Carbohydrate Research, 33 (1974) 35–46
© Elsevier Scientific Publishing Company, Amsterdam – Printed in Belgium

THE SYNTHESIS OF SOME *o*-NITROBENZYLIDENE DERIVATIVES OF ALDOPYRANOSIDES

PETER M. COLLINS AND NATHAN N. OPARAECHE

Chemistry Department, Birkbeck College (University of London), Malet Street, London WC1E 7HX (Great Britain)

(Received July 19th, 1973; accepted for publication October 3rd, 1973)

ABSTRACT

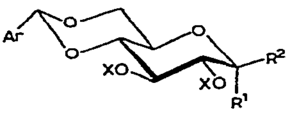
The preparation of the following new compounds is reported: the 4,6-*O*-*o*-nitrobenzylidene derivatives of methyl α- and β-D-glucopyranoside and -D-galactopyranoside, methyl α-D-mannopyranoside, and the corresponding 2,3-diacetates; the 2,3-*O*-*o*-nitrobenzylidene derivatives of methyl 4,6-di-*O*-methyl-β-D-allopyranoside, methyl α-L-rhamnopyranoside and its 4-acetate (**11**), the 3,4-*O*-*o*-nitrobenzylidene derivatives of 1,6-anhydro-2-*O*-methanesulphonyl-D-galactopyranose, methyl β-L-arabinopyranoside, methyl α-L-fucopyranoside, and the 2-*O*-acetyl derivatives (**13** and **15**) of the last two compounds, and 2,3:4,6-di-*O*-*o*-nitrobenzylidene-α-D-mannopyranoside (**19**). The n.m.r. spectra of the *endo* and *exo* forms of four of the dioxolane derivatives, **11**, **13**, **19**, and **15**, are presented. The first three of these compounds have been fractionated into pure *endo* and *exo* forms.

RESULTS AND DISCUSSION

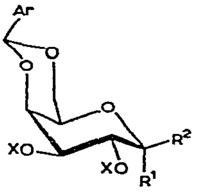
There is an extensive literature on the condensation of polyols with benzaldehyde to give *O*-benzylidene derivatives[1], but there have been few reports about the corresponding *o*-nitrobenzylidene derivatives. Tanasescu and co-workers prepared many di-*O*-*o*-nitrobenzylidene aldoses by heating a mixture of the sugar, *o*-nitrobenzaldehyde, and phosphorus pentaoxide[2–4], but the reported yields of the derivatives were very low (*e.g.*, from rhamnose, mannose, and galactose, they were 10, 20, and 15%, respectively)[3]. These authors extended the reaction to the methyl α-pyranosides of D-galactose[3], D-glucose[2], and D-mannose[5], and they claimed that di-*O*-*o*-nitrobenzylidene derivatives were formed.

We have repeated the reactions involving methyl α-D-mannopyranoside and methyl α-D-glucopyranoside, with a view to adapting them for the synthesis of mono-*O*-*o*-nitrobenzylidene derivatives, but we were unable to form any nitrobenzylidene derivatives from either glycoside under the reported conditions. Consequently, another method of preparation was sought.

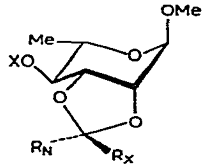
The following preliminary experiments were carried out: methyl α-D-glucopyranoside was stirred at room temperature with *o*-nitrobenzaldehyde dissolved in either benzene, ethyl ether, or *p*-dioxane containing an acid catalyst. Sulphuric acid was used with all three solvents, zinc chloride with the first two, and phosphorus pentaoxide and *p*-tolylsulphonic acid with benzene only. The reactions were monitored by t.l.c. which showed that those in *p*-dioxane were superior, since a high conversion into product was achieved after two hours with sulphuric acid as catalyst and after eight days with zinc chloride. All the other methods yielded little product even after an eight-day reaction period. The product formed in the successful *p*-dioxane–sulphuric acid reaction was isolated in ~70% yield and was shown to be methyl 4,6-*O*-*o*-nitrobenzylidene-α-D-glucopyranoside (**1**). It gave a 2,3-diacetate (**2**), having an n.m.r. spectrum in which all the pyranoid ring protons could be assigned by a first-order analysis (see Table I), and a 2,3-di-*O*-methyl derivative (**3**). This method of acetalation was then applied to eight other glycopyranosides and a 1,6-anhydrohexopyranose derivative.



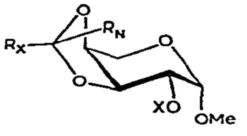
1 $R^1 = OMe, R^2 = H, X = H$
2 $R^1 = OMe, R^2 = H, X = Ac$
3 $R^1 = OMe, R^2 = H, X = Me$
4 $R^1 = H, R^2 = OMe, X = H$
5 $R^1 = H, R^2 = OMe, X = Ac$



6 $R^1 = OMe, R^2 = H, X = H$
7 $R^1 = OMe, R^2 = H, X = Ac$
8 $R^1 = H$ $R^2 = OMe, X = H$
9 $R^1 = H, R^2 = OMe, X = Ac$



