

**Regio- and Stereoselective Syntheses of Chiral Heterocyclic  
Carbohydrate Conjugates; Cesium Fluoride-Celite: A Solid Base for  
Syntheses of Esters, Ethers, Thioesters, Thioethers and Symmetrical  
Disulfides**

**Regio- und stereoselektive Synthesen von chiralen heterozyklischen  
Kohlenhydratkonjugaten; Cäsiumfluorid-Celit: Eine feste Base für die  
Synthese von Estern, Ethern, Thioestern, Thioethern und  
symmetrischen Disulfiden**

**DISSERTATION**

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der Naturwissenschaften**

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**Im Namen Gottes, voller Gnaden und Erbarmen**



**In the Name of Allah, the Most Beneficent, the Most Merciful**

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**Dedicated**  
to my mother

**Ruqaya BiBi (Late)**

Whose praise and encouragement has supported and guided me  
throughout my life

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**ABBREVIATIONS**

Ac	acetyl
AcONa	sodium acetate
aq.	aqueous
<i>as</i>	asymmetric
Bn	benzyl
BuLi	butyl lithium
Bz	benzoyl
cat.	catalytic
conc.	concentrated
d	doublet
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
DEAD	diethylazodicarboxylate
DIPT	diisopropyl tartrate
DMF	<i>N,N'</i> -dimethylformamide
DMSO	dimethyl sulfoxide
eq.	equation
equiv.	equivalent
EtOAc	ethyl acetate
EtOH	ethanol
GASPE	gated spin echo
HMPA	hexamethylphosphoric triamide

h	hour
LDA	lithium diisopropylamide
M	molar
m.p.	melting point
m-CPBA	meta-chloroperbenzoic acid
MeOH	methanol
min	minute
Ms	mesyl
n	normal
NBS	<i>N</i> -bromosuccinimide
NMR	nuclear magnetic resonance
<i>p</i>	para
PPL	porcine pancreatic lipase
Ppm	parts per million
Py	pyridine
rt	room temperature
s	singlet
NaH	sodium hydride
t	triplet
TBDPS	tertiary butyl diphenyl silyl
TBHP	tertiary butyl hydroperoxide
TEA	triethylamine
<i>tert</i>	tertiary
THF	tetrahydrofuran

TLC thin-layer chromatography

TsOH *p*-toluenesulfonic acid

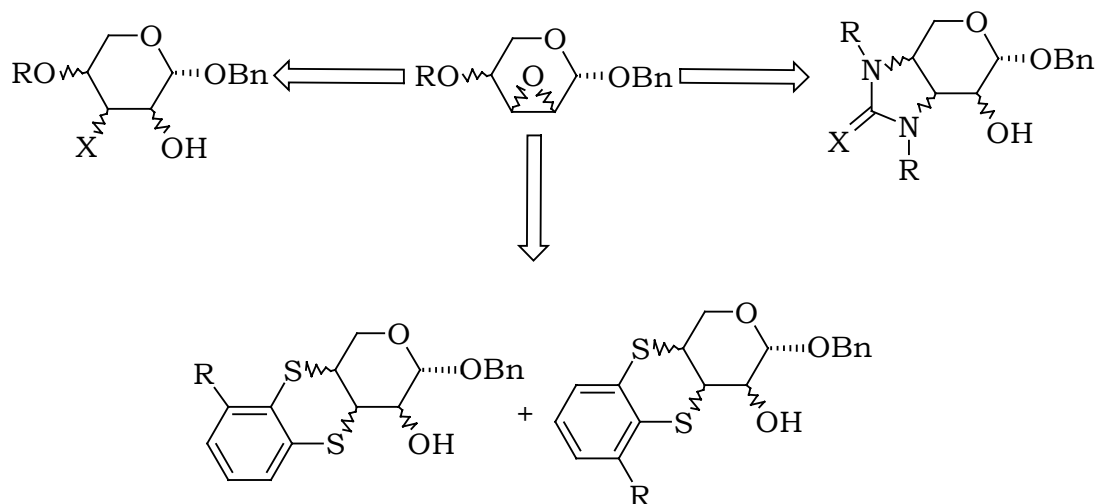
## A. INTRODUCTION

Heterocyclic compounds are the basis for the effectiveness and efficiency of many biochemical processes and pharmaceuticals [1]. Some pharmaceuticals are based on chiral heterocyclic systems [2]. However, the syntheses of chiral heterocycles tend to produce low yields and/or lack of regio- and stereoselectivity. Therefore, complicated procedures are often required to achieve the intended molecule. Thus, there exists the necessity to develop proficient and diastereoselective techniques for the synthesis of chiral heterocyclic systems in enantiopure form, particularly for the medical industry.

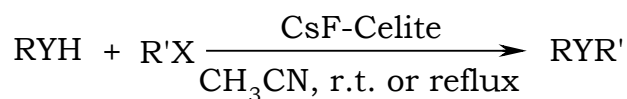
This thesis demonstrates a variety of examples for regio- and stereoselective transformation of 2,3-anhydropentoses delivering a series of chiral heterocyclic systems. Such carbohydrate-derived chiral templates can be further transformed into naturally occurring compounds or to interesting biologically active drugs (Fig. 1). E.g., 1,2-dihydro-(benzyl 3,4-dideoxy- $\alpha$ -D-arabinopyranoso)-[3,4-b]methylbenzo-[1,4]dithiane exhibits a significant *in vitro* toxicity in trypanosomes.

Furthermore, cesium fluoride-Celite is used as a solid base for convenient, efficient, inexpensive and novel syntheses of ethers, esters, thioethers, thioesters and symmetrical disulfides (Fig. 2).





**Fig. 1.** Representation of new targets, synthesized from a 2,3-anhydro-pentose, used as “chiron“ in this thesis.



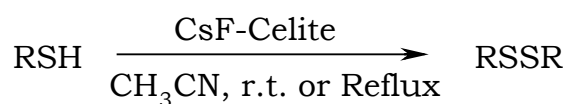
R = alkyl or aryl

Y = O or S

X = Cl, Br or I

R' = alkyl, acyl, benzyl or benzoyl

**a**



**b**

**Fig. 2a.** Scheme for the syntheses of thioethers, thioesters, esters and ethers catalyzed by CsF-Celite. Fig. **2b** Scheme for the syntheses of symmetrical disulfides using CsF-Celite as a solid base.

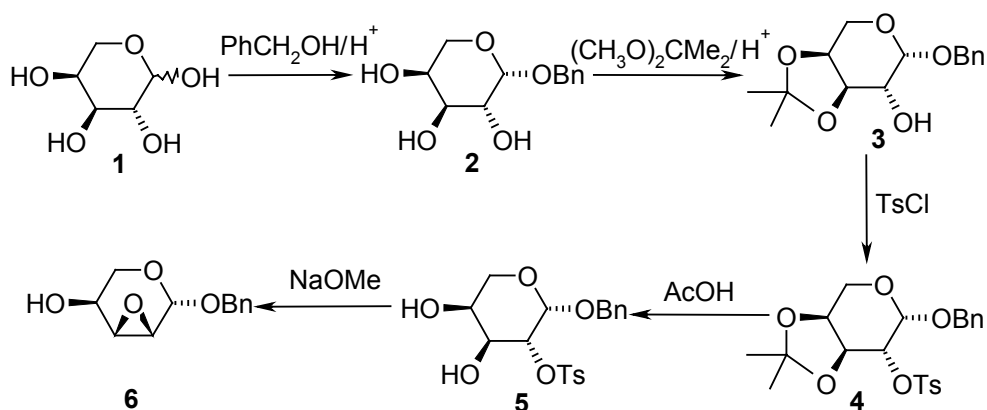
## B. RESULTS AND DISCUSSION

### B.I. 2,3-Anhydropentoses: Synthesis of Starting Materials

This part of the thesis demonstrates a variety of examples for regio- and stereoselective transformations of 2,3-anhydropentoses delivering a series of chiral targets (Fig. 1).

#### B.I.1. Synthesis of benzyl 2,3-anhydro- $\beta$ -L-ribofuranoside (**6**) [3a]

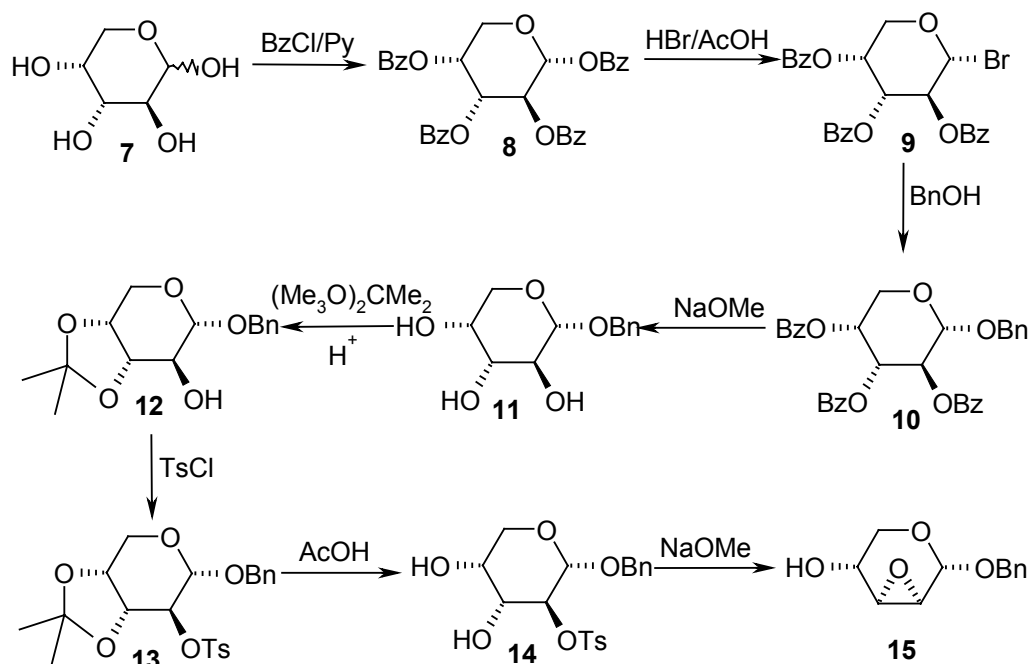
Compound **6** was synthesized in 6 steps, starting from commercially available L-arabinose. Benzylation of L-arabinose in the presence of hydrogen chloride leads to the anomerically protected benzyl  $\beta$ -L-arabinopyranoside (**2**) [4]. The two hydroxyl groups at C-3 and C-4 were protected *via* 2,2-dimethoxypropane and *p*-toluenesulphonic acid in acetone which formed benzyl 3,4-O-isopropylidene- $\beta$ -L-arabinopyranoside (**3**). The left behind free hydroxyl group at C-2 was tosylated with *p*-toluene sulphonyl chloride in pyridine, giving compound **4**. The isopropylidene protecting group was selectively removed from **4** with 90% acetic acid to yield **5** [5]. The target compound **6** was finally obtained by the action of sodium methoxide in methanol on compound **5**, followed by neutralization with dilute hydrochloric acid (Scheme 1).



**Scheme 1.** Synthesis of benzyl 2,3-anhydro- $\beta$ -L-ribofuranoside (**6**) from L-arabinose (**1**) *via* benzyl- $\beta$ -L-arabinopyranoside (**2**), benzyl 3,4-O-isopropylidene- $\beta$ -L-arabinopyranoside (**3**), benzyl 3,4-O-isopropylidene-2-O-*p*-tosylsulphonyl- $\beta$ -L-arabinopyranoside (**4**) and benzyl 2-O-*p*-tosylsulphonyl- $\beta$ -L-arabinopyranoside (**5**).

### B.I.2. Synthesis of benzyl 2,3-anhydro- $\alpha$ -D-ribofuranoside (**15**) [3a]

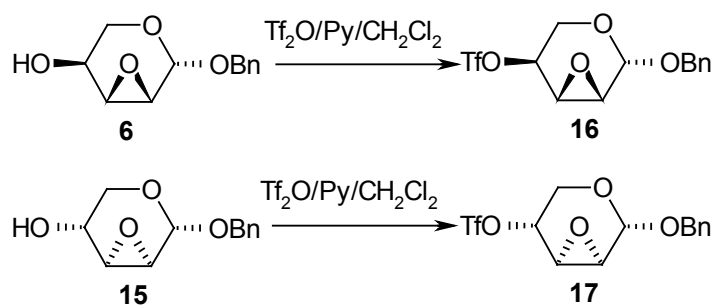
The synthesis of compound **15** was achieved from D-arabinose (**7**), whereby it is known that the direct benzylation does not yield the  $\alpha$ -anomer in high quantity due to the anomeric effect. In order to overcome this problem, one has to follow an alternative procedure (Scheme 3) [6] in which **7** was converted into the tetrabenzoyl derivative **8** by the action of benzoyl chloride in pyridine. The anomeric mixture of compound **8** was treated with hydrogen bromide in 30% acetic acid to furnish **9**, which, *via*  $S_N2$  reaction with benzyl alcohol, affords the  $\alpha$ -D-benzyl glycoside. The benzoyl groups in **10** were removed by sodium methoxide in methanol, to give benzyl  $\alpha$ -D-arabinopyranoside (**11**). The target compound **15** was obtained following analogous reaction sequences as described for the syntheses of compound **6** (Scheme 2) [3a].



**Scheme 2.** Synthesis of benzyl 2,3-anhydro- $\alpha$ -D-ribofuranoside (**15**) *via* D-arabinose (**7**), tetrabenzoyl of benzyl arabinopyranoside (**8**), 2,3,4-tri-O-benzoyl- $\beta$ -D-arabinopyranosyl bromide (**9**), benzyl 2,3,4-tri-O-benzoyl- $\alpha$ -D-arabinopyranoside (**10**), benzyl  $\alpha$ -D-arabinopyranoside (**11**), benzyl 3,4-O-isopropylidene- $\alpha$ -D-arabinopyranoside (**12**), benzyl 3,4-O-isopropylidene-2-O-*p*-tosylsulphonyl- $\alpha$ -D-arabinopyranoside (**13**) and benzyl 2-O-*p*-tosylsulphonyl- $\alpha$ -D-arabinopyranoside (**14**).

### B.I.3. Synthesis of benzyl 2,3-anhydro-4-O-triflylribofuranosides [3a]

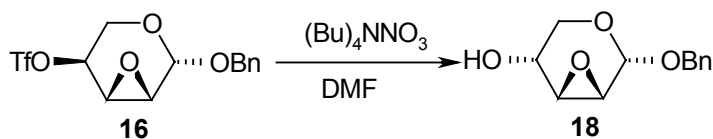
Triflation of the free hydroxyl group in **6** and **15** was successfully achieved at low temperature ( $-20^{\circ}\text{C}$ ) *via* treatment with trifloromethanesulphonic anhydride in dichloromethane. The triflates **16** and **17** were obtained in high yield upon basic work up at  $0^{\circ}\text{C}$  (Scheme 3).



**Scheme 3.** Synthesis of benzyl 2,3-anhydro-4-*O*-triflyl-β-*L*-ribofuranoside (**16**) and benzyl 2,3-anhydro-4-*O*-triflyl-α-*D*-ribofuranoside (**17**) from benzyl 2,3-anhydro-β-*L*-ribofuranoside (**6**) and benzyl 2,3-anhydro-α-*D*-ribofuranoside (**15**), respectively.

#### B.I.4. Synthesis of benzyl 2,3-anhydro-α-*D*-lyxofuranoside (**18**)

The synthesis of compound **18** was achieved from benzyl 2,3-anhydro-β-*L*-ribofuranoside (**6**). Firstly, **6** was converted into **16** with trifloromethanesulphonic anhydride in dichloromethane at low temperature (-20°C). **16** was crystallized from ethanol, and then reacted with tetrabutylammonium nitrate in 98% DMF to produce benzyl 2,3-anhydro-α-*D*-lyxofuranoside (**18**) (Scheme 4).



**Scheme 4.** Synthesis of benzyl 2,3-anhydro-α-*D*-lyxofuranoside (**18**) from benzyl 2,3-anhydro-β-*L*-ribofuranoside (**6**) *via* benzyl 2,3-anhydro-4-*O*-triflyl-β-*L*-ribofuranoside (**16**).

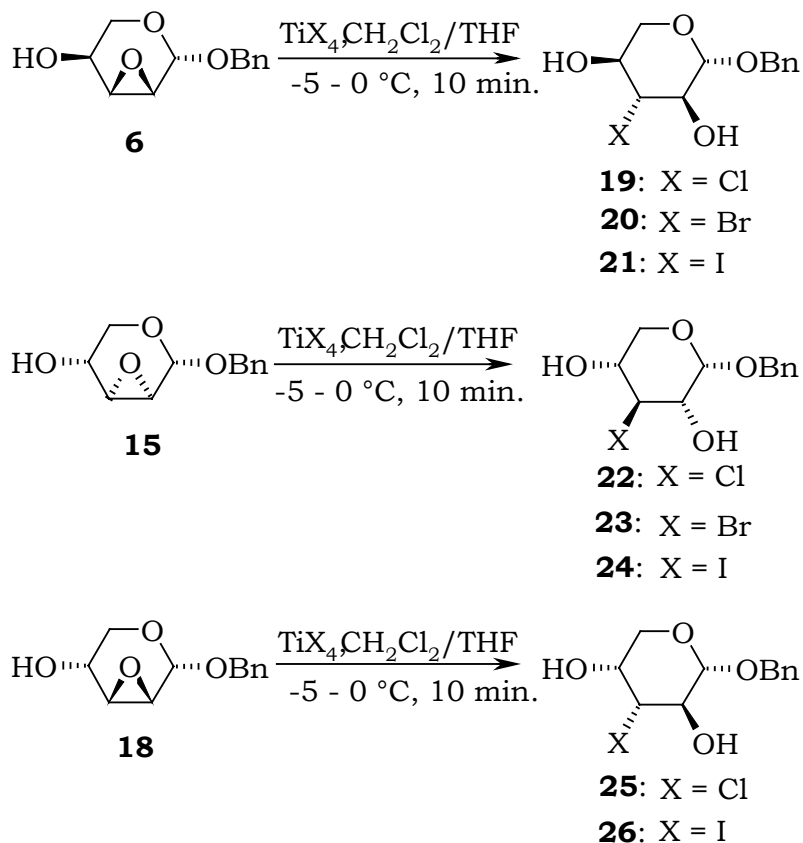
## **B. II. Regioselective Conversion of Anhydro Sugars into Halohydrins and X-Ray Study**

The synthesis of halodeoxy sugars has received continuous interest in recent years because of their key role in the access to deoxy, aminodeoxy and unsaturated sugars [7]. Moreover, anhydro sugars are stable intermediates with unique properties of the oxirane ring to serve, both, as a protective group and readily accessible reaction sites which have led to their extensive exploitation in carbohydrate synthesis. Besides, they have the advantage of convenient removal of protection after the desired synthetic strategy has been accomplished [8-12]. Furthermore, regioselective conversion of epoxides to halohydrins is a useful tool for stereospecific syntheses of various synthons, since optically active epoxides are readily available [13]. A variety of reagents are known to convert epoxides to halohydrins. In particular, metal halides such as  $\text{FeCl}_3$  [14],  $\text{SnCl}_2$ ,  $\text{SnBr}_2$ ,  $\text{SnI}_2$  [15] or  $\text{CoCl}_2$  in the presence of chlorotrimethylsilane [16] catalyse the cleavage of oxiranes. Several other methods are also known for the formation of halohydrins on carbohydrate templates, including Raney nickel(1), sulfuric acid [17], dibromomethyl methyl ether [18], dichloromethylene(dimethyl)ammonium chloride, iron(III) chloride triethylamine and lithium bromide [19] and carbon tetrachloride in the presence of triphenylphosphine [20]. A reaction yielding high regioselectivity is the trans-diaxial opening of oxirane rings of 2,3-anhydro sugars with titanium(IV) halide. The complex has recently

been used by Shimizu *et al.* to achieve epoxide cleavages in a group of halohydrins [21]. Chloro- and iododeoxy sugars were already prepared in high yield from our own laboratory using a dichlorobis(benzonitrile) palladium (II) complex [22] and a titanium isopropoxide reagent in the presence of iodine and samarium iodide [23].

Thus, in continuation of our efforts to synthesize of halodeoxy sugars in high yields and regioselectively, herewith a rapid, easy and regioselective route for the synthesis of halodeoxy sugars in high yields using titanium(IV) halides is reported.

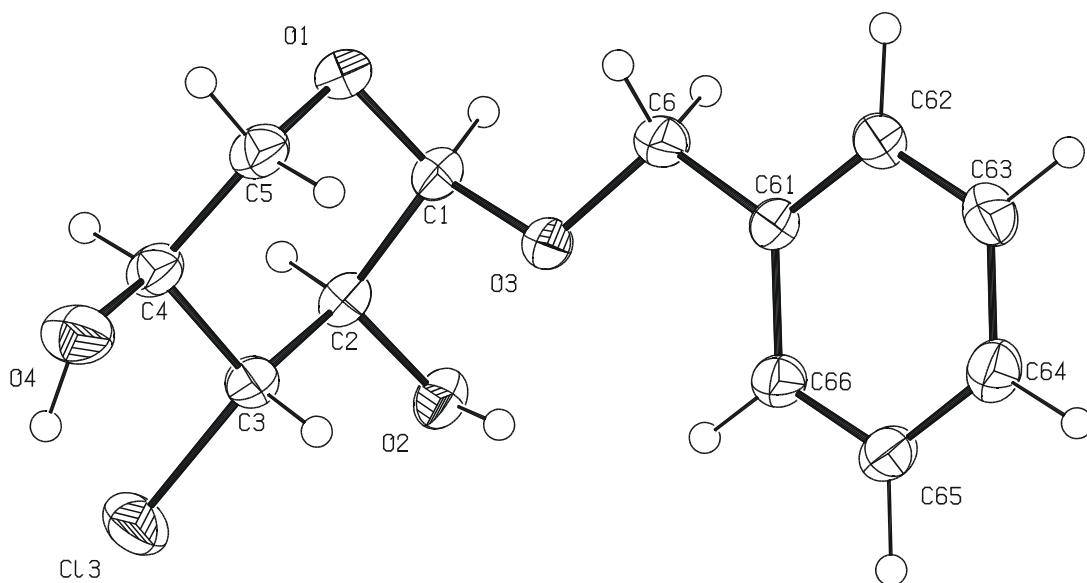
The anhydro sugars **6**, **15**, **18** exist almost entirely in the favoured half-chair conformations  $H^0_5$  and  $H^5_0$  [23-29]. Trans-diaxial opening by the titanium(IV) halide complex leads to benzyl 3-halo-3-deoxy- $\beta$ -L-xylopyranosides **19-21**, benzyl 3-halo-3-deoxy- $\alpha$ -D-xylopyranosides **22-24** and benzyl 3-halo-3-deoxy- $\alpha$ -D-arabinopyranosides **25-26**, respectively. The nucleophilic halide attack at position 3 is also favoured by steric considerations, as position 2 is comparatively blocked by the bulky substituent at C-1. The anhydro sugars benzyl 2,3-anhydro- $\beta$ -L-ribopyranoside (**6**), benzyl 2,3-anhydro- $\alpha$ -D-ribopyranoside (**15**) and benzyl 2,3-anhydro- $\alpha$ -D-lyxopyranoside (**18**) were synthesized according to the literature [30-32]. In the present work it is found that epoxide ring opening in this group of 2,3-anhydrosugars with titanium(IV) halide results in the transformation to the corresponding 3-halo-3-deoxy sugars (Scheme 5).



