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CIRCULAR DICHROISM SPECTRA OF SOME MODEL COMPOUNDS RELATED TO D-GLUCOPYRANOSE AND D-GALACTOPYRANOSE*

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ABSTRACT

C.d. spectra have been measured in aqueous solution to 168 nm for some model compounds related to D-glucopyranose and D-galactopyranose. C.d. difference-spectra reveal the contribution of certain functional groups and confirm contributions for other groups found in earlier work.

INTRODUCTION

Relatively few data are available in the literature concerning the relationship between stereochemistry and circular dichroism (c.d.) of unsubstituted carbohydrates[1–14]. This is because of the difficulty in obtaining c.d. spectra of such compounds, which absorb at wavelengths shorter than 200 nm, and to the lack of definitive data on the chiroptical properties of the chromophores present in the sugars, either isolated or with interactions between them. Further problems arise from the complex equilibria in solution involving different conformational and tautomeric forms.

One approach to investigating the c.d. of the monosaccharides is to study the chromophores present in the sugars with suitable simplified models of fixed stereochemistry. Previous papers on open-chain aliphatic ethers and cyclic ethers permitted the study of electronic transitions related to the ether oxygen atom in the 200–140-nm spectral range[15–17]. The aim of the present report is to investigate the contributions to the c.d. arising from the presence of hydroxyl groups in different stereochemical relationships. For this purpose, we have synthesized several 1,5-anhydroalditols as simplified models and have measured their c.d. in the vacuum-u.v. spectral region with the idea of obtaining information on the relationship between c.d. and structure.

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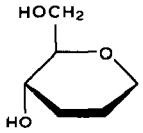
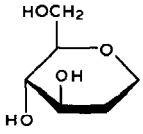
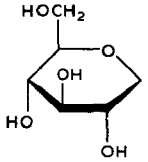
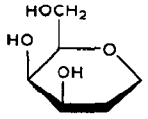
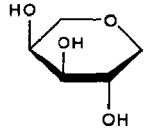
TABLE I

C.D. CHARACTERISTICS OF 1,5-ANHYDROALDITOLS IN WATER SOLUTION

Compound		λ_{max} *(nm)*	$\Delta\varepsilon_{max}$
	(1)	183	+2.4
	(2)	179	+1.6
	(3)	178	+0.5
	(4)	172	−2.1
	(5)	<168	—

RESULTS

Several 1,5-anhydroalditols have been synthesized according to known procedures[18–23] and their c.d. spectra obtained between 210 and 165 nm with water as solvent. These data are summarized in Table I. Monosaccharides are characterized by a complex equilibrium between tautomeric and conformational forms, and so the interpretation of their c.d. spectra is not always obvious. All of our models, however, are pyranoid and the $^4C_1$ conformation of the ring is the predominant one, on the basis of conformational analysis[24,25].

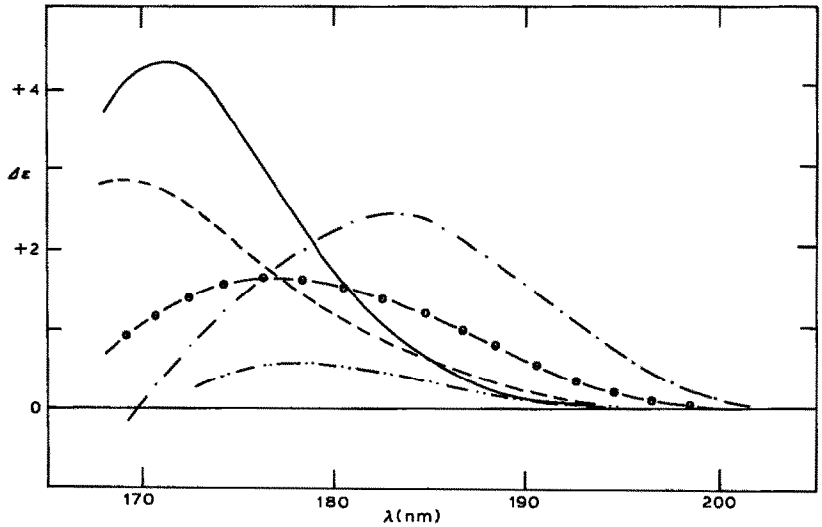


Fig. 1. C.d. spectra of compounds **1** (---), **2** (—·—), and **3** (·····) in water solution. C.d. spectra of α- (——) and β- (·····)-D-glucopyranose. (Spectra of α- and β-glucopyranose from ref. 3, red-shifted by 3 nm to give results in H_2O.)

