Investigation of the base promoted tandem *syn*-elimination–Favorskii rearrangement of levoglucosan sulfonates

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The reaction of various 2,3,4-trisulfonated 1,6-anhydro-β-D-glucopyranoses with alkoxide was investigated. Upon treatment with methoxide the tritosylate† **5**, tris(chlorosulfate) **20** and tris(trifluoromethanesulfonate) **21** all gave 1,5-anhydro-2,3-dideoxy-3-methoxycarbonyl-β-D-*erythro*-pentofuranose **6** in 41–57% yield with the yield increasing with improved leaving group ability. The trimesylate‡ **19** gave the 3,4-epoxide **23** and no rearranged product. Chloroform was found to be the best solvent for obtaining **6**, while alcohol as the solvent only gave epoxide **2**. A study of different bases showed that the yield of the Favorskii product was increased 10–20% by using ethoxide as base. Reaction of the corresponding chlorosulfonated 1,6-anhydrogalactopyranose or anhydromannopyranose gave the same product though in lower yield. The Favorskii product **6** rearranged in the presence of traces of acid to a 1,5′:1′,5-dianhydride.

Introduction

Carbohydrates are potentially useful starting materials in organic synthesis due to three advantages: abundance, chirality and well-defined stereochemistry.[1,2] However the peculiar structure of carbohydrates limits their usefulness towards certain targets. Particularly the fact that carbohydrates consist of linear C-chains makes synthesis of branched structures less straightforward. Methods of readily obtaining branched carbohydrate structures are therefore in demand.

One popular chiral starting material is the 1,6-anhydroglucose **1** (levoglucosan),[3] and its descendants the Cerny epoxides **2** and **3**.[4] Compound **2** is routinely obtained from **1** in two steps: conversion of **1** into the ditosylate **4** followed by epoxidation of **4** *via* treatment with NaOMe.[5,6] The tritosylate **5** is sometimes obtained as a by-product in the tosylation of **1**. Recently we attempted to convert some of the by-product **5** into the epoxide **2** using sodium methoxide, but were surprised to find that only a very small amount of **2** was formed together with a large amount (44%) of the rearranged product **6**.[7] Compound **6** is a useful chiral building block and in this paper we report a full account of the transformation of **5** to **6** as well as a study of the scope and limitations of the reaction (Fig. 1).

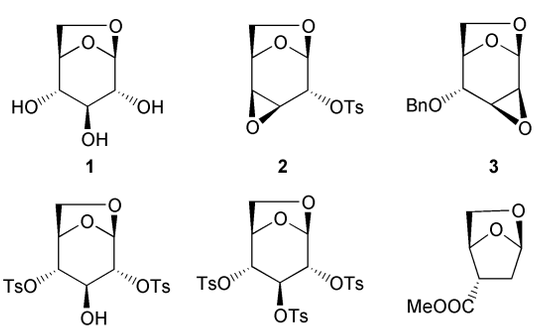
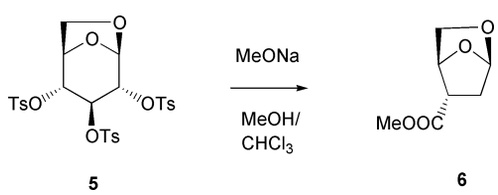


Fig. 1 Levoglucosan **1**, some classical derivatives **2**–**5** and the Favorskii product **6**.

† The IUPAC name for tosylate is toluene-*p*-sulfonate.
‡ The IUPAC name for mesylate is methanesulfonate.

Results and discussion

When the 2,3,4-tri-*O*-tosyl-β-D-glucopyranose **5**[8] was treated with NaOMe in $CHCl_3$ the rearranged product **6** was obtained in 44% yield with small amounts (2–4%) of **5** or **2** also being observed (Scheme 1). The structure of **6** was elucidated from



Scheme 1 Transformation of **5** to **6**.

NMR. Signals at 52 and 178 ppm in the ^{13}C NMR revealed the presence of a methyl ester, while ^{13}C NMR signals at 37 and 45 ppm together with ^{1}H NMR peaks at δ 2.0 and 2.7 showed a deoxygenated CH_2 and a CH. COSY correlations showed an anomeric CH next to CH_2, which was next to CH. This together with HRMS was consistent with the structure **6**. The stereochemistry at C-3 was determined by comparison of the size of the J_{34} coupling constant of **6** (~0 Hz) with the J_{34} values of the 4 possible stereoisomers of peracetylated 1,5-anhydro-β-pentofuranose **7**–**10** (Fig. 2).[9] The *xylo* and *lyxo* isomers **7** and **8**

