

## THE CIRCULAR DICHROISM OF ALKYL-2-ARYLBUTYL SULPHIDES

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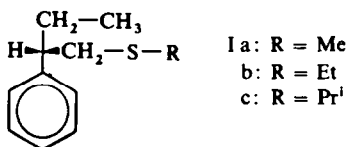
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**Abstract**— The CD spectra of a series of alkyl 2-phenylbutyl sulphides are recorded in various solvents, at room and at low temperature. Whilst the bands corresponding to the  $B_{2u}$  aromatic transitions are very similar to the ones observed in other open chain aromatic derivatives and do not show a significant influence of the sulphide group, the higher energy bands corresponding to sulphur  $A_1 \rightarrow A_2$  and benzene  $B_{1u}$  transitions instead indicate interaction between the two chromophores. These findings seem to confirm the different origins of the optical activity corresponding to the low and high energy transitions of aromatic chromophores.

IN CONNECTION with spectroscopic and chemical physical properties of sulphides mercury(II) chloride complexes<sup>1</sup> and on the CD of aryl-thiiranes<sup>2</sup> and phenylethyl amines,<sup>3</sup> we have synthesized a series of  $\beta$ -aryl-sulphides Ia, b, c.



These compounds, besides their use in the synthesis and study of new types of optically active complexes,<sup>4</sup> are interesting with regards to their optical activity. The low energy CD bands of mono-substituted benzene derivatives at *ca* 260 nm, ( $B_{2u}$ ), show low sensitivity to chemical substitution at the asymmetric centre, allowing the determination of the absolute configuration from the sign of the multiple Cotton effect.<sup>5</sup> On the other hand these bands are very sensitive to substitution at the aromatic ring and the signs of the multiple Cotton effect are inverted by many *para*- and *ortho*-substituents in phenylethyl amines<sup>3</sup> and mandelic acids.<sup>6</sup> The CD of the  $B_{1u}$  benzene-like transition behaves in quite a different way and is very sensitive to the substitution at the asymmetric centre, leading to the conclusion that the optical activity of this transition is likely to involve coupling of the benzene transition moment with those of the substituents.<sup>2, 3</sup>

The direction of the  $B_{1u}$  transition moment does not change by rotation around the bond joining the benzene chromophore to the asymmetric centre (IIa) and its magnitude is reasonably high, while, the  $B_{2u}$  transition moment changes its direction



by rotation (IIb), and has a lower magnitude. On these grounds the different properties of the two CD bands can be explained as arising from different mechanisms of optical activity.<sup>7</sup>

The study of the CD of  $\beta$ -aryl-sulphides can give new indications useful for solving the general problem mentioned above and in addition could add information about the little-studied sulphide chromophore.<sup>8-10</sup>

Derivatives Ia, b, c were synthesized from 99.0% optically pure (+)-(*S*)-1-chloro-2-phenylbutane by reaction with the appropriate mercaptan. The (*S*) configuration is retained because the asymmetric centre is not involved in the reaction which seems to occur without any racemisation, as was proved for analogous reactions.<sup>4, 11</sup> The structures of compounds Ia, b, c are confirmed by NMR spectra (Experimental).

The absorption and CD of derivative Ib are shown in Fig 1. Characteristics of the spectra of derivatives Ia, b, c and of (+)-(*S*)-1-chloro-2-phenylbutane are reported in Table 1.

