Tetrahedron Letters No.29, pp. 3249-3252, 1968. Pergamon Press. Printed in Great Britain.

ABSOLUTE CONFIGURATION AND OPTICAL ROTATORY DISPERSION OF METHYL ALKYL SULFOXIDES

Michael Axelrod, Paul Bickart, Michael L. Goldstein,
Mark M. Green, Anders Kjær and Kurt Mislow

Department of Chemistry, Princeton University, Princeton, New
Jersey, 08540, U.S.A., and Department of Organic Chemistry
Royal Veterinary and Agricultural College, Copenhagen,
Denmark

(Received in USA 4 March 1968; received in UK for publication 22 April 1968)

In a previous communication on this subject (1), we proposed the empirical rule that "(-)-methyl alkyl sulfoxides which do not contain other strongly perturbing groups have negative Cotton effects centered at the strong absorption band near 200 mμ (acetonitrile), and have the (R)-configuration", the sign referring to the rotation at the D-line. In view of the interest which this generalization has recently evoked (2,3), we wish to present briefly some additional studies which substantiate and further extend the above rule, and which also more clearly delineate its limitations.

It had been noted (1) that the short wavelength absorption band of methyl butyl sulfoxide is shifted from 200 mμ in acetonitrile to 205.5 mμ in isooctane. Optical rotatory dispersion (o.r.d.) studies are often conveniently carried out in hydrocarbon solvents, and the proposed rule applies with equal force to such media once account has been taken of the slight (5-10 mμ) bathochromic shift of the Cotton effect. Figure 1 compares the o.r.d. curve in isooctane of (+)-(S)-methyl butyl sulfoxide (1) with that of (-)-(R)-methyl ethyl sulfoxide (prepared from ethylmagnesium chloride and menthyl (R)-methanesulfinate (4)) and of (+)-(S)-3-methylsulfinylpropylamine, the enantiomer of the naturally derived material (5). The o.r.d. curves match the assigned configurations and obey the rule. As shown in Figure 2, branching in the α-position of the alkyl group does not markedly affect either the absorption spectrum or the o.r.d. in isooctane, and all three (-)-(R)-methyl alkyl sulfoxides (prepared from menthyl (R)-methanesulfinate (4) and the appropriate Grignard reagents) exhibit negative Cotton effects centered at 205-210 mμ, in accordance with the rule. We note incidentally that even in the absence of an inherently dissymmetric chromophore (6), the amplitudes of the observed Cotton effects are high (a 200-400), and the corresponding rotational strengths (e.g., R ≈ -2×10^{-39} cgs. for (-)-(R)-methyl tert-butyl sulfoxide, as determined by use of a curve-fitting computer program (7)) intense; the statement (8) that high optical rotatory power may be taken as *prima facie* evidence for the presence of such a chromophore is therefore not applicable in the case of the dialkyl sulfoxides.

When the alkyl group becomes "strongly perturbing", the system exceeds the limitations set by the rule, as may be illustrated for the case of (+)-(R)-methyl allyl sulfoxide (9). Comparison of Figure 3 with Figures 1 and 2 immediately reveals that both in the appearance of its absorption spectrum and that of its o.r.d. curve in isooctane, (+)-(R)-methyl allyl sulfoxide differs grossly from the saturated methyl alkyl analogs but resembles rather closely (+)-(R)-allyl butyl sulfoxide (prepared from menthyl (R)-butanesulfinate (1) and allylmagnesium chloride), a compound with which it shares the allyl grouping. Spectroscopic coupling of a sulfoxide n → d transition (10) and a $\pi \rightarrow \pi^*$ transition of the allyl grouping may be responsible for this phenomenon. With respect to the marked solvent dependence of the Cotton effects, the alkyl allyl sulfoxides resemble the analogous alkyl benzyl sulfoxides (11).

When the alkyl group is itself chiral but not strongly perturbing, the rule still applies. Thus, the absorption spectra of the 4-methylsulfinyl-5α-cholestanes (3) resemble in shape, intensity and band position those of the simpler methyl alkyl sulfoxides, and "strong perturbation" cannot therefore be invoked. In harmony with the proposed rule, the (S)-4α- and (S)-4β-methylsulfinyl isomers have positive Cotton effects centered at 205-210 mμ in hexane (3); similarly the (R)-4α- and (R)-4β-methylsulfinyl isomers have negative Cotton effects centered in the same region (3), the (R)-4α isomer especially bearing a striking resemblance to (+)-(S)-methyl butyl sulfoxide (1), both in the appearance of its absorption spectrum and that of its o.r.d. curve, except of course for sign (12). The intensities of the Cotton effects, to judge by the first extremum, are also in the range (*a* 200-400) observed for the simpler sulfoxides.

Two cautionary notes are in order. First, since the rule is formulated for methyl alkyl sulfoxides, it is by definition inapplicable to molecules in which the sulfoxide grouping is part of a ring system (2, 13). Second, since the rule specifically refers to the short wavelength Cotton effect near 200 mμ, it cannot properly be applied to a correlation of chirality at sulfur with the Cotton effect of the long wavelength transition which is sometimes observed near 230 mμ and which, as has been pointed out (3), is of opposite sign.

