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DIPHENYLMETHYLATION OF CARBOHYDRATE HYDROXYL GROUPS BY THE REACTION WITH DIAZO(DIPHENYL)METHANE

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ABSTRACT

Diphenylmethylation of carbohydrate hydroxyl groups may be effected by the thermal reaction with diazo(diphenyl)methane in the absence of catalysts. Migration of the labile ester groups of methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside and 3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose does not occur during diphenylmethylation by this procedure. The diphenylmethyl group may be readily removed by catalytic hydrogenolysis, and is sufficiently acid-stable to enable the selective hydrolysis of acetal groups. Its use as an O-4 protecting-group and as a non-participating O-2 protecting-group in α-glycoside synthesis has been demonstrated in syntheses of methyl 2,3,6-tri-*O*-methyl-α-D-glucopyranoside and kojibiose octa-acetate, respectively.

INTRODUCTION

There is a continuing need for protecting groups that can be introduced into, and removed from, carbohydrates under mild (preferably neutral) conditions[1]. For example, the usefulness of benzyl ethers as synthetic intermediates was extended by the introduction[2] of benzyl trifluoromethanesulphonate for benzylation under mild conditions.

The use of diazomethane–boron trifluoride etherate for the methylation of carbohydrates has been extensively reported[3]. More recently, it has been shown that certain hydroxyl groups in nucleosides[4] and sugar derivatives[5] undergo highly selective alkylation with diazomethane in the presence of a catalytic quantity of tin(II) chloride dihydrate. Similarly, selective benzylations of nucleosides[6] and glycerol[7] have been achieved by using diazo(phenyl)methane and tin(II) chloride. Although it has been suggested[8] that a Lewis acid catalyst is needed for this type of benzylation, perbenzyl ethers of cellulose have been prepared[9] by the reaction of diazo(phenyl)-methane with cellulose that had been activated with sodium hydroxide. The observation[10,11] that diazo(diphenyl)methane reacts with certain alcohols in the absence of Lewis acid catalysts to give diphenylmethyl ethers suggested that this might be a

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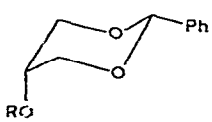
suitable reagent for the protection of hydroxyl groups of carbohydrates under neutral conditions, and we now report on an examination of the scope of this reaction.

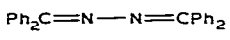
DISCUSSION

Diazo(diphenyl)methane may be prepared as purple crystals, in high yield, by the oxidation of benzophenone hydrazone with yellow mercuric oxide[12], and is stable for long periods when stored at 0° in the dark. The reagent is therefore more convenient than diazo(phenyl)methane, which is an unstable liquid and is normally used as a freshly prepared solution[6,7].

Treatment of *cis*-2-phenyl-1,3-dioxan-5-ol (**1**) with an excess (2.2 mol. equiv.) of diazo(diphenyl)methane in boiling acetonitrile gave *cis*-5-diphenylmethoxy-2-phenyl-1,3-dioxane (**2**, 69%) and benzophenone azine (**3**). These conditions are similar to those used[10] in kinetic studies of the diphenylmethylation of alcohols in which the ethers were not isolated. Although the mechanistic details were not established, the reaction is believed[10] to involve thermolysis of diazo(diphenyl)methane to give diphenylmethylene, which is then involved in electrophilic attack on the alcohol. The consumption of diazo(diphenyl)methane during diphenylmethylation is readily monitored by the purple colour of the solution which changes to yellow when no reagent remains. The yellow colour arises from benzophenone azine, whose formation may[13] be due to attack of diazo(diphenyl)methane by diphenylmethylene.



