72% yield**) as a white solid.



M.W.= 253.25 g.mol^{-1}
$C_{12}H_{15}NO_5$

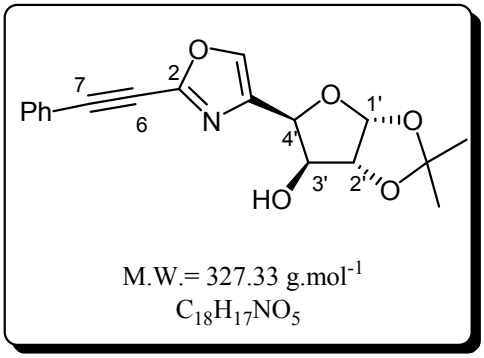
Rf = 0.4 (PE/EtOAc 1:1); $[\alpha]_D$ = - 18 (C=1.0, MeOH); **mp**: 140-142 °C; **MS** (IS): m/z = 254.5 $[M+H]^+$; **I.R.** (NaCl) ν (cm^{-1}) 3498 (OH), 2975, 2923 (CH), 1681 (N=C-O), 1648, 1635 (C=C); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 1.29 (s, 3H, Me), 1.48 (s, 3H, Me), 4.25 (d, 1H, $J_{OH-3'}$= 2.4 Hz, OH), 4.32 (t, 1H, $J_{3'-OH}$ = $J_{3'-4'}$= 2.4 Hz, H-3'), 4.61 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-2'), 5.08 (d, 1H, $J_{3'-4'}$= 2.4 Hz, H-4'), 5.61 (d, 1H, J_{6-7Z}= 11.4 Hz, H-7Z), 5.99 (d, 1H, $J_{1'-2'}$=3.6, H-1'), 6.16 (d, 1H, J_{5-7E}= 17.8 Hz, H-7E), 6.49 (dd, 1H, J_{6-7Z}= 11.4 Hz, J_{6-7E}= 17.8 Hz, H-6), 7.64 (s, 1H, H-5); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 26.2, 26.9 (Me), 73.7 (C-4'), 76.8 (C-3'), 85.1 (C-2'), 105.2 (C-1'), 111.9 (Cq-isop), 122.8 (C-6), 123.6 (C-7), 136.7 (C-4), 137.8 (C-5), 161.5 (C-2).

[241] Silva, S.; Tardy, S.; Routier, S.; Suzenet, F.; Tatibouet, A.; Rauter, A. P.; Rollin, P. *Tetrahedron Lett*. **2008**, *49*, 5583-5586.

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(phenylethynyl)-1,3-oxazole (171)

PROCEDURE

From OXT **100** and phenylacetylene using G.P.4; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compounds **171** (97.3 mg, **77% yield**) and **108** (6.1 mg, **7% yield**) as yellow solids.



M.W.= 327.33 g.mol^{-1}
$C_{18}H_{17}NO_5$

Rf = 0.5 (PE/EtOAc 1:1); $[\alpha]_D$ = - 38 (C=1.0, MeOH); **m.p.** = 128-129°C; **I.R.** (NaCl) ν (cm^{-1}) 3490 (OH), 2984, 2935 (CH), 2224 (C≡C), 1681 (N=C-O), 1643 (C=C), 1594, 1544 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.36 (s, 3H, Me), 1.56 (s, 3H, Me), 3.57 (brs, 1H, O-H), 4.44 (s, 1H, H-3'), 4.69 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-2'), 5.20 (d, 1H, $J_{3'-4'}$= 2.4 Hz, H-4'), 6.06 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-1'), 7.39-7.45 (m, 3H, Ph), 7.59-7.61 (m, 2H, Ph), 7.79 (s, 1H, H-5); **^{13}C NMR** (100MHz, $CDCl_3$) δ 26.3, 26.9

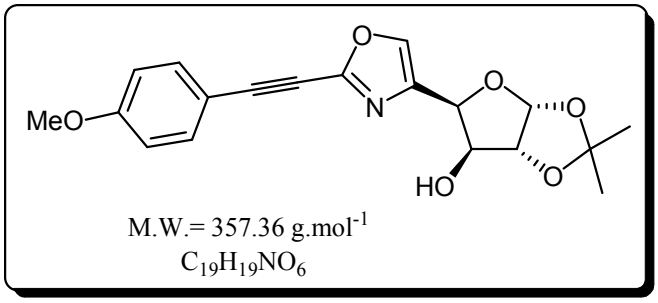
(Me), 74.6 (C-4'), 76.5 (C-3'), 85.0 (C-2'), 92.6 (C-6), 105.2 (C-1'), 112.1 (Cq-isop), 120.3 (C-7), 128.7, 130.4, 132.4 (CH-Ph), 137.3 (C-4), 137.9 (Cq-Ph), 138.9 (C-5), 147.3 (C-2); **HRMS:** calcd for $C_{18}H_{17}NO_5Na$ $[M+Na]^+$ 350.1004, found 350.1017.

[263] Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett.* **2008**, *10*, 853-856.

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(*p*-methoxyphenylethynyl)-1,3-oxazole (172)

PROCEDURE

From OXT **100** and *p*-methoxyphenylacetylene using G.P.4; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compounds **172** (86.9 mg, **63% yield**) and **108** (9.68 mg, **11% yield**) as yellow solids.



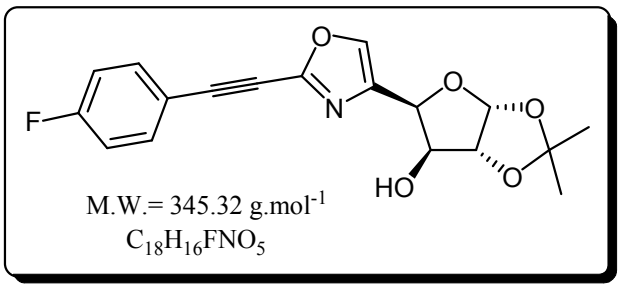
Rf = 0.3 (PE/EtOAc 6:4); $[\alpha]_D$ = - 23 (C=1.0, MeOH); **m.p.** = 139-140°C; **I.R.** (NaCl) ν (cm^{-1}) 3479 (OH), 2976, 2931 (CH), 2222 (C≡C), 1680 (N=C-O), 1649 (C=C), 1592, 1556 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.36 (s, 3H, Me), 1.56 (s, 3H, Me), 3.68 (s, 1H, O-H), 3.84 (s, 3H, OMe), 4.44 (s, 1H, H-3'), 4.68 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-2'), 5.19 (d, 1H, $J_{3'-4'}$= 2.1 Hz, H-4'), 6.06 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-1'), 6.90 (d, 2H, J_{o-m}= 8.9 Hz, H_m-PhOMe), 7.54 (d, 2H, J_{o-m}= 8.9 Hz, H_o-PhOMe), 7.76 (d, 1H, $J_{5-4'}$=0.8, H-5); **^{13}C NMR** (100MHz, $CDCl_3$) δ 26.3, 26.9 (Me), 55.5 (O-Me), 74.6 (C-4'), 76.5 (C-3'), 85.0 (C-2'), 93.0 (C-6), 105.2 (C-1'), 112.1 (Cq-isop), 112.2 (C-7), 114.4 (CH_m-*Ph*OMe), 128.6 (Cq-Ph), 134.1 (CH_o-PhOMe), 137.1 (C-4), 138.6 (C-5), 147.6 (C-2), 161.3 (Cq-PhOMe); **HRMS** calcd for $C_{19}H_{20}NO_6$ $[M+H]^+$ 358.1291, found 358.1293.

