Robinson Annulation on a Carbohydrate Derivative

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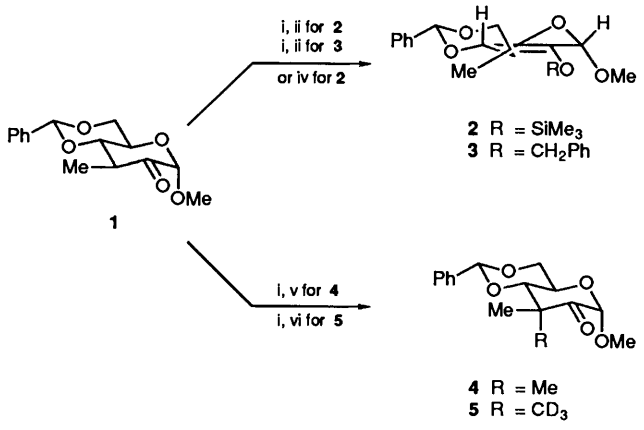
The reactions of an enolate derived from methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-*arabino*-hexopyranosid-2-ulose have been studied; examples of *O*-alkylation, *C*-alkylation and Robinson annulation were observed. In the latter case the structure of the product was confirmed by X-ray crystallography on a crystalline allylic alcohol prepared by reduction of the ketone produced in the reaction.

Carbohydrates provide an ever increasing source of inspiration to the synthetic chemist faced with the task of synthesizing enantiomerically pure compounds.[1] Many important homochiral molecules have been synthesized from carbohydrate precursors using routes in which the practitioner has to forget the special nature of the sugar derivatives and to treat them simply as polyfunctionalised molecules. Some of the major advances in this area have involved the conversion of carbohydrates into carbocyclic molecules, notable examples of this are the Stork prostaglandin synthesis[2] and the discovery, by Fraser-Reid,[3] that carbohydrate derivatives may be annulated in a Diels–Alder reaction. A need arose in our laboratory for a complex chiral cyclohexenone and it appeared that we would be able to prepare this molecule by a Robinson annulation of a sugar methyl ketone. Although extensive studies have revealed that sugar enolates are easily prepared,[4] no report on the reaction of such enolates with Michael acceptors has been published, to the best of our knowledge. It appeared that the conversion of a sugar methyl ketone into an annulated cyclohexenone *via* the Robinson procedure was indeed a novel transformation, and we now present full details of this reaction.[5]



Scheme 1 *Reagents and conditions:* i, LTMP, Et_2O, 0 °C, 1 h; ii, Me_3SiCl, room temp., 1 h; iii, BnBr (7 mol equiv.), HMPA (5 mol equiv.), room temp., 3 h; iv, Me_3SiCl, NEt_3, DMF, room temp., 36 h; v, MeI (7 mol equiv.), HMPA (5 mol equiv.), room temp., 3 h; vi, CD_3I (7 mol equiv.), HMPA (5 mol equiv.), room temp., 3 h

Results and Discussion

The glucose-derived methyl ketone **1** was prepared by the method of Sinay.[6] Surprisingly, the ketone **1** was not deprotonated by lithium diisopropylamide (LDA) but underwent reduction to a 4:1 mixture of equatorial:axial alcohols, respectively. This property of LDA has been previously reported.[7] Deprotonation with lithium 2,2,6,6-tetramethylpiperidide (LTMP) in diethyl ether was far more effective, giving the enolate which then reacted with chlorotrimethylsilane on oxygen to produce the silyl enol ether **2** in 71% yield (Scheme 1). The silyl enol ether **2** was also produced by treatment of ketone **1** with chlorotrimethylsilane and triethylamine. Similarly, the enolate of compound **1** reacted at the oxygen when it was treated with benzyl bromide, thus producing the benzyl enol ether **3**.

C-Alkylation occurred when the enolate of the ketone **1** was treated with iodomethane using hexamethylphosphoric triamide (HMPA) as cosolvent to give the α,α-dimethyl ketone **4** in 66% yield. In order to investigate the stereochemistry of this alkylation we carried out the reaction with iodo[$^2H_3$]methane which give a 49% yield of a deuteriated α,α-dimethyl ketone **5**. The structure of this product was assigned on the basis of NOE results (Fig. 1), there being a 5% enhancement between the C-3 methyl group and the axial proton (4-H) at C-4 and most importantly no enhancement of the 5-H signal. This axial attack of the electrophile is not unexpected,[4d,4e] but what is surprising is that the stereochemistry of the Robinson annulation proved to be different. The enolate of compound **1** reacted cleanly with

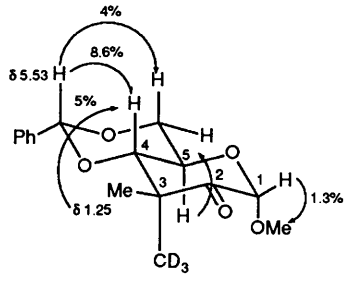
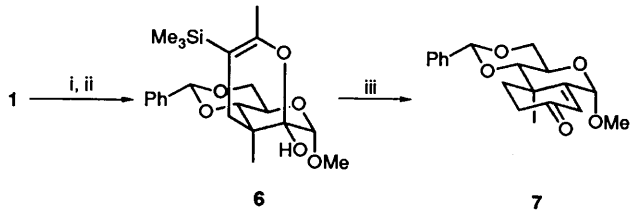


