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REGIOSELECTIVE MONOALKYLATIONS OF THE VICINAL *cis*-DIOL GROUP IN MANNOPYRANOSIDES USING DIARYLDIAZOALKANES–TIN(II) CHLORIDE

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ABSTRACT

Highly regioselective monoalkylations of the *cis*-2,3-diol group in mannopyranosides can be achieved with diaryldiazoalkanes in the presence of catalytic amounts of tin(II) chloride. With diazo(diphenyl)methane (**1**), its 4,4′-dimethyl (**2**) and 4,4′-dichloro (**3**) derivatives, and 9-diazofluorene (**5**), methyl 4,6-*O*-benzylidene-α-D-mannopyranoside gave high yields of the respective 3-diarylmethyl ethers. By contrast, methyl 4,6-*O*-isopropylidene-α-D-mannopyranoside (**11**) gave mainly the 3-[bis(4-methylphenyl)methyl] derivative with **2**, approximately equal amounts of the 2- and 3-ethers with **1** and **3**, and mainly the 2-ether with **5**. With diazo[bis(4-methoxyphenyl)]methane, **11** gave only the 3-ether (61%).

INTRODUCTION

In contrast to the methylation of carbohydrate hydroxyl groups with diazomethane–boron trifluoride[1], diphenylmethylation with diazo(diphenyl)methane[2] occurs in the absence of a Lewis acid catalyst. Generally, these reactions do not show marked selectivity, although hydroxyl groups in ribonucleosides have been selectively methylated with diazomethane in partially aqueous solution[3]. However, in the presence of catalytic amounts of tin(II) chloride, highly regioselective alkylations of hydroxyl groups in carbohydrates and ribonucleosides have been achieved with diazomethane[4–6], diazo(phenyl)methane[7,8], and other aryldiazomethanes[9,10]. Other inorganic salts have also been used[6] as catalysts in selective methylations with diazomethane. We have observed that the use of catalytic amounts of tin(II) chloride in the reactions of some carbohydrate *cis*-diol groups with various diaryldiazomethanes results in highly regioselective, and, in some cases, regiospecific, alkylations, and we now report on these studies.

DISCUSSION

Although diazo(diphenyl)methane (**1**) is stable for long periods at 0° in the

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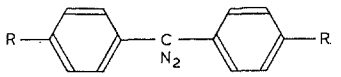
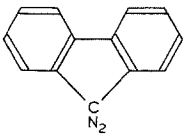
dark, its low melting-point (~29°) makes the reagent inconvenient to handle. Diazo-[bis(4-methylphenyl)]methane (**2**), diazo[bis(4-chlorophenyl)]methane (**3**), diazo-[bis(4-methoxyphenyl)]methane (**4**), and 9-diazofluorene (**5**), which have melting points of ~100°, were therefore considered as alternative reagents for diarylalkylation. Compounds **2–4** were readily prepared in high yield by oxidation of the appropriate ketone hydrazone* with mercuric oxide[11], whereas the best yields of **5** were obtained by oxidation of fluorene hydrazone with silver oxide[13].



1 R = H 3 R = Cl
2 R = Me 4 R = OMe



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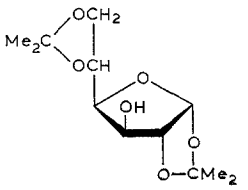

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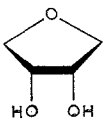

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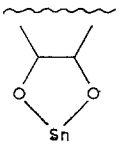

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Treatment of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**6**) with 1 mol. equiv. of the diaryldiazomethanes **2** and **3** in boiling benzene gave the corresponding 3-diarylmethyl ethers, which were isolated in high yield (>80%) after removal of unreacted **6** and the azine by-product by chromatography on silica gel. In each case, catalytic hydrogenolysis of the 3-diarylmethyl ether gave **6** in good yield. These thermal diarylmethylation reactions are therefore exactly analogous to the diphenylmethylation[2] of **6** with diazo(diphenyl)methane (**1**).