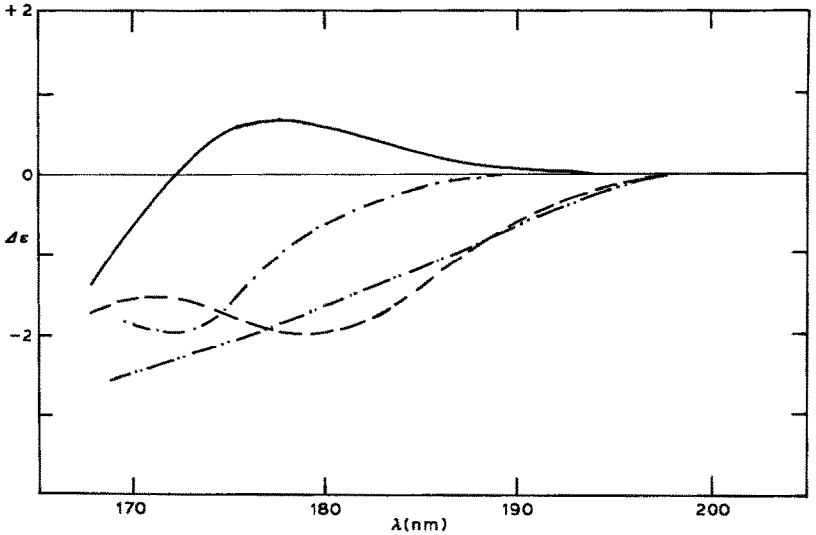


Fig. 2. C.d. spectra of compounds **4** (·····), and **5** (—·—), in water solution. C.d. spectra of α- (——) and β- (— —)-D-galactopyranose. (Spectra of α, and β-galactopyranose from ref. 3, red-shifted by 3 nm to give results in H_2O.)

Compounds **1**, **2**, and **3** constitute simplified models for D-glucopyranose, and they all show a positive band in the 200–168-nm spectral region, as exemplified by the parent compound (Fig. 1). Compounds **4** and **5** may be considered as simplified models of D-galactopyranose, and their c.d. spectra are reported in Fig. 2 together with that of the parent compound. One negative band is observable in the c.d.

