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Aust. J. Chem. **2006**, *59*, 426–433

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An Expansion of the Role of the Corey–Link Reaction for the Synthesis of α-Substituted Carboxylic Acid Esters

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The treatment of 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexos-3-ulose with chloroform under basic conditions has yielded the normal 3-*C*-trichloromethyl-α-D-allofuranose derivative. Under the conditions of the modified Corey–Link reaction but with a nucleophile different from the usual azide, a range of α-substituted carboxylic acid esters (and one amide) has been obtained. A similar addition of bromoform to the ulose has formed the α-bromo methyl ester. Two attempts at forming an 'inositol α-amino acid' from a polyhydroxylated cyclohexanone failed.

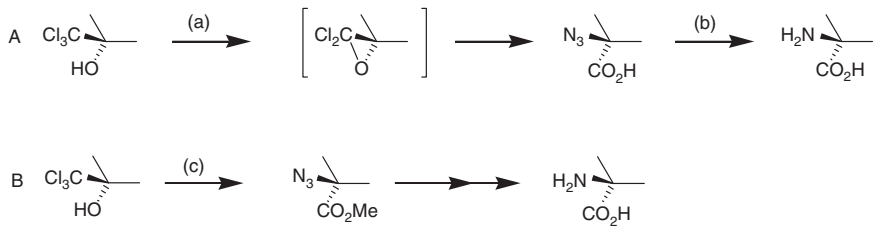
Single-crystal X-ray structure determinations are reported for (3*S*)-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-3-*S*-phenyl-3-thio-α-D-*ribo*-hexose, (3*S*)-1,2:5,6-di-*O*-isopropylidene-3-*S*-phenyl-3-*C*-(phenylthio)-carbonyl-3-thio-α-D-*ribo*-hexose, 3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-*erythro*-hex-3-enofuranose, 4,6-di-*O*-benzyl-2-*C*-trichloromethyl-*scyllo*-inositol 1,3,5-orthoformate, 2,2′-anhydro-4,6-di-*O*-benzyl-2-*C*-dichlorohydroxymethyl-*scyllo*-inositol 1,3,5-orthoformate, 1,3,4,5,6-penta-*O*-benzyl-2-*C*-trichloromethyl-*myo*-inositol, and 2-amino-1,3,4,5,6-penta-*O*-benzyl-2-*C*-cyano-2-deoxy-*myo*-inositol.

Manuscript received: 26 April 2006.
Final version: 3 July 2006.

Introduction

In 1992 Corey and Link reported a general procedure for the synthesis of α-amino acids (Scheme 1A); the starting optically active trichloromethyl alcohols were generally obtained by the stereoselective reduction of a precursor trichloromethyl ketone.[1] Some years later a modification of the procedure was reported, resulting in the formation of α-azido methyl esters, direct precursors of the α-amino acids (Scheme 1B); this time, the starting optically active trichloromethyl alcohols were obtained by the stereoselective addition of chloroform to a ketone.[2] We have applied the modified Corey–Link sequence to a range of carbohydrate ketones, resulting in the formation of intermediate trichloromethyl alcohols that were transformed into α-azido methyl esters, direct precursors of α-amino methyl esters and α-azido acids (for example, Scheme 2).[3] These amines and acids could be coupled together to give a range of novel carbohydrate oligopeptides.[4]

It occurred to us that other nucleophiles (apart from azide) could be used to trap the accepted intermediate dichloro epoxide (Scheme 1A). In the extreme, treatment of the alcohol **1** with just 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in methanol gave the chloro ester **2** (Scheme 3); the addition of a source of bromide ion to the original reaction mixture failed to yield the pure bromo ester **3**, being contaminated with the chloro ester **2**. Treatment of **1** with a source of fluoride ion in the normal reaction mixture gave the fluoro ester **4**, probably owing to the fortuitous precipitation of the less-soluble caesium chloride. Other nucleophiles, namely methoxide, cyanide, and cyanate, provided the methoxy ester **5**, the cyano ester **6**, and the carbamate **7**. The carbamate was the obvious product of methanolysis of an intermediate isocyanate. In an



Scheme 1. (a) (i) NaN_3, NaOH, H_2O, 1,2-dimethoxyethane. (ii) H_3O^+. (b) H_2, Pd/C, MeOH. (c) NaN_3, DBU, [18]crown-6, MeOH.

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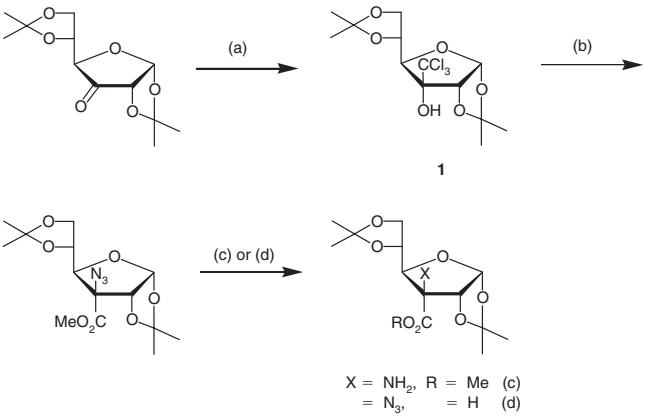
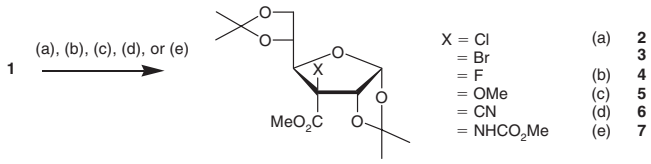
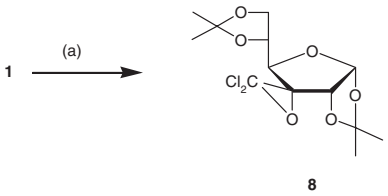


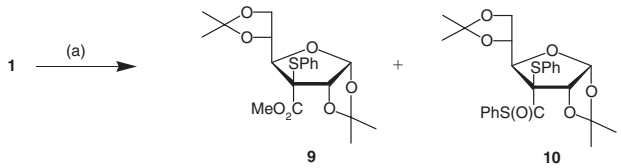
Scheme 2. (a) $LiN(SiMe_3)_2$, $CHCl_3$, THF. (b) NaN_3, DBU, [18]crown-6, MeOH. (c) H_2, Pd/C, MeOH. (d) (i) KOH, MeOH. (ii) H_3O^+.



Scheme 3. (a) DBU, MeOH. (b) CsF, DBU, MeOH. (c) NaOMe, MeOH. (d) NaCN, DBU, MeOH. (e) KOCN, DBU, MeOH.



Scheme 4. (a) KOCN, $KOBu^t$, Bu^tOH.

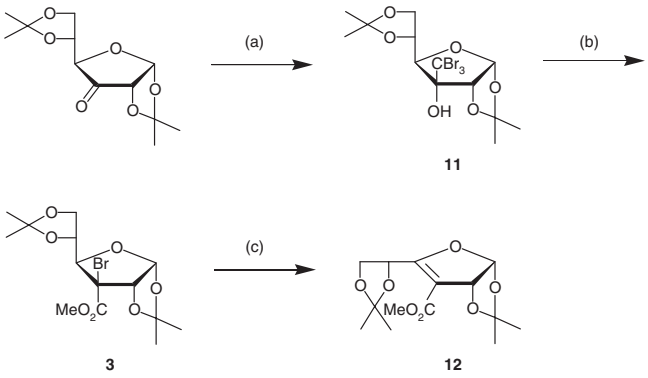


Scheme 5. (a) NaOMe, PhSH, MeOH.