[263] Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett.* **2008**, *10*, 853-856.

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(*p*-fluorophenylethynyl)-1,3-oxazole (173)

PROCEDURE

From OXT **100** and 1-ethynyl-4-fluorobenzene using G.P.4; the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compounds **173** (56.0 mg, **42% yield**) and **108** (18.4 mg, **21% yield**) as yellow solids.



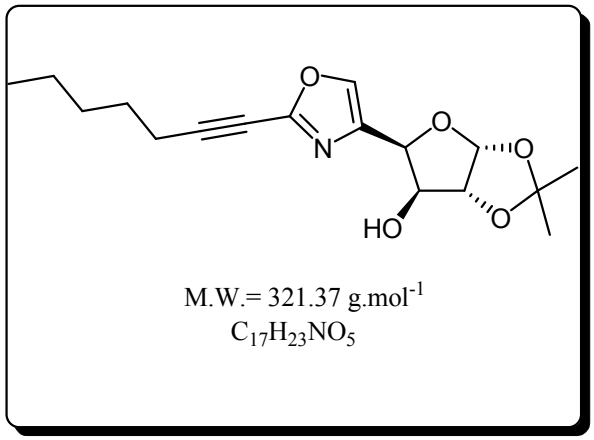
Rf = 0.4 (PE/EtOAc 7:3); $[\alpha]_D$ = - 37 (C=1.0, MeOH); **m.p.** = 103-105°C; **I.R.** (NaCl) ν (cm^{-1}) 3503 (OH), 2986, 2934 (CH), 2177 (C≡C), 1683 (N=C-O), 1650 (C=C), 1567, 1543 (Ph), 1323, 1221 (CF); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.36 (s, 3H, Me), 1.56 (s, 3H, Me), 3.64 (brs, 1H, O-H), 4.44 (d, 1H, $J_{3'-4'}$= 2.4 Hz, H-3'), 4.68 (d, 1H, $J_{1'-2'}$= 3.7 Hz, H-2'), 5.20 (d, 1H, $J_{3'-4'}$= 2.4 Hz, H-4'), 6.06 (d, 1H, $J_{1'-2'}$= 3.7 Hz, H-1'), 7.09 (t, 2H, J_{o-m}= 8.7 Hz, H_m-PhF), 7.58-7.62 (m, 2H, H_o-PhF), 7.79 (d, 1H, $J_{5-4'}$= 0.6 Hz, H-5); **^{13}C NMR** (100MHz, $CDCl_3$) δ 26.3, 26.9 (Me), 74.7 (C-4'), 76.4 (C-3'), 85.0 (C-2'), 91.4 (C-6), 105.2 (C-1'), 112.1 (Cq-isop), 115.8 (C-7), 116.1 (CH_m-*Ph*F), 128.6 (Cq-Ph), 134.6 (CH_o-*Ph*F), 137.3 (C-4), 139.0 (C-5), 147.0 (C-2), 161.7 (Cq-PhF); **HRMS** calcd for $C_{18}H_{16}FNO_5Na$ $[M+Na]^+$ 368.0910, found 368.0914.

[263] Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett*. **2008**, *10*, 853-856.

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(hept-2-ynyl)-1,3-oxazole (174)

PROCEDURE

From OXT **100** and 1-heptyne using G.P.4; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compounds **174** (96.8 mg, **78% yield**) as an orange oil and **108** (10.5 mg, **12% yield**) as a yellow solid.



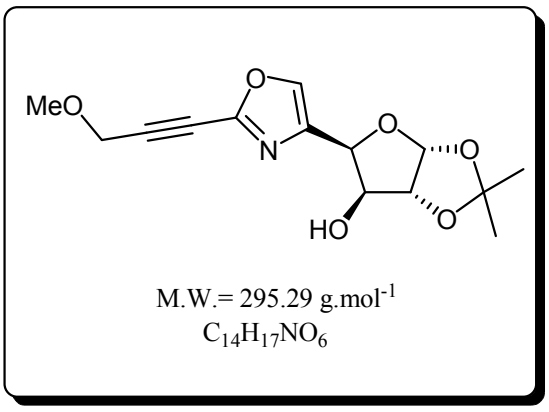
Rf = 0.5 (PE/EtOAc 1:1); $[\alpha]_D$ = - 35 (C=1.0, MeOH); **I.R.** (NaCl) ν (cm^{-1}) 3406 (OH), 2986, 2953 (CH), 2249 (C≡C), 1685 (N=C-O), 1654 (C=C); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.84 (t, 3H, J_{12-11}= 7.2 Hz, Me), 1.23-1.35 (m, 7H, Me, H-11, H-10), 1.47 (s, 3H, Me), 1.52-1.58 (qt, 2H, J_{8-9}= J_{9-10}= 7.1 Hz, H-9), 2.37 (t, 2H, J_{8-9}= 7.1 Hz, H-8), 3.65 (brs, 1H, O-H), 4.33 (d, 1H, $J_{3'-4'}$= 2.4 Hz, H-3'), 4.59 (d, 1H, $J_{1'-2'}$= 3.8 Hz, H-2'), 5.07 (d, 1H, $J_{3'-4'}$= 2.4 Hz, H-4'), 5.96 (d, 1H, $J_{1'-2'}$= 3.8 Hz, H-1'), 7.62 (s, 1H, H-5); **^{13}C NMR** (100MHz, $CDCl_3$) δ 14.0 (C-12), 19.3 (C-8), 22.2 (C-11), 26.2 (C-9), 26.9, 27.5 (Me), 31.1 (C-10), 68.6 (C-7), 74.4 (C-4'), 76.4 (C-3'), 85.0 (C-2'), 95.4 (C-6), 105.2 (C-1'), 112.0 (Cq-isop), 136.6 (C-4), 138.3 (C-5), 147.3 (C-2); **HRMS** calcd for $C_{17}H_{24}NO_5$ $[M]^+$ 322.1654, found 322.1661.

[263] Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett*. **2008**, *10*, 853-856.