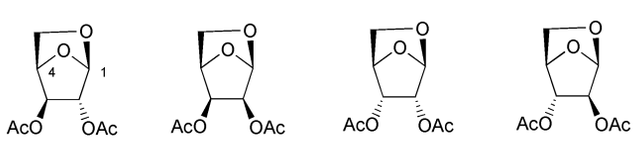


Fig. 2 The four stereoisomers of 1,5-anhydropentofuranose **7**–**10**.

both demonstrated a relatively large coupling (~5 Hz), while the *ribo* and *arabino* isomers **9** and **10** both had a J_{34} value of 0 Hz (Table 1), which suggests that the C-3 of **6** has the same configuration as both **9** and **10**. The spectral data of **7**–**10** were also used to assign the H-2 protons of **6**. The signal at δ 2.1 was assigned to the *exo*-proton, because it had a coupling with H-1 of 2.0 Hz and **8** and **10** have J_{12} values of a similar size

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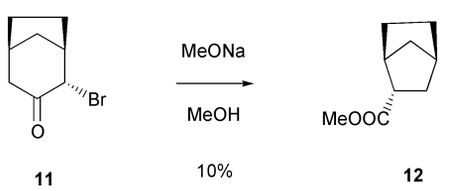
Table 1 ^{1}H-coupling constants for **7**–**10** (from ref. 9)

Compound	J_{12}	J_{23}	J_{34}	J_{45a}	J_{45b}
7	0	1.9	5.0	0	3.2
8	2.4	8.6	4.6	0	3.7
9	0	5.9	0.4	0.4	3.6
10	2.5	1.4	0	(2.5)	(2.5)

(Table 1). In a similar manner the signal at δ 2.0 was assigned to the *endo*-proton, as it had a coupling with H-1 of 0 Hz and both **7** and **9** have J_{12} values of 0 Hz (Table 1). A small inconsistency in this interpretation was found in the size of J_{23}. While J_{2endo3} of **6** (8.5 Hz) is in reasonable agreement with J_{23} of **9**, J_{2exo3} (4.5 Hz) is rather large compared to J_{2endo3} of **10**. This may be explained by the somewhat different conformation of **10** due to steric repulsion between the 2-*O*-acetate and the 1,5-anhydro-bridge. The configuration of **6** was later confirmed by the X-ray crystallographic analysis of a derivative of **6** (see below).

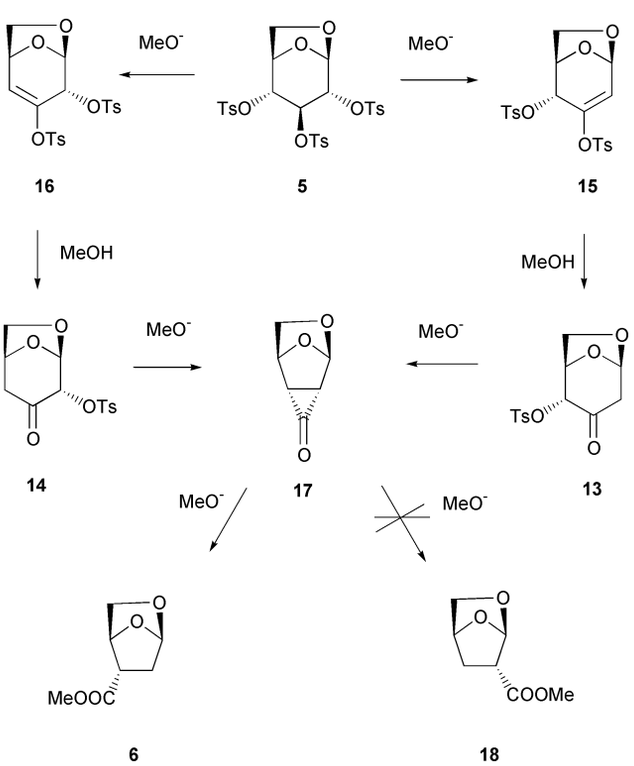
The product **6** seems to be the result of a Favorskii rearrangement due to the presence of the ester and the ring contraction observed. A similar Favorskii reaction was observed on treatment of 2-bromoketone **11** with NaOMe which gave ester **12** in 10% yield (Scheme 2).[10] This reaction also



Scheme 2 Favorskii reaction of haloketone **11** (from ref. 11).

gave a small amount (<1%) of the epimer of **12**, and large amounts of the methoxide substitution products. The stereochemistry of **6** is also consistent with a product of a Favorskii reaction since this reaction is believed to involve a cyclopropanone intermediate which forces the ester and leaving group to be on the same side of the ring in cyclic systems.[11]

If a Favorskii reaction is responsible for the formation of **6** either ketone **13** or **14** has to be an intermediate (Scheme 3).



Scheme 3 Proposed mechanism for the transformation of **5** to **6**.