When **6** was treated with the diaryldiazoalkanes **1–3** and **5** at room temperature in 1,2-dimethoxyethane, in the presence of tin(II) chloride, no alkylation occurred, whereas similar treatment of 1,4-anhydroerythritol (**7**) with an excess of the diaryldiazoalkanes gave high yields of the 2-diarylmethyl ethers of 1,4-anhydro-DL-erythritol (Table I). When treated with diazo(diphenyl)methane (**1**) in boiling benzene, **7** gave the 2,3-bis(diphenylmethyl) ether in 88% yield, which indicates that there is no significant steric hindrance to the introduction of a second, bulky diarylmethyl group. The specific formation of the 2-monoethers of 1,4-anhydro-DL-erythritol matches the monomethylation and monobenzylation of the *cis*-diol system in ribonucleosides achieved with diazomethane[5,6] and diazo(phenyl)methane[7] in the

*The use of hydrazine hydrate in boiling 1-butanol[12] was found to be the most satisfactory procedure for preparing the ketone hydrazones.

TABLE I

REACTION OF 1,4-ANHYDROERYTHRITOL (7) WITH DIARYLDIAZOALKANES–TIN(II) CHLORIDE

Diazo compound	*Ether product*	*Reaction conditions*[a]			*M.p.* *(deg.)*	*Elemental analysis*						
		Temp. *(deg.)*	*Time* *(h)*	*Yield* *(%)*		*Calc.* *C*	*H*	*Cl*	*Formula*	*Found* *C*	*H*	*Cl*
Ph_2CN_2	2-*O*-Diphenylmethyl	17	18	87	77–78[b]	75.5	6.7		$C_{17}H_{18}O_3$	75.3	6.8	
$(4\text{-}MeC_6H_4)_2CN_2$	2-*O*-[Bis(4-methylphenyl)methyl]	~0	18	95	87–88[b]	76.5	7.4		$C_{19}H_{22}O_3$	76.5	7.7	
$(4\text{-}ClC_6H_4)_2CN_2$	2-*O*-[Bis(4-chlorophenyl)methyl]	17	48	62	59–61[b]	60.2	4.75	20.9	$C_{17}H_{16}Cl_2O_3$	60.1	4.8	20.9
9-Diazofluorene	2-*O*-(9-Fluorenyl)	17[c]	72	82	106–107[d]	76.1	6.0		$C_{17}H_{16}O_3$	75.9	5.9	

[a]See Experimental. [b]From ether–light petroleum (b.p. 40–60°). [c]Reaction in 10 mL of 1,2-dimethoxyethane. [d]From ethanol.

TABLE II

PRODUCTS FROM THE ETHERIFICATION OF 4,6-ACETALS OF METHYL α-D-MANNOPYRANOSIDE WITH DIARYLDIAZOALKANES–TIN(II) CHLORIDE

Ether product	*Reaction conditions*			*M.p. (degrees)*	$[\alpha]_D$ *(degrees)* (c *1*, $CHCl_3$)	*Elemental analysis*						
	Temp. (degrees)	*Time (h)*	*Yield (%)*			*Calc. C*	*H*	*Cl*	*Formula*	*Found C*	*H*	*Cl*
4,6-Benzylidene acetal (**9**)[a]												
2-*O*-Diphenylmethyl	17	24	6[b]	130–131[c]	0	72.3	6.3		$C_{27}H_{28}O_6$	72.2	6.5	
3-*O*-Diphenylmethyl			70[b]	glass	+69					71.7	6.4	
3-*O*-[Bis(4-chlorophenyl)methyl]	17	48	81	glass	+70	62.8	5.1	13.7	$C_{27}H_{26}Cl_2O_6$	62.6	5.1	14.0
3-*O*-(9-Fluorenyl)	17	48	65	glass	+48.5	72.6	5.9		$C_{27}H_{26}O_6$	71.8	5.9	
4,6-Isopropylidene acetal (**11**)[d]												
2-*O*-Diphenylmethyl	17	60	38	syrup	+7	69.0	7.05		$C_{23}H_{28}O_6$	68.7	6.8	
3-*O*-Diphenylmethyl			38.5	syrup	+65					—		
2-*O*-[Bis(4-methylphenyl)methyl]	~3	40[e]	8	155–156[c]	−5	70.1	7.5		$C_{25}H_{32}O_6$	70.3	7.8	
3-*O*-[Bis(4-methylphenyl)methyl]			60	syrup	+83					69.8	7.65	
2-*O*-[Bis(4-chlorophenyl)methyl]	17	120	41.5	syrup	+18	58.8	5.55		$C_{23}H_{26}Cl_2O_6$	58.5	5.7	
3-*O*-[Bis(4-chlorophenyl)methyl]			40	syrup	+84					58.6	5.8	
2-*O*-(9-Fluorenyl)	17	192	70	166–167[c]	+18.5	69.3	6.6		$C_{23}H_{26}O_6$	69.2	6.3	
3-*O*(9-Fluorenyl)			~5	syrup	n.d.					—		
3-*O*-[Bis(4-methoxyphenyl)methyl]	−10	3.5[f]	61	syrup	+75	65.2	7.0		$C_{25}H_{32}O_8$	65.3	7.3	