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(methoxypropargyl)-1,3-oxazole (175)

PROCEDURE

From OXT **100** and methylpropargyl ether using G.P.4; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compounds **175** (75.2 mg, **66% yield**) and **108** (20.2 mg, **23% yield**) as yellow solids.



M.W.= 295.29 g.mol^{-1}
$C_{14}H_{17}NO_6$

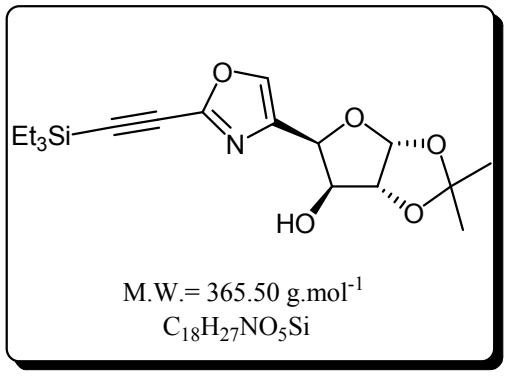
Rf = 0.5 (PE/EtOAc 1:1); $[\alpha]_D$ = - 32 (C=1.0, MeOH); **m.p.** = 85-87°C; **I.R.** (NaCl) ν (cm^{-1}) 3404 (OH), 2991, 2935 (CH), 2224 (C≡C), 1679 (N=C-O), 1643 (C=C); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.36 (s, 3H, Me), 1.55 (s, 3H, Me), 3.46 (s, 3H, O-Me), 3.51 (d, 1H, $J_{OH-3'}$= 1.9 Hz, O-H), 4.34 (s, 2H, H-8), 4.41 (s, 1H, H-3'), 4.67 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-2'), 5.17 (d, 1H, $J_{3'-4'}$= 2.3 Hz, H-4'), 6.04 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-1'), 7.75 (s, 1H, H-5); **^{13}C NMR** (100MHz, $CDCl_3$) δ 26.2 (Me), 26.9 (Me), 58.3 (OMe), 59.9 (C-8), 73.8 (C-7), 74.5 (C-4'), 76.4 (C-3'), 85.0 (C-2'), 89.2 (C-6), 105.2 (C-1'), 112.1 (Cq-isop), 137.1 (C-4), 139.1 (C-5), 146.3 (C-2); **HRMS** calcd for $C_{14}H_{17}NO_6Na$ $[M+Na]^+$ 318.0954, found 318.0961.

[263] Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett.* **2008**, *10*, 853-856.

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(triethylsilylethynyl)-1,3-oxazole (176)

PROCEDURE

From OXT **100** and triethylsilylacetylene using G.P.4; the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compounds **176** (94.5 mg, **67% yield**) as a colourless oil and **108** (18.4 mg, **21% yield**) as a yellow solid.



M.W.= 365.50 g.mol^{-1}
$C_{18}H_{27}NO_5Si$

Rf = 0.4 (PE/EtOAc 8:2); $[\alpha]_D$ = - 26 (C=1.0, MeOH); **I.R.** (NaCl) ν (cm^{-1}) 3404 (OH), 2922, 2853 (CH), 2193 (C≡C), 1689 (N=C-O), 1652 (C=C); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.71 (q, 6H, *J*= 7.5 Hz, $SiCH_2$), 1.04 (t, 9H, *J*= 7.5 Hz, CH_2CH_3), 1.35 (s, 3H, Me), 1.54 (s, 3H, Me), 3.51 (brs, 1H, O-H), 4.41 (d, 1H, $J_{3'-4'}$= 2.5 Hz, H-3'), 4.67 (d, 1H, $J_{2'-1'}$= 3.5 Hz, H-2'), 5.16 (d, 1H, $J_{3'-4'}$= 2.5 Hz, H-4'), 6.04 (d, 1H, $J_{1'-2'}$= 3.5 Hz, H-1'), 7.71 (s, 1H, H-5);

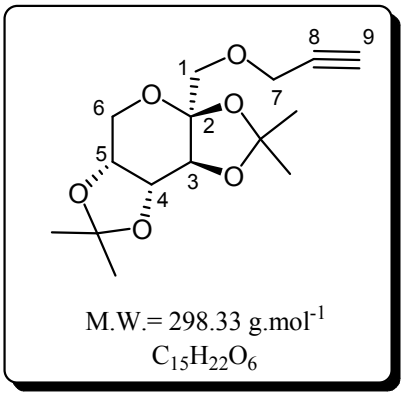
^{13}C NMR (100MHz, $CDCl_3$) δ 4.0 (Si*C*H_2), 7.4 (SiCH$_2$*C*H_3), 26.3, 26.9 (Me), 74.6 (C-4'), 76.4 (C-3'), 85.0 (C-2'), 91.7 (C-6), 98.7 (C-7), 105.2 (C-1'), 112.1 (Cq-isop), 136.9 (C-4), 138.7 (C-5), 146.7 (C-2); **HRMS** calcd for $C_{14}H_{28}NO_5Si$ $[M]^+$ 366.1737, found 366.1745.

[263] Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett.* **2008**, *10*, 853-856.

1-*O*-propargyl-2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose (177)

PROCEDURE

2,3:4,5-di-*O*-isopropylidene-fructopyranose (2.00 g, 7.68 mmol) was dissolved in dry DMF (20 mL) and after cooling at -5ºC, NaH (60% dispersion in oil; 460.8 mg, 11.52 mmol) was added. After stirring until H_2 evolution stopped, propargyl bromide (1.35 mL, 15.36 mmol) was added dropwise. The reaction was stirred overnight at room temperature, then cooled by treating with crushed ice. After extraction with ethyl acetate (3 x 50 mL), the combined organic phase was washed first with water, brine, and finally dried over $MgSO_4$. After filtration and concentration under vacuum, the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compound **177** (2.11 g, **92% yield**), as a colourless oil.

