

## Note

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### Semiempirical, sodium-D molar rotations of pyranosides and other carbohydrate model compounds

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For calculating the Na<sub>D</sub> molar rotations of saccharides, we recently reported a semiempirical method that reproduces the observed dependence of rotation on chemical structure,<sup>1,2</sup>. For the related, but simpler, cyclohexanepolyols, the agreement with experiment is even better<sup>3</sup>. Our model indicates that  $[M]_D$  is largely determined by a single circular dichroic (c.d.) band in the far-vacuum ultraviolet (u.v.). This band has parentage in high-energy transitions, mainly  $\sigma\text{-}\sigma^*$ , associated with CC, CO and CH valence electrons, and is a result of the geometry-dependent interactions among them. Here, we apply the method to a series of methyl pyranosides and other model compounds related to carbohydrates<sup>4–6</sup>.

#### METHODS

Our method of calculating  $[M]_D$  has been described in detail<sup>1–3</sup>. The dominant contribution is taken to be the interaction of the strong electric-dipole transition-moments associated with the high-energy electronic transitions of the CC, CH, and CO valence electrons. If the geometry-dependent, electrostatic interaction between pairs of these transition dipoles is expressed as  $V_{ij}$ , solution of the secular equations

$$\sum_{i=1}^N C_{ik}(V_{ij} - E_k \delta_{ij}) = 0, \text{ where } j = 1, 2, 3, \dots, N,$$

gives coefficients,  $C_{ik}$ , with which interacted transition-moments are given in terms of the original bond-transition moments. By well known equations<sup>7</sup>, rotational strengths are then calculated for a set of c.d. components at energies  $E_k$ . A Kronig–

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TABLE I

CALCULATED AND OBSERVED<sup>a</sup> MOLAR ROTATIONS FOR A SERIES OF METHYL PYRANOSIDES

Compound	Orientation <sup>b</sup>	[M] <sub>D</sub> <sup>calc</sup> (degrees)	[M] <sub>D</sub> <sup>obs</sup> (degrees)
Methyl β-D-mannopyranoside	<i>gt</i>	-42	-136
	<i>gg</i>	-83	
Methyl β-D-xylopyranoside		-27	-108
Methyl β-D-glucopyranoside	<i>gt</i>	-15	-66
	<i>gg</i>	-54	
Methyl β-D-galactopyranoside	<i>gt</i>	+25	0
	<i>tg</i>	+2	
Methyl α-D-mannopyranoside	<i>gt</i>	+86	+154
	<i>gg</i>	+95	
Methyl α-D-xylopyranoside		+152	+253
Methyl α-D-glucopyranoside	<i>gt</i>	+132	+309
	<i>gg</i>	+144	
Methyl α-D-galactopyranoside	<i>gt</i>	+173	+380
	<i>tg</i>	+195	
Methyl β-L-arabinopyranoside		+201	+403

<sup>a</sup>Reference 12. <sup>b</sup> 5-(Hydroxymethyl) group orientation. The 1-methoxyl group was fixed in the *gt* orientation; i.e., O-1-C-7 *gauche* to C-1-O-5 and *trans* to C-1-C-2. The ring was fixed in the <sup>4</sup>C<sub>1</sub>(D) [<sup>1</sup>C<sub>4</sub>(L)] conformation.

Kramers transform<sup>8</sup> of the resulting c.d. produces a calculated optical rotatory dispersion (o.r.d.) spectrum, the 589-nm value of which is [M]<sub>D</sub>. The parameterization originally optimized for saccharide fragments<sup>1</sup> (e.g., CH<sub>2</sub>OH-CH<sub>2</sub>OH) was used unmodified for the present work.

The molecules examined in the present study included a series of methyl pyranosides (see Table I), several cyclic ethers (see Figs. 1 and 2, and Table II), and model compounds related to D-glucose and D-galactose (see Fig. 2, and Table II). Atomic coordinates for the pyranosides and compounds 2-8 were adapted from the <sup>4</sup>C<sub>1</sub> geometry of α-D-glucose reported by Arnott and Scott.<sup>9</sup> Four geometries of compound 1 were considered, based on an electron-diffraction study<sup>10</sup> and conformational-energy calculations<sup>11</sup> for tetrahydrofuran. Two geometries (1a and 1b) are based on the C<sub>2</sub> tetrahydrofuran symmetry, and two (1c and 1d) on C<sub>s</sub> symmetry. Energy differences are small, and all four conformers are likely to be present under most experimental conditions, but in as-yet-unknown relative proportions. Atomic coordinates were adapted from Seip<sup>11</sup>.

