Reactions of Pyranosyl Nitrile Oxides: 1,3-Nucleophilic Addition Reactions in the Synthesis of Novel *C*-Glycosides

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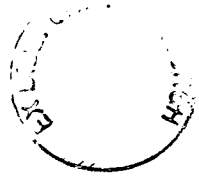

For My Grandparents

Archie and Elizabeth Smellie Richard and Mary Lindsay

Declaration

I declare that this thesis was composed by myself and that it describes my own work, except where specifically stated in the text. The work was carried out between October 2002 and September 2005 in the School of Chemistry at the University of Edinburgh under the supervision of Dr R. M. Paton.

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RSC Perkin Divisional Meeting 2003-Edinburgh University-Poster presented.

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Glossary of Terms, Symbols and Abbreviations

A	Angstrom
[α]	Optical rotation
Ac	Acetate
AIBN	2,2`-Azobisisobutyronitrile
AMP	Adenosine monophospate
Ar	Aryl
Bn	Benzyl
Boc	Butoxycarbonyl
BOM	Benzloxymethyl
Bt	Benzotriazole
Bu	Butyl
Bz	Benzoyl
CAN	Ceric ammonium nitrate
CDI	1,1`-carbonyldiimdazole
cm	centimetre
COSY	COrrelation SpectroscopY
d	Doublet
δ	Chemical shift
DAN	1,8-diaminonapthalene
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCC	1,3-Dicyclohexylcarbodiimide
DCM	Dichloromethane
DMAP	4-Dimethylaminopyridine
DMF	N,N-Dimethylformamide
DMSO	Dimethylsulfoxide
DMTMM	4-(4,6-dimethoxy[1,3,5]triazin-2-yl)-4-methylmorpholonium chloride
EDCI	1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide
Et	Ethyl
Ether	Diethyl ether
FAB	Fast Atom Bombardment
g	gram

hr	hour
HRMS	High Resolution Mass Spectrometry
Hz	Hertz
IR	Infra-red
J	Coupling Constant
Lit	Literature
M	Moles per litre
M	Multiplet
M^+	Molecular Ion
Me	Methyl
mg	milligram
MHz	Megahertz
min	minute
mmole	millimole
mp	melting point
m/z	mass to charge ratio
nd	not determined
NMR	Nuclear Magnetic Resonance
ppm	Parts per million
Pr	Propyl
q	Quartet
s	Singlet
t	Triplet
TDI	Tolylene-2,4-diisocyanate
Tf	Trifluoromethyl
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TMS	Trimethylsilyl
TOCSY	Total Correlation SpectroscopY
Ts	*p*-Toluenesulfonyl
ν	wavelength

Abstract

1,3-Nucleophilic addition reactions of thiols and amines with pyranosylnitrile oxides have been employed in the synthesis of *C*-glycosides. The nitrile oxides were generated by base-induced dehydrochlorination of the corresponding hydroximoyl chlorides **106** and **107**.

D-Glucose derived hydroximoyl chloride **107** was prepared in four steps from D-glucose and employed in collaborative work toward the synthesis of glucosinolate analogues. Reactions of alkyl and aryl thiols with D-xylose nitrile oxide **151** afforded a series of desulfoisoglucosinolates in 55-76% yields.

Reactions of alkyl and aryl amines with the D-xylose and D-glucose derived nitrile oxides **151** and **115** under basic conditions afforded the corresponding *Z*-amidoximes. For example, (Z)-*N*-benzyl-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)formamide oxime (**137**) was prepared from **107** and benzylamine in 88% yield.

The addition of amino acid derived nucleophiles was also investigated. Reaction of the D-xylose and D-glucose nitrile oxides **151** and **115** with L-cysteine derivative **147** under basic conditions afforded thiohydroximates **148** and **150** in high yield. Reaction of the D-xylose nitrile oxide **151** with glycine, L-leucine and L-phenylalanine esters initially afforded amidoximes **152**, **155** and **161**. Cyclisation of **152**, **155** and **161** to form 1,2,4-oxadiazin-6-ones occurred on exposure to silica or prolonged standing. Employing L-proline benzyl ester as the nucleophile led to the formation of predominantly oxadiazinone **163**. Attempts to synthesise pyranosyl-1,2,4-oxathiazin-6-ones were not successful.

6-Amino-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose hydrochloride was prepared from D-galactose in 4 steps, and reaction with D-xylose and D-glucose derived nitrile oxides **151** and **115** afforded (1→6) amidoxime linked pseudo-disaccharides **178** (81%) and **181** (75%). D-Xylose and D-glucose amines **182** and **183** were prepared from the parent aldoses in 5 steps. Reaction of these amines with

D-xylose and D-glucose nitrile oxides **151** and **115** yielded a series of (1→1) amidoxime linked pseudo-disaccharides (31-49% yields). Deprotection of **184** was achieved under basic conditions.

Reaction of *o*-phenylenediamine, *o*-aminothiophenol, *o*-aminophenol with D-glucose nitrile oxide **115** gave access to the corresponding benzimidazole **218**, benzothiazole **215** and benzoxazole **221** in high yields (71-85%). Similarly, reaction with D-xylose nitrile oxide **151** afforded the corresponding xylose benzazoles (68-90%). Deprotection of the pyranosyl benzazoles was achieved under basic conditions. 2-(2,3,5-Tri-*O*-benzoyl-β-D-ribopyranosyl)benzoxazole (**241**) and 2-(2,3,5-tri-*O*-benzoyl-β-D-ribopyranosyl) benzimidazole (**242**) were prepared similarly in 92 and 90% yields respectively. Deprotection of **241** under Zemplen conditions led to an anomeric mixture (β:α, 62:38) of products. Deprotection of **242** on the other hand, gave exclusively 2-β-D-Ribofuranosylbenzimidazole in 91% yield.

Reaction of 1,8-diaminonapthalene with D-xylose derived nitrile oxide **151** at room temperature (16 hours) afforded perimidine **259** in 60% yield. Perimidines derived from D-glucose, D-mannose and D-galactose were prepared similarly (55-65%). Attempts to repeat the reaction at elevated temperature lead to the formation of glycal products **258** and **261**. Glyceraldehyde derived hydroximoyl chloride **265** was prepared in 4 steps from D-mannitol and afforded perimidine **264** under the conditions described above in 61% yield.

Table of Contents

1. Introduction

1.1 Foreword

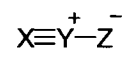
The work presented in this thesis investigates the application of nitrile oxide chemistry as part of a route to novel *C*-glycosides. The synthesis of *C*-glycosides is of great interest due to their importance in biological systems.[1,2] The strategy exploits the ability of nitrile oxides to undergo 1,3-addition reactions with a range of nucleophiles. This introductory section briefly reviews general aspects of nitrile oxide chemistry, the remaining sections cover applications of 1,3-nucleophilic reactions of nitrile oxides in the synthesis of thiohydramates (specifically glucosinolates and their analogues), amidoximes and 5- and 6-membered heterocycles.

1.2 Nitrile oxide chemistry overview

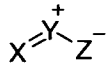
1.2.1 Nitrile Oxides: Background

Nitrile oxides are a member of the nitrilium betaine class of 1,3-dipoles. The existence of nitrile oxides has been known for over 200 years. Mercury and silver fulminate salts (formonitrile oxide salts) were described by Howard *ca* 1800[3] and benzonitrile oxide has been known since 1894.[4] The general nitrile oxide structure was first proposed by Ley in 1899,[5] but not finally elucidated until IR experiments were conducted in the mid 1960s.[6]

1,3-Dipoles are three-atom, 4-π electron systems, which have an overall neutral charge. They are divided into two classes.[7] The allyl class have three sp^2-hybridised atoms, which allow a single π-bond and have a bent structure. The propargyl-allenyl class possess an additional orthogonal π-bond between two sp-hybridised atoms and are therefore linear. Both structural classes are further subdivided according to the nature of the X, Y and Z atoms.

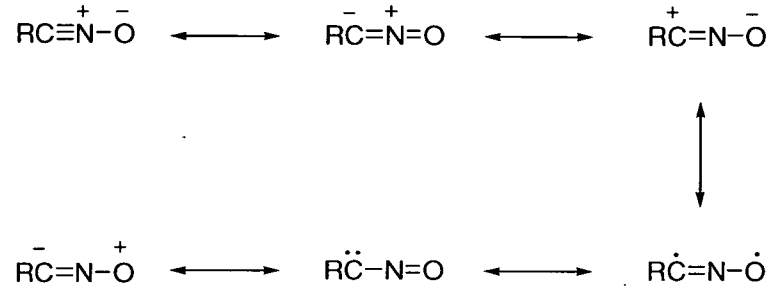


Propargyl-Allenyl Dipole



Allyl Dipole

1,3-Dipolar species such as nitrile oxides are normally represented as having a zwitterionic structure. They are more accurately represented by a resonance hybrid of octet, sextet, diradical and carbene forms (Scheme 1).[8,9] A great deal of work has been conducted in the field of nitrile oxide chemistry over the last 40 years; a number of texts that provide detailed discussions of nitrile oxide structure and reactivity are available.[8-12]

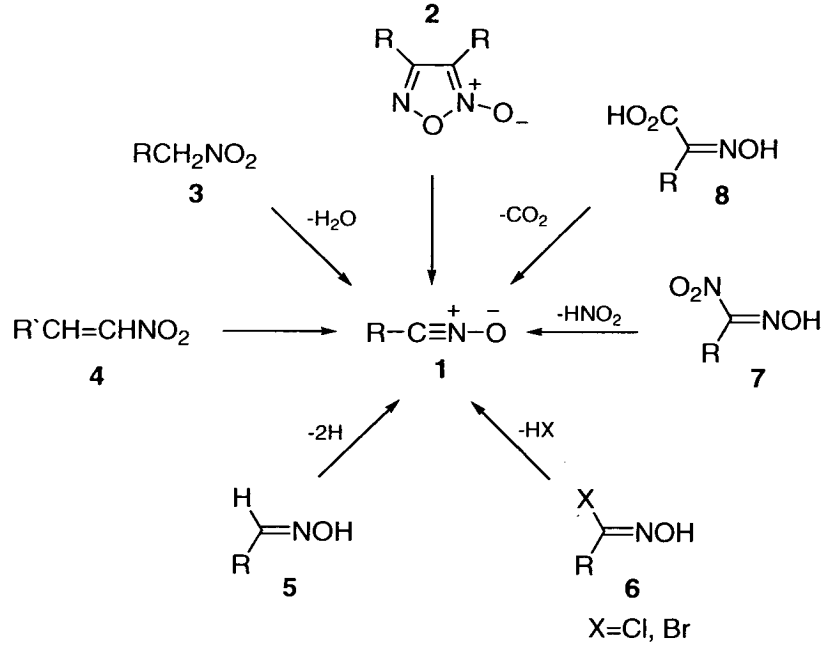


Scheme 1

1.2.2 Nitrile Oxides: Generation

Like many 1,3-dipoles, nitrile oxides **1** are very reactive and are consequently rarely isolated; generation normally takes place *in situ* in the presence of the co-reactant. The key problem in the isolation of nitrile oxides is their ability to dimerise to form 1,2,5-oxadiazole-2-oxides **2** [13,14] (furoxans) (Scheme 2). It should be noted, however, that those with bulky substituents do not readily dimerise and are therefore isolable. Over the years a number of generation strategies have been devised,[12,15] the precursors are most frequently aldoxime derivatives **5-8** [8,9,15] or nitro compounds **3** [8,9,16] (Scheme 2).

The thermal cycloreversion of furoxans **2** also results in the formation of two nitrile oxide molecules.[13] This reaction is not frequently employed in synthetic strategies since high temperatures are usually required (200°C). Furoxans with bulky substituents[18] and ring strained furoxans[19] are observed to undergo cycloreversion at slightly lower temperatures.



Scheme 2

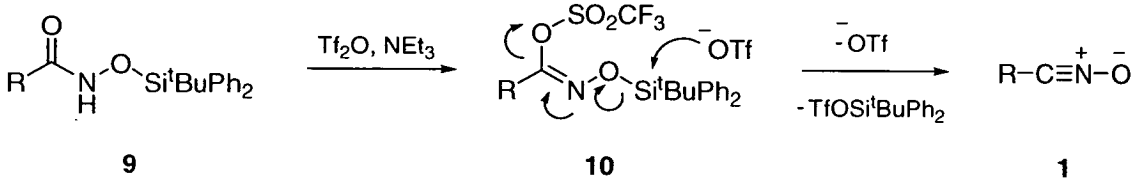
One of the most widely employed strategies is the Mukaiyama dehydration[16] of primary nitro compounds **3**. The reaction is base catalysed and usually employs an isocyanate as a dehydrating agent to generate the nitrile oxide. A variety of dehydrating agents have been employed; these include *t*-Boc anhydride,[17] acid chlorides,[20] phosphorous oxychloride,[21] *p*-toluenesulfonic acid[22] and DAST.[23] A recent publication has reported that Mukaiyama type dehydration takes place under microwave irradiation in the presence of 4-(4,6-dimethoxy[1,3,5]triazin-2-yl)-4-methylmorpholonium chloride (DMTMM).[24] Nitro substituted alkenes **4** are also known to afford nitrile oxides on treatment with organolithium compounds, Grignard reagents or titanium tetrachloride.[25,26]

A number of nitrile oxide generation strategies involve aldoximes **5** or their derivatives as precursors. The most widely used route proceeds *via* base[27-30] or thermally[31] induced dehydrohalogenation of hydroximoyl halides **6**. The hydroximoyl halide precurors are produced from the oxime by direct halogenation[32] or treatment with *N*-chlorosuccinimide[33] or *N*-bromosuccinimide.[34] Hydroximoyl chlorides have also been reported to yield the corresponding nitrile oxide on treatment with silver(I) acetate.[35] Routes based on other aldoxime derivatives have

been reported, these include nitrolic acids **7** [36,37] and α-hydroxyimino carboxylic acids **8**.[38]

Oxidation of aldoximes themselves can also yield the corresponding nitrile oxide. Employing alkaline sodium hypochlorite[39] or ^{t}BuOCl[40] as the oxidising agent affords the respective hydroximoyl halide *in situ*, which may then spontaneously dehydrohalogenate under the basic conditions. A number of other agents are known to afford nitrile oxides from aldoximes; these include chloramine-T[41] manganese dioxide,[42] lead tetraacetate[43] and iodosylbenzene.[44]

A completely novel strategy, that employs *O*-silylated hydroxamic acid precursors **9** has recently been reported by Carreira *et al.*[45] Treatment of the *O*-silylated hydroxamic acid with triflic anhydride leads to an activated intermediate **10** which may undergo de-silylation and C-O bond scission to afford the nitrile oxide **1** (Scheme 3).

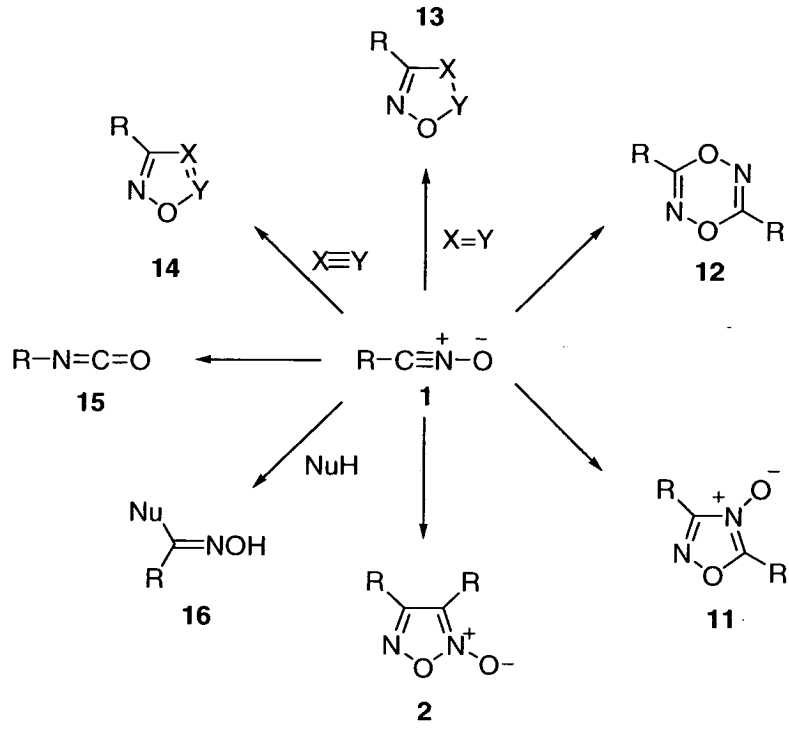


9 **10** **1**

Scheme 3

1.2.3 Nitrile Oxides: Reactions

The reactive character of nitrile oxides allows them to undergo a number of varied reactions (Scheme 4). Generation of nitrile oxides in the absence of any dipolarophile leads to the coupling of two molecules of nitrile oxide. The products of such reactions may be furoxans **2**,[13,14] 1,2,4-oxadiazole-4-oxides **11** or 1,4,2,5-dioxazidines **12**.[14] The furoxan products are well known and are potential synthetic targets.[46] Furoxan formation is also found as a side reaction in cycloadditions of nitrile oxides with less reactive dipolarophiles.[13] Nitrile oxide dimerisation is 2nd order in [RCNO] whereas cycloaddition with dipolarophiles is 1st order.[47] Dimerisation may therefore be limited by *in situ* generation of nitrile oxides, since the concentration of dipole relative to dipolarophile remains low.



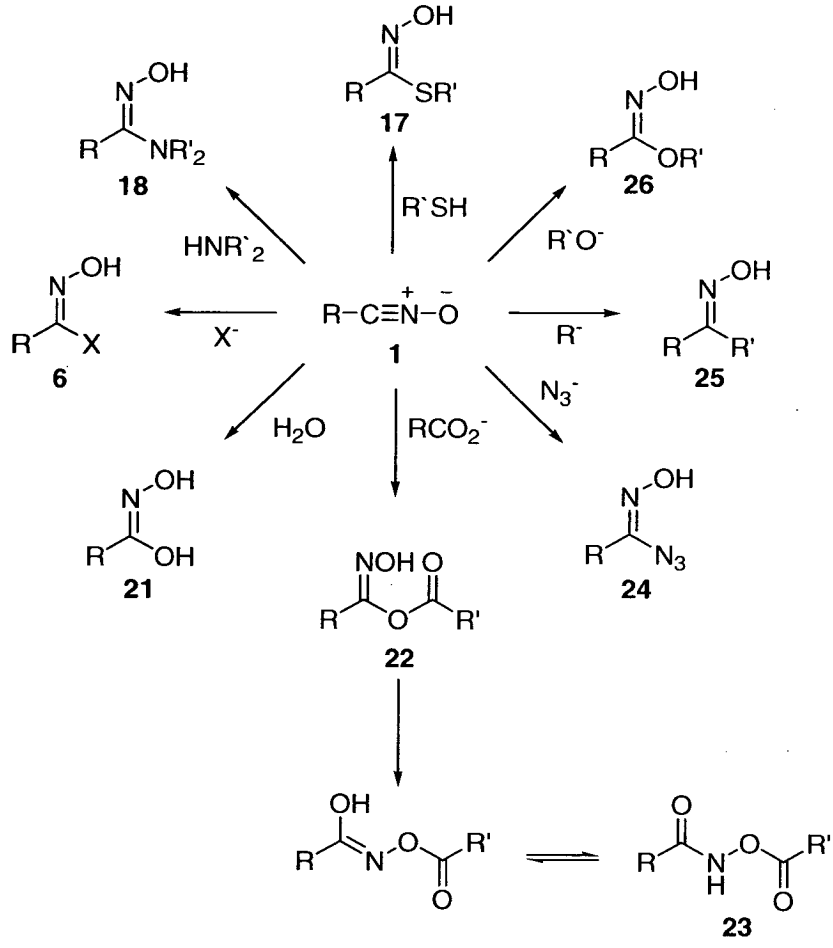
Scheme 4

The most frequently exploited reaction of nitrile oxides is the 1,3-dipolar cycloaddition with alkenes and alkynes (where X=Y=C).[8,9] The products of such reactions are isoxazolines **13** and isoxazoles **14** respectively; the former are frequently employed in natural product synthesis[48,49] and the latter are currently important subjects in the emerging field of "click" chemistry.[50,,51] 1,3-Dipolar cycloadditions with C=N, C=O, C=S and C≡N dipolarophiles are also well known.[8,9] Nitrile oxides also rearrange to isocyanates **15** at temperatures in excess of 110°C.[8,9]

1.2.4 1,3-Addition reactions

The 1,3-addition of nucleophiles to nitrile oxides to afford substituted oximes **16** is a less well-known, yet valuable reaction.[8,9] A large variety of nucleophiles undergo 1,3-additions to nitrile oxides (Scheme 5). Hydroximoyl chlorides are the most convenient nitrile oxide precursors in 1,3-additions since Mukaiyama type conditions do not tolerate nucleophiles[52] and the nitrile oxide concentration may be more readily

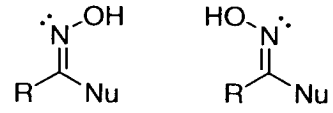
controlled to limit furoxan formation. Arguably the most studied adducts to date have been the thiohydroxamates **17**[53] and amidoximes **18**.[54,55]



Scheme 5

1.2.5 Mechanism of 1,3-addition reactions

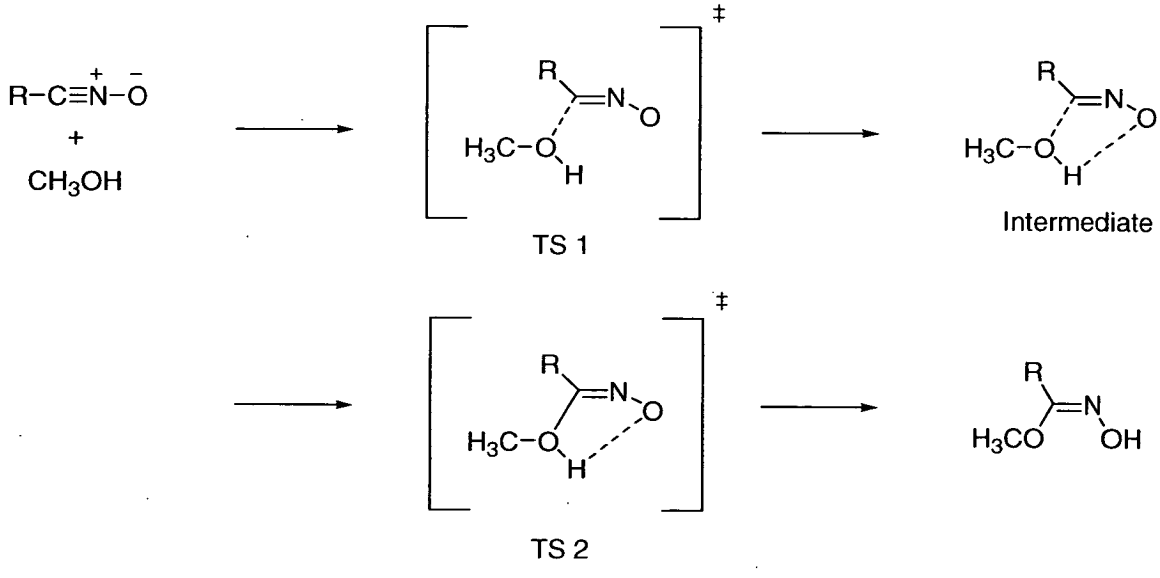
The reactivity of nitrile oxides with nucleophiles stems from the electrophilicity of the nitrilic carbon atom, indeed nitrile oxides may be considered as analogous to nitrilium cations.[56] An interesting facet of the 1,3-addition reactions is that they are stereospecific for the *Z*-oxime **19** (kinetic) product in all cases, despite the fact that many of the *E*-products **20** are thermodynamically favoured.[54,56-66] The formation of the *Z*-oxime is thought to be stereoelectronically favoured; the entering nucleophile and the nitrogen lone pair of electrons adopt a favourable antiperiplanar arrangement, which forces the OH group and nucleophile to be *cis* to each other.



Z-Isomer **19** *E*-Isomer **20**

The specificity of the reaction explains a number of observations that could previously not be fully rationalised. For example addition of carboxylates to nitrile oxides (Scheme 5) does not form the expected oxime derivative **22**, instead as soon as the initial adduct is formed it undergoes a 1,4-acyl migration to form a hydroxamate ester **23**.[57] A second key observation is that addition of azide ion to a nitrile oxide affords exclusively *Z*-azidoxime **24**;[57] if any *E*-isomer was formed it would be expected to cyclise to the corresponding *N*-hydroxytetrazole, and a mixture of products should therefore be observed.

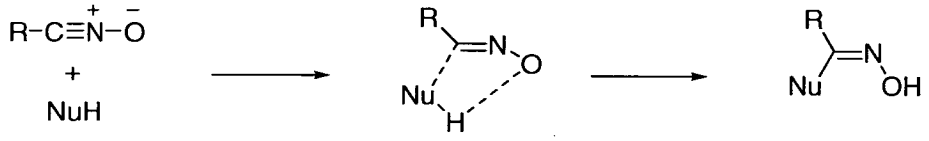
Although the stereochemical outcome of nucleophilic additions is not in doubt there has been some debate as to the mechanistic origins of this specificity. The debate has centred on whether the reaction proceeds in a concerted or a stepwise manner. Work conducted in the mid-1980s by Sharma and Aggarwal[64,65] concluded that the reactions of formonitrile oxide and acetonitrile oxide with methanol proceeded *via* a stepwise addition through two discrete transition states (TS1, TS2, Scheme 6). The findings of this study were based on semi-empirical MNDO calculations.



TS 1 Intermediate TS 2

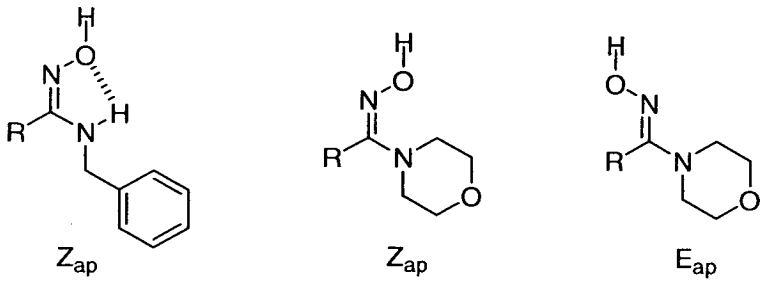
Scheme 6

Hegarty and co-workers[54] have proposed that the 1,3-addition reactions proceed *via* an asynchronous concerted process (Scheme 7). As the nucleophile approaches the nitrile oxide, the dipolar species undergoes heavy-atom rearrangement in a trans fashion, thus establishing the *Z* configuration. Proton transfer is then believed to occur without having to overcome any energy barrier. Hegarty`s conclusions are based on *ab initio* calculations concerning the additions of water, ammonia and methanol to formonitrile oxide. At present, Hegarty`s work appears to have been that accepted, and no subsequent report has so far challenged his findings.

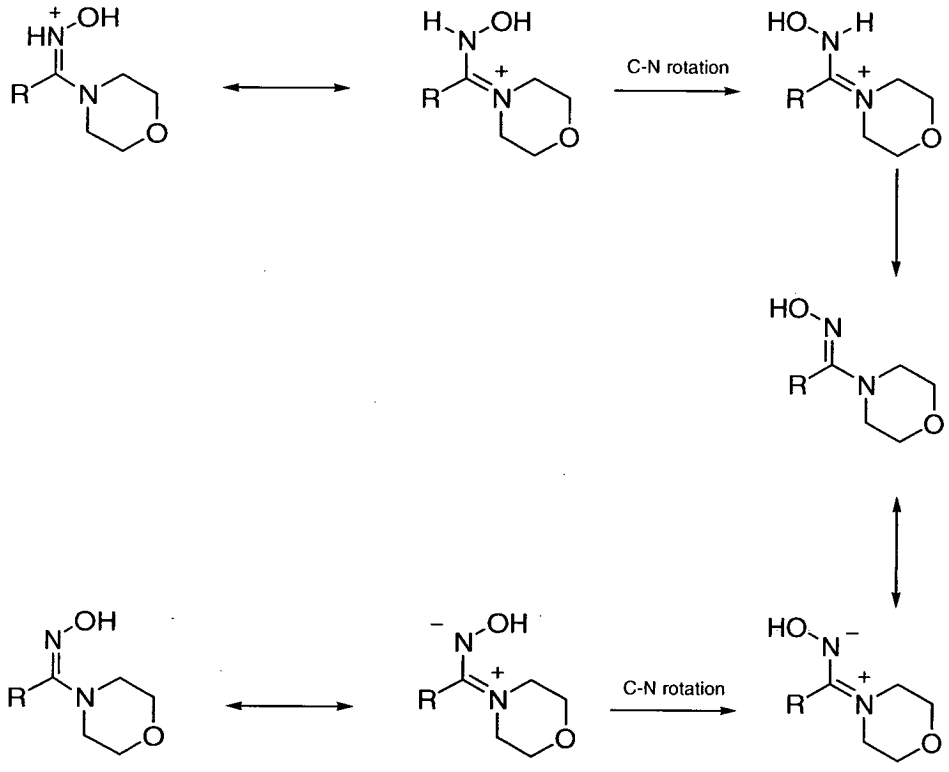


Scheme 7

It was stated above that additions of nucleophiles to nitrile oxides proceeded under kinetic control to afford exclusively *Z*-configured products. It is known, however, that amidoximes produced by such reactions can be obtained only as *E*-configured products.[59-63] *Z* versus *E* specificity has been found to be dependent on the nature of the amine nucleophile. These observations appear to contrast with the theory described previously, and it is therefore necessary to account for this apparent exception. Addition of ammonia or primary amines leads to only *Z*-adducts as isomerisation of such adducts is difficult due to hydrogen bond stabilisation by the "amido" type N-H bond and the oxime oxygen.[62] X-Ray crystallographic studies clearly demonstrate such bonding in non and mono-*N*-substituted amidoximes due to the adoption of a *Z*-antiperiplanar (Z_{ap}) or "*S*-trans" configuration, where the amidic N-H bond faces the oxime OH.[62,66,67] In contrast, *Z* configured *N,N*-di-substituted amidoximes cannot be stabilised as above, and over time isomerise to the thermodynamically favoured *E*-antiperiplanar (E_{ap}) oxime.



Z to *E* isomerisation is promoted by acid and indeed is $>10^5$ times faster[61] than in neutral conditions, the proposed isomerisation mechanisms are illustrated in Scheme 8.



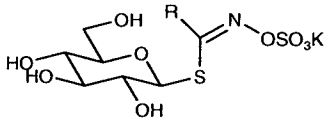
Scheme 8

1.3 Glucosinolates: A natural class of thiohydroximates

1.3.1 Glucosinolates: Background

Glucosinolates are a naturally occurring class of thiosaccharides that are isolated from all members of the botanical family *Cruciferae*.[68-71] A number of familiar brassica crops such as oilseed rape, cabbage, Brussels sprouts and numerous mustards derive their characteristic flavours from the breakdown products of glucosinolates. Glucosinolates are broken down by the enzyme myrosinase (EC 3.2.3.1) to produce a range of degradation products (refer to Scheme 9),[68-71] The most important of these are isothiocyanates (mustard oils). Glucosinolate-derived isothiocyanates possess a range of biological activities; these include toxic, anti-nutritional, goitrogenic, anti-carcinogenic, anti-fungal and anti-bacterial effects in a wide range of mammals (including humans).[68-71] Some glucosinolates are also of interest themselves due to the role they play in host-plant recognition and as egg-laying stimulants for brassica-adapted insects.[72,73]

All glucosinolates conform to the general structure **27**. The structure consists of three fragments: a β-D-glucopyranose unit, an *O*-sulfated thiohydroximate bridge and an aglycon side-chain (R) that varies according to biological origin (Table 1).[68-71]



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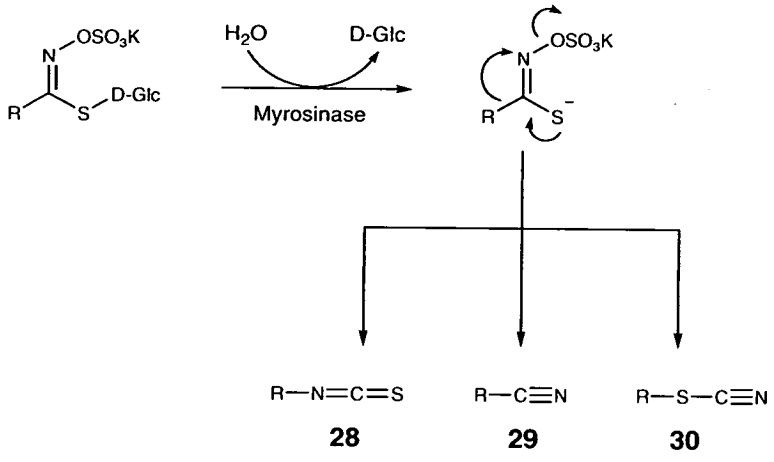
Glucosinolate	Occurrence	Side chain (R)	Biosynthesis from
Sinigrin	Black mustard seeds (*Brassica nigra*)	2-Propenyl-	Homomethionine
Sinalbin	White mustard seeds (*Sinapis alba*)	*p*-Hydroxybenzyl-	Tyrosine
Gluconapin	Rapeseed (*Brassica napus*)	3-Butenyl-	
Glucobrassicanapin	Rapeseed	4-Pentenyl	
Glucotropaeolin	Garden cress (*Lepidium sativum*)	Benzyl-	Phenylalanine
Gluconasturtiin	Watercress (*Nasturtium officinale*)	Phenylethyl-	Homophenylalanine

Table 1: Selected examples of naturally occurring glucosinolates

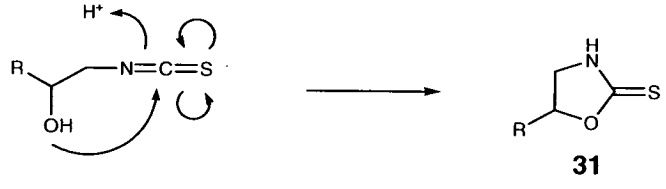
1.3.2 Glucosinolate Hydrolysis

Myrosinase is a naturally occurring β-thioglucosidase enzyme that is found in all known *Cruciferae*.[75-81] It is the only known enzyme that is capable of catalysing the hydrolysis and degradation of glucosinolates. Following hydrolysis, glucosinolates undergo spontaneous Lossen rearrangement to afford a number of degradation products (Scheme 9).[68-70] The major products are isothiocyanates (**28**), nitriles (**29**), thiocyanates (**30**) (Path A) and oxazolidine-2-thiones (**31**) (where the aglycon contains a hydroxy group [Path B]).[68,70]

Path A



Path B

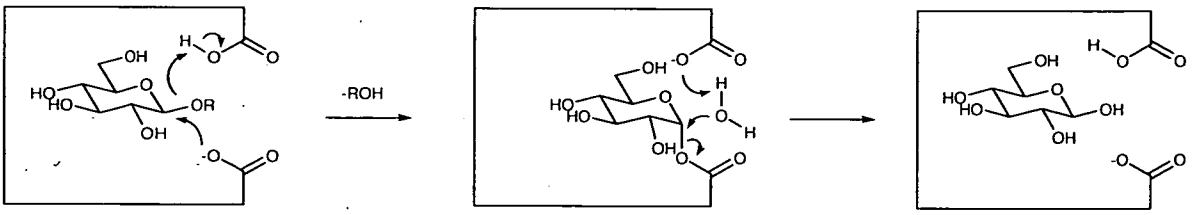


Scheme 9

In Nature the myrosinase and the glucosinolate substrate only come together if plant cells are physically broken by chewing, cutting or grating *etc.*[71] This response is believed to be a plant defence mechanism against herbivores. The breakdown products can be toxic and therefore pose problems to commercial farming.[73,74] Humans do not normally show toxic effects on eating glucosinolate-rich vegetables since cooking destroys myrosinase.

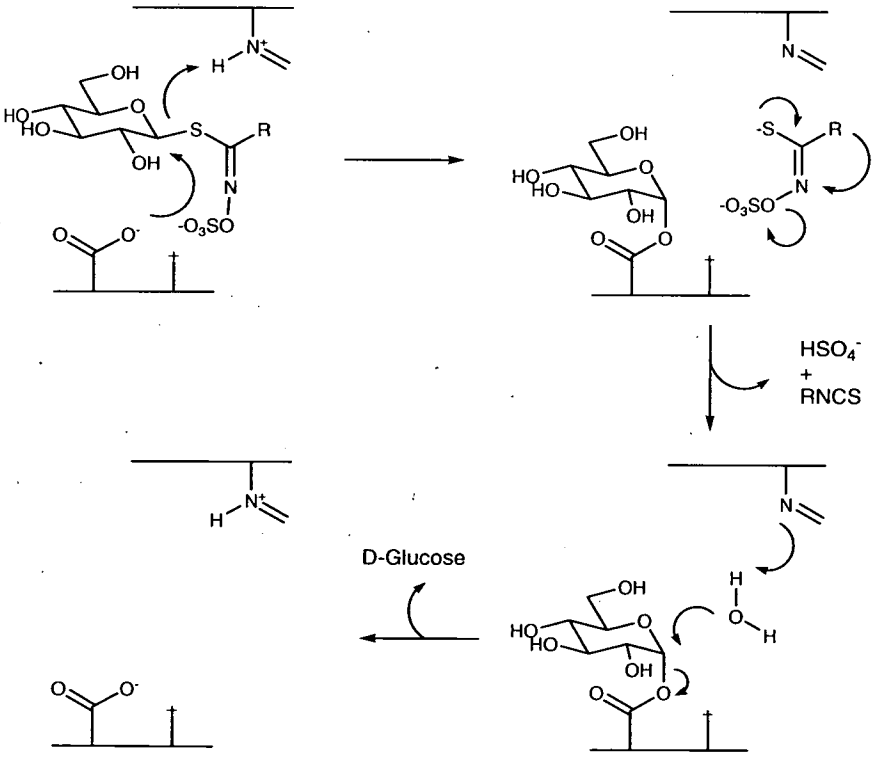
1.3.3 Myrosinase: Mechanism of Action

The mechanism of myrosinase catalysed glucosinolate hydrolysis has been subject to extensive study in recent years.[75-81] The hydrolysis process is believed to resemble the well-established mechanism of (retaining) family 1 *O*-glycosidases (Scheme 10),[76] however there are significant differences. A study by Botting *et al* [75] established that myrosinase is incapable of facilitating transglycosylation. This phenomenon was unexpected since analogous *O*-glycosidases have long been known to mediate transglycosylation.



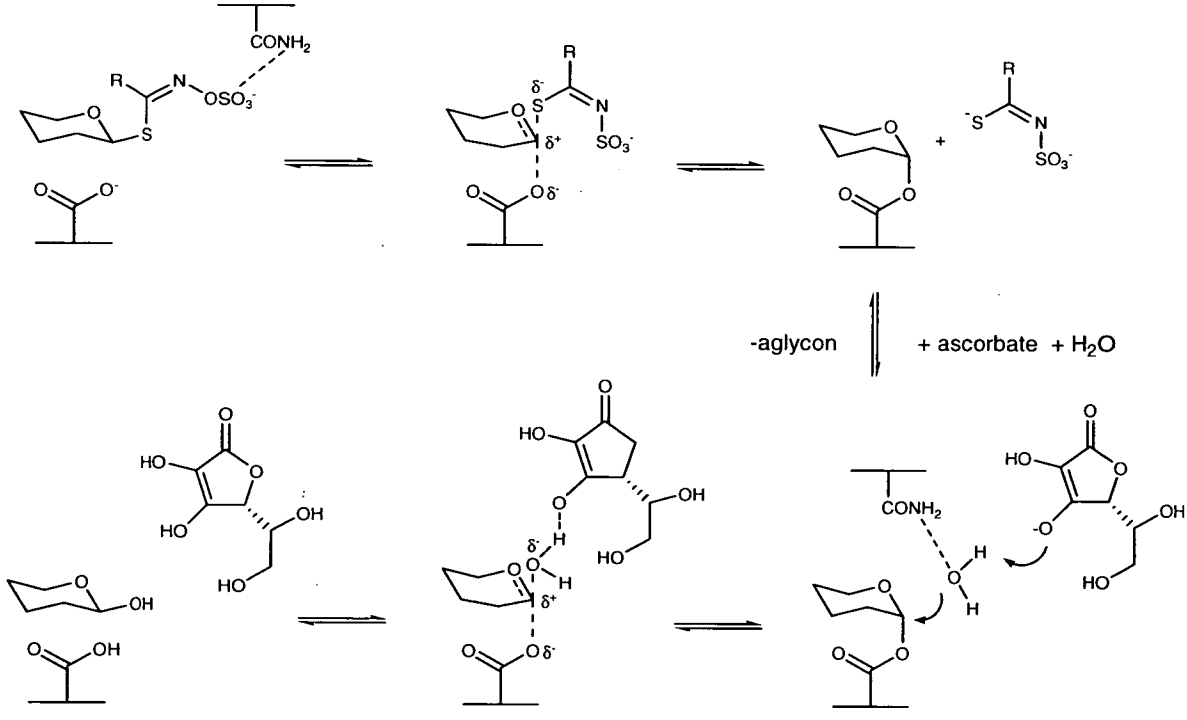
Scheme 10

The catalytic site in myrosinase differs from family 1 *O*-glycosidases by not having two glutamic acid residues, in myrosinase the upper residue is not present.[77] Work with 2-deoxyglucotropaeolin as a myrosinase inhibitor led to a 2-step/double-pocket active site hypothesis being initially put forward for the hydrolysis mechanism (Scheme 11).[78] The first step was believed to be cleavage of the *S*-glycosidic bond to form a covalent intermediate; a histidyl cation was supposed to play the role of the absent glutamic acid residue. The cleavage step was thought to precede an enzyme-independent Lossen rearrangement of the newly formed thiohydroximate-*O*-sulfonate to afford degradation products. The covalent intermediate was then believed to undergo histidine-catalysed hydrolysis.



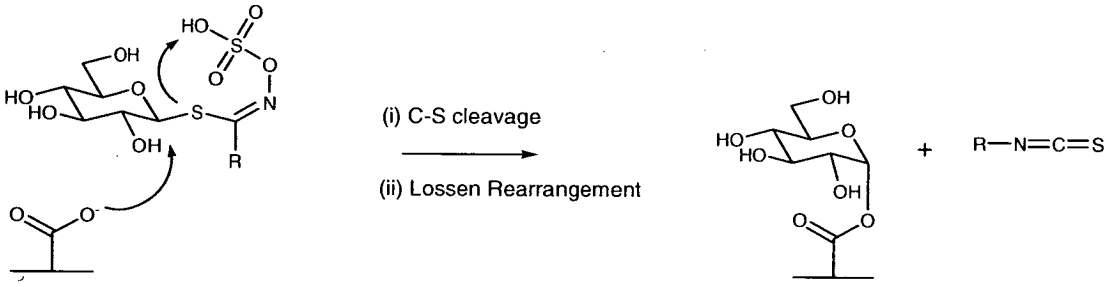
Scheme 11

Subsequent studies with 2-deoxy-2-fluoroglucotropaeolin allowed the resulting glucosyl-enzyme intermediate to be studied by X-ray crystallography.[79] The results of this work have led to a revised mechanism (Scheme 12).[79] The crystal structure showed that the myrosinase active site contains a glutamine residue in place of the glutamic acid found in family 1 *O*-glycosidases, this finding confirmed results obtained by Henrissat *et al.*[77] The glutamine residue assists substrate binding by forming a hydrogen bond to the sulfate group. Its most crucial role, however, is to position an incoming water molecule *via* hydrogen bonding for hydrolysis of the enzyme-substrate intermediate.[79] The water molecule requires a base to initiate hydrolysis, a task normally performed by a glutamate residue.[76] In this case L-ascorbate is found to enter the active site on loss of the aglycon and performs the glutamate role by abstracting a proton from the positioned water molecule, thus initiating the final hydrolysis step.[79] The presence of ascorbate as a co-factor leads to a significantly different hydrolysis process to those outlined in Schemes 10 and 11. The involvement of ascorbate is not entirely surprising since it has previously been reported that myrosinase activity is increased in the presence of ascorbic acid.[75,79]



Scheme 12

The function of the sulfate group is still a matter of debate. The previous studies concluded that the role of the anionic group was to facilitate enzyme-substrate binding. Withers *et al*[80] have proposed that the sulfate acts as a substrate bound acid catalyst, thus removing the need for enzymatic acid catalysis (Scheme 13). According to their proposal, the pendant sulfate would be protonated on entry to the active site, which would then enable spontaneous formation of the enzyme/substrate intermediate and subsequent hydrolysis. Withers *et al* also suggest that the anionic sulfate would lead to poor glucosinolate binding to an *O*-glycosidase type active site, and Nature therefore has removed one of the glutamic acid residues in myrosinase to allow improved substrate binding.[80]

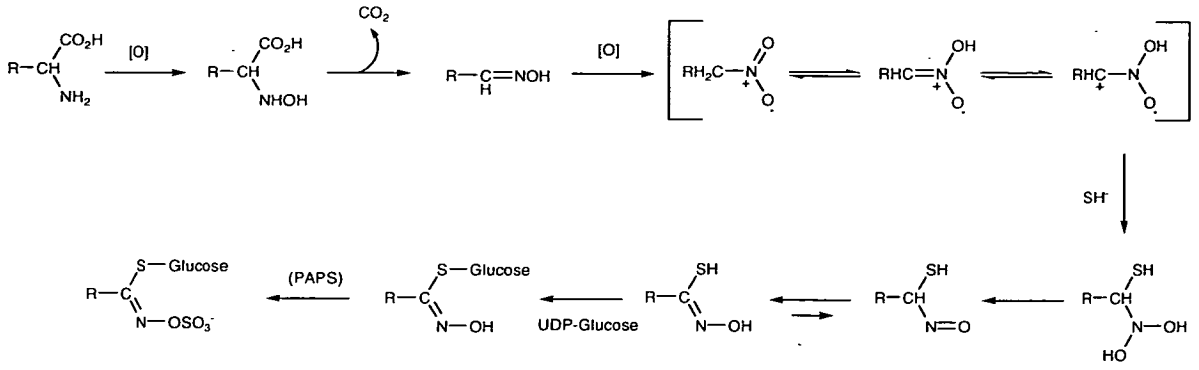


Scheme 13

1.3.4 Synthesis of Glucosinolates

1.3.4.1 Biosynthesis

The biosynthesis of glucosinolates from amino acids has been studied since the early 1970s, and the currently accepted sequence is outlined in Scheme 14.[68-70] The initial step involves P-450 mediated amine hydroxylation of an amino acid and subsequent decarboxylation to afford an aldoxime intermediate. The aldoxime then undergoes a poorly understood conversion to a transient thiohydroximic acid which is glycosylated with UDP-glucose; the resultant desulfoglucosinolate is finally sulfated by 3`-phospho-adenosine-5`-phosphosulfate (PAPS).

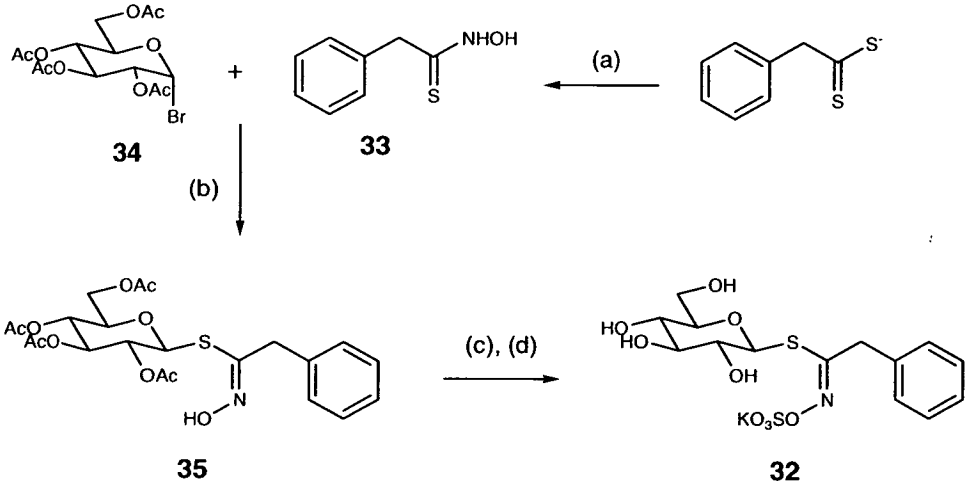


Scheme 14

1.3.4.2 Chemical Synthesis of Glucosinolates

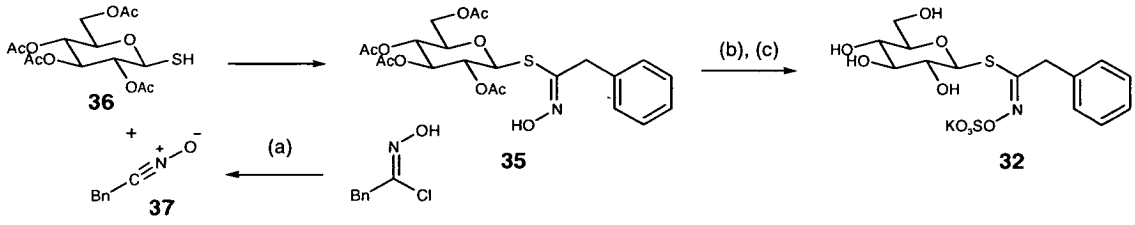
Over a hundred glucosinolates have been isolated from Nature and many are of interest on account of their biological activity.[68,69] To date, extraction procedures have been proven to be problematic and tedious in many cases; therefore synthetic approaches to natural[82-89] and unnatural[90-97] glucosinolates have been pursued.

Pioneering work in the field was conducted by Ettlinger and Lundeen[82] in the late 1950s. They first prepared glucotropaeolin (**32**) (benzyl glucosinolate) by coupling phenylacetothiohydroxamic acid (**33**) with acetylated bromoglucose (**34**) and sulfating the resultant adduct (**35**) (Scheme 15). The sulfated adduct was deacetylated in methanolic ammonia to yield glucotropaeolate **32**. This initial work accomplishes the key glucose-sulfur bond in a similar manner to the natural synthesis.



Scheme 15: (a) $NH_2OH.HCl$, H_2O (b) KOH, MeOH (c) SO_3-Pyridine, (d) NH_3/MeOH

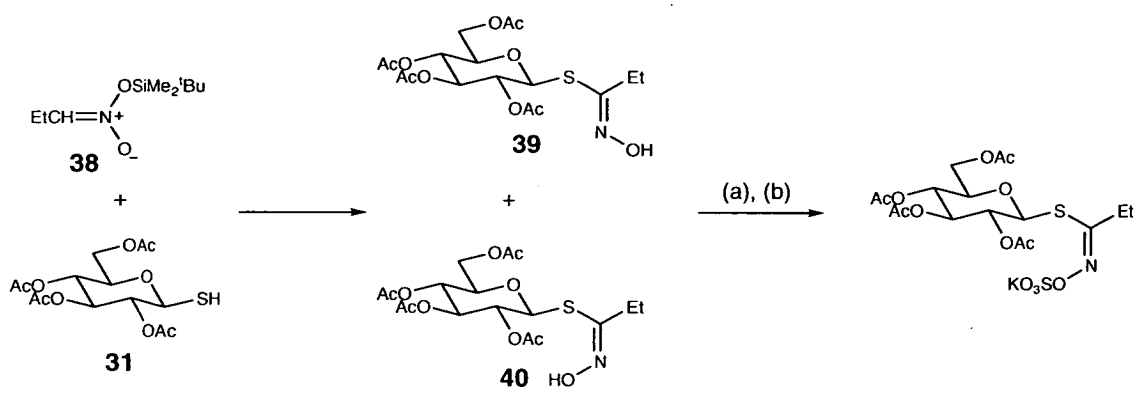
A nitrile oxide based strategy for glucotropaeolin synthesis was first accomplished by Benn[83,84] in the early 1960s (Scheme 16). The key step in the strategy is a 1,3-addition of 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthiol (**36**) to phenylacetonitrile oxide (**37**) to afford thiohydroximate product **35**. *O*-Sulfation of the adduct with sulfur trioxide/pyridine and subsequent deacetylation afforded the desired glucosinolate **32**.



Scheme 16:(a) NEt_3, Et_2O (b) SO_3-Pyridine, $KHCO_3$ (c) NH_3/MeOH

The nitrile oxide based strategy has proved versatile and has been the most widely exploited, indeed Benn,[83,84] Rollin,[85-89] Botting[72,73] and others[53] have employed and extended the nitrile oxide route in the synthesis of a large number of natural and unnatural glucosinolates. The reasons for this are 3-fold; the 1,3-addition of thiols to nitrile oxides is stereospecific for the naturally occurring *Z*-isomer,[68-70] the nitrile oxide precursors can be made by a number of methods, and the products may obtained up to a gram scale if required.[53]

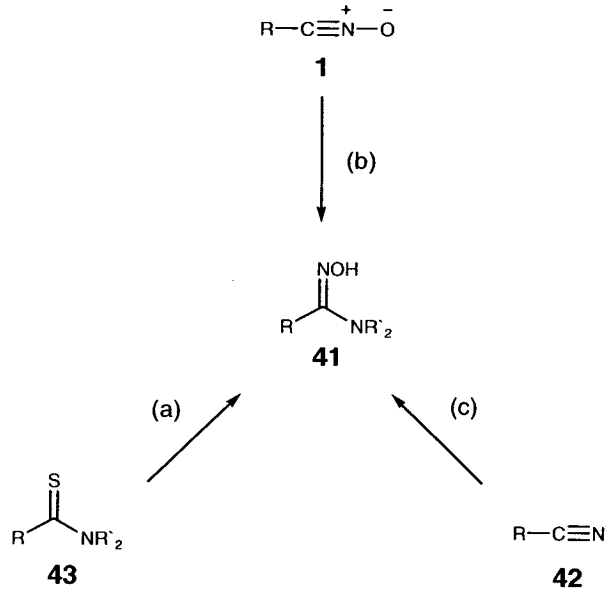
Benn[98] has also proposed a route to glucosinolates that does not require the generation of a nitrile oxide intermediate. A modified version of the Copenhaver reaction is employed (Scheme 17) to couple 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthiol (**31**) with trialkylsilyl nitronate **38** to yield the thiohydroximate product as a 2:1 mixture of *Z* (**39**) and *E* isomers (**40**). The *E*-isomer readily rearranges to the *Z*-isomer under thermal and photochemical conditions (*eg* exposure to visible light at room temperature). *O*-sulfation and deacetylation is achieved by using standard conditions. The reported advantage of this route is the ability to access unnatural *E*-glucosinolates.



Scheme 17: (a) SO_3-Pyridine, $KHCO_3$ (b) NH_3/MeOH

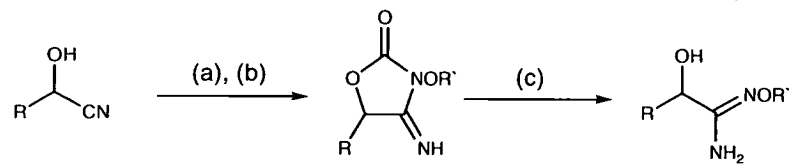
1.4 Amidoximes

Amidoximes constitute a large class of oxime derivatives[55] that adopt the general structure **41** (Scheme 18). Lossen and Schifferdecker first reported the synthesis of an amidoxime in 1873[99] by addition of hydroxylamine to hydrogen cyanide. There are three common modern synthetic routes to amidoximes (Scheme 18);[55] they involve nucleophilic attack by hydroxylamines on nitriles (**43**) and thioamides (**42**), and 1,3-addition of amines to nitrile oxides (**1**). The nitrile oxide based route is particularly amenable to the synthesis of *N*-mono and *N,N*-disubstituted amidoximes. Interest in amidoximes stems from a number of areas; work has primarily focused on medicinal applications, use as ligands for metals and heterocyclic synthesis.



Scheme 18: (a) NH_2OH (b) $NHR`_2$ (c) $NR`_2OH$

The most recent development in amidoxime synthesis is ready access to α-hydroxy variants (Scheme 19).[100] Addition of hydroxylamines and 1,1`-carbonyl-diimidazole (CDI) to cyanohydrins (**44**) results in the formation of 3-hydrox-4-imino-oxazolidin-2-one (**45**) intermediates, which afford the target amidoximes (**46**) on treatment with sodium methoxide.

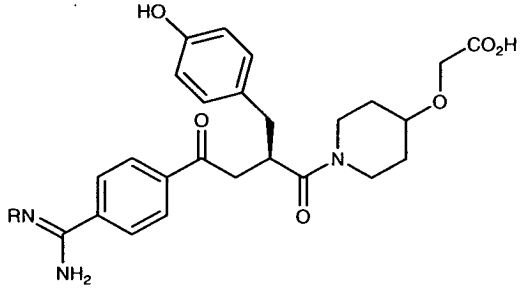


44 45 46

Scheme 19: (a) H_2NOR' (b) CDI (c) NaOMe

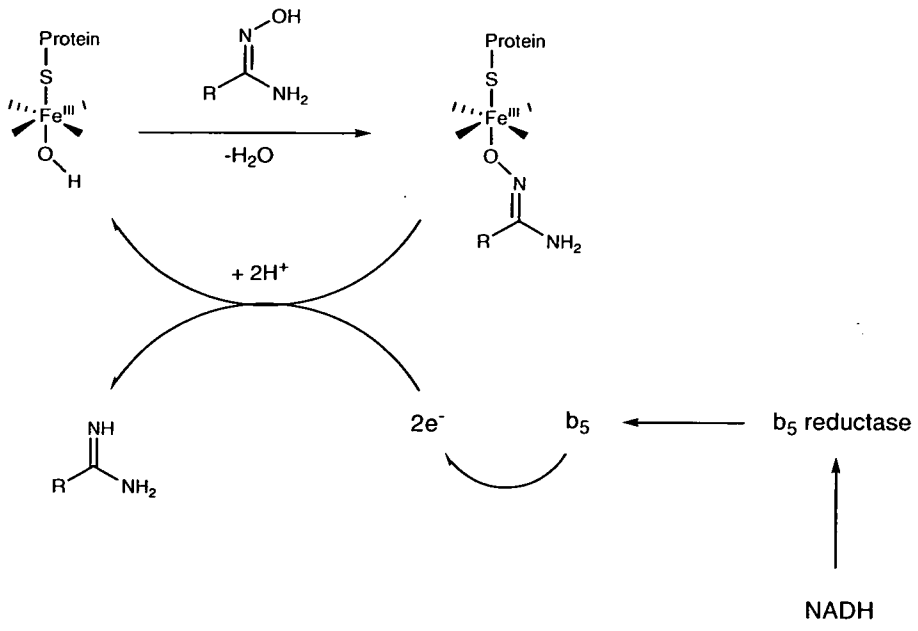
1.4.1 Amidoximes: Bioactivity

Compounds containing the amidine functional group possess a range of biological activity including inhibition of serine protease and nitric oxide synthase.[101-103] Amidine based drugs such as Lamifiban (**47**)[104] serve as anti-thrombotic agents in the treatment of coronary heart disease.



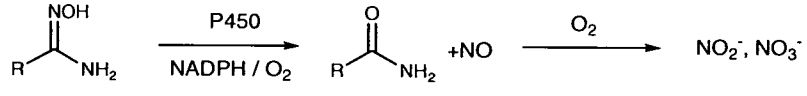
R = H = **47**, R=OH

The amidine group is strongly basic and is therefore protonated under physiological conditions.[105] The protonated species is not readily absorbed from the gastrointestinal tract and as a result the bioactivity of amidine therapeutics may be greatly reduced. Fortunately amidoximes are reduced to amidines *in vivo,*[105]and amidoxime analogues of amidine containing agents have therefore been examined as pro-drugs.[104] The mechanism of *in vivo* amidoxime reduction is the subject of continuing research, the currently proposed mechanism of reduction by b_5, b_5 reductase and a P450 isoenzyme is presented in Scheme 20.[105]



Scheme 20

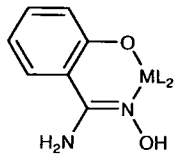
Amidoximes are known to undergo nitric oxide synthase and P-450 dependent oxidative cleavage of the C=N(OH) bond[106-111] (Scheme 21). The resultant product is nitric oxide, therefore interest in amidoximes as potential nitric oxide donors has recently arisen. This research is driven by the major role that NO plays in the cardiovascular, immune and central and peripheral nervous systems.



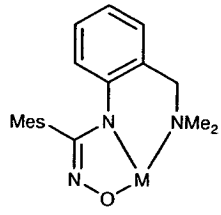
Scheme 21

1.4.2 Amidoximes: Metal ligation

Amidoximes exhibit similar behaviour to oximes in terms of their ability to bind to a number of metal species. Metal binding normally takes place via the oxime nitrogen as is typical of most oximes, although in certain cases binding may take place through the oxime oxygen.[112,113] In general the amido nitrogen is not involved in metal binding, especially if there are other co-ordinating sites available on the ligand (**48**). A recent publication by Barybin *et al*,[112] however, has demonstrated a chelating oximato ligand (**49**) that binds to Cr(III) and Al(III) through the oxime oxygen and the amido nitrogen.

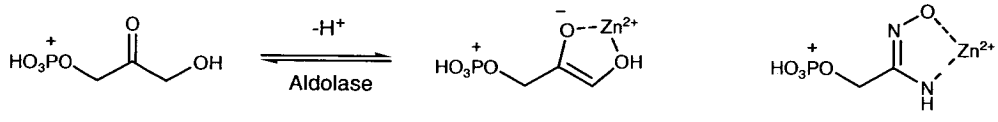


48



49

Amidoximes are known to form complexes with Fe(III), Cr(III), Hg(II), Pd(II), Os(II), Cu(II)[113] and polyoxometalate ions[114,115] (such as $\{Mo_4O_{10}(OMe)2\}^{2+}$), and they are primarily employed in the chelation of heavy metal ions for analytical purposes.[55,113] Amidoximes have found wide application in the extraction of uranium (and other heavy metal ions) from seawater, indeed complexes with dioxouranium (UO_2) are well known.[113] The ability of amidoximes to chelate metal ions has recently been exploited in the design of class II fructose-1,6-bisphospate aldolase inhibitors (Scheme 22),[116] such inhibitors are of interest in the design of antibiotics. Amidoxime **50** was prepared in an attempt to mimic of enolate transition state **51**.



51 50

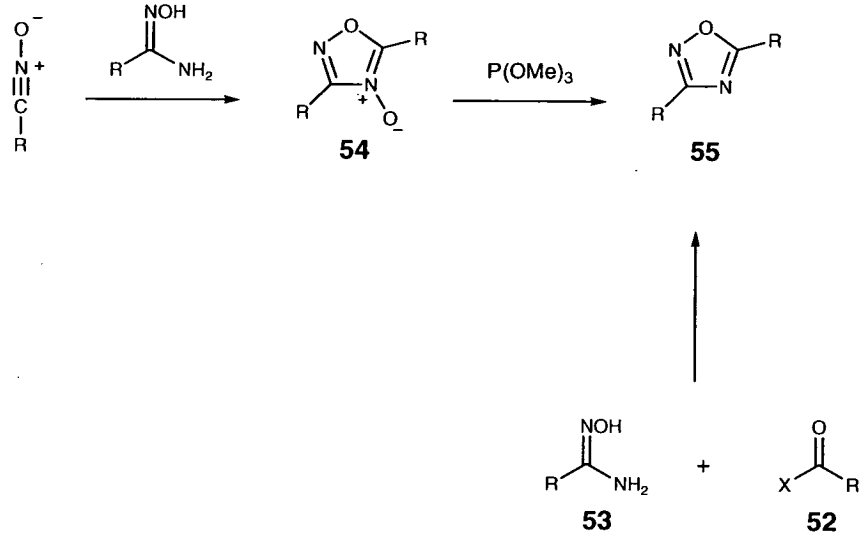
Scheme 22

1.4.3 Amidoximes: Synthesis of Heterocycles

Amidoximes have found applications in heterocycle synthesis for a number of years.[117-124] Much of this work has been devoted to the preparation of 1,2,4-oxadiazoles[117-120] (**55**); these are particularly useful compounds since they function as bioisosteres for esters and amides. Oxadiazoles are more stable than esters and amides and are therefore ideal for use in pharmaceuticals.[117-119]

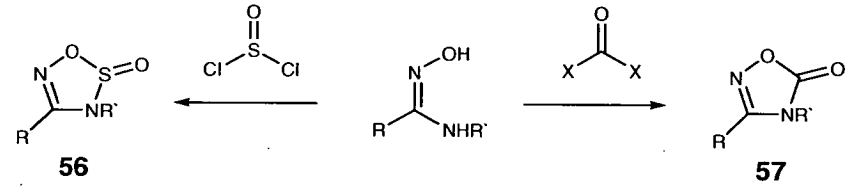
There are two routes to oxadiazoles from amidoximes (Scheme 23). The first involves the condensation of an activated carboxylic acid derivatives (**52**) with an amidoxime (**53**), followed by cyclisation.[117-119] The second route involves 1,3-dipolar cycloaddition of a nitrile oxide (**1**) onto the C=N bond of an amidoxime to afford a 1,2,4-oxadiazole-4-oxide (**54**).[120] Deoxygenation of the product with trimethyl

phosphite yields the desired 1,2,4-oxadiazole (**55**). The second route is not regularly employed since the product(s) are obtained in only moderate yields as a result of extensive by-product formation.



Scheme 23: X = Cl, Br, OR, OAc, OH

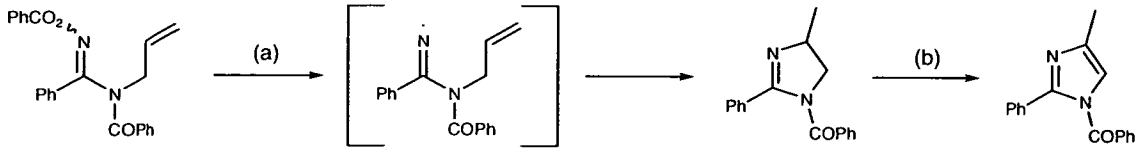
Treatment of unsubstituted and mono-substituted amidoximes with thionyl chloride allows construction of 1,2,3,5-oxathiadiazoles (**56**),[121] similarly reaction with phosgene derivatives affords 1,2,4-oxadiazol-5-ones (**57**) (Scheme 24).[122] 1,2,3,5-Oxathiadiazoles have been examined as antihyperglycemic agents for the treatment of type 2 diabetes.[123] 1,2,3,5-Oxathiadiazoles and 1,2,4-oxadiazol-5-ones have been shown to behave as tetrazole isosteres and are therefore of potential interest in pharmacetical design.[124]



Scheme 24

The products covered so far retain the R`N-C=N-OR unit from the parent amidoxime. Recent work has been directed toward amidoximes as sources of amidine (R`NH-C=NR) containing heterocycles. Zard *et al*[125] have recently reported a conversion amidoximes to imidazolines and/or imidazoles (Scheme 25). The

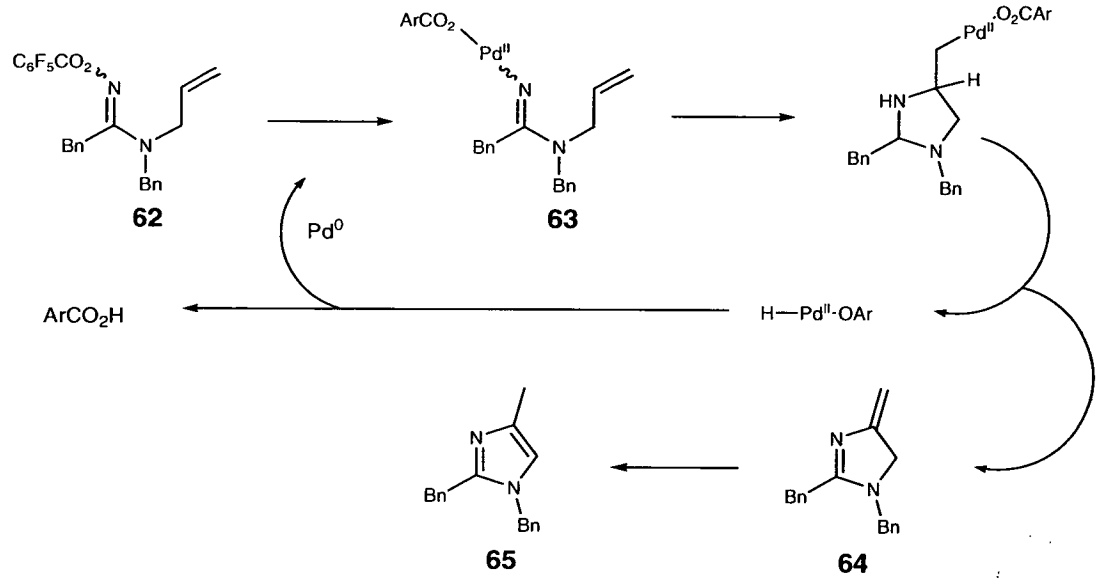
method involves radical cyclisation of *N*-allyl-*O*-benzoylamidoximes (**58**). The key intermediate is believed to be an amidinyl species (**59**) and the cyclic product is an imidazoline (**60**) that can be converted to the corresponding imidazole (**61**) following an oxidation step.



58 **59** **60** **61**

Scheme 25: (a) Bu_3SnH, AIBN, Δ (b) Pd/C, Δ

A similar conversion has been achieved by Abell and co-workers[126] *via* a palladium mediated amino Heck reaction (Scheme 26). *N*-Allyl-*O*-perfluorobenzoylamidoximes (**62**) undergo oxidative addition to Pd(0) to form an alkylideneaminopalladium intermediate (**63**). β-Hydride elimination initially leads to dihydroimidazole species (**64**) which then isomerises to the desired imidazole (**65**).

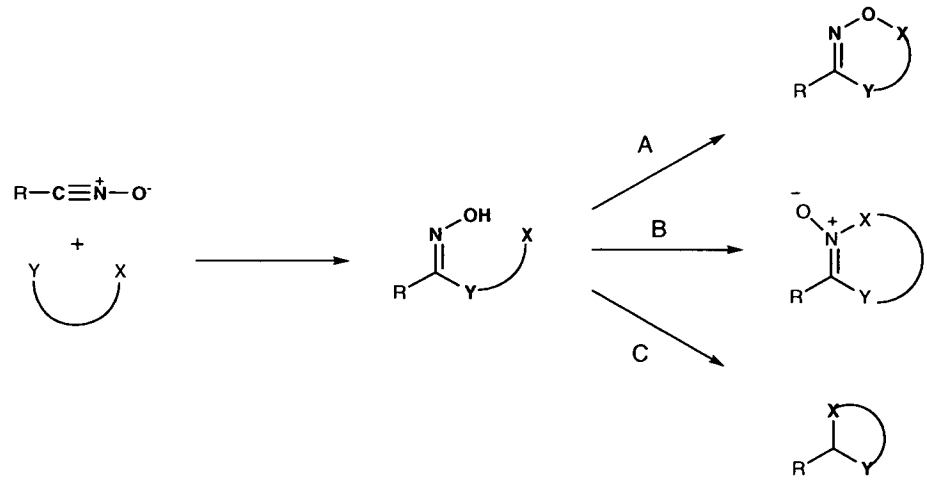


Scheme 26

1.5 1,3-Nucleophilic Addition Reactions to Nitrile Oxides in Heterocyclic Synthesis

As was seen in Section 1.2.3, nitrile oxides are frequently and effectively employed in the synthesis of heterocycles *via* 1,3-dipolar cycloaddition reactions. Nucleophilc addition reactions with nitrile oxides may also result in heterocyclic products *via* a

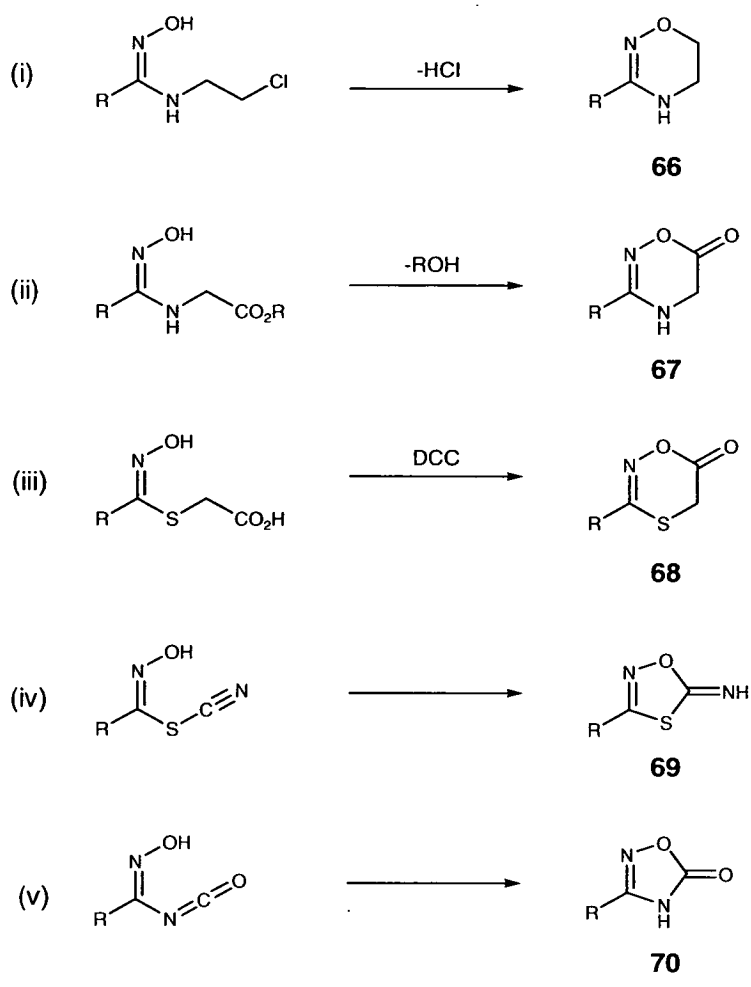
variety of addition-cyclisation processes.[127] A brief overview of the general approaches is presented here (Scheme 27).



Scheme 27

1.5.1 Addition-Cyclisation A: Nucleophilic attack by the oxime hydroxyl

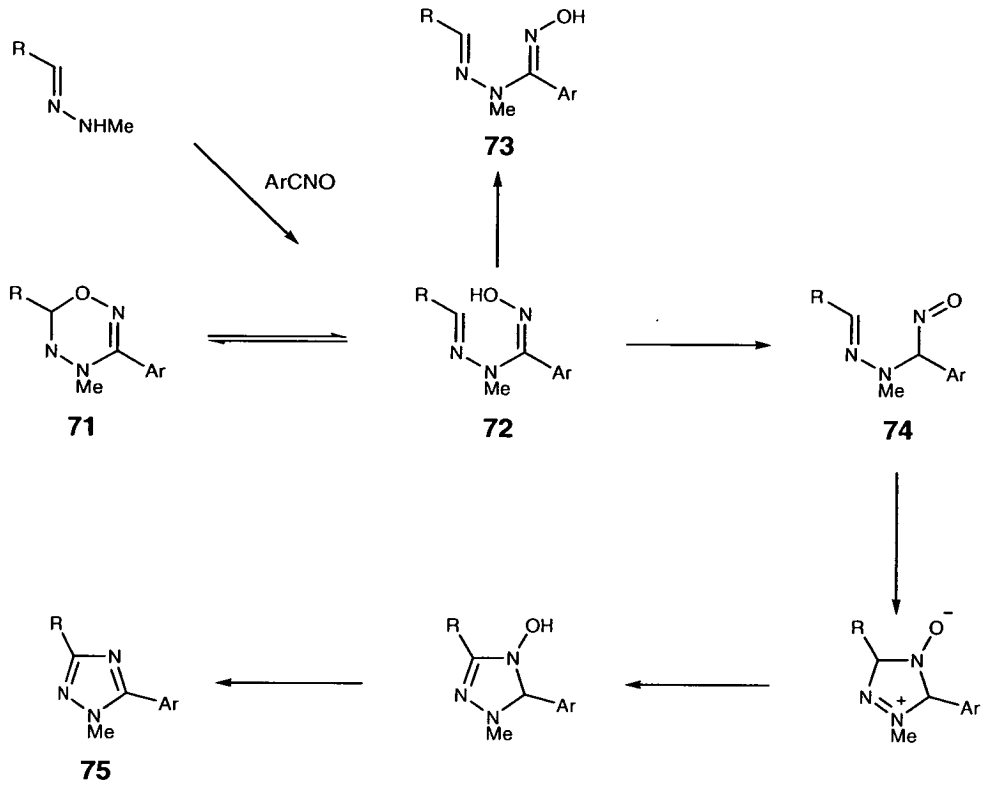
In pathway A (Scheme 27) group X represents an electrophilic carbon centre. Addition of a nucleophile bearing an alkyl halide, followed by cyclisation step affords an 1,2,4-oxadiazine (**66**) [as does addition of an aziridine, Scheme 28 (i)].[128] Similarly, addition of amine and thiol nucleophiles possessing a pendant ester group afford an adduct which may undergo cyclisation to form 1,2,4-oxadiazine-6-ones (**67**)[129] and 1,4,2-oxathiazin-6-one products (**68**)[130,131] respectively [Scheme 28 (ii) and (iii)]. Hussein and co-workers[132] have reported that addition of isocyanate and thiocyanate[133] ions led to formation of 1,2,4-oxadiazol-5-ones (**69**) and 5-imino-1,4,2-oxathiazolines (**70**) [Scheme 28 (iv) and (v)]. There is dispute as to whether isocyanate addition proceeds *via* a 1,3-nucleophilic addition or 1,3-dipolar cycloaddition.[127]



Scheme 28

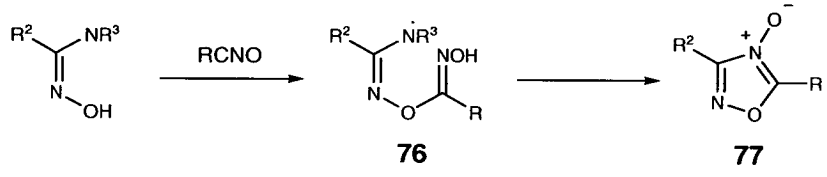
1.5.2 Addition-Cyclisation B: Nucleophilic attack by the oxime nitrogen atom

In pathway B (Scheme 27) group X still represents an electrophilic centre, but the cyclisation occurs via the oxime nitrogen atom; two representative examples are illustrated here. Addition of aryl *N*-methylhydrazones to nitrile oxides[134] initially forms the expected *Z*-oxime **71**, however subsequent reactions are possible, including reversible cyclisation to **72**, isomerisation to *E*-adduct **73** or nitroso compound **74** (Scheme 29). In the presence of silica, cyclisation to triazole (**75**) products occurs.



Scheme 29

Mono-substituted amidoximes have been found to add to nitrile oxides to afford adduct **76**, which on heating may lead to the formation of 1,2,4-oxadiazole-4-oxides (**77**) (Scheme 30).[135]

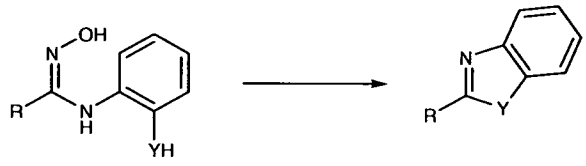


Scheme 30

1.5.3 Addition-Cyclisation C: post 1,3-addition nucleophilic attack on the oxime group

Pathway C (Scheme 27) differs from those above since X in this case is nucleophilic, and addition of ambident nucleophiles leads to the formation of oxime adducts (**78**) which undero attack by the remaining nucleophilic centre with the extrusion of hydroxylamine.[127] *o*-Substituted anilines are known to afford the corresponding

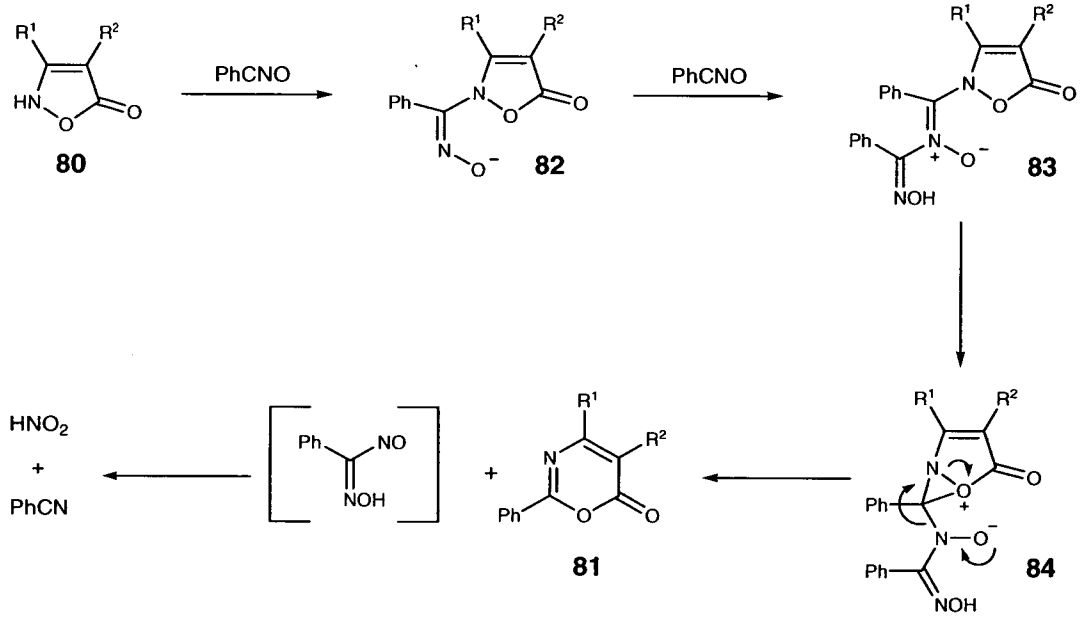
benzazole products (**79**) *via* the described nucleophilic attack/extrusion process (Scheme 31).[136]



78 **79**

Scheme 31: Y = NH, S, O

A related example has been reported in the ring expansion of isoxazol-5-ones (**80**) to 1,3-oxazin-6-ones (**81**),[137] however the extruded species in this case is not hydroxylamine (Scheme 32). Nucleophilic attack on benzonitrile oxide leads to adduct **82**, which may itself react with a further equivalent of nitrile oxide to form intermediate **83**. The isoxazolo oxygen atom is belived to add to the C=N bond of **83** to form shortlived **84**, collapse of which leads to formation of the product (**81**), benzonitrile and nitrous acid.

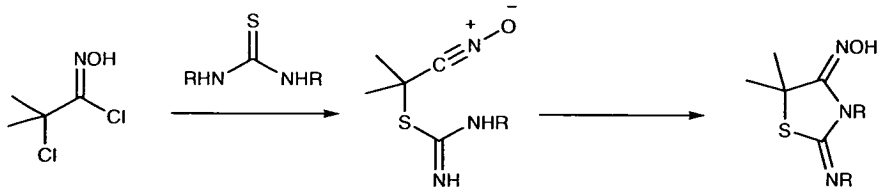


Scheme 32

1.5.4 Addition-Cyclisation D: 1,3 additions with functionalised nitrile oxides

Examples have been reported of nucleophilic addition of ambident nucleophiles to nitrile oxide precursors containing good leaving groups.[127] Cyclisation may occur on generation of nitrile oxide and subsequent intra-molecular addition. The example

illustrated in Scheme 33 involves addition of thioureas to chloro-substituted hydroximoyl chloride **85**, and cyclisation to the 5-membered product **86**.[63]



85 **86**

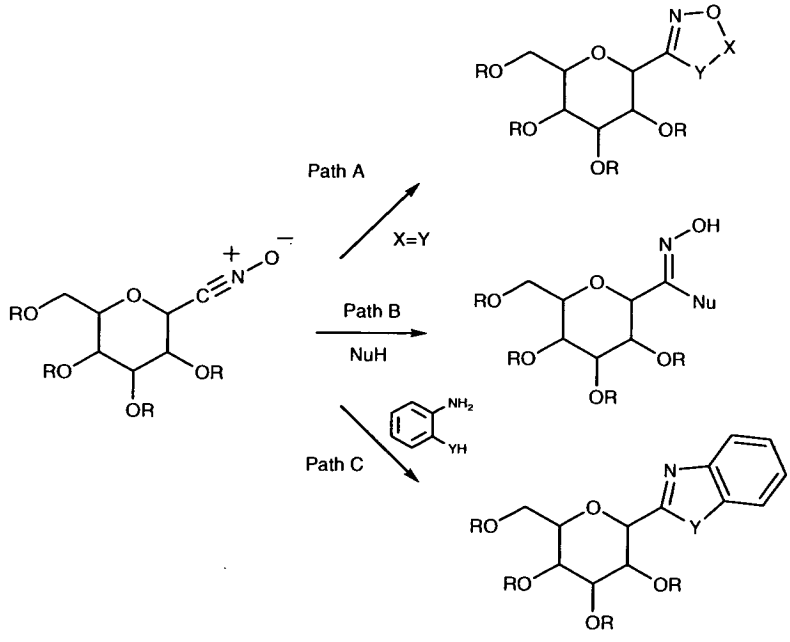
Scheme 33

2. Results and Discussion

The main objective of the present work has been to explore the synthetic potential of the 1,3-nucleophilic addition reactions of pyranosyl nitrile oxides. Additions of thiols have been employed in the synthesis and evaluation of new myrosinase inhibitors. Addition of amines has been applied in the synthesis of novel carbohydrate derived amidoximes, benzazoles and perimidines.

