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A USEFUL MODEL FOR THE OPTICAL ACTIVITY OF DEUTERIUM COMPOUNDS[1]

James H. Brewster

Department of Chemistry, Purdue University, Lafayette, Indiana

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THE empirical Conformational Asymmetry Rule[1,2] permits the assignment of absolute configuration to a number of compounds having both deuterium and hydrogen at the asymmetric center; these configurations are consistent with those assigned on mechanistic grounds.[3] Thus, butane-2-d, in the indicated absolute configuration,[4] would have the three staggered

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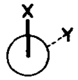
[1] J. H. Brewster, J. Amer. Chem. Soc. 81, 5475 (1959).

[2] The skew system of atoms shown below in Newman projection is dextrorotatory and contributes k•X•Y to $[M]_D$; the constants X and Y appear to be functions of the refractions of atoms X and Y. The atomic refraction of deuterium is less than that of hydrogen; thus the molecular refraction of hexadeutero-benzene is 0.144 lower than that of benzene; C. K. Ingold, C. G. Raisin and C. L. Wilson, J. Chem. Soc. 915 (1936). On this basis, k•X•D will be smaller than k•X•H.



conformations (I_{a-c}) for which molecular rotations would be predicted[2] as shown. Letting the fractional concentration of each gauche form be x, the molecular rotation of a mixture of these three conformations can be expressed:

$$[M]_D = (1-3x)\ k\ (C - H)\ (H - D) \qquad (1)$$

Since the trans form (Ia) predominates, x must be less than 1/3 and expression (1) must be positive. This being the sole expected[1] source of optical activity in this case, we may equate expression (1) with the observed molecular rotation: $[M]_D = +\,0.33 \pm 0.01^\circ$.[3,4] A parallel analysis indicates that 1-phenylbutane-1-d (II) should be ca. 0.33° more dextrorotatory than 1-phenylethane-1-d (III) in the configurations shown; this could occur only if both were dextrorotatory[5] (observed difference: $M_{II} - M_{III} = +\,0.27 \pm 0.11^\circ$). Similarly, the O-alkyl and O-acyl derivatives of benzyl-α-d alcohol (IV) and butanol-1-d (V) should be more dextrorotatory than the parent alcohols[6] in the indicated configurations (O forward); these configurations are the same as those assigned by Streitwieser[3] to the compounds having the rotations shown. The complete agreement between these configurational assignments and those made on mechanistic grounds suggests that this rule can be used to assign an absolute configuration to

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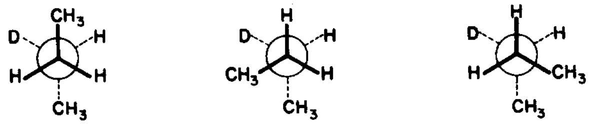
[3] A. Streitwieser, Jr., J. R. Wolfe, Jr. and W. D. Schaeffer, Tetrahedron 6, 338 (1959).

[4] This configuration has been assigned to the (+) isomer; G. K. Helmcamp, C. D. Joel and H. Sharman, J. Org. Chem. 21, 844 (1956).

[5] These absolute configurations have been assigned to the (+) isomers by E. L. Eliel, J. Amer. Chem. Soc. 71, 3970 (1949) (II) and by Streitwieser[3] on mechanistic grounds.

ethanol-1-d.[7]

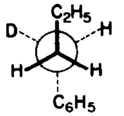


+k(C—H)(H—D) a

-k(C—D)(C—H) b

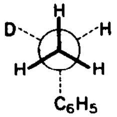
+k(C—H)(C—H) c

I



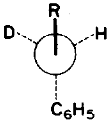
$[M]_D$ + 1·05 ± 0·05

II



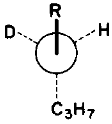
$[M]_D$ + 0·78 ± 0·06

III



R	$[M]^3_D$
-H	-0·780 ± 0·002
$-C_2H_5$	-0·132 ± 0·004
Acetyl	-0·260 ± 0·006
Acid phthalate	+0·538 ± 0·013

IV



R	$[M]^3_D$
-H	-0·139 ± 0·014
Acetyl	+0·56 ± 0·04
$-SO_2C_6H_4NO_2$	+0·332 ± 0·093
$-SO_2C_6H_4Br$	+0·224 ± 0·046
Acid phthalate	+0·85 ± 0·11

V

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[6] We may estimate the magnitude of these shifts by assuming that the steric requirement of a pair of unshared electrons is approximately that of a hydrogen atom. If so, there will be little or no conformational asymmetry about the C*-O bond in the alcohols while the conformational asymmetry in the derivatives will resemble that in I. The rotatory effect of the unshared electron pairs (E) is estimated from the constant (Part II):[1]

$$k\ (C - H)\ (H - E) = +\ 50$$

as follows:

$$\Delta\ [M] = (1 - 3x)\ k\ (R - E)(H - D)$$

On the present basis, butanol-1-*d* (VIb) should be ca. 0.33° more dextrorotatory than ethanol-1-*d* (VIa) in the indicated configurations. Here the magnitudes of rotation indicate that the configurationally related alcohols have *opposite* signs of rotation, *contrary to the assumption of Levy, Loewus and Vennesland.*[7]

