Note

Nitrogen-containing carbohydrate derivatives. Part VI*. Synthesis and circular dichroism of 1,2-dideoxy-1-nitro alcohols†

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INTRODUCTION

In previous papers[1–4], we reported the relationship of the sign of the maxima of the circular dichroism (c.d.) and that of the Cotton effects of the optical rotatory dispersion (o.r.d.) curves of carbohydrate C-nitro alcohols (1-deoxy-1-nitro alcohols) to the configuration at C-2, which is the nearest asymmetric carbon atom to the nitro chromophore group.

The present paper is concerned with the synthesis and the c.d. of 1,2-dideoxy-1-nitro alcohols in which C-2 is not asymmetric and C-3 is the nearest asymmetric carbon to the nitro group. The c.d. and the o.r.d. curves of these compounds were examined and the relationship between the configuration at C-3 and the signs of the c.d. maxima and the Cotton effects is reported.

RESULTS AND DISCUSSION

Five 1,2-dideoxy-1-nitro alcohols, *i.e.*, 1,2-dideoxy-1-nitro-D-*arabino*-hexitol[5] (**1**), 1,2-dideoxy-1-nitro-D-*manno*-heptitol (**2**), 1,2-dideoxy-1-nitro-D-*ribo*-hexitol[6] (**3**), 1,2-dideoxy-1-nitro-D-*xylo*-hexitol (**4**), and 1,2-dideoxy-1-nitro-D-*galacto*-heptitol (**5**) were synthesized according to the methods of Sowden and Fischer,[5] and Shechter *et al.*[7]. In these methods, peracetates of 1-deoxy-1-nitro alcohols are converted into the nitroölefin derivatives of acetoxyalkanes, hydrogenated in the presence of palladium-black[5] or sodium borohydride[7] to peracetates of 1,2-dideoxy-1-nitro alcohols, and then deacetylated.

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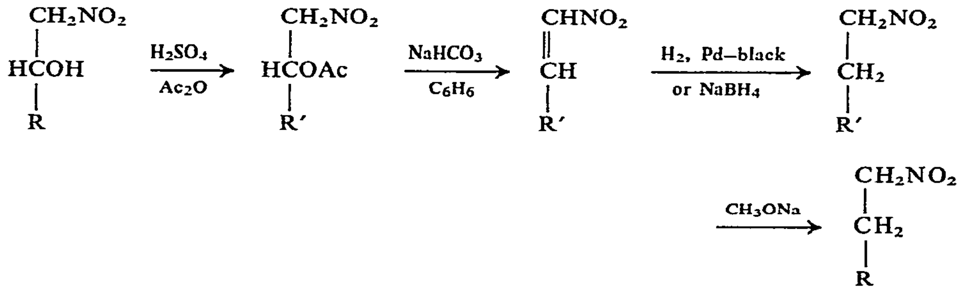


The configuration at C-3 of compounds **1**–**5** is kept unchanged in the final products, C-3 thus becoming the nearest asymmetric carbon to the chromophore group. The presence of the nitro and hydroxyl groups and the absence of the acetoxyl group or the olefinic bond were confirmed by the i.r. and the u.v. absorption spectra.

The u.v. absorption spectra, and c.d. and o.r.d. curves of **1**, **2**, **3**, **4**, and **5** are shown in Fig. 1 and the values of c.d. maxima are reported in Table I. The u.v. absorption spectra of the five compounds show a shoulder in the 260–280 n.m. region. The c.d. curves show two maxima of the same sign at about 310 nm and 265 nm, negative for **1** and **2**, and positive for **3**, **4**, and **5**. The maximum at about 310 nm seems to be associated with the very weak Cotton effect of the o.r.d. curves, but it is difficult to recognize this Cotton effect, especially in the curves of **4** and **5**, since it overlaps with the background curve.

