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A FACILE ROUTE TO STEROIDAL 6-DEOXY-α-L-ALLOPYRANOSIDES

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ABSTRACT: The synthesis of a steroidal 6-deoxy-α-L-allopyranoside from cholestanol and rhamnose is described. The crucial steps in the reaction sequence comprised the transformation of a pseudoglycal into the more steric hindered 2,3-*cis*-diol *via* an intermediate bromohydrin.

The carbohydrate allose occurs in the sugar moiety of several natural glycosides, *e.g.* cardenolide,[1] lignan,[2] iridoid[3] and flavonoid glycosides.[4] The 6-deoxy derivatives of allose, however, are restricted to glycosides of cardenolides and other steroids and triterpenoids,[5] compounds with cardioactive and cytotoxic activity. In these compounds the 6-deoxy-β-allopyranoside derivatives are normally of the D-configuration [*e.g.* as in aspecioside (**1**)[6]] whereas the 6-deoxy-α-allopyranosides are of the L-configuration [*e.g.* as in datiscoside C (**2**)[7]]. 4,6-Dideoxy-α-L-allose also occurs in a modified form in the cardiac glycoside orbicuside A (**3**).[8] Prompted by the

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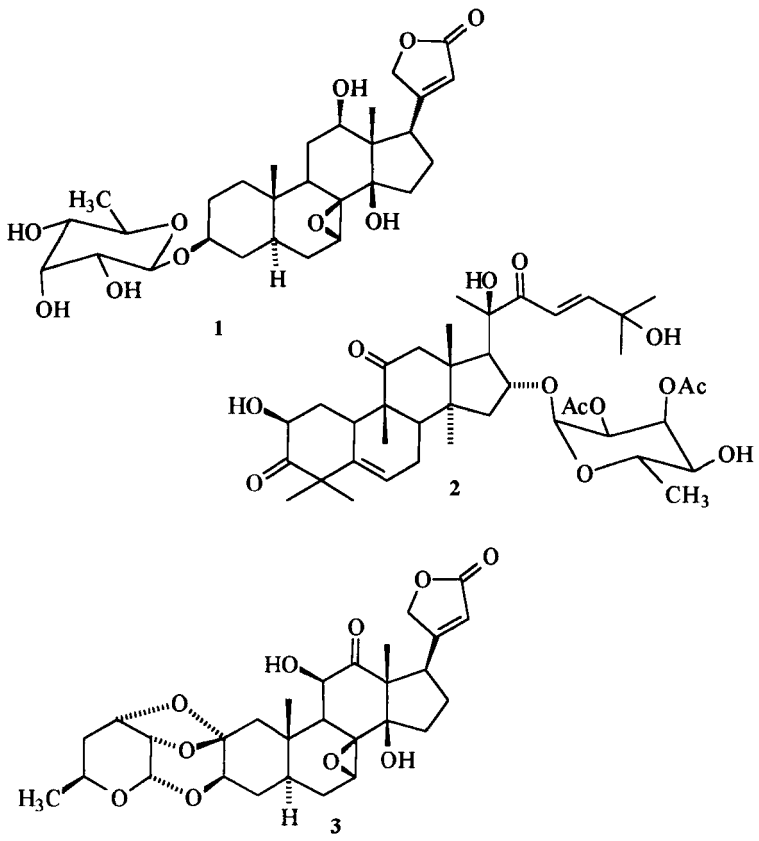
important biological activity of these compounds, we investigated the preparation of 6-deoxy-α-L-allopyranosides.