In 2 the coordinates of the ethyl group were determined by using C-C and C-H bond lengths of 153 and 110 pm, respectively, and tetrahedral bond-angles, by

TABLE II

CALCULATED AND OBSERVED MOLAR ROTATIONS FOR THE COMPOUNDS IN FIGURES 1 AND 2.

Compound	Conformational <sup>b</sup> feature	$[M]_D^{calc}$ (degrees)	$[M]_D^{obs}$ (degrees)
1	C <sub>2</sub> (a)	+4	+26 <sup>b</sup>
	C <sub>2</sub> (b)	+6	
	C <sub>5</sub> (c)	+5	
	C <sub>5</sub> (d)	+8	
2	$\chi = 60$	-2	-10 <sup>c</sup>
	$\chi = 180$	+1	
	$\chi = 300$	-4	
3	$\chi = 60$	-2	+22 <sup>d</sup>
	$\chi = 180$	+5	
	$\chi = 300$	-8	
4	gt	+6	+53 <sup>e</sup>
	gg	+7	
5	gt	-8	+24 <sup>f</sup>
	gg	-5	
6	gt	+9	+69 <sup>g</sup>
	gg	+14	
7	tg	+16	+64 <sup>d</sup>
	gt	+38	
8		+57	+132 <sup>h</sup>

<sup>a</sup>Ring conformation for 1; C-1 substituent of 2 and 3; orientation of C-5 substituent for 4-7. <sup>b</sup>(c 2.79, methanol)<sup>13</sup>. <sup>c</sup>(Neat)<sup>5</sup>. <sup>d</sup>(c 1, water)<sup>14</sup>. <sup>e</sup>(c 0.6, water)<sup>15</sup>. <sup>f</sup>(c 2, water)<sup>16</sup>. <sup>g</sup>(c 0.844, water)<sup>17,18</sup>. <sup>h</sup>(c, 0.88, water)<sup>19</sup>.

placing the methyl protons in staggered positions, and by considering all three of the methylene group orientations, which are staggered with respect to the ring. Those conformations are specified by the O-C-1-C-6-C-7 dihedral angle,  $\chi$ , where  $\chi = 0$  corresponds to the eclipsed conformation, and the direction of rotation is defined as clockwise rotation of C-7 as viewed from C-1. Coordinates of 3 were specified

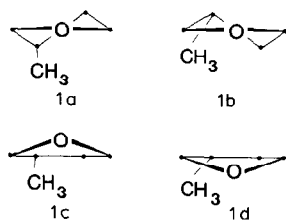


Fig. 1. Four conformations considered for (+)-(R)-3-methyltetrahydrofuran (1).

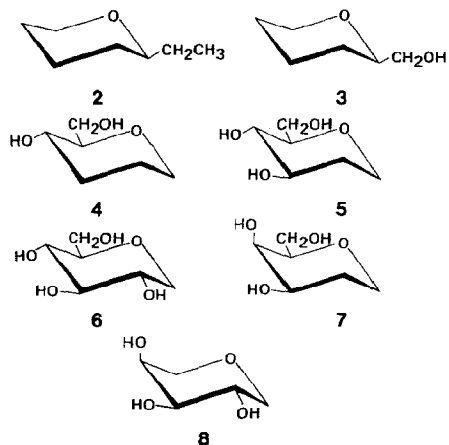


Fig. 2.  ${}^4C_1$  conformations considered for compounds 2-8; (-)-(S)-2-ethyltetrahydropyran (2), (-)-(R) tetrahydro-2-(hydroxymethyl)pyran (3), 1,5-anhydro-2,3-dideoxy-D-*erythro*-hexitol (4), 1,5-anhydro-2-deoxy-D-*arabino*-hexitol (5), 1,5-anhydro-D-glucitol (6), 1,5-anhydro-2-deoxy-D-*lyxo*-hexitol (7), and 1,5-anhydro-L-arabinitol (8).

analogously. Hydroxyl hydrogen atoms do not enter into the calculation; their coordinates need not be specified.