2.1 Synthetic Strategy

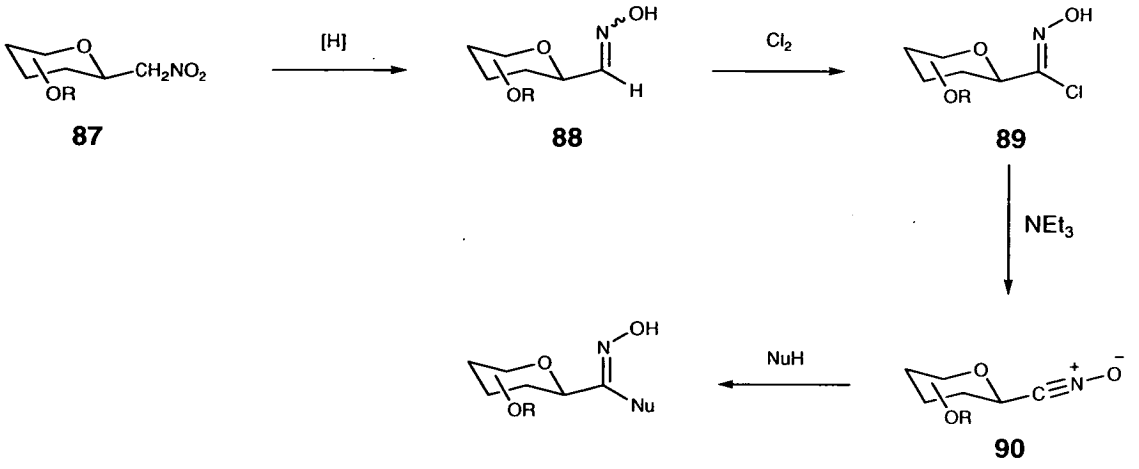
The 1,3-dipolar cycloaddition reactions of pyranosyl nitrile oxides have previously been employed in the synthesis of heterocyclic *C*-glycosides,[138,139] including pyranosyl isoxazolines (Scheme 34, path A). It was anticipated that pyranosyl nitrile oxides would also be able to undergo 1,3-nucleophilic addition reactions, and hence provide routes to novel glycosyl oximes (path B) and glycosyl benzazoles (path C).



Scheme 34

Several synthetically useful routes are available for the generation of nitrile oxides (Section 1.2.2). Reliable and efficient routes to pyranosyl nitrile oxides have been developed within the group in recent years (Scheme 35).[52,140] Pyranosylnitromethanes (**87**) are convenient sources of the corresponding aldoximes

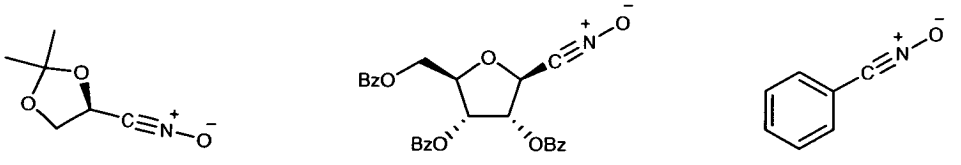
(**88**),[52] these in turn may be efficiently transformed into hydroximoyl chlorides (**89**)[140] and the hydroximoyl chloride may be dehydrohalogenated in the presence of base to generate the required nitrile oxide (**90**). The final stage is addition of the chosen nucleophile to the freshly generated nitrile oxide.[66]



87 **88** **89** **90**

Scheme 35

It was hoped to demonstrate the utility of the methodology by extending it to other carbohydrate scaffolds, many other sugar derived nitrile oxides are known.[138] It was decided that D-glyceraldehyde derived nitrile oxide **91** and D-ribose derived nitrile oxide **92** would be suitable for such studies, since preparations for both had already been described.[141,142] It was also necessary to employ an easily synthesised nitrile oxide for pilot reactions. Benzonitrile oxide **93** was chosen on account of its ease of access from commercially available starting materials.[143]

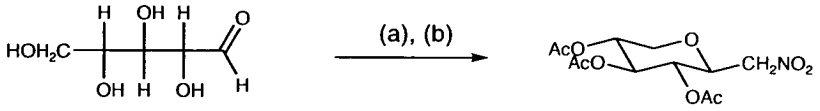


91 **92** **93**

2.2 Synthesis of Pyranosylnitrile Oxide Precursors

2.2.1 Synthesis of Pyranosylnitromethanes

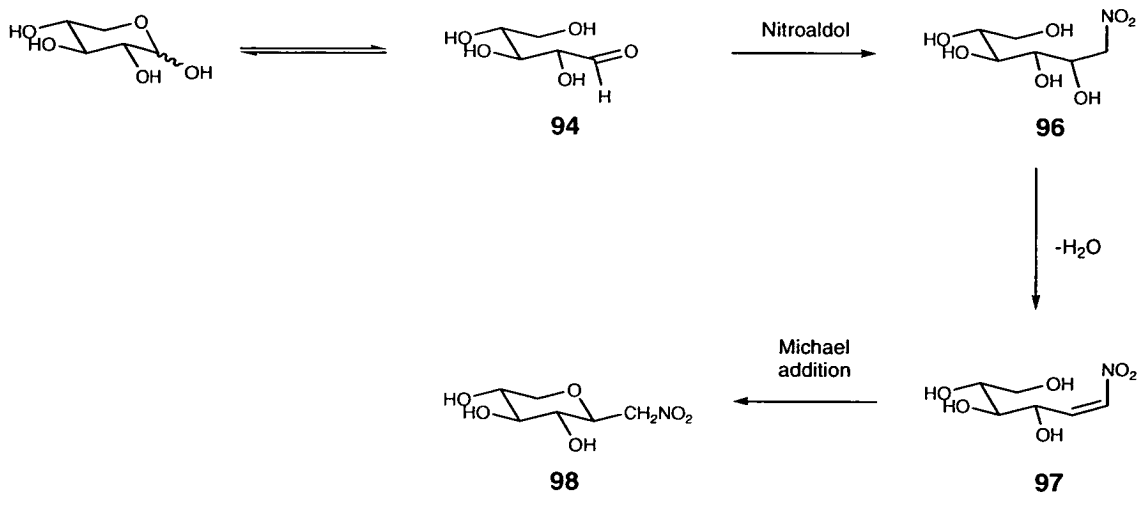
2.2.1.1 3,4,5-Tri-O-acetyl-β-D-xylopyranosylnitromethane (95)



94 **95**

Scheme 36: (a) H_3CNO_2, NaOMe/MeOH (b) Ac_2O, TfOH

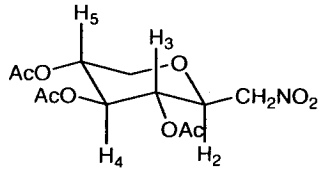
3,4,5-Tri-O-acetyl-β-D-xylopyranosylnitromethane (**95**) was prepared *via* a modified version of the general procedure reported by Koll[144] for the synthesis of pyranosylnitromethanes (Scheme 37). The first stage is a nitroaldol (Henry) reaction between nitromethane and the open chain form of D-xylose (**94**). Dissolving metallic sodium in anhydrous methanol generated sodium methoxide, which was used to deprotonate nitromethane to form its nitronate anion. The aldehyde group of the xylose underwent nucleophilic attack by the nitronate anion to generate a nitroalditol (**96**) intermediate. Sodium ions were removed from the product liquor in an ion-exchange column and residual methanol was removed *in vacuo*. Reflux of the resultant aqueous solution resulted in dehydration of the nitroalditol to form the α,β-unsaturated nitro compound (**97**). Nitroalkene **97** acts as an acceptor in the final step, which is an intramolecular Michael addition.[145]



Scheme 37

The unprotected product (**98**) was acetylated in order to prevent free hydroxyl groups interfering with any of the later reaction steps and to make handling easier. Protection was achieved by dissolving a concentrate of the unprotected sugar in distilled acetic anhydride, adding a catalytic amount of triflic acid before heating the mixture under reflux. Triflic acid is employed as a catalyst in this procedure rather than the traditional basic conditions in order to avoid deprotonation α to the nitro group, and thus any potential side reactions.

Excess acetic anhydride and acetic acid by-product were removed *in vacuo* and the product obtained on crystallisation of the concentrate from ethanol. The product was isolated as white needle-like crystalline solid in moderate yield (40%). ^{1}H NMR spectroscopy indicated that the product (**95**) was obtained as the β-anomer and in the $^{5}C_{2}$ conformation. The vicinal coupling constants involving ring protons H^{2}-H^{5} all fall in the range 9-11 Hz and are consistent with the β $^{5}C_{2}$ conformation (Table 2). The β-anomer is favoured over the α-anomer since the nitro methyl group is bulky and therefore adopts the more favourable equatorial position on cyclisation.[144] ^{1}H and ^{13}C NMR spectroscopy did not indicate that any of the α-anomer, starting material or nitroalditol were present.



95

Coupling	*J* / Hz
H^2-H^3	10.6
H^3-H^4	9.2
H^4-H^5	9.4

Table 2: Vicinal coupling constants for nitromethyl sugar **95**

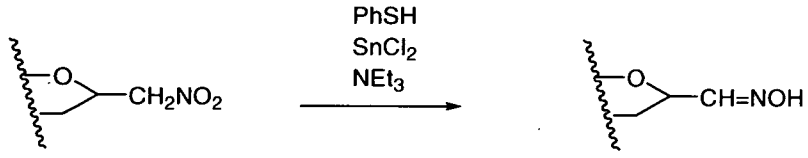
2.2.1.2 3,4,5,7-Tetra-*O*-acetyl-β-D-glucopyranosylnitromethane (99)

3,4,5,7-Tetra-*O*-acetyl-β-D-glucopyranosylnitromethane (**99**) was prepared from D-glucose in 20% overall yield by the approach described above (Section 2.2.1). Previous work[146] has demonstrated that the intermediate nitro sugar cannot be efficiently acetylated *in situ*; the free sugar was therefore isolated by liquid/liquid extraction before the protection stage.

During the course of this work, an alternative route to unprotected D-glucose and L-fucose derived pyranosylnitromethanes was reported by Gross *et al.*[147] This method differs from that above by employing DBU as base and pyridine as solvent. The reported reaction time is slightly shorter than Koll's procedure and the yields obtained are higher (50-60%). It is unclear, however, whether the reaction may be applied to as wide a range of aldoses as Koll's method.

2.2.2 Synthesis of pyranosylaldoximes

Several routes to pyranosylaldoximes have been reported in the last 40 years, many of which require a number of steps and were considered unattractive. The procedure chosen was developed by the group[52] and is based on a study by Bartra *et al.*[148] Bartra's work demonstrated that primary and secondary nitro compounds may be reduced in the presence of a tin (II) complex to their corresponding oximes.

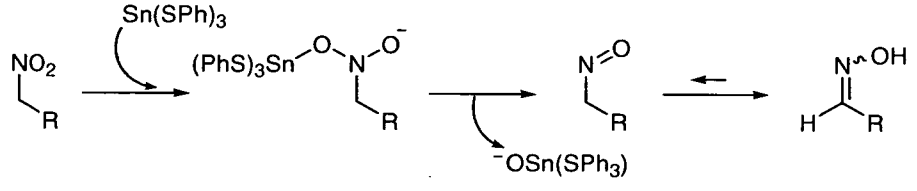


Scheme 38

The reducing species in this instance is believed to be the stannate complex $[Sn(SPh)_3][Et_3NH]$ that is readily generated *in situ* by mixing a solution of tin(II) chloride, thiophenol and triethylamine. The reducing species is believed to be in a rapid equilibrium with the starting reagents since attempts to isolate the complex have been unsuccessful.[148]

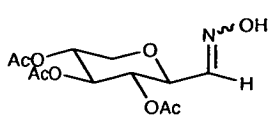
Scheme 39

The proposed mechanism[148] for nitro group reduction is illustrated in Scheme 40. Primary and secondary nitroso intermediates are found to rapidly adopt the oxime tautomer, while tertiary nitroso species undergo further reduction to the corresponding hydroxylamine product.

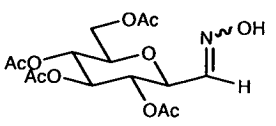


Scheme 40

The above procedure was employed in the synthesis of the pyranosyl oximes (**100**), (**101**) and (**102**) from D-xylose, D-glucose and D-mannose.



100



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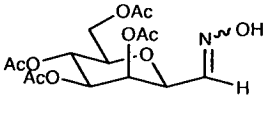
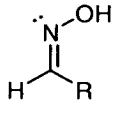
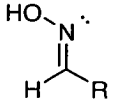


102

The respective pyranosylnitromethanes were treated with tin(II) chloride, thiophenol and triethylamine to afford the aldoxime products as white solids after separation from tin-based by-products by dry-flash chromatography. The reaction was found to proceed in good yields (69-86%) and the products were obtained as a mixture of *E* and *Z* isomers (Table 3).



Z-Isomer



E-Isomer

Aldoxime	% Yield	E: Z isomer ratio
100	86	4:1
101	69	4:1
102	77	2:1

Table 3: Pyranosylaldoxime E:Z ratios

The ^{1}H NMR spectra of the aldoxime products showed characteristic signals for the *E* and *Z* isomers and therefore allowed the *E*:*Z* ratio to be determined; 3,4,5 -tri-*O*-acetyl-β-D-xylopyranosylformaldoxime (**100**) serves as convenient example. The ^{1}H NMR spectrum contains doublets at 6.63 ppm and 7.22 ppm that correspond to the 1-H protons of the *Z*-isomer and *E*-isomer respectively. Broad singlets are observed at 8.62 ppm and 8.88 ppm for the OH proton of the *E*-isomer and *Z*-isomer respectively. The assignment of geometry was based on literature values[52] and NMR studies by Phillips[149] and Lustig.[150] Phillips has proposed that the cis arrangement of

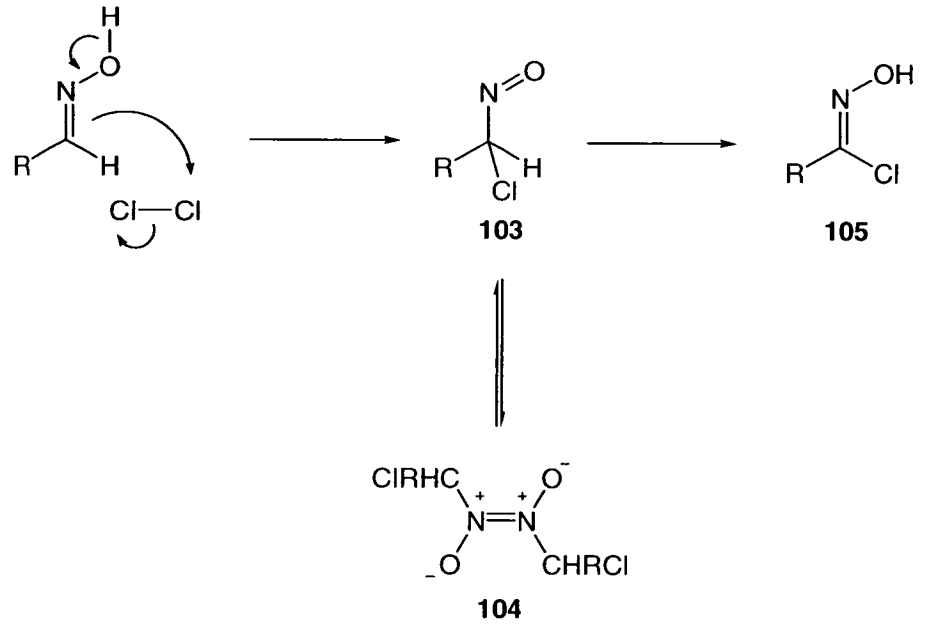
the 1-H proton to the oxime oxygen atom induces a paramagnetic (downfield) shift of the 1-H (*E*-isomer) signal relative to the 1-H (*Z*-isomer) signal.

During the course of this work there have been two significant developments in the field. Somsak and Toth reported a route to pyranosylaldoximes from the corresponding nitriles;[151] this process is outlined in detail in section 2.7.2.3. In a more general case, Carreira *et al* [152] have very recently reported a route to alkyl aldoximes from primary nitro compounds. This method is based on the Kornblum type oxidation of benzyl bromides to aldehydes by reaction with nitronate anions. In the future, application of this latter reaction might be advantageous in the synthesis of pyranosyl aldoximes since it does not lead to the formation of potentially toxic tin by-products.

2.2.3 Synthesis of pyranosyl hydroximoyl chlorides

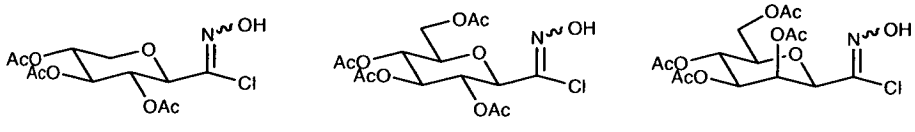
There are two main routes to hydroximoyl chlorides from aldoximes, direct chlorination[32] or a treatment with a "Cl^+" source such as N-chlorosuccinimide (NCS).[33] Direct chlorination is a fairly harsh method, but usually allows straightforward purification. Chlorination of aldoximes is achieved by bubbling chlorine gas through a cooled (-78°C) solution of the substrate in ether or chloroform.

The mechanism of the reaction is understood to be a S_E2' process[7] and involves transient nitroso (**103**) and dimeric (**104**) intermediates (Scheme 41).



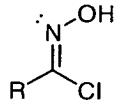
Scheme 41

The nitroso intermediate **103** is believed to be responsible for the characteristic green and blue solutions that are observed over the course of the reaction.[53] The blue colour is due to a strong absorbance at 320 nm that arises from an N=O, π-π^* electron transition.[53] On warming to room temperature the colour disappears indicating that the chloro-oxime (**105**) tautomer has been formed. The products were isolated as white solids on removal of the solvent *in vacuo* and did not require further purification. The D-xylose (**106**), D-glucose (**107**) and D-mannose (**108**) derived products were obtained in 96, 98, and 99% yields respectively.



Although it is theoretically possible to obtain *E* and *Z* isomers from this reaction only a single OH signal in the ^{1}H NMR spectra was observed for each product. Work by Hegarty[56] predicts that the *Z*-isomer is stereoelectronically favoured due to the antiperiplanar relationship between the chlorine atom and the lone pair of electrons (compare with section 1.2.5). It is important to note that the *Z*-isomer is reported to

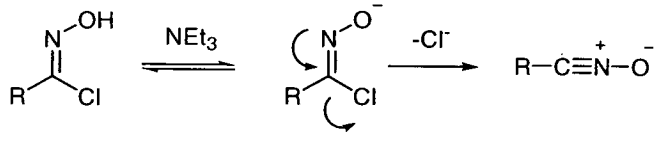
undergo base induced dehydrohalogenation *ca.* 10^7 times faster than the *E*-isomer.[56] This phenomenon is also attributed to the trans relationship between the leaving group and the lone pair of electrons on the oximic nitrogen. The presence of single C=NOH derived signals in the ^1H and ^{13}C NMR spectra in addition to the reactivity of the obtained hydroximoyl chlorides implies that the Z-isomer was obtained exclusively in all cases.[140]



Z-Isomer

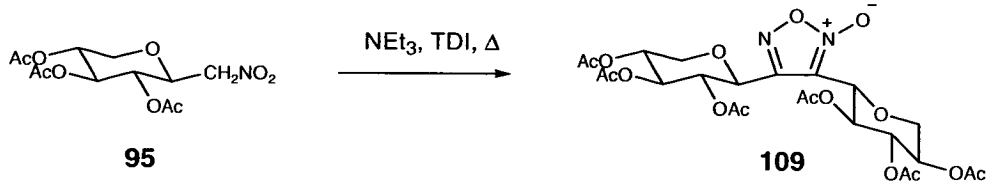
2.2.4 Generation of pyranosyl nitrile oxides

In principle the pyranosyl nitromethanes, aldoximes and hydroximoyl chlorides could all be used to generate the required nitrile oxides, however the hydroximoyl chlorides were ultimately chosen for two reasons. The nitromethyl compound to nitrile oxide transformation is achieved by employing Mukaiyama`s method;[16] this is unsuitable in the presence of nucleophiles since the isocyanate dehydrating agent reacts with thiols, amines and alcohols/phenols.[52] Generation directly from the aldoxime was ruled out due past experience of this method suffering lack of control over the rate of 1,3-dipole formation.[140] Large concentrations of nitrile oxide result in the formation of furoxan dimer. The only remaining option was the well-known Huigsen[27] method (Scheme 42), which involves the base mediated dehydrohalogenation of hydroximoyl chlorides. Huigsen`s method allows control of nitrile oxide concentration by slow addition of base to the hydroximoyl chloride precursor thus minimising the formation of unwanted furoxan. Recent work by Taddei *et al* has described further minimisation of furoxan formation by conducting 1,3-dipolar cycloaddition reactions in ionic liquids.[153,154]



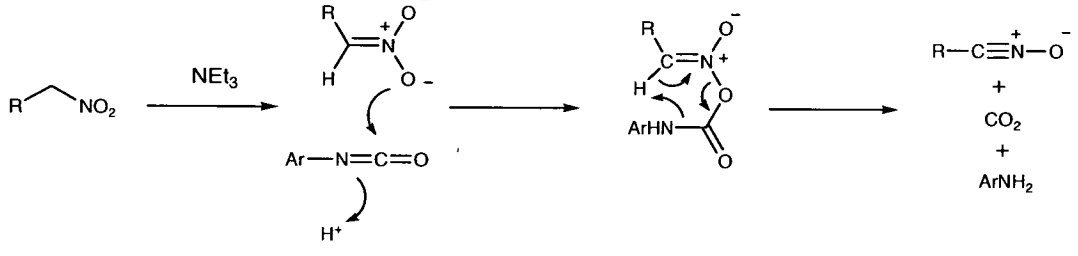
Scheme 42

2.2.5 Synthesis of dipyranosyl-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-1,2,5-oxadiazole-2-oxide (109)



Scheme 43

Dixylopyranosyl furoxan (**109**) was identified as a likely side-product in the proposed programme of 1,3-addition reactions, especially if poorer nucleophiles were employed.[146] An authentic sample of the furoxan was therefore prepared. The target compound was synthesised from the nitromethyl sugar by using a modified version of the Mukaiyama dehydration procedure. The approach employs an isocyanate to achieve dehydration of the primary nitro precursor to form the corresponding nitrile oxide (Scheme 44). The modified procedure of Baker *et al* [140] was employed in this work. This is a modification of the Mukaiyama procedure utilising tolylene diisocyanate (TDI), since a polymeric urea is formed as a co-product and is easily removed by filtration.



Scheme 44

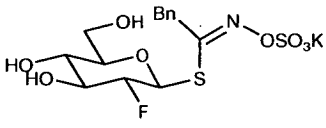
The product was obtained as a white solid in 61 % yield. The ^{1}H NMR spectrum was complex due to the overlap of the signals from the two xylose rings. The anomeric signals, however, were discernable as an overlapped pair of doublets centred at 4.53 ppm. The anomeric protons showed axial-axial couplings ($J_{1,2}$ = 9.5 Hz) to the 2-H protons that are indicative of each ring retaining the β-configuration. The ^{13}C NMR spectrum contained distinctive diagnostic peaks at 153 and 112 ppm that correspond

to the C-4 and C-3 respectively on the 1,2,5-oxadiazole-2-oxide ring. The FAB mass spectrum was also distinctive since a characteristic fragment peak at M-60 was observed; this peak corresponds to loss of N_2O_2 from the 1,2,5-oxadiazole-2-oxide unit.[140]

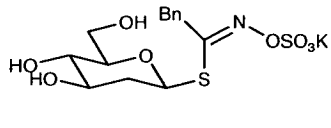
2.3 1,3-Addition reactions: Thiol nucleophiles

2.3.1 Myrosinase inhibition

One of the current challenges in carbohydrate chemistry is a full understanding of the mechanism of glucosinolate hydrolysis catalysed by myrosinase (see section 1.3.3). To date, a considerable amount is known about the mode of action of myrosinase, however some significant gaps still remain. An important goal is to obtain X-ray crystallographic data to establish the nature of the myrosinase-substrate interaction and, in order to achieve this aim a suitable myrosinase inhibitor is required. Several myrosinase inhibitors have been synthesised with varying success.[90-97] There are two main classes. The first function by stabilising the glycosyl-enzyme intermediate. 2-Deoxy-2-fluoroglucotropaeolin (**110**)[93] and 2-deoxyglucotropaeolin (**111**)[96] have both proved to be successful competitive inhibitors of the hydrolysis of glucotropaeolin (**32**) (K_m=1mM). The second class are non-hydrolysable analogues of glucotropaeolin. The *C*-glucoside analogue of glucotropaeolin[91,92] [C-GTL(**112**)] was not recognised by myrosinase and thus ineffective, however the carba-glucotropaeolin (**113**)[90] has been found to exhibit inhibitory behaviour.



110



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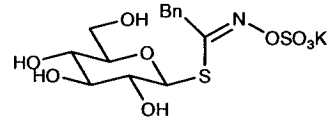
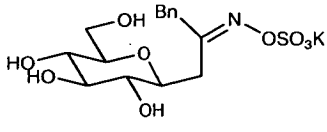


32



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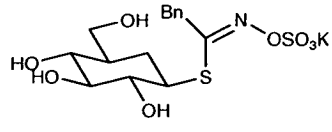

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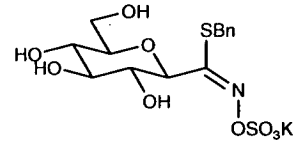
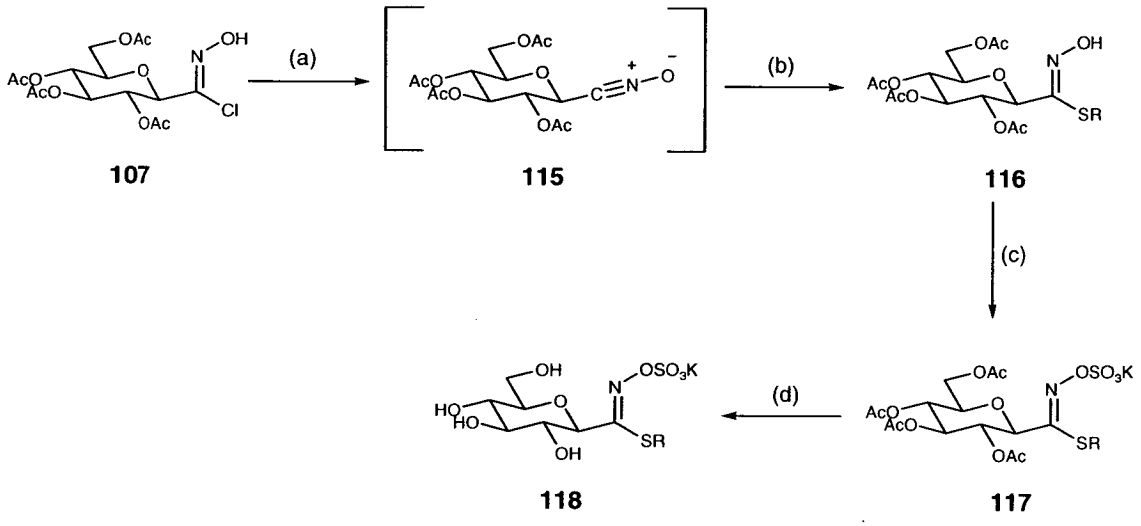


114

One of the best candidates to date is 2-fluoro-2-deoxy-glucotropaeolin (**110**). X-ray studies with this inhibitor have proved valuable (section 1.3.3); however rapid Lossen rearrangement of the aglycon component prevents a full understanding of the nature of the binding between the aglycon part and myrosinase.[79] A non-hydrolysable substrate should enable a fuller analysis of the myrosinase-

glucosinolate interactions. The potential to introduce the thiohydroximate functionality at the anomeric position is of particular interest since the product (**114**) would be a non-hydrolysable *C*-linked glucosinolate analogue. A collaborative project was initiated with Professor Rollin's group at the University of Orléans to investigate the synthesis and biological activity of such "isoglucosinolates". The key steps of the proposed synthesis are outlined in Scheme 45. 1,3-addition of thiols to **115** would deliver desulfoisoglucosinolates (**116**) which, following sulfation steps and deprotection, would afford the target isoglucosinolates (**118**).



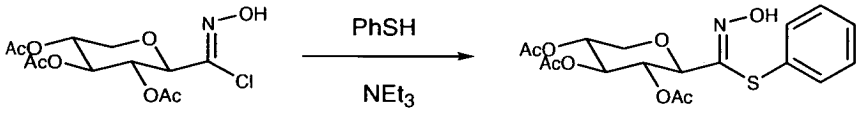
Scheme 45: (a) NEt_3 (b) RSH (c) SO_3-Pyridine, (d) MeOK/MeOH

The D-glucose based precursor **107** was to be prepared in Edinburgh and sent to Orleans for the latter stages. Work in Edinburgh was also to include synthesis of D-xylose analogues of the "isoglucosinolates". It was anticipated that the lack of a C-6 hydroxyl group would alter the ability to bind to myrosinase. In previous studies by Rollin *et al* deoxy-glucosinolates were shown to have varying binding affinities with myrosinase.[78] The results indicated that the presence of the C-2 glycosyl hydroxyl is crucial to allow hydrolysis and that the remaining glycosyl hydroxyls play a secondary binding role. The importance of the C-2 hydroxyl stems from the polarisation it confers to the *S*-glucose bond and in orientation of the glycosyl moiety in the enzyme pocket.[78] The previous observations are based on the fact that 2-

deoxy-glucosinolates function as competitive inhibitors of the hydrolysis of natural glucosinolates.

Preliminary work on 1,3-additions of thiols to pyranosyl nitrile oxides had been conducted within the group by Baker.[146] Pilot reactions with D-glucopyranosyl nitrile oxide **115** and thiophenol were encouraging and thus the reaction was investigated in more detail.

2.3.2 Synthesis of S-Phenyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosylformothiohydroximate (119)



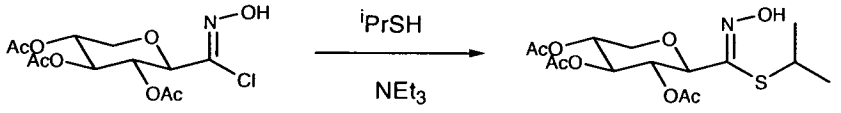
106 **119**

Scheme 46

The nitrile oxide was generated by slowly adding an ethereal solution of triethylamine over 24 hours *via* a syringe to a vigorously stirred solution of **106** in dry ether. The slow addition of base controlled the nitrile oxide concentration thus minimising dimerisation to furoxan **109**. Furthermore, furoxan formation was limited by adding the nucleophile in 3-fold excess. The product (**119**) was isolated as a white solid (75 %) after an aqueous work up and dry-flash chromatography. The product was characterised by ^{1}H and ^{13}C NMR spectroscopy. The ^{1}H NMR spectrum displayed characteristic signals for the pyranose ring protons and aromatic ring derived signals were observed between 7.35 and 7.55 ppm. A doublet was observed at 3.56 ppm due to H-2; this signal is shifted to lower frequency relative to that for the nitrile oxide precursor. The coupling between H-2 and H-3 was found to be 9.94 Hz, thus confirming that the product was obtained as the β-anomer. A broad singlet at 8.81 ppm indicated the presence of the C=NOH group; no significant shift was noted relative to the C=NOH signal of the hydroximoyl chloride. The ^{13}C NMR spectrum displayed the expected aromatic and pyranose ring carbon signals and an oxime (C-1) derived quaternary peak at 148.8 ppm. The C=NOH signal appears at

higher frequency relative to that of the hydroximoyl chloride (136.5 ppm). The appearance of a single oxime signal was consistent with the exclusive formation of a Z-configured product (refer to Section 1.2.5).

2.3.3 Synthesis of S-(2-Propyl) 2,3,4-tri-*O*-acetyl-β-D-xylopyranosylformothiohydroximate (120)



106 **120**

Scheme 47

Following the success of the previous reaction the addition of an alkyl thiol as a nucleophile was attempted. The Rollin group had employed primary thiols with success, therefore a secondary thiol was considered. 2-Propanethiol was easily available and the resultant adduct would constitute a xylose analogue of glucoputranjivin (isopropyl glucosinolate).[68] Using the conditions outlined in Section 2.3.2, 2-propanethiol was reacted with 3,4,5-tri-*O*-acetyl-β-D-xylopyranosyl nitrile oxide to afford the desired adduct (**120**) in 55% yield. Furoxan **109** was also isolated from the reaction mixture in 45% yield. The reaction yield in this case is comparable to earlier work with aromatic nitrile oxides.[8] The bulky isopropyl group is presumably responsible for the observed lower reactivity and thus the formation of by-product. ^{1}H and ^{13}C NMR spectroscopy displayed the characteristic C=NOH derived signals at 8.88 ppm and 147.7 ppm. Signals characteristic of the isopropyl group were also observed in the ^{1}H NMR spectrum. A closely spaced pair of "roofed" doublets at 1.23 and 1.25 ppm is consistent with inequivalence between the two methyl groups. A septet for the isopropyl CH was also present at 3.83 ppm.

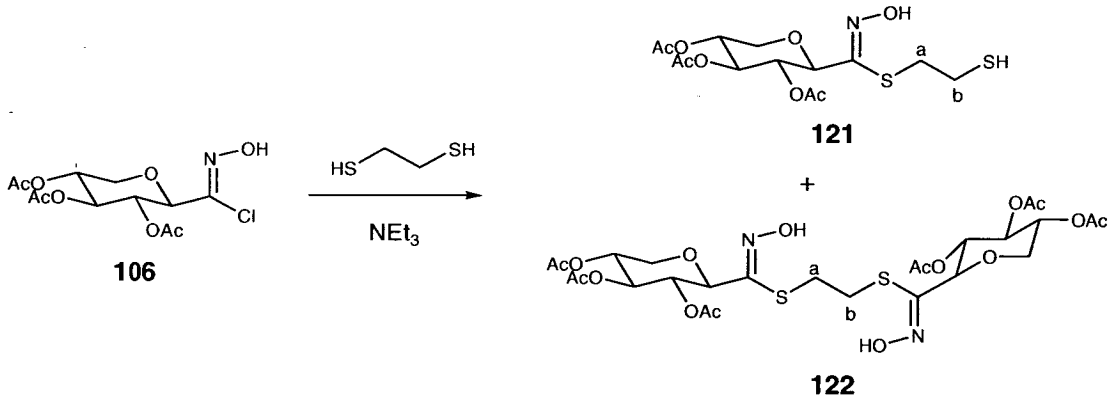
2.3.4 Reaction of 3,4,5-tri-*O*-acetyl-β-D-xylopyranosylnitrile oxide with 1,2-ethanedithiol

As the previous studies had focused on monofunctional thiols, it was decided to examine addition of a difunctional thiol. Initially a similar procedure to that outlined in section 2.3.2 was adopted. The nitrile oxide was present in excess in an attempt to encourage formation of the bridged 2:1 adduct **122**. Both adducts **121** and **122** (Scheme 48) were formed along with a significant amount of furoxan **90** (~65%). The reaction was considered only to be a moderate success, therefore a new addition strategy was attempted.

It was envisaged that adding hydroximoyl chloride **106** dropwise to a solution of nucleophile and triethylamine would allow the concentration of nitrile oxide to be minimised. Adding the nitrile oxide precursor to the nucleophile/base solution afforded **121** and **122** in 40% and 20% yield respectively, with minimal furoxan formation. Following dry-flash chromatography, **121** was isolated as a white solid and the **122** as a semi-solid. ^{1}H and ^{13}C NMR spectroscopy showed that both compounds possessed characteristic C=NOH signals and that the side chain CH_2s were inequivalent. The CH_2 signals appear as a pair of complex multiplets, however the signals are shifted to higher frequency and the separation decreases slightly in the 2:1 adduct **122** (Table 4). The key difference between both adducts is the appearance of an SH resonance at 1.65 ppm in the ^{1}H NMR spectrum. The SH signal appears as a triplet due coupling to the 2 adjacent protons. The identity of the signal was confirmed by a COSY NMR experiment, which showed a cross-peak to the C*H*$_2$SH protons.

	1:1 (**121**)	2:1 (**122**)
CH_2^a (δ_H/ppm)	3.10	3.15
CH_2^b (δ_H/ppm)	2.63	2.82
CH_2^a (δ_C/ppm)	34.7	31.7
CH_2^b (δ_C/ppm)	24.9	31.7
OH (δ_H/ppm)	8.91	9.23
C-1 (δ_C/ppm)	147.6	147.9

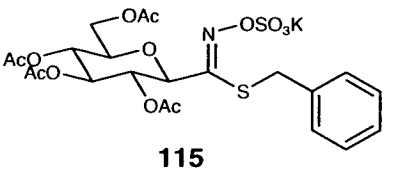
Table 4: Comparison of δ_H and δ_C values for adducts **121** and **122**



Scheme 48

2.3.5 Biological Testing/Postscript

On receipt of several batches of hydroximoyl chloride **107**, the Rollin group was successful in completing the synthesis of a number of "isoglucosinolates". They selected isoglucotropaeolin (**115**) and isoglucolepidiin (**123**) for testing versus the natural substrate, glucotropaeolin. Unfortunately both analogues were not recognised by myrosinase and therefore did not function as planned.



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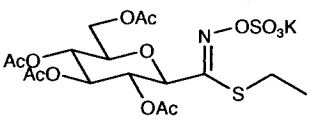
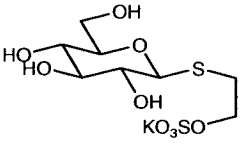


123

This result is not unprecedented, similar results were obtained in studies with the *C*-analogue of glucotropaeolin (**112**).[90,91] The failure of *C*-glucosinolates and isoglucosinolates to inhibit myrosinase indicates that the sulfated thiohydroximate linkage must be intact and linked to the glucose unit through an anomeric sulfur atom, in order to be recognised. These conclusions appear to be partially reinforced by subsequent work conducted independently by Professor Rollin`s group.[81] In an effort to further establish the requirement for the thiohydroximate bridge, compounds such as **124** and **125** were prepared; these retain the anomeric sulfur atom and anionic sulfate group, yet delete the nitrogen atom.



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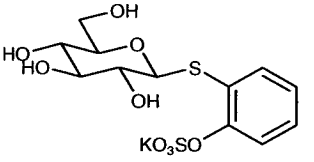
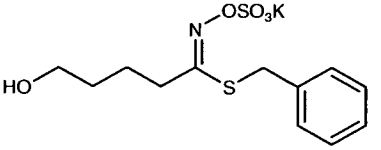


125

Compounds of the type **124** and **125** are found to generally display poor inhibitory properties. Carba-glucotropaeolin (**113**) retains a substrate-like sulfated thiohydroximate bridge and had been found to inhibit myrosinase before the collaboration began.[90] The recent study finally achieved the objective of obtaining an X-crystal structure of a non-hydrolysable glucosinolate analogue bound to myrosinase.[81] The story is certainly not over, however, as recent work[81] has shown that analogues which do not resemble carbohydrates at all (!) such as **126** are actually superior inhibitors than Carba-glucotropaeolin. Clearly, there is more to learn about the glucosinolate/myrosinase couple.



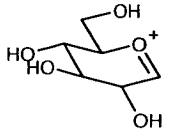
126

2.3.6 Conclusions

It has been shown that thiol nucleophiles successfully undergo 1,3-nucleophilic addition reactions with pyranosyl nitrile oxides to afford the corresponding thiohydroximates. Additions of alkyl and aryl thiols to 3,4,5-tri-*O*-acetyl-β-D-xylopyranosylnitrile oxide were found to give products in satisfactory yields (55 to 75%). Collaborative work with the Rollin group was found to be successful with respect to synthetic aspects, however the targets that were ultimately prepared were found to be biologically inactive. The test results have, however, contributed toward the design of future myrosinase inhibitors.

2.4 Carbohydrate Derived Amidoximes - Introduction

Amidoxime derivatives of monosaccharides have attracted interest as inhibitors of glycosyl hydrolases[155] and transferases.[156,157] Such compounds are known to have similar conformational and electrostatic features to oxocarbonium like species **127** associated with the mechanism of glycosidase action.[155] Amidoximes like **128** have the advantage over their amidrazone and amidine analogues by virtue of increased stability.[155] Glucosyl (**128**), mannosyl and galactosyl amidoximes, in which the oximic unit is part of the carbohydrate ring have been shown to be effective inhibitors of metabolically important glycosidases.[155] *N*-acetylxylosamidoxime **129** has been synthesised as part of a study toward potential inhibitors of N-acetylglucosamine specific glycosyltransferases.[156, 157]



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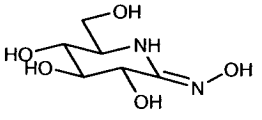

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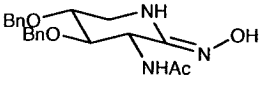
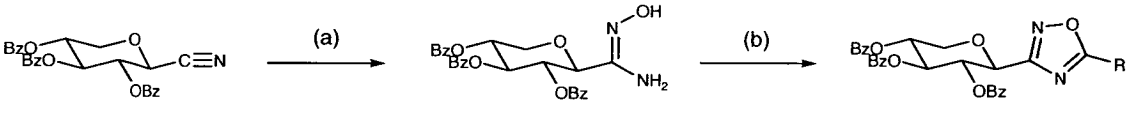


129

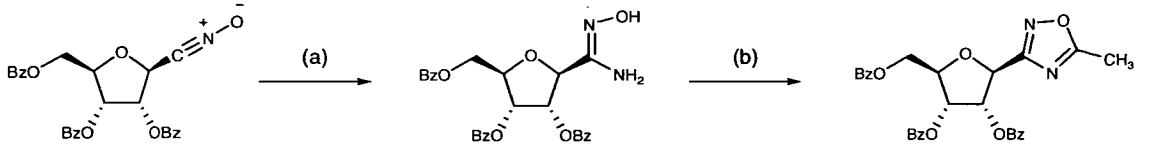
To the authors knowledge, there have been few attempts to install an amidoxime exo to a carbohydrate ring. Zhang *et al*[158] have prepared amidoxime **131** *via* addition of hydroxylamine to nitrile **130** (Scheme 49). This compound was the key intermediate in the synthesis of 3-β-D-xylopyranosyl-1,2,4-oxadiazoles (general structure **132**) that are of interest as potential antibacterial and antitumor agents.[158]



130 **131** **132**

Scheme 49: (a) NH_2OH, MeOH (b) RC(O)Cl

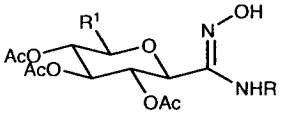
1,3-Nucleophilic addition of ammonia to 3,4,6-tri-*O*-benzoyl-β-D-ribofuranosyl nitrile oxide (**133**) has been reported to afford amidoxime **134**, which was transformed (in a similar manner to above) to 1,2,4-oxadiazole **135**.[159]



133 134 135

Scheme 50: (a) NH_3/MeOH (b) Acetic anhydride, Δ

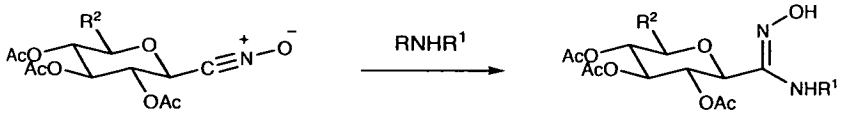
It was envisaged that pyranosyl nitrile oxides would undergo 1,3-additions with amines in a similar manner to the furanosyl analogues (Scheme 50). The resultant amidoximes would be novel *C*-glycosides that could potentially function as NO donors or as ligands for metals (Section 1.4.1).



136

2.4.1 Addition of Primary and Secondary Alkyl Amines

The amidoximes were prepared by a modified version of the procedure employed in the synthesis of the pyranosyl thiohydroximates **121** and **122** (Section 2.3.4). In a typical experiment a solution of the glucopyranosyl-hydroximoyl chloride **107** in dry chloroform was added dropwise over 3 hours to a cooled (0 °C) vigorously stirred solution of benzylamine (3-4 equivalents) and excess triethylamine in chloroform. Removal of the solvent and chromatography of the residue afforded the *N*-benzyl amidoxime **137** (R^1 = Bn, R^2 = H; 80% yield),[66] the furoxan dimer **109** was not detected. Xylopyranosyl-hydroximoyl chloride **106** reacted similarly to yield amidoxime **138** (R^1 = Bn, R^2 = H; 67% yield). The structures of the products were assigned on the basis of their spectroscopic properties. *Eg* for D-xylose-derived amidoxime **138** in the NMR spectra there were, in addition to the expected signals for the carbons and protons of the pyranosyl and benzene rings, distinctive peaks for the oxime unit [δ_C 148.9 ppm (C=N)] and the attached $NHCH_2$ group [δ_H 4.38 ppm, dd, (CHa), 4.39 ppm, dd, (CHb), 5.22 ppm, t, (NH); $J_{NH\text{-}CHa}$ 5.5, $J_{NH\text{-}CHb}$ 6.8, $J_{CHa\text{-}CHb}$ 14.6 Hz; δ_C 46.4 ppm (CH_2)]. Shaking the *N*-benzylamine adducts with D_2O resulted in loss of the NH signal and simplification of the benzyl signals to doublets. Both doublets displayed large geminal coupling constants (14.6 Hz).[66]



Amidoxime	R^1	R^2	%Yield
137	Bn	CH_2OAc	80
138	Bn	H	67
139	Bu	H	63
140	$CH_2CH{=}CH_2$	H	41
141	Ph	H	90
142	Ph	CH_2OAc	80

Table 5: Mono-substituted pyranosyl amidoximes[66]

Hydroximoyl chloride **106** also reacted readily with 1-aminobutane and allylamine to afford corresponding adducts (**139** R^1 = Bu, R^2 = H; 63% yield), and (**140** R^1 = $CH_2CH{=}CH_2$, R^2 = H; 41% yield).[66] It is noteworthy that in the latter case the isolated product results from addition of the nitrile oxide to the amine moiety in allylamine rather than cycloaddition to the alkene. Earlier work has shown that 1,3-addition of propargylamine to benzonitrile oxide has been reported to produce the amidoxime product;[10] in this study it was concluded that the nucleophilic reactivity of the amine was higher than the dipolarophilic activity of the alkyne. It has also been postulated that alkenes are superior to alkynes as dipolarophiles and thus should not lead to significant quantities of amidoxime product.[10] Work by Abell *et al*[126] and Zard *et al*[125] (Section 1.4.3) with alkyl and aryl nitrile oxides, in addition to our own,[66] has clearly shown that the above theory is not necessarily correct.

Having successfully reacted primary alkyl amines with pyranosyl nitrile oxides it was decided to examine the additions of aromatic amines. Hydroximoyl chloride **106** was reacted with aniline according to the procedure employed in the alkyl amine study. Amidoxime **141** was isolated as a white solid in 28 % yield following aqueous work up and dry-flash chromatography. Furoxan by-product **109** was also isolated in

16 % yield. The pilot reaction was disappointing, therefore an improved procedure was attempted based on that of Barbyrin *et* al.[112] Heating a 2:1 mixture of aniline and hydroximoyl chloride **106** in ethanol at reflux for five hours afforded amidoxime **141** (R^1 = Ph, R^2 = H; 90% yield). And the corresponding reaction with D-glucopyranosyl nitrile oxide gave amidoxime **142** (R^1 = Ph, R^2 = CH_2OAc; 80%). Conducting the above reactions at room temperature afforded the same products after 16 hours. In neither case was there any evidence for the formation of the furoxan dimers. The products were characterised by ^1H and ^{13}C NMR spectroscopy. The ^1H and ^{13}C NMR spectra displayed characteristic C=NOH derived signals 7.91 ppm and 146.8 ppm respectively for the D-xylose derived amidoxime. The structure of (*Z*)-*N*-phenyl-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime was established by X-ray crystallography (Figure 1).[66]

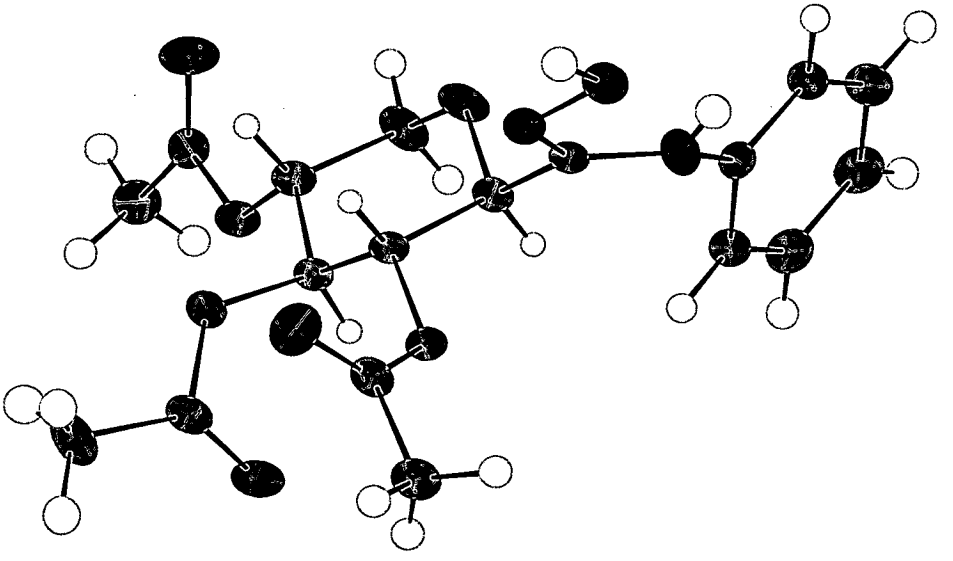


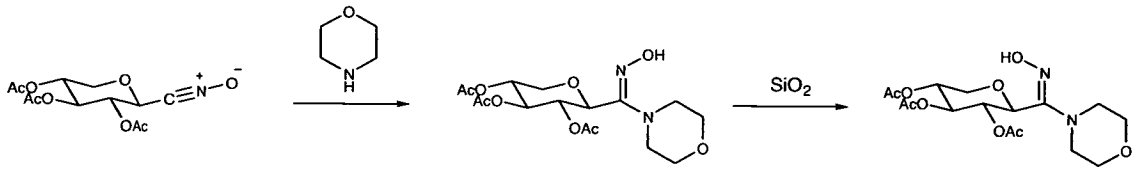
Figure 1- Crystal structure of (Z)-*N*-phenyl-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (**141**)

The structure confirms the *Z*-configuration of the oxime moiety and demonstrates an *s-trans* (Z_{ap}) conformation about the amidic nitrogen with the H of the NHR facing the oxime OH. These results are in accord with previous studies indicating that such additions occur in a concerted, but non-synchronous manner.[54] The near planarity of the NH-C=N-O unit [torsion angle 2.6(3)°] and the short non-bonded distance

between the amidic N and the oxime O [N to O = 2.508(3)Å] are consistent with the existence of an intramolecular H-bond between these atoms.[66, 67]

2.4.2 Addition of morpholine to (3,4,5-tri-O-acetyl-β-D-xylopyranosyl) nitrile oxide

Having successfully reacted primary amines with pyranosyl nitrile oxides, addition of a secondary amine was considered next for study. The procedure outlined for primary amines was employed. Addition of hydroximoyl chloride **106** to a solution of morpholine (4-fold excess) afforded a white solid in 67 % yield. The ^{1}H and ^{13}C NMR spectra displayed characteristic oxime signals [δ_H 8.38 ppm, bs, (OH) and δ_C 154.7 ppm (C=N)]. The OH resonance in $CDCl_3$ was very broad, however using $CD_3S(O)CD_3$ led to a much sharper singlet [δ_H 10.08 ppm]. The data indicated that only one oximic product was present. Signals corresponding to the heterocyclic ring were also apparent in the ^{1}H and ^{13}C NMR spectra. The morpholine protons were observed as three sets of multiplets [3.77-3.81, ppm, m, CH_2; 3.24-3.26 ppm, m, CH_2 and 3.09-3.16 ppm, m, CH_2]. The signal at highest frequency corresponds to the protons adjacent to the ring oxygen atom, and those at lower frequency to the protons adjacent to the morpholine nitrogen. Previous studies[62] on additions of morpholine to *p*-nitrobenzonitrile oxide demonstrated that the *Z*-configured product was obtained initially, which could then undergo acid assisted isomerisation to the *E*-amidoxime. It was found that exposure to silica during chromatography was an acidic enough environment to allow isomerisation. The ^{1}H NMR data quoted above were compared to literature values[62] Hegarty *et al* found the ring CH_2 signals adjacent to nitrogen in the *E*-adduct to appear *ca* 2.91 ppm (i.e similar to morpholine itself) while those of the *Z*-adduct were observed *ca* 3.27 ppm. The signal for the morpholine CH_2s adjacent to the nitrogen in this example is more complex due to the nearby chiral (anomeric) centre, therefore direct comparison is not really possible. The product was purified by dry-flash chromatography and was therefore assumed to adopt an *E*-configuration (**143**), based on previous observations.[62]

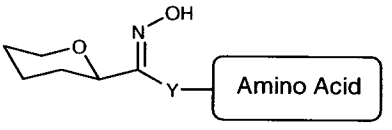


143

Scheme 51

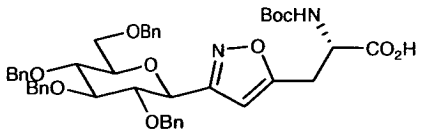
2.4.3 Additions of amino acid derived nucleophiles: Introduction

The success of the reactions of alkyl thiols and amines with pyranosyl nitrile oxides prompted work on addition of amino acid thiol and amine nucleophiles. The resultant adducts of such reactions would each constitute a novel class of *C*-linked glycopeptide analogues.



Y= NH, S

In general *C*-linked analogues of naturally occuring *N*- and *O*-glycosyl amino acids and peptides are of interest since they are resistant to enzymatic cleavage and are therefore useful, eg as probes for various biological processes.[160] The field is large and has been extensively reviewed, [161] a few representative are illustrated overleaf. Isoxazole **144** has been prepared by Dondoni *et al* by 1,3-dipolar cycloaddition of a pyranosyl nitrile oxide with an amino acid derived alkyne.[160] Glycopeptide analogue **145** was made during an investigation into the synthesis of *C*-linked glycosyl asparagines.[162] Glycopeptide analogue **146** has been synthesised and examined as a potential glycoamidase inhibitor.[163] Glycoamidase cleaves the amide linkage between the oligosaccharide and peptide units and is therefore important in the modification of proteins.



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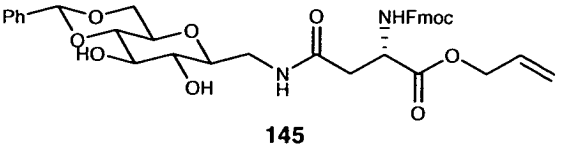

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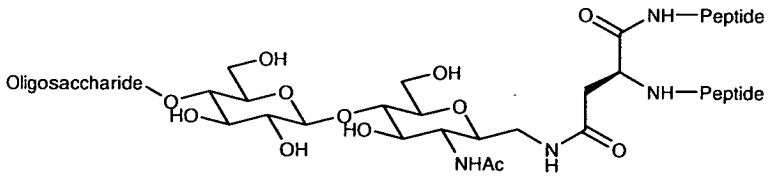


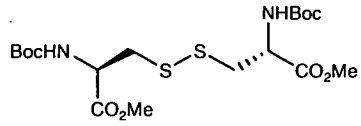
146

2.4.4 Additions of *N*-(tert-butoxycarbonyl)cysteine methyl ester (147) to pyranosylnitrile oxides

L-Cysteine was chosen for study since it is a common constituent in many proteins. A cysteine derivative that possessed carboxyl and amine protection was required in order to prevent side reactions and *N*-Boc protected L-cysteine methyl ester **147** was selected for this purpose. The synthesis was accomplished by following the procedure of Gledhill *et al.*[164] L-Cysteine methyl ester hydrochloride, Boc anhydride and triethylamine were stirred at room temperature for 16 hours. The desired product was obtained as a colourless oil (95% yield). It was feared that on prolonged storage thiol **147** would oxidatively couple to form a disulfide, however it was found that storage in a freezer for more than one year avoided disulfide formation.

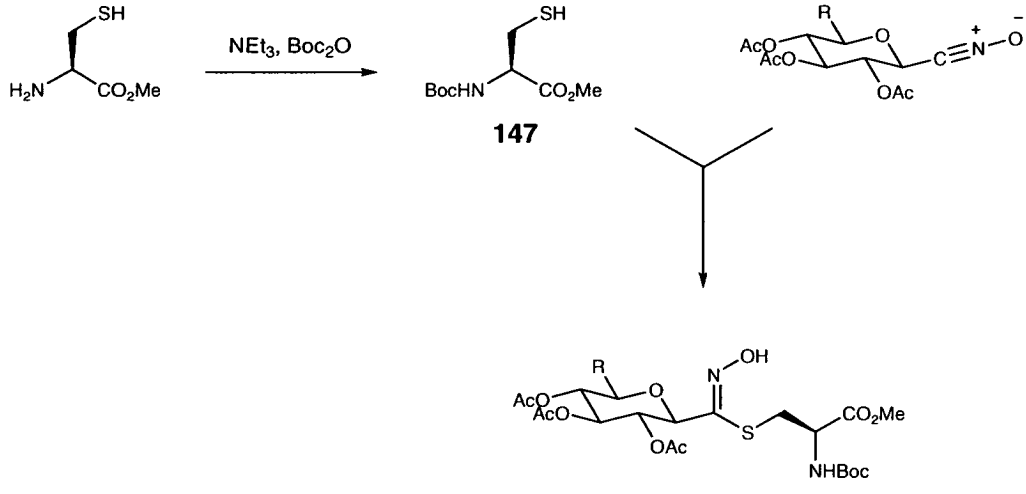
The procedure used was based on that described earlier for addition of amines (section 2.4.1). A solution of D-xylose derived hydroximoyl chloride **106** was added slowly added dropwise to a chloroform solution of cysteine derivative **147** (3 equivalents) and triethylamine (6 equivalents). The target thiohydroximate **148** was obtained as a white solid in 88% yield after purification by dry-flash chromatography (Scheme 52). The ^{1}H and ^{13}C NMR spectra clearly demonstrated that addition had taken place. Signals corresponding to the thiohydroximate linkage and the amino acid unit were observed [δ_H 9.44 ppm (bs, OH), 4.59 ppm (1H, m, cysteine CH), 3.78 ppm (3H, s, methyl ester), 3.35-3.58 ppm (2H, m, cysteine CH_2), 1.47 ppm (9H, s, Boc CH_3) δ_C 147 ppm (C=N), 53.7 ppm (CH), 52.7 ppm (methyl ester), 32.5 ppm

(CH_2), 28.1 ppm (Boc CH_3)] in addition to the pyranosyl ring signals. A second product was obtained as a white crystalline solid after chromatography, the NMR and mass spectrometry data indicated that it was disulfide **149**.[165] Presumably the basic reaction conditions and exposure to air favoured oxidation of the excess thiol to afford **149**.



149

Cysteine derivative **147** was reacted with glucose derived hydroximoyl chloride **107** in a similar fashion to above and the expected adduct **150** was obtained in a comparable yield (85%).



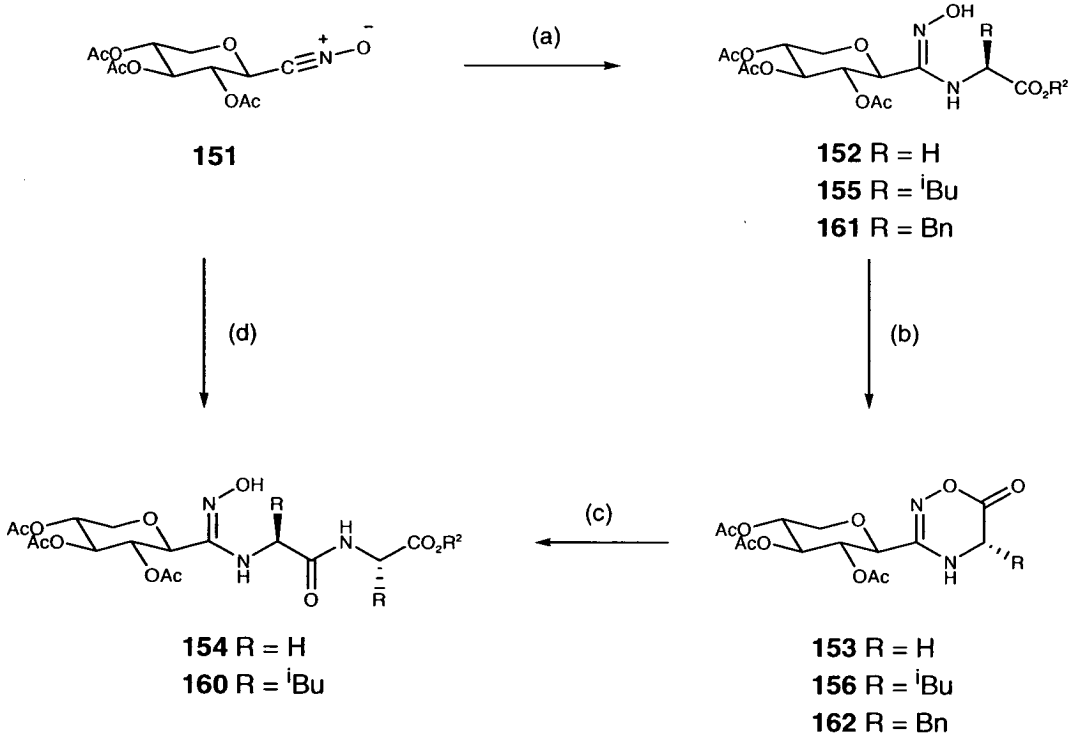
148 R = H, **150** R = CH_2OAc

Scheme 52

2.4.5 Additions of amino acid esters

A larger range of amino acid *N*-nucleophiles were available for the preparation of amidoxime linked glycopeptide analogues; glycine was chosen for initial work since its simple structure would aid analysis of any products. A chloroform solution of D-xylose derived hydroximoyl chloride **106** was added slowly to a stirred and cooled (0 °C) mixture of glycine ethyl ester hydrochloride (3 equivalents) and triethylamine

(18-fold excess) in chloroform.[66] On completion of the addition, the reaction mixture was washed with 0.1 M HCl to remove excess amine. Analysis of the ^{1}H and ^{13}C NMR spectra of the crude product indicated that the expected amidoxime **152** was the major product (Scheme 53). Signals corresponding to the amidoxime linkage and the amino acid unit were evident [δ_H 5.48 ppm (t, NH, $J_{NH\text{-}CH}$ 5.8 Hz), 4.16 ppm (q, Et ester CH_2), 4.07 ppm (d, glycine CH_2), 1.23 ppm (t, Et ester CH_3) δ_C 170. 7 ppm (C=O, Et ester), 148.1 ppm (C=N), 61.7 ppm (Et ester CH_2), 44.7 ppm (glycine CH_2), 14.5 ppm (Et ester CH_3)]. Purification by dry-flash chromatography was attempted, however two major and one minor product were obtained (Scheme 53). The amidoxime **152** was isolated in addition to a second compound which was later identified as oxadiazinone **153**.[66] The NMR spectra indicated that cyclisation had taken place, the ester peaks had been lost and the glycine-derived signals had simplified; [δ_H 5.61 ppm (bs, NH), 3.95 ppm (s, glycine CH_2) δ_C 164.6 ppm (oxadiazinone C=O), 150.4 ppm (C=N), 40.2 ppm (oxadiazinone CH_2)].



Scheme 53: (a) $H_2NCHRCO_2Et.HCl$, NEt_3 (b) SiO_2, $CHCl_3$, Δ or prolonged standing (c) $H_2NCHRCO_2Et.HCl$, NEt_3 (d) glycylglycine.HCl, NEt_3.

Formation of the cyclised product is not entirely surprising since the *Z*-amidoxime geometry puts the nucleophilic OH group in a favourable position to attack the ester carbonyl in a 6-exo-trig process. Similar reactions have been observed for amidoximes in previous studies.[129,166,167] A minor product was also obtained that possessed similar spectroscopic properties to those of amidoxime **152**. Two NH signals were clearly visible in the ^{1}H NMR spectrum in addition to the ethyl ester quartet and triplet [δ_H 7.45 ppm (t, NH, $J_{NH\text{-}CH}$ 7.5 Hz), 5.61 ppm (t, NH, $J_{NH\text{-}CH}$ 6.1 Hz), 4.14 ppm, (q, Et ester CH_2), 1.21 (t, CH_3 Et ester)]. The ^{13}C NMR spectrum showed the diagnostic amidoxime imine signal and side chain attributed to a side chain δ_C 170.9 ppm (Et ester C=O), 147.8 ppm (C=N), 61.0 ppm (Et ester CH_2), 46.2 ppm (CH_2), 40.9 ppm (CH_2), 13.9 ppm (Et ester CH_3)]. The minor product was therefore assigned structure **154**, which results from attack on the oxadiazinone ring by a second equivalent of amino acid.[66] All three products could also be seen in the electrospray mass spectrum of the crude reaction mixture [ES 404 (MH^+, **152**), 358 (MH^+, **153**), 461 (MH^+, **154**)]. Similar results were obtained when the reaction was repeated with L-leucine methyl ester hydrochloride (Scheme 53). It was noted in this case that cyclisation took place to a greater extent before chromatography than in the previous experiment. Studies with L-leucine also found that formation of ring-opened product could be minimised by reducing the amount of amino acid from 3 equivalents to 1.5.

The structures of oxadiazinones **153** and **156** were eventually confirmed by X-ray crystallography. To the author's knowledge these are the first such crystal structures to contain the 1,2,4-oxadiazin-6-one moiety. The crystals of oxadiazinone **153** were found too weakly diffracting and consequently gave poorer quality data than hoped. In contrast, the data obtained for oxadiazinone **156** were suitable for further analysis. Selected bond lengths, bond angles and torsion angles for the oxadiazinone ring system are shown in Table 6.

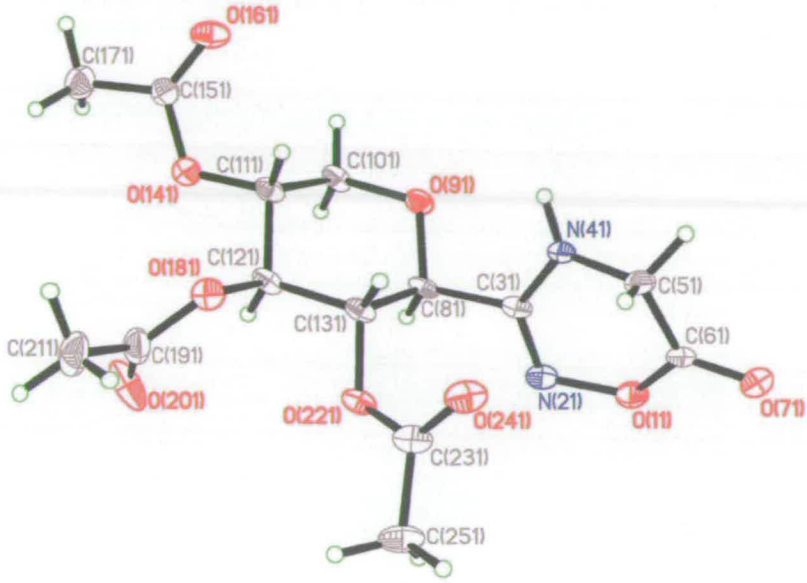


Figure 2- 3-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-1,2,4-oxadiazin-6-one (**153**)

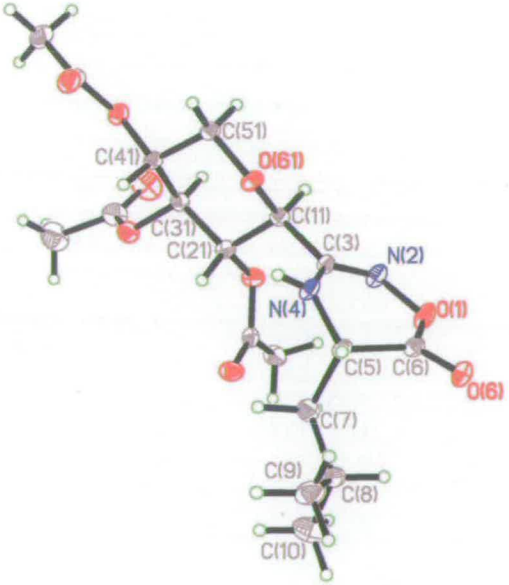
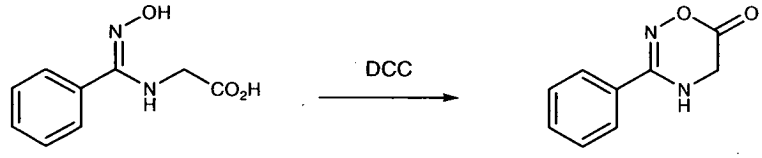


Figure 3- 3-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-5-(isopropyl)-1,2,4-oxadiazin-6-one (**156**)

Bond Lengths/ Å	Bond Angles/ °	Torsion Angles/ °
O(1)-N(2) 1.463(2)	O(1)-N(2)-C(3) 113.96(18)	O(1)-N(2)-C(3)-N(4) -6.10
N(2)-C(3) 1.290(3)	N(2)-C(3)-N(4) 126.71(2)	N(2)-C(3)-N(4)-C(5) -17.80
C(3)-N(4) 1.331(3)	C(3)-N(4)-C(5) 120.12(19)	C(3)-N(4)-C(5)-C(6) 35.65
N(4)-C(5) 1.452(2)	N(4)-C(5)-C(6) 108.28(17)	N(4)-C(5)-C(6)-O(1) -32.68
C(5)-C(6) 1.512(3)	C(5)-C(6)-O(1) 117.82(19)	C(5)-C(6)-O(1)-N(2) 13.14
C(6)-O(1)1.352(3)	C(6)-O(1)-N(2) 122.82(17)	C(6)-O(1)-N(2)-C(3) 7.84

Table 6: Selected bond lengths, bond angles and torsion angles for **156**

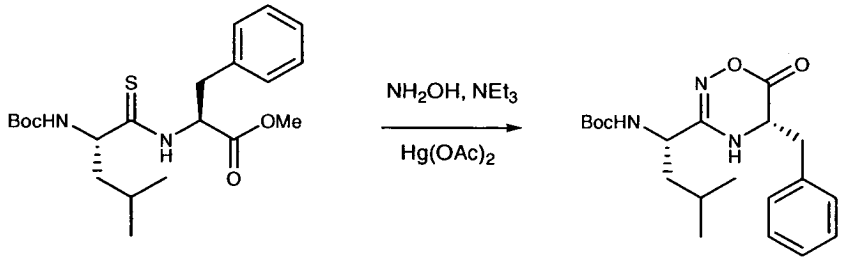
A survey of the literature revealed that 1,2,4-oxadiazin-6-ones are relatively rare heterocycles. The first report of such an oxadiazinone synthesis was made by Takacs and Ajzert,[166] who reported that **157** was formed on reacting glycine carboxymethyl amidoxime **158** with 1,3-dicyclohexylcarbodiimide (DCC) (Scheme 54).



158 **157**

Scheme 54

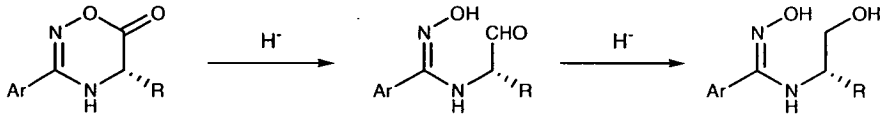
Suave *et al* have reported the formation of oxadiazinone **159** as a by-product under basic conditions whilst attempting to prepare amidoxime analogues of oligopeptides (Scheme 55).[167] they also reported that oxadiazinone formation was avoided by replacing the methyl ester with a ^{t}butyl ester.



159

Scheme 55

The most detailed study to date has been conducted by Hussein and co-workers, [129] who found that the amidoximes from addition of L-valine, L-isoleucine and L-phenylglycine to aryl nitrile oxides spontaneously cyclised in the presence of NEt_3 to the corresponding oxadiazinones. Amino acids with less bulky side chains (such as glycine) afforded only amidoxime products. Hussein *et al* also obtained small amounts of ring-opened products analogous to amidoximes **154** and **160** (Scheme 53). Further ring-opening reactions with sodium borohydride were found to yield amino alcohols via an aldehyde intermediate (Scheme 56).



Scheme 56

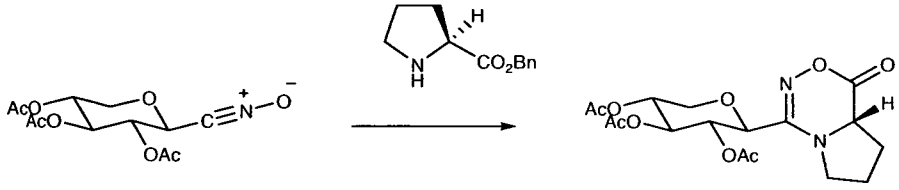
Reactions were therefore attempted to verify some of the observations made in the initial experiments, and by Hussein *et al.* [129] Addition of glycylglycine ethyl ester to D-xylose derived hydroximoyl chloride **106** under the same conditions as in the synthesis of amidoxime **152** afforded the expected amidoxime adduct **154** (43% yield). The analytical and spectroscopic data were identical to those obtained previously. The next stage of the amino acid addition study was to conduct further investigations into the cyclisation reaction.

2.4.6 Cyclisation Reactions

The glycine and L-leucine amidoximes **152** and **155** were found to cyclise (60% and 70% yields respectively) when refluxed in chloroform in the presence of silica for 6-16 hours or over 2-3 days at room temperature (Scheme 53). Hussein had indicated that addition of amino acids with bulkier substituents spontaneously cyclised. The results obtained in this study with L-leucine, however, did not fully support this observation, since amidoxime **155** was the predominant product immediately after amine addition. L-Phenylalanine ethyl ester was selected to examine further the effect of larger substituents. Addition of L-phenylalanine ethyl ester hydrochloride to hydroximoyl chloride **106** afforded exclusively the corresponding amidoxime (**161**)

immediately after addition and dry-flash chromatography. Cyclisation of **161** to oxadiazinone **162** took place when a solution of **161** in chloroform was left to stand in an NMR tube for over a month (Scheme 53), the cyclisation process was slower for pyranosyl amidoximes compared with aryl amidoximes, even when bulky side-chains were present. The NMR data for oxadiazinine **162** were similar to those observed for the previously obtained oxadiazinones.

The fact that the amino group in L-proline is *N,N*-disubstituted made it an interesting experimental candidate for two reasons. Hussein *et al*[129] had claimed that the cyclisation step was faster than potential *Z* to *E* isomerism under basic conditions. The increased tendency of disubstituted amidoximes such as morpholine derived amidoxime **143** to isomerise would challenge the above postulate. The product of L-proline addition and cyclisation would also produce the interesting fused bicyclic product **163** (Scheme 57).



163

Scheme 57

Addition of L-proline benzyl ester hydrochloride to hydroximoyl chloride **106** was conducted according to the procedure employed in the earlier amino acid additions.[13]C NMR analysis of the crude reaction mixture indicated that the major products were oxadiazinone **163** [diagnostic signals δ_C 168.7 ppm (C=O, 151.8 ppm (C=N)], benzyl alcohol and possibly small amounts of amidoxime adduct. The crude mixture was stirred in refluxing chloroform for 2 hours in the presence of silica to ensure cyclisation went to completion, and on work up, the oxadiazinone product was obtained as a white solid in 57%. The rigid ring system is believed to assist cyclisation in this case due to the Thorpe-Ingold effect.[168]

Addition of β-alanine ethyl ester hydrochloride to hydroximoyl chloride **106** was attempted in order to ascertain whether cyclisation to form a 7-membered 1,2,4-

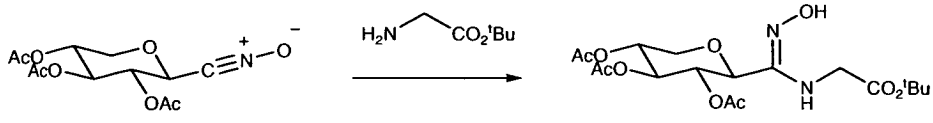
oxadiazepin-7-one would take place under the conditions previously established. The amidoxime **164** was obtained (after chromatographic purification) as a gummy solid in 50% yield (Scheme 58).

164

Scheme 58

The ^{1}H and ^{13}C NMR spectra contained diagnostic signals for the amidoxime group and showed that the ethyl ester protecting group was still present [δ_H 5.36 ppm (t, NH), 4.13 ppm (q, Et ester CH_2), 1.22 ppm (t, Et ester CH_3) δ_C 149.0 ppm (C=N), 61.1 ppm (Et ester CH_2), 14.5 ppm (Et ester CH_3)]. Amidoxime **164** was stirred with silica in refluxing chloroform for >48 hours without any cyclisation being observed on analysis by TLC, ^{1}H NMR or electrospray mass spectrometry. Cyclisation to form a 7-membered ring was found to be unfavourable under the conditions that had allowed access to the 6-membered products.

An attempt was also made to favour exclusive amidoxime formation. It was reasoned that replacing the ethyl or methyl ester protecting groups with a more sterically demanding group would suppress oxadiazinone formation.[167] ^{t}Butyl protection is frequently employed in peptide synthesis, therefore deprotection and subsequent peptide coupling would potentially allow access to chain extended amidoxime linked glycopeptide analogues.



165

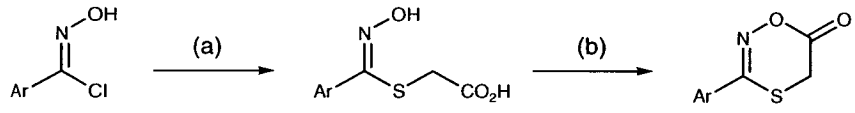
Scheme 59

Amidoxime **165** was obtained (88% yield) in a similar fashion to the original glycine addition procedure (Scheme 59).[66] The ^{1}H and ^{13}C NMR spectra were comparable to

those obtained for addition of glycine ethyl ester. Amidoxime **165** was stirred with silica in refluxing chloroform for >48 hours and the reaction monitored by NMR and electrospray mass spectrometry. No evidence was found for cyclisation having taken place, since the amidoxime imine and ^{t}butyl signals were observed in the ^{13}C NMR spectrum [δ_C 83.2 ppm (Cq) 148.9 ppm (C=N), 30.7 ppm (CH_3)].

2.4.7 Pyranosyl-1,4,2-oxathiazin-6-ones

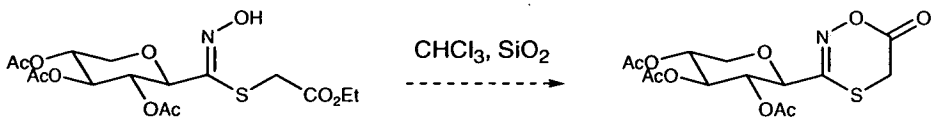
Sulfur analogues of 1,4,2-oxadiazin-6-ones are very rare, indeed, there has only been one publication related to 1,4,2-oxathiazin-6-ones.[130] Johnson and co-workers have accomplished the synthesis of such heterocycles by a two stage process; initial addition of a mercapto carboxylic acids to aromatic nitrile oxides was followed by a DCC mediated 6-exo-trig cyclisation (Scheme 60). The same researchers have also reported the synthesis of 5,6-dihydro-7-1,4,2-oxathiazepin-7-ones by a similar procedure.[131]



Scheme 60: (a) mercatoacetic acid (b) DCC, THF

2.4.8 Attempted synthesis of 3-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-1,4,2-oxathiazin-6-one

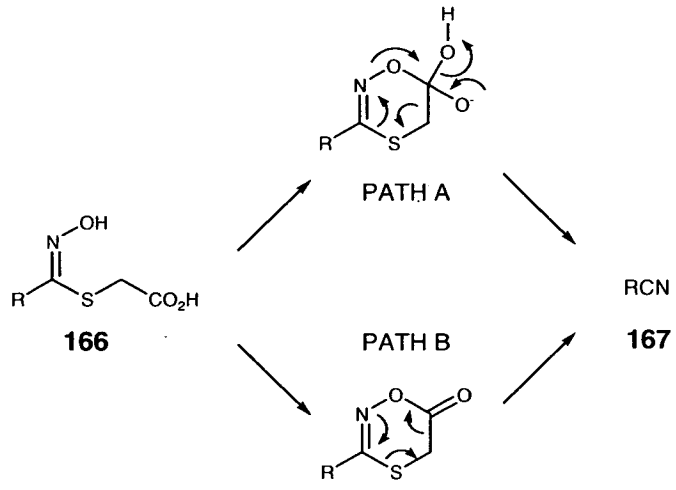
An attempt was made to synthesise pyranosyl-1,4,2-oxathiazin-6-ones from thiohydroximate **166** by the cyclisation procedure employed for pyranosyl-1,2,4-oxadiazin-6-ones.



166

Scheme 61

Thiohydroximate **166** was prepared by reacting methyl thioglycolate with xylose derived hydroximoyl chloride **106** under the conditions described in section 2.4.5. Analysis of the ^{1}H and ^{13}C NMR spectra of the purified product showed diagnostic signals for the thiohydroximate unit and side-chain in addition to the carbohydrate peaks [δ_H 9.39 ppm (bs, OH), 3.82 (1H, d, CH_2b), 3.77 (1H, d, CH_2a) δ_C 148.1 ppm (C=N), 33.3 ppm (CH_2)]. The purified thiohydroximate was stirred with silica in refluxing chloroform for more than 2 days without any cyclisation taking place, so the reaction was repeated in refluxing toluene. A white solid was obtained after dry-flash purification, however the electrospray mass spectrum indicated the mass of the product to be 285 a.m.u rather than the expected 375 a.m.u. The ^{13}C NMR showed a characteristic signal for a nitrile group [δ_C 114.2 ppm (CN)] and the compound was therefore assigned structure **167**. Formation of nitriles is known to arise from oxathiazinone rings in the presence of hydroxide ion (Path A, Scheme 62).[130] In this case, it was thought that cyclisation had taken place and then the product had undergone thermal decomposition to the nitrile (Path B, Scheme 62).[130]



Scheme 62

An attempt was also made to repeat the procedure reported by Johnson et al,[130] Mercapto acetic acid was added to xylose derived nitrile oxide and the resultant thiohydroximate treated with 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDCI). The reaction did not afford any identifiable products, extensive decomposition appeared to have taken place. The reasons for the failure of the reaction remain unclear, although it has been suggested that the stability of oxime acids such as **166** is R dependent.[130] It could be suggested that if **166** was unstable, it may decompose before cyclisation takes place.

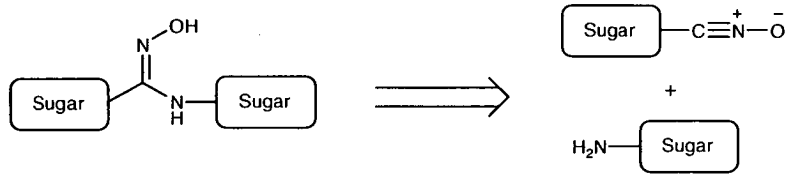
2.4.9 Conclusions/Further Work

Addition of L-cysteine derived thiol **147** to D-xylose and D-glucose nitrile oxides was found to afford novel thiohydroximate linked glycopeptides **148** and **150** in good yield (88% and 85% respectively). Reactions of glycine, L-leucine and L-phenylalanine ester hydrochlorides with hydroximoyl chloride **106** under basic conditions, were found to afford crude amidoximes **152**, **155** and **161**. Attempts to purify **152** and **155** by column chromatography led to the formation of 1,2,4-oxadiazin-6-ones **153** and **156** (60% and 70% yield respectively). Compound **161** was not found to cyclise during purification although, oxadiazinone **162** was obtained after allowing a chloroform solution of **161** to stand for 1 month. In contrast, L-proline benzyl ester hydrochloride afforded predominantly oxadiazinone

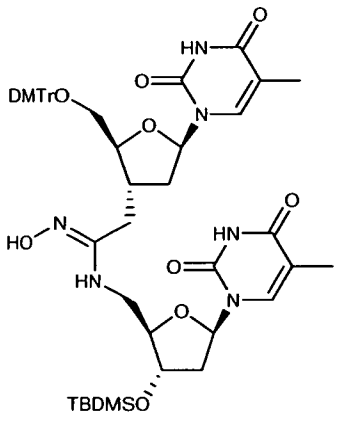
163 before column chromatography. Reaction of β-alanine and glycine ^{t}butyl ester with hydroximoyl chloride **106** in basic conditions afforded amidoximes which did not cyclise. Small amounts of by-products such as **154** were observed, these were the result of ring-opening of the oxadiazinone by residual amino acid. Further work could investigate the ring-opening reaction as a means of making chain extended amidoximes. An alternative chain extension strategy could involve deprotection of adduct **165** and employing classical peptide coupling conditions.