10 R_X or $R_N = Ar$ or $H, X = H$
11A $R_X = Ar, R_N = H, X = Ac$
11B $R_X = H, R_N = Ar, X = Ac$

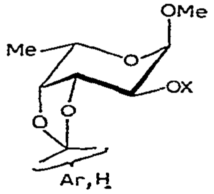


12 R_X or $R_N = Ar$ or $H, X = H$
13A $R_X = Ar, R_N = H, X = Ac$
13B $R_X = H, R_N = Ar, X = Ac$

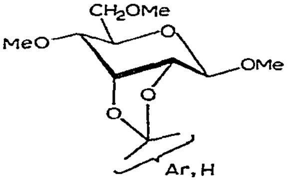
When the methyl hexopyranosides with the β-D-*gluco* and α- and β-D-*galacto* structures were acetalated, they also formed 4,6-*O*-*o*-nitrobenzylidene derivatives (**4**, **6**, and **8**) in yields of 70–90%. These products were converted into 2,3-diacetates (**5**, **7**, and **9**, respectively), the structures of which were established from their elemental analyses and n.m.r. spectra (see Table I). The large values for $J_{1,2}$ observed in the spectra of the β-D-glycoside derivatives **5** and **9** showed that anomerisation had not occurred during the acid-catalysed condensation with the aldehyde. This was also confirmed by the optical rotation data.

Methyl 6-deoxyhexopyranosides having the α-L-*manno* and α-L-*galacto* configurations and methyl β-L-arabinopyranoside all formed dioxolane derivatives in good yield when acetalated, one positional isomer being formed from each sugar. The gross structures of these products were determined from their monoacetates in the usual way. The rhamnoside derivative was shown to be a 2,3-*O*-*o*-nitrobenzylidene-4-acetate (**11**), since the signal assigned to H-4 was at the lowest field of those for the pyranoid ring protons, whereas the arabinoside and fucoside derivatives were 3,4-*O*-*o*-nitrobenzylidene-2-acetates (**13** and **15**) because the signals assigned to H-2 were at the lowest field.

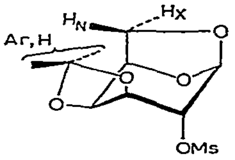
The n.m.r. spectra of these compounds further showed that *endo* and *exo* forms were present, which is not unexpected, since isomers of this type are common with



14 X = H
15 X = Ac



16



17

2-phenyl-1,3-dioxolane derivatives. For example, two forms of methyl 2,3-*O*-benzylidene-β-L-arabinopyranoside are known[6], to which configurations have been assigned[7] by using n.m.r. spectroscopy. Baggett *et al.*[7] showed, from their study of a large number of compounds, that an *exo*-benzylidene proton in these fused bicyclic systems resonates at higher field than an *endo* proton. The assignment of configuration at the *o*-nitrobenzylidene acetal carbon atom was decided by application of this method. The chemical shifts of these protons, in either deuterated benzene or chloroform, for the isomers of the *o*-nitrobenzylidene derivatives **11**, **13**, and **15** are recorded in Table I (the chemical shift data subsequently mentioned are for solutions in $CDCl_3$). They can be classified into two groups: those in the region δ 6.82–6.95 which have been assigned to the *exo* isomers, and those in the region δ 6.50–6.61, to the *endo* isomers.

Although the stereoisomers of the fucoside **15** were not separated, the n.m.r. signals from the two forms could be completely analysed, because the isomers were present in the mixture in unequal, but substantial amounts (see Table I). The rhamnoside **11**, however, was separated into *exo* (**11A**) and *endo* forms (**11B**); the arabinoside isomers **13A** and **13B** were also separated. The structures of these compounds were assigned by the application of n.m.r. spectroscopy.

Dioxolane derivatives were also formed from the condensation of *o*-nitrobenzaldehyde with methyl 4,6-di-*O*-methyl-β-D-alloside and 1,6-anhydro-2-*O*-methanesulphonyl-β-D-galactopyranose. These precursors were partially blocked to avoid the complex mixtures that would otherwise result from condensation at several sites. Two isomeric forms of the 2,3-*O*-*o*-nitrobenzylidene-alloside (**16**) were formed, as indicated by two benzylidene methine signals at δ 6.56 and 6.92, but their relative intensities were 11:1 and consequently the n.m.r. spectrum of only the major isomer was analysed (see Table I). Thus, if the difference in chemical shift between the two nitrobenzylidene methine protons is a reliable method for distinguishing *endo* and *exo* isomers, this results suggests that the *endo* isomer is the preponderant component in this reaction mixture in contrast to compounds **10**, **12**, and **14**, where the *exo* isomer was usually present as the major component.