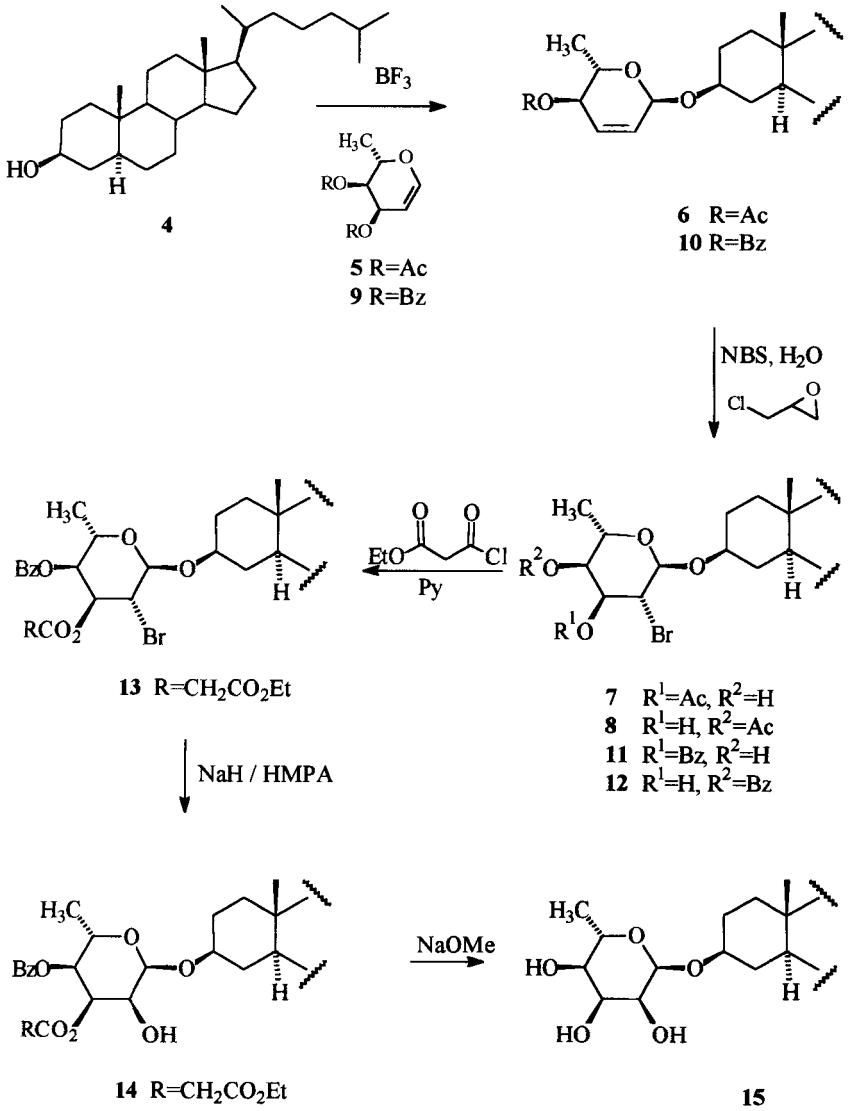


6-Deoxy-D-allopyranosides can be efficiently prepared from alkyl 4,6-*O*-benzylidene-α-D-glucopyranosides by the consecutive selective protection of the 2-hydroxyl function, oxidation of the C-3 hydroxyl to the ketone, reduction of the ketone to yield the axial hydroxyl on C-3, and deprotection of the hydroxyl functions.[9]

Since L-glucose is not readily available, this method cannot be used for the large scale preparation of the analogous L-allopyranosides and, to our knowledge, no other procedure for the preparation of 6-deoxy-α-L-allopyranosides from readily available starting materials has been published. In this report, we describe an efficient synthesis of a steroidal 6-deoxy-α-L-allopyranoside, starting from L-rhamnose and cholestanol (**4**).

Starting from rhamnose, two approaches to a 6-deoxyallopyranoside can be envisaged, *viz.* inversion of both the 2- and 3-hydroxy groups (a double Mitsunobu inversion[10]) or transformation of rhamnose into a pseudorhamnal derivative and subsequent dihydroxylation of the sterically more hindered side. We opted for the second, more direct approach (Scheme 1).

3,4-Di-*O*-acetylrhamnal (**5**) was prepared by the method described Bredenkamp *et al.*[11] and transformed into the corresponding pseudorhamnal **6** by a Ferrier rearrangement in the presence of cholestanol (**4**) and $POCl_3$ as a Lewis acid, using conditions described by Stache *et al.*[12] However, by changing the Lewis acid from phosphorus oxychloride to boron trifluoride, the reaction time was shortened from 24 hours to 2 hours, still retaining a comparable yield. The challenge now was to dihydroxylate the alkene from the sterically more hindered side. Initially the 4-hydroxy was deprotected and oxidation with OsO_4 attempted. It was envisaged that the 4-hydroxy group could coordinate to the osmium and, therefore, direct the attack to the α-face of the sugar, as was found by Wolczunowicz *et al.*[13] using a closely related cyclopentenol derivative. However, only the product resulting from β-attack


BF3
HO
H
4
H3C
O
RO
RO
5 R=Ac
9 R=Bz
6 R=Ac
10 R=Bz
NBS, H2O
Cl
O
EtO
O
O
Cl
Py
BzO
RCO2
Br
13 R=CH2CO2Et
R2O
R1O
7 R1=Ac, R2=H
8 R1=H, R2=Ac
11 R1=Bz, R2=H
12 R1=H, R2=Bz
NaH / HMPA
OH
14 R=CH2CO2Et
NaOMe
HO
15

Scheme 1

was isolated, and it is clear that, in our case, steric hindrance plays a more important role than complexation of the oxygen to the osmium.