1 R = H
2 R = Ph_2CH



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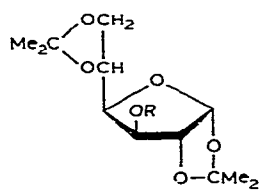


4 R = H
5 R = Ph_2CH

Although the diphenylmethylation of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**4**) could be effected similarly in acetonitrile, better results were obtained with benzene as the solvent. Thus, treatment of **4** with 1.35 mol. equiv. of diazo(diphenyl)methane in boiling benzene gave 3-*O*-diphenylmethyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**5**) and the azine **3** as the main products, and **5** was isolated crystalline (78%) after chromatography on silica gel. The corresponding reaction in acetonitrile was incomplete when all of the reagent had been consumed, although the use of a large excess of diazo(diphenyl)methane gave a 79% yield of crystalline **5** (Table I). In diphenylmethylation reactions, it is desirable to keep the excess of diazo(diphenyl)methane as low as possible in order to minimise the formation of **3** and thereby facilitate isolation of the ether. A high yield (85%) of syrupy **5**, with little formation of azine **3**, was achieved by using 1 mol. equiv. of diazo(diphenyl)-

TABLE I

DATA FOR DIPHENYLMETHYLATION OF COMPOUNDS **4** AND **6–12**

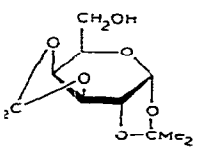
Compound	*Ph_2CN_2 (mol/OH group)*	*Solvent*	*Diphenylmethyl ether*[a]				*Elemental analysis*					*Yield (%) of alcohol by catalytic hydrogenolysis*
			Yield (%)	*M.p. (degrees)*	*$[\alpha]_D$ ($CHCl_3$) (degrees)*	*P.m.r. signal Ph_2CH ($CDCl_3$)*	*Calc. C*	*H*	*Formula*	*Found C*	*H*	
4	4.1	CH_3CN	79	115–116	−31	5.62	70.4	7.1	$C_{25}H_{30}O_6$	70.3	7.1	67.5
4	1.35	C_6H_6	78 ~100 (syrup)									
4	1	C_6H_6	85 (syrup)									
6	4.7	CH_3CN	65	103–104	−61	5.54	70.4	7.1	$C_{25}H_{30}O_6$	70.6	7.2	66
7	2.8	CH_3CN	71	181–182	−19	5.45 5.67	78.15	6.2	$C_{10}H_{38}O_6$	77.85	6.2	—
8	2.45	C_6H_6	84 (syrup)	64–67	+4	5.46 5.25 5.21	80.2	6.4	$C_{48}H_{46}O_6$	80.4	6.5	—
9	2.0	C_6H_6	87	79–80	+132	[b]	64.2	6.2	$C_{26}H_{30}O_9$	64.1	6.1	89
10	1.9	C_6H_6	72	113–115	+118.5	5.54	64.2	6.2	$C_{26}H_{30}O_9$	64.1	6.1	89
11	1.5	C_6H_6	73	syrup	−99.5	5.68 5.41	76.8	6.15	$C_{42}H_{40}O_7$	77.1	6.4	71
12	1.5	C_6H_6	83	glass	+33	5.37 5.30	76.8	6.15	$C_{42}H_{40}O_7$	76.7	6.0	62

[a]The p.m.r. spectra for the ethers were consistent with the assigned structures. [b]Hidden signal.

methane in benzene, but it is generally preferred to ensure complete etherification by using ~2 mol. equiv. of reagent per hydroxyl group and then remove **3** by chromatography on silica gel. The use of pyridine or ethyl acetate as solvent gave incomplete etherification of **4**, and only a trace of **5** was formed in dimethyl sulphoxide or methanol.

Attempts to catalyse the diphenylmethylation of **1** were unsuccessful. Thus, addition of copper, cuprous chloride, or toluene-*p*-sulphonic acid to a mixture of **1** and diazo(diphenyl)methane led to enhanced decomposition of the diazo compound (to give the azine **3**) but no detectable formation of **2**. Moreover, addition of boron trifluoride in the diphenylmethylation of **1** led to complex mixtures. Although it was subsequently found[14] that the use of diazo(diphenyl)methane at room temperature in the presence of a catalytic quantity of tin(II) chloride may lead to the highly regioselective monoalkylation of certain diols, the single hydroxyl group in **4** was not alkylated by this reagent mixture.