The 1,6-anhydrogalactose derivative (**17**) exhibited only one benzylidene methine signal, at δ 6.41. On steric grounds, the *endo* form should be highly disfavoured, consequently the *exo* isomer would be the anticipated product. This conclusion, however, is not compatible with the chemical shift of the benzylidene

TABLE I

N.M.R. PARAMETERS (δ IN P.P.M. AND J IN HZ) OF SOME DERIVATIVES OF *O*-*o*-NITROBENZYLIDENE-GLYCOPYRANOSIDES

Compound	$ArCHO_2$	*H-1*	*H-2*	*H-3*	*H-4*
2[c,e]	6.02 (*s*) 6.12 (*s*)[d]	4.82 (*d*) $J_{1,2}$ 3.5	5.02 (*q*) $J_{2,3}$ 9.5	5.83 (*t*) $J_{3,4}$ 9.5	3.35 (*t*) $J_{4,3}$ 9.5 $J_{4,5}$ 9.5
5[a,b]	6.12 (*s*)	4.50 (*d*) $J_{1,2}$ 8.0	5.0 (*q*) $J_{2,3}$ 8.5	5.27 (*q*) $J_{3,4}$ 9.5	—3.3–
9[a,c]	6.01 (*s*) 6.15 (*s*)[d]	4.18 (*d*) $J_{1,2}$ 8.0	5.68 (*q*) $J_{2,3}$ 10.0	4.98 (*q*) $J_{3,4}$ 3.5	4.08 (*q*) $J_{4,5}$ 1.0
7[c,e]	6.04 (*s*) 6.15 (*s*)[d]	5.10 (*d*) $J_{1,2}$ 3.0	5.50 (*q*) $J_{2,3}$ 11.5 $J_{2,1}$ 3.0	5.55 (*q*) $J_{3,4}$ 3.0 $J_{3,2}$ 11.5	4.27 (*q*) $J_{4,5}$ 1.5
11B[a,c]	6.61 (*s*) 6.58 (*s*)[d]	4.80 (*s*)	4.01 (*d*) $J_{2,3}$ 6.0	4.25 (*q*) $J_{3,4}$ 7.5	4.93 (*q*) $J_{4,5}$ 10.0
11A[a,c]	6.95 (*s*) 6.87 (*s*)[d]	4.80 (*s*)	3.84 (*d*) $J_{2,3}$ 5.5	4.35 (*q*) $J_{3,4}$ 7.5	5.25 (*q*) $J_{4,5}$ 10.0
13A[c,f]	6.82 (*s*) 6.80 (*s*)[d]	4.90 (*d*) $J_{1,2}$ 3.5	5.23 (*q*) $J_{2,3}$ 8.0	4.46 (*q*) $J_{3,4}$ 5.5	3.52 (*q*) broad $J_{4,5e} \sim 1.0$ $J_{4,5a} \sim 3.0$
13B[c,f]	6.54 (*s*) 6.50 (*s*)[d]	4.72 (*d*) $J_{1,2}$ 3.3	4.95 (*q*) $J_{2,3}$ 7.5	4.42 (*q*) $J_{3,4}$ 5.5	3.78 (*q*) broad $J_{4,5e} \sim 1$ $J_{4,5a}$ 3.0
15*endo*[c,e]	6.54 (*s*) 6.57 (*s*)[d]	4.77 (*d*) $J_{1,2}$ 3.5	4.95 (*q*) $J_{2,3}$ 8.0	4.47 (*q*) $J_{3,4}$ 5.5	3.59 (*q*) $J_{4,5}$ 2.7
15*exo*[c,e]	6.82 (*s*) 6.82 (*s*)[d]	4.92 (*d*) $J_{1,2}$ 3.5	5.25 (*q*) $J_{2,3}$ 8.0	4.49 (*q*) $J_{3,4}$ 5.0	3.39 (*q*) $J_{4,5}$ 2.7
18[a,c]	6.17 (*s*) broad 6.16 (*s*)[d]	4.52 (*d*) $J_{1,2}$ 1.5	5.56 (*q*) $J_{2,3}$ 3.5	5.73 (*q*) $J_{3,2}$ 3.5 $J_{3,4}$ 9.0	3.3–4 5
3[a,c]	6.16 (*s*) 6.14 (*s*)[d]	4.60 (*d*) $J_{1,2}$ 3.5	— 3.0–3.9 —		4.08 (*q*) $J_{4,3}$ 10.0 $J_{4,5}$ 2.3
16[a,c]	6.56 (*s*) 6.56 (*s*)[d] 6.92 (*s*)[d]	4.46 (*d*) $J_{1,2}$ 4.0	4.09 (*q*) $J_{2,3}$ 6.5	4.33 (*q*) $J_{3,4} \sim 3$	3.82 (*q*) $J_{4,5} \sim 8$

[a] 60 MHz. [b] $CDCl_3$. [c] C_6D_6. [d] Taken from a 60-MHz spectrum measured in $CDCl_3$. [e] 220 MHz. [f] 100 MHz.