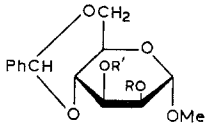
[a]Glycoside **9** (0.5 g, 1.77 mmol) + diaryldiazoalkane (2.66 mmol) in 1,2-dimethoxyethane containing $SnCl_2$ (~20mM). [b]5-g Scale. [c]From ether–light petroleum (b.p. 40–60°). [d]Glycoside **11** (0.5 g, 2.13 mmol) + diaryldiazoalkane (3.2 mmol) in 1,2-dimethoxyethane containing $SnCl_2$ (5mM). [e]Further diaryldiazoalkane (1.5 mmol) added after 24 h. [f]Further diaryldiazoalkane (1 mmol) added after 1.5 h.

presence of tin(II) chloride. This behaviour has been attributed[6,14] to the formation of a cyclic complex, which Smith[14] suggested is a cyclic tin intermediate (**8**) resulting from the reaction of the hydroxyl groups with tin(II) chloride. Only the hydroxyl groups involved in the cyclic complex are activated to alkylation, and, after formation of a monoether, further reaction occurs only when the monoether contains two hydroxyl groups that can form a new complex with tin[15]. For methylation with diazomethane–tin(II) chloride in methanol, Shugar and his co-workers[15,16] concluded that the actual methylation catalyst is $Sn(OMe)_2$ formed by the reaction of tin(II) chloride with methanolic diazomethane.

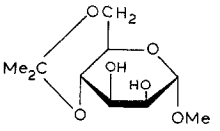
The tin(II)-catalysed monoalkylation of the *cis*-diol system in ribonucleosides gives[5,7] mixtures of the 2′- and 3′-ethers, and the degree of selectivity is usually not high. By contrast, high selectivity was observed in alkylations of hexopyranosides[4] and a xylofuranosyladenine[15]. The selectivity of alkylation by the diaryldiazoalkanes in the presence of tin(II) chloride cannot be assessed from the reaction with 1,4-anhydroerythritol, because the reagent cannot distinguish between the enantiotopic hydroxyl groups, and a single, racemic monoether is formed. However, a high degree of selectivity was observed with methyl 4,6-*O*-benzylidene-α-D-mannopyranoside (**9**), which gave high yields (65–80%) of the 3-diarylmethyl ethers (Table II) on treatment with the diaryldiazoalkanes in the presence of tin(II) chloride. The 2-diarylmethyl ethers were not detected in reactions performed on a 0.5-g scale, but a small proportion (~6%) of the 2-diphenylmethyl ether was isolated from a 5-g reaction. Although this result suggests that the diarylmethylation reactions are probably not regiospecific, the high degree of selectivity facilitates the isolation of the 3-diarylalkyl ethers in good yield.

The structures for the ethers of **9** in Table II were assigned by using n.m.r. spectroscopy and trichloroacetyl isocyanate. In this technique[17], the free hydroxyl group is converted into a carbamate by reaction with the isocyanate, which results in a downfield shift of the n.m.r. signal for the proton on the same carbon atom. The *trans*-fused acetal ring fixes the methyl 4,6-*O*-benzylidene-α-D-mannopyranosides in the $^4C_1$ conformation, so that H-3 and H-4 are axial, whereas H-2 and H-1 are equatorial. The signal for H-3 therefore has a large $J_{3,4}$ value and can be distinguished from the H-2 signal which has small $J_{2,3}$ and $J_{1,2}$ values. For the crystalline, minor diphenylmethyl ether, the n.m.r. signal that is shifted to lower field after addition of trichloroacetyl isocyanate is a doublet of doublets (coupling constants 3.5 and 10.5 Hz). This signal is therefore assigned to H-3, which identifies the compound as the 2-diphenylmethyl ether. For each of the other ethers of **9** in Table II, the shifted signal contains only small couplings and may therefore be assigned to H-2, so that the compounds are all 3-diarylmethyl ethers. Confirmation of the structure of methyl 4,6-*O*-benzylidene-3-*O*-diphenylmethyl-α-D-mannopyranoside was obtained by methylation followed by catalytic hydrogenolysis of the diphenylmethyl group, which gave methyl 4,6-*O*-benzylidene-2-*O*-methyl-α-D-mannopyranoside[18] (**10**) in 35% yield. Because catalytic hydrogenation can also cause debenzylidenation, the reaction was monitored by t.l.c. and stopped when all of the starting material had been con-