Fig. 1 NOE data for compound **5**

3-(trimethylsilyl)but-3-en-2-one[8] to afford the alcohol **6**, which gave the Robinson product **7** upon treatment with 4% methanolic potassium hydroxide, in 58% yield (Scheme 2). Again, since this product was not crystalline we relied upon NOE evidence to assign the stereochemistry at C-3 (Fig. 2). An enhancement (4%) between the 5-H signal and the methyl group



6 **7**

Scheme 2 *Reagents and conditions:* i, see Scheme 1, i; ii, 3-(trimethylsilyl)but-3-en-2-one, −78 °C to room temp., 1 h; iii, KOH (0.3 mol equiv.), MeOH, 80 °C, 6 h

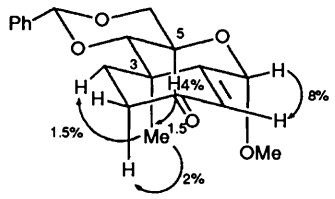
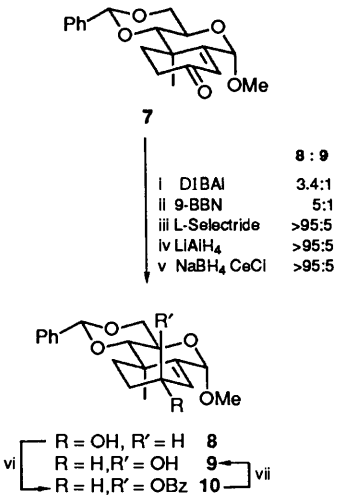


Fig. 2 NOE data for compound **7**



Scheme 3 *Reagents and conditions:* i, Toluene, −78 °C, 2 h; ii, THF, 0 °C, 2 h; iii, THF, −78 °C, 1.5 h; iv, THF, 0 °C, 2 h; v, MeOH, 0 °C, 0.5 h; vi, BzOH, DEAD, PPh_3; vii, K_2CO_3, MeOH, room temp. 3.5 h

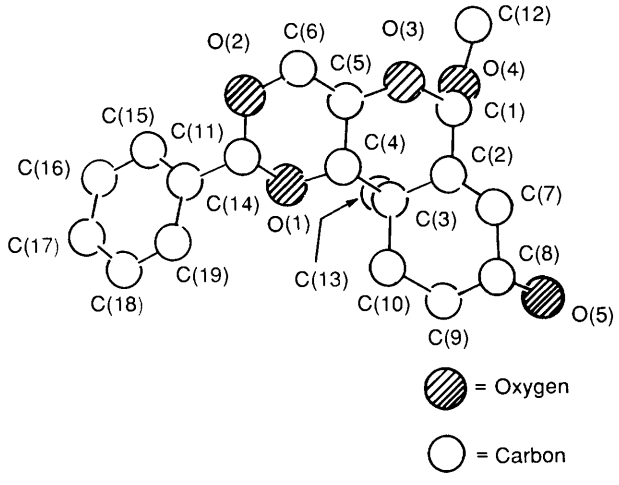


Fig. 3 A view of the X-ray molecular structure of compound **8**. Atoms are represented by circles of arbitrary radius. The hydrogens are not shown.

suggests that this methyl group is axial. We were later able to show that the assignment is correct by obtaining an X-ray crystal structure of the product from reduction of the enone **7**, the allylic alcohol **8** (Scheme 3), which indeed has an axial methyl group at C-3 (Fig. 3). It turned out that we were unduly careful in using normally very selective reducing reagents [*i.e.* potassium tri-sec-butylborohydride (K-Selectride) and diisobutylaluminium hydride (DIBAL)] since lithium aluminium hydride and sodium borohydride/cerium(III) chloride[9] proved to be equally selective. The sense of this selectivity is similar to that of known reductions of cycloenones possessing an axial methyl group at C-4.[10] To be sure that the minor isomer **9** is indeed the axial alcohol we prepared an authentic sample by Mitsunobu inversion[11] of the major isomer.

As yet, we do not know why the stereochemistry of the Robinson annulation is in the opposite sense to that of the methylation result, but since the two electrophiles and the fates of the two adducts are different, it is not too surprising to see such different behaviour. Whatever the reason for the selectivity of the reaction it is, to the best of our knowledge, the first example of a Robinson annulation of a sugar derivative and is a very important step in a projected synthesis of a taxane natural product.

Experimental

90 MHz ^{1}H NMR spectra were recorded on a Varian EM-390 spectrometer. High-field ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Brucker AM-400 spectrometer at the highfield NMR service at the University of Warwick. *J*-Values are given in Hz. Mass spectra were recorded on a Micromass 16B spectrometer. Elemental analysis was carried out by CHN Analysis, Wigston, Leicester. IR spectra were recorded on a Perkin-Elmer 298 spectrometer. M.p.s were determined on a Kofler hot-stage and are uncorrected.

