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The Rotatory Dispersion and Stereochemistry of Organic Compounds. XII.[1] The Circular Dichroism of Hexose Nitrates

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Circular dichroism has been measured of eighteen nitrates of hexoses (glucose, mannose and altrose), and its correlation with the rotatory dispersion as well as the ultraviolet absorption has been established, verifying even a number of suggestions made as regards the sign of some ambiguous Cotton effects (Tsuzuki et al., This Bulletin, **39**, 1391 (1966)), which has eventually led to some significant conclusions.

It was reported for the first time by Mitchell[2] that nitrochromophore ($-NO_2$) is of significance in the studies of rotatory dispersion (RD). Some interesting results were really shown with several nitro-compounds,[3,4] and recently investigations were made on the rotatory dispersion, circular dichroism (CD) and ultraviolet absorption (UV) of a number of compounds containing nitrochromophore.[5,6] Thanks to these studies, the NO_2-chromophore proved to be quite useful in investigating configurational problems for organic compounds. Particularly comparison of CD and UV was found advantageous to the analysis of complex or obscure Cotton effects.

As already reported,[1,7-9] the nitrate chromophore exhibited an optically active absorption and proved to be of great use to the configurational studies of sugars and hydroxy-carboxylic acids, especially with respect to the conformation and optical contribution of the hydroxyl groups.

The rotatory dispersion of compounds with nitrate chromophore exhibits a Cotton effect around 300 mμ, but its absorption is so weak that it becomes often difficult in sugar derivatives to discern the character of the Cotton effect, since it is overlapped by the strong, background optical rotation, particularly due to the C_1- and C_2 groups.

In a previous paper[1] some RD curves were analyzed and the Cotton effects were characterized with the help of the corresponding CD studies. The present authors will deal in this paper with CD measurement of a number of related compounds shown in Table I, whose RD studies were already published, and will confirm their views expressed on the correlation between the rotatory dispersion and stereochemistry of these compounds by studying comparatively the RD and CD curves together with the ultraviolet absorption curves, and further will inquire into the relation between the ultraviolet absorption and the steric influence.

1) Part XI. Y. Tsuzuki, K. Tanabe, K. Okamoto and N. Yamada, This Bulletin, **39**, 1391 (1966).
2) S. Mitchell and R. R. Gordon, *J. Chem. Soc.*, **1936**, 853.
3) N. Kornblum, L. Fishbein and R. A. Smiley, *J. Am. Chem. Soc.*, **77**, 6261 (1955).
4) A. Bowers, M. B. Sanchez and H. T. Ringold, ibid., **81**, 3702 (1959).
5) K. Mislow, E. Bunnenberg, R. Records, K. Wellman and C. Djerassi, ibid., **85**, 1342 (1963).
6) C. Djerassi, H. Wolf and E. Bunnenberg, ibid., **85**, 2835 (1963).
7) Y. Tsuzuki, K. Tanabe and K. Okamoto, This Bulletin, **38**, 274 (1965).
8) Y. Tsuzuki, K. Tanabe and K. Okamoto, ibid., **39**, 1387 (1966).
9) Y. Tsuzuki, K. Tanabe, K. Okamoto and M. Fukubayashi, ibid., **39**, 1391 (1966).

Results and Discussion

In Fig. 1 are given the RD and CD curves of the α-C_1-nitrate of glucopyranose (I), where those of galactopyranoside (II)[1] are reproduced for comparison's sake. The agreement of these two compounds in sign of circular dichroism undoubtedly indicates that the Cotton effect is due to the α-C_1-ONO_2 chromophore. That the peak of CD (II, 263.5 mμ) is a little red-shifted as compared with that of CD (I, 273 mμ) is to be attributed to the steric effect of the C_4-OAc group of L-configuration in the galactoside (II).