sumed; at this stage, **10** was the main product and only a trace of debenzylidenated material was detected. When the n.m.r. spectrum of **10** was recorded after the addition of trichloroacetyl isocyanate, the shifted signal had the pattern (dd, $J_{2,3}$ 3.5, $J_{3,4}$ 11 Hz) expected for H-3 of a mannopyranoside. This result also confirms the correctness of the 2-arylmethyl structures assigned by the trichloroacetyl isocyanate method.



9 R = R' = H
10 R = Me, R' = H
13 R = Me, R' = $CHPh_2$



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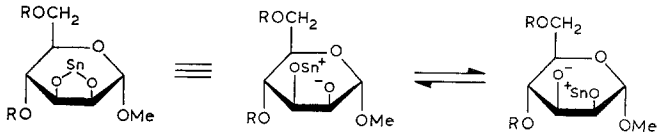

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In considering the usefulness of these selective etherifications in synthesis, attention was turned to methyl 4,6-*O*-isopropylidene-α-D-mannopyranoside (**11**), which has a 4,6-acetal protecting-group that should not be susceptible to hydrogenolysis during removal of diarylmethyl ethers. The monoacetal **11** cannot be prepared by conventional acetonation of methyl α-D-mannopyranoside (which gives[19] the 2,3-acetal and the 2,3:4,6-diacetal), but was conveniently prepared (65% yield) by acetonation with methyl isopropenyl ether under acid conditions. Horton and his co-workers[20] have used this method for the selective, kinetic formation of acetals involving the primary hydroxyl groups of sugars and glycosides. This preparation of **11** is simpler and gave a higher yield than the 2,2-dimethoxypropane procedure[21].

Treatment of **11** with diazo[bis(4-methylphenyl)]methane, in the presence of tin(II) chloride (5mM), gave 60% of the 3-bis(4-methylphenyl)methyl ether and 8% of the 2-ether (plus 24% of an unresolved mixture). Although this preponderant formation of the 3-ether is analogous to the results obtained with methyl 4,6-*O*-benzylidene-α-D-mannopyranoside, the other diaryldiazoalkanes gave very different results (Table II). Thus, **11** gave approximately equal amounts of the 2- and 3-diphenylmethyl ethers and the 2- and 3-bis(4-chlorophenyl)methyl ethers, whereas the reaction with 9-diazofluorene gave 70% of the 2-(9-fluorenyl) ether and only ~5% of the 3-ether (plus 13% of an unresolved mixture). For each reaction, the assignments of structure were based on the trichloroacetyl isocyanate–n.m.r. method, as discussed previously. Thus, the 2-ethers were identified as the products for which

the shifted signal has a large coupling-constant and is therefore assignable to H-3. Each of the 3-ethers has a lower R_F value (t.l.c.) than its 2-isomer, and this behaviour is consistent with the assigned structures, because stronger adsorption of the more acidic HO-2 group to silica gel would be expected.