**Scheme 5.** Syntheses of halodeoxy sugars *via* 2,3-anhydroxyranosides.

It may be concluded from these results that epoxide-opening by titanium(IV) halide competes with other available methods in terms of yields and short preparation time of halodeoxy sugars. The reagent, however, imparts a greater degree of regioselectivity and effective control on epoxide migration. NMR spectroscopy established  ${}^1\text{C}_4$  conformations for the halodeoxy sugars **19-21**, **25** and **26** and  ${}^4\text{C}_1$  conformations for **22-24**. The structure of **19** was further proven unequivocally by X-ray analysis. Fig. 3 shows the ORTEP diagram of benzyl 3-chloro-3-deoxy- $\beta$ -L-xylopyranoside **19**. Crystal data, a summary of experimental details, selected bond lengths and bond angles for compound **19** are given in Tables 1 and 2.





**Fig. 3.** ORTEP diagram of benzyl 3-chloro-3-deoxy- $\beta$ -L-xylopyranoside (**19**).

**Table 1.** Crystal data and structure refinement for compound 19.

Compound	$C_{12}H_{15}ClO_4$
Formula weight	258.69
Temperature	213(2) K
Wavelength	1.54056 Å (Cu $K\alpha$ )
Crystal system / Space group	Orthorhombic/ $P2_12_12_1$
Unit cell dimensions	$a = 5.7958(4)$ Å $\alpha = 90$ deg. $b = 9.1465(18)$ Å $\beta = 90$ deg. $c = 22.148(3)$ Å $\gamma = 90$ deg.
Volume	$1174.1(3)$ Å <sup>3</sup>
$Z$	4
Density (calculated)	1.463 g/cm <sup>3</sup>
Absorption coefficient	2.911 mm <sup>-1</sup>

$F(000)$	544
Crystal size / Colour	0.60 x 0.20 x 0.05 mm / colourless
Theta range for data collection	5.23 to 64.94 deg.
Index ranges	$-6 \leq h \leq 1$ , $-10 \leq k \leq 10$ , $0 \leq l \leq 26$
Reflections collected	2690
Independent reflections	1997 [ $R(\text{int}) = 0.0559$ ]
Reflections observed	1964
Criterion for observation	$I > 2\sigma(I)$
Absorption correction	Psi scans
Max. and min. transmission	0.94275 and 0.67657
Refinement method	Full-matrix least-squares on $F^2$
Data / restraints / parameters	1997 / 0 / 215
Goodness-of-fit on $F^2$	1.115
Final $R$ indices [ $I > 2\sigma(I)$ ]	$R1 = 0.0478$ , $wR2 = 0.1342$
Absolute structure parameter	0.01(3)
Extinction coefficient	0.027(2)
Largest diff. peak and hole	0.253 and -0.375 e.A <sup>-3</sup>

**Table 2.** Bond lengths [ $\text{\AA}$ ] and angles [deg] for compound **19**.

Cl(3)-C(3)	1.795(3)
O(1)-C(1)	1.426(4)
O(1)-C(5)	1.432(4)
O(2)-C(2)	1.428(4)
O(3)-C(1)	1.409(4)

O(3)-C(6)	1.429(4)
O(4)-C(4)	1.414(4)
C(1)-C(2)	1.521(5)
C(2)-C(3)	1.528(4)
C(3)-C(4)	1.516(4)
C(4)-C(5)	1.514(5)
C(6)-C(61)	1.501(5)
C(61)-C(66)	1.388(5)
C(61)-C(62)	1.392(5)
C(62)-C(63)	1.391(5)
C(63)-C(64)	1.384(5)
C(64)-C(65)	1.379(5)
C(65)-C(66)	1.395(5)
C(1)-O(1)-C(5)	112.4(2)
C(1)-O(3)-C(6)	113.3(2)
O(3)-C(1)-O(1)	111.5(3)
O(3)-C(1)-C(2)	107.2(2)
O(1)-C(1)-C(2)	111.1(3)
O(2)-C(2)-C(1)	110.6(3)
O(2)-C(2)-C(3)	112.9(3)
C(1)-C(2)-C(3)	110.0(3)
C(4)-C(3)-C(2)	110.0(3)
C(4)-C(3)-Cl(3)	110.6(2)

C(2)-C(3)-C1(3)	109.9(2)
O(4)-C(4)-C(5)	105.9(3)
O(4)-C(4)-C(3)	113.7(3)
C(5)-C(4)-C(3)	107.7(3)
O(1)-C(5)-C(4)	111.6(3)
O(3)-C(6)-C(61)	110.0(3)
C(66)-C(61)-C(62)	119.3(3)
C(66)-C(61)-C(6)	121.7(3)
C(62)-C(61)-C(6)	119.0(3)
C(63)-C(62)-C(61)	120.3(3)
C(64)-C(63)-C(62)	120.1(3)
C(65)-C(64)-C(63)	119.8(3)
C(64)-C(65)-C(66)	120.4(3)
C(61)-C(66)-C(65)	120.0(3)

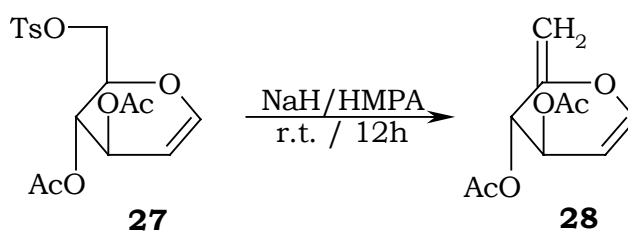
**B. III. Sodium Hydride/Hexamethylphosphoric Triamide: A New Efficient Reagent towards the Synthesis of Protected 1,2- and 5,6-Enopyranosides**

Numerous stable carbohydrate derivatives with an olefinic bond in their carbon skeleton are constituents of a series of naturally occurring compounds. Besides, these unsaturated carbohydrates represent a versatile family of chiral templates that can be further elaborated to useful synthons [33].

The introduction of double bonds in the carbohydrate framework results in the formation of three categories of compounds: alkenes, enols and enediols. Furthermore, the double bond may be exo- or endocyclic with respect to the carbohydrate ring (furanoid or pyranoid). Their various versatile properties and syntheses are reported comprehensively in the literature [33-35]. The normal standard procedure for the synthesis of glycals and 2-hydroxyglucals is the elimination of HBr from acylglycosyl bromides by treatment with Zn/Cu in acetic acid and its improved version [36] with secondary amines [34a,36,37], and, more recently, with the dimeric Ti(III) species  $(\text{Cp}_2\text{TiCl})_2$  [38a] or using sodium hydride in DMF [38b]. Much attention has been focused on the synthesis of 6-deoxy-hex-5-enopyranose derivatives, due to their unique synthetic utility, and on their transformation to cyclohexane (cylitols) and cyclopentane derivatives in which the ring oxygen atom of the sugar is replaced by a methylene group [39-40]. The hex-5,6-enopyranosides, also starting materials for the

synthesis of prostaglandins [40a], are accessible by treating 6-bromo-, 6-iodo-6-deoxyhexopyranosides with NaH/DMF [38], CsF/DMF [41], AgF/pyridine [42], 1,8-diazabicyclo[5.4.0]undec-7-ene(DBU)/CH<sub>3</sub>CN [43], NaI/BuNI/MS4A/DMSO and DBU/DMSO [44] or DBU/DMF [45]. These methods, however, often suffer from low yields or the formation of by-products.

Previously, the cleavage of silyl ethers was reported [46] with sodium hydride (NaH) in hexamethylphosphoric triamide (HMPA) and the selectivity of this reagent towards the cleavage of *tert*-butyldiphenylsilyl ethers in the presence of *tert*-butyldimethylsilyl ethers [47]. In an extension of this work on the reactivity of NaH in HMPA [48], 6-*O-p*-tosylsulphonyl-3,4-di-*O*-acetyl-D-glucal (**27**) was exposed to our reagent with the intention of cleaving the tosyl group, but surprisingly it was found that 3,4-di-*O*-acetyl-5,6-enoglucal was formed as an elimination product in 90% yield (Scheme 6).

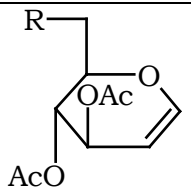
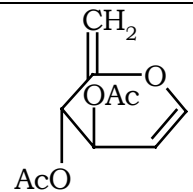
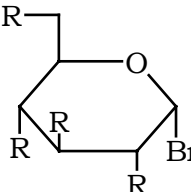
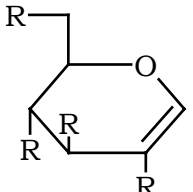


**Scheme 6.** Synthesis of 3,4-di-*O*-acetyl-1,2:5,6-dienopyranoside (**28**) via 6-*O-p*-tosylsulphonyl-3,4-di-*O*-acetyl-D-glucal (**27**).

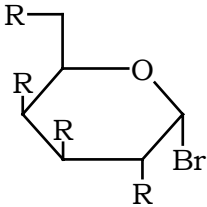
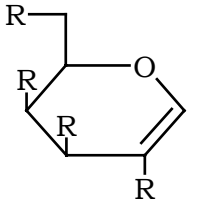
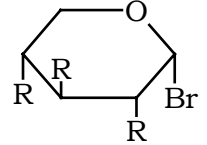
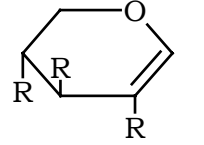
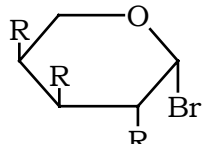
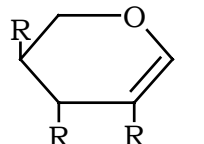
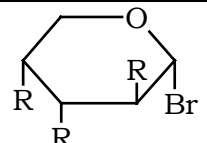
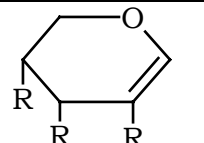
As shown in Table 3, the NaH/HMPA [48] reagent gives higher yields of elimination products compared to the reported NaH/DMF procedure [38], and is also suitable for dehydrotosylations. Using NaH/DMF for

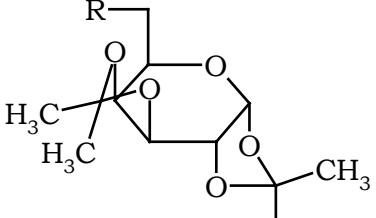
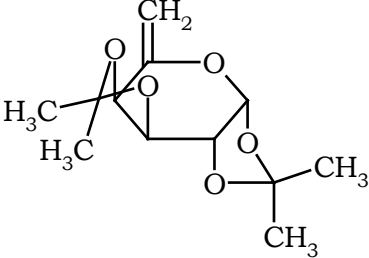
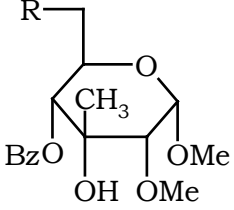
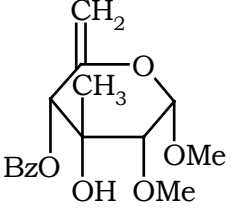
enteries 1,7,8, and 9 yielded less than 5% of elimination products; in addition a complex mixture of non-separable side products was obtained. To determine the general utility of this reagent, several tosylates and halides of different sugars were prepared, reacted with sodium hydride in HMPA and the elimination products in excellent yields isolated (Table 3). In conclusion, NaH in HMPA [48] is a reagent which produces elimination products from halides as well as *p*-toluenesulfonic acid esters in high yields. As this procedure has several advantages it is a valuable addition to existing methods.

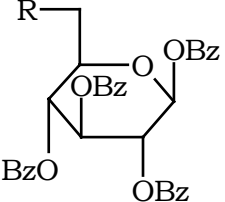
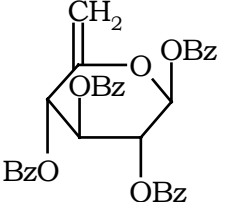
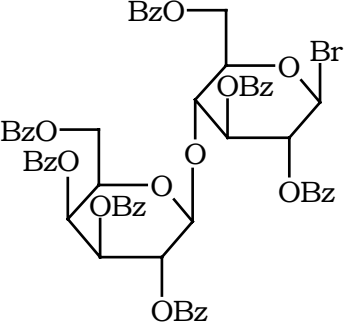
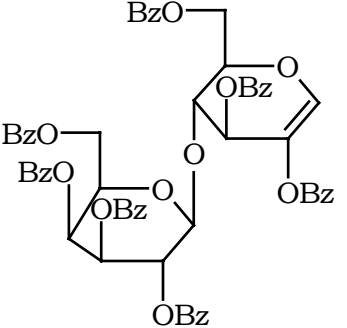
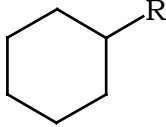
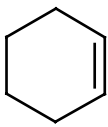
**Table 3.** Elimination of HX and HOTs with NaH in HMPA.

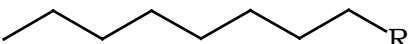
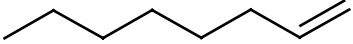
Entry	Starting Material	Product	Reaction time/h	% Yield (isolated)	% Yield (lit.)	Mp (lit.)	[a] <sup>25</sup> <sub>D</sub> <sup>a,b</sup>
1	 <p><b>27</b> R = OTs <b>29</b> R = Br <b>30</b> R = I</p>	 <p><b>28</b></p>	12 13 12	90 96 97	73 [49]	Oil	-176 <sup>a</sup>
2	 <p><b>31</b> R = OAc <b>32</b> R = OBz</p>	 <p><b>33</b> R = OAc <b>34</b> R = OBz</p>	12 12	91 93	56 [50] 78 [51] 53 [52]	64-67 121-122	-21 <sup>a</sup> -77 <sup>a</sup>



3	 <p><b>38</b> R = OAc <b>36</b> R = OBz</p>	 <p><b>37</b> R = OAc <b>38</b> R = OBz</p>	12 12	88 90	89 [53a], 37 [53b] 40 [54], 70 [55]	110-111 Oil	-6 <sup>a</sup> -52 <sup>b</sup>
4	 <p><b>39</b> R = OAc</p>	 <p><b>40</b> R = OAc</p>	12	89	Ref. [48]	81-82	-272 <sup>a</sup>
5	 <p><b>41</b> R = OAc</p>	 <p><b>42</b> R = OAc</p>	18	91	Ref. [48]	125-127	+282 <sup>a</sup>
6	 <p><b>43</b> R = OAc</p>	 <p><b>44</b> R = OAc</p>	24	87	51 [34c]	57-58	+205 <sup>a</sup>

7	 <p> <b>45</b> R = OTs  <b>46</b> R = Br  <b>47</b> R = I </p>	 <p><b>48</b></p>	22	95	70 [38b], 68 [56]	89-90	-135 <sup>b</sup>
8	 <p> <b>49</b> R = OTs  <b>50</b> R = Br  <b>51</b> R = I </p>	 <p><b>52</b></p>	17	90	77 [57]	113-114	+121 <sup>a</sup>

9	 <p><b>53</b> R = OTs <b>54</b> R = Br <b>55</b> R = I</p>	 <p><b>56</b></p>	23	92	67 [58]	131-132	-11 <sup>a</sup>
10	 <p><b>57</b></p>	 <p><b>58</b></p>	16	97	67 [35c]	93	+47 <sup>a</sup>
11	 <p><b>59</b> R = OTs <b>60</b> R = I</p>	 <p><b>61</b></p>	14 12	94 92	82 [59]	Liquid	N.A. <sup>c</sup>

12	 <b>62</b> R = OTs <b>63</b> R = I	 <b>64</b>	13	88	80 [60]	Liquid	N.A. <sup>c</sup>
			14	87			

a = (CHCl<sub>3</sub>, c = 1), b = (acetone, c = 1), c = not applicable.

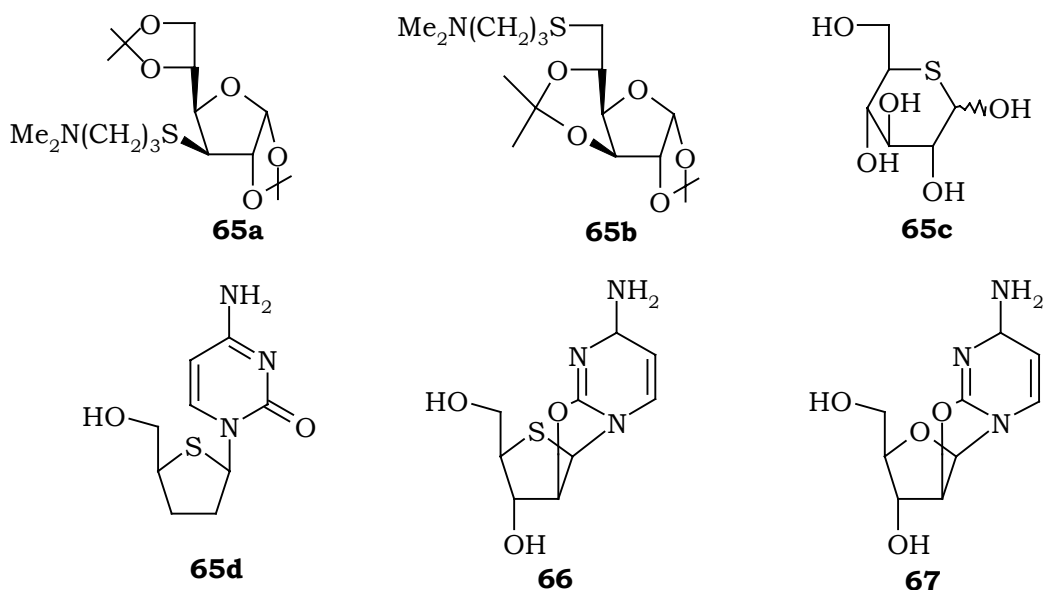
#### **B. IV. A Stereospecific Synthesis of Chiral 2,3-Dihydro-benzo-[1,4]-dithiane and 2,3-Dihydro-methylbenzo-[1,4]-dithiane Derivatives**

The preparations of monosaccharides in which one or more oxygen atoms are replaced by a sulfur atom have received considerable attention, primarily because these compounds provide a route to the synthesis of deoxy sugars [61]. Benzodithiane derivatives of carbohydrates are versatile intermediates for the synthesis of dithiosugars [62] and dideoxy sugars [63]. Many non-carbohydrate organic compounds containing a benzodithiane moiety have been reported to possess interesting biological activities [64]. Furthermore, considerable interest has been focused on the synthesis of thioanhydro- and sulfur- containing sugar derivatives [65].

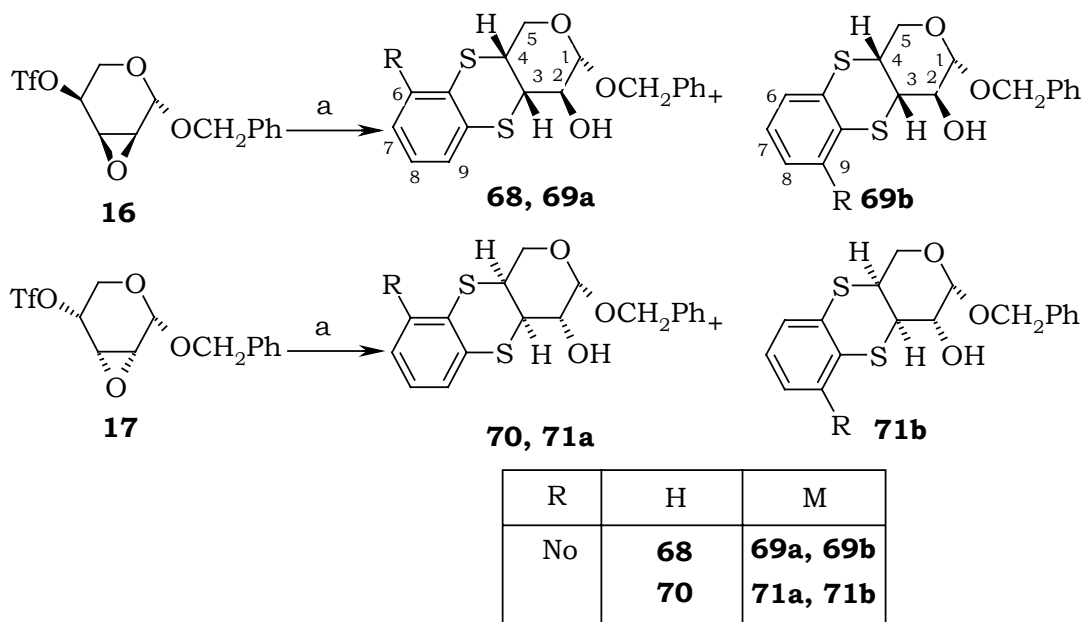
Thio sugars on the other hand, are of interest for, both, the chemical and pharmaceutical point of view. E.g., the 3-thio **65a** 6-thio **65b** derivatives of D-glucose have therapeutic effects on autoimmune disorders [66]. Thio sugars in which the ring oxygen atom is replaced by sulfur atom exhibits also interesting biological activities [67]. Thus, 5-thio-D-glucopyranose (**65c**) inhibits the transport of D-glucose and release of insulin [68], the 4'-thio-2',3'-dideoxynucleoside analogue **65d** shows *in vitro* activity against the human immunodeficiency virus (HIV) [69, 70], and the 4'-thio analogue **66** of 2,2'-anhydro-1- $\beta$ -D-arabinofuranosyl cytosine (**67**) has a comparable antitumor activity to 1- $\beta$ -D-arabinofuranosyl cytosine, which is used clinically against acute leukaemia and lymphoma [71]. However, to the best of our knowledge, no

sugar-embedded benzodithiane has been reported to test its biological activity.

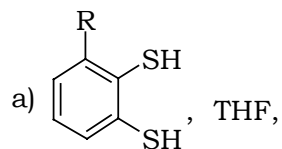
In connection with our interest of developing new synthetic methodologies for regio- and stereoselective syntheses of chiral heterocyclic systems on carbohydrate templates [72-73], herein we report the preparation of chiral 2,3-dihydro-[1,4]-benzodithiane and 2,3-dihydro-methylbenzo-[1,4]-dithiane derivatives with known absolute configurations from the easy accessible chiral synthons, benzyl 4-*O*-trifloxy-2,3-anhydro- $\beta$ -L-ribofuranoside **16** and benzyl 4-*O*-trifloxy-2,3-anhydro- $\alpha$ -D-ribofuranoside **17**.



**Fig. 4.** Some biologically important sulfur-containing compounds and analogues, 3-S-(3-*N,N*-dimethylaminopropyl)-1,2,5,6-*O*-diisopropylidene-3-thio- $\alpha$ -D-glucofuranose (**65a**) [66], 6-S-(6-*N,N*-dimethylaminopropyl)-1,2,3,5-*O*-diisopropylidene-6-thio- $\alpha$ -D-glucofuranose (**65b**) [66], 5-thio-D-glucopyranose (**65c**) [68], 2',3'-dideoxythiocytidine (**65d**) [70], 2,2'-anhydro-4'-thio-1- $\beta$ -D-arabinofuranosyl cytosine (**66**) [71], and 2,2'-anhydro-1- $\beta$ -D-arabinofuranosyl cytosine (**67**) [71].



**Scheme 7.** Synthesis of chiral benzodithiane and methylbenzodithiane derivatives. Reagents and conditions:



For the preparation of the benzodithiane derivatives, the epoxy triflates **16** and **17** were allowed to react with benzene-1,2-dithiol in THF at room temperature to yield after conventional work up the chiral benzodithiane derivatives **68** and **70**, respectively, (Scheme 7).

The preparation of chiral 2,3-dihydro-methylbenzo-[1,4]-dithianes start with the reaction of the epoxy triflates **16** and **17** with the dianion of the 3,4-dimercaptotoluene at 0 °C to yield the corresponding chiral methylbenzo-[1,4]-dithianes **69** and **71**, respectively (Scheme 7).