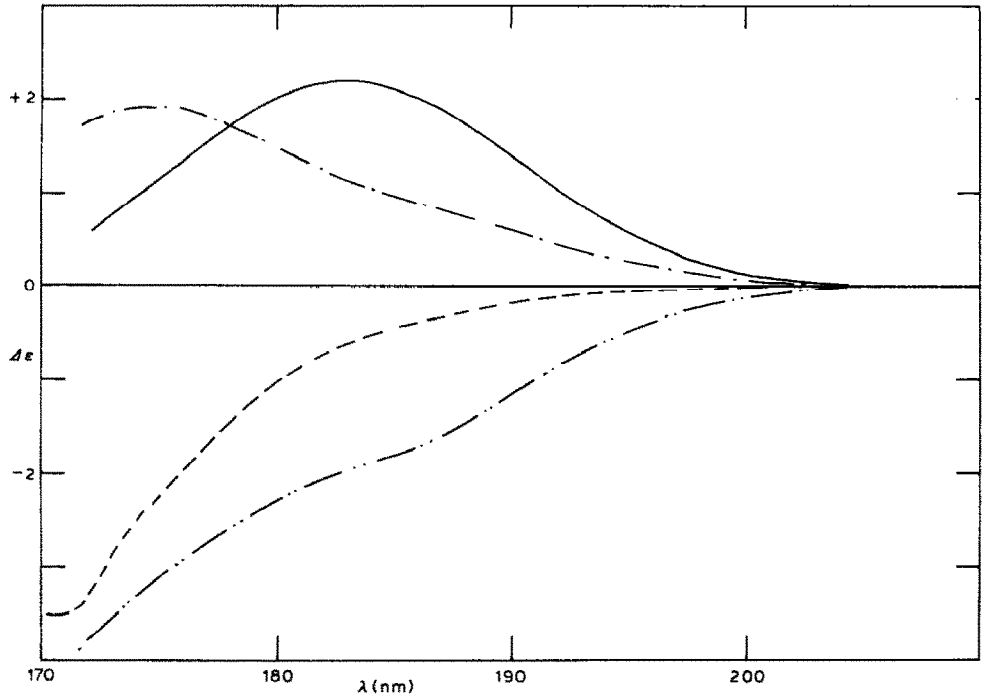


Fig. 3. C.d. spectra of compounds **1** (——), **2** (···), **4** (— —), and **5** (·—·—) in CH_3CN solution.

spectra of **4** and **5**, with a c.d. maximum at 172 nm for **4** and <168 nm for **5**. The c.d. spectrum of D-galactopyranose in water shows one c.d. band at ~175 nm, positive for the α anomer and negative for the β anomer and the equilibrium mixture of anomers[3].

The c.d. spectra of compounds **1, 2, 4**, and **5** were also measured in CH_3CN (Fig. 3). Compound **3** was not sufficiently soluble in this solvent for successful measurements. These spectra and remarkably similar to those obtained in water (Figs. 1 and 2), showing that the c.d. is not very sensitive to the nature of the solvent.

DISCUSSION

At least two transitions have been observed between 200 and 170 nm in the c.d. spectra of glycopyranoses in water, whose energy, sign, and intensity are related to stereochemistry. In particular, the lowest-energy transition has been assigned to the electronic transition of the nonbonding electrons of the ring oxygen atom[4,10]. We analyze here the c.d. results obtained, to seek more information on the contributions arising from fixed stereochemical situations.

The c.d. spectra of these compounds contain detailed information, although proper analysis of the data is not always obvious. However, c.d. difference-spectra between pairs of sugars that differ in stereochemistry at one carbon atom may be

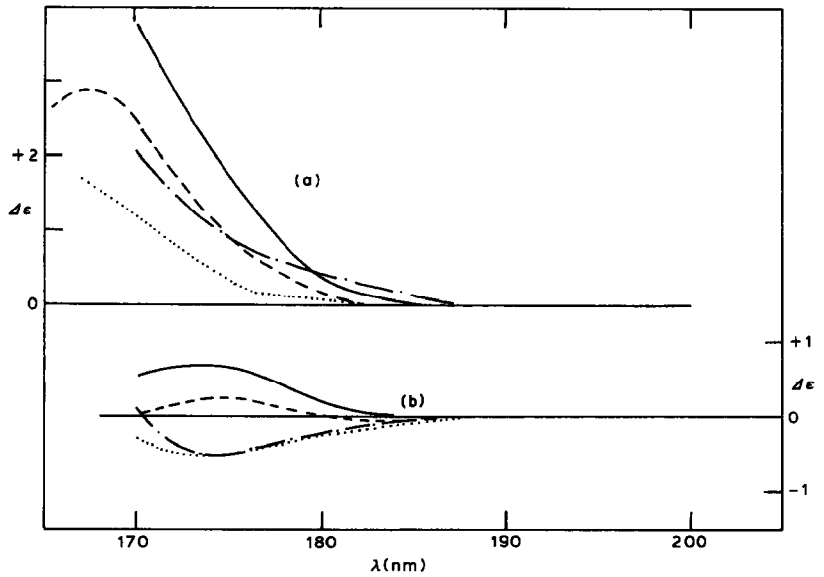
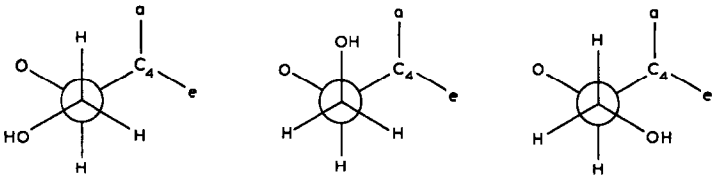