The reasons for the different patterns of reaction of the diaryldiazoalkanes with the acetals **9** and **11** are not understood. A possible pathway for the tin-catalysed diarylalkylation reaction involves the formation of a 2-stanna-1,3-dioxolane intermediate (**12**), as suggested[14,15] for the methylation reaction. Alkylation of **12** would then involve its reaction with the diarylalkyl carbocation formed[22] by reaction of the liberated protons with the diaryldiazoalkane. For the 4,6-*O*-benzylidene derivative **9**, alkylation occurs almost exclusively at O-3, possibly because of the greater steric accessibility of the "equatorial" O-3 position compared with the "axial" O-2. The same argument has been used to explain the almost exclusive attack at the "equatorial" O-3 position in the selective monobenzylation of methyl 4,6-*O*-benzylidene-2,3-*O*-dibutylstannylene-α-D-mannopyranoside with benzyl bromide[18,23]. However, the suggested pathway through **12** does not adequately explain the results obtained in the diarylalkylation of the isopropylidenemannoside **11**. Thus, although alkylation of **11** with the more reactive diaryldiazoalkanes [namely, the 4,4′-dimethoxy and 4,4′-dimethyl derivatives (*cf.* ref. 24)] also occurred mainly at O-3, the less reactive diazo(diphenyl)methane and 4,4′-dichloro derivative (**3**) gave approximately equal amounts of the 2- and 3-ethers and the least reactive member of the series, 9-diazofluorene, gave mainly the 2-ether. The changed selectivity towards O-2 in **11** as the reactivity of the diaryldiazoalkanes decreases may be associated with the greater acidity of HO-2 in sugar glycosides. However, the mechanistic details are not clear and, at present, insufficient data are available to indicate whether the difference in behaviour of the apparently very similar benzylidene (**9**) and isopropylidene (**11**) compounds is primarily of electronic or stereochemical origin.

Despite these mechanistic uncertainties, this method for regioselective monoalkylation is of potential synthetic value, as exemplified by its use in syntheses of 2- and 3-*O*-methyl derivatives of methyl α-D-mannopyranoside. The preparation of methyl 4,6-*O*-benzylidene-2-*O*-methyl-α-D-mannopyranoside (**10**) *via* the 3-*O*-diphenylmethyl derivative has already been described, and methylation of methyl 2-*O*-(9-fluorenyl)-4,6-*O*-isopropylidene-α-D-mannopyranoside followed by catalytic hydrogenolysis of the fluorenyl group gave ready access to methyl 4,6-*O*-isopropylidene-3-*O*-methyl-α-D-mannopyranoside. Nashed[18] has reported convenient syntheses of the 2- and 3-methyl ethers of methyl α-D-mannopyranoside from the 2,3-*O*-dibutylstannylene derivative. Preliminary experiments have indicated that the diaryldiazoalkane–tin(II) chloride method may be of value for the regioselective synthesis of 2′-*O*-alkylnucleosides. Thus, treatment of adenosine with the 4,4′-dimethyl (**2**) and 4,4′-dimethoxy (**4**) reagents in *N*,*N*-dimethylformamide in the presence of tin(II) chloride gave single monoethers (~60%) in each case. Although conclusive proofs of structure have not yet been made, studies of the u.v.-hypochromic effect[7] suggest that the products are the 2′-ethers.

In contrast to its reaction with the mannopyranosides **9** and **11**, diazo(diphenyl)methane–tin(II) chloride is not an effective reagent for the diphenylmethylation of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside. This behaviour presumably reflects the greater difficulty in forming a 5-membered cyclic intermediate with the *trans*-2,3-diol group. Although ready methylation of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside and related glycosides having *trans*-diol groups occurs with diazomethane–tin(II) chloride[4], it may be significant that very large excesses (15–60-fold) of diazomethane were employed, in contrast to the small excess of reagent used in the diphenylmethylation reactions.

EXPERIMENTAL

General methods. — T.l.c. was performed on Kieselgel G (Merck 7731) with detection by iodine vapour or vanillin–sulphuric acid[25]. 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.

Reaction of 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose with diaryldiazomethanes. — (*a*) A solution of diazo[bis(4-methylphenyl)]methane (**2**; 860 mg, 3.87 mmol) and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**6**; 1.0 g, 3.87 mmol) in dry benzene (30 mL) was boiled under reflux for 24 h. The colour of the diazo compound had then been completely discharged, and t.l.c. (9:1 benzene–ether) revealed components having R_F 0.83 (yellow, azine), 0.53, and 0.11 (**6**). After evaporation of the benzene, the residue was fractionated on a column of silica gel (100 g). Elution with benzene removed the azine (0.1 g), and subsequent elution with 9:1 benzene–ether gave 3-*O*-[bis(4-methylphenyl)methyl]-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose as a syrup (1.41 g, 80%), $[\alpha]_D$ −16° (*c* 0.7, ethanol). N.m.r. data: δ 7.32–7.07 (m, 8 H, aromatic), 5.93 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.55 (s, 1 H, OC*H*Ar$_2$), and 2.30 (s, 6 H, 2 Ph*Me*).

