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THE SYNTHESIS OF *C*-FORMYL, BRANCHED-CHAIN CARBOHYDRATE DERIVATIVES BY THE CONVERSION OF NITROMETHYL GROUPS INTO CARBONYL GROUPS*

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ABSTRACT

Addition of the sodium salts of five branched-chain nitromethyl sugars in *N*,*N*-dimethylformamide to aqueous solutions of titanium(III) chloride (at pH 1) produced the respective, *C*-formyl, branched-chain carbohydrate derivatives 3-*C*-formyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, 5-*O*-acetyl-3-deoxy-3-*C*-formyl-1,2-*O*-isopropylidene-α-D-ribofuranose, methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-formyl-α-D-*ribo*-hexopyranoside (**6**), benzyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-formyl-α-D-allopyranoside (**9**), and benzyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-formyl-α-D-*erythro*-hex-2-enopyranoside. The axial formyl groups in **6** and **9** were equilibrated under mild conditions to give the equatorial 3-*C*-formyl epimers methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-formyl-α-D-*arabino*-hexopyranoside and benzyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-formyl-α-D-glucopyranoside (**10**), respectively. The branched chain in **10** was readily elongated by using ethyl 2-(diethoxyphosphoryl)propionate, to give benzyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-(2-ethoxycarbonyl)prop-1-enyl-α-D-glucopyranoside.

INTRODUCTION

A large number of naturally occurring, branched-chain carbohydrates contain a *C*-formyl group[2]. *gem*-Hydroxy-formyl branched-chain derivatives have been obtained by the permanganate oxidation of exocyclic cyanomethylene groups[3]. Addition of vinyl-Grignard reagents[4] or 2-lithio-1,3-dithiane[5,6] to keto-sugars gave derivatives that could also be converted into *gem*-hydroxy-formyl branched-chain carbohydrates. Nucleophilic scission of sugar epoxides with unsaturated organolithium reagents[7] or with the dithianyl anion[8] gave products suitable for conversion into *C*-deoxy-*C*-formyl derivatives. Some *C*-formyl branched-chain sugars have been

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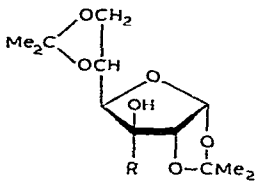
obtained by the oxidation of nitromethyl groups with aqueous permanganate[9,10].

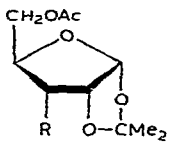
Nitromethyl branched-chain carbohydrates may be obtained by the condensation of nitromethane with suitably protected glycosiduloses[11]. Dehydration and subsequent reduction of the intermediate nitro-olefin may afford the deoxynitromethyl derivatives[11]. Nitromethyl groups in a variety of structural environments have been successfully converted into carbonyl groups with titanium(III) ions in aqueous solution[12–14]. This facile process, in combination with the nitromethane reaction on keto-sugars, provides a convenient route to a variety of *C*-formyl branched-chain carbohydrates, examples of which are described below.

RESULTS AND DISCUSSION

A solution of the sodium salt of the *gem*-hydroxy-nitromethyl-glucofuranose[15] **1** was prepared in *N*,*N*-dimethylformamide with sodium hydride. This solution was added to an aqueous solution of titanium(III) chloride buffered at pH 1. This pH provided optimum conditions for the reaction; at the originally suggested[12] pH of 5, the titanium(III) solution appeared to be unstable and could not be used to effect conversion of the nitromethyl groups. Under the conditions employed, reduction of the nitronate occurred immediately and before protonation of the anion could take place. The resulting imine was rapidly hydrolysed under the acidic conditions, to give the aldehyde, 3-*C*-formyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose[3] (**2**; singlet at δ 9.77), which was isolated in 83% yield.