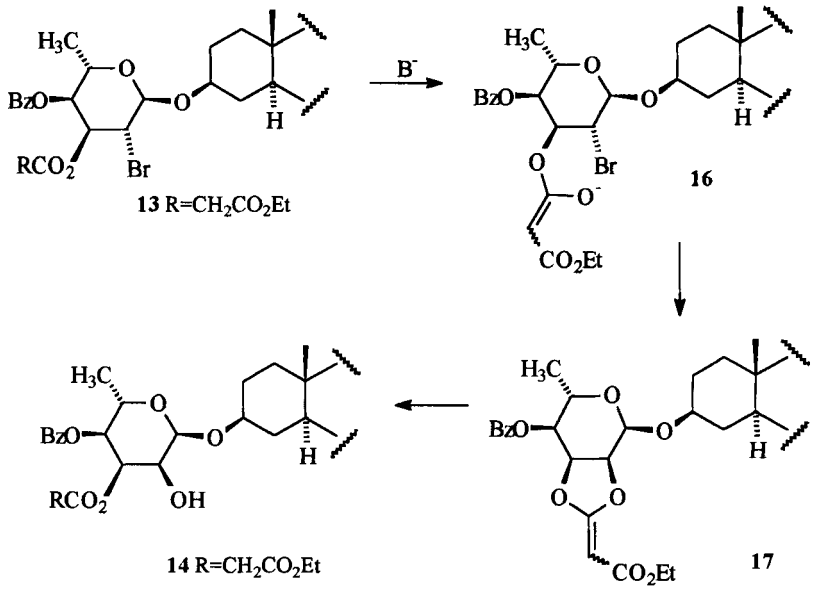
An indirect approach, involving conversion of the alkene into a halohydrin followed by substitution of the halide by an oxygen nucleophile, was first described by Woodward[14] and Corey.[15] Initial attempts to form the bromohydrin by treatment of **6** with NBS in a dimethoxyethane/water mixture resulted in the quantitative hydrolysis of the glycoside, and cholestanol (**4**) was the only product that could be isolated. The hydrolysis was probably facilitated by the HBr formed in the reaction. In addition, neighbouring group participation involving the 2-bromo substituent may have enhanced the rate of hydrolysis. To overcome this problem, epichlorohydrin was added to the reaction as an acid scavenger. Initially, the required product was obtained in a low yield, possibly due to side reactions between the reagents and epichlorohydrin. However, changing the molar ratio of NBS, water and epichlorohydrin, resulted in the quantitative transformation of **6** into two products. These two products had identical R_f-values and separation by chromatography proved to be impossible. From the NMR of the mixture it was clear that it consisted of a mixture of the desired product **7** together with **8** which resulted from the migration of the acetyl group from the 3-oxygen function to the 4-hydroxy group, and that the bromohydrin formation was regioselective.

To overcome the problem of separation, the sequence of reactions described above repeated, but with 3,4-di-*O*-benzoylrhamnal (**9**) replacing the corresponding acetyl derivative as the starting material. Treatment of the pseudoglycal **10** with NBS/H_2O in the presence of epichlorohydrin again resulted in a 54:46 mixture of

products (88%), now separable by chromatography into two compounds identified as **11** and **12**, respectively. Fortunately, the unwanted product **12** could be recycled into **11** by hydrolysis of the ester and selective benzoylation of the equatorial 4-hydroxy *via* a stannylene intermediate. All attempts to substitute the bromide (or the analogous iodide, prepared by using NIS instead of NBS in the abovementioned reaction) with an oxygen nucleophile under the conditions described by Woodward and Brutcher[13] were unsuccessful.

An adaption of the method by Corey and Das,[14] as described by Boyd *et al.*[16] and Begley *et al.*,[17] was used for the stereospecific substitution of the bromide. Treatment of **11** with ethyl (chloroformyl)acetate in the presence of pyridine yielded the mixed ester **13** in an 87% yield. A single product was obtained and there was no evidence of transesterification reactions. The approach to the *cis*-diol is based on the assumption that treatment of **13** with a base would result in the formation of enolate **16** that could participate in an intramolecular substitution reaction to produce a ketene acetal **17**. Hydrolysis of **17** should yield the required product **14** (Scheme 2).

No reaction was observed between of **13** and sodium hydride in THF or DMF, but changing the solvent to HMPA resulted in a quantitative transformation of the starting material. Initially two products were observed on t.l.c., but after chromatography only a single compound, identified as **14**, was isolated in a yield of 89%. The intermediate ketene acetal is presumably very unstable and is quantitatively hydrolysed during the work-up and chromatography of the reaction mixture. In contrast to closely related reactions with non-carbohydrate substrates,[16] only a single positional isomer was obtained. In carbohydrates the 2-hydroxy group is normally



Scheme 2

more nucleophilic than the other secondary hydroxy groups due to the influence of the adjacent acetal, and this enhanced nucleophilicity may favour initial protonation on the C-2 oxygen during the hydrolysis to yield a product containing the mixed ester on C-3. Saponification of **14** with sodium methoxide yielded the required final product **15**.

To our knowledge, this is the first time that the Corey protocol has been applied to a carbohydrate substrate, and it is of interest to compare the reaction with non-carbohydrate substrates. In the formation of the halohydrin, care should be taken to avoid acidic conditions that may lead to hydrolysis of the glycosidic bond. The key reaction, *i.e.* the displacement of the bromide by an adjacent oxygen anion, requires much harsher conditions than with non-carbohydrate substrates,[14,16] and hydrolysis of

the ketene acetal proceeds in a regioselective fashion. In conclusion, we were able to prepare a steroid α-L-allopyranoside in five steps, all in high yield, from readily available starting materials.