Anal. Calc. for $C_{27}H_{34}O_6$: C, 71.4; H, 7.5. Found: C, 71.7; H, 7.3.

Catalytic hydrogenolysis (10% Pd/C, 8 h) of the foregoing ether in ethanol gave **6** (78.5%) identical with an authentic sample.

(*b*) Following the procedure described in (*a*), treatment of **6** with diazo[bis(4-chlorophenyl)]methane gave 3-*O*-[bis(4-chlorophenyl)methyl]-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (80%), m.p. 105–106°, $[\alpha]_D$ −21° (*c* 0.9, ethanol). N.m.r. data: δ 7.27 (s, 8 H, aromatic), 5.93 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), and 5.58 (s, 1 H, OC*H*Ar$_2$).

Anal. Calc. for $C_{25}H_{28}Cl_2O_6$: C, 60.7; H, 5.65. Found: C, 61.0; H, 5.9.

Reactions of 1,4-anhydroerythritol (**7**). — (*a*) *With diazo(diphenyl)methane.* A

solution of diazo(diphenyl)methane (**1**; 600 mg, ~3 mmol) and **7** (104 mg, 1 mmol) in dry benzene (15 mL) was boiled under reflux for 18 h. T.l.c. (benzene) of the colourless solution then showed the absence of **7**, and the solvent was evaporated. The residue was purified by chromatography on a column of silica gel. Elution with benzene gave, first, benzophenone azine, and then a chromatographically homogeneous syrup (385 mg, 88%) that crystallised from ethanol to yield 1,4-anhydro-2,3-bis(diphenylmethyl)erythritol (360 mg), m.p. 101–102°. N.m.r. data: δ 7.5–7.0 (m, 20 H, aromatic), 5.5 (s, 2 H, OC*H*Ph_2), and 4.1–3.7 (m, 6 H, H-1–H-4).

Anal. Calc. for $C_{30}H_{28}O_3$: C, 82.6; H, 6.4. Found: C, 82.5; H, 6.3.

(*b*) *With diazo(diphenyl)methane–tin(II) chloride.* Diazo(diphenyl)methane (485 mg, 2.5 mmol) was added to a solution of **7** (208 mg, 2.0 mmol; 0.4M) in 1,2-dimethoxyethane (5 mL) containing tin(II) chloride (10 mg, ~10mM), and the mixture was kept overnight at room temperature. T.l.c. (ethyl acetate) then showed the absence of **7** (R_F 0.22) and the formation of a single sugar product (R_F 0.78). The solvent was evaporated, and the residue was chromatographed on silica gel (40 g). Elution with 9:1 benzene–ether removed the yellow benzophenone azine, and elution with 4:1 benzene–ether then gave a chromatographically homogeneous syrup (467 mg, 87%) that crystallised from ether–light petroleum (b.p. 40–60°), to give 1,4-anhydro-2-*O*-diphenylmethyl-DL-erythritol, m.p. 77–78°. N.m.r. data: δ 7.32 (s, 10 H, aromatic), 5.48 (s, 1 H, OC*H*Ph_2), 4.23–3.55 (m, 6 H, H-1–H-4), and 2.70 (d, 1 H, $J_{OH,H-3}$ 5 Hz, OH).

Anal. Calc. for $C_{17}H_{18}O_3$: C, 75.5; H, 6.7. Found: C, 75.3; H, 6.8.

(*c*) *With other diaryl(diazo)alkanes–tin(II) chloride.* The reactions of **7** with **2**, **3**, and **5** were performed essentially as described in (*b*). For data, see Table I.

