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The Rotatory Dispersion and Stereochemistry of Organic Compounds. IX.[1] The Nitrates of Glucose

By Yojiro TSUZUKI, Koko TANABE and Kikuhiko OKAMOTO

Department of Chemistry, Tokyo College of Science, Kagurazaka, Shinjuku-ku, Tokyo

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We have measured the rotatory dispersion (RD) and the ultraviolet absorption of twelve nitrates of glucopyranosides carrying a nitrate chromophore, $-O-NO_2$, in the position of the carbon atoms 1, 2, 3, 4, and 6. On the basis of the experimental results and of those results already reported concerning four nitrates,[1] studies have been made as to the correlation between the configuration and the Cotton effect. The sign of the Cotton effect has been determined by the RD curve as well as by the dispersion constant as computed from the dispersion data. A regular relation has been found, namely, irrespective of the position of the nitrate group on the carbon atom, α-glucosides with a nitrate chromophore in the α- or (D)-configuration show negative Cotton effects, while the sign of the Cotton effects of the corresponding β-glucosides is positive. On the contrary, α-glucosides with a nitrate chromophore in the β- or (L)-configuration show positive Cotton effects, while the sign of the Cotton effects of the corresponding β-glucosides is negative.

In a previous preliminary report[1] it has been shown, with some nitrates of glucose, that the $-C-ONO_2$ (nitrate) chromophore has a feeble optically active absorption around 270 mμ ($\varepsilon \sim 20$) and gives rise to a Cotton effect at a region nearly 20 mμ longer than that of the ultraviolet absorption.

In this paper further studies will be reported; these studies were carried out with various nitrates of glucose (Table I) with the object of elucidating the correlation between the configuration and the sign of the Cotton effect, especially the optical rotatory contribution of the functional group attached to each asymmetric center.

Results and Discussion

Figure 1 shows the RD curves of the α- and β-anomers of C_1-nitrates (2, 3, 4, 6-tetraacetyl-α-D-glucopyranose-1-nitrate (I) and the β-anomer (II)). The compound I exhibits a positive Cotton effect which has a peak at 285 mμ, while the compound II shows a negative one, the trough of which lies at 298 mμ. The curve I is positively increased more than the background RD curve XVII (pentaacetyl-α-D-glucopyranose), indicating that the α-C_1-ONO_2 chromophore makes a larger positive rotatory contribution that the C_1-OH group, which is usually expected to make a positive rotatory contribution. (It should, however, be remarked that the C_1-xanthate chromophore has been found to exhibit a distinctly negative Cotton effect,[2] just the opposite effect.)

In a similar, inverse way, the β-C_1-ONO_2 group contributes to the negative rotation of the compound II (Fig. 1), just opposite in sign to the positive effect of the β-C_1-xanthate group.[2]

The compound I, with 1α-$C-ONO_2$, is of the R-configuration according to the rule of Cahn et al.[3]; this is in harmony with the positive Cotton effect, and the absolute configuration of the compound II with β-C_1-ONO_2 is s, in accordance negative effect.

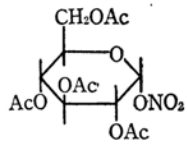
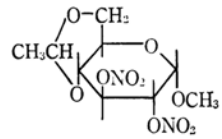
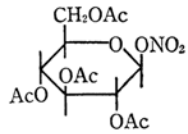
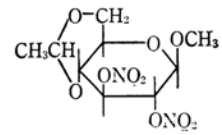
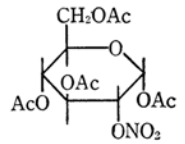
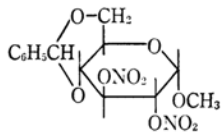
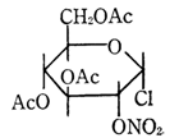
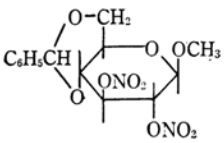
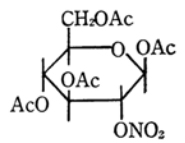
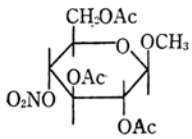
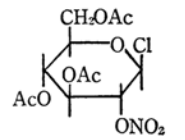
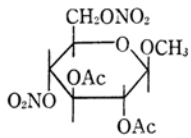
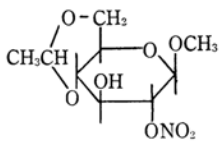
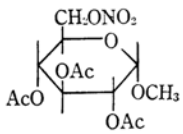
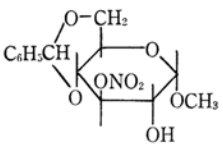
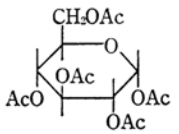
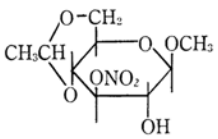
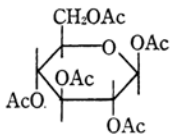
Figure 2 gives the RD curves of a number of various anomers with a nitrate group at the C_2-position. The compounds III and IV in the α-configuration show a weak negative Cotton effect, as has already