Fig. 4. (a) α-D-Xylopyranose (----) calculated as α-D-glucopyranose minus **3** (——) and β-D-xylopyranose (····) calculated as β-D-glucopyranose minus **3** (— —). (b) methyl α-D-xylopyranoside (— —) calculated as methyl α-D-glucopyranoside minus **3** (——), and methyl β-D-xylopyranoside (····) calculated as methyl β-D-glucopyranoside minus **3** (----).

used to simplify the analysis. If we assume that the principle of pairwise interactions is valid, then the c.d. will be given as the sum of the pairwise interactions between the groups. C.d. difference-spectra will then reflect changes in group interactions between the two molecules compared. This approach has been used to obtain fragment spectra and to use these fragments to predict the c.d. of more complex carbohydrates[6].

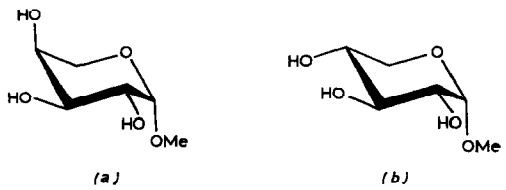
Compound **3** (Table I) represents the hydroxymethyl group as a fragment, because without this group the model compound would be symmetric and show no c.d. Its c.d. spectrum (Fig. 1) is similar to the c.d. fragment-spectrum of the hydroxymethyl derivative given in ref. 6 for the case where HO-4 is equatorial. The c.d. of compound **3** can be used to calculate the c.d. of α- and β-D-xylopyranose, and methyl α- and β-D-xylopyranoside, from data for the glucose analogs. Without the C-1 substituent, the *xylo* compounds are also symmetric. The results in Fig. 4 show good agreement, even to the complicated shape of the low-intensity c.d. for the methyl pyranosides.



gauche-trans *gauche-gauche* *trans-gauche*

Compounds **2** and **4** are epimers and have three substituents on the pyranose ring with the same stereochemistry as D-glucopyranose and D-galactopyranose, respectively. The only difference between **2** and **4** is the absolute configuration at C-4, the hydroxyl group being, for the $^4C_1$ conformation of the ring, equatorial for **2** and axial for **4**. This difference in the relative disposition of the substituents gives a large difference in the c.d. spectra, positive for **2** (λ_{max} 179 nm; $\Delta\varepsilon_{max}$ +1.6) and negative for **4** (λ_{max} 172 nm; $\Delta\varepsilon$ −2.1). Thus it is reasonable to assume that the sign of this c.d. band reflects the absolute configuration of C-4, or the different interaction of the hydroxyl group at C-4 with the neigboring groups in the two molecules. This result agrees with the data of Listowsky *et al.*[1], who studied the c.d. of D-glucose, D-galactose, and their methyl pyranosides, and of Nelson and Johnson[3,4], who extended this study more recently. The relationship between the stereochemistry of the hydroxyl group at C-4 and the sign of the c.d. band has not been completely clarified. However, this has been tentatively related to the conformational equilibrium of rotamers along the C-6–C-5 bond, which is strongly influenced by the orientation of HO-4.

When HO-4 is equatorial, the prevailing conformation is expected to be *gauche-trans,* whereas when HO-4 is axial the prevailing conformation is expected to be *trans-gauche.* To confirm this hypothesis, the authors showed that the sign of the c.d. is independent of the orientation of HO-4 when the hydroxymethyl group is not present, as in the case of methyl β-L-arabinopyranoside (*a*) and methyl α-D-xylopyranoside (*b*).



The effect of interchanging HO-4 from equatorial to axial when there is a hydroxymethyl group at C-5 can be calculated as the c.d. of **4** minus the c.d. of **2**. This is compared in Fig. 5a to the effect calculated from both anomers of D-galactopyranose minus D-glucopyranose. The results are similar for the methyl pyranosides of D-galactose and D-glucose[6]. It is interesting that **4** minus **2** is roughly the average of the somewhat different effect for the α and β anomers. In galactose, the anomerization affects the c.d. because of the hydroxymethyl group, even though these two groups are spatially far apart.

