

A SIMPLE PREPARATION OF THE 2,3:5,6- AND 3,4:5,6-DI-*O*-ISOPROPYLIDENE DERIVATIVES OF D-GLUCOSE DIMETHYL ACETAL*

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ABSTRACT

The title compounds have been prepared in good yield directly from D-glucose. Separation of the isomers is achieved by selective crystallization of their benzoates.

INTRODUCTION AND RESULTS

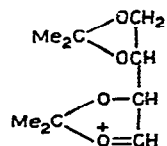
In a preliminary communication¹, it was noted that 3,4:5,6-di-*O*-isopropylidene-D-glucose dimethyl acetal (**1**) and 2,3:5,6-di-*O*-isopropylidene-D-glucose dimethyl acetal (**2**) are formed, together with a number of other products, when D-glucose is treated with an acidified mixture of acetone and methanol. A gas-chromatographic study of this reaction showed that **1** and **2** are formed more rapidly and to a greater extent when a mixture of the methyl D-glucofuranosides is used as the starting material in place of D-glucose. This observation led to a simplified method of preparation. D-Glucose was treated with a solution of sulphuric acid in methanol and, after all of the glucose had dissolved, acetone was added to the mixture. An improved procedure, which results in almost a doubling of the yield of **1** and **2**, involves addition of 2,2-dimethoxypropane instead of acetone to the glycoside solution.

Although **1** and **2** may be separated by chromatography using silica gel as adsorbent, complete resolution has not been achieved and the procedure is tedious. A more satisfactory method, which is well-suited for large-scale preparations, involves conversion of the alcohols into their benzoates, **3** and **4**, respectively, and separation of these by fractional crystallization. From a preparation using 20 g of D-glucose, 15.68 g (34%) of **3**, and 9.58 g (21)% of **4** were obtained by collecting four fractions of crystals for each compound.

Compounds **1** and **2** were identified initially by examination of their p.m.r. spectra and of the p.m.r. spectra of the derived acetates. These spectra showed the presence of two methoxyl groups, two *O*-isopropylidene groups, and one acetate group in each ester. From repeated spacings and the distortion of intensities in the one-proton doublet assigned to H-1 in the spectrum of the acetate derived from **1**, this

*Dedicated to the memory of Dr. Hewitt G. Fletcher, Jr.

compound bears the acetoxy group on C-2, and **1** was tentatively identified as the 3,4:5,6-di-*O*-isopropylidene derivative of D-glucose dimethyl acetal. This compound had been described earlier by Curtis and Jones², who prepared it from the corresponding dimethyl dithioacetal. They also recorded the properties of the benzoic and *p*-toluenesulphonic esters. In the present work, these derivatives were prepared, and although the physical properties of the sulphonate are in reasonable agreement with those recorded, the optical rotations and melting points of the alcohol and benzoate were found to be significantly different. Compounds **1** and **3** were therefore examined further in order to verify their identity. Spin-decoupling experiments on **3** showed conclusively that the low-field doublet of doublets in its p.m.r. spectrum is due to H-2, and signals due to H-3 and H-4 were also identified. This confirms that the free hydroxyl group in **1** is on C-2. Treatment of **3** with a mixture of *p*-dioxane and dilute hydrochloric acid resulted in formation of a more-polar compound (**5**), isolated in high yield using adsorption chromatography. The p.m.r. spectrum of **5** showed the presence of the benzoate group, two methoxyl groups, and one *O*-isopropylidene group. Benzoylation of **5** yielded a liquid benzoate showing no i.r. absorption for hydroxyl. Acetylation of **5** yielded compound **6**, identified as the diacetate of **5** from its n.m.r. spectrum. This spectrum showed two protons, identified as H-2 and H-5, resonating at low field, and the geminal hydrogen atoms on C-6 appeared as the two doublets of doublets typical of a $-\text{CH}_2\text{OAc}$ group with J_{gem} 12.2 Hz. It is evident that the *O*-isopropylidene group removed by hydrolysis involved oxygen atoms on C-5 and C-6. The presence of this *O*-isopropylidene group in **1** and **3** is consistent with the appearance of a high-intensity peak at 101 a.m.u. in the mass spectra of these compounds³. Furthermore, the mass spectrum of **3** shows a peak at 143 a.m.u. (intensity 5% of the base peak) which is consistent with the presence of two contiguous *O*-isopropylidene groups (*cf.* the presence of a peak at 143 a.m.u. in the spectrum⁴ of 1,2:3,4:5,6-tri-*O*-isopropylidene-D-mannitol, arising from the fragment



by loss of acetone). These observations require the oxygen atoms on

C-3 and C-4 to be involved in an *O*-isopropylidene group, thus defining the structure of **1**.