The uncatalysed reaction conditions were then applied to various partially protected carbohydrates (Table I), including 1,2:3,4-di-*O*-isopropylidene-α-D-



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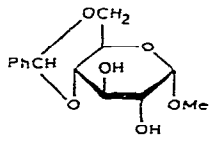

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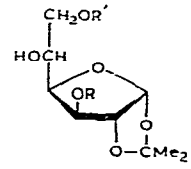
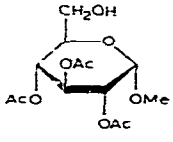


8 R = R′ = H
11 R = Bz, R′ = H
12 R = H, R′ = Bz



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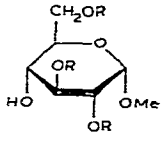
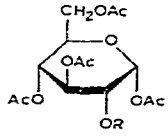
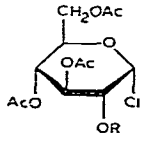


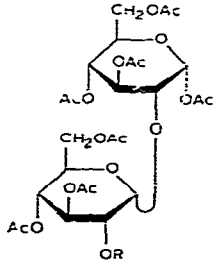
10 R = Ac
13 R = Me



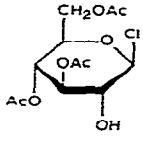
14 R = H
17 R = Ph_2CH



15 R = Ph_2CH
19 R = H



16 R = Ph_2CH



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galactopyranose (**6**; primary OH), methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**7**; two OH groups), and 1,2-*O*-isopropylidene-α-D-glucofuranose (**8**; three OH groups). Use of an excess of the reagent led to complete diphenylmethylation of **6–8** in good yield; with the diol **7** and triol **8**, the use of a deficiency of diazo(diphenyl)-methane gave mixtures of products, and there was no marked selectivity for any particular hydroxyl group. As expected, the acetal groups in **6–8** were stable to the conditions of diphenylmethylation, and **6–8** were recovered by catalytic hydrogenolysis of the respective diphenylmethyl ethers.

Diphenylmethylation of methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (**9**), methyl 2,3,6-tri-*O*-acetyl-α-D-glucopyranoside (**10**), 3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**11**), and 6-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**12**) also proceeded in good yield (Table I) without loss or migration of the ester groups. Thus, in each reaction, diphenylmethylation gave a single product that yielded only the parent sugar acetate or benzoate on catalytic hydrogenolysis. The results for the 2,3,4-triacetate **9** and the 3-benzoate **11** are particularly significant because these compounds readily isomerise[15–17] under acidic or basic conditions, to give **10** and **12**, respectively. For example, the diphenylmethylation of **9** contrasts with its benzylation (silver oxide–benzyl bromide in *N*,*N*-dimethylformamide), which gave[16] a mixture of the 6- and 4-benzyl ethers as a result of acetyl migration. To demonstrate the role of the diphenylmethyl protecting-group in this type of compound in synthesis, methyl 2,3,6-tri-*O*-acetyl-4-*O*-diphenylmethyl-α-D-glucopyranoside was converted into methyl 2,3,6-tri-*O*-methyl-α-D-glucopyranoside (**13**) by application, in sequence, of Zemplén deacetylation, methylation (methyl iodide–sodium hydride), and catalytic hydrogenolysis. The syrupy **13** was characterised as the known[18] *p*-phenylazobenzoate, and this synthesis compares favourably with the multi-stage synthesis of **13** described in the literature[19].

Diphenylmethyl groups are readily hydrogenolysed (~1 atm.) over a palladium–carbon catalyst, and some typical results are summarised in Table I. Treatment of the 3-diphenylmethyl ether **5** with sodium in ethanol gave **4** (54%) as the only carbohydrate product, indicating that this reagent may be of value in the presence of base-stable protecting-groups.