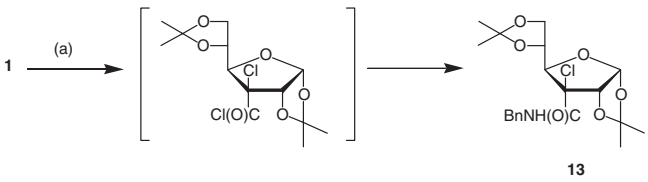
attempt to prepare the related *tert*-butyl carbamate (by replacing methanol with *tert*-butanol and using *tert*-butoxide as the base), only the dichloro epoxide **8** (Scheme 4) was isolated — apparently, potassium cyanate in *tert*-butanol was not soluble enough for a further reaction to occur.

The use of thiophenol in combination with sodium methoxide gave a mixture of the phenylthio ethers **9** and **10** (Scheme 5), the structures being confirmed by single-crystal X-ray structure investigations (Figs 1a and 1b). Further minor experimentation indicated that the methyl ester **9** is first formed, followed by a trans-esterification reaction with the remaining thiophenol to form **10**.

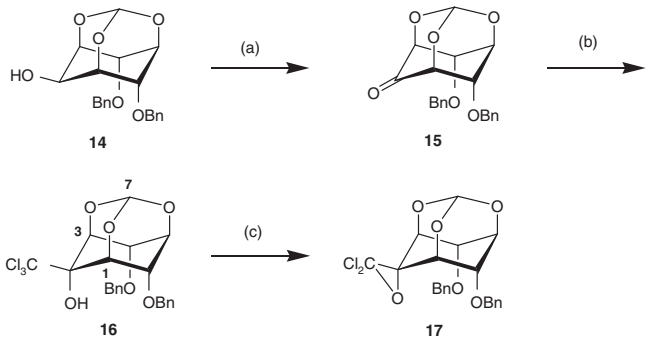
Some interesting observations were made during the above investigations, one being the addition of bromoform to



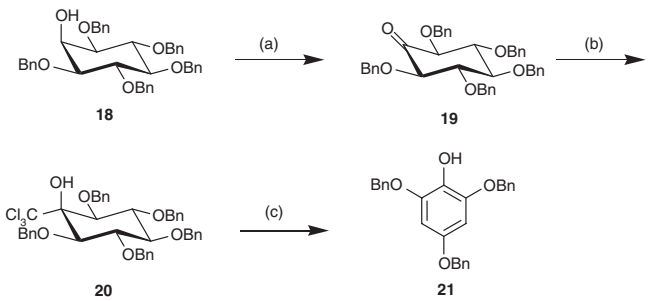
Scheme 6. (a) $LiN(SiMe_3)_2$, $CHBr_3$, THF. (b) DBU, MeOH. (c) DMF, NaN_3.



Scheme 7. (a) DBU, $BnNH_2$, CH_2Cl_2.



Scheme 8. (a) (i) $(COCl)_2$, DMSO, CH_2Cl_2. (ii) Et_3N. (b) $LiN(SiMe_3)_2$, $CHCl_3$, THF. (c) DBU, NaN_3, [18]crown-6, MeOH.



Scheme 9. (a) (i) $(COCl)_2$, DMSO, CH_2Cl_2. (ii) Et_3N. (b) $LiN(SiMe_3)_2$, $CHCl_3$, THF. (c) DBU, NaN_3, [18]crown-6, MeOH.

Scheme 10. (a) (i) NH_3, MeOH, $Ti(OPr^i)_4$. (ii) Me_3SiCN.

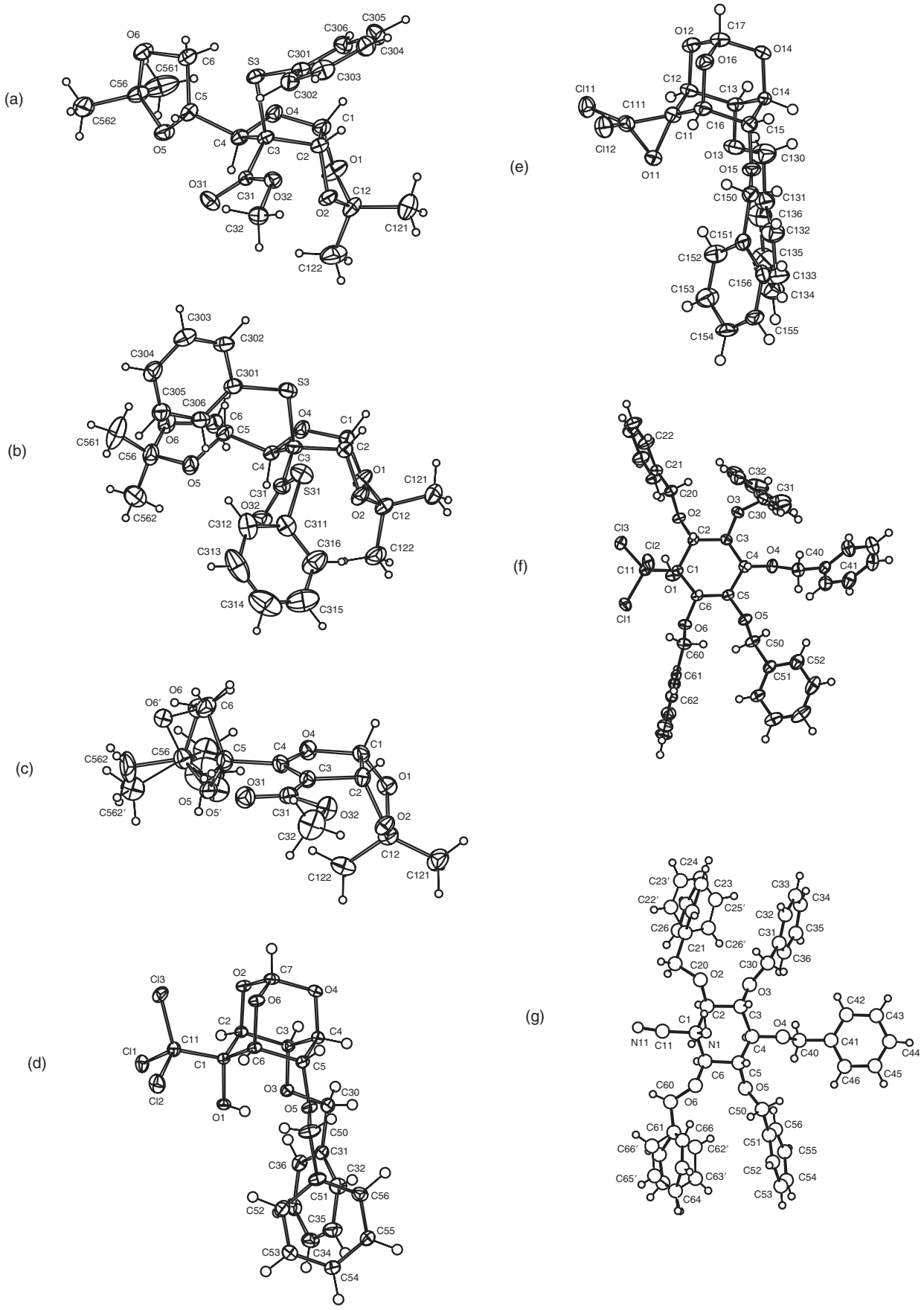


Fig. 1. Molecular projections of (a) **9**, (b) **10**, (c) **12**, (d) **16**, (e) **17** (molecule 1), (f) **20**, and (g) **22**.