Flash chromatography was carried out according to the method of Still *et al.*[12] with silica gel manufactured by Merck and Co., Kiesel 60, 230–400 mesh (ASTM). TLC was conducted on precoated aluminium sheets (60–254) with a 0.2 mm layer thickness, manufactured by Merck and Co.

The concentration of butyllithium was determined by back-titration with 0.1 mol dm^{-3} hydrochloric acid from solutions in 1,2-dibromoethane and water with phenolphthalein as indicator.

Light petroleum refers to the fraction boiling in the range 40–60 °C except where indicated otherwise; both light petroleum and ethyl acetate were distilled prior to use. Tetrahydrofuran (THF) and toluene were distilled from sodium metal in the presence of benzophenone. Diethyl ether was distilled from $LiAlH_4$.

LDA and LTMP were prepared by the addition of butyllithium (1 mmol in hexanes) to diisopropylamine or 2,2,6,6-tetramethylpiperidine (1.1 mmol) in diethyl ether (3 cm^3) at 0 °C under nitrogen. The solutions were stirred for 0.5 h and 1 h, respectively. Unless specified as otherwise, standard aqueous work-up involved addition of aq. ammonium chloride and extraction with diethyl ether (×3). The extracts were dried (Na_2SO_4), and evaporated under reduced pressure.

Treatment of Methyl 4,6-O-*Benzylidene*-3-*deoxy*-3-C-*methyl*-α-D-arabino-*hexopyranosid*-2-*ulose* **1** *with LDA.*—A solution of the ketone **1** (107 mg, 0.385 mmol) in diethyl ether (2 cm^3) was added to the LDA solution (0.385 mmol) at −78 °C. The mixture was allowed to warm to room temperature, and was then quenched with water (10 cm^3). Standard aq. work-up and chromatography [SiO_2; light petroleum–ethyl acetate (1:1 v/v)] gave methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-glucopyranoside and methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-mannopyranoside in the ratio (4:1) (65 mg, 60%) R_f 0.37 [light petroleum–ethyl acetate (1:1 v/v)]; ν_{max}(Nujol mull)/cm^{-1} 3340 (OH), 1305w, 1220w, 1200w, 1183w, 1150m, 1125s, 1075s, 1008s, 960m, 920w, 748s, 725m and 698s; δ_H($CDCl_3$) 1.11 (3 H, d, *J* 6.8, Me manno), 1.17 (3 H, d, *J* 6.4, Me gluco), 1.90–2.06 (2 H, m, 3-H gluco and OH), 2.14–2.26 (1 H, m, 3-H mano), 3.14 (1 H, dd, *J* 10.5 and 8.9, 4-H gluco), 3.33 (1 H, v br m, 2-H), 3.40 (3 H, s, OMe manno), 3.45 (3 H, s, OMe gluco), 3.58 (1 H, dd, *J* 10.4 and 9, 4-H manno), 3.67 (1 H, t, *J* 10.4, 6-H_{ax} gluco), 3.72–3.84 (1 H, m, 5-H manno and gluco), 4.25 (1 H, m, 6-H_{eq} manno and gluco), 4.57 (1 H, d, *J* 1.4, 1-H manno), 4.67 (1 H, d, *J* 3.7, 1-H gluco), 5.49 (1 H, s, PhC*H* gluco), 5.53 (1 H, s, PhC*H* manno) and 7.31–7.50 (5 H, m, Ph gluco and manno), which were identical with the compounds prepared by the literature procedure.[13]

Methyl 4,6-O-*Benzylidene*-3-*deoxy*-2-O-*trimethylsilyl*-3-C-*methyl*-α-D-erythro-*hex*-2-*enopyranoside* **2**.—A solution of the ketone **1** (0.2 g, 0.72 mmol) in diethyl ether (2 cm^3) was added to the solution of LTMP (0.72 mmol) at 0 °C. After 1 h at 0 °C, the mixture was treated with chlorotrimethylsilane (0.27 cm^3, 2.16 mmol) and was then stirred for 1 h at room temperature. Standard aq. work-up and chromatography [SiO_2; light petroleum–ethyl acetate (8:1 v/v)] gave the silyl enol ether **2** as an oil (0.18 g, 71%); $[\alpha]_D^{20}$ 69.6° (*c* 0.8 in $CHCl_3$); R_f 0.67 [light petroleum–ethyl acetate (8:1 v/v)]; δ_H(300 MHz; $CDCl_3$) 0.23 (9 H, s, $SiMe_3$), 1.71 (3 H, t, *J* 1.2, Me), 3.45 (3 H, s, OMe), 3.81 (1 H, dd, *J* 10.3 and 9.8, 6-H_{ax}), 3.94 (1 H, dt, *J* 9.1 and 4.3, 5-H), 4.12 (1 H, d with some splitting, *J* 8.8, 4-H), 4.30 (1 H, dd, *J* 9.8 and 4.3, 6-H_{eq}), 4.61 (1 H, s with some fine splitting, 1-H), 5.58 (1 H, s) and 7.33–7.54 (5 H, m, Ph); δ_C(75 MHz; $CDCl_3$) 0.51 (q, $SiMe_3$), 9.37 (q), 55.63 (q), 64.39 (d), 69.05 (t), 77.80 (d), 97.78 (d), 101.49 (d), 115.55 (s), 126.13 (d), 128.08 (d), 128.76 (d), 137.67 (s) and 142.15 (s); *m/z* 350 (M^+, 1%), 174 (49), 149 (33), 105 (32), 92 (33) and 73 (100).