The physical properties of the preponderating isomer (**2**) and its benzoate agree well with those recorded earlier². Analysis of the p.m.r. spectrum of a solution of **4** in benzene-*d*₆ yielded the spin-coupling constants, including $J_{6,6'}$ whose magnitude of 8.4 Hz is consistent with a methylene group adjacent to one oxygen atom in a five-membered ring⁵. The mass spectrum of **4** included a strong peak at 101 a.m.u., an insignificant peak (0.6% of the base peak) at 143 a.m.u., and a relatively intense peak (3.4% of the base peak) at 335 a.m.u. which is ascribed to the fragment resulting from cleavage of the C-1-C-2 bond with the charge on the C-2 fragment (the peak at 335 a.m.u. in the spectrum of **3** is only 0.03% of the base peak).

DISCUSSION

In detailed examinations of the course of acid-catalyzed methanolysis of aldoses using radio-active labelled compounds, two groups of workers^{6,7} have shown that dimethyl acetals are formed during the glycosidations, although these compounds are evidently not intermediates in glycoside formation. Formation of **1** and **2** from the methyl D-glucofuranosides, as described here, involves displacement of the equilibrium between D-glucose dimethyl acetal and methyl D-glucofuranosides as a result of stabilization of the dimethyl acetal by formation of di-O-isopropylidene derivatives. As the amount of D-glucose dimethyl acetal in a methanolysis reaction of D-glucose is only 1% when 50% of D-glucose has reacted⁶, the formation of ~60% of **1** and **2** in the reaction using 2,2-dimethoxypropane represents a substantial shift of equilibrium. Elsewhere in this issue*, a similar, but less-dramatic, increase in the percentage of D-glucose dimethyl acetal resulting from metal-ion complexing is described.

EXPERIMENTAL

General. — Melting points were determined on a Reichert hot-stage microscope and are uncorrected. I.r. spectra were recorded with a Hitachi EPI G₂ instrument. N.m.r. spectra were obtained by using Varian A60, Jeol JNM-4H-100, and Varian XL-100 instruments. Tetramethylsilane was used as internal reference. Abbreviations used are s, singlet; d, doublet, dd, doublet of doublets, etc. Chemical shifts are in δ values; these and coupling constants are first-order values. G.l.c. was carried out on a custom-built instrument with nitrogen as the carrier gas at 30 ml/min and a flame-ionization detector. The injection block was fitted with a glass sleeve, and the glass column (240 \times 0.3 cm) was packed with 1.5% of LAC-1-R 296 on Chromosorb W (AW/DMCS). T.l.c. was performed on Merck Kieselgel G (Type 60). Optical rotations were determined with a Bendix automatic polarimeter. Mass spectra were recorded using an A.E.I. MS-12 spectrometer operating with an ionizing energy of 70 eV. Microanalyses were performed in the Microanalytical Laboratory in this School. Unless otherwise stated, light petroleum refers to the fraction of b.p. 60–80°. Adsorbents used for column chromatography were silica gel (Merck, 7734, 0.05–0.2 mm, activated at 100° for 1 h) or silicic acid (Mallinckrodt, CC-4, 100–200 mesh, activated).