1) Y. Tsuzuki, K. Tanabe and K. Okamoto, This Bulletin, **38**, 274 (1965).

2) Y. Tsuzuki, K. Tanabe, M. Akagi and S. Tejima, ibid., **37**, 162 (1964).

3) R. S. Cahn, C. K. Ingold and V. Prelog, *Experientia*, **12**, 81 (1956).

Table I. Nitrates of glucose

Compound			Compound		
I	2,3,4,6-Tetra-*O*-acetyl-1-*O*-nitro-α-D-glucopyranose		X	Methyl 4:6-*O*-ethylidene-α-D-glucopyranoside 2:3-dinitrate	
II	2,3,4,6-Tetra-*O*-acetyl-1-*O*-nitro-β-D-glucopyranose		XI	Methyl 4:6-*O*-ethylidene-β-D-glucopyranoside 2:3-dinitrate	
III[1]	1,3,4,6-Tetra-*O*-acetyl-2-*O*-nitro-α-D-glucopyranose		XII[1]	Methyl 4:6-*O*-benzylidene-α-D-glucopyranoside 2:3-dinitrate	
IV[1]	3,4,6-Tri-*O*-acetyl-2-*O*-nitro-α-D-glucopyranosyl chloride		XIII	Methyl 4:6-*O*-benzylidene-β-D-glucopyranoside 2:3-dinitrate	
V	1,3,4,6-Tetra-*O*-acetyl-2-*O*-nitro-β-D-glucopyranose		XIV	Methyl 2,3,6-tri-*O*-acetyl-4-*O*-nitro-β-D-glucopyranoside	
VI	3,4,6-Tri-*O*-acetyl-2-*O*-nitro-β-D-glucopyranosyl chloride		XV	Methyl 2,3-di-*O*-acetyl-4,6-di-*O*-nitro-β-D-glucopyranoside	
VII	Methyl 4:6-*O*-ethylidene-β-D-glucopyranoside 2-nitrate		XVI	Methyl 2,3,4-tri-*O*-acetyl-6-*O*-nitro-α-D-glucopyranoside	
VIII[1]	Methyl 4:6-*O*-benzylidene-α-D-glucopyranoside 3-nitrate		XVII[1]	Pentaacetyl-α-D-glucopyranose	
IX	Methyl 4:6-*O*-ethylidene-β-D-glucopyranoside 3-nitrate		XVIII	Pentaacetyl-β-D-glucopyranose	

been reported,[1] while the corresponding β-anomers (compounds V and VI) show positive Cotton effects, with peaks at 295 and 300 mμ respectively. The ethylidene derivative (VII) of the β-configuration likewise exhibits a positive Cotton effect, with a peak at 300 mμ.

As may be seen from Fig. 2, all the β-anomers show relatively low rotations as a result of the background laevorotatory contribution of the β-glucosidic type (XVIII); this is consistent with the fact that the C_1–OH far surpasses the C_2–OH in rotatory contribution to glucose. A similar interpretation can be made of the RD curves of the nitrates of the α-form (III and IV) and the background α-pentaacetate (XVII), where the discrepancy in rotation is very little except the

