CCCXCIV.—*The Dependence of Rotatory Power on Chemical Constitution. Part XXXIII. The Resolution of* dl-m-*Carboxyphenyl Ethyl Sulphoxide and of* dl-m-*Carboxyphenylethylsulphine*-p-*toluenesulphonylimine.*

By JOSEPH HOLLOWAY, JOSEPH KENYON, and HENRY PHILLIPS.

THE resolution of the sulphoxide (I) and the sulphilimine (II) derived from *m*-carboxyphenyl ethyl sulphide substantiates the

(I) $\bar{O}—\overset{+}{S}<^{C_6H_4\cdot CO_2H}_{C_2H_5}$ $\qquad$ $C_6H_4Me\cdot SO_2\cdot\bar{N}—\overset{+}{S}<^{C_6H_4\cdot CO_2H}_{C_2H_5}$ (II)

results previously recorded (Harrison, Kenyon, and Phillips, J., 1926, 2079; Clarke, Kenyon, and Phillips, J., 1927, 188), which provided independent experimental evidence for the existence of semipolar double bonds.

The brucine salt of m-*carboxyphenyl ethyl sulphoxide*, after recrystallisation from ethyl alcohol until no further increase in rotatory power occurred, had $[\alpha]^{25°}_{5461}$ +70° in chloroform solution. It gave on decomposition with aqueous sodium hydroxide *d-m*-carboxyphenyl ethyl sulphoxide the specific rotatory powers of which are recorded in Table I.

The quinidine salt of the *dl*-sulphoxide, after recrystallisation from benzene, containing a little ethyl alcohol, until constancy of rotatory power—$[\alpha]^{25°}_{5461}$ +102°—was reached, gave on decomposition *l-m*-carboxyphenyl ethyl sulphoxide with $[\alpha]^{25°}_{5461}$ −232° in chloroform solution. The satisfactory agreement between the specific rotatory powers of the two enantiomorphs is good evidence that both were obtained optically pure.

TABLE I.

Specific rotatory powers of *d-m*-carboxyphenyl ethyl sulphoxide in solvents at 25°.

c = g. of sulphoxide in 100 c.c. of solution; l = 2.

		λ				
Solvent.	c.	6708.	5893.	5790.	5461.	4358.
Methyl alcohol	2·7500	+126°	+165°	+171°	+202°	+418°
Chloroform	4·2250	150	202	211	236	445
Ethyl alcohol	4·0985	217	255	260	287	465
Pyridine	1·5750	167	238	251	282	460
Specific rotatory power of the potassium salt of *d-m*-carboxyphenyl ethyl sulphoxide.						
Water *	1·2650	113	153	160	180	355

* This solution was prepared by diluting to the required volume a solution of a known weight of the *d*-sulphoxide in the calculated quantity of standard potassium hydroxide.

The specific rotatory powers of *d-m*-carboxyphenyl ethyl sulphoxide under the experimental conditions employed are all greater than those of *d-m*-carboxyphenyl methyl sulphoxide (Harrison, Kenyon, and Phillips, *loc. cit.*), but in common with the optically active sulphoxide previously described it exhibits complex rotatory dispersion and gives solutions which show no sign of mutarotation even after standing for several months. It can be concluded that the *dl*-sulphoxide is a racemic compound, since its m. p. and its solubilities in various solvents differ widely from those of the optically active enantiomorphs. The *d*-sulphoxide on oxidation yields optically inactive m-*carboxyphenylethylsulphone*.

Under experimental conditions which lead to the replacement of the oxygen atom of the *d*-sulphoxide, racemisation occurs. For example, when the sulphoxide is treated in chloroform solution with hydrogen bromide, the resulting m-*carboxyphenyl ethyl sulphide dibromide* is optically inactive. Further, the rotatory power of a solution of the *d*-sulphoxide in 1·1*N*-hydrobromic acid remains practically unchanged during 1588 hours, but in the same time, owing presumably to more complete reversible replacement of the oxygen atom by bromine, a similar solution in 3·3*N*-hydrobromic acid loses its optical activity as shown in Table II.