H-5a	*H-5e*	*H-6*	*H-6′*	*OMe*	*Blocking groups*
3.70 (*sex*) $J_{5,6'}$ 10.0 $J_{5,4}$ 9.5 $J_{5,6}$ 4.5		3.98 (*q*) $J_{6,6'}$ 10.0 $J_{6,5}$ 4.5	3.40 (*t*) $J_{6',6}$ 10.0 $J_{6',5}$ 10.0	2.94 (*s*)	1.68 (*s*) 1.98 (*s*)
4.1 —		4.40 (*q*) $J_{6,6'}$ 10.0 $J_{6,5}$ 4.5	3.3–4.1	3.64 (*s*)	2.04 (*s*) 2.10 (*s*)
2.62 (*m*)		3.95 (*q*) $J_{6,6'}$ 12.4^d $J_{6,5}$ 1.3	3.40 (*q*) $J_{6',5}$ 2.0	3.25 (*s*)	1.74 (*s*) 1.96 (*s*)
3.00 (*m*)		3.92 (*q*) $J_{6,5}$ 1.5 $J_{6,6'}$ 12.5	3.34 (*q*) $J_{6',5}$ 1.8	2.92 (*s*)	1.59 (*s*) 2.05 (*s*)
4.01 (*o*) $J_{5,6}$ 6.3		1.02 (*d*) $J_{\mathrm{Me},5}$ 6.3		3.02 (*s*)	1.67 (*s*)
3.65 (*o*) $J_{5,\mathrm{Me}}$ 6.3		1.16 (*d*) $J_{\mathrm{Me},5}$ 6.3		3.00 (*s*)	1.71 (*s*)
3.47 (*q*) $J_{5a,4}$ 3.0	3.80 (*q*) broad $J_{5e,5a}$ 13.5 $J_{5e,4}$~1.0			3.02 (*s*)	1.72 (*s*)
3.54 (*q*) $J_{5a,4}$ 3.0	3.87 (*q*) broad $J_{5e,4}$~1 $J_{5e,5a}$ 13.5			2.99 (*s*)	1.67 (*s*)
3.78 (*o*) $J_{5,6}$ 6.5		1.33 (*d*) $J_{\mathrm{Me},5}$ 6.5		2.98 (*s*)	1.65 (*s*)
3.67 (*o*) $J_{5,6}$ 6.5		1.29 (*d*) $J_{\mathrm{Me},5}$ 6.5		3.01 (*s*)	1.71 (*s*)
3.3–4.5		— 3.3–4.5 —		2.93 (*s*)	1.82 (*s*) 1.90 (*s*)
3.0–3.9		— 3.0–3.9 —		3.06 (*s*)	3.32 (*s*) 3.56 (*s*)
3.4–3.7		— 3.4–3.7 —		3.28 (*s*)	3.20

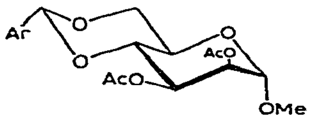
TABLE I (*continued*)

Compound	*ArCHO$_2$*	*H-1*	*H-2*	*H-3*	*H-4*
17^{b,f}	6.41 (*s*)	4.81 (*d*) $J_{1,2}$ 1.2	5 54 (*t*) $J_{2,3}$ 1.9	— 4.52–4.72 (*m*) —	
19B^{c,f}	6.64 (*s*) 6.01 (*s*) 6.65 (*s*)^d 6.08 (*s*)^d	4.61 (*s*)	3.85 (*d*) $J_{2,3}$ 6.0	4.26 (*t*) broad $J_{3,4}$ 7.0	3.91 (*q*) $J_{4,5}$ 4.5
19A^{c,f}	6.92 (*s*) 5.86 (*s*) 6.92 (*s*)^d 6.25(*s*)^d	4.49 (*s*)	3.54 (*d*) $J_{2,3}$ 5.0	4.20 (*t*) $J_{3,4}$ 7.0 $J_{3,2}$ 5.0	— 3.2–

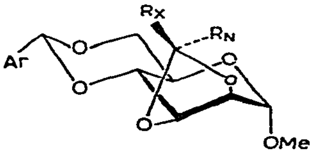
proton, which indicates that the product is the *endo* isomer. As the steric argument and the n.m.r. results are contradictory for compounds **16** and **17**, no assignment of configuration at their benzylidene carbon atoms has been made.

Methyl 4,6-di-*O*-methyl-α-D-allopyranoside and methyl β-L-rhamnopyranoside gave mixtures of products upon acetalation with *o*-nitrobenzaldehyde. One component present in each product was the *O*-*o*-nitrobenzylidene derivative of the corresponding anomer (*i.e.*, **16** and **10**), which was presumably formed by acid-catalysed anomerisation into the more-stable pyranoside modification. This behaviour contrasted with the stability of the methyl β-D-gluco- and β-D-galacto-pyranosides commented on above.

By analogy with its reaction with benzaldehyde[8], the condensation of methyl α-D-mannopyranoside with *o*-nitrobenzaldehyde would be expected to give both 4,6-mono- and 2,3:4,6-di-*O*-*o*-nitrobenzylidene derivatives, with the latter compound existing in *endo* and *exo* forms[7,9]. Treatment of this glycoside with two molar equivalents of *o*-nitrobenzaldehyde, but otherwise under the usual reaction conditions, gave a mixture of products. Analysis of the benzylidene methine-proton region of its n.m.r. spectrum revealed singlets at δ 6.08, 6.16, 6.25, 6.65, and 6.92 in the ratios 1:1.5:1:1:1, and minor signals at δ 6.36, 6.56, and 6.78. Fractionation of the mixture by column chromatography afforded material (R_F 0.35) which was shown to be a mono-*o*-nitrobenzylidene derivative by n.m.r. spectroscopy and by its conversion into a diacetate. The signal for the benzylidene methine proton in the unacetylated



