Stereochemistry of Nucleophilic Substitutions at the Sulphur Atom. The Absolute Configuration of Sulphinamides

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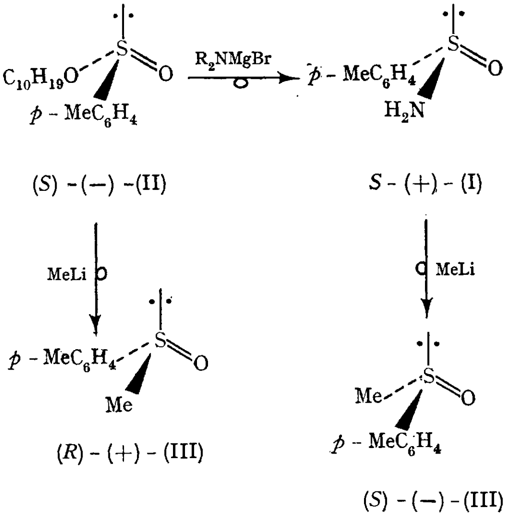
LIKE other three-co-ordinate sulphur compounds, sulphinamides possess pyramidal configuration and can be resolved into optical stereoisomers. This fact was envisaged on the basis of the magnetic non-equivalence of geminal protons adjacent to the sulphinamido-group[1] and received further support from a partial asymmetric synthesis[2] and from the separation of diastereoisomers.[3]

We have prepared (+)-toluene-*p*-sulphinamides (I) from the interaction of bromomagnesium dialkylamides with (−)-menthyl toluene-*p*-sulphinate (II),[4] $[\alpha]_D^{20}$ −196° (acetone, 98·5% optical purity), in diethyl ether–tetrahydrofuran solution at −45°. The products were purified by absorption chromatography on alumina, using diethyl ether–light petroleum as eluent. The yields in isolated product ranged between 40 and 60%.

The dimethyl and diethyl derivatives (I; R = Me, Et) were treated with methyl-lithium in diethyl ether for 2·5 hr. at −70° to yield (*S*)-(−)-*p*-tolyl methyl sulphoxide (III), $[\alpha]^D_{20}$ −113 and −130°, respectively (ethanol, 80 and 92% optical purity based on the highest reported[5] value).† In its turn (−)-menthyl (−)-toluene-*p*-sulphinate (I) was treated with methyl-lithium in diethyl ether at −70° to give (*R*)-(+)-*p*-tolyl methyl sulphoxide (III), $[\alpha]_D^{20}$ +140° (ethanol, 99% optical purity).‡



The combined results of these reactions make it possible to obtain both the enantiomeric sulphoxides starting from a common diastereoisomeric sulphinate ester. The degree of optical purity of (−)-sulphoxides (III) indicates that dimethyl- and diethyl-sulphinamides (I) must also have an optical purity not lower than 80—92%. The sulphinamides appear to be optically stable in the dark, but they racemise when exposed to sunlight. They show very similar o.r.d. curves, with a Cotton effect centred in ethanol at 240—256 mμ (see Table). A red shift of 10—14 mμ was observed when solvent was changed from ethanol to iso-octane.

The position, solvent dependance and large amplitude§ of Cotton effect indicate that the electronic transition at work must be strictly similar to the transitions[5,8] responsible for Cotton effects of menthyl toluene-*p*-sulphinate (II) and *p*-tolyl methyl sulphoxide (III) (centred at 251 and 241 mμ, absolute ethanol). All of these transitions involve an inherently dissymmetric sulphinyl chromophore, and therefore the sign of Cotton effect, which is positive for sulphinamides (I) and negative for the (−)-ester (II) and the (−)-sulphoxide (III), must reflect an opposite chirality at the sulphur atom. On the basis of the known chirality[5] of sulphinate esters and sulphoxides, the absolute chirality of sulphinamides (I) is described by the configurations (*S*)-(+) and (*R*)-(−).¶

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† Di-isopropylsulphinamide (I; R = Pr^i) did not react with methyl-lithium even with a prolonged treatment at higher temperatures. This fact could be explained in terms of steric effects, in agreement with previous observations in other nucleophilic displacements at the sulphur atom.[6] Attempts at converting sulphinamides (I) into sulphoxides (III) by means of methylmagnesium iodide or dimethylcadmium failed.

‡ The reaction of optically pure diastereoisomeric sulphinamides[3] and sulphinate esters[7] with methyl-lithium was recently reported.

§ The much larger amplitude of Cotton effect for di-isopropylsulphinamide with respect to the other sulphinamides points to a reduced conformational freedom and, therefore, the presence of steric interactions responsible for the lack of reaction with methyl-lithium.

¶ For purpose of nomenclature only, the S=O bond of sulphinate esters and related sulphinyl derivatives is treated conventionally as a single bond[5,9] and, consequently, an identical configuration label, *i.e.* (*R*) or (*S*), corresponds to an opposite chirality at the sulphur atom in the cases of sulphinamides and sulphinate esters or sulphoxides.

Optically active toluene-p-sulphinamides[a]

			$[\Phi] = 0$			
R[b]	M.p.	$[\alpha]_D^{20}$	λ (mμ)	$[\Phi]$	λ (mμ)	a
Me	65—66·5°	+157°	240	+11,200 pk −9830!	250 235	+210!
Et	c	+110°	242	+7800 pk −10,000!	250 238	+178!
Pr^i	120—121°	+205°	256	+35,200 pk −98,530 tr	277 240	+1337

[a] Solvent, ethanol; pk = peak; tr = trough; ! = lowest wavelength measured; [b] all the compounds reported gave satisfactory elemental analyses; [c] oil, n_{20}^{D} 1·5320.

The sign of Cotton effect establishes that, in analogy with the conversion (II) → (III),[7] the conversions (II) → (I) and (I) → (III) also occur with inversion of chirality at the sulphur atom. The same trend has been observed in other known instances of stereospecific nucleophilic displacements at the sulphur atom[10] in sulphinate esters, sulphoxides, and sulphoxonium salts. As in most of these cases, the most probable geometry of the transition state[10] appears to be that of a trigonal bipyramid, where both the attacking group and the leaving group are in axial positions, thus closely resembling the geometry of the transition state of the S_N2 reactions at the saturated carbon atom.

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