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SOLVENT EFFECTS ON THE OPTICAL ROTATORY DISPERSION OF SULPHOXIDES

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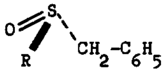
The RD curves of some benzyl-alkyl-sulphoxides (I) have been shown to be strongly dependent on the polarity of the solvent. This characteristic[*] is closely connected with the nature of the alkyl-group, and is also found in other sulphoxides where there is a structural correlation with the compounds (I).

(I)



R = Me, Et, i-Pr, t-Bu, C_6H_4-CH_3-p

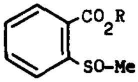
(II) $R\text{-}SO\text{-}CH_2\text{-}CO_2R'$

R = Me, t-Bu, Ph ; R' = H, Me

(III) $R\text{-}SO\text{-}CH_2\text{-}CH_2\text{-}CO_2R'$

R = Me, Ph ; R' = H, Me

(IV)



R = H, Me

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[*] Inversion of sign of rotatory power measured at the D-line in chloroform and ethanol was previously observed (1) for some sulphoxides of low optical purity. In the case of n-propyl-benzyl-sulphoxide plain curves of opposite signs were recorded in the two solvents and in the region 700-350 mμ: these curves are tails of the respective Cotton effects: see in the following and ref. 2.

In ethanol benzyl-alkyl-sulphoxides of equal chirality (2) and of stereoformula (I) show similar RD curves, with a positive Cotton effect centered at 225-228 mμ [peaks at 234-236 mμ, $[\Phi]^{20°}$ = + 19,400° (R = Me), + 19,300° (R = Et), + 28,500° (R = i-Pr), + 51,200° (R = t-Bu); molecular amplitude <u>a</u> within the range + 360! (R = Me) and + 1235 (R = t-Bu) at 20°; shoulders or weak peaks in the region 260-275 mμ, $[\Phi]^{20°}$ approximately + 3,000° (R = Et), + 13,000° (R = t-Bu)]. The Cotton effect is due to a transition n-π^* of the chromophore S=O, probably arising from the promotion of a non-bonding 2p electron of oxygen to an anti-bonding π orbital of the sulphoxide group (3).

In non-protic polar solvents, such as acetonitrile or DMF, the curves of the various compounds are analogous in every respect, except for minor differences in amplitude and in position of the Cotton effects. In changing to protic solvents of lower polarity, such as t-butanol or chloroform, or to non-polar solvents, such as iso-octane, the curve of t-butyl-benzyl-sulphoxide remains practically unchanged, with red-shifts of ~ 10 mμ, as expected for n-π^* transitions. From the other hand, in iso-octane the amplitude of the Cotton effect for the iso-propyl-derivative is noticeably decreased (at 20°, <u>a</u> = + 770!, EtOH; + 300, iso-octane), and for the ethyl- and methyl-derivative the sign becomes inverted (at 20°, <u>a</u> = - 110 and - 175, respectively). The curves in chloroform are similar to those in iso-octane for all compounds (I). In t-butanol the optical activity of the ethyl- and methyl-derivative is fairly low throughout the spectral field [troughs at 250 and 252 mμ; $[\Phi]^{30°}$ = - 960°, - 840°, respectively].*

The RD curves of methylsulphinyl-acetic acid and of the corresponding methyl ester (II, R = CH_3; R' = H, CH_3) show a dependence on the polarity of the solvent similar to that of methyl-benzyl- and ethyl-benzyl-sulphoxide (I). Samples of (II), probably of fairly low optical purity (acid: $[\alpha]^{20°}_{300}$ = + 26°, $CHCl_3$; - 29°, EtOH), gave plain curves down to 250 mµ, which are positive in chloroform and negative in ethanol and acetonitrile.**

The RD curves of (R)(+)p-tolyl-benzyl-sulphoxide (I, R = C_6H_4-CH_3-p; $[\alpha]^{20°}_{D}$ = + 174°, EtOH), of phenylsulphinyl-acetic acid and of the corresponding methyl ester (II, R = Ph, R' = H, CH_3) (acid: $[\alpha]^{20°}_{D}$ = - 178°, EtOH; ester: $[\alpha]^{20°}_{D}$ = - 165°, EtOH), and of t-butylsulphinyl-acetic acid (II, R = t-Bu, R' = H; sample, probably of fairly low optical purity, $[\alpha]^{20°}_{300}$ = - 169°, EtOH; - 169°, $CHCl_3$) are practically insensitive to the polarity of the solvent.

