6. *The Properties of Some Optically Active Sulphonylthioethanes.*

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It has already been shown (J., 1933, 1507) that, when the optically active acid, α-*p*-carboxyphenylsulphonyl-α-*p*-tolylthioethane (IX),* is oxidised, an optically inactive disulphone (X) results:

(IX.) $CO_2H{\cdot}C_6H_4{\cdot}SO_2{\cdot}CHMe{\cdot}S{\cdot}C_7H_7 \longrightarrow CO_2H{\cdot}C_6H_4{\cdot}SO_2{\cdot}CHMe{\cdot}SO_2{\cdot}C_7H_7$ (X.)

The active acid is also racemised by alkali and it seemed of interest to prepare another compound of the same type. dl-α-p-*Carboxyphenylsulphonyl-α-phenylthioethane* (XII) was therefore prepared from α-*p*-carbethoxyphenylsulphonylethyl methyl ketone (VIII) and diphenyl disulphoxide in a similar manner to the corresponding *p*-tolyl compound (IX, p. 1509):

(VIII.) $CO_2Et{\cdot}C_6H_4{\cdot}SO_2{\cdot}CHMe{\cdot}COMe \longrightarrow CO_2H{\cdot}C_6H_4{\cdot}SO_2{\cdot}CHMe{\cdot}S{\cdot}C_6H_5$ (XII.)

* Roman numerals I—XI refer also to J., 1933, 1506—1510.

As in the case of the *p*-tolyl compound, this acid was readily resolved into its optically active components, the *d*-acid being obtained by the crystallisation of the quinine salt, and the *l*-isomeride with the aid of *l*-menthylamine. The active acid was optically stable in chloroform and in acetic acid solutions; when it was dissolved in aqueous alcohol, sodium hydroxide in quantities up to 1 equiv. could be added without causing any racemisation, but amounts above this produced racemisation with a velocity which increased with the quantity of alkali added. When α-*p*-carboxyphenylsulphonyl-α-*p*-tolylthioethane was reinvestigated (*loc. cit.*, p. 1509), similar results were obtained with this acid.

More remarkable still was the racemisation of the methyl esters of (IX) and (XII) by small quantities of sodium methoxide.

These racemisations can only be explained by assuming the formation of a sodium salt from the esters, or from the normal sodium salt of the acid, with excess of alkali, by the displacement of the tertiary hydrogen atom attached to the α-ethane carbon atom. The formation of a salt, –S·CMe:SO(ONa)–, would naturally cause complete racemisation and this might also occur if the salt has the structure –S·CMeNa·SO_2–, the acidic ion being too unstable to retain its tetrahedral configuration. Efforts to isolate a sodium salt of the ester were, however, unsuccessful: when the ester of (XII) was treated with sodium methoxide (1 equiv.) in methyl-alcoholic solution, ether added, and the solution kept over-night, a precipitate separated. This proved to be the normal sodium salt of the acid, hydrolysis of the ester having taken place.

Oxidation of the active acid (XII) and its ester gave an optically inactive disulphone as with the acid (IX).

In order to show still more conclusively that the racemisation of these acids and their esters is due to the presence of a hydrogen atom attached to the α-ethane carbon atom, an acid lacking such a (mobile) hydrogen atom has been prepared. The ethyl ester of (X) was treated with sodium ethoxide and diphenyl disulphoxide in alcoholic solution and the *ethyl* ester of (XIII) was easily isolated; when this was hydrolysed in the usual way with excess of alkali, however, the phenylthio-group was eliminated, presumably as phenylsulphenic acid, and the acid (X) regenerated. On the other hand, by careful hydrolysis with one equivalent of aqueous-alcoholic alkali, the ester yielded dl-α-p-*carboxyphenylsulphonyl*-α-p-*tolylsulphonyl*-α-*phenylthioethane* (XIII), $CO_2H·C_6H_4·SO_2·CMe(SPh)·SO_2·C_7H_7$. This acid was again easily resolved into its optical antimerides, brucine giving the salt of the *l*-isomeride as the more sparingly soluble component, and *l*-menthylamine the salt of the *d*-acid.

As was expected, this acid was optically stable when dissolved in excess of one equivalent of alkali, and was recovered from its sodium salt unchanged in rotatory power: the active esters could not be conveniently examined in alcoholic solution with sodium ethoxide, as they are not sufficiently soluble in that solvent. Careful hydrolysis of the active esters with boiling aqueous-alcoholic alkali, however, gave an active acid of maximum rotation and it is therefore reasonable to suppose that the esters are stable towards sodium ethoxide.

Attempts to oxidise this acid and its esters to the corresponding trisulphone were unsuccessful.

Experimental.

dl-α-p-*Carboxyphenylsulphonyl*-α-*phenylthioethane* (XII) crystallised from acetic acid in prisms, m. p. 167—168° (Found: C, 55·6; H, 4·5. $C_{15}H_{14}O_4S_2$ requires C, 55·8; H, 4·35%). The methyl ester, prepared by the hydrogen chloride method, crystallised from methyl alcohol in prisms, m. p. 72°. No sodium salt of this ester could be obtained. The ester was dissolved in methyl alcohol containing sodium methoxide (1 equiv.), and ether was added: on standing over-night, the sodium salt of the acid was isolated.