All new compounds gave satisfactory (± 0.3%) elemental analyses, and n.m.r. spectra were consistent with the assigned structures.

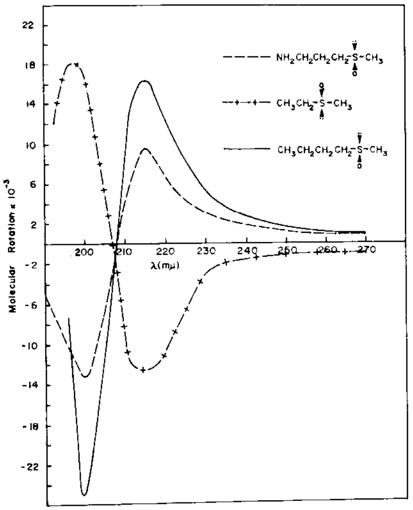

FIG. 1

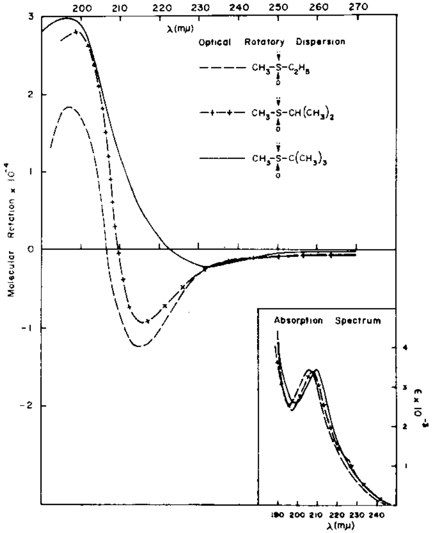

FIG. 2

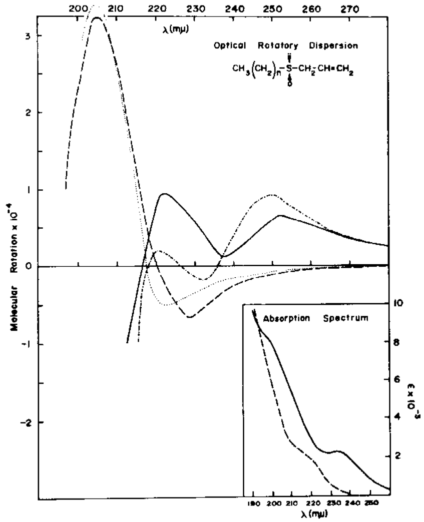

FIG. 3

Captions of Figures

FIG. 1. O.r.d. curves (corrected to optical purity) of methyl n-alkyl sulfoxides in isooctane solution.

FIG. 2. O.r.d. curves (corrected to optical purity) and ultraviolet spectra of (R)-methyl alkyl sulfoxides, all determined in isooctane solution.

FIG. 3. O.r.d. curves (corrected to optical purity) and ultraviolet spectra of (R)-allyl methyl (n = 0) and (R)-allyl n-butyl (n = 3) sulfoxides, determined in isooctane solution (——— for n = 3, and — · — · — for n = 0) and in aqueous solution (— — — for n = 3, and ···· for n = 0). The absorption spectra of the two sulfoxides in each solvent are virtually indistinguishable.

Acknowledgment:

This work was supported by the National Science Foundation under Grant No. GP-3375 and by the Air Force Office of Scientific Research under Grant No. AF-AFOSR-1188-67.

References:

1. K. Mislow, M.M. Green, P. Laur, J.T. Melillo, T. Simmons, and A.L. Ternay, Jr., *J.Amer.Chem.Soc.* **87**, 1958 (1965).
2. R. Nagarajan, B.H. Chollar, and R.M. Dodson, *Chem.Commun.* 550 (1967).
3. D.N. Jones, M.J. Green, M.A. Saeed, and R.D. Whitehouse, *ibid.* 1003 (1967).
4. J. Jacobus and K. Mislow, *J.Amer.Chem.Soc.* **89**, 5228 (1967).
5. K.K. Cheung, A. Kjær, and G.A. Sim, *Chem.Commun.* 100 (1965).
6. P. Crabbé, *Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry*, Holden-Day, San Francisco (1965), Chapter 2 and references cited therein.
7. J.P. Carver, E. Shechter, and E.R. Blout, *J.Amer.Chem.Soc.* **88**, 2550 (1966).
8. A. Moscowitz, K. Mislow, M.A.W. Glass, and C. Djerassi, *J.Amer.Chem.Soc.* **84**, 1945 (1962).
9. P. Bickart, M. Axelrod, J. Jacobus, and K. Mislow, *J.Amer.Chem.Soc.* **89**, 697 (1967).
10. M. Procházka and M. Paleček, *Coll.Czech.Chem.Comm.* **32**, 3049 (1967).
11. U. Folli, F. Montanari, and J. Torre, *Tetrahedron Letters* 5037 (1966).
12. The sign of rotation in the visible of such diastereomers (3) need not however match the sign of the short wavelength Cotton effect, since in some cases it may be dominated by the Cotton effect of opposite sign which is interposed at longer wavelengths (220-230 mμ).
13. P.B. Sollman, R. Nagarajan, and R.M. Dodson, *Chem.Commun.* 552 (1967).