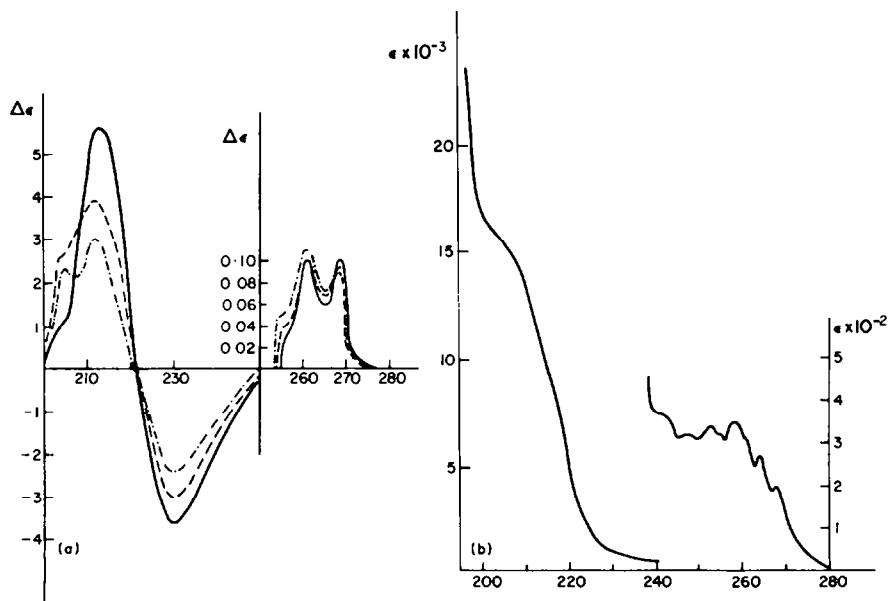



FIG 1. (a) CD of (+)-(*S*)-ethyl-2-phenylbutyl sulphide in *n*-heptane (—), in ethanol (---) and in acetonitrile (-·-·-) (b) UV spectrum of (+)-(*S*)-ethyl-2-phenylbutyl sulphide in *n*-heptane

TABLE I. UV AND CD DATA OF (S)-METHYL-2-PHENYL SULPHIDE AND (S)-1-CHLORO-2-PHENYLBUTANE\*

$\text{CH}_3-\text{CH}_2-\text{CH}-\text{CH}_2-\text{X}$ 	UV		CD					
	$\lambda_{\text{max}}$ nm	$\epsilon$	n-heptane $\lambda$ nm	$\Delta\epsilon$	ethanol $\lambda$ nm	$\Delta\epsilon$	acetonitrile $\lambda$ nm	$\Delta\epsilon$
X = SCH <sub>3</sub>	268.0	130	max 268	+0.08	max 268	+0.08	max 268	+0.09
	264.5	170	max 261	+0.10	max 261	+0.11	max 261	+0.12
	261.0(sh)	180	max 256(sh)	+0.03	max 256(sh)	+0.04	max 255(sh)	+0.05
	258.6	210	max 230	-3.70	max 230	-3.0	max 231	-2.3
	254.8(sh)	170	max 213	+5.30	max 212	+3.7	max 212	+3
	252.7	180	max 204(sh)	+1.90	max 204(sh)	+3.0	max 205	+2.0
	247.5	150						
	242.0(sh)	170						
	216.5(sh)	6880						
	204(sh)	12,280						
X = Cl	267.3	90	max 267	+0.063	max 267	+0.040	max 267	+0.025
	264	150	min 264	+0.050	min 264	+0.033	min 264	+0.020
	260.5(sh)	140	max 261	+0.085	max 261	+0.033	max 261	+0.030
	258	190	min 257	+0.050	min 257	+0.033	min 257	+0.018
	254.3(sh)	130	max 255	+0.060	max 255	+0.040	max 255	+0.020
	252.6	150	max 249(sh)	+0.030	max 248(sh)	+0.018	max 248(sh)	+0.010
	247.5	100	230	0	230	0	230	0
	242(sh)	60	max 215	-1.2	max 214	-1.8	max 214	-0.9
	236.5(sh)	40	min 205	-0.6	min 204	-0.6	min 204	-0.38
	216(sh)	9600	200	-0.8	200	-0.8	200	-0.7

\* Spectroscopic data of the other sulphides do not show significant changes with respect to the ones of the Methyl derivative.

Three bands and one inflection corresponding to four electronic transitions are evident in the spectra:

(i) The extensively studied, but not completely understood (with regards to its optical activity) aromatic transition at *ca* 270 nm. It shows the vibronic structure typical of alkyl monosubstituted benzenes.<sup>5,12</sup> The UV spectrum consists of progressions involving totally symmetric vibrations of 750 and 930  $\text{cm}^{-1}$  and a non-totally symmetric vibration of 520  $\text{cm}^{-1}$ , while the CD shows only the main progression of the breathing vibration (*ca* 930  $\text{cm}^{-1}$ ). The sign of this multiple Cotton effect is related to the absolute configuration of the asymmetric centre: the (*S*) configuration corresponds to positive signs as in (+)-(*S*)-1-chloro-2-phenylbutane (Table 1) and is in agreement with several other examples such as phenylethylamine,<sup>3,5</sup> phenylethanol,<sup>13</sup> phenylbutyric acid,<sup>14</sup> phenyl oxiranes,<sup>15</sup> phenyl thiiranes,<sup>2</sup> and phenyl 1-propanols.<sup>16</sup>