2.5 Additions of carbohydrate derived nucleophiles: Introduction

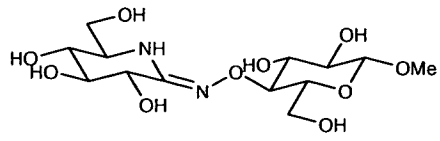
It was envisaged that sugar amines could be employed in 1,3-addition nucleophilic nucleophiles to pyranosyl nitrile oxides to afford a novel class of amidoxime-linked *C*-pseudodisaccharides (Scheme 63). There are few reports of such compounds in the literature; the closest relative known (**168**) was published by Gallos *et al*[169] as part of a study on nucleotide analogues. Oligonucleotides with a backbone that does not contain phosphorous are desirable, since they are resistant to nuclease induced cleavage and are more readily taken up by cells. Vasella *et al*[170] have prepared pyranose examples (eg **169**), which have the amidoxime unit within the carbohydrate ring, as potential glycosidase inhibitors. The Rollin group have reported the synthesis of a series of thiohydroximate-bridged disaccharides (eg **170**), as part of their work on glucosinolate analogues.[95]



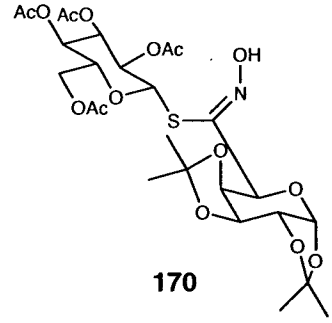
Scheme 63



168

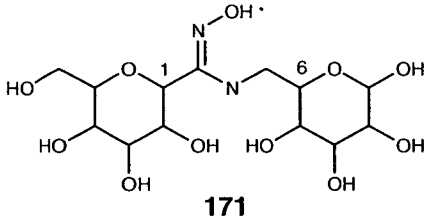


169

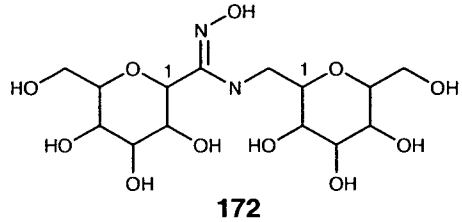


170

Although a number of sugar amines are known in the literature, it was decided to limit the initial study to amines that would result in the (1→6) and (1→1) linked compounds **171** and **172**.

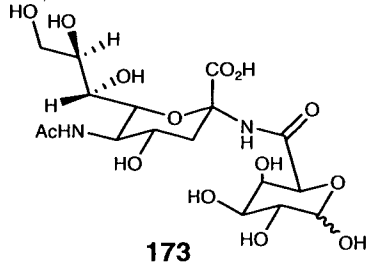


171



172

The proposed structures resemble amide-linked disaccharides. For example, **173** has been studied as a glycosyl mimic.[171] The rationale behind the use of peptide linkages is that they should be resistant to cleavage by glycosidase enzymes. Amidoximes share the same property and as a result have been exploited as amide substitutes.[169, 167, 108]

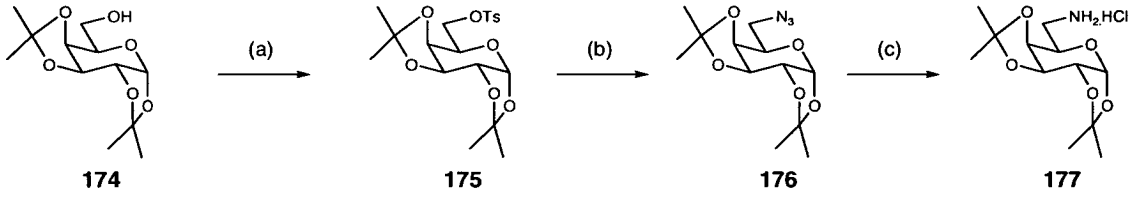


173

2.5.1 Synthesis of (1→6) amidoxime-linked pseudodisaccharides

2.5.1.1 Synthesis of 6-amino-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose Hydrochloride (177)

Galactose derived amine **177** was selected as a suitable nucleophile for addition to pyranosylnitrile oxides. Reitz *et al*[172] had reported a straightforward 3-step synthesis (Scheme 64) from 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**174**), which itself is a well-known precursor in various carbohydrate syntheses.[173]



174 **175** **176** **177**

Scheme 64: (a) TsCl, pyridine, MeCN (b) NaN_3, DMSO (c) H_2, 10% Pd/C, 50:1 EtOH/$CHCl_3$ (20 atm)

Treatment of D-galactose with acetone in the presence of acid and anhydrous $CuSO_4$ gave an oil, which on purification by Kugelrohr distillation afforded the product as a colourless glass in 61% yield. The ^1H and ^{13}C NMR spectra, mass spectra and analytical data were all in agreement with literature values.[174]

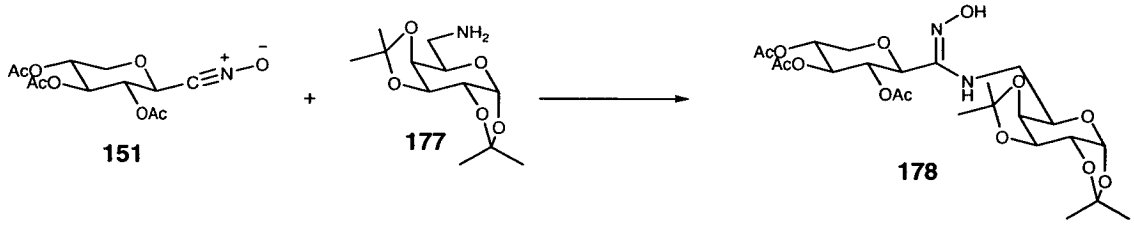
Protected galactose compound **174** was then stirred with *p*-toluenesulfonyl chloride in a 2:1 mixture of pyridine/acetonitrile at room temperature for 6 hours, and the tosylated product **175** isolated as a white solid (67% yield) following washing and trituration. The signals due to the tosyl group were clearly visible in the ^1H NMR spectrum [δ_H 2.37 (1H, s, ArCH_3), 7.73 ppm (2H, d, ArH), 7.26 ppm (2H, d, ArH)].

In the next step, the tosylated galactose derivative **175** and sodium azide were then dissolved in DMSO and heated to 115°C for 24 hours. On cooling, the reaction mixture was washed with water, before isolating the azido sugar **176** as a colourless oil (96% yield). A characteristic absorption for an azide group was observed in the IR spectrum [υ_{max} 2105 cm^{-1}].[175]

The final stage of the synthesis required hydrogenation of azido compound **176** to form the required amine **177**. The original procedure of Reitz and co-workers achieved this transformation by high-pressure (~50 psi) hydrogenation in the presence of 10% palladium on charcoal catalyst, followed by treatment with ethereal HCl to afford the amine as a hydrochloride salt.[172] A paper by Secrist and co-workers[176] had shown that addition of chloroform (~2%) to the reaction mixture allowed the amine hydrochloride salt to be formed *in situ* rather than having to add ether/HCl afterwards. This latter procedure[176] was successfully applied in this case to afford the title compound **177** as a white solid. A very broad signal was observed in the IR spectrum [υ_{max} 3377 cm^{-1}] of the product that is characteristic for amine hydrochloride salts.[175] The ^{1}H and ^{13}C NMR spectra were found to be in agreement with those obtained in the original work.[172]

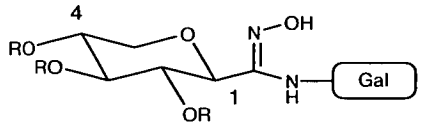
2.5.1.2 Additions of 6-amino-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (177) to pyranosylnitrile oxides

With galactose derived amine **177** in hand, it was possible to proceed with additions to pyranosylnitrile oxides. A solution of xylose derived hydroximoyl chloride **106** was added to a vigorously stirred mixture of amine **177** and triethylamine in chloroform over one hour. The reaction mixture was washed with 0.1 M HCl (to remove residual amine) before being subjected to dry-flash chromatography. The expected amidoxime **178** was obtained as a white solid (81% yield).

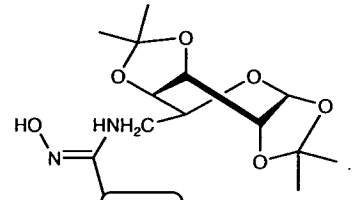


Diagnostic peaks for the amidoxime bridge were observed in the ^{1}H and ^{13}C NMR spectra [δ_H 7.76 ppm (bs, OH) 5.24 ppm (m, NH), δ_C 149 ppm (C=N)]. The ^{1}H NMR spectrum proved to be valuable for characterisation an account of conformation differences for the two carbohydrate rings giving well dispersed and characteristic

signals. The D-xylose ring adopts a $^4C_1$ chair conformation (**179**), whereas the D-galactose ring adopts a skew (twist-boat) conformation **180**, due to the presence of the isopropylidene protecting groups.[174]



179



180

The peaks attributed to the xylose ring were similar to those observed in the amidoxime examples described previously (section 2.4.1). The anomeric proton [δ_H 4.00 ppm (d, 1-H, $J_{H1\text{-}H2}$ 10.1 Hz)] showed a large axial-axial coupling, thus confirming the β-configuration of the xylose component. The remaining xylose ring protons showed the expected large vicinal axial-axial couplings to each other (*ca* 9-10 Hz), with the exception of the axial-equatorial coupling of H-4 to H-5e (equatorial) [δ_H 4.15 ppm (dd, H-5e, $J_{H5e\text{-}H4}$ 5.4 Hz)]. The peaks attributed to the galactose ring were found to have significantly different coupling patterns, since in the skew conformation the protons do not adopt formal axial and equatorial positions. The chemical shifts and coupling constants were found to compare favourably with those of literature compounds.[174] COSY and HSQC NMR experiments were conducted to confirm the identities of each of the carbohydrate ring protons. The ^{13}C NMR spectrum showed the expected 12 carbohydrate skeletal carbon peaks and signals due to the xylose and galactose protecting groups [δ_C (OAc) 170.2, 169.7, 169.3 ppm (3xC=O), (acetal) 109.3, 108.6 ppm (Cq), 25.9, 25.8 , 24.8, 24.3 (CH_3)]. The structure of amidoxime **178** was confirmed by X-ray crystallography.

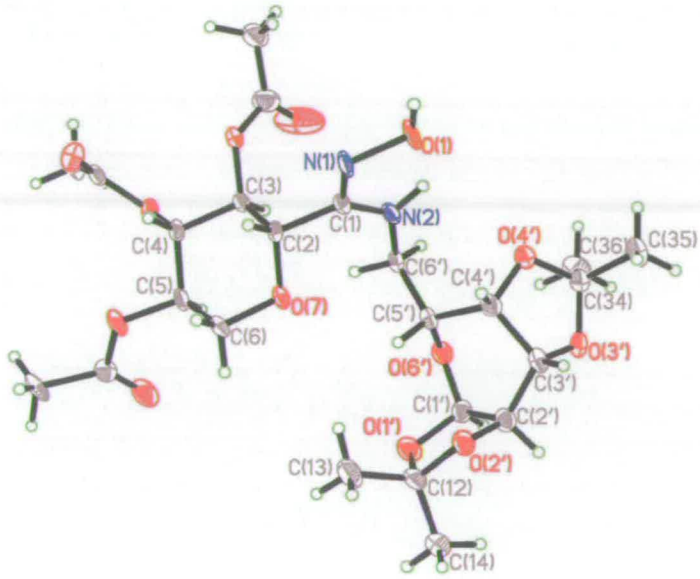


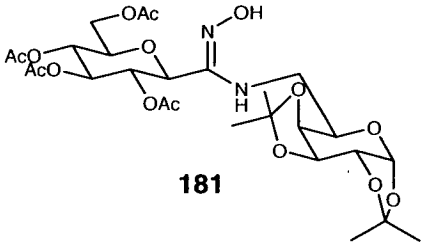
Figure 4 (Z)-*N*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranosyl)-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (**178**)

Each unit cell contained 2 molecules of **178**, one of which is illustrated in Figure 4. The structure shows that the amidoxime unit in pseudo-disaccharide **178** moiety has similar features to those of amidoxime **141**, which was discussed in section 2.4.1. The *Z*-configuration of the oxime and *s-trans* (Z_{ap}) conformation about the amidic nitrogen are again apparent. The existence of an intramolecular H-bond is again observed and is attributed to the near planarity of the NH-C=N-O unit [torsion angle 2.14°] and the short non-bonded distance between the amidic N and the oxime O [N to O = 2.531 Å]. The Cremer and Pople[177] puckering parameters for the two pyranoid rings are given in Table 7. The D-xylose ring has 95% of the puckering of an ideal cyclohexane chair conformation, with Q = 0.600 Å and θ = 5.75° compared with Q = 0.630 Å and θ = 0° for an ideal $^4C_1$ chair. The corresponding values for the D-galactose ring are Q = 0.657 Å and θ = 83.77°, and are consistent with a skew (twist-boat) conformation.

Ring	Atoms	Q / Å	θ / °	ϕ / °
D-Xylose	O(7)-C(2)-C(3)-C(4)-C(5)-C(6)	0.600	5.75	36.42
D-Galactose	O(6`)-C(1`)-C(2`)-C(3`)-C(4`)-C(5`)	0.657	83.77	326.53

Table 7. Cremer and Pople[177] puckering parameters for the pyranoid rings of amidoxime **178**

The above reaction was repeated with glucose derived nitrile oxide **115** and the expected amidoxime **181** was obtained as a white solid in 75% yield. The ^{1}H and ^{13}C NMR spectra were found to be very similar to those obtained for the xylose example **178**.

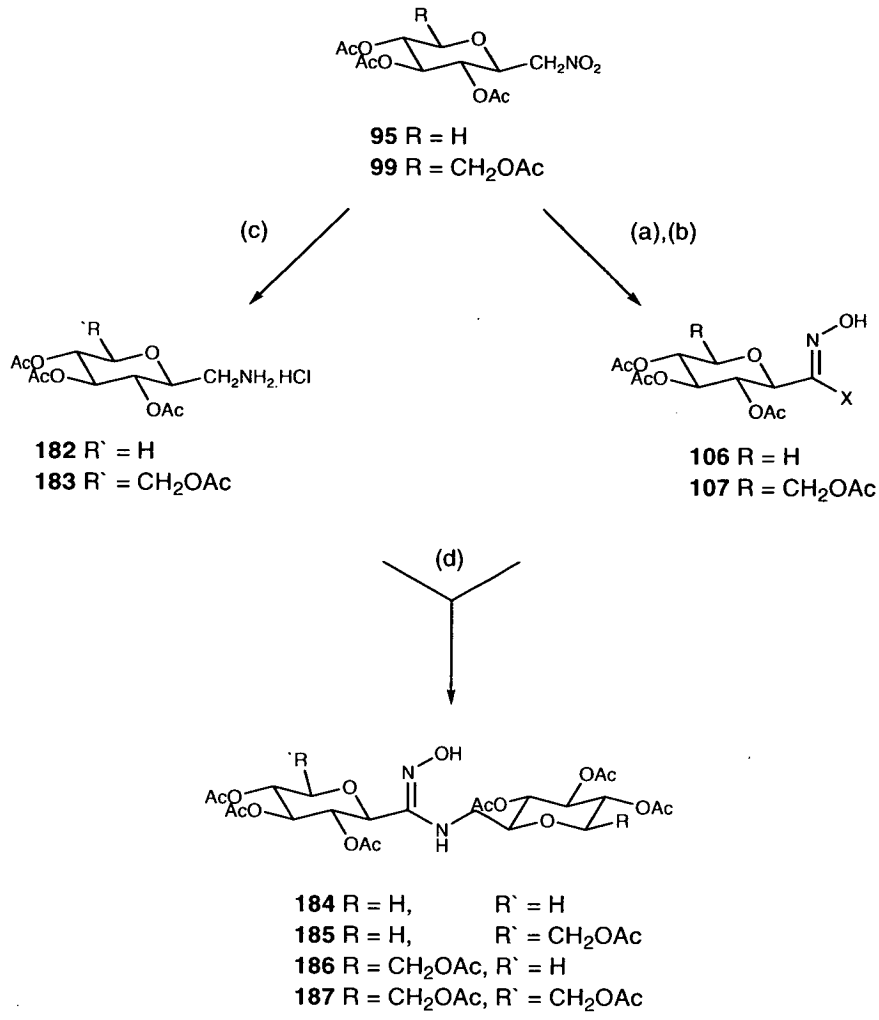


181

2.5.2 Synthesis of (1→1) amidoxime-linked pseudodisaccharides

2.5.2.1 Synthesis of D-xylose and D-glucose derived amines

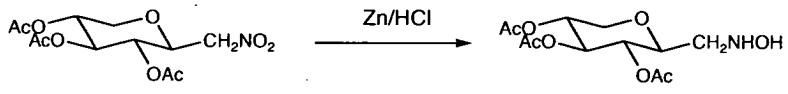
The strategy for the synthesis of (1→1) amidoxime-linked pseudodisaccharides involved a dual role for pyranosylnitromethanes **182** and **183** (Scheme 65). The nitromethyl sugars **95** and **99** were employed as sources of the corresponding amines (for previous examples[178,179]) and nitrile oxides (section 2.2). Secrist *et al*[176] reported that nitro compounds, nitriles and oximes could afford amine hydrochlorides in a similar fashion to azides.



Scheme 65: (a) $SnCl_2$, NEt_3, PhSH (b) Cl_2 (c) H_2, PtO_2, $CHCl_3$/EtOH (d) NEt_3

Nitro sugar **95** was therefore stirred with a catalytic amount of PtO_2 in ethanol/chloroform (50:1) and heated (70°C) under hydrogen (40 atmospheres) in a high-pressure hydrogenation apparatus. The amino sugar **182** was obtained as a white solid after removal of the solvent. The product was water-soluble and again a very broad amine peak was observed in the IR spectrum [υ_{max} 3367 cm^{-1}].[175] The ^{13}C NMR spectrum showed a significant chemical shift change to lower frequency of the exocyclic methylene group relative to that observed in the parent nitro compound [δ_C 40.5 ppm (RCH_2NH_2), δ_C 75.8 ppm (RCH_2NO_2)]. The reaction was found to be capricious; yields and product quality varied from batch to batch. An alternative procedure that involved stirring **95** in a mixture containing Zn/HCl was therefore attempted.[180] A white solid product was obtained, however the ^1H and ^{13}C NMR spectra were not the same as those for the product obtained by high-pressure

hydrogenation. The new compound was identified as hydroxylamine **188**, the product of partial reduction. The electrospray mass spectrum clearly showed formation of **188** (Scheme 66) since the molecular ion peak was 16 mass units heavier than the expected amine. Hydroxylamines of this kind are rare, although recent example was reported by Gross et al.[162]



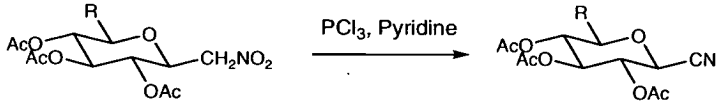
95 **188**

Scheme 66

The troublesome reactions with nitro sugar **95** led to pyranosylnitriles being examined as amine precursors instead. It should be noted that pyranosylaldoximes were not considered (despite their availability) due to the possibility of residual thiol deactivating the catalyst.

2.5.2.2 Alternative synthesis of pyranosylmethylamines

Pyranosyl nitriles are well known and may be prepared by addition of sodium cyanide to glycosyl halides[181,182] or trimethylsilyl cyanide to glycosyl acetates.[183-185] Previous work within the group has used the procedure of Köll *et al*[186] to convert pyranosylnitromethanes to the corresponding nitrile; the latter procedure was chosen for this study (Scheme 67).



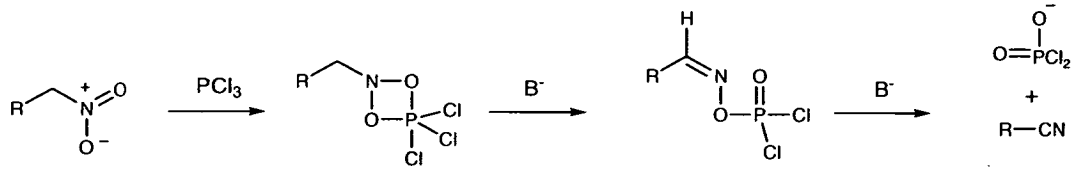
95 R = H
99 R = CH_2OAc

167 R = H
189 R = CH_2OAc

Scheme 67

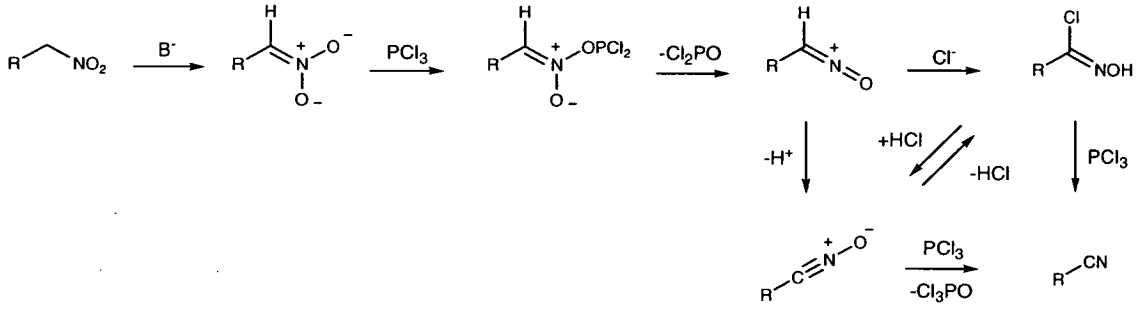
PCl_3 was added to a cooled (0°C) mixture of pyridine and 3,4,5-tri-*O*-acetyl-β-D-xylopyranosylnitromethane (**95**) and the mixture stirred for 3 days at room temperature. On work-up, the target nitrile **167** was obtained as a white solid (75% yield) after dry-flash chromatography. A diagnostic signal was observed in the ^{13}C NMR [δ_C 114.2 ppm (CN)] and analytical data were in agreement with literature.[186] The glucose derived nitrile **189** was obtained by the same procedure in 82% yield.

The procedure described above has been known for over 25 years. The mechanism was believed to proceed by the addition/elimination sequence illustrated in Scheme 68. [186]



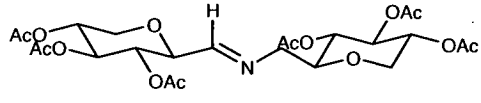
Scheme 68

This mechanism has been challenged very recently in a study by Yao and co-workers.[187] The new proposal is of particular interest since the key step involves deoxygenation of a nitrile oxide intermediate (Scheme 69).



Scheme 69

Nitriles **167** and **189** were hydrogenated under similar conditions to those employed in Section 2.5.1.1 (although lower temperatures and pressures were required) and the desired amine salts **182** and **183** were obtained in 99% and 90% yields respectively. In-situ generation of the amine as a hydrochloride salt was particularly important when nitriles were employed for two reasons; O→N-acetyl migration could possibly occur[183] and/or formation of aldimines such as **190**,[188] if free amine was formed.

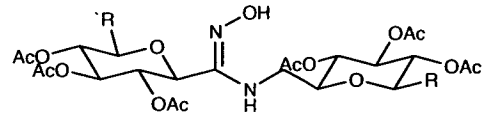


190

2.5.2.3 Additions of xylose and glucose derived amines 182 and 183 pyranosylnitrile oxides

Amines **182** and **183** were reacted with the D-xylose and D-glucose nitrile oxides **115** and **151** in the presence of triethylamine as outlined in section 2.5.1.2. All of the

four possible products were purified by dry-flash chromatography and the expected amidoximes were obtained as white solids (Table 8).



Compound	R`	R	Yield (%)
184	H	H	44
185	CH_2OAc	H	40
186	H	CH_2OAc	31
187	CH_2OAc	CH_2OAc	49

Table 8: (1→1) linked pseudodisaccharides

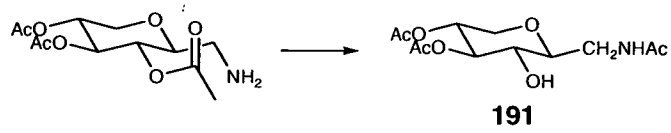
The ^1H and ^{13}C NMR spectra of the products showed characteristic signals for the amidoxime linkage; (Z)-*N*-(3,4,5-tri-*O*-acetyl-β-D-xylopyranosylmethyl)-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (**184**) serves as a typical example. The ^1H NMR spectra were expected to be more complicated than those obtained for the (1→6)-linked amidoximes since both carbohydrate rings adopted $^4C_1$ chair conformations and would probably lead to overlap of both sets of signals. A 600 MHz ^1H NMR experiment was required to obtain the required peak dispersion to achieve a full structural analysis, and D_6-DMSO was needed to get the sample to fully dissolve. Diagnostic amidoxime OH and NH signals were clearly observed [δ_H 9.97 ppm (bs, OH), 5.26-5.29 ppm (m, NH)] in the ^1H NMR. The anomeric protons [δ_H 4.27 ppm (d, 1-H, $J_{H1\text{-}H2}$ 10.1 Hz), 3.62 ppm (ddd, 2`-H, $J_{H2`\text{-}H3`}$ 9.6 Hz)] both exhibited large axial-axial coupling with the adjacent ring protons, thus confirming the β-configuration had been retained in each of the xylose components. The identities of the remaining carbohydrate ring protons were established by COSY and 2D-TOCSY ^1H NMR experiments.

The ^{13}C NMR spectrum displayed peaks associated with the acetyl protecting groups, in addition to the 12 peaks that corresponded to the carbohydrate framework. The

most diagnostic signals were those from the amidoxime unit and exo-methylene group [δ_C 147.3 ppm (C=N), 42.4 ppm (C-1`)]. Of the remaining ten signals, two corresponded, as expected, to the xylose ring methylene carbons [$\delta_C$ 65.2 ppm (C-6`), 65.1 ppm (C-5)].

2.5.2.4 By-product formation

A polar by-product was identified on analysis by TLC (R_f <0.1 EtOAc), the formation of which was belived to responsible for the lower yields (31-49%) of the (1→1) linked pseudodisaccharides. Attempts to isolate and analyse the by-product were unsuccessful, however it was thought to be compound **191** resulting from O→N acetyl migration.[183] An authentic sample of the migration product was therefore prepared by hydrogenation of nitro sugar **95** under a balloon of hydrogen in the presence of Raney nickel.[162] A colourless oil was obtained from the reaction mixture, following filtration and solvent removal. The ^1H and ^{13}C NMR spectra indicated the acetate group had migrated from the 2-hydroxyl to the amino group since signals corresponding to a hydroxyl group [δ_H 4.60 ppm (bs, OH)] and amide group were observed [δ_C 174.7 ppm (C=O)]. The IR spectrum was particularly convincing since OH and amide C=O stretching frequencies were clearly visible, in addition to a signal attributed to N-H bending. [υ_{max} 3364 cm^{-1} (OH), 1742 cm^{-1} (C=O ester), 1651 cm^{-1} (C=O amide), 1550 cm^{-1} (NH bend)].[175] Unfortunately the migration product **191** was never isolated from any of the addition reactions, although TLC analysis of reaction mixture versus the authentic migrated product indicated that migration could have occurred. Amide **191** is believed to be formed by intramolecular nucleophilic acyl substitution reaction between the amine group and the adjacent acetyl ester at C-2.

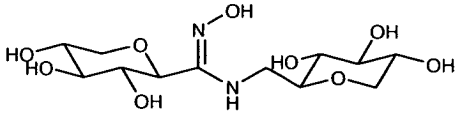


191

Scheme 70

2.5.2.5 Synthesis of deprotected (1→1) amidoxime-linked pseudodisaccharide

An attempt was made to deprotect amidoxime **184** by stirring the disaccharide in a triethylamine/methanol mixture at room temperature.[189] Analysis of the reaction mixture after two days by electrospray mass spectrometry showed that the reaction was taking place rather slowly. Peaks were observed for successive acetate loss [ES 591 (MH^+, 6Ac), 549 (MH^+, 5Ac), 507 (MH^+, 4Ac), 465 (MH^+, 3Ac), 423 (MH^+, 2Ac), 382 (MH_2^+, Ac), 340 (MH_2^+, 0Ac)] from the fully protected form, right through to the desired fully deprotected compound **192**.



192

The reaction was driven to completion within 6 hours by heating the reaction mixture to afford the product as a viscous oil (95% yield). A full analysis of **192** by ^{1}H NMR spectroscopy proved difficult since at 360 MHz all 12 ring proton signals overlapped and appeared as a large multiplet. A 600 MHz ^{1}H NMR experiment was attempted to disperse the ring proton signals, however the resultant spectrum was too broad to be of any use. The ^{1}H NMR spectra did show, however, that the acetyl groups had been removed. The ^{13}C NMR spectrum showed that the 12 expected carbons were present, the most diagnostic being those due to the amidoxime unit and the exo-methylene group [δ_C 153.7 ppm (C=N), 44.2 ppm (C-1`)].

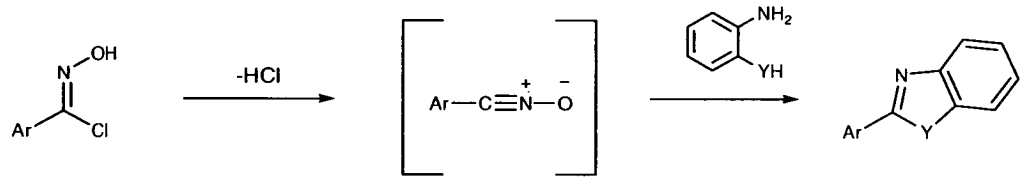
2.5.2.6 Conclusions/Further Work

Reaction of galactose amine **177** with nitrile oxides **115** and **151** under basic conditions afforded (1→6) linked pseudo-disaccharides **178** and **181** in good yield (81% and 75% respectively). Reactions of xylose and glucose amines (**182** and **183**) under similar conditions afforded (1→1) linked pseudo-disaccharides **184**, **185**, **186** and **187** (31-49% yield). The lower yields of the (1→1) linked products were attributed to the formation of **191**. Future work would be directed toward preventing formation of **191**. This could be achieved by employing benzoyl protected amines.

Deprotection of the pseudo-disaccharides would allow biological testing to be conducted, their potential function as nitric oxide donors would be of particular interest (Section 1.4.1).

2.6 Ambident nucleophile additions 2-pyranosylbenzazole synthesis

A logical extension of the work with amines was to examine the reactivity of a variety of ambident nucleophiles. A survey of the literature revealed work in this field by Sasaki *et al*,[136] and latterly by Parkanyi[190] and Risitano.[191] They reported that addition of *o*-phenylenediamine, *o*-aminophenol and *o*-aminothiophenol to aryl nitrile oxides offered a mild and high yielding method of synthesising 2-arylbenzimidazoles, benzoxazoles and benzothiazoles (Scheme 71).



Scheme 71: Y= S, O, NH

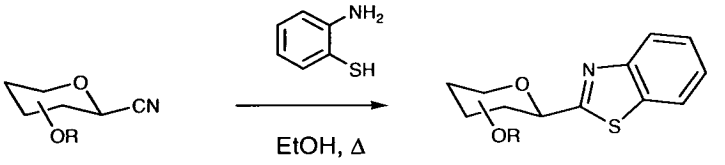
This procedure has not received great attention since there are more accessible precursors for the synthesis of 2-arylbenzazoles; typically aromatic carboxylic acids or aldehydes are employed in the synthesis of such compounds.[192-194]

It was envisaged that the Sasaki procedure might provide a convenient route to 2-pyranosylbenzothiazoles, benzimidazoles and benzoxazoles. The traditional routes are not as amenable to the synthesis of such compounds since the corresponding carboxylic acids and aldehydes are not easily accessed and/or the reaction conditions can be harsh. A brief survey of the current routes to pyranosylbenzazoles is presented below.

2.6.1 Synthesis of 2-pyranosylbenzothiazoles

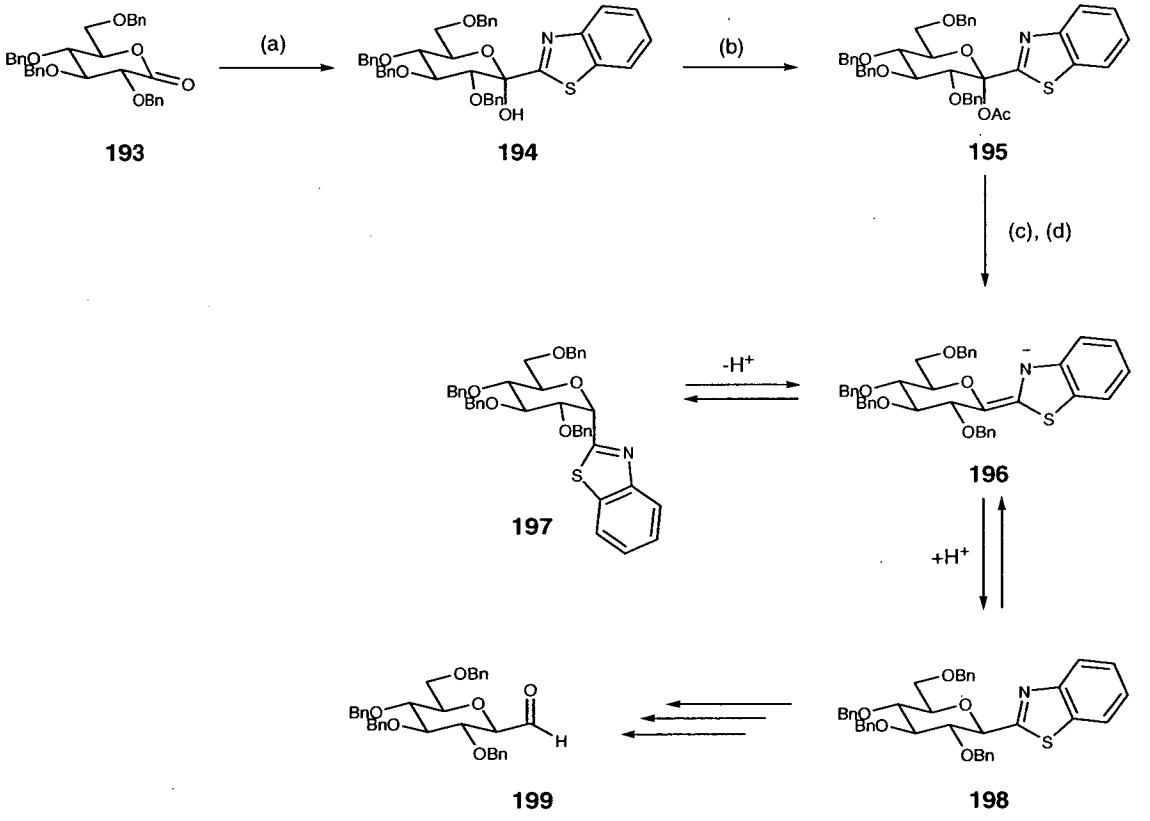
2-Pyranosylbenzothiazoles have been known for over 25 years,[195] and have received attention as β-D-galactosidase[196] and glycogen phosphorylase inhibitors.[197] There are currently two major routes to 2-pyranosylbenzothiazoles: the first procedure involves addition of *o*-aminothiophenol to 2,6-anhydro-aldononitriles and subsequent cyclisation. Farkas[195] and Somsak[198] have employed this route in the synthesis of 2-β-D- xylo, galacto, gluco, arabino and ribopyranosylbenzothiazoles. The Farkas procedure is relatively straightforward; the relevant acetylated glycosyl nitrile and 2-

aminothiophenol are heated at reflux in ethanol under a nitrogen atmosphere for 4 hours, (Scheme 72) and the products obtained by crystallisation in 57-77 % yield.[195]



Scheme 72

The second route, which was reported recently by Dondoni *et al*,[199] begins with addition of 2-lithiobenzothiazole to tetra-*O*-benzyl-D-gluconolactone (**193**) to afford a hemiacetal product **194** as a single isomer in 78% yield. Subsequent acetylation and deoxygenation leads to a 6:4 mixture of benzothiazole products (**197** and **198**); the α compound is transformed into the more stable β anomer **198** on treatment with NaOMe (80% combined yield on crystallisation).

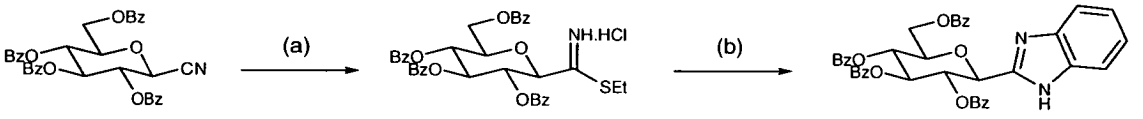


Scheme 73: (a) 2-lithiobenzothiazole, THF, -65°C (b) Ac_2O, NEt_3 (c) Et_3SiH, TMSOTf, (d) NaOMe, MeOH.

To date this procedure has not been extended to other monosaccharides. The benzothiazole may function as a masked aldehyde, on further manipulation hydrolysis of the heterocycle may be effected to afford the formyl *C*-glucoside **199** (Scheme 73).

2.6.2 Synthesis of 2-pyranosylbenzimidazoles

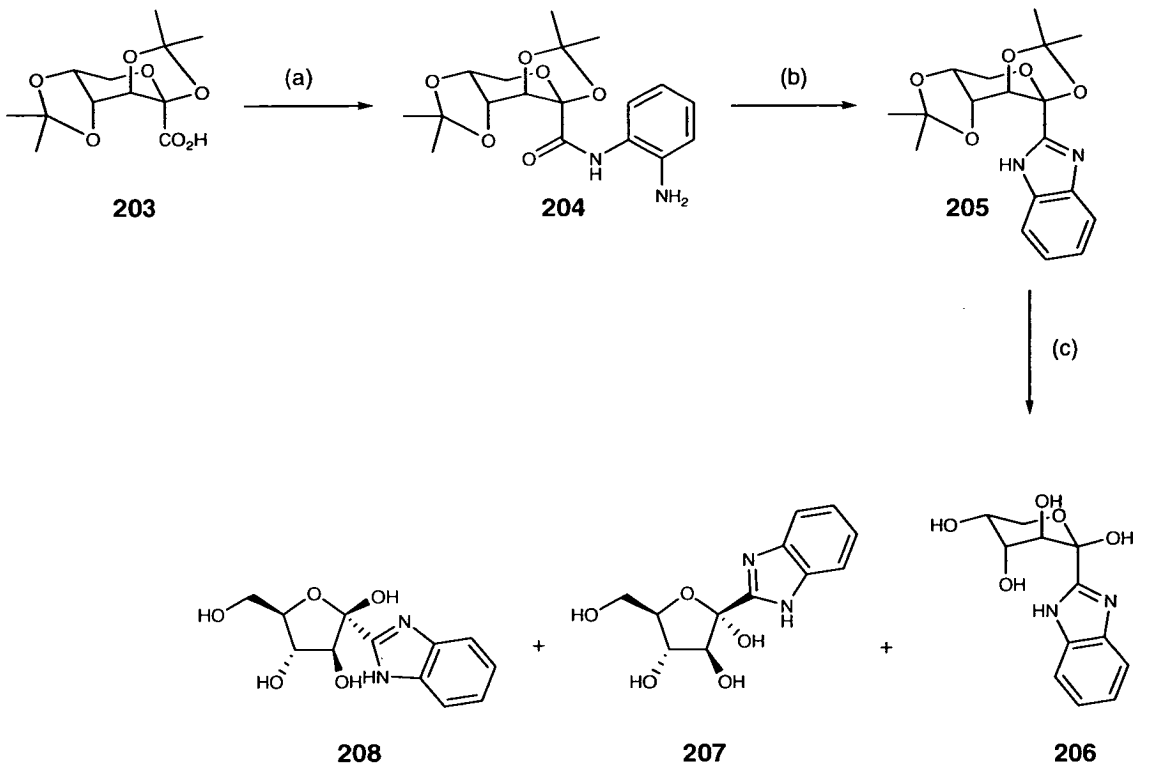
Establishing a route to 2-pyranosylbenzimidazoles has proven to be more challenging, however a recent synthesis of 2-β-D-glucopyranosylbenzimidazole has been accomplished by Somsak *et al* (Scheme 74).[197] Somsak's route requires addition of ethanethiol to nitrile **200** to afford a thioimidate intermediate **201**, which was transformed into the target **202** in a modest yield (34%) on treatment with *o*-phenylenediamine.



200 **201** **202**

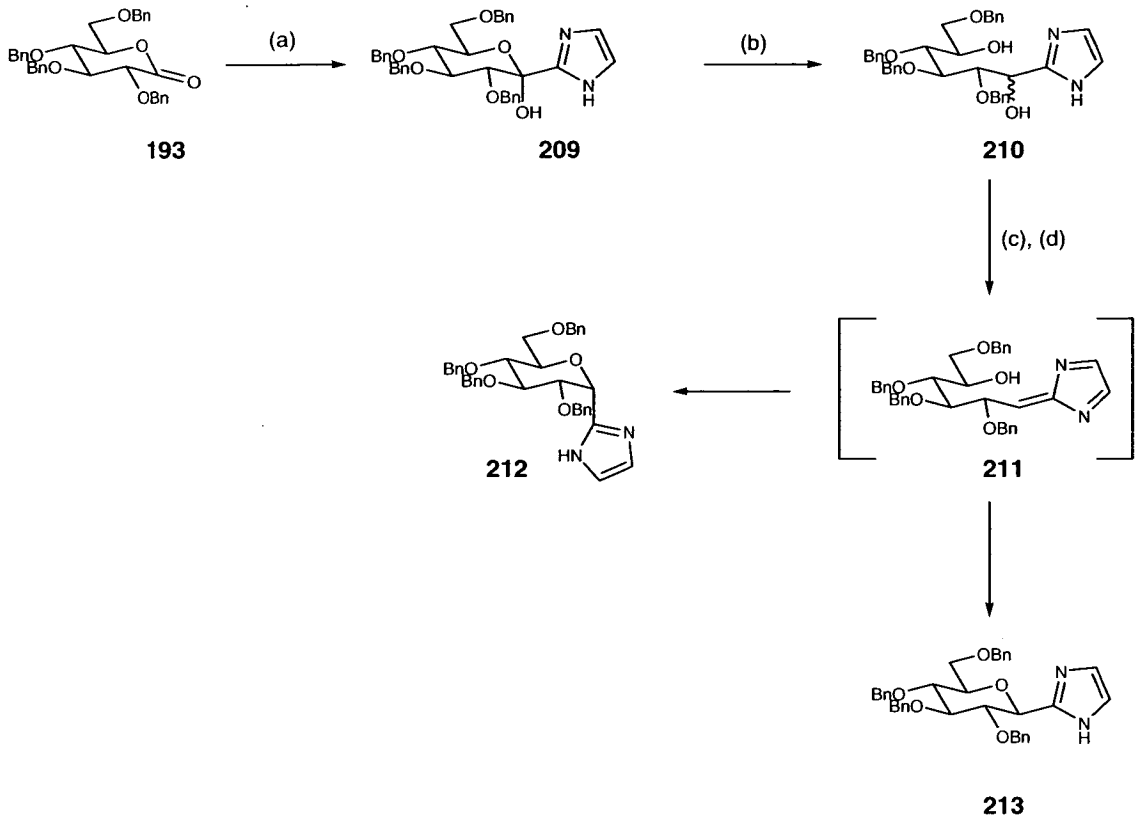
Scheme 74: (a) EtSH, Et_2O/HCl, 0°C, (b) 1,2-diaminobenzene, pyridine.

The only other route known was reported by Chapleur and Castro 25 years ago (Scheme 75).[200] Coupling of ulosonic acid derivative **203** with *o*-phenylenediamine was achieved by employing Castro's reagent. The resultant amide **204** was found to cyclise in refluxing diglyme (160°C) in the presence of Na_2CO_3 to give benzimidazole **205** in 75% yield. Acid-induced hydrolysis then afforded a mixture of furanose and pyranosebenzimidazole products **206-208**, the relative proportions of which were found to be solvent dependent.



Scheme 75: (a) 1,2-aminobenzene, $BtOP^{+}(NMe)_3.PF_6^{-}$, NEt_3 (b) Na_2CO_3, Diglyme, (c) TFA, H_2O.

2-Pyranosyimidazoles are also rare. 2-α-D-Glucopyranosylimidazole and 2-β-D-glucopyranosylimidazole have been synthesised by Vasella and Granier (Scheme 76)[201] but, to the author's knowledge, no group has attempted to employ this methodology to prepare the analogous benzimidazoles. Vasella's route is similar to that of Dondoni (scheme 73); addition of 2-lithio-1-(dimethylamino)methyl-1*H*-imidazole to tetra-*O*-benzyl-D-gluconolactone affords hemiacetal **209** (68%). Reduction of **209** formed a 12:88 mixture of diols **210** which, after chromatographic separation and dehydration, cyclised to the desired heterocyclic products **212** and **213** (80% yield).



Scheme 76: (a) BuLi, 1-(Me_2NCH_2)Im, THF (b) $NaBH_4$, dioxane, H_2O, AcOH (c) 3,5-dinitrobenzoyl chloride, pyridine (d) NaH, DMF.

2.6.3 Synthesis of 2-pyranosylbenzoxazoles

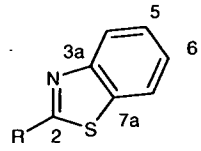
At the outset of this work, 2-pyranosylbenzoxazoles were believed to be unknown, however rare examples of furanosyl analogues had been prepared.[202] The synthesis of these compounds is outlined later, in section 2.7.1.

2.6.4 Nitrile oxide route to pyranosylbenzazoles

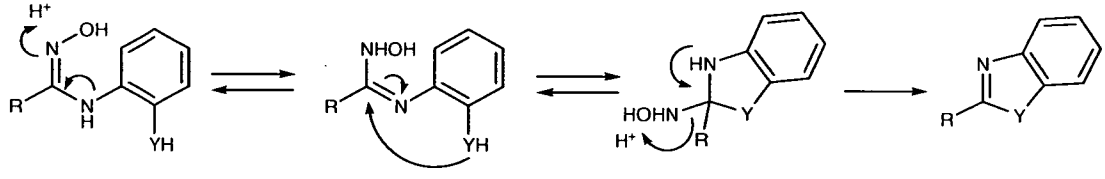
2.6.4.1 2-Pyranosylbenzothiazoles

Pilot work was conducted with D-xylose derived nitrile oxide **151**, following a procedure based on that of Sasaki *et al.*[136] Stirring the hydroximoyl chloride **106** with 2.5 equivalents of *o*-aminothiophenol in refluxing ethanol afforded 2-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)benzothiazole (**214**, 90% yield) on cooling, or after dry-flash chromatography. Distinctive NMR signals corresponding to the pyranosyl ring protons were observed. The coupling between H-1` and H-2` was found to be 9.5 Hz, which demonstrated that the expected β-anomer was obtained. Signals characteristic

for the heterocyclic ring were also observed in the ^{1}H and ^{13}C NMR spectra [δ_H 7.36-7.44 (2H, m, Ar), 7.81-7.96 (2H, m, Ar), δ_C 166.6 ppm (C-2), 152.5 ppm (C-3a), 134.7 ppm (C-7a)]. D-Glucose derived benzothiazole **215** was synthesised in a similar fashion (81% yield). The products of both reactions were found to have similar analytical and spectroscopic properties to those in the literature.[198]

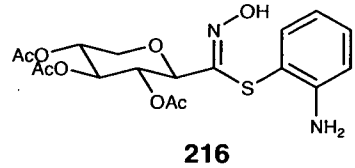


The proposed reaction mechanism is outlined in Scheme 77.[136] One equivalent of amine is believed to dehydrochlorinate the hydroximoyl chloride to form a nitrile oxide, attack by a second equivalent of amine leads to amidoxime formation, and finally this intermediate can expel hydroxylamine and cyclise to the benzazole. In the case of benzothiazole formation, the possibility of initial attack by the thiol was considered unlikely on account of previous observations by the Sasaki group,[136] presumably the neutral conditions do not allow formation of the more nucleophilic thiolate anion. Risitano *et al*[191] have isolated the postulated amidoxime intermediates when studying additions of *o*-phenylenediamine to aryl nitrile oxides.



Scheme 77

S-2-aminophenyl-2,3,4-tri-*O*-acetyl-β-D-xylopyranosylformothiohydroximate (**216**) was prepared by stirring *o*-aminothiophenol with hydroximoyl chloride **106** in the presence of triethylamine (78% yield).



216

The ^{1}H and ^{13}C NMR spectra were reminiscent of the thiophenol adduct, except for the presence of a broad singlet at 4.35 ppm due to the primary amino group. The structure of **216** was confirmed by X-ray crystallography (see Figure 5). The crystal

structure clearly displayed that the thiohydroximate moiety exclusively adopted the expected Z-configuration. Stirring the thiohydroximate in refluxing ethanol over 5 hours did not lead to any benzothiazole formation; this observation therefore also appeared to favour a mechanism involving initial attack on the nitrile oxide by the amino group.

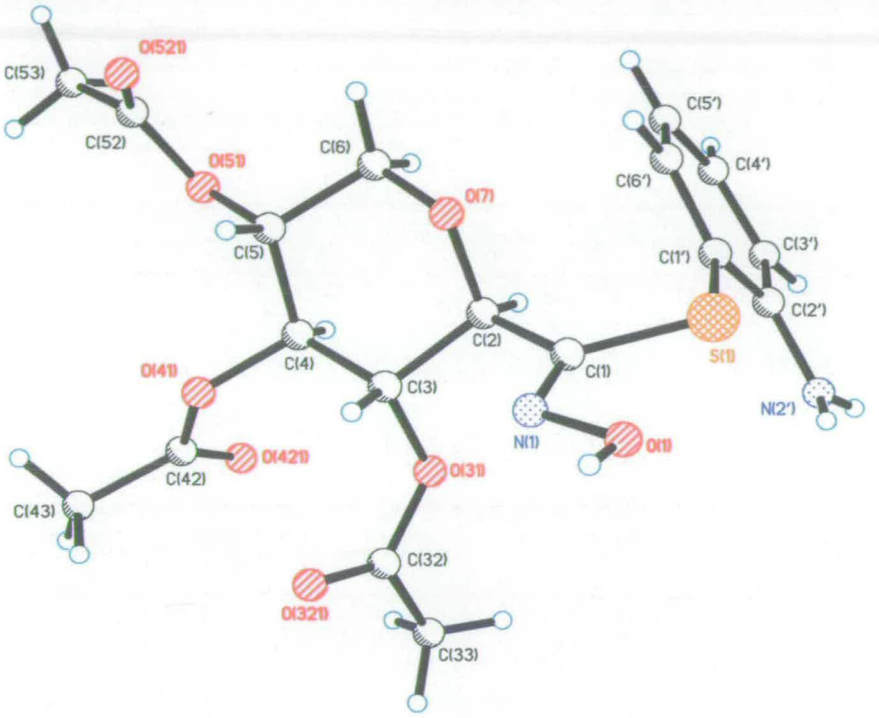


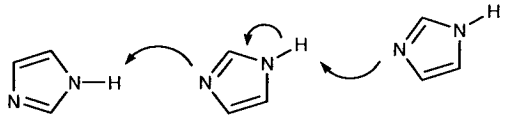
Figure 5- Crystal structure of S-2-aminophenyl-2,3,4-tri-*O*-acetyl-β-D-xylopyranosylformothiohydroximate (**216**)

The work by Sasaki[136] and Parkanyi[190] indicated that the reaction proceeded under milder conditions. For example, stirring benzohydroximoyl chloride with 2 equivalents of *o*-aminothiophenol at room temperature for 3 hours afforded the corresponding benzothiazole in 95% yield. Attempts to employ such conditions with D-xylose and D-glucose derived hydroximoyl chlorides **106** and **107** proved to be unsuccessful.

2.6.4.2 Synthesis of 2-pyranosylbenzimidazoles

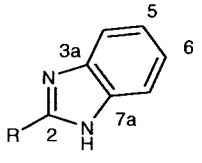
Reaction of hydroximoyl chloride **106** with *o*-phenylenediamine in refluxing ethanol in a similar manner to above (section 2.6.4.1) afforded the expected benzimidazole **217** (83% yield). Unlike the previous cases, the reaction was also found to proceed

cleanly and efficiently when the starting materials were stirred at room temperature for 12-16 hours. In pilot studies the product was separated from excess starting material by dry-flash chromatography. The original work-up was found to be tedious, but was greatly improved by diluting the reaction mixture with DCM and washing with 4% $CuSO_4$ solution. The washing step led to the formation of an insoluble lilac precipitate, which was attributed to the copper (II) ions chelating out the residual *o*-phenylenediamine. Purified material was obtained after filtration through a silica pad and crystallisation from ethylacetate/hexane. The ^{1}H and ^{13}C NMR data provided useful structural information for identification of the product, since both were simpler than those obtained for the benzothiazoles. This phenomenon was attributed to certain positions becoming magnetically equivalent due to rapid proton exchange between N-1 and N-3, Such prototropic tautomerism is well known to occur in $CDCl_3$ solutions of imidazoles and benzimidazoles (Scheme 78).[193]



Scheme 78

The ^{1}H NMR spectrum for D-xylose derived benzimidazole **217** showed a distinctive broad signal corresponding to H-4 and H-7 [δ_H 7.50 ppm (2H, vbs)], while the ^{13}C NMR spectrum showed only two major (heterocyclic) peaks (C-2 148.8 ppm, C-5,6 123.4 ppm). The remaining quaternary carbons, C-4 and C-7 gave very broad signals *c.f* 2-methylbenzimidazole. The D-glucose analogue **218** was prepared similarly (89% yield).



The structure of **217** was confirmed by X-ray crystallography (Figure 6, ethyl acetate solvent has co-crystallised).

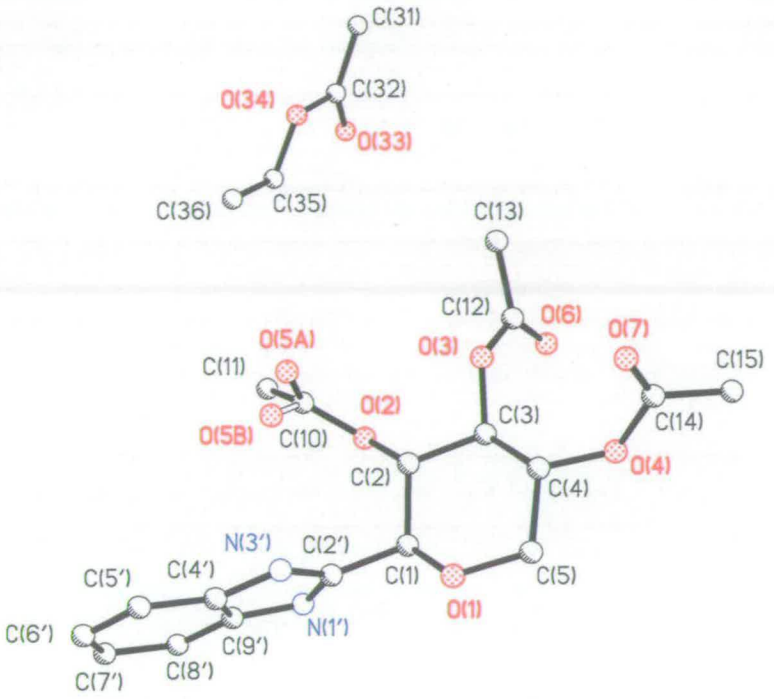


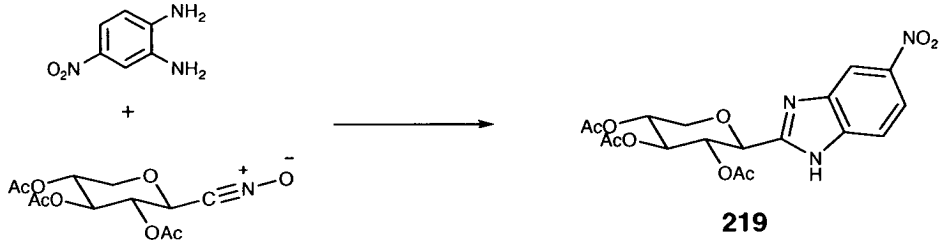
Figure 6- Crystal structure of 2-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)benzimidazole (**217**)

Selected bond lengths are compared with benzimidazole itself in Table 9.[203] All bond distances are not significantly different (within 3σ), with the exception of N1A-C9A, which is somewhat shorter than expected. This may be a direct result of the poor quality of the diffraction data. The distances quoted above were freely refined, whereas the benzene ring was constrained to be a perfect hexagon. No comparison was made with 2-methylbenzimidazole since the proton in this crystal structure is disordered over the two N atoms and this results in bond distances being averaged.

	Bond Length/ Å (**217**)	Bond Length/ Å Benzimidazole[203]
N3A-C2A	1.313(9)	1.311(5)
N3A-C4A	1.380(9)	1.395(3)
N1A-C2A	1.331(10)	1.346(4)
N1A-C9A	1.346(8)	1.372(4)

Table 9: Comparison of bond lengths in **217** and Benzimidazole

A number of substituted 1,2-diaminobenzenes are commercially available, therefore it was decided to investigate the possibility of subjecting such nucleophiles to the reaction conditions established in section 2.6.4.1. 4-Nitro-1,2-diaminobenzene was selected as a candidate due to the reduced nucleophilicity of the amino groups. It was believed that if this reaction was successful, other less electron poor nucleophiles (such as halogenated 1,2-diaminobenzenes) could be employed. Stirring hydroximoyl chloride **106** with 4-nitro-1,2-diaminobenzene in refluxing ethanol afforded crude benzimidazole **219** (Scheme 80). In this case washing the reaction mixture with 4% $CuSO_4$ solution did not efficiently chelate out the residual amine. Attempted purification by dry-flash and wet-flash chromatography was not completely successful, a red material was obtained which was estimated to be ~90% benzimidazole by ^{1}H NMR.



219

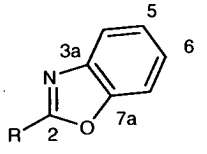
Scheme 80

The pyranosyl ring region of the ^{1}H NMR spectrum resembled those of the unsubstituted benzimidazoles although all of the ring proton signals were shifted to higher frequency. The aromatic region contained distinctive signals for each of the 3 protons on the benzo-fused component [δ_H 8.64 ppm (d, 4-H, $J_{H4\text{-}H6}$ 1.8 Hz), 8.28, (dd, 6-H, $J_{H6\text{-}H7}$ 8.8 Hz), 7.89, (d, 7-H, $J_{H4\text{-}H6}$ 1.8 Hz), 6.60 ppm (dd, H-4, $J_{H4\text{-}H5}$ 7.3 Hz, $J_{H4\text{-}H6}$ 0.6 Hz), 6.58 ppm (dd, H-9, $J_{H9\text{-}H8}$ 7.3 Hz, $J_{H9\text{-}H7}$ 0.6 Hz)]. Although the product was not fully purified, the experiment demonstrated that an electron poor 1,2-diaminobenzene would indeed react under the established conditions.

2.6.4.3 Synthesis of 2-pyranosylbenzoxazoles

The success of the previous reactions encouraged attempts to prepare the hitherto unknown 2-pyranosylbenzoxazoles. Reaction of D-xylose nitrile oxide **151** with *o*-

aminophenol in refluxing ethanol, in a similar manner to that outlined in section 2.6.4.1, afforded the expected benzoxazole **220** in 68% yield. The reaction was also found to proceed with no reduction of yield at room temperature after stirring for 16 hours. Dry-flash chromatography was avoided by diluting the reaction mixture with DCM, as the phenol was found to be insoluble in chlorinated solvents. The solid was filtered off before removing any residual *o*-aminophenol with a 0.1 M HCl wash. Purified material was obtained after filtration through a silica pad and crystallisation from ethyl acetate/hexane. Again, the D-glucose analogue **221** was prepared similarly (71% yield). Distinctive NMR signals corresponding to the pyranosyl ring protons were observed in each case. Signals characteristic for the heterocyclic ring were also observed in the ^{1}H and ^{13}C NMR spectra [δ_H 7.64-7.68 (1H, m, Ar), 7.49-7.52 (1H, m, Ar) 7.27-7.32 (2H, m, Ar), δ_C 159.9 ppm (C-2), 150.6 ppm (C-7a), 140.2 ppm (C-3a)]. The NMR data for both products were found to correlate with those found for 2-alkylbenzoxazoles.[194]



2.6.5 Deprotection studies

On completion of the peracetylated series of pyranosyl heterocycles, it was decided to investigate deprotection of **217**, **218** and **220**. Many conditions are available for deprotection: The classic Zemplen method (NaOMe/MeOH) was considered too harsh[204] and methanolic ammonia was regarded as being inconvenient.[204] Milder conditions were ultimately employed. Treatment of the acetylated substrates with triethylamine in methanol,[189] or (as recently reported by Field *et al*[205]) 4Å molecular sieves in methanol, allowed efficient deprotection in all cases (refer to Table 11, section 2.6.7). The latter conditions were found to achieve deprotection more rapidly.

NMR spectra were obtained in D_2O and D_3COD, however d_6-DMSO was found to give superior resolution. The ^{1}H and ^{13}C spectra of deprotected benzoxazole **222** were not significantly different from the acetylated precursors, although coupling was observed between the pyranosyl ring protons and the ring OHs ($J_{H\text{-}OH}$ 5.0-5.9

Hz) and hence more complex coupling patterns than expected were observed for the ring protons. The ^{1}H and ^{13}C spectra of the deprotected benzimidazoles **223** and **224**, however, were markedly different from their acetylated derivatives, The D-glucose derived product **224** serves as a convenient example. The ^{1}H NMR spectrum no longer showed H-4 and H-7 as broad signals and the ^{13}C NMR contained individual signals for the aromatic CHs and quaternary carbons. The NMR data indicated that proton exchange between N-1 and N-3 had been limited in DMSO and hence any previously magnetically/chemically atoms were no longer so. The structure of **224** was confirmed by X-ray crystallography (Figure 7).

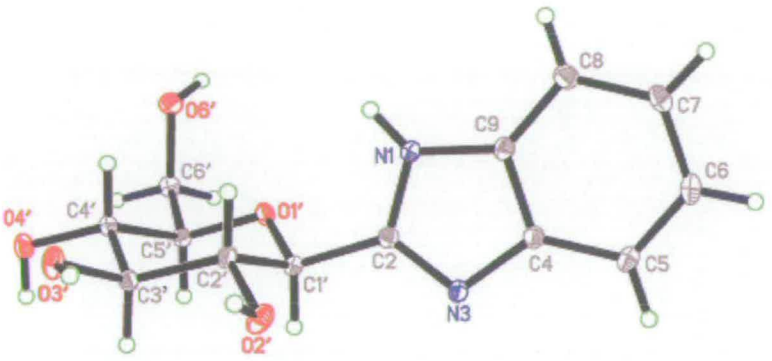


Figure 7- Crystal structure of 2-β-D-glucopyranosylbenzimidazole (**224**)

Selected bond lengths for compound **224** are compared with benzimidazole in Table 10. The bond lengths were found to be in good agreement with those of benzimidazole (within 3σ).

	Bond Length/ Å (**224**)	Bond Length/ Å Benzimidazole
N3A-C2A	1.314(2)	1.311(5)
N3A-C4A	1.395(2)	1.395(3)
N1A-C2A	1.360(2)	1.346(4)
N1A-C9A	1.384(2)	1.372(4)

Table 10: Comparison of bond lengths in **224** and benzimidazole

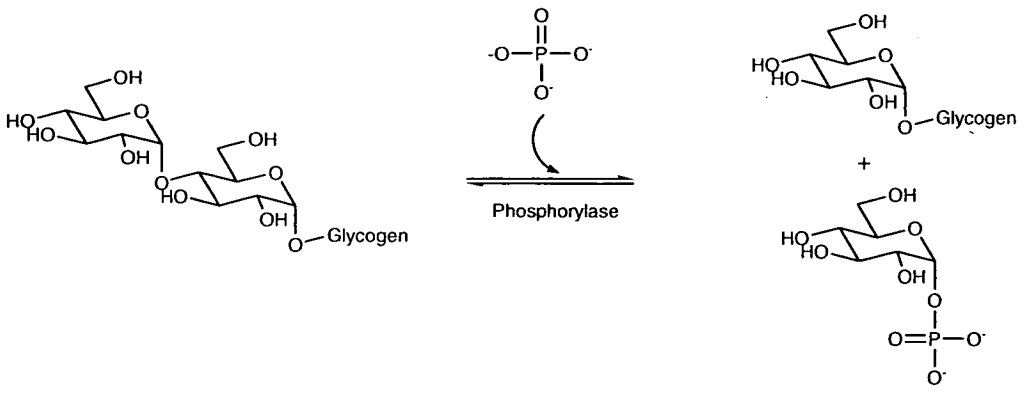
As in the benzoxazoles case, coupling was observed between the pyranosyl ring protons and the OHs ($J_{H\text{-}OH}$ 5-5.9 Hz) and again the ring protons gave rise to more complex splitting patterns. A COSY ^{1}H NMR experiment allowed a full assignment of the spectrum.

2.6.6 Biological activity

During the course of the project, 2-β-D-glucopyranosylbenzimidazole was reported to inhibit glycogen phosphorylase (K_i 8.6 μM).[197] This enzyme is currently a target for hypoglycemic drugs to treat impaired insulin production (type 2 diabetes). The function of glycogen phosphorylase is outlined below.

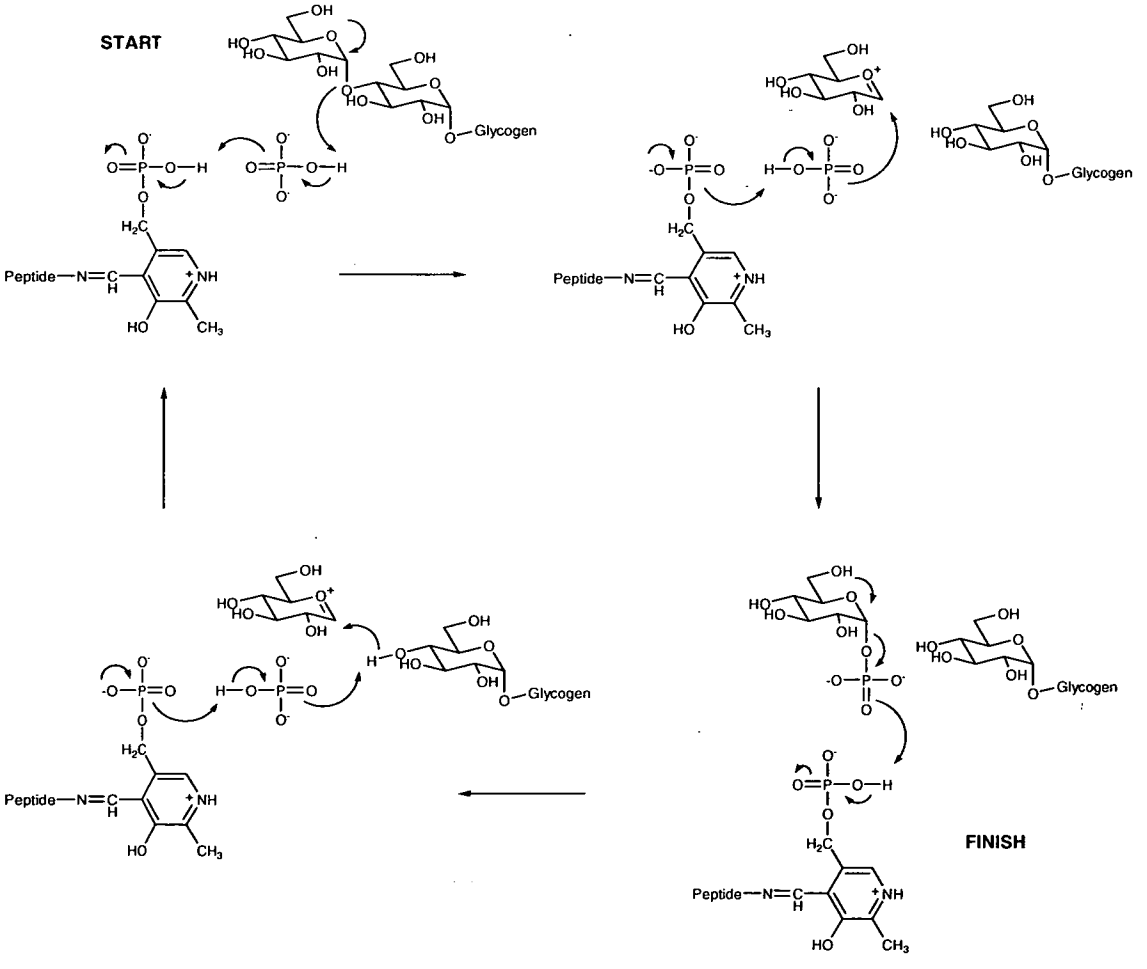
2.6.6 Glycogen phosphorylase function

Glycogen phosphorylase (GP) catalyses the breakdown of glycogen to glucose-1-phosphate (Glc-1-P) (glycogenolysis), the process is illustrated in scheme 80.[206]



Scheme 80

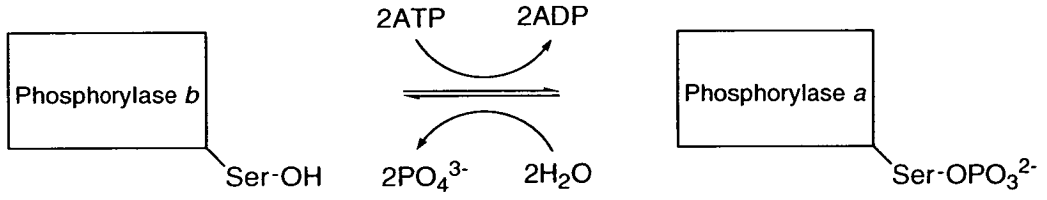
The mechanism of phospholytic cleavage of glycogen has been established by Helmreich and co-workers (Scheme 81).[207] Pyridoxal phosphate is believed to function as an acid/base catalyst for orthophosphate, orthophosphate donates a proton to the departing "OR" group and then attacks the glucosyl cation to form α-glucose-1-phosphate.



Scheme 81

As indicated in Schemes 80 and 81, the process is reversible, as the glycogen 4-OH can displace the Glc-1-P phosphate group to reform chain extended glycogen.

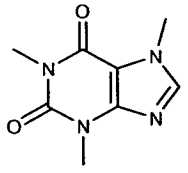
Glycogen phosphorylase exists in two forms, Phosphorylase *b* is usually inactive and Phosphorylase *a* is active. Phosphorylase *b* is transformed into the *a* form by phosphorylation of the serine 14-residue on each subunit (Scheme 82).[206,208]



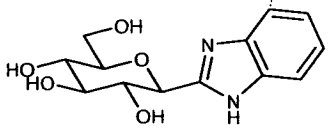
Scheme 82

Both Phosphorylase *a* and *b* are structurally different, *a* exists in an R-state (relaxed) while *b* exists in a T-state (tense). The glycogen binding site is 30 Å from the catalytic site, they are connected by a tunnel, which is blocked in the T state.[206] Molecules that would stabilise the inactive T-form of GP*b*, and thus inhibit glycogenolysis, have become drug targets for controlling blood glucose levels.

The presence of glucose and caffeine (**225**) are known to favour the inactive form, with glucose binding to the active site and caffeine to a site nearby.[209] Analogues of glucose and caffeine have therefore been investigated as GP inhibitors.[209] Adenosine mono phosphate (AMP) is a known allosteric activator of GP, and as a result inhibitors of AMP have also received attention.[209,210] In the last five years new allosteric sites have been identified through X-ray studies with novel inhibitors, and these sites offer potentially new drug targets.[209,210]



225



224

An X-ray crystal structure of a 2-β-D-glucopyranosylbenzimidazole/enzyme complex has demonstrated that this inhibitor primarily binds to the catalytic site.[211]

Binding was also found to take place at the indole/caffeine site and a previously unknown binding site, but it is unclear whether this new site will be of interest as a future drug target.

2.6.7 Conclusions/Further Work

2-β-D-Pyranosyl benzoxazoles, benzimidazoles and benzothiazoles have been synthesised in good yields (Table 11). The key addition/cyclisation reaction proceeds under mild and neutral conditions, which do not necessitate resilient protecting groups and chromatographic purification is largely avoided. Pilot experiments have indicated that substituted benzazoles could also be accessible by this methodology. Addition of halogenated *o*-hydroxy, thio or amino anilines could afford benzazoles which could be manipulated further using Pd(II) chemistry.

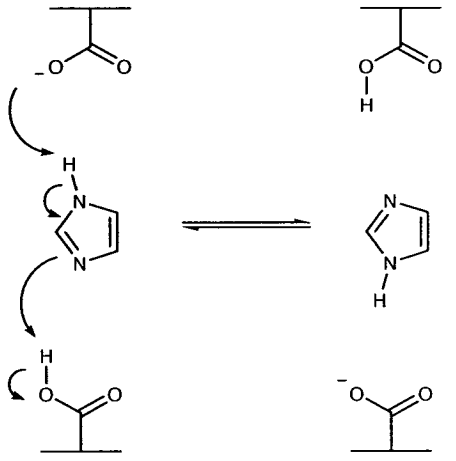
Hydroximoyl Chloride	X	R	Y	Yield %
214	H	Ac	S	90
215	CH_2OAc	Ac	S	81
217	H	Ac	NH	88
218	CH_2OAc	Ac	NH	85
220	H	Ac	O	68
221	CH_2OAc	Ac	O	71
222	H	H	O	92
223	H	H	NH	93
224	CH_2OH	H	NH	95

Table 11: Summary of Benzazole Results

2.6.7.1 Potential glycosidase inhibition

The Vasella group have synthesised 2-β-D-glucopyranosylimidazole (**213**) (see section 2.6.2),[201] and found that this compound inhibits sweet almond glucosidase (K_i 640μM). Glycosidase inhibitors have many therapeutic applications, including: antiviral activity,[212] anticancer activity,[213] treatment of diabetes,[214] treatment of

obesity,[215] amongst others. The mode of action of retaining-β-*O*-glycosidases was outlined in section 2.6.1. Imidazoles such as **213** are believed to inhibit glycosidases by shuttling a proton between the glutamate residues in the glycosidase catalytic site (Scheme 83), thus preventing entry and binding of the substrate.[170] In principle, there is no reason why 2-β-D-glucopyranosylbenzimidazole or derivatives could not be employed in a similar capacity.



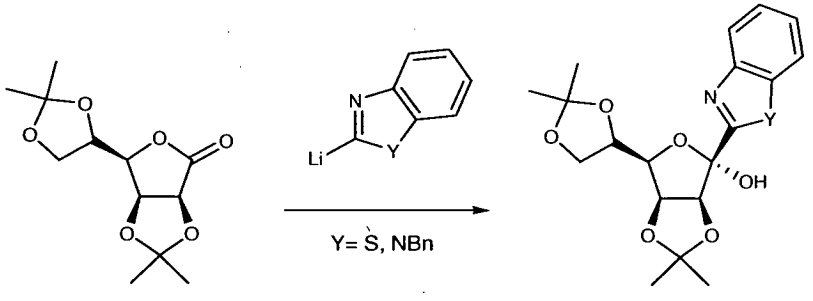
Scheme 83

2.7 Ambident nucleophile additions 2-furanosylbenzazole synthesis

Whilst investigating 2-pyranosylbenzazole chemistry, it was realised that the same methodology could be applied to the synthesis of furanosyl analogues. Such *C*-nucleoside analogues are of great interest, particularly in the design of antiviral compounds.[216,217] 2-Furanosylbenzimidazoles, benzoxazoles, and benzothiazoles have been the subject of a recent patent, held by Celltech,[218] who report them to be potential therapeutic agents for cystic fibrosis. A brief overview of the available methods for making 2-β-furanosylbenzazoles is provided below.

2.7.1 Synthesis of 2-furanosylbenzazoles

Early research in this area examined additions of *o*-substituted anilines to aldonic acids,[219] such procedures required harsh conditions (reflux in the presence of mineral acids), which could result in anomeric mixtures of products. Addition of lithiated heterocycles to sugar lactones featured in section 2.6.1 in syntheses of 2-pyranosylbenzazoles, and the most successful approaches to furanosyl analogues also employ this method. Early work by Ogura and Takahashi[220] examined addition of lithiobenzothiazole and 1-benzylbenzimidazole to lactones such as the D-gulose derived compound **226** (Scheme 84). The heterocyclic unit in resultant hemiacetals **227** was found to occupy the β-position (40-70%). Disappointingly, however, attempts to remove the anomeric OH group with trimethylammonium formate proved to be unsuccessful.

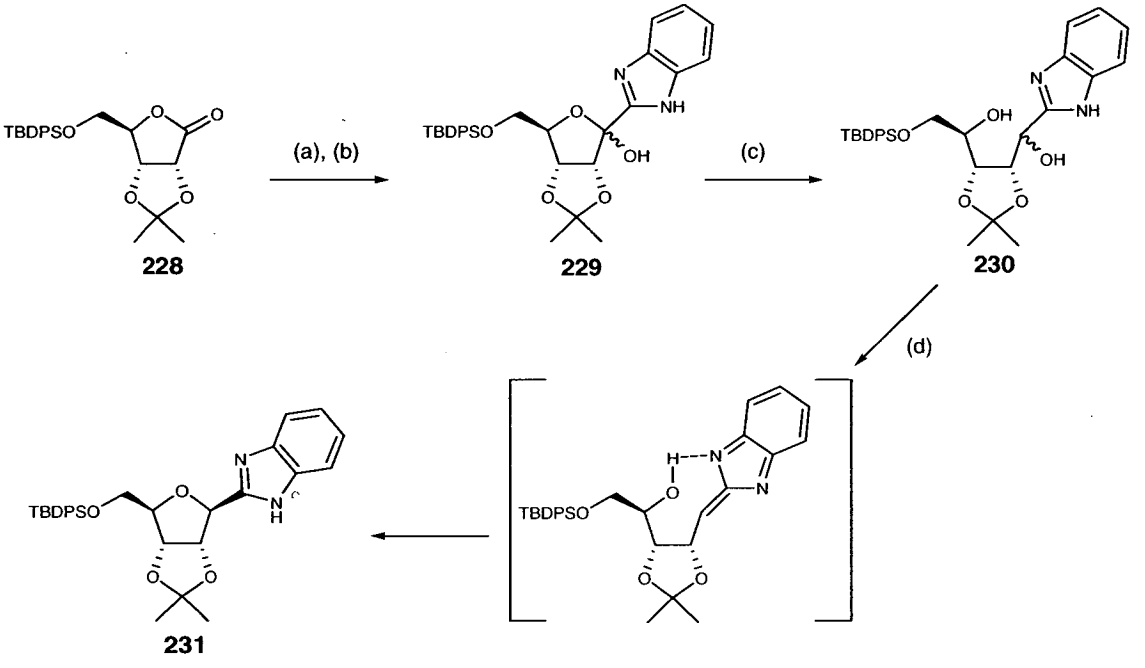


226 **227**

Scheme 84

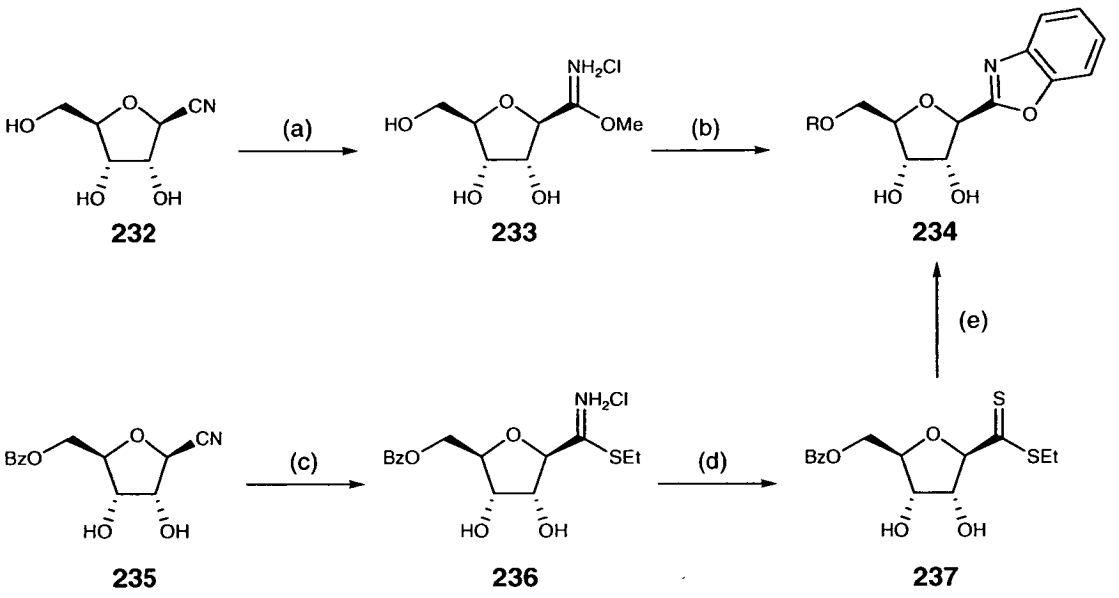
Ogura's methodology has been revisited in recent years by Benhida et al (Scheme 85).[221, 222] The initial stage in the updated method still features addition of a lithiated heterocycle to a furanosyl lactone, however the anomeric OH is removed by a successive reduction / Mitsunobu cyclisation strategy. Addition of benzyloxymethyl

(BOM) protected 2-lithiobenzimidazole to ribose derived-lactone **228** afforded hemiacetal **229** in 75% yield as a mixture of anomers (45:55). Subsequent hydrogenation and borohydride reduction afforded a diastereomeric mixture (~1/1 ratio) of diols **230**, which was converted to 2-β-D-ribofuranosyl derivative **231**, in 90% yield, by a stereocontrolled Mitsunobu type cyclisation.



Scheme 85: (a) NBOM benzimidazole, LDA, THF, -50°C (b) H_2 (60 psi), Pd/C, MeOH, THF (c) $NaBH_4$, MeOH (d) DEAD, PPh_3, MeOH.

2-α-D-Ribofuranosylbenzimidazoles have also been made by this method. Performing a Felkin-Ahn controlled borohydride reduction before heterocycle deprotection afforded a diastereomeric mixture of diols, where the *S* diol (C*) was the major product (95:5, *S*:*R*). Ring-closure was achieved in a similar fashion. There have been no reports to date that employ Benhida's procedure to prepare benzothiazole or benzoxazole derivatives.



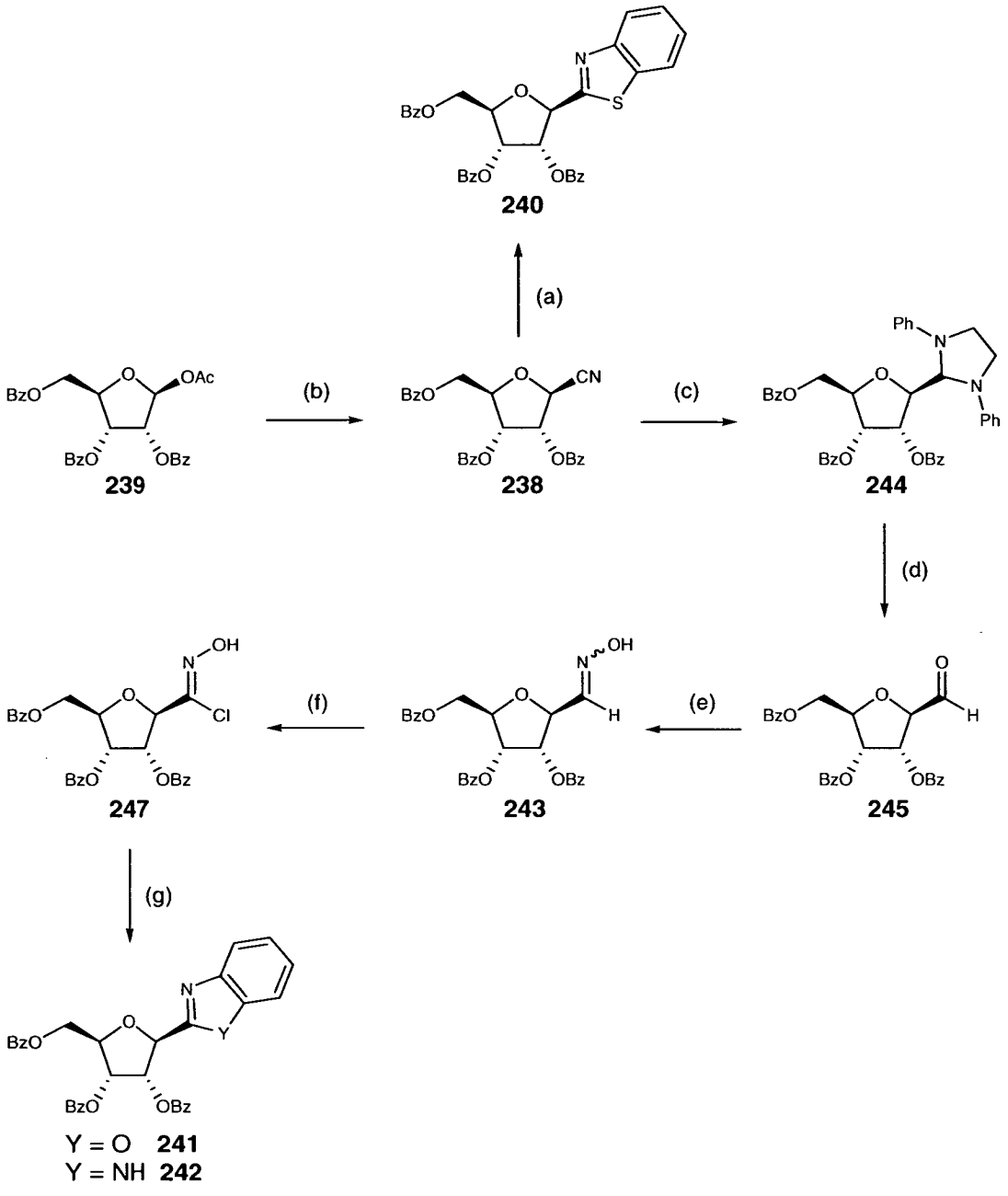
Scheme 86: (a) NaOMe (b) o-aminophenol, MeOH (c) EtSH, HCl (d) H_2S, pyridine (e) o-aminophenol, EtOH.

It was stated in section 2.6.3 that furanosylbenzazoles were rare. The only synthesis reported until recently, was achieved by Kawai and El Khadem (Scheme 86).[202] β-D-Ribofuranosyl cyanide **232** was converted to acetimidate **233**, which was found to be highly hygroscopic and therefore required handling in a glove box. Refluxing **233** and *o*-aminophenol in methanol for 2 hours afforded benzoxazole **234** in 20% yield. A second approach was attempted based on dithioate intermediate **237**. Refluxing dithioate **237** with *o*-aminophenol in ethanol for 36 hours afforded benzoxazole **234** in 24% yield. The low yields, careful handling and toxic reagents associated with the above procedures probably account for the limited use of this process.