*Reactions of methyl 4,6-*O*-benzylidene-α-*D*-mannopyranoside* (**9**). — (*a*) *With diazo[bis(4-methylphenyl)]methane* (**2**). Compound **2** (595 mg, 2.66 mmol) was added to a cooled solution (~0°) of **9** (500 mg, 1.77 mmol) in 1,2-dimethoxyethane (10 mL) containing tin(II) chloride (40 mg, ~20mM), and the mixture was kept at ~3°. After 1.5 h, when the colour of the diazo compound had disappeared, t.l.c. (1:1 benzene–ether) revealed a single sugar product (R_F 0.71) and only a trace of **9** (R_F 0.13). The solvent was then evaporated, and the residue was chromatographed on silica gel (100 g). Elution with 19:1 benzene–ether (200 mL) followed by 9:1 benzene–ether removed the azine by-product and then gave methyl 4,6-*O*-benzylidene-3-*O*-[bis(4-methylphenyl)methyl]-α-D-mannopyranoside as a chromatographically homogeneous glass (681 mg, 80%), $[\alpha]_D$ +65° (*c* 1, chloroform). N.m.r. data: δ 7.56–6.97 (m, 13 H, aromatic), 5.70, 5.57 (2 s, 2 H, OC*H*Ph and OC*H*Ar_2), 4.70 (s, 1 H, H-1), 4.30–3.68 (m, 6 H, H-2–H-6), 3.30 (s, 3 H, OMe), 2.66 (bs, 1 H, OH), 2.31 and 2.28 (2 s, 6 H, 2 Ph*Me*); after addition of trichloroacetyl isocyanate: (*inter alia*) δ 4.30–3.55 (m, 5 H, H-3–H-6) and 5.35 (dd, 1 H, $J_{1,2}$ 3, $J_{2,3}$ 6.5 Hz, H-2).

Anal. Calc. for $C_{29}H_{32}O_6$: C, 73.1; H, 6.8. Found: C, 73.0; H, 6.7.

(*b*) *With other diaryldiazoalkanes.* The reactions of **9** with **1**, **3**, and **5** were performed as described in (*a*), but with the reaction times and temperatures listed in Table II. For data on the products, see Table II.

Methyl 4,6-O-isopropylidene-α-D-mannopyranoside (**11**). — Methyl isopropenyl ether (3.66 g, 51.5 mmol) was added to a solution of methyl α-D-mannopyranoside (5.0 g, 25.8 mmol) and toluene-*p*-sulphonic acid (10 mg) in *N*,*N*-dimethylformamide (25 mL, dried over Drierite) cooled below 5° with an ice bath. The mixture was stirred for 12 h at 0–5°, and t.l.c. (ethyl acetate) then revealed components having R_F 0.52 (major), 0.71 (trace), and 0.87 (minor), and only traces of starting material (R_F 0.1). After the addition of anhydrous sodium carbonate (~5 g), the mixture was stirred for 0.5 h and filtered, the solvent was evaporated at ~55° under diminished pressure, and xylene 2 × 10 mL was evaporated from the residue. A solution of the oily residue in chloroform (50 mL) was washed with water (4 × 50 mL) and t.l.c. then indicated that the major product (R_F 0.52) had been extracted into the aqueous layer, leaving the other products in the chloroform layer. The combined, aqueous extracts were concentrated to ~50 mL and continuously extracted with chloroform overnight. Evaporation of the dried ($MgSO_4$) extract gave an oily residue (6 g) that crystallised from chloroform–light petroleum, to give **11** (3.95 g, 65.5%), m.p. 99–101°, $[\alpha]_D$ +73° (*c* 1, chloroform); lit.[21] m.p. 98–99°, $[\alpha]_D$ +73° (chloroform).

Reactions of methyl 4,6-O-isopropylidene-α-D-mannopyranoside (**11**) *with diaryldiazoalkanes–tin(II) chloride.* — Each diaryldiazoalkane (Table II, 3.2 mmol) was added to a solution of **11** (2.13 mmol) in 1,2-dimethoxyethane (10 mL) containing tin(II) chloride (10 mg, 5mM), and the mixture was kept at room temperature until the colour of the diazo compound had been discharged. T.l.c. (1:1 benzene–ether) then showed the formation of two new sugar components {only one for diazo[bis(4-methoxyphenyl)]methane} and a small proportion of **11**. The products were isolated by chromatography on silica gel, as described for the reaction of **9**. For data on the products, see Table II.

Methyl 2-O-methyl-α-D-mannopyranoside. — A solution of methyl 4,6-*O*-benzylidene-3-*O*-diphenylmethyl-α-D-mannopyranoside (1 g) in methyl iodide (10 mL) was treated with freshly prepared silver oxide (8.8 g) added in 4 portions during 1 day. The mixture was stirred for 4 days, with further additions of silver oxide (3 g) and methyl iodide (10 mL) after 2 days. T.l.c. then showed completion of the reaction, and, after filtration, the methyl iodide was evaporated. The residue was chromatographed on silica gel (100 g) with 9:1 benzene–ether, to yield syrupy methyl 4,6-*O*-benzylidene-3-*O*-diphenylmethyl-2-*O*-methyl-α-D-mannopyranoside (**13**; 662 mg, 64%), $[\alpha]_D^{22}$ +63.5° (*c* 0.4, ethanol). N.m.r. data: δ 7.5–7.1 (m, 15 H, aromatic), 5.72, 5.58 (2 s, 2 H, C*H*Ph and OC*H*Ar_2), 4.67 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 4.30–3.54 (m, 9 H, OMe and H-2–H-6), and 3.31 (s, 3 H, OMe).