Although the diphenylmethyl group is acid-labile, it is sufficiently stable to enable selective removal of acetal groups by acid hydrolysis. Thus, mild hydrolysis (~0.2M HCl, 35°, 18 h) of methyl 4,6-*O*-benzylidene-2,3-di-*O*-diphenylmethyl-α-D-glucopyranoside gave methyl 2,3-di-*O*-diphenylmethyl-α-D-glucopyranoside (80%) characterised by conversion into methyl 4,6-di-*O*-benzoyl-α-D-glucopyranoside by sequential benzoylation and hydrogenolysis. This selective cleavage of the acetal group contrasts with the selective removal of diphenylmethyl groups by catalytic hydrogenolysis (Table I), and demonstrates the versatility of the diphenylmethyl protecting-group. Similarly, treatment of **5** with 70% acetic acid for 60 h at room temperature gave 3-*O*-diphenylmethyl-1,2-*O*-isopropylidene-α-D-glucofuranose (95%), which was characterised as 5,6-di-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose following benzoylation and catalytic hydrogenolysis of the diphenyl-

methyl group. More drastic conditions of hydrolysis led to loss of the diphenylmethyl group as well as hydrolysis of the 1,2-acetal group. This behaviour contrasts with that of 3-*O*-benzyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, which is readily converted into 3-*O*-benzyl-D-glucose by acid hydrolysis[20], and accords with the expected greater acid-lability of the diphenylmethyl group compared with the benzyl group.

In the synthesis of α-linked disaccharides and oligosaccharides, there is a need[2,21] for non-participating, O-2 protecting-groups that can be introduced into such sugars as 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose without causing loss or migration of acetyl groups. The possible role of the diphenylmethyl group in such syntheses has been examined in a synthesis of 2-*O*-α-D-glucopyranosyl-α-D-glucopyranose (α-kojibiose) octa-acetate. Thus, treatment of 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose (**14**) with 0.96 mol. equiv. of 3,4,6-tri-*O*-acetyl-2-*O*-diphenylmethyl-α-D-glucopyranosyl chloride (**15**) by the silver perchlorate–ether procedure[21] gave a mixture of α-kojibiose hepta-acetate 2′-diphenylmethyl ether (**16**) and minor proportions of unreacted **14** and an unidentified hydrolysis product of **15**. Compound **16** (27%) was isolated by crystallisation, and the α configuration of the glycosidic linkage was shown by the low value (4 Hz) for $J_{1',2'}$. Completion of the synthesis by hydrogenolysis of the diphenylmethyl group followed by acetylation gave α-kojibiose octa-acetate (20% overall yield). Although the yield in this reaction has not been optimised, the use of 2 mol. equiv. of **15** gave **16** in 45% yield together with an increased proportion of the unidentified hydrolysis product and only traces of **14**. The formation of the α-linked disaccharide **16** is consistent with the findings of Igarashi *et al.*[21], who did not give a detailed, mechanistic rationalisation of their results, but obtained very high ratios of α- to β-glycosides when ether was used as solvent in the silver perchlorate procedure.

Our first approach to the synthesis of **15** was unsuccessful. Thus, although diphenylmethylation of 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose (**14**) proceeded without acetyl migration, to give a high yield of the 2-diphenylmethyl ether **17**, attempts to convert **17** into **15** by treatment with hydrogen chloride at 0°, or with titanium tetrachloride[22], resulted in extensive de-diphenylmethylation. These reactions have been successfully applied[22,23] to 2-*O*-benzyl analogues of **17**, and the results accord with the greater acid-lability of the diphenylmethyl group when compared with the benzyl group, as already noted.