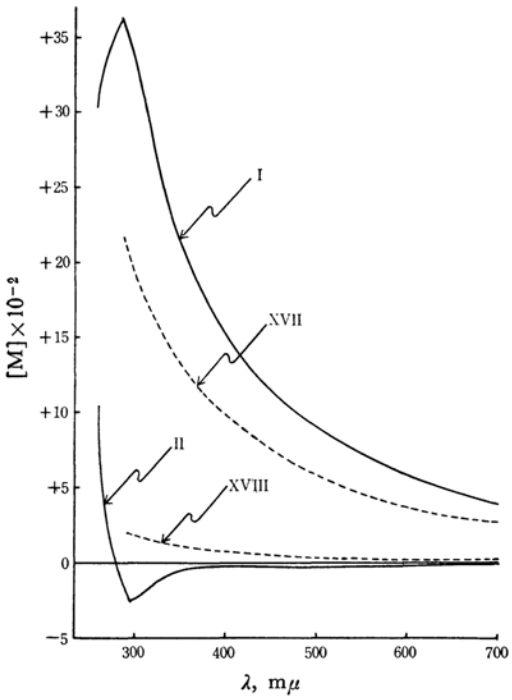


Fig. 1. RD of α- and β-1-nitrates of glucose.

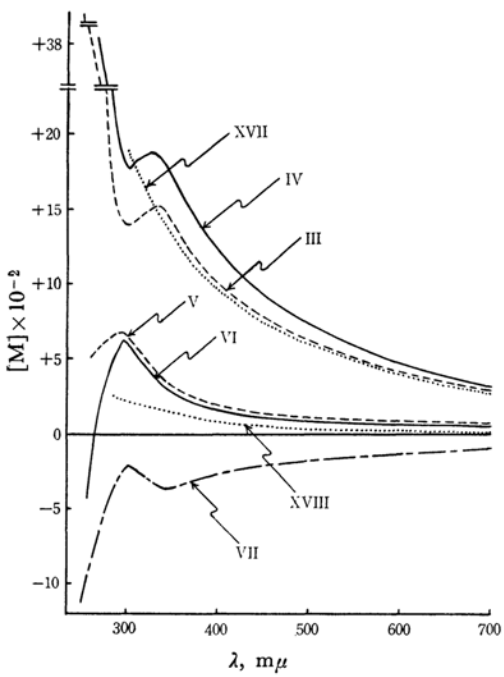


Fig. 2. RD of α- and β-2-nitrates of glucose.

feeble Cotton effects of the former due to the nitrate chromophore.

The rule of Cahn et al. does not appear to hold with the C_2-nitrates(R), since the α-forms (III and IV) show negative Cotton effects.

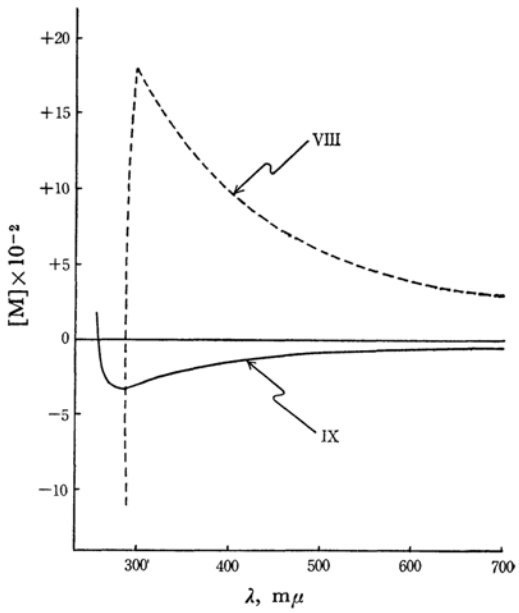


Fig. 3. RD of α- and β-3-nitrates of glucose.

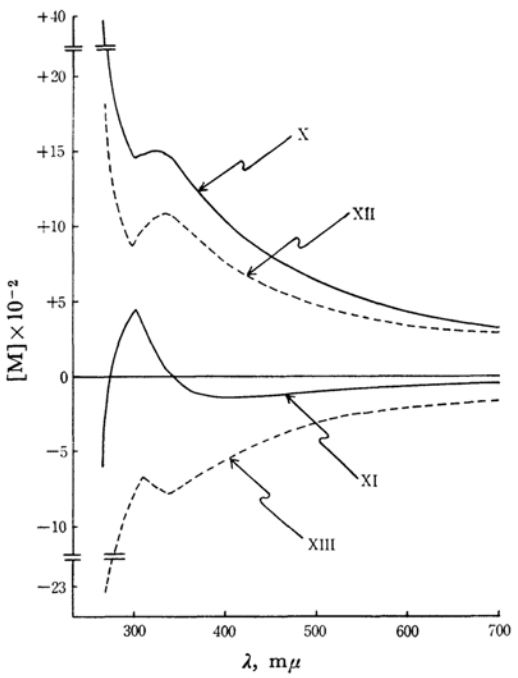


Fig. 4. RD of α- and β-2:3-dinitrates of glucose.