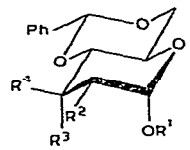
1 R = CH_2NO_2
2 R = CHO



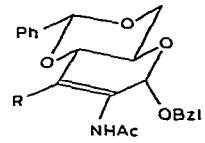
3 R = CH_2NO_2
4 R = CHO

Similarly, treatment of the deoxy-*C*-nitromethyl-ribofuranose[16] **3** with titanium(III) chloride produced 5-*O*-acetyl-3-deoxy-3-*C*-formyl-1,2-*O*-isopropylidene-α-D-ribofuranose (**4**) in 82% yield. The n.m.r. spectrum of **4** showed a singlet (δ 9.80) for the aldehyde proton. If the Karplus relationship is valid, the dihedral angle of the aldehyde proton and the vicinal H-3 should be approximately 90° for minimal coupling[17], which would require the carbonyl group to be almost eclipsed by C-2 or C-4. The preferred rotamer for simple aldehydes is considered to be[18] that in which the carbonyl group is eclipsed by a neighbouring alkyl substituent. Other rotamers would produce a *vicinal* coupling constant larger than zero.

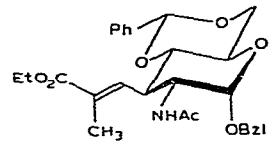
Addition of the sodium salt of the deoxy-*C*-nitromethyl derivative[11] **5**, prepared in *N*,*N*-dimethylformamide with sodium hydride, to aqueous titanium(III) chloride (at pH 1) produced methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-formyl-α-D-*ribo*-



5 R^1 = Me, R^2 = H, R^3 = CH_2NO_2, R^4 = H
6 R^1 = Me, R^2 = H, R^3 = CHO, R^4 = H
7 R^1 = Me, R^2 = H, R^3 = H, R^4 = CHO
8 R^1 = Bzl, R^2 = NHAc, R^3 = CH_2NO_2, R^4 = H
9 R^1 = Bzl, R^2 = NHAc, R^3 = CHO, R^4 = H
10 R^1 = Bzl, R^2 = NHAc, R^3 = H, R^4 = CHO



11 R = CH_2NO_2
12 R = CHO
13 R = CH_2OH



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hexopyranoside (**6**) in 71% yield. The n.m.r. spectrum of **6** showed a one-proton doublet at δ 10.15 ($J_{3,3'}$ 2.5 Hz) for the aldehyde proton. The *ribo* configuration was assigned on the basis of a $J_{3,4}$ value of 4.5 Hz, indicating a synclinal relationship. Treatment of **6** with methanolic sodium methoxide caused equilibration to the *arabino*-epimer **7** in 40% isolable yield. This was evident from the upfield shift to δ 9.85 ($J_{3,3'}$ 1.5 Hz) of the signal for the aldehyde proton of **7**; the proton signals for equatorial formyl groups usually occur[19] at higher field than those for axial formyl groups.

Application of the titanium(III) reduction to the benzyl 3-*C*-nitromethyl-allopyranoside[11] **8** produced a mixture of epimers (**9** and **10**) in a ratio of ~4:1 as judged by the signals for aldehyde protons at δ 10.07 and 9.62. Equilibration of this mixture with potassium carbonate in moist benzene produced benzyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-formyl-α-D-glucopyranoside (**10**) in 73% yield (overall from **8**). The n.m.r. signal of the formyl proton of **10** was a doublet at δ 9.62 ($J_{3,3'}$ 4.8 Hz).

Similarly, α,β-unsaturated aldehydes may also be prepared by the titanium(III) reduction of appropriate nitromethyl sugar derivatives. Treatment of the sodium salt of the 3-*C*-nitromethyl-hex-2-enopyranoside[11] **11** with aqueous titanium(III) chloride (at pH 1) produced the conjugated aldehyde benzyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-formyl-α-D-*erythro*-hex-2-enopyranoside (**12**) in 98% yield. The aldehyde group of **12** could be reduced with lithium aluminium hydride in tetrahydrofuran or with sodium borohydride in pyridine, to give benzyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-hydroxymethyl-α-D-*erythro*-hex-2-enopyranoside (**13**). Attempts to hydrogenate the conjugated double-bond in **13** catalytically resulted in removal of protecting groups.

Elongation of the branched chain is possible. Addition of the ethyl 2-(diethoxyphosphoryl)propionate carbanion[20] to the aldehyde **10** in *N*,*N*-dimethylformamide produced the conjugated ester benzyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-(2-ethoxycarbonyl)prop-1-enyl-α-D-glucopyranoside (**14**) in 67% yield. Since the *trans* isomer generally preponderates[20] under the conditions of the Wadsworth–Emmons reaction[21], it is assumed that the configuration of the double bond in ester **14** is *trans*.