2.7.2 Nitrile oxide based strategy

The first route examined the preparation of 2-β-D-ribofuranosylbenzazoles (Scheme 87). The key difference between the strategy to be employed for the ribose-derived benzazoles and that for pyranose derivatives, was the use of a nitrile precursor, rather than a nitromethyl sugar. This decision was made since previous work within the group,[223] and by others,[224] had found the preparation of nitromethylribose in large quantities to be arduous and low yielding. In contrast, the ribose derived nitrile **238**

was well known[184,185,225-230] and readily accessible from commercially available **239** (Scheme 87).



Scheme 87: (a) *o*-aminothiophenol, EtOH (b) TMSCN, $BF_3.Et_2O$,MeCN (c) $PhNHCH_2CH_2NHPh$, Raney Ni, NaH_2PO_2, pyridine/AcOH/H_2O (d) TsOH (e) NH_2OH. HCl, pyridine (f) Cl_2 (f) Y=NH, *o*-phenylenediamine; EtOH, Y=O, *o*-aminophenol.

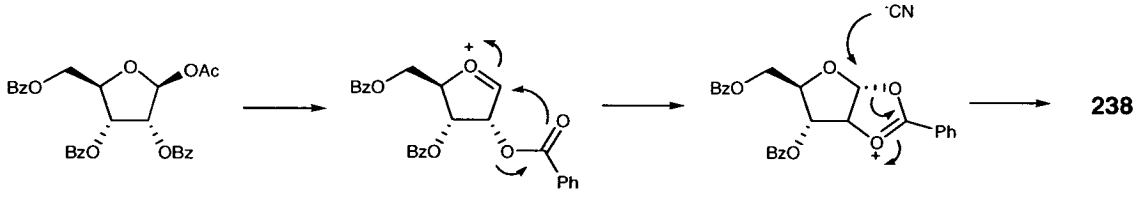
The proposed strategy was also believed to be particularly advantageous over previous strategies because all three possible β-D-ribofuranosylbenzazoles could be

made from the same starting material. The benzothiazole **240** could be accessed from nitrile **238** directly *via* the previously mentioned procedure of Farkas and co-workers.[195] The focus of the current work was to prepare the benzoxazole **241** and benzimidazole **242** by the nitrile oxide methodology (section 87).

2.7.2.1 Ribose Nitrile Oxide Precursors

2.7.2.2 Synthesis of 3,4,5-tri-*O*-benzoyl-β-D-ribofuranosyl cyanide (238)

A survey of the literature revealed many methods for the preparation of the title compound,[184,185,225-230] The method of Morelli *et al*[225] is representative and was ultimately chosen. β-D-Ribofuranosyl acetate **239** was reacted with trimethylsilyl cyanide (TMSCN) in the presence of catalytic boron trifluoride etherate to afford an amber solution after 5 minutes. The reaction mixture was quenched with aqueous $NaHCO_3$ and the target nitrile isolated in 86% yield after wet-flash chromatography. The reaction was found to proceed without reduction of yield when attempted on a gram scale. The ^1H NMR spectrum was in agreement with the literature[225] and the ^{13}C NMR spectrum showed characteristic signals [δ_C 115.6 ppm (C≡N)]. The reaction is stereospecific for the required β-configured product, an effect attributed to neighbouring group participation of the benzoyl ester at C-2 (scheme 88).[185]



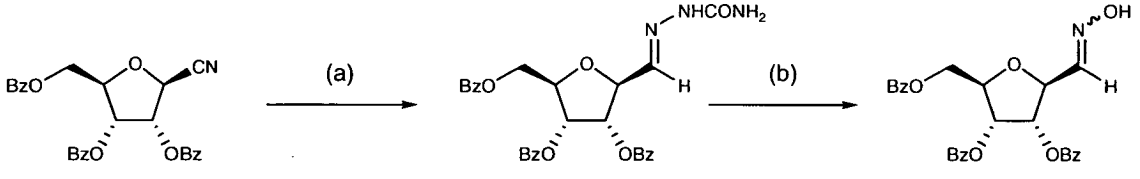
Scheme 88

2.7.2.3 Synthesis of 2,5-anhydro-3,4,6-tri-*O*-benzoyl-β-D-allose oxime (243)

Some years ago Moffat and co-workers reported a three-step synthesis of the title compound **243** from nitrile **238**.[231] The first step involved conversion of the nitrile to imidazoline **244**, which on treatment with *p*-toluenesulfonic acid afforded formyl-*C*-furanoside **245**. Crude **245** was reacted with hydroxylamine hydrochloride to obtain the required oxime. A modified version of Moffat's procedure was employed in the current synthesis. 3,4,5-Tri-*O*-benzoyl-β-D-ribofuranosyl cyanide was stirred with

Raney nickel, *N,N*-diphenylethylenediamine (Wanzlick's reagent) and sodium hypophosphite in aqueous acetic acid and pyridine. Imidazoline **244** was isolated in 59% yield after wet-flash chromatography. The separation between the product and diamine proved to be very small by TLC (ΔR_f = ~0.025, 30% EtOAc in hexane), which made purification more difficult than expected. In addition to the expected signals for the carbohydrate ring and its benzoyl protecting groups and the imidazoline *N*-phenyls, peaks corresponding to the imidazoline moiety itself were observed [δ_C 48.0 ppm (NCH_2), 48.4 ppm (NCH_2), 84.2 ppm (C-2), δ_H 3.62-3.77 ppm (2H, m, NCH_2), 3.81-3.96 ppm (2H, m, NCH_2), 5.97 ppm (1H, s, 2-H)]. The signal for H-2 appears as a singlet, an observation consistent with the product being obtained as the β-anomer. Treatment of imidazoline **244** with *p*-toluenesulfonic acid afforded crude aldehyde **245**, which was immediately reacted with hydroxylamine hydrochloride and pyridine. The title compound (45% yield) was finally obtained as a 4:1 mixture of isomers (*E*:*Z*) after purification by dry-flash chromatography. Diagnostic peaks for the oxime unit were seen in the NMR spectra [δ_C 148.3 ppm (C=N), δ_H), 8.88 ppm, bs (OH) (*E*)),], and the analytical data were consistent with literature values.[142]

Although the required oxime **243** was obtained, the procedure was not considered satisfactory if larger scale syntheses were to be accomplished. Particular concerns included: the final yields of oxime and imidazoline were lower than expected, extensive chromatographic purification was required, and it was thought desirable to avoid the aldehyde intermediate if possible. The previously mentioned Somsak/Toth procedure[151] (section 2.2.2) for pyranosylaldoxime synthesis offered a viable alternative to that described above.



238 **246** **243**

Scheme 89: (a) semicarbazide.HCl, KOH, Raney Ni, NaH_2PO_2, pyridine/AcOH/H_2O (b) NH_2OH. HCl, pyridine

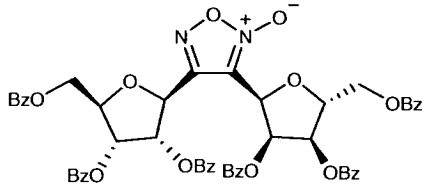
The alternative procedure is essentially a modified version of that reported by Moffat *et al.*[231] Somsak demonstrated[151] that sugar nitriles could be converted under reducing conditions into semicarbazones by reaction with semicarbazide and that these semicarbazones were found to efficiently undergo transimination with hydroxylamine to afford the corresponding aldoximes. Crucially, the aldehyde formation step is avoided and it was hoped that crude semicarbazone **246** could be employed in the final step and hence eliminate tedious purification steps. A mixture of 3,4,5-tri-*O*-benzoyl-β-D-ribofuranosyl cyanide (**238**) Raney nickel, semicarbazide hydrochloride, KOH, sodium hypophosphite in aqueous acetic acid and pyridine was heated to 40 °C for 4 hours. The reaction mixture was washed successively with 1 M HCl, saturated $NaHCO_3$ and water before isolating the crude semicarbazone as a light brown solid. Diagnostic peaks for the semicarbazone unit were seen in the NMR spectra [δ_C 157.4 ppm (C=O), 138.6 ppm (C=N) δ_H), 9.85 ppm, bs, (OH), 7.13 ppm, d, (C<u>H</u>=N), $J_{H1\text{-}H2}$ 5.2 Hz]. The crude material was taken on to the next step immediately. Hydroxylamine hydrochloride was added to a solution of crude semicarbazone in acetonitrile / pyridine and the reaction stirred at room temperature under argon for 16 hours. Purification by wet-flash chromatography afforded the title compound as a colourless oil (81% yield). The NMR data and physical properties were identical to those obtained previously by the original route. The second procedure was judged to be the more suitable of the two and allowed attempts to prepare ribose-derived hydroximoyl chloride **247**.

2.7.2.4 Attempted synthesis of ribose derived hydroximoyl chloride (247)

It was envisaged that the procedures outlined in section 2.2.3 for the synthesis of pyranosylhydroximoyl chlorides would also be suitable for the required ribofuranose analogue. It was known that Moffat *et al* [142] had used a similar procedure in the preparation of **247** toward the synthesis of β-D-ribofuranosylisoxazoles. Repeated chlorinations were conducted in the manner described previously, but were disappointingly only partly successful. The ^1H and ^{13}C NMR spectra of the product were more complex than expected, indicating that more than one species was present after chlorination. Peaks corresponding to hydroximoyl chloride **247** could be

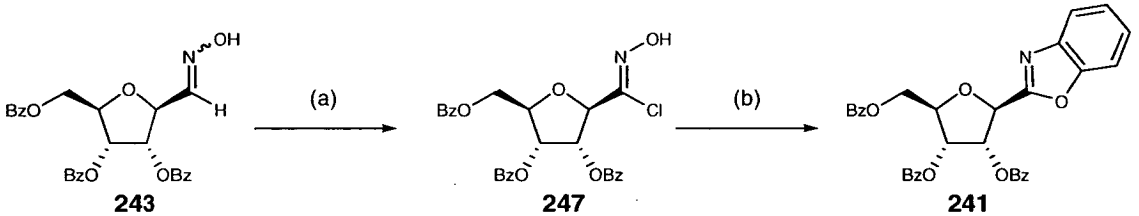
identified [δ_C 137.2 ppm (C=N), δ_H 9.81 ppm, bs, (OH)], however they appeared to make up the minor component of the mixture. The identity of the other substance remains unclear.

A milder chlorination procedure employing *N*-chlorosuccinimide [33] was attempted in order to avoid by-product formation. A pilot reaction with the aim of making the furoxan dimer **248** was employed to establish the usefulness of the new conditions. A mixture of oxime **243**, *N*-chlorosuccinimide and pyridine in chloroform was heated to 40°C for *ca* 45 minutes. On cooling, triethylamine was added and the mixture stirred for 1 hour. Dry-flash chromatography afforded furoxan **248** as a colourless gum (107 mg, 72%). The formation of furoxan in high yield was a good indication that the NCS method was the better way of obtaining the desired nitrile oxide precursor **247**. The newer method also had the advantage of being a one-pot procedure.



248

2.7.2.5 Synthesis of 2-(2,3,5-Tri-*O*-benzoyl-β-D-ribopyranosyl)benzoxazole (241)



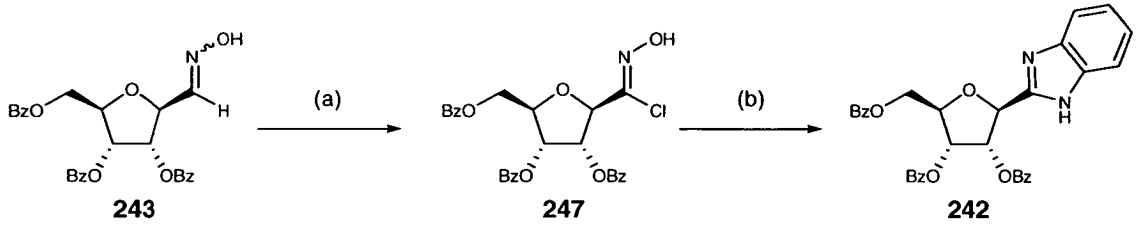
243 **247** **241**

Scheme 90: (a) NCS, pyridine (b) *o*-aminophenol, EtOH

A mixture of oxime **243**, *N*-chlorosuccinimide and pyridine in chloroform was heated to 40°C for *ca* 45 minutes and, after cooling, the solvent was removed *in vacuo*. A solution of the resulting hydroximoyl chloride and *o*-aminophenol in ethanol was heated at reflux for 5 hours. The reaction mixture was washed with 1 M

HCl before dry-flash chromatography afforded **241** as a colourless gum (92% yield). Diagnostic peaks corresponding to the benzoxazole moiety were observed in the ^{13}C NMR spectra [δ_C 162.5 ppm (C-2), 152.0 ppm (C-7a), 141.7 ppm (C-3a)].

2.7.2.6 Synthesis of 2-(2,3,5-Tri-*O*-benzoyl-β-D-ribopyranosyl)benzimidazole (242)

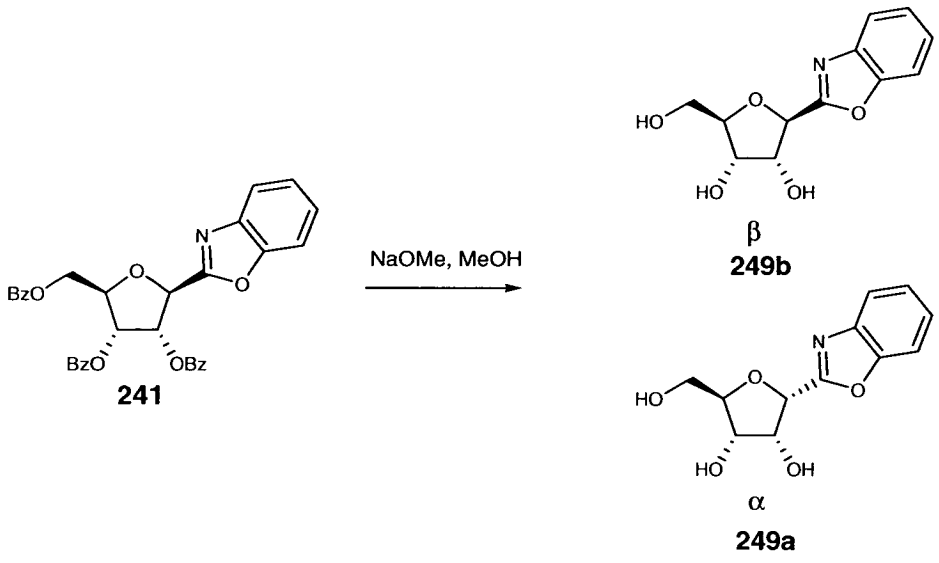


243 **247** **242**

Scheme 91: (a) NCS, pyridine (b) *o*-phenylenediamine, EtOH

A mixture of oxime **243**, *N*-chlorosuccinimide and pyridine in chloroform was heated to 40°C for *ca* 45 minutes. On cooling, the solvent was removed *in vacuo*. The residue and *o*-phenylenediamine were refluxed in ethanol for 5 hours. The reaction mixture was washed with 4% $CuSO_4$ solution before dry-flash chromatography afforded **242** as a colourless gum (90% yield). The ^1H and ^{13}C NMR spectra showed a distinctive benzimidazole signals that were reminiscent of the pyranosyl analogues [δ_H 7.90-7.94 ppm (2H, m), 7.23-7.27 ppm (2H, m)], while the ^{13}C NMR showed only two major peaks [δ_C 151.3 ppm (C-2), 123.2 ppm C-5, C-6)]. Tautomerism of the benzimidazole ring led the C-4 and C-7 signals being broadened out in an analogous fashion to the pyranosylbenzimidazoles in section 2.6.4.2.

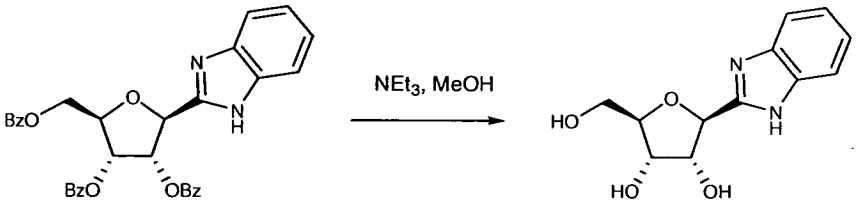
2.7.2.7 Deprotection of 2-(2,3,5-Tri-*O*-benzoyl-β-D-ribopyranosyl)benzoxazole (241)



Scheme 92

Studies were conducted to establish efficient deprotection conditions. Benzoate esters are known to be more resilient than their acetyl counterparts,[204] therefore Zemplen deprotection of 2-(2,3,5-tri-*O*-benzoyl-β-D-ribopyranosyl)benzoxazole (**241**) with methanolic sodium methoxide was attempted.[204] The benzoxazole was stirred in freshly prepared sodium methoxide/methanol solution for 16 hours. The reaction was quenched with Amberlite 120(H^+) resin before purification by wet-flash chromatography. The product was obtained as a mixture of anomers. A COSY ^1H NMR experiment allowed the carbohydrate ring protons for both isomers to be identified. The most distinctive signals for each were the anomeric [δ_H 4.47 ppm, d, (1-Hβ), 5.08 ppm, d, (1-Hα)] protons, which were assigned α (**249a**) and β (**249b**) by comparison with analogous compounds in the literature.[221] The anomeric integrals were measured and hence the isomer ratio calculated (β:α, 62:38). The aromatic protons were observed as a large set of multiplets between 6.92 and 7.67 ppm. The conditions used were evidently too harsh, therefore milder conditions were sought. Time precluded any further work with the benzoxazoles, consequently the remaining stock of benzimidazole **242** was used for further deprotection reactions.

2.7.2.8 Deprotection of 2-(2,3,5-Tri-*O*-benzoyl-β-D-ribopyranosyl)benzimidazole (242)



242 **250**

Scheme 93

Stocks of benzimidazole **242** were limited and it was therefore impossible to investigate the effect on anomeric ratio by diluting the NaOMe solution or shortening the reaction time. It was therefore decided to employ the milder method of Bazin *et al.*[189] Benzimidazole **242** was dissolved in triethylamine and methanol, and heated to 50°C for 4 days. After removal of the solvent and wet-flash chromatography, 2-β-D-ribofuranosylbenzimidazole (**250**) was obtained as a white foam (91% yield). The ^{1}H NMR spectrum showed diagnostic peaks for the benimidazole ring [δ_H 7.07-7.10 ppm (2H, m), 7.35-7.41 ppm (2H, m)] in addition to the expected carbohydrate ring signals. A comparison with literature ^{1}H NMR values[231] was made in order to confirm that the β-anomer had indeed been prepared (Table 12). None of the α-isomer was detected in the crude reaction mixture.

	δ_H (ppm)	$J_{1'\text{-}2'}$ (Hz)
Literature α[231]	5.21	8.0
Literature β[231]	5.06	5.0
250	4.92	5.3

Table 12 Comparison of literature δ_H / *J* values with benzimidazole **250**

The benzimidazole ring signals in the ^{13}C NMR spectrum [δ_C 152.9 ppm (C-2), 123.2 ppm C-5, C-6)] were reminiscent of the protected compound **242**; a very broad signal *ca* 115 ppm was attributed to C-4 and C-7.

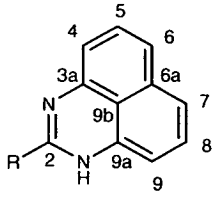
2.7.3 Conclusions/Further Work

A revised route to D-ribose derived hydroximoyl chloride **247** has been established. Reaction of nitrile **238** with semicarbazide afforded crude semicarbazone **246** in ~85% yield and was transformed to oxime **243** by treatment with hydroxylamine hydrochloride. Hydroximoyl chloride **247** was initially prepared by chlorination, however the reaction was unsatisfactory due to formation of an unidentified by-product. Treatment of **243** with NCS was found to afford crude hydroximoyl chloride in almost quantitative yield. Reaction of D-ribose derived nitrile oxide **92** with *o*-phenylenediamine and *o*-aminophenol afforded benzimidazole **242** and benzoxazole **241** in 90% and 92% yield respectively. An attempt to deprotect **241** under Zemplen conditions led to a 62:38 mixture of 2-β-D-ribofuranosylbenzoxazole (**249b**) and 2-α-D-ribofuranosylbenzoxazole (**249a**). 2-β-D-Ribofuranosylbenzimidazole (**250**) was prepared in 91% yield by reacting **242** under mild conditions. The products obtained in this section are *C*-nucleoside analogues and may therefore be of interest as anti-viral agents, The established route offers a mild and stereocontrolled approach to future candidates for the treatment of cystic fibrosis.

2.8 Perimidine chemistry

2.8.1 Introduction

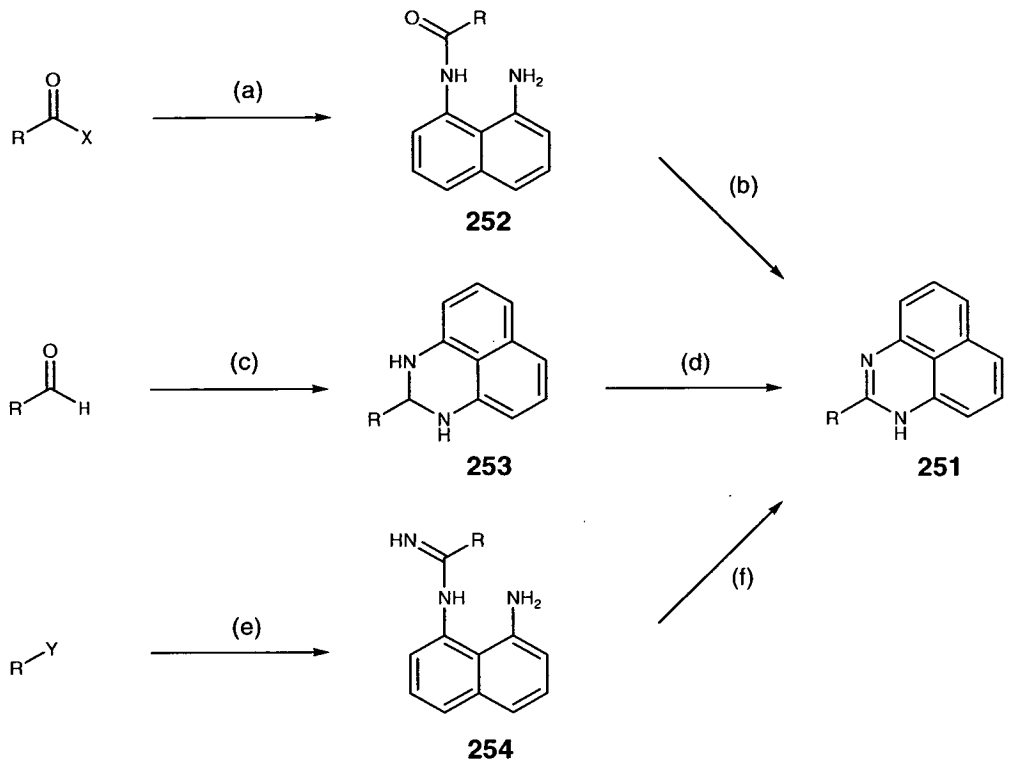
Perimidines (**251**) are *peri*-naptho-fused derivatives of pyrimidine. The chemistry of perimidines has been already been reviewed[232-234] and therefore only a brief overview of their synthesis and applications is presented here.



251

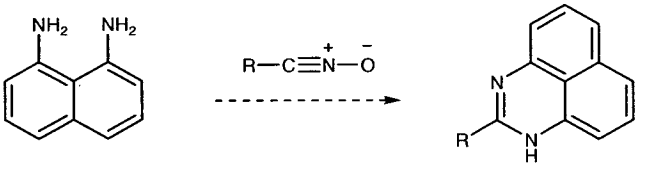
Perimidines and their derivatives have found a variety of applications; they have been used in dyestuffs[232-234] for many years and more recently in the manufacture of polyester fibres[232-234] and antistatics.[235] The biological activity of perimidines and their derivatives have also been examined; they are believed to intercalate DNA, and have therefore been tested as antitumor agents.[236,237] They have also been found to possess antiulcer, antimicrobial and antifungal activity.[232-234]

A range of substituents have been installed at the 2-position of perimidines; these include alkyl, aryl and heterocyclic groups. In contrast, no report of a pyranosyl substituted perimidine has been made to date. The majority of the methods of 2-perimidine (**251**) synthesis use 1,8-diaminonaphthalene (DAN) as the starting material, the most common routes are outlined in (Scheme 94).[232-234] Addition of DAN to carboxylic acid derivatives leads to amide intermediates (**252**), which cyclise in refluxing acid (4 M HCl or formic acid for example). The corresponding reaction with aldehydes affords 2,3-dihydroperimidine products (**253**), oxidation of which yield the desired 2-perimidine. Milder conditions[232] have been developed which involve cyclisation of amidine intermediates (**254**).



Scheme 94: (a) [X = halide, OR, COR, OH] 1,8-diaminonapthalene (b) H^+ reflux (c) 1,8-DAN (d) Pd/C or DDQ (e) [Y = CN, HN=COR, HN=CNH_2] DAN (f) H^+.

The rigid nature of 1,8-diaminonapthalene confers a reactivity similar to that of *o*-phenylenediamine,[232] and it was therefore proposed that addition of DAN to nitrile oxides would provide a new and mild method of constructing 2-perimidines (Scheme 95).

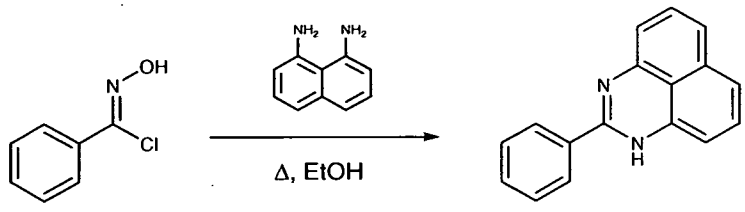


Scheme 95

2.8.2 Pilot studies

As 2-phenylperimidine had previously been synthesised and fully characterised,[238] it was chosen as a target for pilot work. Benzohydroximoyl chloride (**255**), the precursor for benzonitrile oxide (**93**), was prepared by passing chlorine gas through a chloroform solution of syn-benzaldoxime.[143] The product was obtained as a white solid in 74% yield. The procedure that had been successfully applied to benzazoles

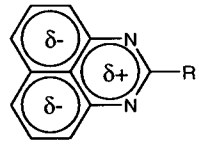
was employed in the attempted perimidine synthesis. A mixture of benzohydroximoyl chloride (**255**) and DAN was stirred in refluxing ethanol for 5 hours, before washing the reaction mixture with 4% $CuSO_4$ solution. The washing procedure was found to work well, although the resultant mixture required more extensive purification by comparison with the benzimidazole syntheses. 2-Phenylperimidine (**256**) was obtained in 68% yield as an orange crystalline solid.



255 **256**

Scheme 96

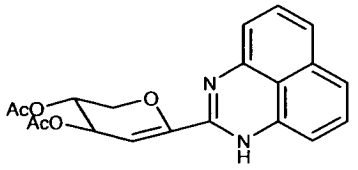
The ^1H NMR spectrum and analytical data agreed with those in the literature.[238] The coloured nature of the product is also consistent with the perimidine ring being present, and the electronic structure of the heterocycle. Perimidines have 14π-electrons delocalised over 13 atoms,[232-234] the electron density is not uniform and this results in an electron deficient heterocyclic ring and an electron rich napthalene component (**257**).[232-234] The observed colour is attributed to a π-π charge transfer absorption, which is derived from electron transition from the naphthalene ring to the heterocyclic ring.[233]



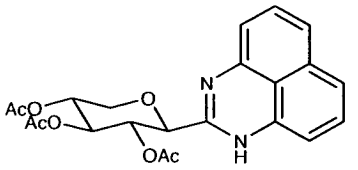
257

2.8.3 Synthesis of 2-pyranosylperimidines

The results of the pilot reaction were encouraging enough to attempt to transfer the procedure to carbohydrate scaffolds. D-Xylose derived hydroximoyl chloride **106** was stirred with DAN in refluxing ethanol for 5 hours. Two compounds were isolated from the reaction mixture by chromatography. The least polar fraction (R_f [Et_2O] = 0.35) was found to contain glycal perimidine **258**, the remaining fraction (R_f [Et_2O] = 0.27) afforded the expected pyranosyl perimidine **259**.

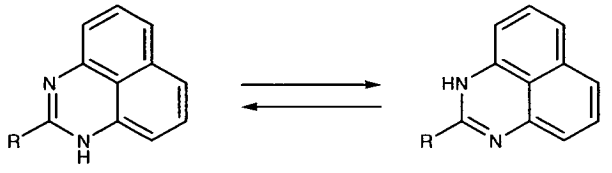


258



259

The glycal derivative **258** was found to be the major product of the reaction (**258** 43%, **259** 16%, **258**:**259** = 2.68:1, Table 16). The ^{1}H NMR spectra of both compounds in $CDCl_3$ had broad signals in the aromatic region due to annular tautomerism in a similar fashion to that observed in benzimidazoles (Scheme 97).[239]



Scheme 97

Repeating the NMR experiments in D_6-DMSO appeared to suppress or sufficiently slow the interconversion to obtain well-resolved signals in the aromatic region; the same effect was observed on cooling below -40 °C by Yavari *et al.*[239] In both cases in D_6-DMSO, the heteroatomic ring CH protons were observed at lower frequency than those of the naphthyl unit. Values from glycal perimidine **258** are representative [δ_H 7.47-7.51 ppm (4H, m, H-5, H-6, H-7, H-9), 6.60 ppm (dd, H-4, $J_{H4\text{-}H5}$ 7.3 Hz, $J_{H4\text{-}H6}$ 0.6 Hz), 6.58 ppm (dd, H-9, $J_{H9\text{-}H8}$ 7.3 Hz, $J_{H9\text{-}H7}$ 0.6 Hz)]. The NH was clearly defined [δ_H 10.49 ppm (bs, OH)]. In both **258** and **259** the perimidine derived signals in the ^{13}C NMR could be assigned by comparison with data from a detailed study by Claramunt et al;[240] representative data sets from glycal perimidine **258** and pyranosyl perimidine **259** are presented in Table 13.

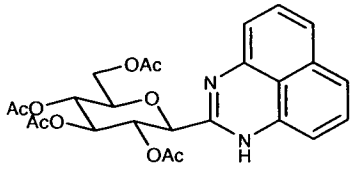
C-X	2	3a	4	5	6	6a	7	8	9	9a	9b
259 δ_C/ppm	154.0	145.8	115.0	130.3	121.1	136.6	119.2	129.5	104.1	139.4	123.6
258 δ_C/ppm	150.1	145.9	115.2	130.4	121.0	136.6	119.5	129.5	104.7	139.2	123.8

Table 13: Comparison of ^{13}C chemical shifts of glycal perimidine **258** and pyranosyl perimidine **259**

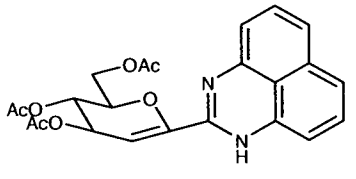
Several key features in the ^{1}H and ^{13}C NMR spectra indicated that glycal **258** had been formed. Only two peaks corresponding to the acetyl protecting groups were observed [δ_H 2.12, 2.10 ppm (2x CH_3); δ_C 171.0, 170.9 ppm (2x C=O); 22.3, 22.2 ppm (2x CH_3)] and no signal appeared in anomeric proton region. In contrast, in the case of pyranosyl perimidine **259**, three acetyl signals were observed [δ_H 2.05, 2.03, 1.93 ppm (3x CH_3); δ_C 171.2, 171.1 170.7 ppm (3x C=O); δ_C 22.0, 21.9, 21.8 ppm (3x CH_3)] and the anomeric peak appeared as a doublet [δ_H 4.24 ppm (d, H-1`, $J_{H1`-H2`}$ 9.7 Hz)]. Glycals are known to adopt a half-chair conformation,[146] therefore the carbohydrate ring signals differ from those observed for a chair conformer. The coupling constant between the 2`-H and 3`-H protons [$J_{2,3}$ 5.1 Hz] was smaller than that observed in pyranosyl perimidine **259** [$J_{2,3}$ 9.6 Hz]. The remaining signals are observed as complex multiplets rather than discrete doublets of doublets with large coupling constants. The alkene signals in the ^{13}C NMR spectrum were particularly apparent, the chemical shift of the anomeric carbon atom being significantly higher than that in perimidine **259** [**258** δ_C C-1` 149.2 ppm, **259** $\delta_C$ C-1` 78.8 ppm].

The expected pyranosyl perimidine was a green/yellow colour, which is consistent with literature data for similar compounds.[232-234] The glycal was orange in colour, this shift to lower frequency is probably due to conjugation of the heterocycle with the double bond in the carbohydrate ring. On repeating the above reaction at room temperature for 16 hours, the major product was found to be **259** (60%) together with traces of **258** (TLC).

When D-glucose hydroximoyl chloride **107** was reacted in ethanol at room temperature, similar results were obtained to the xylose case (pyranosyl perimidine **260** 65% yield, traces of glycal perimidine **261**). Perimidine **260** was found to be the major product (**260** 34%, **261** 16%, **260**:**261** = 2.13:1, Table 16) when the reaction was attempted in refluxing ethanol.



260



261

Both products **260** and **261** had similar ^{1}H and ^{13}C NMR spectra to the xylose analogues. The structure of pyranosyl perimidine **260** was confirmed by X-ray crystallography. Selected bond lengths and bond angles are compared with 2-(anthr-9-yl)perimidine[240] and were found to be in good agreement (Tables 14 and 15).

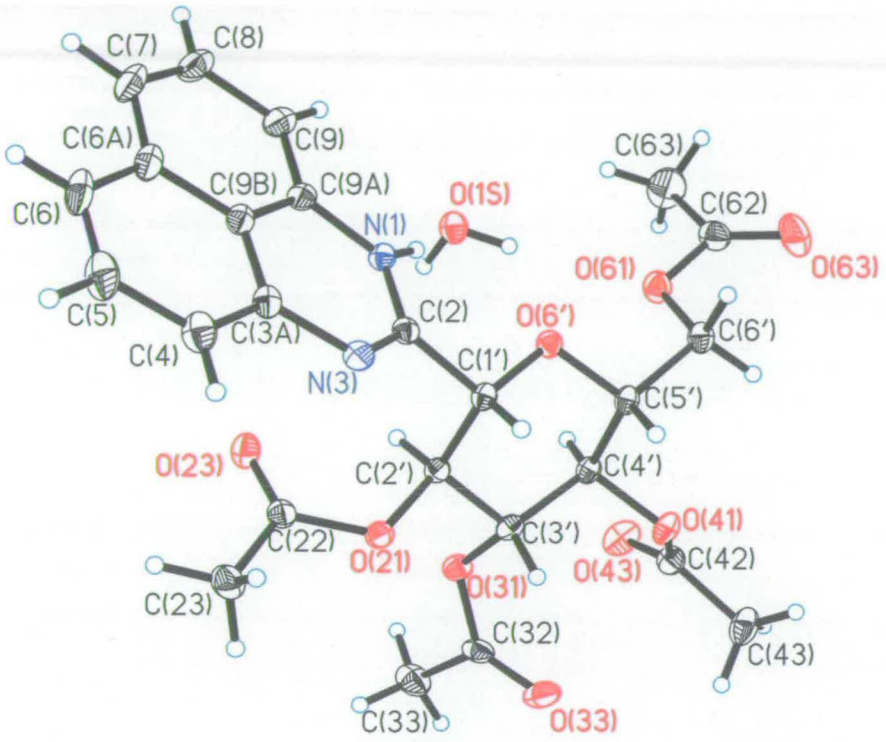


Figure 8- Crystal structure of 2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)perimidine (**260**)

The mechanism of glycal formation was proposed to occur *via* an E1cB elimination process due to charge delocalisation onto the heterocycle. Deprotonation would have to occur by the basic DAN nucleophile or a molecule of the newly formed perimidine. The pK_a of DAN is known to be *ca* 5, whereas the pK_a of 2-perimidines is *ca* 6.[232] Clearly, the perimidine would be more basic than DAN and might be expected to be more able to deprotonate the anomeric position, however the pK_a values of the anomeric proton of **259** or **260** are currently unknown.

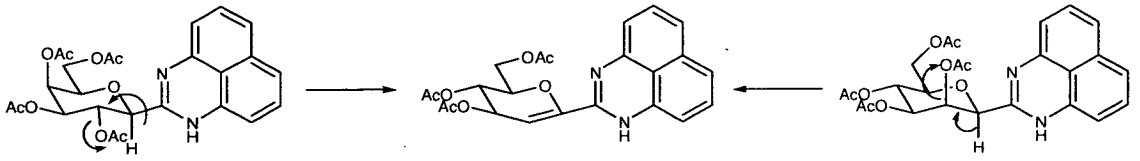
	Bond length/Å **260**	Bond length/Å 2-(Anthr-9-yl)perimidine[240]
N(1)-C(2)	1.351(3)	1.352(2)
N(1)-C(9a)	1.396(3)	1.398(2)
N(3)-C(2)	1.300(2)	1.301(2)
N(3)-C(3a)	1.410(3)	1.408(2)
C(3a)-C(4)	1.377(3)	1.378(3)
C(4)-C(5)	1.409(4)	1.404(3)
C(5)-C(6)	1.359(4)	1.358(4)
C(6)-C(6a)	1.420(4)	1.416(3)
C(6a)-C(7)	1.413(4)	1.412(3)
C(7)-C(8)	1.367(4)	1.355(3)
C(8)-C(9)	1.412(3)	1.408(3)
C(9)-C(9a)	1.378(3)	1.374(3)
C(9a)-C(9b)	1.414(3)	1.412(2)
C(9b)-C(6a)	1.426(3)	1.420(2)
C(3a)-C(9b)	1.425(3)	1.416(2)

Table 14: Comparison of bond lengths in **260** and 2-(anthr-9-yl)perimidine

	Bond Angle/° **260**	Bond Angle/° 2-(Anthr-9-yl)perimidine[240]
N(1)-C(2)-N(3)	125.57(18)	124.4(2)
C(2)-N(3)-C(3a)	116.94(18)	117.5(1)
N(3)-C(3a)-C(9b)	120.96(18)	120.8(1)
C(3a)-C(9b)-C(9a)	119.57(18)	119.4(2)
C(9b)-C(9a)-N(1)	116.08(18)	116.0(2)
C(9a)-C(N1)-C(2)	121.21(17)	121.9(1)

Table 15: Comparison of bond angles in **260** and 2-(anthryl)perimidine

In order to provide further evidence for the reaction pathway, an attempt was made to prepare mannopyranosyl perimidine **262**. In the mannose case, the OAc group would be anti-periplanar to the anomeric anion and thus ideally placed to undergo E2 elimination in addition to E1cB and thus likely to favour formation of glycal **261**. The glucopyranosyl perimidine **260** also afforded glycal **261**, but the elimination was sluggish since only E1cb elimination is possible (Scheme 98).



260 **261** **262**

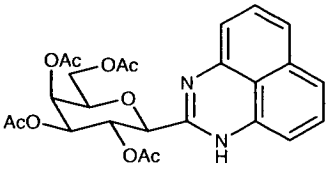
Scheme 98

Conducting the reaction of DAN with D-mannose hydroximoyl chloride **108** in ethanol at room temperature afforded pyranosyl perimidine **262** (55%) with traces of glycal **261**. When the reaction was conducted in refluxing ethanol, glycal **261** was indeed the predominant product (**261** 34%, **262** 4%, **261**:**262** = 8.5:1, Table 16). The ^{1}H and ^{13}C NMR spectra of **261** and **262** were comparable with those of the D-xylose and D-glucose analogues. The observation that the proportion of glycal perimidine **261** is significantly higher from perimidine **262** is consistent with the tandem elimination processes taking place.

Carbohydrate Substituent	Reaction Temperature/ °C	% Yield Pyranosyl Perimidine	% Yield Glycal Perimidine	Glycal perimidine : Pyranosyl perimidine
D-Xylose	25	60	<1	-
D-Xylose	80	16	43	2.68:1
D-Glucose	25	65	<1	-
D-Glucose	80	34	16	1:2.13
D-Mannose	25	55	<1	-
D-Mannose	80	4	34	8.5:1

Table 16: Glycal perimidine to pyranosyl perimidine ratios

The range of carbohydrate substituents was extended further with the room temperature synthesis of 2-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)perimidine (**263**) in 69% yield. The preparation of perimidine **263** and its precursors was completed in association with Andreas Fromm.[241]



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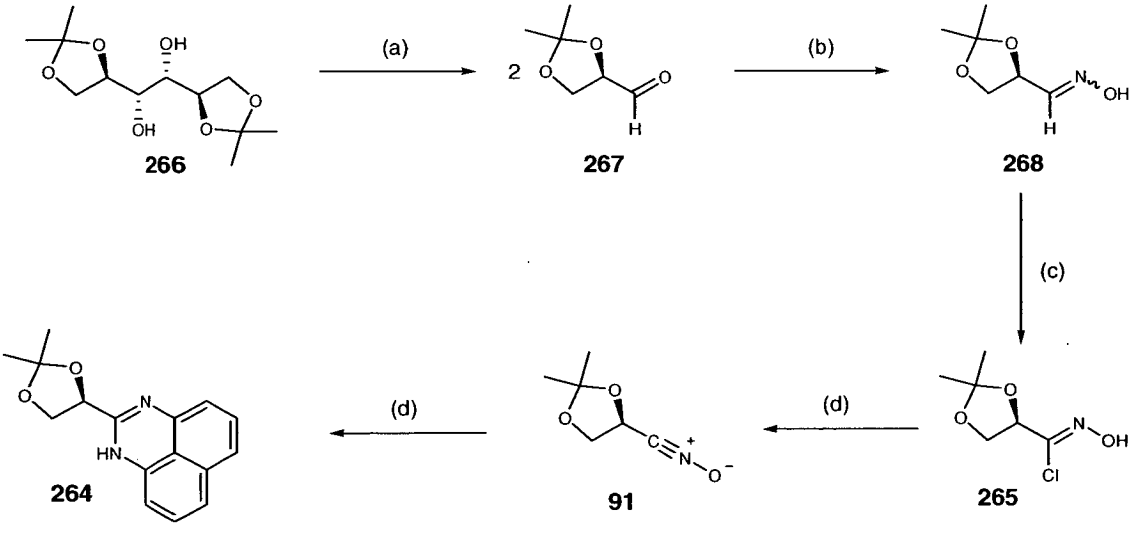
2.8.4 Preparation of D-glyceraldehyde derived perimidine

The success of the perimidine methodology encouraged an attempt to synthesise a perimidine with an acyclic carbohydrate substituent. D-Glyceraldehyde derived perimidine **264** was selected as a target since the precursor nitrile oxide (**91**) was known.[141] The nitrile oxide is generated by dehydrochlorination of hydroximoyl chloride **265**, which is accessible from D-mannitol derivative **266** *via* aldehyde **267** and oxime **268** (Scheme 99).[242,243]



Scheme 99: (a) $NaIO_4$ (b) $NH_2OH.HCl$, $NaCO_3$ (c) Cl_2 (d) DAN, Δ

1,2:5,6-Di-*O*-isopropylidene-D-mannitol (**266**) was oxidatively cleaved with sodium periodate to form two equivalents of aldehyde **267**. Treatment of the crude aldehyde with hydroxylamine hydrochloride and sodium carbonate afforded oxime **268** as a mixture of isomers (*E*:*Z* 3:1) in 63% yield. The ^1H NMR spectrum showed

diagnostic peaks for the *E* and *Z* isomers [δ_H 9.18 ppm (*Z*- isomer, bs, OH), 8.89 ppm (*E*- isomer, bs, OH)]. Oxime **268** was dissolved in ether and treated with chlorine gas to afford hydroximoyl chloride **265** as a grey solid (98% yield).[141] The product was immediately taken on to the next stage to avoid the risk of decomposition on standing at room temperature. Hydroximoyl chloride **265** was stirred with DAN in refluxing ethanol for 5 hours to afford the target perimidine **264** as a yellow/green solid (61% yield). The aromatic region of the ^1H and ^{13}C NMR spectra (in D_6-DMSO), were found to mirror those observed in the pyranosyl series. The signals in the ^1H and ^{13}C NMR spectra corresponding to the acyclic component were clearly visible [δ_H 4.67 ppm (t, CH), 4.02 ppm (d, CH_2); δ_C 73.9 ppm (CH), 66.6 ppm (CH_2)].

2.8.5 Conclusions / Further work

A new and mild method for the preparation of perimidines has been established. For example, reaction of 1,8-diaminonapthalene (DAN) with D-xylose derived hydroximoyl chloride **106** at room temperature afforded pyranosyl perimidine **259** in 60% yield. Reaction of D-Glucose, D-mannose and D-galactose derived hydroximoyl chlorides with DAN proceeded in a similar fashion (55-65% yield). Reaction of D-glucose hydroximoyl chloride **107** with DAN in refluxing ethanol afforded a 2.1:1 mixture of pyranosyl perimidine **260** and glycal perimidine **261**. Under the same conditions, D-mannose hydroximoyl chloride **108** afforded a 1:8.5 mixture of perimidine **262** and glycal perimidine **261**. Application of the method to the D-glyceraldehyde hydroximoyl chloride **265** was also successful in delivering the corresponding perimidine **264** (61% yield). Future work in this area could include extension of the methodology to a ribose scaffold and an examination of the products as potential antiviral agents. The methodology could also be extended to the synthesis of substituted perimidines by reaction with derivatives of DAN.

3. Experimental

3.1 General

3.1.1 Instumentation

All ^{1}H and ^{13}C NMR spectra were recorded on a Varian WP200SY, Bruker ARX250 and Bruker avance 360 instruments by Mr J. R. A. Millar, Stewart Wharton and the author. High field ^{1}H NMR was conducted on a Varian inova 600 instrument by Dr I. H. Sadler. 2D NMR spectra were obtained from the Bruker avance 360 and Varian inova 600 instruments. Chemical shifts (δ) in all spectra are measured in parts per million (p.p.m), using tetramethylsilane ($\delta = 0.0$) as a reference signal.

FAB mass spectra and exact mass measurements were recorded on a Kratos MS50TC instrument using either glycerol or thioglycerol as a matrix by Mr A. Taylor.

Melting points were measured on a Gallenkamp capillary tube apparatus and are uncorrected. Optical rotations were measured on an Optical Activity Polaar 20 polarimeter using 2 cm^3 of filtered solution. IR spectra were obtained as liquid films or nujol mulls on a Perkin Elmer Paragon 1000 FT-IR spectrometer and are quoted in wavenumbers (cm^{-1}). Infrared spectra were recorded on a Jasco FT/IR-460 using sodium chloride plates.

Diffraction data were collected with graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å) on a Bruker Apex CCD diffractometer equipped with an Oxford Cryosystems low-temperature device operating at 150K. X-ray structural analysis of **141**, **153**, **156**, **178**, **216**, **217**, **224**, **260** by Dr S. Parsons, Dr I. Oswald, Mr S. Moggach, Miss F. Fabbiani and Mr F. White.

High pressure hydrogenation was conducted using a Parr 4842 apparatus.

3.1.2 Chromatography

Analytical TLC was carried out on Merck aluminium-backed plates with Kieselgel GF_{254} silica (0.2 mm).

Dry flash chromatography was performed using a variety of sinters with different diameters filled with Kieselgel GF_{254} silica and eluted under a vacuum supplied by a water pump.

3.1.3 Solvents and reagents

All reagents and solvents were standard laboratory grade and were used as supplied unless specifically stated.

Dichloromethane, chloroform and acetonitrile were purified by distillation from and stored over calcium hydride.
Pyridine was purified by distillation from and stored over potassium hydroxide.
Acetic anhydride was purified by fractional distillation and dried over 4A molecular sieves.
THF was purified by distillation over calcium hydride.
Toluene and ether were dried over sodium wire.

3.2 Synthesis of pyranosylnitrile oxide precursors

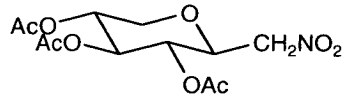
3.2.1 Synthesis of pyranosylnitromethanes

3.2.2.1 3,4,5-Tri-O-acetyl-β-D-xylopyranosylnitromethane (95)

Sample code: IAS001

Molecular formula: $C_{12}H_{17}NO_9$

Molecular weight: 319



Solid sodium (2.5 g, 108 mmol) was dissolved in methanol (90 ml) under an atmosphere of N_2. Sodium methoxide (90 ml in methanol) was added to a stirred solution of D-(+)-xylose (13.5 g, 83 mmol), nitromethane (45 ml, 0.83 mol) and dry methanol (30 ml). The solution was stirred for 24 h. The resultant brown solid was filtered, washed with ice-cold methanol, and dissolved in ice-cold deionised water (200 ml). The solution was rapidly forced through an amberlite 120 (H^+) ion-exchange column. Excess nitromethane was removed *in vacuo*, and the residual liquid was heated at reflux for 48 h. Charcoal (5 g) was added to the solution and the mixture was heated at reflux for 2 h. The charcoal was filtered through celite and the filtrate concentrated *in vacuo* to yield an orange oil. The oil was dissolved in dry acetic anhydride (140 ml) (under an atmosphere of N_2), cooled to 0 °C, triflic acid (0.1 ml) was added, and the mixture stirred for 14 h. The resultant solution was added to ice-water (100 ml), extracted with chloroform (3 x 40 ml), washed with $NaHCO_3$ (3 x 40 ml) and the combined extracts dried ($MgSO_4$). The dried extract was concentrated *in vacuo* (residual water was co-evaporated with toluene) to afford an orange oil. The oil was dissolved in chloroform (100 ml) and activated charcoal (2 g) was added. The solution was heated under reflux for 30 minutes, charcoal was filtered over celite and the filtrate concentrated *in vacuo* to yield an orange oil which was crystallised from ethanol. The purified product (**95**) was isolated as a white crystalline solid (10.48 g, 40%); M.p 163-165 °C (lit.[144] 164-165 °C); δ_H (250 MHz, $CDCl_3$) 2.40 (9H, 3s, 3x$COCH_3$), 3.72 (1H, dd, 6b-H), 4.41 (1H, dd, 6a-H), 4.55 (1H, m, 2-H), 4.74 (1H, dd, 1b-H), 4.81 (1H, dd, 1a-H), 5.20 (1H, dd, 3-H), 5.36 (1H, m, 5-H), 5.61 (1H, dd, 4-H); *J*(x-y)/Hz 1a-1b 13.3, 1a-2 8.8, 1b-2 2.9, 2-3 10.6,

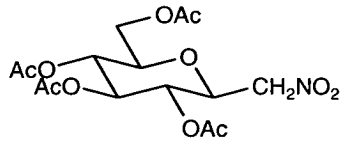
3-4 9.3, 4-5 9.4, 5-6a 10.6, 5-6b 5.8, 6a-6b 11.3; δ_C (63 MHz, $CDCl_3$) 21.1, 21.2, 21.4 (3x$COCH_3$), 66.1, 68.5, 69.3, 72.9, 74.8, (C-6, C-2, C-3, C-4, C-5), 75.8 (C-1), 170.1, 170.2, 170.6 (3x$COCH_3$)

3.2.2 3,4,5,7-Tetra-*O*-acetyl-β-D-glucopyranosylnitromethane (99)

Sample code: IAS004

Molecular formula: $C_{15}H_{21}NO_{11}$

Molecular weight: 391



Solid sodium (2.5 g, 108 mmol) was dissolved in methanol (90 ml) under an atmosphere of N_2. Sodium methoxide (90 ml in methanol) was added to a stirred solution of D-(+)-glucose (15.1 g, 84 mmol), nitromethane (45 ml, 0.83 mol) and dry methanol (30 ml). The solution was stirred for 24 h. The resultant brown solid was filtered, washed with ice-cold methanol, and dissolved in ice-cold deionised water (200 ml). The solution was rapidly forced through an amberlite 120 (H^+) ion-exchange column. Excess nitromethane was removed *in vacuo*, and the residual liquid was heated at reflux for 48 h. Charcoal (5 g) was added to the sugar solution and the mixture was heated at reflux for 2 h. The charcoal was filtered through celite and the filtrate concentrated *in vacuo* to yield an orange oil. The product was isolated as a white solid by continuous liquid/liquid extraction using ethyl acetate/water (48 hours), followed by concentration of the organic layer *in vacuo*. The resultant solid was dissolved in dry acetic anhydride (50 ml) (under an atmosphere of N_2), cooled to 0 °C , triflic acid (0.2 ml) was added, and the mixture stirred for 14 h. The resultant solution was added to ice-water (100 ml), extracted with chloroform (3 x 40 ml), washed with $NaHCO_3$ (3 x 40 ml) and the combined extracts dried ($MgSO_4$). The dried extract was concentrated *in vacuo* (residual water was co-evaporated with toluene) to afford an orange oil. The oil was dissolved in chloroform (100 ml) and activated charcoal (2 g) was added. The solution was heated under reflux for 30 minutes, charcoal was filtered over celite and the filtrate concentrated *in vacuo* to yield an orange oil which was crystallised from hexane/ethanol. The purified product (**99**) was isolated as a white crystalline solid. (6.72 g, 20%); M.p 143-145 °C (lit.[144]

144-145 °C); δ_H (250 MHz, $CDCl_3$) 1.96,1.98, 2.00 (12H, 4s, 4x$COCH_3$), 3.67 (1H, ddd, 6-H), 3.98 (1H, dd, 7a-H), 4.21 (1H, dd, 7b-H), 4.22-4.27 (1H, m, 2-H), 4.34 (1H, dd, 1b-H), 4.47 (1H, dd, 1a-H), 4.87 (1H, dd, 3-H), 5.01 (1H, dd, 5-H) 5.21 (1H, dd, 4-H); *J*(x-y)/Hz 1a-1b 13.7, 1a-2 2.8, 1b-2 8.9, 2-3 9.3, 3-4 9.3, 4-5 9.6, 5-6 9.98, 6-7a 2.21, 6-7b 4.97, 7a-7b 12.5; δ_C (63 MHz, $CDCl_3$) 20.4, 20.4 (4x$COCH_3$), 61.4 (C-7) 67.7, 69.3, 72.7, 73.4, 74.2 (C-2, C-3, C-4, C-5, C-6), 75.5 (C-1) 169.2, 169.5, 169.9, 170.4 (4x$COCH_3$).

3.2.3 Synthesis of pyranosyloximes

The acetylated D-gluco, D-xylo and D-mannose (provided by Mr A. Fromm) derived nitromethanes were reduced to their respective oximes using a modified version of the procedure of Bartra *et al*[52].

3.2.3.1 Pyranosyloximes- General Procedure

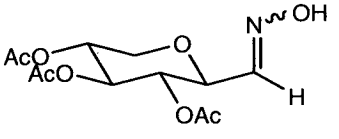
Triethylamine (5 equivalents) and thiophenol (4.5 equivalents) were added to a cooled (0 °C) solution of tin (II) chloride (1.5 equivalents) and acetylated pyranosylnitromethane (1 equivalent) in dry THF (5 ml) under nitrogen. The resulting yellow mixture was stirred for 16 hours. After removal of THF *in vacuo*, the residue was washed with hexane to remove excess thiophenol. The product was separated by dry-flash chromatography (silica / 0-100 % ether in hexane; gradient elution).

3.2.3.2 3,4,5-Tri-*O*-acetyl-β-D-xylopyranosylformaldoxime (100)

Sample code: IAS005

Molecular formula: $C_{12}H_{17}NO_8$

Molecular weight: 303

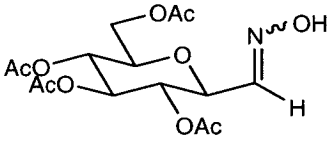


3,4,5-Tri-*O*-acetyl-β-D-xylopyranosylnitromethane (**95**) (1.5 g, 3.13 mmol) was added to a cooled (0 °C) solution of tin (II) chloride (1.34 g, 4.7 mmol), triethylamine (3.3 ml, 15.7 mmol), and thiophenol (1.5 ml, 14.1 mmol) as outlined in

the general procedure above. The product (**100**) was isolated by dry-flash chromatography as a white solid (1.2 g, 86 %). Oxime **100** was recrystallised from a 60:40 ether/hexane mix. The oxime was obtained as a mixture of E/Z isomers in a 4:1 ratio; M.p 128-130°C (lit.[52] 135-137 °C); δ_H (250 MHz, $CDCl_3$); 1.95, 1.97, 1.98 (9H, 3s, 3x$COCH_3$), 3.29 (1H, dd, 6a-H), 3.92 (1H, dd, 2-H), 4.08 (1H, dd, 6b-H), 4.85-4.93 (1H, m, 5-H), 4.99 (1H, dd, 3-H), 5.19 (1H, dd, 4-H), 6.63 (1H, d, 1-H (*Z*)), 7.72 (1H, d, 1-H (*E*)), 8.62 (1H, bs, OH (*E*)), 8.88 (1H, bs, OH (*Z*)); *J*(x-y)/Hz 1-2 6.6, 2-3 9.8, 3-4 9.4, 4-5 9.5, 5-6a 10.2, 5-6b 5.6, 6a-6b 11.2; δ_C (63 MHz, $CDCl_3$) 20.4, 20.5 (3x$COCH_3$), 66.5 (C-6), 68.8, 69.6, 72.9, 75.9 (C-2, C-3, C-4, C-5), 146.7 (C-1),169.7, 169.8, 170.3 (3x$COCH_3$)

3.2.3.3 3,4,5,7-Tetra-*O*-acetyl-β-D-glucopyranosylformaldoxime (101)

Sample code: IAS002/007
Molecular formula: $C_{15}H_{21}NO_{10}$
Molecular weight: 375



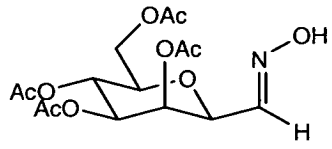
3,4,5,7-Tetra-*O*-acetyl-β-D-glucopyranosylnitromethane (**99**) (1.1 g, 3.84 mmol) was added to a cooled (0 °C) solution of tin (II) chloride (1.1 g, 5.76 mmol), triethylamine (3.3 ml, 19.2 mmol), and thiophenol (2.1 ml, 17.3 mmol) as outlined in the general procedure above. The product (**101**) was isolated by dry- flash chromatography as a white solid (660 mg, 69 %). Oxime **101** was recrystallised from a 60:40 ether/hexane mix. The oxime was obtained as a mixture of E/Z isomers in a 4:1 ratio; M.p 158-160°C (lit.[52] 155-157 °C); δ_H (250 MHz, $CDCl_3$) 1.94, 1.95, 1.97, 2.02 (12H, 4s, 4x$COCH_3$), 3.66 (1H, ddd, 6-H), 4.03 (1H, dd, 2-H), 4.08 (1H, dd, 7b-H), 4.21 (1H, dd, 7a-H), 5.06 (1H, dd, 3-H), 5.08 (1H, dd, 5-H), 5.20 (1H, dd, 4-H), 6.8 (1H, d, 1-H (*Z*)), 7.41 (1H, d, 1-H(*E*)), 8.35 (1H, bs, OH (*E*)), 8.53 (1H, bs, OH (*Z*)); *J*(x-y)/Hz 1-2 6.9, 2-3 9.9, 3-4 9.1, 4-5 9.8, 5-6 9.6, 6-7a 2.06, 6-7b 4.7, 7a-7b 12.5; δ_C (63 MHz, $CDCl_3$) 20.5 (4x$COCH_3$), 61.9 (C-7), 68.0, 69.4, 73.4, 75.7, 75.7 (C-2, C-3, C-4, C-5, C-6), 146.7 (C-1) 169.4, 169.6, 170.2, 170.6 (4x$COCH_3$).

3.2.3.4 3,4,5,7-Tetra-*O*-acetyl-β-D-mannopyranosylformaldoxime (102)

Sample code: IAS088

Molecular formula: $C_{15}H_{21}NO_{10}$

Molecular weight: 375



3,4,5,7-Tetra-*O*-acetyl-β-D-mannopyranosylnitromethane (supplied by A. Fromm) (1.57 g, 4.2 mmol) was added to a cooled (0 °C) solution of tin (II) chloride (1.15 g, 6.28 mmol), triethylamine (2.8 ml, 20.9 mmol), and thiophenol (1.85 ml, 18.8 mmol) as outlined in the general procedure above. The product (**102**) was isolated by dry-flash chromatography as a white solid (1.16 g, 77 %). Oxime **102** was recrystallised from a 60:40 ether/hexane mix. The oxime was obtained as a mixture of E/Z isomers in a 2:1 ratio; M.p 151-152 °C (lit.[52] 152-154 °C); δ_H (360 MHz, $CDCl_3$) 2.00, 2.01 2.08, 2.13, 2.14, 2.17, 2.19 (24H, 4s, 4x$COCH_3$), 3.71-3.75 (2H, m, 6-H(*E*), 6-H(*Z*)), 4.19 (2H, dd, 7a-H(*E*), 7b-H(*Z*)), 4.25 (2H, dd, 7b-H(*E*), 7b-H(*Z*)), 4.40 (1H, d, 2-H(*E*)), 4.86 (1H, d, 2-H(*Z*)), 5.11-5.19 (2H, m, 4-H(*E*), 4-H(*Z*)), 5.24-5.33 (2H, m, 5-H(*E*), 5-H(*Z*)), 5.54 (1H, dd, 3-H (*E*)), 5.85 (1H, dd, 3-H(*Z*)), 6.75 (1H, d, 1-H(*Z*)), 7.35 (1H, d, 1-H(*E*)), 8.67 (1H, bs, OH (*E*)), 8.94 (1H, bs, OH (*Z*)); *E*-isomer *J*(x-y)/Hz 1-2 5.5, 2-3 3.2, 3-4 nd, 4-5 nd, 5-6 nd, 6-7a 2.1, 6-7b 5.7, 7a-7b 12.3, *Z*-isomer *J*(x-y)/Hz 1-2 4.0, 2-3 1.3, 3-4 nd, 4-5 nd, 5-6 nd, 6-7a 2.1, 6-7b 5.7, 7a-7b 12.3.

3.2.4 Synthesis of pyranosylhydroximoyl chlorides

3.2.4.1 Hydroximoyl chlorides-General procedure

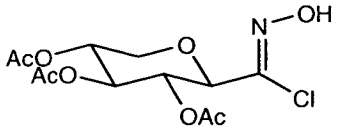
Dry chlorine gas was bubbled through a cooled (-78 °C) solution of pyranosylformaldoxime, in dry chloroform (under nitrogen) until the solution turned emerald green. Nitrogen gas was bubbled through the solution and it was allowed to warm to room temperature. On warming, the solution became green, blue, then colourless and the solvent was removed *in vacuo* to afford an oily solid. The product was obtained as a white solid on trituration with ice-cold ether.[32]

3.2.4.2 3,4,5, -Tri-*O*-acetyl-2,6-anhydro-1-deoxy-1-chloro-1-hydroxyimino-D-*xylo*-D-*gulo*-hexitol (106)

Sample code: IAS008

Molecular formula: $C_{12}H_{16}NO_8Cl$

Molecular weight: 337.5



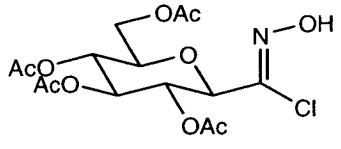
Following the procedure above, 3,4,5-tri-*O*-acetyl-β-D-xylopyranosylformaldoxime (**100**) (550 mg, 1.6 mmol) was converted to the corresponding hydroximoyl chloride. The product (**106**) was obtained as a white solid (600 mg, 98%); M.p 147-149°C; δ_H (250 MHz, $CDCl_3$); 1.92, 1.95, 1.98 (9H, 3s, 3x$COCH_3$), 3.34 (1H, dd, 6a-H), 4.12 (1H, dd, 6b-H), 4.17 (1H, d, 2-H), 5.01 (1H, td, 5-H), 5.15 (1H, dd, 3-H), 5.22 (1H, dd, 4-H), 8.80 (1H, bs, OH; *J*(x-y)/Hz 2-3 9.3, 3-4 9.2, 4-5 8.0, 5-6a 10.8, 5-6b 6.1, 6a-6b 11.3; δ_C (63 MHz, $CDCl_3$) 20.4, 20.6 (3x$COCH_3$), 66.5 (C-6), 68.5, 68.9, 73.1, 78.8 (C-3, C-4, C-5, C-2), 136.5 (C-1) 169.3, 169.9, 170.5 (3x$COCH_3$); *m/z* (FAB) 338 (M^++1); HRMS (FAB) Found: M^++1 338.06427. $C_{15}H_{21}NO_{10}{}^{35}Cl$ requires M^++1 338.06442.

3.2.4.3 3,4,5,7 -Tetra-*O*-acetyl-2,6-anhydro-1-deoxy-1-chloro-1-hydroxyimino-D-*glycero*-D-*gulo*-heptitol (107)

Sample code: IAS003

Molecular formula: $C_{15}H_{20}NO_{10}Cl$

Molecular weight: 409.5



Following the procedure above, 3,4,5,7-tetra-*O*-acetyl-β-D-glucopyranosylformaldoxime (**101**) (600 mg, 1.5 mmol) was converted to the corresponding hydroximoyl chloride. The product (**107**) was obtained as a white solid (620 mg, 99%); M.p 158-160°C (lit.[140] 157-159°C); υ_{max}/cm^{-1} (Nujol) 3311 (OH), 1747 (C=O); $[\alpha]_D{}^{18}$ -5.0 (c = 1.0, $CHCl_3$); δ_H (250 MHz, $CDCl_3$); 2.14, 2.25, 2.30, 2.35 (12H, 4s, 4x$COCH_3$), 3.73 (1H, ddd, 6-H), 4.08 (1H, dd, 7a-H), 4.17 (1H, dd, 7b-H), 4.24 (1H, dd, 2-H), 5.07 (1H, dd, 3-H), 5.19 (1H, dd, 5-H), 5.30 (1H, dd,

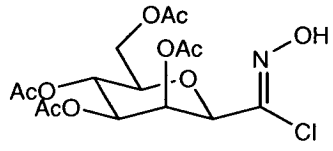
4-H), 8.78 (1H, bs, OH); *J*(x-y)/Hz 2-3 9.8, 3-4 9.3, 4-5 9.4, 5-6 9.5, 6-7a 2.4, 6-7b 4.6, 7a-7b 12.5; δ_C (63 MHz, $CDCl_3$) 20.4, 20.5, 20.6 (4x$COCH_3$), 61.8 (C-7), 67.8, 68.7, 73.7, 75.7, 78.3 (C-3, C-4, C-5, C-6, C-2), 136.5 (C-1) 169.4, 169.6, 170.2, 170.6 (4x$COCH_3$); *m/z* (FAB) 410 (M^+ +1) HRMS (FAB) Found M^++1 410.08565, $C_{15}H_{21}NO_{10}{}^{35}Cl$ requires M^++1 410.08540.

3.2.4.4 3,4,5,7 -Tetra-*O*-acetyl-2,6-anhydro-1-deoxy-1-chloro-1-hydroxyimino-D-*glycero*-D-*galacto*-heptitol (108)

Sample code: IAS089

Molecular formula: $C_{15}H_{20}NO_{10}Cl$

Molecular weight: 409.5



Following the procedure above, 3,4,5,7-tetra-*O*-acetyl-β-D-mannopyranosylformaldoxime (**102**) (200 mg, 0.48 mmol) was converted to the corresponding hydroximoyl chloride. The product (**108**) was obtained as a white solid (210 mg, 96%).

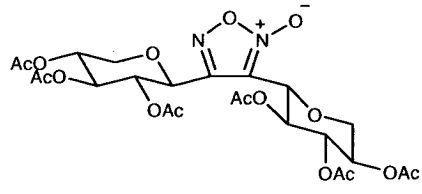
M.p 101 °C (lit,[140] 102-103 °C); δ_H (250 MHz, $CDCl_3$); 1.97, 2.04, 2.08, 2.10 (12H, 4s, 4x$COCH_3$), 3.78 (1H, m, 6-H), 4.17 (1H, dd, 7a-H), 4.26 (1H, dd, 7b-H), 5.09-5.34 (3H, m, 2-H, 4-H, 5-H), 5.71 (1H, dd, 3-H), 9.76 (1H, bs, OH); *J*(x-y)/Hz 2-3 nd, 3-4 3.3, 4-5 nd, 5-6 nd, 6-7a 2.3, 6-7b 5.7, 7a-7b 12.2; δ_C (63 MHz, $CDCl_3$) 20.9, 21.1, 21.1 (4x$COCH_3$), 62.9 (C-7), 63.2, 66.1, 68.4, 72.2, 76.9 (C-3, C-4, C-5, C-6, C-2), 134.8 (C-1) 170.1, 170.6, 170.8, 171.3 (4x$COCH_3$); *m/z* (FAB) 410 (M^+ +1) HRMS (FAB) Found M^++1 410.08551, $C_{15}H_{21}NO_{10}{}^{35}Cl$ requires M^++1 410.08540.

3.2.4.5 Dipyranosyl-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-1,2,5-oxadiazole-2-oxide (109)

Sample code: IAS006

Molecular formula: $C_{24}H_{32}N_2O_{16}$

Molecular weight: 602



3,4,5-Tri-*O*-acetyl-β-D-xylopyranosylnitromethane (**95**) (1 g, 3.13 mmol) was dissolved in dry toluene (30 cm^3) with stirring. Triethylamine (0.5 ml) and TDI (1.56 ml, 10.9mmol) were added and the resulting mixture was heated under reflux (85 °C) for 7 days. The mixture was stirred at room temperature for 1 h before cooling to 0 °C. The reaction was quenched with ethylenediamine (0.3 ml) and allowed to stir for 18 h. Polymeric urea by-product was filtered off over celite, washed with toluene and chloroform and the filtrate was concentrated *in vacuo*. Dry flash chromatography (0-100 % ether in hexane; gradient elution) of the residue yielded the product (**109**) as a white solid (568 mg, 61%); M.p 186-189°C (lit.[140] 190 °C); δ_H (250 MHz, $CDCl_3$); 1.90, 1.93, 1.94, 1.95, 1.97 (18H, 6s, 6x$COCH_3$), 3.35-3.43 (2H, m,), 4.19-4.27 (2H, m), 4.54 (2H, 2 x d, 1'-H, 1"-H), 4.93-4.97 (2H, m), 5.20-5.31 (4H, m); *J*(x-y)/Hz 1'-2' 9.5, 1"-2" 9.1; δ_C (63 MHz, $CDCl_3$) 20.3, 20.5, 20.1 (6x $COCH_3$), 66.8, 66.9 (C-6', C6") 68.3, 69.8, 70.3, 71.7, 72.4, 72.5, 73.9 (C-1'-C-5', C-1"-C-5"), 112.7 (C-3), 153.7 (C-4), 169.3, 169.5, 169.7, 169.9, 169.9 (6x $COCH_3$).

3.3 Synthesis of the pyranosylthiohydroximates

3.3.1 Thiohydroximates- General procedures

General procedure A

To a cooled solution (0 °C) of the pyranosyl hydroximoyl chloride (0.6 mmol, 1 equivalent) and thiol (1.2 mmol, 2 equivalents) in dry ether (5 ml), a solution of triethylamine (1.8 mmol, 3 equivalents) in dry ether (30 ml) was added dropwise *via* a syringe and the solution left to stir overnight. The mixture was then poured into water, the organic layer separated and the aqueous layer extracted with chloroform (3 x 50 ml). The combined organic layers were dried ($MgSO_4$) and the solvent removed *in vacuo* to yield the crude product, which was purified by dry-flash chromatography (silica, hexane/Et_2O gradient elution).

General procedure B

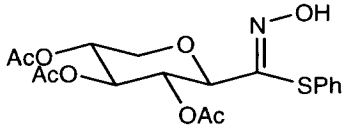
A solution of the hydroximoyl chloride (1 equivalent) in dry ether or chloroform (35 ml) was added dropwise over 1 hour to a cooled (0°C) and stirred solution of the nucleophile (2 equivalents) and triethylamine (3 equivalents) in dry ether or chloroform (5 ml) under N_2. After stirring for 1 hour the mixture was poured into water (50 ml), extracted with DCM (3 x 50 ml), the combined organic layers dried ($MgSO_4$), and the solvent removed *in vacuo*. The product was isolated by dry-flash chromatography (silica, hexane/Et_2O gradient elution).

3.3.1.1 S-Phenyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosylformothiohydroximate (119)

Sample code: IAS009

Molecular formula: $C_{18}H_{21}N_2O_8S$

Molecular weight: 411



To D-xylose derived hydroximoyl chloride (**106**) (200 mg, 0.6 mmol) in dry ether (5 ml) was added thiophenol (0.12 ml, 1.2 mmol) followed by triethylamine (0.25 ml, 1.8 mmol) in accordance to the general procedure A. Dry-flash chromatography

yielded (in order of elution) residual thiophenol, the title compound (**119**) as a white solid (180 mg, 75%) and a trace amount of furoxan by-product (<5 mg).

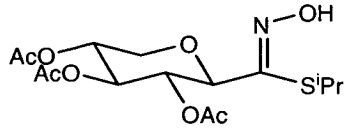
M.p 177-178 °C (from Et_2O/hexane); $[\alpha]_D^{20}$ 7.3 (c = 0.8, $CHCl_3$); δ_H (250 MHz, $CDCl_3$); 1.89, 1.97 (9H, 3s, 3x$COCH_3$), 2.40 (1H, dd, 5a-H), 3.56 (1H, d, 1-H) 3.81 (1H, dd, 5e-H), 4.80 (1H, td, 4-H), 4.84 (1H, dd, 2-H), 5.34 (1H, dd, 3-H), 7.20-7.58 (5H, m, ArH) 8.75 (1H, bs, OH); *J*(x-y)/Hz 1-2 9.9, 2-3 9.2, 3-4 9.8, 4-5a 10.2, 4-5e 5.3, 5a-5e 11.3; δ_C (63 MHz, $CDCl_3$) 20.6 (3x$COCH_3$), 66.1 (C-5), 68.6, 69.2, 73.8, 75.2 (C-2, C-3, C-4, C-1), 127.3, 128.9, 129.8 (ArCH), 136.4 (ArC), 148.9 (C=N), 169.5, 169.6, 170.6 (3x$COCH_3$); *m/z* (FAB) 412 (M^++1); HRMS (FAB) Found: M^++1 412.10629. $C_{18}H_{21}NO_8S$ requires M^++H 412.10661.

3.3.1.2 S-(2-Propyl) 2,3,4-tri-*O*-acetyl-β-D-xylopyranosylformothiohydroximate (120)

Sample code: IAS010

Molecular formula: $C_{15}H_{23}NO_8S$

Molecular weight: 377



To D-xylose derived hydroximoyl chloride (**106**) (200 mg, 0.6 mmol) in dry ether (5 ml) was added 2-propane thiol (0.11 ml, 1.2 mmol) followed by triethylamine (0.25 ml, 1.8 mmol) in accordance to general procedure A. Dry-flash chromatography yielded (in order of elution) residual 2-propane thiol, the title compound (**120**) as a white solid (120 mg, 55%) and furoxan by-product (80 mg, 45%)

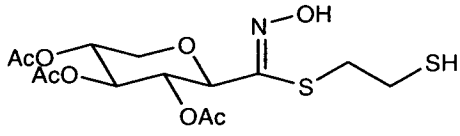
M.p 97-98 °C; δ_H (250 MHz, $CDCl_3$); 1.23 (3H, d, CH_3), 1.25 (3H, d, CH_3), 1.95, 1.97 (9H, 3s, 3x$COCH_3$), 3.27 (1H, dd, 5a-H), 3.83 (1H, septet, CH) 4.11 (1H, d, 1-H) 4.13 (1H, dd, 5e-H), 5.00 (1H, td, 4-H), 5.17 (1H, dd, 2-H), 5.32 (1H, dd, 3-H), 8.88 (1H, bs, OH); *J*(x-y)/Hz 1-2 9.4, 2-3 9.3, 3-4 9.5, 4-5a 10.3, 4-5e 5.5, 5a-5e 11.2 ; δ_C (63 MHz, $CDCl_3$) 20.0 (3x$COCH_3$), 22.9, 23.8 (CH_3), 36.1 (CH), 66.1 (C-5), 68.1, 69.2, 73.2, 78.7 (C-2, C-3, C-4, C-1), 147.8 (C=N), 168.9, 169.3, 169.9 (3x$COCH_3$); *m/z* (FAB) 378 (M^++1); HRMS (FAB) Found: M^++1 378.12198. $C_{18}H_{21}NO_8S$ requires M^++H 378.12226.

3.3.1.3 S-Mercaptoethyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosylformothiohydroximate (121)

Sample code: IAS011.1

Molecular formula: $C_{14}H_{21}NO_8S_2$

Molecular weight: 395



To a stirred mixture of 1,2-ethanedithiol (0.24 ml, 3 mmol) and triethylamine (0.31 ml, 2.2 mmol) in dry ether (10 ml), D-xylose derived hydroximoyl chloride (**106**) (250 mg, 0.7 mmol) was added in accordance to general procedure B. Dry-flash chromatography yielded (in order of elution) residual 1,2-ethanedithiol, the title compound (**121**) as a white solid (112 mg, 40%) and 2:1 adduct **122** as a viscous oil (57 mg, 22%).

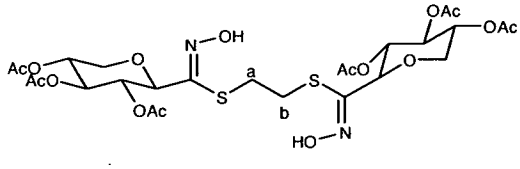
M.p 144-146 °C; $[\alpha]_D^{20}$ -48 (c = 0.5,$CHCl_3$); δ_H (250 MHz, $CDCl_3$); 1.65 (1H, t, SH), 1.95, 1.97 (9H, 3s, 3x$COCH_3$), 2.63 (2H, m, CH_2^b), 3.10 (2H, m, CH_2^a), 3.26 (1H, dd, 5a-H), 4.02 (1H, d, 1-H), 4.06 (1H, dd, 5e-H), 4.99 (1H, dt, 4-H), 5.18 (1H, dd, 2-H), 5.32 (1H, dd, 3-H), 8.91 (1H, bs, OH); *J*(x-y)/Hz 1-2 9.6, 2-3 9.3, 3-4 9.52, 4-5a 10.3, 4-5e 5.5, 5a-5e 11.0, SH-CH_2 8.5; δ_C (63 MHz, $CDCl_3$) 20.6 (3x$COCH_3$), 24.9 (CH_2^b), 34.7 (CH_2^a) 66.5 (C-5), 68.6, 69.4, 73.5, 78.8 (C-2, C-3, C-4, C-1), 147.6 (C=N) 169.5, 169.8, 170.4 (3x$COCH_3$); *m/z* (FAB) 396 (M^++1); HRMS (FAB) Found: M^++1 396.07842. $C_{18}H_{21}NO_8S$ requires M^++H 396.07869.

3.3.1.4 2:1 adduct (122)

Sample code: IAS011.2

Molecular formula: $C_{26}H_{36}N_2O_{16}S_2$

Molecular weight: 696



δ_H (250 MHz, $CDCl_3$); 1.93, 1.98 (18H, 6s, 6x$COCH_3$), 2.82 (2H, m, CH_2^b), 3.15 (2H, m, CH_2^a) 3.31 (1H, dd, 5a-H), 4.10 (1H, dd, 5e-H) 4.15 (1H, d, 1-H), 5.01 (1H, dt, 4-H), 5.18 (1H, dd, 2-H), 5.29 (1H, dd, 3-H), 9.23 (1H, bs, OH); *J*(x-y)/Hz 1-2 9.52, 2-3 9.3, 3-4 9.6, 4-5a 10.2, 4-5e 5.2, 5a-5e 10.8; δ_C (63 MHz, $CDCl_3$) 21.1

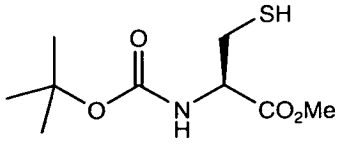
(6xCOCH$_3$), 31.7 (CH$_2^b$), 38.9 (CH$_2^a$), 66.9 (C-5), 69.1, 70.0, 74.0, 79.3 (C-2, C-3, C-4, C-1), 147.9 (C=N) 170.4, 170.9 (6x*C*OCH$_3$); *m/z* (FAB) 697 (M$^+$+1); HRMS (FAB) Found: M$^+$+1 697.15834. $C_{18}H_{21}NO_8S$ requires M$^+$+H 697.15833.

3.3.1.5 *N*-(tert-Butoxycarbonyl)cysteine methyl ester (147)

Sample code: IAS038

Molecular formula: $C_9H_{17}NO_4S$

Molecular weight: 235



Triethylamine (1.01 g, 10 mmol) was added to a well stirred slurry of L-cysteine methyl ester hydrochloride (1.72 g, 10 mmol) in DCM (20 ml), followed after 10 minutes by di-tert-butyl dicarbonate (2.18 g, 10 mmol). The mixture was stirred for 16 hours at room temperature, washed with water and dried ($MgSO_4$). Evaporation of the solvent afforded the target (**147**) as a colourless oil (2.26 g, 95 %).

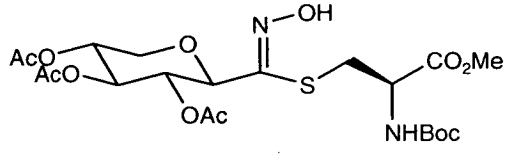
δ_H (250 MHz, $CDCl_3$); 1.45 (9H, s, 3xCH$_3$), 2.95-2.99 (2H, m, CH$_2$), 3.76 (3H, s, OCH$_3$), 4.60 (1H, dt, CH), 5.48 (1H, d, NH), *J*(x-y)/Hz CH-CH$_2$ 4.1, CH-NH 7.0; δ_C (63 MHz, $CDCl_3$) 27.1 (CH$_2$), 28.1 (3x<u>C</u>H$_3$), 52.5 (O<u>C</u>H$_3$), 54.7 (CH), 80.0 (C Boc), 154.9 (C=O Boc) 170.6 (<u>C</u>O$_2$CH$_3$); *m/z* (FAB) 236 (M$^+$+1); HRMS (FAB) Found: M$^+$+1 236.09575 $C_9H_{18}NO_4S$ requires M$^+$+H 236.09566.

3.3.1.6 S-2-Methoxycarbonyl-2-^{t}butoxycarbonylamino-2,3,4-tri-*O*-acetyl-β-D-xylopyranosylformothiohydroximate (148)

Sample code: IAS040

Molecular formula: $C_{21}H_{32}N_2O_{12}S$

Molecular weight: 536



To a stirred mixture of *N*-(tert-butoxycarbonyl)-L-cysteine methyl ester (350 mg, 1.5 mmol) and triethylamine (0.31 ml, 2.2 mmol) in dry chloroform (10 ml), D-xylose derived hydroximoyl chloride (**106**) (150 mg, 0.4 mmol) was added in accordance to general procedure B. Dry-flash chromatography yielded (in order of elution) *N,N*-

bis(tert-Butoxy)carbonyl-L-cystine dimethyl ester (**149**, 107 mg, 31% recovery) and the title compound (**148**) as a white solid (209 mg, 88%).

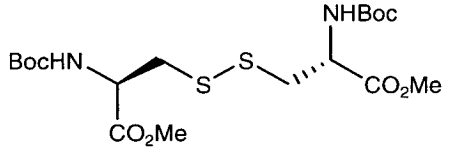
M.p 94-96 °C; $[\alpha]_D^{20}$ -39 (c = 1.0 ,$CHCl_3$); δ_H (250 MHz, $CDCl_3$); 1.47 (9H, s, 3xCH_3), 1.97, 2.03, 2.05 (9H, 3s, 3x$COCH_3$), 3.35-3.58 (3H, m, 5a-H, CH_2 a,b), 3.78 (3H, s, OCH_3), 4.16 (1H, d, 1-H), 4.18 (1H, dd, 5e-H), 4.59 (1H, m, CH), 5.03 (1H, dt, 4-H), 5.23 (1H, dd, 2-H), 5.39 (1H, dd, 3-H), 9.44 (1H, bs, OH; *J*(x-y)/Hz 1-2 9.6, 2-3 9.4, 3-4 9.4, 4-5a 10.2, 4-5e 5.4, 5a-5e 11.3; δ_C (63 MHz, $CDCl_3$) 20.5 (3x$COCH_3$), 28.1 (3xCH_3), 32.5 (CH_2), 52.7 (OCH_3), 53.7 (CH), 66.4 (C-5), 68.6, 69.3, 73.5, 78.4 (C-1, C-2, C-3, C-4), 80.3 (C Boc), 147.0 (C=N) 155.2 (C=O Boc), 169.5, 169.7, 170.3 (3x*C*OCH_3), 170.7 (*C*O_2CH_3); *m/z* (FAB) 537 (M^++1); HRMS (FAB) Found: M^++1 537.17542 $C_{21}H_{33}N_2O_{12}S$ requires M^++H 537.17542.