Table 2 Yield of **6**, **24** or **25** from reactions of **5**, **19**–**21** with different alkoxides in $CHCl_3$.

Substrate	Base		
NaOMe (%)	NaOEt (%)	NaOPr (%)	
6	44	55	50[b]
19	0[a]	—	—
20	46	61	—
21	57	75	—

[a] Epoxide **23** was formed. [b] Yield of impure (90% pure) material. Treatment of **5** with NaOiPr gave only alkenes **15** and **16**, while treatment with $NaNH_2$ gave only epoxide **2**.

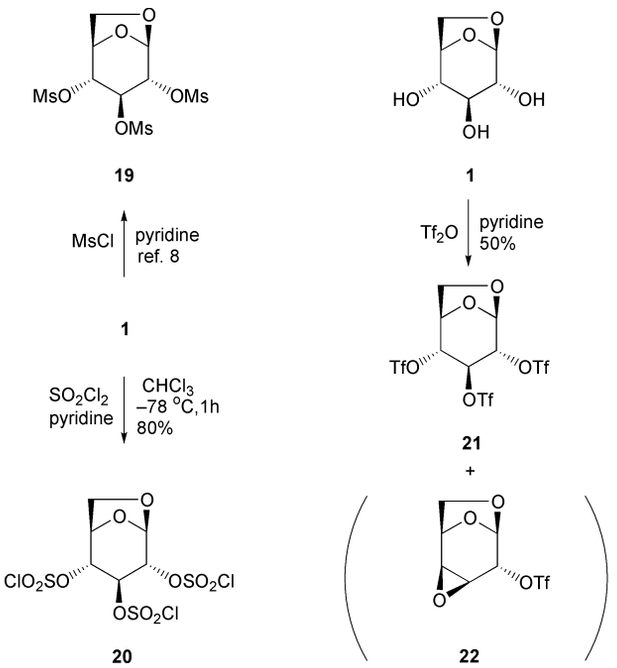
Epoxide **2**, which could conceivably lead to ketone **14**, was however found not to be an intermediate, as **2** was entirely stable towards prolonged treatment with NaOMe in chloroform.

The ketones **13** and **14** can on the other hand be formed by elimination of a 2- or 4-tosylate respectively followed by transtosylation between the resulting enol tosylates **15** and **16** and methanol. The alkenes **15** and **16** were indeed formed in 90% yield (2 : 3) when **5** was treated with DBU in $CHCl_3$. It is likely that the elimination of the tosylate groups from **5** occurs by an E2 *syn*-elimination process since a conventional E2 *anti*-elimination not is possible. Such an elimination requires that the tosylate leaving groups and H-3 are eclipsed, which is not the case in compounds that have a $^1C_4$ conformation of the monosaccharide ring. It has been suggested however that **5** and similar 3-substituted derivatives of levoglucosan are forced into a boat conformation due to steric repulsion between the 3-substituent and the 1,6-anhydro bridge.[12] This would facilitate a *syn*-elimination.

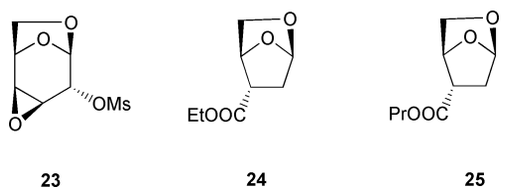
We therefore propose the mechanism outlined in Scheme 3 for the reaction. According to this mechanism four reactions occur: 1) *syn*-elimination leads to either **15** or **16**, 2) base-catalysed trans-esterification of the enol tosylates of **15** and **16** gives ketones **13** and **14** respectively, 3) base induced formation of the Favorskii intermediate **17** and 4) opening of the cyclopropanone with alkoxide to give **6**. There is much evidence for **17** being an intermediate in the Favorskii reaction.[11,13] It is curious, however, that the regioisomeric ester **18** is not formed in the reaction. This must be due to the electron withdrawing power of the acetal functionality which makes negative charge accumulation on C-2 more favourable than C-3. This effect of electron withdrawing substituents is known in the Favorskii reaction as phenylacetone gives 3-phenylpropionates and not methylphenylacetates on treatment with base.[13]

Since several of the steps of this mechanism could be improved by changing the leaving groups, a study of the effect of the leaving groups was undertaken. From levoglucosan **1** a series of analogues of **5**, **19**–**21**, was prepared. Known trimesylate **19** was prepared as described in the literature,[8] while known tris(chlorosulfate) **20** was prepared by an improvement of the literature procedure[14] which allowed its preparation in 80% yield (Scheme 4). The tris(trifluoromethanesulfonate) **21** was prepared in a similar fashion using Tf_2O (7 eq.) in CH_2Cl_2–pyridine (15 : 1) at −78 °C, but the yield was lower due to some formation of epoxide **22**. Presumably the epoxide formation is so fast in this case that it is competes with the sulfonylation of the hindered 3-OH. Epoxide **22** could be isolated in 50% yield after chromatography (EtOAc–pentane 1 : 4).

