Rearrangement of Carbohydrate Epoxides to Amino Sugars Using a Trichloroacetimidoyl Neighboring Group

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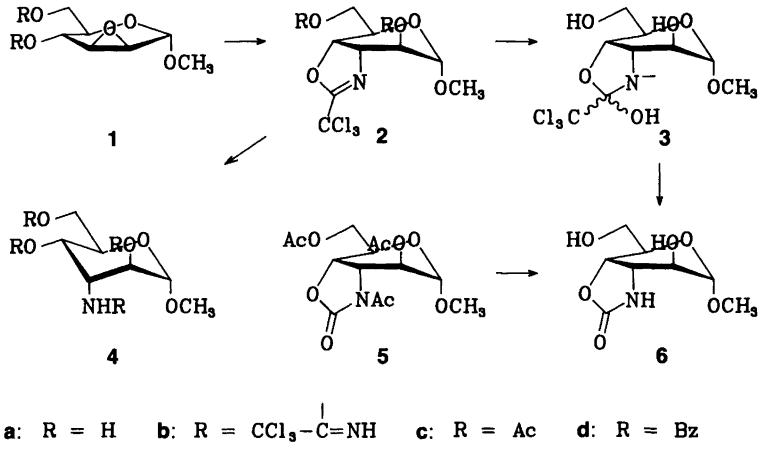
When glycosides containing an epoxide functionality are treated with trichloroacetonitrile and sodium hydride, the free hydroxy groups are converted into trichloroacetimidates, which subsequently open the epoxide ring to give amino-sugar derivatives. The reaction was carried out on manno-, altro-, gulo- and galacto-pyranosides, manno-, gulo-, altro- and galacto-1,6-anhydropyranoses, and lyxo- and arabino-pyranosides, and it was found, that the reaction takes place with vicinal *trans*-substituted epoxide trichloroacetimidates to give oxazoline derivatives.

In a recent paper[1] it was shown that neighbouring-group participation from a trichloroacetimidoyl group can be utilized in the regiospecific *trans*-opening of carbohydrate benzoxonium ions, to give amino sugars. Trichloroacetimidates have also been used as neighboring groups in iodocyclization reactions on allylic and homoallylic trichloroacetimidates to give a regiospecific conversion into amino-alcohol derivatives.[2] The present paper describes the nucleophilic opening of carbohydrate epoxides by a neighboring trichloroacetimidoyl group. Bernet and Vasella[3] have shown in a synthesis of sphingosine that an electrophilic opening (with triethylaluminium) of an epoxide with a neighboring trichloroacetimidoyl group leads only to one of the two possible products.

For the introductory studies of the conversion of trichloroacetimodoyl-substituted epoxides to amino sugars was chosen methyl 2,3-anhydro-α-D-mannopyranoside (**1**), which is easily prepared from methyl α-D-glucopyranoside.[4] Treatment of this epoxide with sodium hydride and trichloroacetonitrile gave methyl 3-amino-3-deoxy-2,6-di-*O*-trichloroacetimidoyl-α-D-altropyranoside 3-*N*,4-*O*-trichloroacetimidate (**2b**) as an unstable syrup, which rapidly turned cloudy, probably as a result of precipitation of the trichloroacetamide liberated in the facile hydrolysis of the 2,6-iminoester substituents.

In order to avoid handling the moisture-sensitive trichloroacetimidates, the reaction mixture was hydrolysed with sodium hydroxide in methanol and acetylated. This resulted in two products. The minor product (23 %) was the expected methyl 3-acetamido-3-deoxy-2,4,6-tri-*O*-acetyl-α-D-altropyranoside (**4c**) already described by Myers and Robertson[5] as the sole product obtained on acetylation of methyl 3-amino-3-deoxy-α-D-altropyranoside (**4a**). The major product (50 %) contained only three acetyl groups, but four carbonyl groups, of which one had a chemical shift of 152.4 ppm and a very long relaxation time, as seen from the ^1H and ^{13}C NMR spectra. These observations combined with an elemental analysis corresponding to the formula $C_{13}H_{19}NO_7$ and absorptions in the IR spectrum at 1807, 1748 and 1712 cm^{-1}, indicated the carbamate structure (**5**) for the major product. *N*-Acetyl-2-oxazolidinone, which contains the same cyclic *N*-acyl carbamate structure as **5**, shows IR absorptions at 1776 and 1698 cm^{-1}.[6] *N*-Benzoyl-4,5-tetramethylene-2-oxazolidone absorbs at 1791 and 1677 cm^{-1}.[7]

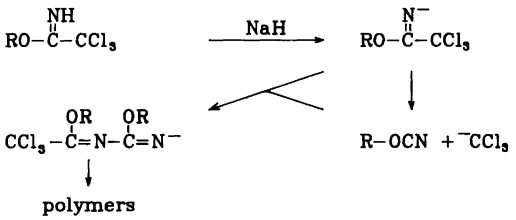
The formation of **5** may involve a reaction between the liberated aminoglycoside and carbon



Scheme 1.

dioxide (either from the atmosphere or from contaminating sodium carbonate in the sodium hydroxide) to give the *N*-carbamate, which to some extent survives neutralization and cyclizes on being acetylated. Alternatively the trichloroacetimidate itself may be the source of the carbamate. When trichloroacetamides are treated with sodium hydroxide isocyanates are formed with the elimination of chloroform.[8] This type of reaction can be visualized for the cyclic trichloroacetimidate (**2a**), which on being attacked by the hydroxide ion gives **3**, which subsequently decomposes to the enol form of the cyclic carbamate (**6**).

