Carbohydrate Research, 167 (1987) 9–17
Elsevier Science Publishers B.V., Amsterdam - Printed in The Netherlands

RELATIONSHIP BETWEEN CIRCULAR DICHROISM AND STRUCTURE OF ACETYL DERIVATIVES OF DEOXYPYRANOSES*

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(Received August 13th, 1986; accepted for publication, December 12th, 1986)

ABSTRACT

The relationship between the c.d. of some acetyl derivatives of deoxypyranoses and their stereochemistry in solution has been deduced. The contribution to the c.d. arising from the pair interaction of the acetyl groups accounts for the observed signal.

INTRODUCTION

Many sugar derivatives contain chromophoric groups that absorb in the range of commercially available instruments. For the "transparent" sugars, absorbing chromophoric groups have been added in order to make c.d. spectra easier to measure and interpret. In this way, the c.d. of several biological and synthetic derivatives of carbohydrates have been studied[1–12]. Acetyl derivatives have attracted study because this chromophoric moiety is present in some biologically important sugars, such as components of bacterial walls[10,11]. However, a direct correlation between the c.d. of these carbohydrates and their stereochemistry is complicated by the presence of several interacting groups in the molecule.

An approach to the problem is the study of suitable model compounds which reproduce local stereochemical situations in order to identify the most important contributions to the optical activity. We now report on the absorption and c.d. spectra allied to the $n \rightarrow \pi^*$ transition of the acetyl chromophore in the acetylated deoxyhexopyranose derivatives **1–8**.

RESULTS AND DISCUSSION

Absorption and c.d. measurements. — The data in Table I were obtained for solutions of compounds **1–8** in ethanol at room temperature in the range 260–190

* Presented at the XIIIth International Carbohydrate Symposium, Ithaca, August 10–15, 1986.
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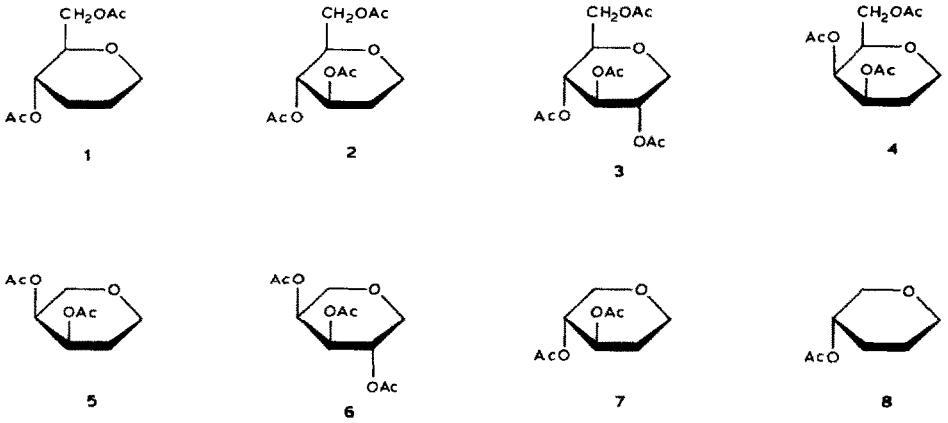


nm. In the u.v. spectrum, a low intensity broad band is present at 210 nm and the tail of a stronger band at higher energy. In the same region, the c.d. spectrum shows a band, the sign and intensity of which remarkably depend on the structure of the compound. This band, due to the $n \rightarrow \pi^*$ transition of the acetyl chromophore[13], exhibits a favourable *g factor* ($\Delta\epsilon/\epsilon$), and hence is easily detectable even when the intensity is low. The results in Fig. 1 show that there is no effect on the c.d. of **6** and **7** on changing the solvent (trifluoroethanol or acetonitrile) even if a blue shift is obtained with more polar solvents, as expected for a $n \rightarrow \pi^*$ transition.