The results of the reaction of the sulfonates **19**–**21** with 4 equivalents of NaOMe in $CHCl_3$–MeOH (7 : 1) is shown in Table 2 (column 2). It is clearly seen that the yield of the Favorskii product **6** is increased when the leaving group ability is increased *i.e.* OTf > OSO_2Cl > OTs > OMs. The reaction completely fails with mesylate leaving groups (substrate **19**), where only the epoxide **23** was formed (Fig. 3). This may be due to the



Scheme 4 Synthesis of trisulfonated analogues of **1**.



23 **24** **25**

Fig. 3 Epoxide **23** and Favorskii products **24** and **25**.

somewhat poorer leaving group ability of mesylate compared to tosylate, but perhaps also because attack on sulfur, which leads to epoxide, is less hindered in the mesylate case.

It is known that ethoxide or isopropoxide often gives higher yields in the Favorskii reaction than methoxide.[13] We therefore also investigated the effect of using different alkoxides (Table 2). The yield of the Favorskii product **24** when using NaOEt was increased in all the substrates investigated. NaOPr and NaOiPr were also tried, but treatment of **5** with these bases led to the isolation of alkenes **15** and **16**. When the propoxide was used **25** was also obtained, but only **15** and **16** were obtained with the more hindered isopropoxide. These experiments suggest that attack on the enol sulfonates in **15** or **16** becomes a more difficult step when the more hindered alkoxides are used.

$NaNH_2$ is also known to react with α-haloketones to give a Favorskii rearrangement in 15–20% yield.[13] However reaction of $NaNH_2$ with **5** in THF–NH_3 only gave epoxide **2**.

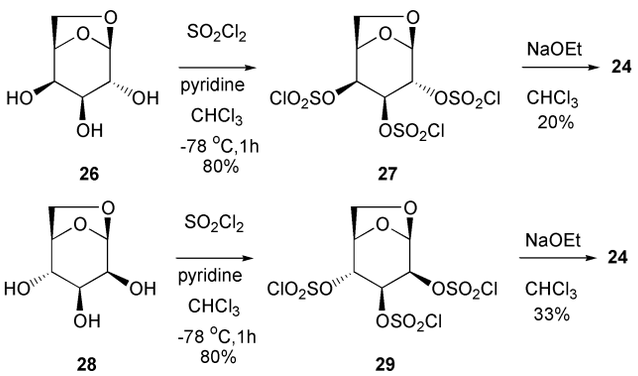
It is particularly interesting to note that **5** has been reacted by Miljkovic *et al.* with NaOMe in THF to give **2** in 30% yield.[12] We therefore also investigated the effect of the cosolvent (Table 3). When the reaction between **5** and NaOMe or NaOEt was carried out, but chloroform was exchanged for THF, EtOAc or MeOAc, formation of **6** or **24** was still observed, but in reduced yields. Thus the reaction is favoured using a non-polar reaction medium. When no cosolvent was used, *i.e.* the reaction was carried out in pure MeOH or EtOH, only the epoxide **2** was isolated. We believe that in these protic solvents the alkoxide is not a strong enough base to cause the *syn*-elimination of a tosylate, therefore the reaction follows another path.

We also investigated the reaction of readily available stereoisomers of levoglucosan **26**[15] and **28**.[16] The chlorosulfates **27**[14] and **29** were obtained from **26** and **28** by the same method and with the same yield as the conversion of **1** to **20** (Scheme 5).

Table 3 Yield of **6** from reactions of **5** with NaOMe or NaOEt with different cosolvents. The cosolvent constituted 88% (v/v) of the solution, the remaining being MeOH or EtOH.

Cosolvent	Base	
	NaOMe (%)	NaOEt (%)
$CHCl_3$	44	55
EtOAc	—	46
MeOAc	44	—
THF	15	20
MeOH	0[a]	—
EtOH	—	0[a]

[a] Epoxide **2** was formed.



Scheme 5 The Favorskii reaction of stereoisomers of **20**.

Treatment of **27** with NaOEt in $CHCl_3$–EtOH (7 : 1) gave a 20% yield of **24**, while similar treatment of **29** gave a 33% yield of **24**. Somewhat surprisingly no stereoisomers of **24** were detected. Since **24** can only be formed from the intermediate ketone **17**, **27** must undergo preferential *syn*-elimination of the equatorial 4-chlorosulfate to form alkene **16** while **29** must undergo preferential *syn*-elimination of the equatorial 2-chlorosulfate to form an alkene similar to **15**. This supports the hypothesis that the chlorosulfate analogues of **15** and **16** can lead to Favorskii products, and that the reaction follows both paths in Scheme 3.