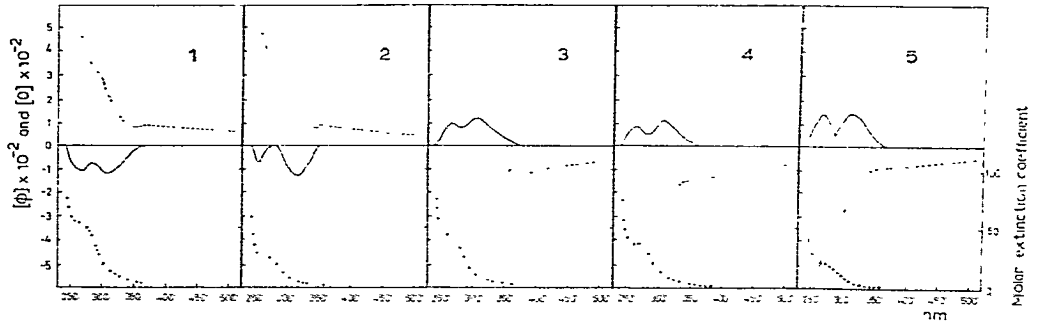


Fig. 1. Circular dichroism (————), optical rotatory dispersion (— — — —), and ultraviolet absorption (+ — + — + —) curves of 1,2-dideoxy-1-nitro-D-*arabino*-hexitol (**1**), 1,2-dideoxy-1-nitro-D-*manno*-heptitol (**2**), 1,2-dideoxy-1-nitro-D-*ribo*-hexitol (**3**), 1,2-dideoxy-1-nitro-D-*xylo*-hexitol (**4**), and 1,2-dideoxy-1-nitro-D-*galacto*-heptitol (**5**) in water.

In **1** and **2**, the hydroxyl group at C-3 is on the left in the conventional Fischer projection formula, whereas in **3**, **4**, and **5**, it is on the right. Thus, the following rules relating the signs of the c.d. maxima of these compounds to the configuration at C-3 may be established, as it was previously done for the configuration at C-2 of 1-deoxy-1-nitro alcohols[1–4]:

1. 1,2-Dideoxy-1-nitro alcohols that have a hydroxyl group on the left side of C-3 in the conventional Fischer projection formula show negative c.d. maxima at

TABLE I

CIRCULAR DICHROISM MOLECULAR ELLIPTICITY OF 1,2-DIDEOXY-1-NITRO ALCOHOLS

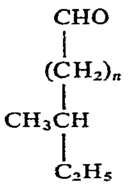
1,2-Dideoxy-1-nitro derivative	*Wavelength (nm)*	$[\theta]$
D-*arabino*-Hexitol (**1**)	308	−116
	266	−106
D-*manno*-Heptitol (**2**)	315	−127
	255	−70
D-*ribo*-Hexitol (**3**)	304	+122
	265	+100
D-*xylo*-Hexitol (**4**)	308	+115
	265	+86
D-*galacto*-Heptitol (**5**)	308	+146
	265	+146

about 310 nm and 265 nm, whereas those having the hydroxyl group on the right side show positive c.d. maxima.

2. The configuration of other asymmetric centers do not contribute significantly to the sign of the ellipticity.

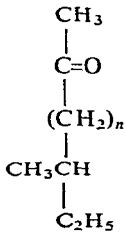
However, the values of the ellipticity of these compounds are from one tenth to one twentieth of those of 1-deoxy-1-nitro alcohols. This decrease of the ellipticity suggests that the decrease of the contribution of the configuration at C-3 to the nitro chromophore is due to the presence of two methylene groups between the nitro chromophore and the nearest asymmetric carbon atom (C-3).

Similar observations have been reported[8] for the o.r.d. curves of acyclic aldehydes and ketones. Djerassi *et al.*[8] synthesized a homologous series of acyclic aldehydes (**6**) and ketones (**7**) having the asymmetric carbon in the *S*-configuration, and examined their o.r.d. curves.



$\mathrm{CHO{-}(CH_2)_n{-}CH_3CH{-}C_2H_5}$

6



$\mathrm{CH_3{-}C{=}O{-}(CH_2)_n{-}CH_3CH{-}C_2H_5}$

7

Whereas the first ($n = 0$) and second ($n = 1$) members of the aldehyde series exhibited marked positive and negative Cotton effects, respectively, in their o.r.d. curves, the higher homologous aldehyde ($n = 2$) showed only a weak Cotton effect overlapping with the positive background curve. In the ketone series **7**, the anomalous nature of the dispersion curve becomes less pronounced as the distance between the asymmetric center and the ketonic chromophore group increases, and the higher homologs ($n = 3, 4$) showed only plain curves. This effect was named the "distance factor".

As the contribution of the configuration of the asymmetric centers of 1,2-dideoxy-1-nitro alcohols is very small, it is understandable that the sign of the ellipticity or of the Cotton effect of 1-deoxy-1-nitro alcohols depends on the configuration at C-2 and is relatively independent of the configurations of the other asymmetric centers[1,4].

