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Note

Far-u.v. circular-dichroism spectra, at 145–220 nm, of some cyclic ethers as model compounds for carbohydrates

CARLO BERTUCCI, RAFFAELLO LAZZARONI,

Centro di Studio del C.N.R. per le Macromolecole Stereoordinate ed Otticamente Attive, Istituto di Chimica Organica dell'Universitá, Facoltà di Science M.F.N., 56100 Pisa (Italy)

AND W. CURTIS JOHNSON, JR.

Department of Biochemistry and Biophysics, Oregon State University, Corvallis, Oregon 97331 (U.S.A.)

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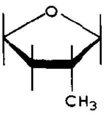
One limitation in obtaining a direct correlation between circular dichroism (c.d.) and the conformation of carbohydrates in solution is the lack of definitive data on the optical activity of the chromophoric portions, either isolated or interacting, that are present in the sugars. Thus, it is important to obtain the c.d. of suitable, simplified models[1]. The ether chromophore has been studied in acyclic, aliphatic ethers[2] and in polyethers[3]. Here, we have extended this concept to a study of some cyclic ethers and hydroxy-substituted cyclic ethers that are more closely related to sugars.

We now report the electronic absorption and c.d. spectra, between 145 and 220 nm, of tetrahydro-(+) –(*R*)-3-methylfuran[4] (**1**), (–)-(*S*)-2-ethyltetrahydropyran (**2**), and tetrahydro-(–)-(*R*)-2-(hydroxymethyl)pyran (**3**) in different solvents. The results obtained indicated that the nature of the solvent markedly affects the c.d. spectra, and that, at least, the longest-wavelength c.d. band of the carbohydrates is related to the ether chromophore.



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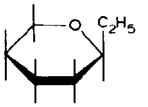

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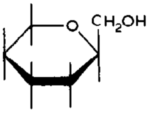

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RESULTS AND DISCUSSION

Synthesis. — Compound **1** was obtained from (+)-(*R*)-methylsuccinic acid (**4**), according to a procedure reported in the literature[4], and **2** was prepared in quantitative yield from tetrahydro-(+)-(*R*)-2-vinylpyran (**5**) by hydrogenation in the presence of Adams's catalyst; **5** $\{[\alpha]_D^{20}$ +6.69° (neat); enantiomeric excess

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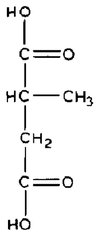
(e.e.) 90%} was procured by resolution of tetrahydro-(*R*),(*S*)-2-vinylpyran with a chiral, platinum complex, as described[5]. The enantiomeric excess of **2** ($[\alpha]_D^{20}$ −8.93°, neat) was assumed to be the same as that of **5**, owing to the complete stereospecificity of the sequence adopted[6].

Compound **3** was prepared by treating **5** with ozonized oxygen. The crude ozonide, without characterization, was decomposed with $LiAlH_4$. After hydrolysis, a chemically pure sample of **3**, having $[\alpha]_D^{25}$ +14.67° (*c* 0.9, H_2O), was isolated.

Absorption and c.d. measurements. — In Figs. 1 and 2, absorption and c.d. spectra of **1** and **2** are depicted for solutions in pentane, perfluorohexane (PFH), and hexafluoro-2-propanol (HFIP). Three major absorption bands were found in the spectral region examined, in analogy to the literature data on the u.v. spectra



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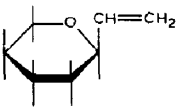

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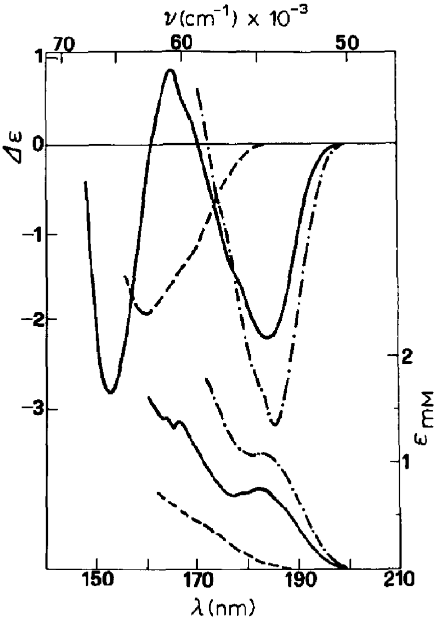

Fig.1. Absorption (lower curves) and c.d. (upper curves) spectra of **1** in PFH (——), pentane (–·–·–·), and HFIP (-------) solution at room temperature. [C.d. data are corrected for 100% optical purity of the sample.]

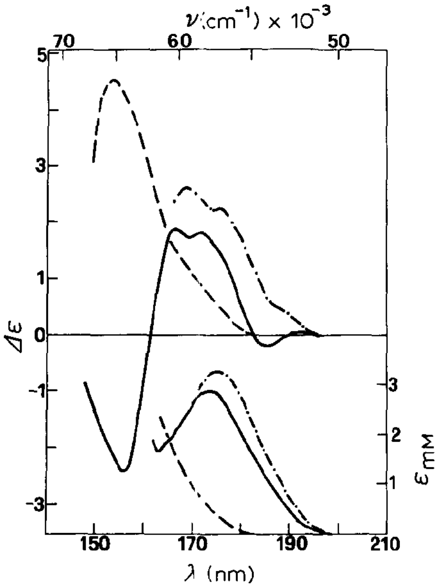

Fig. 2. Absorption (lower curves) and c.d. (upper curves) spectra of **2** in PFH (——), pentane (–·–·–), and HFIP (-------) solution at room temperature. [C.d. data are corrected for 100% enantiomeric excess of the sample.]

of tetrahydropyran and tetrahydrofuran in the gas phase. The nature of the electronic transitions related to the absorptions observed has been extensively studied[7]. In particular, the lowest-energy band in the c.d. spectra of unsubstituted saccharides has been related to a $\sigma^*/3\ s \leftarrow n$ transition originating from the nonbonding orbital of every oxygen atom, including the ring-oxygen atom[8].