Alternatively the ketone **1** (0.234 g, 0.84 mmol), triethylamine (281 mm^3, 2.02 mmol), and freshly distilled chlorotrimethylsilane (320 mm^3, 2.53 mmol) were stirred in dimethylformamide (DMF) (3 cm^3) under nitrogen for 36 h at room temperature. Standard aq. work-up and chromatography [SiO_2; light petroleum–ethyl acetate (8:1 v/v)] gave the silyl enol ether **2** as an oil (0.257 g, 87%), and was identical with the sample previously described.

Methyl 2-O-*Benzyl*-4,6-O-*benzylidene*-3-*deoxy*-3-C-*methyl*-α-D-erythro-*hex*-2-*enopyranoside* **3**.—A solution of the ketone **1** (0.2 g, 0.72 mmol) in diethyl ether (2 cm^3) was added to a solution of LTMP (0.72 mmol) at 0 °C. After 1 h at 0 °C the diethyl ether was removed by means of a vacuum pump, whilst maintaining a nitrogen atmosphere. THF (2 cm^3) was then added to the stirred mixture, followed by benzyl bromide (600 mm^3, 5.04 mmol) and HMPA (63 mm^3, 0.36 mmol). The mixture was stirred for 3 h at room temperature. Standard aq. work-up, chromatography [light petroleum–ethyl acetate (10:1 v/v)], and recrystallisation (from diisopropyl ether) gave the *benzyl ether* **3** (142 mg, 54%) as a crystalline solid, m.p. 125–127 °C; $[\alpha]_D^{20}$ 24.6° (*c* 2.4 in $CHCl_3$); R_f 0.63 [light petroleum–ethyl acetate (7:1 v/v)] (Found: C, 71.4; H, 6.6. $C_{22}H_{24}O_5$ requires C, 71.7; 6.57%); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 2940m, 2920m, 1090s, 1060s, 1038s and 1010s; δ_H(300 MHz; $CDCl_3$) 1.77 (3 H, t, *J* 1.2, Me), 3.47 (3 H, s, OMe), 3.80 (1 H, t, *J* 10.0, 6-H_{ax}), 3.96 (1 H, dt, *J* 10.0 and 4.4, 5-H), 4.09 (1 H, d with some fine splitting, *J* 9, 4-H), 4.30 (1 H, dd, *J* 10.0 and 4.4, 6-H_{eq}), 4.83 (1 H, s, 1-H) overlapping with 4.81 (1 H, d, *J* 11.5), 4.89 (1 H, d, *J* 11.5), 5.56 (1 H, s) and 7.28–7.52 (5 H, m, Ph); δ_C(75 MHz; $CDCl_3$) 9.27 (q), 55.55 (q, OMe), 64.03 (d), 68.96 (t), 73.26 (t), 77.45 (d), 96.94 (d), 101.58 (d), 120.42 (s), 126.06 (d), 127.46 (d), 127.67 (d), 128.02 (d), 128.23 (d), 128.75 (d), 137.46 (s), 137.51 (s) and 145.95 (s); *m/z* 368 (M^+, 2), 224 (53), 202 (13), 174 (26), 159 (17), 105 (81) and 91 (100).

Methyl 4,6-O-*Benzylidene*-3-*deoxy*-3,3-C-*dimethyl*-α-D-erythro-*hexopyranosid*-2-*ulose* **4**.—The ketone **1** (0.2 g, 0.72 mmol) was treated in a similar manner as in the preparation of the ether **3**, except that iodomethane was used in place of benzyl bromide, to give the α,α-*dimethyl ketone* **4** (120 mg, 57%) as an oil; $[\alpha]_D^{20}$ 16.3° (*c* 3.5 in EtOH); R_f 0.48 [light petroleum–ethyl acetate (8:1 v/v)] (Found: C, 65.7; H, 7.0. $C_{16}H_{20}O_5$ requires C, 65.7; H, 6.96%); ν_{max}(film)/cm^{-1} 2980s, 2960s, 2860br s, 1730s (C=O), 1460s, 1405s, 1380s, 1368s, 1330s, 1310s, 1292s, 1220s, 1150s, 1110s, 1048s, 995s, 750s and 700s; δ_H(300 MHz; $CDCl_3$) 1.25 (3 H, s, Me), 1.33 (3 H, s, Me), 3.44 (3 H, s, OMe), 3.52 (1 H, d, *J* 9.6, 4-H), 3.73 (1 H, t, *J* 10.1, 6-H_{ax}), 4.27 (1 H, dt, *J* 9.7 and 5.2, 5-H), 4.39 (1 H, dd, *J* 10.1 and 5.2, 6-H_{eq}), 4.59 (1 H, s, 1-H), 5.51 (1 H, s) and 7.3–7.52 (5 H, m, Ph); δ_C(75 MHz; $CDCl_3$) 18.89 (q), 20.72 (q), 48.18 (s, C-3), 55.96 (q, OMe), 59.89 (d), 69.16 (dd, C-6), 83.44 (d), 101.19 (d), 101.29 (d), 126.05 (d), 128.19 (d), 128.93 (d), 137.3 (s) and 203.85 (s, C-2); *m/z* 292 (M^+, 3%), 148 (93), 135 (8), 120 (20), 107 (37), 105 (44) and 98 (100).