As seen in VII, the original Atomic Asymmetry Rule[1,8] gives correct predictions in five of the seven systems to which it might be applied. Apparently, however, the hydroxy and amino groups must be assigned

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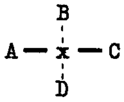
$$= (1 - 3x)\left[k(C - H)(H - E) + k(C - H)(R - H)\right] \frac{k\ (C - H)(H - D)}{k\ (C - H)(C - H)}$$

On this basis, when R is alkyl $\Delta\,[M]$ is ca. + 0.60°, when R is acetyl $\Delta\,[M]$ is ca. + 0.77°. These values are reasonably close to those observed. The large shifts shown by the acid phthalates suggest that the phenyl group contributes to the rotation too.

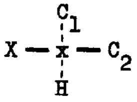
[7] H. R. Levy, F. A. Loewus and B. Vennesland, *J. Amer. Chem. Soc.* *79*, 2949 (1957).

[8] An asymmetric atom is dextrorotatory in the configuration:

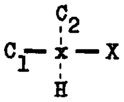


$$\begin{array}{ccc} & B & \\ A\ — & x & —\ C \\ & D & \end{array}$$

when the four *attachment atoms* can be ranked: $A > B > C > D$ in accord with the sequence: $I > Br > SH > Cl > CN > C_6H_5 > CO_2H > CH_3 > NH_2 > OH > H > D$. It was pointed out in Part I that unique assignments of rotational rank could not (at that time) be made to the hetero substituents (other than Cl) but that each must either rank above the carbon sequence or between that sequence and hydrogen. This ambiguity arises because the two configurations:



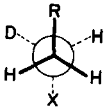
$$\begin{array}{ccc} & C_1 & \\ X\ — & x & —\ C_2 \\ & H & \end{array}$$

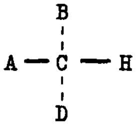


$$\begin{array}{ccc} & C_2 & \\ C_1\ — & x & —\ X \\ & H & \end{array}$$

are identical; rotational rank was therefore assigned on the basis of conformational rotatory power and atomic refraction. Such ambiguity does not occur in compounds of series VII; by using these compounds A can unambiguously be assigned a higher rank than B when configuration VII is dextrorotatory.

rotational rank higher than the carbon sequence when they are a- to a phenyl group. This amendment of the empirical Atomic Asymmetry Rule necessitates no changes in the treatment of the compounds considered in Part I, except for the case of (+) atrolactic acid (VIII) where the amended rule indicates that the asummetric atom makes a positive contribution to $[M]_D$. It is, perhaps, pertinent in this regard to point out that the phenyl group is reported not to produce rotation anomalies near its absorption band at about 265 mμ in hydrocarbons and acids[9] but does produce

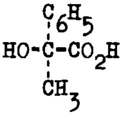




$$\begin{array}{ccc} & B & \\ A\,— & C & —\,H \\ & D & \end{array}$$

	R	X	$[M]_D^3$
a.	H	OH	-0.13 ± 0.02
b.	C_2H_5	OH	+0.139 ± 0.014
c.	C_2H_5	NH_2	-0.028 ± 0.009*
d.	C_2H_5	Cl	+0.37 ± 0.03

VI



$$\begin{array}{c} C_6H_5 \\ HO\text{-}C\text{-}CO_2H \\ CH_3 \end{array}$$

VIII

A	B	$[M]_D^3$
CH_3	OH	+0.13 ± 0.02
CH_3	NH_2	ca. +0.33**
Cl	CH_3	ca. +0.07**
C_6H_5	CH_3	+0.78 ± 0.06
Br	C_6H_5	+1.06 ± 0.34
OH	C_6H_5	+0.780 ± 0.002
NH_2	C_6H_5	+1.110 ± 0.016

VII

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[*] Calculated from the data of A. Streitwieser, Jr. and W. D. Schaeffer, J. Amer. Chem. Soc. **78**, 5597 (1957), assuming the value shown above for optically pure alcohol.

such anomalies in the α-phenylethyl amines and alcohols[10,11] and in certain β-phenylethyl alcohols as well,[12] suggesting the occurrence of a rotationally significant interaction of hetero substituents with phenyl groups.

[**] Estimated from rotations given in VI, letting expression (1)=0.30.

[9] A. Rothen and P. A. Levene, J. Chem. Phys. **7**, 975 (1939).

[10] G. G. Lyle, Abstracts of Papers, 136th Meeting of the American Chemical Society, Atlantic City, N. J., Sept. 1959, p. 71P.

[11] J. H. Brewster, S. F. Osman and G. Asato, unpublished.

[12] J. L. Mateos and D. J. Cram, J. Amer. Chem. Soc. **81**, 2756 (1959).