Figure 3 shows the RD curves of the anomers of the C_3-nitrates of glucose. While the α-anomer (VIII) clearly exhibits a positive Cotton effect,[1] quite in harmony with the R-configuration of the carbon 3, the β-glucoside (IX) shows an anomalous RD curve, and the Cotton effect with a trough at 290 mμ is indistinct in sign,

Figure 4 gives the RD curves of the 2 : 3-dinitrates

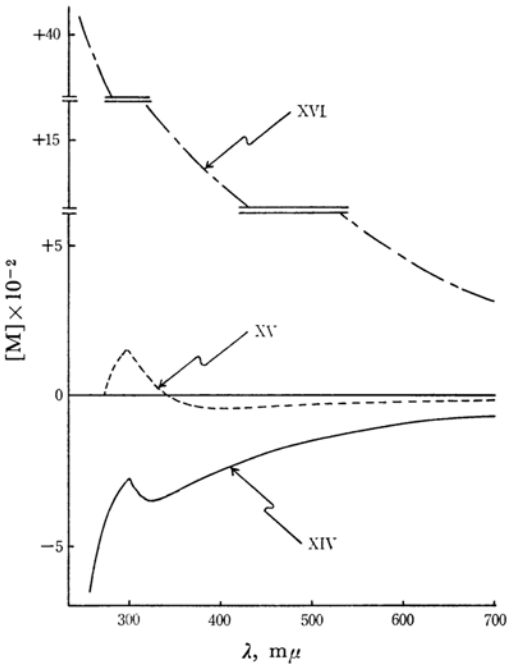


Fig. 5. RD of 4-, 6- and 4:6-dinitrates of glucose.

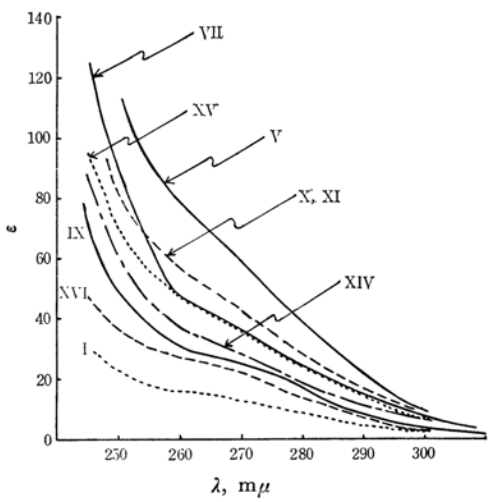


Fig. 6. UV absorption spectra of nitrates of glucose.

(X–XIII). The benzylidene derivatives (XII) show a negative Cotton effect, as has already been reported.[1] Here the rotatory contribution of the carbon 2 is greater than that of the carbon 3, so a negative Cotton effect results in the compound XII.

On the contrary, the β-anomer (XIII) shows a positive Cotton effect, indicating that the C_2-nitrate group also predominates over the C_3-chromophore. This is reasonable when we consider that the C_2-nitrates of the β-form (V–VII) all show positive Cotton effects.

A similar contrast in RD between the α- and β-

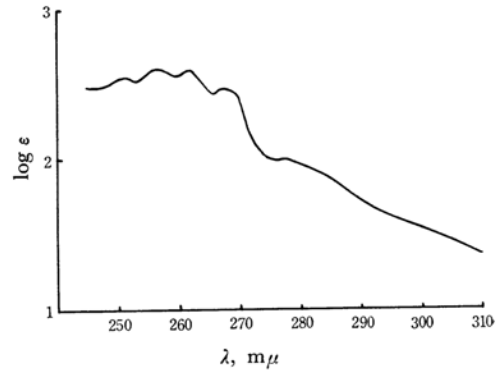


Fig. 7. UV absorption spectrum of XIII.

anomers can be seen in the α- and β-ethylidene derivatives (X and XI). It may, however, be seen in Fig. 4 that the ethylidene derivatives show more distinct Cotton effects than the benzylidene derivatives. Mention should also be made of how the sharper contrast between the former anomers can be used as a means of identification.