18



19A Rx=Ar RN=H
19B Rx=H RN=Ar

H-5a	*H-5e*	*H-6*	*H-6′*	*OMe*	*Blocking groups*
	4.42 (*t*) broad $J_{5,6}$ 5.0 $J_{5,4}$ 7–8	3.81 (*d*) $J_{6,6'}$ 7.5	3.45 (*q*) broad $J_{6,5}$ 5.0		3.15 (*s*)
3.44 (*quint*) $J_{5,6}$ 4.5 $J_{5,6'}$ 9.0		3.61 (*q*) $J_{6,6'}$ 9.0 $J_{6,5}$ 4 5	3.20 (*t*) $J_{6',6}$ 9.0 $J_{6',5}$ 9.0	2.83 (*s*)	
3.9 —		— 3.2–3.9 —		2.70 (*s*)	

compound appeared at δ 6.16. The product could be a 2,3- or a 4,6-*O*-*o*-nitrobenzylidene diacetate; a decision in favour of the latter structure was made from the n.m.r. data (Table I), which showed, in particular, signals for H-2 and H-3 at low field indicative of a 2,3-diacetate (*i.e.*, **18**).

A crystalline fraction (R_F 0.6) was also obtained, and the elemental analysis, i.r. spectrum (OH absorption absent), and n.m.r. spectrum showed it to be a di-*O*-*o*-nitrobenzylidene derivative (*B*). In particular, the benzylidene proton resonances appeared at δ 6.65 and 6 08. The mother liquor, which contained less than 10% of isomer *B*, was purified by further column chromatography to give another di-*O*-*o*-nitrobenzylidene derivative (*A*), the n.m.r. spectrum of which, apart from indicating its gross structure, showed that it differed from *B* in having signals for benzylidene protons at δ 6.92 and 6.25.

The chemical shifts of the benzylidene protons recorded in Table I show that those on a dioxane ring (*e.g.*, compounds **2**, **3**, **5**, **7**, **9**, and **18**) appear in the range δ 6.12–6.16, whereas those on a dioxolane ring (*e.g.*, compounds **11**, **13**, **15**, **16**, and **17**) appear at lower field, in the range δ 6.41–6.92. These observations agree with those of Baggett *et al.*[10], who were the first to report a difference of this type for benzylidene derivatives. Consequently, the benzylidene methine proton signals at δ 6.92 and 6.65 in the n.m.r. spectra of *A* and *B*, respectively, can be assigned to the dioxolane ring which is fused to C-2 and C-3 of the pyranoside. Therefore, *A* must be the *exo* isomer (**19A**) and *B* the *endo* isomer (**19B**)[7].

A small amount of a third fraction (R_F 0.5) was also obtained by column chromatography. Its n.m.r. spectrum was poorly resolved, but the integrated peak areas of the signals for the aromatic protons relative to those of the aliphatic protons showed that it was a mono-*O*-*o*-nitrobenzylidene derivative. The chemical shifts of the benzylidene protons (δ 6.37 and 6.60) are close to the region at which these signals appear when attached to dioxolane rings. Therefore it is possible that this fraction contains the mono-2,3-*O*-*o*-nitrobenzylidene derivatives.

The compounds obtained in this work with *o*-nitrobenzaldehyde closely resemble the products formed by condensing the corresponding sugar derivatives with benzaldehyde, but they differ, in the cases where a comparison may be made, from the previously reported *O*-*o*-nitrobenzylidene derivatives. For example, good yields of 4,6-*O*-*o*-nitrobenzylidene derivatives were obtained from the glucopyranosides and galactopyranosides in this work, in contrast with the 2,3:4,6-di-*O*-*o*-nitrobenzylidene derivatives reported to be formed by the phosphorus pentaoxide method[2,3]. Furthermore, a mixture of products was formed almost quantitatively from methyl α-D-mannopyranoside, whereas Tanasescu and co-workers reported only one product (m.p. 125–130°) that crystallised directly in low yield from the reaction mixture and was claimed to be a di-*O*-*o*-nitrobenzylidene derivative from its elemental analysis. We also found that a di-*O*-*o*-nitrobenzylidene derivative could be crystallised from the reaction mixture without recourse to chromatography, but the material was the pure *exo*-isomer **19A** (m.p. 194–195°).

EXPERIMENTAL

I.r. spectra were measured for solids dispersed in potassium bromide discs and for gums smeared on sodium chloride plates, with a Perkin–Elmer Infracord model 137; optical rotations were measured on 1% solutions in chloroform with a Bellingham and Stanley polarimeter. N.m.r. spectra at 60 and 220 MHz were measured on A60D and HA220 Varian Associates instruments, respectively, and at 100 MHz on a Jeol-MH-100 instrument. Unless stated otherwise, the reported spectra were measured in $CDCl_3$ at 60 MHz.

Thin-layer chromatography (t.l.c.) on Silica Gel G (Merck) employed the following benzene–ethyl acetate mixtures: *A* 4:1; *B* 3:2. The compounds were located with an anisaldehyde–sulphuric acid–ethanol spray at elevated temperatures.