## RESULTS

In our calculational model,  $[M]_D$  is largely determined by a vacuum-u.v. c.d. component that is well separated from higher-energy components<sup>1,2</sup>. That c.d. component is calculated to be in the region 157-165 nm for pyranosides, and 134-137 nm for compounds 1-8. Calculated values of  $[M]_D$  are given in Tables I and II, and in Fig. 3, compared with experimental values. The experimental values reflect conformational averaging; the calculated value for each conformation considered is shown separately. The dashed line in Fig. 3 indicates a linear, least-squares fit to the results; for that purpose, the calculated rotations of the conformations considered for each molecule were averaged (see Tables I and II).

## DISCUSSION

In the correlation of calculated and observed  $[M]_D$  values (see Fig. 3), the general dependence of rotation on chemical structure is reproduced, but the calculated values are consistently too low. The approximately two-fold discrepancy between calculated and observed rotations found here is not uncommon in attempts to calculate optical activity, and was previously discussed in detail<sup>1</sup>. In the present case, it most probably arises from the limitations in Kirkwood's polarizability theory of optical activity, which includes the  $\mu$ - $\mu$  coupling contribution to optical activity, but neglects the  $\mu$ - $m$  coupling between electric-dipole and intrinsic magnetic-dipole

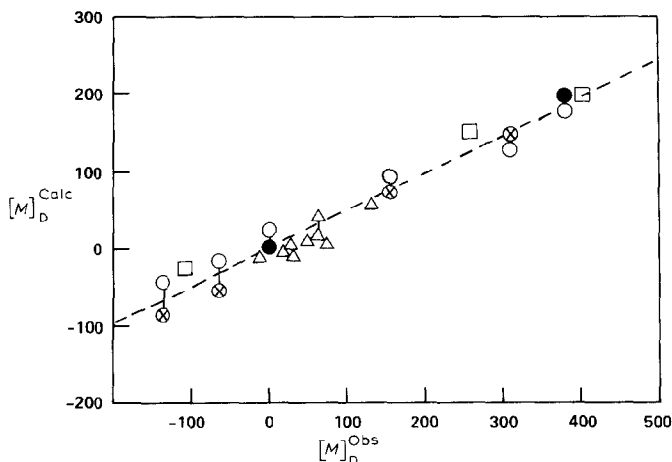


Fig. 3. Correlation of calculated NaD rotations ( $[M]_D^{\text{calc}}$ ) and experimental values ( $[M]_D^{\text{obs}}$ ). Units are  $\text{deg. cm}^2 \cdot \text{dmol}^{-1}$ . Compounds can be identified by data in Table I (hexopyranosides: O, *gt*; x, *gg*; •, *tg*) (pentopyranosides: □) and Table II (Δ). The dashed line is a linear, least-squares fit:  $[M]_D^{\text{calc}} = 0.49 [M]_D^{\text{obs}} - 1$ ; stand dev. 22.

transition-moments. In this context, it may be significant that, in recent *ab initio* calculations of the optical activity of methyl derivatives of cyclopropane, Bohan and Bouman<sup>20</sup> found the  $\mu$ - $\mu$  coupling to make, consistently, the largest contribution to rotational strength, but the  $\mu$ - $m$  coupling contribution, in the cases examined, was of the same sign and order of magnitude. An intriguing possibility is that, for reasons not now known, that finding holds generally for saturated hydrocarbons and, perhaps, also for saturated oxo compounds. In such a case, it would justify an empirical "correction" of the model described here with a factor of two, which would result in nearly quantitative accuracy (see Fig. 3).

The scatter in Fig. 3 is such that small differences in calculated rotations cannot be used to draw conclusions concerning the favored orientation of the 5-(hydroxymethyl) group; *e.g.*, the rotations calculated for the *gt* and *gg* rotamers of methyl  $\beta$ -D-mannopyranoside are not significantly different. On the other hand, the calculated rotation is more sensitive to orientation of the methoxyl group on C-1, at least for the  $\alpha$ -D- and  $\beta$ -L-pyranosides. Fig 3 shows the correlation between calculated and observed rotations for the *gt* methoxyl rotamers already known to be favored, *i.e.*, *gauche* to C-1-O-5 and *trans* to C-1-C-2. The calculated rotations for the (less-stable) methoxyl group rotamers do not fall close to the correlation line of Fig. 3, which provides additional grounds for excluding those disfavored conformations from consideration.