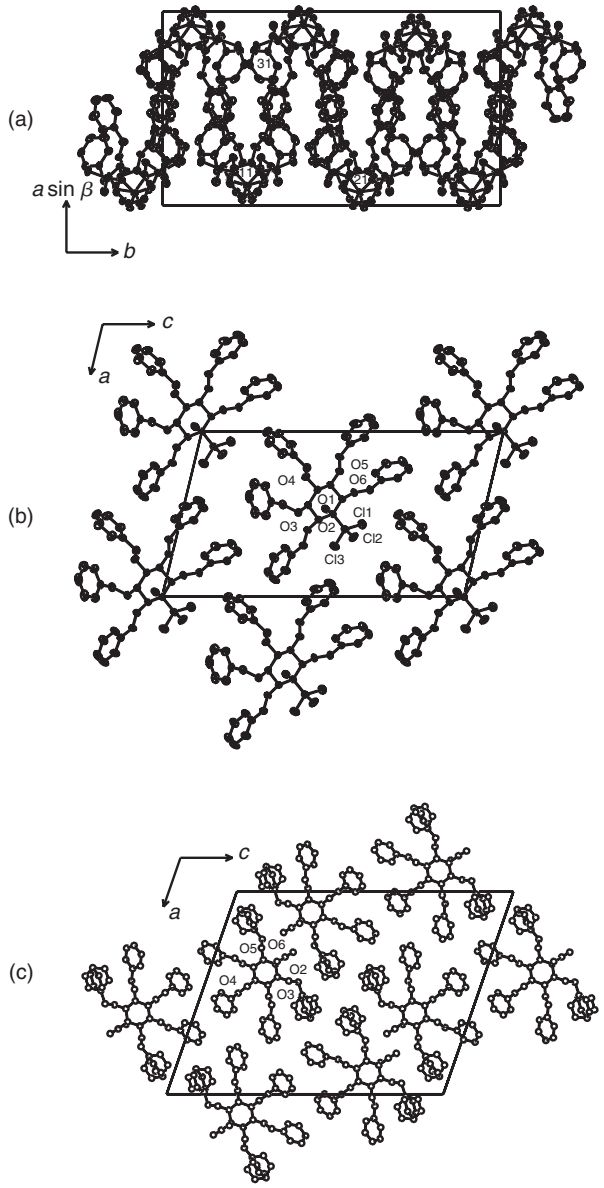


Fig. 2. Unit cell projections of (a) **17** down the *c*-axis, (b) **20** down the *b*-axis, and (c) **22** down the *b*-axis.

1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexos-3-ulose to provide the pure bromo ester **3** (Scheme 6), via the alcohol **11**. An attempt to replace the bromine atom in **3** with azide, hopefully with inversion of configuration, gave only the alkene **12**, the structure of which was confirmed by a single crystal X-ray structure investigation (Fig. 1c).

One final experiment, with benzylamine, converted the alcohol **1** into the amide **13** (Scheme 7) — apparently, the chloro acid chloride is formed and is subsequently trapped by the (weakly nucleophilic) amine.

We were always interested in seeing if the Corey–Link reaction could be used for the synthesis of 'inositol α-amino acids'; to the best of our knowledge this is a new class of molecule. Therefore, the easily prepared ortho ester **14** was oxidized and the resulting ketone **15** converted into the trichloromethyl alcohol **16** (Scheme 8), the expected configuration of which was confirmed by a single-crystal X-ray structure investigation (Fig. 1d). The treatment of **16** under the conditions of the modified Corey–Link reaction failed to yield the desired azido ester — only the dichloro epoxide **17** was (again) obtained, the structure of which was confirmed by a single-crystal X-ray investigation (Fig. 1e). It seems that the trajectory of approach for a successful displacement by the azide ion is blocked in this rigid tricyclic framework.

An alternative approach was from the alcohol **18** (Scheme 9). Although oxidation to the ketone **19** and subsequent addition of chloroform yielded the alcohol **20**, the basic conditions of the modified Corey–Link reaction yielded only the phenol **21**. This sort of elimination process is not without precedent.[5] We were ultimately able to form a precursor to an inositol amino acid but not by the chosen route — treatment of the ketone **19** under modern Strecker conditions gave the amino nitrile **22**, the hydrolysis of which proved impossible in our hands (Scheme 10). The configuration of **20** and **22** were again confirmed by single-crystal X-ray structure investigations (Figs 1f and 1g).

The results described here show that the conditions of the modified Corey–Link reaction can be used for the synthesis of a range of α-substituted carboxylic acid esters (and amides).

Structural Comment

The results of the seven single crystal X-ray studies are consistent, in terms of stoichiometry, connectivity and stereochemistry (Fig. 1), with those given above for **9**, **10**, **12**, **16**, **17**, **20**, and **22**, the determinations being of diverse degrees of precision; absolute configurations, where assignable (at relatively low levels of confidence on the basis of the presence of Cl or S), are consistent with those expected. With the exception of **17**, one formula unit devoid of crystallographic symmetry comprises the asymmetric unit of each structure; in **17**, three similar molecules comprise the asymmetric unit, the structure overall displaying an interesting packing as sheets parallel to the *ac*-plane (Fig. 2). In both **20** and **22**, the packing of the molecules is also of interest, in both cases, stacking being found up the short (*b*) axes. The conformations of the fused dioxolane rings of **9** and **10** (Table 1) are similar, as are those of the parent furanoses, which are envelopes with O4 the flaps; in **12** with the incorporation of the double bond, the ring is flattened, while the dioxolane rings, also envelopes with C12 the flaps, have the latter atoms directed 'outwards' in **9**, and in **10** turned 'inwards', with methyl substituent C122 lying over the furanose ring. The conformations of the pendant dioxolane rings are similar in **9** and **10**; in **12**, disorder is resolved and refinable in the oxygen atoms, the minor components conforming to the conformation found in **9** and **10**, while the major component now differs. A concomitant of this is that in the major component H5 may lie marginally more distant from O31 (with which it is 'coplanar') than H5′, which lies at the van der Waals distance; there seems to be no compelling intramolecular imperative why the disposition of H5, H5′ should be thus, relative to O31.

All six-membered rings in **16**, **17**, **20**, and **22**, are 'chairs' (Table 2), relatively undistorted by fusion into the

trioxaadamantane systems of **16** and **17**, and by the epoxide in **17**, although the rings in **20** and **22**, are 'flatter' than their counterparts in **16** and **17** (Table 2); in **16** and **17**, ring torsions involving the apical carbon, C7, are slightly greater than elsewhere in the trioxaadamantane array.

Table 1. Five-membered ring conformational descriptors, torsion angles

Compound	**9**	**10**	**12**
C_5O rings			
O4–C1–C2–C3	−2.5(11)	2.1(9)	−5.8(7)
C1–C2–C3–C4	22.8(10)	20.3(8)	4.3(9)
C2–C3–C4–O4	−35.8(9)	−36.0(7)	−1.0(10)
C3–C4–O4–C1	36.5(10)	40.0(9)	−3.1(10)
C4–O4–C1–C2	−21.6(11)	−26.6(9)	5.6(8)
1,2-Fused dioxolane rings			
O1–C1–C2–O2	−4.0(12)	−0.1(9)	−7.4(7)
C1–C2–O2–C12	21.0(12)	19.5(9)	−9.9(7)
C2–O2–C12–O1	−30.2(12)	−31.1(9)	22.6(7)
O2–C12–O1–C1	28.3(13)	30.7(9)	−27.8(6)
C12–O1–C1–C2	−14.9(12)	−18.5(9)	21.9(6)
4-Pendant dioxolane rings[A]			
O5–C5–C6–O6	29.4(11)	38.9(10)	−22.7(9), 37(2)
C5–C6–O6–C56	−34.3(11)	−32.4(12)	33.6(8), −43(1)
C6–O6–C56–O5	26.0(12)	13.5(1)	−31.9(9), 36(2)
O6–C56–O5–C5	−6.1(12)	12.3(12)	16.9(11), −12(3)
C56–O5–C5–C6	−14.5(11)	−31.4(11)	3.3(11), 15(3)

[A] The two entries for **12** are for the major (unprimed) and minor (primed) ring components of the disordered array, respectively (Fig. 1c).