Resolution of dl-α-p-*Carboxyphenylsulphonyl*-α-*phenylthioethane*.—The *quinine* salt of the acid was first obtained crystalline from a mixture of absolute alcohol and petroleum (b. p. 60—80°) and was afterwards fractionated from alcohol, from which it separated in needles. The acid (33 g.) and quinine (33 g.) in alcohol (200 c.c.) deposited 40 g. of the quinine salt, m. p. 122—126°. $[\alpha]_{5461}$ —128° in chloroform (c = 1). After six crystallisations from alcohol, 20 g. of product were obtained, m. p. 136—138°. $[\alpha]_{5461}$ —97° in chloroform (c = 1·06). These values were unchanged by further crystallisation and refer to specimens dried at 80° in a vacuum

[Found : H_2O, 2·4, 2·9. $C_{15}H_{14}O_4S_2,C_{20}H_{24}O_2N_2,H_2O$ requires H_2O, 2·7%. Found : N (after drying at 80°), 4·4. Required, 4·3%]. The *d*-acid was obtained from the final fraction by dissolving the salt in acetic acid and adding water. It had m. p. 164—165° (Found : C, 56·0; H, 4·7%), $[\alpha]_{5780}$ + 113°, $[\alpha]_{5461}$ + 134° in chloroform (c = 0·75).

The acid recovered from the initial mother-liquors was dissolved in alcohol, and 1 equiv. of *l*-menthylamine hydrochloride and sodium hydroxide added successively. A menthylamine salt was precipitated which, after crystallisation from alcohol, was finally obtained in fine needles, m. p. 182—183°, $[\alpha]_{5461}$ − 95° in chloroform (c = 0·5). The acid from this had $[\alpha]_{5461}$ − 134° in chloroform.

The following weights of acid were dissolved in 5 c.c. of alcohol, the specified quantity of sodium hydroxide (N/10-solution) added, and the solution made up to 20 c.c. with water and examined at once in a 2 dcm. polarimeter tube. The values of [α] are calculated on the weight of acid taken.

Wt. of acid, g.	Equivs. of sodium hydroxide.	$[\alpha]_{5461}$.	Approximate time from addition of alkali.
0·1177	0·99	+123°	2 mins. and 12 hrs.
0·1032	0·997	+120	,, ,, ,,
0·1612	1·035	+100	1·5 mins.
		+ 80	13 mins.
		+ 27	86 mins.
		0	18 hrs.
0·2450	1·39	+ 20	1 min.
		+ 10	2 mins.
		0	3 mins.

The acid was stable in pyridine solution, showing $[\alpha]_{5461}$ + 122·5°.

The d- and the l-*methyl* ester, prepared in the usual way, crystallised from methyl alcohol or petroleum in needles, m. p. 73—74° (Found : C, 57·4; H, 5·1. $C_{16}H_{16}O_4S_2$ requires C, 57·2; H, 4·8%), $[\alpha]_{5780}$ ± 123°, $[\alpha]_{5461}$ ± 145° in chloroform (c = 0·3), $[\alpha]_{5780}$ + 128°, $[\alpha]_{5461}$ + 148° in methyl alcohol (c = 0·5).

The first two series of the following figures show the racemisation of the *d*-ester in the presence of sodium methoxide, the methyl-alcoholic solution (made up to 20 c.c.) being examined in a 2 dcm. tube, whilst the third series refers similarly to the *l*-methyl ester of (IX) :

Wt. of ester, g.	Atoms of sodium.	$[\alpha]_{5461}$.	Approximate time, mins., after addition of sodium methoxide.
0·1303	0·08	+119°	1
		+ 88	5
		+ 29	21
		0	56
0·1251	0·68	+ 57	1·5
		+ 10	4
		0	5·5
0·0528	0·435	−127	1
		− 53	10
		0	27

The *dl*-ester was recovered from the solution in each case.

α-p-*Carboxyphenylsulphonyl*-α-*phenylsulphonylethane*.—This was obtained by oxidising the corresponding *dl*-thio-acid with hydrogen peroxide in acetic acid solution on the water-bath during 2 hours. It crystallised from acetic acid; m. p. 244°. The *methyl* ester, prepared by esterification of this acid or by the oxidation of the thio-ester, crystallised from methyl alcohol in small prisms, m. p. 128—129° (Found : C, 52·4; H, 4·7. $C_{16}H_{16}O_6S_2$ requires C, 52·2; H, 4·4%). The ethyl ester had m. p. 84°.

The active acid and methyl esters gave inactive products when they were oxidised in acetic acid with hydrogen peroxide on the water-bath or with permanganate at the ordinary temperature.