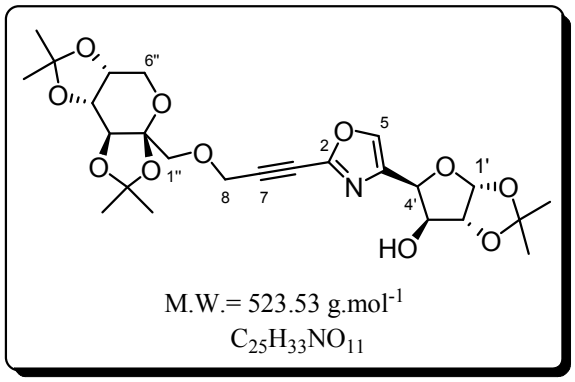


Rf = 0.7 (PE/EtOAc 7:3); $[\alpha]_D$ = - 27 (C=0.4, CHCl3); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 1.34 (s, 3H, Me), 1.42 (s, 3H, Me), 1.47 (s, 3H, Me), 1.53 (s, 3H, Me), 2.41 (t, 1H, $J_{7A\text{-}9}$= $J_{7B\text{-}9}$= 2.3 Hz, H-9), 3.62-3.67 (m, 2H, H-3, H-5), 3.74 (d, 1H, $J_{6A\text{-}6B}$= 13.1 Hz, H-6B), 3.91 (dd, 1H, $J_{5\text{-}6A}$= 2.0 Hz, $J_{6A\text{-}6B}$= 13.1 Hz, H-6A), 4.19-4.31 (m, 3H, H-4, H-7A, H-7B), 4.36 (d, 1H, $J_{1A\text{-}1B}$= 7.6 Hz, H-1B), 4.59 (d, 1H, $J_{1A\text{-}1B}$= 7.6 Hz, H-1B); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 24.2, 25.4, 26.0, 26.7 (Me), 59.2 (C-7), 61.2 (C-6), 70.3 (C-4), 70.4 (C-3), 71.1 (C-5), 71.3 (C-1), 74.6 (C-8), 79.5 (C-9), 102.7 (C-2), 108.7, 109.1 (Cq-isop); **HRMS**: calcd. for $C_{15}H_{22}O_6Na$ $[M+Na]^+$ 321.1314, found 321.1313.

4-[(4*R*)-1,2-*O*-isopropylidene-*α*-D-threofuranos-4-*C*-yl]-2-(2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranosyl-1-oxypropargyl)-1,3-oxazole (178)

PROCEDURE

From OXT **100** and ether **177** using G.P.4; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **178** (117.2 mg, **58% yield**) as a colourless oil and **108** (21.0 mg, **24% yield**) as a yellow solid.



M.W.= 523.53 g.mol^{-1}
$C_{25}H_{33}NO_{11}$

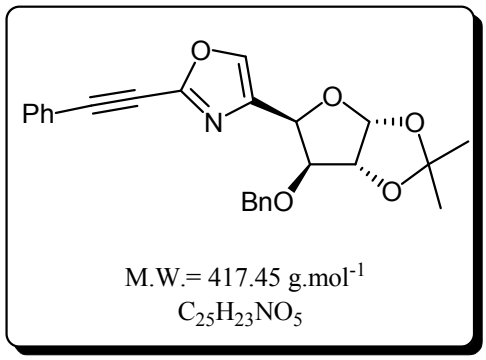
Rf = 0.2 (PE/EtOAc 7:3); $[\alpha]_D$ = - 33 (C=1.0, MeOH); **I.R.** (NaCl) ν (cm^{-1}) 3497 (OH), 2986, 2930 (CH), 2212 (C≡C), 1681 (N=C-O), 1664 (C=C); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.33 (s, 3H, Me), 1.35 (s, 3H, Me), 1.42 (s, 3H, Me), 1.46 (s, 3H, Me), 1.54-1.55 (m, 6H, Me), 3.51 (d, 1H, $J_{OH-3'}$= 2.6 Hz, O-H), 3.72-3.76 (m, 3H, H-1", H-6"B), 3.91 (dd, 1H, $J_{6"A-5"}$= 1.9 Hz, $J_{6"A-6"B}$= 13.1 Hz, H-6"A), 4.23 (dd, 1H, $J_{5"-6"A}$= 1.9 Hz, $J_{5"-4"}$= 8.0 Hz, H-5"), 4.36 (d, 1H, $J_{3"-4"}$= 2.6 Hz, H-3"), 4.41 (t, 1H, $J_{3'-4'}$= $J_{3'-OH}$= 2.6 Hz, H-3'), 4.47 (d, 1H, J_{8A-8B}= 16.3 Hz, H-8B), 4.53 (d, 1H, J_{8A-8B}= 16.3 Hz, H-8A), 4.60 (dd, 1H, $J_{3"-4"}$= 2.6 Hz, $J_{4"-5"}$= 8.0 Hz, H-5"), 4.66 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-2'), 5.16 (d, 1H, $J_{3'-4'}$= 2.4 Hz, H-4'), 6.04 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-1'), 7.74 (s, 1H, H-5); **^{13}C NMR** (100MHz, $CDCl_3$) δ 24.2, 25.4, 26.0, 26.2, 26.7, 26.9 (Me), 59.3 (C-8), 61.2 (C-6"), 70.3 (C-4"), 70.4 (C-3"), 71.0 (C-5"), 71.8 (C-1"), 73.8 (C-6), 74.4 (C-4'), 76.4 (C-3'), 85.0 (C-2'), 89.0 (C-7), 102.5 (C-2"), 105.2 (C-1'), 108.8, 109.2, 112.1 (Cq-isop), 137.1 (C-4), 139.1 (C-5), 146.3 (C-2); **HRMS** calcd for $C_{25}H_{33}NO_{11}Na$ $[M+Na]^+$ 546.1951, found 546.1971.

[263] Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett.* **2008**, *10*, 853-856.

4-[(4*R*)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-threofuranos-4-*C*-yl]-2-(phenylethynyl)-1,3-oxazole (179)

PROCEDURE

From OXT **87** and phenylacetylene using G.P.4; the residue was purified by column chromatography (PE/EtOAc 9:1) to afford compounds **179** (95.5 mg, **80% yield**) as a white solid and **109** (4.5 mg, **5% yield**) as a yellow oil.



M.W.= 417.45 g.mol^{-1}
$C_{25}H_{23}NO_5$

Rf = 0.5 (PE/EtOAc 7:3); $[\alpha]_D$ = - 48 (C=1.0, MeOH); **m.p.** = 130-132°C; **I.R.** (NaCl) ν (cm^{-1}) 2986, 2925 (CH), 2224 (C≡C), 1680 (N=C-O), 1658 (C=C), 1543, 1456 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.35 (s, 3H, Me), 1.53 (s, 3H, Me), 4.20 (d, 1H, $J_{3'-4'}$= 3.0 Hz, H-3'), 4.40 (d, 1H, J_{A-B}= 11.8 Hz, OCH_2Ph), 4.52 (d, 1H, J_{A-B}= 11.8 Hz, OCH_2Ph), 4.69 (d, 1H, $J_{1'-2'}$= 3.8 Hz, H-2'), 5.30 (d, 1H, $J_{3'-4'}$= 3.0 Hz, H-4'), 6.04 (d, 1H, $J_{1'-2'}$= 3.8 Hz, H-1'), 7.14-7.38 (m, 10H, Ph), 7.72 (s, 1H, H-5); **^{13}C NMR** (100MHz, $CDCl_3$) δ 26.4, 27.0 (Me), 72.8 (OCH_2Ph), 77.2 (C-4'), 82.4 (C-3'), 83.1 (C-2'), 91.6 (C-6), 105.0 (C-1'), 112.2 (Cq-isop), 120.7 (C-7), 127.8, 128.0, 128.6 (CH-Ph), 128.6 (Cq-Ph), 128.7, 130.1, 132.3

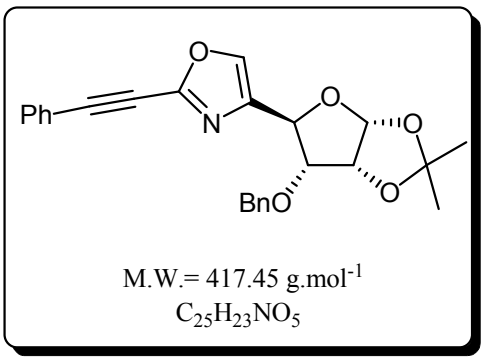
(CH-Ph), 137.3 (Cq-Ph), 137.9 (C-4), 138.4 (C-5), 146.5 (C-2); **HRMS** calcd for $C_{25}H_{24}NO_5$ $[M+H]^+$ 418.1654, found 418.1669.