3,4:5,6- and 2,3:5,6-di-O-isopropylidene-D-glucose dimethyl acetals. — (a) D-Glucose (20 g, ground using a hammermill to pass through a 120-mesh sieve) was added to a mixture of conc. sulphuric acid (6 ml) in methanol (300 ml, distilled but not otherwise dried). The mixture, which was stirred at ~22°, became homogeneous after 7.5 h and, after 10 h, 2,2-dimethoxypropane (200 ml) and conc. sulphuric acid (4 ml) were added. The mixture was kept at 25° for 2.5 h, and then cooled in an ice-water bath and neutralized with gaseous ammonia. The residue left on concen-

*F. W. Parrish, S. J. Angyal, M. E. Evans, and A. L. Mills, *Carbohydr. Res.*, 45 (1975) 73–83.

tration of the mixture was shaken with water (250 ml) and chloroform (100 ml). After extracting the aqueous phase with chloroform (2×50 ml), the combined extracts were concentrated, benzene was added to the residue, and the solution was concentrated. Traces of solvent were removed at $55^\circ/0.2$ mmHg to give a light brown liquid (28 g), a solution of which in 70 ml of light petroleum was added to a column (52×2.8 cm) of silica gel (140 g) packed in 1% of acetone in light petroleum. The column was developed initially using 1% of acetone in light petroleum, and 50-ml fractions were collected. Fraction 8 gave a positive residue test, and g.l.c. showed only compounds of short retention time (T) in fractions 8–16. Fraction 17 contained **1** and **2** plus a small amount of a compound of short retention time, identified as 1,2:3,4:5,6-tri-*O*-isopropylidene-1-methoxy-D-glucitol¹ (**7**) by comparison of T values (at 175° , **7** had T 3.0 min, cf. 5.7 and 7.9 min, respectively, for **1** and **2**). After fraction 17 had been collected, the eluent was changed to acetone–light petroleum (1:19), and after fraction 38 had been collected the eluent was changed to acetone–light petroleum (1:9). Fraction 53 contained only a trace of **2** plus larger amounts of compounds of longer retention time. Concentration of fractions 17–52 left 22.10 g of liquid after heating at $55^\circ/0.2$ mmHg. G.l.c. of this material revealed a small amount of **7** together with **1** and **2** in the ratio 1:1.7 (assuming equal detector responses). Correcting for the presence of **7** gives the total yield of **1** and **2** as 21.8 g (64%).

(b) The procedure in (a) was repeated, but the amount of silica gel was reduced to 70 g and no attempt was made to remove **7** from **1** and **2**. The silica gel was packed in 2% of acetone in light petroleum, and this solvent mixture was used for the initial elution. Fractions of 100 ml were collected and, after the second fraction, the eluent was changed to acetone–light petroleum (1:19). Only a trace of **1** and **2** appeared in fraction 16. Concentration of fractions 2–15 (fraction 1 gave no residue) gave 23.6 g of liquid containing (g.l.c.) **7**, **2**, and **1**. Correcting for the presence of **7** gave 22.3 g of **1** + **2**.

(c) The procedure in (b) was used, except that acetone (200 ml) was used instead of 2,2-dimethoxypropane. The crude products (16.7 g) were chromatographed over 50 g of silica gel. Only fractions 2–7 contained **1** and **2**, and concentration gave 10.7 g of products. G.l.c. revealed **7**, **1**, and **2** in the ratios 7:50:90. Assuming equal detector responses, this gives 10.2 g (30%) for the yield of **1** and **2**.

Separation of benzoates 3 and 4 by fractional crystallization. — Anhydrous pyridine (100 ml, distilled from P_2O_5) was added to the mixture of **1** and **2** from (a) above. Benzoyl chloride (15 ml) was added to the solution at $\sim 0^\circ$, and the mixture was kept thereat for 10 min, then for 3 h at 22° , and finally for 1 h at 40° . To the cooled ($\sim 0^\circ$) mixture, water (10 ml) was added to destroy excess reagent and the mixture was shaken with chloroform (150 ml) and 0.5M sulphuric acid (700 ml). After extracting the aqueous layer with chloroform (2×50 ml), the combined extracts were washed with 1.5M sulphuric acid (200 ml) and saturated aqueous sodium hydrogen carbonate, filtered through a 5-cm bed of silicic acid (10 g), and concentrated. The residue was dissolved in benzene and the solution was concentrated. Traces of solvent were removed from the liquid products by warming at 0.2 mmHg.