Partial, rather than complete, hydrolysis of **2b** is possible if methanol is added to the reaction mixture and the resulting methanol–methoxide solution is neutralized with carbon dioxide. In this way aqueous work-up is avoided and methyl 3-amino-3-deoxy-α-D-altropyranoside 3-*N*-,4-*O*-trichloroacetimidate (**2a**) can be isolated (89 %) by evaporation, extraction and flash chromatography. The syrupy cyclic imidate (**2a**) is sufficiently stable to be isolated in analytical purity, however isolation (43 %) as the crystalline 2,6-di-*O*-benzoate (**2d**) is more convenient. Alternatively, hydrolysis with trifluoroacetic acid–water yields methyl 3-amino-3-deoxy-α-D-altropyranoside hydrochloride (**4a** · HCl; 57 %), which on being acetylated gives methyl 3-acetamido-3-deoxy-2,4,6-tri-*O*-acetyl-α-D-altropyranoside (**4c**; 73 %).



Scheme 2.

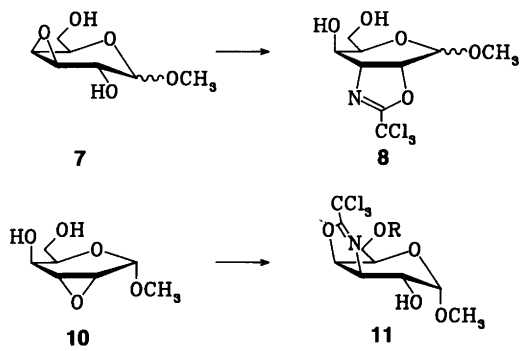
Based on the experience gained from the experiments with the anhydromannoside (**1**) the reaction was then extended to a variety of anhydromonosaccharides. The results, given in Table 1, show the outcome of rearrangement to cyclic imino esters followed by immediate deacylation to remove the trichloroacetimidoyl groups. In this manner the compounds isolated were the cyclic imidate and recovered starting material. In several cases a considerable amount of epoxide was recovered even after reaction times of 4 h at room temperature; this result does not however indicate that a higher yield of rearranged product is obtained by increasing the reaction time or temperature. Attempts to increase conversion further only led to destruction of the product already formed and no substantial decrease in the amount of recovered epoxide was observed. One possible explanation is that the trichloroacetimidate, formed initially from the hydroxy epoxide, undergoes a competing reaction to give the cyanate, which may not be able to rearrange or may react to give di- or poly-meric products as shown in Scheme 2; products which on deacylation

Table 1. Conversion of epoxy sugars to amino sugar *O,N*-trichloroacetimidates.

Starting material	Time/h	Temp./°C	Recovered st. mat./%	Product (yield/%)
Methyl 2,3-anhydro-α-D-mannopyranoside (**1**)	1	0	0	**2a** (89)
Methyl 3,4-anhydro-α-D-galactopyranoside (α-**7**)	1	20	79	–
Methyl 3,4-anhydro-β-D-galactopyranoside (β-**7**)	1	0	0	β-**8** (53)
Methyl 2,3-anhydro-α-D-gulopyranoside (**10**)	1	0	0	**11a** (31), **11b** (24)
1,6:2,3-Dianhydro-β-D-gulopyranose (**13**)	4	20	35	**14** (34)
1,6:3,4-Dianhydro-β-D-altropyranose (**16**)	4	20	51	**17** (29)
1,6:3,4-Dianhydro-β-D-galactopyranose (**19**)	4	20	61	**20** (3)
1,6:2,3-Dianhydro-β-D-mannopyranose (**22**)	4	20	65	**23** (6)
Methyl 2,3-anhydro-α-D-lyxopyranoside (**25**)	1	0	0	**26** (84)
Methyl 3,4-anhydro-α-D-arabinopyranoside (**28**)	1	0	0	**29** (73)
5,6-Anhydro-1,2-*O*-isopropylidene-α-D-glucofuranoside (**31**)	4	20	66	–
Benzyl 3,4-anhydro-β-D-altropyranoside (**32**)	4	20	56	**33** (8)

would all lead to recovery of the starting material. An analogy to the first step in this reaction sequence is found in the afore mentioned use of trichloroacetamides as a source of isocyanates.[8]

Examination of the outcome of the individual reactions in Table 1 reveals that the α-galacto epoxide (α-**7**) is attacked neither by the 2- nor the 6-*O*-trichloroacetimidoyl group. The failure of the attack by the 2-*O*-trichloroacetimidoyl group may be due to 1,3-diaxial steric interactions within the methyl glycoside, since the corresponding β-galacto epoxide (β-**7**) is opened by the 2-*O*-trichloroacetimidoyl group to give methyl 3-amino-3-deoxy-β-D-gulopyranoside 2-*O*,3-*N*-trichloroacetimidate (β-**8**), although in this case, the 6-*O*-trichloroacetimidoyl group



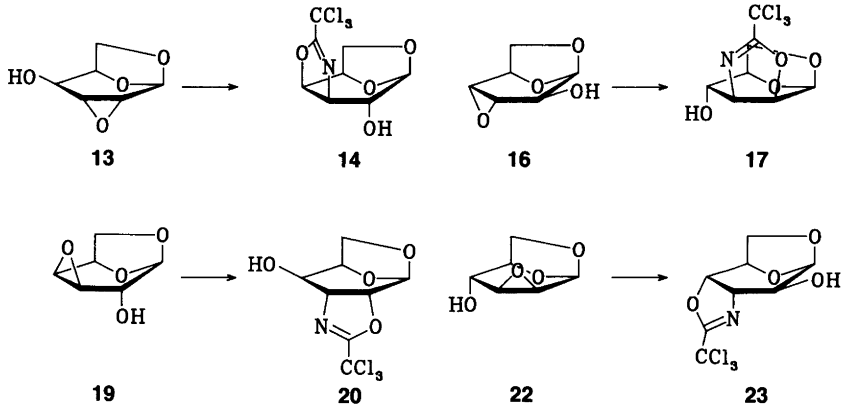
a: R = H **b**: R = CCl_3–C(=NH)–

Scheme 3.