[263] Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett*. **2008**, *10*, 853-856.

4-[(4*R*)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-*C*-yl]-2-(phenylethynyl)-1,3-oxazole (180)

PROCEDURE

From OXT **95** and phenylacetylene using G.P.4; the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compounds **180** (90.7 mg, **76% yield**) as a colourless oil and **110** (7.3 mg, **8% yield**) as a yellow oil.



M.W.= 417.45 g.mol^{-1}
$C_{25}H_{23}NO_5$

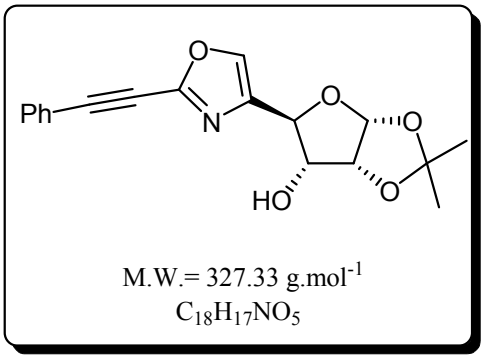
Rf = 0.5 (PE/EtOAc 7:3); $[\alpha]_D$ = + 87 (C=1.0, MeOH); **I.R.** (NaCl) ν (cm^{-1}) 2995, 2933 (CH), 2222 (C≡C), 1680 (N=C-O), 1653 (C=C), 1567, 1451 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.39 (s, 3H, Me), 1.66 (s, 3H, Me), 4.22 (dd, 1H, $J_{3'-2'}$= 4.3 Hz, $J_{3'-4'}$= 8.9 Hz, H-3'), 4.54 (d, 1H, J_{A-B}= 12.0 Hz, OCH_2Ph), 4.64-4.66 (m, 2H, H-2', OCH_2Ph), 4.99 (d, 1H, $J_{3'-4'}$= 8.9 Hz, H-4'), 5.87 (d, 1H, $J_{1'-2'}$= 3.6 Hz, H-1'), 7.25-7.40 (m, 10H, Ph), 7.62 (s, 1H, H-5); **^{13}C NMR** (100MHz, $CDCl_3$) δ 26.5, 27.0 (Me), 72.4 (C-4'), 72.8 (OCH_2Ph), 77.8 (C-2'), 81.0 (C-3'), 91.7 (C-6), 104.2 (C-1'), 113.2 (Cq-isop), 120.6 (C-7), 128.0 (Cq-Ph), 128.0, 128.1, 128.4, 128.7, 130.2, 132.3, (CH-Ph), 137.5 (C-4), 137.7 (Cq-Ph), 138.6 (C-5), 147.3 (C-2); **HRMS** calcd for $C_{25}H_{24}NO_5$ $[M+H]^+$ 418.1654, found 418.1659.

[263] Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett*. **2008**, *10*, 853-856.

4-[(4*R*)-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-*C*-yl]-2-(phenylethynyl)-1,3-oxazole (181)

PROCEDURE

From OXT **101** and phenylacetylene using G.P.4; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compounds **181** (92.2 mg, **73% yield**) and **111** (5.3 mg, **6% yield**) as yellow solids.



M.W.= 327.33 g.mol^{-1}
$C_{18}H_{17}NO_5$

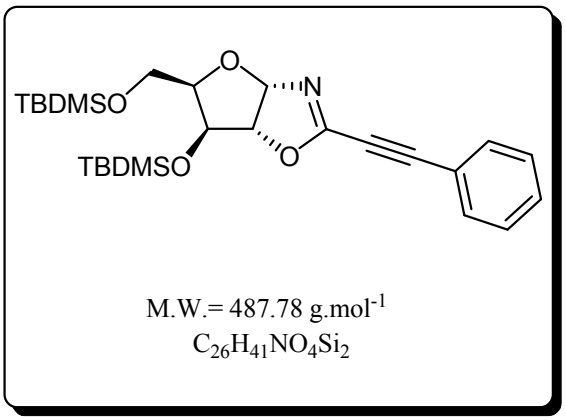
Rf = 0.5 (PE/EtOAc 1:1); $[\alpha]_D$ = + 44 (C=1.0, MeOH); **m.p.** = 119-120°C; **I.R.** (NaCl) ν (cm^{-1}) 3494 (OH), 2998, 2967 (CH), 2217 (C≡C), 1680 (N=C-O), 1646 (C=C), 1576, 1553 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.41 (s, 3H, Me), 1.64 (s, 3H, Me), 2.57 (d, 1H, $J_{3'\text{-OH}}$= 9.8 Hz, OH), 4.26-4.35 (m, 1H, H-3'), 4.70 (m, 1H, $J_{2'\text{-}1'}$= 4.0 Hz, $J_{2'\text{-}3'}$= 4.8 Hz, H-2'), 4.75 (d, 1H, $J_{3'\text{-}4'}$= 8.6 Hz, H-4'), 5.96 (d, 1H, $J_{1'\text{-}2'}$= 3.9 Hz, H-1'), 7.38-7.43 (m, 3H, Ph), 7.57-7.61 (m, 2H, Ph), 7.72 (s, 1H, H-5); **^{13}C NMR** (100MHz, $CDCl_3$) δ 26.7, 26.7 (Me), 74.8 (C-4'), 75.4 (C-3'), 78.6 (C-2'), 91.9 (C-6), 104.3 (C-1'), 113.1 (Cq-isop), 120.6 (C-7), 128.1 (Cq-Ph), 128.7, 130.2, 132.4, 138.0 (C-5), 138.8 (C-4), 147.5 (C-2); **HRMS** calcd for $C_{18}H_{17}NO_5Na$ $[M+Na]^+$ 350.1004 , found 350.1018.

[263] Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett.* **2008**, *10*, 853-856.