The Favorskii esters **6** and **24** were observed to undergo dimerisation or oligomerisation on prolonged standing in the dry state, occasionally even during silica gel chromatography or in a chloroform solution. Thus refluxing **6** in $(CH_2Cl)_2$ solution led to trans-acetalisation to give a 35% yield of 1,5′:5,1′ diacetal **30** (Scheme 6), which was characterised by 1H and 13C NMR spectra and X-ray crystallography (Fig. 4). Similarly

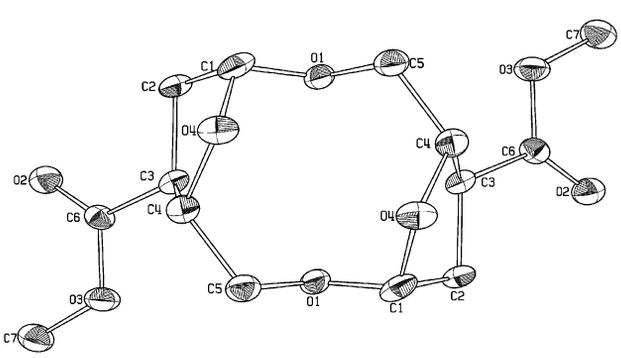
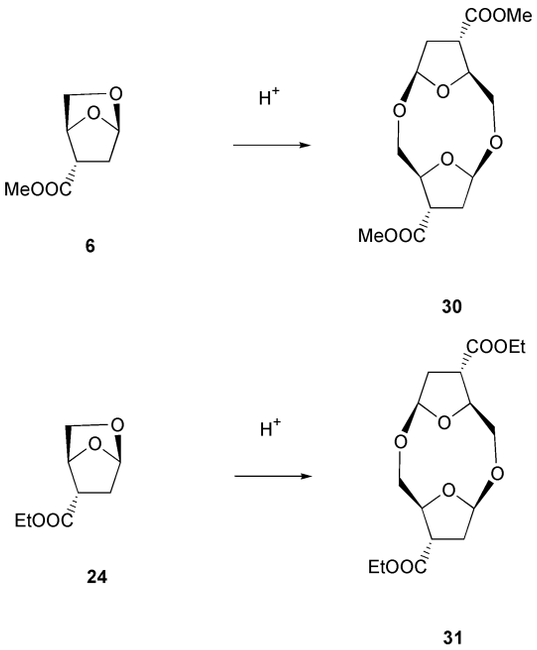


Fig. 4 X-Ray structure of **30**.

1,5′:5,1′ diacetals of other ribofuranoses are known.[17–19] Dimerisation was accompanied by formation of higher oligomers and the process could be promoted by addition of acid or heat. Similarly **24** could dimerise to **31**. The dimerisation can be prevented by adding a small amount of Et_3N to the eluent



Scheme 6 Dimerisation of **6** and **24**.

during chromatography and storing **6** or **24** in a solution containing a small amount of Et_3N.

In summary it has been found that the chiral building blocks **6** and **24** are obtained by addition of NaOMe or NaOEt to persulfonylated 1,6-anhydrohexoses in chloroform. The best overall yield of Favorskii product is obtained by chlorosulfonation of **1** and subsequent treatment of the chlorosulfate **20** with NaOEt in $CHCl_3$. Though the tris-trifluorosulfonate **21** provides a better yield in the Favorskii reaction the fact that **21** cannot be obtained in good yield makes it a less than ideal intermediate. The compounds **6** and **24** are available from starch in just three steps and will be useful building blocks for the synthesis of many chiral compounds.

Experimental

General

Solvents were distilled under anhydrous conditions. All reagents were used as purchased without further purification. Pyridine was dried over potassium hydroxide before use. Evaporation was carried out on a rotatory evaporator with the temperature kept below 40 °C. Glassware used for waterfree reactions was dried for a minimum of 2 hours at 130 °C before use. Columns were packed with silica gel 60 (230–400 mesh) as the stationary phase. TLC-plates (Merck, 60, F_{254}) were visualized by spraying with cerium sulfate (1%) and molybdic acid (1.5%) in 10% H_2SO_4 and heating until coloured spots appeared. ^{1}H-NMR, ^{13}C-NMR and COSY were carried out on a Varian Gemini 200 instrument. Mass spectra were carried out on a Micromass LC-TOF instrument. Specific optical rotations were measured on a Perkin Elmer 241 polarimeter in units of 10^{-1} deg cm^2 g^{-1}.