Experimental

*Structure Determinations of **9**, **10**, **12**, **16**, **17**, **20**, and **22***

Full spheres of CCD area-detector diffractometer data were measured (Bruker AXS instrument, ω-scans, monochromatic $Mo_{K\alpha}$ radiation, λ 0.7107_3 Å; T ca. 153 or 298 K) yielding $N_{t(otal)}$ reflections, these merging to N unique (R_{int} cited) after 'empirical'/multiscan absorption correction (proprietary software), N_o with $F > 4\sigma(F)$ being employed in the full matrix least-squares refinements on $|F^2|$ (**12**, **17**) or $|F|$ (the remainder), anisotropic displacement parameter forms being refined for the non-hydrogen atoms, $(x,y,z,U_{iso})_H$ being constrained at estimates (hydroxylic hydrogens excepted, which were positioned from difference maps). Conventional residuals R, R_w on $|F|$ are cited at convergence (weights: $(\sigma^2(F^2) + n_wF^2)^{-1}$ or $\sigma^2(F) + 0.000n_wF^2)^{-1}$; for the non-centrosymmetric structures containing Cl or S, Friedel data were retained distinct and the absolute structure refined. Neutral atom complex scattering factors were employed within the context of the *Xtal 3.7* program system.[6] Pertinent results are given below and in the Table and Figures, the latter showing 50% (153 K) or 20% (298 K) probability amplitude envelopes for the non-hydrogen atoms, hydrogen atoms having arbitrary radii of 0.1 Å. Individual variations in procedure are cited under 'variata'; data quality across this series of compounds was, in general, quite poor in consequence of deficiencies in crystal quality and/or size. Full CIF depositions, excluding structure factor amplitudes, are deposited with the Cambridge Crystallographic Data Centre, CCDC no. 603019–603025.

Crystal/Refinement Data

Compound **9**, $C_{20}H_{26}O_7S$, M 410.5. Monoclinic, space group $C2$ (C_2^3, no. 5), a 21.566(7), b 7.077(2), c 14.873(4) Å, β 103.149(5)°, V 2210 Å^3. D_c (Z 4) 1.23_3 g cm^{-3}. μ_{Mo} 0.18 mm^{-1}; specimen: $0.54 \times 0.23 \times 0.18$ mm^3; 'T'$_{min/max}$ 0.69. $2\theta_{max}$ 50°; N_t 7993, N 2134

Table 2. Six-membered ring conformational descriptors, torsion angles

Compound/mol.	**16**	**17**/1	**17**/2	**17**/3	**20**	**22**
Cyclohexane rings						
C6–C1–C2–C3	62.4(1)	57.3(6)	58.1(5)	58.6(5)	48.0(5)	−59(2)
C1–C2–C3–C4	−60.1(1)	−55.0(9)	−56.3(5)	−54.9(5)	−45.7(6)	50(2)
C2–C3–C4–C5	57.7(1)	57.9(3)	58.5(5)	57.6(5)	48.6(6)	−45(2)
C3–C4–C5–C6	−56.8(1)	−58.8(6)	−59.3(5)	−59.6(5)	−57.1(6)	48(2)
C4–C5–C6–C1	59.1(1)	57.6(5)	58.0(5)	58.4(5)	63.1(6)	−55(2)
C5–C6–C1–C2	−61.8(1)	−58.7(6)	−59.9(5)	−59.8(5)	−56.5(5)	60(2)
	16	**17**/1	**17**/2	**17**/3	Mean	
1,3-Dioxane rings						
(a) O2, O6 ring						
C6–C1–C2–O2	−54.9(1)	−58.5(6)	−57.9(5)	−58.1(5)	−58.2(3)	
C1–C2–O2–C7	59.5(1)	59.5(1)	59.6(5)	60.4(5)	59.8(5)	
C2–O2–C7–O6	−61.5(1)	−63.9(6)	−63.9(5)	−65.2(5)	−64.3(8)	
O2–C7–O6–C6	60.8(1)	62.7(6)	64.4(5)	63.2(5)	63.4(9)	
C7–O6–C6–C1	−58.6(1)	−58.9(6)	−61.0(5)	−58.7(5)	−59.5(13)	
O6–C6–C1–C2	54.6(1)	58.5(6)	59.1(5)	58.1(5)	58.6(5)	
(b) O2, O4 ring						
O2–C2–C3–C4	59.3(1)	59.1(5)	59.1(5)	60.1(5)	59.4(6)	
C2–C3–C4–O4	−60.0(1)	−59.9(5)	−59.4(5)	−60.9(5)	−60.1(8)	
C3–C4–O4–C7	61.4(1)	61.3(6)	60.4(6)	62.4(6)	61.4(10)	
C4–O4–C7–O2	−63.1(1)	−62.1(6)	−60.7(6)	−62.3(6)	−61.7(9)	
O4–C7–O2–C2	63.2(1)	60.6(5)	60.6(5)	60.1(5)	60.4(3)	
C7–O2–C2–C3	−60.9(1)	−59.1(6)	−59.2(6)	−59.2(6)	−59.2(1)	
(c) O4, O6 ring						
O6–C6–C5–C4	−60.4(1)	−58.6(6)	−59.0(5)	−58.8(5)	−58.8(2)	
C6–C5–C4–O4	60.5(1)	58.5(5)	59.1(6)	58.1(56)	58.6(5)	
C5–C4–O4–C7	−60.3(1)	−60.9(5)	−62.2(3)	−60.8(6)	−61.3(8)	
C4–O4–C7–O6	61.7(1)	62.5(6)	63.0(6)	63.0(6)	62.8(3)	
O4–C7–O6–C6	−63.7(1)	−62.0(5)	−60.3(5)	−62.5(5)	−61.6(12)	
C7–O6–C6–C5	61.8(1)	60.5(6)	59.3(5)	60.7(5)	60.2(8)	

(R_{int} 0.051), N_o 1546; R 0.072, R_w 0.094 (n_w 7); $|\Delta\rho_{max}|$ 0.40(4) e Å^{-3}. x_{abs} 0.1(3).

Compound **10**, $C_{25}H_{28}O_6S_2$, M 488.6. Monoclinic, space group $P2_1$ (C_2^2, no. 4), a 6.973(2), b 17.219(5), c 10.756(2) Å, β 103.868(4)°, V 1254 Å^3. D_c (Z 2) 1.29$_4$ g cm^{-3}. μ_{Mo} 0.25 mm^{-1}; specimen: 0.54 × 0.20 × 0.15 mm^3; 'T'$_{min/max}$ 0.64. $2\theta_{max}$ 52.6°; N_t 10852, N 2652 (R_{int} 0.035), N_o 2014; R 0.070, R_w 0.086 (n_w 3); $|\Delta\rho_{max}|$ 0.50(3) e Å^{-3}. x_{abs} 0.1(2).

Compound **12**, $C_{14}H_{20}O_7$, M 360.1. Monoclinic, space group $P2_1$, a 9.232(2), b 9.051(2), c 9.932(2) Å, β 113.019(3)°, V 763.$_8$ Å^3. D_c (Z 2) 1.30$_6$ g cm^{-3}. μ_{Mo} 0.11 mm^{-1}; specimen: 0.35 × 0.25 × 0.25 mm^3; 'T'$_{min/max}$ 0.82. $2\theta_{max}$ 58°; N_t 7041, N 2012 (R_{int} 0.098), N_o 1422; R 0.070, R_w 0.14 (n_w 0.16); $|\Delta\rho_{max}|$ 0.31(4) e Å^{-3}. x_{abs} not refined.

Variata. Atoms O5, O6, C561, C562 of the pendant ring were modelled as disordered over pairs of sites, occupancies refining to 0.78(1) and complement.

Compound **16**, $C_{22}H_{21}Cl_3O_6$, M 487.8. Triclinic, space group $P\bar{1}$ (C_i^1, no. 2), a 8.075(2), b 8.726(2), c 16.131(4) Å, α 85.438(5), β 89.692(5), γ 65.606(5)°, V 1031 Å^3. D_c (Z 2) 1.57$_0$ g cm^{-3}. μ_{Mo} 0.48 mm^{-1}; specimen: 0.38 × 0.33 × 0.30 mm^3; 'T'$_{min/max}$ 0.89. $2\theta_{max}$ 75°; N_t 20253, N 10562 (R_{int} 0.027), N_o 8337; R 0.044, R_w 0.069 (n_w 3); $|\Delta\rho_{max}|$ 1.07(5) e Å^{-3}.