In Fig. 2 are shown the RD and CD curves of 1, 3, 4, 6-tetra-*O*-acetyl-2-*O*-nitro-α-D-glucopyranoside (III) and those of its anomer (IV). The CD (III) has a negative sign, which confirms the view[7] that the RD curve (III) shows a negative Cotton effect. The CD (IV) exhibits a positive sign in agreement with the positive Cotton effect (IV). The CD curves III and IV are nearly equal in optical rotatory strength, both originating in the C_2-ONO_2 chromophore of D-type, but they are opposite in sign, that is undoubtedly attributed to the respective α- and β-form of the C_1-OAc

Table I. Nitrate compounds

Number	Name
I[1]	2,3,4,6-Tetra-*O*-acetyl-1-*O*-nitro-α-D-glucopyranose
II[8]	2,3,4,6-Tetra-*O*-acetyl-1-*O*-nitro-α-D-galactopyranose
III[7]	1,3,4,6-Tetra-*O*-acetyl-2-*O*-nitro-α-D-glucopyranose
IV[8]	1,3,4,6-Tetra-*O*-acetyl-2-*O*-nitro-β-D-glucopyranose
V[8]	Methyl 4 : 6-*O*-ethylidene-β-D-glucopyranoside 3-nitrate
VI[1]	1,2:5,6-Diisopropylidene-3-*O*-nitro-α-D-glucofuranose
VII[1]	Methyl 4 : 6-*O*-benzylidene-α-D-altropyranoside 3-nitrate
VIII[8]	Methyl 2,3,6-tri-*O*-acetyl-4-*O*-nitro-β-D-glucopyranoside
IX[8]	Methyl 2,3,4-tri-*O*-acetyl-6-*O*-nitro-α-D-glucopyranoside
X[8]	Methyl 4 : 6-*O*-ethylidene-α-D-glucopyranoside 2 : 3-dinitrate
XI[8]	Methyl 4 : 6-*O*-ethylidene-β-D-glucopyranoside 2 : 3-dinitrate
XII[1]	Methyl 4 : 6-*O*-ethylidene-α-D-mannopyranoside 2 : 3-dinitrate
XIII[1]	Methyl 4 : 6-*O*-benzylidene-α-D-altropyranoside 2 : 3-dinitrate
XIV[1]	Methyl 6-*O*-acetyl-2,3,4-tri-*O*-nitro-β-D-glucopyranoside
XV[8]	Methyl 2,3-di-*O*-acetyl-4 : 6-di-*O*-nitro-β-D-glucopyranoside
XVI[1]	Methyl 2,3,4,6-tetra-*O*-nitro-β-D-glucopyranoside
XVII[1]	Methyl 2,3,4,6-tetra-*O*-nitro-α-D-glucopyranoside
XVIII	1,2,3,4,6-Penta-*O*-nitro-α-D-glucopyranose

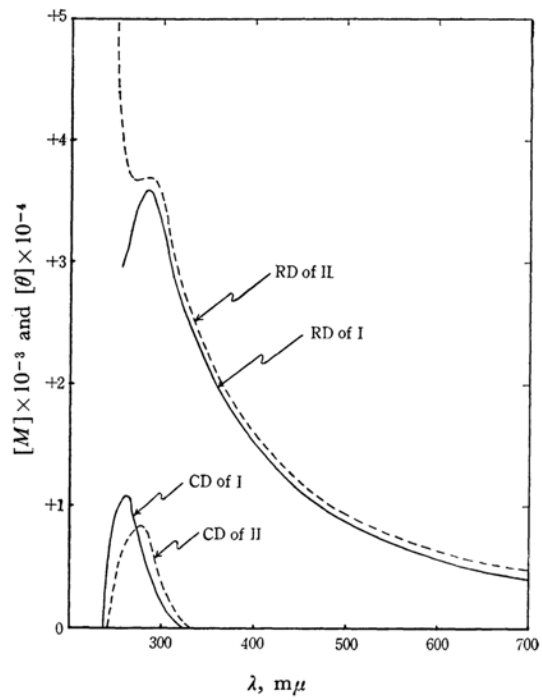

Fig. 1. RD and CD of C_3-nitrates of glucose (I) and galactose (II).