The <sup>13</sup>C NMR spectra of the benzodithiane derivatives **68** and **70**, show two methylene carbons (C-3, C-4) resonating at (47.5, 44.6), (44.3,

43.4), two methylene carbons (C-3, C-4) of **69** and **71** resonating at (47.3, 44.5), (44.0, 44.4), ppm, respectively. The predominant conformation of these compounds is extracted from the coupling constants of the  $^1\text{H}$  NMR spectra: For compounds **68** and **69** the  $\text{H}_1/\text{H}_2$  coupling constant of  $J = 6.1$  Hz, indicates a diaxial relationship, therefore, the predominant conformation is  $^1\text{C}_4$ . In the  $^1\text{H}$  NMR spectra of compounds **70** and **71**  $\text{H}_1/\text{H}_2$  a coupling of  $J = 3.3$  Hz is observed indicating a diequatorial relationship, and thus a  $^4\text{C}_1$  conformation.

#### **C.IV.1. Bioactivity of methylbenzodithiane (69) against trypanosomes**

Trypanosomes exist since more than 300 million years and are microscopic unicellular protozoa, almost ubiquitously found in insects, plants, birds, bats, fish, amphibians and mammals. Because of their early appearance on earth, they and their natural hosts have evolved together to ensure their mutual survival. Trypanosomes can be found mainly in tropical regions. Fortunately, only few species of trypanosomes are pathogenic.

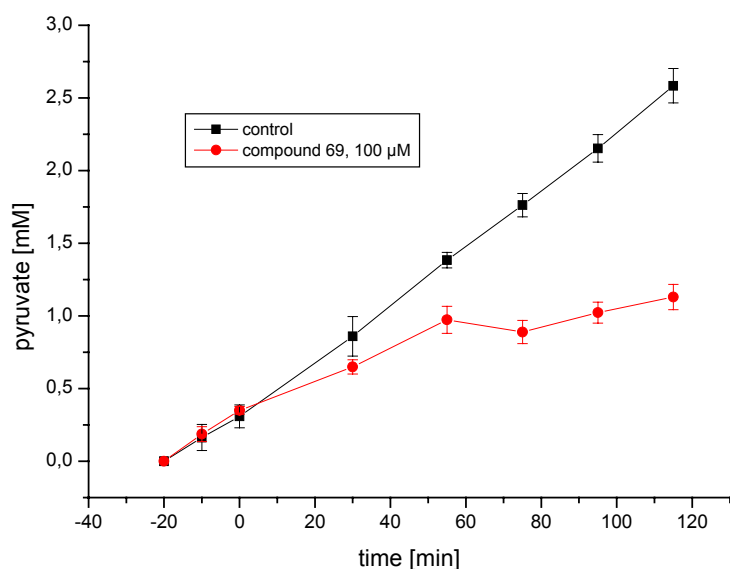
Trypanosomes are generally associated with diseases in Africa and South America. African trypanosomiasis is commonly known as sleeping sickness in humans and nagana ('loss of spirit' in Zulu language) in cattle. *Trypanosoma cruzi* causes Chagas' Diseases, a chronic human infection prevalent throughout Latin America, extending to the southern borders of the USA. Due to the lack of appropriate drugs, work has been in progress



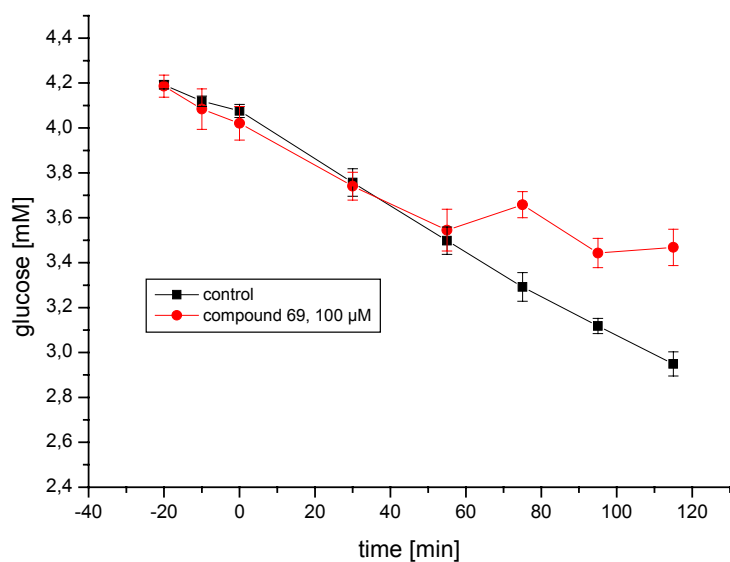
since many years to develop novel compounds that might prevent these partly lethal diseases from spreading even further.

#### **C. IV.2. In *vitro* toxicity of compound 69 in trypanosomes**

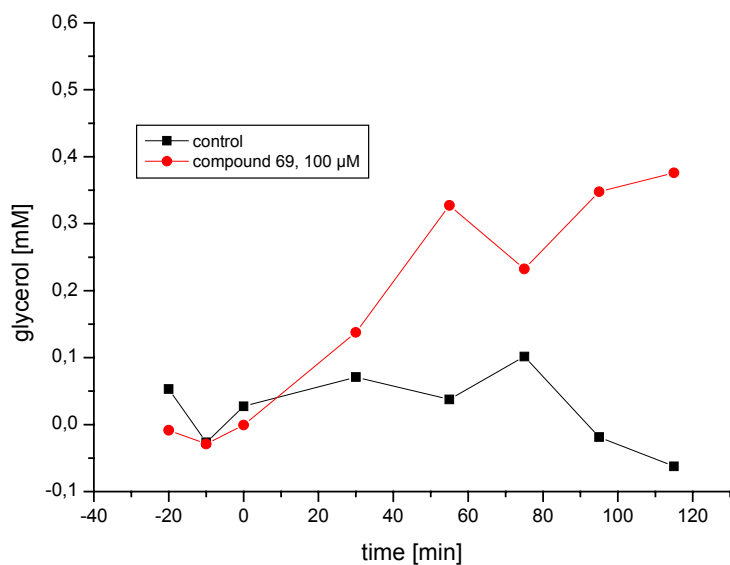
Obviously, the analyzed compound **69** exhibits a significant *in vitro* toxicity in trypanosomes. As the examination of their energy metabolism reveals, the cells reduce their pyruvate production prior to cell death. In the bloodstream form of *Trypanosoma brucei*, pyruvate is the end product of glycolysis, which is released into the medium. Therefore, it can be considered a measure of the parasites' metabolic activity. However, glucose consumption remains constant during the initial phase of the reduction of pyruvate production, whereas a significant production of glycerol commences. In bloodstream form of *T. brucei*, the major part of glycolysis takes place within characteristic organelles termed glycosomes. NADH produced by GAPDH reaction must be reoxidized *via* reduction of DHAP to glycerol-3-phosphate which is subsequently reoxidized by molecular oxygen under catalysis of the mitochondrial alternative oxidase, an enzyme specific to kinetoplasts. Inhibition of this enzyme eventually leads to a production of glycerol *via* the glycerol kinase reaction. The glycerol is then released into the surroundings of the cell and can be measured easily.



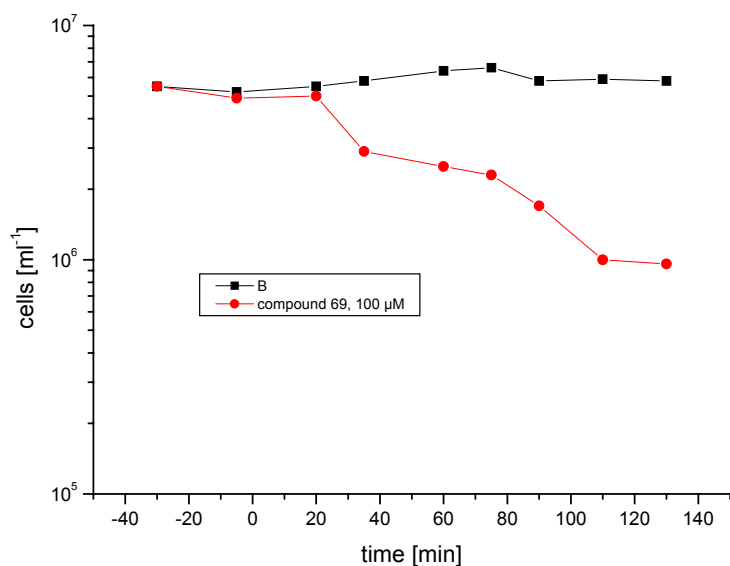
**Fig. 5.** Concentration of pyruvate in the medium of BF-221 during incubation with compound **69** (100  $\mu\text{M}$ ). Determination of pyruvate: Optical assay in 96-well plates employing lactate dehydrogenase and NADH; measured value:  $\text{OD}_{340}$ .



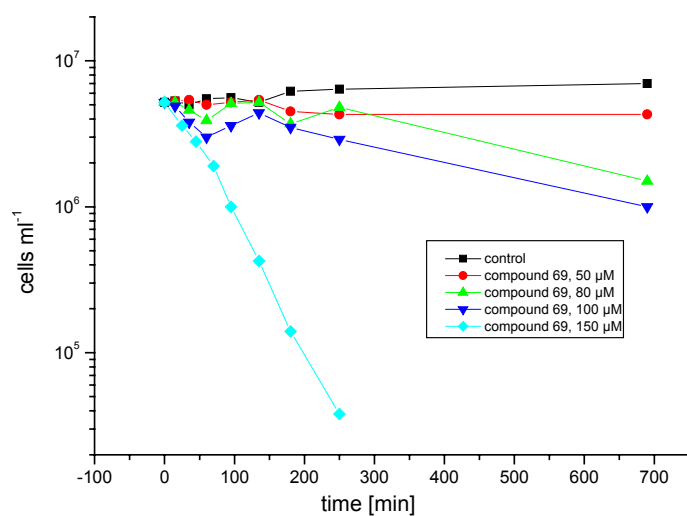
**Fig. 6.** Concentration of glucose in the medium of BF-221 during incubation with compound **69** (100  $\mu\text{M}$ ) (initial glucose conc.: 4.2). Determination of glucose: Coupled optical assay in 96-well plates with  $\text{NADP}^+$ , hexokinase, and glucose-6-phosphate dehydrogenase; measured value:  $\text{OD}_{340}$ .



**Fig. 7.** Concentration of glycerol in the medium of BF-221 during incubation with compound **69** (100  $\mu\text{M}$ ). Determination of glycerol: Coupled optical assay in 96-well plates with  $\text{NAD}^+$ , glycerokinase, and glycerol-3-phosphate dehydrogenase; measured value:  $\text{OD}_{340}$ .



**Fig. 8.** Cell density of BF-221 during incubation with compound **69** (100  $\mu\text{M}$ ). Cells were incubated at a density of  $5 \times 10^6$   $\text{ml}^{-1}$  under culture conditions at a concentration of 120  $\mu\text{M}$  of compound **69** in medium containing 4 mM glucose. Although cell density remains fairly high during the entire experiment, the cells cease to produce pyruvate and to consume glucose (as shown in figs 5 and 6).



**Fig. 9.** Cell density of bloodstream form *T. brucei* (BF-221) during incubation with different concentrations of compound **69** in culture medium. Cells were incubated at a density of  $5 \times 10^6 \text{ ml}^{-1}$  under culture conditions at a concentration of  $120 \mu\text{M}$  of the compound in medium containing  $4 \text{ mM}$  glucose.

Thus, the observed metabolic effects might suggest the alternative oxidase as one of the possible targets of compound **69**. Further studies to examine the effects of the drug are in progress. Above experiments present a significant toxic effect of compound **69** in *Trypanosoma brucei* in the low micromolar range (Figs 5-9).

## **B. V. An Efficient Synthetic Approach towards Thioesters and Thioethers Using CsF-Celite as a Solid Base**

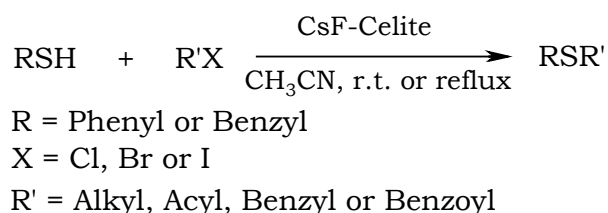
Protection of thiol groups is important in many areas of organic research, particularly in peptide, protein and  $\beta$ -lactam synthesis [74, 75a]. A free SH group can be protected as thioether, thioester or, after oxidation, as disulfide, from which it can be regenerated by reduction. Thioethers are, in general, formed by reaction of thiols or thiophenols under basic conditions with alkyl or benzyl halides. Thioesters are formed and cleaved in the same way as oxygen esters; they are more reactive against nucleophilic substitution [75b] and used as "activated esters".

The conversion of thiols to thioethers is usually achieved by reaction of thiolate with organic halides [76]. The yields and reaction conditions depend on the solvent, the basic catalyst and the acidity of thiol. These reactions require very long refluxing time and yields obtained were low [76].

Several other methods were employed for preparing thioethers which include palladium(0)-mediated alkylation [78], phase transfer catalysis [79], platinum(II) complex with bis(diphenylphosphino)methane [80], bis(diphenylstannyl)telluride [81], tin sulfides with aryl halides [82], ligand transfer reactions [83], organometallic sulfides [84], montmorillonite clay catalysis [85] and trifluoroacetic acid [86]. Recently, Yin and Pidgeon [87] reported a high yield method for the preparation of unsymmetrical sulfides by using very strong basic *n*-butyllithium.

In continuation of the interest in developing new organic synthetic methodologies [88], very recently the *N*-alkylation [89] of amines using CsF-Celite as a solid base was reported. In extension of this work on the reactivity of CsF-Celite, the utility of CsF-Celite for the synthesis of thioethers and thioesters in good yields is reported (Scheme 8).

The CsF-Celite-assisted coupling of aliphatic and aromatic thiols with various alkyl, acyl, benzyl and benzoyl halides resulted in thioethers and thioesters (Tables 4 and 5).



**Scheme 8.** Synthesis of thioesters and thioethers using CsF-Celite as a solid base.

In a typical reaction, to a mixture of thiol (1.0 mol) and CsF-Celite (1.5 mol) in 20 ml of acetonitrile, alkyl, acyl, benzyl, or benzoyl halides (2.0 mol) were added. Then, the mixture was stirred at room temperature or refluxed up to completion of the reaction, indicated by tlc monitoring. The reaction mixture was filtered and the solvent evaporated. The product was purified, whenever necessary, by column chromatography on silicagel using appropriate solvent systems like dichloromethane and petroleum ether etc. as eluents, to afford pure thioether or thioester products. The physical properties and NMR spectra of compounds agreed with those reported in the literature [90-108] and were furthermore identified by comparing the data with those of authentic samples. The unknown

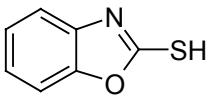
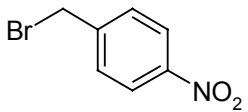
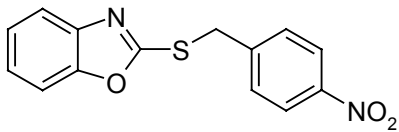
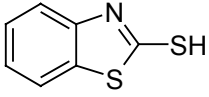
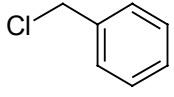
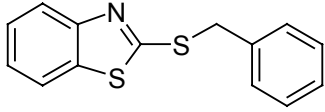
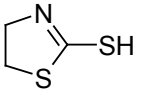
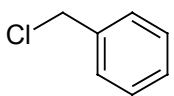
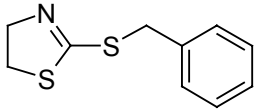
compounds were characterized by different spectroscopic techniques and their elemental analyses.

In conclusion, CsF-Celite-assisted reactions provide an easy access to thioethers as well as thioesters in good yields. As this methodology has several advantages, it is a valuable addition to existing methods. In short, this is an efficient, convenient, inexpensive, non-corrosive and practical method for preparing thioethers and thioesters.

**Table 4.** Synthesis of thioethers using CsF-Celite.

Entry	Substrate	Reagent	Product	Comp.	% Yield	Mp (lit.)
1	CH <sub>3</sub> CH <sub>2</sub> SH	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> Br	CH <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub> CH <sub>2</sub> SCH <sub>2</sub> CH <sub>3</sub>	<b>72</b>	60 <sup>b</sup>	Liquid [93]
2	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> SH	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Cl	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> SCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	<b>73</b>	81 <sup>b</sup>	Liquid [94]
3	C <sub>6</sub> H <sub>5</sub> SH	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Br	C <sub>6</sub> H <sub>5</sub> SCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	<b>74</b>	85 <sup>b</sup>	42-43, (43-44) [95]
4	C <sub>6</sub> H <sub>5</sub> SH	CH <sub>3</sub> CHICH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> SCH(CH <sub>3</sub> ) <sub>2</sub>	<b>75</b>	78 <sup>b</sup>	Liquid [96]
5	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SH	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Br	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	<b>76</b>	81 <sup>b</sup>	48-50, (48-49) [97]
6	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> SH	CH <sub>3</sub> CHICH <sub>3</sub>	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> SCH(CH <sub>3</sub> ) <sub>2</sub>	<b>77</b>	61 <sup>b</sup>	46-47, (46-47) [98]
7	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> SH	CH <sub>2</sub> =CHCH <sub>2</sub> Br	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> SCH <sub>2</sub> CH=CH <sub>2</sub>	<b>78</b>	75 <sup>b</sup>	38-39, (38-39) [99]
8	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> SH	CH <sub>3</sub> CH <sub>2</sub> I	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> SCH <sub>2</sub> CH <sub>3</sub>	<b>79</b>	60 <sup>b</sup>	40-42, (42-43) [90]
9	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> SH	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Cl	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> SCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	<b>80</b>	77 <sup>b</sup>	128-129, (128-129) [97]
10	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SH	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Cl	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SCH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> OCH <sub>3</sub> -4	<b>81</b>	86 <sup>b</sup>	90-91, (90) [100]

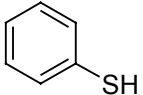
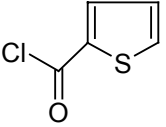
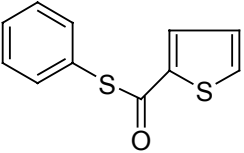
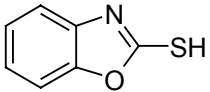
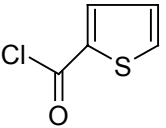
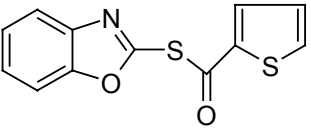
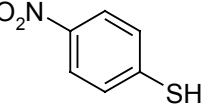
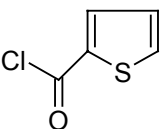
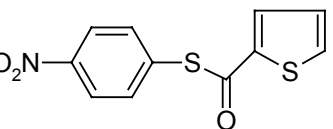


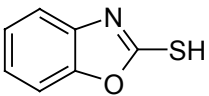
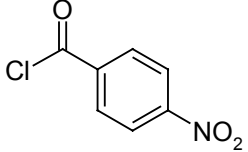
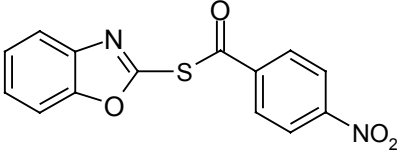
11				<b>82</b>	90 <sup>b</sup>	112-114, (114-115) [101]
12				<b>83</b>	74 <sup>a</sup>	38-40, (39-40)[ 102]
13				<b>84</b>	81 <sup>a</sup>	Liquid [103]

a = room temp. for 1 to 8h, b = reflux at 82 °C for 2 to 48 h.

**Table 5.** Synthesis of thioesters using CsF-Celite.

Entry	Substrate	Reagent	Product	Comp.	% Yield	Mp (lit.)
1	C <sub>6</sub> H <sub>5</sub> SH	C <sub>6</sub> H <sub>5</sub> COCl	C <sub>6</sub> H <sub>5</sub> SOC <sub>6</sub> H <sub>5</sub>	<b>85</b>	88 <sup>a</sup>	55-56, (55-57) [104]
2	C <sub>6</sub> H <sub>5</sub> SH	CH <sub>3</sub> COCl	C <sub>6</sub> H <sub>5</sub> SOCCH <sub>3</sub>	<b>86</b>	85 <sup>a</sup>	Liquid, [105, 106]
3	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SH	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> COCl	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SOC(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> CH <sub>3</sub>	<b>87</b>	89 <sup>b</sup>	Liquid
4	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SH	CH <sub>3</sub> COCl	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SCO <sub>2</sub> CH <sub>3</sub>	<b>88</b>	88 <sup>b</sup>	Liquid [107]

5	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SH	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>5</sub> COCl	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SOCC <sub>6</sub> H <sub>5</sub> OCH <sub>3</sub> -4	<b>89</b>	81 <sup>b</sup>	134-137, (134-136) [104]
6	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SH	C <sub>6</sub> H <sub>5</sub> COCl	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SOCC <sub>6</sub> H <sub>5</sub>	<b>90</b>	71 <sup>b</sup>	96-98, (97.5-99) [104]
7	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> SH	C <sub>6</sub> H <sub>5</sub> COCl	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> SOCC <sub>6</sub> H <sub>5</sub>	<b>91</b>	49 <sup>b</sup>	125-127, (126-127) [104]
8				<b>92</b>	83 <sup>b</sup>	60-62, (59-60) [108]
9				<b>93</b>	79 <sup>b</sup>	110-112
10				<b>94</b>	75 <sup>b</sup>	139-141

11				<b>95</b>	80 <sup>b</sup>	Liquid
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a = room temp. for 1 to 8h, b = reflux at 82 °C for 2 to 48 h.

## **B.VI. Cesium Fluoride-Celite: A Solid Base For Efficient Syntheses of Aromatic Esters and Ethers**

Hydroxyl groups are present in a number of compounds of biological and synthetic interests, including nucleosides, carbohydrates, steroids and alkaloids etc. During oxidation, acylation, halogenation with phosphorus or hydrogen halides, or dehydration reactions of these compounds, a hydroxyl group must be protected. Ethers and esters are among the most used protective groups in organic synthesis which were formed and removed under a wide variety of conditions [109]. However, these methods suffer serious limitations, when the substrates have acid or base labile moieties in their skeletons.

Yin et. al., [110] reported protection of hydroxyl groups as ethers using allyl bromide- and potassium fluoride-impregnated alumina. Hijfte and Little reported [111] *O*-alkylation of primary alcohols with benzyl bromide and  $\text{Ag}_2\text{O}$  in DMF, however, use of benzyl and benzoyl halides for the protection of primary and secondary alcohols is more often used in carbohydrate synthesis [112]. Although acylation of alcohols and phenols is routinely carried out using acid anhydrides or acyl halides in the presence of tertiary amines such as triethylamine and pyridine [113]. Vedejs and co-workers reported tributylphosphine as a catalyst for acylation of alcohols [114]. However, there is still a demand for base catalysts to generate ethers and esters *via* an environmentally friendly process. Herewith a practical and convenient method for the preparation

of ethers and esters is reported using cesium fluoride-Celite as a solid base which can overcome such types of limitations. Also the utility of CsF-Celite/CH<sub>3</sub>CN for the syntheses of ethers and esters is demonstrated using the reaction conditions, presented below.

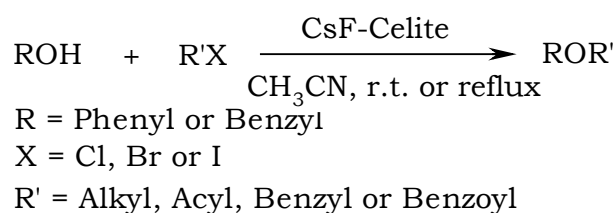
The importance of the fluoride ion as a catalyst for the promotion of various types of base catalyzed reactions in organic synthesis has been previously recognized [115]. The work of Clark and Miller, in particular, revealed that fluoride ion has an effect on coupling reaction because of its high capability of hydrogen-bond formation [116]. As reagents generating fluoride ion in these reactions, potassium, cesium and tetraalkylammonium fluorides are generally used so far. However, it is not easy to handle these hygroscopic reagents and the reproducibility of these reactions are invariably poor. Previously, poorly hygroscopic reagents generating a fluoride ion were designed by allowing cesium fluoride to be absorbed on celite [117]. The effect of cesium fluoride might be two-fold: (a) activation of the hydroxyl group by fluoride ion, whose ionic character is larger owing the low charge/surface area ratio of cesium cation and (b) activation of alkyl or acyl halide group by lewis acid type effect [118].