EXPERIMENTAL

General. — Melting points are uncorrected. The o.r.d. and c.d. of 1,2-dideoxy-1-nitro alcohols were measured in aqueous solutions with a JASCO Model ORD/UV-5 automatic recording spectropolarimeter, Nippon Bunko. The u.v. absorption spectra of the same solutions were measured with a Hitachi recording spectrophotometer (Type EPS-2U).

*3,4,5,6-Tetra-*O*-acetyl-1,2-dideoxy-1-nitro-*D-arabino*-hexitol* (**8**). — According to the method of Sowden and Fischer[5], 3,4,5,6-tetra-*O*-acetyl-1-nitro-D-*arabino*-1-hexene[5] (2 g) was reduced in 2:1 (v/v) abs. ethanol–tetrahydrofuran (120 ml) with hydrogen in the presence of palladium-black (200 mg) at room temperature and atmospheric pressure. After one mole of hydrogen had been absorbed, the catalyst was filtered off, and evaporation gave 1.1 g (55%) of crystalline **8**, m.p. 89–91°, after 3 crystallizations from ether, u.v. datum: λ_{max}^{EtOH} 278 nm (ε 40). The u.v. absorption spectrum showed that compound **8** has one nitro but no nitroölefin group (λ_{max}^{EtOH} 230 nm).

Anal. Calc. for $C_{14}H_{21}NO_{10}$: C, 46.27; H, 5.78; N, 3.85. Found: C, 46.63; H, 5.56; N, 3.89.

*1,2-Dideoxy-1-nitro-*D-arabino*-hexitol* (**1**). — To a solution of **8** (700 mg) in methanol (50 ml) was added 0.1M sodium methoxide (1.5 ml), and the mixture was kept for 45 h at room temperature. After addition of water (50 ml), the mixture was neutralized with Dowex-50 (H^+) resin, and the resin was filtered off. Evaporation *in vacuo* of the filtrate gave crystalline **1** (184 mg, 49%), m.p. 124–126° after recrystallization from ethanol; u.v. datum: $\lambda_{shoulder}^{H_2O}$ 280–260 nm (ε 47–55).

Anal. Calc. for $C_6H_{13}NO_6$: C, 36.92; H, 6.72; N, 7.17. Found: C, 36.72; H, 6.52; N, 7.10.

*3,4,5,6,7-Penta-*O*-acetyl-1,2-dideoxy-1-nitro-*D-manno*-heptitol* (**9**). — 3,4,5,6,7-Penta-*O*-acetyl-1-nitro-D-*manno*-1-heptene[9] (1 g) in ethanol (70 ml) was hydrogenated as just described for **8** and the catalyst was filtered off. Evaporation of the filtrate gave a colorless syrup which was dissolved in a small volume of methanol. The solution was kept in the cold, and the crystals appearing were filtered off and washed with methanol–petroleum ether to give crude **9** (770 mg, 73%), showing m.p. 98–99° after 2 recrystallizations from ethanol; u.v. datum: $\lambda_{shoulder}^{dioxane}$ 280–265 nm (ε 47–51).

Anal. Calc. for $C_{17}H_{25}NO_{12}$: C, 46.88; H, 5.79; N, 3.22. Found: C, 47.03; H, 5.71; N, 3.26.

*1,2-Dideoxy-1-nitro-*D-manno*-heptitol* (**2**). — Crude crystalline **9** (2 g) was dissolved in hot methanol (150 ml). To the cooled solution was added 0.2M sodium methoxide (1.4 ml), and the mixture was kept for 20 h at room temperature. It was added to water (150 ml) and neutralized with Dowex-50 (H^+) resin. The resin was filtered off, and the filtrate and washings were evaporated to a syrup which was kept in the cold. The crystals were filtered off, washed with ethanol (840 mg, 81%), and recrystallized from ethanol, m.p. 116–117°; u.v. datum: $\lambda_{max}^{H_2O}$ 273–265 (ε 25).

Anal. Calc. for $C_7H_{15}NO_7$: C, 37.33; H, 6.71; N, 6.21. Found: C, 37.69; H, 6.62; N, 6.25.