Inversion in sign of the Cotton effect, recorded both in RD and in CD in the case of asymmetrically perturbed carbonyl chromophores, have been

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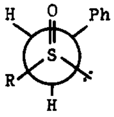
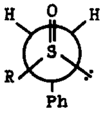
* The addition of 1-100 mole equivalents of trifluoro-acetic acid to a solution 10^{-6} M in iso-octane causes blue-shifts, but no sign-inversion in the Cotton effects of the various compounds. Also, o-methylsulphinyl-benzoic acid (IV) ($[\alpha]^{20°}_{D}$ = + 230°, EtOH) (4) gives curves which are essentially identical in alcohol and chloroform to those of the corresponding methyl ester , although infra-red spectra show that the SO-group is strongly perturbed (unpublished observations from this laboratory).

** Because of the high concentration of the solutions it was not possible to carry out measurements at shorter wave-lenghts.

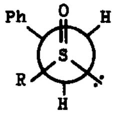
attributed (5) either to variations of conformational equilibria, or to variations of solvational equilibria, or to more complex combinations of the two. In the case of sulphoxides one must also take into account the possibility of equilibria between dimeric and monomeric species in non-polar solvents (6, 7). The data available at this stage do not afford us the choice between the possible causes; for the variation of the steric factor in passing from the t-butyl-(or aryl-)-derivatives to the iso-propyl-, ethyl- and methyl-derivatives can equally influence the relative populations of the various conformers, as the equilibria of solvation and the eventual monomer-dimer equilibria. It does however seem likely that, apart from the concurrent presence of equilibria of solvation and association, conformational equilibria play an important rôle in the cases examined.



(Ia)



(Ib)



(Ic)

In system (I) the staggered conformations (Ia), (Ib), (Ic) show substantial differences in steric and electrostatic interactions among the substituents. Unfavourable steric interactions should be minimised in conformation (Ia), which should dominate when group R is bulky. Accordingly the amplitude of the Cotton effect is greatest in the t-butyl- and p-tolyl-derivative and, apart from the sign constancy, is practically insensitive to the variations of solvent. By assuming that the sign of the Cotton effect associated with conformation (Ia) is the same independently of R, the analogy between the RD curves in the polar solvents seems to indicate that the population of this conformation is high in these solvents and for all the alkyl compounds of the series.

The electrostatic interactions between the substituents, small in polar solvents, in less polar solvents must be more prominent and compete more with steric interactions. If unfavourable electrostatic interactions are less important in conformations (Ib) and (Ic), the relative population of the latter should increase in respect of (Ia) passing to less polar solvents, when R is sufficiently small. Therefore, the variations in amplitude and sign of the Cotton effect could perhaps be associated with variations of the conformational equilibrium (Ia)...(Ic) determined by the polarity of the solvent.*

A similar conformational equilibrium exists in compounds (II), where CH_2-CO_2R substitutes the benzyl-group. It is worth noticing that the RD curves of methylsulphinyl- and phenylsulphinyl-propionic acids (III) and of the corresponding esters (acids: R = Me, $[\alpha]_{300}^{20°} = +\ 360°$, EtOH; R = Ph, $[\alpha]_{D}^{20°} = -\ 185°$, EtOH) do not depend on the solvent, in agreement with the greater degree of rotational freedom, and thus with the more complex con-

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* Measurements taken in ethanol at temperatures in the range + 62°, + 2° showed that, as the temperature decreases, there is a steady increase in molecular rotation (R = Me, $[\Phi]_{236}^{62°} = +\ 11{,}080°$, $[\Phi]_{236}^{2°} = +\ 20{,}$[illegible]$90°$; R = t-Bu, $[\Phi]_{236}^{62°} = +\ 37{,}900°$, $[\Phi]_{236}^{2°} = +\ 54{,}530°$). In solvents of lower polarity the process is more complex, indicating the likely presence of more than two species in equilibrium.

formational equilibrium.*

The (+)alkyl-benzyl-sulphoxides (I, R = Alk) and (R)(+)p-tolyl-benzyl-sulphoxide (I, R = C_6H_4-CH_3-p) were prepared by reaction of l-menthyl phenyl-methane-sulphinate with alkyl- or aryl-magnesium halides, as recently described (2, 8).

Methylsulphinyl-acetic acid (9) and t-butylsulphinyl-acetic acid (10) (II, R =Me, t-Bu) were resolved through the brucine and quinine salts, respectively; phenylsulphinyl-acetic acid (11) (II, R = Ph) and methylsulphinyl-propionic acid (III, R = Me) through the cinconidine salts. (-)Phenylsulphinyl-propionic acid (12) (III, R = Ph) was obtained by hydrogenation with di-imide of (+) cis-phenylsulphinyl-acrylic acid (resolved through the quinine salt).

The rotation data refer to the highest optical purities obtained, not necessarily to optically pure enantiomers. The curves were recorded with a Perkin-Elmer spectropolarimeter mod. P-22.

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* The (S)(+)methyl-n-butyl-sulphoxide, which is essentially dimeric in solutions 0.018-0.055 M in cyclohexane, and monomeric in ethanol and acetonitrile, shows only differences in position and amplitude, not in sign, of the Cotton effect in these solvents (7).

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