*Methyl 2,3-di-*O*-acetyl-4,6-*O*-*o*-nitrobenzylidene-α-D-glucoside* (**2**). — Methyl α-D-glucopyranoside (40 g), *o*-nitrobenzaldehyde (20 g), and conc. sulphuric acid (8 ml) in *p*-dioxane (200 ml) were stirred together at 20° for 8 h. The solution was then diluted with dichloromethane (300 ml), neutralised with solid sodium carbonate, filtered, and evaporated under diminished pressure to yield a mobile oil, a solution of which in dichloromethane was washed with water and then dried. Evaporation of the solvent gave methyl 4,6-*O*-*o*-nitrobenzylidene-α-D-glucoside (**1**) as a yellow solid (47 g, 70%), m.p. 162–163° (from ethyl acetate), $[\alpha]_D$ +137°, ν_{max} 1530, 3330 cm^{-1} (NO_2 and OH). N.m.r. data: δ 4.75 (*d*, H-1), 6.13 (*s*, PhC*H*), 3.40 (*s*, OMe), 7.3–8.4 (4H, aromatic), 3.16 (2OH), 3.45–4.34 (6H).

Anal. Calc. for $C_{14}H_{17}NO_8$: C, 51.7; H, 5.2; N, 4.3. Found: C, 51.3; N, 4.1; H, 5.2.

The glucoside **1** (2.5 g) was acetylated during 18 h with acetic anhydride (4 ml) in anhydrous pyridine (20 ml) to give **2** (3 g, 96%), m.p. 120–121° (from ethyl acetate), $[\alpha]_D$ +194°, ν_{max} 1530, 1740 cm^{-1} (NO_2 and Ac). For n.m.r. data, see Table I.

Anal. Calc. for $C_{18}H_{21}NO_{10}$: C, 52.6; H, 5.2; N, 3.4. Found: C, 53.1; H, 5.3; N, 3.4.

*Methyl 2,3-di-*O*-methyl-4,6-*O*-o-nitrobenzylidene-α-*D*-glucopyranoside* (**3**). — Compound **1** (7 g) was heated under reflux in *N,N*-dimethylformamide (150 ml) with methyl iodide (20 g) and barium oxide (20 g) for 4 days. The usual work-up gave **3** (6 g, 83%), m.p. 131–132° (from ethanol), $[\alpha]_D$ +91°.

Anal. Calc. for $C_{16}H_{21}NO_8$: C, 54.1; H, 6.0; N, 3.9. Found: C, 54.2; H, 6.0; N, 4.1.

*Methyl 2,3-di-*O*-acetyl-4,6-*O*-o-nitrobenzylidene-β-*D*-glucoside* (**5**). — Methyl β-D-glucopyranoside (5 g) was acetalated as described above with the aldehyde (3 g) and acid (2 ml) in *p*-dioxane (50 ml) for 4 h to give methyl 4,6-*O*-*o*-nitrobenzylidene-β-D-glucoside (**4**; 7.7 g, 90%), m.p. 176–178° [from ethyl acetate–light petroleum (b.p. 60–80°)], ν_{max} 1530 cm^{-1}.

Acetylation of **4** (2 g) gave **5** (2.4 g, 95%), m.p. 181–182° (from ethanol–light petroleum), $[\alpha]_D$ +30°. For n.m.r. data, see Table I.

Anal. Calc. for $C_{18}H_{21}NO_{10}$: C, 52.6; H, 5.2; N, 3.4. Found: C, 52.9; H, 5.2; N, 3.5.

*Methyl 2,3-di-*O*-acetyl-4,6-*O*-o-nitrobenzylidene-α-*D*-galactoside* (**7**). — Methyl α-D-galactopyranoside (4 g) was acetalated as described above to give the nitrobenzylidene galactoside **6** (3.5 g, 79% based on the aldehyde consumed), which after acetylation gave **7** (62%), m.p. 135–136°, $[\alpha]_D$ +16°. For n.m.r. data, see Table I.

Anal. Calc. for $C_{18}H_{21}NO_{10}$: C, 52.6; H, 5.2; N, 3.4. Found: C, 52.8; H, 5.2; N, 3.4.

*Methyl 2,3-di-*O*-acetyl-4,6-*O*-o-nitrobenzylidene-β-*D*-galactoside* (**9**). — Methyl β-D-galactopyranoside (15 g) was acetalated as described above to give the nitrobenzylidene galactoside **8** (20 g, 79%), m.p. 189–190°, which was then acetylated to give **9** (73%), m.p. 199–201°, $[\alpha]_D$ −85°. For n.m.r. data, see Table I.

Anal. Calc. for $C_{18}H_{21}NO_{10}$: C, 52.6; H, 5.2; N, 3.4. Found: C, 52.2; H, 5.2; N, 3.3.

*Methyl 4-*O*-acetyl-*endo- (**11B**) *and* -exo-*2,3-*O*-o-nitrobenzylidene-α-*L*-rhamnopyranoside* (**11A**). — Methyl α-L-rhamnopyranoside (6.2 g) was acetalated for 2 h as described above. Unreacted *o*-nitrobenzaldehyde was removed by washing a solution of the reaction mixture in dichloromethane with aqueous sodium metabisulphite. This gave, after work-up, the nitrobenzylidene-rhamnopyranoside **10**, as a 7:4 *exo,endo*-mixture (5.7 g, 62%), m.p. 190–191°. N.m.r. data: δ 6.82 (*s*) and 6.55 (*s*) (relative intensity 7:4, PhC*H*), 5.0 (*s*) and 4.95 (*s*) (relative intensity 4:7, H-1), 3.41 (*s*) and 3.39 (*s*) (relative intensity 7:4, OMe), 1.23 (*d*) and 1.35 (*d*) ($J_{Me,5}$ 6.5 Hz, relative intensity 7:4), 7.3–8.0 (4H, aromatic), 3.0–4.5 (5H).