2-phenylethynyl-4,5-dihydro (1,2-dideoxy-3,5-di-*O-tert*-butyldimethylsilyl-α-D-xylofuranoso)-[1,2-*d*]-1,3-oxazole (182)

PROCEDURE

From OZT **L$_3$** and phenylacetylene using G.P.4; the residue was purified by column chromatography (PE/EtOAc 95:5) to afford compound **182** (94.8 mg, **82% yield**) as a colourless oil.



M.W.= 487.78 g.mol^{-1}
$C_{26}H_{41}NO_4Si_2$

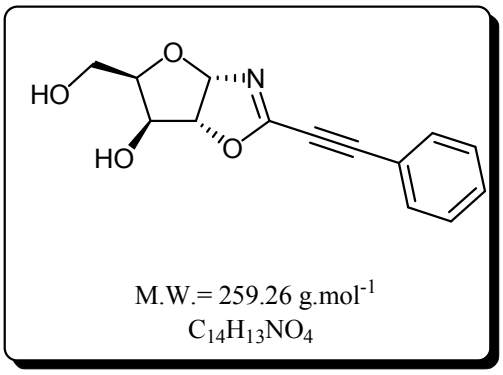
Rf = 0.5 (PE/EtOAc 9:1); $[\alpha]_D$ = + 45 (C=1.0, MeOH); **I.R.** (NaCl) ν (cm^{-1}) 2977, 2954 (CH), 2221 (C≡C), 1682 (N=C-O), 1576, 1553, 1478 (Ph), 1215, 1210 ($Si(CH_3)_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.05 (s, 3H, $Si(CH_3)_2$), 0.06 (s, 3H, $Si(CH_3)_2$), 0.13 (s, 3H, $Si(CH_3)_2$), 0.16 (s, 3H, $Si(CH_3)_2$), 0.88 (s, 9H, *t*-Bu), 0.91 (s, 9H, *t*-Bu), 3.45 (dd, 1H, $J_{4\text{-}5B}$= 8.2 Hz, $J_{5A\text{-}5B}$= 10.5 Hz, H-5B), 3.66 (dd, 1H, $J_{4\text{-}5A}$= 4.8 Hz, $J_{5A\text{-}5B}$= 10.5 Hz, H-5A), 3.95-3.99 (m, 1H, $J_{4\text{-}5B}$= 8.2 Hz, $J_{4\text{-}5A}$= 4.8 Hz, $J_{4\text{-}3}$= 2.0 Hz, H-4), 4.46 (d, 1H, $J_{3\text{-}4}$= 1.8 Hz, H-3), 4.75 (dd, 1H, $J_{1\text{-}2}$= 6.2 Hz, $J_{2\text{-}3}$= 1.0 Hz, H-2), 6.13 (d, 1H, $J_{1\text{-}2}$= 6.2 Hz, H-1), 7.31-7.46 (m, 5H, Ph); **^{13}C NMR** (100MHz, $CDCl_3$) δ -5.3, -5.2, -4.7, -4.7 (Si $(CH_3)_2$), 18.2, 18.5 (Cq, *t*-Bu), 25.9, 26.1 ($(CH_3)_3C$), 62.3 (C-5), 77.4 (C-3), 86.5 (C-4), 89.1 (C-2), 91.5 (C-2'), 101.0 (C-1), 120.0 (C-3'), 128.0 (Cq-Ph), 128.7, 130.6, 132.8 (CH-Ph), 152.3 (C-1'); **HRMS** calcd for $C_{26}H_{42}NO_4Si_2$ $[M+H]^+$ 488.2652, found, 488.2652.

[263] Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett*. **2008**, *10*, 853-856.

2-phenylethynyl-4,5-dihydro (1,2-dideoxy-3,5-dihydroxy-α-D-xylofuranoso)-[1,2-*d*]-1,3-oxazole (183)

PROCEDURE

From OZT **L4** and phenylacetylene using G.P.4; the residue was purified by column chromatography (PE/EtOAc 2:8) to afford compound **183** (77.4 mg, **57% yield**) as a yellow oil.



M.W.= 259.26 g.mol^{-1}
$C_{14}H_{13}NO_4$

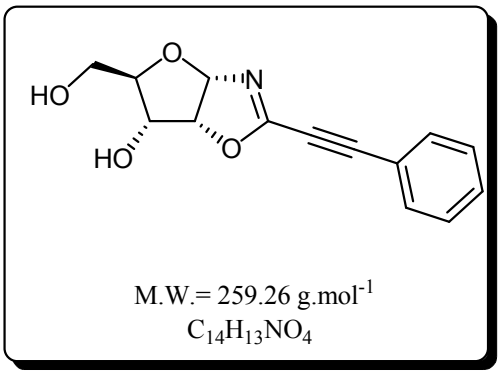
Rf = 0.3 (EtOAc); $[\alpha]_D$ = + 83 (C=1.0, MeOH); **I.R.** (NaCl) ν (cm^{-1}) 3504 (OH), 2996, 2978 (CH), 2227 (C≡C), 1681 (N=C-O), 1545, 1498 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.73 (brs, 2H, O-H), 3.72-3.74 (m, 1H, J_{3-4}= 2.9 Hz, H-4), 4.10 (dd, 1H, J_{4-5B}= 2.6 Hz, J_{5A-5B}= 12.5 Hz, H-5B), 4.19 (dd, 1H, J_{4-5A}= 3.8 Hz, J_{5A-5B}= 12.5 Hz, H-5A), 4.47 (d, 1H, J_{3-4}= 2.8 Hz, H-3), 4.85 (d, 1H, J_{1-2}= 5.6 Hz, H-2), 6.29 (d, 1H, J_{1-2}= 5.6 Hz, H-1), 7.36-7.40 (m, 3H, Ph), 7.56-7.58 (m, 2H, Ph); **^{13}C NMR** (100MHz, $CDCl_3$) δ 60.8 (C-5), 76.6 (C-3), 77.3 (C-4), 87.0 (C-2), 92.4 (C-2'), 100.0 (C-1), 119.8 (C-3'), 128.7 (Cq-Ph), 128.8, 130.8, 132.8 (CH-Ph), 153.2 (C-1'); **HRMS** calcd for $C_{14}H_{14}NO_4$ $[M+H]^+$ 260.0923, found 260.0924.

[263] Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett*. **2008**, *10*, 853-856.

2-phenylethynyl-4,5-dihydro (1,2-dideoxy-3,5-dihydroxy-α-D-ribofuranoso)-[1,2-*d*]-1,3-oxazole (184)

PROCEDURE

From OZT **L5** and phenylacetylene using G.P.4; the residue was purified by column chromatography (PE/EtOAc 2:8) to afford compound **184** (82.9 mg, **61% yield**) as a yellow solid.