Methyl 4,6-O-*Benzylidene*-3-*deoxy*-3-C-*methyl*-3-C-[$^2H_3$]-*methyl*-α-D-erythro-*hexopyranosid*-2-*ulose* **5**.—The ketone **1** (0.1 g, 0.36 mmol) was treated in a similar manner as in the preparation of the ether **4**, except that iodo[$^2H_3$]methane was used in place of iodomethane, to give the deuteriated ketone **5** as an oil (52 mg, 49%); R_f 0.5 [light petroleum–ethyl acetate (8:1 v/v)]; δ_H(400 MHz; $CDCl_3$) 1.25 (3 H, s), 3.46 (3 H, s, OMe), 3.54 (1 H, d, *J* 9.6, 4-H), 3.72 (1 H, t, *J* 10.3, 6-H_{ax}), 4.28 (1 H, dt, *J* 9.7 and 5.2, 5-H), 4.41 (1 H, dd, *J* 10.3 and 5.2, 6-H_{eq}), 4.60 (1 H, s, 1-H), 5.53 (1 H, s) and 7.34–7.50 (5 H, m, Ph); the signal at δ 5.53 shows an NOE to that of δ 3.54 (4-H, 8.6%), and to that at δ 3.72 (6-H_{ax}, 4%); signal at δ 4.60 (1-H) shows an NOE to that at δ 3.46 (OMe, 1.3%); signal at δ 1.25 (Me) shows an NOE to that at δ 3.54 (4-H, 5%); signal at δ 4.28 (5-H) shows an NOE to that at δ 4.41 (6-H_{eq}); *m/z* 295 (M^+, 1), 151 (100), 120 (19), 119 (2), 105 (67) and 101 (98).

Methyl 4,6-O-*Benzylidene*-2,3-*dideoxy*-3-C-*methyl*-3,2-C-(3′-*oxobutan*-1′-*yl*-4′-*ylidene*)-α-D-arabino-*hexopyranoside* **7**.—A solution of the ketone **1** (1.15 g, 4.13 mmol) in diethyl ether (12 cm^3) was added to the stirred LTMP solution (4.14 mmol) at 0 °C. After a further 1 h the enolate solution was concentrated by removal of *ca.* one-half of the solvent by means of a vacuum pump. 3-(Trimethylsilyl)but-3-en-2-one[8] (0.82 g, 5.79 mmol) was then added to the stirred enolate solution at −78 °C. The mixture was then allowed to warm to room temperature and then was stirred for 1 h before being poured into water (100 cm^3) and extracted with diethyl ether (3 × 150 cm^3). The extracts were washed with saturated brine (100 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography [SiO_2; light petroleum–ethyl acetate (8:2 v/v)] gave the alcohol **6** as a viscous oil; R_f 0.49 [light petroleum–ethyl acetate (8:2 v/v)]; δ_H(300 MHz; $CDCl_3$) 0.07 (9 H, s, $SiMe_3$), 1.20 (3 H, s, Me), 1.83 (s with some fine splitting, Me), 1.89 (1 H, dq, *J* 16.7 and 2.3), 2.08 (1 H, br d, *J* 16.7), 3.14 (1 H, s), 3.42 (3 H, s), 3.46 (1 H, d, *J* 9.6, 4-H), 3.68 (1 H, t, *J* 10.0, 6-H_{ax}), 3.91 (1 H, dt, *J* 10.0 and 4.9, 5-H), (1 H, dd, *J* 10.0 and 4.9, 6-H_{eq}), 4.42 (1 H, s, 1-H), 5.40 (1 H, s) and 7.27–7.42 (5 H, m, Ph); δ_C(75 MHz; $CDCl_3$) 0.34 (q), 16.79 (q), 20.00 (q), 28.47 (t), 37.01 (s), 55.84 (q), 60.04 (d), 69.33 (t), 77.27 (d), 94.88 (s), 97.94 (s), 101.47 (d), 102.85 (d), 125.97 (d), 128.10 (d), 128.76 (d), 137.74 (s) and 150.15 (s); *m/z* 420 (M^+, 2), 389 (1), 350 (3), 277 (3), 204 (10), 149 (100) and 105 (18).