The conversion of carbohydrate nitromethyl groups into formyl groups with aqueous titanium(III) chloride is of importance in general carbohydrate chemistry. It should be possible to prepare C-formyl branched-chain derivatives of both general types (R-C-OH and R-C-H) from a common keto-sugar precursor. The introduction of the branch proceeds in a stereochemically predetermined manner[11], and either of the possible epimers of a deoxy-*C*-formyl branched-chain sugar can be prepared.

EXPERIMENTAL

General. — Melting points were taken in capillary tubes in a Büchi silicone oil-bath apparatus and are uncorrected. I.r. spectra of solids were recorded for KBr disks with a Perkin–Elmer 257 grating spectrophotometer; for liquids, films on KBr disks were used. N.m.r. spectra were recorded with a Varian EM-360 spectrometer, with tetramethylsilane as internal standard. Optical rotations were determined with a Perkin–Elmer 141 polarimeter. T.l.c. was performed on Silica Gel F (precoated plates, Merck) with detection by u.v. light or with 0.5% $KMnO_4$ in M NaOH. Mass spectra were recorded with an A.E.I. MS-9 spectrometer. Microanalyses were performed by Dr. Franz Pascher (Bonn, West Germany).

Aqueous titanium(III) chloride (pH 1). — A solution of titanium(III) ions in aqueous hydrochloric acid at pH 1 was prepared by the cautious addition of 35% aqueous ammonium acetate (10 ml) to a solution of titanium trichloride (10 mmol) in 4% hydrochloric acid (10 ml). The solution was freshly prepared before each reaction.

3-C-Formyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose[3] (**2**). — To a solution of 1,2:5,6-di-*O*-isopropylidene-3-*C*-nitromethyl-α-D-glucofuranose[15] (**1**; 229 mg, 0.75 mmol) in anhydrous *N*,*N*-dimethylformamide (2 ml) at 0° was added a dispersion of sodium hydride in mineral oil (60%; 30 mg, 0.75 mmol), and stirring was continued until gas evolution ceased (~30 min). The solution was added to a well-stirred, buffered solution of titanium(III) chloride (pH 1, 20 ml). Stirring was continued for 2 min and the mixture was poured into dichloromethane (50 ml). The organic phase was washed with saturated, aqueous sodium hydrogencarbonate (5 ml) and water (15 ml), dried (Na_2SO_4), and concentrated, to give **2** as a homogeneous (t.l.c.; benzene–ethyl acetate, 10:1), colorless oil (180 mg, 83%); ν_{max}^{liquid} 1725 cm^{-1}. N.m.r. data: δ 1.23, 1.33, and 1.60 (3 s, 12 H, 4 Me), 3.80 (bs, 1 H, OH; exchangeable with D_2O), 4.0–4.6 (m, 4 H), 4.43 (d, 1 H, $J_{2,1}$ 3.4 Hz, H-2), 5.97 (d, 1 H, H-1), and 9.77 (s, 1 H, CHO). These data correspond with those reported[3] for **2**.

5-O-Acetyl-3-deoxy-3-C-formyl-1,2-O-isopropylidene-α-D-ribofuranose (**4**). — To a solution of 5-*O*-acetyl-3-deoxy-1,2-*O*-isopropylidene-3-*C*-nitromethyl-α-D-ribofuranose[16] (**3**; 200 mg, 0.73 mmol) in anhydrous *N*,*N*-dimethylformamide (3 ml) at −10° was added sodium hydride (60% dispersion in mineral oil; 30 mg, 0.75

mmol). Stirring was continued at −10° until gas evolution ceased (~20 min), and the mixture was then added at ~1 drop/sec. to a buffered solution of titanium(III) chloride (pH 1) kept at 0°. Stirring was continued for 45 min at room temperature. The mixture was worked-up, as described for **2**, to leave a syrup that was eluted from a column of silica gel 60 (70–230 mesh, Merck) with chloroform, to give **4** as a colorless syrup (146 mg, 82%), $[\alpha]_D^{23}$ +49° (*c* 0.5, chloroform); ν_{max}^{liquid} 2760, 1750, 1735, and 1465 cm^{-1}. N.m.r. data: δ 1.33 and 1.42 (2 s, 6 H, Me_2C), 2.05 (s, 3 H, AcO), 2.90 (dd, 1 H, $J_{3,4}$ 9.7 Hz, H-3), ~4.27 (m, 2 H, H-5,5'), 4.67 (m, 1 H, H-4), 5.10 (dd, 1 H, $J_{2,3}$ 6 Hz, H-2), 5.90 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), and 9.80 (unresolved d, $J_{3,3'}$ <1 Hz, CHO). Mass spectrum: *m/e* 229 [M^+ − 15] (Found: 229.070783. $C_{10}H_{13}O_6$ calc.: 229.071205).