The position and the relative intensity of the bands are strongly affected by the nature of the solvent, and the marked blue shift observed when changing from a nonprotic to a protic solvent is shown in both the absorption and the c.d. spectra (see Figs. 1 and 2) of solutions in pentane, perfluorohexane (PFH), and hexafluoro-2-propanol (HFIP). This sensitivity of the c.d. to the nature of the solvent is particularly evident for the longest-wavelength portion of the c.d. spectrum of **2** (see Fig. 2). Indeed, the c.d. spectrum of **2** in perfluorohexane shows bands of opposite sign between 200 and 180 nm, whereas only one shoulder is observed for the pentane solution. The behavior of the c.d. spectra on changing the nature of the solvent confirms that the c.d. in this spectral region is largely related to the transition of the nonbonding electrons of the oxygen atom, as pointed out for the acyclic aliphatic ethers[2b].

Because model compounds **1** and **2** have only a ring-oxygen atom as the chromophore, the present results suggest that the ether chromophore contributes markedly to the c.d. of carbohydrates, at least in the long-wavelength portion of the spectrum. This hypothesis[8] is strongly supported by comparison of the c.d.

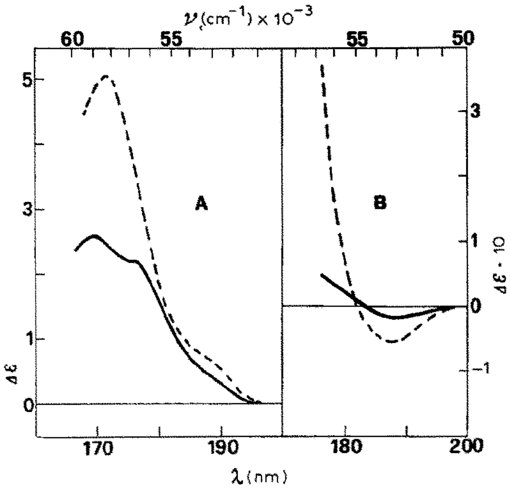

Fig. 3. C.d. spectra of **2** (——) and **3** (------) in pentane (A) and water (B) solution. [C.d. data are corrected for 100% enantiomeric excess of the samples.]

spectra of **2** and **3** in pentane and in water solution (see Fig. 3). Compound **3** is closely related to **2**, but has a hydroxyl group on the side chain of the tetrahydropyran ring. This hydroxyl group does not affect, to a significant extent, the c.d. spectrum or its behavior on changing the nature of the solvent.

EXPERIMENTAL

Synthesis

Tetrahydro-(+)-(R)-3-methylfuran (**1**). — A chemically pure sample of **1**, obtained from **4** {$[\alpha]_D^{25}$ +15.24° (*c* 5.32, ethanol)} according to a procedure reported in the literature[4], showed $[\alpha]_D^{25}$ +12.52° (*c* 2.65, methanol) {lit.[4] $[\alpha]_D^{25}$ max. +30.09° (*c* 2.79, methanol)}.

(−)-(S)-*2-Ethyltetrahydropyran* (**2**). — A mixture of 0.6 g (5.36 mmol) of **5** {$[\alpha]_D^{20}$ +6.69° (neat), e.e. 90%} and Adams's catalyst (50 mg, 0.4 mmol) in absolute ethanol (20 mL) was stirred under hydrogen during 6 h at room temperature. Quantitative hydrogenation of **5** to **2** was obtained, as shown by g.l.c. analysis (2-m SE 30 column, 100°) of the reaction mixture. A chemically pure sample of **2**, recovered from the alcoholic solution by fractional distillation and by preparative g.l.c., showed the following physical constants: b.p. 128°; n_D^{25} 1.4288; $[\alpha]_D^{20}$ −8.93° (neat), e.e. 90%.

Tetrahydro-(−)-(R)-*2-(hydroxymethyl)pyran* (**3**). — Ozonized oxygen was passed through a solution of **5** {0.96 g, 8.6 mmol; $[\alpha]_D^{20}$ +5.75° (neat), e.e. 77%} in dichloromethane for 15 min at −60°. The solvent was carefully removed *in vacuo*, and the crude ozonide was decomposed in ethereal solution (100 mL) with $LiAlH_4$ (2 g, 52 mmol). After hydrolysis, the ethereal layer was dried, and evaporated *in vacuo*. By distillation of the residue, compound **3** (0.871 g, 7.5 mmol) was obtained (b.p. 98–100°/3.33 kPa; $[\alpha]_D^{25}$ +14.67° (*c* 0.9, H_2O); lit.[9] b.p. 90–91°/2.66 kPa; $[\alpha]_D^{25}$ +19.2° (*c* 1, H_2O).

Absorption and c.d. measurements

Absorption and c.d. spectra were recorded with a vacuum ultraviolet spectrometer[10], using standard, cylindrical quartz cells of 50- and 10-μm path-length for most of the measurements. Sandwich-type cells with aluminum-foil spacers were also used, to extend the spectra farther into the vacuum u.v. Suprasil windows were used for measurements above, and CaF_2 windows for measurements below, 160 nm. Pentane, perfluorohexane (PFH), hexafluoro-2-propanol (HFIP), and water solutions (0.5–1 g/L) were used. In all cases, the total optical absorbance of the cell, solvent, and sample was kept below 1.0. The spectral slit-width was a constant 1.6 nm.

ACKNOWLEDGMENTS

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