In an alternative route, diphenylmethylation of the less-readily available 3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl chloride (**19**) gave **15** in 70% yield. Compound **19** may be prepared by the anomerisation of 3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl chloride[24] (**18**), which occurs on storage in dry acetone[25]. Diphenylmethylation of **18** also gave **15** (40%), as a result of anomerisation of the initially formed 2-diphenylmethyl ether of **18** during chromatography on silica gel. Although **15** appeared to be homogeneous by t.l.c. and n.m.r. spectroscopy, the syrupy product was not obtained analytically pure, and was characterised by catalytic hydrogenolysis to give **19** (80%).

The acid-lability of the diphenylmethyl group and the syrupy nature of **15** (which hindered its purification), together with the ready availability[26] of per-*O*-

benzylglycosyl halides, suggest that the usefulness of the diphenylmethyl group as a non-participating protecting-group in α-glycoside synthesis would be confined to cases where it is necessary to generate, selectively, a free HO-2 group after glycosidation.

EXPERIMENTAL

General methods. — T.l.c. was performed on Kieselgel G (Merck 7731) with detection by iodine vapour or vanillin–sulphuric acid[27]. Kieselgel 60 (Merck 7734) was used for column chromatography. Evaporations were effected under diminished pressure at <40°. Melting points are uncorrected. Light petroleum refers to the fraction having b.p. 60–80°. ^{1}H-N.m.r. spectra were recorded with a Perkin–Elmer R14 (100 MHz) spectrometer for solutions in deuteriochloroform with tetramethylsilane as the internal reference; the couplings given are first-order spacings. Optical rotations were measured at ambient temperature with a Perkin–Elmer 141 polarimeter.

Diphenylmethylation reactions. — (*a*) cis-*2-Phenyl-1,3-dioxan-5-ol*[28] (**1**). A solution of diazo(diphenyl)methane (1.2 g, 6.2 mmol) and **1** (0.5 g, 2.8 mmol) in dry acetonitrile (15 mL) was boiled under reflux for 16 h. After being cooled, the yellow solution was filtered to remove benzophenone azine (**3**, 0.24 g), the solvent was evaporated under diminished pressure, and the residue was crystallised from chloroform–hexane, to give *cis*-5-diphenylmethoxy-2-phenyl-1,3-dioxane (**2**; 0.67 g, 69%), m.p. 138–140°. After recrystallisation, **2** had m.p. 142–143°. N.m.r. data: δ 5.63 (s, 1 H, OC*H*Ph$_2$) and 5.59 (s, 1 H, PhC*H*).

Anal. Calc. for $C_{23}H_{22}O_3$: C, 79.75; H, 6.4. Found: C, 79.8; H, 6.7.

(*b*) *1,2:5,6-Di-O-isopropylidene-α-*D*-glucofuranose* (**4**). A solution of diazo(diphenyl)methane (1.0 g, 5.15 mmol) and **4** (1.0 g, 3.8 mmol) in dry benzene (30 mL) was boiled under reflux for 20 h. The purple colour had then been discharged, and t.l.c. (benzene) showed that all of **4** (R_F 0.05) had reacted, giving 3-*O*-diphenylmethyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**5**, R_F 0.2) and two yellow components [R_F 0.5 (faint) and 0.55 (**3**)]. The solvent was evaporated under diminished pressure, and the resulting, yellow syrup (2.2 g) was purified on a column of silica gel. Elution with benzene removed the yellow components, and subsequent elution with benzene–ether (1:1) gave a chromatographically homogeneous syrup (1.63 g, ~100%) that crystallised from light petroleum (b.p. 40–60°), to give **5** (1.275 g, 78%), m.p. 115–116°, $[\alpha]_D^{19}$ −31° (*c* 0.7, chloroform). N.m.r. data: δ 7.36 (m, 10 H, aromatic), 5.93 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 5.62 (s, 1 H, OC*H*Ph$_2$), 4.55 (d, 1 H, H-2), 1.46, 1.41, 1.37, and 1.29 (4 s, 12 H, 4 Me).

Anal. Calc. for $C_{25}H_{30}O_6$: C, 70.4; H, 7.1. Found: C, 70.3; H, 7.1.