Elimination of 5

The tritosylate **5** (512 mg, 0.79 mmol) was dissolved in $CHCl_3$ (5 ml) and DBU (600 mg) was added. The mixture was stirred for 18 h at room temperature. The solution was concentrated to a residue using rotary evaporation, redissolved in CH_2Cl_2 (20 ml), washed with Na_2CO_3 solution (10 ml, 5%), dried and concentrated. The residue was then subjected to flash-chromatography in EtOAc–CH_2Cl_2, 1 : 9 to give 338 mg (90%) of a mixture of **15** and **16** (2 : 3). Repeated chromatography (EtOAc–pentane, 1 : 3) allowed a small amount of pure **16** to be isolated. **16**: R_f 0.3 (EtOAc–pentane, 1 : 3); ^{1}H NMR ($CDCl_3$): δ 2.4 (s, 6H, Ts's), 3.6 (m, 2H, H-6a, H-6b), 4.2 (d, 1H, H-2, $J_{1,2}$ 1.9), 4.8 (dd, 1H, H-5, $J_{4,5}$ 5.3, $J_{5,6}$ 4.0), 5.55 (d, 1H, H-1), 6.0 (d, 1H, H-4), 7.2–7.8 (m, 8H, Ts's); MS(ES) *m*/*z* 475.6 (M + Na). **15**: R_f 0.2 (EtOAc–pentane, 1 : 3); ^{1}H NMR ($CDCl_3$): δ 2.4 (s, 6H, Ts's), 3.25 (dd, 1H, H-6a, $J_{5,6a}$ 6.3, $J_{6a,6b}$ 8.7), 3.85 (dd, 1H, H-6b, $J_{5,6b}$ 2.3), 4.4 (d, 1H, H-4, $J_{4,5}$ 1.5), 4.7 (ddd, 1H, H-5), 5.6 (d, 1H, H-1, $J_{1,2}$ 4.1), 5.75 (d, 1H, H-2), 7.2–7.8 (m, 8H, Ts's).

Chlorosulfonation of 1,6-anhydropyranoses

The reaction proceeded under a nitrogen atmosphere and freshly distilled dichloromethane was used. To a solution of 1,6-anhydropyranose (0.47 g, 2.92 mmol) in pyridine (1.8 ml, 22.3 mmol) was added dichloromethane (20 ml). The mixture was cooled to −78 °C (approx. 20 min) and, while stirring vigorously, sulfuryl chloride (1.64 ml, 20.4 mmol) was added dropwise over a period of 20 minutes. Stirring was continued at −78 °C for 1 hour followed by addition of 10% sulfuric acid (5 ml) with heating to 25 °C over a period of no more than 10 minutes. The organic layer was separated and washed twice with a saturated aqueous solution of sodium bicarbonate (2 × 5 ml) and finally with water (5 ml). The organic layer was dried ($MgSO_4$) and concentrated affording the tris(chlorosulfate) as a yellow–white syrup–semisolid (1.07 g, 80%). These compounds were unstable and were used without further purification.

1,6-Anhydro-2,3,4-tris-*O*-chlorosulfonyl-β-D-glucopyranose (20)[14]. R_f 0.43 (EtOAc–pentane, 1 : 4); ^{1}H NMR ($CDCl_3$): δ 3.95 (dd, 1H, H-6a, $J_{6,5}$ 5.2, $J_{6a,6b}$ 8.2), 4.2 (d, 1H, H-6b), 4.8 (d, 1H, H-2, $J_{2,3}$ 0.8), 4.95 (d, 1H, H-4, $J_{3,4}$ 0.8), 4.95 (d, 1H, H-5), 5.25 (t, 1H, H-3), 5.75 (s, 1H, H-1); ^{13}C NMR ($CDCl_3$): δ 65.3 (C-6), 73.1, 75.8, 77.0 and 77.9 (C-2, C-3, C-4 and C-5), 97.9 (C-1).

1,6-Anhydro-2,3,4-tris-*O*-chlorosulfonyl-β-D-galactopyranose (27)[14]. R_f 0.43 (EtOAc–pentane, 1 : 4); ^{1}H NMR ($CDCl_3$): δ 3.9 (dd, 1H, H-6a, $J_{6,5}$ 4.8, $J_{6a,6b}$ 8.9), 4.35 (d, 1H, H-6b), 4.85 (t, 1H, H-4, $J_{4,3}$ 4.8, $J_{4,5}$ 4.8), 5.05 (d, 1H, H-2, $J_{2,3}$ 1.9), 5.2 (t, 1H, H-5), 5.35 (dd, 1H, H-3), 5.7 (s, 1H, H-1); ^{13}C NMR ($CDCl_3$): δ 65.0 (C-6), 71.7, 73.2, 77.0 and 78.8 (C-2, C-3, C-4 and C-5), 98.1 (C-1).