Compound **17**, $C_{22}H_{20}Cl_2O_6$, M 451.3. Monoclinic, space group $P2_1/c$ (C_{2h}^5, no. 14), a 15.986(3), b 27.010(6), c 14.480(3) Å, β 104.217(4)°, V 6060 Å^3. D_c (Z 12) 1.48$_4$ g cm^{-3}. μ_{Mo} 0.36 mm^{-1}; specimen: 0.28 × 0.20 × 0.04 mm^3; 'T'$_{min/max}$ 0.81. $2\theta_{max}$ 50°; N_t 55706, N 10581 (R_{int} 0.13), N_o 6858; R 0.078, R_w 0.14 (n_w 4.5); $|\Delta\rho_{max}|$ 1.0(2) e Å^{-3}.

Compound **20**, $C_{42}H_{41}Cl_3O_6$, M 748.2. Monoclinic, space group Pn (C_s^2, no. 7 variant), a 13.623(2), b 5.7876(9), c 24.173(4) Å, β 103.529(2)°, V 1853 Å^3. D_c (Z 2) 1.14$_5$ g cm^{-3}. μ_{Mo} 0.30 mm^{-1}; specimen: 0.26 × 0.24 × 0.16 mm^3; 'T'$_{min/max}$ 0.93. $2\theta_{max}$ 56°; N_t 17281, N 4229 (R_{int} 0.027), N_o 3637; R 0.050, R_w 0.069 (n_w 5); $|\Delta\rho_{max}|$ 0.37(5) e Å^{-3}. x_{abs} 0.30(8).

Compound **22**, $C_{42}H_{42}N_2O_5$, M 654.9. Monoclinic, space group $P2_1/n$ (C_{2h}^5, no. 14 variant), a 24.05(2), b 4.945(4), c 31.06(2) Å, β 109.13(1)°, V 3490 Å^3. D_c (Z 4) 1.24$_6$ g cm^{-3}. μ_{Mo} 0.08 mm^{-1}; specimen: 0.68 × 0.04 × 0.02 mm^3; 'T'$_{min/max}$ 0.68. $2\theta_{max}$ 50°; N_t 17850, N 5946 (R_{int} 0.18), N_o 1885; R 0.17, R_w 0.25 (n_w 0.042); $|\Delta\rho_{max}|$ 1.05(9) e Å^{-3}.

Variata. Weak and limited data would support meaningful displacement parameter refinement for C,N,O only with the isotropic form; phenyl rings 2,6 were modelled as disordered over pairs of sites, rotationally related about the pendant axis, site occupancies set at 0.5 after trial refinement.

General

^{1}H and ^{13}C NMR spectra were obtained on a Varian Gemini 200 (200 MHz for ^{1}H), a Bruker AM 300 (300 MHz for ^{1}H and 75.5 MHz for ^{13}C), a Bruker ARX500 (500 MHz for ^{1}H and 125.7 MHz for ^{13}C), or a Bruker AV600 (600 MHz for ^{1}H and 150.8 MHz for ^{13}C) spectrometer. Unless stated otherwise, deuterated chloroform ($CDCl_3$) was used as the solvent with $CHCl_3$ (δ_H 7.26) or $CDCl_3$ (δ_C 77.0) being employed as internal standards. NMR spectra run in D_2O used internal CH_3OH (δ_H 3.34, δ_C 49.0) as the standard.

Melting points were determined on a Reichert hot stage melting point apparatus. Optical rotations were performed with a Perkin–Elmer 141 Polarimeter in a microcell (1 mL, 10 cm path length) in $CHCl_3$ at room temperature, unless otherwise stated. Mass spectra were recorded with a VG-Autospec spectrometer using the fast atom bombardment (FAB) technique, with 3-nitrobenzyl alcohol as a matrix, unless otherwise stated. Microanalyses were performed by the Microanalytical Unit, Australian National University, Canberra.

Flash chromatography was performed on BDH silica gel or Geduran silica gel 60 with the specified solvents. Thin-layer chromatography (TLC) was effected on Merck silica gel 60 F_{254} aluminium-backed plates that were stained by heating (>200°C) with 5% sulfuric acid in EtOH.

Percentage yields for chemical reactions as described are quoted only for those compounds that were purified by recrystallization or by column chromatography and the purity assessed by TLC or ^{1}H NMR spectroscopy.

All solvents except DMF and MeCN were distilled before use and dried according to the methods of Burfield and Smithers.[7]

'Usual workup' refers to dilution with water, repeated extraction into an organic solvent, sequential washing of the combined extracts with hydrochloric acid (1 M, where appropriate), saturated aqueous sodium bicarbonate and brine solutions, followed by drying over anhydrous magnesium sulfate, filtration, and evaporation of the solvent by means of a rotary evaporator at reduced pressure.

*(3*S*)-3-Chloro-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-*arabino*-hexose* **2**

DBU (0.90 mL, 6.0 mmol) was added to the alcohol **1** (200 mg, 0.53 mmol) in MeOH (10 mL) and the solution stirred at 50°C (1 h) before being diluted with saturated NH_4Cl solution. A usual workup (EtOAc) gave a yellow residue that was subjected to flash chromatography (EtOAc/petrol 1/9) to yield the chloride **2** as a solid (148 mg, 83%), mp 68–70°C, $[\alpha]_D$ +54.4°. δ_H (300 MHz) 1.23, 1.25, 1.35, 1.45 (12H, 4s, CH_3), 3.75 (s, CO_2CH_3), 4.03 (2H, d, H6), 4.28 (ddd, $J_{4,5}$ 6.0, $J_{5,6}$ 5.6, 5.6, H5), 4.68 (d, $J_{1,2}$ 3.4, H2), 4.72 (d, H4), 5.88 (d, H1). δ_C (75.5 MHz) 24.82, 25.91, 26.34, 26.67 (4C, CH_3), 53.09 (CO_2CH_3), 66.13 (C6), 73.67 (C3), 74.26, 81.19, 88.15 (C2,C4,C5), 104.44 (C1), 109.19, 113.44 (2C, OCO), 165.39 (CO_2CH_3). *m/z* (HR-MS FAB) 337.1044; $[M+H]^+$ requires 337.1054.

*(3*S*)-3-Bromo-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-*arabino*-hexose* **3**

DBU (1.0 mL, 6.7 mmol) was added to the alcohol **11** (1.1 g, 2.2 mmol) in MeOH (30 mL) and the mixture stirred at 50°C (1 h) before being diluted with saturated NH_4Cl solution. A usual workup (EtOAc) gave a yellow residue that was subjected to flash chromatography (EtOAc/petrol 1/9) to afford the bromide **3** as an oil (690 mg, 82%), $[\alpha]_D$ +57.7°. δ_H (500 MHz) 1.26, 1.30, 1.40, 1.46 (12H, 4s, CH_3), 3.79 (s, CO_2CH_3), 4.07 (dd, $J_{6,6}$ 8.7, $J_{5,6}$ 6.6, H6), 4.10 (dd, $J_{5,6}$ 5.0, H6), 4.33 (ddd, $J_{4,5}$ 5.1, H5), 4.55 (d, H4), 4.90 (d, $J_{1,2}$ 3.5, H2), 5.93 (d, H1). δ_C (125.8 MHz) 24.95, 26.02, 26.50, 26.73 (4C, CH_3), 53.23 (CO_2CH_3), 65.93 (C6), 66.10 (C3), 76.09, 81.20, 88.20 (C2,C4,C5), 104.34 (C1), 109.15, 113.54 (2C, OCO), 165.71 (CO_2CH_3). *m/z* (HR-MS FAB) 381.0536; $[M+H]^+$ requires 381.0549.