TABLE II.

Specific rotatory powers of *d-m*-carboxyphenyl ethyl sulphoxide in 3·3*N*-hydrobromic acid solution at 25°.

c = 1·4400 g.; l = 2; t = time in hours.

.....	0	48	72	144	312	480	648	816	1084	1588
$[\alpha]_{5790}$ ...	144°	121°	115°	95°	71°	45°	27°	22°	14°	0°
$[\alpha]_{5461}$ ...	160	135	128	107	80	51	31	25	16	0

m - *Carboxyphenylethylsulphine* - p - *toluenesulphonylimine.* — The brucine salt of *dl-m*-carboxyphenylethylsulphine-*p*-toluenesulphonylimine on recrystallisation from acetone changed rapidly in rotatory power and when optically pure had $[\alpha]^{25°}_{5461}$ −157° in ethyl-alcoholic solution. On decomposition of this salt with dilute hydrochloric acid l-m-*carboxyphenylethylsulphine*-p-*toluenesulphonylimine* was obtained, the specific rotatory powers of which are recorded in Table III.

TABLE III.

Specific rotatory powers of *l-m*-carboxyphenylethylsulphine-*p*-toluenesulphonylimine in solvents at 25°.

$l = 2$; c = g. of *l*-sulphilimine in 100 c.c. of solution.

		λ				
Solvent.	*c.*	6708.	5893.	5790.	5461.	4359.
Ethyl alcohol	2·7725	−226°	−308°	−324°	−373°	−690°
Ethyl acetate	0·8980	213	286	307	343	640
Chloroform	1·2315	243	300	322	365	678
,, ...	0·6380	—	—	305	345	642
,, ...	0·5600	204	272	286	330	621
Glacial acetic acid ...	1·9185	233	280	306	334	643
Pyridine	2·5695	200	290	307	344	670

Specific rotatory power of the sodium salt of *l-m*-carboxyphenylethylsulphine-*p*-toluenesulphonylimine.

Water *	1·7950	—	—	318	363	662

* This solution was prepared by diluting to the required volume a solution of a known weight of the *l*-sulphilimine in the calculated quantity of standard sodium hydroxide.

The more soluble portions of the brucine salt on decomposition gave a sulphilimine with $[\alpha]_{5461}$ +270°. This sulphilimine was combined with strychnine, and the strychnine salt crystallised repeatedly from ethyl alcohol until its rotatory power remained unchanged. It then had $[\alpha]^{25°}_{5461}$ +152° and on decomposition gave *d-m*-carboxyphenylethylsulphine-*p*-toluenesulphonylimine with $[\alpha]^{25°}_{5461}$ +373° in ethyl-alcoholic solution.

The physical properties of both optically active and the inactive sulphilimines are similar, in marked contrast to the wide divergence between the physical properties of the optically active and inactive sulphoxides. Hence the *dl*-sulphilimine is probably a mixture of the two enantiomorphs and not a racemic compound. The specific rotatory power of the optically active sulphilimine is but slightly influenced by solvents and remains unchanged when the solutions are kept for several months. The rotatory dispersion is less complex than that exhibited in corresponding solvents by the sulphoxide: in ethyl-alcoholic solution the sulphilimine exhibits simple rotatory

dispersion, since a straight line is obtained when $1/\alpha$ is plotted against λ^2.

d + *dl-m*-Carboxyphenylethylsulphine - *p* - toluenesulphonylimine was converted by the action of dilute hydrochloric acid into a mixture of *p*-toluenesulphonamide, *m*-carboxyphenyl ethyl sulphide, and *dl-m*-carboxyphenyl ethyl sulphoxide, and with hydrogen peroxide the *dl*-sulphilimine gave as sole products *p*-toluenesulphonamide and *m*-carboxyphenylethylsulphone.

EXPERIMENTAL.