Conformational analysis. — The $^4C_1$ conformation is assumed to be preponderant for **1–4**, **6**, and **8** on the basis of conformational analysis[14,15] and ^{1}H-n.m.r. data[16–19]. Conformational analysis of **5** shows the two chair forms to be similar in energy, but the $^4C_1$ conformation should be preferred because there is only one 1,3-diaxial AcO/H interaction. The ^{1}H-n.m.r. data for **5** do not allow a definite assignment of the preponderant conformation. The $^4C_1$ conformation has been suggested as preponderant for **7** on the basis of conformational analysis[14,15]. The

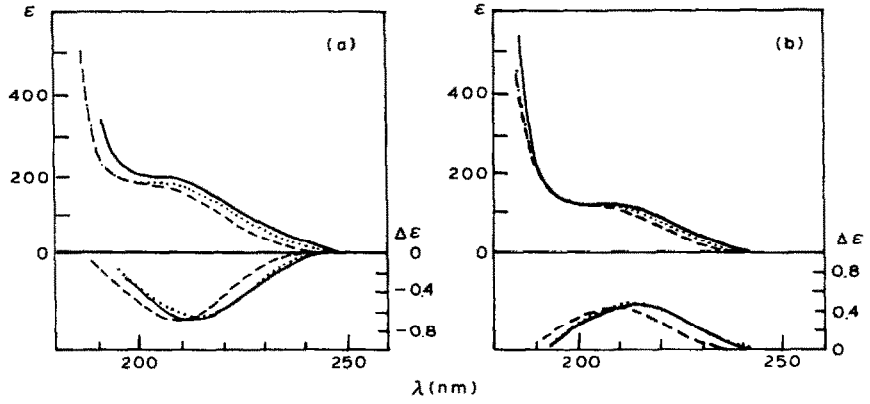


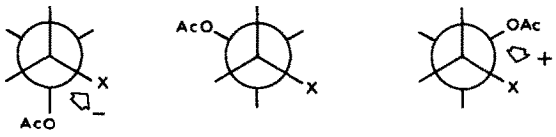
Fig. 1. C.d. spectra of **6** (a) and **7** (b) in acetonitrile (————), ethanol (· · · · · · ·), and trifluoroethanol (— — — — — —) at 20°.

TABLE I

U.V. AND C.D. DATA FOR SOLUTIONS OF ACETYLDEOXYPYRANOSES **1–8** IN ETHANOL AT 20°

Compound	*U.v.*	*C.d.*	
	ϵ_{max} (λ_{max})	λ_{max}	$\Delta\epsilon_{max}$
1	180 (210, sh)	210	−0.99
2	180 (210)	210	−0.54
3	250 (210, sh)	210	−1.04
4	220 (210, sh)	210	+0.20
5	120 (212)	215	−0.20
6	200 (210, sh)	212	−0.66
7	150 (210)	215	+0.47
8	120 (210, sh)	222	+0.03

^{1}H-n.m.r. data ($CDCl_3$) support this suggestion since the $J_{3,4}$ value of 7.5 Hz is that expected[20] for diaxial disposition of H-3,4. Further support for the preponderance of the $^4C_1$ conformation for all the compounds studied is provided by applying the empirical rule proposed by Boren *et al.*[11,12] to the c.d. data, which suggests that the sign of the lowest energy c.d.-band due to the ester chromophore is related to the contributions arising from the interaction of pairs of oxygen atoms linked on vicinal chiral carbons. Considering the Newman-type projections for pairs of carbon atoms of the pyran ring and assuming negative and positive contributions to the c.d. for projections **9** and **10**, respectively, it is possible to predict the sign of the c.d. band for acetyl derivatives of carbohydrates. It was also assumed[11,12] that there is no contribution to the c.d. from projection **11**, and that the intensity depends on the nature of X, decreasing in the sequence $CH_2OH \geq CH_2OAc >> O > OH > MeO > AcO$. When this empirical rule is applied to **1–7**, the c.d. sign predicted for a $^4C_1$ conformation is the same as that found experimentally (Table II).



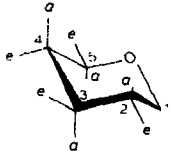
9 **11** **10**

X = O, OH, OMe, OAc, CH_2OAc, CH_2OH

C.d. and the configuration of the ring asymmetric centres. — According to the principle of pairwise interaction[21] and considering the near-neighbor approximation, it has been suggested that preponderant contributions to the c.d. for compounds with two or more ether, ester, or alcohol chromophores arise from the interactions of vicinal oxygens[11,12,22]. The differences observed between the c.d. spectra of two different molecules reflect the changes in group interactions in the molecular framework[22]. A c.d. band of only low intensity was observed for **8**, which contains an isolated acetate group (Table I). The c.d. spectra of **5** and **7** (Fig. 2) each