Figure 5 shows the RD curves of C_4-nitrate (XIV), 4, 6-dinitrates (XV) and 6-nitrate (XVI). The 4-nitrate exhibits a distinctly positive Cotton effect, even though in the negative domain, the peak of which is located at 300 mμ. The negative background rotation of IV undoubtedly arises from the β-methylglucoside. The RD curve of the compound XV shows a more strongly positive Cotton effect, thus showing the effect of the C_4–ONO_2 group. The 6-nitrate (XVI) does not appear to exhibit any Cotton effect, presumably because the carbon 6 is not asymmetric. The strongly positive background rotation is, naturally, due to the α-form of the glucoside.

The ultraviolet absorption spectra of these nitrates are assembled in Fig. 6, except for the spectrum of XI, which is shown in Fig. 7. As may be seen in Fig. 6, all the spectra show slightly visible shoulders in a region from 265 to 280 mμ, though they are not as distinct as those of alkyl nitrates.[4]

As in the case already elucidated,[1] in these cases a red shift of 5 to 25 mμ is also observed between the ultraviolet absorption and the peak of the Cotton effect. The ultraviolet absorption spectrum of the compound XI shows exceptionally a fine structure and relatively large extinction coefficients (Fig. 7), but it exerts almost no influence on the position of the Cotton effect.

Dispersion Constants

The dispersion data have been found to conform more suitably to the simplified two-term equation of Drude (1), than to the normal two-term equation (2).

4) H. E. Ungade and R. A. Smiloy, *J. Org. Chem.*, **21**, 993 (1956).

Table II. Dispersion data

$$[M] = \frac{A}{\lambda^2-\lambda_0^2} + \frac{B}{\lambda^2}$$

Compound	Drude's equation			λ_{RD}, μ	Sign of Cotton effect	Configuration of C_1
	A	B	λ_0, μ			
I	+20.75	+172.9	0.285	0.285	+	α
II	− 2.58	+ 2.37	0.287	0.298	−	β
III	− 2.35	+159.1	0.298	0.300	−	α
IV	− 2.83	+186.0	0.295	0.295	−	α
V	+ 7.60	+ 17.22	0.265	0.295	+	β
VI	+ 3.62	+ 20.66	0.277	0.300	+	β
VII	+ 2.05	− 45.54	0.283	0.300	+	β
VIII	+20.18	+108.4	0.259	0.300	+	α
IX	−0.565	− 24.16	0.271	0.290	−	β
X	−6.69	+162.8	0.306	0.300	−	α
XI	+5.43	− 28.00	0.291	0.2975	+	β
XII	−3.72	+124.7	0.291	0.295	−	α
XIII	+1.40	− 77.30	0.278	0.308	+	β
XIV	+0.185	− 36.22	0.290	0.300	+	β
XV	+3.45	− 18.43	0.291	0.295	+	β

$$[M] = \frac{A}{\lambda^2-\lambda^2{}_0} + \frac{B}{\lambda^2} \quad (1)$$

$$[M] = \frac{A_1}{\lambda^2-\lambda^2{}_1} + \frac{A_2}{\lambda^2-\lambda^2{}_2} \quad (2)$$

The results of the computation are given in Table II, together with the sign of the Cotton effect.

As may be seen in Table II, the term A invariably agrees with the Cotton effect in sign, indicating that A represents the Cotton effect indeed, the values of λ_0 nearly coincide with the values of λ_{RD}, the optically active absorption maxima observed from the RD, although in some cases the former are 10 to 30 mμ shorter.

The term B without doubt represents the rotatory strength of the non-chromophoric contributions; its value is in general far greater than the corresponding A value. This means that the nitrate chromophore is a feeble contributor to the Cotton effect and, hence, to the optical rotation, and that the dominant rotation originates in the residue of the molecule, mainly in the asymmetry of the carbon 1.

As may be seen in Table II, the values of B are always positive with the α-anomers, while with the β-anomers they are negative in sign, with a few exceptions. However, even with these exceptions (II, V and VI), the positive values are comparatively small.

Conclusion

The results of the above studies are summarized in Table III, where some regular correlations can be seen between the configurations of the carbon atom carrying the nitrate chromophore, as well as the glucosidic carbon atom C_1, and the sign of the Cotton effect.