3.3.1.7 *N, N*-bis(tert-Butoxy)carbonyl-L-cystine dimethyl ester (149)

Sample code: IAS039

Molecular formula: $C_{18}H_{32}N_2O_8S_2$

Molecular weight: 468



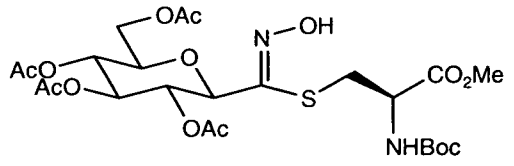
M.p 89-90 °C (lit 96-97°C); δ_H (250 MHz, $CDCl_3$); 1.45 (18H, 2xs, 6xCH_3), 3.16 (4H, 2xd, 2xCH_2), 3.77 (6H, 2xs, 2xOCH_3), 4.60 (2H, 2xdt, 2xCH), 5.41 (2H, 2xd, 2xNH), *J*(x-y)/Hz CH-CH_2 5.2, CH-NH 7.0; δ_C (63 MHz, $CDCl_3$) 28.2 (6xCH_3), 41.1 (2xCH_2) 52.5 (2xOCH_3) 52.6 (2xCH), 80.2 (2xC Boc), 154.9 (2xC=O Boc), 171.0 (2xCO_2CH_3); *m/z* (FAB) 469 (M^++1); HRMS (FAB) Found: M^++1 469.16810 $C_{18}H_{33}N_2O_8S_2$ requires M^++H 469.16784.

3.3.1.8 S-2-Methoxycarbonyl-2-^{t}butoxycarbonylamino-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylformothiohydroximate (150)

Sample code: IAS042

Molecular formula: $C_{24}H_{36}N_2O_{14}S$

Molecular weight: 608



To a stirred mixture of *N*-(tert-Butoxycarbonyl)cysteine methyl ester (260 mg, 1.1 mmol) and triethylamine (0.31 ml, 2.2 mmol) in dry chloroform (10 ml), D-glucose derived hydroximoyl chloride (**107**) (150 mg, 0.36 mmol) was added in accordance to general procedure B. Dry-flash chromatography yielded (in order of elution) *N, N*-bis(tert-Butoxy)carbonyl-L-cystine dimethyl ester (101 mg, 39% recovery) and the title compound (**150**) as a white solid (145 mg, 85%).

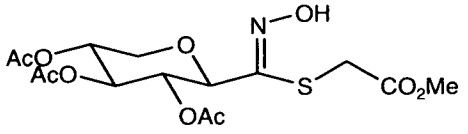
M.p 145-147 °C; $[\alpha]_D^{20}$ -15 (c = 1.0 ,$CHCl_3$); δ_H (250 MHz, $CDCl_3$); 1.40 (9H, s, 3xCH_3), 1.90, 1.93, 1.97, 2.03 (12H, 4xs, 4x$COCH_3$), 3.35 (1H, dd, CH_2a), 3.54 (1H, dd, CH_2b), 3.73 (3H, s, OCH_3), 3.93-3.78 (1H, m, 5-H), 4.11-4.17 (2H, m, 6a-H, 6b-H), 4.22 (1H, d, 1-H), 4.53 (1H, m, CH), 5.06 (1H, dd, 2-H), 5.17 (1H, dd, 4-H), 5.39 (1H, dd, 3-H), 5.62 (1H, dd, NH), 9.63 (1H, bs, OH; *J*(x-y)/Hz 1-2 9.8, 2-3 9.6, 3-4 9.3, 4-5 9.2, 5-6a nd, 5-6b nd, 6a-6b nd ; δ_C (63 MHz, $CDCl_3$) 20.5 (4x$COCH_3$), 29.5 (3xCH_3), 32.1 (CH_2), 52.6 (OCH_3), 53.7 (CH), 62.0 (C-6), 65.7, 67.8, 69.1, 74.1, 75.6 (C-1, C-2, C-3, C-4, C-5), 80.3 (C Boc), 146.4 (C=N) 155.1 (C=O Boc), 169.4, 170.3, 170.5 (4x$COCH_3$), 170.6 (CO_2CH_3); *m/z* (FAB) 609 (M^++1); HRMS (FAB) Found: M^++1 609.19777 $C_{24}H_{37}N_2O_{14}S$ requires M^++H 609.19655.

3.3.1.9 S-Carbmethoxymethyl-2,3,4-tri-*O*-acetyl-β-D-xylopyranosylformothiohydroximate (166)

Sample code: IAS067

Molecular formula: $C_{15}H_{21}N\,O_{10}S$

Molecular weight: 407



To a stirred mixture of methyl thioglycolate (0.08 ml, 0.9 mmol) and triethylamine (0.25 ml, 1.8 mmol) in dry chloroform (30 ml), D-xylose derived hydroximoyl chloride (**106**) (100 mg, 0.3 mmol) was added in accordance to general procedure B. Dry-flash chromatography yielded (in order of elution) residual methyl thioglycolate, and the title compound (**166**) as a white solid (85 mg, 70%)

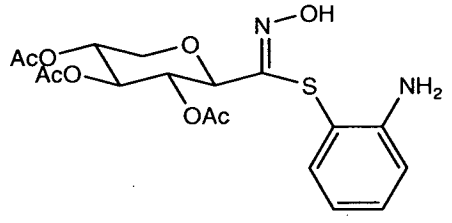
M.p 144-145°C; δ_H (360 MHz, $CDCl_3$); 1.98, 2.04, 2.05 (9H, 3s, 3x$COCH_3$), 3.38 (1H, dd, 5a-H), 3.75 (1H, d, CH_2a), 3.77 (3H, s, $CO_2\underline{CH_3}$), 3.82 (1H, d, CH_2b), 4.14 (1H, dd, 5e-H), 4.29 (1H, d, 1-H), 5.01-5.08 (1H, m, 4-H), 5.25 (1H, dd, 2-H), 5.41 (1H, dd, 3-H), 9.39 (1H, bs, OH; *J*(x-y)/Hz 1-2 9.6, 2-3 9.3, 3-4 9.5, 4-5a 10.6, 4-5e 5.6, 5a-5e 11.2, 2a'-2b' 15.8; δ_C (93 MHz, $CDCl_3$) 21.7, 21.8 (3x$COCH_3$), 33.3 ($SCH_2CO_2CH_3$) 53.9 (CO_2CH_3) 67.5 (C-5), 69.7, 70.4, 74.6, 79.2 (C-1, C-2, C-3, C-4), 148.1 (C=N) 170.8, 170.9, 171.1 (3x$COCH_3$), 171.7 (CO_2CH_3); *m/z* (ES) 408 (MH^+).

3.3.1.10 S-2-Aminophenyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosylformothiohydroximate (216)

Sample code: IAS021

Molecular formula: $C_{18}H_{22}N_2O_8S$

Molecular weight: 426



To a stirred mixture of 2-amino-thiophenol (225 mg, 1.8 mmol) and triethylamine (0.25 ml, 1.8 mmol) in dry ether (10 ml), D-xylose derived hydroximoyl chloride **106** (200mg, 0.6 mmol) was added in accordance to general procedure B. Dry-flash chromatography yielded (in order of elution) residual 2-amino-thiophenol , and the title compound (**216**) as a white solid (196 mg, 78%).

M.p 97-98°C ; $[\alpha]_D^{20}$ 30 (c = 0.5 ,$CHCl_3$); δH (250 MHz, $CDCl_3$); 1.91, 1.92, 1.98 (9H, 3s, 3x$COCH_3$), 2.41 (1H, dd, 5a-H), 3.59 (1H, d, 1-H) 3.80 (1H, dd, 5b-H), 4.35 (2H, bs, NH_2), 4.84 (1H, td, 4-H), 4.90 (1H, dd, 2-H), 5.34 (1H, dd, 3-H), 6.64-6.73 (2H, m, ArH), 7.14-7.18 (1H, m, ArH), 7.36 (1H, dd, Ar); *J*(x-y)/Hz 1-2 9.9, 2-3 8.9, 3-4 10.0, 4-5a 10.3, 4-5b 5.6, 5a-5b 11.1; δC (63 MHz, $CDCl_3$) 21.0, 21.1 (3x$COCH_3$), 66.6 (C-5), 69.2, 69.6, 74.5, 75.6 (C-2, C-3, C-4, C-1), 110.2 (Ar*C*-SR) 115.7, 118.7, 132.3, 138.9 (ArCH) 148.6 (C=N) 150.3 (Ar*C*-NH_2)) 170.1, 170.2, 171.1 (3x*C*OCH_3); m/z (FAB) 427 (M^+ +1) HRMS (FAB) Found M^++1 427.1167, $C_{18}H_{22}N_2O_8S$ requires M^++H 427.1175.

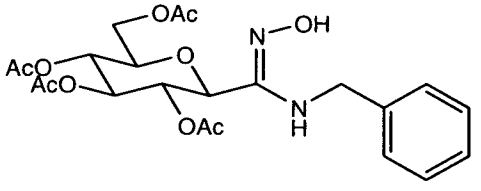
3.4 Synthesis of the pyranosylamidoximes

3.4.1 Alkyl/Aryl Amidoximes- General procedure

A solution of the hydroximoyl chloride (1 equivalent) in chloroform (35-50 ml) was added dropwise over 2 hours to a cooled (0°C) and stirred solution of the amine (2 equivalents) and triethylamine (3-18 equivalents) in chloroform (3-5 ml) under N_2. After stirring for 1 hour the mixture was poured into water (50 ml), extracted with DCM (3 x 50 ml), the combined organic layers dried ($MgSO_4$), and the solvent removed *in vacuo*. The product was isolated by dry-flash chromatography (silica, hexane/Et_2O gradient elution).

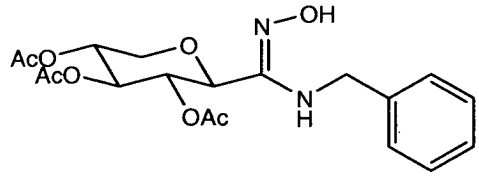
3.4.1.1 (Z)-*N*-Benzyl-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)formamide oxime (137)

Sample code: IAS061
Molecular formula: $C_{22}H_{28}N_2O_{10}$
Molecular weight: 480



To a stirred mixture of benzylamine (0.18 ml, 1.6 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (3 ml), D-glucose derived hydroximoyl chloride **107** (200 mg, 0.5 mmol) was added in accordance to the general procedure above. Dry-flash chromatography yielded the title compound (**137**) as a white solid (205 mg, 88%).
M.p. 128-129 °C ; $[\alpha]_D^{20}$ -12 (c = 1 $CHCl_3$); δ_H (360 MHz, $CDCl_3$) 1.85, 1.95, 1.98 (12H, 4s, 4x$COCH_3$), 3.59 (1H, ddd, 5'-H), 4.00 (1H, d, 2'-H), 4.02 (1H, dd, 6a'-H), 4.06 (1H, dd, 6b'-H), 4.36 (1H, dd, Bna-H), 4.49 (1H, dd, Bnb-H), 5.02 (1H, dd, 3'-H), 5.13 (1H, dd, 5'-H), 5.30 (1H, t, NH), 5.35 (1H, dd, 4'-H) 7.18-7.29 (5H, m, PhH), 8.55 (1H, bs, OH); *J*(x-y)/Hz 1'-2' 10.3, 2'-3' 9.8, 3'-4' 9.7, 4'-5' 9.9, 5'-6a' 2.4, 5'-6b' 4.7, 6a-6b 12.5 Bna-Bnb 14.5, Bna-NH 7.0, Bnb-NH 6.8; δ_C (93 MHz, $CDCl_3$) 21.5, 21.6, 21.7, (4x$COCH_3$), 47.5 (PhCH_2), 63.0 (C-6'), 69.0, 69.5, 74.3, 75.0, 76.6 (C-1',C-2',C-3', C-4', C-5'), 128.4, 129.9, (5xPhCH), 140.0 (PhC), 149.7 (C=N), 170.5, 170.7, 171.4, 171.7 (4x$COCH_3$); *m/z* (FAB) 481 (M^++1) HRMS (FAB) Found M^++1 481.18263, $C_{22}H_{28}N_2O_{10}$ requires M^++1 481.18222.

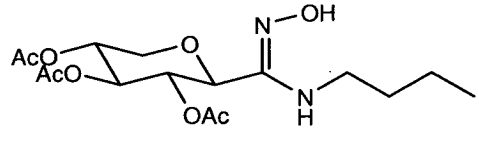
3.4.1.2 (Z)-*N*-Benzyl-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (138)



Sample code: IAS023
Molecular formula: $C_{19}H_{24}N_2O_8$
Molecular weight: 408

To a stirred mixture of benzylamine (0.14 ml, 1.3 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (3 ml), D-xylose derived hydroximoyl chloride **106** (150 mg, 0.4 mmol) was added in accordance to the general procedure above. Dry-flash chromatography yielded the title compound (**138**) as a white solid (121 mg, 67%). M.p. 64-66 °C ; $[\alpha]_D^{20}$ -3.7 (c = 0.54 $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 1.95, 1.96, 1.97 (9H, 3s, 3x$COCH_3$), 3.19 (1H, dd, 5a'-H), 3.89 (1H, d, 1'-H), 4.07 (1H, dd, 5e'-H), 4.38 (1H, dd, Bna-H), 4.39 (1H, dd, Bnb-H), 4.92 (1H, ddd, 4'-H), 5.11 (1H, dd, 3'-H), 5.22 (1H, t, NH), 5.29 (1H, dd, 2'-H), 7.14-7.31 (5H, m, PhH); *J*(x-y)/Hz 1'-2' 10.0, 2'-3' 9.2, 3'-4' 9.5, 4'-5a' 10.4, 4'-5e' 5.6, 5a'-5e' 11.2, Bna-Bnb 14.6, Bna-NH 5.5, Bnb-NH 6.8; δ_C (63 MHz, $CDCl_3$) 20.5 (3x$COCH_3$), 46.4 (PhCH_2), 67.7 (C-5'), 68.6, 68.7, 73.5, 76.1 (C-1',C-2',C-3', C-4'), 127.3, 127.4, 128.6 (5xPhCH), 138.8 (PhC), 148.9 (C=N), 169.5, 169.7, 170.2 (3x$COCH_3$); *m/z* (FAB) 409 (M^+ +1) HRMS (FAB) Found M^++1 409.16095, $C_{19}H_{24}N_2O_8$ requires M^++1 409.16109.

3.4.1.3 (Z)-*N*-Butyl-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (139)



Sample code: IAS016
Molecular formula: $C_{16}H_{26}N_2O_8$
Molecular weight: 374

To a stirred mixture of *n*-butylamine (0.21 ml, 2.2 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (5 ml), D-xylose derived hydroximoyl chloride **106**

(250 mg, 0.75 mmol) was added in accordance to the general procedure above. Dry-flash chromatography yielded the title compound (**139**) as a white solid (169 mg, 63%).

M.p 111-113 °C; $[\alpha]_D^{20}$ –41 (c = 0.8 ,$CHCl_3$); δ_H (250 MHz, $CDCl_3$); 1.91, 1.96, 1.97 (9H, 3s, 3x$COCH_3$), (3H, t, CH_3,), (6H, m, CH_2), 3.21 (1H, dd, 5a'-H), 3.86 (1H, d, 1'-H), 4.10 (1H, dd, 5e'-H), 4.93 (1H, td, 4'-H), 5.12 (1H, dd, 2'-H), 5.24 (1H, dd, 3'-H), 8.57 (1H, bs, OH); *J*(x-y)/Hz 1'-2' 9.8, 2'-3' 9.3, 3'-4' 9.3, 4'-5a' 10.7, 4'-5e' 6.0, 5a'-5e' 11.1; δ_C (63 MHz, $CDCl_3$) 14.1 (CH_3), 20.1 (CH_2), 20.9 (3x$COCH_3$), 33.3 (CH_2), 42.4 (CH_2), 67.1 (C-5'), 69.2, 70.7, 73.9, 77.6 (C-1', C-2', C-3', C-4'), 149.5 (C=N) 169.9, 170.2, 170.6 (3x$COCH_3$) ; *m/z* (FAB) 375 (M^+ +1) HRMS (FAB) Found M^++1 375.17622, $C_{16}H_{26}N_2O_8$ requires M^++1 375.17674.

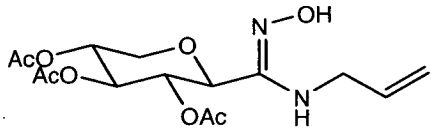
3.4.1.4 (*Z*)-N-Propenyl-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl) formamide oxime (140)

This experiment was done in collaboration with Miss K. S. Horner

Sample code: KH09

Molecular formula:

$C_{15}H_{22}N_2O_8$Molecular weight: 358

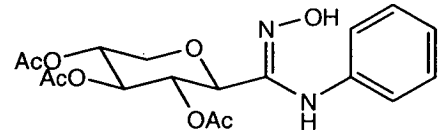


To a stirred mixture of allylamine (0.13 ml, 1.8 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (3 ml), D-xylose derived hydroximoyl chloride **106** (150 mg, 0.4 mmol) was added in accordance to the general procedure above. Dry-flash chromatography yielded the title compound (**140**) as a white solid (66 mg, 41%).

Mp 52-54 °C; $[\alpha]_D^{20}$ = -3.5 (c = 0.34, $CHCl_3$); δ_H (250 MHz, $CDCl_3$); 1.99, 2.01 (9H, 3s, 3x$COCH_3$), 3.24 (1H, dd, 5a-H), 3.85 (2H, d, CH_2), 3.88 (1H, d, 1-H), 4.09 (1H, dd, 5b-H), 4.95 (1H, m, 4-H), 5.11 (2H, dd, CH_2), 5.13 (1H, dd, 2-H), 5.26 (1H, dd, 3-H), 5.83 (1H, m, CH), 8.71 (1H, bs, OH); *J*(x-y)/Hz 1-2 9.8, 2-3 9.5, 3-4 5.4, 4-5a 10.8, 4-5b 11.2; δ_C (63 MHz, $CDCl_3$); 20.0 ($COCH_3$), 44.3 (CH_2), 66.2 (C-5), 68.0, 68.1, 72.9, 75.3 (C-2, C-3, C-4, C-1), 115.5 (CH_2), 134.7 (CH), 148.4 (C=N), 168.9, 169.2, 169.6 ($COCH_3$); *m/z* (FAB) 359 (M^+ +1) HRMS (FAB) Found M^++1 359.14514, $C_{15}H_{22}N_2O_8$ requires M^++1 359.14544.

3.4.1.5 (Z)-*N*-Phenyl-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (141)

Procedure A



Sample code: IAS014

Molecular formula: $C_{18}H_{22}N_2O_8$

Molecular weight: 394

To a stirred mixture of aniline (0.24 ml, 1.8 mmol) and triethylamine (0.25 ml, 1.8 mmol) in dry chloroform (5 ml), D-xylose derived hydroximoyl chloride **106** (200 mg, 0.6 mmol) was added in accordance to the general procedure above. Dry-flash chromatography yielded the title compound (**141**) as a crystalline solid (65 mg, 28%).

Procedure B

Xylose derived hydroximoyl chloride **106** (200 mg, 0.6 mmol) and aniline (0.12 ml, 1.5 mmol) were dissolved in ethanol (10 ml) and the mixture stirred under an atmosphere of nitrogen at room temperature for 16 h or heated under reflux for 5 hours. The reaction mixture was concentrated *in vacuo* to afford the crude product, which was purified by dry-flash chromatography (silica, hexane/Et_2O gradient elution). The title compound (**141**) was obtained as a crystalline solid (211 mg, 90%)

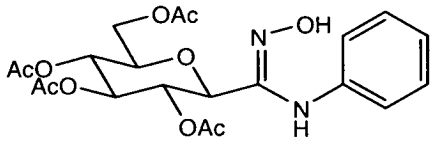
M.p 179-180°C; $[\alpha]_D^{20}$ –82 (c = 1, $CHCl_3$); δ_H (250 MHz, $CDCl_3$); 1.93, 1.95 (9H, 3s, 3x$COCH_3$), 3.07 (1H, dd, 5a'-H), 4.05 (1H, dd, 5e'-H) 4.09 (1H, d, 1'-H), 4.95 (1H, td, 4'-H), 5.02 (1H, dd, 2'-H), 5.35 (1H, dd, 3'-H), 6.94 (1H, b.s, NH), 7.04-7.31 (5H, m, Ar), 7.91 (1H, bs, OH); *J*(x-y)/Hz 1'-2' 10.0, 2'-3' 9.1, 3'-4' 9.9, 4'-5a' 10.1, 4'-5b' 5.45, 5a'-5b' 11.00; δ_C (63 MHz, $CDCl_3$) 20.60 (3x$COCH_3$), 66.53 (C-5), 68.59, 69.17, 73.31, 73.83 (C-1, C-2, C-3, C-4), 123.59, 124.84, 129.14 (ArCH), 138.11 (ArC), 146.77 (C=N) 169.25, 169.61, 170.38 (3x*C*OCH_3); *m/z* (FAB) 395 (M^+ +1) HRMS (FAB) Found M^++1 395.14526, $C_{18}H_{22}N_2O_8$ requires M^++1 395.14544.

3.4.1.6 (Z)-*N*-Phenyl-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)formamide oxime (142)

Sample code: IAS060

Molecular formula: $C_{21}H_{26}N_2O_{10}$

Molecular weight: 466



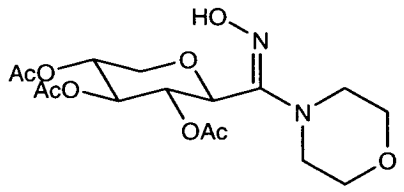
D-Glucose derived hydroximoyl chloride **107** (200 mg, 0.5 mmol) and aniline (0.11 ml, 1.2 mmol) were dissolved in ethanol (10 ml) and the mixture stirred under an atmosphere of nitrogen at room temperature for 16 h or heated under reflux for 5 hours. The reaction mixture was concentrated *in vacuo* to afford the crude product, which was purified by dry-flash chromatography (silica, hexane/Et_2O gradient elution). The title compound (**142**) was obtained as a crystalline solid (190 mg, 83%) M.p 55-56°C; $[\alpha]_D^{20}$ –79 (c = 1, $CHCl_3$); δ_H (360 MHz, $CDCl_3$); 1.91, 1.93, 1.94, 1.98 (12H, 4s, 4x$COCH_3$), 3.48 (1H, dd, 5'-H), 4.01 (1H, dd, 6a'-H), 4.08 (1H, dd, 6b'-H), 4.15 (1H, d, 1'-H), 4.97 (1H, dd, 3'-H), 5.03 (1H, dd, 5'-H), 5.40 (1H, dd, 4'-H), 7.04 (1H, b.s, NH), 7.10-7.30 (5H, m, ArH), 8.30 (1H, bs, OH); *J*(x-y)/Hz 1'-2' 10.2, 2'-3' 9.5, 3'-4' 9.3, 4'-5' 10.1, 5'-6a' 2.3, 5`-6b 6.1, 6a'-6b' 12.4; $\delta_C$ (93 MHz, $CDCl_3$) 20.3, 20.4, 20.6, 20.9 (4x$COCH_3$), 62.4 (C-6`), 68.0, 68.6, 72.7, 74.3, 75.8 (C-2`, C-3`, C-4`, C-5`, C-1`), 123.6, 124.9, 129.1 (ArCH), 138.1 (ArC), 146.4 (C=N) 170.4, 171.3, 171.5, 171.7 (4x$COCH_3$); *m/z* (FAB) 467 (M^+ +1) HRMS (FAB) Found M^++1 467.16695, $C_{21}H_{26}N_2O_{10}$ requires M^++1 467.16657.

3.4.1.7 (*E*)-*N*-Morpholino-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (143)

Sample code: IAS018

Molecular formula: $C_{16}H_{24}N_2O_9$

Molecular weight: 388



To a stirred mixture of morpholine (0.26 ml, 3 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (5 ml), D-xylose derived hydroximoyl chloride **106** (250 mg, 0.75 mmol) was added in accordance to the general procedure above. Dry-flash chromatography yielded the title compound (**143**) as a white solid (192 mg, 67%). M.p 108-111 °C $[\alpha]_D^{20}$ 16 (c = 0.5 ,$CHCl_3$); δ_H (250 MHz, $CDCl_3$); 2.06, 2.10, 2.11 (9H, 3s, 3x$CO\underline{C}H_3$), 3.09-3.16 (2H, m, morpholine CH_2), 3.24-3.36 (2H, m, morpholine CH_2), 3.39 (1H, dd, 5a'-H), 4.24 (1H, dd, 5e'-H) 3.77-3.81 (4H, m, morpholine CH_2), 5.12-5.16 (2H, m, 4'-H, 1'-H), 5.31-5.36 (2H, m, 2'-H, 3'-H), 8.33 (1H, bs, OH); *J*(x-y)/Hz 1'-2' 9.9, 2'-3', nd, 3'-4' nd, 4'-5a' 10.9, 4'-5e' 5.6, 5a'-5e' 11.3; δ_C (63 MHz, $CDCl_3$) 20.5 (3x$COCH_3$), 47.4 (CH_2), 65.7 (CH_2), 66.8 (C-5'), 68.6, 69.3, 73.3, 77.1 (C-1', C-2', C-3', C-4'), 154.7 (C=N) 169.3, 169.6, 170.4 (3x$COCH_3$); *m/z* (FAB) 389 (M^+ +1) HRMS (FAB) Found M^++1 389.15644, $C_{26}H_{24}N_2O_9$ requires M^++1 389.15601.

3.4.2 General procedure –Amidoxime linked glycopeptide analogues

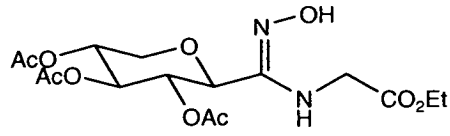
A solution of the hydroximoyl chloride (1 equivalent) in chloroform (35-50 ml) was added dropwise over 2 hours to a cooled (0 °C) and stirred solution of the amino acid ester (1.5-2 equivalents) and triethylamine (18 equivalents) in chloroform (3-5 ml) under N_2. On completion of addition, the mixture was diluted with DCM (50 ml), washed with 0.1 M HCl (2 x 50 ml) and the organic layers dried ($MgSO_4$). The products were isolated by dry-flash chromatography (silica, hexane/Et_2O gradient elution).

3.4.2.1 (Z)-*N*-Carbethoxymethyl-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (152)

Sample code: IAS019

Molecular formula: $C_{16}H_{24}N_2O_{10}$

Molecular weight: 404



To a stirred mixture of glycine ethyl ester hydrochloride (186 mg, 1.125 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (5 ml), D-xylose derived hydroximoyl chloride **106** (250 mg, 0.75 mmol) was added in accordance to the general procedure above. Dry-flash chromatography (silica, hexane/EtOAc gradient elution) yielded the title compound (**152**) as a gum (156 mg, 52%).

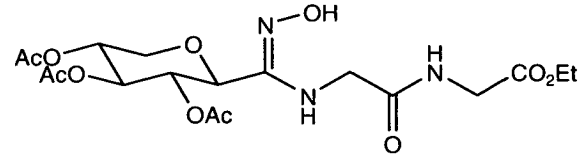
δ_H (250 MHz, $CDCl_3$) 1.23 (3H, t, $CO_2CH_2CH_3$), 1.96, 1.97, 1.98 (9H, 3s, $3xCOCH_3$), 3.28 (1H, dd, 5a'-H), 3.85 (1H, d, 1'-H), 4.07 (2H, d, CH_2), 4.06 (1H, dd, 5e'-H), 4.16 (2H, q, $CO_2CH_2CH_3$), 4.8-5.0 (1H, m, 4'-H), 5.1-5.2 (2H, m, 2'-H & 3'H), 5.48 (1H, t, NH); *J*(x-y)/Hz 1'-2' 9.8, 2'-3' 9.2, 3'-4' nd, 4'-5a' 10.2, 4'-5e' 5.5, 5a'-5e' 11.5, CH_2-NH 5.8; δ_C (63 MHz, $CDCl_3$) 14.5 ($CO_2CH_2CH_3$), 21.0 ($3xCOCH_3$), 44.7 (CH_2), 61.7 ($CO_2CH_2CH_3$), 67.1 (C-5'), 68.9, 69.1, 73.6, 76.9 (C-4',C-2',C-3', C-1'), 148.1 (C=N), 170.1, 170.2, 170.5 ($3xCOCH_3$), 170.7 ($CO_2CH_2CH_3$); *m/z* (FAB) 405 (M^+ +1) HRMS (FAB) Found M^++1 405.15194, $C_{16}H_{24}N_2O_{10}$ requires M^++1 405.151092.

3.4.2.2 2:1 Adduct (154)

Sample code: IAS051

Molecular formula: $C_{18}H_{27}N_3O_{11}$

Molecular weight: 461



Procedure A

To a stirred mixture of glycyl glycine ethyl ester hydrochloride (120 mg, 0.6 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (5 ml), D-xylose derived hydroximoyl chloride **106** (150 mg, 0.4 mmol) was added in accordance to the general procedure above. Dry-flash chromatography (silica, hexane/EtOAc gradient elution) yielded the title compound (**154**) as a gum (88 mg, 43%).

Procedure B

To a cooled (0°C) and stirred mixture of glycine ethyl ester hydrochloride (188 mg, 1.4 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (5 ml), D-xylose derived hydroximoyl chloride (**106**) (300 mg, 0.9 mmol) in chloroform (45 ml) was added dropwise over 2 hours. On completion of addition the mixture was allowed to stir for 16 hours. The mixture was diluted with DCM (50 ml), washed with 0.1 M HCl (2 x 50 ml) and the organic layers dried ($MgSO_4$). The organic layers were concentrated *in vacuo* and the residue subjected to dry-flash chromatography (silica, hexane/EtOAc gradient elution) to yield the product (**154**) as a white solid (82 mg, 20%).

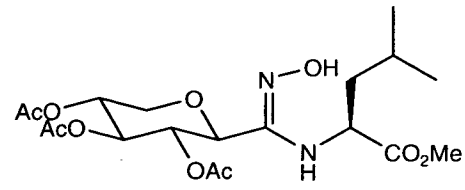
$[\alpha]_D^{20}$ –35 (c = 1.0 ,$CHCl_3$); δ_H (250 MHz, $CDCl_3$) 1.21 (3H, t, $CO_2CH_2CH_3$), 1.92, 1.95, 1.97 (9H, 3s, 3x$COCH_3$), 3.29 (1H, dd, 5a-H), 3.90 (1H, d, 1-H), 3.98-4.08 (5H, m, 5e-H, CH_2a, CH_2b), 4.14 (2H, q, $CO_2CH_2CH_3$), 4.86-5.39 (3H, m, 4-H, 3-H, 2-H), 5.61 (1H, t, NH), 7.45 (1H, t, NH); *J*(x-y)/Hz 1-2 9.6, 2-3 nd, 3-4 nd, 4-5a 10.8, 4-5e nd, 5a-5e 11.0, CH_2-NH 5.8; δ_C (63 MHz, $CDCl_3$) 13.9 ($CO_2CH_2CH_3$), 20.4 (3x$COCH_3$), 40.9 (CH_2), 46.2 (CH_2), 61.0 ($CO_2CH_2CH_3$), 66.5 (C-5), 68.5, 69.7, 73.0, 76.1 (C-1, C-2, C-3, C-4), 147.8 (C=N), 169.7, 169.9, 170.0 (3x$COCH_3$), 170.9 ($CO_2CH_2CH_3$); *m/z* (FAB) 462 (M^+ +1) HRMS (FAB) Found M^++1 462.17268, $C_{17}H_{28}N_2O_{10}$ requires M^++1 462.17238.

3.4.2.3 (Z)-*N*-Carbmethoxymethyl-2-^{i}butyl-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (155)

Sample code: IAS046A

Molecular formula: $C_{19}H_{30}N_2O_{10}$

Molecular weight: 446



To a stirred mixture of L-leucine methyl ester hydrochloride (110 mg, 0.6 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (5 ml), D-xylose derived hydroximoyl chloride **106** (150 mg, 0.4 mmol) was added in accordance to the general procedure above. Dry-flash chromatography (silica, hexane/EtOAc gradient elution) yielded the title compound (**155**) as a colourless gum (105 mg, 53%).

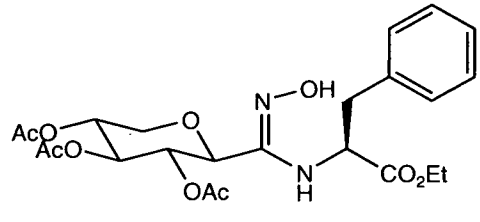
δ_H (250 MHz, $CDCl_3$) 0.88, 0.91 (6H, 2s, CH_3(iPr)), 1.48-1.57 (2H, m, CH_2(iPr)), 1.60-1.78 (1H, m, CH(iPr)) 1.89, 1.97, 1.99 (9H, 3s, 3x$COCH_3$), 3.29 (1H, dd, 5a-H), 3.66 (3H, s, CO_2CH_3), 3.85 (1H, d, 1-H), 4.04 (1H, dd, 5e-H), 4.16-4.27 (1H, m, CH), 4.86-5.03 (1H, m, 4-H), 5.09-5.31 (3H, m, 2-H, 3-H, NH) ; *J*(x-y)/Hz 1-2 9.8, 2-3 nd, 3-4 nd, 4-5a 10.8, 4-5e 5.7, 5a-5e 11.2, CH_2-NH 5.6; δ_C (63 MHz, $CDCl_3$) 20.5, 21.2, 21.3 (3x$COCH_3$), 24.0, 24.7 (CH_3(^{i}Pr)), 40.8 (CH_2(^{i}Pr)), 48.8 (CO_2CH_3), 66.5 (C-5), 68.4, 68.9, 72.2, 74.7 (C-1, C-2, C-3, C-4), 149.8 (C=N), 169.6, 169.7, 169.8 (3x$COCH_3$), 173.0 (CO_2CH_3); *m/z* (FAB) 447 (M^+ +1) HRMS (FAB) Found M^++1 447.19823, $C_{19}H_{30}N_2O_{10}$ requires M^++1 447.19787.

3.4.2.4 (Z)-*N*-Carbethoxymethyl-2-benzyl-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (161)

Sample code: IAS045

Molecular formula: $C_{23}H_{30}N_2O_{10}$

Molecular weight: 494



To a stirred mixture of L-phenylalanine ethyl ester hydrochloride (306 mg, 0.6 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (5 ml), D-xylose derived hydroximoyl chloride **106** (150 mg, 0.4 mmol) was added in accordance to the general procedure above. Dry-flash chromatography (silica, hexane/EtOAc gradient elution) yielded the title compound (**161**) as a gum (115 mg, 52%).

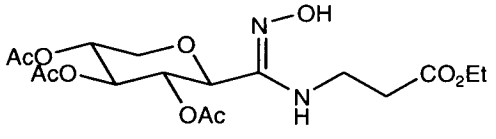
M.p 209-210 °C; $[\alpha]_D^{20}$ –161 (c = 1.0 ,$CHCl_3$); δ_H (250 MHz, $CDCl_3$) 1.12 (3H, t, $CO_2CH_2C\underline{H}_3$), 1.89, 1.97, 1.98 (9H, 3s, 3x$COCH_3$), 3.01 (1H, dd, CH_2a), 3.09 (1H, dd, CH_2b), 3.21 (1H, dd, 5a-H), 3.82 (1H, d, 1-H), 4.00-4.09 (3H, m, $CO_2C\underline{H}_2CH_3$, 5b-H), 4.46-4.55 (1H, m, CH), 4.86-4.97 (1H, m, 4-H), 5.09-5.20 (2H, m, 2-H, 3-H), 5.26 (1H, d, NH), 7.08-7.39 (5H, m, PhH); *J*(x-y)/Hz 1-2 9.5, 2-3 nd, 3-4 nd, 4-5a 10.7, 4-5e nd, 5a-5e 10.8., CH-NH 10.0; δ_C (63 MHz, $CDCl_3$) 13.9 ($CO_2CH_2\underline{C}H_3$), 20.5 (3x$CO\underline{C}H_3$), 39.8 ($PhCH_2$), 56.2 (CH), 61.1 ($CO_2\underline{C}H_2CH_3$), 66.5 (C-5), 68.6, 69.1, 73.3, 76.2 (C-1, C-2, C-3, C-4), 126.9, 128.4, 129.3 (ArCH), 135.6 (ArC), 147.1 (C=N), 169.4, 169.7, 170.2 (3x$\underline{C}OCH_3$), 172.1 ($\underline{C}O_2CH_2H_3$); *m/z* (FAB) 495 (M^+ +1) HRMS (FAB) Found M^++1 495.19803, $C_{23}H_{31}N_2O_{10}$ requires M^++1 495.19787.

3.4.2.5 (Z)-*N*-Carbethoxyethyl-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime beta alanine (164)

Sample code: IAS049

Molecular formula: $C_{17}H_{27}N_2O_{10}$

Molecular weight: 418



To a stirred mixture of β-alanine ethyl ester hydrochloride (92 mg, 0.6 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (5 ml), D-xylose derived hydroximoyl chloride **106** (150 mg, 0.4 mmol) was added in accordance to the general procedure above. Dry-flash chromatography (silica, hexane/EtOAc gradient elution) yielded the title compound (**164**) as a gum (90 mg, 50%)

M.p 110-112 °C; $[\alpha]_D^{20}$ –35 (c = 1.0 ,$CHCl_3$); δ_H (360 MHz, $CDCl_3$); 1.22 (3H, t, $CO_2CH_2C\underline{H}_3$), 1.94, 1.98, 2.01 (9H, 3s, 3x$COC\underline{H}_3$), 2.53 (2H, t, $CH_2\underline{C}H_2CO_2Et$), 3.29 (1H, dd, 5a'-H), 3.53 (2H, m, $C\underline{H}_2CH_2CO_2Et$), 3.91 (1H, d, 1-H), 4.12 (1H, dd,

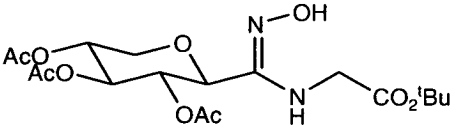
5e'-H), 4.13 (3H, q, $CO_2C\underline{H}_2CH_3$), 4.96 (1H, ddd, 4-H), 5.18 (1H, dd, 2-H), 5.24 (1H, dd, 3'-H), 5.36 (1H, t, NH); *J*(x-y)/Hz 1-2 9.3, 2-3 9.4, 3-4 9.0, 4-5a 10.8, 4-5e 5.4, 5a-5e 11.2; δ_C (93 MHz, $CDCl_3$) 14.5 ($CO_2CH_2\underline{C}H_3$), 20.9, 21.0 (3x$COCH_3$), 36.1 ($CH_2\underline{C}H_2CO_2Et$), 38.9 ($\underline{C}H_2CH_2CO_2Et$), 61.1 ($CO_2\underline{C}H_2CH_3$), 67.14 (C-5), 69.0, 69.2, 73.9, 76.9 (C-1, C-2, C-3, C-4), 149.0 (C=N) 170.0, 170.2, 170.60 (3x$\underline{C}OCH_3$) 170.3 ($\underline{C}O_2CH_2CH_3$); *m/z* (FAB) 419 (M^+ +1) HRMS (FAB) Found M^++1 419.16741, $C_{17}H_{28}N_2O_{10}$ requires M^++1 419.16657.

3.4.2.6 (Z)-*N*-Carb^{t}butoxymethyl-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (165)

Sample code: IAS050

Molecular formula: $C_{18}H_{28}N_2O_{10}$

Molecular weight: 432



To a stirred mixture of glycine tertiarybutyl ester.AcOH (115 mg, 0.6 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (5 ml), D-xylose derived hydroximoyl chloride **106** (150 mg, 0.4 mmol) was added in accordance to the general procedure above. Dry-flash chromatography (silica, hexane/EtOAc gradient elution) yielded the title compound (**165**) as a colourless gum (170 mg, 88%).

$[\alpha]_D^{20}$ –49 (c = 1.35 ,$CHCl_3$) δ_H (360 MHz, $CDCl_3$) 1.45, (9H, s, CH_3), 1.97, 2.02, 2.03 (9H, 3s, 3x$COCH_3$), 3.32 (1H, dd, 5a-H), 3.87 (1H, d, 1-H), 3.92 (1H, dd, CH_2a), 4.04 (1H, dd, CH_2b), 4.16 (1H, dd, 5e-H), 4.97-5.04 (1H, m, 4-H), 5.18-5.22 (2H, m, 2-H & 3H), 5.49 (1H, t, NH) ; *J*(x-y)/Hz 1-2 9.8, 2-3 nd, 3-4 nd, 4-5a 10.8, 4-5e 5.6, 5a-5e 11.2, CH_2-NH 5.8; δ_C (93 MHz, $CDCl_3$) 21.7, 21.8 (3x$COCH_3$), 30.7 (CH_3), 45.8 (CH_2), 67.8 (C-5'), 69.6, 69.9, 74.3, 77.9 (C-4',C-2',C-3', C-1'), 83.2 (Cq), 148.9 (C=N), 170.4, 170.8, 171.0 (3x$\underline{C}OCH_3$), 171.3 ($\underline{C}O_2{}^t$Bu); *m/z* (FAB) 433 (M^+ +1) HRMS (FAB) Found M^++1 433.18226, $C_{16}H_{24}N_2O_{10}$ requires M^++1 433.18222.

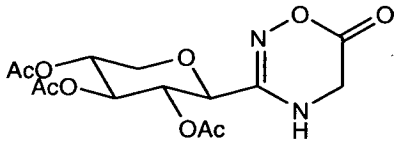
3.4.3 Cyclisation Reactions

3.4.3.1 3-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-1,2,4-oxadiazin-6-one (153)

Sample code: IAS020

Molecular formula: $C_{14}H_{18}N_2O_9$

Molecular weight: 358



(Z)-*N*-Carbethoxymethyl-(2',3',4'-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (**152**) (156 mg, 0.4 mmol) was dissolved in chloroform (15 ml), stirred with silica (500 mg) and heated under reflux for 32 hours. On cooling, the product was obtained as a crystalline solid (83 mg, 60%) after dry-flash chromatography (silica, hexane/Et_2O gradient elution).

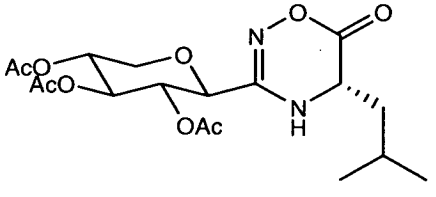
M.p. 165 °C (decomp.) (from hexane-EtOAc), $[\alpha]_D^{20}$ –151 (c = 2.25, $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 1.98, 1.99, 2.00 (9H, 3s, 3x$COCH_3$), 3.37 (1H, dd, 5a'-H), 3.94 (1H, d, 1'-H), 3.95 (2H, s, CH_2), 4.14 (1H, dd, 5e'-H), 4.93 (1H, ddd, 4'-H), 4.98 (1H, dd, 3'-H), 5.26 (1H, t, 2'H), 5.61 (1H, br s, NH); *J*(x-y)/Hz 1'-2' 9.7, 2'-3' 9.4, 3'-4' 9.9, 4'-5a' 10.3, 4'-5e' 6.2, 5a'-5e' 11.6; δ_C (63 MHz, $CDCl_3$) 20.4 (3x$COCH_3$), 40.2 (CH_2), 66.5 (C-5'), 68.4, 69.1, 71.7 (C-2',C-3',C-4'), 74.9 (C-1'), 150.4 (C=N), 164.6 (C=O), 169.7, 169.8, 170.1 (3x$COCH_3$); *m/z* (FAB) 359 (M^+ + 1) HRMS (FAB) Found M^++ 1 359.10950, $C_{14}H_{18}N_2O_9$ requires M^+ + 1, 359.10906.

3.4.3.2 3-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-5-(isopropyl)-1,2,4-oxadiazin-6-one (156)

Sample code: IAS046B

Molecular formula: $C_{18}H_{26}N_2O_9$

Molecular weight: 414



Amidoxime **155** (199 mg, 0.44 mmol) was dissolved in chloroform (15 ml), stirred with silica (500 mg) and heated under reflux for 32 hours. On cooling, the product

(**156**) was obtained as a crystalline solid (130 mg, 70%) after dry-flash chromatography (silica, hexane/Et_2O gradient elution).

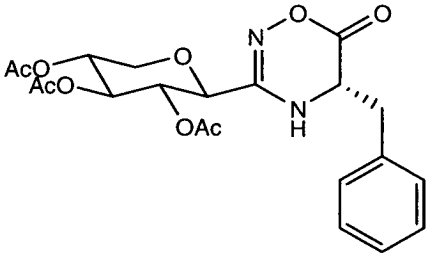
M.p 182-184 °C; $[\alpha]_D^{20}$ –107 (c = 1.0 ,$CHCl_3$); δ_H (360 MHz, $CDCl_3$) 0.95, 0.99 (6H, 2d, CH_3(iPr)), 1.72-1.81 (2H, m, CH_2(iPr)), 2.04, 2.05 (9H, 3s, 3x$COCH_3$), 3.41 (1H, dd, 5a'-H), 3.99-4.03 (2H, m, CH, 1'-H), 4.21 (1H, dd, 5e'-H), 5.00 (1H, m, 4'-H), 5.02 (1H, dd, 2'-H), 5.28 (1H, dd, 3'-H); *J*(x-y)/Hz 1'-2' 9.8, 2'-3' 9.5, 3'-4' 9.6, 4'-5a' 10.8, 4'-5e' 5.6, 5a'-5e' 11.4; δ_C (93 MHz, $CDCl_3$) 21.7, 22.4 (3x$COCH_3$), 23.7, 25.2 ($CH_3(^iPr)$), 41.9 ($CH_2(^iPr)$), 50.0 (C-5), 67.7 (C-5'), 69.6, 70.0, 73.3, 75.8 (C-1', C-2', C-3', C-4'), 151.0 (C=N), 168.6 (C=O) 170.8, 170.9, 171.0 (3x*C*OCH_3); *m/z* (FAB) 415 (M^+ +1) HRMS (FAB) Found M^++1 415.17168, $C_{18}H_{27}N_2O_9$ requires M^++1 415.17166.

3.4.3.3 3-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-5-(benzyl)-1,2,4-oxadiazin-6-one (162)

Sample code: IAS068

Molecular formula: $C_{21}H_{24}N_2O_9$

Molecular weight: 448



Amidoxime **161** (115 mg, 0.23 mmol) was allowed to stand in an N.M.R tube for ~ 6 months at room temperature, after which time, the solvent was removed *in vacuo* to afford the title compound (**162**) as a white solid (104 mg, 98%).

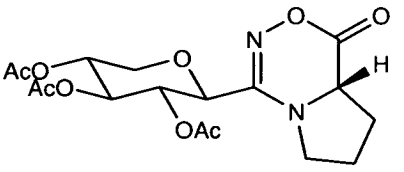
M.p 82-84 °C; $[\alpha]_D^{20}$ –24 (c = 5.1 ,$CHCl_3$); δ_H (360 MHz, $CDCl_3$) 2.08, 2.11, 2.14 (9H, 3s, 3x$COCH_3$), 3.04 (1H, dd, CH_2a), 3.38 (1H, dd, 5a'-H), 3.45 (1H, dd, CH_2b), 3.97 (1H, d, 1'-H), 4.12 (1H, dd, 5e'-H), 4.23 (1H, ddd, 5-H), 4.93 (1H, ddd, 4'-H), 5.03 (1H, dd, 2'-H), 5.08 (1H, d, NH), 5.32 (1H, dd, 3'-H) ; *J*(x-y)/Hz 1'-2' 9.8, 2'-3' 9.6, 3'-4' 9.6, 4'-5a' 10.8, 4'-5e' 5.7, 5a'-5e' 11.4., CH-NH 1.8; δ_C (93 MHz, $CDCl_3$) 21.7, 21.8, 22.0 (3x$COCH_3$), 39.7 (CH_2Ph), 52.9 (C-5), 67.2 (C-5'), 67.7, 69.6, 73.1, 75.8 (C-1', C-2', C-3', C-4'), 128.8, 129.7, 130.3 (PhCH), 136.3 (PhC), 150.4 (C=N), 167.6 (C=O) 170.9, 171.0, 171.2 (3x*C*OCH_3); *m/z* (FAB) 449 (M^+ +1) HRMS (FAB) Found M^++1 449.15613, $C_{21}H_{25}N_2O_9$ requires M^++1 449.15601.

3.4.3.4 6-*S*-2-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-4-oxa-1,3-diazabicyclo[4.3.0]non-2-en-5-one (163)

Sample code: IAS053

Molecular formula: $C_{17}H_{22}N_2O_9$

Molecular weight: 398



To a cooled (0°C) and stirred mixture of L-proline benzyl ester hydrochloride (326 mg, 1.4 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (5 ml), D-xylose derived hydroximoyl chloride **106** (300 mg, 0.9 mmol) in chloroform (45 ml) was added dropwise over 2 hours. On completion of addition, the mixture was diluted with DCM (50 ml), washed with 0.1 M HCl (2 x 50 ml) and the organic layers dried ($MgSO_4$). The organic layers were concentrated *in vacuo* and the residue subjected to dry-flash chromatography (silica, hexane/Et_2O gradient elution) to remove residual amino acid. The amidoxime/oxadiazinone mixture was dissolved in chloroform (15 ml), stirred with silica (500 mg) and heated under reflux for 2 hours. On cooling, the product (**163**) was obtained as a white solid (200 mg, 57%) after dry-flash chromatography (silica, hexane/Et_2O gradient elution).

M.p 71-73 °C; $[\alpha]_D^{20}$ –99 (c = 1.0 ,$CHCl_3$); δ_H (360 MHz, $CDCl_3$) 2.03, 2.07 (9H, 3s, 3x$COCH_3$), 2.01-2.37 (4H, m, 2xproline CH_2), 3.39 (1H, dd, 5a'-H), 3.72-3.80 (2H, m, proline CH_2), 3.85-3.91 (1H, m, proline CH), 4.03 (1H, d, 1'-H), 4.18 (1H, dd, 5e'-H), 5.02 (1H, ddd, 4'-H), 5.10 (1H, dd, 3'-H), 5.32 (1H, dd, 2'-H); *J*(x-y)/Hz 1'-2' 10.3, 2'-3' 9.6, 3'-4' 9.6, 4'-5a' 10.8, 4'-5e' 5.7, 5a'-5e' 11.3; δ_C (93 MHz, $CDCl_3$) 20.3, 20.4 (3x$COCH_3$), 24.1 (CH_2), 26.8 (CH_2), 47.1 (CH_2), 54.8 (CH), 66.6 (C-5'), 68.0, 68.6, 72.2, 75.7 (C-1', C-2', C-3', C-4'), 151.8 (C=N), 168.7 (C=O) 169.5, 169.7, 170.1 (3x$COCH_3$); *m/z* (FAB) 399 (M^+ +1) HRMS (FAB) Found M^++1 399.14027, $C_{17}H_{23}N_2O_9$ requires M^++1 399.14036.

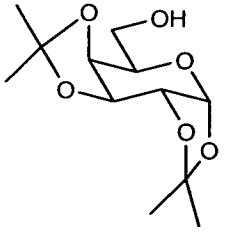
3.5 Synthesis of Pyranosylamines

3.5.1 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (174)

Sample code: IAS034

Molecular formula: $C_{12}H_{20}O_6$

Molecular weight: 260



D-Galactose (20 g, 0.11 mol), anhydrous $CuSO_4$ (43.7 g, 0.27 mol) and dry acetone (440 ml) were stirred at room temperature under nitrogen. Concentrated H_2SO_4 ((2.2 ml) was added with vigourous stiring, the resulting mixture was left to stir for 24 hours. The mixture was filtered, the resultant yellow filtrate was stirred with $CaOH_2$ (15 g) for 24 hours. The mixture was filtered and the filtrate was concentrated *in vacuo* to afford an amber coloured oil that contained crude product. The crude material was purified by kügelrohr distillation, the product (**174**) was obtained as a colourless glass (17.5 g, 61%)

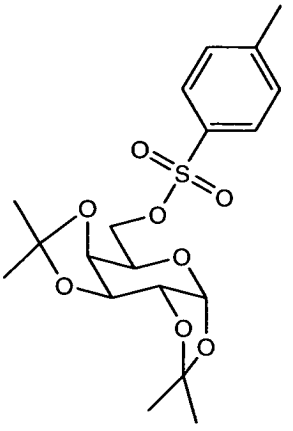
$[\alpha]_D^{20}$ –56 (c = 3 ,$CHCl_3$) (lit.[173] $[\alpha]_D^{20}$ -59 (c = 3, $CHCl_3$)); δ_H (360 MHz, $CDCl_3$); 1.32, 1.44, 1.52, (12H, 4s, 4xCH_3), 2.38 (1H, bs, OH), 3.71 (1H, dd, 6a-H) 3.80-3.88 (2H, m, 6b-H, 5-H), 4.25 (1H, dd, 4-H), 4.31 (1H, dd, 2-H), 4.59 (1H, dd, 3-H), 5.55 (1H, d, 1-H); *J*(x-y)/Hz 1-2 5.0, 2-3 2.4, 3-4 7.9, 4-5 1.6, 5-6a 3.4, 5-6b 6a-6b 10.4; δC (63 MHz, $CDCl_3$) 24.2, 24.8, 25.8, 25.9 (4xCH_3), 62.2 (C-6), 68.4, 70.7, 70.8, 71.6 (C-2, C-3, C-4, C-5), 96.2 (C-1), 108.5, 109.3, (2xC); *m/z* (FAB) 261 (M^++1); HRMS (FAB) Found: M^++1 261.13366. $C_{12}H_{20}O_6$ requires M^++1 261.13381.

3.5.2 6-*O*-(*p*-Tolylsulfonyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (175)

Sample code: IAS030

Molecular formula: $C_{19}H_{26}O_8S$

Molecular weight: 414



1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (**174**) (5 g, 19 mmol) and p-toluenesulfonyl chloride (4.2 g, 22 mmol) were dissolved in a 2:1 mixture of pyridine:acetonitrile (60 ml) and stirred for 6 hours. The reaction mixture was mixed with ether (80 ml), washed 3 times water (70 ml) and once with 0.2 M HCl (80 ml) before drying over $MgSO_4$. The mixture was filtered and concentrated *in vacuo* to yield an oil. The oil was chilled in ice until it became a gum, and was vigourously triturated with 9:1 hexane:ethyl acetate (5 ml) to afford the title compound (**175**) as a white solid (5.3 g, 67 %).

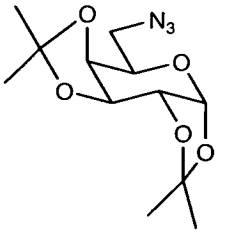
δ_H (250 MHz, $CDCl_3$); 1.21, 1.24, 1.27, 1.43 (12H, 4s, 4xCH_3), 2.37 (1H, s, ArCH_3), 3.94-4.05 (2H, m, 6a-H, 6b-H) 4.10-4.16 (2H, m, 5-H, 4-H), 4.22 (1H, dd, 2-H), 4.52 (1H, dd, 3-H), 5.38 (1H, d, 1-H), 7.26 (2H, d, ArH) 7.73 (2H, d, ArH) ; *J*(x-y)/Hz 1-2 4.9, 2-3 2.5, 3-4 7.9, 4-5 nd, 5-6a nd, 5-6b nd, 6a-6b nd; δC (63 MHz, $CDCl_3$) 21.5 (ArMe), 24.2, 24.7, 25.6 (4xCH_3), 68.0 (C-6), 65.7, 70.1, 70.2, 70.3 (C-2, C-3, C-4, C-5), 96.0 (C-1), 108.8, 109.4, (2xC), 127.9, 129.0, 132.6 (ArCH) 144.6 (ArC); *m/z* (FAB) 412 (M^++1); HRMS (FAB) Found: M^++1 414.14292. $C_{19}H_{26}O_8S$ requires M^++1 414.14267.

3.5.3 6-Azido-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (176)

Sample code: IAS031

Molecular formula: $C_{12}H_{19}N_3O_5$

Molecular weight: 285



6-*O*-(*p*-tolylsulfonyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**175**) (1 g, 2.4 mmol) was dissolved in DMSO (10 ml) before adding sodium azide (315 mg, 5 mmol). The mixture was heated to 115°C under reflux for 24 hours. On cooling, water (50 ml) and ether (50 ml) were added and the mixture was allowed to partition. The aqueous layer was extracted with ether (2x 50 ml) and the combined organic layers dried over $MgSO_4$. The solution was filtered and concentrated *in vacuo* to afford the title compound (**176**) as a colourless oil (663 mg, 96%).

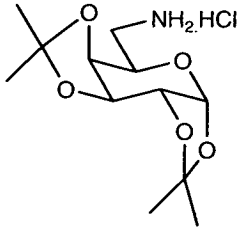
υ_{max}/cm^{-1} (Nujol) 2105 (N_3); δ_H (250 MHz, $CDCl_3$); 1.27, 1.39, 1.48 (12H, 4s, 4xCH_3), 3.29 (1H, dd, 6a-H), 3.44 (1H, dd, 6b-H) 3.79-3.88 (2H, m, 5-H), 4.13 (1H, dd, 4-H), 4.26 (1H, dd, 2-H), 4.56 (1H, dd, 3-H), (1H, d, 1-H); *J*(x-y)/Hz 1-2 5.0, 2-3 2.5, 3-4 7.9, 4-5 2.0, 5-6a 5.4, 5-6b 7.8, 6a-6b 12.7; δC (63 MHz, $CDCl_3$) 24.2, 24.7, 25.8, 25.9 (4xCH_3), 50.5 (C-6), 66.9, 70.2, 70.6, 71.0 (C-2, C-3, C-4, C-5), 96.2 (C-1), 108.6, 109.5, (2xC); *m/z* (FAB) 286 (M^++1); HRMS (FAB) Found: M^++1 286.14094. $C_{12}H_{19}N_3O_5$ requires M^++1 286.14030.

3.5.4 6-Amino-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose Hydrochloride (177)

Sample code: IAS033

Molecular formula: $C_{12}H_{21}NO_5Cl$

Molecular weight: 295.5



6-azido-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**176**) (660 mg, 2 mmol) was dissolved in a mixture of ethanol (50 ml) and chloroform (1 ml) and stirred vigourously with 10% Pd/C (110 mg) for 16 hours under an atmosphere of

hydrogen gas (20 bar) in a Parr high pressure hydrogenator. The Pd catalyst was filtered off through a celite pad and the filtrate removed *in vacuo* to afford the title compound (**177**) as a white solid (611 mg, 89%).

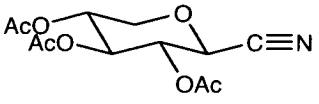
υ_{max}/cm^{-1} (Nujol) 3377 v.broad (NH_2); δ_H (250 MHz, D_2O); 1.39, 1.48, 1.56 (12H, 4s, 4xCH_3), 3.14-3.30 (2H, m, 6a-H, 6b-H), 4.08-4.16 (1H, m, 5-H) 4.46 (1H, dd, 4-H), 4.57 (1H, dd, 2-H), 4.71-4.88 (1H, m, 3-H), 5.70 (1H, d, 1-H); *J*(x-y)/Hz 1-2 5.0, 2-3 2.4, 3-4 7.9, 4-5 1.6, 5-6a nd, 5-6b nd, 6a-6b nd; δC (63 MHz, D_2O) 23.7, 24.3, 25.3 (4xCH_3), 40.2 (C-6), 64.8, 70.2, 70.6, 71.5 (C-2, C-3, C-4, C-5), 96.3 (C-1), 110.4, 110.9, (2xC); *m/z* (FAB) 260 (M^++1); HRMS (FAB) Found: MH^+ 260.14998. $C_{12}H_{22}NO_5$ requires MH^+ 260.14980.

3.5.5 2,6-Anhydro-3,4,5-tri-*O*-acetyl-β-D-xylopyranosylnitrile (167)

Sample code: IAS043

Molecular formula: $C_{12}H_{15}N\,O_7$

Molecular weight: 285



3,4,5-Tri-O-acetyl-β-D-xylopyranosylnitromethane (**95**) (1.5 g, 4.7 mmol) was dissolved in pyridine (30 ml) and cooled in an ice bath. PCl_3 (1 ml) was added and the mixture stirred for 3 days at room temperature. Ice-cold 1 M HCl (30 ml) was added to the solution and the mixture stirred for 1 hour. The solution was extracted with chloroform (3 x 50 ml) and the combined organic layers were washed with $NaHCO_3$ (2 x 50 ml) and water before drying over $MgSO_4$. The solvent was co-evaporated with water (to remove residual pyridine) to afford crude product as a gummy solid. The title compound (**167**) was obtained as a white solid (1.34 g, 75%) after dry-flash chromatography.

M.p 128-130°C (lit.[186] 131-132°C); υ_{max}/cm^{-1} (Nujol) 2257 (CN) 1759 (C=O); δ_H (250 MHz, $CDCl_3$); 2.02, 2.04, 2.06 (9H, 3s, 3x$COCH_3$), 3.54 (1H, dd, 6a-H), 4.17 (1H, dd, 6b-H), 4.46 (1H, d, 2-H), 4.82-4.89 (1H, m, 5-H), 5.00-5.08 (2H, m, 3-H, 4-H); *J*(x-y)/Hz 2-3 6.7, 3-4 nd, 4-5 nd, 5-6a 6.8, 5-6b 4.0, 6a-6b 12.4; δ_C (63 MHz, $CDCl_3$) 20.41, 20.58 (3x$COCH_3$), 65.1 (C-6), 65.3, 66.7, 67.7, 68.7 (C-3, C-4, C-5,

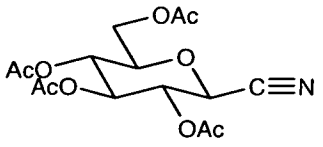
C-2), 114.2 (CN) 168.7, 169.2, 169.3 (3x$COCH_3$); *m/z* (FAB) 286 (M^++1); HRMS (FAB) Found: M^++1 286.09240. $C_{12}H_{15}NO_7$ requires M^++1 286.09268.

3.5.6 2,3,4,6-Tetra-*O*-acetyl-1-deoxy-1-β-D-glucopyranosylnitrile (189)

Sample code: IAS057

Molecular formula: $C_{15}H_{19}N\,O_9$

Molecular weight: 357



2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosylnitromethane (**99**) (1.5 g, 4.2 mmol) was dissolved in pyridine (30 ml) and cooled in an ice bath. PCl_3 (1 ml) was added and the mixture stirred for 3 days at room temperature. Ice-cold 1 M HCl (30 ml) was added to the solution and the mixture stirred for 1 hour. The solution was extracted with chloroform (3 x 50 ml) and the combined organic layers were washed with $NaHCO_3$ (2 x 50 ml) and water before drying over $MgSO_4$. The solvent was co-evaporated with water (to remove residual pyridine) to afford crude product as a gummy solid. The title compound (**189**) was obtained as a white solid (1.2 g, 82%) after dry-flash chromatography.

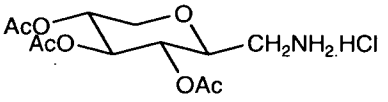
M.p 114°C (lit.[186] 114-115°C); υ_{max}/cm^{-1} (Nujol) 2257 (CN), 1753 (C=O); δ_H (250 MHz, $CDCl_3$); 1.96, 1.97, 2.05 (12H, 4s, 4x$COCH_3$), 3.67 (1H, ddd, 6-H), 4.07 (1H, dd, 7a-H), 4.17 (1H, dd, 7b-H), 4.29 (1H, dd, 2-H), 5.04 (1H, dd, 3-H), 5.12 (1H, dd, 5-H), 5.25 (1H, dd, 4-H), 8.78 (1H, bs, OH); *J*(x-y)/Hz 2-3 9.9, 3-4 9.2, 4-5 9.7, 5-6 9.0, 6-7a 2.2, 6-7b 4.7, 7a-7b 12.7; δ_C (63 MHz, $CDCl_3$) 20.7, 20.8, 21.0 (4x$COCH_3$), 61.7 (C-7), 66.68, 67.5, 69.2, 73.1, 76.9 (C-2, C-3, C-4, C-5, C-6,), 114.5 (C-1) 169. 1, 169.5, 170.3, 170.8 (4x$COCH_3$); *m/z* (ES) 358 (MH^+)

3.5.7 (3,4,5-Tri-*O*-acetyl-β-D-xylopyranosyl) methylamine hydrochloride (182)

Sample code: IAS036

Molecular formula: $C_{12}H_{20}N_2O_7Cl$

Molecular weight: 325.5



2,6-Anhydro-3,4,5-tri-*O*-acetyl-β-D-xylopyranosylnitrile (**167**) (500 mg, 1.8 mmol) was dissolved in a mixture of ethanol (50 ml) and chloroform (1 ml) and stirred vigourously with PtO_2 (Adam`s catalyst) (60 mg) for 16 hours under an atmosphere of hydrogen gas (20 bar) in a Parr high pressure hydrogenator. The catalyst was filtered off through a celite pad and the filtrate removed *in vacuo* to afford the title compound as a white solid (**182**) (565 mg, 99%).

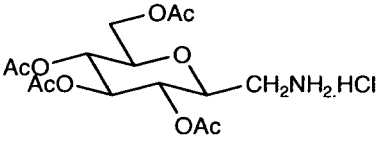
υ_{max}/cm^{-1} (Nujol) 3364 (NH_2), 1745 (C=O); $[\alpha]_D^{20}$ 129 (c = 1.5 , D_2O); M.p 183-184°C, $[\alpha]_D^{18}$ -38 (c = 1.6, D_2O); δ_H (250 MHz, D_2O); 2.01, 2.04 (9H, 3s, 3x$COCH_3$), 3.02 (1H, dd, 1a-H), 3.18-3.25 (1H, m, 1b-H), 3.45 (1H, dd, 6a-H), 3.79-3.86 (1H, m, 2-H), 4.13 (1H, dd, 6e-H), 4.90 (1H, dd, 3-H), 4.95-5.06 (1H, m, 5-H), 5.25 (1H, dd, 4-H); *J*(x-y)/Hz 1a-2 8.8, 1b-2 nd, 1a-1b 13.5, 2-3 9.6, 3-4 9.3, 4-5 9.1, 5-6a 10.7, 5-6e 5.9, 6a-6e 11.4; δ_C (63 MHz, D_20) 20.6 (3x$COCH_3$), 40.5 (C-1), 66.2 (C-6), 69.3, 70.6, 74.2 (C-2, C-3, C-4, C-5), 173.3, 173.7 (3x$COCH_3$); *m/z* (FAB) 290 (M^++1); HRMS (FAB) Found: M^++1 290.12351. $C_{12}H_{19}NO_7$ requires M^++1 290.12398.

3.5.8 (3,4,5,7-Tetra-*O*-acetyl-β-D-glucopyranosyl) methylamine hydrochloride (183)

Sample code: IAS058

Molecular formula: $C_{15}H_{23}NO_9$

Molecular weight: 397.5



2,3,4,6-Tetra-*O*-acetyl-1-deoxy-1-β-D-glucopyranosylnitrile (**189**) (500 mg, 4.2 mmol) was dissolved in a mixture of ethanol (50 ml) and chloroform (1 ml) and stirred vigourously with PtO_2 (Adam`s catalyst) (60 mg) for 16 hours under an atmosphere of hydrogen gas (20 bar) in a Parr high pressure hydrogenator. The catalyst was filtered off through a celite pad and the filtrate removed *in vacuo* to afford the title compound (**183**) as a waxy solid (476 mg, 90%).

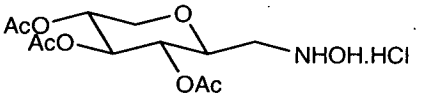
υ_{max}/cm^{-1} (Nujol) 3367 (NH_2), 1742 (C=O); $[\alpha]_D^{18}$ -5.0 (c = 0.2, D_2O); δ_H (250 MHz, D_2O); 2.03, 2.07, 2.08 (12H, 4s, 4x$COCH_3$), 3.08 (1H, dd, 1a-H), 3.24-3.32 (1H, m, 1b-H), 3.81-4.03 (1H, dd, 2-H, 6-H), 4.18-4.24 (1H, m, 7a-H), 4.41 (1H, dd, 7b-H), 4.97 (1H, dd, 3-H), 5.11 (1H, dd, 5-H), 5.36 (1H, dd, 4-H); *J*(x-y)/Hz 1a-2 9.1, 1b-2 nd, 1a-1b 13.5, 2-3 9.1, 3-4 10.1, 4-5 10.2, 5-6 9.2, 6-7a nd, 6-7b 3.6, 7a-7b 12.7; δ_C (63 MHz, D_20) 20.5 (4x$COCH_3$), 40.5 (C-1), 62.4 (C-7), 68.5, 70.4, 73.7, 74.5, 75.3 (C-2, C-3, C-4, C-5, C-6,), 173. 2, 173.7, 174.1 (4x$COCH_3$); *m/z* (FAB) 362 (M^++1) HRMS (FAB) Found M^++1 362.14517, $C_{15}H_{19}NO_9$ requires M^++1 362.14511.

3.5.9 (3,4,5-Tri-*O*-acetyl-β-D-xylopyranosyl) methylhydroxylamine hydrochloride (188)

Sample code: IAS054

Molecular formula: $C_{12}H_{19}NO_8$

Molecular weight: 341.5



Nitromethyl compound **95** (312 mg, 1 mmol) was dissolved in a mixture of THF (75 ml), conc HCl (3 ml), glacial acetic acid (16 ml) and water (30 ml). The mixture was cooled (0°C) and stirred before adding Zn dust (1.57 g, 24 mmol). On completion of the reaction (2 hours) the Zn was filtered off through a celite pad and the filtrate diluted with DCM (50 ml). The solution was washed with $NaHCO_3$ (2x 50 ml) and water before drying over $MgSO_4$ The solvent was removed *in vacuo* and the title compound (**188**) was afforded as a white solid (565 mg, 98%) on treatment with 1 M ethereal HCl.

M.p 156-157°C, $[\alpha]_D^{18}$ -39 (c = 1, D_2O); δ_H (250 MHz, D_2O); 1.90, 1.95 (9H, 3s, 3x$COCH_3$), 3.21-3.40 (3H, m, 1a-H, 1b-H, 6a-H), 3.89-3.96 (1H, m, 2-H), 4.02 (1H,

dd, 6e-H), 4.85 (1H, dd, 3-H), 4.86-4.91 (1H, m, 5-H), 5.15 (1H, dd, 4-H); *J*(x-y)/Hz 1a-2 nd, 1b-2 nd, 1a-1b nd, 2-3 9.1, 3-4 10.2, 4-5 10.1, 5-6a nd, 5-6e 5.6, 6a-6e 11.5; δ_C (63 MHz, D_2O) 20.6 (3x$COCH_3$), 51.7 (C-1), 66.2 (C-6), 69.3, 70.5, 71.5, 74.2 (C-2, C-3, C-4, C-5), 173. 2, 173.3, 174.7 (3x$COCH_3$); *m/z* (FAB) 306 (M^++1) HRMS (FAB) Found M^++1 306.11864, $C_{12}H_{19}NO_8$ requires M^++1 306.11889.

3.6 Synthesis of amidoxime-linked pseudodisaccharides

3.6.1 Amidoxime linked pseudo-disaccharides- General procedure

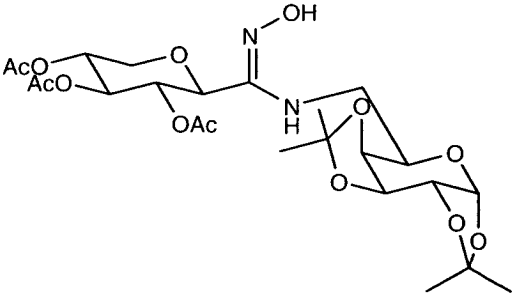
A solution of the hydroximoyl chloride (1 equivalent) in dry chloroform (40 ml) was added dropwise over 2 hours to a cooled (0°C) and stirred solution of the pyranosyl amine (1.5 equivalents) and triethylamine (1 ml, 18 equivalents) in dry chloroform (3 ml) under N_2. The mixture was diluted with DCM (50 ml), washed with 0.1 M HCl (2 x 50 ml) and the combined organic layers were dried over $MgSO_4$. The product was isolated by dry-flash chromatography (silica, hexane/Et_2O gradient elution).

3.6.1.1 (Z)-*N*-(6-Deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranosyl)-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (178)

Sample code: IAS041

Molecular formula: $C_{24}H_{36}N_2O_{13}$

Molecular weight: 560



To a stirred mixture of D-galactose amine **177** (395 mg, 1.3 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (3 ml), D-xylose derived hydroximoyl chloride **106** (150 mg, 0.4 mmol) was added in accordance to the general procedure above. Dry-flash chromatography yielded the title compound (**178**) as a white solid (201 mg, 81%).

M.p 167-168°C; $[\alpha]_D^{20}$ -74 (c = 1.0 ,$CHCl_3$); δ_H (360 MHz, $CDCl_3$); 1.33, 1.38, 1.49, 1.53 (12H, 4s, 4xCH_3), 1.97, 2.04, 2.05 (9H, 3s, 3x$CO\underline{C}H_3$), 3.33 (1H, dd, 5a-H), 3.34-3.59 (2H, m, 6a'-H, 6b'-H), 3.84-3.89 (1H, m, 5'-H), 4.00 (1H, d, 1-H), 4.15 (1H, dd, 5e-H), 4.29-4.34 (2H, m, 4'-H, 2'-H) 4.63 (1H, dd, 3'-H), 5.04 (1H, ddd, 4-H), 5.20 (1H, dd, 3-H), 5.24 (1H, m, NH), 5.40 (1H, dd, 2-H), 5.53 (1H, d, 1'-H), 7.76 (1H, bs, OH); *J*(x-y)/Hz 1-2 10.1, 2-3 9.4, 3-4 9.4, 4-5a 9.0, 4-5e 5.4, 5a-5e 11.2, 1'-2' 5.0, 2'-3' 2.5, 3'-4' 7.9, 4'-5' nd, 5'-6a' nd, 5'-6b' nd, 6a'-6b' nd; δ_C (93 MHz, $CDCl_3$) 20.6 (3x$CO\underline{C}H_3$), 24.3, 24.8, 25.8, 25.9 (acetal 4xCH_3), 42.6 (C-6'),

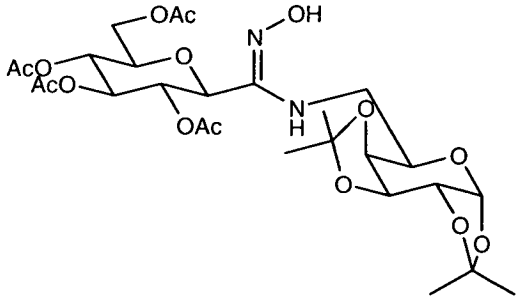
66.7 (C-5), 67.4, 68.6, 68.7, 70.4, 70.6, 70.9, 73.7, 76.2 (C-1, C-2, C-3, C-4, C-2', C-3', C-4', C-5'), 96.1 (C-1'), 108.6, 109.3 (2xC), 149.0 (C=N), 169.3, 169.7, 170.2 (3x*C*OCH$_3$); *m/z* (FAB) 561 (M^++1) HRMS (FAB) Found M^+ +1 561.22821, $C_{24}H_{36}N_2O_{13}$ requires M^+ +1 561.22919.

3.6.1.2 (Z)-*N*-(6-Deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranosyl)-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)formamide oxime (181)

Sample code: IAS044

Molecular formula: $C_{27}H_{40}N_2O_{15}$

Molecular weight: 632



To a stirred mixture of D-galactose amine **177** (395 mg, 1.3 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (3 ml), D-xylose derived hydroximoyl chloride **107** (150 mg, 0.36 mmol) was added in accordance to the general procedure above. Dry-flash chromatography yielded the title compound (**181**) as a white solid (173 mg, 75%).

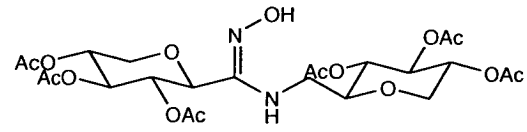
M.p 110-111 °C; $[\alpha]_D^{20}$ -48 (c = 1.0 ,$CHCl_3$); δ_H (360 MHz, $CDCl_3$); 1.35, 1.40, 1.47, 1.49 (12H, 4s, 4xCH_3), 1.94, 1.98, 2.01, 2.06 (12H, 4s, 4xCO$\underline{C}H_3$), 3.38 (1H, ddd, 6a'-H), 3.58 (1H, ddd, 6b'-H), 3.68 (1H, dt, 5-H), 3.78-3.82 (1H, m, 5'-H), 4.08 (1H, d, 1-H), 4.13-4.18 (2H, m, 6a-H, 6b-H), 4.27 (1H, dd, 2'-H), 4.32 (1H, dd, 4'-H), 4.61 (1H, dd, 3'-H), 5.11 (1H, dd, 4-H), 5.18 (1H, dd, 3-H), 5.17-5.20 (1H, m, NH), 5.45 (1H, dd, 2-H), 5.50 (1H, d, 1'-H), 7.78 (1H, bs, OH); *J*(x-y)/Hz 1-2 10.1, 2-3 9.2, 3-4 9.5, 4-5 9.7, 5-6a nd, 5-6b nd, 6a-6b nd, 1'-2' 5.0, 2'-3' 2.7, 3'-4' 8.0, 4'-5' 1.8, 5'-6a' 6.5, 5'-6b' 6.8, 6a'-6b' 13.2; δ_C (93 MHz, $CDCl_3$) 20.5 (3xCO*C*H$_3$), 24.2, 24.7, 25.9 (acetal 4xCH_3), 42.5 (C-6'), 61.8 (C-6), 67.3, 67.8, 68.3, 70.4, 70.6, 70.8, 74.2, 75.6, 75.7 (C-1, C-2, C-3, C-4, C-5, C-2', C-3', C-4', C-5'), 96.2 (C-1'), 108.5, 109.3 (2xC), 148.7 (C=N), 169.3, 170.1, 170.6 (3x*C*OCH$_3$); *m/z* (FAB) 633 (M^++1) HRMS (FAB) Found M^+ +1 633.25026, $C_{27}H_{40}N_2O_{15}$ requires M^+ +1 633.25069

3.6.1.3 (Z)-*N*-(3,4,5-Tri-*O*-acetyl-β-D-xylopyranosyl methyl)-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (184)

Sample code: IAS037

Molecular formula: $C_{24}H_{34}N_2O_{15}$

Molecular weight: 590



To a stirred mixture of D-xylose derived amine (**182**) (215 mg, 0.7 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (3 ml), D-xylose derived hydroximoyl chloride **106** (150 mg, 0.4 mmol) was added in accordance to the general procedure above. Dry-flash chromatography yielded the title compound (**184**) as a white solid (115 mg, 44%).

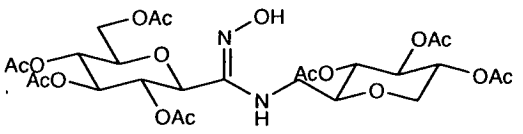
M.p 140-141 °C; δ_H (600 MHz, $CD_3S(O)CD_3$); 1.89, 1.96, 1.97, 1.98, 1.99, 2.04 (18H, 6s, 6x$COCH_3$), 3.03 (1H, ddd, 1a'-H), 3.44-3.51 (2H, m, 1b'-H, 6a'-H), 3.62 (1H, ddd, 2'-H), 3.94 (1H, dd, 5e-H), 3.98 (1H, dd, 6e'-H), 4.27 (1H, d, 1-H) 4.73 (1H, dd, 3'-H), 4.79-4.85 (2H, m, 4-H, 5'-H), 5.15 (1H, dd, 2-H), 5.22 (1H, dd, 3-H), 5.23 (1H, dd, 4'-H), 5.26-5.29 (1H, m, NH), 9.97 (1H, bs, OH); *J*(x-y)/Hz 2-3 9.9, 3-4 9.5, 4-5 9.5, 5-6a nd, 5-6e 5.5, 6a-6e 10.9, 1a'-2' 3.6, 1b'-2 2.6, 1a'-1b' 11.3, 2'-3' 9.6, 3'-4' 9.6, 4'-5' 9.5, 5'-6a' nd, 5'-6e' 5.6, 6a'-6e' 11,0; δ_C (63 MHz, $CD_3S(O)CD_3$) 20.5 (6x$COCH_3$), 42.4 (C-1'), 65.1, 65.2 (C-5, C-6'), 68.2, 68.6, 69.6, 72.6, 72.9, 74.3, 76.7 (C-1, C-2, C-3, C-4, C-2', C-3', C-4', C-5'), 147.3 (C=N), 168.4, 169.4, 169.5 (6x*C*OCH_3); *m/z* (FAB) 591 (M^++1) HRMS (FAB) Found M^+ +1 591.20377, $C_{24}H_{34}N_2O_{15}$ requires M^+ +1 591.20374.

3.6.1.4 (Z)-*N*-(3,4,5-Tri-*O*-acetyl-β-D-xylopyranosyl methyl)-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)formamide oxime (185)

Sample code: IAS055

Molecular formula: $C_{27}H_{38}N_2O_{17}$

Molecular weight: 662



To a stirred mixture of D-xylose derived amine **182** (200 mg, 0.7 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (3 ml), D-glucose derived hydroximoyl chloride **107** (150 mg, 0.36 mmol) was added in accordance to the general procedure above. Dry-flash chromatography yielded the title compound (**185**) as a white solid (100 mg, 40%).

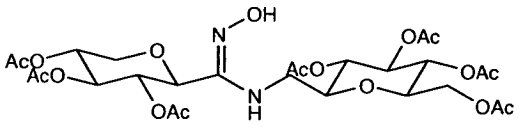
M.p 141-143 °C; $[\alpha]_D^{20}$ -36 (c = 1.0 ,$CHCl_3$); δ_H (600 MHz, $CDCl_3$); 1.93, 1.95, 1.98, 1.99, 2.00, 2.03, 2.04 (21H, 7s, 7x$COCH_3$), 3.17 (1H, ddd, 1a'-H), 3.26 (1H, dd, 6a'-H), 3.43 (1H, ddd, 2'-H), 3.54 (1H, ddd, 1b'-H), 3.64 (1H, ddd, 5-H), 4.03 (1H, d, 1-H) 4.04-4.07 (1H, m, 6a-H), 4.09 (1H, m, 6e'-H), 4.14 (1H, dd, 6b-H), 4.85 (1H, dd, 3'-H), 4.89-4.93 (1H, m, 5'-H), 4.95 (1H, dd, 4-H), 5.14-5.19 (2H, m, 4'-H, 3-H), 5.25 (1H, dd, 2-H), 5.34 (1H, dd, NH); *J*(x-y)/Hz 1-2 10.2, 2-3 9.6, 3-4 9.7, 4-5 9.9, 5-6a 2.2, 5-6b 5.8, 6a-6e 12.4, 1a'-2' 6.6, 1b'-2 2.6, 1a'-1b' 11.1, 2'-3' 9.6, 3'-4' 9.6, 4'-5' 9.9, 5'-6a' 10.9, 5'-6e' 5.8, 6a'-6e' 11,2; δ_C (93 MHz, $CDCl_3$) 20.4, 20.5, 20.6 (7x$COCH_3$), 43.2 (C-1'), 62.2 (C-6), 65.2 (C-6'), 68.0, 68.2, 68.9, 70.0, 73.1, 73.8, 75.1, 75.9, 77.5 (C-1, C-2, C-3, C-4, C-5, C-2', C-3', C-4', C-5'), 147.8 (C=N), 169.3, 169.7, 170.1, 170.4 (7x$COCH_3$); *m/z* (FAB) 663 (M^++1) HRMS (FAB) Found M^+ +1 663.22504, $C_{27}H_{38}N_2O_{17}$ requires M^+ +1 663.22487.

3.6.1.5 (Z)-*N*-(3,4,5,7-Tetra-*O*-acetyl-β-D-glucopyranosyl methyl)-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (186)

Sample code: IAS059

Molecular formula: $C_{27}H_{38}N_2O_{17}$

Molecular weight: 662



To a stirred mixture of D-glucose derived amine **183** (240 mg, 0.6 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (3 ml), D-xylose derived hydroximoyl chloride **106** (150 mg, 0.4 mmol) was added in accordance to the general procedure above. Dry-flash chromatography yielded the title compound **186** as a white solid (76 mg, 31%).

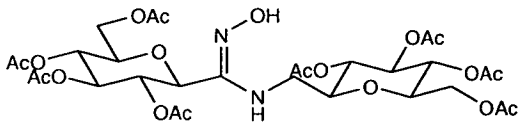
M.p 193-194°C; δ_H (360 MHz, $CD_3S(O)CD_3$); 1.91, 1.97, 1.98, 2.00, 2.01, 2.03, 2.06 (21H, 7s, 7x$COCH_3$), 3.02-3.09 (1H, m, 1a'-H), 3.45-3.52 (2H, m, 1b'-H, 5a-H), 3.76 (1H, ddd, 2'-H), 3.95-4.08 (3H, m, 6'-H, 5e-H, 7a'-H), 4.14 (1H, dd, 7b'-H), 4.35 (1H, d, 1-H) 4.77 (1H, dd, 3'-H), 4.87 (1H, dd, 5'-H), 4.82-4.88 (1H, m, 4-H), 5.17 (1H, dd, 2-H), 5.23 (1H, dd, 3-H), 5.32 (1H, dd, 4'-H), 5.36 (1H, dd, NH), 9.79 (1H, bs, OH); *J*(x-y)/Hz 1-2 9.5, 2-3 10.0, 3-4 9.6, 4-5a 10.7, 4-5e nd, 5a-5e 11.0, 1a'-2' 7.4, 1b'-2 2.5, 1a'-1b' nd, 2'-3' 9.7, 3'-4' 9.5, 4'-5' 9.8, 5'-6' 9.7, 6'-7a' nd, 6'-7b' 6.1, 7a'-7b' 12.3; δ_C (93 MHz, $CD_3S(O)CD_3$) 21.8 (7x$COCH_3$), 44.2 (C-1'), 63.8 (C-6), 67.2 (C-6'), 70.1, 70.2, 70.3, 71.3, 74.9, 75.0, 76.0, 76.4, 77.9 (C-1, C-2, C-3, C-4, C-5, C-2', C-3', C-4', C-5'), 149.2 (C=N), 170. 0, 170.7, 170.9, 171.0, 171.4 (7x$COCH_3$); *m/z* (FAB) 663 (M^++1) HRMS (FAB) Found M^+ +1 663.22507, $C_{27}H_{38}N_2O_{17}$ requires M^+ +1 663.22487.