TABLE II

PREPONDERANT CONFORMATION OF ACETYLDEOXYPYRANOSES **1–7** AS DETERMINED BY C.D. AND ^{1}H-N.M.R. SPECTROSCOPY



($^4C_1$)

Compound					*Sign of c.d. at 210 nm*		*Preponderant conformation*	
No.	*AcO-2*	*AcO-3*	*AcO-4*	*AcOCH$_2$-5*	*Calc.*[a]	*Found*[b]	*Molecular model conf. analysis*	*^{1}H-N.m.r. data*[c]
1			*e*	*e*	–	–	$^4C_1$	$^4C_1$
2		*e*	*e*	*e*	–	–	$^4C_1$	$^4C_1$
3	*e*	*e*	*e*	*e*	–		$^4C_1$	$^4C_1$
4		*e*	*a*	*e*	+	+	$^4C_1$	$^4C_1$
5		*e*	*a*		–	–	$^4C_1 \rightleftarrows {}^1C_4$	
6	*e*	*e*	*a*		–	–	$^4C_1$	$^4C_1 \rightleftarrows {}^1C_4$
7		*e*	*e*		+	+	$^4C_1$	$^4C_1$

[a]According to the literature[12] for a $^4C_1$ conformation. [b]In ethanol at 20°. [c]Compounds **1–4** and **6** from refs. 16–19; **7**, present investigation.

contain one band at 215 nm, but the c.d. band for **5** is negative whereas that for **7** is positive. Compounds **5** and **7** differ in the absolute configuration at C-4 and show a different relative disposition of the two acetyl groups (*cis* for **5** and *trans* for **7**). The influence of an additional chromophore at C-5 is shown by comparing the c.d. spectra of **2** and **4** (Fig. 3). These compounds differ in the absolute configuration at C-4 and different signs are observed for the c.d band at 210 nm. The interaction of $AcOCH_2$-5 and AcO-4 dominates the c.d. spectrum. The c.d. spectra (Fig. 3) for **2** and **4** are of opposite sign compared to those of the structurally related compounds **5** and **7**, which lack $AcOCH_2$-5 and have AcO-3,4 *cis* and *trans*, respectively. The importance of $AcOCH_2$-5 is indicated by the larger negative c.d. of **1** (Fig. 3) where the sequence *e*AcO-4/*e*$AcOCH_2$-5 is isolated. The same result is obtained from a comparison of the c.d. spectra of **5** and **4** (Figs. 2 and 3). These two structurally related molecules differ in the presence of $AcOCH_2$-5. The c.d. band is negative for **5** and positive for **4**, suggesting a dominant contribution for the interaction *e*AcO-4/*e*$AcOCH_2$-5, which gives a positive c.d..

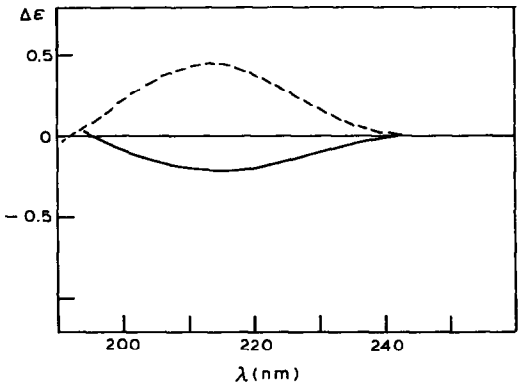


Fig. 2. C.d. spectra of **5** (————) and **7** (— — — — — —) in ethanol at 20°.

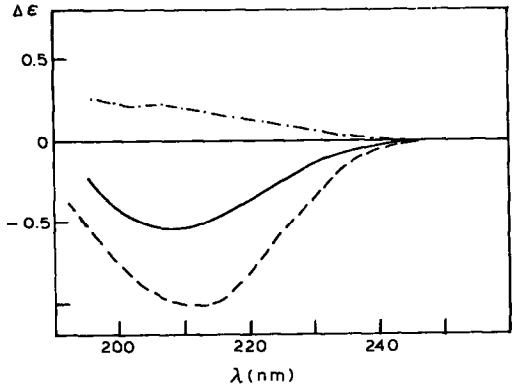


Fig. 3. C.d. spectra of **1** (— — — — — —), **2** (————), and **4** (— · — · —) in ethanol at 20°.