Table III. The Configurations and signs of the Cotton effect of nitrates

Configuration of C-O-NO_2	C_1-Configuration	Sign of the Cotton effect
D or α	α-anomer	negative
D or α	β-anomer	positive
L or β	α-anomer	positive
L or β	β-anomer	negative

Experimental

The nitrates of glucose were prepared according to the literature. The rotatory dispersion was measured with a Rudolph spectropolarimeter over the region from 250 to 700 mμ. The ultraviolet absorption was measured with a self-recording spectrophotometer of the Hitachi EPU-II type. The dispersion constants of the Drude equation were calculated from the data by means of the least-square method with an electronic computer of the Fuji FACOM 201 type.

2, 3, 4, 6-Tetra-*O*-acetyl-1-*O*-nitro-α-D-glucopyranose (Compound I).[5]—Colorless prisms and plates; m. p. 150.5—151°C. The RD was measured at 21°C in chloroform (c 1.0100). $[\alpha]_{700}^{21}$ +103°, $[\alpha]_{589}$ +151°, $[\alpha]_{500}$ +222°, $[\alpha]_{400}$ +382°, $[\alpha]_{300}$ +832°, $[\alpha]_{285}$ +921° (peak), $[\alpha]_{270}$ +844°, $[\alpha]_{260}$ +790°.

2, 3, 4, 6-Tetra-*O*-acetyl-1-*O*-nitro-β-D-glucopyranose (Compound II).[5]—Colorless needles; m. p. 86°C. The RD was measured at 21°C in chloroform (c 1.142). $[\alpha]_{650}^{21}$ −0.110°, $[\alpha]_{589}$ −1.37°, $[\alpha]_{500}$ −1.52°, $[\alpha]_{400}$ −4.50°, $[\alpha]_{300}$ −60.4° (trough), $[\alpha]_{280}$ +2.63°, $[\alpha]_{260}$ +262°.

1, 3, 4, 6-Tetra-*O*-acetyl-2-*O*-nitro-β-D-glucopyranose (Compound V).[6]—Colorless needles; m. p. 121—122°C. The RD was measured at 21°C in chloroform (c 1.3930). $[\alpha]_{700}^{21}$ +13.2°, $[\alpha]_{600}$ +19.1°, $[\alpha]_{589}$ +20.2°, $[\alpha]_{500}$ +27.6°, $[\alpha]_{400}$ +48.9°, $[\alpha]_{300}$ +165°, $[\alpha]_{290}$ 173° (peak), $[\alpha]_{270}$ +149°.

5) E. Fischer and E. F. Armstrong, *Ber.*, **34**, 975 (1901).
6) M. L. Wolfrom, A. Thompson and O. R. Lineback, *J. Org. Chem.*, **28**, 1930 (1963).

3,4,6-Tri-*O*-acetyl-2-*O*-nitro-β-D-glucopyranosyl Chloride (Compound VI).[7]—Colorless needles; m. p. 138°C. The RD was measured at 21°C in chloroform (*c* 0.9006). $[\alpha]_{700}^{21}$ +14.0°, $[\alpha]_{589}$ +19.1°, $[\alpha]_{500}$ +27.9°, $[\alpha]_{400}$ +49.3°, $[\alpha]_{300}$ +159°, $[\alpha]_{295}$ +165°(peak), $[\alpha]_{270}$ +5.55°, $[\alpha]_{260}$ −100°.

Methyl 4:6-*O*-Ethylidene-β-D-glucopyranoside 2-Nitrate (Compound VII).[8]—Colorless needles; m. p. 143—144°C. The RD was measured at 21°C in chloroform (*c* 0.5880). $[\alpha]_{700}^{21}$ −34.1°, $[\alpha]_{589}$ −44.6°, $[\alpha]_{400}$ −101°, $[\alpha]_{340}$ −131° (broad extreme), $[\alpha]_{305}$ −83.7°(peak), $[\alpha]_{280}$ −183°, $[\alpha]_{265}$ −402°.

Methyl 4:6-*O*-Ethylidene-β-D-glucopyranoside 3-nitrate (Compound IX).[8]—Colorless needles; m. p. 145.5—146°C. The RD was measured at 21°C in chloroform (*c* 0.8740). $[\alpha]_{700}^{21}$ −19.3°, $[\alpha]_{589}$ −26.0°, $[\alpha]_{500}$ −37.9°, $[\alpha]_{400}$ −61.2°, $[\alpha]_{300}$ −111°, $[\alpha]_{290}$ −118°(trough), $[\alpha]_{260}$ −44.6°.