The viscous oil **6** was heated at 80 °C for 6 h in a mixture of methanol (18 cm^3) and potassium hydroxide (1.9 cm^3 of a 4% aq. solution, 1.36 mmol). The methanol was then removed under reduced pressure. Standard aq. work-up and chromatography [SiO_2; light petroleum–ethyl acetate (8:2 v/v)] gave the *enone* **7** (0.79 g, 58%) as a viscous oil; $[\alpha]_D^{20}$ −38° (*c* 3.3 in $CHCl_3$); R_f 0.4 [light petroleum–ethyl acetate (7:3 v/v)] (Found: C, 69.0; H, 6.65. $C_{19}H_{22}O_5$ requires C, 69.07; H, 6.7%); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1685s (C=O), 1555s, 1125s, 1110s, 1095s, 1076s, 1050s, 1035s and 970s; δ_H(300 MHz; $CDCl_3$) 1.48 (3 H, s), 1.87 (1 H, br dt, *J* 14 and 5, 1′-H_{ax}), 2.25 (1 H, ddd, *J* 13.5, 5.0 and 2.6, 1′-H_{eq}), 2.43 (1 H, dddd, *J* 17.5, 5.0, 2.6 and 0.8, 2′-H_{eq}), 2.55 (1 H, ddd, *J* 17.5, 14.6 and 5.0 Hz, 2′-H_{ax}), 3.38–3.41 (1 H, d) overlapping with 3.41 (3 H, s), 3.71 (1 H, t, *J* 10.2, 6-H_{ax}), 4.19 (1 H, dt, *J* 9.8 and 5.2, 5-H), 4.34 (1 H, dd, *J* 10.2 and 5.2, 6-H_{eq}), 4.89 (1 H, s, 1-H), 5.54 (1 H, s), 5.86 (1 H, s) and 7.32–7.51 (5 H, m, Ph); signal at δ 1.48 shows an NOE to that at δ 2.25 (1′-H_{eq}, 1.5%), 2.55 (2′-H_{ax}, 2%), 4.19 (5-H, 4%); signal at δ

Table 1 Crystallographic data for compound **8**. Fractional atomic co-ordinates for the allyl alcohol **8**, $C_{19}H_{24}O_5$, with standard deviations in parentheses

Atom	*x*	*y*	*z*
C(1)	0.011 2(7)	0.035 20(25)	1.225 4(16)
C(2)	−0.115 9(7)	0.059 72(23)	1.153 1(14)
C(3)	−0.102 6(7)	0.099 73(24)	0.992 5(14)
C(4)	0.014 1(6)	0.129 38(24)	1.076 1(16)
C(5)	0.139 6(7)	0.100 49(26)	1.108 0(18)
C(6)	0.250 5(7)	0.132 16(28)	1.181 9(18)
C(7)	−0.230 5(7)	0.047 19(22)	1.236 8(14)
C(8)	−0.361 9(7)	0.070 41(24)	1.194 6(15)
C(9)	−0.357 0(7)	0.100 63(23)	0.993 8(17)
C(10)	−0.228 0(6)	0.129 30(23)	1.004 4(17)
C(11)	0.144 0(8)	0.194 56(25)	1.005 8(19)
C(12)	0.154 7(7)	−0.027 08(25)	1.144 1(18)
C(13)	−0.077 7(8)	0.083 93(23)	0.759 2(14)
C(14)	0.158 6(6)	0.233 29(18)	0.844 9(11)
C(15)	0.263 4(6)	0.235 06(18)	0.694 5(11)
C(16)	0.263 3(6)	0.268 52(18)	0.528 1(11)
C(17)	0.158 4(6)	0.300 18(18)	0.512 1(11)
C(18)	0.053 6(6)	0.298 39(18)	0.662 5(11)
C(19)	0.053 7(6)	0.264 95(18)	0.828 9(11)
O(1)	0.039 8(5)	0.166 28(15)	0.926 0(10)
O(2)	0.263 6(5)	0.169 51(17)	1.027 9(13)
O(3)	0.115 0(5)	0.067 44(18)	1.274 4(10)
O(4)	0.052 1(5)	0.003 39(16)	1.063 5(10)
O(5)	−0.466 8(4)	0.036 87(16)	1.169 6(10)

4.19 (5-H) shows an NOE to that at δ 1.48 (1.5%); signal at δ 4.89 (1-H) shows an NOE to that at δ 5.86 (1-H, 8%); δ_C(75 MHz; $CDCl_3$) 16.60 (q), 33.53 (t), 34.61 (t), 37.81 (s), 55.16 (q), 59.71 (d), 69.13 (dd), 85.32 (d), 101.47 (d), 125.96 (d), 127.15 (d), 128.04 (d), 128.87 (d), 137.27 (s), 157.95 (s) and 198.56 (s); *m/z* 330 (M^+, 5), 299 (3), 181 (42), 152 (100), 121 (31), 105 (19) and 91 (25).