again did not participate in the epoxide opening. That the 1,3-diaxial interactions mentioned above are not prohibitive, can be inferred from the reactions of 1,6:2,3-dianhydro-β-D-gulopyranose (**13**) and 1,6:3,4-dianhydro-β-D-altropyranose (**16**), which in spite of two 1,3-diaxial interactions do undergo epoxide opening, although a substantial part of the starting material is converted into side products which revert to starting material upon work-up. This difference in behavior may be ascribed to the flattening of the half-chair conformations adopted by carbohydrate epoxides caused by the 1,6-anhydro bridge.[9]

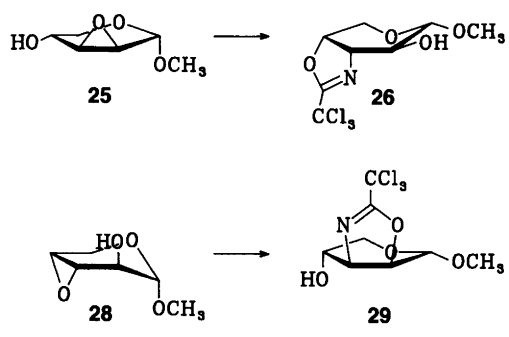
When 5,6-anhydro-1,2-di-*O*-isopropylidene-α-D-glucofuranose (**31**) is treated with trichloroacetonitrile and sodium hydride no 3,5-fused dihydrooxazine derivative is formed, again an indication that neighboring-group participation in the form of a six-membered ring is not operative.

Treatment of methyl 2,3-anhydro-α-D-gulopyranoside (**10**) with trichloroacetonitrile and sodium hydride leads to rearrangement to methyl 3-amino-3-deoxy-α-D-galactopyranoside 3-*N*,4-*O*-trichloroacetimidate (**11a**), isolated partly as the corresponding 6-*O*-trichloroacetimidate (**11b**) owing to the low solubility of this latter compound preventing its complete methanolysis under the standard conditions employed. The outcome of this reaction is a *trans* diequatorial opening of the epoxide ring, a reaction path usually considered unfavorable compared with the *trans* diaxial (Fürst–Plattner) opening. In spite of this, no trace was found of attack at C-2, al-



Scheme 4.

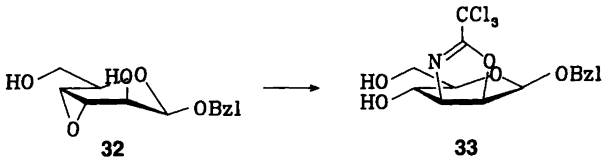
though this reaction would in principle be possible. The *trans* diequatorial opening is also observed in the case of methyl 3,4-anhydro-α-D-arabinopyranoside (**28**), which reacts to give the 2-*O*,3-*N*-trichloroacetimidate of methyl 3-amino-3-deoxy-α-D-lyxopyranoside (**29**). In the case of 1,6:3,4-dianhydro-β-D-galactopyranose (**19**) and 1,6:2,3-dianhydro-β-D-mannopyranose (**22**), two further prospects for the unusual diequatorial opening of the epoxide ring, the main product is recovered starting material resulting from reversible side reactions on the trichloroacetimidoyl group. A small amount of rearranged product was isolated in both cases and was indeed the result of diequatorial opening. However, the diequatorial opening of the epoxide ring competes with the side reactions leading to recovered starting material, with much less success than was the case with the diaxial opening of **13** and **16**, which were already at a disadvantage as regards competition with the side reactions, owing to their 1,3-diaxial interactions. A similar result is found on treatment of benzyl 3,4-anhydro-β-D-altropyranoside (**32**) with trichloroacetonitrile and sodium hydride resulting in recovery of 56 % of the starting material and isolation of only 8 % of the rearranged product, benzyl 3-amino-3-deoxy-β-D-mannopyranoside 2-*O*,3-*N*-trichloroacetimidate (**33**).



Scheme 5.

The *trans* hydroxy epoxides used in the reactions described above could all be expected to undergo epoxide migration under the alkaline reaction conditions employed.[10] However no such products were observed, which may indicate further reaction of rearranged epoxides. Furthermore, the recovered epoxides were starting material only, and in no case was any rearranged epoxide observed. The reason for this is that the first step of the reaction, the formation of an *O*-trichloroacetimidate, is much faster than the rearrangement of the epoxide, and thus blocks this side reaction, even in cases where the subsequent nucleophilic opening of the epoxide by the trichloroacetimidate is slow.

In one case, 1,6:3,4-dianhydro-β-D-galactopyranose (**19**), the opening of an epoxide by a neighboring trichloroacetimidoyl group can be compared directly with the corresponding opening of a benzoxonium ion. When 1,6-anhydro-3,4-*O*-benzylidene-2-*O*-trichloroacetimidoyl-β-D-galactopyranose was oxidized with NBS a rapid and complete conversion to 3-amino-1,6-anhydro-4-*O*-benzoyl-3-deoxy-β-D-gulopyranose 2-*O*,3-*N*-trichloroacetimidate



Scheme 6.

took place,[1] while, in the reaction described here, rearrangement of the epoxide was slow and led only to traces of the amino sugar. In spite of the lower reactivity of the epoxides, this type of rearrangement is a useful supplement to the benzoxonium-ion rearrangements, since the contrasting nature of the reagents employed makes the two reactions compatible for a variety of substituents and protecting groups present in the substrates. Secondly, the availability of the starting materials, epoxides and benzylidene compounds, will influence the choice of method.

The structure of the products obtained was determined by high-field NMR spectroscopy. Since the fused oxazoline ring forces the pyranose ring to adopt a half-chair conformation, making interpretation of the spectra of the cyclic imidates difficult, al' products were hydrolysed with aqueous trifluoroacetic acid to the free amino sugars and isolated as such or as the hydrochlorides, to enable straightforward interpretation of the NMR spectra. The cyclic imidates showed coupling between the vicinal protons on the oxazoline ring in the range 9.3–10.3 Hz, in agreement with the value previously found[11] for substituted 2-trichloromethyloxazolines; J_{cis} 9.5 Hz and J_{trans} 5–6 Hz.