Removal of diphenylmethyl groups. — (*a*) *Catalytic hydrogenolysis.* A solution of methyl 2,3,4-tri-*O*-acetyl-6-*O*-diphenylmethyl-α-D-glucopyranoside (200 mg) in ethanol (50 mL) was shaken with 10% palladium-on-carbon (50 mg) under hydrogen (1 atm.) for 3 h. T.l.c. (ether) then showed the absence of the starting material (R_F 0.95) and formation of a single product (R_F 0.5; **9**). The catalyst was removed by filtration, the solvent was evaporated, and the syrupy residue was chromatographed

on a column of silica gel. Elution with benzene removed diphenylmethane, and subsequent elution with ether gave a chromatographically homogeneous syrup (120 mg, 89%) that crystallised from ether–light petroleum (b.p. 60–80°) to give the 2,3,4-triacetate **9**, m.p. 110°, mixture m.p. 110°, $[\alpha]_D$ +145.5° (*c* 0.5, chloroform); lit.[29] m.p. 111°, $[\alpha]_D$ +147° (chloroform).

(*b*) The diphenylmethyl ethers listed in Table I were hydrogenolysed as described in (*a*). In each reaction, only the parent alcohol was detected, and the yields of the recovered alcohols are listed in Table I.

(*c*) *With sodium in ethanol.* Sodium (3 g) in small pieces was added to a solution of 3-*O*-diphenylmethyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**5**, 200 mg) in ethanol (30 mL); during the addition, ethanol (60 mL) was added to keep the product in solution. The cooled solution was then diluted with water, made neutral (solid CO_2), and concentrated to dryness. Column chromatography of the residue (R_F 0.4; t.l.c., 1:1 benzene–ether) on silica gel (9:1 benzene–ether) gave **4** (65 mg, 54%) that was identical with an authentic sample.

Methyl 2,3,6-tri-O-methyl-α-D-glucopyranoside. — A solution of methyl 2,3,6-tri-*O*-acetyl-4-*O*-diphenylmethyl-α-D-glucopyranoside (940 mg; Table I) in dry methanol (80 mL) containing sodium methoxide (from ~10 mg of sodium) was kept at room temperature for 16 h and then treated with solid carbon dioxide. The methanol was evaporated, the residue was extracted with warm acetone, and, after filtration, the acetone was evaporated, to give a chromatographically homogeneous syrup (540 mg, 77.5%), $[\alpha]_D$ +132° (*c* 1.4, chloroform).

A solution of the foregoing syrup (400 mg) in dry 1,2-dimethoxyethane (6 mL) was stirred with sodium hydride (200 mg) at 0° for 20 min. Methyl iodide (0.64 mL) was then added and stirring was continued for a further 1.5 h. T.l.c. (ether) then revealed the absence of starting material, and the mixture was poured into ice–water. A solution of the resulting, semi-solid precipitate in chloroform (25 mL) was washed with water and dried (Na_2SO_4), and the chloroform was evaporated. The residue (340 mg, 75%) was recrystallised from ethanol, to give methyl 4-*O*-diphenylmethyl-2,3,6-tri-*O*-methyl-α-D-glucopyranoside, m.p. 74–77°, $[\alpha]_D$ +170° (*c* 0.6, chloroform). N.m.r. data: δ 7.10 (m, 10 H, aromatic), 5.67 (s, 1 H, C*H*Ph_2), 4.69 (d, 1 H, $J_{1,2}$ 6 Hz, H-1), 3.36, 3.31, 3.25, and 2.97 (4 s, 12 H, 4 OMe).

Anal. Calc. for $C_{23}H_{30}O_6$: C, 68.6; H, 7.5. Found: C, 68.6; H, 7.5.

A solution of the foregoing 2,3,6-trimethyl ether (280 mg) in ethanol (30 mL) was hydrogenolysed over Pd/C (50 mg), by the procedure already described, to give methyl 2,3,6-tri-*O*-methyl-α-D-glucopyranoside (**13**) as a chromatographically homogeneous, colourless syrup (134 mg, 82%), $[\alpha]_D$ +142° (*c* 2.6, methanol); lit.[30] $[\alpha]_D$ +149° (methanol).