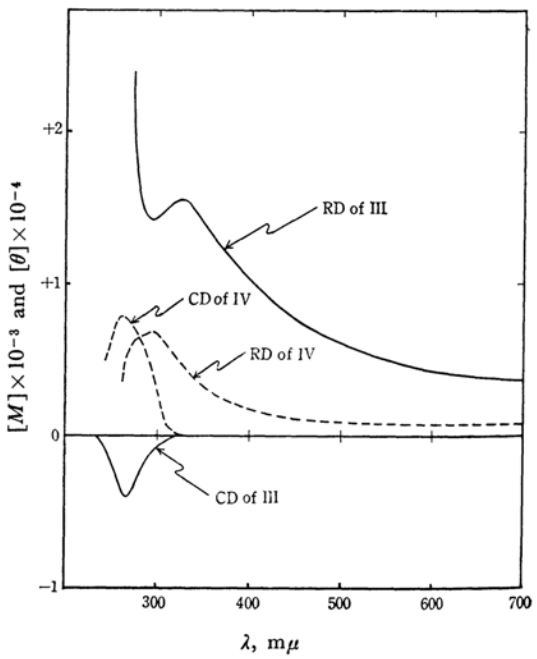

Fig. 2. RD and CD of C_2-nitrate of glucose.

group, which predominates over others in optical rotation.

Figure 3 shows the CD curves of three C_3-nitrates (V–VII), and reproduces their RD curves. Small as its ellipticity is, the CD curve (V) of methyl 4 : 6-*O*-ethylidene-*β*-D-glucopyranoside is negative in sign. The RD curve was discussed in a previous paper[8] to have a negative Cotton effect by analyzing the curve with the help of Drude equation as well as configurational studies.

The positive CD (VI) of 1, 2 : 5. 6-diisopropylidene-3-*O*-nitro-*α*-D-glucofuranose is consistent

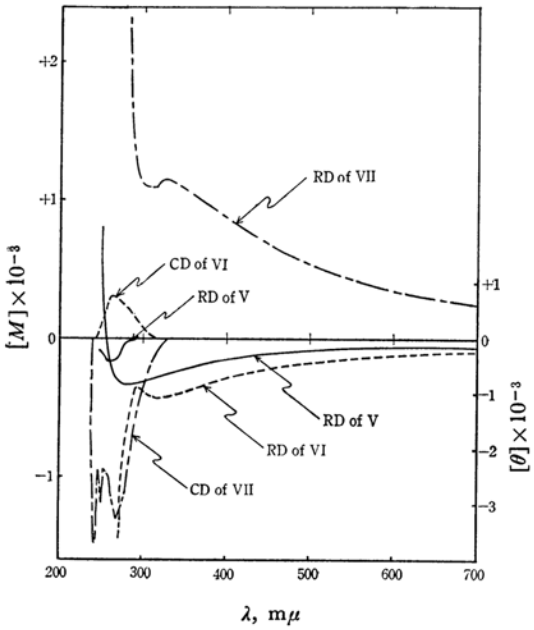

Fig. 3. RD and CD of C_3-nitrate of hexoses.

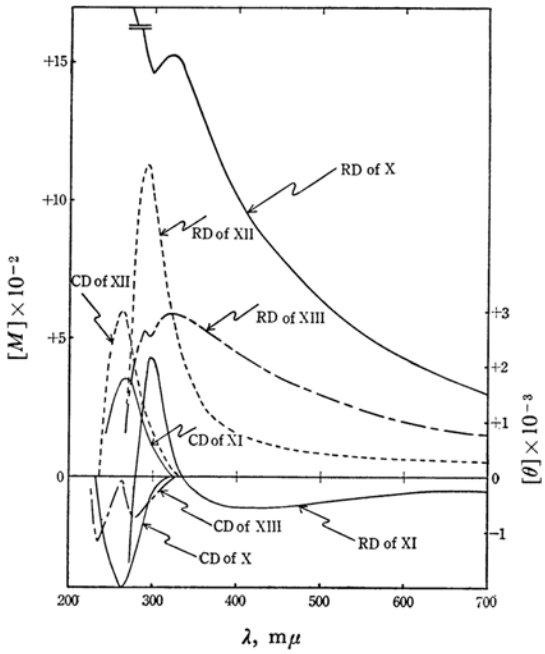

Fig. 5. RD and CD of 2,3-dinitrates of hexoses.