The effect of interchanging the orientation of HO-4 when there is no substituent at O-5 is embodied in the c.d. of **5**, as the compound having HO-4 equatorial is not asymmetric. In contrast to the difference between methyl β-L-arabinopyranoside and methyl α-D-xylopyranoside, a large c.d. is observed (Fig. 5b). Comparing the results in Fig. 5 shows that, in this case, the hydroxy-

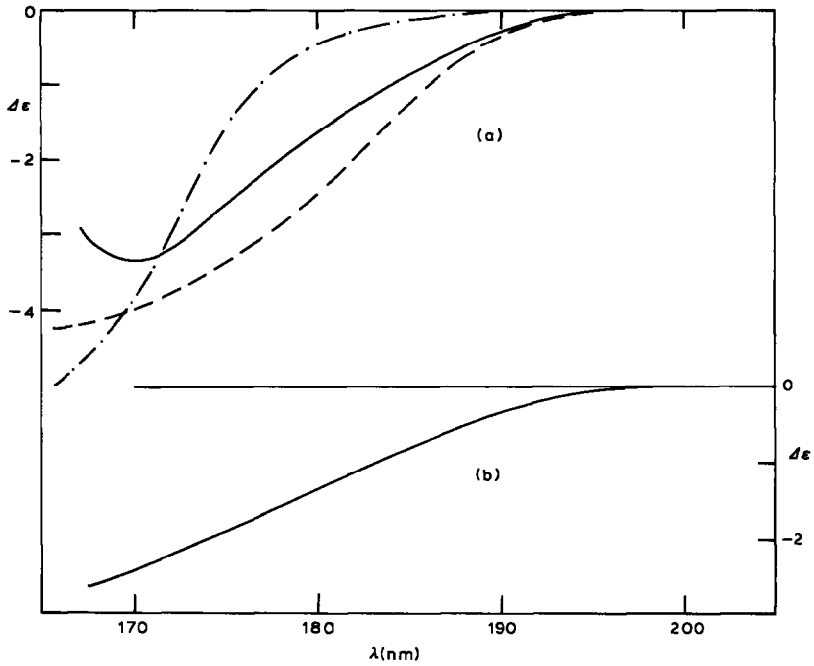


Fig. 5. (a) Compound **4** minus **2** (——), α-D-galactopyranose minus α-D-glucopyranose (···), and β-D-galactopyranose minus β-D-glucopyranose (— —). (b) C.d. spectrum of **5** in water solution.

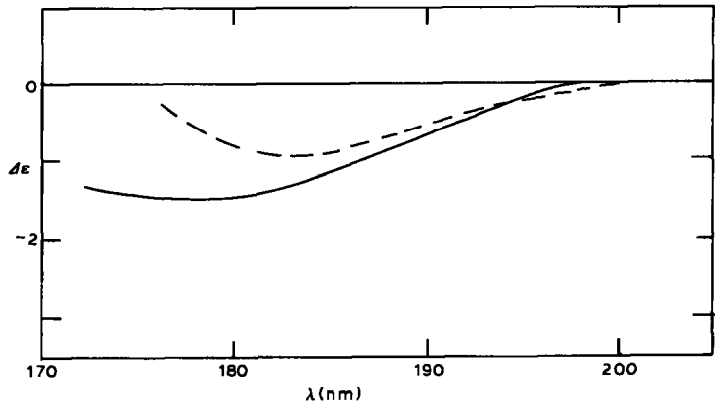


Fig. 6. Compound **3** minus **2** (——) and methyl α-D-glucopyranoside minus methyl 2-deoxy-α-D-*arabino*-hexopyranoside (— —).

methyl group appears to have no net effect. The c.d. of **5** (with the sign reversed) would be the effect of changing HO-2 from equatorial to axial, as the two compounds are enantiomeric.