The reaction catalyzed by cesium fluoride-Celite are usually carried out under mild conditions with good yields and simple workup of these reactions; only filtration is required to remove the catalyst and evaporation of the filtrate afforded pure products. Previously in a short communication [117], esters of acids were prepared from carboxylic acids and alkyl halides *via* CsF-Celite catalysis, however, this report is limited only to the

formation of esters from acids, whereas, they have also used the alcoholic moieties in their reactions, but they overlooked the utility of this solid base in the same reaction conditions for the protection of an alcohol as an ether or ester. In this thesis the utility of the CsF-Celite system as an efficient, inexpensive and non-corrosive and environmentally friendly reagent is explored for the protection of a hydroxy function to an ether or ester depending upon the substrate used.

Several examples of CsF-Celite-assisted couplings of aromatic hydroxyl groups with various alkyl or acyl halides, resulting in alkylation, acylation benzoylation and benzoylation are presented in Tables 6 and 7.

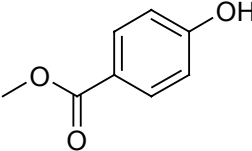
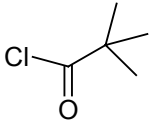
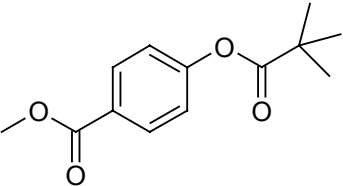
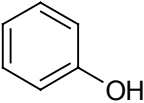
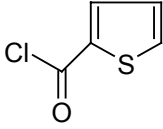
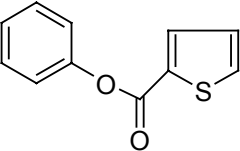
In a typical reaction, a mixture of alcohol (1.0 mol), CsF-Celite (1.5 mol) and alkyl or acyl halide (2.0 mol) in acetonitrile is stirred at room temperature or under reflux. The completion of reaction was monitored by TLC. After completion of reaction, the reaction mixture was filtered and the filtrate evaporated to afford the pure product.



**Scheme 9.** Synthesis of esters and ethers using CsF-Celite as a solid base.

**Table 6.** O-Acylation of hydroxyl groups using CsF-Celite.

<b>Entry</b>	<b>Substrate</b>	<b>Reagent</b>	<b>Product</b>	<b>Comp.</b>	<b>% Yield</b>	<b>Mp (lit.)</b>
1	C <sub>6</sub> H <sub>5</sub> OH	CH <sub>3</sub> COCl	C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> CH <sub>3</sub>	<b>96</b>	89 <sup>a</sup>	Liquid [119]
2	C <sub>6</sub> H <sub>5</sub> OH	C <sub>6</sub> H <sub>5</sub> COCl	C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	<b>97</b>	88 <sup>b</sup>	Liquid [120]
3	C <sub>6</sub> H <sub>5</sub> OH	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> COCl	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	<b>98</b>	84 <sup>a</sup>	128-129, (128-129) [121]
4	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OH	C <sub>6</sub> H <sub>5</sub> COCl	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	<b>99</b>	78 <sup>a</sup>	Liquid [122]
5	CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> OH	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> COCl	CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> NO <sub>2</sub> -4	<b>100</b>	76 <sup>b</sup>	96-98, (96.5-97.5) [121]
6	4-C <sub>6</sub> H <sub>5</sub> C <sub>6</sub> H <sub>4</sub> OH	C <sub>6</sub> H <sub>5</sub> COCl	4-C <sub>6</sub> H <sub>4</sub> C <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	<b>101</b>	63 <sup>b</sup>	149-151, (149-150) [123]
7	2-C <sub>6</sub> H <sub>5</sub> C <sub>6</sub> H <sub>4</sub> OH	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> COCl	2-C <sub>6</sub> H <sub>5</sub> C <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> (CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> CH <sub>3</sub>	<b>102</b>	59 <sup>b</sup>	Liquid [124]
8	4-C <sub>6</sub> H <sub>5</sub> C <sub>6</sub> H <sub>4</sub> OH	CH <sub>3</sub> COCl	4-C <sub>6</sub> H <sub>5</sub> C <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> CH <sub>3</sub>	<b>103</b>	78 <sup>b</sup>	87-88, (87-88) [125]

9				<b>104</b>	82 <sup>b</sup>	Liquid [126]
10				<b>105</b>	73 <sup>b</sup>	44-45, (44-45) [127]

a = room temp., b = reflux at 82 °C.

**Table 7.** O-Alkylation of hydroxyl groups using CsF-Celite.

Entry	Substrate	Reagent	Product	Comp	% Yield	Mp (lit.)
1	C <sub>6</sub> H <sub>5</sub> OH	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Br	C <sub>6</sub> H <sub>5</sub> OCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	<b>106</b>	91 <sup>a</sup>	39-40, (39) [128]
2	C <sub>6</sub> H <sub>5</sub> OH	CH <sub>2</sub> =CHCH <sub>2</sub> Br	C <sub>6</sub> H <sub>5</sub> OCH <sub>2</sub> CH=CH <sub>2</sub>	<b>107</b>	77 <sup>b</sup>	Liquid [129]



3	$C_6H_5OH$	$4-NO_2C_6H_4CH_2Cl$	$4-NO_2C_6H_4CH_2OC_6H_5$	<b>108</b>	71 <sup>b</sup>	90-91, (91) [130]
4	$C_6H_5CH_2OH$	$4-NO_2C_6H_4CH_2Br$	$4-NO_2C_6H_4CH_2OCH_2C_6H_5$	<b>109</b>	82	Liquid [131]
5	$3,5-(CH_3O)_2C_6H_3OH$	$CNCH_2CH_2Br$	$3,5-(CH_3O)_2C_6H_3OCH_2CH_2CN$	<b>110</b>	67 <sup>b</sup>	Liquid [132]
6	$4-C_6H_5C_6H_4OH$	$CH_3CH_2O_2CCH_2I$	$4-C_6H_5C_6H_4OCH_2CO_2CH_2CH_3$	<b>111</b>	89 <sup>b</sup>	60-61, (60) [133]
7	$4-C_6H_5C_6H_4OH$	$C_2H_5O_2CCH=CHCH_2Br$	$4-C_6H_5C_6H_4OCH_2CH=CHCO_2C_2H_5$	<b>112</b>	64 <sup>b</sup>	69-70
8	$2-C_6H_5C_6H_4OH$	$CH_2=CHCH_2Br$	$2-C_6H_5C_6H_4OCH_2CH=CH_2$	<b>113</b>	62 <sup>b</sup>	Liquid [134]
9	$4-NO_2C_6H_4OH$	$4-NO_2C_6H_4CH_2Br$	$4-NO_2C_6H_4OCH_2C_6H_4NO_2-4$	<b>114</b>	85 <sup>b</sup>	187, (187.4) [135]

10				<b>115</b>	88 <sup>b</sup>	Liquid
11		$\text{CH}\equiv\text{CCH}_2\text{Br}$		<b>116</b>	60	Liquid
12				<b>117</b>	54 <sup>b</sup>	Liquid [136]
13		$\text{CH}_2=\text{CHCH}_2\text{Br}$		<b>118</b>	68 <sup>b</sup>	Liquid [137]
14				<b>119</b>	81 <sup>b</sup>	Liquid [138]

a = room temp., b = reflux at 82 °C.

## **B. VII. A Novel Method for the Syntheses of Symmetrical Disulfides Using CsF-Celite as a Solid Base**

Disulfides are useful reagents in organic synthesis [139-140]. Disulfides are also used in sulphenylation of enolates and other anions [141], and they are essential moieties of biologically active compounds for peptide and protein stabilization [142]. As disulfides are relatively more stable to organic reactions, such as oxidation, alkylation and acylation compared to the corresponding free thiols, the thiol group can conveniently be protected as a disulfide. The desired thiol can be generated from the disulfide either by reduction or by other sulfur-sulfur bond cleavage reactions such as  $\text{CN}^-$ ,  $\text{OH}^-$  or hydrazines [143]. Various reagents for oxidative coupling of thiols to disulfides are described, e.g. iodine/hydrogen iodide [144], neat bromine [145],  $\text{FeCl}_3/\text{NaI}$  [146],  $\text{KMnO}_4/\text{CuSO}_4$  [147] and hydrogen peroxide in tetrafluoroethanol [148]. Furthermore, some of the non-metallic reagents like  $\text{Br}_2$  [149], DMSO [150] also accomplish thiol coupling, but they encounter the difficulty of product handling and isolation. Enzymatic [151] and electrochemical [152] methods are also known to perform this oxidative transformation. However, there is still an interest to develop a clean, mild and efficient method to synthesize aliphatic, aromatic and heteroaromatic disulfides.

In connection with studies, described before, on the synthesis of ethers, esters, thioethers and thioesters [153] using cesium fluoride-Celite as a solid base, the utility by preparing disulfides using similar reaction

conditions is explored. Moreover, the importance of the fluoride ion as a catalyst for the promotion of various types of base-catalyzed reactions in organic synthesis has been previously recognized [115]. In particular, the work of Clark and Miller revealed that the fluoride ion has an effect on coupling reactions because of its high capability of hydrogen-bond formation [116]. As reagents for generating the fluoride ion in these reactions, potassium, cesium and tetraalkylammonium fluorides were generally used so far. However, it is not easy to handle these hygroscopic reagents and the reproducibility of these reactions are invariably poor. Previously, poorly hygroscopic reagents generating fluoride ions were designed by allowing cesium fluoride to be absorbed on Celite [89, 117]. The effect of cesium fluoride-Celite might be two-fold: (a) activation of thiol groups by the fluoride ion, whose ionic character is increased owing to the low charge/surface area ratio of the cesium cation and (b) activation of the alkyl group by a Lewis acid type effect [118].

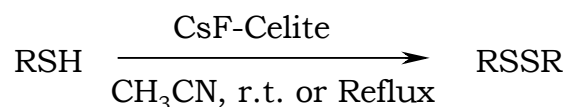
The present method is equally applicable for the oxidative coupling of alkyl, aryl and heterocyclic thiols, and the efficiency of the procedure is demonstrated also by coupling of long chain thiols (entries, 1-3). We have noticed that the coupling of dithiol compounds resulted in the formation of cyclic tetrasulfide products (compounds **131** and **132**).

The reactions catalyzed by cesium fluoride-Celite are usually carried out under mild conditions with good yields and simple workup; only filtration is required to remove the catalyst and often evaporation of the filtrate afforded pure products. The utility of the CsF-Celite system as an

efficient, inexpensive and non-corrosive reagent for the synthesis of disulfides and cyclic tetrasulfides is explored, depending upon the substrate used. Several examples of CsF-Celite-assisted couplings of aliphatic, aromatic and heteroaromatic thiols into disulfides are presented in Tables 8 and 9.

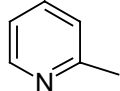
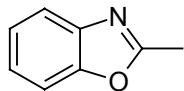
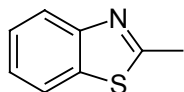
In a typical reaction, a mixture of thiol (1.0 mol), CsF-Celite (1.5 mol) in acetonitrile is stirred at room temperature or under reflux. The completion of reaction is monitored by TLC. After completion of the reaction, the reaction mixture is filtered and the filtrate evaporated to afford the pure product. The physical properties and NMR spectra of compounds agreed with those reported in the literature [147, 151, 154-160] and were furthermore identified by comparing the data with those of authentic samples. The unknown compounds were characterized by different spectroscopic techniques and their elemental analyses.

In conclusion, CsF-Celite-assisted reactions provide an easy access for the syntheses of disulfides in good yields. As this methodology has several advantages, it is a valuable addition to existing methods. In short, this approach is an efficient, convenient, inexpensive, non-corrosive and practical method for preparing symmetrical disulfides.



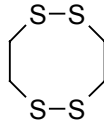
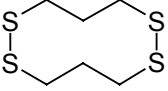
**Scheme 10.** Synthesis of symmetrical disulfides using CsF-Celite as a solid base.

**Table 8.** Synthesis of disulfides using CsF-Celite.

Entry	R	Compound	% Yield	Mp °C (lit.)
1	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> -	<b>120</b>	81 <sup>a</sup>	Liquid [147]
2	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>7</sub> -	<b>121</b>	81 <sup>a</sup>	Liquid [154]
3	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>11</sub> -	<b>122</b>	81 <sup>a</sup>	30-31, (30-31) [154]
4	C <sub>6</sub> H <sub>5</sub> -	<b>123</b>	78 <sup>a</sup>	59-61, (61) [155]
5	HOCH <sub>2</sub> CH <sub>2</sub> -	<b>124</b>	85 <sup>a</sup>	Liquid [155]
6	HOC <sub>6</sub> H <sub>4</sub> -	<b>125</b>	75 <sup>b</sup>	149-151, (149-150) [156]
7	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> -	<b>126</b>	81 <sup>a</sup>	40-42, (42-44) [151]
8	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> -	<b>127</b>	92 <sup>a</sup>	177-178, (177-178) [147]
9		<b>128</b>	90 <sup>b</sup>	57-58, (57) [155]
10		<b>129</b>	74 <sup>b</sup>	110-111, (110) [157]
11		<b>130</b>	81 <sup>a</sup>	183-184, (182-183.5) [158]

a = room temp. for 1 to 24h, b = reflux at 82 °C for 2 to 12h.

**Table 9.** Synthesis of cyclic tetrasulfides using CsF-Celite.

Entry	Product	Compound	% Yield	Mp °C (lit.)
1		<b>131</b>	79 <sup>a</sup>	100-101, (100) [159]
2		<b>132</b>	84 <sup>a</sup>	53-54, (53-54) [160]

a = room temp. for 1 to 24h.

## **C. EXPERIMENTAL PART**

### **Standard Experimental Procedures**

All chemicals and reagents were obtained from commercial suppliers and used as such without further purification. Solvents were dried and distilled according to standard procedures. The reactions were monitored by thin-layer chromatography, carried out on 0.25 mm silica gel plates (60 F-254, Merck, Darmstadt, Germany). Plates were visualized under UV light (where appropriate), sprayed with an orcinol/H<sub>2</sub>SO<sub>4</sub>/FeCl<sub>3</sub> solution and heated to develop. Column chromatography was performed on silica gel 60 (0.063-0.200 mm, Merck, Darmstadt, Germany) using the indicated solvent system. <sup>1</sup>H and <sup>13</sup>C NMR spectra were obtained in CDCl<sub>3</sub> on a Bruker AC 250 (<sup>1</sup>H NMR: 250 MHz, <sup>13</sup>C NMR: 63 MHz) or a Bruker WM 400 spectrometer (<sup>1</sup>H NMR: 400 MHz, <sup>13</sup>C NMR: 100 MHz). The chemical shifts are reported in parts per million (ppm) on a δ scale from TMS as internal standard. The EI, FAB and FD mass spectra were recorded on a Finnigan MAT 312 mass spectrometer connected to a PDO 11/34 (DEC) computer system. Optical rotations were obtained with an LEP AZ polarimeter (Zeiss, Jena) at 546 nm. All melting points are uncorrected.

### **C.I. Synthesis of Starting Materials**

#### **C.I.1. Benzyl 2,3-anhydro-β-L-ribofuranosides (6)**

**C.I.1.1. Benzyl  $\beta$ -L-arabinopyranoside (2)**

**2** was prepared from 50 g (0.33 mol) of L-arabinose (**1**) and 250 ml benzyl alcohol and 1L of abs. ether as described in ref. [3a]: Yield 73 g (91%); m.p. 171-172°C (ethanol/water), ref. [3a]: 168-171°C (ethanol);  $[\alpha]_D^{20} = +208^\circ$  (c = 1, water), ref. [3a]:  $+206^\circ$  (c = 0.3, water).

C<sub>12</sub>H<sub>16</sub>O<sub>5</sub> (240.23)

Calculated: C 59.99 H 6.7%,

Found: C 59.55 H 6.50%.

**C.I.1.2. Benzyl 3,4-O-isopropylidene- $\beta$ -L-arabinopyranoside (3)**

**3** was prepared from 70 g of benzyl- $\beta$ -L-arabinopyranoside (**2**) (0.29 mol), 500 ml 2,2-dimethoxypropane and 1.0 g. *p*-toluenesulphonic acid in 500 ml acetone. The resultant product **3** was used as such for the next step. Yield: 53 g (89%).

**C.I.1.3. Benzyl 3,4-O-isopropylidene-2-O-*p*-tolylsulphonyl- $\beta$ -L-arabinopyranoside (4)**

**4** was prepared from 75 g (0.27 mol) of **3**, in 500 ml pyridine and 200 g *p*-toluenesulphonyl chloride as described in ref. [3a]. Yield: 110 g (93%); m.p. 92°C (ethanol/water), ref. [3a]: 93-94°C (ethanol/water);  $[\alpha]_D^{20} = +185^\circ$  (c = 1, CHCl<sub>3</sub>), ref. [3a]:  $+183^\circ$  (c = 1, CHCl<sub>3</sub>).

C<sub>22</sub>H<sub>26</sub>O<sub>7</sub>S (434.47)

Calculated: C 60.81 H 7.37%,



Found: C 60.61 H 7.15%.

#### **C.I.1.4. Benzyl 2-O-*p*-tolylsulphonyl- $\beta$ -L-arabinopyranoside (5)**

**5** was prepared from 135 g (0.31 mol) of **4** and 100 ml 90% acetic acid as described in ref. [3a]. Yield: 110.4 g (90%);  $[\alpha]_D = +125^\circ$  (c = 1, CHCl<sub>3</sub>), ref. [3a]:  $+134^\circ$  (c = 1, CHCl<sub>3</sub>).

C<sub>19</sub>H<sub>22</sub>O<sub>7</sub>S (394.41)

Calculated: C 51.81 H 8.12%,

Found: C 57.71 H 8.05%.

#### **C.I.1. Benzyl 2,3-anhydro- $\beta$ -L-ribopyranosides (6)**

**6** was prepared from 110 g (0.28 mol) of **5**, 1.2 L methanol and 8.9 g (0.37 mol) sodium. as described in ref. [3a]. Yield: 39.7 g (67%); m.p. 77°C (EE), 76-77°C (EE);  $[\alpha]_D = -15^\circ$  (c = 1, EE), ref. [3a]:  $-13^\circ$  (c = 1, EE).

C<sub>12</sub>H<sub>14</sub>O<sub>4</sub> (222.22)

Calculated: C 64.86 H 6.34%,

Found: C 64.32 H 6.32%.

#### **C.I.2. Benzyl 2,3-anhydro- $\alpha$ -D-ribopyranoside (15)**

##### **C.I.2.1. Tetrabenzoate of $\beta$ -D-arabinopyranoside (8)**

**8** was prepared from 50 g (0.33 mol) D-arabinose (**7**) and 300 ml CH<sub>2</sub>Cl<sub>2</sub>, 100 ml pyridine and 250 ml benzoyl chloride as described in ref. [3a].

Yield 170 g (90%); m.p. 172°C (ethanol), ref. [3]: 175°C (ethanol);  $[\alpha]_D = -318^\circ$  (c = 1, CHCl<sub>3</sub>), ref. [3a]:  $-321^\circ$  [c = 0.3, CHCl<sub>3</sub>].

C<sub>33</sub>H<sub>26</sub>O<sub>9</sub> (566.56)

Calculated: C 69.96 H 4.63%,

Found: C 70.35 H 4.52%.

### C.I.2.2. 2,3,4-Tri-O-benzoyl-β-D-arabinopyranosyl bromide (9)

**9** was prepared from 173 g (0.30 mol) **8**, 200 ml CH<sub>2</sub>Cl<sub>2</sub> and 325 ml HBr/acetic acid as reported in ref. [3a]. Yield 125 g (79%); m.p. 142°C (CH<sub>2</sub>Cl<sub>2</sub>/EE), ref. [6]: 146-148°C (EE);  $[\alpha]_D = -348^\circ$  (c = 1, CHCl<sub>3</sub>), ref. [6]:  $-353^\circ$  [c = 1.4, CHCl<sub>3</sub>].

C<sub>26</sub>H<sub>21</sub>BrO<sub>9</sub> (566.56)

Calculated: C 59.44 H 4.03 Br 15.21%,

Found: C 59.68 H 4.00 Br 15.09%.

### C.I.2.3. Benzyl 2,3,4-tri-O-benzoyl-α-D-arabinopyranoside (10)

**10** was prepared from 125 g (0.22 mol) of **9**, 1 L benzyl alcohol, as described in ref. [6]. Yield 110 g (86%); m.p. 145°C (ethanol), ref. [6]: 143-144°C (ethanol);  $[\alpha]_D = -143^\circ$  (c = 1, CHCl<sub>3</sub>), ref. [6]:  $-146.7^\circ$  [c = 2.11, CHCl<sub>3</sub>].

C<sub>33</sub>H<sub>28</sub>O<sub>8</sub> (552.55)

Calculated: C 71.73 H 5.11%,

Found: C 72.26 H 5.07%.

**C.I.2.4. Benzyl  $\alpha$ -D-arabinopyranoside (11)**

**11** was prepared from 110 g (0.20 mol) of **10**, 365 ml CH<sub>2</sub>Cl<sub>2</sub> and 250 ml MeOH as described in ref. [3]. Yield 45 g (93%); m.p. 137°C (ethanol), ref. [3a]: 140-141°C (ethanol); [ $\alpha$ ]<sub>D</sub> = +13° (c = 1, water), ref.[3a]: +12.3° (c = 1.4, water).

C<sub>12</sub>H<sub>16</sub>O<sub>5</sub> (240.23)

Calculated: C 59.99 H 6.71%,

Found: C 59.80 H 6.50%.

**C.I.2.5. Benzyl 3,4-O-isopropylidene- $\alpha$ -D-arabinopyranoside (12)**

**12** was prepared from 47 g (0.18 mol) of **11**, 500 ml acetone, 300 ml 2,2-dimethoxypropane and 1.0 g. *p*-toluenesulphonic acid as described in ref. [1a]. Yield: 50 g (90%). The product was used directly for the next step.

C<sub>15</sub>H<sub>20</sub>O<sub>5</sub> (280.31)

**C.I.2.6. Benzyl 3,4-O-isopropylidene-2-O-tolylsulphonyl- $\alpha$ -D-arabinopyranoside (13)**

**13** was prepared from 50 g of **12**, 600 ml pyridine and 190 g *p*-toluenesulphonyl chloride as described in ref. [3a]. Yield 66 g (83%); m.p. 80°C (ethanol/water), ref. [3a]: 80-82°C (ethanol/water); [ $\alpha$ ]<sub>D</sub> = -8° (c = 1, CHCl<sub>3</sub>), ref.[3a]: -7° [c = 1, CHCl<sub>3</sub>].

C<sub>22</sub>H<sub>26</sub>O<sub>7</sub>S (434.47).

Calculated: C 60.81 H 6.02 S 7.37%,

Found: C 61.02 H 6.00 S 7.20%.

**C.I.2.7. Benzyl 2-O-tolylsulphonyl- $\alpha$ -D-arabinopyranoside (14)**

**14** was prepared from 50 g (0.112 mol) of **13**, 110 ml 90% acetic acid as described in ref. [3a]. Yield: 42 g (86%); m.p. 118°C (ethanol/water), ref. [3a]: 115-117°C (ethanol/water);  $[\alpha]_D^{25} = +22^\circ$  (c = 1, CHCl<sub>3</sub>), ref. [3a]:  $+25^\circ$  [c = 1, CHCl<sub>3</sub>].