Methyl 4,6-O-*Benzylidene*-2,3-*dideoxy*-3,2-C-[(3′R)-3′-*hydroxybutan*-1′-*yl*-4′-*ylidene*]3-C-*methyl*-α-D-arabino-*hexopyranoside* **8**.—L-Selectride (203 mm^3, 0.203 mmol) was added to a stirred solution of the enone **7** (67 mg, 0.203 mmol) in THF (1 cm^3) at −78 °C under nitrogen. After 1.5 h, when TLC showed no starting material, sodium hydroxide (122 mm^3 of a 2 mol dm^{-3} solution, 0.24 mmol) and hydrogen peroxide (55 mm^3 of a 33% solution, 0.487 mmol) were added and the mixture was stirred for 1 h at room temperature. Standard aq. work-up and chromatography [SiO_2; light petroleum–ethyl acetate (1:1, v/v)] and recrystallisation (60–80 light petroleum) yielded the *alcohol* **8** as needles (55 mg, 82%), m.p. 125–126 °C; $[\alpha]_D^{20}$ 8° (*c* 1.5 in EtOH) (Found: C, 68.9; H, 7.4. $C_{19}H_{24}O_5$ requires C, 68.65; H, 7.28%); R_f 0.4 [(1:1) light petroleum–ethyl acetate]; ν_{max}(Nujol)/cm^{-1} 3440br m (OH), 1100s, 1070s, 1042s, 1030s, 990s, 955s and 700s; δ_H(300 MHz; $CDCl_3$) 1.40 (3 H, s, Me) overlapping with 1.4–1.52 (1 H, m) overlapping with 1.56 (1 H, tdd, *J* 14.3, 9.5 and 2.5), 1.73 (1 H, br s, OH), 1.89–1.97 (1 H, m), 2.01–2.09 (1 H, m), 3.27 (1 H, d, *J* 9.5, 4-H), 3.38 (3 H, s, OMe), 3.68 (1 H, t, *J* 10.2, 6-H_{ax}), 4.12 (1 H, dt, *J* 9.7 and 5.0, 5-H), 4.23 (1 H, br t, *J* 5, 3′-H), 4.30 (1 H, dd, *J* 10.2 and 5.0, 6-H_{eq}), 4.78 (1 H, s, 1-H), 5.51 (1 H, s), 5.72 (1 H, s with some fine splitting, 4′-H) and 7.31–7.49 (5 H, m, Ph); δ_C(75 MHz; $CDCl_3$) 18.98 (q), 28.19 (t), 34.37 (t), 17.33 (s, C-3), 54.87 (q, OMe), 60.42 (q), 67.41 (d), 69.59 (t, C-6), 86.74 (d), 101.53 (d), 103.27 (d), 126.13 (d), 128.14 (d), 128.87 (d), 131.73 (d), 137.79 (s) and 139.33 (s).

Crystal Data for Compound **8**.—$C_{19}H_{24}O_5$, M = 332.39, orthorhombic, space group $P2_12_12_1$, *a* = 10.053(1), *b* = 28.748(2), *c* = 6.079(16) Å, *V* = 1753.4 $Å^3$, *Z* = 4, μ = 0.54 cm^{-1}, λ(Mo-Kα) = 0.7107 Å, *F*(000) = 712.0, D_x = 1.259 g cm^{-3}.

The unit-cell parameters were determined from an oscillation photograph for the rotation axis *c*, and from refined positional data of zone-layer reflections for *a* and *b*. The intensities of 3182 unique reflections with $2q < 52$ and $(+h, \pm k, +l)$ were measured on a Stoe STADI-2 Weissenberg diffractometer, with graphite-monochromated Mo-Kα radiation, using an ω-scan technique. The data were corrected for Lorentz and polarisation effects to yield 1180 reflections with $I > 3\sigma(I)$.

The structure was solved by using the TREF option of SHELXS 84.[14] All subsequent calculations were carried out using the program SHELX 76.[15]

Hydrogen atoms were included in calculated positions (C–H = 1.08 Å). All non-hydrogen atoms were refined as anisotropic. Final cycles of refinement employed a weighting parameter *g* (0.000 54)$\{w = 1/[\sigma^2(F) + g(F)^2]\}$ and gave the final indices $R = \{\Sigma||F_o| - |F_c||/\Sigma|F_o|\} = 0.062$ and $R_w\{=[\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{0.5}\} = 0.059$. The final difference Fourier map was featureless and an analysis of the weighting scheme over $|F_o|$ and sin θ/λ was satisfactory.

The geometry of the molecule is shown in Fig. 3. Final non-H-atomic positions are listed in Table 1; bond lengths and angles and thermal parameters together with the coordinates for the hydrogen atoms have been deposited as supplementary material with the Cambridge Crystallographic Data Centre.*