EXPERIMENTAL

M.p.s. were determined on a Kofler hotplate apparatus and are uncorrected. IR spectra were obtained as dilute solutions in spectroscopic grade chloroform using a Perkin Elmer 881 instrument. ^1H (200 MHz) and ^{13}C (50 MHz) NMR data were recorded on a Varian VXR 200 NMR spectrometer in $CDCl_3$ solution with tetramethylsilane as internal standard. Mass spectra were recorded on a Finnigan - MAT 8200 spectrometer at an electron impact of 70 eV.

3β-(4-*O*-Acetyl-2,3-dideoxy-2,3-dihydro-α-L-rhamnopyranosyloxy)-5α-cholestane (6): A solution of 3,4-di-*O*-acetyl-L-rhamnal (**5**, 500 mg, 2.3 mmol) and 5α-cholestan-3β-ol (**4**, 363 mg, 0.9 mmol) in THF (10 ml) was cooled to 0°C under a N_2 atmosphere and $POCl_3$ (15 μl, 0.16 mmol) was added. The reaction mixture was stirred at 25°C for 24 h. A saturated $NaHCO_3$ solution (10 ml) and CH_2Cl_2 (20 ml) were added. After shaking the mixture thoroughly, the two layers were separated. The organic layer was dried over anhydrous Na_2SO_4 and the solvent removed *in vacuo*. Chromatography (hexane-EtOAc, 8:1) of the residue afforded the pseudoglycal **6** (421 mg, 86%), m.p. 100-103 °C (hexane-Et_2O), $[\alpha]_D^{20}$ -64.7 (*c* 1.00 in $CHCl_3$); IR: ν_{max} 1738, 1652 cm^{-1}; ^1H NMR: δ 2.04 (s, 3H, OAc), 3.58 (ddt, 1H, *J* 16.1, 11.1 and 5.1, 3-H), 3.99 (dq, 1H, *J* 9.1 and 6.2, 5'-H), 5.02 (dd, *J* 9.2 and 1.3, 4'-H), 5.08 (s, 1H, 1'-H), 5.73 (dt, 1H, *J* 10.2 and 2.2, 2'-H) 5.81 (d, 1H, *J* 10.4, 3'-H); ^{13}C NMR: δ 12.08, (C-18), 12.24 (C-19), 17.99 (C-6'), 18.69 (C-21), 21.02 (OAc), 21.26 (C-11), 22.55 (C-26), 22.79 (C-27), 23.86 (C-23), 24.23 (C-15), 28.00 (C-25), 28.24 (C-16), 28.89 (C-6), 29.86 (C-2), 32.12 (C-7), 34.74 (C-4), 35.55 (C-8),35.65 (C-10), 35.80 (C-20), 36.21 (C-22), 37.23 (C-1), 39.54 (C-24),40.10 (C-12),42.64 (C-13),44.91 (C-5), 54.46 (C-9), 56.37 (C-17), 56.54 (C-14), 64.58 (C-5'), 71.08 (C-4'), 77.32 (C-3), 92.6 (C-1'), 128.52 (C-2'), 129.33 (C-3'), 170.48 (OAc); FAB-MS: *m/z* 543 (M^+ +1), EI-MS: *m/z* 498 (15 %), 456 (5), 371 (16).

3β-(3-*O*-Acetyl-2-bromo-2,6-dideoxy-α-L-altropyranosyloxy)-5α-cholestane (7) and 3β-(4-*O*-Acetyl-2-bromo-2,6-dideoxy-α-L-altropyranosyloxy)-5α-cholestane (8): H_2O (203 μl, 11.3 mmol), epichlorohydrin (221 μl, 2.8 mmol) and NBS (1.006 g, 5.6 mmol) were added sequentially to a solution of **6** (300 mg, 0.55 mmol) in 1,2-dimethoxyethane (12 ml) at 0°C. The mixture was stirred for 30 min at 0 °C and then for 2 h at 25 °C.The reaction mixture was diluted with Et_2O (150 ml) and extracted with a saturated $NaHCO_3$ solution (150 ml) containing sodium thiosulphate (892 g,

5.64 mmol). The organic layer was washed with H_2O (2 × 50 ml), dried over anhydrous $MgSO_4$ and the solvent removed under reduced pressure. Chromatography (hexane-EtOAc, 5:1) of the residue yielded an inseparable 1:1 mixture (333 mg, 91%) of two compounds that was provisionally identified as **7** and **8**.