C<sub>19</sub>H<sub>22</sub>O<sub>7</sub>S (394.41).

Calculated: C 57.81 H 5.61 S 8.12%,

Found: C 57.64 H 5.60 S 8.02%.

**C.I.2. Benzyl 2,3-anhydro- $\alpha$ -D-ribose (15)**

**15** was prepared from 40 g (0.102 mol) of **14**, 910 ml methanol and 3.0 g sodium as described in ref. [3a]. Yield: 21 g (72%); m.p. 97°C (EE/PE), ref. [3a]: 97-98°C (PE);  $[\alpha]_D^{25} = +190^\circ$  (c = 1, EE), ref. [3a]:  $+188^\circ$  [c = 1, EE].

C<sub>12</sub>H<sub>14</sub>O<sub>4</sub> (222.22)

Calculated: C 64.86 H 6.34%,

Found: C 64.56 H 6.22%.

**C.I.3. Benzyl 2,3-anhydro-4-O-triflyl- $\beta$ -L-ribose (16) and Benzyl 2,3-anhydro-4-O-triflyl- $\alpha$ -D-ribose (17)**

**16** and **17** were prepared from 2.22 g (10 mmol) **6** and **15** respectively, 75 ml CH<sub>2</sub>Cl<sub>2</sub>, 2 ml pyridine and 1.8 ml (10.97 mmol) trifloromethanesulphonic anhydride as described in ref. [3a].

**C.I.3.1. Benzyl 2,3-anhydro-4-O-triflyl- $\beta$ -L-ribofuranoside (16)**

Yield: 3.2 g (91%); m.p. 81°C (ethanol), ref. [3a]: 82-83°C (ethanol);  $[\alpha]_D^{25} = +15^\circ$  (c = 1, CHCl<sub>3</sub>), ref. [3a] :  $+16^\circ$  [c = 1, CHCl<sub>3</sub>].

C<sub>13</sub>H<sub>13</sub>F<sub>3</sub>O<sub>6</sub>S (354.29)

Calculated: C 44.07 H 3.69 S 9.04%,

Found: C 43.85 H 3.60 S 9.25%.

**C.I.3.2. Benzyl 2,3-anhydro-4-O-triflyl- $\alpha$ -D-ribofuranoside (17)**

Yield: 3.3 g (94.3%); m.p. 65°C (ethanol), ref. [3a]: 66-68°C (ethanol);  $[\alpha]_D^{25} = +129^\circ$  (c = 1, CHCl<sub>3</sub>), ref. [3a]:  $+128^\circ$  [c = 1, CHCl<sub>3</sub>].

C<sub>13</sub>H<sub>13</sub>F<sub>3</sub>O<sub>6</sub>S (354.29)

Calculated: C 44.07 H 3.69 S 9.04%,

Found: C 43.85 H 3.60 S 9.25%.

**C.I.4. Benzyl 2,3-anhydro- $\alpha$ -D-lyxofuranoside (18)**

Yield: 3.3 g (72 %); m.p. 66°C (ether/PE), ref. [3c]: 65-66°C (ether/PE);  $[\alpha]_D^{25} = +60.1^\circ$  (c = 1, CHCl<sub>3</sub>), ref. [3c]  $+60.1^\circ$  [c = 1, CHCl<sub>3</sub>].

C<sub>12</sub>H<sub>14</sub>O<sub>2</sub> (222.22)

Calculated: C 64.85 H 6.35

Found: C 64.36 H 6.31

## C.II. General Procedure for the Preparation of Halodeoxy Sugars [16b]

To a stirred solution of the 2,3-anhydro sugars 1-3 (354 mg, 1 mmol) in 20 ml dry THF, 2 equivalents of the corresponding titanium(IV) halide was added dropwise to the stirred mixture at 0 °C under argon. Stirring was continued at 0 °C for 5-20 min, until TLC showed no starting 2,3-anhydro sugar. The reaction mixture was then quenched with ice-cold water and extracted with ethyl acetate (3 x 20 ml). The organic layer was then collected, washed with water (30 ml), brine (30 ml), finally with water and the solvent evaporated in *vacuo*. The resulting crude solid was then collected and purified on a column of silica gel (20% ethyl acetate/dichloromethane).

### C.II.1. Benzyl 3-chloro-3-deoxy- $\beta$ -L-xylopyranoside (19)

Colourless needles; yield 97%. - M.p. 152 °C (lit. 152 °C [17]).; -  $[\alpha]_D = +6.85^\circ$  ( $c = 0.13$ ,  $\text{CHCl}_3$ ). -  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ ):  $\delta = 128.6$ - $128.2$  (Ar-C), 97.11 (C-1), 69.7 (C-2), 72.3 (C-4), 70.6 (OCH<sub>2</sub>Ph), 66.2 (C-5), 62.3 (C-3). - MS (FD):  $m/z = 258$ . -  $\text{C}_{12}\text{H}_{15}\text{ClO}_4$  (258.5): calcd. C 55.74, H 5.88; found: C 55.73, H 5.76.

### C.II.2. Benzyl 3-bromo-3-deoxy- $\beta$ -L-xylopyranoside (20)

Colourless needles; yield 82%. - M.p. 128-129 °C.; -  $[\alpha]_D = +85.10^\circ$  ( $c = 0.04$ ,  $\text{CHCl}_3$ ). -  $^1\text{H}$  NMR (250 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta = 7.31$ - $7.25$  (m, 5H, Ar-H), 4.86 (d, 1H,  $J = 11.1$  Hz, OCHHPh), 4.56 (d, 1H,  $J = 11.1$  Hz, OCHHPh),

4.28 (d, 1H,  $J = 7.0$  Hz, H-1), 4.01 (dd, 1H,  $J = 4.8, 11.2$  Hz, H-5), 3.68-3.92 (m, 2H, H-3, H-4), 3.57 (dd, 1H,  $J = 9.7, 7.0$  Hz, H-2), 3.18 (dd, 1H,  $J = 11.3, 9.1$  Hz, H-5). -  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ ):  $\delta = 128.1-128.6$  (Ar-C), 102.5 (C-1), 73.8 (C-2), 71.7 (C-4), 71.2 ( $\text{OCH}_2\text{Ph}$ ), 66.85 (C-5), 59.69 (C-3). - MS (FD):  $m/z = 303$ . -  $\text{C}_{12}\text{H}_{15}\text{BrO}_4$  (303.15): calcd. C 47.48 H 4.97; found: C 47.59, H 5.02.

### **C.II.3. Benzyl 3-iodo-3-deoxy- $\beta$ -L-xylopyranoside (21)**

Colourless needles; yield 91%. - M.p. 144-145 °C (lit. 145 °C [16]);  $[\alpha]_{\text{D}} = +156.45^\circ$  ( $c = 0.14$ ,  $\text{CHCl}_3$ ). -  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ ):  $\delta = 128.1-128.6$  (Ar-C), 102.5 (C-1), 74.2 (C-2), 71.89 (C-4), 71.5 ( $\text{OCH}_2\text{Ph}$ ), 67.4 (C-5), 40.4 (C-3). - MS (FD):  $m/z = 350$ . -  $\text{C}_{12}\text{H}_{15}\text{IO}_4$  (350.9): calcd. C 41.16; H 4.32; found: C 41.14, H 4.34.

### **C.II.4. Benzyl 3-chloro-3-deoxy- $\alpha$ -D-xylopyranoside (22)**

Colourless needles; yield 92%. - M.p. 158-160 °C (lit. 159-160 °C [17]); -  $[\alpha]_{\text{D}} = +18.45^\circ$  ( $c = 0.20$ ,  $\text{CHCl}_3$ ) -  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ ):  $\delta = 128.1-128.6$  (Ar-C), 97.2 (C-1), 72.4 (C-2), 71.5 (C-4), 69.8 ( $\text{OCH}_2\text{Ph}$ ), 66.4 (C-5), 62.4 (C-3). - MS (FD):  $m/z = 258$ . -  $\text{C}_{12}\text{H}_{15}\text{ClO}_4$  (258.5): calcd. C 55.68, H 5.84; found: C 55.61, H 5.75.

### **C.II.5. Benzyl 3-bromo-3-deoxy- $\alpha$ -D-xylopyranoside (23)**

Colourless needles; yield 75%. - M.p. 125-126 °C.; -  $[\alpha]_D = +139.13^\circ$  ( $c = 0.42$ ,  $\text{CHCl}_3$ ). -  $^1\text{H NMR}$  (250 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta = 7.24\text{-}7.40$  (m, 5H, Ar-H), 4.71\* (d, 1H,  $J = 11.91$  Hz, OCHHPH), 4.53 (d, 1H,  $J = 11.90$  Hz, OCHHPH), 4.65 (d, 1H,  $J = 7.4$  Hz, H-1), 4.02 (dd, 1H,  $J = 9.8, 10.4$  Hz, H-5), 3.47-3.77(m, 4H, H-2, H-3, H-4, H-5'). -  $^{13}\text{C NMR}$  (62.9 MHz,  $\text{CDCl}_3$ ):  $\delta = 128.1\text{-}128.6$  (Ar-C), 99.0 (C-1), 74.0 (C-2), 72.2 (C-4), 72.3 (OCH<sub>2</sub>Ph), 64.0 (C-5), 60.4 (C-3). - MS (FD):  $m/z = 303$ . -  $\text{C}_{12}\text{H}_{15}\text{BrO}_4$  (303.15): calcd. C 47.54, H 4.99; found: C 47.52, H 5.00.

#### **C.II.6. Benzyl 3-iodo-3-deoxy- $\alpha$ -D-xylopyranoside (24)**

Colourless needles; yield 81%. - M.p. 75-76 °C (lit. 75 °C [16]); -  $[\alpha]_D = +56.55^\circ$  ( $c = 0.12$ ,  $\text{CHCl}_3$ ). -  $^{13}\text{C NMR}$  (62.9 MHz,  $\text{CDCl}_3$ ):  $\delta = 128.1\text{-}128.6$  (Ar-C), 96.7 (C-1), 73.8 (C-2), 71.5 (C-4), 69.8 (OCH<sub>2</sub>Ph), 62.4 (C-5), 42.5 (C-3). - MS (FD):  $m/z = 350$ . -  $\text{C}_{12}\text{H}_{15}\text{IO}_4$  (350.9): calcd. C 41.16, H 4.32; found: C 41.20, H 4.28.

#### **C.II.7. Benzyl 3-chloro-3-deoxy- $\alpha$ -D-arabinopyranoside (25)**

Colourless needles; yield 94%. - M.p. 142-143 °C (lit. 142 °C [17]); -  $[\alpha]_D = +95.12^\circ$  ( $c = 0.18$ ,  $\text{CHCl}_3$ ). -  $^{13}\text{C NMR}$  (62.9 MHz,  $\text{CDCl}_3$ ):  $\delta = 128.1\text{-}128.6$  (Ar-C), 96.6 (C-1), 73.3 (C-2), 71.5 (C-4), 69.8 (OCH<sub>2</sub>Ph), 62.4 (C-5), 59.4 (C-3). - MS (FD):  $m/z = 258$ . -  $\text{C}_{12}\text{H}_{15}\text{ClO}_4$  (258.5): calcd. C 55.68, H 5.84; found: C 55.62, H 5.90.



**C.II.8. Benzyl 3-iodo-3-deoxy- $\alpha$ -D-arabinopyranoside (26)**

Colourless needles; yield 87%. - M.p. 160 °C (lit. 160 °C [16]).; -  $[\alpha]_D = -48.92^\circ$  ( $c = 12$ , MeOH). -  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ ):  $\delta = 128.1-128.5$  (Ar-C), 102.5 (C-1), 72.5 (C-2), 70.8 ( $\text{OCH}_2\text{Ph}$ ), 70.4 (C-4), 67.2 (C-5), 37.8 (C-3). - MS (FD):  $m/z = 350$ . -  $\text{C}_{12}\text{H}_{15}\text{IO}_4$  (350.9): calcd. C 41.03, H 4.30; found: C 41.10, H 4.37.

**C.III. General Procedure for Dehydrohalogenation and Dehydrotosylation [37b]**

To a suspension of oil-free NaH (2.2 molar equivalent) in anhydrous HMPA (1 ml per mmol) under argon was added at 0 °C dropwise halogenated or tosylated sugar (1 molar equivalent) in anhydrous HMPA (1 ml per mmol). The reaction mixture was then allowed to stir at room temperature for a given time period. After completion of the reaction (TLC analysis), quenching was performed with ether (10 ml per mmol) and filtered through a pad of Celite. The filtrate was washed with water to remove HMPA and then with a 1 % aqueous solution of HCl for neutralization. The organic phase was dried over anhydrous sodium sulfate and concentrated under vacuum. The residue was purified by short column chromatography (silica gel 60, Merck, mesh 0.063-0.200 mm).

**C.III.1. 2,3,4,6-Tetra-O-acetyl-2-hydroxy-D-glucal (33)**

Starting with 0.411 g (1 mmol) of **31**, after a reaction time of 18 h and column chromatography (ethyl acetate/hexane) pure **33** as white needles was collected. Yield 0.3 g (91%), ref. [38b] -25°; m.p. 64-67 °C, ref. [38b] 64-65 °C;  $[\alpha]^{25}_{\text{D}} = -21^{\circ}$  (CHCl<sub>3</sub>, c=1), ref. [38b] -20° (CHCl<sub>3</sub>, c=1); <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$ =6.5 (1H, s, H-1), 5.46 (1H, d,  $J_{3,4}=4.4$  Hz, H-3), 5.14 (1H, dd,  $J_{4,3}=4.4$ ,  $J_{4,5}=5.3$  Hz, H-4), 4.34 (1H, dd,  $J_{6,5}=6.4$ ,  $J_{6,6}=11.0$  Hz, H-6), 4.29 (1H, ddd,  $J_{5,4}=5.3$ ,  $J_{5,6}=6.4$ ,  $J_{5,6}=2.9$  Hz, H-5), 4.14 (1H, dd,  $J_{6,5}=2.9$ ,  $J_{6,6}=11.0$  Hz, H-6), 2.01, 2.00, 1.98, 1.97 (4 x 3H, s, COCH<sub>3</sub>); <sup>13</sup>C NMR (63 MHz, CDCl<sub>3</sub>):  $\delta$ =170.3, 169.9, 169.4, 169.3 (COCH<sub>3</sub>), 139.2 (C-1), 127.3 (C-2), 74.0 (C-5), 67.4 (C-4), 66.2 (C-3), 60.9 (C-6), 20.7, 20.7, 20.6, 20.5, 20-2 (COCH<sub>3</sub>).

C<sub>14</sub>H<sub>18</sub>O<sub>9</sub> (330.29)

Calculated: C 50.91 H 5.49%,

Found: C 50.87 H 5.62%.

### C.III.2. 2,3,4,6-Tetra-O-benzoyl-2-hydroxy-D-glucal (**34**)

Starting with 0.659 g (1 mmol) of **32**, after a reaction time of 16 h and column chromatography (ethyl acetate/hexane) pure **34** as white needles was collected. Yield 0.538 g (93%), ref. [38b] 70 %; m.p. 121-122 °C, ref. [38b]: 124 °C;  $[\alpha]^{25}_{\text{D}} = -77^{\circ}$  (CHCl<sub>3</sub>, c=1), ref. [38b] -86° (CHCl<sub>3</sub>, c=2.11); <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$ =8.14-7.35 (H,m, Ph), 6.98 (1H, s, H-1), 6.13 (1H, d,  $J_{3,4}=4.06$  Hz, H-3), 5.86 (1H, t,  $J_{4,3}=J_{4,5}=4.06$  Hz, H-4), 4.91 (2H, m, H-5,6), 4.72 (1H, m, H-6); <sup>13</sup>C NMR (63 MHz, CDCl<sub>3</sub>):  $\delta$ =166.1, 165.5, 165.4, 165.1 (PhCOO), 133.6, 129.2, 129.1, 129.0, 129.0, 128.5 (Ph), 128.5 (Ph),

128.4 (C-1), 128.4 (C-1), 127.5 (C-2), 73.9 (C-5), 68.3 (C-4), 66.6 (C-3), 61.6 (C-6).

$C_{39}H_{26}O_9$  (578.57)

Calculated: C 70.58 H 4.53%,

Found: C 70.41 H 4.62%.

### C.III.3. 2,3,4,6-Tetra-O-acetyl-2-hydroxy-D-galactal (37)

Starting with 0.411 g (1 mmol) of **35**, after a reaction time of 20 h and column chromatography (ethyl acetate/hexane) pure **37** as white needles was collected. Yield 0.29 g (85%), ref. [38b] 32 %; m.p. 110-111 °C, ref. [38b]: 110-112 °C;  $[\alpha]^{25}_D = 6^\circ$  ( $CHCl_3$ ,  $c=1$ ), ref. [38b]  $-5^\circ$  ( $CHCl_3$ ,  $c=1$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta=7.21-7.35$  (1H, d,  $J_{1,3}=1.2$ ) 5.77 (1H, td,  $J_{3,1}=1.2$ ,  $J_{3,4}=4.8$  Hz, H-3), 5.41 (1H, dd,  $J_{4,3}=4.8$   $J_{4,5}=2.1$  Hz, H-4), 4.32 (1H, m, H-5), 4.16 (1H, dd,  $H=5.1$ ,  $J_{6,6} 11.3$ , Hz, H-6), 2.02, 2.00, 1.97, 1.92 (4x3H, s,  $COCH_3$ );  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta=170.4$ , 169.9, 169.8, 169.3 ( $COCH_3$ ), 138.8 (C-1), (C-2), 73.3 (C-6), 64.0 (C-5), 63.9 (C-4), 61.3 (C-3), 20.7, 20.6, 20.5, 20.4 ( $COCH_3$ ).

$C_{14}H_{18}O_9$

Calculated: C 50.91 H 5.49%,

Found: C 50.79 H 5.56%.

### C.III.4. 2,3,4-Tri-O-acetyl-2-hydroxy-D-xylal (40)

Starting with 0.336 g (1 mmol) of **39**, after a reaction time of 12 h and column chromatography (ethyl acetate/hexane) pure **40** as white needles

was collected. Yield 0.23 g (89%), ref. [34a]: 24%; m.p. 81-82 °C; ref. [34a]: 81-82 °C;  $[\alpha]^{25}_{\text{D}} = +272^{\circ}$  ( $\text{CHCl}_3$ ,  $c=1$ ), ref. [34a]:  $-280^{\circ}$  ( $\text{CHCl}_3$ )  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta=6.66$  (1H, s, H-1), 5.27 (1H, t,  $J_{3,4}=J_{3,5}=1.8$  Hz, H-3), 4.89 (1H, dd,  $J_{4,3}=1.8$   $J_{4,5}=2.4$  Hz, H-4), 4.16 (1H, ddd,  $J_{5,3}=1.8$   $J_{5,4}=2.4$ ,  $J_{5,5}=12.5$  Hz, H-5), 3.88 (1H, dd,  $J_{5,4}=1.5$ ,  $J_{5,5}=12.5$  Hz, H-5), 2.02, 2.01, 1.99 (3x 3H, s,  $\text{COCH}_3$ );  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta=169.9$ , 169.9, 169.8 ( $\text{COCH}_3$ ), 141.3 (C-1), 127.4 (C-2), 67.3 (C-5), 64.2 (C-4), 63.3 (C-3), 20.9, 20.8, 20.6 ( $\text{COCH}_3$ ).

$\text{C}_{11}\text{H}_{14}\text{O}_7$  (258.22)

Calculated: C 51.17 H 5.47%,

Found: C 51.25 H 5.38%.

### **C.III.5. 2,3,4-Tri-O-acetyl-2-hydroxy-L-xylal (42)**

Starting with 0.336 g (1 mmol) of **41**, after a reaction time of 12 h and column chromatography (ethyl acetate/hexane) pure **42** as white needles was collected. Yield 0.237 g (92%), m.p. 125-127 °C;  $[\alpha]^{25}_{\text{D}} = +282^{\circ}$  ( $\text{CHCl}_3$ ,  $c=1$ ),  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta=6.67$  (1H, s, H-1), 5.27 (1H, t,  $J_{3,4}=1.8$  Hz, H-3), 4.89 (1H, dd,  $J_{3,4}=1.8$   $J_{4,5}=3.2$  Hz, H-4), 4.16 (1H, ddd,  $J_{5,3}=1.8$   $J_{5,4}=3.2$ ,  $J_{5,5}=2.5$  Hz, H-5), 3.89 (1H, dd,  $J_{5,4}=1.8$ ,  $J_{5,5}=12.5$  Hz, H-5), 2.02, 2.01, 1.99 (3x 3H, s,  $\text{COCH}_3$ );  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta=169.9$ , 169.9, 169.8 ( $\text{COCH}_3$ ), 141.3 (C-1), 127.4 (C-2), 67.3 (C-5), 64.2 (C-4), 63.3 (C-3), 20.9, 20.8, 20.6 ( $\text{COCH}_3$ ).

$\text{C}_{11}\text{H}_{14}\text{O}_7$  (258.22)

Calculated: C 51.17 H 5.47%,

Found: C 51.25 H 5.38%.

### C.III.6. 2,3,4-Tri-O-acetyl-2-hydroxy-L-arabinal (**44**)

Starting with 0.336 g (1 mmol) of **43** after a reaction time of 12 h and column chromatography (ethyl acetate/hexane) pure **44** as white needles was collected. Yield 0.25 (87 %) m.p 55-57 °C, ref[34c]: 59-60 °C;  $[\alpha]^{25}_D = +205^\circ$  (CHCl<sub>3</sub>, c=1), ref.[34c]:  $+202^\circ$  (CHCl<sub>3</sub>, c=2.5). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta=6.61$  (1H, s, H-1),  $5.65$  (1H, dd,  $J_{3,4}=4.1$ ,  $J_{3,5}=1.3$  Hz, H-3),  $5.22$  (1H, td,  $J_{4,3}=J_{4,5}=4.1$   $J_{4,5}=10.4$  Hz, H-4),  $3.97$  (ddd, 1H,  $J_{5,3}=1.3$ ,  $J_{5,4}=4.1$ ,  $J_{5,5}=10.4$  Hz, H-5),  $3.86$  (1H, t,  $J_{5,4}=J_{5,5}=10.4$  Hz, H-5),  $2.03$ ,  $2.01$ ,  $1.99$  (3x 3H, s, COCH<sub>3</sub>); <sup>13</sup>C NMR (63 MHz, CDCl<sub>3</sub>):  $\delta=141.2$ , (C-1),  $127.0$  (C-2), (C-5),  $64.4$  (C-4),  $62.6$  (C-3),  $20.8$ ,  $20.6$ ,  $20.5$  (COCH<sub>3</sub>).

C<sub>11</sub>H<sub>14</sub>O<sub>7</sub> (258.22)

Calculated: C 51.17 H 5.47%,

Found: C 51.10 H 5.59%.

### C.III.7. 6-Deoxy-1,2,3,4-di-O-isopropylidene-L-arabinohex-5-enopyranoside (**48**)

Starting with 0.411, 0.323 g (1 mmol) of **45**, **46** or **47**, after a reaction time of 31 h and column chromatography (ethyl acetate/hexane) pure **48** as white needles was collected. Yield 0.2-0.209 g (84-85 %) ref. [38b]: 0-70-78 %; m.p 89-90 °C, ref [38b]: 86-87 °C;  $[\alpha]^{25}_D = -135^\circ$  (CHCl<sub>3</sub>, c=1), ref.[38b]:  $-152^\circ$  CDCl<sub>3</sub>, c=1.86); <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta=5.52$  (1H, d,

$J_{1,2}=5.0\text{Hz}$ , H-14.95-4.71 (2H, m, H-6,6), 4.59 (1H, dd,  $J_{3,2}=2.4$ ,  $J_{4,3}=7.9$  Hz, H-3), 4.30 (1H, dd  $J_{2,2}=5.0$ ,  $J_{2,3}=2.4$  Hz, H-2), 4.25(1H, d,  $J_{4,3}=7.9$  Hz, H-4), 1.51, 1.44, 1.32, 1.24 (4x 3H, s, CH<sub>3</sub>).