Methyl 3,2-C-[(3′S)-3-*Benzoyloxybutan*-1′-*yl*-4′-*ylidene*]-4,6-O-*benzylidene*-2,3-*dideoxy*-3-C-*methyl*-α-D-arabino-*hexopyranoside* **10**.—A solution of the alcohol **8** (0.30 g, 0.9 mmol) and triphenylphosphine (0.237 g, 0.9 mmol) in diethyl ether (10 cm^3) was added to a solution of benzoic acid (0.11 g, 0.9 mmol) and diethyl azodicarboxylate (DEAD) (0.157 g, 0.9 mmol) in diethyl ether (5 cm^3). The mixture was stirred for 3 h, the precipitate was filtered off, and the filtrate was evaporated under reduced pressure. Chromatography [SiO_2; diethyl ether–light petroleum–methanol (4:5:1 v/v/v)] gave the *benzoate* **10** (0.312 g, 80%) as a solid, m.p. 47–55 °C; R_f 0.64 [diethyl ether–light petroleum–methanol (4:5:1 v/v/v)]; $[\alpha]_D^{20}$ −112° (*c* 1.6 in MeOH) (Found: C, 71.4; H, 6.5. $C_{26}H_{28}O_6$ requires C, 71.5; H, 6.46%); $\nu_{max}(CH_2Cl_2)$/cm^{-1} 3040m, 2940m, 2820m, 1705m (C=O), 1600w, 1450w, 1375w, 1275m and 1235w; δ_H(300 MHz; $CDCl_3$) 1.37 (3 H, s, Me), 1.75–1.85 (1 H, br m, 1′-H), 1.95–2–05 (3 H, br m, 1′-H and 2′-H_2), 3.40 (3 H, s, OMe), overlying 3.40 (1 H, d, *J* 9.5, 4-H), 3.71 (1 H, t, *J* 10.1, 6-H_{ax}), 4.18 (1 H, dt, *J* 9.7 and 5.2, 5-H), 4.32 (1 H, dd, *J* 10.1 and 5.2, 6-H_{eq}), 5.5 (1 H, br m, 3′-H), 5.56 (1 H, s, C*H*Ph), 5.96 (1 H, d, *J* 4.6, 4′-H and 7.30–8.15 (10 H, m, 2 × Ph); δ_C(75 MHz; $CDCl_3$) 14.41 (q), 17.67 (q), 24.44 (t), 30.99 (t), 37.35 (s), 55.02 (q), 60.24 (d), 66.58 (d), 69.54 (t), 86.40 (d), 101.57 (d), 103.09 (d), 125.14 (d), 126.14 (d), 128.18 (d), 128.30 (d), 129.60 (d), 130.12 (d), 132.92 (d), 133.56 (s), 143.36 (s) and 165.96 (s); *m/z* 436 (M^+, 5%), 405 (24), 404 (64), 287 (30), 137 (20), 136 (80), 121 (67), 105 (86) and 104 (100).

Methyl 4,6-O-*Benzylidene*-2,3-*dideoxy*-3,2-C-[(3′S)-3′-*hydroxybutan*-1′-*yl*-4′-*ylidene*]-3-C-*methyl*-α-D-arabino-*hexopyranoside* **9**.—Potassium carbonate (0.3 g, 2.2 mmol) was added to a solution of the benzoate **10** (0.835 g, 2.5 mmol) in methanol (50 cm^3) and the mixture was stirred at room temperature for 3.5 h. The solvent was removed under reduced pressure, and standard aq. work-up and chromatography [SiO_2; diethyl ether–light petroleum–methanol (4:5:1 v/v/v)] gave the alcohol **9** (0.581 g, 91%) as an oil, R_f 0.38 [ether–petroleum ether–methanol (4:5:1 v/v/v)]; $[\alpha]_D^{20}$ 18° (*c* 3.2 in MeOH) (Found: C, 68.6; H, 7.3. $C_{19}H_{24}O_5$ requires C 68.65; H, 7.28%): $\nu_{max}(CH_2Cl_2)$/cm^{-1}

* For details see the 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, 1991, Issue 1.

3600 (OH), 3940m, 3850m, 1360s and 1050s; δ_H(300 MHz; $CDCl_3$) 1.32 (3 H, s, Me), 1.62–1.70 (1 H, br m, 1′-H), 1.75–1.90 (2 H, br m, 1′ and 2′-H), 1.97 (1 H, br s, 2′-H), 3.37 (1 H, d, *J* 9.5, 4-H), 3.39 (3 H, s, OMe), 3.68 (1 H, t, *J* 10.1, 6-H_{ax}), 4.11 (1 H, dt, *J* 9.6 and 5.4, 5-H), 4.15 (1 H, br m, 3′-H), 4.30 (1 H, dd, *J* 10.1 and 5.4, 6-H_{eq}), 4.81 (1 H, s, 1-H), 5.53 (1 H, s, PhC*H*), 5.84 (1 H, d, *J* 4.4, 4′-H), and 7.34–7.49 (5 H, m, Ph); δ_C(75 MHz; $CDCl_3$) 17.78 (q), 27.23 (t), 30.06 (t), 37.28 (s), 54.86 (q), 60.16 (d), 63.11 (d), 69.50 (t), 86.28 (d), 101.48 (d), 103.21 (d), 126.08 (d), 128.10 (d), 128.83 (d), 128.89 (d), 137.70 (s) and 140.96 (s); *m/z* 332 (M^+), 302 (28), 301 (87), 165 (37), 154 (24), 151 (30), 149 (41), 138 (33) and 105 (100).

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