*(3*S*)-3-Deoxy-3-fluoro-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-*arabino*-hexose* **4**

DBU (0.90 mL, 6.0 mmol) was added to the alcohol **1** (200 mg, 0.53 mmol) and CsF (400 mg, 2.6 mmol) in MeOH (10 mL) and the mixture stirred at 50°C (1 h) before being diluted with saturated NH_4Cl solution. A usual workup (EtOAc) gave a yellow residue that was subjected to flash chromatography (EtOAc/petrol 1/9) to afford the fluoride **4** as fine needles (145 mg, 85%), mp 66–68°C, $[\alpha]_D$ +55.3°. δ_H (300 MHz) 1.26, 1.29, 1.35, 1.50 (4C, CH_3), 3.80 (s, CO_2CH_3), 4.00–4.10 (2H, m, H6), 4.16–4.25 (m, H5), 4.55–4.70 (m, H2,H4), 5.96 (d, $J_{1,2}$ 3.9, H1). δ_C (75.5 MHz) 24.84, 26.13, 26.43, 26.78 (4C, CH_3), 53.00 (d, $J_{C,F}$ 55.0, CO_2CH_3), 66.72 (C6), 72.03 (d, $J_{C5,F}$ 6.3, C5), 81.82 (d, $J_{C2,F}$ 20.5, C2), 84.81 (d, $J_{C4,F}$ 37.4, C4), 98.87 (d, $J_{C3,F}$ 196.7, C3), 105.36 (C1), 109.73, 113.63 (2C, OCO), 165.37 (d, $J_{C,F}$ 24.1, CO_2CH_3). *m/z* (HR-MS FAB) 321.1383; $[M+H]^+$ requires 321.1350.

*1,2:5,6-Di-*O*-isopropylidene-3-*C*-methoxycarbonyl-3-*O*-methyl-α-D-glucose* **5**

Sodium methoxide (560 mg, 10.6 mmol) in MeOH (5 mL) was added to the alcohol **1** (200 mg, 0.53 mmol) in MeOH (5 mL) and the mixture stirred at 50°C (0.5 h) before being diluted with saturated NH_4Cl solution. A usual workup (EtOAc) gave a yellow residue that was subjected to flash chromatography (EtOAc/petrol 3/17) to afford the ether **5** as an oil (95 mg, 54%), $[\alpha]_D$ +55.1°. δ_H (500 MHz) 1.32, 1.35, 1.43, 1.53 (12H, 4s, CH_3), 3.58 (s, OCH_3), 3.81 (s, CO_2CH_3), 4.03–4.07 (2H,

m, H6), 4.35 (ddd, $J_{4,5}$ 6.4, $J_{5,6}$ 6.1, 6.0, H5), 4.65 (d, H4), 4.72 (d, $J_{1,2}$ 3.8, H2), 5.88 (d, H1). δ_C (125.8 MHz) 25.28, 26.26, 26.72, 26.74 (4C, CH_3), 52.08 (CO_2CH_3), 54.93 (OCH_3), 66.64 (C6), 72.98, 82.29, 82.96 (C2,C4,C5), 87.52 (C3), 104.61 (C1), 109.02, 112.82 (2C, OCO), 107.79 (CO_2CH_3). *m/z* (HR-MS FAB) 333.1559; $[M+H]^+$ requires 333.1550.

*(3*R*)-3-*C*-Cyano-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-*arabino*-hexose **6***

DBU (0.90 mL, 6.0 mmol) was added to the alcohol **1** (200 mg, 0.53 mmol) and NaCN (130 mg, 2.6 mmol) in MeOH (10 mL) and the mixture stirred at 50°C (1 h) before being diluted with saturated NH_4Cl solution. A usual workup (EtOAc) gave a yellow residue that was subjected to flash chromatography (EtOAc/petrol 1/9) to afford the nitrile **6** as fine needles (140 mg, 80%), mp 107–109°C (EtOAc/pentane), $[\alpha]_D$ +75.5°. δ_H (300 MHz) 1.30, 1.37, 1.50 (12H, 3s, CH_3), 3.82 (s, CO_2CH_3), 4.05 (dd, $J_{6,6}$ 9.0, $J_{5,6}$ 3.6, H6), 4.15 (dd, $J_{5,6}$ 6.2, H6), 4.25 (ddd, $J_{4,5}$ 8.7, H5), 4.57 (d, H4), 5.00 (d, $J_{1,2}$ 3.8, H2), 6.00 (d, H1). δ_C (75.5 MHz) 24.75, 25.93, 25.95, 26.85 (4C, CH_3), 53.61 (CO_2CH_3), 56.41 (C3), 67.13 (C6), 74.75, 80.79, 85.76 (C2,C4,C5), 105.11 (C1), 110.31, 113.98 (2C, OCO), 114.86 (CN), 161.99 (CO_2CH_3). *m/z* (HR-MS FAB) 328.1391; $[M+H]^+$ requires 328.1396.

*(3*S*)-3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-3-methoxycarbonylamino-α-D-*arabino*-hexose **7***

DBU (0.90 mL, 6.0 mmol) was added to the alcohol **1** (200 mg, 0.53 mmol) and KOCN (215 mg, 2.70 mmol) in MeOH (30 mL) and the mixture stirred at 50°C (1 h) before being diluted with saturated NH_4Cl solution. A usual workup (EtOAc) gave a yellow residue that was subjected to flash chromatography (EtOAc/petrol 7/13) to afford the carbamate **7** as an oil (100 mg, 50%), $[\alpha]_D$ +56.8°. δ_H (300 MHz) 1.26, 1.35, 1.50 (12H, 3s, CH_3), 3.65, 3.75 (6H, 2s, CO_2CH_3), 3.97–4.02 (2H, m, H6), 4.18–4.26 (m, H5), 4.74 (d, $J_{4,5}$ 6.7, H4), 5.09 (d, $J_{1,2}$ 3.7, H1), 5.67 (bs, NH), 6.07 (d, H1). δ_C (75.5 MHz) 24.82, 25.98, 26.15, 26.52 (4C, CH_3), 52.37, 52.77 (2C, CO_2CH_3), 66.11 (C6), 69.95 (C3), 73.47, 82.07, 85.47 (C2,C4,C5), 105.51 (C1), 109.22, 112.48 (2C, OCO), 155.79 (C(O)NH), 167.94 (CO_2CH_3). *m/z* (HR-MS FAB) 376.1610; $[M+H]^+$ requires 376.1608.

*3,3′-Anhydro-1,2:5,6-di-*O*-isopropylidene-3-*C*-dichlorohydroxymethyl-α-D-allose **8***

The alcohol **1** (500 mg, 1.33 mmol) was added to KOCN (430 mg, 5.4 mmol) and KOBu^t (500 mg, 5.4 mmol) in *tert*-butanol (20 mL) and the mixture stirred at 30°C (0.5 h). The mixture was concentrated before being diluted with EtOAc/petrol (1/4, 50 mL) and then filtered. Concentration of the filtrate gave a brown residue that was subjected to flash chromatography (EtOAc/petrol 1/9) to afford **8** as a colourless oil (350 mg, 77%), $[\alpha]_D$ +109.8°. δ_H (500 MHz) 1.36, 1.46, 1.53, 1.57 (12H, 4s, CH_3), 4.05 (dd, $J_{6,6}$ 8.7, $J_{5,6}$ 6.1, H6), 4.13 (dd, $J_{5,6}$ 7.1, H6), 4.40 (d, $J_{4,5}$ 3.3, H4), 4.45 (ddd, H5), 4.92 (d, $J_{1,2}$ 4.5, H2), 6.04 (d, H1). δ_C (125.8 MHz) 24.86, 26.19, 26.75, 27.85 (4C, CH_3), 65.93 (C6), 75.33 (C3), 75.73, 79.07, 80.71 (C2,C4,C5), 87.60 (CCl_2), 104.47 (C1), 110.53, 115.50 (2C, OCO). *m/z* (HR-MS FAB) 341.0541; $[M+H]^+$ requires 341.0559.