Preparation and Resolution of dl-m-*Carboxyphenyl Ethyl Sulphoxide.*

m-*Ethylthiolbenzoic Acid.*—*m*-Thiolbenzoic acid (78 g.), prepared by the reduction of *m*-chlorosulphonylbenzoic acid (Smiles and Stewart, J., 1921, **119**, 1792), was dissolved in sodium hydroxide solution (1000 c.c. of 10%) and added to a solution of ethyl *p*-toluenesulphonate (200 g.) in ethyl alcohol (500 c.c.). The mixture was heated under reflux on a steam-bath until a sample remained clear on dilution with water (6—8 hrs.). m-*Ethylthiolbenzoic acid*, precipitated from the cold reaction mixture by hydrochloric acid, was recrystallised twice from aqueous alcohol, from which it (73 g.) separated as shining leaflets, m. p. 99—100° (Found: equiv., by titration, 181. $C_9H_{10}O_2S$ requires equiv., 182).

dl-m-*Carboxyphenyl Ethyl Sulphoxide.*—*m*-Ethylthiolbenzoic acid (78 g.) and 2*N*-nitric acid (780 c.c.) were heated on a steam-bath until solution was almost complete and the evolution of nitrous fumes had ceased. The cold filtered solution was extracted several times with chloroform. The dl-m-*carboxyphenyl ethyl sulphoxide* obtained on evaporation of the dried chloroform extract was crystallised from either benzene or a mixture of chloroform and ligroin; it (52 g.) then had m. p. 104—106° (Found: C, 54·6; H, 5·1; S, 16·2; equiv., by titration, 199. $C_9H_{10}O_3S$ requires C, 54·5; H, 5·0; S, 16·1%; equiv., 198). It is moderately easily soluble in hot water, more easily soluble in warm alcohol, acetone, or chloroform, and fairly readily soluble in warm benzene, cold chloroform, or cold alcohol.

d-m-*Carboxyphenyl Ethyl Sulphoxide.*—When a solution of the *dl*-sulphoxide (27·5 g.) and brucine (55 g.) in hot ethyl alcohol (50 c.c. of 99%) was allowed to cool, the brucine salt, m. p. 98—101°, separated as rosettes of needles. After five recrystallisations from alcohol, subsequent recrystallisation produced no further change in the rotatory power of the salt, which then had m. p. 125—126° (after desiccation for 3 days) and $[\alpha]_{5461}$ +69° ($c = 2{\cdot}145$, $l = 2$) in chloroform solution.

The brucine salt was decomposed with dilute sodium hydroxide

solution, the liberated brucine removed by filtration, and the filtrate acidified and extracted three times with chloroform. *d-m*-Carboxyphenyl ethyl sulphoxide, obtained from the dried chloroform extract, set to a hard mass of crystalline needles, m. p. 71°, and $[\alpha]_{5461}^{25°}$ +236° ($l = 2$, $c = 2{\cdot}230$) in chloroform solution.

l-m-*Carboxyphenyl Ethyl Sulphoxide.*—The *dl*-sulphoxide (15 g.) and quinidine (25 g.) were dissolved in hot benzene (150 c.c.) containing a few drops of ethyl alcohol. The quinidine salt (10 g.), which separated on standing, had m. p. 189°, $[\alpha]_{5461}$ +130° ($l = 2$, $c = 1{\cdot}25$) in chloroform solution. After five further recrystallisations, the optically pure salt was obtained with m. p. 198—199° and $[\alpha]_{5461}$ +102° ($l = 2$, $c = 1{\cdot}25$) in chloroform solution. *l-m*-Carboxyphenyl ethyl sulphoxide, obtained by the decomposition of this quinidine salt, had $[\alpha]_{5461}^{25°}$ −232°, $[\alpha]_{5790}^{25°}$ −207°, $[\alpha]_{4379}^{25°}$ −440° ($l = 2$, $c = 1{\cdot}25$) in chloroform solution.