The mixture **10** was acetylated, without prior purification, to give the crystalline *exo,endo*-mixture (**11A, B**) (91%). Fractional crystallisation of part (5.2 g) of this product from ethyl ether at 0° gave first the *endo* isomer **11B** (2.6 g, 40%), m.p. 126–127°, $[\alpha]_D$ −80°. For n.m.r. data, see Table I.

Anal. Calc. for $C_{16}H_{19}NO_8$: C, 54.5; H, 5.4; N, 4.0. Found: C, 54.8; H, 5.5; N, 4.0.

As a second fraction, the *exo* isomer **11A** was obtained (1.5 g, 23%), m.p. 101–102°, $[\alpha]_D$ −47°. For n.m.r. data, see Table I.

Anal. Calc. for $C_{16}H_{19}NO_8$: C, 54.4; H, 5.4; N, 4.0. Found: C, 54.3; H, 5.6; N, 4.0.

Methyl 2-O-acetyl-3,4-O-o-nitrobenzylidene-β-L-arabinoside (**13**). — Methyl β-L-arabinoside (7.5 g), when acetalated in the usual way for 16 h, gave a syrupy *endo,exo*-mixture of *o*-nitrobenzylidene derivatives **12** (7.0 g, 55%). N.m.r. data: δ 6.79 (*s*) and 6.53 (*s*) (relative intensity 2:1, PhC*H*), 4.76 (*d*) and 4.65 (*d*) ($J_{1,2}$ 3.5 Hz, relative intensity 1:2, H-1), 3.42 (*s*, OMe), 7.4–8.1 (4H, aromatic), 3.5–4.5 (5H). The isomer ratio varied with reaction time.

Acetylation of the crude product **12** gave a 1:2 *endo,exo*-mixture of *o*-nitrobenzylidene acetates **13** as a syrup, $[\alpha]_D$ +60°.

Anal. Calc. for $C_{15}H_{17}NO_8$: C, 53.1; H, 5.1; N, 4.1. Found: C, 53.9; H, 5.0; N, 4.0.

Upon addition of ethyl ether to the foregoing syrup, a solid precipitated which was recrystallised from ethanol to yield the *exo* isomer **13A** (2.0 g), m.p. 192–193°, $[\alpha]_D$ +66° (*c* 0.3). For n.m.r. data, see Table. I.

The ether solution was evaporated to a gum, which was then crystallised from methanol–light petroleum (b.p. 40–60°) at 0° to give the *endo* isomer **13B** (1.7 g), m.p. 116–118°, $[\alpha]_D$ +18° (*c* 0.2). For n.m.r. data, see Table I.

Methyl 2-O-acetyl-3,4-O-o-nitrobenzylidene-α-L-fucopyranoside (**15**). — Methyl α-L-fucopyranoside (2.5 g) gave, after the usual acetalation reaction, a syrupy *endo,exo*-mixture of *o*-nitrobenzylidene-fucosides **14** (2.9 g, 67%). N.m.r. data: δ 6.83 (*s*) and 6.57 (*s*) (relative intensity 2:1, PhC*H*), 4.82 (*d*) and 4.72 (*d*) ($J_{1,2}$ 3.5 Hz, relative intensity 2:1), 3.46 (OMe), 1.4 (*d*) and 1.3 (*d*) ($J_{Me,5}$ 6.5 Hz; relative intensity 2:1), 7.5–8.2 (4H, aromatic), 2.8 broad (OH), 3.5–4.6 (4H).

Acetylation of this product gave a 1:2 *endo,exo*-mixture of the *o*-nitrobenzylidene acetates **15** (96%) as a syrup which, when purified by column chromatography with solvent *A*, had $[\alpha]_D$ +60°. For n.m.r. data, see Table I.

Anal. Calc. for $C_{16}H_{19}NO_8$: C, 54.4; H, 5.4; N, 3.9. Found: C, 54.7; H, 5.6; N, 3.5.

Methyl 4,6-di-O-methyl-2,3-O-o-nitrobenzylidene-β-D-alloside (**16**). — Methyl 4,6-*O*-benzylidene-α-D-allopyranoside (10 g) was converted into its 2,3-di-*O*-benzyl derivative (m.p. 94–95°), which was then heated at 64° for 12 h in 2% aqueous methanol in the presence of Amberlite IR-120(H^+) resin. This afforded methyl 2,3-di-*O*-benzyl-β-D-allopyranoside which was methylated and reductively debenzylated to give methyl 4,6-di-*O*-methyl-β-D-alloside as a syrup (62%). N.m.r. data: δ 4.58 (*d*, $J_{1,2}$ 7.50 Hz, H-1).

Methyl 4,6-di-*O*-methyl-β-D-alloside (1.5 g) was acetalated as described above to give **16** (1.6 g, 88%), $[\alpha]_D$ +106°. For n.m.r. data, see Table I.

Anal. Calc. for $C_{16}H_{21}NO_8$: C, 54.1; H, 5.9; N, 3.9. Found: C, 54.0; H, 5.5; N, 4.3.

When methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-alloside (1.3 g) was hydrolysed in 40% aqueous acetic acid at 55° for 3 h and the crude product methylated and hydrogenolysed as described above for the β anomer, the 2,3-dihydroxy compound was obtained as an oil (0.33 g). N.m.r. data: δ 4.80 (*d*, $J_{1,2}$ 4.0 Hz, H-1), 4.33 (*t*, $J_{3,2}$ and $J_{3,4}$ 3.5 Hz, H-3), 3.9–3.1 (7H), 3.42 (2OMe), 3.45 (OMe). Treatment of this crude material with *o*-nitrobenzaldehyde, under the usual conditions, afforded a product which appeared to be composed of a mixture of anomers of methyl 4,6-di-*O*-methyl-2,3-*O*-*o*-nitrobenzylidene-β-D-alloside.

*1,6-Anhydro-2-*O*-methanesulphonyl-3,4-*O*-*o*-nitrobenzylidene-β-D-galactopyranose* (**17**). — 1,6-Anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose[11] (1.1 g) was converted into the 2-methanesulphonate (m.p. 149–150°; lit.[12] m.p. 156°) and then hydrolysed to give the 3,4-dihydroxy 2-sulphonate in 85% overall yield, m.p. 152–153° (from ethanol).

The sulphonate (1 g) was acetalated in the usual way to give **17** as a gum (1.3 g, 81%), $[\alpha]_D$ +56°. For n m.r. data, see Table I. The assignment of signals in the n.m.r. spectrum was aided by published results on the unsubstituted anhydride[13].

*Methyl 2,3-di-*O*-acetyl-4,6-*O*-*o*-nitrobenzylidene-α-D-mannopyranoside* (**18**) *and methyl* exo- (**19A**) *and* endo-*2,3:4,6-di-*O*-*o*-nitrobenzylidene-α-D-mannopyranoside* (**19B**). — Methyl α-D-mannopyranoside (6.0 g) was treated with *o*-nitrobenzaldehyde (8 g), as described above, to give a crude product (11.7 g) which afforded crystalline **19B** (2.4 g, R_F 0.6) from benzene–ethyl acetate. The remaining, crude product was fractionated by column chromatography to give a fraction (4.0 g, R_F 0.6–0.5), from which more **19B** (0.8 g) crystallised, having m.p. 194–195°, $[\alpha]_D$ −100°. For n.m.r. data, see Table I.

Anal. Calc. for $C_{21}H_{20}N_2O_{10}$: C, 54.8; H, 4.4; N, 6.1. Found: C, 55.0; H, 4.4; N, 6.0.

A second fraction (2.5 g) had R_F 0.35 and on acetylation gave **18**, m.p. 125–126° [from ethyl ether–light petroleum (b.p. 40–60°)], $[\alpha]_D$ +129°. For n.m.r. data, see Table I.

Anal. Calc. for $C_{18}H_{21}NO_{10}$: C, 52.6; H, 5.2; N, 3.4. Found: C, 53.1; H, 5.1; N, 3.5.

The mother liquor of **19B** was rechromatographed into two fractions, one of which was **19A** (2 0 g), $[\alpha]_D$ +10°. For n.m.r. data, see Table I.

Anal. Calc. for $C_{21}H_{20}N_2O_{10}$: C, 54.8; H, 4.4; N, 6.1. Found: C, 54.9; H, 4.4; N, 6.0. The second fraction (0.9 g) contained mainly **19A** contaminated with ~20% of **18**.

ACKNOWLEDGMENTS

We thank the S.R.C. for support of n.m.r. spectroscopic measurements made by the P.C.M.U. at Harwell, and Professor W. G. Overend for his encouragement.

REFERENCES

1 A. N. de Belder, *Advan. Carbohyd. Chem.*, 20 (1965) 219.
2 I. Tanasescu and M. Ionescu, *Bull. Soc. Chim. Fr.*, (1936) 1511.
3 I. Tanasescu and E. Craciunescu, *Bull. Soc. Chim. Fr.*, (1936) 581.
4 I. Tanasescu and M. Ionescu, *Bull. Soc. Chim. Fr.*, (1940) 77.
5 I. Tanasescu, *Bull. Soc. Chim. Fr.*, (1936) 1517.
6 M. A. Oldham and J. Honeyman, *J. Chem. Soc.*, (1946) 986.
7 N. Baggett, K. W. Buck, A. B. Foster, and J. M. Webber, *J. Chem. Soc.*, (1965) 3401.
8 W. Alberda van Ekenstein and J. J. Blanksma, *Rec. Trav. Chim. Pays-Bas*, 25 (1906) 153.
9 G. J. Robertson, *J. Chem. Soc.*, (1934) 330.
10 N. Baggett, K. W. Buck, A. B. Foster, M. H. Randall, and J. M. Webber, *J. Chem. Soc.*, (1965) 3395.
11 R. M. Hann and C. S. Hudson, *J. Amer. Chem. Soc.*, 64 (1942) 2435.
12 S. P. James, F. Smith, M. Stacey, and L. F. Wiggins, *J. Chem. Soc.*, (1946) 625.
13 K. Heyns and J. Weyer, *Ann.*, 718 (1968) 224.