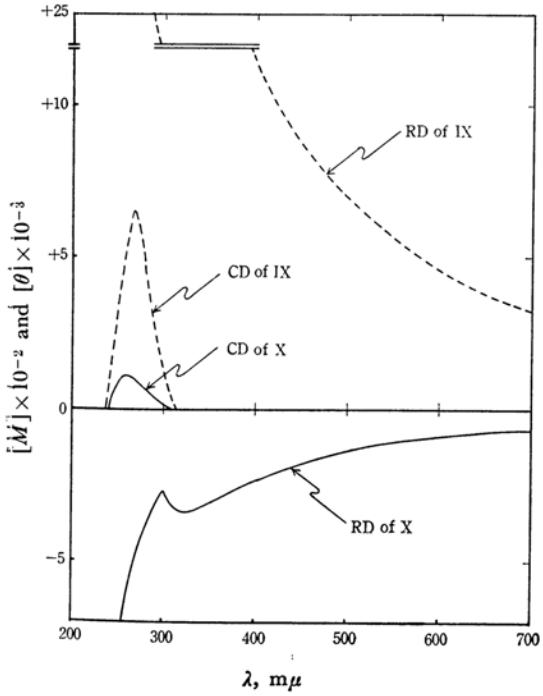

Fig. 4. RD and CD of C_4-nitrate (VIII) and C_5-nitrate (IX) of glucose.

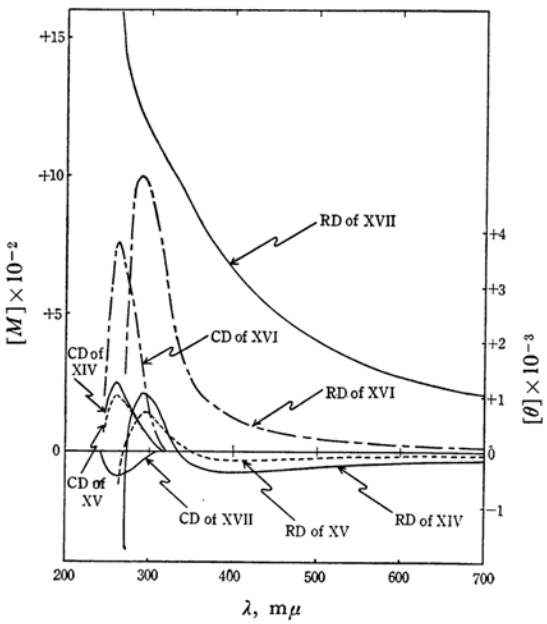

Fig. 6. RD and CD of di-(XV), tri-(XIV) and tetranitrates (XVI, XVII) of methyl glucopyranosides.

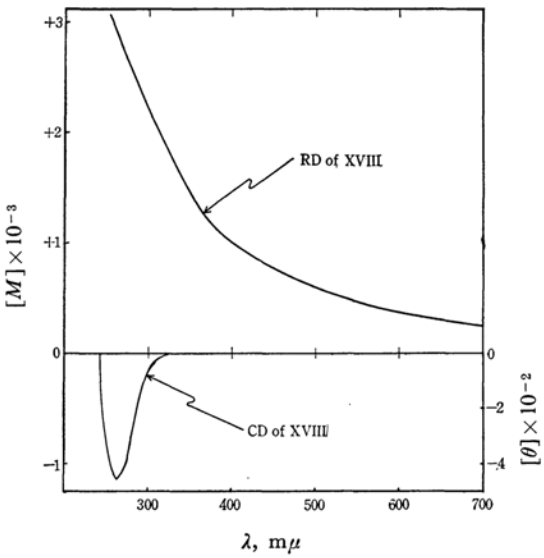

Fig. 7. RD and CD of pentanitrates of glucopyranose.

with the weakly positive Cotton effect (RD VI). The ellipticity is smaller in C_3-nitrates (V and VI) than in C_1-nitrate (Fig. 1) and in C_2-nitrate (Fig. 2). The complex circular dichroism of 4 : 6-*O*-benzylidene-α-D-altropyranoside 3-nitrate (VII) has a negative sign, one of the peaks of which (270 mμ) may be associated with the negative Cotton effect appearing in the RD curve as already demonstrated.[1] The negative maximum 242 mμ exhibited in the CD curve (VII) is due to the benzylidene radical, qualified by the D-configuration of C_4.[10]

In Fig. 4 are exhibited the RD and CD of glucopyranose C_4-nitrate (VIII) and C_6-nitrate (IX). The positive circular dichroism (VIII) now justifies the dicision of the weak Cotton effect (RD VIII) to be positive in sign.[8]

As already reported, the C_6-nitrate (IX) shows a nearly plain dispersion curve[8] and only a shoulder in the UV absorption spectrum in the region 265 to 280 mμ, but displays a distinct circular dichroism of positive sign at 267 mμ. This suggests the existence of an optically active absorption in this region, although hidden by the strong background rotation of α-methylglucopyranoside.