(ii) A band at *ca* 230 nm without corresponding maximum in the isotropic absorption. The low temperature CD shows that we are not dealing with a band caused by conformational effect (Fig 2).<sup>17</sup> It is connected with the electrically forbidden transition of the sulphide chromophore at *ca* 230 nm, which is detectable with difficulty in the UV spectra of alkyl sulphides<sup>9-10</sup> and is here completely hidden under the more intense  $B_{1u}$  aromatic transition. The rotational strength of this band

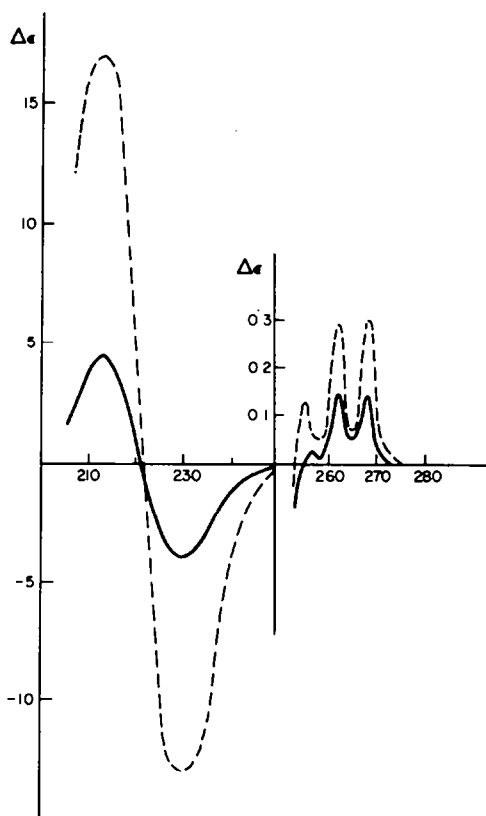


FIG 2. CD of (+)-*S*-isopropyl-2-phenylbutyl sulphide in  $P_3M_1$  at +22° (—) and -155° (-----)

for Ic at  $-155^\circ$  (in methyl cyclohexane-isopentane) has the value of  $-13 \cdot 10^{-40}$  c.g.s.u. which is about two orders of magnitude greater than that observed in alkyl 2-methylbutyl sulphide in the same experimental conditions.<sup>18</sup>

(iii) A band at *ca* 212 nm corresponding to the  $B_{1u}$  benzene-like transition whose rotational strength is considerably enhanced with respect to the corresponding band of analogous open chain benzene derivatives<sup>3</sup> and of (+)-(*S*)-1-chloro-2-phenylbutane.

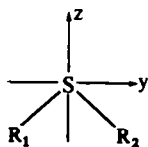
(iv) An inflection at *ca* 205 nm, more evident in polar solvents (Fig 1), corresponding to an inflection in the absorption, related to the allowed sulphide transition at *ca* 205 nm (in solution).

By cooling down to  $-155^\circ$  the CD spectrum of Ic shows a considerable increase in intensity of all bands.

The (*S*) absolute configuration in this series of sulphides can be correlated to the negative band at *ca* 230 nm and to the positive one at *ca* 210 nm, and as described above to the positive bands at 270 nm.

The UV spectrum of alkyl sulphides has been investigated by few authors.<sup>8-10</sup> A very weak transition is observed at *ca* 230 nm in solution for dimethyl sulphide with molar decadic extinction coefficient in the range 15-20, which becomes stronger in unsymmetrical sulphides. A second stronger transition appears at *ca* 220 nm in the vapour and is shifted to the blue in solution, where it appears as a shoulder of the higher energy band, the shift increasing with the polarity of the solvent. Other transitions appear at *ca* 200 and 195 nm, but are not discussed here as they lie outside the region investigated in the CD.

The absorption at *ca* 230 nm is assigned to an  $A_1 \rightarrow A_2$  ( $nb_1 \rightarrow b_2^*$ ) symmetry in group  $C_{2v}$ .<sup>8,9</sup> All the authors assign it to a  $3p_x(S) \rightarrow b_2^*$  transition where for the first group<sup>8</sup>  $b_2^*$  is an antibonding orbital with relevant  $3p_x(S)$  contribution: the transition is "strongly analogous to the  $n \rightarrow \pi^*$  in carbonyl". It is electrically forbidden and magnetically allowed with magnetic transition moment along the *z*-axis (III).