C<sub>12</sub>H<sub>18</sub>O<sub>5</sub> (242.27)

Calculated: C 59.50 H 7.49%,

Found: C 59.38 H 7.40%.

**C.III.8. Methyl 4-O-benzyl-6-deoxy-3-C-methyl-2-O-methyl- $\alpha$ -D-ribohex-5-enopyranoside (52)**

Starting with 0.477, 0.389 or 436 g (1 mmol) of **49**, **50** or **51**, after a reaction time of 24 h and column chromatography (ethyl acetate/hexane) pure **52** as white needles was collected. Yield 0.247 g (80 %)ref. [57]: 77 %; m.p 113-114 °C, ref [57]: 112-113°C;  $[\alpha]^{25}_{\text{D}} = +121^{\circ}$  (CHCl<sub>3</sub>, c=1), ref.[ 57]:  $+126^{\circ}$  (CDCl<sub>3</sub>); <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta=8.2-7.58$  (5H, m, Ph), 5.45 (1H, d,  $J_{4,6}=2.3$ , Hz, H-4), 5.11 (1H, d,  $J_{1,2}=4$  Hz, H-1), 4.80 (2H, dd  $J_{6,6}=9.1$ , Hz,  $J_{6,4}=2.3$  Hz, H-6,6), 3.55 (6H, s, 2OCH<sub>3</sub>), 3.40, (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (63 MHz, CDCl<sub>3</sub>):  $\delta=150.7$  (C-5), 99.2 (C-6), 98.4 (C-1), 81.0 (C-2), 75.0 (C-3), 73.9 (C-4), 58.9, 56.9 (2OMe), 23.0 (Me).

C<sub>16</sub>H<sub>20</sub>O<sub>6</sub> (308.33)

Calculated: C 62.33 H 6.54%,

Found: C 62.45 H 6.49%.

**C.III.9. 1,2,3,4-Tetra-O-benzoyl-6-deoxy- $\beta$ -D-xylohex-5-enopyranoside (56)**

Starting with 0.747, 0.659 or 0.706 g (1 mmol) of **53**, **54** or **55**, after a reaction time of 27 h and column chromatography (ethyl acetate/hexane) pure **56** as white needles was collected. Yield 0.405-0.433 g (70-75 %) ref. [39c]: 77 %; m.p 131-132 °C, ref [39c]:129-130 °C;  $[\alpha]^{25}_D = -11^\circ$  (CHCl<sub>3</sub>, c=1), ref.[ 39c]:  $-8^\circ$  (CDCl<sub>3</sub>); <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta=8.6-7.4$  (20H, m, Ph), 6.69 (1H, d,  $J_{1,2}=2.9$ , Hz, H-1), 6.2 (1H, m, H-4), 5.91 (1H, t  $J_{4,9}$  Hz, H-3) 5.75 (1H, dd,  $J_{2,1}=2.9$ ,  $J_{2,3}=4.9$  (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (63)MHz, CDCl<sub>3</sub>):  $\delta=150.7$  (C-5), 99.2 (C-6), Hz, H-2), 5.1-4.9 (2H, m, H-6,6).

C<sub>34</sub>H<sub>26</sub>O<sub>9</sub> (578.57)

Calculated: C 70.60 H 4.53%,

Found: C 70.12 H 4.53%.

### C.III.10. 3,4-Di-O-acetyl-hex-1,2:5,6-dienopyranoside (28)

Starting with 0.381, 0.293 or 0.340 g (1 mmol) of **27**, **29** or **30**, after a reaction time of 12 h and column chromatography (ethyl acetate/hexane) pure **28** as white needles was collected. Yield 0.19-.02 g (90-95 %) m.p 64-65 °C,  $[\alpha]^{25}_D = -21^\circ$  (CHCl<sub>3</sub>, c=1), <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta=6.54$  (1H, dd,  $J_{1,2}=5.1$ ,  $J_{1,3} 0.6$  Hz, H-1), 5.42 (1H, dd,  $J_{4,6}=1.7$ ,  $J_{4,3}=3.1$  Hz, H-4), 5.10 (1H,dd,  $J_{3,4}=3.1$ ,  $J_{3,2}=1.4$  Hz, H-3), 5.08 (1H, dd,  $J_{2,1}=5.1$ ,  $J_{2,3}=1.4$  Hz, H-2), 4.91 (1H, d,  $J_{6,6}=1.6$ , H-6), 4.65 (1H, dt,  $J_{6,4}=1.7$ ,  $J_{6,6}=1.7$ ,  $J_{6,6}= 1.6$  Hz, H-6).

C<sub>10</sub>H<sub>12</sub>O<sub>5</sub> (212.29)

Calculated: C 56.61 H 5.70%,

Found: C 65.48 H 5.59%.

**C.III.11. 2,3,6-Tri-O-benzoyl-4-O-(2,3,4,5-tetra-O-benzoyl- $\beta$ -D-galactopyranosyl)-1,5-anhydro-D-arabinohex-1-enitol (58)**

Starting with 1.133 g (1 mmol) of **57**, after a reaction time of 13 h and column chromatography (ethyl acetate/hexane) pure **58** as white needles was collected. Yield 0.9255 g (88 %) m.p 93 °C, ref. [35c]: 91 %; m.p. 93-94 °C, ref. [35c]: 94-95 °C  $[\alpha]^{25}_D = +47^\circ$  (CHCl<sub>3</sub>, c=1), ref. [35c]:  $+52^\circ$  (CHCl<sub>3</sub>, c=1). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$ =7.99-7.07 (35H, m, Ph), 6.75 (1H, d, J=0.64 Hz, H-1), 6.23 (1H, d, J=4.46 Hz, H-3), 5.82 (1H, d, J=3.39 Hz, H-4), 5.76 (1H, dd, J=7.76, 10.39 Hz, H-2), 5.48 (1H, dd, J=3.40, 10.38 Hz, H-3), 5.10 (1H, d, J=7.97 Hz H-1), 4.56-4.11 (7H, m, H-4, 5,6,6); <sup>13</sup>C NMR (63 MHz, CDCl<sub>3</sub>):  $\delta$ =165.7, 165.5, 165.2, 165.1 (PhCO<sub>2</sub>), 139.9-127.1 (Ph), 139.9 (C-1) 127.2 (C-2), 101.9 (C-1), 75.4 (C-2), 74.9 (C-3), 71.9 (C-5), 71.7 (C-4), 69.9 (C-5), 67.9 (C-3), 68.8 (C-4), 61.8 (C-6), 61.4 (C-6).

**C.IV. General Procedure for the Preparation of Chiral Benzodithiane and Methylbenzodithiane**

To a suspension of 50 mg of NaH (2.3 mmol, 65% mineral oil) in dry THF (20 ml) at 0 °C under argon were added 2.5 mmol of benzene-1,2-dithiol or 3,4-dimercaptotoluene. After stirring at the same temperature, a solution of 254 mg (1 mmol) of the triflate sugar 16 or 17 in 10 ml of THF was added and the mixture was stirred for additional 2 h. The temperature was allowed to rise to rt and the mixture was stirred until the TLC shows the completion of the triflate. The reaction was quenched by addition of



saturated  $\text{NH}_4\text{Cl}$ , extracted with (3 x 30 ml) EtOAc, dried over  $\text{Na}_2\text{SO}_4$ , and concentrated under reduced pressure. Purification of the oil residue by column chromatography using 10% Petether/ $\text{CH}_2\text{Cl}_2$  yielded the title compounds.

**C.IV.1. 1,2-Dihydro-(benzyl 3,4-dideoxy- $\alpha$ -D-arabinopyranoso)-[3,4-b]-benzo-[1,4]-dithiane (68)**

White solid, m.p. 148-149 °C; (91% yield);  $[\alpha]^{20}_{\text{D}} = -163.1^\circ$  (c = 0.08,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.09$ -7.22 (m, 5H,  $\text{C}_6\text{H}_5$ ), 6.84-6.94 (m, 4H, H-7, H-8, H-9, H-10), 4.76 (d, J = 11.5 Hz, 1H, OCHHPH), 4.44 (d, J = 11.5 Hz, 1H, OCHHPH), 4.31 (d, J = 6.1 Hz, 1H, H-1), 4.02 (dd, J = 3.3, 9.1 Hz, 1H, H-5), 3.56 (dd, J = 3.3, 7.6 Hz, 1H, H-3), 3.72 (ddd, J = 2.7, 3.3, 10.1 Hz, 1H, H-4), 3.69 (dd, J = 6.5, 9.7 Hz, 1H, H-2), 3.27 (dd, J = 3.6, 8.95 Hz, 1H, H-5'), 2.48 (bs, 1H, O-H).  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta = 47.5$  (C-3), 44.6 (C-4), 65.8 (C-5), 70.0 (C-2), 70.6 (OCH<sub>2</sub>Ph), 102.7 (C-1), 125.8-129.5, ( $\text{C}_6\text{H}_5$ , C-7-10). FAB-MS: m/z = 346 [ $\text{M}^+ + 1$ ],  $\text{C}_{18}\text{H}_{18}\text{O}_3\text{S}_2$  (346.47).

**C.IV.2. 1,2-Dihydro-(benzyl 3,4-dideoxy- $\beta$ -L-arabinopyranoso)-[3,4-b]-benzo-[1,4]-dithiane (70)**

White solid, m.p. 128-130 °C; (87% yield);  $[\alpha]^{20}_{\text{D}} = 170.2^\circ$  (c = 0.10,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 6.99$ -7.17 (m, 5H,  $\text{C}_6\text{H}_5$ ), 6.80-6.87 (m, 4H, H-7, H-8, H-9, H-10), 4.86 (d, J = 3.3 Hz, 1H, H-1), 4.63 (d, J = 11.5 Hz, 1H, OCHHPH), 4.40 (d, J = 11.5 Hz, 1H, OCHHPH), 4.05 (dd, J =

2.75, 12.25 Hz, 1H, H-5), 3.45 (dd,  $J = 2.4, 6.1$  Hz, 1H, H-3), 3.53-3.63 (m, 2H, H-4, 5'), 3.99 (dd,  $J = 3.3, 8.5$  Hz, 1H, H-2), 2.10 (bs, 1H, O-H).  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta = 44.3$  (C-3), 43.4 (C-4), 61.6 (C-5), 68.0 (C-2), 69.4 ( $\text{OCH}_2\text{Ph}$ ), 97.0 (C-1), 124.9-139.3 ( $\text{C}_6\text{H}_5$ , C-7-10). FAB-MS:  $m/z = 346$  [ $\text{M}^{++1}$ ],  $\text{C}_{18}\text{H}_{18}\text{O}_3\text{S}_2$  (346.47).

**C.IV.3. 1,2-Dihydro-(benzyl 3,4-dideoxy- $\alpha$ -D-arabinopyranoso)-[3,4-b]-methylbenzo-[1,4]-dithiane (69)**

White solid, m.p. 96-97 °C; (72% yield);  $[\alpha]^{20}_{\text{D}} = -47.2^\circ$  ( $c = 0.18$ ,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.09$ -7.35 (m, 5H,  $\text{C}_6\text{H}_5$ ), 6.83-6.87 (m, 3H, H-8, H-9, H-10), 4.88 (d,  $J = 11.5$  Hz, 1H,  $\text{OCHHPH}$ ), 4.56 (d,  $J = 11.9$  Hz, 1H,  $\text{OCHHPH}$ ), 4.43 (d,  $J = 6.6$  Hz, 1H, H-1), 4.13 (dd,  $J = 2.2, 5.7$  Hz, 1H, H-5), 3.36 (m, 1H, H-3), 3.67 (ddd,  $J = 3.1, 7.5, 4.0$  Hz, 1H, H-4), 3.78 (dd,  $J = 2.6, 9.2$  Hz, 1H, H-2), 3.85 (dd,  $J = 2.2, 5.7$  Hz, 1H, H-5'), 2.24 (s, 3H,  $\text{CH}_3$ ) 2.58 (bs, 1H, O-H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 20.7$  ( $\text{CH}_3$ ), 47.3 (C-3), 44.5 (C-4), 65.7 (C-5), 69.6 (C-2), 70.4 ( $\text{OCH}_2\text{Ph}$ ), 102.6 (C-1), 120.7, 126.7, 126.8, 127.0 (C-7-10), 127.8-136.9, ( $\text{C}_6\text{H}_5$ ). FAB-MS:  $m/z = 360$  [ $\text{M}^{++1}$ ],  $\text{C}_{19}\text{H}_{20}\text{O}_3\text{S}_2$  (360.50).

**C.IV.4. 1,2-Dihydro-(benzyl 3,4-dideoxy- $\beta$ -L-arabinopyranoso)-[3,4-b]-methylbenzo-[1,4]-dithiane (71)**

White solid, m.p. 140-141 °C; (76% yield);  $[\alpha]^{20}_{\text{D}} = 54^\circ$  ( $c = 0.12$ ,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.28$ -7.37 (m, 5H,  $\text{C}_6\text{H}_5$ ), 6.82-7.13 (m, 3H, H-,

H-9, H-10), 4.79 (d,  $J = 11.4$  Hz, 1H, OCHHPH), 4.56 (d,  $J = 11.4$  Hz, 1H, OCHHPH), 4.36 (d,  $J = 3.3$  Hz, 1H, H-1), 4.20 (dd,  $J = 2.6, 12.3$  Hz, 1H, H-5), 3.67 (ddd,  $J = 3.1, 7.5, 4.0$  Hz, 1H, H-4), 4.03 (dd,  $J = 3.1, 9.7$  Hz, 1H, H-2), 3.85 (dd,  $J = 2.2, 5.7$  Hz, 1H, H-5'), 3.58-3.77 (m, 1H, H-3,4, 5'), 2.24 (s, 3H, CH<sub>3</sub>) 2.58 (bs, 1H, O-H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 20.7$  (CH<sub>3</sub>), 44.0 (C-3), 44.4 (C-4), 62.1 (C-5), 68.2 (C-2), 69.8 (OCH<sub>2</sub>Ph), 97.5 (C-1), 125.1-136.7 (C-7-10, C<sub>6</sub>H<sub>5</sub>). FAB-MS:  $m/z = 360$  [M<sup>++1</sup>], C<sub>19</sub>H<sub>20</sub>O<sub>3</sub>S<sub>2</sub> (360.50).

#### **C.IV.5.1. Cultivation of trypanosomes**

Bloodstream form of *Trypanosoma brucei* (BF-221) were seeded from frozen perms in modified Dulbecco's Eagle Medium (DMEM) at a density of approximately  $2 \times 10^5$  cells/ml and cultivated at 37°C under an atmosphere containing 5 % CO<sub>2</sub>. After the cells had grown up to a density of approximately  $8 \times 10^6$ , they were diluted to the initial density to yield a higher volume of the cell culture. Cells were spun down at late log-phase and resuspended in fresh medium to perform the assays. Determination of the cell density was achieved by counting in a modified Neubauer hemacytometer.

#### **C.IV.5.2. Determination of metabolites**

Cells were incubated at a density of  $5 \times 10^6$  ml<sup>-1</sup> under culture conditions at a concentration of 120  $\mu$ M of the compound in medium containing 4.2 mM glucose. For each time point, about  $1 \times 10^6$  cells were lysed by addition of

perchloric acid up to a final concentration of 3-5% and precipitated overnight at 4°C. Determination of metabolites of glycolysis was achieved via optical assays in a 96-well plates (MRX II Revelation ELISA) reader from Dynex as follows:

Determination of pyruvate: Optical assay in 96-well plates employing lactate dehydrogenase and NADH; measured value: OD<sub>340</sub>.

Determination of glucose: Coupled optical assay in 96-well plates with NADP<sup>+</sup>, hexokinase, and glucose-6-phosphate dehydrogenase; measured value: OD<sub>340</sub>.

Determination of glycerol: Coupled optical assay in 96-well plates with NAD<sup>+</sup>, glycerokinase, and glycerol-3-phosphate dehydrogenase; measured value: OD<sub>340</sub>.

#### **C.V. General Procedure for Syntheses of Thioethers and Thioesters**

[153b]

To a stirred solution of thiol compound (1.0 mol) and CsF-Celite (1.5 mol) in 20 ml of acetonitrile, alkyl, acyl, benzyl, or benzoyl halide (2.0 mol) was added. Then the mixture was continued for stirring at room temperature or reflux up to completion of the reaction, indicated by tlc monitoring. The reaction mixture was filtered, the solvent evaporated and the residue

dissolved in ethyl acetate. Precipitates were filtered off, washed with ethyl acetate (20 ml) and the filtrate evaporated under reduced pressure. The product was purified, whenever necessary, by column chromatography on silica gel using various solvent systems like dichloromethane, and petroleum ether etc. as eluents, to afford pure thioether or thioester products.

**C.V.1. Benzyl phenyl sulfide (74)** [95]

Solid; m.p. 42-43 °C; <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 4.3 (s, 2H), 7.45-7.25 (m, 10H); <sup>13</sup>C NMR (63 MHz, CDCl<sub>3</sub>): δ 125.35, 125.71, 127.92, 127.95, 128.44, 128.43, 128.89, 128.81, 129.25, 129.23, 130.51; EIMS, m/z = 200.30; anal. calcd. for C<sub>13</sub>H<sub>10</sub>OS: C = 77.95, H = 6.04, S = 16.01, found: C = 77.80, H = 6.09, S = 16.11.

**C.V.2. 2-Propyl 4-nitrophenyl sulfide (77)** [98]

Solid; 46-47 °C; <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 1.40 (d, *J* = 6.65 Hz, 6H), 3.60 (m, 1H), 7.45 (d, *J* = 8.92 Hz, 2 H), 8.23 (d, *J* = 8.92 Hz, 2H); <sup>13</sup>C NMR (63 MHz, CDCl<sub>3</sub>): δ 22.15, 36.64, 124.38, 127.62, 145.13, 147.55; EIMS, m/z = 197.05; anal. calcd. for C<sub>9</sub>H<sub>11</sub>NO<sub>2</sub>S: C = 54.80, H = 5.62, N = 7.10, O = 16.22, S = 16.25, found: C = 54.89, H = 5.73, N = 7.01, O = 16.12, S = 16.24.

**C.V.3. Allyl 4-nitrophenyl sulfide (78)** [99]

Solid; m.p. 38-39 °C; <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 3.72 (ddd, *J* = 6.50, 1.41, 1.01 Hz, 2H), 5.14 (ddd, *J* = 10.04, 1.41, 1.15 Hz, 1H), 5.25 (ddd, *J* =

16.90, 1.15, 1.04 Hz, 1H), 5.84 (ddd,  $J = 16.93, 10.10, 6.54$  Hz, 1H), 7.24 (d,  $J = 9.10$  Hz, 2H), 8.08 (d,  $J = 9.12$  Hz, 2H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta$  53.12, 119.01, 123.54, 125.92, 131.71, 145.00, 146.58; EIMS,  $m/z = 195.035$ ; anal. calcd. for  $\text{C}_9\text{H}_9\text{NO}_2\text{S}$ : C = 55.37, H = 4.65, N = 7.17, O = 16.39, S = 16.42; found: C = 55.57, H = 4.80, N = 7.02, O = 16.39, S = 16.22.

#### **C.V.4. Ethyl 4-nitrophenyl sulfide (79) [90]**

Solid; m.p. 40-42 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.40 (t,  $J = 7.53$  Hz, 3H), 3.00 (q,  $J = 7.36$  Hz, 2H), 7.31 (d,  $J = 8.93$  Hz, 2H), 8.21 (d,  $J = 8.80$  Hz, 2H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta$  13.73, 25.15, 123.77, 126.29, 144.63, 147.81; EIMS,  $m/z = 183.03$ ; anal. calcd. for  $\text{C}_8\text{H}_9\text{NO}_2\text{S}$ : C = 52.44, H = 4.95, N = 7.64, O = 17.46, S = 17.50, found: C = 52.55, H = 4.91, N = 7.64, O = 17.50, S = 17.49.

#### **C.V.5. Benzyl 4-nitrophenyl sulfide (80) [97]**

Solid; m.p. 128-129 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  4.22 (s 2H), 7.36 (d,  $J = 9.10$  Hz, 2H), 7.00-7.51 (m, 5H), 8.43 (d,  $J = 8.67$  Hz, 2H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta$  37.41, 122.80, 126.35, 127.62, 129.27, 128.88, 135.42, 145.22, 147.35; EIMS,  $m/z = 245.05$ ; anal. calcd. for  $\text{C}_{13}\text{H}_{11}\text{NO}_2\text{S}$ : C = 63.65, H = 4.52, N = 5.71, O = 13.04, S = 13.07, found: C = 63.20, H = 4.40, N = 5.74, O = 13.01, S = 13.19.

#### **C.V.6. Phenylthio acetate (86) [105-106]**

Liquid;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.41 (s, 3H), 7.41-7.43 (m, 5H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta$  30.11, 127.87, 129.12, 129.35, 134.37, 193.90; EIMS,  $m/z$  = 152.22; anal. calcd. for  $\text{C}_8\text{H}_8\text{OS}$ : C = 63.13, H = 5.30, O = 10.51, S = 21.06, found: C = 63.14, H = 5.29, O = 10.50, S = 21.07.

#### **C.V.7. 4-Methoxyphenylthio benzoate (90) [104]**

Solid; mp 96-98 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.80 (s, 3H), 6.96-7.41 (m, 4H, H-2,3,5,6), 7.45-7.60 (m, 3H, H-3',4',5');  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta$  55.45, 115.15, 117.53, 127.42, 128.34, 133.35, 135.59, 136.59, 160.84, 190.95; EIMS,  $m/z$  = 231.30; anal. calcd. for  $\text{C}_{13}\text{H}_{11}\text{O}_2\text{S}$ : C = 67.51, H = 4.79, O = 13.83, S = 13.86; found: C = 67.83, H = 4.81, O = 13.51, S = 13.84.

#### **C.V.8. 4-Nitrophenylthio benzoate (91) [104]**

Solid; m.p. 125-127 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.58-7.66 (m, 3H, H-3',4',5'), 7.72 (m, 2H, H-2,6), 8.03 (m, 2H, H-2',6'), 8.30 (m, 2H, H-3,5);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta$  123.88, 127.78, 128.69, 135.10, 135.80, 135.85, 136.25, 148.30, 188.01; EIMS,  $m/z$  = 259.29; anal. calcd. for  $\text{C}_{13}\text{H}_9\text{NO}_3\text{S}$ : C = 60.22, H = 3.50, N = 5.40, O = 18.51, S = 12.37; found: C = 60.01, H = 3.45, N = 5.45, O = 18.72, S = 12.37.

### **C.VI. General Procedure for Syntheses of Ethers and Esters [153a]**

To a stirred solution of phenol compound (1.0 mol) and CsF-Celite (1.5 mol) in 20 ml of acetonitrile, alkyl, acyl, benzyl, or benzoyl halide (2.0 mol)

was added. Then the mixture was continued for stirring at room temperature or reflux up to completion of the reaction, indicated by tlc monitoring. The reaction mixture was filtered, the solvent evaporated and the residue dissolved in ethyl acetate. Precipitates were filtered off, washed with ethyl acetate (20 ml) and the filtrate evaporated under reduced pressure. The product was purified, whenever necessary, by column chromatography on silica gel using various solvent systems like dichloromethane, and petroleum ether etc. as eluents, to afford pure ester or ether products.

#### **C.VI.1. Phenyl acetate (96) [119]**

Liquid;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.20(s, 3H), 6.92-7.28 (m, 5H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta$  16.9, 121.5, 122.1, 127.2, 152.1, 168.5; EIMS,  $m/z = 229.24$ ; anal. calcd. for  $\text{C}_8\text{H}_8\text{O}_2$ : C = 70.58, H = 5.92, found: C = 70.67, H = 5.89.