The semicarbazone of **4** had m.p. 182–183° (from ethyl acetate–light petroleum).

Anal. Calc. for $C_{12}H_{19}N_3O_6$: C, 47.84; H, 6.36; N, 13.95. Found: C, 47.62; H, 6.36; N, 13.94.

*Methyl 4,6-O-benzylidene-2,3-dideoxy-3-C-formyl-α-*D-ribo-*hexopyranoside* (**6**). — A solution of methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-nitromethyl-α-D-*ribo*-hexopyranoside[11] (**5**; 773 mg, 2.5 mmol) in anhydrous *N*,*N*-dimethylformamide (10 ml) at 0° was treated with sodium hydride (60% dispersion in mineral oil; 100 mg, 2.5 mmol) as described above. The solution was added dropwise during 3 min to a solution of buffered titanium(III) chloride (pH 1, 50 ml) at 0°, which was stirred for another 3 min and then poured into dichloromethane (250 ml). After work-up, as described for **2**, the resulting oil, which gave one spot in t.l.c. (benzene–ethyl acetate, 10:1), crystallised spontaneously (492 mg, 71%). Recrystallisation from ether–light petroleum gave needles of **6** (440 mg), m.p. 119–120° (dec.), $[\alpha]_D^{23}$ +147° (*c* 0.7, chloroform); ν_{max} 2850 and 1725 cm^{-1}. N.m.r. data: δ 2.10 (m, 2 H, H-2,2'), 2.74 (ddd, 1 H, H-3), 3.34 (s, 3 H, MeO), 3.85 (dd, 1 H, $J_{4,3}$ 4.5, $J_{4,5}$ 8 Hz, H-4), 3.7–4.45 (m, 3 H), 4.68 (m, 1 H, H-1), 5.55 (s, 1 H, PhC*H*), 7.40 (m, 5, Ph), and 10.15 (d, 1 H, $J_{3,3'}$ 2.5 Hz, CHO).

Anal. Calc. for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.87; H, 6.74.

*Methyl 4,6-O-benzylidene-2,3-dideoxy-3-C-formyl-α-*D-arabino-*hexopyranoside* (**7**). — To a solution of **6** (50 mg, 0.18 mmol) in methanol (2 ml) at 0° was added sodium methoxide (10 mg, 0.5 mmol). The mixture was stirred for 30 min, added to 1% aqueous acetic acid (50 ml), and extracted with dichloromethane (10 ml), and the extract was washed with saturated, aqueous sodium hydrogencarbonate (2 ml) and water (4 ml), dried (Na_2SO_4), and concentrated. The residual oil (20 mg, 40%), after washing with light petroleum to remove traces of benzaldehyde, gave a single spot in t.l.c. (benzene–ethyl acetate, 10:1). N.m.r. data: δ 2.05 (m, 2 H, H-2,2'), 3.20 (m, 1 H, H-3), 3.37 (s, 3 H, MeO), 3.6–4.4 (m, 4 H), 4.77 (m, 1 H, H-1), 5.57 (s, 1 H, PhC*H*), 7.40 (m, 5 H, Ph), and 9.85 (d, 1 H, $J_{3,3'}$ 1.5 Hz, CHO). Mass spectrum: *m/e* 278 [M^+] (Found: 278.115425. $C_{15}H_{18}O_5$ calc.: 278.115414).