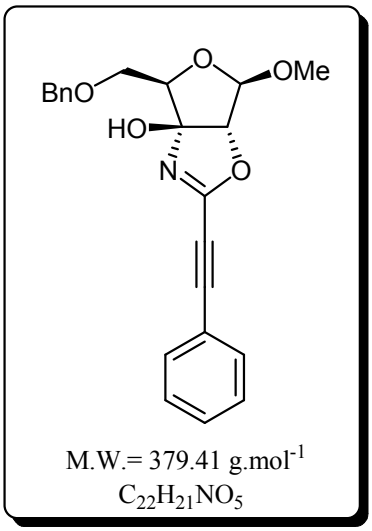
Rf = 0.2 (EtOAc); $[\alpha]_D$ = - 71 (C=0.5, MeOH); **m.p.** = 189-190°C; **I.R.** (NaCl) ν (cm^{-1}) 3485 (OH), 2972, 2955 (CH), 2219 (C≡C), 1680 (N=C-O), 1538, 1479 (Ph); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.45 (ddd, 1H, $J_{3\text{-}4}$= 6.8 Hz, $J_{4\text{-}5A}$= 1.9 Hz, $J_{4\text{-}5B}$= 4.5 Hz, H-4), 3.66 (dd, 1H, $J_{4\text{-}5B}$= 4.5 Hz, $J_{5A\text{-}5B}$= 12.4 Hz, H-5B), 3.88 (dd, 1H, $J_{4\text{-}5A}$= 1.9 Hz, $J_{5A\text{-}5b}$= 12.4 Hz, H-5A), 4.13 (dd, 1H, $J_{3\text{-}2}$= 5.6 Hz, $J_{3\text{-}4}$= 9.3 Hz, H-3), 4.92 (t, 1H, $J_{1\text{-}2}$= $J_{2\text{-}3}$= 5.6 Hz, H-2), 6.04 (d, 1H, $J_{1\text{-}2}$= 5.6 Hz, H-1), 7.43-7.63 (m, 5H, Ph); **^{13}C NMR** (100MHz, $CDCl_3$) δ 61.3 (C-5), 72.5 (C-3), 80.3 (C-4), 83.0 (C-2), 93.3 (C-2′), 100.1 (C-1), 120.9 (C-3′), 129.5 (Cq-Ph), 130.0, 132.1, 133.7 (CH-Ph), 149.7 (C-1′); **HRMS** calcd for $C_{14}H_{14}NO_4$ $[M+H]^+$ 260.0923, found 260.0934.

[263] Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett*. **2008**, *10*, 853-856.

2-phenylethynyl-4,5-dihydro[methyl (2-deoxy-5-*O*-benzyl)-β-D-xylofuranosid][3,2-d]-1,3-oxazole (185)

PROCEDURE

From OZT **33** and phenylacetylene using G.P.4; the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **185** (86.5 mg, **71% yield**) as a yellow oil.

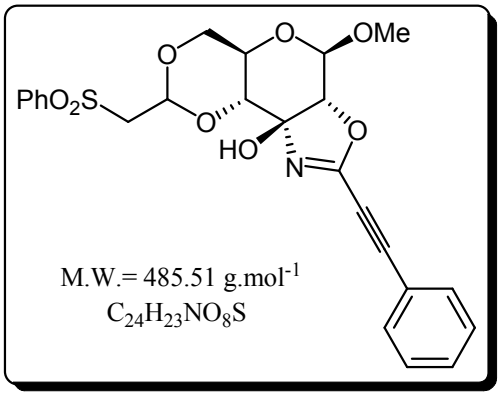


Rf = 0.4 (PE/EtOAc 7:3); $[\alpha]_D$ = - 38 (C=0.3, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3485 (OH), 2998, 2965, 2913 (CH), 2224 (C≡C), 1678 (N=C-O), 1529, 1505, 1461, 1456 (Ph); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 3.37 (s, 3H, OMe), 3.72 (dd, 1H, $J_{4\text{-}5B}$= 4.5 Hz, $J_{5A\text{-}5B}$= 9.2 Hz H-5B), 4.02 (t, 1H, $J_{4\text{-}5A}$= $J_{5A\text{-}5B}$= 9.2 Hz, H-5A), 4.31-4.37 (m, 1H, H-4), 4.58 (d, 1H, $J_{A\text{-}B}$= 11.8 Hz, O*C*H_2Ph), 4.63 (d, 1H, $J_{A\text{-}B}$= 11.8 Hz, O*C*H_2Ph), 4.67 (s, 1H, H-2), 4.73 (brs, 1H, OH), 4.98 (s, 1H, H-1), 7.31-7.46 (m, 10H, Ph); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 55.3 (OMe), 70.2 (C-5), 73.7 (O*C*H_2Ph), 83.7 (C-4), 90.6 (C-2), 91.5 (C-2′), 108.3 (C-1), 108.4 (C-3), 120.0 (C-3′), 127.9, 128.1, 128.7, 128.8, 130.6, 132.8 (CH-Ph), 137.3, 137.9 (Cq-Ph), 147.3 (C-1′); **HRMS**: calcd. for $C_{22}H_{22}NO_5$ $[M+H]^+$ 380.1498, found 380.1496.

2-phenylethynyl-4,5-dihydro{methyl [2-deoxy-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[3,2-d]-1,3-oxazole (186)

PROCEDURE

From OZT **58** and phenylacetylene using G.P.4; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **186** (100.2 mg, **86% yield**) as a colourless oil.