Experimental

Thin layer chromatography (TLC) was performed on silica gel PF_{254} (Merck). For preparative work, 1 mm layers were used on 20×40 cm plates. Melting points are uncorrected. Optical rotations were measured on a Perkin–Elmer 241 polarimeter. ^{1}H NMR spectra were recorded on Bruker HXE 90 or AM 500 instruments and ^{13}C NMR spectra on a Bruker WH 90 at 22.63 MHz. IR spectra were recorded on a Perkin–Elmer 1720 Fourier transform spectrometer. Flash chromatography was carried out as described by Still, Kahn and Mitra.[12]

*Methyl 3-amino-3-deoxy-2,6-di-*O*-trichloroacetimidoyl- α-*D*-altropyranoside 3-*N*,4-*O*-trichloroacetimidate* (**2b**). Compound **1**[4] (528 mg), trichloroacetonitrile (1.13 ml) and imidazole (68 mg) were dissolved in THF and cooled to 0 °C and NaH (300 mg; 50 % suspension in mineral oil) was added. The suspension was stirred at 0 °C for 1 h and was then poured into a rapidly stirred mixture of H_2O, $CHCl_3$ and ice. After having been neutralized with AcOH to pH 6, the $CHCl_3$ layer was separated and the aqueous phase extracted with $CHCl_3$ (3×). The organic phases were washed with aqueous $NaHCO_3$, dried ($MgSO_4$), treated with charcoal and subjected to flash chromatography [AcOEt–hexane (1:2)] to give 1588 mg of **2b** as a syrup, which rapidly became turbid owing to hydrolysis of the trichloroacetimidoyl groups. ^{1}H NMR (500 MHz; $CDCl_3$): δ 4.98 (H1), 5.48 (H2), 4.61 (H3), 5.09 (H4), 4.11 (H5), 4.60 (H6), 4.52 (H6′), 3.45 (OMe); $J_{1,2}$ = 1.2, $J_{2,3}$ = 2.5, $J_{3,4}$, $J_{4,5}$ = 9.0, $J_{5,6}$ = 2.5, $J_{5,6'}$ = 5.5, $J_{6,6'}$ = 12.0 Hz.

Hydrolysis of **2b** *with NaOH.* Crude **2b** was prepared as described above, dissolved in MeOH (50 ml) and refluxed with NaOH (2.02 g) for 2 h, whereupon it was evaporated to dryness, neutralized with aqueous HCl, evaporated to dryness and acetylated with Ac_2O (10 ml) in pyridine (25 ml) overnight at 20 °C. Work-up of the reaction mixture in the usual manner followed by flash chromatography of the crude product (AcOEt) gave two products. The slower-eluting component was identified as **4c** (155 mg), m.p. 155–165 °C. The faster-eluting product was methyl 3-acetamido-3-*N*,4-*O*-carbonyl-3-deoxy-2,6-di-*O*-acetyl-α-D-altropyranoside **5**; 570 mg). Recrystallization of this from AcOEt–hexane gave m.p. 117–118 °C, $[\alpha]_D^{20}$ +184° (*c* 0.9, $CHCl_3$), anal. $C_{13}H_{19}NO_7$: C, H, N, IR (KBr): 1807, 1748, 1712 cm^{-1} (C=O). ^{1}H NMR (500 MHz; $CDCl_3$): δ 4.74 (H1), 5.24 (H2), 4.63 (H3, H4), 4.15 (H5), 4.35 (H6), 4.30 (H6′), 3.42 (OMe), 2.48 (NAc), 2.12, 2.08 (OAc); $J_{1,2}$ = 4.2, $J_{5,6}$ = 3.9,

$J_{5,6'}$ = 5.6, $J_{6,6'}$ = 12.2 Hz. ^{13}C NMR (22.63 MHz; $CDCl_3$): δ 170.4, 170.1, 169.7 (Ac), 152.4 (NCOO), 98.8 (C1), 69.6, 69.1, 66.9 (C2, C4, C5), 63.0 (C6), 55.4 (OMe), 53.7 (C3), 23.4, 20.5, 20.4 (Ac).

*Methyl 3-amino-2,6-di-*O*-benzoyl-3-deoxy-α-*D*-altropyranoside 3-*N*,4-*O*-trichloroacetimidate* (**2d**). Compound **2a** (656 mg) was benzoylated with benzoyl chloride (1.0 ml) in pyridine (10 ml) overnight, and worked up without the use of mineral acid, i.e. by hydrolysis of the excess benzoyl chloride with a few drops of H_2O for 15 min, dilution with H_2O and $CHCl_3$ and extraction of the organic phase with dilute aqueous $NaHCO_3$. Drying ($MgSO_4$) and evaporation of the organic phase to dryness (<0.1 mmHg) gave 1008 mg of a product which still smelt of pyridine. Crystallization of this from Et_2O–pentane gave 595 mg of **2d**, m.p. 103–110 °C. Flash chromatography [AcOEt–hexane (1:3)] of the mother liquors gave a further 196 mg of **2d**, m.p. 113–115 °C. Recrystallization from AcOEt–hexane gave m.p. 115–116 °C, $[\alpha]_D^{20}$ +39° (*c* 1.0, $CHCl_3$), anal. $C_{23}H_{20}Cl_3NO_7$: C, H, Cl, N. ^{1}H NMR (500 MHz; $CDCl_3$): δ 4.91 (H1), 5.56 (H2), 4.62 (H3), 5.12 (H4), 4.19 (H5), 4.66 (H6), 4.59 (H6'), 3.46 (OMe); $J_{1,2}$ = 2.3, $J_{2,3}$ = 3.6, $J_{3,4}$, $J_{4,5}$ = 9.0, $J_{5,6}$ = 3.6, $J_{5,6'}$ = 5.5, $J_{6,6'}$ = 11.8 Hz.