m-*Carboxyphenylethylsulphone.*—The calculated quantity of perhydrol was added to a solution of *m*-ethylthiolbenzoic acid in aqueous potassium carbonate. When reaction was complete, the solution was cooled, filtered, and acidified with concentrated hydrochloric acid. The precipitated m-*carboxyphenylethylsulphone*, after crystallisation from hot water, had m. p. 162—164° (Found: equiv., by titration, 210. $C_9H_{10}O_4S$ requires equiv., 214), and was identical with the inactive sulphone, prepared in a similar manner from *d-m*-carboxyphenyl ethyl sulphoxide.

m-*Carboxyphenyl ethyl sulphide dibromide* separated as clusters of yellowish-red needles, m. p. 102°, when bromine (13 g.) was added to *m*-ethylthiolbenzoic acid (9 g.) in carbon disulphide (100 c.c.) (Found: Br, 45·3. $C_9H_{10}O_2SBr_2$ requires Br, 46·8%). Its bromine content decreases on exposure to air.

Preparation and Resolution of dl-m-*Carboxyphenylethylsulphine*-p-*toluenesulphonylimine.*

dl-m-*Carboxyphenylethylsulphine*-p-*toluenesulphonylimine.*—To a solution of *m*-ethylthiolbenzoic acid (110 g.) in warm alcohol (550 c.c.), made just alkaline to phenolphthalein by the addition of 3*N*-sodium hydroxide, chloramine-T (197 g.; 1·1 mols.) in warm water (550 c.c.) was added, and the mixture heated under reflux on a steam-bath for 2 hours. Dilute hydrochloric acid was added to the resulting solution when cold; dl-m-*carboxyphenylethylsulphine*-p-*toluenesulphonylimine* (100 g.) separated, and was obtained as small needles, m. p. 149°, by crystallisation from aqueous alcohol (Found: C, 54·8; H, 4·8; N, 3·9; S, 18·0; equiv., by titration, 349. $C_{16}H_{17}O_4NS_2$ requires C, 54·7; H, 4·8; N, 4·0; S, 18·2%; equiv., 351).

l-m-*Carboxyphenylethylsulphine*-p-*toluenesulphonylimine*.—To the *dl*-sulphonylimine (45 g.) in acetone (150 c.c.) containing a little ethyl alcohol, brucine (55 g.) was added, and the mixture warmed until solution was complete. The brucine salt, which crystallised in rosettes of fine needles, m. p. 160—161°, on cooling, was recrystallised from four successive quantities (about 150 c.c. in each case) of acetone containing a little alcohol. Subsequent recrystallisation produced no further alteration in the rotatory power of this salt, which then had m. p. 161°, and $[\alpha]_{5461}^{20^\circ}$ −157° and $[\alpha]_{4359}^{20^\circ}$ −287° ($l = 2$, $c = 1{\cdot}100$) in ethyl-alcoholic solution.

The brucine salt, dissolved in warm alcohol, was added to dilute hydrochloric acid, and a current of air drawn through the resulting clear solution. The l-m-*carboxyphenylethylsulphine*-p-*toluenesulphonylimine* which separated crystallised from alcohol in small prismatic needles, m. p. 149—150°, and had $[\alpha]_{5461}^{25^\circ}$ −368° ($l = 2$, $c = 2{\cdot}543$) in ethyl-alcoholic solution (Found: C, 54·8; H, 4·8%).