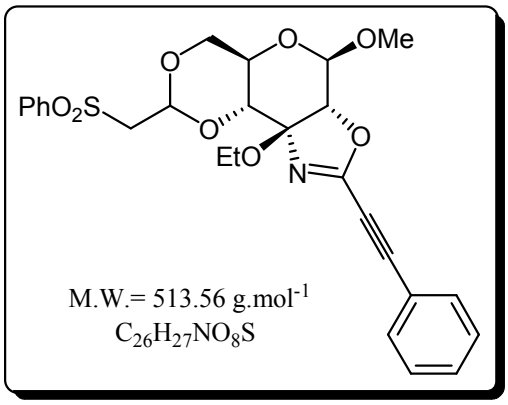


Rf = 0.5 (PE/EtOAc 1:1); $[\alpha]_D$ = - 34 (C=0.6, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 3479 (OH), 2979, 2932 (CH), 2225 (C≡C), 1684 (N=C-O), 1554, 1456, 1445 (Ph) 1367, 1307 (SO_2); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 3.32 (s, 3H, OMe), 3.41-3.53 (m, 3H, H-5, H-6B, H-8B), 3.65 (dd, 1H, $J_{7\text{-}8A}$= 4.9 Hz, $J_{8A\text{-}8B}$= 15.1 Hz, H-8A), 4.04 (dd, 1H, $J_{5\text{-}6A}$=4.3 Hz, $J_{6A\text{-}6B}$= 10.3 Hz, H-6A), 4.25 (d, 1H, $J_{4\text{-}5}$= 9.8 Hz, H-4), 4.65 (d, 1H, $J_{1\text{-}2}$= 3.1 Hz, H-2), 4.77 (d, 1H, $J_{1\text{-}2}$= 3.1 Hz, H-1), 5.14 (dd, 1H, $J_{7\text{-}8A}$= 4.9 Hz, $J_{7\text{-}8B}$= 4.4 Hz, H-7), 7.36-7.60 (m, 10H, Ph); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 55.5 (OMe), 59.3 (C-8), 64.1 (C-5), 68.3 (C-6), 77.2 (C-4), 85.7 (C-2), 90.1 (C-3), 96.8 (C-7), 98.9 (C-2'), 100.5 (C-1), 119.4 (C-3'), 127.9, 128.5, 128.6, 129.3, 129.7, 131.3 (CH-Ph), 137.5, 139.2 (Cq-Ph), 148.4 (C-1'); **HRMS**: calcd. for $C_{24}H_{24}NO_8S$ $[M+H]^+$ 486.1223, found 486.1221.

2-phenylethynyl-4,5-dihydro{methyl [2-deoxy-3-*O*-ethyl-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[3,2-d]-1,3-oxazole (187)

PROCEDURE

From OZT **59** and phenylacetylene using G.P.4; the residue was purified by column chromatography (PE/EtOAc 7:3) to afford compound **187** (102.3 mg, **89% yield**) as a colourless oil.

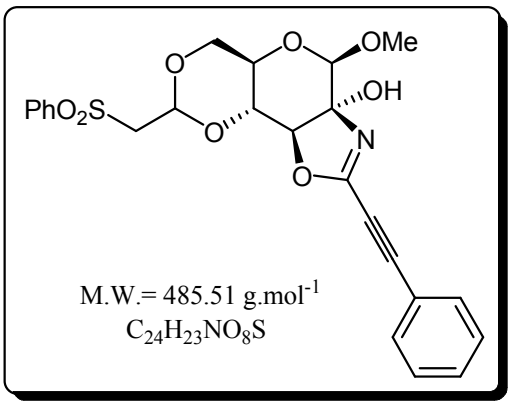


Rf = 0.6 (PE/EtOAc 1:1); $[\alpha]_D$ = - 23 (C=0.7, $CHCl_3$); **I.R.** (NaCl) ν (cm^{-1}) 2957, 2941 (CH), 2229 (C≡C), 1680 (N=C-O), 1535, 1467, 1458 (Ph) 1370, 1304 (SO_2); **^{1}H NMR** (400 MHz, DMSO) δ 1.09 (t, 3H, $J_{CH2-CH3}$= 6.9 Hz, $OCH_2\mathit{CH_3}$), 3.23-3.28 (m, 1H, H-5), 3.34 (s, 3H, OMe), 3.40-3.55 (m, 3H, $O\mathit{CH_2}CH_3$, H-6B), 3.68 (dd, 1H, $J_{7\text{-}8B}$= 5.3 Hz, $J_{8A\text{-}8B}$= 14.9 Hz, H-8B), 3.75 (dd, 1H, $J_{7\text{-}8A}$= 4.5 Hz, $J_{8A\text{-}8B}$= 14.9 Hz, H-8A), 3.97 (dd, 1H, $J_{5\text{-}6A}$=4.9 Hz, $J_{6A\text{-}6B}$= 10.2 Hz, H-6A), 4.38 (d, 1H, $J_{4\text{-}5}$= 10.1 Hz, H-4), 4.98 (d, 1H, $J_{1\text{-}2}$= 2.5 Hz, H-2), 4.76 (d, 1H, $J_{1\text{-}2}$= 2.5 Hz, H-1), 5.15 (t, 1H, $J_{7\text{-}8A}$=$J_{7\text{-}8B}$= 4.5 Hz, H-7), 7.35-7.70 (m, 10H, Ph); **^{13}C NMR** (100 MHz, DMSO) δ 15.3 ($OCH_2\mathit{CH_3}$), 55.2 (OMe), 58.4 ($O\mathit{CH_2}CH_3$), 58.7 (C-8), 63.9 (C-5), 68.2 (C-6), 77.3 (C-4), 81.8 (C-2), 90.5 (C-3), 96.6 (C-7), 98.4 (C-2'), 99.2 (C-1), 118.4 (C-3'), 127.9, 128.5, 128.9, 129.8, 131.1, 131.7 (CH-Ph), 137.3, 139.4 (Cq-Ph), 150.4 (C-1'); **HRMS**: calcd. for $C_{26}H_{28}NO_8S$ $[M+H]^+$ 514.1536, found 514.1545.

2-phenylethynyl-4,5-dihydro{methyl [3-deoxy-4,6-*O*-(2-phenylsulfonyl)ethylidene]-β-D-glucopyranosid}[2,3-d]-1,3-oxazole (188)

PROCEDURE

From OZT **60** and phenylacetylene using G.P.4; the residue was purified by column chromatography (PE/EtOAc 1:1) to afford compound **188** (100.2 mg, **82% yield**) as a yellow solid.



Rf = 0.5 (PE/EtOAc 3:7); $[\alpha]_D$ = - 104 (C= 0.4, $CHCl_3$); **mp**: 166-167 °C; **I.R.** (NaCl) ν (cm^{-1}) 3502 (OH), 2983, 2962 (CH), 2217 (C≡C), 1681 (N=C-O), 1550, 1459, 1451 (Ph) 1370, 1305 (SO_2); **^{1}H NMR** (400 MHz, $CHCl_3$) δ 3.38 (s, 3H, OMe), 3.47-3.50 (m, 3H, H-8A, H-8B, H-5), 4.07 (d, 1H, $J_{3\text{-}4}$= 7.9 Hz, H-3), 4.15-4.20 (m, 3H, H-4, H-6A, H-6B), 4.70 (s, 1H, H-1), 4.82 (brs, 1H, O-H), 5.08 (t, 1H, $J_{7\text{-}8A}$= $J_{7\text{-}8B}$= 5.1 Hz, H-7), 7.31-7.49 (m, 10H, Ph); **^{13}C NMR** (100 MHz, $CHCl_3$) δ 56.1 (OMe), 59.8 (C-8), 63.2 (C-5), 69.5 (C-6), 77.1 (C-4), 79.2 (C-3), 83.9 (C-2), 96.9 (C-7), 97.8 (C-2'), 101.7 (C-1), 119.9 (C-3'), 128.0, 128.3, 128.5, 129.2, 129.4, 132.3 (CH-Ph), 137.2, 139.7 (Cq-Ph), 162.7 (C-1'); **HRMS**: calcd. for $C_{24}H_{24}NO_8S$ $[M+H]^+$ 486.1223, found 486.1217.

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