*Benzyl 2-acetamido-4,6-O-benzylidene-2,3-dideoxy-3-C-formyl-α-*D-*glucopyranoside* (**10**). — A solution of benzyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-nitromethyl-α-D-allopyranoside[11] (**8**; 442 mg, 1 mmol) in anhydrous *N*,*N*-dimethyl-

formamide (10 ml) at 0° was treated with sodium hydride (60% dispersion in mineral oil; 40 mg, 1 mmol). After gas evolution had ceased (~30 min), the solution was added dropwise during 5 min to a well-stirred solution of titanium(III) chloride (pH 1, 50 ml). Work-up after 15 min, as described for **2**, gave an epimeric mixture of **9** and **10** (330 mg). N.m.r. data: δ 1.87 (s, 0.2 H, AcN, *gluco*-epimer), 1.95 (s, 0.8 H, AcN, *allo*-epimer), 2.90 (m, 1 H, H-3), 5.68 (d, 0.2 H, NH, *gluco*-epimer), 6.30 (d, 0.8 H, NH, *allo*-epimer), 9.62 (d, 0.2 H, CHO, *gluco*-epimer), and 10.07 (m, 0.8 H, CHO, *allo*-epimer).

The mixture of epimers was treated with boiling, moist benzene (10 ml containing 2 drops of water) together with powdered potassium carbonate (300 mg) for 12 h. The solvent was removed *in vacuo* and the residue was partitioned between chloroform (100 ml) and water (20 ml). The organic layer was separated, washed with water (10 ml), dried (Na_2SO_4), and concentrated. Recrystallisation of the residue from acetone–light petroleum gave **10** (300 mg, 73%) as colorless needles, showing one spot in t.l.c. (chloroform–*p*-dioxane, 95:5); m.p. 262–264° (dec.), $[\alpha]_D^{23}$ +63° (*c* 1, chloroform); ν_{max} 3300, 2750, 1735, 1660, and 1565 cm^{-1}. N.m.r. data: δ 1.87 (s, 1 H, AcN), 2.93 (m, 1 H, H-3), 3.7–4.4 (m, 4 H), 4.63 (dd, 2 H, J_{AB} 11 Hz, $\Delta\nu_{AB}$ 4 Hz, PhCH_2O), 4.85 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 5.55 (s, 1 H, PhC*H*), 5.75 (d, 1 H, $J_{NH,2}$ 9.4 Hz, NH), 7.33 (m, 10 H, 2 Ph), and 9.62 (d, 1 H, $J_{3,3}$ 4.8 Hz, CHO).

Anal. Calc. for $C_{23}H_{25}NO_6$: C, 67.14; H, 6.12; N, 3.40. Found: C, 66.93; H, 6.13; N, 3.45.

*Benzyl 2-acetamido-4,6-O-benzylidene-2,3-dideoxy-3-C-formyl-α-*D-erythro-*hex-2-enopyranoside* (**12**). — To a solution of benzyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-nitromethyl-α-D-*erythro*-hex-2-enopyranoside[11] (**11**; 284 mg, 0.65 mmol) in anhydrous *N*,*N*-dimethylformamide (3 ml) at −10° was added sodium hydride (60% dispersion in mineral oil; 26 mg, 0.65 mmol), and stirring was continued for 45 min at this temperature. Treatment of the mixture with titanium(III) chloride and work-up, as described for **2**, gave a colorless solid (260 mg, 98%) that showed a single spot in t.l.c. (chloroform), but crystallised in low yield (~100 mg) from chloroform–ethyl acetate, to give **12**, m.p. 181–182°, $[\alpha]_D^{23}$ +34° (*c* 1, chloroform); ν_{max} 2900, 1750(w), 1720(s), 1670, and 1610 cm^{-1}. N.m.r. data: δ 2.15 (s, 3 H, AcN), 3.8–4.3 (m, 3 H), 4.58 (d, 1 H, $J_{4,5}$ 8 Hz, H-4), 4.78 (s, 2 H, PhCH_2O), 5.65 (s, 1 H, PhCHO_2), 6.35 (s, 1 H, H-1), 7.35 (m, 10 H, 2 Ph), 9.65 (s, 1 H, CHO), and 11.77 (bs, 1 H, NH).

Anal. Calc. for $C_{23}H_{23}NO_6$: C, 67.47; H, 5.66; N, 3.42. Found: C, 67.30; H, 5.65; N, 3.40.