Methyl 4:6-*O*-Ethylidene-α-D-glucopyranoside 2:3-Dinitrate (Compound X).[9]—Colorless needles; m. p. 100—101°C. The RD was measured at 21°C in chloroform (*c* 2.492). $[\alpha]_{700}^{21}$ +98.6°, $[\alpha]_{589}$ +141°, $[\alpha]_{500}$ +201°, $[\alpha]_{400}$ +330°, $[\alpha]_{320}$ +494° (broad extreme), $[\alpha]_{300}$ +477°, (peak), $[\alpha]_{270}$ +1261°.

Methyl 4:6-*O*-Ethylidene-β-D-glucopyranoside 2:3-Dinitrate (Compound XI).[9]—Colorless prisms; m. p. 88—89°C. The RD was measured at 20.5°C in chloroform (*c* 1.0182). $[\alpha]_{700}^{20.5}$ −15.3°, $[\alpha]_{589}$ −21.6°, $[\alpha]_{500}$ −28.5°, $[\alpha]_{400}$ −38.7°(broad extreme), $[\alpha]_{330}$ +8.15°, $[\alpha]_{297.5}$ +142°(peak), $[\alpha]_{280}$ +19.6°, $[\alpha]_{270}$ −189°.

Methyl 4:6-*O*-Benzylidene-β-D-glucopyranoside 2:3-Dinitrate (Compound XIII).—This compound was obtained by the same procedure as was used in the case of compound XII,[1] but the reaction temperature was from −5 to −10°C. The compound was identified by means of its ultraviolet spectrum, its infrared spectrum and its analytical value. Colorless prisms; m. p. 163°C. The RD was measured at 21°C in tetrahydrofuran (*c* 1.2756). $[\alpha]_{700}^{21}$ −40.3°, $[\alpha]_{589}$ −59.0°, $[\alpha]_{500}$ −80.2°, $[\alpha]_{400}$ −140°, $[\alpha]_{337.5}$ −201° (broad extreme), $[\alpha]_{308}$ 178° (peak), $[\alpha]_{300}$ −192°, $[\alpha]_{270}$ −772°.

Methyl 2,3,6-Tri-*O*-acetyl-4-*O*-nitro-β-D-glucopyranoside (Compound XIV).[9]—Colorless needles; m. p. 113.5°C. The RD was measured at 20.8°C in chloroform (*c* 1.0644). $[\alpha]_{700}^{20.8}$ −19.8°, $[\alpha]_{589}$ −26.3°, $[\alpha]_{500}$ −39.8°, $[\alpha]_{400}$ −64.3°, $[\alpha]_{325}$ −90.5° (broad extreme), $[\alpha]_{300}$ −76.1°(peak), $[\alpha]_{280}$ −106°, $[\alpha]_{265}$ −181°.

Methyl 2,3-Di-*O*-acetyl-4,6-di-*O*-nitro-β-D-glucopyranoside (Compound XV).[10]—Colorless needles; m. p. 116°C. The RD was measured at 21°C in chloroform (*c* 1.7118). $[\alpha]_{700}^{21}$ −8.00°, $[\alpha]_{589}$ −10.2°, $[\alpha]_{500}$ −13.4°, $[\alpha]_{420}$ −16.2°(broad extreme), $[\alpha]_{350}$ −5.26°, $[\alpha]_{300}$ +77.7°, $[\alpha]_{295}$ +82.4°(peak), $[\alpha]_{275}$ +3.51°.

Methyl 2,3,4-Tri-*O*-acetyl-6-*O*-nitro-α-D-glucopyranoside (Compound XVI)[11]—Colorless prisms; m. p. 112—113°C. The RD was measured at 21°C in chloroform (*c* 1.1437). $[\alpha]_{700}^{21}$ +89.9°, $[\alpha]_{589}$ +131°, $[\alpha]_{500}$ +190°, $[\alpha]_{400}$ +316°, $[\alpha]_{300}$ +589°, $[\alpha]_{250}$ +1159°.

Pentaacetyl-β-D-glucopyranose (Compound XVIII).[12]—Colorless needles; m. p. 132°C. The RD was measured at 21°C in chloroform (*c* 2.1320). $[\alpha]_{700}^{21}$ +4.36°, $[\alpha]_{589}$ +6.47°, $[\alpha]_{500}$ +9.05°, $[\alpha]_{400}$ +16.8°, $[\alpha]_{300}$ +44.2°.

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