Analysis of our c.d. data also contributes to an understanding of the c.d. arising from the presence of a hydroxyl group at O-2. Fig. 6 compares the c.d. of

compounds **2** and **3**. The bands are positive for both compounds between 200 and 170 nm, but the intensity is lower for **3**, where an equatorial hydroxyl group is present at C-2. The contribution of the hydroxyl group at C-2 is investigated with c.d. difference-spectra of **3** with **2** in Fig. 6. A negative c.d. is observed between 200 and 170 nm, as expected for an equatorial HO-2 group. It compares well with the difference between methyl α-D-glucopyranoside and methyl 2-deoxy-α-D-*arabino*-hexopyranoside shown in the same figure.

The results obtained stimulate the use of c.d. fragment-spectra to predict the c.d. of more-complex carbohydrates.

EXPERIMENTAL

Syntheses. — *1,5-Anhydro-2,3-dideoxy*-D-erythro-*hexitol* (**1**). 4,6-Di-*O*-acetyl-1,5-anhydro-2,3-dideoxy-D-*erythro*-hexitol [0.86 g, 4.2 mmol, $[\alpha]_D^{25}$ +3.75° (*c* = 1.66, EtOH)], prepared by a literature procedure[26], was deacetylated by the method of Zemplén[18]. A chemically pure sample of **1** (0.28 g, 2.1 mmol), recovered from the methanolic solution by fractional distillation, had b.p. 60–63°/0.7 mmHg, $[\alpha]_D^{25}$ +41.0° (*c* 0.87, water); lit.[19] b.p. 62–64°/0.7 mmHg, $[\alpha]_D^{25}$ +40° (*c* 0.6, water).

1,5-Anhydro-2-deoxy-D-arabino-*hexitol* (**2**). A chemically pure sample of **2** (0.42 g, 3 mmol) obtained from 3,4,5-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hexitol [4.0 g, 3.5 mmol, $[\alpha]_D^{25}$ +34.5° (*c* 1.24, ethanol)] by the Zemplén method[18], and crystallized from ethyl acetate, had m.p. 86–88°, $[\alpha]_D^{25}$ +16.2° (*c* 2.24, water); lit.[20] m.p. 87–88°, $[\alpha]_D^{25}$ +16° (*c* 2, water).

1,5-Anhydro-D-*glucitol* (**3**). A chemically pure sample of **3** (2.5 g, 15.5 mmol) obtained from tetra-*O*-acetyl-α-D-glucopyranosyl bromide[21], had m.p. 141–142°, $[\alpha]_D^{25}$ +42.1° (*c* 0.9, water); lit.[21,22] m.p. 142–142°, $[\alpha]_D^{25}$ +42.3° (*c* 0.844, water).

1,5-Anhydro-2-deoxy-D-lyxo-*hexitol* (**4**). Compound **4** was synthesized (0.4 g, 2.6 mmol) by the procedure of Lemieux and Martin[23], from 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*lyxo*-hexitol (1.0 g, 3.6 mmol), and was purified by crystallization from ethyl acetate; m.p. 128–129°: $[\alpha]_D^{25}$ +43.4° (*c* 1.35, chloroform); $[\alpha]_D^{25}$ +42.9° (*c* 1.0, water); lit.[23] m.p. 128–129°, $[\alpha]_D^{25}$ +43.1° (*c* 1.0, water).

1,5-Anhydro-L-arabino-*pentitol* (**5**). Reduction tri-*O*-acetyl-β-L-*arabino*-pyranosyl bromide (10 g, 29.5 mmol) with $LiAlH_4$ afforded **5**, which was purified by crystallization from absolute ethanol; yield 2.2 g (16.2 mmol), m.p. 94–95°, $[\alpha]_D^{25}$ +99.2° (*c* 1.01, water); lit.[27] m.p. 95–96°, $[\alpha]_D^{25}$ −98.6° (*c* 0.88) for the D enantiomer.

C.d. measurements. — C.d. measurements were recorded with a vacuum-u.v. spectrometer using standard, cylindrical quartz cells of 50- and 10-μm pathlength for most of the measurements. To obtain c.d. curves at wavelengths <170 nm, we placed a small drop between CaF_2 or Suprasil windows with no spacer. Water and acetonitrile solutions (5–30 g/L) were used. In all cases, the total optical absorbances of the cell, solvent, and sample was kept below 1.0. The spectral slitwidth was a constant 1.6 nm.

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