1,6-Anhydro-2,3,4-tris-*O*-chlorosulfonyl-β-D-mannopyranose (29). R_f 0.69 (EtOAc–pentane, 1 : 4); ^{1}H NMR ($CDCl_3$): δ 4.0 (dd, 1H, H-6a, $J_{6a,5}$ 5.3, $J_{6a,6b}$ 9.2), 4.25 (d, 1H, H-6b), 4.95 (dd 1H, H-2, $J_{2,3}$ 5.3, $J_{2,1}$ 1.5), 5.95 (dd, 1H, H-5, $J_{5,4}$ 2.0), 5.15 (t, 1H, H-4), 5.35 (dd, 1H, H-3), 5.75 (d, 1H, H-1); ^{13}C NMR ($CDCl_3$): δ 65.9 (C-6), 73.6 (C-5), 75.4 (C-2), 77.2 (C-4), 80.9 (C-3), 98.1 (C-1).

Trifluoromethanesulfonylation of levoglucosan (1)

A solution of **1** (473 mg, 2.92 mmol) in pyridine (1.8 ml, 22.3 mmol) and dichloromethane (30 ml) was cooled to −78 °C (approx. 20 min) and, while stirring vigorously, trifluoromethanesulfonic anhydride (4.25 ml, 20.4 mmol) was added dropwise. Stirring was continued at −78 °C for 1 hour followed by addition of 10% sulfuric acid (5 ml) with heating to 25 °C over a period of no more than 10 minutes. The organic layer was separated and washed twice with a saturated aqueous solution of sodium bicarbonate (2 × 5 ml) and finally with water (5 ml). The organic layer was dried ($MgSO_4$) and concentrated. The crude product was chromatographed (EtOAc–pentane, 1 : 4) affording a colourless syrup containing 1,6-anhydro-2,3,4-tris-*O*-[(trifluoromethyl)sulfonyl]-β-D-glucopyranose (**21**, 802 mg, 50%), which was unstable and was used immediately without further purification. R_f 0.81 (EtOAc–pentane, 1 : 4); ^{1}H

NMR ($CDCl_3$): δ 3.9 (dd, 1H, H-6a, $J_{6a,6b}$ 8.9, $J_{6a,5}$ 5.5), 4.11 (d, 1H, H-6b), 4.65(d, 1H, H-4, $J_{4,3}$ 1.3), 4.81 (d, 1H, H-2, $J_{2,3}$ 1.3), 4.82 (d, 1H, H-5), 5.0 (t, 1H, H-3), 5.65 (s, 1H, H-1); ^{13}C NMR ($CDCl_3$): δ 65.7 (C-6), 74.0, 76.0, 77.9 and 78.3 (C-2, C-3, C-4 and C-5), 98.7 (C-1), 119.1 (q, 3 × OSO_2CF_3).

Elimination–Favorskii rearrangement

General procedure. To a solution of trisulfate (0.57 mmol) in chloroform (7 ml) a solution of sodium (50 mg) in alcohol (1 ml, HPLC quality) was added. The reaction proceeded for 30 min at room temperature followed by addition of a mixture of water (3 ml) and a saturated solution of ammonium chloride (0.5 ml). The phases were separated, and the organic layer dried ($MgSO_4$), concentrated and chromatographed in diethyl ether–pentane (1 : 4) to give the product.

*1,5-Anhydro-2,3-dideoxy-3-methoxycarbonyl-β-D-erythro-pentofuranose (**6**).* R_f 0.35 (EtOAc–pentane, 1 : 4); $[\alpha]_D^{25}$: −50.4 (*c* 3.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 2.0 (d, 1H, H-2*endo*, $J_{2endo,2exo}$ 12.0), 2.1 (ddd, 1H, H-2*exo*, $J_{2exo,1}$ 2.0), 2.7 (dd, 1H, H-3, $J_{2endo,3}$ 8.5, $J_{2exo,3}$ 4.5), 3.5 (m, 2H, H-5a and H-5b); 3.6 (s, 3H, OCH_3), 5.0 (t, 1H, H-4, $J_{4,5}$ 2.7), 5.65 (d, 1H, H-1); ^{13}C NMR ($CDCl_3$): δ 36.6 (C-2), 44.7 (C-3), 52.2 (OCH_3), 68.6 (C-5), 78.1 (C-4), 100.4 (C-1), 172.6 (CO_2CH_3);. MS(ES) *m*/*z* 181.0483. Calc. for $C_7H_{10}O_4$ + Na: 181.0477.