III

For the second group<sup>9</sup>  $b_2^*$  is an antibonding orbital which is practically a  $3d_{yz}(S)$  ( $-0.9995$  is the coefficient), giving in this way only a very small magnetic moment.<sup>19</sup> The first interpretation without however excluding a small contribution of  $3d_{yz}(S)$  to the  $b_2^*$  excited orbital,<sup>20</sup> can be used to explain the optical activity of  $\beta$ -aryl sulphides. The optical activity corresponding to the sulphur 230 nm and phenyl 210 nm transitions, which are strongly enhanced with respect to open chain alkyl sulphides and alkyl benzenes and the opposite signs of the two CD bands, indicate interactions between the two groups. Such interactions cannot be measured in the absorption spectra, because of the strong overlapping of the bands; however the inflections correspond to definite bands of the isolated chromophores without relevant shifts in the wavelengths.<sup>21</sup> Unfortunately it is impossible to know the conformation of the molecules under investigation and consequently to perform significant calculation

of the optical activity; one can have tentative interpretations by inspecting the order of magnitude of rotational strengths, calculated in a few limiting cases. The approaches used both assume direct analogy of the sulphur transition at *ca* 230 nm with ketone  $n \rightarrow \pi^*$  transition.

Following the dynamic approach<sup>7,22</sup> the sulphur  $A_1 \rightarrow A_2$  transition can couple with the benzene  $B_{1u}$  transition through interaction between the transient quadrupole  $\theta_{xy}$  on the sulphur and the electric dipole transition moment on the benzene molecule. If we take the product  $i\theta_{xy} \cdot m_z = 5 \cdot 10^{-46}$  c.g.s.u. where  $m_z$  is the magnetic moment of the  $A_1 \rightarrow A_2$  transition as given in Ref.<sup>22</sup> for ketones, then, using the value of the electric transition moment of toluene,  $R$  ranges from  $30 \cdot 10^{-40}$  c.g.s.u., at a distance between the centre of the sulphide group and the centre of benzene of 3.5 Å, to  $6 \cdot 10^{-40}$  c.g.s.u. for a distance of 5 Å, assuming in both cases favourably oriented electric and magnetic transition moments.

Following the static approach,<sup>23</sup> a small overlap of the sulphur  $3p_x$  with carbon  $p_x$  orbitals of the benzene ring mixes the magnetically allowed  $A_1 \rightarrow A_2$  sulphur transition with an allowed  $\pi \rightarrow \pi^*$  transition of the extended  $\pi$  system. Using first order perturbation theory to express the partial delocalisation of sulphur  $3p_x$  electrons

$$n = 3p_x(S) + \lambda\pi$$

one obtains<sup>24</sup>

$$R \approx \lambda \mu^\pi \cdot m(S)$$

where  $\mu^\pi$  is the electric dipole transition moment of the homoconjugated system and  $m(S)$  is the magnetic moment of the sulphur  $A_1 \rightarrow A_2$  transition. Even in conformations having the sulphide group far from the benzene ring the overlap between sulphur  $3p_x$  orbital and the nearest  $p_x$  carbon of benzene (0.005 at 4 Å calculated assuming the values 1.625 and 1.680 for orbital exponents of  $2p_x$  and  $3p_x$  respectively) can be sufficient to obtain values of the rotational strength of the same order of magnitude as the experimental, always assuming favourable orientation of the magnetic and electric transition moments.

It is therefore impossible to decide which one of the two explanations is more appropriate in the present case. The right answer can probably be given by the study of a compound having the phenyl and the sulphide groups in a fixed geometrical relation. A synthesis of derivatives of this type is at the moment in progress.

## EXPERIMENTAL

Optical rotations were measured with an automatic NPL Bendix polarimeter. UV spectra were recorded on a Cary 14 spectrophotometer. CD spectra were measured with a Jouan CD 185 dichrograph. <sup>1</sup>H NMR spectra were measured with a Jeol 60 ML spectrometer with TMS as internal standard. Chemical shifts are given in ppm.

*Preparation.* (-)-(+)-1-Chloro-2-phenylbutane, b.p. 61–62°/0.5 mmHg,  $[\alpha]_D +9.71$  ( $c = 1.03$ , EtOH 95°),  $\alpha_D +5.85$  (neat,  $l = 1$ ), was obtained as described<sup>24</sup> from (+)-2-phenylbutanoic acid via reduction to (+)-2-phenylbutanol and subsequent halogenation. The NMR spectrum (neat) shows the following signals: 0.71 (3H, t, CH<sub>3</sub>  $\delta$ ), 1.67 (2H, m, CH<sub>2</sub>  $\gamma$ ), 2.75 (1H, m, CH  $\beta$ ), 3.52 (2H, d, CH<sub>2</sub>  $\alpha$ ), 7.17 (5H, m, C<sub>6</sub>H<sub>5</sub>).