*Methyl 3-acetamido-3-deoxy-2,4,6-tri-*O*-acetyl-α-*D*-altropyranoside* (**4c**). Compound **2a** (789 mg) was hydrolysed with CF_3COOH (2 ml)–H_2O (2 ml) overnight at 20 °C. Evaporation of the reaction mixture to dryness, evaporation of the residue with H_2O (2×) and acetylation with Ac_2O (10 ml) and AcONa (1.0 g) gave **4c** (787 mg), m.p. 165–170 °C. Recrystallization of this from AcOEt–$CHCl_3$ gave m.p. 171–172 °C, $[\alpha]_D^{25}$ +35.5° (*c* 1.2, $CHCl_3$) (lit. m.p. 177 °C,[5] 171–172 °C,[13] $[\alpha]_D$ +34.1°,[5] 42.2° [13]).

Conversion of carbohydrate epoxides to amino sugar trichloroacetimidates: general procedure. The carbohydrate epoxide (3 mol), trichloroacetonitrile (1.25 mmol for each epoxy and hydroxy group) and imidazole (1 mmol) were suspended or dissolved in 10 ml of dry THF, sodium hydride (60 % suspension in mineral oil; 1 mol for each hydroxy group) was added and the reaction mixture was stirred at the temperature and time specified for the individual compounds (see below), after which 10 ml of dry MeOH and 10 drops of 1 M MeONa were added and the solution was stirred for 10 min at 25 °C. The resulting reaction mixture was neutralized with gaseous CO_2 (10 min), evaporated to dryness, redissolved in $CHCl_3$, filtered through charcoal, evaporated to dryness, and flash chromatographed in AcOEt to give the products stated below, followed, in some cases, by recovered starting material.

*Methyl 2,3-anhydro-α-*D*-mannopyranoside* (**1**). Compound **1**[4] (528 mg) gave, after 1 h at 0 °C, 855 mg (89 %) of methyl 3-amino-3-deoxy-α-*D*-altropyranoside 2-*O*,3-*N*-trichloroacetimidate (**2a**) as a syrup, $[\alpha]_D^{20}$ +39° (*c* 1.0, $CHCl_3$), anal. $C_9H_{12}Cl_3NO_5$: C, H, N, Cl. ^{1}H NMR (500 MHz; $CDCl_3$): δ 4.67 (H1), 3.86 (H2), 4.39 (H3), 5.06 (H4), 3.7–4.0 (H5, H6); $J_{1,2}$ = 5.0, $J_{2,3}$ = 7.4, $J_{3,4}$ = 9.8, $J_{4,5}$ = 8.8 Hz.

*Methyl 3,4-anhydro-α-*D*-galactopyranoside* (α-**7**). Compound α-**7**[14] (528 mg) gave, after 45 min at 20 °C, a dark brown crude product, which crystallized from AcOEt to give 211 mg (40 %) of impure recovered α-**7**. Flash chromatography of the mother liquors gave further 204 mg (39 %) of α-**7**. Recrystallization of the combined products gave m.p. 115–116 °C (lit.,[14] 118–119 °C), identical (NMR) with the starting material.

*Methyl 3,4-anhydro-β-*D*-galactopyranoside* (β-**7**). Compound β-**7**[15] (528 mg) gave, after 1 h at 0 °C, 513 mg (53 %) of methyl 3-amino-3-deoxy-β-*D*-gulopyranoside 2-*O*,3-*N*-trichloroacetimidate (β-**8**), m.p. 120–123 °C. Two recrystallizations of this from AcOEt–hexane gave m.p. 125–126 °C, $[\alpha]_D^{20}$ −20° (*c* 1.3, $CHCl_3$), anal. $C_9H_{12}Cl_3NO_5$: C, H, N, Cl. ^{1}H NMR (500 MHz; $CHCl_3$): δ 4.86 (H1), 4.96 (H2), 4.69 (H3), 4.16 (H4), 3.83 (H5), 3.85–3.90 (H6), 3.59 (OMe); $J_{1,2}$ = 2.6, $J_{2,3}$ = 9.6, $J_{3,4}$ = 2.4, $J_{4,5}$ = .2.5, $J_{5,6}$ = 6 and 5 Hz.

*Methyl 2,3-anhydro-α-*D*-gulopyranoside* (**10**). Compound **10**[16] (396 mg) gave 2 products after 1 h at 0 °C. The faster-eluting compound, 254 mg (24 %), was methyl 3-amino-3-deoxy-6-*O*-trichloroacetimidoyl-α-*D*-galactopyranoside 3-*N*,4-*O*-trichloroacetimidate (**11b**), m.p. 169–171 °C from Et_2O. Recrystallization of this from AcOEt–hexane gave m.p. 172–173 °C, $[\alpha]_D^{20}$ +13° (*c* 1.1, $CHCl_3$), anal. $C_{11}H_{12}Cl_6N_2O_5$: C, H, Cl, N. ^{1}H NMR (500 MHz; $CDCl_3$): δ 4.70 (H1),

4.40 (H2), 4.79 (H3), 5.08 (H4), 4.58 (H5), 4.53 (H6), 4.45 (H6'), 3.55 (OMe); $J_{1,2}$ = 4.5, $J_{2,3}$ = 3.5, $J_{3,4}$ = 9.7, $J_{4,5}$ = 1.5, $J_{5,6}$ = 4.5, $J_{5,6'}$ = 7.8, $J_{6,6'}$ = 11.3 Hz. Deacylation of 50 mg of **11b** with MeONa in MeOH overnight gave 30 mg **11a** (see below), m.p. 130–131 °C. The slower-eluting compound, 221 mg (31 %), was methyl 3-amino-3-deoxy-α-D-galactopyranoside 3-*N*,4-*O*-trichloroacetimidate (**11a**), m.p. 125–128 °C. Recrystallization of this from AcOEt–hexane gave m.p. 130–131 °C, $[\alpha]_D^{20}$ +31° (*c* 0.9, $CHCl_3$), anal. $C_9H_{12}Cl_3NO_5$: C, H, Cl, N. ^{1}H NMR (500 MHz; $CDCl_3$): δ 4.70 (H1), 4.36 (H2), 4.75 (H3), 5.02 (H4), 4.32 (H5), 3.80 (H6), 3.89 (H6'), 3.55 (OMe); $J_{1,2}$ = 4.5, $J_{2,3}$ = 3.6, $J_{3,4}$ = 9.6, $J_{4,5}$ = 1.6, $J_{5,6}$ = 4.5, $J_{5,6'}$ = 7.5, $J_{6,6'}$ = 11.4 Hz.