#### **C.VI.2. Phenyl benzoate (97) [120]**

Liquid;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.20 (s, 3H), 3H), 6.92-7.55 (m, 9H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta$  16.9, 118.2, 121.5, 127.5, 129.8, 126.7, 130.2, 131.9, 130.6 134.1, 138.4, 152.5, 164.0; EIMS,  $m/z = 228.29$ ; anal. calcd. for  $\text{C}_{15}\text{H}_{16}\text{O}_2$ : C = 78.92, H = 7.06, found: C = 78.73, H = 7.17.

#### **C.VI.3. 4-Biphenyl benzoate (101) [123]**



Solid; mp 149-151 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.10-7.38 (m, 9H), 7.41-8.15 (m, 5H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  118.2, 121.5, 127.5, 129.8, 126.7, 130.2, 131.9, 130.6, 134.1, 138.4, 152.5, 167.0, EIMS,  $m/z$  = 290.37; anal. calcd. for  $\text{C}_{20}\text{H}_{18}\text{O}_2$ : C = 82.73, H = 6.25, found: C = 82.64, H = 6.31.

#### **C.VI.4. Benzyl phenyl ether (106)** [128]

Solid; mp 39-40 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.20, (s, 2H,  $\text{CH}_2$ ), 6.77-6.19 (m, 10H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.8, 114.1, 114.1, 120.8, 125.7, 127.9, 128.4, 129.5, 129.5, 162.0; EIMS,  $m/z$  = 184.24; anal. calcd. for  $\text{C}_{13}\text{H}_{12}\text{O}$ : C = 84.75, H = 6.57, found: C = 84.59, H = 6.65.

#### **C.VI.5. Benzyl 4-nitrophenyl ether (108)** [130]

Solid; mp 90-91 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.10 (s, 2H), 6.95 (m, 3H), 7.28 (m, 2H), 7.52 (d,  $J$  = 9 Hz, 2H), 8.15 (d,  $J$  = 9 Hz, 2H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta$  29.5, 117.2, 124.4, 125.8, 128.1, 128.8, 140.0, 141.6, 164.1; EIMS,  $m/z$  = 229.24; anal. calcd. for  $\text{C}_{13}\text{H}_{11}\text{NO}_3$ : C = 68.11, H = 4.84, N = 6.11, found: C = 67.97, H = 4.96, N = 5.99.

#### **C.VI.6. Ethyl *p*-phenylphenoxyacetate (112)** [133]

Solid; mp 60-61 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.36 (t,  $J$  = 6.7 Hz, 3H), 4.24 (q,  $J$  = 6.9 Hz, 2H), 4.85 (s, 2H), 6.75-7.52 (m, 9H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ ):  $\delta$  13.8, 76.0, 113.8, 127.8, 127.6, 128.8, 128.9, 136.8, 162.4,

169.5; EIMS,  $m/z = 256.30$ ; anal. calcd. for  $C_{16}H_{16}O_3$ : C = 74.98, H = 6.29, found: C = 75.09, H = 6.31.

### **C.VII. General Procedure for the Preparation of Symmetrical Disulfides** [146b]

To a stirred solution of aromatic or open chain thiol compounds (1.0 mol) in 20 ml of acetonitrile, CsF-Celite (1.5 mol) was added. Then the mixture was continued for stirring at room temperature or reflux up to completion of the reaction, indicated by tlc monitoring. The reaction mixture was filtered, the solvent evaporated and the residue dissolved in ethyl acetate. The reaction mixture was washed with ethyl acetate (20 ml) and the filtrate evaporated under reduced pressure. The product was purified, whenever necessary, by column chromatography on silica gel using various solvent systems like dichloromethane, and petroleum ether etc. as eluents, to afford pure symmetrical disulfides products.

#### **C.VII.1. Dipentyl disulfide (120)** [147]

Liquid; EIMS,  $m/z = 206.41$ ; anal. calcd. for  $C_{10}H_{22}S_2$  C = 58.19 H = 10.74; found: C = 58.11 H = 10.82.

#### **C.VII.2. Diheptyl disulfide (121)** [154]

Liquid; EIMS,  $m/z = 262.52$ ; anal. calcd. for  $C_{14}H_{30}S_2$  C = 54.05 H = 11.52; found: C = 54.99 H = 11.58.

**C.VII.3. Didodecyl disulfide (122)** [154]

Solid; mp 30-31 °C; EIMS,  $m/z = 374.74$ ; anal. calcd. for  $C_{22}H_{46}S_2$  C = 70.51 H = 4.62; found: C = 70.47 H = 4.66.

**C.VII.4. Diphenyl disulfide (123)** [155]

Solid; mp 59-61 °C; EIMS,  $m/z = 218.34$ ; anal. calcd. for  $C_{12}H_{10}S_2$  C = 66.01 H = 4.62; found: C = 66.08 H = 4.55.

**C.VII.5. Bis(p-methoxyphenyl) disulfide (126)** [113c]

Solid; mp 40-42 °C; EIMS,  $m/z = 278.39$ ; anal. calcd. for  $C_{14}H_{14}O_2S_2$  C = 60.40 H = 5.07; found: C = 60.42 H = 5.09.

**C.VII.6. Bis(p-nitrophenyl) disulfide (127)** [147]

Solid; mp 177-178 °C; EIMS,  $m/z = 308.34$ ; anal. calcd. for  $C_{12}H_8N_2O_4S_2$  C = 46.75 H = 2.62; found: C = 46.67 H = 2.70.

**C.VII.7. Dipyradyl disulfide (128)** [155]

Solid; mp 60-61 °C; EIMS,  $m/z = 220.32$ ; anal. calcd. for  $C_{10}H_8N_2S_2$  C = 54.52, H = 3.66; found: C = 54.61, H = 3.57.

**C.VII.8. Bis(benzoxazol-2-yl) disulfide (129)** [157]

Solid; mp 110-111 °C; EIMS,  $m/z = 300.36$ ; anal. calcd. for  $C_{14}H_8N_2O_2S_2$  C = 55.98 H = 2.68; found: C = 55.03 H = 2.62.

**C.VII.9. Bis(benzothiazol-2-yl) disulfide (130)** [158]

Solid; mp 183-184 C; EIMS,  $m/z = 332.49$ ; anal. calcd. for  $C_{14}H_8N_2S_4$  C = 50.57 H = 2.43; found: C = 50.66 H = 2.34.

## D. ABSTRACT

This thesis describes the application of carbohydrates as “chiral synthons” for the regio- and stereoselective syntheses of new classes of compounds. Combination of the natural chirality and inherent topology of cyclic sugar derivatives allowed to design a strategy for the regio- and stereoselective synthesis of 3-halo-3-deoxy sugars and 2,3-dihydrobenzo-[1,4]-dithiane derivatives. Furthermore, in this thesis, cesium fluoride-Celite is used as a solid base for convenient, efficient, inexpensive and novel syntheses of ethers, esters, thioethers, thioesters and symmetrical disulfides.

Chapter I describes synthesis of starting materials benzyl 2,3-anhydro-4-O-triflylribopyranosides *via* benzyl 2,3-anhydroribopyranosides from L- and D-arabinose.

In chapter II, a rapid, easy, regio- and stereoselective synthesis of 3-halo-3-deoxy sugars using titanium tetrahalides is described. To fully confirm the stereochemistry of the synthetic products, the X-ray structure of benzyl 3-chloro-3-deoxy- $\beta$ -L-xylopyranoside was determined.

Chapter III describes a new method for the elimination of hydrogen halides and *p*-toluenesulfonic acid from sugar moieties using sodium hydride (NaH) in hexamethylphosphoric triamide (HMPA) at room temperature. NaH/HMPA has several advantages compared to NaH/DMF: elimination products are produced in high yields even from sterically hindered starting materials and not only from halides, but also tosylates.

In chapter IV, a convenient and novel method for the stereospecific synthesis of chiral 2,3-dihydro-benzo[1,4]dithiane and 2,3-dihydro-methylbenzo[1,4]dithiane from anhydrosugars is described.

In chapter V, syntheses of thioethers and thioesters of aliphatic, aromatic and heterocyclic compounds, bearing thiol groups are accomplished by reacting alkyl, acyl, benzyl or benzoyl halides in acetonitrile in the presence of cesium fluoride-Celite. In this manner, compounds like ethanethiol, 1-pentanethiol, thiophenol, 4-methoxythiophenol, 4-nitrothiophenol, 2-mercaptobenzoxazole 2-mercaptobenzothiazole or 2-mercapto-2-thiazoline can be successfully alkylated, acylated, benzylated or benzoylated. This procedure is convenient, efficient and practical for the preparation of thioethers and thioesters.

In chapter VI, coupling reactions of a number of alcohols and phenols with alkyl, acyl or benzoyl halides in acetonitrile in the presence of cesium fluoride-Celite are described. It has been found that CsF-Celite combinations provide an efficient, convenient and practical method for syntheses of both, ethers and esters.

In chapter VII, oxidative couplings of aliphatic, aromatic and heteroaromatic thiols to disulfides using cesium fluoride-Celite is reported. CsF-Celite provides an efficient, convenient and practical method for the syntheses of symmetrical disulfides.

## E. ZUSAMMENFASSUNG

Die Doktorarbeit beschreibt die Anwendung von Kohlenhydraten als chirale Synthone für die regio- und stereoselektive Synthese neuer Moleküle. Die Kombination natürlicher Chiralität und inhärenter Topologie bei zyklischen Zuckerderivaten ermöglichte es, eine neue Strategie zur regio- und stereoselektiven Synthese von 3-Halo-3-desoxyzuckern und 2,3-Dihydrobenzo[1,4]dithian-Derivaten zu entwickeln. Weiterhin wird in dieser Doktorarbeit Cäsiumfluorid-Celit als Festphase zur bequemen, effizienten und kostengünstigen Herstellung von Ethern, Estern, Thioethern, Thioestern und symmetrischen Disulfiden eingesetzt.

Kapitel I beschreibt die Synthese der Benzyl-2,3-anhydro-4-O-triflylribo-pyranoside als Ausgangsstoffe aus L- und D-Arabinose.

In Kapitel II wird eine einfache regio- und stereoselektive Synthese von 3-Halo-3-desoxyzuckern unter Verwendung von Titanetrahalogeniden vorgestellt. Um die Stereochemie der Syntheseprodukte zu bestätigen, wurde die Struktur von Benzyl-3-desoxy-3-chlor- $\beta$ -L-xylopyranosid röntgenkristallographisch bestimmt.

Kapitel III beschreibt eine neue Methode zur Eliminierung von Halogenwasserstoff und p-Toluolsulfonsäure aus Zuckerderivaten durch NaH/HMPA bei Raumtemperatur. NaH/HMPA ist in vielerlei Hinsicht NaH/DMF überlegen: Eliminierungen finden selbst bei sterisch gehinderten

Ausgangsstoffen unter großen Ausbeuten statt. Auch Tosylate lassen sich umsetzen.

In Kapitel IV wird eine leicht realisierbare und neue Methode für die stereoselektive Synthese von chiralem 2,3-Dihydrobenzo[1,4]dithianen und 2,3-Dihydromethylbenzo[1,4]dithianen aus Anhydrozuckern beschrieben.

In Kapitel V wird die Synthese von Thioethern und Thioestern aus aliphatischen, aromatischen und heterozyklischen Thiolverbindungen durch Reaktion mit Alkyl-, Acyl-, Benzyl- oder Benzoylhalogeniden in Acetonitril mit Hilfe von Cäsiumfluorid-Celit erreicht. Auf diesem Weg können Verbindungen wie Ethanthiol, 1-Pentanthiol, Thiophenol, 4-Methoxythiophenol, 4-Nitrothiophenol, 2-Mercaptobenzoxazol, 2-Mercaptobenzothiazol oder 2-Mercapto-2-thiazolin erfolgreich alkyliert, acyliert, benzyliert oder benzoiliert werden. Dieses Verfahren ist für die Darstellung von Thioethern und -estern effizient, praktisch und einfach durchführbar.

In Kapitel VI werden Kopplungsreaktionen verschiedener Alkohole und Phenole mit Alkyl-, Acyl- oder Benzoylhalogeniden in Acetonitril in Gegenwart von Cäsiumfluorid-Celit durchgeführt, ein Verfahren durch welches Ether und Ester in einfacher Weise zugänglich sind.

In Kapitel VII wird über die oxidative Kopplung aliphatischer, aromatischer und heteroaromatischer Thiole zu Disulfiden unter Verwendung von CsF-Celit berichtet, welche die effektive Darstellung symmetrischer Disulfide erlaubt.



**F. REFERENCES**

- [1] F. Pozharskii, A. T. Soldatenkoc, A. R. Katritzky, In “*Heterocycles in Life and Society. An Introduction to Heterocyclic Chemistry and Biochemistry and the Role of Heterocycles in Science, Technology, Medicine and Agriculture*”, John Wiley and Sons Ltd., New York, (1997).
- [2] R. B. Silvermann, In “*The Organic Chemistry of Drug Design and Drug Action*”, Academic Press, San Diego, (1992).
- [3] a) W. Kowollik, In Ph. D. thesis, University of Tuebingen, (1987). b) F. Wold, *J. Org. Chem.*, **26**, 197, (1961). c) W. Kowollik, A. Malik, N. Afza, W. Voelter, *J. Org. Chem.* **50**, 3325 (1985).
- [4] E. Fischer, *Chem. Ber.*, **28**, 1895 (1895).
- [5] A. Holý, F. Šorm, *Collect. Czech. Chem. Commun.*, **34**, 3383 (1969).
- [6] a) H. G. Fletcher, Jr., C. S. Hudson, *J. Am. Chem. Soc.*, **72**, 4173 (1950). b) H. G. Fletcher, Jr., C. S. Hudson, *J. Am. Chem. Soc.*, **72**, 1145 (1947).
- [7] B. T. Lawton, W. A. Szarek, J. K. N. Jones, *Carbohydr. Res*, **15**, 397 (1970).
- [8] a) T. H. Al-Tel, M. Meisenbach, W. Voelter, *Ann. Liebigs*. 689 (1995). b) T. H. Al-Tel, Y. Al-Abed, W. Voelter, *J. Chem. Soc., Chem Commun.* 1735 (1994). c) Y. Al-Abed, T. H. Al-Tel, W. Voelter, *Tetrahedron*, **41**, 9295 (1993).

- [9] a) Y. Al-Abed, F. Zaman, M. S. Shekhani, A. Fatima, W. Voelter, *Tetrahedron Lett.*, **33**, 3305 (1992). b) Y. Al-Abed, N. Naz, K. M. Khan, W. Voelter, *Angew. Chem. Int. Ed. Engl.*, **35**, 523 (1996).
- [10] R. A. Al-Qawasmeh, T. H. Al-Tel, R. J. Abdel-Jalil, R. Thürmer, W. Voelter, *Polish J. Chem.*, **73**, 71 (1999).
- [11] R. J. Abdel-Jalil, R. A. Al-Qawasmeh, Y. Al-Abed, W. Voelter, *Tetrahedron Lett.*, **39**, 6155 (1998).
- [12] R. J. Abdel-Jalil, R. A. Al-Qawasmeh, Y. Al-Abed, W. Voelter, *Tetrahedron Lett.*, **39**, 7703 (1998).
- [13] T. Katsuki, K. B. Sharpless, *J. Am. Chem. Soc.*, **102**, 5974 (1980).
- [14] J. Kagan, B. E. Firth, N. Y. Shih, C. G. Boyanjan, *J. Org. Chem.*, **42**, 343 (1977).
- [15] C. Einhorn, J.-L. Luche, *J. Chem. Soc. Chem. Commun.*, 1368 (1986).
- [16] a) J. Iqbal, M. A. Khan, *Chem. Lett.*, 1157 (1988). b) Regioselective Conversion of Anhydro Sugars into Halohydrins and X-Ray Studies; S. T. A. Shah, R. J. Abdel-Jalil, K. M. Khan, A. M. Heinrich and W. Voelter; *Z. Naturforsch.* **58b** (2003) (Accepted).
- [17] D. M. Dean, W. A. Szarek, J. K. N. Jones, *Carbohydr. Res.*, **33**, 383 (1974).
- [18] K. Bock, C. Pedersen, *Carbohydr. Res.*, **73**, 85 (1979).
- [19] A. Klemer, B. Brandt, *Ann. Liebigs Chem.*, 932 (1986).
- [20] G. Ritzmann, R. S. Klein, D. H. Hollenberg, J. J. Fox, *Carbohydr. Res.*, **39**, 227 (1975).

- [21] M. Shimizu, A. Yoshida, T. Fujisawa, *Synth. Lett.*, 204 (1991).
- [22] N. Afza, A. Malik, W. Voelter, *Chimia* **37**, 422 (1983).
- [23] N. Khan, Y. Al-Abed, H-J. Kohlbau, F. L. Ansari, W. Kowollik, W. Voelter, *Z. Naturforsch.*, **51b**, 1781 (1996).
- [24] D. H. Buss, L. Hough, L. D. Hall, J. F. Manville, *Tetrahedron*, **21**, 69 (1965).
- [25] W. R. Jackson, A. Zurqiyah, *J. Chem. Soc., B*, 49 (1966).
- [26] B. Ottar, *Acta. Chem. Scand.*, **1**, 283 (1947).
- [27] J. G. Buchanan, R. Fletcher, K. Parry, W. A. Thomas, *J. Chem. Soc., B*, 377 (1969).
- [28] W. Kowollik, A. Malik, N. Afza, W. Voelter, *J. Org. Chem.*, **50**, 3325 (1985).
- [29] A. Malik, W. Kowollik, P. Scheer, N. Afza, W. Voelter, *J. Chem. Soc. Chem. Commun.*, **18**, 1229 (1984).
- [30] A. Holy, F. Sorm, *Collect. Czech. Chem. Commun.* **34**, 3383 (1969).
- [31] J. G. Buchanan, D. M. Clode, N. Vethaviasar, *J. Chem. Soc. Perkin Trans.*, 1, 1449 (1976).
- [32] R. Kimmich, W. Voelter, *Ann Liebigs. Chem.*, 1100 (1981).
- [33] a) R. J. Ferrier, *Adv. Carbohydr. Chem.*, **20**, 67 (1965). b) S. Hanessian, *Adv. Carbohydr. Chem.*, **21**, 143 (1966). c) R. F. Butterworth, S. Hanessian, *Adv. Carbohydr. Chem.*, **26**, 279 (1971). d) M. G. Blair, *Adv. Carbohydr. Chem.*, **9**, 279 (1954). e) R. J. Ferrier, In *The Carbohydrates, Chemistry and Biochemistry*, 2nd edn., Academic Press, New York, Vol. **IB.**, pp. 843-879 (1980).

- [34] a) R. J. Ferrier, G. H. Sankey, *J. Chem. Soc., (C)*, 2339 (1966). b) R. J. Ferrier, G. H. Sankey, *J. Chem. Soc., (C)*, 2345 (1966). c) K. Bock, C. Pedersen, *Acta, Chem. Scand.*, **24**, 2465 (1970).
- [35] a) F. W. Lichtenthaler, E. S. H. El Ashry, V. H. Göckel, *Tetrahedron Lett.*, **21**, 1429 (1980). b) F. W. Lichtenthaler, P. Jarglis, *Tetrahedron Lett.*, **21**, 1425 (1980). c) F. W. Lichtenthaler, E. Kaji, S. Weprek, *J. Org. Chem.*, **50**, 3505 (1985). d) F. W. Lichtenthaler, P. Jarglis, *Chem. Ber.*, **113**, 489 (1980). e) F. W. Lichtenthaler, T. Sakakibara, E. Egert, *Chem. Ber.*, **113**, 471 (1980).
- [36] (a) C. L. Forbes, R. W. Franck, *J. Org. Chem.*, **64**, 1424 (1999). b) M. G. Blair, *Methods in Carbohydr. Chem.*, **2**, 411 (1963). c) H. G. Fletcher Jr., C. S. Hudson, *J. Am. Chem. Soc.*, **69**, 921 (1947). d) R. T. Major, E. W. Cook, *J. Am. Chem. Soc.*, **58**, 2333 (1936).
- [37] a) R. U. Lemieux, D. R. Lineback, *Can. J. Chem.*, **43**, 94 (1965). b) K. M. Khan, S. Perveen, S. T. A. Shah, M. S. Shekhani and W. Voelter; *New J. Chem.*; **25**, 896-898. (2001).
- [38] a) C. L. Cavallaro, J. Schwartz, *J. Org. Chem.*, **60**, 7055 (1995). b) F. Chrétien, *Synth. Commun.*, **19**, 1015 (1989).
- [39] a) P. I. Dialko, P. Sinaÿ, *Angew. Chem. Int. Ed.*, **38**, 773 (1999) and references quoted there in. b) S. K. Das, J.-M. Mallet, P. Sinaÿ, *Angew. Chem. Int. Ed.*, **36**, 493 (1997). c) R. J. Ferrier, S. Middleton, *Chem. Rev.*, **93**, 2779 (1993). d) M. Sollogoub, J.-M. Mallet, P. Sinaÿ, *Tetrahedron Lett.*, **39**, 3471 (1998).

- [40] (a) R. J. Ferrier, P. Prasit, *J. Chem. Soc. Chem. Commun.*, 983 (1981). (b) R. A. Farr, N. P. Peet, M. S. Kang, *Tetrahedron Lett.*, **31**, 7109 (1990). (c) R. J. Ferrier, R. H. Furneaux, P. Prasit, P. C. Tyler, K. L. Brown, G. J. Gainsford, J. W. Diehl, *J. Chem. Soc. Perkin Trans. I.*, 1621 (1983). d) B. Bernet, A. Vasella, *Helv. Chem. Acta.*, **62**, 2400 (1979). e) B. Bernet, A. Vasella, *Helv. Chem. Acta.*, **62**, 2411 (1979).
- [41] I. D. Blackburne, P. M. Frederick, R. D. Guthrie, *Aust. J. Chem.*, **29**, 381 (1976).
- [42] M. G. Blair, *Methods in Carbohydr. Chem.*, **2**, 415 (1963).
- [43] T. F. Gallagher, D. Horton, *Carbohydr. Res.*, **116**, 227 (1983).
- [44] K-I, Sato, N. Kubo, R. Takada, A. Aqeel, H. Hashimoto, J. Yoshimura, *Chem. Lett.*, 1703 (1988).
- [45] S. Adam, *Tetrahedron Lett.*, **29**, 6589 (1988).
- [46] M. S. Shekhani, K. M. Khan, K. Mahmood, *Tetrahedron Lett.*, **29**, 6161 (1988).
- [47] M. S. Shekhani, K. M. Khan, K. Mahmood, P. M. Shah, S. Malik, *Tetrahedron Lett.*, **31**, 1669 (1990).
- [48] This is not an improvement in an existing method [38b]; rather, it is a new method for dehyrosylation and dehydrohalogenation. Until now there was no existing method that could eliminate both HOTs and HX. Due to theses elimination properties of a single reagent, the toxicity of HMPA could be compromised.