Isolation of d-m-*Carboxyphenylethylsulphine*-p-*toluenesulphonylimine*.—(a) *By means of cinchonidine*. The *d* + *dl*-*m*-carboxyphenylethylsulphine-*p*-toluenesulphonylimine recovered from the alcohol–acetone mother-liquor from the first crystallisation of the brucine salt described above had $[\alpha]_{5461}$ +243°. That obtained from a second preparation of the brucine salt had $[\alpha]_{5461}$ +279°. These two lots (17·8 g.) of highly dextrorotatory sulphilimine, together with cinchonidine (14·9 g.), were dissolved in hot alcohol (500 c.c.). On cooling, the cinchonidine salt separated in bulky clusters of prismatic needles. It was recrystallised eight times from alcohol, but purification was rather slow and, towards the end, somewhat erratic. The almost optically pure *l*-cinchonidine *d*-*m*-carboxyphenylethylsulphine-*p*-toluenesulphonylimine obtained had m. p. 198—199° and $[\alpha]_{5461}^{20^\circ}$ +50° ($l = 2$, $c = 1{\cdot}050$) in chloroform solution. On decomposition, as previously described, it gave *d* + *dl*-*m*-carboxyphenylethylsulphine-*p*-toluenesulphonylimine, m. p. 149—150°, $[\alpha]_{5461}^{20^\circ}$ +364° ($l = 2$, $c = 2{\cdot}070$) in ethyl-alcoholic solution.

(b) *By means of strychnine*. On cooling a solution of the *d* + *dl*-sulphilimine (5·3 g.; $[\alpha]_{5461}$ +270°) and strychnine (5·0 g.) in alcohol (20 c.c.), the strychnine *d*-salt, m. p. 165°, separated. It was recrystallised ten times from alcohol (90—50 c.c.), its rotatory power then being constant, and was thus obtained as glistening prismatic needles, m. p. 174° (decomp.), $[\alpha]_{5461}^{25^\circ}$ +152° ($l = 2$, $c = 0{\cdot}9566$) in ethyl-alcoholic solution. On decomposition with dilute sulphuric acid it gave *d*-*m*-carboxyphenylethylsulphine-*p*-toluenesulphonylimine, m. p. 150—151°, $[\alpha]_{6790}^{25^\circ}$ +323°, $[\alpha]_{5461}^{25^\circ}$ +373°, $[\alpha]_{4359}^{25^\circ}$ +689° ($l = 2$, $c = 2{\cdot}3425$) in ethyl-alcoholic solution.

It is somewhat curious that, although strychnine forms a beauti-

fully crystalline salt—hard rosettes of fine needles—m. p. 162—164°, with the *dl*-sulphilimine, yet crystallisation of this salt from methyl alcohol effects no separation of the diastereoisomeric forms.

The Interaction of l + dl-m-*Carboxyphenylethylsulphine*-p-*toluenesulphonylimine and Hydrochloric Acid.*—The clear, deep red solution obtained by heating *l* + *dl*-sulphilimine (6 g.) with concentrated hydrochloric acid (18 c.c.) on a steam-bath for 5 minutes was neutralised with sodium carbonate solution, and the precipitated *p*-toluenesulphonamide (2·5 g., m. p. 138°) removed. The filtrate was acidified and the *m*-ethylthiolbenzoic acid liberated (1 g.), after crystallisation from aqueous alcohol, had m. p. 99°. By extraction five times with chloroform, the *m*-carboxyphenyl ethyl sulphoxide (1·0 g., m. p. 102—104°) remaining in the filtrate was isolated: 0·5 g. made up to 20 c.c. with chloroform gave a solution which was optically inactive when examined in a 2-dcm. tube in light of λ5461. The total yield of hydrolytic products was 75% of the calculated quantity.

The Interaction of dl-m-*Carboxyphenylethylsulphine*-p-*toluenesulphonylimine and Hydrogen Peroxide.*—A mixture of the *dl*-sulphilimine (4 g.) and perhydrol (35 c.c.), heated on a steam-bath with occasional shaking, gave a clear solution in 15 minutes. The crystalline material (3 g., m. p. indefinite) which separated on cooling was recrystallised from a small bulk of ethyl alcohol, glistening leaflets (1·5 g., m. p. 162—164°) of *m*-carboxyphenylethylsulphone being obtained. After dilution, the filtrate yielded a second crop of crystals (0·5 g.) which proved to be *p*-toluenesulphonamide, m. p. 138°.

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BATTERSEA POLYTECHNIC, S.W. 11. [*Received, September 20th*, 1928.]