A solution of the products in methanol (40 ml) at $\sim 40^\circ$ was cooled to $\sim 20^\circ$ and was seeded with highly purified **4** (see below); it is essential to avoid contamination by crystals of **3**. After crystallization of **4** had taken place overnight, the solution was kept at 0° for 5 h. The crystals were collected, and washed with 8 ml of methanol to yield **4** (11.10 g). The mother liquor plus washings was warmed to $\sim 40^\circ$, cooled to $\sim 10^\circ$, seeded with **3**, and stored at $\sim 0^\circ$ for 10 h. The crystals were collected and washed as for **4**, yielding **3** (6.43 g). The homogeneity of **3** and **4** was established by t.l.c. (ether–light petroleum, 1:3; double development, migration distances: **3** 1.8, **4** 2.8 cm) or g.l.c. (220° , T 7.7 and 10.4 min for **3** and **4**, respectively). The mother liquor and washings from **3** were concentrated, and the residue was crystallised from methanol (20 ml) as described above, 4-ml portions of methanol being used for washing, to give homogeneous **4** (2.92 g) and **3** (2.04 g). The procedure was repeated using 8 ml of methanol for crystallization and 2-ml portions of methanol for washing to give **4** (1.21 g) and **3** (0.75 g). Fourth crops of **4** (0.45 g) and **3** (0.36 g) were obtained from 3 ml of methanol. The combined crops of **4** (15.68 g, 34.4%) were recrystallized from methanol (30 ml) to give 13.90 g of **4** (second crop of 1.26 g from 6 ml of methanol); each solution was seeded with purified **4** and stored at $\sim 0^\circ$ for 1 day after much crystallization had occurred at room temperature. Final recrystallization from methanol gave 4-*O*-benzoyl-2,3:5,6-di-*O*-isopropylidene- β -D-glucose dimethyl acetal, m.p. $101\text{--}102^\circ$, $[\alpha]_D^{22} -3^\circ$ (*c* 3.5, chloroform), $+3^\circ$ (*c* 3.7, ethanol); lit.² m.p. $101.5\text{--}102^\circ$, $[\alpha]_D -5.8^\circ$ (chloroform) (Found: C, 61.2; H, 7.5. $\text{C}_{21}\text{H}_{30}\text{O}_8$ calc.: C, 61.5; H, 7.4). P.m.r. data (100 MHz, C_6D_6): 8.18–7.0 (5 H, aromatic), 5.89 (dd, 1 H, $J_{3,4}$ 1.9, $J_{4,5}$ 5.9 Hz, H-4), 4.59 (dd, 1 H, $J_{2,3}$ 7.3, $J_{3,4}$ 1.9 Hz, H-3), 4.46 (ddd, 1 H, $J_{4,5}$ 5.9, $J_{5,6}$ 6.0, $J_{5,6'}$ 6.3 Hz, H-5), 4.23 (dd, 1 H, $J_{5,6}$ 6.0, $J_{6,6'}$ 8.4 Hz, H-6), 4.31 (d, 1 H, $J_{1,2}$ 5.2 Hz, H-1), 4.175 (dd, 1 H, $J_{1,2}$ 5.2, $J_{2,3}$ 7.3 Hz, H-2), 3.99 (dd, 1 H, $J_{5,6'}$ 6.3, $J_{6,6'}$ 8.4 Hz, H-6'), 3.18, 3.21 (2 s, 6 H, 2 MeO), 1.28, 1.32, 1.41, 1.45 (4 s, 12 H, 4 CMe). Mass spectrum: m/e (%) 395 (11), 379 (0.4), 337 (1.4), 335 (3.4), 309 (0.2), 277 (1.5), 251 (1), 147 (2.5), 143 (0.6), 141 (2.4), 129 (2.5), 115 (3.3), 113 (1.7), 105 (38), 101 (10.3), 91 (4.5), 85 (4), 77 (10), 75 (100), 73 (8), 59 (2), 43 (21).