*1,5-Anhydro-2,3-dideoxy-3-ethoxycarbonyl-β-D-erythro-pentofuranose (**24**).* R_f 0.40 (EtOAC–pentane, 1 : 4). $[\alpha]_D^{25}$: −42.3 (*c* 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.25 (t, 3H, CH_3, $J_{OCH2,CH3}$ 7.0), 2.1 (d, 1H, H-2*endo*, $J_{2endo,2exo}$ 12.0), 2.2 (ddd, 1H, H-2*exo*, $J_{2exo,1}$ 2.0), 2.8 (dd, 1H, H-3, $J_{3,2endo}$ 8.5, $J_{3,2exo}$ 4.5), 3.6 (m, 2H, H-5a, H-5b), 4.2 (q, 2H, OCH_2), 5.1 (t, 1H, H-4, $J_{4,5}$ 2.7), 5.75 (d, 1H, H-1); ^{13}C NMR ($CDCl_3$): δ 14.3 (OCH_2CH_3), 36.8 (C-2), 45.1 (C-3), 61.4 (OCH_2), 68.9 (C-5), 78.5 (C-4), 100.6 (C-1), 172.4 (CO_2CH_3); MS(ES) *m*/*z* 195.0629. Calc. for $C_8H_{12}O_4$ + Na: 195.0633.

Bis(2,3-dideoxy-3-methoxycarbonyl-β-D-*erythro*-pentofuranose) 1,5′:5,1′-dianhydride (30)

The Favorskii product **6** (50 mg) was dissolved in 1,2-dichloroethane (5 ml) and refluxed for 2 h. The solution was concentrated and subjected to chromatography in pentane–EtOAc to give **30** (21 mg, 35%). $[\alpha]_D^{25}$: −42.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 2.2 (dt, 2H, H-2a, $J_{2a,3}$ = $J_{2a,2b}$ 12 Hz, $J_{1,2a}$ 4 Hz), 2.25 (dd, 2H, H-2b, $J_{2b,3}$ 8 Hz), 3.6 (dt, 2H, H-3, $J_{3,4}$ 8 Hz), 3.7 (s, 6H, OCH_3), 3.8 (m, 4H, H-5a, H-5b), 4.2 (d, 2H, H-4), 5.1 (d, 2H, H-1 $J_{1,2a}$ 4); MS(ES) *m*/*z* 339.1061. Calc. for $C_{14}H_{20}O_8$ + Na: 339.1056.

Bis(2,3-dideoxy-3-ethoxycarbonyl-β-D-*erythro*-pentofuranose)-1,5′:5,1′-dianhydride (31)

Anhydride **24** (50 mg) was heated to 70 °C for 1.5 h without solvent present. The resulting syrup was chromatographed in EtOAc–pentane 1 : 4 to give **31** (10 mg, 20%, R_f 0.28). Slower moving polymeric compounds could not be obtained in a pure form. ^{1}H NMR ($CDCl_3$): δ 1.45 (t, 6H, Me's, *J* 7 Hz), 2.2 (dt, 2H, H-2a, $J_{2a,3}$ = $J_{2a,2b}$ 12 Hz, $J_{1,2a}$ 4 Hz), 2.35 (dd, 2H, H-2b, $J_{2b,3}$ 8 Hz), 2.65 (dt, 2H, H-3, $J_{3,4}$ 8 Hz), 3.8 (m, 4H, H-5a, H-5b), 4.25 (d, 2H, H-4), 4.45 (q, 4H, CH_2's), 5.15 (d, 2H, H-1 $J_{1,2a}$ 4); MS(ES) *m*/*z* 367.1367. Calc. for $C_{16}H_{24}O_8$ + Na: 367.1369.

X-Ray work §

The crystal structure of **30**, bis(2,3-dideoxy-3-methoxycarbonyl-β-D-*erythro*-pentofuranose) 1,5′:5,1′-dianhydride, $C_{14}H_{20}O_8$, MW = 316.31, was solved using data collected at 120 K from a colourless needle on a SIEMENS SMART CCD diffractometer. The crystals are monoclinic, space group C_2, with unit cell: a = 16.975(2) Å, b = 5.1909(6) Å, c = 8.569(1) Å, β = 92.386(3)°, V = 754.4(2) Å^3, Z = 2, μ = 0.115, R_{int} = 0.081, for 2433 measured reflections giving 1210 independent. Direct methods were applied[20] for the structure solution, and the structure refined by least squares methods to a final R = 0.078, R_w = 0.100, GoF = 1.72 for 932 reflections with $I > 3\sigma(I)$ and 99 parameters. The floating origin was fixed by not refining the y coordinate of O1, but the standard errors are correct because they are calculated using the full matrix. The absolute configuration was assumed from the starting materials, but no anomalous scattering was considered since all atoms are too light to give any effect with Mo radiation.

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§ CCDC reference number 178389. See http://www.rsc.org/suppdata/p1/b2/b200064b/ for crystallographic files in .cif. or other electronic format.

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