1,6:2,3-Dianhydro-β-D-gulopyranose (**13**). Crude **13**, prepared as described in Ref. 17, was purified by benzoylation, recrystallization of the benzoate from EtOH, and debenzoylation with MeONa in MeOH overnight, to give a ca. 70 % recovery of a product with m.p. 121–123 °C. Compound **13** (436 mg) then gave 184 mg (21 %) of 3-amino-1,6-anhydro-3-deoxy-β-D-galactopyranose 3-*N*,4-*O*-trichloroacetimidate (**14**), m.p. 143–145 °C, after flash chromatography in AcOEt–hexane (3:1). Recrystallization of this from AcOEt–hexane gave m.p. 145–146 °C, $[\alpha]_D^{25}$ −39° (*c* 1.1, $CHCl_3$), anal. $C_8H_8Cl_3NO_4$: C, H, Cl, N. ^{1}H NMR (500 MHz; $CDCl_3$): δ 5.49 (H1), 4.16 (H2), 4.37 (H3), 5.33 (H4), 4.66 (H5), 4.06 (H6), 3.70 (H6'); $J_{1,2}$, $J_{2,3}$ ~ 0, $J_{3,4}$ = 10.3, $J_{5,6}$ = 6.5, $J_{5,6'}$ = 5.0, $J_{6,6'}$ = 8.9 Hz. Further fractions were eluted which contained mixtures of **14** and recovered **13** amounting to a further 13 % of **14** and 35 % of **13**, as estimated from the ^{1}H NMR spectrum of the combined fractions.

1,6:3,4-Dianhydro-β-D-altropyranose (**16**). Compound **16**[18] (434 mg) gave, after 4 h at 20 °C, a crude product, which on being crystallized from AcOEt gave 143 mg (33 %) of recovered **16**. Flash chromatography of the mother liquors yielded 251 mg (29 %) of 3-amino-1,6-anhydro-β-D-mannopyranose 2-*O*,3-*N*-trichloroacetimidate (**17**), m.p. 167–171 °C. Two recrystallizations of this from AcOEt–hexane gave m.p. 174–175 °C, $[\alpha]_D^{25}$ +6.4° (*c* 1.0, $CHCl_3$), anal. $C_8H_8Cl_3NO_4$: C, H, Cl, N. ^{1}H NMR (90 MHz; $CDCl_3$): δ 5.47 (H1), 4.92 (H2), 4.33 (H3), 4.27 (H4), 4.64 (H5), 3.8 (H6, H6'); $J_{1,2}$ = 3.0, $J_{2,3}$ = 9.0, $J_{3,4}$ ~ 1 Hz.

1,6:3,4-Dianhydro-β-D-galactopyranose (**19**). Compound **19**[19] (432 mg) gave, after 4 h at 20 °C, a crude product, which, when examined by NMR spectroscopy, revealed a trace (3 %) of 3-amino-1,6-anhydro-3-deoxy-β-D-gulopyranose 2-*O*,3-*N*-trichloroacetimidate (**20**).[1] Flash chromatography of the crude product yielded 262 mg (61 %) of **19**, m.p. 57–63 °C (the starting material had m.p. 65–66 °C).

1,6:2,3-Dianhydro-β-D-mannopyranose (**22**). Compound **22**[18] (432 mg) gave, after 4 h at 20 °C, 53 mg (6 %) of 3-amino-1,6-anhydro-3-deoxy-β-D-altropyranose 3-*N*,4-*O*-trichloroacetimidate (**23**) as a syrup. ^{1}H NMR (500 MHz; $CDCl_3$): δ 5.48 (H1), 3.57 (H2), 4.33 (H3), 4.76 (H4), 4.97 (H5), 3.92 (H6), 3.88 (H6'); $J_{1,2}$ = 3.0, $J_{2,3}$ = 4.9, $J_{3,4}$ = 9.3, $J_{4,5}$ = 1.0, $J_{5,6}$ = 5.5, $J_{5,6'}$ = 1.3, $J_{6,6'}$ = 8.2 Hz. The main product of the reaction was the slower-eluting **22** (280 mg, 65 %).

Methyl 2,3-anhydro-α-D-lyxopyranoside (**25**). Compound **25**[20] (438 mg) gave, after 1 h at 0 °C, 732 mg (84 %) of methyl 3-amino-3-deoxy-α-D-arabinopyranoside 3-*N*,4-*O*-trichloroacetimidate (**26**), m.p. 87–91 °C. Recrystallization of this from AcOEt–hexane gave m.p. 92–93 °C, $[\alpha]_D^{20}$ −65° (*c* 1.1, $CHCl_3$), anal. $C_8H_{10}Cl_3NO_4$: C, H, Cl, N. ^{1}H NMR (500 MHz; $CDCl_3$): δ 4.32 (H1), 3.59 (H2), 4.31 (H3), 4.92 (H4), 4.27 (H5), 3.94 (H5'), 3.51 (OMe); $J_{1,2}$ = 6.7, $J_{2,3}$ = 7.5, $J_{3,4}$ = 9.4, $J_{4,5}$ = 5.4, $J_{4,5'}$ = 4.5, $J_{5,5'}$ = 13.5 Hz.