- [49] R. Blattner, R. J. Ferrier, *J. Chem. Soc., Perkin Trans. 1*, 1523 (1980).
- [50] Y. E. Tsvetkov, N. É. Byramova, L. V. Backinowsky, *Carbohydr. Res.*, **115**, 254 (1983).
- [51] S. Jain, S. N. Suryawanshi, S. Misra, D. S. Bhakuni, *Indian J. Chem., Sect. B*, **27**, 866 (1988).
- [52] D. Loganathan, G. K. Trivedi, *Carbohydr. Res.*, **162**, 117 (1987).
- [53] (a) O. Varela, G. M. De Fina, R. M. De Lederkremer, *Carbohydr. Res.*, **167**, 187 (1987.) b) H. Paulsen, J. Thiem, *Chem. Ber.*, **106**, 132 (1973).
- [54] P. Kovác, R. B. Taylor, *Carbohydr. Res.*, **167**, 153 (1987).
- [55] E. Kaji, Y. Osa, K. Takahashi, S. Zen, *Chem. Pharm. Bull.*, **44**, 15 (1996).
- [56] F. S-García, F. J. L-Herrera, M. S. P. González, *Tetrahedron*, **51**, 5491 (1995).
- [57] L. E. S. Barata, A. J. Marasaioli, L. Valente, A. Olesker, G. Lukacs, T. T. Thang, *Carbohydr. Res.*, **90**, 326 (1981).
- [58] R. Blattner, R. J. Ferrier, P. C. Tyler, *J. Chem. Soc., Perkin Trans. 1*, 1535 (1980).
- [59] N. Ishikawa, T. Kitazume, T. Yamazaki, Y. Mochida, T. Tatsuno, *Chem. Lett.*, 761 (1981).
- [60] J-J. Brunet, P. Gallois, P. Caubere, *J. Org. Chem.*, **45**, 1937 (1980).

- [61] A. L. Raymond, In "*Advances in Carbohydrate Chemistry*", Vol. **1**, Academic Press Inc., New York, pp. 129 (1945). b) G. E. McCasl, A. B. Zanlungo, L. J. Durham, *J. Org. Chem.*, **39**, 1462 (1974).
- [62] S. M. Iqbal, L. N. Owen, *J. Chem. Soc.*, 1030 (1960).
- [63] G. P. McSweeney, L. F. Wiggins, *Nature*, **168**, 874 (1951).
- [64] W. Watanabe, K. Sudo, R. Sato, T. Kajiyashiki, K. Konno, S. Shigeta, T. Yokota, *Biochem. and Biophys. Res. Commun.*, **249**, 922-926 (1998).
- [65] E. Breitmeier, W. Voelter, In *<sup>13</sup>C NMR Spectroscopy*, Verlag Chemie, Weinheim, Germany (1974).
- [66] D. Horton, J. D. Wander, In *The Carbohydrates Chemistry and Biochemistry*, ed.; W. Pigman, D. Horton, J. D. Wander, Academic Press, New York, pp. 799-841 (1980).
- [67] Z. J. Witczak, *Adv. Carbohydr. Chem. Biochem.*, Academic Press, New York, **44**, 91-145 (1986).
- [68] P. Vanleemmens, D. Postel, G. Ronco, P. Villa, *Carbohydr. Res.*, **289**, 171-178 (1996).
- [69] J. Brånalt, I. Kvarnström, S. C. T. Svensson, B. Classon, B. Samuelsson, *J. Org. Chem.*, **59**, 4430-4432 (1994).
- [70] N. Ototani, R. L. Whistler, *J. Med. Chem.*, **17**, 535-537 (1974).
- [71] M. R. Dyson, P. L. Coe, R. T. Walker, *J. Med. Chem.*, **34**, 2782-2786 (1991).
- [72] J. A. Secrist III, R. M. Riggs, K. N. Tiwari, J. A. Montgomery, *J. Med. Chem.*, **35**, 533-538 (1992).

- [73] M. Bobek, A. Bloch, R. Parthasarathy, R. L. Whistler, *J. Med. Chem.*, **18**, 784-787 (1975).
- [74] F. Cavelier, J. Daunis, R. Jacquier, *Bull. Soc. Chim. Fr.*, **127**, 210 (1990).
- [75] a) H. Wild, In *The Organic Chemistry of  $\beta$ -Lactams*; I. Georg., Ed. *Protective Groups in  $\beta$ -lactam Chemistry*; VCH: Weinheim, pp. 1-38 (1993). b) W. Yang, D. G. Drueckhammer, *J. Am. Chem. Soc.*, **123**, 11004 (2001).
- [76] For a review, see: M. E. Peach, In *The Chemistry of the Thiol Groups*; S. Patai., Ed. *Thiols as nucleophiles*; John Wiley & Sons: London, pp. 721-756 (1974).
- [77] S.-I. Yunoki, K. Takimiya, Y. Aso, T. Otsubo, *Tetrahedron Lett.*, **38**, 3017 (1997).
- [78] C. Goux, P. Lhoste, D. Sinou, *Tetrahedron Lett.*, **33**, 8099 (1992).
- [79] A. W. Herriott, D. Picker, *J. Am. Chem. Soc.*, **97**, 2345 (1975).
- [80] P. C. B. Page, S. S. Klair, M. P. Brown, M. M. Harding, C. S. Smith, S. J. Maginn, S. Mulley, *Tetrahedron Lett.*, **29**, 4477 (1988).
- [81] C.-J. Li, D. N. Harpp, *Tetrahedron Lett.*, **33**, 7293 (1992).
- [82] M. Kosugi, T. Ogata, M. Terada, H. Sano, T. Migita, *Bull. Chem. Soc. Jpn.*, **58**, 3657 (1985).
- [83] a) F. D. Toste, I. W. J. Still, *Tetrahedron Lett.*, **36**, 4361 (1995). b) F. D. Toste, F. Laronde, I. W. J. Still, *Tetrahedron Lett.*, **36**, 2949 (1995).



- [84] a) D. N. Harpp, M. Gingras, *J. Am. Chem. Soc.*, **110**, 7737 (1988).  
b). d) M. Gingras, T. H. Chan, D. N. Harpp, *J. Org. Chem.*, **55**, 2078 (1990).
- [85] T.-S. Li, A.-X. Li, *J. Chem. Soc., Perkin. Trans. 1*, 1913 (1998).
- [86] L. S. Richter, J. C. Marsters, Jr., T. R. Gadek, *Tetrahedron Lett.*, **35**, 1631 (1994).
- [87] J. Yin, C. Pidgeon, *Tetrahedron Lett.*, **38**, 5953 (1997).
- [88] a) F. Iqbal, M. S. Shekhani, A. Malik, M. Parvez, U. Riaz, Z. Ali, K. M. Khan, *Z. Naturforsch.*, **55b**, 317 (2000). b) M. Saeed, M. Abbas, K. M. Khan, W. Voelter, *Z. Naturforsch.*, **56b**, 325 (2001). c) S. Hayat, Atta-ur-Rahman, M. I. Choudhary, K. M. Khan, E. Bayer, *Tetrahedron Lett.*, **42**, 1647 (2001). d) J. H. Zaidi, F. Naeem, R. Iqbal, M. I. Choudhary, K. M. Khan, S. T. A. Shah, S. Hayat, W. Voelter, *Z. Naturforsch.*, **56b**, 689 (2001).
- [89] S. Hayat, Atta-ur-Rahman, M. I. Choudhary, K. M. Khan, W. Schumann, E. Bayer, *Tetrahedron*, **57**, 9951 (2001).
- [90] D. J. Pasto, F. Cottard, L. Jumelle, *J. Am. Chem. Soc.*, **116**, 8978 (1994).
- [91] D. J. Pasto, F. Cottard, *J. Org. Chem.*, **59**, 4642 (1994).
- [92] S. Perumal, G. Vasuki, V. Vijayabaskar, S. Selvaraj, D. W. Boykin, *Mag. Reson. Chem.*, **36**, 720 (1998).
- [93] M. S. Karasch, C. F. Fuchs, *J. Org. Chem.*, **13**, 97 (1948).
- [94] J. Büchi, M. Prost, H. Eichenberger, R. Leiberherr, *Helv. Chem. Acta.*, **35**, 1527 (1952).

- [95] J. Drabowicz, M. Mikolajczyk, *Synthesis*, 542 (1978).
- [96] J. Drabowicz, M. Mikolajczyk, *Synthesis*, 527 (1978).
- [97] H. Harayama, T. Nagahama, T. Kozera, M. Kimura, K. Fugami, S. Tanaka, Y. Tamaru, *Bull. Chem. Soc. Jpn.*, **70**, 445 (1997).
- [98] P. Cogolli, L. Testaferri, M. Tingoli, M. Tiecco, *J. Org. Chem.*, **44**, 2636 (1979).
- [99] D. G. Foster, E. E. Reid, *J. Am. Chem. Soc.*, **46**, 1936 (1924).
- [100] I. I. Lapkin, N. V. Bogoslovskii, N. F. Mozhova, *Chem. Abstr.*, **64**, 11115 (1966).
- [101] J. E. Cranham, D. Greenwood, H. A. Stevenson, *J. Sci. Food Agric.*, **9**, 147 (1958).
- [102] K. Maekawa, K. Narasaka, T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, **46**, 3478 (1973).
- [103] E. Fujita, Y. Nagao, K. Seno, S. Takao, T. Miyasaka, M. Kimura, W. H. Watson, *J. Chem. Soc. Perkin Trans. 1*, 914 (1981).
- [104] G. Cilento, *J. Am. Chem. Soc.*, **75**, 3748 (1953).
- [105] J. C. Sheehan, C. W. Beck, *J. Am. Chem. Soc.*, **77**, 4875 (1955).
- [106] G. Cilento, W. F. Walter, *J. Am. Chem. Soc.*, **76**, 4469 (1954).
- [107] H. Pelster, W. Hahn, K. Goliash, W. Behrenz, *Chem. Abstr.*, **64**, 6573 (1966).
- [108] Y. V. Gulevich, N. A. Bumagin, I. P. Beletskaya, *J. Org. Chem.*, (USSR), **24**, 1918 (1988).
- [109] T. W. Greene, P. G. M. Wuts, In "Protective Groups in Organic Synthesis", Int, Ed., John Wiley: New York, (1991).

- [110] H. Yin, R. W. Frank, S-S. Chen, G. J. Wuigley, L. Todaro, *J. Org. Chem.*, **57**, 644-651 (1992).
- [111] L. V. Hijfte, R. D. Little, *J. Org. Chem.*, **50**, 3940-3942 (1985).
- [112] a) F. J. Wold, *J. Org. Chem.*, **26**, 197 (1961). b) In “*Vogel’s Text book of Pratical Organic Chemistry*”; 5<sup>th</sup> ed.; Addison Wesley Longman, London, pp. 646 (1994).
- [113] a) R. I. Zhdanov, S. M. Zhenodarova, *Synthesis*, 222 (1975). b) D. Horton, *Org. Synth. Coll. Vol.*, **5**, 1 (1973).
- [114] a) E. Vedejs, S. T. Diver, *J. Am. Chem. Soc.*, **115**, 3358 (1993). b) E. Vedejs, N. S. Bennett, L. M. Conn, S. T. Diver, M. Gingrass, S. Lin, P. A. Oliver, M. J. Peterson, *J. Org. Chem.*, **48**, 7286 (1993).
- [115] J. M. Miller, K-H. So, J. H. Clark, *J. Chem. Soc., Chem. Commun.*, 466-467 (1978).
- [116] J. H. Clark, *J. Chem. Soc., Chem. Commun.*, 789-791 (1978) and references cited therein.
- [117] J. C. Lee, Y. Choi, *Synth. Commun.*, **28**, 2021-2026 (1998).
- [118] a) M. Yamada, S. Yahiro, T. Yamano, V. Nakatani, G. Wurisson, *Bull. Soc. Chim. Fr.*, **127**, 824-829 (1990). b) W. H. Kruizinga, R. M. Kellogg, *J. Am. Chem. Soc.*, **103**, 5183 (1981).
- [119] P. B. D. de al. Mare, N. S. Isaacs, M. J. McGlone, *J. Chem. Soc., Perkin Trans. 1*, 784-786 (1976).
- [120] G. Cilento, *J. Am. Chem. Soc.*, **75**, 3748-3750 (1953).
- [121] F. M. Menger, J. H. Smith, *J. Am. Chem. Soc.*, **94**, 8324-8325 (1972).

- [122] K. Williams, B. Halpern, *Synthesis*, 727 (1974).
- [123] D. S. Tarbell, J. A. Price, *J. Org. Chem.*, **22**, 245-248 (1957).
- [124] *Chem. Abstr.*, **63**, 17909c (1965).
- [125] H. Kataoka, *Chem. Abstr.*, **64**, 8058 (1966).
- [126] W. A. Reckhow, D. S. Tarbell, *J. Am. Chem. Soc.*, **14**, 4968 (1952).
- [127] C. D. Hurd, K. L. Kreuz, *J. Am. Chem. Soc.*, **27**, 5543 (1950).
- [128] E. Baciocchi, A. Piermattei, C. Rol, R. Ruzziconi, G. V. Sebastiani, *Tetrahedron*, **45**, 7049 (1989).
- [129] H. C. Brown, O. J. Cope, *J. Am. Chem. Soc.*, **86**, 1801-1807 (1964).
- [130] P. Maslak, R. D. Guthrie, *J. Am. Chem. Soc.*, **108**, 2628-2636 (1986).
- [131] R. L. Huang, K. H. Lee, *J. Am. Chem. Soc.*, **86** 5963-5969 (1964).
- [132] A. V. R. Rao, A. S. Gaitonde, K. R. C. Parkash, S. P. Rao, *Tetrahedron lett.*, **35**, 6347-6350 (1994).
- [133] K. Raman, H. K. Singh, S. K. Salzman, S. S. Parmar, *J. Pharm. Sci.*, **82**, 167-169 (1993).
- [134] Buu-Hoi, Hiong-ki-wie, R. Royer, *Bull. Soc. Chim. Fr.*, **12**, 866-869 (1945).
- [135] J. A. Lyman, E. E. Reid, *J. Am. Chem. Soc.*, **42**, 615 (1920).
- [136] R. S. Coleman, W. Chen, *Org. Lett.*, **3**, 1141-1144 (2001).
- [137] N. V. Maatschappij, *Chem. Abstr.*, **59**, 2721 (1963).
- [138] E. Hayashi, H. Yamanaka, K. Shimizu, *Chem. Pharm. Bull.*, **7**, 146-148 (1959).

- [139] A. Ogawa, Y. Nishiyama, N. Kambe, S. Murai, N. Sonoda, *Tetrahedron Lett.*, **28**, 3271-3274 (1987).
- [140] S. Antebi, H. Apler, *Tetrahedron Lett.*, **26**, 2609-2612 (1985).
- [141] Bischoff, C. David, L. Martin, H. Meudal, B-P. Roques, M-C. Fournié-Zaluski, *J. Org. Chem.*, **62**, 4848-4850 (1997).
- [142] M. Bodanszky, In *Principles of Peptide Synthesis*, 307 (1984).
- [143] S. N. Maiti, P. Spevak, M. P. Singh, R. G. Micetich, *Synth. Commun.*, **18**, 575-581 (1988).
- [144] T. Aida, T. Akasaka, N. Furukawa, S. Oae, *Bull. Chem. Soc. Jpn.*, **49**, 1441-1442 (1976).
- [145] X. Wu, R. D. Rieke, L. Zhu, *Synth. Commun.*, **26**, 191-196 (1996).
- [146] a) N. Iranpoor, B. Zeynizadeh, *Synthesis*, 49-50 (1999). b) A Novel Method for the Syntheses of Symmetrical Disulfides Using CsF-Celite as a Solid Base; S. T. A. Shah, K. M. Khan, M. Fecker and W. Voelter (Submitted to *Tetrahedron lett.*) 2003.
- [147] N. A. Noureldin, M. Caldwell, J. Hendry, D. G. Lee, *Synthesis*, 1587-1589 (1998).
- [148] V. Kesavan, D. Bonnet-Delpon, J.-P. Bégué, *Synthesis*, 223-225 (2000).
- [149] J. Drabowicz, M. Mikolajczyk, *Synthesis*, 32-34 (1980).
- [150] J. P. Tam, C-R. Wu, W. Liu, J-W. Zhang, *J. Am. Chem. Soc.*, **113**, 6657-6662 (1991).
- [151] M. Sridhar, S. K. Vadivel, U. T. Bhalerao, *Synth. Commun.*, **28**, 1499-1502 (1998).

- [152] S. L. S. Leite, V. L. Pardini, H. Viertler, *Synth. Commun.*, **20**, 393-397 (1990).
- [153] a) S. T. A. Shah, K. M. Khan, A. M. Heinrich, M. I. Choudhary, W. Voelter, *Tetrahedron Lett.*, **43**, 8603-8606 (2002). b) S. T. A. Shah, K. M. Khan, A. M. Heinrich, M. I. Choudhary, W. Voelter, *Tetrahedron Lett.*, **43**, 8281-8283 (2002).
- [154] Y. Huang, Y. Zhang, Y. Wang, *Synth. Commun.*, **27**, 1043-1047 (1997).
- [155] H. M. Meshram, A. Bandyopadhyay, G. S. Reddy, J. S. Yadav, *Synth. Commun.*, **30**, 701-706 (2000).
- [156] S. Oae, M. Yoshihara, *Bull. Chem. Soc. Jpn.*, **41**, 2082-2086 (1968).
- [157] A. S. Demir, A. C. Idgir, A. S. Mahasneh, *Tetrahedron*, **55**, 12399-12404 (1999).
- [158] L. Field, J. E. Lawson, *J. Am. Chem. Soc.*, **80**, 838-841 (1958).
- [159] Q. T. Do, D. Elothmani, J. Simonet, G. L. Guillanton, *Bull. Soc. Chim. Fr.*, **133**, 273-281 (1996).
- [160] D. Ghiringhelli, *Synthesis*, 580-582 (1982).

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## PUBLICATIONEN

1. An Alternative Approach Towards the Syntheses of Thioethers and Thioesters Using CsF-Celite in Acetonitrile; **Syed Tasadaque Ali Shah**, Khalid M. Khan, A. M. Heinrich and W. Voelter; *Tetrahedron Lett.*, **43**, 8281-8283 (2002).
2. An Efficient Approach towards Ethers and Esters Syntheses Using CsF-Celite as a Solid Base; **Syed Tasadaque Ali Shah**, Khalid M. Khan, A. M. Heinrich, and W. Voelter; *Tetrahedron Lett.*, **43**, 8603-8606 (2002).
3. Synthesis, Antibacterial, Cytotoxic and Antifungal Effects of New 3-Carboxy-1-phenacylpyridinium Salts; Khalid Mohammed Khan, Zafar Saeed Saify, **Syed Tasadaque Ali Shah**, Mansoor Ahmed, Muhammad Saeed, Safdar Hayat, Muhammad Abbas and Wolfgang Voelter; *Arzneimittel Forschung/Drug Research* **52**, 286-293, (2002).
4. Synthesis, Characterization and Biological Studies of Di- and Tri Organotin (IV) Complexes with 2,4-Difluoro-4-hydroxy-[1,1]-biphenyl-3-carboxylic acid: crystal structure of  $[(\text{CH}_3)_3\text{Sn}(\text{C}_{13}\text{H}_7\text{F}_2)]$ ;

- F. Ahmed, S. Ali, M. Parvez, A. Munir, M. Mazhar, K. M. Khan and **Syed Tasadaque Ali Shah**; *Heteroatom Chem.*, **13**, 638-649 (2002).
5. Isolation and Structure Elucidation of Two New Xanthenes from *Gentiana azurium* Bunge (Fam. Gentianaceae); O. Purev, Kh. Oyun, G. Odontuya, A. M. Tankhaeva, G. G. Nikolaeva, Khalid M. Khan, **Syed Tasadaque Ali Shah** and Wolfgang Voelter; *Z. Naturforsch.*, **57b**, 331-334, (2002).
6. Synthesis of Naturally Occurring Anthraquinones: Isochrysophanol,  $\omega$ -Hydroxyisochrysophanol, Isozyganein, Morindaparvin and Biological Evaluation; Javed H. Zaidi, Fazal Naeem, Rashid Iqbal, M. Iqbal Choudhary, Khalid Mohammed Khan, **Syed Tasadaque Ali Shah**, Safdar Hayat and Wolfgang Voelter; *Z. Naturforsch.*, **56b**, 689-696, (2001).
7. Sodium Hydride/Hexamethylphosphoric Triamide: A New Efficient Reagent towards the Synthesis of Protected 1,2- and 5,6-Enopyranosides; Khalid Mohammed Khan, Shahnaz Perveen, **Syed Tasadaque Ali Shah**, Mohammed Saleh Shekhani and Wolfgang Voelter; *New J. Chem.*, **25**, 896-898. (2001).
8. Syntheses and Evaluation of the Analgesic Activity of Some 4-Acetyl-4-phenylepiperidine and 4-Hydroxy-4-phenylepiperidine Derivatives; Z. S. Saify, K. M. Khan, S. M. Haider, Zeeshan, **Syed Tasadaque Ali Shah**, M. Saeed, Mohammed Saleh Shekhani and W. Voelter; *Z. Naturforsch.*, **54b**, 1327-1336 (1999).

9. Regioselective Conversion of Anhydro Sugars into Halohydrins and X-Ray Studies; **Syed Tasadaque Ali Shah**, Raid Abdel-Jalil, Khalid M. Khan, Angelica M. Heinrich and W. Voelter; *Z. Naturforsch.*, **58b** (accepted 2003).
10. A Novel Method for the Syntheses of Symmetrical Disulfides Using CsF-Celite as a Solid Base; **Syed Tasadaque Ali Shah**, Khalid M. Khan, Miriam Fecker and W. Voelter; *Tetrahedron Lett.*, (accepted 2003).
11. A Stereospecific Synthesis of Chiral Tetrahydroquinoxaline, 2,3-Dihydro-benzo-[1,4]-dioxin and 2,3-Dihydro-naphtho-[2,3-b]-[1,4]-dioxin Derivatives; Raid J. Abdel-Jalil, **Syed Tasadaque Ali Shah**, Muhammed Saeed, Miriam Fecker and Wolfgang Voelter (submitted to *Organic Lett.*, 2002).
12. A Novel Route towards the Synthesis of Stereospecific *N*-substituted Chiral Morpholines; Raid Abdel-Jalil, **Syed Tasadaque Ali Shah**, Muhammed Saeed and Wolfgang Voelter (submitted to *Tetrahedron Lett.*, 2002).
13. A Convenient and Stereospecific Synthesis of Chiral 2-Imidazolidinethione from Anhydro sugars; **Syed Tasadaque Ali Shah** and Wolfgang Voelter (under preparation).
14. A Stereospecific Synthesis of Chiral 2,3-Dihydro-benzo-[1,4]-dithiane and 2,3-Dihydro-methylbenzo-[1,4]-dithiane Derivatives; **Syed Tasadaque Ali Shah**, Michael Duszenko and Wolfgang Voelter (to be submitted).

**KURZFASSUNGEN VON INTERNATIONALEN SYMPOSIEN**

1. A Novel and Efficient Cyclization Access to Optically Pure 1,4,5,6-Tetrahydro-*as*-triazines, Fused to Carbohydrates; Raid J. Abdel-Jalil, **Syed Tasadaque Ali Shah**, Hans-Jürgen Machulla and Wolfgang Voelter; 12<sup>th</sup> European Carbohydrate Symposium, Grenoble, France (2003).
2. An Alternative Method for S-Alkylation and Acylation Using CsF-Celite in Acetonitrile; **Syed Tasadaque Ali Shah**, Khalid M. Khan, Safdar Hayat, Muhammad Abbas, Angelika Martinez and Wolfgang Voelter; 7<sup>th</sup> Euroasia Conference on Chemical Sciences, Karachi, Pakistan (2002).
3. Asymmetric Total Synthesis of Lactone Ketone from Amino Acid Template, **Syed Tasadaque Ali Shah**, Naheed Kausar, Khalid Mohammed Khan, Zeeshan, Zia-Ullah Khattak; 8<sup>th</sup> International Symposium on Natural Product Chemistry, Karachi, Pakistan (2000).
4. Some Azaindole Derivatives of Potential Biological Activities, Z. S. Saify, Khalid M. Khan, Nousheen Mushtaq, Fozia Noor, **Syed Tasadaque Ali Shah** and M. Arif; 8<sup>th</sup> International Symposium on Natural Product Chemistry, Karachi, Pakistan (2000).