3.6.1.6 (Z)-*N*-(3,4,5,7-Tetra-*O*-acetyl-β-D-glucopyranosyl methyl)-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)formamide oxime (187)

Sample code: IAS062

Molecular formula: $C_{30}H_{42}N_2O_{19}$

Molecular weight: 734



To a stirred mixture of D-glucose derived amine **183** (240 mg, 0.6 mmol) and triethylamine (1 ml, 7.2 mmol) in dry chloroform (3 ml), D-glucose derived hydroximoyl chloride **107** (150 mg, 0.36 mmol) was added in accordance to the general procedure above. Dry-flash chromatography yielded the title compound **187** as a white solid (131 mg, 49%).

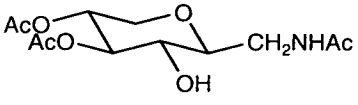
M.p 180-181 °C; $[\alpha]_D^{20}$ -12 (c = 1.0 ,$CHCl_3$); δ_H (360 MHz, $CDCl_3$); 1.90, 1.91, 1.93, 1.94, 1.95, 2.01, 2.02, 2.04 (24H, 8s, 8x$COCH_3$), 3.13-3.20 (1H, m, 1a'-H), 3.47-3.51 (1H, m, 2'-H), 3.53-3.68 (3H, m, 5-H, 6'-H, 1b'-H), 4.01-4.18 (5H, m, 1-H, 6a-H, 6b-H, 7a'-H, 7b'-H), 4.87-4.97 (3H, m, 4-H, 3'-H, 5'-H), 5.09-5.27 (3H, m, 2-H, 3-H, 4'-H) 5.36 (1H, dd, NH), 8.09 (1H, bs, OH); *J*(x-y)/Hz 1-2 nd, 2-3 nd, 3-4 nd, 4-5 nd, 5-6a nd, 5-6b nd, 6a-6e nd, 1a'-2' nd, 1b'-2 nd, 1a'-1b' nd, 2'-3' nd, 3'-4' nd, 4'-5' nd, 5'-6' nd, 6'-7a' nd, 6'-7b' nd, 7a'-7b'nd; δ_C (93 MHz, $CDCl_3$) 21.6, 21.7, 21.8 (8x$COCH_3$), 44.1 (C-1'), 63.2, 63.4 (C-6, C-7'), 69.3, 69.4, 70.0, 70.7, 74.4, 74.8, 75.0, 76.2, 76.6, 77.1, 78.3 (C-1, C-2, C-3, C-4, C-5, C-2', C-3', C-4', C-5', C-6'), 149.3 (C=N), 170.7, 170.8, 170.9, 171.3, 171.5, 171.6, 171.9 (8x*C*OCH_3); *m/z* (FAB) 735 (M^++1) HRMS (FAB) Found M^+ +1 735.24605, $C_{30}H_{42}N_2O_{19}$ requires M^+ +1 735.24600.

3.6.2 *N*-Acetyl(4,5-di-*O*-acetyl-β-D-xylopyranosyl) methylamine (191)

Sample code: IAS081

Molecular formula: $C_{12}H_{19}NO_7$

Molecular weight: 289



Nitromethyl compound **95** (300 mg, 1 mmol) was vigourously stirred in methanol (8 ml) (THF added to improve solubility) with Raney nickel (500 mg) (stored under methanol-not water!) under a balloon of hydrogen gas for 16 hours. The mixture was filtered through a pad of celite and washed with methanol and DCM, before removing the solvent *in vacuo* to afford the title compound (**191**) as a colourless oil (260 mg, 96%).

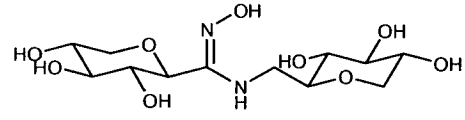
υ_{max}/cm^{-1} (Nujol) 3364 (OH), 1742 (C=O ester), 1651 (C=O amide), 1550 (NH bend); $[\alpha]_D^{18}$ 129 (c = 1.5, $CHCl_3$); δ_H (360 MHz, $CHCl_3$); 1.99, 2.03, 2.05 (9H, 3s, 2x$CO\underline{C}H_3$, 1x$CONHCH_3$), 3.16-3.31 (3H, m, 1a-H, 2-H, 3-H), 3.22 (1H, dd, 6a-H), 3.86 (1H, ddd, 1b-H), 4.01 (1H, dd, 6e-H), 4.60 (1H, bs, OH), 4.83 (1H, dt, 5-H), 5.09 (1H, dd, 4-H); *J*(x-y)/Hz 1a-2 2.9, 1b-2 8.2, 1a-1b 11.0, 2-3 nd, 3-4 9.4, 4-5 10.7, 5-6a 10.9, 5-6e 5.7, 6a-6e 11.0; δ_C (63 MHz, $CHCl_3$) 20.6, 20.7 (2x$COCH_3$), 22.6 (1x$CONHCH_3$) 39.8 (C-1), 66.2 (C-6), 68.4, 69.3, 74.4, 79.5 (C-3, C-5, C-4, C-2), 170.1, 170.5 (2x$COCH_3$) 172.5 (1x$CONHCH_3$); *m/z* (FAB) 290 (M^++1) HRMS (FAB) Found M^++1 290.12351, $C_{12}H_{19}NO_7$ requires M^++1 290.12398.

3.6.3 (Z)-*N*-(β-D-xylopyranosylmethyl)-(β-D-xylopyranosyl)formamide oxime (192)

Sample code: IAS086

Molecular formula: $C_{12}H_{22}N_2O_9$

Molecular weight: 338



pseudodisaccharide **184** (110 mg, mmol) and triethylamine (0.05 ml, mmol) were stirred in methanol (5 ml) and the mixture heated (65 °C), for 16 hours. On cooling, the reaction mixture was concentrated *in vacuo* to yield the title compound (**192**) as a viscous oil (60 mg, 95%).

δ_C (93 MHz, D_2O); 44.2 (C-1'), 70.0 (C-5), 70.1 (C-6'), 70.3, 70.5, 71.7, 72.2, 77.3, 78.1, 78.4, 80.9 (C-1, C-2, C-3, C-4, C-2', C-3', C-4', C-5'), 153.7 (C=N); *m/z* (ES) 340 (MH_2^+).

3.7 Synthesis of pyranosylbenzazoles

3.7.1 Benzothiazoles - General procedure

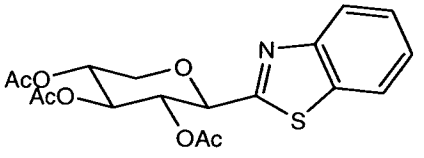
Pyranosyl hydroximoyl chloride (1 equivalent) and *o*-aminothiophenol (2.5 equivalents) were dissolved in ethanol (10 ml) and the mixture refluxed (80 °C) under an atmosphere of nitrogen for 5 h. The products were usually found to crystallize on cooling, although, an alternative work-up could be employed, this proceeded as follows: The reaction mixture was diluted with DCM (50 ml) and washed with 0.1 M HCl (50 ml), the aqueous layer was further extracted with DCM (2x 50 ml), and the combined organic layers dried ($MgSO_4$). Removal of the solvent *in vacuo* afforded the crude product which was purified by dry-flash chromatography (silica, hexane/Et_2O gradient elution).

3.7.1.1 2-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)benzothiazole (214)

Sample code: IAS024

Molecular formula: $C_{18}H_{19}NO_7S$

Molecular weight: 393



Xylose derived hydroximoyl chloride **106** (200 mg, 0.6 mmol) and *o*-amino thiophenol (185 mg, 1.5 mmol) were added according to the general procedure above. The title compound (**214**) was obtained as a white solid (220 mg, 90%) after dry-flash chromatography.

M.p 160-161 °C (lit.[195] 161-162 °C); $[\alpha]_D^{20}$ = -36 (c = 0.6, $CHCl_3$); δ_H (250 MHz, $CDCl_3$); 1.91, 1.97, 2.00 (9H, 3s, 3x$COCH_3$), 3.48 (1H, dd, 5a`-H), 4.28 (1H, dd, 5e`-H), 4.76 (1H, d, 1`-H), 5.06 (1H, m, 4`-H), 5.19 (1H, dd, 2`-H), 5.34 (1H, dd, 3`-H), 7.36-7.44 (2H, m, Ar), 7.81-7.96 (2H, m, Ar); *J*(x-y)/Hz 1-2 9.5, 2-3 9.4, 3-4 9.3, 4-5a 10.5, 4-5e 5.5, 5a-5e 11.2; δ_C (63 MHz, $CDCl_3$); 20.5 (3x$COCH_3$), 66.9 (C-5`), 68.8, 71.4, 72.8, 77.9 (C-1`, C-2`, C-3`, C-4`), 121.8, 123.2, 125.4, 126.1 (C-7, C-6, C-5, C-4), 134.7 (C-7a), 152.5 (C-3a), 166.6 (C-2), 169.3, 169.7, 170.1 (3x$COCH_3$);

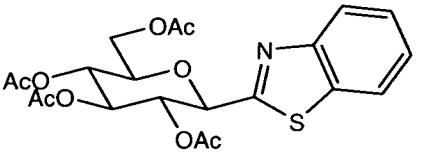
m/z (FAB) 393 (M^+ +1) HRMS (FAB) Found M^++1 393.09568, $C_{18}H_{20}NO_7S$ requires M^++1 393.09605.

3.7.1.2 2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)benzothiazole (215)

Sample code: IAS027

Molecular formula: $C_{21}H_{23}NO_9S$

Molecular weight: 465



Glucose derived hydroximoyl chloride **107** (200 mg, 0.5 mmol) and *o*-aminothiophenol (188 mg, 1.5 mmol) were added according to the general procedure above. The title compound (**215**) was obtained as a white solid (185 mg, 81%) after dry-flash chromatography.

M.p 128-129 °C (lit.[198] 129-130 °C); $[\alpha]_D^{20}$ = -24 (c = 1, $CHCl_3$); δ_H (250 MHz, $CDCl_3$); 1.99, 2.05, 2.10, 2.14 (12H, 4s, 4x$COCH_3$), 3.99 (1H, m, 5`-H), 4.28 (1H, dd, 6b`-H), 4.37 (1H, dd, 6a`-H), 4.97 (1H, d, 1`-H), 5.30 (1H, dd, 2`-H), 5.37 (1H, dd, 4`-H), 5.47 (1H, dd, 3`-H) 7.39-7.54 (2H, m, Ar), 7.89-8.56 (2H, m, Ar); *J*(x-y)/Hz 1-2 9.5, 2-3 9.2, 3-4 9.3, 4-5 9.5, 5-6a 4.7, 5-6b 2.5, 6a-6b 12.4; $\delta_C$ (63 MHz, $CDCl_3$); 20.2, 20.3, 20.4 (4x$COCH_3$), 61.7 (C-6`), 67.9, 71.1, 73.3, 76.1, 76.4 (C-1`, C-2`, C-3`, C-4`), 121.6, 123.1, 125.3, 125.9 (C-7, C-6, C-5, C-4), 134.6 (C-7a), 152.4 (C-3a), 166.2 (C-2), 168.9, 169.1, 169.9, 170.3 (4x$COCH_3$); *m/z* (FAB) 466 (M^+ +1) HRMS (FAB) Found M^++1 466.11680, $C_{21}H_{24}NO_9S$ requires M^++1 466.11718.

3.7.2 Benzimidazoles-General procedures

General Procedure A

Pyranosyl hydroximoyl chloride (1 equivalent) and *o*-phenylenediamine (2.5 equivalents) were dissolved in ethanol (10 ml) and the mixture stirred under an atmosphere of nitrogen at room temperature for 16 h. The reaction mixture was diluted with DCM (50 ml) and washed with 4% $CuSO_4$ solution (50 ml), the aqueous layer was further extracted with DCM (2x 50 ml), and the combined organic layers dried ($MgSO_4$). Removal of the solvent *in vacuo* afforded the crude product which was purified by filtration through a silica pad.

General Procedure B

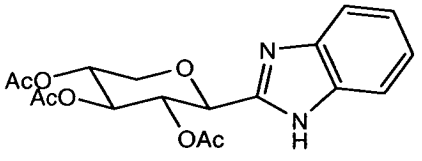
Pyranosyl hydroximoyl chloride (1 equivalent) and *o*-phenylenediamine (2.5 equivalents) were dissolved in ethanol (10 ml) and the mixture refluxed (80 °C) under an atmosphere of nitrogen for 5 h. The reaction mixture was diluted with DCM (50 ml) and washed with 4% $CuSO_4$ solution (50 ml), the aqueous layer was further extracted with DCM (2x 50 ml), and the combined organic layers dried ($MgSO_4$). Removal of the solvent *in vacuo* afforded the crude product which was purified by filtration through a silica pad.

3.7.2.1 2-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)benzimidazole (217)

Sample code: IAS025

Molecular formula: $C_{18}H_{20}N_2O_7$

Molecular weight: 376



Xylose derived hydroximoyl chloride **106** (200 mg, 0.6 mmol) and *o*-phenylenediamine (162 mg, 1.5 mmol) were added according to general procedures A or B. The title compound (**217**) was obtained as a white solid (185 mg, 83%) after dry-flash chromatography.

M.p 152-153 °C; $[\alpha]_D^{20} = -78$ (c = 1, $CHCl_3$); δ_H (250 MHz, $CDCl_3$); 1.89, 1.98, 2.01 (9H, 3s, 3x$COCH_3$), 3.46 (1H, dd, 5a`-H), 4.18 (1H, dd, 5e`-H), 4.70 (1H, d, 1`-H),

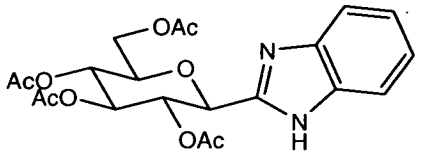
5.03 (1H, m, 4`-H), 5.21 (1H, dd, 2`-H), 5.35 (1H, dd, 3`-H), 7.13-7.72 (2H, m, Ar), 7.50 (2H, bs, Ar); *J*(x-y)/Hz 1-2 9.7, 2-3 9.4, 3-4 9.6, 4-5a 10.4, 4-5e 5.6, 5a-5e 11.3; $\delta_C$ (63 MHz, $CDCl_3$); 20.5, 20.5, 20.6 (3x$COCH_3$), 67.0 (C-5`), 68.9, 70.6, 72.7, 75.1 (C-1`, C-2`, C-3`, C-4`), 122.9 (C-5, C-6), 148.6 (C-2), 169.8, 169.9, 170.0 (3x$COCH_3$); *m/z* (FAB) 377 (M^+ +1) HRMS (FAB) Found M^++1 377.13424, $C_{18}H_{21}N_2O_7$ requires M^++1 377.13488.

3.7.2.2 2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)benzimidazole (218)

Sample code: IAS032

Molecular formula: $C_{21}H_{24}N_2O_9$

Molecular weight: 448



Glucose derived hydroximoyl chloride **107** (350 mg, 0.8 mmol) and *o*-phenylenediamine (231 mg, 1.9 mmol) were added according to general procedures A or B. The title compound (**218**) was obtained as a white solid (292 mg, 89%) after dry-flash chromatography.

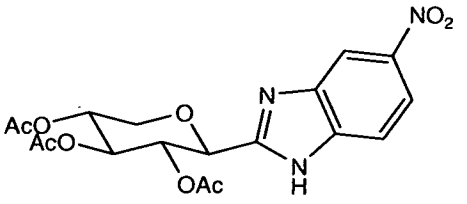
M.p 171-172 °C; $[\alpha]_D^{20}$ = -20 (c = 1, $CHCl_3$); δ_H (250 MHz, $CDCl_3$); 2.14, 2.21, 2.25 (12H, 4s, 4x$COCH_3$), 4.12 (1H, m, 5`-H), 4.33 (1H, dd, 6b`-H), 4.51 (1H, dd, 6a`-H), 5.04 (1H, d, 1`-H), 5.36 (1H, dd, 2`-H), 5.50 (1H, dd, 4`-H), 5.61 (1H, dd, 3`-H) 7.41-7.48 (2H, m, Ar), 7.76 (2H, bs, Ar); *J*(x-y)/Hz 1-2 9.7, 2-3 9.5, 3-4 9.1, 4-5 10.1, 5-6a 5.2, 5-6b 2.0, 6a-6b 12.5; $\delta_C$ (63 MHz, $CDCl_3$); 20.9, 21.0, 21.0, 21.1 (4x$COCH_3$), 62.5 (C-6`), 66.2, 68.7, 70.9, 73.8, 75.1 (C-1`, C-2`, C-3`, C-4`), 123.4 (C-5, C-6), 148.8 (C-2), 170.0, 170.5, 169.9, 171.1 (4x$COCH_3$); *m/z* (FAB) 449 (M^+ +1) HRMS (FAB) Found M^++1 449.15606, $C_{21}H_{24}N_2O_9$ requires M^++1 449.15601.

3.7.2.3 2-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-5-nitro-benzimidazole (219)

Sample code: IAS076

Molecular formula: $C_{18}H_{19}N_3O_9$

Molecular weight: 421



Xylose derived hydroximoyl chloride **106** (200 mg, 0.6 mmol) and 4-nitro-1,2-diamino benzene (230 mg, 1.5 mmol) were added according to general procedure B. The title compound (**219**) was obtained in a crude form (reddish solid) which resisted attempts at purification by dry and wet-flash chromatography.

δ_H (250 MHz, DMSO); 2.03, 2.19, 2.22 (9H, 3s, 3x$COCH_3$), 3.98 (1H, dd, 5a`-H), 4.36 (1H, dd, 5e`-H), 5.25 (1H, d, 1`-H), 5.19-5.34 (1H, m, 4`-H), 5.47 (1H, dd, 2`-H), 5.70 (1H, dd, 3`-H), 7.89 (1H, d, 7-H), 8.28 (1H, dd, 6-H), 8.64 (1H, d, 4-H); *J*(x-y)/Hz 1`-2` 9.7, 2`-3` 9.4, 3`-4` 9.5, 4`-5a` 10.6, 4`-5e` 5.6, 5a`-5e` 11.0, 4-6 1.8, 6-7 8.8; *m/z* (FAB) 422 (M^+ +1) HRMS (FAB) Found M^++1 422.11996, $C_{18}H_{19}N_3O_9$ requires M^++1 422.11995.

3.7.3 Benzoxazoles - General procedures

General procedure A

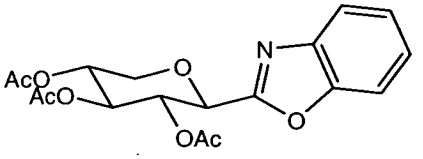
Pyranosyl hydroximoyl chloride (1 equivalent) and *o*-aminophenol (2.5 equivalents) were dissolved in ethanol (10 ml) and the mixture stirred under an atmosphere of nitrogen at room temperature for 16 h. The reaction mixture was diluted with DCM (50 ml) and washed with 0.1 M HCl (50 ml), the aqueous layer was further extracted with DCM (2x 50 ml), and the combined organic layers dried ($MgSO_4$). Removal of the solvent *in vacuo* afforded the crude product which was purified by filtration through a silica pad.

General procedure B

Pyranosyl hydroximoyl chloride (1 equivalent) and *o*-aminophenol (2.5 equivalents) were dissolved in ethanol (10 ml) and the mixture refluxed (80 °C) under an atmosphere of nitrogen at for 5 h. The reaction mixture was diluted with DCM (50 ml) and washed with 0.1 M HCl (50 ml), the aqueous layer was further extracted with DCM (2x 50 ml), and the combined organic layers dried ($MgSO_4$). Removal of the solvent *in vacuo* afforded the crude product which was purified by filtration through a silica pad.

3.7.3.1 2-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)benzoxazole (220)

Sample code: IAS026
Molecular formula: $C_{18}H_{19}NO_8$
Molecular weight: 377



Xylose derived hydroximoyl chloride **106** (185 mg, 0.6 mmol) and *o*-aminophenol (164 mg, 1.5 mmol) were added according to general procedures A or B. The title compound (**220**) was obtained as a white solid (140 mg, 68%) after dry-flash chromatography.

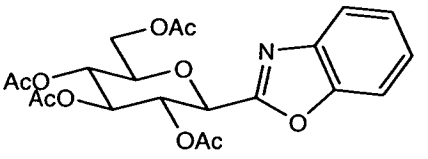
M.p 155-156 °C; $[\alpha]_D^{20}$ = -74 (c = 1, $CHCl_3$); δ_H (250 MHz, $CDCl_3$);); 1.84, 1.97, 2.00 (9H, 3s, 3x$COCH_3$), 3.47 (1H, dd, 5a`-H), 4.26 (1H, dd, 5e`-H), 4.68 (1H, d, 1`-H), 5.08 (1H, m, 4`-H), 5.31 (1H, dd, 2`-H), 5.43 (1H, dd, 3`-H), 7.27-7.32 (2H, m, Ar), 7.47-7.51 (1H, m, Ar), 7.64-7.68 (1H, m, Ar); *J*(x-y)/Hz 1-2 10.2, 2-3 9.1, 3-4 9.2, 4-5a 10.3, 4-5e 5.5, 5a-5e 11.3; δ_C (63 MHz, $CDCl_3$); 20.5, 20.6 (3x$COCH_3$), 66.9 (C-5`), 68.5, 69.9, 72.6, 73.9 (C-1`, C-2`, C-3`, C-4`), 110.8, 120.4, 124.6, 125.8 (C-7, C-4, C-6, C-5), 140.2 (C-3a), 150.6 (C-7a), 159.9 (C-2), 169.1, 169.6, 170.1 (3x$COCH_3$); *m/z* (FAB) 378 (M^+ +1) HRMS (FAB) Found M^++1 378.11935, $C_{18}H_{20}NO_8$ requires M^++1 378.11889.

3.7.3.2 2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)benzoxazole (221)

Sample code: IAS029

Molecular formula: $C_{21}H_{24}NO_{10}$

Molecular weight: 465



Glucose derived hydroximoyl chloride **107** (200 mg, 0.5 mmol) and *o*-aminophenol (110 mg, 1.0 mmol) were added according to general procedures A or B. The title compound (**221**) was obtained as a white solid (156 mg, 71%) after dry-flash chromatography.

M.p 174-175 °C; $[\alpha]_D^{20}$ = -36 (c = 1, $CHCl_3$); δ_H (250 MHz, $CDCl_3$); 1.81, 1.97, 1.99, 2.01 (12H, 4s, 4x$COCH_3$), 3.86 (1H, m, 5`-H), 4.09 (1H, dd, 6b`-H), 4.25 (1H, dd, 6a`-H), 4.76 (1H, d, 1`-H), 5.19 (1H, dd, 2`-H), 5.33 (1H, dd, 4`-H), 5.51 (1H, dd, 3`-H) 7.28-7.33 (2H, m, Ar), 7.49-7.52 (1H, m, Ar), 7.65-7.69 (1H, m, Ar); *J*(x-y)/Hz 1-2 10, 2-3 9.5, 3-4 9.3, 4-5 9.9, 5-6a 4.8, 5-6b 2.2, 6a-6b 12.6; $\delta_C$ (63 MHz, $CDCl_3$); 20.7, 20.9, 21.0, 21.1 (4x$COCH_3$), 62.3 (C-6`), 68.3, 69.5, 70.2, 73.9, 76.9 (C-1`, C-2`, C-3`, C-4`), 111.5, 120.9, 125.1, 126.4 (C-7, C-4, C-6, C-5), 140.7 (C-3a), 151.2 (C-7a), 159.9 (C-2), 169.3, 169.7, 170.6, 171.0 (4x$COCH_3$); *m/z* (FAB) 450 (M^+ +1) HRMS (FAB) Found M^++1 450.14098, $C_{21}H_{24}NO_{10}$ requires M^++1 450.14002.

3.7.4 Deprotections

Procedure A

The acetylated substrate (1 equivalent) and triethylamine (1.33 mmol) were stirred in methanol (5 ml) at room temperature, under nitrogen for 36h. The reaction mixture was concentrated *in vacuo* to yield the crude product, which were crystallised from ice-cold methanol.

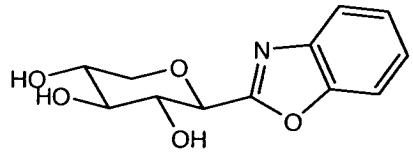
Procedure B

The acetylated substrate (1 equivalent) and powdered 4A molecular sieves (equal mass to that of substrate) were stirred in warm (40 °C) HPLC grade methanol (5 ml) for 12-24h. On completion of the reaction, the mixture was filtered through celite and

concentrated *in vacuo* to afford the crude product. The deprotected products were crystallised from ice-cold methanol.

3.7.4.1 2-β-D-Xylopyranosylbenzoxazole (222)

Sample code: IAS047
Molecular formula: $C_{12}H_{13}NO_5$
Molecular weight: 251

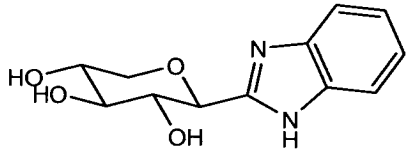


2-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)benzoxazole (**220**) (100 mg, 0.3 mmol) was deacetylated according to deprotection A to afford the title compound (**222**) as a white solid (61 mg, 92%).

M.p 192-194 °C; $[\alpha]_D^{20}$ = -26 (c = 1, MeOH); δ_H (360 MHz, DMSO); 3.22 (1H, dd, 5a`-H), 3.24 (1H, td, 3`-H), 3.39 (1H, d, 4`-H), 3.60 (1H, td, 2`-H), 3.78 (1H, dd, 5e`-H), 4.32 (1H, d, 1`-H), 5.09 (1H, d, OH), 5.12 (1H, d, OH), 5.29 (1H, d, OH), 7.29-7.40 (2H, m, Ar), 7.62-7.71 (2H, m, Ar); *J*(x-y)/Hz 1-2 9.8, 2-3 8.6, 3-4 nd, 4-5a 10.4, 4-5e 5.2, 5a-5e 10.9; δ_C (93 MHz, DMSO); 69.3 (C-3`), 70.0 (C-5`), 71.9 (C-2`), 75.8 (C-1`), 77.5 (C-4`), 110.8, 119.8, 124.4, 125.4 (C-7, C-4, C-6, C-5), 140.1 (C-7a), 149.9 (C-3a), 162.8 (C-2); *m/z* (FAB) 252 (M^+ +1) HRMS (FAB) Found M^++1 252.08679, $C_{12}H_{14}NO_5$ requires M^++1 252.08720.

3.7.4.2 2-β-D-Xylopyranosylbenzimidazole (223)

Sample code: IAS048
Molecular formula: $C_{12}H_{14}N_2O_4$
Molecular weight: 250



2-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)benzimidazole (**217**) (100 mg, 0.3 mmol) was deacetylated according to deprotections A or B to afford the title compound (**223**) as a white solid (62 mg, 93%).

M.p 232-233 °C; $[\alpha]_D^{20}$ = -17 (c = 1, MeOH); δ_H (360 MHz, DMSO) 3.20 (1H, dd, 5a`-H), 3.25 (1H, dd, 3`-H), 3.42 (1H, ddd, 4`-H), 3.59 (1H, dd, 2`-H), 3.81 (1H, dd,

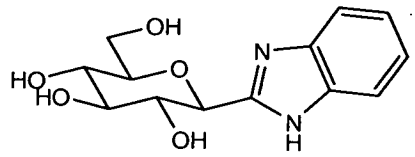
5e`-H), 4.25 (1H, d, 1`-H), 5.12 (3H, bs, OH), 7.09-7.13 (2H, m, Ar), 7.45-7.49 (2H, m, Ar); *J*(x-y)/Hz 1-2 9.7, 2-3 8.7, 3-4 9.1, 4-5a 10.7, 4-5e 5.2, 5a-5e 10.9; δ_C (93 MHz, DMSO); 69.4 (C-3`), 70.0 (C-5`), 72.6 (C-2`), 76.8 (C-1`), 77.8 (C-4`), 111.2, 118.6, 121.0, 122.0 (C-4, C-5, C-6, C-7), 134.6 (C-7a), 142.2 (C-3a), 152.2 (C-2); *m/z* (FAB) 251 (M^+ +1) HRMS (FAB) Found M^++1 251.10372, $C_{12}H_{15}N_2O_4$ requires M^++1 251.10318.

3.7.4.3 2-β-D-Glucopyranosylbenzimidazole (224)

Sample code: IAS063

Molecular formula: $C_{13}H_{16}N_2O_5$

Molecular weight: 280



2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)benzimidazole (**218**) (150 mg, 0.3 mmol) was deacetylated according to deprotection B to afford the title compound (**224**) as a white solid (89 mg, 95%).

M.p 253-254 °C; $[\alpha]_D^{20}$ = 21 (c = 1, MeOH); δ_H (360 MHz, DMSO) 3.24 (1H, dt, 4`-H), 3.33 (1H, dt, 3`-H), 3.37 (1H, m, 5`-H), 3.49 (1H, dt, 6b`-H), 3.67 (1H, dt, 2`-H), 3.75 (1H, ddd, 6a`-H), 4.37 (1H, d, 1`-H), 4.58 (1H, t, OH), 5.12 (1H, d, OH), 5.16 (1H, d, OH), 5.19 (1H, d, OH), 7.12-7.26 (2H, m, Ar), 7.46-7.65 (2H, m, Ar); *J*(x-y)/Hz 1-2 9.8, 2-3 9.2, 3-4 9.3, 4-5 9.0, 5-6a 1.4, 5-6b 5.8, 6a-6b 11.9; $\delta_C$ (93 MHz, DMSO); 62.9 (C-6`), 71.6, 74.3, 77.5, 79.3 (C-2`, C-3`, C-4`, C-5`), 83 (C-1`), 112.8, 120.2, 122.6, 123.7 (C-4, C-5, C-6, C-7), 135.5 (C-7a), 144.0 (C-3a), 154.0 (C-2); *m/z* (FAB) 281 (M^+ +1) HRMS (FAB) Found M^++1 281.11362, $C_{13}H_{17}N_2O_5$ requires M^++1 281.11375.

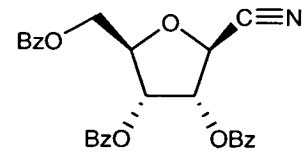
3.8 Synthesis of furanosylbenzazoles

3.8.1 3,4,5-Tri-*O*-benzoyl-β-D-ribofuranosyl cyanide (238)

Sample code: IAS077

Molecular formula: $C_{27}H_{21}NO_7$

Molecular weight: 471



To a stirred solution of tri-*O*-benzoyl-β-D-ribofuranosyl acetate **239** (450 mg, 1 mmol), trimethylsilyl cyanide (0.5 ml, 4 mmol) and dry acetonitrile (15 ml) a few drops (0.2 ml) of $BF_3.Et_2O$ were added. The reaction mixture was stirred under argon at room temperature for 10 minutes. The reaction mixture was quenched with $NaHCO_3$ (10 ml), the mixture extracted with ether (3 x 30 ml) and the organic layers were dried over $MgSO_4$. The solvent was removed *in vacuo*, the resultant oil was purified by wet-flash chromatography (silica, 25% ethyl acetate in hexane) to afford the title compound (**238**) as a white solid (360 mg, 86%).

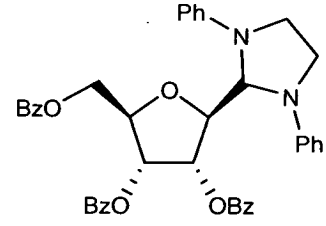
M.p 78-80 °C (lit.[225] 77-80 °C); $[\alpha]_D^{20}$ 21 (c = 0.5 ,$CHCl_3$) (lit $[\alpha]_D^{20}$ 23.9 (c = 0.5 , $CHCl_3$)); δ_H (250 MHz, $CDCl_3$); 4.51 (1H, dd, 5a-H), 4.61-4.69 (2H, m, 4-H, 5b-H) 4.91 (1H, d, 1-H), 5.78 (1H, dd, 3-H), 5.93 (1H, dd, 2-H), 7.27-7.53 (9H, m, ArH), 7.82-8.06 (6H, m, ArH); *J*(x-y)/Hz 1-2 4.3, 2-3 5.0, 3-4 5.4, 4-5a 4.7, 4-5b nd 5a-5b 13.2; δC (63 MHz, $CDCl_3$) 63.0 (C-5), 69.3, 71.7, 74.3, (C-2, C-3, C-4,) 80.7 (C-1) 115.6 (CN), 128.4, 129.7 (ArCH), 133.3, 133.7, 133.9 (ArC), 164.7, 164.9, 166.0 (3x*C*OPh); *m/z* (ES) 472 (MH^+).

3.8.2 1,3-Diphenyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl) imidazoline (244)

Sample code: IAS078

Molecular formula: $C_{26}H_{30}N_2O_7$

Molecular weight: 482



Raney nickel (2 g) was added to a vigourously stirred solution of pyridine (8 ml), glacial acetic acid (6 ml) and water (6 ml). $NaH_2PO_2.H_2O$ (1 g) was added, along with *N,N*-diphenylethylenediamine (550 mg) and D-ribose derived nitrile **238** (550 mg, 2.5 mmol). The reaction was stirred for 16 hours. The resultant mixture was filtered through a pad of celite and the filter cake was washed thoroughly with DCM. The filtrate was washed with water (~200 ml), extracted with DCM (2 x 50 ml) and the combined organic layers were dried over $MgSO_4$. The solvent was co-evaporated with water (to remove residual pyridine) to yield a gum. The gum was dissolved in DCM (5 ml), acetic anhydride (4.72 ml) and triethylamine (8.3 ml) and the reaction mixture was stirred for 16 hours. The mixture was diluted with DCM (20 ml) and stirred with water (20 ml) for 20 minutes before extracting with DCM (2 x 10 ml). The combined organic layers were washed with $NaHCO_3$ (20 ml) and dried over $MgSO_4$. Dry-flash chromatography (silica, hexane/Et_2O gradient elution) afforded the product (**244**) as a colourless oil, which solidified on addition of methanol (295 mg, 59%).

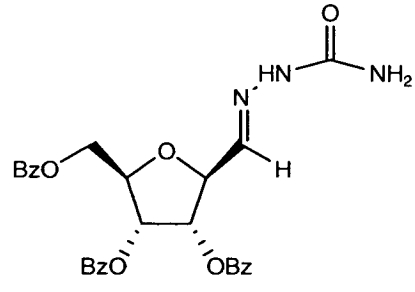
$[\alpha]_D^{20}$ 10 (c = 0.1 ,$CHCl_3$) (lit.[231] $[\alpha]_D^{20}$ 11.2 (c = 0.1 ,$CHCl_3$)); δ_H (360 MHz, $CDCl_3$); 3.62-3.77 (2H, m, NCH_2), 3.81-3.96 (2H, m, NCH_2), 4.48 (1H, dd, 5a`-H), 4.57-4.61 (1H, m, 4`-H) 4.66 (1H, dd, 5b`-H), 4.92 (1H, d, 1`-H), 5.61 (1H, dd, 3`-H), 5.81 (1H, dd, 2`-H), 5.97 (1H, s, 2-H), 6.79-6.97 (4H, m, ArH), 7.26-7.68 (15H, m, ArH), 7.82-8.06 (6H, m, ArH); *J*(x-y)/Hz 1`-2` 5.4, 2`-3` 5.7, 3`-4` 5.8, 4`-5a` 4.7, 4`-5b` 3.2 5a-5b 11.6; δC (93 MHz, $CDCl_3$) 48.0 (NCH_2), 48.4 (NCH_2), 65.3 (C-5`), 73.4, 73.8, 74.4, (C-2`, C-3`, C-4`,) 80.6 (C-1`) 84.2 (C-2), 114.2, 114.6, 119.1, 128.5, 130.85 (ArCH), 134.1, 134.4, 134.5 (ArC), 166.5, 166.6, 167.2 (3x*C*OPh); *m/z* (ES) 483 (MH^+).

3.8.3 2,5-Anhydro-3,4,6-tri-*O*-benzoyl-β-D-allose semicarbazone (246)

Sample code: IAS084

Molecular formula: $C_{28}H_{25}N_3O_8$

Molecular weight: 531



Raney nickel (3.75 g) was added to a vigourously stirred solution of pyridine (10 ml), glacial acetic acid (9 ml) and water (5 ml). $NaH_2PO_2.H_2O$ (1.85 g) was added, followed by semicarbazide hydrochloride (550 mg) and KOH (285 mg) in water (5 ml) and D-ribose derived nitrile **238** (1.05 g) in pyridine (5 ml). The reaction was heated to 40°C for 4 hours. The resultant mixture was filtered through a pad of celite and the filter cake was washed thoroughly with DCM. The filtrate was washed with water (~200 ml), extracted with DCM (2 x 50 ml) and the combined organic layers were dried over $MgSO_4$. The solvent was co-evaporated with water (to remove residual pyridine) to yield a gum. The mixture was diluted with DCM (50 ml) and washed with 1 M HCl (2 x 30 ml), $NaHCO_3$ (2 x 30 ml) and dried over $MgSO_4$. removal of the solvent *in vacuo* to afford crude semicarbazone (**246**) as a brown foam (~1 g, ~85%).

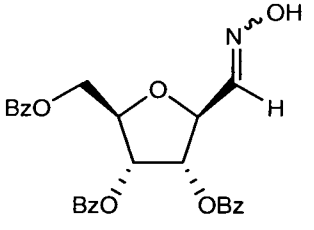
δ_H (250 MHz, $CDCl_3$); 4.43 (1H, dd, 5a-H), 4.51-4.64 (2H, m, 4-H, 5b-H) 4.76 (1H, d, 1-H), 5.67 (1H, dd, 3-H), 5.87 (1H, dd, 2-H), 7.13 (HC=N(NHCONH$_2$)), 7.22-7.49 (9H, m, ArH), 7.82-8.03 (6H, m, ArH), 9.85 (1H, bs, OH); *J*(x-y)/Hz 1-2 5.7, 2-3 5.2, 3-4 4.7, 4-5a 3.6, 4-5b nd 5a-5b 11.4; δC (63 MHz, $CDCl_3$) 63.8 (C-5), 67.7, 72.6, 72.8, (C-2, C-3, C-4,) 79.9 (C-1), 128.2, 128.3, 128.8, 129.2, 129.5 (ArCH), 133.1, 133.3, 133.6 (ArC), 138.6 (HC=N(NHCONH$_2$), 157.4 (HC=N(NHCONH$_2$), 165.1, 165.2, 166.0 (3x*C*OPh); *m/z* (ES) 532 (MH^+).

3.8.4 2,5-Anhydro-3,4,6-tri-*O*-benzoyl-β-D-allose oxime (243)

Sample code: IAS080

Molecular formula: $C_{27}H_{23}NO_8$

Molecular weight: 489



Procedure A

TsOH (212 mg, mmol) was added to a solution of D-ribose derived imidazoline **244** in DCM (4.5 ml), and the mixture stirred at room temperature under nitrogen for 45 minutes. The resultant mixture was filtered and the filter cake washed with DCM,

before concentrating the filtrate *in vacuo* (the water bath temperature did not exceed 30°C!). The residue was dissolved in ethanol (2.5 ml) and pyridine (2.25 ml), hydroxylamine hydrochloride (160 mg) was added, and the mixture heated to 95°C under reflux for 2.5 hours.On cooling, the reaction mixture was diluted with DCM (50 ml) and washed with saturated $NHCO_3$ solution (50 ml), water (50 ml) and 1 M HCl (50 ml) and the organic layer dried over $MgSO_4$. Dry-flash chromatography (silica, hexane/Et_2O gradient elution) afforded the title compound (**243**) as a colourless oil (100 mg, 45%).

Procedure B

Hydroxylamine hydrochloride (278 mg) was added to crude semicarbazone **246** (~500 mg) dissolved in acetonitrile (12.5 ml) and pyridine (4.2 ml), the resulting mixture was stirred at room temperature under argon for 16 hours. The mixture was diluted with ethyl acetate (30 ml) and washed with 1 M HCl (3 x 30 ml), $NaHCO_3$ (3x 30 ml) and brine (30 ml), before drying the organic layer over $MgSO_4$. Wet-flash chromatography (silica, 25% ethyl acetate in hexane) afforded the title compound (**243**) as a colourless oil (236 mg, 81%).

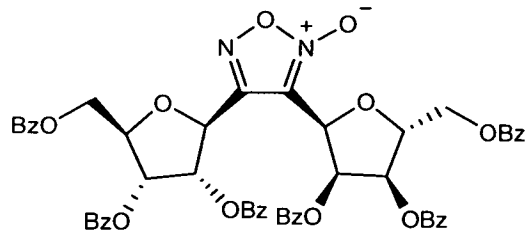
$[\alpha]_D^{20}$ 14 (c = 0.2 ,MeOH) (lit.[142] $[\alpha]_D^{20}$ 12.9 (c = 0.2, MeOH)); δ_H (360 MHz, $CDCl_3$); 4.61 (1H, dd, 5a-H), 4.66-4.71 (1H, m, 4-H), 4.77 (1H, dd, 5b-H), 4.95 (1H, dd, 1-H(*E*)), 5.53 (1H, dd, 1-H(*Z*)), 5.75 (1H, dd, 3-H(*Z*)), 5.80-5.84 (2H, m, 3-H, 2-H(*E*)) 5.92 (1H, dd, 2-H(*Z*)), 6.99 (1H, d, *H*C=NOH(*Z*)), 7.31-7.61 (19H, m, *H*C=NOH(*E*)), ArH), 7.92-8.22 (12H, m, ArH), 8.88 (1H, bs, OH (*E*)); *J*(x-y)/Hz 1-2 5.5, 2-3 nd, 3-4 nd, 4-5a 4.3, 4-5b 3.2 5a-5b 11.7; (*Z*) *J*(x-y)/Hz 1-2 4.7, 2-3 5.5, 3-4 5.2, 4-5a nd, 4-5b nd 5a-5b nd; δC (93 MHz, $CDCl_3$) 64.9 (C-5(*Z*)), 65.2 (C-5(*E*)), 73.4, 73.6, 74.6, 75.1, 78.5, 79.6, (C-2, C-3, C-4 (*E* and *Z*) 80.2 (C-1(*Z*)), 80.4 (C-1(*E*)), 129.5, 129.6, 129.9, 130.1, 130.4, 130.5, 130.8, 130.9, 131.2 (ArCH), 134.4, 134.6, 134.7 (ArC), 148.8 (C=N), 166.3, 166.4, 166.5, 167.4 (6x*C*OPh); *m/z* (ES) 490 (MH^+).

3.8.5 Difuranosyl-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,5-oxadiazole-2-oxide (248)

Sample code: IAS083

Molecular formula: $C_{54}H_{42}N_2O_{16}$

Molecular weight: 974



A stirred mixture of ribose derived oxime **243** (150 mg, 0.3 mmol), *N*-chlorosuccinimide (41 mg, 0.3 mmol), pyridine (0.01 ml) and chloroform (2.5 ml) was heated to 40°C under nitrogen for 45 minutes. On cooling, triethylamine (0.3 ml) was added and the mixture stirred for 1 hour. The solution was diluted with DCM (40 ml), 1 M HCl (40 ml) and dried over $MgSO_4$. Dry-flash chromatography (silica, hexane/Et_2O gradient elution) afforded the title compound (**248**) as a colourless gum (107 mg, 72%).

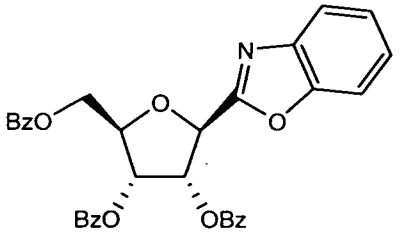
$[\alpha]_D^{20}$ -7.4 (c = 5.65 ,$CHCl_3$); δ_H (250 MHz, $CDCl_3$); 4.45-4.63 (6H, m, 5a-H, 5b-H, 5a`-H, 5b`-H, 4-H, 4`-H), 5.37 (2H, d, 1-H), 5.46 (2H, d, 1`-H) 5.73-5.77 (2H, m, 3-H, 3`H), 6.03 (1H, dd, 2-H), 6.15 (1H, dd, 2`-H), 7.21-7.45 (18H, m, ArH), 7.81-8.18 (12H, m, ArH); *J*(x-y)/Hz 1-2 5.4, 2-3 6.1, 3-4 nd, 4-5a nd, 4-5b nd 5a-5b nd, 1`-2` 4.7, 2`-3` 5.3, 3`-4` nd, 4`-5a` nd, 4`-5b` nd 5a`-5b` nd; δC (63 MHz, $CDCl_3$) 63.6 (C-5), 63.8 (C-5`), 71.9, 72.4, 72.6, 73.9, 74.4, 76.0 (C-2, C-2`,C-3, C-3`, C-4, C-4`) 80.6 (C-1), 80.3 (C-1`) 112.6 (C=N), 128.9, 129.1, 129.2, 129.7, 129.8, 130.0, 130.2 (ArCH), 133.7, 134.1 (ArC), 155.0 ($C=N^+$), 165.6, 165.8, 166.4, 166.6 (6x*C*OPh); HRMS (FAB) Found: M^++1 975.26020. $C_{54}H_{42}N_2O_{16}$ requires M^++H 975.26126.

3.8.6 2-(2,3,5-Tri-*O*-benzoyl-β-D-ribopyranosyl)benzoxazole (241)

Sample code: IAS085

Molecular formula: $C_{33}H_{25}NO_8$

Molecular weight: 563



A stirred mixture of ribose derived oxime **243** (150 mg, 0.3 mmol), *N*-chlorosuccinimide (41 mg, 0.3 mmol), pyridine (0.01 ml) and chloroform (2.5 ml) was heated to 40°C under nitrogen for 45 minutes. The solvent was removed *in vacuo* before adding ethanol (10 ml) and *o*-aminophenol (85 mg, 0.75 mmol) and the mixture was heated to reflux for 5 hours. On cooling, the solvent was removed *in vacuo* and DCM added to precipitate out excess *o*-aminophenol. The solution was washed with 1 M HCl (20 ml) and dried over $MgSO_4$. Dry-flash chromatography (silica, hexane/Et_2O gradient elution) afforded the title compound (**241**) as a colourless gum (155 mg, 92%).

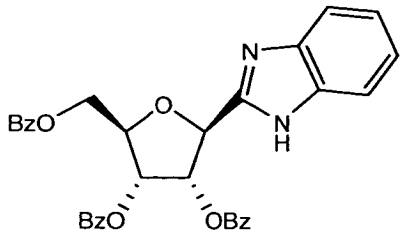
$[\alpha]_D^{20}$ -125 (c = 2.9 ,$CHCl_3$); δ_H (360 MHz, $CDCl_3$); 4.66 (1H, dd, 5a`-H), 4.83-4.92 (2H, m, 4`-H, 5b`-H) 5.62 (1H, d, 1`-H), 6.11 (1H, dd, 3`-H), 6.28 (1H, dd, 2`-H), 7.30-7.41 (10H, m, ArH), 7.53-7.58 (3H, m, ArH), 7.72-7.74 (1H, m, ArH), 7.98-8.12 (5H, m, ArH); *J*(x-y)/Hz 1-2 4.6, 2-3 4.9, 3-4 5.4, 4-5a 3.0, 4-5b nd 5a-5b 11.5; δC (93 MHz, $CDCl_3$) 61.4 (C-5`), 64.6, 73.6, 75.7, (C-2`, C-3`, C-4`,) 81.6 (C-1`) 112.0 (C-7), 121.7 (C-4), 125.7 (C-6), 126.9 (C-5) 129.4, 129.5, 129.8, 129.9, 130.6, 130.9 (ArCH), 131.0, 134.2, 134.6 (ArC), 141.7 (C-3a), 152.0 (C-7a), 162.5 (C-2), 166.2, 166.3, 167.2 (3x*C*OPh); *m/z* (FAB) 564 (M^++1); HRMS (FAB) Found: M^++1 564.16656 $C_{33}H_{25}NO_8$ requires M^++H 564.16584.

3.8.7 2-(2,3,5-Tri-*O*-benzoyl-β-D-ribopyranosyl) benzimidazole (242)

Sample code: IAS087

Molecular formula: $C_{33}H_{26}N_2O_7$

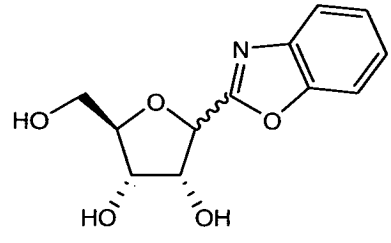
Molecular weight: 562



A stirred mixture of ribose derived oxime **243** (150 mg, 0.3 mmol), *N*-chlorosuccinimide (41 mg, 0.3 mmol), pyridine (0.01 ml) and chloroform (2.5 ml) was heated to 40°C under nitrogen for 45 minutes. The solvent was removed *in vacuo* before adding ethanol (10 ml) and *o*-phenylenediamine (85 mg, 0.75 mmol) and the mixture was heated to reflux for 5 hours. On cooling, the reaction mixture was diluted with DCM (50 ml) and washed with 4% $CuSO_4$ solution (50 ml), the aqueous layer was further extracted with DCM (2x 50 ml), and the combined organic layers dried ($MgSO_4$). Dry-flash chromatography (silica, hexane/Et_2O gradient elution) afforded the title compound (**242**) as a colourless gum (152 mg, 90%).
$[\alpha]_D^{20}$ -106 (c = 3.65 ,$CHCl_3$); δ_H (360 MHz, $CDCl_3$); 4.78-4.88 (3H, dd, 5a`-H, 4`-H, 5b`-H) 5.72 (1H, d, 1`-H), 5.80 (1H, dd, 3`-H), 6.09 (1H, dd, 2`-H), 7.23-7.27 (2H, m, ArH), 7.33-7.59 (11H, m, ArH), 7.90-7.94 (2H, m, ArH), 8.03-8.08 (4H, m, ArH); *J*(x-y)/Hz 1-2 4.4, 2-3 4.8, 3-4 5.3, 4-5a nd, 4-5b nd 5a-5b nd; δC (93 MHz, $CDCl_3$) 64.6 (C-5`), 72.6, 76.5, 78.9 (C-2`, C-3`, C-4`,) 80.9 (C-1`) 114.2.-118.7 (bs, C-4, C-7), 123.2 (C-5, C-6) 128.9, 129.0, 129.2, 129.3, 129.6, 130.2 (ArCH), 130.3, 133.9 (ArC), 151.3 (C-2), 165.7, 167.2 (3x*C*OPh); *m/z* (FAB) 563 (M^++1); HRMS (FAB) Found: M^++1 563.18113. $C_{33}H_{26}N_2O_7$requires M^++H 563.18183.

3.8.8 2-β-D-Ribofuranosylbenzoxazole/2-α-D-Ribofuranosylbenzoxazole (249b/249a)

Sample code: IAS094
Molecular formula: $C_{12}H_{13}NO_5$
Molecular weight: 251



Ribose derived benzoxazole **241** (169 mg, 0.3 mmol) was stirred in methanol (8 ml) at room temperature. Freshly prepared 1 M NaOMe (7 ml) solution was added, and the reaction stirred for 16 hours. Amberlite 120(H^+) resin was added in portions until the solution was neutral to pH paper. All solids were filtered off and the filtrate concentrated *in vacuo* to afford a residue. Following wet-flash chromatography (silica, 10% methanol in ethyl acetate), the title compounds were obtained as an inseperable mixture of anomers (**249b** β : **249a** α, 62:38) (colourless foam, 65 mg, 87%).

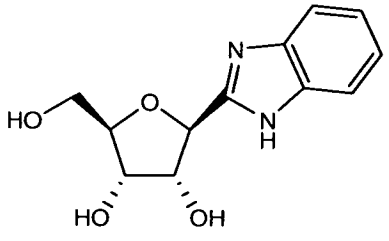
δ_H (360 MHz, D_2O); β-anomer carbohydrate signals, 3.74 (1H, dd, 5a`-H), 3.89 (1H, dd, 5b`-H) 4.05-4.09 (1H, m, 4`-H), 4.11-4.16 (1H, m, 3`-H), 4.34 (1H, dd, 2`-H), 4.47 (1H, d, 1`-H), α-anomer carbohydrate signals, 3.71 (1H, dd, 5a`-H), 3.82 (1H, dd, 5b`-H) 4.11-4.16 (1H, m, 4`-H), 4.26 (1H, dd, 3`-H), 4.53 (1H, dd, 2`-H), 5.08 (1H, d, 1`-H), aromatic signals, 6.92-6.96 (2H, m, ArH), 7.12-7.14 (1H, m, ArH), 7.38-7.44 (3H, m, ArH), 7.59-7.67 (2H, m, ArH); β-anomer *J*(x-y)/Hz 1`-2` 3.3, 2`-3` 4.6, 3`-4` nd, 4`-5a` 4.1, 4`-5b` 2.9 5a`-5b` 12.7; α-anomer *J*(x-y)/Hz 1`-2` 5.3, 2`-3` 5.2, 3`-4` 5.2, 4`-5a` 5.3, 4`-5b` 3.44 5a`-5b` 12.6; δC (63 MHz, D_2O) 60.6, 61.8 (C-5`α, C-5`β), 70.5, 71.5, 74.8, 74.9, 78.0, 83.3, 83.4, 85.1 (C-1`α, C-2`α, C-3`α, C-4`α, C-1`β, C-2`β, C-3`β, C-4`β), 111.5, 116.6, 119.8, 120.9, 123.4, 125. 5, 126.5, 128.3 (ArCH), 139.6, 149.3, 150.8 (ArC) 164.1 (C=N); *m/z* (FAB) 252 (M^++1); HRMS (FAB) Found: M^++1 252.08755. $C_{12}H_{14}NO_5$ requires M^++H 252.08720.

3.8.9 2-β-D-Ribofuranosylbenzimidazole (250)

Sample code: IAS095

Molecular formula: $C_{12}H_{14}N_2O_4$

Molecular weight: 250



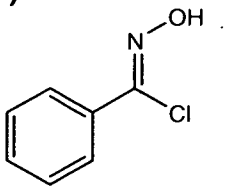
Ribose derived benzimidazole (**242**) (90 mg, 0.16 mmol) was stirred in a mixture of methanol (5 ml) and triethylamine (0.8 ml, 5.7 mmol) which was heated to 50°C for 4 days. On cooling, the mixture was purified by wet-flash chromatography (silica, 10% methanol in ethyl acetate) to afford the title compound (**250**) as a colourless foam (43 mg, 91%).

δ_H (250 MHz, D_2O); 3.61 (1H, dd, 5a`-H), 3.76 (1H, dd, 5b`-H) 3.98-4.05 (2H, m, 3`-H, 4`-H), 4.21 (1H, dd, 2`-H), 4.92 (1H, d, 1`-H), 7.07-7.10 (2H, m, ArH), 7.35-7.41 (2H, m, ArH); *J*(x-y)/Hz 1-2 5.3, 2-3 4.4, 3-4 4.7, 4-5a 3.8, 4-5b 2.0 5a-5b 12.3; δC (63 MHz, D_2O) 61.7 (C-5`), 71.2, 75.7, 78.9, 84.7 (C-3`, C-2`, C-1`), 115.3 (broad) (C-4, C-7), 123.2 (C-5, C-6), 152.9 (C-2); *m/z* (FAB) 251 (M^++1); HRMS (FAB) Found: M^++1 251.10318. $C_{12}H_{15}N_2O_4$ requires M^++H 251.10318.

3.9 Synthesis of Pyranosylperimidines

3.9.1 Synthesis of perimidine precursors

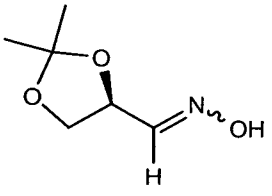
3.9.1.1 Benzohydroximoyl chloride (255)



Sample code: IAS017
Molecular formula: $C_7H_6NO_3Cl$
Molecular weight: 155.5

Syn-benzaldoxime (5 g, 33 mmol) was dissolved in dry chloroform (60 ml) and cooled in a dry-ice/acetone bath. Chlorine gas was passed through the solution until the colour changed from blue, through green, to yellow. The solvent was removed *in vacuo* to afford an oil, which gave the title compound (**255**) as a white solid (4.1 g 74%) on trituration with pentane.; 49-50 °C (lit.[143] 50-51 °C).

3.9.1.2 2,2-Dimethyl-4-formyl-1,3-dioxolane oxime (268)



Sample code: IAS072
Molecular formula: $C_6H_{11}NO_3$
Molecular weight: 145

1,2:5,6-Di-*O*-isopropylidene-D-mannitol (**266**) (5.00 g, 20 mmol) in THF (48 ml) was added to a stirred solution of water (7 ml), THF (10 ml) and $NaIO_4$ (4.56 g, 21.3 mmol). The resulting mixture was stirred vigorously for 2 h before adding Et_2O (70 ml) and filtering of the resultant white flocculate. The filtrate was concentrated and extracted into DCM (2x 50 ml), dried ($MgSO_4$) and the solvent removed in vacuo to afford crude 2,2-Dimethyl-4-formyl-1,3-dioxolane (**267**) (*ca* 4 g). Na_2CO_3 (3.00 g, 27.5 mmol) was added in portions to a stirred solution of $NH_2OH.HCl$ (3.74 g, 54 mmol) in water (40 ml). aldehyde **267** was added and the mixture stirred for 16 h. The reaction mixture was partitioned between water (20 ml) and Et_2O (50 ml) and aqueous layer was extracted with Et_2O (2 x 50 ml). The combined layers were dried

($MgSO_4$) and the solvent removed *in vacuo* to afford the title compound as an oil (3.48 g, 63%) (3:1 mixture of *E:Z* isomers).

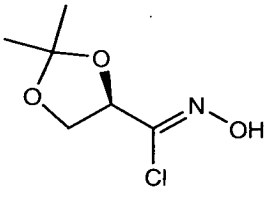
E-isomer δ_H (250 MHz, $CDCl_3$); 1.43, 1.48 (6H, s, CH_3), 3.91 (1H, dd, 5a-H), 4.20 (1H, dd, 5b-H), 4.67 (1H, q, 4-H), 7.42 (1H, d, H-1`-H), 8.89 (1H, bs, OH); *J*(x-y)/Hz 1`-4 6.9, 4-5a 6.3, 4-5b 6.5, 5a-5b 8.6; (63 MHz $CDCl_3$); 24.8, 25.8 (CH_3), 66.7 (C-5), 72.5 (C-4), 109.7 (C-2), 149.0 (C-1`); *Z*-isomer $\delta_H$ (250 MHz, $CDCl_3$); 1.43, 1.48 (6H, s, $CH_3$), 3.84 (1H, dd, 5a-H), 4.40 (1H, dd, 5b-H), 5.15 (1H, m, 4-H), 6.99 (1H, d, H-1`-H), 9.18 (1H, bs, OH); *J*(x-y)/Hz 1`-4 4.1, 4-5a 6.7, 4-5b 7.1, 5a-5b 8.5; (63 MHz $CDCl_3$); 24.6, 25.4 (CH_3), 67.2 (C-5), 70.0 (C-4), 109.1 (C-2), 152.1 (C-1); *m/z* (ES) 146.

3.9.1.3 2,2-Dimethyl-4-formyl-1,3-dioxolane Chloro-oxime (265)

Sample code: IAS073

Molecular formula: $C_6H_{11}NO_3$

Molecular weight: 179.5



(E,Z) 2,2-Dimethyl-4-formyl-1,3-dioxolane oxime (**268**) (1.00 g) was dissolved in dry Et_2O (60 ml) and cooled to -78°C. Dry Cl_2 gas was bubbled through the stirred solution for 20 minutes. The solution initially turned blue and then to emerald green. Nitrogen gas was bubbled through the solution and it was allowed to warm to room temperature. On warming, the solution became colourless and the solvent was removed *in vacuo* to afford an oily solid. The product was obtained as a grey solid (1.20 g, 98%) on trituration with cold pentane. The freshly prepared 2,2-Dimethyl-4-formyl-1,3-dioxolane Chloro-oxime (**265**) was taken on to the next step immediately. δ_H (250 MHz, $CDCl_3$); 1.68, 1.76 (6H, s, CH_3), 4.35-4.50 (2H, m, 5a-H, 5b-H), 5.08 (1H, dd, 4-H), 8.61 (1H, bs, OH); *J*(x-y)/Hz 4-5a 6.3, 4-5b 6.5, 5a-5b nd; (63 MHz $CDCl_3$); 26.2, 26.7 (CH_3), 67.7 (C-5), 76.9 (C-4), 112.1 (C-2), 140.1 (C-1).

3.9.2 Synthesis of perimidines

General Procedure A

Hydroximoyl chloride (1 equivalent) and 1,8-diaminonapthalene (2.5 equivalents) were dissolved in ethanol (10 ml) and the mixture stirred under an atmosphere of nitrogen at room temperature for 16 h. The reaction mixture was diluted with DCM (50 ml) and firstly shaken with saturated K_2CO_3 (50 ml), and then with 4% $CuSO_4$ solution (50 ml) until a dark precipitate was observed, the combined layers were filtered through a pad of celite. The organic layer was separated off, dried ($MgSO_4$) and the solvent removed *in vacuo*. The product was isolated by dry-flash chromatography (silica, hexane/Et_2O gradient elution).

General Procedure B

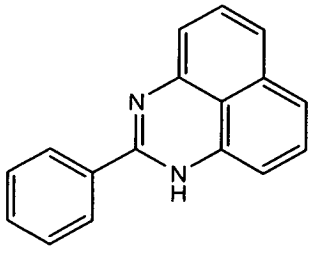
Hydroximoyl chloride (1 equivalent) and 1,8-diaminonapthalene (2.5 equivalents) were stirred in refluxing ethanol (10 ml) under an atmosphere of nitrogen for 5 h. On cooling, the reaction mixture was diluted with DCM (50 ml) and firstly shaken with saturated K_2CO_3 (50 ml), and then with 4% $CuSO_4$ solution (50 ml) until a dark precipitate was observed, the combined layers were filtered through a pad of celite. The organic layer was separated off, dried ($MgSO_4$) and the solvent removed *in vacuo*. The product was isolated by dry-flash chromatography (silica, hexane/Et_2O gradient elution).

3.9.2.1 2-(Phenyl)perimidine (256)

Sample code: IAS066

Molecular formula: $C_{17}H_{12}N_2$

Molecular weight: 244



Benzohydroximoyl chloride (200 mg, 1.3 mmol) and 1,8-diaminonapthalene (402 mg, 2.5 mmol) were added according to general procedure B. The title compound was obtained as an orange crystalline solid (214 mg, 68%) after dry-flash chromatography.

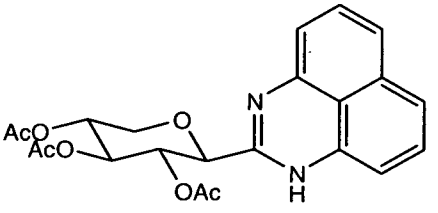
M.p 187-188 °C (lit.[238] 187-188 °C); δ_H (360 MHz, $CDCl_3$); 6.65 (2H, br s, 9-H, 4-H), 7.14-7.26 (4H, m, ArH), 7.47-7.55 (3H, m, ArH), 7.85-7.90 (2H, m, ArH); *m/z* (EI) 244 (M^+) HRMS (EI) Found M^+ 244.10036, $C_{17}H_{12}N_2$ requires M^+ 244.10005.

3.9.2.2 2-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)perimidine (259)

Sample code: IAS065

Molecular formula: $C_{22}H_{22}N_2O_7$

Molecular weight: 426



D-Xylose derived hydroximoyl chloride **106** (120 mg, 0.35 mmol) and 1,8-diaminonapthalene (170 mg, 1 mmol) were added according to general procedure A. In order of elution, glycal **258** (trace) was obtained as an orange solid and the title compound (**259**) was obtained as a yellow/green solid (92 mg, 60%) after dry-flash chromatography.

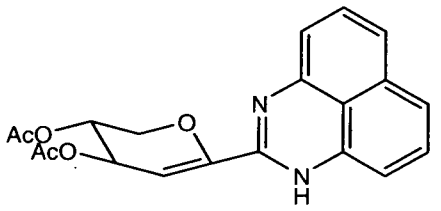
M.p 169-170 °C; $[\alpha]_D^{20}$ = -40 (c = 0.2, $CHCl_3$); δ_H (360 MHz, $CD_3S(O)CD_3$); 1.93, 2.03, 2.05 (9H, 3s, 3x$COCH_3$), 3.67 (1H, dd, 5`a-H), 4.10 (1H, dd, 5`e-H), 4.24 (1H, d, 1`-H), 5.02 (1H, m, 4`-H), 5.24 (1H, dd, 2`-H), 5.41 (1H, dd, 3`-H), 6.42 (1H, dd, 9-H), 6.54 (1H, dd, 4-H), 6.99-7.17 (4H, m, H-5, H-6, H-7, H-8), 10.48 (1H, bs, NH); *J*(x-y)/Hz 1`-2` 9.7, 2`-3` 9.6, 3`-4` 9.5, 4`-5`a 10.9, 4`-5`e 5.5, 5`a-5`e 11.0, 4-5 7.5, 4,6 1.1, 9-8 7.2, 9-7 0.9; δ_C (93 MHz, $CD_3S(O)CD_3$); 21.8, 21.9, 22.0 (3x$COCH_3$), 66.8 (C-5`), 69.8, 71.2, 73.6, 78.8 (C-2`, C-3`, C-4`, C-1`), 104.1 (C-9), 115.0 (C-4), 119.2 (C-7), 121.1 (C-6), 123.6 (C-9b), 129.5 (C-8), 130.3 (C-5), 136.6 (C-6a), 139.4 (C-9a), 145.8 (C-3a), 154.0 (C-2), 170.7, 171.1, 171.2 (3x$COCH_3$); *m/z* (FAB) 427 (M^+ +1) HRMS (FAB) Found M^++1 427.15109, $C_{22}H_{22}N_2O_7$ requires M^++1 427.15053.

3.9.2.3 2-(3,4-Di-*O*-acetyl-2-deoxy-1,2-didehydro-D-*threo*-pento-pyranosyl)perimidine (258)

Sample code: IAS064

Molecular formula: $C_{20}H_{18}N_2O_5$

Molecular weight: 366



D-Xylose derived hydroximoyl chloride **106** (150 mg, 0.4 mmol) and 1,8-diaminonapthalene (170 mg, 1 mmol) were added according to general procedure B. In order of elution, the title compound (**258**) was obtained as an orange solid (70 mg, 43%) and perimidine **259** (31 mg, 16%) after dry-flash chromatography.

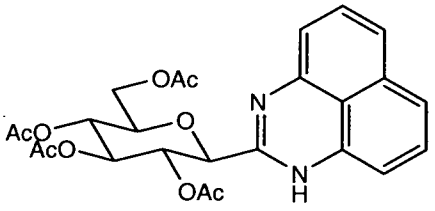
M.p 148-149 °C; $[\alpha]_D^{20} = -113$ (c = 0.15, $CHCl_3$); δ_H (360 MHz, $CD_3S(O)CD_3$); 2.10, 2.12 (6H, 2s, 2x$COCH_3$) 4.14 (1H, dd, 5`a-H), 4.48 (1H, dd, 5`b-H), 5.04 (1H, m, 3`-H), 5.12 (1H, m, 4`-H), 6.02 (1H, d, 2`-H), 6.58 (1H, dd, 9-H), 6.60 (1H, dd, 4-H), 7.47-7.51 (4H, m, H-5, H-6, H-7, H-8), 10.49 (1H, bs, NH); *J*(x-y)/Hz 2`-3` 5.13, 3`-4` nd, 4`-5`a nd, 4`-5`e nd, 5`a-5`e 12.3, 4-5 7.3, 4-6 0.6, 9-8 7.3, 9-7 0.6; $\delta_C$ (93 MHz, $CD_3S(O)CD_3$); 22.2, 22.3 (2x$COCH_3$), 64.5, 66.2, 67.6 (C-3`, C-5`, C-4`), 99.9 (C-2`), 104.7 (C-9), 115.2 (C-4), 119.5 (C-7), 121.0 (C-6), 123.8 (C-9b), 129.5 (C-8), 130.4 (C-5), 136.6 (C-6a), 139.2 (C-9a), 145.9 (C-3a), 149.2 (C-1`), 150.1 (C-2), 170.9, 171.0 (2x$COCH_3$); *m/z* (FAB) 367 (M^+ +1) HRMS (FAB) Found M^++1 367.12985, $C_{20}H_{18}N_2O_5$ requires M^++1 367.12940.

3.9.2.4 2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)perimidine (260)

Sample code: IAS069

Molecular formula: $C_{23}H_{26}N_2O_9$

Molecular weight: 498



D-Glucose derived hydroximoyl chloride **107** (150 mg, 0.4 mmol) and 1,8-diaminonapthalene (170 mg, 1 mmol) were added according to general procedure A.

In order of elution, glycal **261** (trace) was obtained as an orange solid and the title compound (**260**) was obtained as a yellow solid (120 mg, 65%) after dry-flash chromatography.

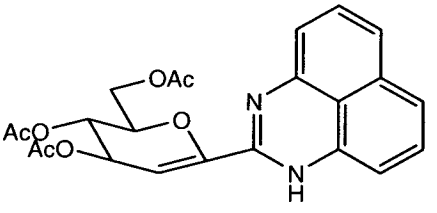
M.p 105-106 °C; $[\alpha]_D^{20}$ = -233 (c = 0.15, $CHCl_3$); δ_H (360 MHz, $CD_3S(O)CD_3$); 1.91, 1.99, 2.05 (12H, 4s, 4x$COCH_3$), 4.08-4.19 (3H, m, 6`a-H, 6`b-H, 5`-H), 4.33 (1H, d, 1`-H), 5.05 (1H, dd, 2`-H), 5.35 (1H, dd, 4`-H), 5.45 (1H, dd, 3`-H), 6.38 (1H, d, 9-H), 6.55 (1H, d, 4-H), 6.94-7.21 (4H, m, H-5, H-6, H-7, H-8), 10.44 (1H, bs, NH); *J*(x-y)/Hz 1`-2` 9.7, 2`-3` 8.9, 3`-4` 9.5, 4`-5` 8.6, 5`-6`a nd, 5`-6`b nd, 6`a-6`b nd, 4-57.2, 9-8 7.3; $\delta_C$ (93 MHz, $CD_3S(O)CD_3$); 21.8, 21.9, 22.0 (4x$COCH_3$), 63.9 (C-6`), 69.5, 70.9, 74.1, 75.8, 78.2 (C-2`, C-3`, C-4`, C-5`, C-1`), 104.0 (C-9), 115.3 (C-4), 119.3 (C-7), 121.3 (C-6), 123.5(C-9b), 129.5 (C-8), 130.3 (C-5), 136.6 (C-6a), 139.3 (C-9a), 145.7 (C-3a), 153.8 (C-2), 170.6, 171.0, 171.1, 171.7 (4x*C*OCH_3); *m/z* (FAB) 499 (M^+ +1) HRMS (FAB) Found M^++1 499.17171, $C_{25}H_{26}N_2O_9$ requires M^++1 499.17166.

3.9.2.5 2-(3,4,6-Tri-*O*-acetyl-2-deoxy-1,2-didehydro-D-*arabino*-hexo-pyranosyl)perimidine (261) (*via* Glucose derived hydroximoyl chloride)

Sample code: IAS070

Molecular formula: $C_{23}H_{22}N_2O_7$

Molecular weight: 438



D-Glucose derived hydroximoyl chloride **107** (150 mg, 0.4 mmol) and 1,8-diaminonapthalene (170 mg, 1 mmol) were added according to general procedure B. In order of elution, The title compound (**261**) was obtained as an orange solid (40 mg, 16 %) and perimidine **260** was obtained as a yellow solid (100 mg, 34%) after dry-flash chromatography.

M.p 154-155 °C; $[\alpha]_D^{20}$ = 175 (c = 0.2, $CHCl_3$); δ_H (360 MHz, $CD_3S(O)CD_3$); 2.06, 2.07 (9H, 3s, 3x$COCH_3$), 4.24 (1H, dd, 6`a-H), 4.59 (1H, dd, 6`b-H), 4.69 (1H, m, 5`-H), 5.22 (1H, m, 3`-H), 5.44 (1H, dd, 4`-H), 5.92 (1H, d, 2`-H), 6.56 (1H, d, 9-H),

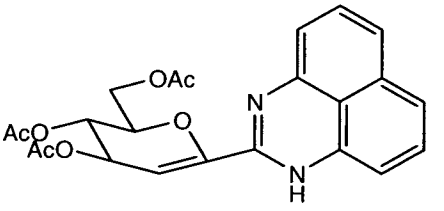
6.58 (1H, d, 4-H), 7.00-7.18 (4H, m, H-5, H-6, H-7, H-8), 10.28 (1H, bs, NH); *J*(x-y)/Hz 2`-3` 3.8, 3`-4` nd, 4`-5` nd, 5`-6`a 3.1, 5`-6`b 5.5, 6`a-6`b 12.3, 4-5 7.2, 9-8 7.3; δ_C (93 MHz, $CD_3S(O)CD_3$); 21.8, 22.1, 22.2 (3x$COCH_3$), 61.6 (C-6`), 69.7, 69.7, 76.1 (C-3`, C-4`, C-5`), 99.9 (C-2`), 104.6 (C-9), 115.3 (C-4), 119.5 (C-7), 121.1 (C-6), 123.7 (C-9b), 129.5 (C-8), 130.4 (C-5), 136.6 (C-6a), 139.1 (C-9a), 145.8 (C-3a), 148.1 (C-1`), 148.6 (C-2), 170.7, 171.3, 171.6 (3x$COCH_3$); *m/z* (FAB) 439 (M^+ +1) HRMS (FAB) Found M^++1 439.15068, $C_{23}H_{22}N_2O_7$ requires M^++1 439.15053.

3.9.2.6 2-(3,4,6-Tri-*O*-acetyl-2-deoxy-1,2-didehydro-D-*arabino*-hexopyranosyl)perimidine (261) (*via* mannose derived hydroximoyl chloride)

Sample code: IAS070

Molecular formula: $C_{23}H_{22}N_2O_7$

Molecular weight: 438



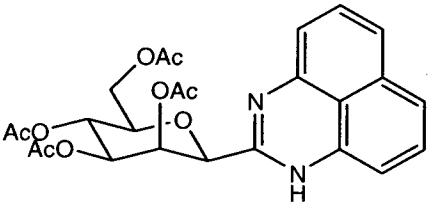
D-Mannose derived hydroximoyl chloride **108** (250 mg, 0.6 mmol) and 1,8-diaminonapthalene (242 mg, 1.5 mmol) were added according to general procedure B. In order of elution, The title compound (**261**) was obtained as an orange solid (90 mg, 34%) and perimidine **262** was obtained as a yellow solid (12 mg, 4%) after dry-flash chromatography.

3.9.2.7 2-(2,3,4,6-Tetra-*O*-acetyl-β-D-mannopyranosyl)perimidine (262)

Sample code: IAS090

Molecular formula: $C_{23}H_{26}N_2O_9$

Molecular weight: 498



Mannose derived hydroximoyl chloride **108** (250 mg, 0.6 mmol) and 1,8-diaminonapthalene (242 mg, 1.5 mmol) were added according to general procedure A. In order of elution, glycal **261** (trace) was obtained as an orange solid and the title compound (**262**) was obtained as a yellow solid (170 mg, 55%) after dry-flash chromatography.

M.p 120-121 °C; $[\alpha]_D^{20} = -193$ (c = 0.75, $CHCl_3$); δ_H (360 MHz, $CD_3S(O)CD_3$); 2.00, 2.04, 2.08 (12H, 4s, 4x$COCH_3$), 4.09 (1H, m, 5`-H), 4.14 (1H, dd, 6`a-H), 4.34 (1H, dd, 6`b-H), 4.83 (1H, d, 1`-H), 5.17 (1H, dd, 4`-H), 5.36 (1H, dd, 3`-H), 5.67 (1H, dd, 2`-H) 6.50 (1H, d, 9-H), 6.60 (1H, d, 4-H), 7.03-7.19 (4H, m, H-5, H-6, H-7, H-8), 10.06 (1H, bs, NH); *J*(x-y)/Hz 1`-2` 1.1, 2`-3` 3.4, 3`-4` 10.1, 4`-5` 10.0, 5`-6`a 2.5, 5`-6`b, 5.7, 6`a-6`b 12.2, 4-5 6.8, 9-8 6.4; $\delta_C$ (93 MHz, $CD_3S(O)CD_3$); 21.8, 21.9, 22.0, 22.2 (4x$COCH_3$), 63.1 (C-6`), 68.4, 69.0, 72.3, 75.3, 78.0 (C-2`, C-3`, C-4`, C-5`, C-1`), 104.5 (C-9), 114.8 (C-4), 119.5 (C-7), 120.8 (C-6), 123.4(C-9b), 129.4 (C-8), 130.3 (C-5), 136.6 (C-6a), 139.0 (C-9a), 145.6 (C-3a), 153.8 (C-2), 171.2, 171.7 (4x$COCH_3$); *m/z* (FAB) 499 (M^+ +1) HRMS (FAB) Found M^++1 499.17133, $C_{25}H_{26}N_2O_9$ requires M^++1 499.17166.

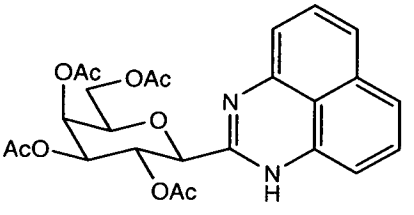
3.9.2.8 2-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)perimidine (263)

This experiment was done in collaboration with Mr A. Fromm

Sample code: AF015

Molecular formula: $C_{23}H_{26}N_2O_9$

Molecular weight: 498



D-Galactose derived hydroximoyl chloride (150 mg, 0.36 mmol) and 1,8-diaminonapthalene (145 mg, 0.9 mmol) were added according to general procedure B. The title compound (**263**) was obtained as a yellow/orange glass (126 mg, 69%) after dry-flash chromatography.

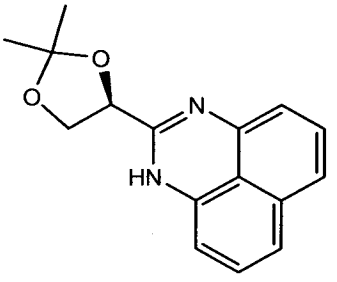
Yellow/orange glass (%); $[\alpha]_D^{20}$ = -120 (c =, $CHCl_3$); δ_H (360 MHz, $CD_3S(O)CD_3$); 1.95, 1.98, 2.04, 2.21 (12H, 4s, 4x$COCH_3$), 4.13 (1H, dd, 6`a-H), 4.18 (1H, dd, 6`b-H), 4.26 (1H, d, 1`-H), 4.39 (1H, dd, 4`-H), 5.22-5.42 (3H, m, 2`-H, 3`-H, 5`-H), 6.55 (2H, d, (9-H, 4-H), 7.04-7.13 (4H, m, 5-H, 6-H, 7-H, 8-H), 10.42 (1H, bs, NH); *J*(x-y)/Hz 1`-2` 8.6, 2`-3` nd, 3`-4` 6.3, 4`-5` 6.4, 5`-6`a 7.14, 5`-6`b, 5.77, 6`a-6`b 11.53, 4-5 7.3, 9-8 7.3; $\delta_C$ (93 MHz, $CD_3S(O)CD_3$); 21.8, 21.9, 22.0, 22.2 (4x$COCH_3$), 63.2 (C-6`), 68.4, 69.0, 72.3, 75.3, 78.0 (C-1`, C-2`, C-3`, C-4`, C-5`), 104.4 (C-9), 115.0 (C-4), 119.3 (C-7), 121.1 (C-6), 123.6(C-9b), 129.4 (C-8), 130.3 (C-5), 136.6 (C-6a), 139.3 (C-9a), 145.7 (C-3a), 153.6 (C-2), 170.2, 171.1, 171.5, 171.6 (4x$COCH_3$); *m/z* (FAB) 499 (M^+ +1) HRMS (FAB) Found M^++1 499.17217, $C_{25}H_{26}N_2O_9$ requires M^++1 499.17166.

3.9.2.9 2-(2,2-Dimethyl-1,3-dioxolan-4-yl)perimidine (264)

Sample code: IAS074

Molecular formula: $C_{16}H_{16}N_2O_2$

Molecular weight: 268



D-glyceraldehyde derived hydroximoyl chloride **265** (150 mg, 0.8 mmol) and 1,8-diaminonapthalene (316 mg, 2 mmol) were added according to general perimidine procedure B. The title compound (**264**) was obtained as a yellow/green solid (137 mg, 61%) after dry-flash chromatography.

M.p 101-102 °C; $[\alpha]_D^{20}$ = 60 (c = 0.2, $CHCl_3$); δ_H (250 MHz, $CD_3S(O)CD_3$); 1.21, 1.26 (6H, s, CH_3), 4.02 (2H, d, 5`a-H, 5`b-H), 4.67 (1H, t, 4`-H), 6.37 (2H, d, 9-H, 4-H), 6.68-7.04 (4H, m, , H-5, H-6, H-7, H-8), 10.13 (1H, bs, NH); *J*(x-y)/Hz 4`-5`a 6.4, 4`-5`b 6.4, 5`a-5b 6.4, 4-5 7.2, 9-8 7.2; (63 MHz, $CD_3S(O)CD_3$); 25.2, 25.6 (CH_3), 66.6 (C-2`), 73.9 (C-1`), 102.7 (C-9), 109.8 (acetal Cq) 113.1 (C-4), 117.6 (C-7), 119.0 (C-6), 121.8 (C-9b), 127.7 (C-8), 128.5 (C-5), 134.9 (C-6a), 137.5 (C-9a), 144.3 (C-3a), 155.5 (C-2); *m/z* (FAB) 268 (M^+) HRMS (FAB) Found M^+ 268.12111, $C_{16}H_{16}N_2O_2$ requires M^+ 268.12118.

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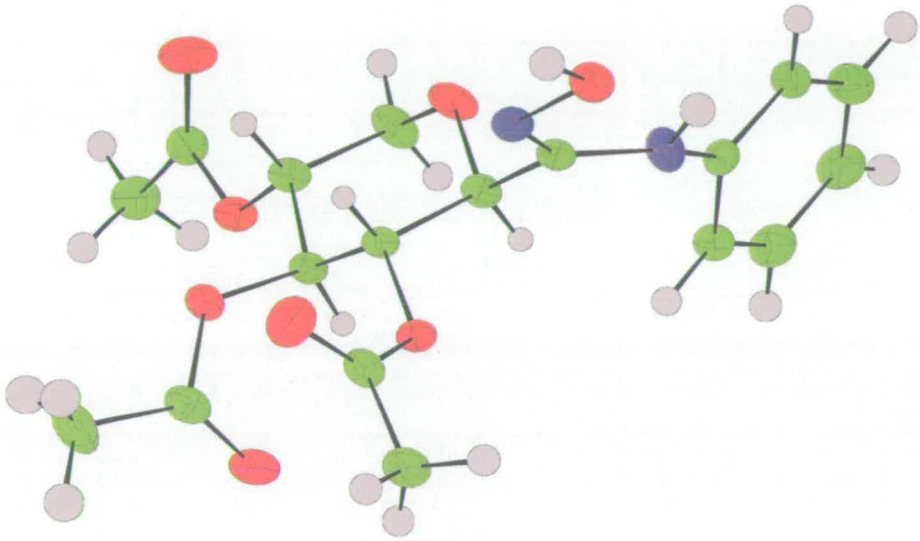
Appendix 1

(Z)-*N*-phenyl-(2',3',4'-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (141)



Appendix 1

Table 1. Crystal data and structure refinement for CRYSTALS_cif.

Contact	Stephen Moggach, S.Moggach@ed.ac.uk
A. CRYSTAL DATA	
Empirical formula	C18 H22 N2 O8 C18 H22 N2 O8
Formula weight	394.38
Wavelength	0.71073 A
Temperature	150 K
Crystal system	Monoclinic
Space group	P 1 21 1
Unit cell dimensions	a = 9.440(3) A alpha = 90 deg. b = 8.007(2) A beta = 103.711(4) deg. c = 12.932(4) A gamma = 90 deg.
Volume	949.6(5) A^3
Number of reflections for cell	3805 (4.839 < theta < 56.847 deg.)
Z	2
Density (calculated)	1.379 Mg/m^3
Absorption coefficient	0.110 mm^-1
F(000)	416.000
B. DATA COLLECTION	
Crystal description	colourless block
Crystal size	0.35 x 0.35 x 0.94 mm
Instrument	Bruker smart apex
Theta range for data collection	2.221 to 28.510 deg.
Index ranges	-11<=h<=12, -10<=k<=10, -17<=l<=14
Reflections collected	5834
Independent reflections	2377 [R(int) = 0.02]
Scan type	\f & \w scans
Absorption correction	Semi-empirical from equivalents (Tmin= 0.819585, Tmax=1.00)
C. SOLUTION AND REFINEMENT.	
Solution	direct methods
Refinement type	Full-matrix least-squares on F
Program used for refinement	CRYSTALS
Hydrogen atom placement	geom
Hydrogen atom treatment	mixed

Data	2368
Parameters	253
Goodness-of-fit on F^2	1.0108
R	0.0397
RW	0.1056
Final maximum delta/sigma	0.008215
Weighting scheme	Chebychev Polynomial
Largest diff. peak and hole	0.48 and -0.27 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for ias014. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	-1256(2)	-584(3)	-8902(2)	22
N(1)	-2561(2)	-801(3)	-9443(1)	25
C(2)	-1075(2)	-45(3)	-7765(2)	22
N(2)	-52(2)	-916(3)	-9304(1)	28
C(3)	-2315(2)	1071(3)	-7595(2)	21
C(4)	-2074(2)	1424(3)	-6408(2)	21
C(5)	-1851(2)	-187(3)	-5765(2)	24
C(6)	-662(3)	-1236(3)	-6054(2)	32
O(7)	-1044(2)	-1553(2)	-7171(1)	30
C(10)	1427(2)	-1113(3)	-8736(2)	23
C(11)	2131(2)	-2554(3)	-8912(2)	28
O(11)	-2543(2)	-1481(2)	-10455(1)	28
C(12)	3593(3)	-2803(4)	-8417(2)	36
C(13)	4341(3)	-1597(4)	-7743(2)	37
C(14)	3645(3)	-138(4)	-7573(2)	36
C(15)	2185(2)	126(3)	-8087(2)	30
O(31)	-2180(2)	2608(2)	-8145(1)	23
C(32)	-3417(2)	3417(3)	-8616(2)	26
O(33)	-4598(2)	2896(3)	-8594(2)	39
C(34)	-3116(3)	5019(3)	-9116(2)	36
O(41)	-3325(2)	2250(2)	-6176(1)	25
C(42)	-3235(3)	3934(3)	-6041(2)	30
O(43)	-2236(2)	4759(2)	-6170(2)	43
C(44)	-4550(4)	4580(4)	-5716(3)	51
O(51)	-1413(2)	349(2)	-4669(1)	25
C(52)	-1454(2)	-798(3)	-3912(2)	27
O(53)	-1842(2)	-2208(2)	-4108(2)	42
C(54)	-945(3)	-57(4)	-2830(2)	34

Table 3. Bond lengths [A] and angles [deg] for ias014.