Methyl 3,4-anhydro-α-D-arabinopyranoside (**28**). Compound **28**[20] (292 mg) gave, after 1 h at 0 °C, 427 mg (73 %) of methyl 3-amino-3-deoxy-α-D-lyxopyranoside 2-*O*,3-*N*-trichloroacetimidate (**29**), which slowly crystallized from Et_2O–pentane, m.p. 61–65 °C. Attempted purification by further recrystallization was unsuccessful. ^{1}H NMR (500 MHz; $CDCl_3$): δ 4.80 (H1), 4.87 (H2), 4.60 (H3), 4.02 (H4), 3.95 (H5), 3.90 (H5'), 3.53 (OMe); $J_{1,2}$ = 1.9, $J_{2,3}$ = 9.3, $J_{3,4}$ = 3.5, $J_{4,5}$ = 4.2, $J_{4,5'}$ = 3.1, $J_{5,5'}$ = 12.0, $J_{3,5}$ = 1.1 Hz.

5,6-Anhydro-1,2-O-isopropylidene α-D-glucofuranose (**31**). Compound **31**[21] (606 mg) gave, after 4 h at 20 °C, a crude product containing only starting material (NMR spectroscopy). Crystallization of this from benzene gave m.p. 121–123 °C, slightly lower than that of the starting material (127–128 °C, lit.,[21] 133.5 °C).

Benzyl 3,4-anhydro-β-D-altropyranoside (**32**). Compound **32**[22] (522 mg) gave, after 4 h at 20 °C, 69 mg (8 %) of benzyl 3-amino-3-deoxy-β-D-mannopyranoside 2-*O*,3-*N*-trichloroacetimidate (**33**) as a syrup, ^{1}H NMR (500 MHz; $CDCl_3$): δ 5.09 (H1), 4.96 (H2), 4.39 (H3), 4.34 (H4), 3.65 (H5), 3.79 (H6), 3.76 (H6′), 4.83, 4.66 ($ArCH_2$); $J_{1,2}$ = 3.8, $J_{2,3}$ = 10.0, $J_{3,4}$ = 8.3, $J_{4,5}$ = 9.5, $J_{5,6}$ = 4.1, $J_{5,6'}$ = 4.6, $J_{6,6'}$ = 11.5 Hz, followed by 293 mg (56 %) of recovered **32**.

Hydrolysis of the cyclic trichloroacetimidates to amino sugar glycosides: general procedure. The cyclic imidate (3 mmol) was dissolved in CF_3COOH (2 ml) and diluted with the same volume of water. The reaction mixture was left at 20 °C overnight, evaporated to dryness and re-evaporated with 3×10 ml of water. The residue was dissolved in water and stirred for 5 min with 5 ml of IRA-400 (OH^-) ion-exchange resin and passed through a short column containing a further 5 ml of the same resin. The column was eluted with water until the eluate was neutral. Concentration of the eluate gave the free aminoglycoside. If the aminoglycoside did not crystallize directly, it was redissolved in water, neutralized with HCl (methyl red), evaporated to a small volume and crystallized from EtOH. The individual compounds are described below.

Methyl 3-amino-3-deoxy-α-D-altropyranoside (**4a**). Compound **2** (845 mg) gave 393 mg of **4a** · HCl, m.p. 188 °C (decomp.), $[\alpha]_D^{25}$ +91° (*c* 1.1, H_2O) (lit. m.p. 208 °C,[23] $[\alpha]_D$ +88.2°,[23] +84°[24]). ^{1}H NMR (500 MHz; D_2O): δ 4.02 (H2), 3.64 (H3), 4.17 (H4), 3.84 (H5), 3.90 (H6), 3.81 (H6′), 3.47 (OMe); $J_{1,2}$ = 2.7, $J_{2,3}$ = 5.0, $J_{3,4}$ = 4.8, $J_{4,5}$ = 8.8, $J_{5,6}$ = 2.3, $J_{5,6'}$ = 6.0, $J_{6,6'}$ = 11.5 Hz. ^{13}C NMR (22.63 MHz; D_2O): δ 100.7 (C1), 70.5, 67.0, 61.6, 61.5 (C2, C4, C5, C6), 56.2 (OMe), 53.4 (C3).

Methyl 3-amino-3-deoxy-β-D-gulopyranoside (**9**). Compound **8** (314 mg) gave 220 mg of **9** · HCl as a syrup. ^{1}H NMR (500 MHz; D_2O): δ 4.66 (H1), 4.00 (H2), 3.72 (H3), 4.16 (H4), 4.04 (H5), 4.84 (H6), 3.56 (OMe); $J_{1,2}$ = 6.2, $J_{2,3}$ = 4.6, $J_{3,4}$ = 6.0, $J_{4,5}$ = 3.3, $J_{5,6}$ = 6.2 Hz. ^{13}C NMR (22.63 MHz; D_2O): δ 101.9 (C1), 75.3, 66.2, 65.8, 61.7, 61.4 (C2, C4, C5, C6), 57.6 (OMe), 53.7 (C3).

Methyl 3-amino-3-deoxy-α-D-galactopyranoside (**12**). Compound **11** (155 mg) gave 100 mg of **12**, m.p. 96–99 °C. ^{13}C NMR (22.63 MHz; D_2O): δ 99.9 (C1), 72.2 (C5), 70.0, 69.7 (C2, C4), 62.1 (C6), 55.8 (OMe), 52.1 (C3). Conversion into the hydrochloride (**12** · HCl) gave m.p. 197 °C (decomp.), $[\alpha]_D^{20}$ +159° (*c* 0.3, H_2O) (lit.,[25] m.p. 219–221 °C, $[\alpha]_D$ + 146.5). ^{1}H NMR (500 MHz; D_2O): δ 4.90 (H1), 4.01 (H2), 3.60 (H3), 4.16 (H4), 3.96 (H5), 3.76 (H6), 3.46 (OMe); $J_{1,2}$ = 3.9, $J_{2,3}$ = 11.0, $J_{3,4}$ = 3.4, $J_{4,5}$ ~ 1, $J_{5,6}$ = 6.5 Hz. ^{13}C NMR (22.63 MHz; D_2O): δ 99.2 (C1), 70.9 (C5), 66.4, 65.9 (C2, C4), 61.6 (C6), 56.0 (OMe), 53.2 (C3).