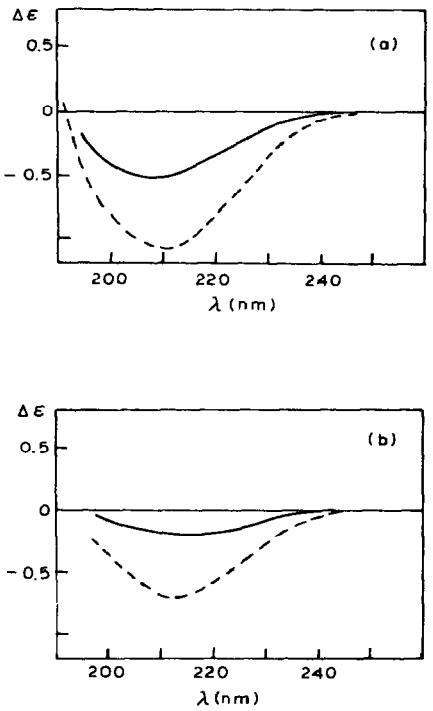


Fig. 4. C.d. spectra in ethanol at 20° of (a) **2** (————) and **3** (— — — — — —); (b) **5** (————) and **6** (— — — — — —).

The analysis of the c.d. results also provides information about the contribution of an *e*AcO-2. Fig. 4 compares the c.d. spectra of **2** and **3** with those of **5** and **6**. For a fixed relative disposition of AcO-3,4, either *e/e* (**2** and **3**) and *e/a* (**5** and **6**), *e*AcO-2 makes a negative contribution. The value of $\Delta\epsilon_{max}$ changes from −0.20 to −0.68 on changing **5** into **6**, and from −0.54 to −1.04 on changing **2** into **3**. This suggests a negative contribution for the *e*AcO-2/*e*AcO-3 which is unaffected by the absolute configuration of C-4. Indeed, comparison of the c.d. spectra of 2,3,4-tri-*O*-acetyl-D-gluco-, -D-manno-, and -D-galacto-pyranans[23] suggests that the sign of the c.d. band due to the acetyl $n\rightarrow\pi^*$ electronic transition reflects the relative disposition of AcO-2, being positive for the D-*manno* compound and negative for the other two polysaccharides[23].

Empirical evaluation of the c.d. at 210 nm. — The preceding data can be used for an empirical evaluation of the c.d. band at 210 nm. Taking into account the contribution from each pair of vicinal acetyl groups and considering these contributions as additive, the sign and, to a good approximation, the intensity of the $n\rightarrow\pi^*$ c.d. band can be calculated for the compounds examined. Table III summarises the results obtained by applying the following procedure. The $\Delta\epsilon_{max}$ values for **1**, **5**, and **7** are considered to be the basic set because these compounds contain vicinal acetyl groups and hence represent a single pair interaction. These data have been used to

TABLE III

EMPIRICAL EVALUATION OF THE C.D. SIGNAL AT 210 NM

Compound	*Couples*	*Contribution*	$\Delta\epsilon_{max}$ (*calc.*)	$\Delta\epsilon_{max}$ (*exptl.*)
1	*e*AcO-4/*e*AcOCH$_2$-5	−0.99		−0.99
5	*e*AcO-3/*a*AcO-4	−0.20		−0.20
7	*e*AcO-3/*e*AcO-4	+0.47		+0.47
2	*e*AcO-3/*e*AcO-4	+0.47	−0.52	−0.54
	*e*AcO-4/*e*AcOCH$_2$-5	−0.99		
3	*e*AcO-2/*e*AcO-3	−0.47[a]	−0.99	−1.04
	*e*AcO-3/*e*AcO-4	+0.47		
	*e*AcO-4/*e*AcOCH$_2$-5	−0.99		
6	*e*AcO-2/*e*AcO-3	−0.47[a]	−0.67	−0.68
	*e*AcO-3/*e*AcO-4	−0.20		

[a]Enantiomer of 7.