C(1)-N(2)	1.384(3)
C(1)-C(2)	1.503(3)
C(1)-N(1)	1.277(3)
N(1)-O(11)	1.420(2)
H(1)-O(11)	0.908
C(2)-H(21)	1.000
C(2)-O(7)	1.427(3)
C(2)-C(3)	1.529(3)

N(2)-C(10)	1.424(3)
N(2)-H(2)	0.909
C(3)-H(31)	1.000
C(3)-O(31)	1.443(3)
C(3)-C(4)	1.523(3)
C(4)-H(41)	0.999
C(4)-O(41)	1.446(2)
C(4)-C(5)	1.522(3)
C(5)-H(51)	1.001
C(5)-O(51)	1.444(2)
C(5)-C(6)	1.519(3)
C(6)-H(62)	0.999
C(6)-H(61)	1.000
C(6)-O(7)	1.427(3)
C(10)-C(15)	1.384(3)
C(10)-C(11)	1.377(3)
C(11)-H(111)	1.000
C(11)-C(12)	1.392(3)
C(12)-H(121)	0.999
C(12)-C(13)	1.378(4)
C(13)-H(131)	1.001
C(13)-C(14)	1.383(4)
C(14)-H(141)	1.000
C(14)-C(15)	1.397(3)
C(15)-H(151)	1.002
O(31)-C(32)	1.348(3)
C(32)-C(34)	1.493(3)
C(32)-O(33)	1.197(3)
C(34)-H(343)	1.001
C(34)-H(342)	0.999
C(34)-H(341)	0.999
O(41)-C(42)	1.360(3)
C(42)-C(44)	1.494(4)
C(42)-O(43)	1.195(3)
C(44)-H(443)	1.003
C(44)-H(442)	1.000
C(44)-H(441)	0.999
O(51)-C(52)	1.349(3)
C(52)-C(54)	1.491(3)
C(52)-O(53)	1.196(3)
C(54)-H(543)	1.000
C(54)-H(542)	1.000
C(54)-H(541)	0.999

N(2)-C(1)-C(2)	120.67(18)
N(2)-C(1)-N(1)	122.67(19)
C(2)-C(1)-N(1)	116.54(18)
O(11)-N(1)-C(1)	109.65(16)
H(21)-C(2)-O(7)	113.382
H(21)-C(2)-C(3)	105.594
O(7)-C(2)-C(3)	109.59(16)
H(21)-C(2)-C(1)	109.740
O(7)-C(2)-C(1)	105.45(17)
C(3)-C(2)-C(1)	113.26(16)
C(10)-N(2)-H(2)	109.531
C(10)-N(2)-C(1)	128.28(17)
H(2)-N(2)-C(1)	112.984
H(31)-C(3)-O(31)	111.872
H(31)-C(3)-C(4)	109.090
O(31)-C(3)-C(4)	109.25(17)
H(31)-C(3)-C(2)	112.570
O(31)-C(3)-C(2)	105.49(15)
C(4)-C(3)-C(2)	108.46(16)
H(41)-C(4)-O(41)	110.846
H(41)-C(4)-C(5)	110.790
O(41)-C(4)-C(5)	106.74(17)
H(41)-C(4)-C(3)	106.230
O(41)-C(4)-C(3)	111.08(16)

C(5)-C(4)-C(3)	111.23(18)
H(51)-C(5)-O(51)	112.114
H(51)-C(5)-C(6)	106.831
O(51)-C(5)-C(6)	110.43(17)
H(51)-C(5)-C(4)	112.324
O(51)-C(5)-C(4)	104.81(18)
C(6)-C(5)-C(4)	110.40(18)
H(62)-C(6)-H(61)	109.542
H(62)-C(6)-O(7)	109.673
H(61)-C(6)-O(7)	109.584
H(62)-C(6)-C(5)	109.660
H(61)-C(6)-C(5)	109.508
O(7)-C(6)-C(5)	108.86(17)
C(6)-O(7)-C(2)	111.25(18)
C(15)-C(10)-C(11)	120.0(2)
C(15)-C(10)-N(2)	122.5(2)
C(11)-C(10)-N(2)	117.4(2)
H(111)-C(11)-C(12)	119.673
H(111)-C(11)-C(10)	119.720
C(12)-C(11)-C(10)	120.6(2)
H(1)-O(11)-N(1)	102.018
H(121)-C(12)-C(13)	120.190
H(121)-C(12)-C(11)	120.199
C(13)-C(12)-C(11)	119.6(3)
H(131)-C(13)-C(14)	119.933
H(131)-C(13)-C(12)	119.963
C(14)-C(13)-C(12)	120.1(2)
H(141)-C(14)-C(15)	120.007
H(141)-C(14)-C(13)	119.761
C(15)-C(14)-C(13)	120.2(2)
H(151)-C(15)-C(10)	120.365
H(151)-C(15)-C(14)	120.241
C(10)-C(15)-C(14)	119.4(2)
C(32)-O(31)-C(3)	117.69(16)
C(34)-C(32)-O(33)	125.7(2)
C(34)-C(32)-O(31)	112.01(19)
O(33)-C(32)-O(31)	122.3(2)
H(343)-C(34)-H(342)	109.424
H(343)-C(34)-H(341)	109.459
H(342)-C(34)-H(341)	109.608
H(343)-C(34)-C(32)	109.359
H(342)-C(34)-C(32)	109.523
H(341)-C(34)-C(32)	109.453
C(42)-O(41)-C(4)	116.84(18)
C(44)-C(42)-O(43)	125.7(3)
C(44)-C(42)-O(41)	110.4(2)
O(43)-C(42)-O(41)	123.9(2)
H(443)-C(44)-H(442)	109.289
H(443)-C(44)-H(441)	109.384
H(442)-C(44)-H(441)	109.599
H(443)-C(44)-C(42)	109.341
H(442)-C(44)-C(42)	109.552
H(441)-C(44)-C(42)	109.665
C(52)-O(51)-C(5)	117.30(18)
C(54)-C(52)-O(53)	126.1(2)
C(54)-C(52)-O(51)	110.6(2)
O(53)-C(52)-O(51)	123.3(2)
H(543)-C(54)-H(542)	109.439
H(543)-C(54)-H(541)	109.507
H(542)-C(54)-H(541)	109.537
H(543)-C(54)-C(52)	109.401
H(542)-C(54)-C(52)	109.431
H(541)-C(54)-C(52)	109.518

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for ias014. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	25(1)	17(1)	24(1)	1(1)	4(1)	2(1)
N(1)	30(1)	23(1)	22(1)	-1(1)	4(1)	-2(1)
C(2)	23(1)	19(1)	22(1)	1(1)	2(1)	3(1)
N(2)	24(1)	36(1)	21(1)	-6(1)	2(1)	2(1)
C(3)	21(1)	17(1)	23(1)	2(1)	3(1)	1(1)
C(4)	20(1)	18(1)	24(1)	0(1)	3(1)	1(1)
C(5)	30(1)	21(1)	18(1)	1(1)	1(1)	0(1)
C(6)	43(1)	29(1)	22(1)	3(1)	3(1)	16(1)
O(7)	47(1)	20(1)	22(1)	3(1)	4(1)	10(1)
C(10)	24(1)	24(1)	22(1)	3(1)	7(1)	-1(1)
C(11)	27(1)	26(1)	32(1)	-5(1)	8(1)	-2(1)
O(11)	29(1)	30(1)	23(1)	-6(1)	1(1)	-3(1)
C(12)	27(1)	29(1)	50(1)	-1(1)	7(1)	2(1)
C(13)	23(1)	39(2)	47(1)	1(1)	2(1)	-4(1)
C(14)	31(1)	38(1)	38(1)	-7(1)	6(1)	-11(1)
C(15)	31(1)	26(1)	34(1)	-5(1)	11(1)	-4(1)
O(31)	26(1)	18(1)	25(1)	4(1)	5(1)	1(1)
C(32)	31(1)	24(1)	23(1)	3(1)	5(1)	8(1)
O(33)	27(1)	43(1)	46(1)	19(1)	4(1)	10(1)
C(34)	47(1)	25(1)	36(1)	9(1)	13(1)	10(1)
O(41)	24(1)	22(1)	28(1)	0(1)	6(1)	3(1)
C(42)	38(1)	23(1)	27(1)	1(1)	6(1)	6(1)
O(43)	57(1)	23(1)	54(1)	-6(1)	22(1)	-4(1)
C(44)	56(2)	43(2)	60(2)	-2(2)	26(1)	20(2)
O(51)	32(1)	21(1)	21(1)	-1(1)	3(1)	-1(1)
C(52)	28(1)	27(1)	25(1)	2(1)	6(1)	2(1)
O(53)	67(1)	25(1)	32(1)	3(1)	11(1)	-7(1)
C(54)	46(1)	35(1)	22(1)	-1(1)	9(1)	-3(1)

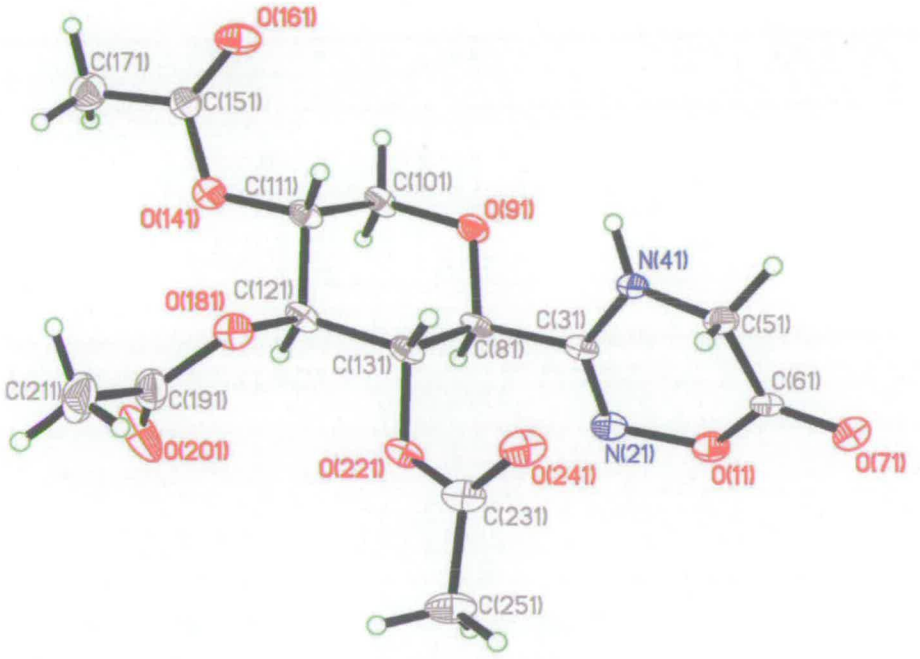
Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for ias014.

	x	y	z	U(eq)
H(1)	-3507	-1650	-10745	50
H(2)	-250	-1629	-9868	50
H(21)	-168	638	-7536	26
H(31)	-3296	546	-7858	25
H(41)	-1190	2149	-6213	25
H(51)	-2751	-893	-5902	28
H(61)	285	-617	-5863	37
H(62)	-564	-2317	-5657	37
H(111)	1587	-3429	-9400	34
H(121)	4098	-3851	-8548	43
H(131)	5388	-1777	-7376	44
H(141)	4192	732	-7081	43
H(151)	1693	1201	-7987	37
H(341)	-4058	5577	-9454	44
H(342)	-2560	4784	-9668	44
H(343)	-2526	5767	-8556	44
H(441)	-4471	5816	-5619	64
H(442)	-5445	4305	-6279	64
H(443)	-4616	4042	-5029	64
H(541)	-983	-922	-2280	41

H(542)	-1591	902	-2751	41
H(543)	80	349	-2734	41

Appendix 2

3-(2',3',4'-Tri-*O*-acetyl-β-D-xylopyranosyl)-1,2,4-oxadiazin-6-one (152)



Appendix 2

able 1. Crystal data and structure refinement for ias020.

Contact	Simon Parsons, S.Parsons@ed.ac.uk
A. CRYSTAL DATA	
Empirical formula	C14 H18 N2 O9 C14 H18 N2 O9
Formula weight	358.30
Wavelength	0.71073 A
Temperature	150 K
Crystal system	Monoclinic
Space group	P 1 21 1
Unit cell dimensions	a = 5.3400(6) A alpha = 90 deg. b = 17.884(2) A beta = 92.321(6) deg. c = 18.154(2) A gamma = 90 deg.
Volume	1732.3(3) A^3
Number of reflections for cell	1007 (3 < theta < 28 deg.)
Z	4
Density (calculated)	1.374 Mg/m^3
Absorption coefficient	0.116 mm^-1
F(000)	752
B. DATA COLLECTION	
Crystal description	colourless block
Crystal size	0.37 x 0.18 x 0.16 mm
Instrument	Bruker SMART
Theta range for data collection	1.123 to 28.543 deg.
Index ranges	-7<=h<=7, -23<=k<=23, -23<=l<=23
Reflections collected	15939
Independent reflections	2255 [R(int) = 0.031]
Scan type	\w
Absorption correction	Sadabs (Tmin= 0.622, Tmax=1.000)
C. SOLUTION AND REFINEMENT.	
Solution	direct (SIR92 (Altomare et al, 1994))
Refinement type	Full-matrix least-squares on F^2
Program used for refinement	SHELXL-97
Hydrogen atom placement	geom

Hydrogen atom treatment	mixed
Data / restraints / parameters	3118/477/451
Goodness-of-fit on F^2	0.9748
Conventional R [F>4sigma(F)]	R1 = 0.0835 [2673 data]
Weighted R (F^2 and all data)	wR2 = 0.1936
Final maximum delta/sigma	0.009153
Weighting scheme	Sheldrick weights.
Largest diff. peak and hole	0.54 and -0.45 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for ias020. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(11)	407(7)	1061(3)	-2586(2)	45
N(21)	312(7)	753(3)	-1842(3)	32
C(31)	-1946(7)	635(3)	-1642(2)	24
N(41)	-4063(7)	792(3)	-2008(3)	28
C(51)	-4054(8)	1369(3)	-2571(3)	34
C(61)	-1578(7)	1400(4)	-2929(3)	33
O(71)	-1271(9)	1711(4)	-3498(3)	46
C(81)	-2104(9)	299(4)	-878(2)	27
O(91)	-4157(9)	-205(3)	-901(3)	32
C(101)	-4433(15)	-571(4)	-217(4)	31
C(111)	-5069(14)	5(4)	370(4)	31
C(121)	-3030(14)	580(4)	442(4)	28
C(131)	-2594(14)	918(4)	-307(4)	29
O(141)	-5177(10)	-355(3)	1088(3)	37
C(151)	-7308(16)	-711(5)	1225(4)	34
O(161)	-9065(10)	-756(4)	786(4)	44
C(171)	-7240(20)	-1024(6)	1980(5)	52
O(181)	-3787(10)	1170(3)	924(3)	36
C(191)	-2399(19)	1296(5)	1544(5)	45
O(201)	-444(16)	988(5)	1691(4)	73
C(211)	-3470(20)	1910(6)	1974(5)	61
O(221)	-464(10)	1401(3)	-234(3)	33
C(231)	-556(15)	2052(4)	-621(5)	35
O(241)	-2275(11)	2220(3)	-1035(4)	43
C(251)	1754(17)	2506(5)	-472(6)	46
O(12)	2125(6)	-1098(3)	-2095(2)	37
N(22)	1733(7)	-825(3)	-2855(2)	32
C(32)	-618(7)	-720(3)	-3038(2)	23
N(42)	-2571(7)	-888(3)	-2659(2)	24
C(52)	-2277(8)	-1431(3)	-2071(3)	30
C(62)	272(7)	-1385(4)	-1710(2)	29
O(72)	744(8)	-1592(3)	-1091(3)	41
C(82)	-1078(9)	-401(4)	-3803(2)	26
O(92)	-3181(9)	78(3)	-3777(2)	26
C(102)	-3789(14)	449(4)	-4460(4)	30
C(112)	-4545(13)	-132(4)	-5041(4)	27
C(122)	-2478(14)	-703(4)	-5113(4)	26
C(132)	-1753(13)	-1028(4)	-4358(4)	24
O(142)	-4923(10)	194(3)	-5754(3)	30
C(152)	-7126(14)	552(4)	-5876(4)	28
O(162)	-8609(10)	676(3)	-5406(3)	34
C(172)	-7470(18)	773(5)	-6657(4)	43

O(182)	-3366(10)	-1311(3)	-5565(3)	32
C(192)	-2179(18)	-1402(5)	-6207(4)	40
O(202)	-527(15)	-1023(4)	-6407(4)	69
C(212)	-3280(20)	-2051(6)	-6622(6)	54
O(222)	376(9)	-1509(3)	-4462(3)	30
C(232)	389(14)	-2180(4)	-4110(5)	32
O(242)	-1088(12)	-2348(3)	-3668(3)	43
C(252)	2570(18)	-2640(5)	-4326(6)	50

Table 3. Bond lengths [A] and angles [deg] for ias020.

O(11)-N(21)	1.462(5)
O(11)-C(61)	1.351(5)
N(21)-C(31)	1.291(5)
C(31)-N(41)	1.318(5)
C(31)-C(81)	1.517(6)
N(41)-C(51)	1.453(5)
N(41)-H(41)	0.911
C(51)-C(61)	1.497(5)
C(51)-H(511)	0.991
C(51)-H(512)	0.972
C(61)-O(71)	1.191(6)
C(81)-O(91)	1.419(6)
C(81)-C(131)	1.548(9)
C(81)-H(811)	0.976
O(91)-C(101)	1.416(9)
C(101)-C(111)	1.530(11)
C(101)-H(1011)	0.980
C(101)-H(1012)	0.983
C(111)-C(121)	1.500(10)
C(111)-O(141)	1.456(9)
C(111)-H(1111)	0.981
C(121)-C(131)	1.514(11)
C(121)-O(181)	1.438(9)
C(121)-H(1211)	0.983
C(131)-O(221)	1.429(9)
C(131)-H(1311)	0.983
O(141)-C(151)	1.337(10)
C(151)-O(161)	1.208(10)
C(151)-C(171)	1.480(12)
C(171)-H(1711)	0.980
C(171)-H(1712)	0.978
C(171)-H(1713)	0.976
O(181)-C(191)	1.342(10)
C(191)-O(201)	1.202(12)
C(191)-C(211)	1.476(13)
C(211)-H(2111)	0.969
C(211)-H(2112)	0.984
C(211)-H(2113)	0.980
O(221)-C(231)	1.360(10)
C(231)-O(241)	1.202(10)
C(231)-C(251)	1.492(12)
C(251)-H(2511)	0.970
C(251)-H(2512)	0.974
C(251)-H(2513)	0.992
O(12)-N(22)	1.469(5)
O(12)-C(62)	1.337(5)
N(22)-C(32)	1.299(5)
C(32)-N(42)	1.308(5)
C(32)-C(82)	1.513(5)
N(42)-C(52)	1.447(5)
N(42)-H(42)	0.909
C(52)-C(62)	1.489(5)
C(52)-H(521)	0.970
C(52)-H(522)	0.993
C(62)-O(72)	1.200(5)

C(82)-O(92)	1.415(6)
C(82)-C(132)	1.540(9)
C(82)-H(821)	0.978
O(92)-C(102)	1.432(9)
C(102)-C(112)	1.524(10)
C(102)-H(1021)	0.975
C(102)-H(1022)	0.983
C(112)-C(122)	1.514(10)
C(112)-O(142)	1.426(9)
C(112)-H(1121)	0.983
C(122)-C(132)	1.523(10)
C(122)-O(182)	1.432(9)
C(122)-H(1221)	0.980
C(132)-O(222)	1.445(8)
C(132)-H(1321)	0.982
O(142)-C(152)	1.350(9)
C(152)-O(162)	1.207(9)
C(152)-C(172)	1.478(11)
C(172)-H(1721)	0.982
C(172)-H(1722)	0.983
C(172)-H(1723)	0.976
O(182)-C(192)	1.359(9)
C(192)-O(202)	1.181(11)
C(192)-C(212)	1.493(13)
C(212)-H(2121)	0.980
C(212)-H(2122)	0.979
C(212)-H(2123)	0.980
O(222)-C(232)	1.359(10)
C(232)-O(242)	1.186(10)
C(232)-C(252)	1.492(12)
C(252)-H(2521)	0.971
C(252)-H(2522)	0.973
C(252)-H(2523)	0.985

N(21)-O(11)-C(61)	122.56(9)
O(11)-N(21)-C(31)	112.91(9)
N(21)-C(31)-N(41)	128.01(7)
N(21)-C(31)-C(81)	114.13(7)
N(41)-C(31)-C(81)	117.82(8)
C(31)-N(41)-C(51)	118.61(9)
C(31)-N(41)-H(41)	119.715
C(51)-N(41)-H(41)	121.641
N(41)-C(51)-C(61)	111.05(9)
N(41)-C(51)-H(511)	109.014
C(61)-C(51)-H(511)	107.761
N(41)-C(51)-H(512)	110.467
C(61)-C(51)-H(512)	109.273
H(511)-C(51)-H(512)	109.221
C(51)-C(61)-O(11)	118.35(7)
C(51)-C(61)-O(71)	123.23(8)
O(11)-C(61)-O(71)	118.41(7)
C(31)-C(81)-O(91)	107.26(9)
C(31)-C(81)-C(131)	110.3(5)
O(91)-C(81)-C(131)	108.8(5)
C(31)-C(81)-H(811)	110.767
O(91)-C(81)-H(811)	110.033
C(131)-C(81)-H(811)	109.623
C(81)-O(91)-C(101)	112.1(4)
O(91)-C(101)-C(111)	109.5(6)
O(91)-C(101)-H(1011)	110.031
C(111)-C(101)-H(1011)	109.234
O(91)-C(101)-H(1012)	109.883
C(111)-C(101)-H(1012)	109.017
H(1011)-C(101)-H(1012)	109.172
C(101)-C(111)-C(121)	110.0(6)
C(101)-C(111)-O(141)	110.1(6)
C(121)-C(111)-O(141)	106.3(6)
C(101)-C(111)-H(1111)	110.031

C(121)-C(111)-H(1111)	110.139
O(141)-C(111)-H(1111)	110.242
C(111)-C(121)-C(131)	109.5(6)
C(111)-C(121)-O(181)	109.6(6)
C(131)-C(121)-O(181)	108.1(6)
C(111)-C(121)-H(1211)	109.955
C(131)-C(121)-H(1211)	109.597
O(181)-C(121)-H(1211)	110.107
C(81)-C(131)-C(121)	110.6(6)
C(81)-C(131)-O(221)	109.8(6)
C(121)-C(131)-O(221)	108.0(6)
C(81)-C(131)-H(1311)	109.724
C(121)-C(131)-H(1311)	109.047
O(221)-C(131)-H(1311)	109.651
C(111)-O(141)-C(151)	116.2(6)
O(141)-C(151)-O(161)	123.6(8)
O(141)-C(151)-C(171)	111.3(7)
O(161)-C(151)-C(171)	125.1(8)
C(151)-C(171)-H(1711)	109.223
C(151)-C(171)-H(1712)	108.953
H(1711)-C(171)-H(1712)	109.612
C(151)-C(171)-H(1713)	109.263
H(1711)-C(171)-H(1713)	109.821
H(1712)-C(171)-H(1713)	109.950
C(121)-O(181)-C(191)	118.3(7)
O(181)-C(191)-O(201)	123.7(8)
O(181)-C(191)-C(211)	110.9(9)
O(201)-C(191)-C(211)	125.2(9)
C(191)-C(211)-H(2111)	109.549
C(191)-C(211)-H(2112)	108.645
H(2111)-C(211)-H(2112)	110.064
C(191)-C(211)-H(2113)	108.947
H(2111)-C(211)-H(2113)	110.434
H(2112)-C(211)-H(2113)	109.167
C(131)-O(221)-C(231)	117.2(6)
O(221)-C(231)-O(241)	123.3(7)
O(221)-C(231)-C(251)	111.1(7)
O(241)-C(231)-C(251)	125.6(8)
C(231)-C(251)-H(2511)	109.961
C(231)-C(251)-H(2512)	109.319
H(2511)-C(251)-H(2512)	110.861
C(231)-C(251)-H(2513)	108.306
H(2511)-C(251)-H(2513)	109.327
H(2512)-C(251)-H(2513)	109.019
N(22)-O(12)-C(62)	122.53(9)
O(12)-N(22)-C(32)	112.83(9)
N(22)-C(32)-N(42)	127.94(7)
N(22)-C(32)-C(82)	114.15(7)
N(42)-C(32)-C(82)	117.81(8)
C(32)-N(42)-C(52)	118.53(9)
C(32)-N(42)-H(42)	120.049
C(52)-N(42)-H(42)	121.386
N(42)-C(52)-C(62)	110.95(9)
N(42)-C(52)-H(521)	110.908
C(62)-C(52)-H(521)	109.161
N(42)-C(52)-H(522)	109.286
C(62)-C(52)-H(522)	107.295
H(521)-C(52)-H(522)	109.156
C(52)-C(62)-O(12)	118.29(7)
C(52)-C(62)-O(72)	123.28(8)
O(12)-C(62)-O(72)	118.43(7)
C(32)-C(82)-O(92)	107.23(9)
C(32)-C(82)-C(132)	110.6(5)
O(92)-C(82)-C(132)	107.3(5)
C(32)-C(82)-H(821)	111.046
O(92)-C(82)-H(821)	110.252
C(132)-C(82)-H(821)	110.297
C(82)-O(92)-C(102)	113.8(4)

O(92)-C(102)-C(112)	109.1(6)
O(92)-C(102)-H(1021)	109.835
C(112)-C(102)-H(1021)	109.603
O(92)-C(102)-H(1022)	109.499
C(112)-C(102)-H(1022)	109.173
H(1021)-C(102)-H(1022)	109.602
C(102)-C(112)-C(122)	110.3(6)
C(102)-C(112)-O(142)	112.0(6)
C(122)-C(112)-O(142)	105.9(6)
C(102)-C(112)-H(1121)	109.901
C(122)-C(112)-H(1121)	109.276
O(142)-C(112)-H(1121)	109.388
C(112)-C(122)-C(132)	109.9(6)
C(112)-C(122)-O(182)	109.7(6)
C(132)-C(122)-O(182)	107.0(6)
C(112)-C(122)-H(1221)	109.672
C(132)-C(122)-H(1221)	110.119
O(182)-C(122)-H(1221)	110.490
C(82)-C(132)-C(122)	110.8(6)
C(82)-C(132)-O(222)	110.8(5)
C(122)-C(132)-O(222)	106.4(5)
C(82)-C(132)-H(1321)	109.797
C(122)-C(132)-H(1321)	109.299
O(222)-C(132)-H(1321)	109.727
C(112)-O(142)-C(152)	115.6(6)
O(142)-C(152)-O(162)	124.3(7)
O(142)-C(152)-C(172)	111.0(6)
O(162)-C(152)-C(172)	124.7(7)
C(152)-C(172)-H(1721)	109.265
C(152)-C(172)-H(1722)	109.346
H(1721)-C(172)-H(1722)	109.072
C(152)-C(172)-H(1723)	109.981
H(1721)-C(172)-H(1723)	109.643
H(1722)-C(172)-H(1723)	109.515
C(122)-O(182)-C(192)	115.3(6)
O(182)-C(192)-O(202)	125.2(8)
O(182)-C(192)-C(212)	109.7(8)
O(202)-C(192)-C(212)	125.1(9)
C(192)-C(212)-H(2121)	109.543
C(192)-C(212)-H(2122)	109.647
H(2121)-C(212)-H(2122)	109.586
C(192)-C(212)-H(2123)	109.058
H(2121)-C(212)-H(2123)	109.466
H(2122)-C(212)-H(2123)	109.527
C(132)-O(222)-C(232)	117.0(6)
O(222)-C(232)-O(242)	123.4(7)
O(222)-C(232)-C(252)	110.6(7)
O(242)-C(232)-C(252)	125.9(8)
C(232)-C(252)-H(2521)	109.426
C(232)-C(252)-H(2522)	108.978
H(2521)-C(252)-H(2522)	110.769
C(232)-C(252)-H(2523)	108.302
H(2521)-C(252)-H(2523)	109.758
H(2522)-C(252)-H(2523)	109.563

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for ias020. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12

O(11)	23(2)	66(4)	45(3)	6(3)	1(2)	-7(3)
N(21)	24(2)	27(4)	44(3)	-3(3)	1(2)	3(3)
C(31)	23(2)	11(3)	38(3)	-9(2)	-2(2)	3(3)
N(41)	20(2)	32(3)	32(3)	0(2)	-1(2)	-4(3)
C(51)	25(3)	38(4)	40(4)	6(3)	-1(3)	-6(3)
C(61)	25(3)	38(4)	36(3)	-1(3)	0(2)	-13(3)
O(71)	44(3)	54(4)	42(3)	7(3)	5(2)	-15(3)
C(81)	14(3)	30(3)	37(3)	-4(2)	-10(2)	4(2)
O(91)	36(3)	26(3)	33(2)	3(2)	-9(2)	-8(2)
C(101)	40(4)	18(3)	34(3)	5(2)	-15(3)	0(3)
C(111)	28(4)	26(3)	37(3)	3(2)	-11(3)	2(2)
C(121)	30(4)	19(3)	35(3)	-2(2)	-12(3)	5(2)
C(131)	25(3)	26(3)	36(3)	-1(2)	-10(3)	1(2)
O(141)	35(3)	42(3)	33(2)	1(2)	-1(2)	-3(2)
C(151)	38(3)	27(4)	36(3)	-7(3)	3(2)	-1(3)
O(161)	28(3)	39(3)	65(4)	3(3)	-4(2)	1(3)
C(171)	65(6)	51(6)	42(4)	4(4)	7(4)	-13(5)
O(181)	36(3)	27(3)	44(3)	-5(2)	4(2)	5(2)
C(191)	63(5)	42(5)	30(4)	-5(3)	7(3)	-4(4)
O(201)	93(5)	76(5)	48(4)	-23(4)	-33(4)	22(4)
C(211)	94(8)	51(6)	40(5)	-14(4)	28(5)	-10(5)
O(221)	28(3)	27(2)	41(3)	-8(2)	-7(2)	-1(2)
C(231)	27(3)	23(3)	56(5)	-7(3)	1(3)	5(3)
O(241)	32(3)	34(3)	63(4)	10(3)	-1(2)	4(3)
C(251)	34(4)	26(4)	77(7)	0(4)	0(4)	-3(3)
O(12)	22(2)	46(4)	42(3)	6(2)	0(2)	-3(2)
N(22)	22(2)	36(4)	37(3)	-3(3)	0(2)	-2(3)
C(32)	23(2)	18(3)	28(3)	-7(2)	6(2)	5(3)
N(42)	18(2)	26(3)	29(3)	-3(2)	3(2)	7(3)
C(52)	19(3)	33(4)	38(4)	5(3)	0(2)	1(3)
C(62)	21(3)	31(4)	36(3)	5(3)	-2(2)	4(3)
O(72)	37(3)	51(4)	34(2)	8(3)	-5(2)	5(3)
C(82)	24(3)	24(3)	32(3)	-1(2)	3(2)	1(2)
O(92)	26(2)	26(3)	27(2)	-3(2)	0(2)	3(2)
C(102)	31(4)	30(4)	28(3)	0(2)	-2(3)	2(3)
C(112)	25(3)	26(3)	29(3)	2(2)	5(3)	-4(2)
C(122)	28(3)	22(3)	27(3)	2(2)	6(2)	-5(2)
C(132)	24(3)	24(3)	25(2)	1(2)	10(2)	0(2)
O(142)	33(3)	29(3)	29(2)	-1(2)	1(2)	5(2)
C(152)	28(3)	30(4)	26(3)	-6(3)	-1(2)	1(3)
O(162)	33(3)	34(3)	36(3)	7(3)	7(2)	8(2)
C(172)	59(6)	38(5)	31(3)	5(4)	-3(3)	11(4)
O(182)	34(3)	28(3)	33(2)	-3(2)	-1(2)	0(2)
C(192)	56(5)	34(4)	29(3)	-1(3)	1(3)	2(3)
O(202)	92(6)	68(5)	50(4)	-20(4)	38(4)	-24(4)
C(212)	66(6)	51(5)	45(5)	-18(4)	-10(5)	5(4)
O(222)	22(2)	27(2)	40(3)	-2(2)	6(2)	0(2)
C(232)	25(3)	28(3)	41(4)	-1(3)	-3(3)	0(3)
O(242)	47(3)	32(3)	49(4)	8(3)	9(2)	2(3)
C(252)	42(5)	38(5)	70(7)	1(5)	10(4)	11(4)

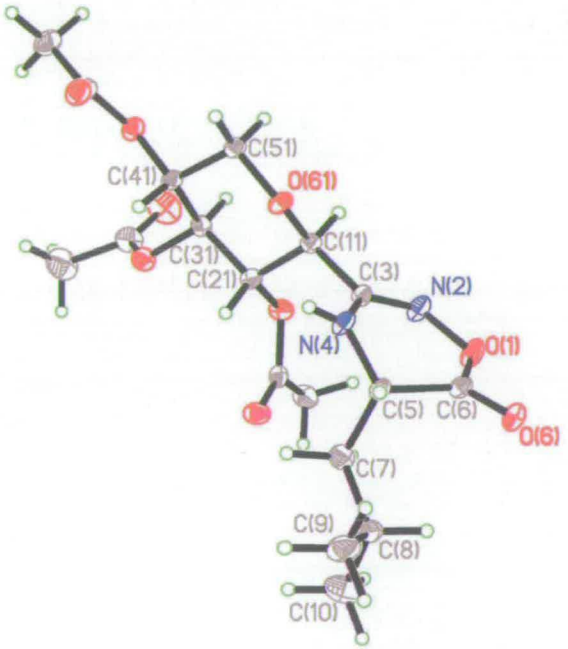
Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for ias020.

	x	y	z	U(eq)
H(41)	-5498	550	-1893	35
H(42)	-4084	-678	-2777	30
H(511)	-5353	1250	-2959	41
H(512)	-4412	1855	-2360	41
H(811)	-559	34	-737	34
H(1011)	-5782	-942	-261	39
H(1012)	-2860	-824	-65	39

H(1111)	-6677	245	238	38
H(1211)	-1474	348	638	34
H(1311)	-4078	1210	-467	36
H(1711)	-8834	-1276	2064	66
H(1712)	-6992	-616	2334	66
H(1713)	-5864	-1382	2033	66
H(2111)	-2440	1992	2419	76
H(2112)	-5181	1770	2103	76
H(2113)	-3540	2363	1671	76
H(2511)	1666	2964	-757	58
H(2512)	1928	2613	54	58
H(2513)	3218	2208	-619	58
H(521)	-2556	-1935	-2256	38
H(522)	-3502	-1322	-1688	38
H(821)	383	-123	-3961	34
H(1021)	-2339	729	-4619	36
H(1022)	-5198	794	-4394	36
H(1121)	-6088	-387	-4903	34
H(1221)	-1020	-467	-5327	31
H(1321)	-3156	-1323	-4181	30
H(1721)	-9090	1027	-6731	53
H(1722)	-7456	324	-6970	53
H(1723)	-6121	1108	-6793	53
H(2121)	-2429	-2114	-7086	68
H(2122)	-5073	-1962	-6728	68
H(2123)	-3068	-2504	-6322	68
H(2521)	2555	-3115	-4066	61
H(2522)	2465	-2718	-4857	61
H(2523)	4118	-2364	-4189	61

Appendix 3

3-(2',3',4'-Tri-*O*-acetyl-β-D-xylopyranosyl)-5-(isopropyl)-1,2,4-oxadiazin-6-one (156)



Appendix 3

Table 1. Crystal data and structure refinement for ias046.

Contact	Simon Parsons, S.Parsons@ed.ac.uk
A. CRYSTAL DATA	
Empirical formula	C18 H26 N2 O9 C18 H26 N2 O9
Formula weight	414.41
Wavelength	0.71073 A
Temperature	150 K
Crystal system	Monoclinic
Space group	C 2
Unit cell dimensions	a = 28.1300(9) A alpha = 90 deg. b = 5.3729(2) A beta = 123.387(2) deg. c = 16.9066(5) A gamma = 90 deg.
Volume	2133.57(13) A^3
Number of reflections for cell	6621 (2 < theta < 31 deg.)
Z	4
Density (calculated)	1.290 Mg/m^3
Absorption coefficient	0.104 mm^-1
F(000)	880
B. DATA COLLECTION	
Crystal description	colourless slab
Crystal size	2.60 x 0.72 x 0.18 mm
Instrument	Bruker SMART Apex CCD
Theta range for data collection	1.734 to 30.541 deg.
Index ranges	-40<=h<=38, -7<=k<=7, -23<=l<=23
Reflections collected	17968
Independent reflections	3455 [R(int) = 0.046]
Scan type	\w
Absorption correction	Semi-empirical from equivalents (Tmin= 0.75, Tmax=0.98)
C. SOLUTION AND REFINEMENT.	
Solution	direct (SIR92 (Altomare et al., 1994))
Refinement type	Full-matrix least-squares on F^2
Program used for refinement	CRYSTALS
Hydrogen atom placement	geom

Hydrogen atom treatment	mixed
Data	3455
Parameters	266
Goodness-of-fit on F^2	0.8769
Conventional R [F>4sigma(F)]	R1 = 0.0451 [2730 data]
Rw	0.1143
Final maximum delta/sigma	0.000711
Weighting scheme	Sheldrick Weights
Largest diff. peak and hole	0.39 and -0.26 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for ias046. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(1)	10049(1)	5053(3)	3837(1)	41
N(2)	9493(1)	4715(4)	3703(2)	36
C(3)	9358(1)	2418(4)	3699(2)	26
N(4)	9646(1)	422(4)	3723(2)	29
C(5)	10067(1)	645(4)	3483(1)	26
C(6)	10360(1)	3134(4)	3838(2)	28
O(6)	10840(1)	3562(4)	4081(1)	34
C(7)	9801(1)	443(5)	2412(2)	34
C(8)	10225(1)	270(5)	2118(2)	35
C(9)	10526(1)	-2223(6)	2377(2)	49
C(10)	9924(2)	758(8)	1061(2)	67
C(11)	8820(1)	2000(4)	3686(1)	26
C(21)	8302(1)	1493(4)	2681(1)	27
O(12)	8152(1)	3751(3)	2131(1)	30
C(22)	8209(1)	3788(4)	1388(1)	29
O(22)	8407(1)	2110(4)	1192(1)	37
C(32)	7996(1)	6198(5)	858(2)	41
C(31)	7796(1)	827(4)	2733(1)	28
O(13)	7331(1)	37(4)	1807(1)	35
C(23)	6817(1)	1115(7)	1468(2)	47
O(23)	6747(1)	2913(5)	1811(2)	65
C(43)	6360(1)	-374(10)	640(2)	72
C(41)	7942(1)	-1316(4)	3415(1)	27
O(14)	7456(1)	-1566(3)	3484(1)	31
C(24)	7419(1)	-3705(5)	3864(2)	32
O(24)	7781(1)	-5288(3)	4174(1)	37
C(34)	6879(1)	-3810(6)	3834(2)	50
C(51)	8474(1)	-685(4)	4373(1)	27
O(61)	8932(1)	-142(3)	4254(1)	27

Table 3. Bond lengths [A] and angles [deg] for ias046.

O(1)-N(2)	1.463(2)
O(1)-C(6)	1.352(3)
N(2)-C(3)	1.290(3)
C(3)-N(4)	1.331(3)
C(3)-C(11)	1.517(3)
N(4)-C(5)	1.452(2)

N(4)-H(4)	0.77(4)
C(5)-C(6)	1.512(3)
C(5)-C(7)	1.536(3)
C(5)-H(51)	1.005
C(6)-O(6)	1.198(2)
C(7)-C(8)	1.528(3)
C(7)-H(71)	1.001
C(7)-H(72)	1.000
C(8)-C(9)	1.515(4)
C(8)-C(10)	1.522(3)
C(8)-H(81)	0.999
C(9)-H(91)	1.002
C(9)-H(92)	1.001
C(9)-H(93)	0.997
C(10)-H(101)	1.002
C(10)-H(102)	1.002
C(10)-H(103)	0.996
C(11)-C(21)	1.536(3)
C(11)-O(61)	1.419(3)
C(11)-H(111)	1.001
C(21)-O(12)	1.443(3)
C(21)-C(31)	1.519(3)
C(21)-H(211)	1.000
O(12)-C(22)	1.353(2)
C(22)-O(22)	1.197(3)
C(22)-C(32)	1.499(3)
C(32)-H(321)	1.003
C(32)-H(322)	0.997
C(32)-H(323)	1.000
C(31)-O(13)	1.445(2)
C(31)-C(41)	1.517(3)
C(31)-H(311)	1.002
O(13)-C(23)	1.359(3)
C(23)-O(23)	1.198(4)
C(23)-C(43)	1.508(5)
C(43)-H(431)	0.999
C(43)-H(432)	0.995
C(43)-H(433)	1.005
C(41)-O(14)	1.440(2)
C(41)-C(51)	1.520(3)
C(41)-H(411)	1.001
O(14)-C(24)	1.349(3)
C(24)-O(24)	1.202(3)
C(24)-C(34)	1.494(3)
C(34)-H(341)	0.998
C(34)-H(342)	1.000
C(34)-H(343)	1.005
C(51)-O(61)	1.439(2)
C(51)-H(511)	1.001
C(51)-H(512)	1.000

N(2)-O(1)-C(6)	122.82(17)
O(1)-N(2)-C(3)	113.96(18)
N(2)-C(3)-N(4)	126.7(2)
N(2)-C(3)-C(11)	115.47(19)
N(4)-C(3)-C(11)	117.82(19)
C(3)-N(4)-C(5)	120.12(19)
C(3)-N(4)-H(4)	117(2)
C(5)-N(4)-H(4)	122(2)
N(4)-C(5)-C(6)	108.28(17)
N(4)-C(5)-C(7)	112.33(17)
C(6)-C(5)-C(7)	109.59(18)
N(4)-C(5)-H(51)	109.037
C(6)-C(5)-H(51)	108.574
C(7)-C(5)-H(51)	108.968
C(5)-C(6)-O(1)	117.51(17)
C(5)-C(6)-O(6)	124.9(2)
O(1)-C(6)-O(6)	117.5(2)

C(5)-C(7)-C(8)	115.27(17)
C(5)-C(7)-H(71)	107.897
C(8)-C(7)-H(71)	108.037
C(5)-C(7)-H(72)	107.972
C(8)-C(7)-H(72)	108.138
H(71)-C(7)-H(72)	109.433
C(7)-C(8)-C(9)	111.8(2)
C(7)-C(8)-C(10)	110.1(2)
C(9)-C(8)-C(10)	110.7(2)
C(7)-C(8)-H(81)	108.144
C(9)-C(8)-H(81)	108.006
C(10)-C(8)-H(81)	108.010
C(8)-C(9)-H(91)	109.461
C(8)-C(9)-H(92)	109.348
H(91)-C(9)-H(92)	109.241
C(8)-C(9)-H(93)	109.653
H(91)-C(9)-H(93)	109.532
H(92)-C(9)-H(93)	109.591
C(8)-C(10)-H(101)	109.397
C(8)-C(10)-H(102)	109.235
H(101)-C(10)-H(102)	109.170
C(8)-C(10)-H(103)	109.682
H(101)-C(10)-H(103)	109.695
H(102)-C(10)-H(103)	109.645
C(3)-C(11)-C(21)	111.91(16)
C(3)-C(11)-O(61)	105.25(16)
C(21)-C(11)-O(61)	109.07(17)
C(3)-C(11)-H(111)	109.979
C(21)-C(11)-H(111)	110.323
O(61)-C(11)-H(111)	110.180
C(11)-C(21)-O(12)	109.13(17)
C(11)-C(21)-C(31)	109.03(15)
O(12)-C(21)-C(31)	106.45(16)
C(11)-C(21)-H(211)	110.780
O(12)-C(21)-H(211)	110.668
C(31)-C(21)-H(211)	110.669
C(21)-O(12)-C(22)	117.90(16)
O(12)-C(22)-O(22)	123.8(2)
O(12)-C(22)-C(32)	110.81(19)
O(22)-C(22)-C(32)	125.38(19)
C(22)-C(32)-H(321)	109.182
C(22)-C(32)-H(322)	109.654
H(321)-C(32)-H(322)	109.439
C(22)-C(32)-H(323)	109.571
H(321)-C(32)-H(323)	109.265
H(322)-C(32)-H(323)	109.715
C(21)-C(31)-O(13)	108.87(15)
C(21)-C(31)-C(41)	110.62(16)
O(13)-C(31)-C(41)	107.80(18)
C(21)-C(31)-H(311)	109.916
O(13)-C(31)-H(311)	109.763
C(41)-C(31)-H(311)	109.838
C(31)-O(13)-C(23)	116.72(18)
O(13)-C(23)-O(23)	124.1(3)
O(13)-C(23)-C(43)	109.4(3)
O(23)-C(23)-C(43)	126.4(3)
C(23)-C(43)-H(431)	109.518
C(23)-C(43)-H(432)	109.525
H(431)-C(43)-H(432)	109.934
C(23)-C(43)-H(433)	109.189
H(431)-C(43)-H(433)	109.171
H(432)-C(43)-H(433)	109.488
C(31)-C(41)-O(14)	105.02(16)
C(31)-C(41)-C(51)	109.69(18)
O(14)-C(41)-C(51)	110.78(15)
C(31)-C(41)-H(411)	110.077
O(14)-C(41)-H(411)	110.482
C(51)-C(41)-H(411)	110.653

C(41)-O(14)-C(24)	116.35(18)
O(14)-C(24)-O(24)	122.81(19)
O(14)-C(24)-C(34)	111.1(2)
O(24)-C(24)-C(34)	126.1(2)
C(24)-C(34)-H(341)	109.795
C(24)-C(34)-H(342)	109.638
H(341)-C(34)-H(342)	109.635
C(24)-C(34)-H(343)	109.398
H(341)-C(34)-H(343)	109.278
H(342)-C(34)-H(343)	109.082
C(41)-C(51)-O(61)	109.08(14)
C(41)-C(51)-H(511)	109.536
O(61)-C(51)-H(511)	109.505
C(41)-C(51)-H(512)	109.682
O(61)-C(51)-H(512)	109.628
H(511)-C(51)-H(512)	109.393
C(51)-O(61)-C(11)	112.19(15)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for ias046. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
O(1)	43(1)	21(1)	75(1)	-5(1)	42(1)	-5(1)
N(2)	38(1)	22(1)	63(1)	-2(1)	37(1)	0(1)
C(3)	27(1)	22(1)	32(1)	1(1)	18(1)	1(1)
N(4)	31(1)	18(1)	51(1)	2(1)	30(1)	-1(1)
C(5)	24(1)	22(1)	36(1)	1(1)	19(1)	1(1)
C(6)	30(1)	23(1)	35(1)	5(1)	21(1)	0(1)
O(6)	29(1)	31(1)	42(1)	4(1)	19(1)	-5(1)
C(7)	26(1)	39(1)	33(1)	-3(1)	13(1)	1(1)
C(8)	39(1)	37(1)	36(1)	0(1)	24(1)	0(1)
C(9)	63(2)	39(2)	70(2)	0(1)	51(2)	4(1)
C(10)	79(2)	80(3)	41(1)	2(2)	34(2)	8(2)
C(11)	27(1)	24(1)	33(1)	0(1)	20(1)	3(1)
C(21)	31(1)	22(1)	31(1)	3(1)	19(1)	4(1)
O(12)	37(1)	24(1)	34(1)	4(1)	22(1)	7(1)
C(22)	30(1)	24(1)	30(1)	-1(1)	14(1)	-3(1)
O(22)	50(1)	31(1)	41(1)	2(1)	31(1)	5(1)
C(32)	57(2)	29(1)	35(1)	5(1)	24(1)	5(1)
C(31)	24(1)	28(1)	31(1)	-2(1)	15(1)	1(1)
O(13)	28(1)	40(1)	33(1)	-3(1)	14(1)	1(1)
C(23)	29(1)	64(2)	41(1)	2(1)	15(1)	5(1)
O(23)	40(1)	77(2)	64(1)	-2(1)	19(1)	24(1)
C(43)	36(1)	105(3)	56(2)	-17(2)	13(1)	-5(2)
C(41)	25(1)	27(1)	34(1)	-1(1)	20(1)	1(1)
O(14)	26(1)	31(1)	43(1)	-2(1)	23(1)	0(1)
C(24)	33(1)	35(1)	35(1)	-8(1)	22(1)	-7(1)
O(24)	41(1)	30(1)	48(1)	0(1)	29(1)	-1(1)
C(34)	45(1)	58(2)	67(2)	-7(2)	43(1)	-10(1)
C(51)	26(1)	28(1)	33(1)	1(1)	20(1)	1(1)
O(61)	24(1)	28(1)	35(1)	5(1)	20(1)	3(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for ias046.

	x	y	z	U(eq)
H(4)	9550(13)	-850(70)	3790(20)	43(9)
H(51)	10358	-708	3815	33
H(71)	9558	1951	2104	39
H(72)	9556	-1079	2177	39
H(81)	10519	1593	2463	45
H(91)	10800	-2265	2175	68
H(92)	10740	-2460	3080	68
H(93)	10240	-3583	2053	68
H(101)	10206	646	876	80
H(102)	9755	2470	914	80
H(103)	9617	-496	700	80
H(111)	8747	3469	3968	33
H(211)	8386	125	2373	33
H(321)	8043	6175	311	48
H(322)	8219	7608	1288	48
H(323)	7584	6406	613	48
H(311)	7677	2310	2943	33
H(431)	5980	408	392	77
H(432)	6437	-422	132	77
H(433)	6359	-2116	855	77
H(411)	8000	-2876	3154	35
H(341)	6859	-5406	4116	68
H(342)	6864	-2377	4197	68
H(343)	6545	-3705	3158	68
H(511)	8581	-2135	4812	35
H(512)	8399	798	4647	35

Appendix 4

(Z)-*N*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranosyl)-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (178)

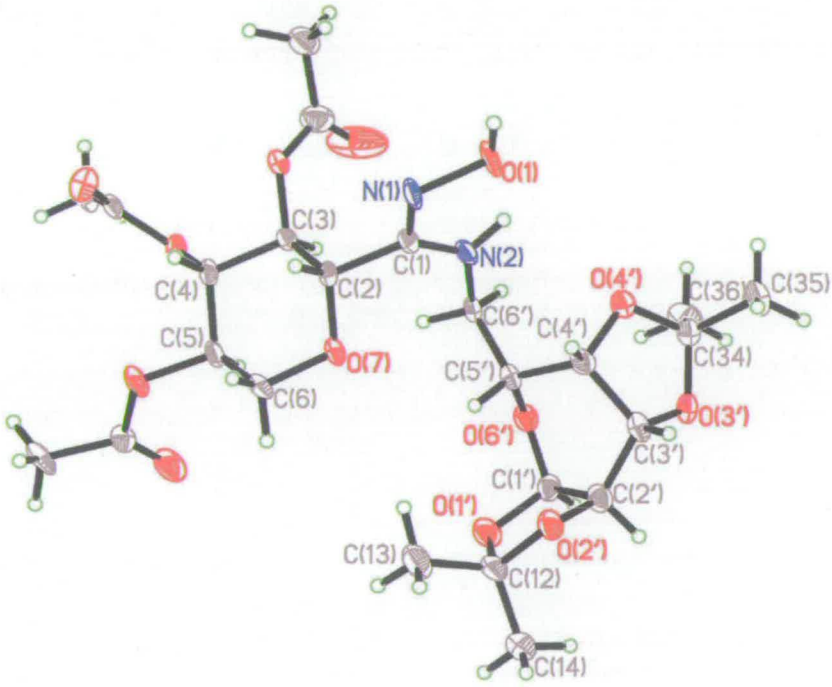


Table 1. Crystal data and structure refinement for mp0502.

Contact	Stephen Moggach, s.moggach@ed.ac.uk
A. CRYSTAL DATA	
Empirical formula	C52 H80 N4 O28 2(C24 H36 N2 O13), C4 H8 O2
Formula weight	1209.20
Wavelength	0.71073 A
Temperature	150(2) K
Crystal system	Triclinic
Space group	P 1
Unit cell dimensions	a = 7.3600(4) A alpha = 91.927(3) deg. b = 11.6820(6) A beta = 91.103(3) deg. c = 18.9910(10) A gamma = 108.254(3) deg.
Volume	1549.03(14) A^3
Number of reflections for cell	5822 (4 < theta < 59 deg.)
Z	1
Density (calculated)	1.296 Mg/m^3
Absorption coefficient	0.106 mm^-1
F(000)	644
B. DATA COLLECTION	
Crystal description	colourless block
Crystal size	0.54 x 0.35 x 0.15 mm
Theta range for data collection	1.07 to 23.26 deg.
Index ranges	-8<=h<=8, -12<=k<=12, -20<=l<=21
Reflections collected	15677
Independent reflections	8344 [R(int) = 0.0436]
Scan type	?
Absorption correction	Semi-empirical from equivalents (Tmin= 0.724652, Tmax=1.00)
C. SOLUTION AND REFINEMENT.	
Solution	direct (SHELXS-97 (Sheldrick, 1990))
Refinement type	Full-matrix least-squares on F^2
Program used for refinement	SHELXL-97
Hydrogen atom placement	geom

Appendix 4

Hydrogen atom treatment	mixed
Data / restraints / parameters	8344/3/773
Goodness-of-fit on F^2	1.124
Conventional R [F>4sigma(F)]	R1 = 0.0674 [7800 data]
Weighted R (F^2 and all data)	wR2 = 0.1756
Absolute structure parameter	2.4(12)
Final maximum delta/sigma	0.114

Weighting scheme
calc w=1/[\s^2^(Fo^2^)+(0.0935P)^2^+0.6247P] where P=(Fo^2^+2Fc^2^)/3

Largest diff. peak and hole 0.439 and -0.312 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for mp0502. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C1'1	-2119(8)	-533(5)	6078(3)	40(1)
O11	-899(6)	-2311(3)	2690(2)	53(1)
N11	-606(6)	-1035(4)	2640(2)	41(1)
C11	21(7)	-488(4)	3239(3)	32(1)
O1'1	-2469(5)	601(3)	6019(2)	49(1)
N21	398(6)	-1050(4)	3816(2)	39(1)
C2'1	-4032(8)	-1447(5)	5859(3)	43(1)
C21	487(7)	859(4)	3210(3)	32(1)
O2'1	-4979(5)	-782(3)	5457(2)	43(1)
O3'1	-3020(5)	-3171(3)	5839(2)	45(1)
C3'1	-3845(7)	-2504(5)	5412(3)	39(1)
C31	2662(7)	1512(4)	3200(3)	32(1)
O4'1	-1401(6)	-2940(3)	4817(2)	51(1)
C4'1	-2456(7)	-2104(5)	4813(3)	38(1)
O41	3436(5)	1088(3)	2599(2)	36(1)
C4A1	4619(8)	443(6)	2699(4)	56(2)
C41	2938(7)	2844(4)	3125(3)	34(1)
C5'1	-1130(7)	-818(4)	4931(3)	33(1)
O51	4967(4)	3505(3)	3206(2)	35(1)
C5B1	5851(7)	4085(4)	2629(3)	37(1)
C5A1	5227(9)	45(6)	2026(4)	57(2)
O5A1	5056(11)	214(8)	3279(3)	130(3)
C51	1935(8)	3305(5)	3704(3)	38(1)
C6'1	709(7)	-593(5)	4534(3)	35(1)
O6'1	-611(5)	-570(3)	5650(2)	38(1)
O61	2069(5)	4532(3)	3534(2)	43(1)
C6C1	2258(7)	5329(5)	4086(3)	38(1)
C6B1	7865(8)	4801(5)	2833(3)	51(2)
O6B1	5089(5)	4033(4)	2071(2)	51(1)
C61	-157(8)	2538(5)	3722(3)	42(1)
C7C1	2489(9)	6567(5)	3829(3)	54(2)
O7C1	2289(7)	5063(4)	4672(3)	67(1)
O71	-263(5)	1309(3)	3800(2)	39(1)
C121	-4376(8)	415(5)	5764(3)	45(1)
C131	-4318(10)	1292(6)	5189(4)	63(2)
C141	-5650(9)	514(6)	6351(4)	61(2)
C341	-1810(8)	-3641(5)	5431(3)	45(1)
C351	-2832(9)	-4936(5)	5184(4)	57(2)

C361	-44(10)	-3501(7)	5850(4)	65(2)
C12	-1292(7)	-2917(4)	10647(3)	32(1)
C1'2	-3596(8)	-2963(5)	7794(3)	45(1)
O1'2	-5081(6)	-4059(4)	7883(2)	53(1)
O12	-369(6)	-1108(3)	11204(2)	55(1)
N12	-1339(6)	-2383(4)	11245(2)	43(1)
N22	-404(6)	-2355(4)	10085(2)	41(1)
C2'2	-4511(8)	-2004(5)	7983(3)	46(1)
O2'2	-6041(5)	-2601(3)	8411(2)	43(1)
C22	-2172(7)	-4279(4)	10656(3)	35(1)
C3'2	-3207(8)	-920(5)	8402(3)	42(1)
O3'2	-1735(6)	-318(4)	7943(2)	52(1)
C32	-674(7)	-4926(4)	10674(3)	32(1)
O42	565(5)	-4524(3)	11282(2)	40(1)
C4A2	2414(8)	-3877(6)	11192(3)	54(2)
C4'2	-2157(8)	-1268(5)	9005(3)	41(1)
O4'2	-254(6)	-462(3)	8980(2)	52(1)
C42	-1710(7)	-6276(4)	10749(3)	37(1)
C5A2	3450(9)	-3476(6)	11865(4)	59(2)
O5A2	3026(7)	-3631(8)	10620(3)	136(3)
C5'2	-2176(7)	-2577(5)	8947(2)	35(1)
C52	-3258(8)	-6725(4)	10166(3)	39(1)
O52	-358(5)	-6938(3)	10664(2)	39(1)
C5B2	10(7)	-7511(4)	11233(3)	38(1)
C6'2	-557(7)	-2806(5)	9350(3)	37(1)
O6'2	-2002(5)	-2909(3)	8230(2)	42(1)
C62	-4528(7)	-5956(5)	10153(3)	41(1)
O62	-4319(5)	-7944(3)	10334(2)	46(1)
C6C2	-4859(8)	-8769(5)	9802(3)	46(1)
C6B2	1318(8)	-8212(5)	11037(3)	49(1)
O6B2	-652(6)	-7464(4)	11797(2)	53(1)
O72	-3421(5)	-4721(3)	10066(2)	37(1)
C7C2	-5859(9)	-9990(5)	10043(4)	56(2)
O7C2	-4547(8)	-8523(4)	9200(3)	81(2)
C122	-6722(8)	-3835(6)	8148(3)	52(2)
C132	-7466(9)	-4658(6)	8737(4)	59(2)
C142	-8162(10)	-3964(7)	7541(4)	70(2)
C342	-62(10)	198(6)	8349(3)	55(2)
C352	1623(10)	65(7)	7948(4)	69(2)
C362	229(12)	1516(6)	8571(4)	75(2)
O33	-6110(10)	-6610(5)	-2904(3)	88(2)
O53	-3086(10)	-5777(7)	-3122(4)	113(2)
C43	-4297(16)	-6278(8)	-2717(5)	90(3)
C13	-8798(15)	-6896(10)	-3754(7)	133(4)
C23	-6722(15)	-6377(8)	-3589(5)	95(3)
C53	-3810(20)	-6513(10)	-2022(6)	127(4)

Table 3. Bond lengths [A] and angles [deg] for mp0502.

C1'1-O6'1	1.399(6)
C1'1-O1'1	1.434(7)
C1'1-C2'1	1.517(8)
C1'1-H1'1	1.0000
O11-N11	1.445(5)
O11-H11	0.8400
N11-C11	1.288(6)
C11-N21	1.364(6)
C11-C21	1.505(7)
O1'1-C121	1.424(7)
N21-C6'1	1.436(7)
N21-H21	0.8800
C2'1-O2'1	1.424(6)
C2'1-C3'1	1.517(8)
C2'1-H2'1	1.0000
C21-O71	1.415(6)
C21-C31	1.544(6)

C21-H21	1.0000
O2'1-C121	1.428(7)
O3'1-C3'1	1.397(6)
O3'1-C341	1.414(7)
C3'1-C4'1	1.530(8)
C3'1-H3'1	1.0000
C31-O41	1.426(6)
C31-C41	1.517(7)
C31-H31	1.0000
O4'1-C4'1	1.425(6)
O4'1-C341	1.428(7)
C4'1-C5'1	1.520(7)
C4'1-H4'1	1.0000
O41-C4A1	1.333(7)
C4A1-O5A1	1.203(8)
C4A1-C5A1	1.471(9)
C41-O51	1.453(6)
C41-C51	1.511(7)
C41-H41	1.0000
C5'1-O6'1	1.405(6)
C5'1-C6'1	1.516(7)
C5'1-H5'1	1.0000
O51-C5B1	1.372(6)
C5B1-O6B1	1.180(6)
C5B1-C6B1	1.492(8)
C5A1-H5A11	0.9800
C5A1-H5A21	0.9800
C5A1-H5A31	0.9800
C51-O61	1.454(6)
C51-C61	1.521(8)
C51-H51	1.0000
C6'1-H6'11	0.9900
C6'1-H6'21	0.9900
O61-C6C1	1.353(6)
C6C1-O7C1	1.168(7)
C6C1-C7C1	1.501(8)
C6B1-H6B11	0.9800
C6B1-H6B21	0.9800
C6B1-H6B31	0.9800
C61-O71	1.426(6)
C61-H6A1	0.9900
C61-H6B1	0.9900
C7C1-H7C11	0.9800
C7C1-H7C21	0.9800
C7C1-H7C31	0.9800
C121-C141	1.496(8)
C121-C131	1.513(9)
C131-H13A1	0.9800
C131-H13B1	0.9800
C131-H13C1	0.9800
C141-H14A1	0.9800
C141-H14B1	0.9800
C141-H14C1	0.9800
C341-C361	1.473(9)
C341-C351	1.517(9)
C351-H35A1	0.9800
C351-H35B1	0.9800
C351-H35C1	0.9800
C361-H36A1	0.9800
C361-H36B1	0.9800
C361-H36C1	0.9800
C12-N12	1.283(7)
C12-N22	1.342(6)
C12-C22	1.519(7)
C1'2-O6'2	1.406(6)
C1'2-O1'2	1.418(7)
C1'2-C2'2	1.514(8)
C1'2-H1'2	1.0000

O1'2-C122	1.411(7)
O12-N12	1.442(5)
O12-H12	0.8400
N22-C6'2	1.465(7)
N22-H22	0.8800
C2'2-O2'2	1.414(7)
C2'2-C3'2	1.517(8)
C2'2-H2'2	1.0000
O2'2-C122	1.439(7)
C22-O72	1.412(6)
C22-C32	1.520(7)
C22-H22	1.0000
C3'2-O3'2	1.424(7)
C3'2-C4'2	1.505(8)
C3'2-H3'2	1.0000
O3'2-C342	1.393(8)
C32-O42	1.428(6)
C32-C42	1.535(7)
C32-H32	1.0000
O42-C4A2	1.351(7)
C4A2-O5A2	1.195(8)
C4A2-C5A2	1.459(9)
C4'2-O4'2	1.425(7)
C4'2-C5'2	1.526(7)
C4'2-H4'2	1.0000
O4'2-C342	1.433(7)
C42-O52	1.447(6)
C42-C52	1.529(7)
C42-H42	1.0000
C5A2-H5A12	0.9800
C5A2-H5A22	0.9800
C5A2-H5A32	0.9800
C5'2-O6'2	1.422(6)
C5'2-C6'2	1.501(7)
C5'2-H5'2	1.0000
C52-O62	1.443(6)
C52-C62	1.486(8)
C52-H52	1.0000
O52-C5B2	1.356(6)
C5B2-O6B2	1.192(6)
C5B2-C6B2	1.491(8)
C6'2-H6'12	0.9900
C6'2-H6'22	0.9900
C62-O72	1.434(6)
C62-H6A2	0.9900
C62-H6B2	0.9900
O62-C6C2	1.337(7)
C6C2-O7C2	1.196(7)
C6C2-C7C2	1.479(8)
C6B2-H6B12	0.9800
C6B2-H6B22	0.9800
C6B2-H6B32	0.9800
C7C2-H7C12	0.9800
C7C2-H7C22	0.9800
C7C2-H7C32	0.9800
C122-C132	1.497(9)
C122-C142	1.521(9)
C132-H13A2	0.9800
C132-H13B2	0.9800
C132-H13C2	0.9800
C142-H14A2	0.9800
C142-H14B2	0.9800
C142-H14C2	0.9800
C342-C352	1.513(9)
C342-C362	1.529(9)
C352-H35A2	0.9800
C352-H35B2	0.9800
C352-H35C2	0.9800

C362-H36A2	0.9800
C362-H36B2	0.9800
C362-H36C2	0.9800
O33-C43	1.306(11)
O33-C23	1.430(11)
O53-C43	1.206(10)
C43-C53	1.420(13)
C13-C23	1.479(14)
C13-H1A3	0.9800
C13-H1B3	0.9800
C13-H1C3	0.9800
C23-H2A3	0.9900
C23-H2B3	0.9900
C53-H5A3	0.9800
C53-H5B3	0.9800
C53-H5C3	0.9800

O6'1-C1'1-O1'1	109.9(4)
O6'1-C1'1-C2'1	114.1(4)
O1'1-C1'1-C2'1	103.2(4)
O6'1-C1'1-H1'1	109.8
O1'1-C1'1-H1'1	109.8
C2'1-C1'1-H1'1	109.8
N11-O11-H11	109.5
C11-N11-O11	109.7(4)
N11-C11-N21	123.9(4)
N11-C11-C21	112.4(4)
N21-C11-C21	123.4(4)
C121-O1'1-C1'1	110.3(4)
C11-N21-C6'1	128.0(4)
C11-N21-H21	116.0
C6'1-N21-H21	116.0
O2'1-C2'1-C3'1	109.8(4)
O2'1-C2'1-C1'1	104.4(4)
C3'1-C2'1-C1'1	113.3(5)
O2'1-C2'1-H2'1	109.8
C3'1-C2'1-H2'1	109.8
C1'1-C2'1-H2'1	109.8
O71-C21-C11	109.9(4)
O71-C21-C31	108.7(4)
C11-C21-C31	112.3(4)
O71-C21-H21	108.6
C11-C21-H21	108.6
C31-C21-H21	108.6
C2'1-O2'1-C121	106.1(4)
C3'1-O3'1-C341	109.2(4)
O3'1-C3'1-C2'1	107.8(4)
O3'1-C3'1-C4'1	104.9(4)
C2'1-C3'1-C4'1	112.5(4)
O3'1-C3'1-H3'1	110.5
C2'1-C3'1-H3'1	110.5
C4'1-C3'1-H3'1	110.5
O41-C31-C41	108.2(4)
O41-C31-C21	109.4(4)
C41-C31-C21	107.3(4)
O41-C31-H31	110.6
C41-C31-H31	110.6
C21-C31-H31	110.6
C4'1-O4'1-C341	110.2(4)
O4'1-C4'1-C5'1	110.9(4)
O4'1-C4'1-C3'1	103.4(4)
C5'1-C4'1-C3'1	112.5(4)
O4'1-C4'1-H4'1	109.9
C5'1-C4'1-H4'1	109.9
C3'1-C4'1-H4'1	109.9
C4A1-O41-C31	118.7(4)
O5A1-C4A1-O41	122.0(6)
O5A1-C4A1-C5A1	126.4(6)

O41-C4A1-C5A1	111.6(5)
O51-C41-C51	107.3(4)
O51-C41-C31	108.7(4)
C51-C41-C31	110.3(4)
O51-C41-H41	110.2
C51-C41-H41	110.2
C31-C41-H41	110.2
O6'1-C5'1-C6'1	107.0(4)
O6'1-C5'1-C4'1	110.4(4)
C6'1-C5'1-C4'1	112.3(4)
O6'1-C5'1-H5'1	109.0
C6'1-C5'1-H5'1	109.0
C4'1-C5'1-H5'1	109.0
C5B1-O51-C41	117.1(4)
O6B1-C5B1-O51	124.1(5)
O6B1-C5B1-C6B1	126.7(5)
O51-C5B1-C6B1	109.1(5)
C4A1-C5A1-H5A11	109.5
C4A1-C5A1-H5A21	109.5
H5A11-C5A1-H5A21	109.5
C4A1-C5A1-H5A31	109.5
H5A11-C5A1-H5A31	109.5
H5A21-C5A1-H5A31	109.5
O61-C51-C41	106.0(4)
O61-C51-C61	109.8(4)
C41-C51-C61	110.6(4)
O61-C51-H51	110.1
C41-C51-H51	110.1
C61-C51-H51	110.1
N21-C6'1-C5'1	113.1(4)
N21-C6'1-H6'11	109.0
C5'1-C6'1-H6'11	109.0
N21-C6'1-H6'21	109.0
C5'1-C6'1-H6'21	109.0
H6'11-C6'1-H6'21	107.8
C1'1-O6'1-C5'1	114.3(4)
C6C1-O61-C51	116.5(4)
O7C1-C6C1-O61	122.9(5)
O7C1-C6C1-C7C1	126.6(5)
O61-C6C1-C7C1	110.4(5)
C5B1-C6B1-H6B11	109.5
C5B1-C6B1-H6B21	109.5
H6B11-C6B1-H6B21	109.5
C5B1-C6B1-H6B31	109.5
H6B11-C6B1-H6B31	109.5
H6B21-C6B1-H6B31	109.5
O71-C61-C51	109.1(4)
O71-C61-H6A1	109.9
C51-C61-H6A1	109.9
O71-C61-H6B1	109.9
C51-C61-H6B1	109.9
H6A1-C61-H6B1	108.3
C6C1-C7C1-H7C11	109.5
C6C1-C7C1-H7C21	109.5
H7C11-C7C1-H7C21	109.5
C6C1-C7C1-H7C31	109.5
H7C11-C7C1-H7C31	109.5
H7C21-C7C1-H7C31	109.5
C21-O71-C61	111.1(4)
O2'1-C121-O1'1	104.7(4)
O2'1-C121-C141	110.2(5)
O1'1-C121-C141	111.2(5)
O2'1-C121-C131	108.8(5)
O1'1-C121-C131	108.4(5)
C141-C121-C131	113.3(5)
C121-C131-H13A1	109.5
C121-C131-H13B1	109.5
H13A1-C131-H13B1	109.5

C121-C131-H13C1	109.5
H13A1-C131-H13C1	109.5
H13B1-C131-H13C1	109.5
C121-C141-H14A1	109.5
C121-C141-H14B1	109.5
H14A1-C141-H14B1	109.5
C121-C141-H14C1	109.5
H14A1-C141-H14C1	109.5
H14B1-C141-H14C1	109.5
O3'1-C341-O4'1	106.4(4)
O3'1-C341-C361	108.3(5)
O4'1-C341-C361	110.7(5)
O3'1-C341-C351	110.9(5)
O4'1-C341-C351	107.3(5)
C361-C341-C351	113.1(5)
C341-C351-H35A1	109.5
C341-C351-H35B1	109.5
H35A1-C351-H35B1	109.5
C341-C351-H35C1	109.5
H35A1-C351-H35C1	109.5
H35B1-C351-H35C1	109.5
C341-C361-H36A1	109.5
C341-C361-H36B1	109.5
H36A1-C361-H36B1	109.5
C341-C361-H36C1	109.5
H36A1-C361-H36C1	109.5
H36B1-C361-H36C1	109.5
N12-C12-N22	124.0(4)
N12-C12-C22	113.1(4)
N22-C12-C22	122.6(5)
O6'2-C1'2-O1'2	110.0(4)
O6'2-C1'2-C2'2	113.6(4)
O1'2-C1'2-C2'2	103.6(5)
O6'2-C1'2-H1'2	109.8
O1'2-C1'2-H1'2	109.8
C2'2-C1'2-H1'2	109.8
C122-O1'2-C1'2	110.8(4)
N12-O12-H12	109.5
C12-N12-O12	109.6(4)
C12-N22-C6'2	128.7(4)
C12-N22-H22	115.7
C6'2-N22-H22	115.7
O2'2-C2'2-C3'2	108.3(4)
O2'2-C2'2-C1'2	103.9(5)
C3'2-C2'2-C1'2	114.3(4)
O2'2-C2'2-H2'2	110.1
C3'2-C2'2-H2'2	110.1
C1'2-C2'2-H2'2	110.1
C2'2-O2'2-C122	106.2(4)
O72-C22-C12	110.8(4)
O72-C22-C32	109.1(4)
C12-C22-C32	112.6(4)
O72-C22-H22	108.1
C12-C22-H22	108.1
C32-C22-H22	108.1
O3'2-C3'2-C4'2	104.3(4)
O3'2-C3'2-C2'2	106.5(4)
C4'2-C3'2-C2'2	112.8(5)
O3'2-C3'2-H3'2	111.0
C4'2-C3'2-H3'2	111.0
C2'2-C3'2-H3'2	111.0
C342-O3'2-C3'2	108.1(4)
O42-C32-C22	110.1(4)
O42-C32-C42	106.8(4)
C22-C32-C42	108.1(4)
O42-C32-H32	110.6
C22-C32-H32	110.6
C42-C32-H32	110.6

C4A2-O42-C32	118.8(4)
O5A2-C4A2-O42	121.6(6)
O5A2-C4A2-C5A2	126.4(6)
O42-C4A2-C5A2	111.9(5)
O4'2-C4'2-C3'2	104.3(4)
O4'2-C4'2-C5'2	110.9(4)
C3'2-C4'2-C5'2	113.4(4)
O4'2-C4'2-H4'2	109.4
C3'2-C4'2-H4'2	109.4
C5'2-C4'2-H4'2	109.4
C4'2-O4'2-C342	109.2(4)
O52-C42-C52	107.8(4)
O52-C42-C32	109.3(4)
C52-C42-C32	109.4(4)
O52-C42-H42	110.1
C52-C42-H42	110.1
C32-C42-H42	110.1
C4A2-C5A2-H5A12	109.5
C4A2-C5A2-H5A22	109.5
H5A12-C5A2-H5A22	109.5
C4A2-C5A2-H5A32	109.5
H5A12-C5A2-H5A32	109.5
H5A22-C5A2-H5A32	109.5
O6'2-C5'2-C6'2	106.4(4)
O6'2-C5'2-C4'2	109.6(4)
C6'2-C5'2-C4'2	113.6(4)
O6'2-C5'2-H5'2	109.0
C6'2-C5'2-H5'2	109.0
C4'2-C5'2-H5'2	109.0
O62-C52-C62	110.8(4)
O62-C52-C42	105.5(4)
C62-C52-C42	110.6(4)
O62-C52-H52	109.9
C62-C52-H52	109.9
C42-C52-H52	109.9
C5B2-O52-C42	117.0(4)
O6B2-C5B2-O52	124.2(5)
O6B2-C5B2-C6B2	126.1(5)
O52-C5B2-C6B2	109.7(5)
N22-C6'2-C5'2	112.4(4)
N22-C6'2-H6'12	109.1
C5'2-C6'2-H6'12	109.1
N22-C6'2-H6'22	109.1
C5'2-C6'2-H6'22	109.1
H6'12-C6'2-H6'22	107.8
C1'2-O6'2-C5'2	114.2(4)
O72-C62-C52	110.2(4)
O72-C62-H6A2	109.6
C52-C62-H6A2	109.6
O72-C62-H6B2	109.6
C52-C62-H6B2	109.6
H6A2-C62-H6B2	108.1
C6C2-O62-C52	117.7(4)
O7C2-C6C2-O62	122.5(5)
O7C2-C6C2-C7C2	124.9(5)
O62-C6C2-C7C2	112.6(5)
C5B2-C6B2-H6B12	109.5
C5B2-C6B2-H6B22	109.5
H6B12-C6B2-H6B22	109.5
C5B2-C6B2-H6B32	109.5
H6B12-C6B2-H6B32	109.5
H6B22-C6B2-H6B32	109.5
C22-O72-C62	110.1(3)
C6C2-C7C2-H7C12	109.5
C6C2-C7C2-H7C22	109.5
H7C12-C7C2-H7C22	109.5
C6C2-C7C2-H7C32	109.5
H7C12-C7C2-H7C32	109.5

H7C22-C7C2-H7C32	109.5
O1'2-C122-O2'2	104.4(4)
O1'2-C122-C132	109.1(5)
O2'2-C122-C132	110.2(5)
O1'2-C122-C142	108.7(5)
O2'2-C122-C142	109.8(5)
C132-C122-C142	114.1(5)
C122-C132-H13A2	109.5
C122-C132-H13B2	109.5
H13A2-C132-H13B2	109.5
C122-C132-H13C2	109.5
H13A2-C132-H13C2	109.5
H13B2-C132-H13C2	109.5
C122-C142-H14A2	109.5
C122-C142-H14B2	109.5
H14A2-C142-H14B2	109.5
C122-C142-H14C2	109.5
H14A2-C142-H14C2	109.5
H14B2-C142-H14C2	109.5
O3'2-C342-O4'2	106.8(5)
O3'2-C342-C352	109.2(5)
O4'2-C342-C352	109.4(5)
O3'2-C342-C362	112.7(5)
O4'2-C342-C362	107.1(5)
C352-C342-C362	111.5(6)
C342-C352-H35A2	109.5
C342-C352-H35B2	109.5
H35A2-C352-H35B2	109.5
C342-C352-H35C2	109.5
H35A2-C352-H35C2	109.5
H35B2-C352-H35C2	109.5
C342-C362-H36A2	109.5
C342-C362-H36B2	109.5
H36A2-C362-H36B2	109.5
C342-C362-H36C2	109.5
H36A2-C362-H36C2	109.5
H36B2-C362-H36C2	109.5
C43-O33-C23	121.2(8)
O53-C43-O33	120.8(10)
O53-C43-C53	121.4(11)
O33-C43-C53	117.7(9)
C23-C13-H1A3	109.5
C23-C13-H1B3	109.5
H1A3-C13-H1B3	109.5
C23-C13-H1C3	109.5
H1A3-C13-H1C3	109.5
H1B3-C13-H1C3	109.5
O33-C23-C13	115.5(9)
O33-C23-H2A3	108.4
C13-C23-H2A3	108.4
O33-C23-H2B3	108.4
C13-C23-H2B3	108.4
H2A3-C23-H2B3	107.5
C43-C53-H5A3	109.5
C43-C53-H5B3	109.5
H5A3-C53-H5B3	109.5
C43-C53-H5C3	109.5
H5A3-C53-H5C3	109.5
H5B3-C53-H5C3	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for mp0502.
The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C1'1	49(3)	30(3)	34(3)	0(2)	2(2)	5(2)
O11	92(3)	9(2)	51(2)	-1(2)	-4(2)	7(2)
N11	59(3)	13(2)	49(3)	7(2)	2(2)	8(2)
C11	38(3)	18(3)	36(3)	-1(2)	2(2)	6(2)
O1'1	51(2)	32(2)	61(2)	-9(2)	0(2)	9(2)
N21	64(3)	25(2)	34(2)	3(2)	3(2)	23(2)
C2'1	58(3)	37(3)	35(3)	4(2)	1(2)	18(3)
C21	36(3)	16(3)	38(3)	5(2)	5(2)	1(2)
O2'1	42(2)	28(2)	54(2)	0(2)	2(2)	5(2)
O3'1	58(2)	30(2)	47(2)	15(2)	12(2)	9(2)
C3'1	45(3)	24(3)	45(3)	0(2)	-5(2)	6(2)
C31	43(3)	21(3)	32(3)	1(2)	4(2)	10(2)
O4'1	74(3)	33(2)	50(2)	10(2)	20(2)	21(2)
C4'1	49(3)	32(3)	31(3)	-4(2)	-3(2)	13(2)
O41	47(2)	21(2)	42(2)	5(2)	8(2)	11(2)
C4A1	49(3)	61(4)	64(4)	-2(3)	9(3)	25(3)
C41	40(3)	17(3)	40(3)	7(2)	3(2)	2(2)
C5'1	42(3)	21(3)	36(3)	3(2)	-6(2)	11(2)
O51	37(2)	23(2)	42(2)	8(2)	1(2)	3(1)
C5B1	43(3)	18(3)	52(3)	1(2)	5(3)	11(2)
C5A1	53(3)	40(4)	75(4)	-5(3)	14(3)	11(3)
O5A1	175(7)	223(9)	63(4)	-5(4)	-11(4)	169(7)
C51	57(3)	20(3)	39(3)	8(2)	3(2)	15(2)
C6'1	44(3)	22(3)	40(3)	8(2)	4(2)	10(2)
O6'1	44(2)	28(2)	39(2)	-3(2)	-3(2)	8(2)
O61	62(2)	14(2)	49(2)	-4(2)	-7(2)	10(2)
C6C1	40(3)	26(3)	42(3)	-8(2)	-5(2)	2(2)
C6B1	45(3)	20(3)	82(4)	16(3)	5(3)	0(2)
O6B1	51(2)	49(3)	46(2)	13(2)	1(2)	6(2)
C61	53(3)	22(3)	55(3)	0(2)	8(3)	17(2)
C7C1	67(4)	20(3)	75(4)	-13(3)	-18(3)	19(3)
O7C1	107(4)	40(3)	57(3)	-15(2)	-5(2)	29(2)
O71	46(2)	15(2)	53(2)	5(2)	10(2)	7(2)
C121	47(3)	27(3)	61(4)	-3(3)	10(3)	12(2)
C131	63(4)	35(4)	91(5)	2(3)	4(3)	17(3)
C141	64(4)	44(4)	79(4)	2(3)	18(3)	22(3)
C341	57(3)	33(3)	46(3)	7(2)	10(3)	13(3)
C351	67(4)	32(3)	70(4)	10(3)	-2(3)	13(3)
C361	77(4)	62(5)	60(4)	-9(3)	-6(3)	29(4)
C12	34(2)	17(3)	41(3)	7(2)	-3(2)	5(2)
C1'2	58(3)	48(4)	31(3)	-7(2)	-9(2)	22(3)
O1'2	53(2)	38(2)	67(3)	-14(2)	-6(2)	13(2)
O12	91(3)	7(2)	53(2)	0(2)	1(2)	-3(2)
N12	60(3)	12(2)	51(3)	5(2)	2(2)	1(2)
N22	46(2)	23(2)	42(3)	3(2)	0(2)	-7(2)
C2'2	52(3)	47(4)	44(3)	0(3)	-2(3)	22(3)
O2'2	50(2)	33(2)	48(2)	1(2)	6(2)	15(2)
C22	49(3)	19(3)	34(3)	4(2)	-1(2)	7(2)
C3'2	52(3)	36(3)	43(3)	4(2)	8(2)	23(3)
O3'2	67(3)	44(3)	46(2)	10(2)	1(2)	16(2)
C32	41(3)	19(3)	32(3)	2(2)	3(2)	5(2)
O42	49(2)	24(2)	42(2)	6(2)	-3(2)	6(2)
C4A2	35(3)	63(4)	59(4)	2(3)	16(3)	9(3)
C4'2	55(3)	25(3)	42(3)	-1(2)	15(2)	11(2)
O4'2	63(2)	31(2)	55(2)	6(2)	-7(2)	6(2)
C42	44(3)	16(3)	52(3)	2(2)	8(2)	10(2)
C5A2	57(4)	45(4)	72(4)	-9(3)	-16(3)	14(3)
O5A2	45(3)	235(9)	71(4)	-28(4)	19(3)	-36(4)
C5'2	44(3)	29(3)	30(3)	2(2)	7(2)	8(2)
C52	54(3)	14(3)	44(3)	1(2)	2(2)	4(2)
O52	48(2)	21(2)	48(2)	5(2)	5(2)	11(2)
C5B2	39(3)	17(3)	52(3)	4(2)	-4(3)	2(2)

C6'2	47(3)	24(3)	38(3)	4(2)	4(2)	6(2)
O6'2	52(2)	36(2)	38(2)	-3(2)	6(2)	15(2)
C62	37(3)	27(3)	48(3)	3(2)	-6(2)	-4(2)
O62	57(2)	18(2)	52(2)	-4(2)	13(2)	-4(2)
C6C2	54(3)	28(3)	51(4)	-8(3)	5(3)	8(3)
C6B2	49(3)	31(3)	68(4)	11(3)	11(3)	11(3)
O6B2	65(3)	54(3)	50(3)	14(2)	12(2)	31(2)
O72	40(2)	18(2)	47(2)	2(2)	-9(2)	1(1)
C7C2	57(3)	24(3)	75(4)	-8(3)	22(3)	-4(2)
O7C2	119(4)	37(3)	57(3)	-13(2)	4(3)	-18(3)
C122	48(3)	45(4)	65(4)	-11(3)	-2(3)	17(3)
C132	56(4)	43(4)	76(4)	-2(3)	5(3)	14(3)
C142	68(4)	68(5)	72(5)	-17(4)	-16(3)	20(4)
C342	78(4)	37(4)	56(4)	13(3)	12(3)	26(3)
C352	75(4)	53(4)	73(5)	-5(3)	11(4)	12(3)
C362	98(5)	26(4)	100(6)	14(3)	12(4)	13(3)
O33	101(4)	43(3)	109(5)	-1(3)	-2(3)	7(3)
O53	95(4)	121(6)	119(5)	24(4)	17(4)	25(4)
C43	109(7)	55(5)	113(7)	14(5)	38(6)	35(5)
C13	106(8)	75(7)	194(12)	-38(7)	-13(8)	1(6)
C23	119(7)	53(5)	103(7)	-14(4)	0(5)	15(5)
C53	197(13)	98(8)	114(8)	30(6)	27(8)	82(9)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for mp0502.

	x	y	z	U(eq)
H1'1	-1793	-643	6579	47
H11	-1224	-2657	2291	79
H21	458	-1785	3738	46
H2'1	-4777	-1749	6286	51
H21	-124	1045	2772	38
H3'1	-5128	-3018	5222	47
H31	3308	1379	3644	39
H4'1	-3185	-2187	4355	45
H41	2436	2982	2653	41
H5'1	-1808	-248	4772	39
H5A11	6185	-360	2117	86
H5A21	5783	746	1741	86
H5A31	4117	-518	1771	86
H51	2590	3302	4170	45
H6'11	1382	286	4541	42
H6'21	1549	-978	4781	42
H6B11	8742	4562	2522	77
H6B21	8138	4650	3322	77
H6B31	8037	5662	2788	77
H6A1	-778	2816	4122	50
H6B1	-835	2616	3280	50
H7C11	2334	7090	4222	80
H7C21	1517	6516	3459	80
H7C31	3767	6903	3639	80
H13A1	-3768	2120	5383	94
H13B1	-5620	1173	5005	94
H13C1	-3527	1150	4807	94
H14A1	-5675	-98	6694	92
H14B1	-6949	387	6161	92
H14C1	-5161	1319	6583	92
H35A1	-3956	-4968	4889	85
H35B1	-3240	-5430	5594	85
H35C1	-1961	-5247	4910	85
H36A1	807	-3833	5577	97
H36B1	-364	-3935	6286	97
H36C1	602	-2644	5965	97

H1'2	-3220	-2904	7290	54
H12	-173	-786	11612	82
H22	373	-1617	10169	49
H2'2	-5017	-1737	7546	55
H22	-2938	-4474	11091	42
H3'2	-3930	-373	8571	50
H32	78	-4790	10234	38
H4'2	-2731	-1123	9459	49
H42	-2297	-6417	11222	45
H5A12	4824	-3148	11783	89
H5A22	3217	-4162	12172	89
H5A32	3005	-2850	12090	89
H5'2	-3417	-3108	9122	42
H52	-2653	-6724	9699	47
H6'12	-751	-3684	9338	45
H6'22	658	-2410	9116	45
H6A2	-5485	-6236	9760	49
H6B2	-5221	-6024	10599	49
H6B12	2612	-7656	10982	74
H6B22	861	-8669	10591	74
H6B32	1340	-8770	11408	74
H7C12	-6370	-10539	9634	84
H7C22	-6914	-9958	10343	84
H7C32	-4958	-10282	10314	84
H13A2	-7630	-5492	8579	88
H13B2	-8701	-4588	8879	88
H13C2	-6553	-4431	9140	88
H14A2	-7504	-3541	7136	105
H14B2	-9149	-3613	7688	105
H14C2	-8759	-4820	7409	105
H35A2	1517	-791	7896	104
H35B2	2815	503	8208	104
H35C2	1627	398	7481	104
H36A2	333	1994	8151	113
H36B2	1404	1830	8864	113
H36C2	-866	1568	8842	113
H1A3	-9076	-6684	-4230	199
H1B3	-9512	-6572	-3413	199
H1C3	-9181	-7775	-3730	199
H2A3	-6023	-6697	-3945	114
H2B3	-6351	-5492	-3635	114
H5A3	-4977	-6925	-1776	190
H5B3	-3131	-5749	-1768	190
H5C3	-2981	-7026	-2042	190

Appendix 5

S-2-Aminophenyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosylformothiohydroximate (216)

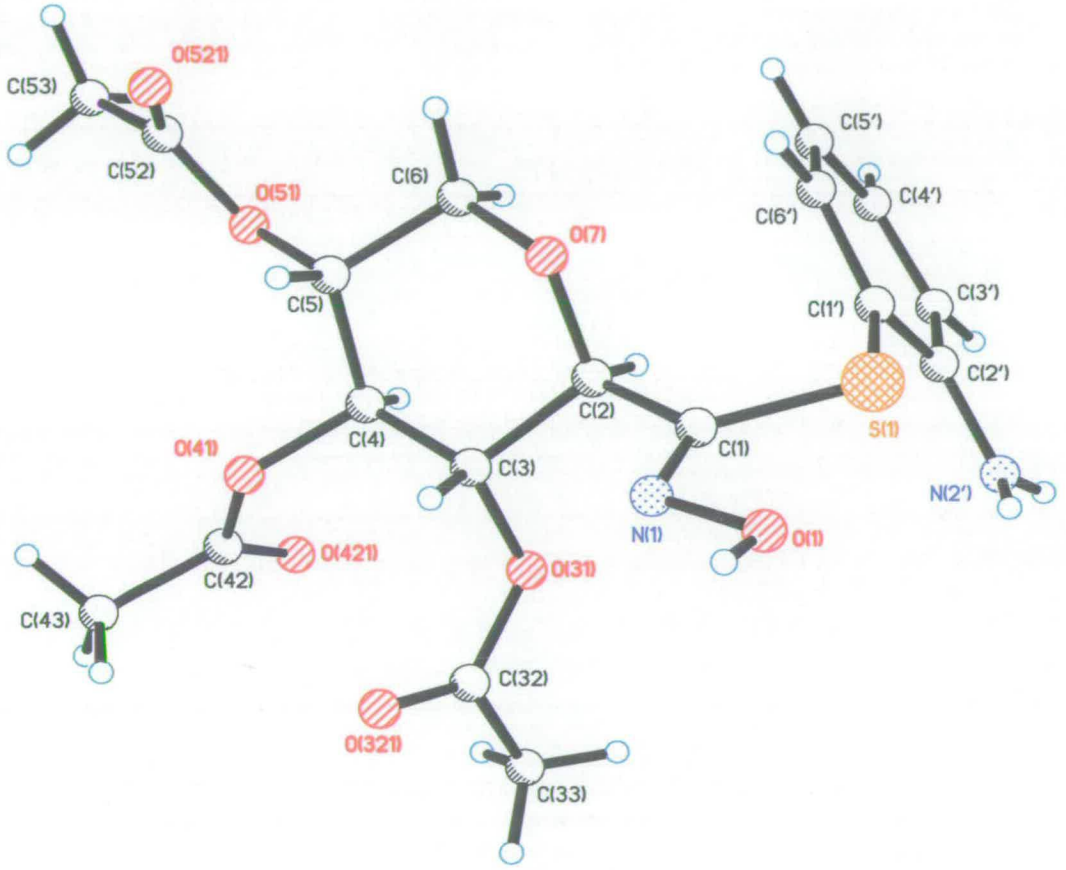


Table 1. Crystal data and structure refinement for ias021.