The positive sign of this "hidden" Cotton effect can be expected from the rule proposed by the present authors in a previous paper,[1] which states that the Cotton effect due to a nitrate of the β-configuration in α-glucosides is positive, for the C_6-nitrate in this case is linked to the β-configurated C_5-atom.

In Fig. 5 are given the RD and CD curves of some C_2, C_3-dinitrates of hexose derivatives (X-XIII). As already demonstrated[1,8] the sign of the Cotton effect due to the chromophore is controlled and determined in di-, tri- as well as tetranitrates always by the configuration of the asymmetric center, which contributes most strongly to optical rotation. The rotatory dispersion of methyl 4 : 6 - *O* -ethylidene - α - D-glucopyranoside 2 : 3-dinitrate (X) exhibits a weakly negative Cotton effect[8] because of the C_2-chromophore of D-configuration in the α-series, regularly contributing to negative rotation. And the distinct, negative circular dichroism really supports this conclusion.

On the contrary its anomer (XI) shows a positive Cotton effect,[8] being dominated by the C_2-chromophore in the β-series, quite in harmony with the positive circular dichroism (XI).

By comparing the compounds X and XI with each other in circular dichroism, it will be noted that their CD curves take a form of symmetry, because they are associated primarily with the optically active absorption due to the C_2-chromophore. However, methyl 4 : 6-*O*-ethylidene-α-D-mannopyranoside 2 : 3-dinitrate (XII) exhibits a positive Cotton effect,[1] which is further evidenced by the positive circular dichroism (Fig. 5).

The ellipticity of compound XII is large as compared with that of compound XI, since the C_2- and C_3-chromophores both contribute to positive rotation in compound II, while the C_2- and C_3-chromophores of compound XI are respectively a positive and a negative contributor, so that its circular dichroism becomes less positive.

In Fig. 5 are reproduced the RD and CD curves of methyl 4 : 6-*O*-benzylidene-α-D-altropyranoside 2 : 3-dinitrate (XIII) already reported.[1] Here it should be pointed out that a negative maximum appears in circular dichroism at 240 mμ characteristic of the benzylidene group, which may be due to the C_4-contribution, as observed in another benzylidene derivative (VII, Fig. 3).

Figure 6 exhibits the RD and CD curves of the di-, tri- and tetra-nitrates of glucopyranose (XIV—XVII). The positive circular dichroism (XIV) confirms the sign of the Cotton effect (RD XIV) of methyl 6-*O*-acetyl-2, 3, 4-tri-*O*-nitro-β-D-glucopyranoside (XIV) which was determined to be positive. This rotatory dispersion was dominated by the dextro-rotatory C_2-chromophore, which is characteristic of the D-configuration in the β-glucoside. Methyl 2, 3-di-*O*-acetyl-4, 6-di-*O*-nitro-β-D-glucopyranoside (XV) also shows a positive Cotton effect, the sign of which is verified by the positive circular dichroism (XV). This Cotton effect can be explained in the following way: in the α-glucoside the D-configurated C_4-chromophore contributes to positive rotation, and although the C_5-asymmetric center contributes to negative one, as may be expected from the behavior of

10) The RD of compounds containing benzene ring has recently been reported to display Cotton effect in the region 258 to 260 mμ. L. Verbit, *J. Am. Chem. Soc.*, **87**, 1617 (1965).

C_6-nitrate (IX), the former predominates over the latter in the absorption region. The positive Cotton effect of methyl 2, 3, 4, 6-tetra-*O*-nitro-β-D-glucopyranoside (XVI)[1] agrees, as shown in Fig. 6, with the CD (XVI) in sign, and its anomer (XVII) on the contrary exhibits a negative circular dichroism (267 mμ). Although the RD curve (XVII) presents only a slight shoulder in the region from 285 to 325 mμ, it was interpreted to have a negative Cotton effect due to the C_2–ONO_2 chromophore overlapped by the stronger α-glucosidic positive rotation. Thus the interpretation has now been confirmed by the CD measurement.