3,4-Di-*O*-benzoylrhamnal (9): K_2CO_3 (18 mg, 0.13 mmol) was added to a solution of di-*O*-acetyl-L-rhamnal (**5**, 2.79 g, 13.0 mmol) in MeOH (15 ml) and the mixture was stirred for 24 hours at room temperature. The mixture was filtered through a short silica gel column, the solvent evaporated under reduced pressure and the residue purified by crystallisation (hexane) to give pure L-rhamnal (1.64 g, 78%) as white crystals, m.p. 71 - 74°C; $[\alpha]_D^{23}$ +20.4 (*c* 1.00 in $CHCl_3$); IR: ν_{max} 3432 cm^{-1}; ^1H NMR: δ 1.28 (d, 3H, *J* 6.3, 6-H), 3.25 (dd, 1H, *J* 9.8 and 6.9, 4-H), 3.72 (dq, 1H, *J* 9.8 and 6.4, 5-H), 4.07 (dt, 1H, *J* 6.9 and 1.7, 3-H), 4.62 (dd, 1H, *J* 6.1 and 2.0, 2-H) and 6.23 (dd, 1H, *J* 6.0 and 1.7, 1-H); ^{13}C NMR: δ 17.7 (C-6), 70.4 (C-3), 75.6 (C-5), 75.9 (C-4), 105.2 (C-2) and 144.2 (C-1); MS: *m/z* 130 (M^+ - 2 × OH, 13%) and 73 (100). Pyridine (2.24 ml, 27.7 mmol) and benzoyl chloride (3.22 ml, 27.7 mmol) were added to a solution of L-rhamnal (1.64 g, 12.6 mmol) in CH_2Cl_2 (20 ml) at 0°C and the mixture stirred for 24 hours at room temperature. CH_2Cl_2 (40 ml) and H_2O (40 ml) were added, the mixture was shaken, the organic layer dried over anhydrous Na_2SO_4 and the removed under reduced pressure. Chromatography of the residue (hexane-ethyl acetate, 4:1) gave 3,4-di-*O*-benzoyl-L-rhamnal (**9**, 3.57 g, 84%) as a colourless oil; $[\alpha]_D^{20}$ +204.8 (*c* 1.00 in $CHCl_3$); IR:ν_{max} 1219 (C-O), 1529 (C=C), 1659 (C=C) and 1699 (C=O)cm^{-1}; ^1H NMR: δ 1.43 (d, 3H, *J* 6.6, CH_3), 4.34 (q, 1H, *J* 6.8, 5-H), 4.99 (dd, 1H, *J* 6.1 and 2.9, 2-H), 5.49 (dd, 1H, *J* 7.8 and 6.0, 4-H), 5.68 - 5.73 (m, 1H, 3-H), 6.52 (dd, 1H, *J* 6.1 and 1.4, 1-H), 7.35 - 7.58 (m, 6H, *m*, *p*-Ph) and 7.96 - 8.09 (m, 4H, *o*-Ph); ^{13}C NMR: δ 16.7 (C-6), 68.8 (C-3), 72.1 (C-4), 72.7 (C-5), 98.8 (C-2), 128.3, 128.4, 129.7 and 129.8 (*ortho*- and *meta*-Ph), 129.5 and 129.9 (*ipso*-Ph), 133.1 and 133.3 (*para*-Ph), 146.1 (C-1), 165.4 and 166.0 (2 x $C_6H_5CO_2$); MS: *m/z* 217 (M^+ - $OCOC_6H_5$, 9%), 201 (4) and 105 (100).

3β-(4-*O*-Benzoyl-2,3-dideoxy-2,3-dihydro-α-L-rhamnopyranosyloxy)-5α-cholestane (10): A solution of 3,4-di-*O*-benzoyl-L-rhamnal **9** (1.58 g, 4.7 mmol) and 5α-cholestan-3β-ol (**4**, 1.8 g, 4.7 mmol) in CH_2Cl_2 (20 ml) was cooled to 0°C under a N_2 atmosphere and BF_3.OEt (115 μl, 0.93 mmol) was added. The reaction mixture was stirred at 0°C for 40 min. A saturated $NaHCO_3$ solution (25 ml) and CH_2Cl_2 (50 ml) were added. After shaking the mixture thoroughly, the two layers were separated. The organic layer was dried over anhydrous Na_2SO_4 and all the solvent removed *in vacuo*. Chromatography (hexane-EtOAc, 10:1) of the residue afforded the pseudoglycal **10** (2.13 g, 77%) as a colourless glass, $[\alpha]_D^{20}$ -70.1 (*c* 1.00 in $CHCl_3$); IR: ν_{max} 1728, 1655 cm^{-1}; ^1H NMR:δ 3.65 (ddd, 1H, *J* 16.0, 11.0 and 5.0, 3-H), 4.19 (dq, 1H, *J* 9.2 and 6.2, 5'-H), 5.17 (s, 1H, 1'-H), 5.32 (ddd, 1H, *J* 9.3, 3.1 and 1.6, 4'-H), 5.82 (dt, 1H, *J* 10.2 and 2.5, 2'-H), 5.95 (d, 1H, *J* 10.4, 3'-H), 7.39-7.47 (m, 2H, *m*-Ph), 7.53-7.62 (m, 1H, *p*-Ph), 8.00-8.07 (m, 2H, *o*-Ph); ^{13}C NMR: δ 12.09 (C-18), 12.25 (C-19), 18.09 (C-6'), 18.69 (C-21), 21.27 (C-11), 22.54 (C-26), 22.78 (C-27),