*3,4,5,6-Tetra-*O*-acetyl-1,2-dideoxy-1-nitro-*D-ribo-*hexitol* (**10**). — According to the method of Shechter *et al.*[7], a solution of 3,4,5,6-tetra-*O*-acetyl-1-nitro-D-*ribo*-1-hexene[5] (1 g) in 2:3 (v/v) tetrahydrofuran–ethanol (25 ml) was added to a stirred suspension of sodium borohydride (180 mg) in tetrahydrofuran (10 ml) at 0°. The mixture was stirred for 2.5 h at 0° and then acidified at 0° with an aqueous solution (2.5 ml) of acetic acid and urea, obtained[10] by dissolving urea (20.5 g) in 20% aqueous acetic acid (100 ml). After evaporation, a small portion of water was added to the residual syrup and the mixture was extracted with ether. The ether extract was dried with sodium sulfate and then evaporated to give a colorless syrup (785 mg); u.v. datum: λ_{max}^{EtOH} 282 nm (ε 49).

*1,2-Dideoxy-1-nitro-*D-ribo-*hexitol* (3). — To a cooled solution of syrupy **10** (720 mg) in ethanol (20 ml) was added M sodium methoxide (8 ml). The mixture turned yellow and an amorphous precipitate appeared. After 20 h, water (30 ml) was added to the cooled mixture. The resulting mixture was passed through a column (2 x 8 cm) of Dowex-50 (H^+) resin, the effluent and washings were combined, decolorized with charcoal, and evaporated *in vacuo* to a syrup. After repeated additions of ethanol to the syrup and subsequent evaporations *in vacuo*, the syrup crystallized. The crystals were washed with ethanol–ether to give **3** (340 mg, 88%) and were recrystallized twice from ethanol, m.p. 106–107°, u.v. datum: $\lambda_{schoulder}^{H_2O}$ 272 nm (ε 41).

Anal. Calc. for $C_6H_{13}NO_6$: C, 36.92; H, 6.72; N, 7.17. Found: C, 36.84; H, 6.69; N, 7.10.

*3,4,5,6-Tetra-*O*-acetyl-1,2-dideoxy-1-nitro-*D-xylo-*hexitol* (**11**). — A solution of 3,4,5,6-tetra-*O*-acetyl-1-nitro-D-*xylo*-1-hexene[5] (3 g) in 1:2 (v/v) tetrahydrofuran–ethanol (75 ml) was added dropwise to a stirred suspension of sodium borohydride (360 mg) in tetrahydrofuran (30 ml) at 0° over a period of 45 min. The mixture was stirred for 2.5 h at 0°, and then acidified with an aqueous acetic acid–urea solution (7 ml) at 0° within 10 min. A pale-yellow syrup (2.1 g) having λ_{max}^{EtOH} 290 nm was obtained after treatment of the reaction mixture as just described for **10**.

*1,2-Dideoxy-1-nitro-*D-xylo-*hexitol* (4). — To a cooled solution of syrupy **11** (2.0 g) in ethanol (140 ml) was added 0.2M sodium methoxide (100 ml). The mixture was treated as just described for **3**, and the crystals were filtered off and washed with ethanol to give hygroscopic crystals of **4** (640 mg, 60%), m.p. 43–44° (dec.), u.v. datum: $\lambda_{max}^{H_2O}$ 273–260 nm (ε 37).

Anal. Calc. for $C_6H_{13}NO_6$: C, 36,92; H, 6.72; N, 7.17. Found: C, 36.64; H, 6.61; N, 7.08.

*3,4,5,6,7-Penta-*O*-acetyl-1,2-dideoxy-1-nitro-*D-galacto-*heptitol* (**12**). — 3,4,5,6,7-

Penta-*O*-acetyl-1-nitro-D-*galacto*-1-heptene[11] (2 g) in tetrahydrofuran (80 ml) was treated as just described for **9** to give crude crystalline **12** (1.5 g, 75%) which was recrystallized from ethanol, m.p. 158°, u.v. datum: λ_{max}^{EtOH} 289 nm.

Anal. Calc. for $C_{17}H_{25}NO_{12}$: C, 46.88; H, 5.79; N, 3.22. Found: C, 47.00; H, 5.73; N, 3.19.

*1,2-Dideoxy-1-nitro-*D-galacto-*heptitol* (**5**). — Compound **12** (1 g) was deacetylated as just described for **8** and crystalline **5** (264 mg, 51%) was recrystallized from ethanol, m.p. 142–145°, u.v. datum: $\lambda_{max}^{H_2O}$ 272–265 (ε 23).

Anal. Calc. for $C_7H_{15}NO_7$: C, 37.33; H, 6.71; N, 6.21. Found: C, 37.72; H, 6.60; H, 6.25.

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