In Fig. 7 is given the RD curve of penta-*O*-nitro-α-D-glucopyranose (XVIII), which shows a more or less apparent anomaly about 285 to 315 mμ, though no distinct Cotton effect can be observed. The compound XVIII exhibits a negative circular dichrosim (Fig. 7), probably because the dominant C_2–ONO_2 effect in this α-glucoside series becomes negative in sign.

As may be seen from Figs. 5, 6 and 7 the C_2-chromophore always determines the circular dichroism as well as the rotatory dispersion excepting the cases where steric hindrance interferes, since the C_2-group is most influential in the optical rotation of these sugars.

Conclusions

1) Anomalous rotatory dispersion curves of sugar nitrates have been analyzed and verified by CD measurement, the wavelength of CD_{max} always coinciding with the region of the ultraviolet absorption.

2) The CD_{max} of sugar nitrates lies in the region 260 to 270 mμ, and is red-shifted by steric hindrance.

3) The C_6-nitrates of the α-series (glycosides) exhibit positive circular dichroism, in accordance with the rule found by the present authors,[1] since the C_5-configuration is of L-type.

4) Each anomer has an ellipticity of nearly equal strength.

5) The contribution to the ellipticity conforms to the order of the rotatory contribution, namely,

$$C_2 > C_3 > C_4 > C_5$$

Experimental

The circular dichroism was measured with a JASCO optical rotatory dispersion recorder of the ORD/UV-5 type at 25° to 30°C in chloroform (but XVIII in ethanol) in the wavelength region from 350 to 230 mμ. The rotatory dispersion was measured with a Rudolph spectropolarimeter.

2, 3, 4, 6-Tetra-*O*-acetyl-1-*O*-nitro-α-D-galactopyranose (compound I): $[\theta]_{330}$ 0, $[\theta]_{300}$ +9.37, $[\theta]_{270}$ +25.4, $[\theta]_{250}$ +4.67, $[\theta]_{248}$ 0 (*c*, 0.2356).

2, 3, 4, 6-Tetra-*O*-acetyl-1-*O*-nitro-α-D-glucopyranose (compound II): $[\theta]_{330}$ 0, $[\theta]_{300}$ +18.1, $[\theta]_{267}$ +64.1, $[\theta]_{250}$ +25.7, $[\theta]_{240}$ 0 (*c*, 0.3901).

1, 3, 4, 6-Tetra-*O*-acetyl-2-*O*-nitro-α-D-glucopyranose (compound III): $[\theta]_{315}$ 0, $[\theta]_{300}$ −7.35, $[\theta]_{266}$ −56.7, $[\theta]_{250}$ −42.9, $[\theta]_{240}$ 0 (*c* 0.3205).

1, 3, 4, 6-Tetra-*O*-acetyl-2-*O*-nitro-β-D-glucopyranose (compound IV): $[\theta]_{330}$ 0, $[\theta]_{300}$ +17.2, $[\theta]_{260}$ +39.5, $[\theta]_{250}$ +33.4 (*c* 0.7534).

Methyl 4 : 6-*O*-ethylidene-β-D-glucopyranoside 3-nitrate (compound V): $[\theta]_{290}$ 0, $[\theta]_{270}$ −1.93, $[\theta]_{260}$ −2.42 (*c* 0.4382).

1, 2 : 5, 6-Diisopropylidene-3-*O*-nitro-α-D-glucofuranose (compound VI): $[\theta]_{320}$ 0, $[\theta]_{300}$ +2.91, $[\theta]_{262}$ +26.3, $[\theta]_{250}$ +8.30, $[\theta]_{248}$ 0, (*c* 0.7362).

Methyl 4 : 6-*O*-benzylidene-α-D-altropyranoside 3-nitrate (compound VII): $[\theta]_{330}$ 0, $[\theta]_{300}$ −4.45, $[\theta]_{270}$ −12.4, $[\theta]_{255}$ −6.68, $[\theta]_{244}$ −14.2, $[\theta]_{240}$ 0 (*c* 0.3681).

Methyl 2,3,6-tri-*O*-acetyl-4-*O*-nitro-β-D-glucopyranoside (compound VIII): $[\theta]_{315}$ 0, $[\theta]_{300}$ +5.00, $[\theta]_{260}$ +31.5 (*c* 0.4755).