*(3*S*)-1,2:5,6-Di-*O*-isopropylidene-3-*S*-phenyl-3-*C*-(phenylthio)carbonyl-3-thio-α-D-*ribo*-hexose **10** and (3*S*)-1,2:5,6-Di-*O*-isopropylidene-3-*C*-methoxycarbonyl-3-*S*-phenyl-3-thio-α-D-*ribo*-hexose **9***

Sodium methoxide (560 mg, 10.6 mmol) and PhSH (0.12 mL, 1.1 mmol) in MeOH (5 mL) were added to the alcohol **1** (200 mg, 0.53 mmol) in MeOH (5 mL) and the mixture stirred at 50°C (5 min) before being diluted with saturated NH_4Cl solution. A usual workup (EtOAc) gave a yellow residue that was subjected to flash chromatography (EtOAc/petrol 1/9) to afford the thio ester **10** as plates (90 mg, 31%), mp 74–76°C (EtOAc/pentane), $[\alpha]_D$ +168.7°. δ_H (500 MHz) 1.25, 1.33, 1.43, 1.53 (12H, 4s, CH_3), 4.15 (dd, $J_{6,6}$ 8.6, $J_{5,6}$ 5.6, H6), 4.17 (dd, $J_{5,6}$ 6.4, H6), 4.59 (d, $J_{1,2}$ 4.6, H2), 4.66 (ddd, $J_{4,5}$ 6.2, H5), 4.92 (d, H4), 5.59 (d, H1), 7.38–7.48, 7.77–7.79 (10H, 2m, Ph). δ_C (125.8 MHz) 25.31, 26.13, 26.79, 26.89 (4C, CH_3), 66.97 (C6), 71.92 (C3), 74.44, 82.05, 85.75 (C2,C4,C5), 104.38 (C1), 109.48, 113.18 (2C, OCO), 128.70–136.88 (Ph), 192.20 (C=O). *m/z* (HR-MS FAB) 489.1393; $[M+H]^+$ requires 489.1406.

Next to elute was the methyl ester **9** as plates (100 mg, 46%), mp 98–100°C (EtOAc/pentane), $[\alpha]_D$ +71.9°. δ_H (500 MHz) 1.26, 1.40, 1.49 (12H, 3s, CH_3), 3.62 (s, CO_2CH_3), 4.17 (dd, $J_{6,6}$ 8.4, $J_{5,6}$ 6.7, H6), 4.24 (dd, $J_{5,6}$ 5.8, H6), 4.60 (d, $J_{1,2}$ 3.4, H2), 4.74 (ddd, $J_{4,5}$ 3.6, H5), 4.86 (d, H4), 5.94 (d, H1), 7.36–7.59 (Ph). δ_C (125.8 MHz) 25.23, 26.21, 26.85, 26.94 (4C, CH_3), 52.18 (CO_2CH_3), 64.22 (C3), 65.79 (C6), 74.71, 81.37, 84.81 (C2,C4,C5), 104.04 (C1), 108.79, 112.95 (2C, OCO), 128.45–137.51 (Ph), 167.89 (CO_2CH_3). *m/z* (HR-MS FAB) 411.1476; $[M+H]^+$ requires 411.1478.

*1,2:5,6-Di-*O*-isopropylidene-3-*C*-tribromomethyl-α-D-allose **11***

Lithium bis(trimethylsilyl)amide in THF (1.0 M, 14.0 mL, 14 mmol) was added dropwise to 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuran-3-ulose (2.5 g, 8.9 mmol) and $CHBr_3$ (1.3 mL, 15 mmol) in THF (50 mL) at −78°C. The resulting solution was stirred at −78°C (1 h) before being diluted with saturated $NaHCO_3$ solution. A usual workup (EtOAc) followed by flash chromatography (EtOAc/petrol 1/9) yielded the alcohol **11** as plates (4.0 g, 81%), mp 119–121°C, $[\alpha]_D$ +26.8°. δ_H (500 MHz) 1.37, 1.47, 1.65 (12H, 3s, CH_3), 3.91 (dd, $J_{6,6}$ 8.4, $J_{5,6}$ 7.4, H6), 4.00 (s, CO_2CH_3), 4.18 (dd, $J_{5,6}$ 5.8, H6), 4.23 (d, $J_{4,5}$ 8.1, H4), 4.77 (d, $J_{1,2}$ 4.5, H2), 4.81–4.86 (m, H5), 5.97 (d, H1). δ_C (125.8 MHz) 25.74, 26.38, 26.65, 27.11 (4C, CH_3), 46.21 (CBr_3), 68.06 (C6), 71.37, 83.05, 85.42 (C2,C4,C5), 86.30 (C3), 103.02 (C1), 110.02, 113.32 (2C, OCO). *m/z* (HR-MS FAB) 508.8755; $[M+H]^+$ requires 508.8810.

*3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-*erythro*-hex-3-enofuranose **12***

Sodium azide (34 mg, 0.52 mmol) was added to the bromo ester **3** (100 mg, 0.26 mmol) in DMF (1 mL) and the mixture heated at 70°C (24 h). A usual workup (CH_2Cl_2) gave a yellow residue that was subjected to flash chromatography (EtOAc/petrol 3/17) to yield the alkene **12** as plates (63 mg, 80%), mp 94–96°C, $[\alpha]_D$ +34.4°. δ_H (500 MHz) 1.40, 1.46, 1.48, 1.49 (12H, 4s, CH_3), 3.78 (s, CO_2CH_3), 3.97 (dd, $J_{6,6}$ 8.6, $J_{5,6}$ 5.3, H6), 4.25 (dd, $J_{5,6}$ 7.0, H6), 5.42 (d, $J_{1,2}$ 5.2, H2), 5.62 (dd, H5), 6.16 (d, H1). δ_C (125.8 MHz) 25.47, 25.68, 27.71, 27.97 (4C, CH_3), 51.63 (CO_2CH_3), 67.49 (C6), 69.76, 82.28 (C2,C5), 107.04 (C1), 107.19 (C3), 111.15, 113.82 (2C, OCO), 164.41 (CO_2CH_3), 170.32 (C4). *m/z* (HR-MS FAB) 301.1294; $[M+H]^+$ requires 301.1287.

*(3*S*)-3-Chloro-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-benzylaminocarbonyl-α-D-*arabino*-hexose **13***

DBU (0.50 mL, 3.3 mmol) was added to the alcohol **1** (200 mg, 0.53 mmol) in a mixture of benzylamine/CH_2Cl_2 (1/2, 3 mL) and the solution heated at 40°C (0.5 h). A usual workup (EtOAc) followed by flash chromatography (EtOAc/petrol 3/17) gave the amide **13** as a colourless gum (80 mg, 37%), $[\alpha]_D$ +32.9°. δ_H (500 MHz) 1.07, 1.24, 1.38, 1.57 (12H, 4s, CH_3), 4.04 (dd, $J_{6,6}$ 9.0, $J_{5,6}$ 5.5, H6), 4.19 (dd, $J_{5,6}$ 6.2, H6), 4.38–4.43 (m, H5), 4.47 (d, $J_{4,5}$ 8.3, H4), 4.46–4.48 (2H, m, CH_2Ph), 4.99 (d, $J_{1,2}$ 3.2, H2), 5.86 (d, H1), 7.27–7.38 (Ph), 7.94 (br t, NH). δ_C (125.8 MHz) 24.91, 25.59, 26.70, 26.91 (4C, CH_3), 44.13 (CH_2Ph), 67.84 (C6), 73.36, 80.27, 88.32 (C2,C4,C5), 75.92 (C3), 103.34 (C1), 110.57, 113.85 (2C, OCO), 127.63–137.24 (Ph), 164.35 (C=O). *m/z* (HR-MS FAB) 412.1519; $[M+H]^+$ requires 412.1527.