Contact Iain.Oswald@ed.ac.uk

A. CRYSTAL DATA

Empirical formula C18 H22 N2 O8 S
C18 H22 N2 O8 S

Formula weight 426.44

Wavelength 0.71073 A

Temperature 150(2) K

Crystal system Orthorhombic

Space group P2(1)2(1)2(1)

Unit cell dimensions a = 9.1358(5) A alpha = 90 deg.
b = 13.3082(7) A beta = 90 deg.
c = 17.5321(9) A gamma = 90 deg.

Volume 2131.6(2) A^3

Number of reflections for cell 9029 (2 < theta < 29 deg.)

Z 4

Density (calculated) 1.329 Mg/m^3

Absorption coefficient 0.197 mm^-1

F(000) 896

B. DATA COLLECTION

Crystal description COLOURLESS BLOCK

Crystal size 0.46 x 0.40 x 0.31 mm

Theta range for data collection 1.92 to 28.72 deg.

Index ranges -11<=h<=12, -17<=k<=17, -23<=l<=23

Reflections collected 19133

Independent reflections 5175 [R(int) = 0.0256]

Scan type \f &\w scans

Absorption correction Semi-empirical from equivalents (Tmin= 0.921, Tmax=1.000)

C. SOLUTION AND REFINEMENT.

Solution direct (SHELXS-97 (Sheldrick, 1990))

Refinement type Full-matrix least-squares on F^2

Program used for refinement SHELXL-97

Hydrogen atom placement geom

Hydrogen atom treatment mixed

Data / restraints / parameters 5175/0/278

Goodness-of-fit on F^2 1.094

Conventional R [F>4sigma(F)] R1 = 0.0380 [4960 data]

Weighted R (F^2 and all data) wR2 = 0.0964

Absolute structure parameter 0.04(7)

Final maximum delta/sigma 0.007

Weighting scheme
calc w=1/[\s^2^(Fo^2^)+(0.0490P)^2^+0.4805P] where P=(Fo^2^+2Fc^2^)/3

Largest diff. peak and hole 0.364 and -0.216 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for IAS021. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	7573(2)	5714(1)	8513(1)	23(1)
N(1)	7086(2)	6436(1)	8915(1)	30(1)
O(1)	6418(2)	7169(1)	8462(1)	38(1)
C(2)	8191(2)	4821(1)	8936(1)	21(1)
C(3)	8945(2)	5117(1)	9685(1)	22(1)
O(31)	10308(1)	5593(1)	9450(1)	27(1)
C(32)	10870(2)	6307(1)	9907(1)	33(1)
O(321)	10241(2)	6613(1)	10465(1)	44(1)
C(33)	12346(3)	6642(2)	9644(1)	47(1)
C(4)	9307(2)	4187(1)	10154(1)	22(1)
O(41)	9688(1)	4483(1)	10924(1)	27(1)
C(42)	11118(2)	4517(1)	11108(1)	29(1)
O(421)	12091(1)	4322(1)	10675(1)	36(1)
C(43)	11298(2)	4858(2)	11918(1)	49(1)
C(5)	7985(2)	3504(1)	10227(1)	25(1)
O(51)	8516(1)	2601(1)	10590(1)	31(1)
C(52)	7518(2)	2062(2)	10983(1)	34(1)
O(521)	6246(2)	2288(1)	11020(1)	37(1)
C(53)	8201(3)	1173(2)	11352(2)	71(1)
C(6)	7391(2)	3265(1)	9438(1)	27(1)
O(7)	6963(1)	4191(1)	9089(1)	25(1)
S(1)	7307(1)	5710(1)	7514(1)	28(1)
C(1')	8224(2)	4605(1)	7213(1)	26(1)
C(2')	9501(2)	4709(2)	6779(1)	32(1)
N(2')	10061(2)	5627(2)	6584(1)	47(1)
C(3')	10234(2)	3818(2)	6565(1)	44(1)
C(4')	9719(3)	2892(2)	6781(1)	51(1)
C(5')	8431(3)	2800(2)	7187(1)	47(1)
C(6')	7668(2)	3655(2)	7387(1)	36(1)

Table 3. Bond lengths [A] and angles [deg] for IAS021.

C(1)-N(1)	1.272(2)
C(1)-C(2)	1.511(2)
C(1)-S(1)	1.7673(16)
N(1)-O(1)	1.399(2)
C(2)-O(7)	1.425(2)
C(2)-C(3)	1.534(2)
C(3)-O(31)	1.4564(19)
C(3)-C(4)	1.523(2)

O(31)-C(32) 1.345(2)
C(32)-O(321) 1.206(3)
C(32)-C(33) 1.493(3)
C(4)-O(41) 1.4477(19)
C(4)-C(5) 1.517(2)
O(41)-C(42) 1.346(2)
C(42)-O(421) 1.197(2)
C(42)-C(43) 1.501(3)
C(5)-O(51) 1.443(2)
C(5)-C(6) 1.520(2)
O(51)-C(52) 1.349(2)
C(52)-O(521) 1.202(2)
C(52)-C(53) 1.486(3)
C(6)-O(7) 1.430(2)
S(1)-C(1') 1.7725(17)
C(1')-C(6') 1.396(3)
C(1')-C(2') 1.401(3)
C(2')-N(2') 1.367(3)
C(2')-C(3') 1.412(3)
C(3')-C(4') 1.373(4)
C(4')-C(5') 1.381(4)
C(5')-C(6') 1.380(3)

N(1)-C(1)-C(2) 116.88(14)
N(1)-C(1)-S(1) 120.26(13)
C(2)-C(1)-S(1) 122.37(12)
C(1)-N(1)-O(1) 111.34(14)
O(7)-C(2)-C(1) 105.10(13)
O(7)-C(2)-C(3) 110.06(13)
C(1)-C(2)-C(3) 112.71(13)
O(31)-C(3)-C(4) 108.68(13)
O(31)-C(3)-C(2) 104.68(12)
C(4)-C(3)-C(2) 110.58(13)
C(32)-O(31)-C(3) 117.73(14)
O(321)-C(32)-O(31) 122.72(18)
O(321)-C(32)-C(33) 125.44(19)
O(31)-C(32)-C(33) 111.83(18)
O(41)-C(4)-C(5) 106.06(13)
O(41)-C(4)-C(3) 109.55(13)
C(5)-C(4)-C(3) 111.03(13)
C(42)-O(41)-C(4) 117.76(13)
O(421)-C(42)-O(41) 124.19(17)
O(421)-C(42)-C(43) 125.69(17)
O(41)-C(42)-C(43) 110.10(16)
O(51)-C(5)-C(4) 105.56(13)
O(51)-C(5)-C(6) 110.32(14)
C(4)-C(5)-C(6) 109.49(13)
C(52)-O(51)-C(5) 116.18(15)
O(521)-C(52)-O(51) 123.22(18)
O(521)-C(52)-C(53) 125.5(2)
O(51)-C(52)-C(53) 111.23(19)
O(7)-C(6)-C(5) 107.83(13)
C(2)-O(7)-C(6) 111.85(12)
C(1)-S(1)-C(1') 103.46(8)
C(6')-C(1')-C(2') 120.75(17)
C(6')-C(1')-S(1) 120.95(14)
C(2')-C(1')-S(1) 118.28(14)
N(2')-C(2')-C(1') 122.36(18)
N(2')-C(2')-C(3') 120.43(19)
C(1')-C(2')-C(3') 117.17(18)
C(4')-C(3')-C(2') 121.2(2)
C(3')-C(4')-C(5') 121.0(2)
C(6')-C(5')-C(4') 119.2(2)
C(5')-C(6')-C(1') 120.5(2)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for IAS021.
The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	22(1)	24(1)	22(1)	0(1)	2(1)	-2(1)
N(1)	37(1)	25(1)	29(1)	-2(1)	3(1)	6(1)
O(1)	52(1)	29(1)	33(1)	0(1)	7(1)	19(1)
C(2)	22(1)	20(1)	22(1)	-3(1)	0(1)	-1(1)
C(3)	21(1)	23(1)	23(1)	-4(1)	-1(1)	-4(1)
O(31)	26(1)	28(1)	28(1)	0(1)	-2(1)	-9(1)
C(32)	35(1)	26(1)	37(1)	4(1)	-10(1)	-11(1)
O(321)	51(1)	38(1)	44(1)	-14(1)	-5(1)	-14(1)
C(33)	42(1)	50(1)	48(1)	10(1)	-10(1)	-24(1)
C(4)	21(1)	25(1)	21(1)	-2(1)	-3(1)	-2(1)
O(41)	24(1)	36(1)	21(1)	-3(1)	-2(1)	-3(1)
C(42)	27(1)	32(1)	27(1)	-1(1)	-6(1)	-2(1)
O(421)	25(1)	49(1)	35(1)	-5(1)	-4(1)	0(1)
C(43)	33(1)	84(2)	30(1)	-13(1)	-8(1)	-6(1)
C(5)	23(1)	25(1)	27(1)	3(1)	-1(1)	-2(1)
O(51)	28(1)	31(1)	36(1)	11(1)	-4(1)	-3(1)
C(52)	36(1)	36(1)	31(1)	7(1)	-6(1)	-10(1)
O(521)	35(1)	40(1)	36(1)	3(1)	3(1)	-10(1)
C(53)	51(1)	68(2)	94(2)	57(2)	-14(2)	-10(1)
C(6)	29(1)	21(1)	30(1)	1(1)	-5(1)	-5(1)
O(7)	23(1)	25(1)	28(1)	2(1)	-5(1)	-4(1)
S(1)	30(1)	31(1)	22(1)	0(1)	0(1)	10(1)
C(1')	29(1)	28(1)	22(1)	-5(1)	-3(1)	5(1)
C(2')	28(1)	36(1)	31(1)	-5(1)	-2(1)	5(1)
N(2')	36(1)	40(1)	66(1)	-1(1)	20(1)	3(1)
C(3')	35(1)	47(1)	49(1)	-16(1)	7(1)	11(1)
C(4')	60(2)	38(1)	54(1)	-20(1)	-4(1)	17(1)
C(5')	75(2)	29(1)	38(1)	-9(1)	-1(1)	-2(1)
C(6')	45(1)	34(1)	29(1)	-6(1)	2(1)	-5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic
displacement parameters (A^2 x 10^3) for IAS021.

	x	y	z	U(eq)
H(2)	8901	4456	8601	26
H(3)	8324	5594	9983	27
H(33A)	13090	6172	9831	70
H(33B)	12548	7315	9843	70
H(33C)	12368	6657	9085	70
H(4)	10139	3813	9915	27
H(43A)	12335	4826	12060	73
H(43B)	10730	4419	12255	73
H(43C)	10948	5550	11968	73
H(5)	7213	3829	10547	30
H(53A)	8685	1382	11825	106
H(53B)	8925	878	11006	106
H(53C)	7445	675	11469	106
H(6A)	8152	2930	9127	32
H(6B)	6538	2809	9478	32
H(3')	11100	3861	6266	52
H(4')	10255	2306	6648	61
H(5')	8075	2155	7328	57

H(6') 6757 3597 7644 43
H(1'1) 10770(40) 5600(20) 6259(18) 65(9)
H(1'2) 9550(30) 6151(18) 6685(13) 34(6)
H(1) 6060(30) 7500(20) 8753(16) 45(7)

Appendix 6

2-(2`,3`,4`-Tri-*O*-acetyl-β-D-xylopyranosyl)benzimidazole (217)

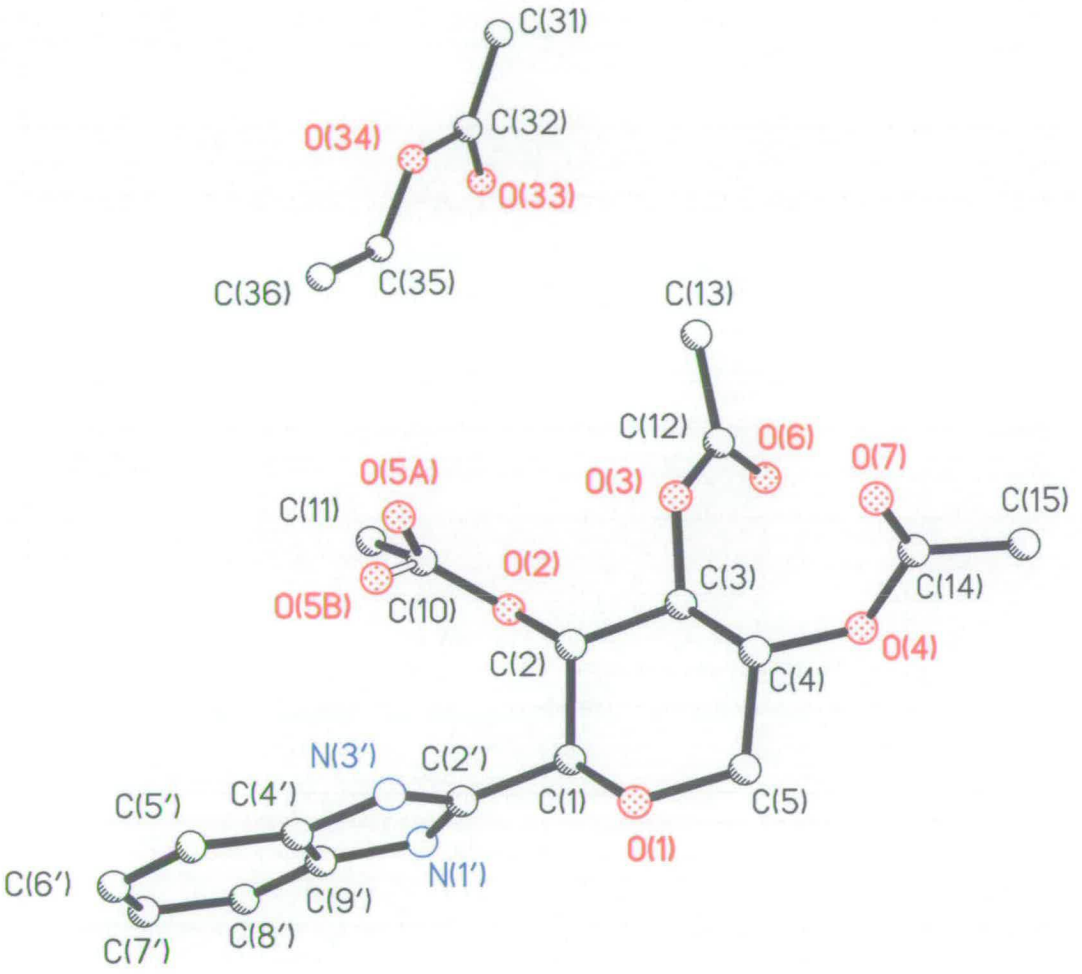


Table 11. Crystal data and structure refinement for ias025.

Contact	F.P.A.Fabbiani@ed.ac.uk
A. CRYSTAL DATA	
Empirical formula	C22 H28 N2 O9 C18 H20 N2 O7, C4 H8 O2
Formula weight	464.46
Wavelength	0.71073 A
Temperature	150(2) K
Crystal system	Hexagonal
Space group	P6(5)
Unit cell dimensions	a = 12.1781(2) A alpha = 90 deg. b = 12.1781(2) A beta = 90 deg. c = 28.1631(6) A gamma = 120 deg.
Volume	3617.18(11) A^3
Number of reflections for cell	7363 (2.41 < theta < 23.43 deg.)
Z	6
Density (calculated)	1.279 Mg/m^3
Absorption coefficient	0.100 mm^-1
F(000)	1476
B. DATA COLLECTION	
Crystal description	clolourless block
Crystal size	0.97 x 0.66 x 0.24 mm
Theta range for data collection	1.93 to 24.99 deg.
Index ranges	-14<=h<=14, -14<=k<=14, -33<=l<=33
Reflections collected	21712
Independent reflections	2060 [R(int) = 0.0673]
Scan type	omega scans
Absorption correction	Multiscan (Tmin= 0.924, Tmax=0.976)
C. SOLUTION AND REFINEMENT.	
Solution	direct (SHELXS-97 (Sheldrick, 1990))
Refinement type	Full-matrix least-squares on F^2
Program used for refinement	SHELXL-97
Hydrogen atom placement	geom
Hydrogen atom treatment	noref
Data / restraints / parameters	2060/15/295

Goodness-of-fit on F^2	1.214
Conventional R [F>4sigma(F)]	R1 = 0.1049 [1810 data]
Weighted R (F^2 and all data)	wR2 = 0.2658
Absolute structure parameter	-2(4)
Final maximum delta/sigma	0.000

Weighting scheme
calc w=1/[\s^2^(Fo^2^)+(0.1307P)^2^+2.0931P] where P=(Fo^2^+2Fc^2^)/3

Largest diff. peak and hole 0.344 and -0.239 e.A^-3

Table 12. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for ias025. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(1)	10850(6)	11602(6)	68(2)	64(2)
O(2)	8142(5)	8798(5)	-447(2)	55(1)
O(3)	7021(6)	10186(7)	-98(2)	69(2)
O(4)	8814(7)	12955(6)	-106(2)	75(2)
C(11)	7028(16)	6646(10)	-616(4)	101(4)
O(6)	6447(11)	10701(13)	-763(4)	131(4)
O(7)	7574(11)	12655(12)	516(3)	117(3)
N(3A)	10657(10)	9066(9)	228(2)	81(3)
N(1A)	11022(6)	9184(7)	-540(2)	53(2)
C(1)	10182(9)	10503(8)	-244(2)	57(2)
C(2)	8793(8)	9900(8)	-142(2)	54(2)
C(2A)	10653(7)	9611(8)	-174(2)	52(2)
C(3)	8314(8)	10797(8)	-233(2)	56(2)
C(4)	9099(9)	12012(9)	48(3)	64(2)
C(5)	10488(10)	12522(9)	-33(3)	68(2)
C(4A)	11044(7)	8213(6)	109(2)	74(3)
C(5A)	11209(9)	7357(8)	383(2)	104(4)
C(6A)	11581(9)	6565(8)	169(2)	95(4)
C(7A)	11787(8)	6629(7)	-318(2)	94(3)
C(8A)	11621(7)	7485(7)	-592(2)	76(3)
C(9A)	11250(6)	8277(6)	-378(2)	58(2)
C(10)	7547(12)	7662(11)	-237(2)	87(3)
O(5A)	7205(15)	7470(14)	176(4)	69(5)
O(5B)	7940(30)	7570(20)	142(5)	97(6)
C(12)	6177(12)	10170(13)	-388(4)	87(3)
C(13)	4866(13)	9370(20)	-212(7)	129(6)
C(14)	8041(13)	13193(15)	162(5)	93(4)
C(15)	7926(18)	14246(16)	-66(6)	121(5)
O(34)	1264(12)	4060(15)	-1173(5)	162(5)
C(31)	-634(18)	4120(20)	-1312(9)	195(12)
C(32)	563(15)	4228(15)	-1501(6)	147(7)
C(35)	2359(18)	4070(30)	-1374(7)	178(9)
C(36)	3070(20)	3950(30)	-951(8)	217(16)
O(33)	1010(30)	4430(30)	-1889(6)	510(40)

Table 13. Bond lengths [A] and angles [deg] for ias025.

O(1)-C(5)	1.423(12)
O(1)-C(1)	1.461(10)
O(2)-C(10)	1.336(11)

O(2)-C(2)	1.450(10)
O(3)-C(12)	1.305(12)
O(3)-C(3)	1.416(11)
O(4)-C(14)	1.346(13)
O(4)-C(4)	1.422(12)
C(11)-C(10)	1.513(16)
O(6)-C(12)	1.196(16)
O(7)-C(14)	1.172(18)
N(3A)-C(2A)	1.313(9)
N(3A)-C(4A)	1.380(9)
N(1A)-C(2A)	1.331(10)
N(1A)-C(9A)	1.346(8)
C(1)-C(2A)	1.473(13)
C(1)-C(2)	1.497(13)
C(2)-C(3)	1.496(12)
C(3)-C(4)	1.523(12)
C(4)-C(5)	1.500(14)
C(4A)-C(5A)	1.3900
C(4A)-C(9A)	1.3900
C(5A)-C(6A)	1.3900
C(6A)-C(7A)	1.3900
C(7A)-C(8A)	1.3900
C(8A)-C(9A)	1.3900
C(10)-O(5B)	1.199(10)
C(10)-O(5A)	1.217(9)
C(12)-C(13)	1.48(2)
C(14)-C(15)	1.50(2)
O(34)-C(32)	1.342(9)
O(34)-C(35)	1.441(10)
C(31)-C(32)	1.495(9)
C(32)-O(33)	1.192(10)
C(35)-C(36)	1.520(10)

C(5)-O(1)-C(1)	110.6(6)
C(10)-O(2)-C(2)	117.4(6)
C(12)-O(3)-C(3)	120.0(8)
C(14)-O(4)-C(4)	118.8(9)
C(2A)-N(3A)-C(4A)	105.0(6)
C(2A)-N(1A)-C(9A)	107.8(5)
O(1)-C(1)-C(2A)	110.6(6)
O(1)-C(1)-C(2)	108.0(6)
C(2A)-C(1)-C(2)	112.0(7)
O(2)-C(2)-C(3)	110.1(6)
O(2)-C(2)-C(1)	107.6(6)
C(3)-C(2)-C(1)	111.6(7)
N(3A)-C(2A)-N(1A)	112.6(7)
N(3A)-C(2A)-C(1)	126.1(6)
N(1A)-C(2A)-C(1)	121.0(6)
O(3)-C(3)-C(2)	107.9(7)
O(3)-C(3)-C(4)	111.3(7)
C(2)-C(3)-C(4)	109.6(7)
O(4)-C(4)-C(5)	107.4(7)
O(4)-C(4)-C(3)	109.7(7)
C(5)-C(4)-C(3)	110.6(7)
O(1)-C(5)-C(4)	111.9(8)
N(3A)-C(4A)-C(5A)	131.4(4)
N(3A)-C(4A)-C(9A)	108.6(4)
C(5A)-C(4A)-C(9A)	120.0
C(6A)-C(5A)-C(4A)	120.0
C(5A)-C(6A)-C(7A)	120.0
C(8A)-C(7A)-C(6A)	120.0
C(7A)-C(8A)-C(9A)	120.0
N(1A)-C(9A)-C(8A)	134.0(4)
N(1A)-C(9A)-C(4A)	106.0(4)
C(8A)-C(9A)-C(4A)	120.0
O(5B)-C(10)-O(5A)	41.1(12)
O(5B)-C(10)-O(2)	117.3(14)
O(5A)-C(10)-O(2)	125.3(12)

O(5B)-C(10)-C(11)	124.9(14)
O(5A)-C(10)-C(11)	123.6(12)
O(2)-C(10)-C(11)	108.9(7)
O(6)-C(12)-O(3)	122.9(12)
O(6)-C(12)-C(13)	124.4(12)
O(3)-C(12)-C(13)	112.6(12)
O(7)-C(14)-O(4)	123.5(13)
O(7)-C(14)-C(15)	127.9(11)
O(4)-C(14)-C(15)	108.6(13)
C(32)-O(34)-C(35)	112.5(10)
O(33)-C(32)-O(34)	113.7(12)
O(33)-C(32)-C(31)	132.3(14)
O(34)-C(32)-C(31)	114.0(12)
O(34)-C(35)-C(36)	105.0(12)

Symmetry transformations used to generate equivalent atoms:

Table 14. Anisotropic displacement parameters (A^2 x 10^3) for ias025. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

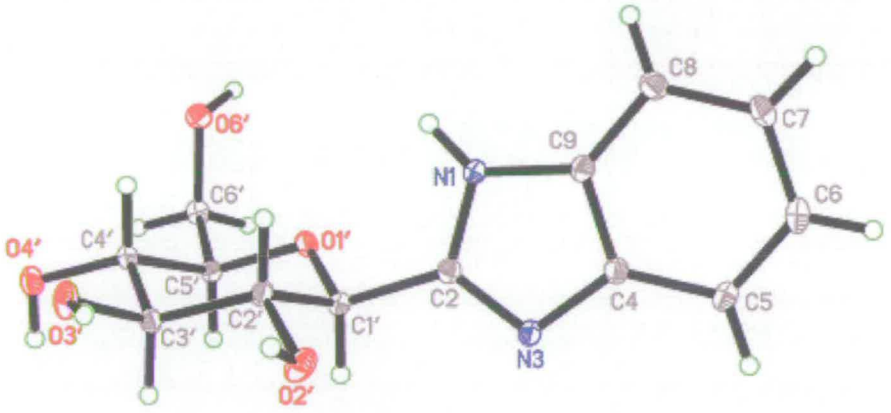
	U11	U22	U33	U23	U13	U12
O(1)	62(3)	86(4)	41(3)	-6(2)	-8(2)	36(3)
O(2)	72(3)	67(3)	27(2)	-2(2)	-9(2)	36(3)
O(3)	75(4)	95(4)	41(3)	-12(3)	-13(3)	44(3)
O(4)	106(5)	65(4)	61(3)	-4(3)	-16(3)	48(4)
C(11)	158(12)	63(6)	70(6)	4(5)	-6(7)	45(7)
O(6)	111(7)	212(12)	114(7)	16(8)	-36(6)	113(8)
O(7)	136(8)	171(10)	84(6)	-9(6)	13(5)	107(8)
N(3A)	136(7)	122(7)	27(3)	31(4)	30(4)	96(6)
N(1A)	44(3)	102(5)	23(3)	21(3)	7(2)	44(3)
C(1)	77(5)	81(5)	16(3)	7(3)	-1(3)	41(5)
C(2)	72(5)	62(4)	27(3)	4(3)	-3(3)	34(4)
C(2A)	51(4)	75(5)	24(3)	5(3)	9(3)	27(4)
C(3)	62(5)	75(5)	28(3)	-2(3)	-10(3)	33(4)
C(4)	87(6)	71(5)	34(4)	-3(3)	-2(4)	38(5)
C(5)	84(6)	68(5)	50(4)	2(4)	-10(4)	36(5)
C(4A)	99(7)	90(6)	40(4)	32(4)	27(4)	52(6)
C(5A)	154(11)	139(10)	46(5)	46(6)	45(6)	95(10)
C(6A)	112(9)	118(9)	88(7)	41(7)	30(6)	83(8)
C(7A)	99(8)	126(10)	77(7)	-4(6)	12(6)	72(8)
C(8A)	83(6)	113(8)	60(5)	10(5)	7(4)	70(6)
C(9A)	39(4)	105(6)	34(3)	7(4)	16(3)	40(4)
C(10)	136(10)	82(7)	37(4)	13(4)	-17(5)	50(7)
O(5A)	59(8)	49(7)	48(7)	22(5)	-2(6)	-12(7)
O(5B)	117(16)	77(11)	67(10)	15(7)	-22(10)	27(13)
C(12)	109(9)	121(9)	66(6)	-23(6)	-27(6)	85(8)
C(13)	77(8)	186(17)	140(12)	-41(11)	-13(8)	78(10)
C(14)	100(8)	125(10)	80(7)	-38(7)	-11(6)	78(8)
C(15)	153(13)	124(11)	132(11)	-9(9)	-1(10)	103(11)
O(34)	136(11)	153(11)	165(12)	-28(9)	0(9)	49(9)
C(31)	210(30)	116(15)	220(30)	38(16)	80(20)	55(15)
C(32)	140(16)	145(16)	110(12)	3(11)	-10(12)	36(12)
C(35)	129(16)	200(20)	180(20)	23(18)	59(16)	68(16)
C(36)	140(20)	300(40)	140(19)	-20(20)	25(15)	60(20)
O(33)	790(120)	320(50)	320(50)	190(40)	160(60)	210(60)

Table 15. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for ias025.

	x	y	z	U(eq)
H(11A)	6589	5808	-466	152
H(11B)	7728	6719	-811	152
H(11C)	6432	6753	-817	152
H(1A)	11102	9448	-836	64
H(1)	10337	10800	-581	69
H(2)	8634	9624	197	65
H(3)	8387	11003	-580	67
H(4)	8903	11841	394	77
H(5A)	10694	12796	-368	82
H(5B)	10980	13274	171	82
H(5A1)	11069	7313	716	124
H(6A)	11694	5980	356	114
H(7A)	12040	6088	-464	113
H(8A)	11762	7529	-925	91
H(13A)	4884	9041	103	194
H(13B)	4391	8668	-431	194
H(13C)	4454	9888	-190	194
H(15A)	8422	14508	-360	182
H(15B)	8247	14968	153	182
H(15C)	7033	13949	-138	182
H(31A)	-694	3944	-970	293
H(31B)	-1363	3428	-1474	293
H(31C)	-628	4918	-1366	293
H(35A)	2896	4877	-1546	214
H(35B)	2101	3357	-1596	214
H(36A)	3833	3956	-1063	325
H(36B)	2521	3156	-784	325
H(36C)	3310	4668	-735	325

Appendix 7

2-β-D-Glucopyranosylbenzimidazole (224)



Appendix 7

Table 1. Crystal data and structure refinement for mp0501.

Contact	Fraser J. White, f.j.white@sms.ed.ac.uk
A. CRYSTAL DATA	
Empirical formula	C13 H16 N2 O5 C13 H16 N2 O5
Formula weight	280.28
Wavelength	0.71073 A
Temperature	150(2) K
Crystal system	Monoclinic
Space group	P 21
Unit cell dimensions	a = 6.2177(2) A alpha = 90 deg. b = 9.6686(3) A beta = 92.6760(10) deg. c = 10.6720(3) A gamma = 90 deg.
Volume	640.86(3) A^3
Number of reflections for cell	8993 (5.5 < theta < 58.5 deg.)
Z	2
Density (calculated)	1.452 Mg/m^3
Absorption coefficient	0.113 mm^-1
F(000)	296
B. DATA COLLECTION	
Crystal description	block Colourless
Crystal size	0.40 x 0.27 x 0.16 mm
Instrument	Bruker Smart Apex CCD
Theta range for data collection	1.91 to 28.27 deg.
Index ranges	-7<=h<=8, -12<=k<=12, -14<=l<=14
Reflections collected	18479
Independent reflections	1680 [R(int) = 0.0328]
Scan type	Omega and Phi scans
Absorption correction	Semi-empirical from equivalents (Tmin= 0.815, Tmax=0.98)
C. SOLUTION AND REFINEMENT.	
Solution	direct (SHELXS-97 (Sheldrick, 1990))
Refinement type	Full-matrix least-squares on F^2
Program used for refinement	SHELXL-97
Hydrogen atom placement	geom

Hydrogen atom treatment	mixed
Data	1680
Restraints	1
Parameters	201
Goodness-of-fit on F^2	1.071
Conventional R [F>4sigma(F)]	R1 = 0.0330 [1604 data]
Rw	0.0842
Absolute structure parameter	0(10)
Final maximum delta/sigma	0.001
Weighting scheme	Sheldrick Weights
Largest diff. peak and hole	0.328 and -0.225 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for mp0501. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
N(1)	-1546(2)	441(2)	-2386(1)	19(1)
C(2)	118(3)	874(2)	-1688(2)	17(1)
N(3)	1069(2)	2018(2)	-2155(1)	19(1)
C(4)	-81(3)	2363(2)	-3253(2)	18(1)
C(5)	146(3)	3440(2)	-4108(2)	23(1)
C(6)	-1362(3)	3484(2)	-5106(2)	25(1)
C(7)	-3021(3)	2498(2)	-5249(2)	28(1)
C(8)	-3223(3)	1427(2)	-4405(2)	24(1)
C(9)	-1717(3)	1371(2)	-3385(2)	18(1)
O(1')	1150(2)	1196(1)	445(1)	18(1)
C(1')	955(3)	171(2)	-512(2)	17(1)
O(2')	2762(2)	-1541(2)	-1632(1)	25(1)
C(2')	3134(3)	-515(2)	-705(2)	17(1)
O(3')	6149(2)	-1623(2)	459(1)	24(1)
C(3')	4003(3)	-1122(2)	541(2)	18(1)
O(4')	4853(2)	-565(2)	2737(1)	23(1)
C(4')	4059(3)	-21(2)	1564(2)	17(1)
C(5')	1830(3)	635(2)	1642(1)	17(1)
O(6')	3183(2)	2887(1)	2198(1)	22(1)
C(6')	1764(3)	1815(2)	2572(2)	19(1)

Table 3. Bond lengths [A] and angles [deg] for mp0501.

N(1)-C(2)	1.314(2)
N(1)-C(9)	1.395(2)
C(2)-N(3)	1.360(2)
C(2)-C(1')	1.500(2)
N(3)-C(4)	1.384(2)
N(3)-H(3)	0.88(3)
C(4)-C(5)	1.396(2)
C(4)-C(9)	1.400(2)
C(5)-C(6)	1.387(2)
C(5)-H(5)	0.9500

C(6)-C(7)	1.407(3)
C(6)-H(6)	0.9500
C(7)-C(8)	1.382(3)
C(7)-H(7)	0.9500
C(8)-C(9)	1.404(2)
C(8)-H(8)	0.9500
O(1')-C(1')	1.4246(19)
O(1')-C(5')	1.4338(18)
C(1')-C(2')	1.531(2)
C(1')-H(1')	1.0000
O(2')-C(2')	1.412(2)
O(2')-H(2')	0.85(3)
C(2')-C(3')	1.529(2)
C(2')-H(2'1)	1.0000
O(3')-C(3')	1.426(2)
O(3')-H(3')	0.86(3)
C(3')-C(4')	1.524(2)
C(3')-H(3'1)	1.0000
O(4')-C(4')	1.4248(19)
O(4')-H(4')	0.84(3)
C(4')-C(5')	1.530(2)
C(4')-H(4'1)	1.0000
C(5')-C(6')	1.514(2)
C(5')-H(5')	1.0000
O(6')-C(6')	1.430(2)
O(6')-H(6')	0.87(3)
C(6')-H(6'1)	0.9900
C(6')-H(6'2)	0.9900

C(2)-N(1)-C(9)	104.92(14)
N(1)-C(2)-N(3)	113.30(15)
N(1)-C(2)-C(1')	124.26(16)
N(3)-C(2)-C(1')	122.42(14)
C(2)-N(3)-C(4)	106.86(14)
C(2)-N(3)-H(3)	121.1(17)
C(4)-N(3)-H(3)	131.3(17)
N(3)-C(4)-C(5)	131.98(17)
N(3)-C(4)-C(9)	105.31(15)
C(5)-C(4)-C(9)	122.70(15)
C(6)-C(5)-C(4)	116.06(17)
C(6)-C(5)-H(5)	122.0
C(4)-C(5)-H(5)	122.0
C(5)-C(6)-C(7)	121.90(17)
C(5)-C(6)-H(6)	119.0
C(7)-C(6)-H(6)	119.0
C(8)-C(7)-C(6)	121.71(16)
C(8)-C(7)-H(7)	119.1
C(6)-C(7)-H(7)	119.1
C(7)-C(8)-C(9)	117.16(17)
C(7)-C(8)-H(8)	121.4
C(9)-C(8)-H(8)	121.4
N(1)-C(9)-C(4)	109.60(14)
N(1)-C(9)-C(8)	129.93(17)
C(4)-C(9)-C(8)	120.46(16)
C(1')-O(1')-C(5')	112.74(12)
O(1')-C(1')-C(2)	107.40(13)
O(1')-C(1')-C(2')	110.62(12)
C(2)-C(1')-C(2')	110.97(13)
O(1')-C(1')-H(1')	109.3
C(2)-C(1')-H(1')	109.3
C(2')-C(1')-H(1')	109.3
C(2')-O(2')-H(2')	108(2)
O(2')-C(2')-C(3')	112.30(14)
O(2')-C(2')-C(1')	106.37(13)
C(3')-C(2')-C(1')	109.12(13)
O(2')-C(2')-H(2'1)	109.7
C(3')-C(2')-H(2'1)	109.7
C(1')-C(2')-H(2'1)	109.7

C(3')-O(3')-H(3')	111.7(18)
O(3')-C(3')-C(4')	106.90(13)
O(3')-C(3')-C(2')	111.72(13)
C(4')-C(3')-C(2')	110.51(14)
O(3')-C(3')-H(3'1)	109.2
C(4')-C(3')-H(3'1)	109.2
C(2')-C(3')-H(3'1)	109.2
C(4')-O(4')-H(4')	107.5(18)
O(4')-C(4')-C(3')	111.52(14)
O(4')-C(4')-C(5')	112.49(13)
C(3')-C(4')-C(5')	109.74(13)
O(4')-C(4')-H(4'1)	107.6
C(3')-C(4')-H(4'1)	107.6
C(5')-C(4')-H(4'1)	107.6
O(1')-C(5')-C(6')	106.39(13)
O(1')-C(5')-C(4')	109.79(12)
C(6')-C(5')-C(4')	113.59(13)
O(1')-C(5')-H(5')	109.0
C(6')-C(5')-H(5')	109.0
C(4')-C(5')-H(5')	109.0
C(6')-O(6')-H(6')	108.6(19)
O(6')-C(6')-C(5')	109.14(13)
O(6')-C(6')-H(6'1)	109.9
C(5')-C(6')-H(6'1)	109.9
O(6')-C(6')-H(6'2)	109.9
C(5')-C(6')-H(6'2)	109.9
H(6'1)-C(6')-H(6'2)	108.3

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for mp0501. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
N(1)	19(1)	18(1)	20(1)	0(1)	-4(1)	0(1)
C(2)	16(1)	17(1)	17(1)	-1(1)	0(1)	1(1)
N(3)	19(1)	19(1)	18(1)	1(1)	-4(1)	-3(1)
C(4)	18(1)	19(1)	17(1)	-3(1)	-2(1)	2(1)
C(5)	26(1)	21(1)	21(1)	1(1)	1(1)	-1(1)
C(6)	32(1)	26(1)	17(1)	5(1)	1(1)	3(1)
C(7)	28(1)	36(1)	19(1)	1(1)	-7(1)	3(1)
C(8)	24(1)	27(1)	21(1)	-2(1)	-7(1)	-2(1)
C(9)	19(1)	18(1)	18(1)	-1(1)	-2(1)	1(1)
O(1')	21(1)	16(1)	15(1)	1(1)	-2(1)	3(1)
C(1')	17(1)	17(1)	17(1)	1(1)	-2(1)	-1(1)
O(2')	21(1)	28(1)	25(1)	-11(1)	-4(1)	2(1)
C(2')	16(1)	18(1)	18(1)	-1(1)	-3(1)	1(1)
O(3')	22(1)	29(1)	21(1)	-5(1)	-4(1)	12(1)
C(3')	18(1)	16(1)	18(1)	1(1)	-2(1)	3(1)
O(4')	24(1)	27(1)	18(1)	5(1)	-5(1)	3(1)
C(4')	17(1)	18(1)	15(1)	2(1)	-1(1)	2(1)
C(5')	18(1)	18(1)	15(1)	2(1)	-1(1)	0(1)
O(6')	22(1)	17(1)	27(1)	-2(1)	1(1)	2(1)
C(6')	20(1)	20(1)	18(1)	-1(1)	3(1)	4(1)

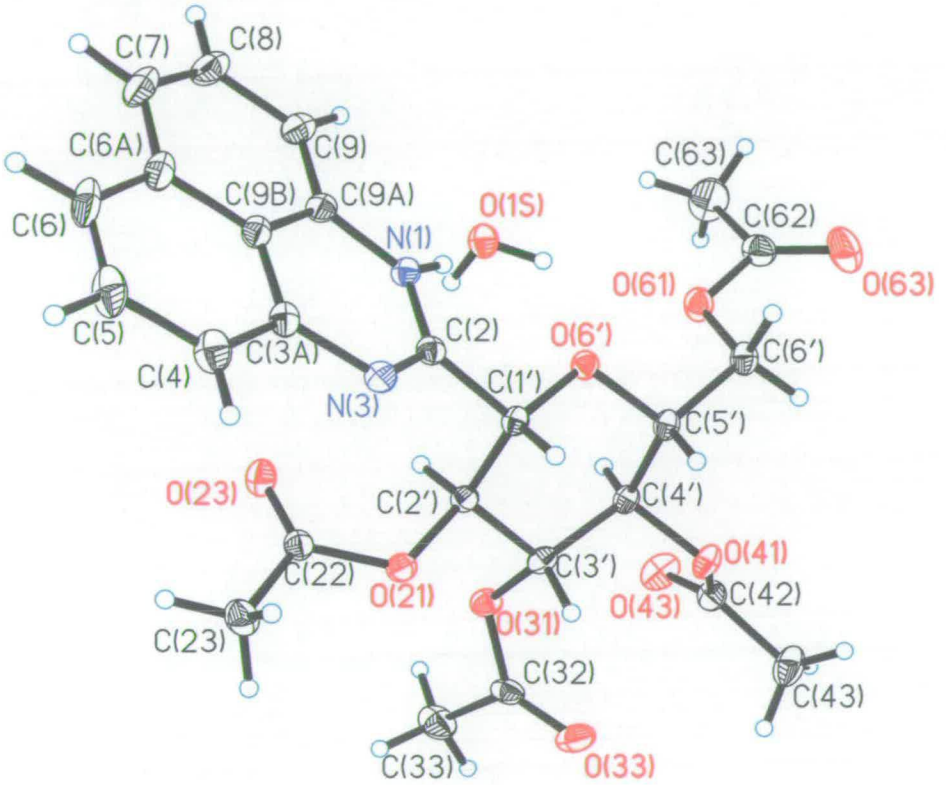
Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for mp0501.

Appendix 7

	x	y	z	U(eq)
H(5)	1268	4104	-4012	27
H(6)	-1273	4200	-5711	30
H(7)	-4028	2571	-5943	34
H(8)	-4333	756	-4511	29
H(1')	-100	-549	-264	20
H(2'1)	4169	187	-1009	21
H(3'1)	3050	-1899	789	21
H(4'1)	5075	720	1313	20
H(5')	782	-93	1882	20
H(6'1)	278	2178	2598	23
H(6'2)	2214	1482	3421	23
H(6')	2530(40)	3680(40)	2260(30)	40(7)
H(3)	2080(40)	2460(30)	-1720(20)	28(6)
H(4')	3960(40)	-1160(30)	2970(20)	33(7)
H(3')	6350(40)	-2000(30)	-260(30)	47(8)
H(2')	3960(50)	-1750(40)	-1940(30)	48(8)

Appendix 8

2-(2`,3`,4`,6`-Tetra-*O*-acetyl-β-D-glucopyranosyl)perimidine (260)



Appendix 8

Table 1. Crystal data and structure refinement for ias069.

Contact	Stephen Moggach, s.moggach@ed.ac.uk
A. CRYSTAL DATA	
Empirical formula	C25 H28 N2 O10 C25 H26 N2 O9, H2 O
Formula weight	498.48
Wavelength	0.71073 A
Temperature	150(2) K
Crystal system	Orthorhombic
Space group	P 21 21 21
Unit cell dimensions	a = 9.9570(9) A alpha = 90 deg. b = 13.8850(12) A beta = 90 deg. c = 18.0620(18) A gamma = 90 deg.
Volume	2497.1(4) A^3
Number of reflections for cell	4478 (4.510 < theta < 60.405 deg.)
Z	4
Density (calculated)	1.326 Mg/m^3
Absorption coefficient	0.102 mm^-1
F(000)	1048
B. DATA COLLECTION	
Crystal description	yellow block
Crystal size	0.50 x 0.36 x 0.20 mm
Theta range for data collection	1.85 to 30.31 deg.
Index ranges	-13<=h<=14, -19<=k<=17, -15<=l<=24
Reflections collected	16966
Independent reflections	7043 [R(int) = 0.0323]
Scan type	\w
Absorption correction	Semi-empirical from equivalents (Tmin= 0.86, Tmax=1.00)
C. SOLUTION AND REFINEMENT.	
Solution	direct (SHELXS-97 (Sheldrick, 1990))
Refinement type	Full-matrix least-squares on F^2
Program used for refinement	SHELXL-97
Hydrogen atom placement	geom
Hydrogen atom treatment	mixed

Data / restraints / parameters	7043/4/350
Goodness-of-fit on F^2	1.112
Conventional R [F>4sigma(F)]	R1 = 0.0546 [6329 data]
Weighted R (F^2 and all data)	wR2 = 0.1302
Absolute structure parameter	1.3(9)
Final maximum delta/sigma	0.051

Weighting scheme
calc w=1/[\s^2^(Fo^2^)+(0.0509P)^2^+0.7065P] where P=(Fo^2^+2Fc^2^)/3

Largest diff. peak and hole 0.310 and -0.244 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for ias069. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
N(1)	1653(2)	2364(1)	10807(1)	24(1)
C(1')	2706(2)	2223(1)	9597(1)	23(1)
C(2)	2499(2)	2764(1)	10311(1)	24(1)
C(2')	1606(2)	2510(1)	9040(1)	23(1)
N(3)	3046(2)	3611(1)	10368(1)	26(1)
C(3')	1655(2)	1907(1)	8339(1)	24(1)
C(3A)	2634(2)	4189(2)	10968(1)	28(1)
C(4)	3040(3)	5135(2)	11015(1)	38(1)
C(4')	1842(2)	834(1)	8496(1)	24(1)
C(5)	2607(3)	5707(2)	11614(2)	46(1)
C(5')	2931(2)	678(1)	9085(1)	24(1)
C(6)	1814(3)	5344(2)	12159(2)	44(1)
O(6')	2585(1)	1218(1)	9733(1)	24(1)
C(6')	3135(2)	-353(2)	9312(1)	29(1)
C(6A)	1354(2)	4376(2)	12137(1)	35(1)
C(7)	527(2)	3943(2)	12679(1)	43(1)
C(8)	93(3)	3015(2)	12603(1)	42(1)
C(9)	452(2)	2456(2)	11980(1)	34(1)
C(9A)	1277(2)	2854(2)	11450(1)	27(1)
C(9B)	1761(2)	3807(2)	11520(1)	27(1)
O(21)	1813(2)	3494(1)	8822(1)	27(1)
C(22)	1120(2)	4177(2)	9205(1)	28(1)
O(23)	273(2)	3986(1)	9657(1)	34(1)
C(23)	1573(3)	5164(2)	8989(1)	40(1)
O(31)	373(2)	2084(1)	7985(1)	28(1)
C(32)	336(3)	2149(1)	7237(1)	31(1)
O(33)	1283(2)	2004(1)	6843(1)	41(1)
C(33)	-1040(3)	2441(2)	6984(2)	46(1)
O(41)	2351(2)	376(1)	7836(1)	30(1)
C(42)	1467(2)	-37(2)	7364(1)	30(1)
O(43)	293(2)	-115(1)	7500(1)	43(1)
C(43)	2143(3)	-346(2)	6669(2)	45(1)
O(61)	1912(2)	-697(1)	9660(1)	34(1)
C(62)	1918(3)	-1642(2)	9844(1)	37(1)
O(63)	2829(2)	-2164(1)	9691(1)	56(1)
C(63)	654(4)	-1940(2)	10217(2)	69(1)
O(1S)	72(2)	647(1)	10594(1)	32(1)

Table 3. Bond lengths [A] and angles [deg] for ias069.

N(1)-C(2)	1.351(3)
N(1)-C(9A)	1.396(3)
N(1)-H(1)	0.898(16)
C(1')-O(6')	1.422(2)
C(1')-C(2)	1.506(3)
C(1')-C(2')	1.539(3)
C(1')-H(1')	1.0000
C(2)-N(3)	1.300(2)
C(2')-O(21)	1.438(2)
C(2')-C(3')	1.519(3)
C(2')-H(2')	1.0000
N(3)-C(3A)	1.410(3)
C(3')-O(31)	1.448(2)
C(3')-C(4')	1.529(3)
C(3')-H(3')	1.0000
C(3A)-C(4)	1.377(3)
C(3A)-C(9B)	1.425(3)
C(4)-C(5)	1.409(4)
C(4)-H(4)	0.9500
C(4')-O(41)	1.443(2)
C(4')-C(5')	1.533(3)
C(4')-H(4')	1.0000
C(5)-C(6)	1.359(4)
C(5)-H(5)	0.9500
C(5')-O(6')	1.432(2)
C(5')-C(6')	1.503(3)
C(5')-H(5')	1.0000
C(6)-C(6A)	1.420(4)
C(6)-H(6)	0.9500
C(6')-O(61)	1.450(3)
C(6')-H(6'1)	0.9900
C(6')-H(6'2)	0.9900
C(6A)-C(7)	1.413(4)
C(6A)-C(9B)	1.426(3)
C(7)-C(8)	1.367(4)
C(7)-H(7)	0.9500
C(8)-C(9)	1.412(3)
C(8)-H(8)	0.9500
C(9)-C(9A)	1.378(3)
C(9)-H(9)	0.9500
C(9A)-C(9B)	1.414(3)
O(21)-C(22)	1.362(2)
C(22)-O(23)	1.202(3)
C(22)-C(23)	1.494(3)
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
O(31)-C(32)	1.355(2)
C(32)-O(33)	1.199(3)
C(32)-C(33)	1.500(4)
C(33)-H(33A)	0.9800
C(33)-H(33B)	0.9800
C(33)-H(33C)	0.9800
O(41)-C(42)	1.353(3)
C(42)-O(43)	1.199(3)
C(42)-C(43)	1.489(3)
C(43)-H(43A)	0.9800
C(43)-H(43B)	0.9800
C(43)-H(43C)	0.9800
O(61)-C(62)	1.354(3)
C(62)-O(63)	1.193(3)
C(62)-C(63)	1.486(4)
C(63)-H(63A)	0.9800
C(63)-H(63B)	0.9800
C(63)-H(63C)	0.9800
O(1S)-H(1S)	0.862(16)
O(1S)-H(2S)	0.866(17)

C(2)-N(1)-C(9A)	121.21(17)
C(2)-N(1)-H(1)	118.4(16)
C(9A)-N(1)-H(1)	120.3(17)
O(6')-C(1')-C(2)	109.29(15)
O(6')-C(1')-C(2')	107.80(14)
C(2)-C(1')-C(2')	109.45(15)
O(6')-C(1')-H(1')	110.1
C(2)-C(1')-H(1')	110.1
C(2')-C(1')-H(1')	110.1
N(3)-C(2)-N(1)	125.57(18)
N(3)-C(2)-C(1')	117.46(18)
N(1)-C(2)-C(1')	116.64(16)
O(21)-C(2')-C(3')	106.85(15)
O(21)-C(2')-C(1')	108.88(15)
C(3')-C(2')-C(1')	112.32(16)
O(21)-C(2')-H(2')	109.6
C(3')-C(2')-H(2')	109.6
C(1')-C(2')-H(2')	109.6
C(2)-N(3)-C(3A)	116.94(18)
O(31)-C(3')-C(2')	104.26(15)
O(31)-C(3')-C(4')	110.76(15)
C(2')-C(3')-C(4')	112.69(16)
O(31)-C(3')-H(3')	109.7
C(2')-C(3')-H(3')	109.7
C(4')-C(3')-H(3')	109.7
C(4)-C(3A)-N(3)	120.3(2)
C(4)-C(3A)-C(9B)	119.4(2)
N(3)-C(3A)-C(9B)	120.26(18)
C(3A)-C(4)-C(5)	119.7(2)
C(3A)-C(4)-H(4)	120.2
C(5)-C(4)-H(4)	120.2
O(41)-C(4')-C(3')	108.54(16)
O(41)-C(4')-C(5')	105.22(15)
C(3')-C(4')-C(5')	110.64(15)
O(41)-C(4')-H(4')	110.8
C(3')-C(4')-H(4')	110.8
C(5')-C(4')-H(4')	110.8
C(6)-C(5)-C(4)	121.7(2)
C(6)-C(5)-H(5)	119.2
C(4)-C(5)-H(5)	119.2
O(6')-C(5')-C(6')	107.92(16)
O(6')-C(5')-C(4')	108.82(15)
C(6')-C(5')-C(4')	114.81(16)
O(6')-C(5')-H(5')	108.4
C(6')-C(5')-H(5')	108.4
C(4')-C(5')-H(5')	108.4
C(5)-C(6)-C(6A)	121.2(2)
C(5)-C(6)-H(6)	119.4
C(6A)-C(6)-H(6)	119.4
C(1')-O(6')-C(5')	110.65(14)
O(61)-C(6')-C(5')	108.56(16)
O(61)-C(6')-H(6'1)	110.0
C(5')-C(6')-H(6'1)	110.0
O(61)-C(6')-H(6'2)	110.0
C(5')-C(6')-H(6'2)	110.0
H(6'1)-C(6')-H(6'2)	108.4
C(7)-C(6A)-C(6)	124.9(2)
C(7)-C(6A)-C(9B)	118.1(2)
C(6)-C(6A)-C(9B)	117.0(2)
C(8)-C(7)-C(6A)	121.0(2)
C(8)-C(7)-H(7)	119.5
C(6A)-C(7)-H(7)	119.5
C(7)-C(8)-C(9)	121.3(2)
C(7)-C(8)-H(8)	119.4
C(9)-C(8)-H(8)	119.4
C(9A)-C(9)-C(8)	119.0(2)
C(9A)-C(9)-H(9)	120.5

C(8)-C(9)-H(9)	120.5
C(9)-C(9A)-N(1)	122.8(2)
C(9)-C(9A)-C(9B)	121.1(2)
N(1)-C(9A)-C(9B)	116.08(18)
C(9A)-C(9B)-C(3A)	119.57(18)
C(9A)-C(9B)-C(6A)	119.5(2)
C(3A)-C(9B)-C(6A)	120.9(2)
C(22)-O(21)-C(2')	116.75(15)
O(23)-C(22)-O(21)	123.10(19)
O(23)-C(22)-C(23)	126.2(2)
O(21)-C(22)-C(23)	110.65(19)
C(22)-C(23)-H(23A)	109.5
C(22)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(22)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5
C(32)-O(31)-C(3')	118.41(17)
O(33)-C(32)-O(31)	124.0(2)
O(33)-C(32)-C(33)	125.6(2)
O(31)-C(32)-C(33)	110.3(2)
C(32)-C(33)-H(33A)	109.5
C(32)-C(33)-H(33B)	109.5
H(33A)-C(33)-H(33B)	109.5
C(32)-C(33)-H(33C)	109.5
H(33A)-C(33)-H(33C)	109.5
H(33B)-C(33)-H(33C)	109.5
C(42)-O(41)-C(4')	118.61(16)
O(43)-C(42)-O(41)	122.9(2)
O(43)-C(42)-C(43)	126.0(2)
O(41)-C(42)-C(43)	111.10(19)
C(42)-C(43)-H(43A)	109.5
C(42)-C(43)-H(43B)	109.5
H(43A)-C(43)-H(43B)	109.5
C(42)-C(43)-H(43C)	109.5
H(43A)-C(43)-H(43C)	109.5
H(43B)-C(43)-H(43C)	109.5
C(62)-O(61)-C(6')	114.96(18)
O(63)-C(62)-O(61)	122.3(2)
O(63)-C(62)-C(63)	125.5(2)
O(61)-C(62)-C(63)	112.2(2)
C(62)-C(63)-H(63A)	109.5
C(62)-C(63)-H(63B)	109.5
H(63A)-C(63)-H(63B)	109.5
C(62)-C(63)-H(63C)	109.5
H(63A)-C(63)-H(63C)	109.5
H(63B)-C(63)-H(63C)	109.5
H(1S)-O(1S)-H(2S)	106(2)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for ias069. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
N(1)	27(1)	23(1)	23(1)	-3(1)	-1(1)	-2(1)
C(1')	21(1)	23(1)	24(1)	-4(1)	0(1)	-1(1)
C(2)	23(1)	24(1)	24(1)	-1(1)	-4(1)	2(1)
C(2')	24(1)	22(1)	22(1)	-1(1)	2(1)	-1(1)
N(3)	26(1)	25(1)	26(1)	-2(1)	-3(1)	-2(1)

C(3')	24(1)	27(1)	21(1)	-3(1)	1(1)	-3(1)
C(3A)	24(1)	29(1)	30(1)	-6(1)	-7(1)	2(1)
C(4)	37(1)	32(1)	45(1)	-9(1)	-6(1)	-2(1)
C(4')	22(1)	25(1)	24(1)	-6(1)	1(1)	-2(1)
C(5)	44(1)	33(1)	61(2)	-19(1)	-15(1)	0(1)
C(5')	20(1)	25(1)	28(1)	-5(1)	1(1)	-1(1)
C(6)	38(1)	44(1)	50(1)	-26(1)	-11(1)	14(1)
O(6')	26(1)	22(1)	24(1)	-3(1)	-1(1)	1(1)
C(6')	27(1)	27(1)	34(1)	-6(1)	-1(1)	1(1)
C(6A)	29(1)	43(1)	34(1)	-15(1)	-9(1)	11(1)
C(7)	33(1)	63(2)	32(1)	-20(1)	-1(1)	14(1)
C(8)	33(1)	64(2)	28(1)	-5(1)	6(1)	5(1)
C(9)	31(1)	44(1)	28(1)	-1(1)	1(1)	0(1)
C(9A)	24(1)	33(1)	23(1)	-2(1)	-5(1)	3(1)
C(9B)	24(1)	32(1)	27(1)	-5(1)	-6(1)	6(1)
O(21)	32(1)	23(1)	24(1)	0(1)	3(1)	-1(1)
C(22)	30(1)	27(1)	25(1)	-2(1)	-5(1)	2(1)
O(23)	30(1)	33(1)	41(1)	-4(1)	5(1)	4(1)
C(23)	51(2)	27(1)	41(1)	1(1)	-2(1)	1(1)
O(31)	28(1)	33(1)	24(1)	-1(1)	-3(1)	-1(1)
C(32)	49(1)	21(1)	24(1)	2(1)	-5(1)	-6(1)
O(33)	59(1)	40(1)	25(1)	1(1)	6(1)	-8(1)
C(33)	61(2)	39(1)	38(1)	-2(1)	-17(1)	2(1)
O(41)	27(1)	34(1)	29(1)	-12(1)	4(1)	-1(1)
C(42)	35(1)	27(1)	29(1)	-6(1)	-2(1)	-1(1)
O(43)	36(1)	54(1)	40(1)	-11(1)	-1(1)	-15(1)
C(43)	43(1)	52(1)	41(1)	-22(1)	-1(1)	6(1)
O(61)	36(1)	25(1)	41(1)	0(1)	7(1)	1(1)
C(62)	50(1)	27(1)	36(1)	-1(1)	-4(1)	0(1)
O(63)	54(1)	32(1)	82(2)	7(1)	2(1)	9(1)
C(63)	85(2)	41(2)	81(2)	13(2)	36(2)	-5(2)
O(1S)	28(1)	31(1)	38(1)	-3(1)	-1(1)	1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for ias069.

	x	y	z	U(eq)
H(1)	1300(20)	1784(13)	10704(14)	33(7)
H(1')	3613	2371	9389	27
H(2')	704	2442	9278	27
H(3')	2398	2141	8013	29
H(4)	3609	5401	10645	46
H(4')	975	533	8654	28
H(5)	2876	6362	11637	55
H(5')	3800	931	8887	29
H(6)	1563	5745	12561	52
H(6'1)	3346	-752	8873	35
H(6'2)	3894	-400	9664	35
H(7)	269	4303	13103	51
H(8)	-460	2740	12975	50
H(9)	129	1816	11928	41
H(23A)	1072	5644	9275	59
H(23B)	1408	5263	8459	59
H(23C)	2535	5231	9091	59
H(33A)	-1120	3144	7002	69
H(33B)	-1716	2151	7309	69
H(33C)	-1183	2219	6475	69
H(43A)	1645	-884	6449	68
H(43B)	3062	-552	6780	68
H(43C)	2166	193	6319	68
H(63A)	-31	-2082	9843	104
H(63B)	339	-1417	10538	104
H(63C)	820	-2517	10516	104

H(1S)	-560(20)	857(19)	10312(14)	44(8)
H(2S)	560(30)	280(20)	10317(16)	69(11)

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Synthesis of pyranosyl amidoximes by addition of amines to pyranosyl nitrile oxides

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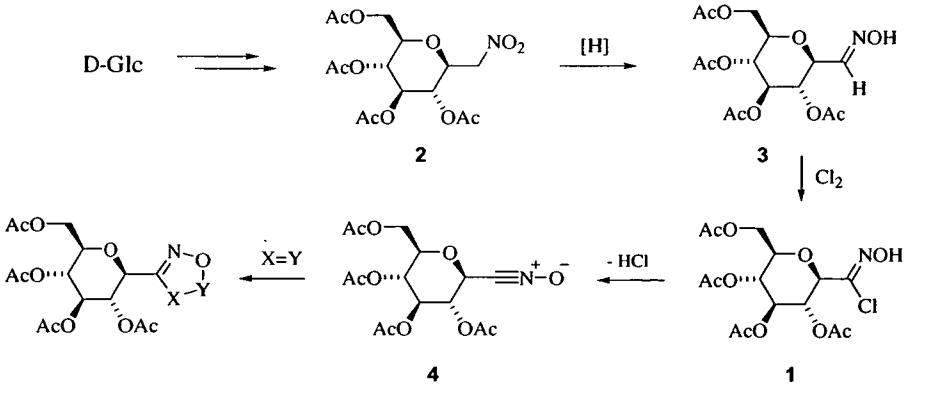
Abstract—Addition of amines to pyranosyl nitrile oxides, generated by base-induced dehydrochlorination of the corresponding hydroximoyl chloride, affords pyranosyl *N*-alkyl/aryl-formamide oximes (41–90%). Reaction with amino acid esters yields the corresponding amidoximes and/or 3-pyranosyl-1,2,4-oxadiazin-6-ones. The structure of *N*-phenyl-*C*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime was established by X-ray crystallography.

We have recently reported a short and efficient synthetic route from monosaccharides to pyranosyl hydroximoyl chlorides.[1–3] The approach, which is illustrated in Scheme 1 for the D-glucose-derived compound **1**, involves addition of nitromethane to D-glucose and acetylation to afford the pyranosylnitromethane **2**, followed by reduction to oxime **3**, and finally reaction with chlorine. The hydroximoyl chorides were then used as a source of the corresponding nitrile oxide, for example, **4**, from which a variety of novel *C*-glycosides were prepared by cycloaddition to dipolarophiles X=Y.

We now report that dehydrochlorination of these hydroximoyl chlorides in the presence of a primary or secondary amine provides easy access to a range of novel pyranosyl amidoximes (Scheme 2). 1,3-Addition of amines to arene nitrile oxides has been known for many years[4,5] and the resulting amidoximes have been shown to have a variety of useful properties. These include metal ligation[6–8] and biological activity, for example, as nitric oxide donors[9] and amidine prodrugs.[10] Less attention, however, has been paid to carbohydrate analogues; rare examples include cyclic amidoximes as



Scheme 1.

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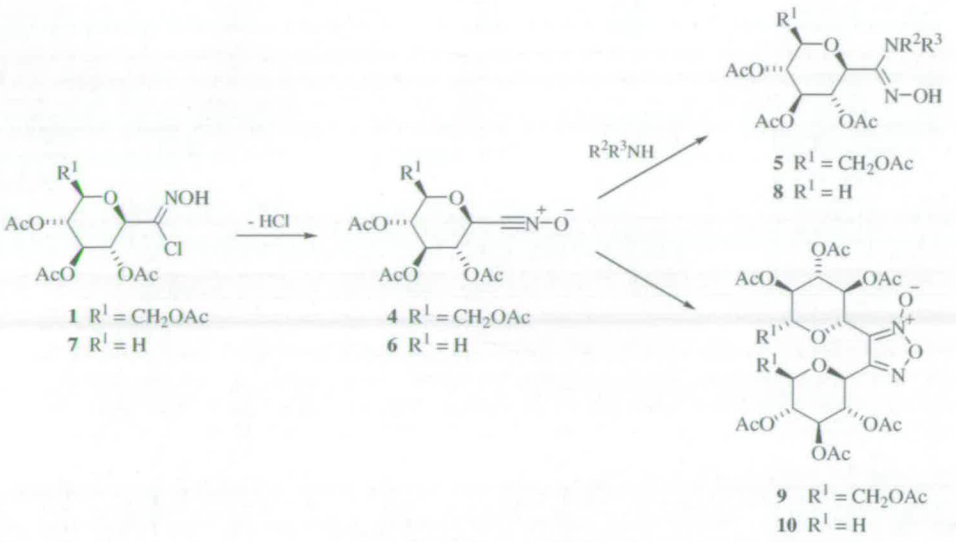


Scheme 2.

glycosidase and glycosyl transferase inhibitors[11,12] and amidoxime-linked nucleosides.[13]

In the present work the pyranosyl nitrile oxides were generated by dehydrochlorination of the corresponding hydroximoyl chlorides in situ in order to minimise dimerisation to 1,2,5-oxadiazole *N*-oxides (furoxans), which are often formed as by-products in reactions involving nitrile oxides.[3,14] In a typical experiment a solution of the glucopyranosyl-hydroximoyl chloride **1** (0.44 mmol) in dry chloroform (40 ml) was added dropwise over 3 h to a cooled (0 °C) vigorously stirred solution of benzylamine (1.32 mmol) and dry triethylamine (7.1 mmol) in dry chloroform (5 ml) under nitrogen. Removal of the solvent and chromatography of the residue (silica, hexane–EtOAc) afforded the *N*-benzyl amidoxime **5** (R^2 = Bn, R^3 = H) in 80% yield. The furoxan dimer **9** was not detected. D-Xylopyranosyl nitrile oxide **6**, generated from the hydroximoyl chloride **7**, reacted similarly to yield amidoxime **8** (R^2 = Bn, R^3 = H) (67%). The structures of the products were assigned on the basis of their spectroscopic properties; for example, in the NMR spectrum of D-xylose-derived amidoxime **8** (R^2 = Bn, R^3 = H) there are, in addition to the expected signals for the carbons and protons of the pyranosyl and benzene rings,[15] distinctive peaks for the oxime unit [δ_C 148.9 ppm (C=N)] and the attached $NHCH_2$ group [δ_H 4.38 (CH_a), 4.39 ppm (CH_b), 5.22 (NH); J_{NH-CH_a} 5.5, J_{NH-CH_b} 6.8, $J_{CH_a-CH_b}$ 14.6 Hz; δ_C 46.4 ppm (CH_2)].

Nitrile oxide **6** also reacted readily with 1-aminobutane, morpholine and allylamine to afford the corresponding adducts (**8** R^2 = Bu, R^3 = H; 63%), (**8** R^2R^3 = $CH_2CH_2OCH_2CH_2$; 67%) and (**8** R^2 = $CH_2CH{=}CH_2$, R^3 = H; 41%). It is noteworthy that in the latter case the isolated product results from addition of the nitrile oxide to the amine moiety in allylamine rather than cycloaddition to the alkene.

More forcing conditions were used for the corresponding reactions with aniline. Heating a 2:1 mixture of aniline and D-glucopyranosyl-hydroximoyl chloride **1** in ethanol at reflux for 5 h afforded amidoxime **5** (R^2 = Ph, R^3 = H) in 80% yield. The corresponding reaction with D-xylopyranosyl nitrile oxide **6** gave amidoxime **8** (R^2 = Ph, R^3 = H) (90%). In neither case was there any evidence for the formation of the furoxan dimer (**9**,**10**). However, reaction with aniline in the presence of triethylamine as dehydrochlorinating agent afforded a mixture (~1:3) of the amidoxime and the furoxan.

The structure of the adduct **8** (R^2 = Ph, R^3 = H) formed by 1,3-addition of aniline to nitrile oxide **6** was established by X-ray crystallography (Fig. 1).[16] Of particular note are the *Z*-configuration of the oxime moiety and the *s-trans* conformation about the amidic nitrogen with the H of the NHR facing the oxime OH. These results are in accord with previous studies indicating that such additions occur in a concerted, but nonsynchronous manner.[17] The near planarity of the NH–C=N–O unit [torsion angle 2.6(3)°] and the short nonbonded distance between the amidic N and the oxime O [N to O = 2.508(3) (Å)] are consistent with the existence of an intramolecular H-bond between these atoms.[17,18]

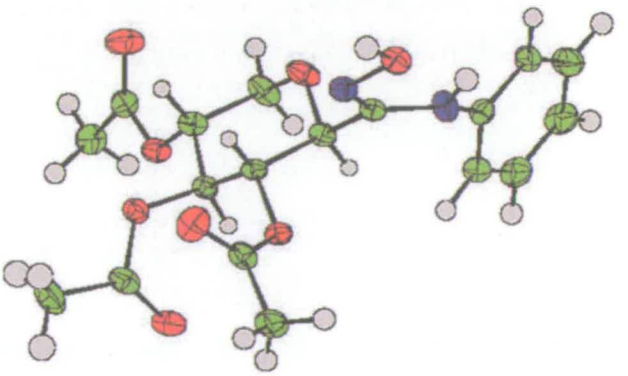
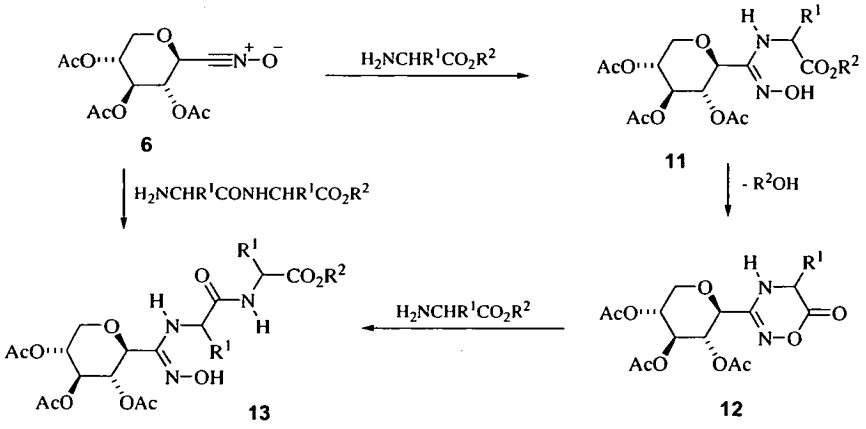


Figure 1. X-ray crystal structure of amidoxime **8** (R^2 = Ph, R^3 = H) showing the *Z-s-trans* arrangement.



Scheme 3.

Having established that simple amines such as aniline and benzylamine add readily to the pyranosyl nitrile oxides, the corresponding reactions with amino acid esters were examined. The resulting adducts were considered of interest as they would contain an unusual amidoxime sugar/amino acid linkage, and extension of the reaction to oligopeptides might provide access to novel glycopeptide analogues.

Reaction of hydroximoyl chloride **7** with glycine ethyl ester hydrochloride and triethylamine (1:1.5:15 molar ratio) at 0 °C afforded a mixture of three products, two of which were isolated and characterised (Scheme 3). The first (40%) proved to be the amidoxime **11** (R^1 = H, R^2 = Et)[19] resulting from the expected addition of glycine ethyl ester to nitrile oxide **6**; the other major product was identified from its spectroscopic properties[20] as the 1,2,4-oxadiazin-6-one **12** (R^1 = H) [δ_H 3.95 (CH_2), 5.61 ppm (NH); δ_C 40.2 (CH_2), 150.4 (C=N), 164.6 ppm (C=O)], and the third was provisionally assigned structure **13** (R^1 = H, R^2 = Et) on the basis of its NMR and mass spectra. In contrast, when the reaction was repeated under the same conditions with glycine *t*-butyl ester the amidoxime **11** (R^1 = Pr^i, R^2 = Bu^t) (88%) was the only isolated product. The corresponding reaction with L-leucine ethyl ester afforded 53% of amidoxime **11** (R^1 = CH_2CHMe_2, R^2 = Et) (53%) as the main product, which readily cyclised to oxadiazinone **12** (R^1 = CH_2CHMe_2) (71%). Reaction with β-alanine ethyl ester, for which cyclisation would result in a seven-membered ring, afforded only the expected amidoxime **8** (R^2 = $CH_2CH_2CO_2Et$, R^3 = H) (50%).

These results are consistent with nucleophilic addition of the amino acid ester to nitrile oxide **6** forming adduct **11**, followed by intramolecular cyclisation with expulsion of ethanol to afford oxadiazinone **12**, and finally nucleophilic ring opening to form dipeptide amidoxime **13** (Scheme 3). Similar facile cyclisations of amino acid amidoximes have been reported previously for adducts from benzonitrile oxide,[21] and for oligopeptides incorporating amidoxime links.[22]

Support for the pathway shown in Scheme 3 was the observation that, in the presence of silica, amidoxime **11** (R^1 = H, R^2 = Et) was smoothly converted to oxadiazinone **12** (R^1 = H) (~6 h in $CHCl_3$ at reflux, 2–3 days at room temperature). Furthermore, reaction of nitrile oxide **6** with glycylglycine ethyl ester afforded the dipeptide amidoxime **13** (R^1 = H, R^2 = Et) directly (43%), thus confirming the identity of the 2:1 adduct in the glycine ethyl ester reaction described above.

In conclusion, an efficient route to pyranosyl amidoximes has been established based on 1,3-addition of amines to pyranosyl nitrile oxides, which were generated from readily accessible hydroximoyl chlorides. The adducts resulting from the addition of amino acid esters cyclised to afford 3-pyranosyl-1,2,4-oxadiazin-6-ones; the feasibility of using the oxadiazinones as precursors for pyranosyl oligopeptides is currently under investigation.

Acknowledgements

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15. (*Z*)-*N*-benzyl-(2′,3′,4′-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (**8**, R^2 = Bn, R^3 = H): mp 64–66 °C (from hexane–EtOAc). $[\alpha]_D^{20}$ −3.7 (*c* = 0.54 $CHCl_3$). δ_H (250 MHz, $CDCl_3$) 1.95, 1.96, 1.97 (9H, 3s, 3 × $COCH_3$), 3.19 (1H, dd, 5a′-H), 3.89 (1H, d, 1′-H), 4.07 (1H, dd, 5e′-H), 4.38 (1H, dd, Bn-H_a), 4.39 (1H, dd, Bn-H_b), 4.92 (1H, ddd, 4′-H), 5.11 (1H, dd, 3′-H), 5.22 (1H, t, NH), 5.29 (1H, dd, 2′-H); *J*(X-Y)/Hz 1′–2′ 10.0, 2′–3′ 9.2, 3′–4′ 9.5, 4′–5a′ 10.4, 4′–5e′ 5.6, 5a′–5e′ 11.2, Bna-Bnb 14.6, Bna-NH 5.5, Bnb-NH 6.8; δ_C (63 MHz, $CDCl_3$) 20.5 (3 × $COCH_3$), 46.4 ($BnCH_2$), 67.7 (C-5′), 68.6, 68.7, 73.5 (C-2′,C-3′,C-4′), 76.1 (C-1′), 127.3, 127.4, 128.6 (5 × PhCH), 138.8 (PhC), 148.9 (C=N), 169.5, 169.7, 170.2 (3 × C=O). FAB-HRMS $[M + H]^+$ calculated for $C_{19}H_{24}N_2O_8$: 409.16109; found: 409.16095.
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19. (*Z*)-*N*-Carbethoxymethyl-(2′,3′,4′-tri-*O*-acetyl-β-D-xylopyranosyl)formamide oxime (**11**, R^1 = H, R^2 = Et): δ_H (250 MHz, $CDCl_3$) 1.23 (3H, t, CH_3), 1.96, 1.97, 1.98 (9H, 3s, 3 × $COCH_3$), 3.28 (1H, dd, 5a′-H), 3.85 (1H, d, 1′-H), 4.07 (2H, d, CH_2), 4.06 (1H, dd, 5e′-H), 4.16 (2H, q, OCH_2), 4.85–5.02 (1H, m, 4′-H), 5.12–5.21 (2H, m, 2′-H & 3′H), 5.48 (1H, t, NH); *J*(X-Y)/Hz 1′–2′ 9.8, 2′–3′ 9.2, 3′–4′ nd, 4′–5a′ 10.2, 4′–5e′ 5.5, 5a′–5e′ 11.5, CH_2-NH 5.8; δ_C (63 MHz, $CDCl_3$) 14.5 (CH_3), 21.0 (3 × CH_3), 44.7 (CH_2), 61.7 (OCH_2), 67.1 (C-5′), 68.9, 69.1, 73.6 (C-2′,C-3′,C-4′), 76.9 (C-1′), 148.1 (C=N), 170.1, 170.2, 170.5, 170.7 (4 × C=O). FAB-HRMS $[M + H]^+$ calculated for $C_{16}H_{24}N_2O_{10}$: 405.15092; found: 405.15194.
20. 3-(2′,3′,4′-Tri-*O*-acetyl-β-D-xylopyranosyl)-1,2,4-oxadiazin-6-one (**12**, R^1 = H): mp 165 °C (decomp.) (from hexane–EtOAc). δ_H (250 MHz, $CDCl_3$) 1.98, 1.99, 2.00 (9H, 3s, 3 × $COCH_3$), 3.37 (1H, dd, 5a′-H), 3.94 (1H, d, 1′-H), 3.95 (2H, s, CH_2), 4.14 (1H, dd, 5e′-H), 4.93 (1H, ddd, 4′-H), 4.98 (1H, dd, 3′-H), 5.26 (1H, t, 2′H), 5.61 (1H, br s, NH); *J*(X-Y)/Hz 1′–2′ 9.7, 2′–3′ 9.4, 3′–4′ 9.9, 4′–5a′ 10.3, 4′–5e′ 6.2, 5a′–5e′ 11.6; δ_C (63 MHz, $CDCl_3$) 20.4 (3 × $COCH_3$), 40.2 (CH_2), 66.5 (C-5′), 68.4, 69.1, 71.7 (C-2′,C-3′,C-4′), 74.9 (C-1′), 150.4 (C=N), 164.6 (C=O), 169.7, 169.8, 170.1 (3 × C=O). FAB-HRMS $[M + H]^+$ calculated for $C_{14}H_{18}N_2O_9$: 359.10906; found 359.10950. The structure of oxadiazinone **12** has been confirmed by X-ray crystallography (Parsons, S.; Paton, R. M.; Smellie, I. A. S. unpublished observations).
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