23.86 (C-23), 24.23 (C-15), 28.00 (C-25), 28.24 (C-16), 28.89 (C-6), 29.86 (C-2), 32.13 (C-7), 34.80 (C-4), 35.56 (C-8), 35.65 (C-10), 35.79 (C-20), 36.21 (C-22), 37.24 (C- 1), 39.54 (C-24), 40.10 (C-12), 42.65 (C-13), 44.92 (C-5), 54.46 (C-9), 56.37 (C-17), 56.54 (C-14), 64.79 (C-5'), 71.47 (C-4'), 77.49 (C-3), 92.77 (C-1'), 128.39 (COPh), 128.60 (C- 2'), 129.51 (C-3'), 129.69 (COPh), 130.01 (COPh), 133.13 (COPh), 165.01 (COPh); FAB -MS: *m/z* 605 ($M^+ + 1$, 11%), EI-MS 604 (M^+, 1%), 560 (67), 498 (8), 388 (36), 370 (21), 307 (16), 190 (100), 149 (34)..

3β-(4-*O*-Benzoyl-2-bromo-2,6-dideoxy-α-L-altropyranosyloxy)-5α-cholestane (11): H_2O (415 μl, 23 mmol), epichlorohydrin (451 μl, 5.77 mmol) and NBS (2.05 g, 11.5 mmol) were added sequentially to a solution of **10** (683 mg, 1.2 mmol) in 1,2-dimethoxyethane (30 ml) at 0 °C. The mixture was stirred for 30 minutes at 0 °C and then for a further 2 h at 25 °C. The reaction mixture was diluted with Et_2O (100 ml) and extracted with a 2% sodium thiosulphate solution (50 ml) The organic layer was washed with H_2O (2 × 50 ml), dried over anhydrous and the solvent removed under reduced pressure. Chromatography (hexane-EtOAc, 6:1) of the residue gave **11** (362 mg, 46%) and **12** (335, 42%). *3β-(4-O-Benzoyl-2-bromo-2,6-dideoxy-α-L-altropyranosyloxy)-5α-cholestane* (**11**) had $[\alpha]_D^{20}$ -53.2 (*c* 1.00 in $CHCl_3$); IR: ν_{max} 1727, 1121 cm^{-1} ; ^1H NMR: δ 3.56-3.70 (m, 2H, 2-H and OH), 4.19 (dd, 1H, *J* 3.7 and 1.5, 2'-H), 4.27-4.37 (m, 2H, 3'-H, 5'-H), 5.14 (s, 1H, 1-H), 5.39 (dd, 1H, *J* 9.9 and 3.1, 4'-H), 7.38-7.48 (m, 2H, *m*-Ph), 7.49-7.70 (m, 1H, *p*-Ph), 8.03-8.07 (m, 2H, *o*-Ph); ^{13}C NMR: δ 12.07 (C-18), 12.20 (C-19), 17.48 (C-6'), 18.68 (C-21), 21.25 (C-11), 22.54 (C-26), 22.79 (C-27), 23.84 (C-23), 24.21 (C-15), 28.00 (C-25), 28.22 (C-16), 28.78 (C-6), 29.28 (C-2), 32.03 (C-7), 33.98 (C-4), 34.49 (C-8), 35.61 (C-10), 35.78 (C-20), 36.19 (C-22), 37.01 (C-1), 39.52 (C-24), 40.03 (C-12), 42.62 (C-13), 44.66 (C-5), 47.41 (C-2'), 54.33 (C-9), 56.33 (C-17), 56.47 (C-14), 62.75 (C-5'), 69.92 (C-3'), 71.52 (C-4'), 77.96 (C-3), 97.90 (C-1'), 128.40 (COPh), 129.81 (COPh), 130.01 (COPh), 133.19 (COPh), 165.64 (COPh); FAB-MS: *m/z* 700 (M^+), EI-MS: *m/z* 371 (42%), 105 (100).