*4,6-Di-*O*-benzyl-2-*C*-trichloromethyl-*scyllo*-inositol 1,3,5-Orthoformate **16***

(a) Dimethyl sulfoxide (1.7 mL, 24 mmol) in CH_2Cl_2 (5 mL) was added dropwise to oxalyl chloride (1.0 mL, 11 mmol) in CH_2Cl_2 (20 mL) at −55°C and the solution stirred (0.5 h). The alcohol **14** (1.8 g, 4.9 mmol) in CH_2Cl_2 (5 mL) was then added dropwise and the resulting solution stirred at −55°C (1.5 h). The solution was warmed to −30°C, followed by the dropwise addition of Et_3N (8.0 mL, 57 mmol). The solution was

then warmed to room temperature and a usual workup (CH_2Cl_2) presumably yielded the ketone **15** (1.7 g) that was used in the next step without any purification.

(b) Lithium bis(trimethylsilyl)amide in THF (1.0 M, 6.0 mL, 6.0 mmol) was added dropwise to the above ketone **15** (1.7 g) and $CHCl_3$ (1.0 mL, 12 mmol) in THF (30 mL) at −78°C. The resulting solution was stirred at −78°C (1 h) before being diluted with saturated $NaHCO_3$ solution. A usual workup (EtOAc) followed by flash chromatography (EtOAc/petrol 1/9) yielded the alcohol **16** as prisms (1.4 g, 63%), mp 154–156°C (EtOAc/pentane) (Found: C 54.1, H 4.5. $C_{22}H_{21}Cl_3O_6$ requires C 54.2, H 4.3%). δ_H (300 MHz) 4.55–4.63, 4.93–4.97 (2m, H1,H3,H4,H5,H6), 4.61, 4.76 (4H, ABq, *J* 10.8, CH_2Ph), 5.55, 6.04 (2s, H7, OH), 7.24–7.35 (10H, m, Ph). δ_C (75.5 MHz) 67.65 (C2/C5), 69.07 (C1/4,C3/6), 71.80 (*C*H_2Ph), 74.80 (C4/1,C6/3), 74.89 (C5/C2), 102.10 (C7), 103.78 (CCl_3), 128.11–136.06 (Ph). *m/z* (HR-MS FAB) 487.0488; $[M + H]^+$ requires 487.0482.

2,2′-Anhydro-4,6-di-O-*benzyl-2*-C-*dichlorohydroxymethyl*-scyllo-*inositol 1,3,5-Orthoformate* ***17***

DBU (0.90 mL, 6.0 mmol) was added to the alcohol **16** (1.0 g, 2.1 mmol), NaN_3 (270 mg, 4.1 mmol) and [18]crown-6 (10 mg) in MeOH (30 mL) and the mixture stirred at 50°C (1 h) before being diluted with saturated NH_4Cl solution. A usual workup (EtOAc) gave a yellow residue that was subjected to flash chromatography (EtOAc/petrol 1/9) to afford the epoxide **17** as plates (860 mg, 93%), mp 80–82°C (EtOAc/pentane). δ_H (300 MHz) 4.44–4.48 (m, H1,H3,H4,H6), 4.60–4.63 (m, H5), 4.64–4.66 (4H, m, CH_2Ph), 5.68 (s, H7), 7.32–7.40 (10H, m, Ph). δ_C (75.5 MHz) 63.21, 68.02 (C2,C5), 68.47, 72.47 (C1,C3,C4,C6), 71.30 (*C*H_2Ph), 88.21 (CCl_2), 102.87 (C7), 127.63–137.06 (Ph). *m/z* (HR-MS FAB) 451.0680; $[M + H]^+$ requires 451.0715.

1,3,4,5,6-Penta-O-*benzyl-2*-C-*trichloromethyl*-myo-*inositol* ***20***

(a) Dimethyl sulfoxide (0.55 mL, 7.7 mmol) in CH_2Cl_2 (2 mL) was added dropwise to oxalyl chloride (0.35 mL, 4.0 mmol) in CH_2Cl_2 (10 mL) at −55°C and the solution stirred (0.5 h). The alcohol **18** (800 mg, 1.27 mmol) in CH_2Cl_2 (5 mL) was then added dropwise and the resulting solution stirred at −55°C (1.5 h). The solution was warmed to −30°C, followed by the dropwise addition of Et_3N (2.5 mL, 18 mmol). The solution was then warmed to room temperature and a usual workup (CH_2Cl_2) presumably yielded the ketone **19** (780 mg) that was used in the next step without any purification.

(b) Lithium bis(trimethylsilyl)amide in THF (1.0 M, 1.5 mL, 1.5 mmol) was added dropwise to the above ketone **19** (780 mg) and $CHCl_3$ (0.20 mL, 2.5 mmol) in THF (15 mL) at −78°C. The resulting solution was stirred at −78°C (1 h) before being diluted with saturated $NaHCO_3$ solution. A usual workup (EtOAc) followed by flash chromatography (EtOAc/petrol 1/9) afforded the alcohol **20** as plates (810 mg, 86%), mp 128–130°C (EtOAc/pentane). δ_H (300 MHz) 3.94 (dd, $J_{4,5} \approx J_{5,6}$ 9.8, H5), 4.14 (dd, $J_{1/3,6/4} \approx J_{6/4,5}$ 9.8, H4,H6), 4.44 (d, H1,H3), 4.61 (s, OH), 4.84 (s, CH_2Ph), 4.86, 4.95 (4H, ABq, *J* 11.2, CH_2Ph), 4.96, 5.05 (4H, ABq, *J* 11.2, CH_2Ph), 7.35–7.45 (25H, m, Ph). δ_C (75.5 MHz) 73.54 (*C*H_2Ph), 74.27 (*C*H_2Ph), 74.38 (*C*H_2Ph), 78.90 (2C, C1/6,C3/4), 81.09 (C2/5), 81.29 (2C, C6/1,C4/3), 82.93 (C5/2), 105.26 (CCl_3), 127.43–137.92 (Ph). *m/z* (HR-MS FAB) 747.2076; $[M + H]^+$ requires 747.2047.

2,4,6-Tri(phenylmethyloxy)phenol ***21***

DBU (0.10 mL, 0.66 mmol) was added to the alcohol **20** (100 mg, 0.13 mmol), NaN_3 (25 mg, 0.38 mmol) and [18]crown-6 (1 mg) in MeOH (10 mL) and the mixture stirred at 50°C (1 h) before being diluted with saturated NH_4Cl solution. A usual workup (EtOAc) gave a yellow residue that was subjected to flash chromatography (toluene) to afford the phenol **21** as colourless needles (32 mg, 58%). The spectral data of **21** were consistent with those previously reported.[5]

2-Amino-1,3,4,5,6-penta-O-*benzyl-2*-C-*cyano-2-deoxy*-myo-*inositol* ***22***

Titanium(IV) isopropoxide (0.30 mL, 1.0 mmol) was added to the ketone **19** (550 mg, 0.87 mmol) in NH_3/MeOH (7 M, 15 mL) and the solution stirred at r.t. (5 h). Trimethylsilyl cyanide (0.12 mL, 0.90 mmol) was added and the solution stirred (5 h) before being diluted with H_2O and concentrated, to leave a yellow residue. Flash chromatography (toluene/Et_3N 99/1) afforded the amine **22** as fine needles (480 mg, 82%), mp 135–138°C (EtOAc/pentane). δ_H (300 MHz) 2.30 (br s, NH_2), 3.68 (dd, $J_{4,5} \approx J_{5,6}$ 9.5, H5), 3.82 (d, $J_{1/3,6/4}$ 9.5, H1,H3), 4.21 (dd, H4,H6), 4.96, 5.03 (4H, ABq, *J* 10.8, CH_2Ph), 5.04 (s, CH_2Ph), 5.06, 5.11 (4H, ABq, *J* 10.3, CH_2Ph) 7.40–7.55 (25H, m, Ph). δ_C (75.5 MHz) 57.09 (C5), 75.77 (*C*H_2Ph), 75.84 (*C*H_2Ph), 76.29 (*C*H_2Ph), 80.99, 81.34 (C1,C3,C4,C6), 82.68 (C2), 122.40 (C≡N), 127.53–138.22 (Ph). *m/z* (HR-MS FAB) 655.3132; $[M + H]^+$ requires 655.3172.

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