*Benzyl 2-acetamido-4,6-O-benzylidene-2,3-dideoxy-3-C-hydroxymethyl-α-*D-erythro-*hex-2-enopyranoside* (**13**). — (*a*) *With lithium aluminium hydride.* To a stirred solution of **12** (150 mg, 0.37 mmol) in anhydrous tetrahydrofuran (5 ml) was added lithium aluminium hydride (15 mg, 0.41 mmol). Stirring was continued at room temperature for 2 h. Excess of hydride was then decomposed with ice (~50 mg), the mixture was filtered through Celite, and the residue was washed with chloroform (10 ml). The organic phase was then washed with water (5 ml), dried (Na_2SO_4), and concentrated. The residue crystallised from ethyl acetate–light petroleum, to

give needles (120 mg, 80%) of **13**, m.p. 188–189°. N.m.r. data: δ 1.92 (s, 3 H, AcN), 3.23 (bs, 1 H, OH; exchangeable with D_2O), 3.7–4.5 (m, 4 H), 4.13 (s, 2 H, $HOCH_2$), 4.63 (dd, 2 H, J_{AB} 11.8 Hz, $\Delta\nu_{AB}$ 16.6 Hz, $PhCH_2O$), 5.13 (s, 1 H, H-1), 5.53 (s, 1 H, $PhCHO_2$), 6.83 (bs, 1 H, NH), and 7.2–7.5 (m, 10 H, 2 Ph).

Anal. Calc. for $C_{23}H_{25}NO_6$: C, 67.14; H, 6.12; N, 3.40. Found: C, 67.27; H, 6.23; N, 3.46.

(*b*) *With sodium borohydride in pyridine.* To a stirred solution of **12** (150 mg, 0.37 mmol) in freshly distilled, anhydrous pyridine (5 ml) was added sodium borohydride (20 mg, 0.53 mmol). Stirring was continued at room temperature for 5 h, and the mixture was then poured into ice–water (50 ml). Excess of borohydride was decomposed with acetic acid (~0.3 ml), and the product was extracted with dichloromethane (50 ml). The organic phase was washed in succession with ice-cold 5% hydrochloric acid (50 ml), saturated, aqueous sodium hydrogencarbonate (10 ml), and water (20 ml), dried (Na_2SO_4), and concentrated. The residue was crystallised from ethyl acetate–light petroleum, to give **13** (100 mg, 67%), m.p. and mixture m.p. 183–185°.

Benzyl 2-acetamido-4,6-O-benzylidene-2,3-dideoxy-3-C-(2-ethoxycarbonyl)prop-1-enyl-α-D-glucopyranoside (**14**). — To a stirred solution of ethyl 2-(diethoxyphosphoryl)propionate[20] (100 mg, 0.42 mmol) in anhydrous *N,N*-dimethylformamide (1.5 ml) at 0° was added sodium hydride (60% dispersion in mineral oil: 18 mg, 0.45 mmol), and stirring was continued until gas evolution ceased (~40 min). This solution was added dropwise during 3 min to a stirred solution of **10** (150 mg, 0.36 mmol) in anhydrous *N,N*-dimethylformamide (3 ml). Stirring was continued for 2 h and the mixture was then poured into 1% acetic acid (30 ml). The product was extracted with dichloromethane (20 ml). The organic phase was washed with saturated, aqueous sodium hydrogencarbonate (5 ml) and water (10 ml), dried (Na_2SO_4), and concentrated. The residue was crystallised from ethanol, to give **14** (121 mg, 67%) as colorless crystals which gave one spot in t.l.c. (chloroform–*p*-dioxane, 95:5) and had m.p. 223–224°; ν_{max} 3300, 1715, and 1660 cm^{-1}. N.m.r. data: δ 1.25 (t, 3 H, J_{AX} 6.8 Hz, CH_3CH_2O), 1.85 (s, 6 H, AcN and MeC), ~3.93 (m, 1 H, H-3), 3.1–4.4 (m, 5 H), 4.15 (dd, 2 H, CH_3CH_2O), 4.63 (dd, 2 H, J_{AB} 11.2 Hz, $\Delta\nu_{AB}$ 18.5 Hz, $PhCH_2O$), 5.47 (d, 1 H, $J_{NH,2}$ 9.2 Hz, NH), 5.47 (s, 1 H, $PhCHO_2$), 6.43 (m, 1 H, H-3'), and 7.2–7.5 (m, 10 H, 2 Ph).

Anal. Calc. for $C_{28}H_{33}NO_7$: C, 67.86; H, 6.71; N, 2.83. Found: C, 67.58; H, 6.70; N, 2.79.

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