α-p-*Carboxyphenylsulphonyl*-α-p-*tolylsulphonyl*-α-*phenylthioethane*.—The ethyl ester of (X) gave with sodium ethoxide (1 mol.) in warm alcohol a yellow colour, which was immediately discharged by the addition of diphenyl disulphoxide (1 mol.). After about 1 minute on the water-bath a crystalline solid had separated and the solution was neutral. Water was added, and the crystalline material filtered off and washed with water, m. p. 165°. It was recrystallised from alcohol, in which it was sparingly soluble, and from which it separated in fine needles, m. p. 173° (Found : C, 57·3; H, 4·8. $C_{24}H_{24}O_6S_3$ requires C, 57·2; H, 4·75%).

This *ester* was hydrolysed with excess of alkali in aqueous-alcoholic solution, and the resulting liquid acidified; the acid (X), m. p. and mixed m. p. 233° (ethyl ester, m. p. and mixed m. p. with authentic specimen, 121°), was precipitated. From the mother-liquors, on standing, a small quantity of diphenyl disulphide, m. p. and mixed m. p. 62°, separated. In another experiment the mother-liquors were evaporated and phenylsulphinic acid, m. p. 80°, isolated; this gave diphenyl disulphoxide, m. p. and mixed m. p. 45°, on heating in solution with hydriodic acid. Presumably a sulphenic acid is the first product of hydrolysis and this then gives a disulphide and a sulphinic acid, $3Ph{\cdot}S{\cdot}OH \rightarrow Ph{\cdot}S{\cdot}S{\cdot}Ph + Ph{\cdot}SO_2H + H_2O$. Hydrolysis of the ester without further decomposition was effected by using the theoretical amount of alkali, and an acid was then precipitated on acidification, m. p. 190°. After crystallisation from acetic acid it had m. p. 145—147° (Found: C, 53·8; H, 4·9. $C_{22}H_{20}O_6S_3,C_2H_4O_2$ requires C, 53·8; H, 4·5%). The acetic acid in these crystals could not be removed by heating in a vacuum. Crystallisation from methyl alcohol gave fine needles, m. p. 186—190° (decomp.) depending on the rate of heating (Found: C, 55·2; H, 4·5. $C_{22}H_{20}O_6S_3$ requires C, 55·5; H, 4·2%). Recrystallised from acetic acid, this specimen melted at 145°, resolidified, and melted again at 186°. The ethyl ester prepared from this acid had m. p. 173° and was identical with the ester described above.

Resolution of α-p-*Carboxyphenylsulphonyl*-α-p-*tolylsulphonyl*-α-*phenylthioethane*.—The acid (27 g.) and brucine (25 g.) were mixed in alcoholic solution and the sparingly soluble salt which separated (39 g.) was filtered off. It had m. p. 165—170°, $[\alpha]_{5461}$ − 2·75° in chloroform (c = 6·67). This salt was repeatedly extracted with hot alcohol insufficient to dissolve it and after six such extractions the residue (6 g.) finally crystallised in prisms, m. p. 171—172° (Found: C, 60·7; H, 5·7; loss at 80° in a vacuum, 2·0. $C_{22}H_{20}O_6S_3,C_{23}H_{26}O_4N_2,H_2O$ requires C, 60·7; H, 5·4; H_2O, 2·0%). $[\alpha]_{5461}$ + 14·1°. Further extraction did not alter these values. The acid was obtained from this final fraction by solution in acetic acid, followed by the addition of water. It had a variable m. p. (decomp.) 192—205° according to the rate of heating [Found: C, 55·9, 55·7; H, 4·7, 4·8 (dried at 60° in a vacuum). $C_{22}H_{20}O_6S_3$ requires C, 55·5; H, 4·2%]. $[\alpha]_{5461}$ − 16·1° in acetone (c = 3·5). The acid obtained from the salt from the original mother-liquor gave $[\alpha]_{5461}$ + 15·0° in acetone (c = 4·8). The *d*-acid can also be obtained with the aid of the *l*-menthylamine salt, which crystallises finally from alcohol in small needles, m. p. 220°. The acid from this gave $[\alpha]_{5461}$ + 15·5° in acetone (c = 0·67). The *l*-acid, dissolved in *N*-sodium hydroxide (1·9 equivs.), gave $[\alpha]_{5461}$ + 12·2° (calc. on acid, c = 1·7). No racemisation took place during 18 hours and the recovered acid showed $[\alpha]_{5461}$ − 15·4° in acetone.

The *l*- and the *d*-ethyl ester, prepared in the usual way, crystallised from alcohol in needles, m. p. 148°, $[\alpha]_{5461}$ − 3·2° (c = 1·55) and + 4·24° (c = 4·8) respectively in chloroform. When equal weights in hot alcohol were mixed, the *dl*-ester, m. p. 173—174°, crystallised at once. The *d*-ester, dissolved in chloroform with the addition of sodium ethoxide, was recovered unchanged after an hour. The ester was hydrolysed by aqueous-alcoholic sodium hydroxide (1 equiv.), and the pure active acid recovered unchanged. By using larger quantities of alkali, *p*-carboxyphenylsulphonyl-α-*p*-tolylsulphonylethane, m. p. 233° (ester, m. p. 121°), was obtained.

Attempts to oxidise the acid and the ester with permanganate and hydrogen peroxide were unsuccessful, as they were either unchanged or broken down into substances soluble in water.

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