The combined crops (9.58 g, 21.0%) of **3** were recrystallized from methanol (20 ml) to give 6.95 g of **3** (second crop of 2.23 g from 4 ml of methanol); conditions as for **4**. Final recrystallization from methanol gave 2-*O*-benzoyl-3,4:5,6-di-*O*-isopropylidene- β -D-glucose dimethyl acetal, m.p. $80\text{--}81^\circ$, $[\alpha]_D^{22} +25^\circ$ (*c* 2.2, chloroform), $+27^\circ$ (*c* 2.6, ethanol); lit.² m.p. $71\text{--}72.5^\circ$, $[\alpha]_D -40.8^\circ$ (chloroform) (Found: C, 61.8; H, 7.6. $\text{C}_{21}\text{H}_{30}\text{O}_8$ calc.: C, 61.5; H, 7.4). P.m.r. data (100 MHz), *A* in $\text{Me}_2\text{CO}-d_6$: 8.20–7.40 (5 H, aromatic), 5.424 (dd, 1 H, $J_{1,2}$ 7.8, $J_{2,3}$ 1.7 Hz, H-2), 4.674 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.41 (dd, 1 H, $J_{2,3}$ 1.7, $J_{3,4}$ 7.5 Hz, H-3), 4.24–3.78 (3 H, H-5,6,6'), 3.70 (dd, 1 H, $J_{3,4}$ 7.5, $J_{4,5}$ 7.5 Hz, H-4), 3.30, 3.44 (2 s, 6 H, 2 MeO), 1.39 (s, 9 H, 3 CMe), 1.29 (s, 3 H, CMe). On irradiation at 5.424, H-1 appeared as a singlet and H-3 as a doublet (J 7.5 Hz); on irradiation at 4.41, H-2 appeared as a doublet (J 7.8 Hz) and H-4 as a doublet (J 7.5 Hz); *B* in C_6D_6 : 5.91 (dd, 1 H, H-2), 4.98 (d, 1 H, H-1), 4.72 (m, 1 H, H-3), 4.10–3.7 (m, 4 H, H-4,5,6,6'), 3.19, 3.27

(2 s, 6 H, 2 MeO), 1.25, 1.37, 1.45, 1.55 (4 s, 12 H, 4 CMe); *C* in CDCl_3 : 5.47 (dd, 1 H, H-2), 4.71 (d, 1 H, H-1), 4.40 (dd, 1 H, H-3), 3.71 (dd, 1 H, H-4), 4.21–3.88 (3 H, H-5,6,6'), 3.34, 3.47 (2 s, 6 H, 2 MeO), 1.44 (s, 6 H, 2 CMe), 1.42, 1.34 (2 s, 6 H, 2 CMe). Mass spectrum: *m/e* (%) 395 (6.6), 379 (1.1), 337 (0.6), 335 (0.03), 309 (6.0), 277 (0.4), 251 (3.7), 143 (5.1), 142 (2.2), 141 (2.2), 129 (6.7), 115 (0.5), 113 (1), 105 (40), 101 (8), 91 (0.24), 85 (3), 77 (7.2), 75 (100), 73 (7.3), 59 (4), 43 (24).

Benzoylation of the mixture of **1** and **2** from (b) and fractional crystallization as described above gave four successive crops of **4** of 9.21, 3.90, 1.83, and 0.34 g (total yield 15.28 g, 33.5%). The four successive crops of **3** were 4.69, 2.69, 1.38, and 0.08 g (total yield 8.84 g, 19.4%). Recrystallization as described above then gave two crops of **4** (13.41 and 1.45 g, total 32.5%) and **3** (6.15 and 2.24 g, total 18.4%).

Chromatographic separation of 1 and 2. — A solution of a mixture of **1** and **2** (2 g) prepared as in (c) was added to a column (2.8 × 36.5 cm) of silica gel packed in acetone–light petroleum (1:19) and eluted (25-ml fractions) with the same solvent mixture. Fractions were examined by g.l.c. (185°, carrier gas at 45 ml/min); *T* 2.9 and 3.8 min, respectively, for **1** and **2**. Fractions 13–15 contained **7** (0.04 g), 44–51 **1** (0.25 g), 52–79 **1** and **2** (1.31 g, ratio 1:2.3), and 80–114 **2** plus a trace of **1** (0.27 g, ratio 33:1). The products were used for the preparation of pure benzoates **3** and **4**.