Methyl 2,3,4-tri-*O*-acetyl-6-*O*-nitro-α-D-glucopyranoside (compound IX): $[\theta]_{310}$ 0, $[\theta]_{290}$ +4.42, $[\theta]_{267}$ +9.95, $[\theta]_{250}$ +5.54, $[\theta]_{240}$ 0 (*c* 4.944).

Methyl 4 : 6-*O*-ethylidene-α-D-gluxopyranoside 2 : 3-dinitrate (compound X): $[\theta]_{320}$ 0, $[\theta]_{300}$ −6.83, $[\theta]_{263}$ −61.1, $[\theta]_{250}$ −50.8, $[\theta]_{240}$ −17.6 (*c* 0.6358).

Methyl 4 : 6-*O*-ethylidene-β-D-glucopyranoside 2 : 3-dinitrate (compound XI): $[\theta]_{325}$ 0, $[\theta]_{300}$ +13.4, $[\theta]_{265}$ +55.2, $[\theta]_{250}$ +44.2, $[\theta]_{240}$ +22.7 (*c* 0.6610).

Methyl 4 : 6-*O*-ethylidene-α-D-mannopyranoside 2 : 3-dinitrate (compound XII): $[\theta]_{330}$ 0, $[\theta]_{300}$ +17.4, $[\theta]_{261}$ +90.5, $[\theta]_{250}$ +66.7, $[\theta]_{240}$ 0 (*c* 0.4293).

Methyl 4 : 6-*O*-benzylidene-α-D-altropyranoside 2 : 3-dinitrate (compound XIII): $[\theta]_{310}$ 0, $[\theta]_{300}$ −2.84, $[\theta]_{280}$ −11.2, $[\theta]_{267}$ −2.65, $[\theta]_{258}$ +2.00, $[\theta]_{250}$ −9.86, $[\theta]_{240}$ −74.0, $[\theta]_{235}$ 0 (*c* 0.9829).

Methyl 6-*O*-acetyl-2, 3, 4-tri-*O*-nitro-β-D-glucopyranoside (compound XIV): $[\theta]_{330}$ 0, $[\theta]_{300}$ +6.65, $[\theta]_{260}$ +32.7, $[\theta]_{253}$ +30.4 (*c* 0.6596).

Methyl 2, 3-di-*O*-acetyl-4, 6-di-*O*-nitro-β-D-glucopyranoside (compound XV): $[\theta]_{340}$ 0, $[\theta]_{300}$ +6.04, $[\theta]_{258}$ +31.4, $[\theta]_{254}$ +30.9 (*c* 0.7627).

Methyl 2, 3, 4, 6-tetra-*O*-nitro-α-D-glucopyranoside (compound XVI): $[\theta]_{310}$ 0, $[\theta]_{300}$ −3.19, $[\theta]_{270}$ −20.2, $[\theta]_{250}$ −16.0, $[\theta]_{243}$ 0 (*c* 0.5860).

Methyl 2, 3, 4, 6-tetra-*O*-nitro-β-D-glucopyranoside (compound XVII): $[\theta]_{322}$ 0, $[\theta]_{300}$ +8.68, $[\theta]_{260}$ +30.8 (*c* 0.4740).

1, 2, 3, 4, 6-Penta-*O*-nitro-α-D-glucopyranose (compound XVIII):[11] Colorless syrup. The RD was measured at 22°C in ethanol (*c* 0.9852). $[\alpha]^{22}_{700}$ +69.7°, $[\alpha]_{589}$ +99.1°, $[\alpha]_{500}$ +143°, $[\alpha]_{400}$ +244°, $[\alpha]_{360}$ +318°, $[\alpha]_{320}$ +439°, $[\alpha]_{300}$ +524°, $[\alpha]_{290}$ +556°, $[\alpha]_{280}$ +597°.

$[\theta]_{312}$ 0, $[\theta]_{310}$ −13.8, $[\theta]_{290}$ −138, $[\theta]_{260}$ −468, $[\theta]_{245}$ 0.

The authors owe the CD measurement to the Japan Spectroscopic Co., Ltd.

11) W. Will and F. Lenze, *Ber.*, **31**, 74 (1898).