3β-(3-O-Benzoyl-2-bromo-2,6-dideoxy-α-L-altropyranosyloxy)-5α-cholestane (**12**) had m.p. 153-155 °C (hexane-Et_2O), $[\alpha]_D^{20}$ -18.6 (*c* 1.00 in $CHCl_3$); IR: ν_{max} 1730, 1118 cm^{-1} ; ^1H NMR: δ 3.50-3.65 (m, 1H, 3-H), 4.06 (dd, 1H, *J* 8.9 and 3.2, 4'-H), 4.20 (dq, 1H, *J* 9.0 and 6.3, 5'-H), 4.26 (dd, 1H, *J* 3.7 and 1.4, 2'-H), 5.07 (s, 1H, 1'-H), 5.46 (t, 1H, *J* 3.5, 3'-H), 7.38-7.46 (m, 2H, *m*-Ph), 7.53-7.61 (m, 1H, *p*-Ph); ^{13}C NMR: δ 12.07 (C-18), 12.20 (C-19), 17.48 (C-6'), 18.69 (C-21), 21.25 (C-11), 22.55 (C-26), 22.80 (C-27), 23.85 (C-23), 24.21 (C-15), 28.01 (C-25), 28.23 (C-16), 28.79 (C-6), 29.43 (C-2), 32.05 (C-7), 34.24 (C-4), 35.60 (C-10), 35.79 (C-20), 36.2 (C-22), 36.51 (C-8), 37.10 (C-1), 39.53 (C-24), 40.06 (C-12), 42.62 (C-13), 44.65 (C-5), 46.62 (C-2'), 54.35 (C-9), 56.34 (C-17), 56.48 (C-14), 63.35 (C-4'), 65.79 (C-5'), 72.79 (C-3'), 77.23 (C-3), 97.47 (C-1'), 128.36 (COPh), 129.82 (COPh), 130.01 (COPh), 133.42 (COPh), 166.02 (COPh); FAB-MS: *m/z* 700 (M^+), EI-MS: *m/z* 371 (58%), 105 (100).

3β-[4-*O*-Benzoyl-2-bromo-2,6-dideoxy-3-*O*-(ethoxycarbonyl)acetyl-α-L-altropyranosyloxy]-5α-cholestane (13): Pyridine (35 μl, 0.43 mmol) and ethyl (chloroformyl)acetate (55 μl, 0.43 mmol) was added to a solution of **10** (250 mg, 0.36 mmol) in CH_2Cl_2 (4 ml) at 0°C under a N_2 atmosphere. The mixture was stirred for 18 h at room temperature. CH_2Cl_2 (50 ml) was added and the solution washed successively with a cold 10% HCl solution (1 ml), H_2O (2 × 20 ml), the organic layer dried over anhydrous Na_2SO_4 and the solvent removed under reduced pressure at room temperature. Chromatography (hexane-EtOAc, 6:1) of the residue gave the mixed malonyl ester **13** (253 mg, 87%) as a colourless glass, $[\alpha]_D^{20}$ -49.2 (*c* 1.00 in $CHCl_3$); IR: ν_{max} 1724, 1455 cm^{-1}; ^1H NMR: δ 3.31 (d, 1H, *J* 15.4, $COCH_2CO$), 3.39 (d, 1H, *J* 15.2, $COCH_2CO$), 3.56 (m, 1H, 3-H), 4.08 (q, 2H, *J* 7.2, CH_2), 4.20 (dd, 1H, *J* 4.9 and 3.1, 2'-H), 4.40 (dq, 1H, *J* 7.0 and 6.6, 5'-H), 5.07 (d, 1H, *J* 2.9, 1'-H), 5.42 (d, 2H, *J* 5.9, 3'-H, 4'-H), 7.37-7.45 (m, 2H, *m*-Ph), 7.51-7.60 (m, 1H, *p*-Ph) 7.98-8.11 (m, 2H, *o*-Ph); ^{13}C NMR: δ 12.07 (C-19), 12.29 (C-18), 13.98 (OCH_2CH_3), 17.06 (C-6'), 18.68 (C-21), 21.27 (C-11), 22.53 (C-26), 22.78 (C-27), 23.84 (C-23), 24.22 (C-15), 27.99 (C-25), 28.22 (C-16), 28.84 (C-6), 29.30 (C-2), 32.08 (C-7), 34.15 (C-8), 35.44 (C-4), 35.52 (C-10), 35.77 (C-20), 36.19 (C-22), 37.06 (C-1), 39.52 (C-24), 40.06 (C-12), 41.45 ($COCH_2CO$), 42.63 (C-13), 44.73 (C-5), 46.48 (C-2'), 54.40 (C-9), 56.32 (C-17), 56.50 (C-14), 61.49 (OCH_2CH_3), 65.15 (C-5'), 70.03 (C-4'), 71.49 (C-3'), 77.55 (C-3), 97.46 (C-1'), 128.41 (Ph), 129.50 (Ph), 129.82 (Ph), 133.32 (Ph), 165.37 (CO), 165.55 (CO), 165.70 (CO); MS: *m/z* 702 (M^+-OBz, 3%), 387 (2), 371 (48).