A solution of the foregoing product (500 mg) in ethanol (50 mL) was shaken with 10% palladium-on-carbon under hydrogen (1 atm.) for 2.25 h. T.l.c. (1:1 benzene–ether) then showed the absence of **13** and the formation of products having R_F 0.43 (major) and 0.06 (trace). After filtration and evaporation of the solvent, the residue was chromatographed on silica gel (60 g) with 1:1 benzene–ether, to give methyl 4,6-*O*-benzylidene-2-*O*-methyl-α-D-mannopyranoside (175 mg, 55%), R_F 0.43,

m.p. 111–112°, $[\alpha]_D^{22}$ +33.5° (*c* 1, chloroform); lit.[18] m.p. 111.5–112°, $[\alpha]_D^{25}$ +32.7° (chloroform). N.m.r. data ($CDCl_3$, after the addition of trichloroacetyl isocyanate): δ (*inter alia*) 5.35 (dd, 1 H, $J_{2,3}$ 3.5, $J_{3,4}$ 11 Hz, H-3) and 4.35–3.70 (m, 5 H, H-2 and H-4–H-6); no OH signal.

Methyl 2-O-(9-fluorenyl)-4,6-O-isopropylidene-3-O-methyl-α-D-mannopyranoside. — A solution of methyl 2-*O*-(9-fluorenyl)-4,6-*O*-isopropylidene-α-D-mannopyranoside (800 mg) in methyl iodide (15 mL) was treated with freshly prepared silver oxide (7.5 g) added in 4 portions during 1 day. The mixture was stirred for 5 days, with further additions of silver oxide (3 g) and methyl iodide (15 mL) after 2 days. T.l.c. then showed completion of the reaction, and, after filtration, the methyl iodide was evaporated. The residue was chromatographed on silica gel (100 g) with 9:1 benzene–ether, to yield a chromatographically homogeneous syrup (690 mg, 83.5%) that crystallised from ethanol–water to give the title compound, m.p. 137–138°, $[\alpha]_D$ +8° (*c* 0.6, ethanol). N.m.r. data: δ 7.82–7.18 (m, 8 H, aromatic), 5.73 (s, 1 H, OC*H*Ar_2), 4.60 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 4.11–3.38 (m, 6 H, H-2–H-6), 3.34, 3.21 (2 s, 6 H, 2 OMe), 1.58 and 1.45 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_{24}H_{28}O_6$: C, 69.9; H, 6.8. Found: C, 69.8; H, 6.5.

Methyl 4,6-O-isopropylidene-3-O-methyl-α-D-mannopyranoside. — A solution of methyl 2-*O*-(9-fluorenyl)-4,6-*O*-isopropylidene-3-*O*-methyl-α-D-mannopyranoside (500 mg) in ethanol (50 mL) was shaken with 10% palladium-on-carbon (100 mg) under hydrogen (1 atm.) for 1 h. After filtration and evaporation of the solvent, the residue was chromatographed on silica gel (40 g) with benzene–ether (1:2), to give the title compound as a syrup (210 mg, 70%), $[\alpha]_D$ +42.5° (*c* 0.7, chloroform). N.m.r. data ($CDCl_3$): δ 4.74 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.15–3.55 (m, 6 H, H-2–H-6), 3.51, 3.38 (2 s, 6 H, 2 OMe), 2.60 (bs, 1 H, OH), 1.54 and 1.44 (2 s, 6 H, CMe_2); after addition of trichloroacetyl isocyanate: δ (*inter alia*) 5.35 (dd, 1 H, $J_{1,2}$ 2, $J_{2,3}$ 3.5 Hz, H-2) and 4.12–3.58 (m, 5 H, H-3–H-6).

Anal. Calc. for $C_{11}H_{20}O_6$: C, 53.2; H, 8.1. Found: C, 53.1; H, 8.3.

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