calculate the c.d. of **2**, **3**, and **6**. Thus, for **2**, the c.d. is related to the presence of the two pair interactions *e*AcO-4/*e*AcO-3 and *e*AcOCH$_2$-5/*e*AcO-4. These interactions are present in **7** and **1**, respectively, and $\Delta\epsilon$(calc.) for **2** is then obtained by adding the experimental $\Delta\epsilon_{max}$ observed for **7** and **1**. This gives a calculated $\Delta\epsilon_{max}$ of −0.52, which is in good agreement with the experimental value (−0.54). Likewise, a value of −0.67 is calculated for **6**, which agrees well with the experimental value ($\Delta\epsilon_{max}$ −0.68). For **3**, the contribution to the c.d. can be considered as due to the interaction *e*AcOCH$_2$-5/*e*AcO-4, because the contributions of the other possible pair interactions [*e*AcO-4/*e*AcO-3 ($\Delta\epsilon_{max}$ +0.47); *e*AcO-3/*e*AcO-2 ($\Delta\epsilon_{max}$ −0.47)] cancel each other. The $\Delta\epsilon$(calc.) for **3**, considered equal to the experimental value for **1** ($\Delta\epsilon_{max}$ −0.99), is in a very good agreement with that ($\Delta\epsilon_{max}$ −1.04) measured.

Even though limited to a few compounds, the above analysis appears promising for the empirical evaluation of the c.d. of saccharides.

EXPERIMENTAL

General. — Spectra were recorded with a Jasco Uvidec 710 or J-500C c.d. spectrometer, using standard, cylindrical cells of 1–0.1-mm path length and solutions (6.5–30.4 g/L) in acetonitrile, trifluoroethanol, and ethanol. Optical rotations were measured on solutions (0.7–2.0 g/100 mL) in $CHCl_3$ and EtOH with a Perkin-Elmer 241 polarimeter (1-dm cell) at 25°. ^{1}H-N.m.r. spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) with a Varian XL-100 spectrometer. G.l.c. was carried out with a Dani 6800 gas chromatograph (flame-ionisation detector) equipped with columns packed with SE-30, and a Perkin-Elmer F21 preparative gas chromatograph equipped with a 2-m column packed with SE-30.

Synthesis. — The following componds were prepared by literature procedures.

4,6-Di-*O*-acetyl-1,5-anhydro-2,3-dideoxy-D-*erythro*-hexitol (**1**), purified by g.l.c. at 175°, b.p. 88–90°/0.7 mmHg, $[\alpha]_D^{25}$ +37.5° (*c* 1.7, ethanol); lit.[24] b.p.

89–90°/0.7 mmHg, $[\alpha]_D^{25}$ +37.1° (ethanol).

3,4,6-Tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hexitol (**2**), b.p. 102–104°/0.01 mmHg, $[\alpha]_D^{25}$ +33° (*c* 1.2, ethanol); lit.[25] b.p. 129–130°/0.7 mmHg; lit.[16] $[\alpha]_D^{25}$ +34.5° (ethanol).

2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-glucitol (**3**), m.p. 72–74° (from ether–pentane), $[\alpha]_D^{25}$ +40° (*c* 0.7, ethanol); lit.[26] m.p. 73–74°, $[\alpha]_D^{25}$ +38.9° (ethanol).

3,4,6-Tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*lyxo*-hexitol (**4**), b.p. 140–143°/0.02 mmHg, $[\alpha]_D^{25}$ +43° (*c* 1.35, chloroform); lit.[17] $[\alpha]_D^{25}$ +43.7° (chloroform).

3,4-Di-*O*-acetyl-1,5-anhydro-2-deoxy-L-*erythro*-pentitol (**5**), b.p. 60–62°/0.002 mmHg, $[\alpha]_D^{25}$ −45.5° (*c* 1, chloroform); lit.[27] b.p. 86–90°/0.2 mmHg; lit.[28] $[\alpha]_D^{25}$ −45.1° (chloroform).

2,3,4-Tri-*O*-acetyl-1,5-anhydro-L-arabinitol (**6**), m.p. 50–53° (from ether–pentane), $[\alpha]_D^{25}$ +73° (*c* 2, chloroform); lit.[29] m.p. 50–52°, $[\alpha]_D^{25}$ +73.6° (chloroform).

3,4-Di-*O*-acetyl-1,5-anhydro-2-deoxy-D-*threo*-pentitol (**7**), b.p. 64–66°/0.001 mmHg, $[\alpha]_D^{25}$ −37.5° (*c* 0.9, chloroform); lit.[27] $[\alpha]_D^{25}$ −38° (chloroform).

(3*S*)-3-Acetoxytetrahydropyran (**8**), b.p. 75–77°/0.1 mmHg, $[\alpha]_D^{25}$ −22° (neat liquid); lit.[30] $[\alpha]_D^{25}$ −21.7°.

ACKNOWLEDGMENT

We thank Professor W. Curtis Johnson, Jr., for criticism of the manuscript.

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