3-Amino-1,6-anhydro-3-deoxy-β-D-galactopyranose (**15**). Compound **14** (349 mg) gave 130 mg of **15** · HCl, m.p. 190–200 °C (decomp.), $[\alpha]_D^{20}$ −5.6° (*c* 1.0, H_2O) (lit.,[26] m.p. 180–185 °C (decomp.), $[\alpha]_D$ −9.0°). ^{1}H NMR (90 MHz; D_2O): δ 5.53 (H1), 3.96 (H2), 3.57 (H3), 4.39 (H4), 4.64 (H5), 4.17 (H6), 3.70 (H6′); $J_{1,2}$, $J_{2,3}$ = 1.7, $J_{3,4}$ = 7.5, $J_{4,5}$ = 5.3, $J_{5,6}$ ~ 0, $J_{5,6'}$ = 4.5, $J_{6,6'}$ = 8.9, $J_{1,3}$, $J_{3,5}$, $J_{4,6}$ ~ 1 Hz.

3-Amino-1,6-anhydro-3-deoxy-β-D-mannopyranose (**18**). Compound **17** (289 mg) gave 172 mg of **18**. ^{1}H NMR (90 MHz; D_2O): δ 5.43 (H1), 3.85 (H2), 3.14 (H3), 3.93 (H4), 4.58 (H5), 4.09 (H6), 3.75 (H6′); $J_{1,2}$ = 2.0, $J_{2,3}$ = 6.4, $J_{3,4}$, $J_{4,5}$ ~ 2, $J_{5,6}$ ~ 1, $J_{5,6'}$ = 5.4, $J_{6,6'}$ = 8.5, $J_{1,3}$, $J_{3,5}$ ~ 1 Hz. Conversion into the hydrochloride and crystallization from EtOH and MeOH gave **18** · HCl, m.p. 187 °C (decomp.), $[\alpha]_D^{25}$ −102° (*c* 0.7, H_2O), anal. $C_6H_{12}ClNO_4$: C, H, Cl, N. ^{1}H NMR (500 MHz; D_2O): δ 5.51 (H1), 4.12 (H2), 3.61 (H3), 4.13 (H4), 4.68 (H5), 4.08 (H6), 3.86 (H6′); $J_{1,2}$ = 2.0, $J_{2,3}$ = 6.6, $J_{3,4}$ = 2.1, $J_{5,6}$ ~ 1, $J_{5,6'}$ = 5.2, $J_{6,6'}$ = 9.0, $J_{1,3}$, $J_{3,5}$ ~ 1 Hz.

Methyl 3-amino-3-deoxy-α-D-arabinopyranoside (**27**). Compound **26** (302 mg) gave 156 mg of **27**, m.p. 165–185 °C. Recrystallization of this from EtOH gave m.p. 190–195 °C (decomp.), $[\alpha]_D^{25}$ −17.5° (*c* 1.0, H_2O), anal. $C_6H_{13}NO_4$: C, H, N. ^{1}H NMR (500 MHz; D_2O): δ 4.25 (H1), 3.35 (H2), 2.76 (H3), 3.87 (H4), 3.91 (H5), 3.70 (H5′), 3.53 (OMe); $J_{1,2}$ = 7.5, $J_{2,3}$ = 10.0, $J_{3,4}$ = 3.3, $J_{4,5}$ = 2.2, $J_{4,5'}$ = 1.3, $J_{5,5'}$ = 12.8 Hz. ^{13}C NMR (22.63 MHz; D_2O): δ 105.3 (C1), 72.4, 68.9, 68.7 (C2, C4, C5), 57.8 (OMe), 55.8 (C3).

Methyl 3-amino-3-deoxy-α-D-lyxopyranoside (**30**). Compound **29** (288 mg) gave 144 mg of **30** as a syrup. Conversion of this into the hydrochloride and two recrystallizations from AcOEt–EtOH gave 30 mg of **30** · HCl, m.p. 194 °C (decomp.), $[\alpha]_D^{25}$ +42° (*c* 0.8, H_2O), anal. $C_6H_{14}ClNO_4$: C, H, N, Cl. ^1H NMR (500 MHz; D_2O): δ 4.09 (H2), 3.44 (H3), 4.03 (H4), 3.81 (H5), 3.55 (H5′), 3.43 (OMe); $J_{1,2}$ = 1.9, $J_{2,3}$ = 3.2, $J_{3,4}$ = 10.5, $J_{4,5}$ = 5.7, $J_{4,5'}$ = 10.5, $J_{5,5'}$ = 11.4 Hz.

Benzyl 3-amino-3-deoxy-β-D-altropyranoside (**33**). Compound **32** (81 mg) gave 44 mg of **33** as a syrup. Conversion of this into the hydrochloride and crystallization from EtOH gave 25 mg of **33** · HCl, which decomposes at 200–250 °C, $[\alpha]_D^{25}$ −72° (*c* 0.5, D_2O), anal. $C_{13}H_{20}ClNO_5$: C, H, N; Found: Cl, 11.17, Calc: Cl, 11.60 %. ^1H NMR (500 MHz; D_2O): δ 4.60 (H1), 3.94 (H2), 3.21 (H3), 3.62 (H4), 3.31 (H5), 3.78 (H6), 3.61 (H6′), 4.77, 4.59 ($ArCH_2$); $J_{1,2} \sim 1$, $J_{2,3}$ = 3.2, $J_{3,4}$ = 10.5, $J_{4,5}$ = 9.8, $J_{5,6}$ = 2.5, $J_{5,6'}$ = 6.0, $J_{6,6'}$ = 12.5 Hz.

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