3β-[4-*O*-Benzoyl-6-deoxy-3-*O*-(ethoxycarbonyl)acetyl-α-L-allopyranosyloxy]-5α-cholestane (14): NaH (4 mg, ~75% pure, ~0.13 mmol) was added under a N_2 atmosphere to a solution of **13** (100 mg, 0.15 mmol) in HMPA (9 ml) at room temperature. The mixture was stirred for 5 minutes at room temperature and then for a further 6 h at 60°C. T.l.c. indicated that the starting material was transformed quantitavely to two more polar compounds. Et_2O (50 ml) was added to the reaction mixture, and it was then extracted with H_2O (2 x 25 ml), the organic layer dried over anhydrous Na_2SO_4 and the solvent evaporated under reduced pressure. Chromatography (hexane-EtOAc, 4:1) of the residue gave a single product (**14**, 82 mg, 89%) as a colourless glass, $[\alpha]_D^{20}$ -48.7 (*c* 1.00 in $CHCl_3$); IR: ν_{max} 1730, 1455 cm^{-1}; ^1H NMR: δ 1.25 (t, 3H, *J* 7.1, OCH_2CH_3), 3.35 (d, 1H, *J* 15.9, $COCH_2CO$), 3.48 (d, 1H, *J* 16.1, $COCH_2CO$), 3.52 (m, 1H, 3-H), 3.84 (t, 1H, *J* 3.8, 2'-H), 4.19 (q, 2H, *J* 7.1, OCH_2CH_3), 4.25 (dq, 1H, *J* 10.3 and 6.5, 5'-H), 4.87 (dd, 1H, *J* 10.1 and 2.9, 4'-H), 4.95 (d, 1H, *J* 4.4, 1'-H), 5.70 (t, 1H, *J* 3.2, 3'-H), 7.36-7.44 (m, 2H, *m*-Ph), 7.49-7.58 (m, 1H, *p*-Ph), 7.93-7.97 (m, 2H, *o*-Ph); ^{13}C NMR: δ 12.01 (C-19), 12.32 (C-18), 14.11 (OCH_2CH_3), 17.00 (C-6'), 18.70 (C-21), 21.30 (C-11), 22.55 (C-26), 22.79 (C-27), 23.86 (C-23), 24.23 (C-15), 28.01 (C-25), 28.24 (C-16), 28.84 (C-6), 29.64 (C-2), 32.09 (C-7), 34.46 (C-8), 35.56 (C-4), 35.65 (C-10), 35.80 (C-20), 36.21 (C-22), 37.09 (C-1), 39.54 (C-24), 40.08 (C-12), 41.56 ($COCH_2CO$), 42.64 (C-13), 44.73 (C-5), 54.40 (C-9), 56.36 (C-17), 56.50 (C-14), 61.03 (C-5'), 61.67 (OCH_2CH_3), 66.97 (C-2'), 71.27 (C-4'), 71.72 (C-3'), 77.98 (C-3), 96.16 (C-1'),

128.39 (Ph), 129.61 (Ph), 129.72 (Ph), 133.21 (Ph), 165.22 (CO), 165.75 (CO), 166.73 (CO); MS: *m/z* 708 (1%), 664 (1), 649 (1).

3β-(6-Deoxy-α-L-allopyranosyloxy)-5α-cholestane (15): NaH (22 mg, ~75% pure, ~0.69 mmol) was dissolved in MeOH (20 ml) under a N_2 atmosphere. 4 ml of this solution was added to a solution of **14** (50 mg, 0.07 mmol) in toluene (3 ml) at 0 °C. The reaction was stirred for 80 minutes at room temperature. CH_2Cl_2 (25 ml) was added and the mixture was extracted with H_2O (10 ml), the organic layer dried over anhydrous Na_2SO_4 and the solvent removed under reduced pressure at room temperature. Chromatography ($CHCl_3$-MeOH, 10:1) of the residue gave *3β-(6-deoxy-α-L-allopyranosyloxy)-5α-cholestane* (**15**, 24 mg, 68%), m.p. 204-205 °C (hexane-Et_2O), $[\alpha]_D^{20}$ -48.7 (*c* 1.00 in $CHCl_3$); IR: ν_{max} 1041 cm^{-1} ; ^1H NMR ($CDCl_3$): δ 3.14 (dd, 1H, *J* 9.8 and 3.2, 4'-H), 3.56 (t, 1H, *J* 3.5, 2'-H), 3.49-3.73 (m, 2H, 3-H, 5'-H), 3.97 (dd, 1H, *J* 2.9, 3'-H), 4.95 (d, 1H, *J* 3.4, 1'-H); ^{13}C NMR: δ 12.06 (C-19), 12.30 (C-18), 17.30 (C-6'), 18.68 (C-21), 21.27 (C-11), 22.53 (C-26), 22.77 (C-27), 23.85 (C-23), 24.21 (C-15), 28.21 (C-16), 28.75 (C-6), 29.56 (C-2), 29.99 (C-25), 32.03 (C-7), 34.15 (C-8), 35.50 (C-4), 35.60 (C-10), 35.77 (C-20), 36.19 (C-22), 37.00 (C-1), 39.53 (C-24), 40.04 (C-12), 42.62 (C-13), 44.67 (C-5), 54.35 (C-9), 56.35 (C-17), 56.47 (C-14), 63.81 (C-5'), 67.96 (C-4'), 72.44 (C-2'), 72.56 (C-3'), 78.17 (C-3), 97.70 (C-1'); FAB-MS *m/z* 535 (M^++1), EI-MS: *m/z* 475 (2%), 461 (1), 443 (4).

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