Compound **13** was characterised as the 4-*p*-phenylazobenzoate[18], m.p. 87–88°, $[\alpha]_D$ +25° (*c* 0.2, chloroform); lit.[18] m.p. 89.6–90°, $[\alpha]_{6438}$ +25° (chloroform).

3,4,6-Tri-O-acetyl-2-O-diphenylmethyl-α-D-glucopyranosyl chloride (**15**). — (*a*) A solution of diazo(diphenyl)methane (10 g, 51 mmol) and 3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl chloride[25] (**19**; 4 g, 12 mmol) in dry benzene (200 mL) was boiled

under reflux for 17 h. T.l.c. then showed that no starting material remained, and the benzene was evaporated. A solution of the resulting syrup in hot, dry acetonitrile deposited the azine **3** (5.5 g) on cooling, and evaporation of the solvent gave a syrup that was chromatographed on silica gel. Elution with dry benzene–ether (9:1) gave **15** as a chromatographically homogeneous syrup (4.2 g, 70%), $[\alpha]_D$ +91° (*c* 0.5, chloroform). N.m.r. data: δ 7.30 (m, 10 H, aromatic), 5.88 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.51 (s, 1 H, C*H*Ph$_2$), 5.60, 5.00 (2 t, 2 H, $J_{2,3} = J_{3,4} = J_{4,5} = 9$ Hz, H-3,4), 3.95–3.75 (dd, 1 H, H-2), 2.01, 2.00, and 1.90 (3 s, 9 H, 3 OAc).

Anal. Calc. for $C_{25}H_{27}ClO_8$: C, 59.3; H, 5.3. Found: C, 60.5; H, 5.1.

Compound **15** was not obtained analytically pure and was therefore characterised by hydrogenolysis over Pd/H$_2$ (by the procedure already described), to give 3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl chloride (80%) that was identical with the starting material.

(*b*) *Attempted diphenylmethylation of 3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl chloride*[24] (**18**). Diazo(diphenyl)methane (0.8 g, 4.1 mmol) was added to a suspension of **18** (0.5 g, 1.5 mmol) in dry benzene (100 mL), and the mixture was boiled under reflux for 17 h, and then processed, as described in (*a*), to give the α-chloride **15** (0.3 g, 40%), $[\alpha]_D$ +89° (*c* 0.5, chloroform), whose n.m.r. spectrum was indistinguishable from that of **15** prepared in (*a*).

The n.m.r. signal (δ 5.37, $J_{1,2}$ 8 Hz) for H-1 of the crude product (R_F 0.7) indicated that it was the β-chloride, which then underwent anomerisation to **15** during chromatography on silica gel.

Kojibiose octa-acetate. — (*a*) A solution of silver perchlorate (260 mg, 1.25 mmol) in anhydrous ether (20 mL) at 0° was added, with stirring, to **15** (590 mg, 1.2 mmol). After ~2 min, a solution of 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose[31] (**14**; 200 mg, 0.57 mmol) and 2,4,6-trimethylpyridine (145 mg, 1.1 mmol) in dry ether was added, and the mixture was stirred at 0° for 4 h. T.l.c. (benzene–ether, 1:1) then revealed components with R_F 0.6 (minor), 0.5, and 0.25 (**14**, trace); no **15** was detected. After filtration, the solvent was evaporated, a solution of the residue in acetonitrile (20 mL) was washed with light petroleum (5 × 80 mL), and the solvent was evaporated. The resulting colourless syrup (503 mg) was chromatographed on silica gel (benzene–ether, 9:1) to give a syrup (255 mg, R_F 0.5) that was crystallised from ethanol to give α-kojibiose hepta-acetate 2′-diphenylmethyl ether (**16**; 205 mg, 45%), m.p. 157–158°, $[\alpha]_D$ +142° (*c* 1, chloroform). N.m.r. data: δ 7.40–7.05 (m, 10 H, aromatic), 6.36 (d, 1 H, $J_{1',2'}$ 4 Hz, H-1′), 3.92–3.53 (2 dd, 2 H, H-2,2′), and 2.15–1.80 (m, 21 H, 7 OAc).