Optical activity measurements in the long-wavelength region have historically played an important role in the conformational analysis of carbohydrates<sup>21</sup>, especially after the empirical treatments of Whiffen<sup>22</sup>, Brewster<sup>23</sup>, and Lemieux and Brewer<sup>24</sup> became available. The present model provides a theoretical foundation for

these empirical treatments<sup>1-3</sup>, and gives support to the extension of those treatments to establishing the inter-residue linkage geometries in polymers, as Rees and co-workers originally proposed<sup>25-27</sup>.

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#### REFERENCES

- 1 E. S. STEVENS AND B. K. SATHYANARAYANA, *Carbohydr. Res.*, **166** (1987) 181-193.
- 2 E. S. STEVENS AND B. K. SATHYANARAYANA, *Biopolymers*, **27** (1988) 415-421.
- 3 B. K. SATHYANARAYANA AND E. S. STEVENS, *J. Org. Chem.*, **52** (1987) 3170-3171.
- 4 R. G. NELSON AND W. C. JOHNSON, JR., *J. Am. Chem. Soc.*, **98** (1976) 4296-4301.
- 5 C. BERTUCCI, R. LAZZARONI, AND W. C. JOHNSON, JR., *Carbohydr. Res.*, **133** (1984) 152-156.
- 6 C. BERTUCCI, P. SALVADORI, G. ZULLINO, D. PINI, AND W. C. JOHNSON, JR., *Carbohydr. Res.*, **149** (1986) 299-307.
- 7 I. TINOCO, R. W. WOODY, AND D. F. BRADLEY, *J. Chem. Phys.*, **38** (1963) 1317-1325.
- 8 A. MOSCOWITZ, IN C. DIERASSI (ED.), *Optical Rotatory Dispersion*, McGraw-Hill, New York, 1950, pp. 150-177.
- 9 S. ARNOTT AND S. E. SCOTT, *J. Chem. Soc., Perkin Trans. 2*, (1972) 324-335.
- 10 A. ALMENNIGEN, H. M. SEIP, AND T. WILLADSEN, *Acta Chem. Scand.*, **23** (1969) 2748-2753.
- 11 H. M. SEIP, *Acta Chem. Scand.*, **23** (1969) 2741-2747.
- 12 F. J. BATES, *Polarimetry, Saccharimetry and the Sugars*, Natl. Bur. Stand. Circular C440, U.S. Gov't. Printing Office, Washington, D.C., 1942.
- 13 R. ROSSI, P. DIVERSI, AND G. INGROSSO, *Gazz. Chim. Ital.*, **98** (1968) 1391-1399.
- 14 R. U. LEMIEUX AND J. C. MARTIN, *Carbohydr. Res.*, **13** (1970) 139-161.
- 15 R. U. LEMIEUX, A. A. PAVIA, J. C. MARTIN, AND K. A. WATANABE, *Can. J. Chem.*, **47** (1969) 4427-4439.
- 16 A. B. FOSTER, M. STACEY, AND S. V. VARDHEIM, *Acta Chem. Scand.*, **12** (1958) 1819-1824.
- 17 R. K. NESS, H. G. FLETCHER, JR., AND C. S. HUDSON, *J. Am. Chem. Soc.*, **72** (1950) 4547-4549.
- 18 H. G. FLETCHER, JR., *J. Am. Chem. Soc.*, **69** (1947) 706-707.
- 19 H. G. FLETCHER, JR., AND C. S. HUDSON, *J. Am. Chem. Soc.*, **69** (1947) 1672-1674.
- 20 S. BOHAN AND T. D. BOUMAN, *J. Am. Chem. Soc.*, **108** (1986) 3261-3266.
- 21 C. S. HUDSON, *J. Am. Chem. Soc.*, **47** (1925) 268-280.
- 22 D. H. WHIFFEN, *Chem. Ind. (London)*, (1956) 964-968.
- 23 J. H. BREWSTER, *J. Am. Chem. Soc.*, **81** (1959) 5483-5493.
- 24 R. U. LEMIEUX AND J. T. BREWER, IN H. S. ISBELL (ED.), *Carbohydrates in Solution*, *Adv. Chem. Ser.*, **117** (1973) 121-146.
- 25 D. A. REES, *J. Chem. Soc., B*, (1970) 877-884.
- 26 D. A. REES AND W. E. SCOTT, *J. Chem. Soc., B*, (1971) 469-479.
- 27 D. A. REES AND D. THOM, *J. Chem. Soc., Perkin Trans. 2*, (1977) 191-201.