Chromatographic separation of 3 and 4. — A solution of **3** (0.5 g) and **4** (0.8 g) in ether (3 ml) was diluted with light petroleum (6 ml) and added to a column (1.9 × 19 cm) of silicic acid (26 g) packed in ether–light petroleum (1:9) and eluted with the same solvent mixture (20-ml fractions). The fractionation was monitored by t.l.c. (ethyl acetate–light petroleum, 1:4); *R_F* values, **3** 0.28, **4** 0.42. Fractions 14–35 contained **3** (0.431 g), 36–48 contained **3** and **4** (0.166 g). Elution of **4** was completed by using ether–light petroleum (1:2) after fraction 51 had been collected. Fractions 49–61 contained **4** (0.705 g).

3,4:5,6-Di-O-isopropylidene-D-glucose dimethyl acetal from 3. — To a solution of **3** (4.1 g) in 95% ethanol (40 ml), a solution of sodium hydroxide (2 g) in water (10 ml) was added and the mixture was kept at 50° for 2 h. The residue left on concentration of the reaction mixture was shaken with chloroform (50 ml) and water (60 ml), and the organic phase was washed with water (60 ml), filtered, and concentrated. The residue was dissolved in benzene and the solution was concentrated to give a product (3.02 g) which was recrystallized from a small volume of light petroleum (30–40°) to give stout needles of **1**, m.p. 49–50°, $[\alpha]_D^{22} +22^\circ$ (*c* 2.5, chloroform), $+35^\circ$ (*c* 3.2 methanol); lit.² m.p. 88–89° $[\alpha]_D -9^\circ$ (*c* 4.2 methanol). Sublimation at 44–45° (bath)/0.2 mmHg gave needles, m.p. 50–51° (Found: C, 55.2; H, 8.55. $\text{C}_{14}\text{H}_{26}\text{O}_7$ calc.: C, 54.9; H, 8.55). P.m.r. data (60 MHz, C_6D_6): 4.59 (d, 1 H, H-1), 3.8–4.45 (6 H, H-2 to H-6'), 3.32, 3.33 (2 s, 6 H, 2 MeO), 2.85 (d, 1 H, OH), 1.28, 1.40, 1.42, 1.48 (4 s, 12 H, 4 CMe). The mass spectrum included an intense peak at *m/e* 291 (*M*–15).

Conventional acetylation of **1**, using acetic anhydride and pyridine, yielded an oil, short-path distilled at 0.01 mmHg/∼80° (bath), $[\alpha]_D^{22} +3^\circ$ (*c* 1.9, chloroform). P.m.r. data (60 MHz, C_6D_6): 5.52 (dd, 1 H, H-2), 4.75 (d, 1 H, H-1), 4.55 (dd, 1 H,

H-3), 3.7–4.6 (4 H, H-4 to H-6'), 3.27, 3.22 (2 s, 6 H, 2 MeO), 1.83 (s, 3 H, OAc), 1.25, 1.36, 1.45, 1.50 (4 s, 12 H, 4 CMe).

Toluene-*p*-sulphonylation² of **1** yielded the 2-sulphonate, m.p. 116–118° (from benzene–light petroleum), $[\alpha]_D^{22} + 9^\circ$ (*c* 2.5, chloroform); lit.² m.p. 109–111°, $[\alpha]_D + 10.4^\circ$ (*c* 2.5, chloroform).

2,3:5,6-Di-O-isopropylidene-D-glucose dimethyl acetal from 4. — Saponification of **4** (8.2 g), as described for **3**, gave **2** (6.05 g) as a colourless liquid, $[\alpha]_D^{22} - 15^\circ$ (*c* 3.1, methanol); lit.² $[\alpha]_D - 15.9^\circ$ (*c* 3.5, methanol). P.m.r. data (60 MHz, C₆D₆): 3.6–4.5 (7 H, H-1 to H-6'), 3.25, 3.28 (2 s, 6 H, 2 MeO), 2.50 (s, 1 H, OH), 1.40 (s, 9 H, 3 CMe), 1.33 (s, 3 H, CMe).

Conventional acetylation of **2** yielded a liquid acetate, short-path distilled at 0.01 mmHg/∼80° (bath), $[\alpha]_D^{22} + 5^\circ$ (*c* 1.5, chloroform). P.m.r. data (60 MHz, C₆D₆): 5.47 (dd, 1 H, H-4), 4.43 (dd, 1 H, H-3), 3.9–4.33 (5 H, H-1,2,5,6,6'), 3.25, 3.23 (2 s, 6 H, 2 MeO), 1.80 (s, 3 H, OAc), 1.42 (s, 6 H, 2 CMe), 1.37, 1.30 (2 s, 6 H, 2 CMe).