Sulphides were prepared by reaction of the chloride with alkyl mercaptans in NaOEt according to the following general procedure. Ethyl mercaptan (0.13 mol) was added at  $-10^\circ$  to a soln of NaOEt (0.13 mol) in EtOH (60 ml). (+)-(+)-1-Chloro-2-phenylbutane (0.06 mol) was then added dropwise at room temp.

The mixture was stirred (8 hr) and refluxed for a further 4 hr. The soln diluted with water was then steam distilled, the product extracted with ether and the extract washed with 10% NaOH aq and water, dried over  $\text{Na}_2\text{SO}_4$  and distilled. The sulphides were characterized by GLC, NMR and analysis.

(-)-(*S*)-Methyl-2-phenylbutyl sulphide, b.p. 91–92°/2.2 mmHg, yield 77%,  $n_D^{25}$  1.5360,  $[\alpha]_D^{24}$  -1.75 ( $c = 1.312$ , EtOH 95°),  $\alpha_D - 2.6$  (neat,  $l = 1$ ). The NMR spectrum shows four signals:  $\delta$  0.80 (3H, t,  $\text{CH}_3 \delta$ ), 1.75 (2H, m,  $\text{CH}_2 \gamma$ ) partially overlapped to 1.92 (3H, s,  $\text{CH}_3 \alpha'$ ), 2.7 (3H, m,  $\text{CH}-\text{CH}_2 \alpha$ ), 7.2 (5H, m,  $\text{C}_6\text{H}_5$ ). With respect to (+)-(*S*)-1-chloro-2-phenylbutane spectrum a shift to high field of the doublet of  $\text{CH}_2 \alpha$  with consequent overlapping with the multiplet  $\text{CH} \beta$  at 2.7 ppm was observed. The same overlapping was observed in all sulphides. (Found: C, 73.7; H, 9.15; S, 17.15.  $\text{C}_{11}\text{H}_{16}\text{S}$  requires: C, 73.25; H, 8.95; S, 17.8%.)

(+)-(*S*)-Ethyl-2-phenylbutyl sulphide, b.p. 83–85°/0.7 mmHg, yield 86%,  $n_D^{25}$  1.5287,  $[\alpha]_D^{24}$  +6.19 ( $c = 1.150$ , EtOH 95°),  $\alpha_D + 6.55$  (neat,  $l = 1$ ). The NMR spectrum shows the signals in the range 0.5–3 ppm partially overlapped:  $\delta$  0.80 (3H, t,  $\text{CH}_3 \delta$ ), 1.17 (3H, t,  $\text{CH}_3 \alpha'$  of S-Et), 1.7 (2H, m,  $\text{CH}_2 \gamma$ ), 2.4 (2H, q,  $\text{CH}_2 \alpha'$ ), 2.7 (3H, m,  $\text{CH}-\text{CH}_2 \alpha$ ), 7.18 (5H, m,  $\text{C}_6\text{H}_5$ ). (Found: C, 75.05; H, 9.55; S, 15.95.  $\text{C}_{12}\text{H}_{18}\text{S}$  requires: C, 74.15; H, 9.35; S, 16.5%.)

(+)-(*S*)-Isopropyl-2-phenylbutyl sulphide, b.p. 80.5–81.5°/0.5 mmHg, yield 51%,  $n_D^{25}$  1.5202,  $[\alpha]_D^{24}$  +7.81 ( $c = 0.778$ , EtOH 95°). NMR signals:  $\delta$  0.80 (3H, t,  $\text{CH}_3 \delta$ ), 1.2 (6H, d,  $2\text{CH}_3 \beta'$ ), 1.75 (2H, m,  $\text{CH}_2 \gamma$ ), 2.72 (4H, m,  $\text{CH}-\text{CH}_2-\text{S}-\text{CH}$ ) overlapped,<sup>25</sup> 7.2 (5H, m,  $\text{C}_6\text{H}_5$ ). (Found: C, 74.85; H, 9.6; S, 15.4.  $\text{C}_{13}\text{H}_{20}\text{S}$  requires: C, 74.95; H, 9.65; S, 15.4%.)

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