Anal. Calc. for $C_{39}H_{46}O_{18}$: C, 58.35; H, 5.7. Found: C, 58.3; H, 6.0.

Hydrogenolysis of **16** over Pd/C, by the procedure already described, gave a single product (syrup, 180 mg; 90%) that was conventionally acetylated with acetic anhydride–sodium acetate (reflux, 1.5 h), to give α-kojibiose octa-acetate (80%), m.p. 170° (from ethanol), $[\alpha]_D$ +150° (*c* 0.5, chloroform); lit.[31] m.p. 168–168.5°, $[\alpha]_D$ +152.5° (chloroform).

(*b*) When the reaction in (*a*) was repeated with a 1:1 ratio of **15**:**14**, the crude

product contained less of the unidentified hydrolysis product (R_F 0.6) of **15**, but the isolated yield of **16** was only 27%.

Methyl 2,3-di-O-diphenylmethyl-α-D-glucopyranoside. — A solution of the 2,3-bis(diphenylmethyl) ether of **7** (3.2 g) in a mixture of acetone (225 mL), water (15 mL), and concentrated HCl (5.2 mL) was kept at 35° overnight, and then neutralised ($NaHCO_3$). The solvents were evaporated, the residue was extracted with acetone, and the extract was chromatographed on a column of silica gel (benzene–ether, 9:1), to give the title compound as a glass (2.2 g, 80%), $[\alpha]_D$ −95.5° (*c* 0.8, chloroform). N.m.r. data: δ 7.52–7.07 (m, 20 H, aromatic), 5.92, 5.38 (2 s, 2 H, Ph_2CH), 4.48 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), and 3.28 (s, 3 H, OMe).

Anal. Calc. for $C_{33}H_{34}O_6$: C, 75.3; H, 6.5. Found: C, 75.2; H, 6.3.

Conventional benzoylation of the foregoing product with benzoyl chloride–pyridine gave methyl 4,6-di-*O*-benzoyl-2,3-di-*O*-diphenylmethyl-α-D-glucopyranoside as a syrup (56%), $[\alpha]_D$ −69° (*c* 0.3, chloroform).

Anal. Calc. for $C_{47}H_{42}O_8$: C, 76.8; H, 5.8. Found: C, 76.6; H, 5.6.

Catalytic hydrogenolysis (Pd/C) of the foregoing dibenzoate, by the procedure already described, gave methyl 4,6-di-*O*-benzoyl-α-D-glucopyranoside (90%), m.p. and mixture m.p. 132–133°.

5,6-Di-O-benzoyl-1,2-O-isopropylidene-α-D-glucofuranose. — A suspension of **5** (1 g) in 70% aqueous acetic acid (60 mL) was shaken at room temperature for 60 h. T.l.c. (benzene–ether, 1:1) then revealed a single product (R_F 0.35) and the absence of **5** (R_F 0.85). Evaporation of the solvents gave syrupy 3-*O*-diphenylmethyl-1,2-*O*-isopropylidene-α-D-glucofuranose (860 mg, 95%), $[\alpha]_D$ −70° (*c* 1.3, chloroform).

Conventional benzoylation (benzoyl chloride–pyridine) of this product, followed by catalytic hydrogenolysis (Pd/C) of the resulting, syrupy dibenzoate, gave 5,6-di-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (725 mg, 76%) which, when crystallised from ether–light petroleum, had m.p. 117°, $[\alpha]_D$ +40° (*c* 0.5, chloroform); lit.[32] m.p. 118°, $[\alpha]_D$ +41.4° (chloroform).

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