2-O-Benzoyl-3,4-O-isopropylidene-D-glucose dimethyl acetal (5). — 0.1M Hydrochloric acid (10 ml) was added to a solution of **3** (3 g) in *p*-dioxane (30 ml), and the mixture was kept at 25° for 12 h. More (5 ml) of 0.1M hydrochloric acid was then added and the solution was kept at 25° for 48 h. T.l.c. (ethyl acetate–light petroleum, 1:1) showed the presence of a small amount of starting material (*R*_F 0.8), a much larger amount of material having *R*_F 0.2, together with a trace of material which remained at the origin. The solution was deionised with Amberlite IRA-400 (HCO₃[−]) resin and concentrated, the residue was dissolved in benzene–ethanol, and the solution was concentrated. Light petroleum (7.5 ml) was added to a solution of the residue in ethyl acetate (2.5 ml), and the mixture was added to a column (2.3 × 21 cm) of silicic acid (40 g), packed in ethyl acetate–light petroleum (1:4), which was eluted with the same solvent mixture (20-ml fractions). Fractions 6–9 contained **3** (0.31 g). After fraction 13, the eluent was changed to ethyl acetate–light petroleum (1:2), and to ethyl acetate–light petroleum (1:1) after fraction 38. Fractions 17–44 yielded **5** as a colourless liquid (2.45 g, ∼100%), *v*_{max} 3450 (s), 1725 (vs); short-path distilled at 0.01 mmHg/∼140° (bath); $[\alpha]_D^{22} + 10^\circ$ (*c* 2.6, chloroform). P.m.r. data (100 MHz, Me₂CO-*d*₆): 8.15–7.4 (5 H, aromatic), 5.45 (dd, 1 H, H-2), 4.70 (d, 1 H, H-1), 4.50 (dd, 1 H, H-3), 4.2–3.5 (complex m), 3.47, 3.32 (2 s, 6 H, 2 MeO), 1.41 (s, 6 H, CMe).

The 5,6-diacetate crystallized from light petroleum. Recrystallization from light petroleum gave prisms, m.p. 63–64°, $[\alpha]_D^{22} + 46.6^\circ$ (*c* 2.16, chloroform) (Found: C, 58.3; H, 6.4. C₂₂H₃₀O₁₀ calc.: C, 58.1; H, 6.7). P.m.r. data (100 MHz, Me₂CO-*d*₆): 5.33 (dd, 1 H, *J*_{1,2} 7.4, *J*_{2,3} 2.3 Hz, H-2), 5.21 (ddd, 1 H, *J*_{4,5} 6.7, *J*_{5,6} 3.1, *J*_{5,6'} 5.8 Hz, H-5), 4.68 (d, 1 H, *J*_{1,2} 7.4 Hz, H-1), 4.52 (dd, 1 H, *J*_{5,6} 3.1, *J*_{6,6'} 12.2 Hz, H-6), 4.43 (dd, 1 H, *J*_{2,3} 2.3, *J*_{3,4} 7.5 Hz, H-3), 4.04 (dd, 1 H, *J*_{5,6'} 5.8, *J*_{6,6'} 12.2 Hz, H-6'), 4.03 (dd, 1 H, *J*_{3,4} 7.5, *J*_{4,5} 6.7 Hz, H-4), 3.46, 3.32 (2 s, 6 H, 2 MeO), 2.08, 1.95 (2 s, 6 H, 2 AcO), 1.40 (s, 6 H, CMe₂); on irradiation at 5.32, H-1 appeared as a singlet and H-3 as a doublet.

2,3:5,6-Di-O-isopropylidene-4-O-p-nitrobenzoyl-D-glucose dimethyl acetal. — Treatment of **2** (0.25 g) with *p*-nitrobenzoyl chloride (0.2 g) and pyridine (4 ml) at 25° for 14 h, followed by isolation of the product in the usual way and recrystallization from 95% ethanol, gave the title compound as needles (0.23 g), m.p. 106–107.5°; lit.⁸ m.p. 106–107°.

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