Asymmetric Synthesis of Amidothiosulphites. Substitution at Sulphur with Retention of Configuration

By Marian Mikołajczyk* and Józef Drabowicz

(*Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Department of Organic Sulphur Compounds, 90–362 Łódź, Boczna 5, Poland*)

Summary The reaction of (—)-t-butyl dimethylamidothiosulphite with mercury(II) chloride leading to optically active dimethylaminosulphinyl chloride proceeds with retention of configuration at the sulphinyl centre.

Although the scission of the sulphur–sulphur bond in organosulphur compounds containing a labile S(O)S-group has been thoroughly investigated,[1] stereochemical studies are limited to the synthesis and acid- and nucleophile-catalysed racemization of optically active thiosulphinates (**1**).[2]

$$\underset{(\mathbf{1})}{\mathrm{R{-}S(:O){-}SR}} \qquad \underset{(\mathbf{2})}{\mathrm{R^1_2N{-}S(:O){-}SR^2}}$$

Using an approach described for the synthesis of optically active amidosulphites[3] we have now prepared the hitherto unknown optically active amidothiosulphites (**2**) (50—90% yields) by treatment (ether: room temp.; *ca.* 2—3 h) of a mixture of (+)-α-phenylethyl isothiocyanate and the sulphurous diamide with an equimolar amount of the achiral thiol [reaction (1)]. The optical rotations of (**2**)

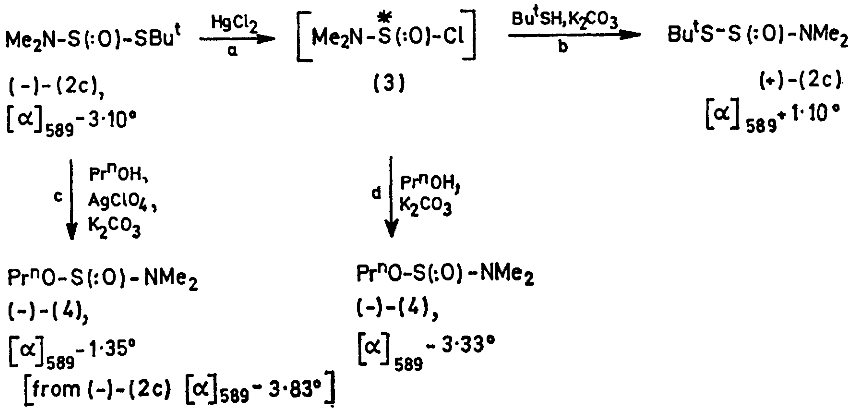
$$(+)\text{-Ph}\overset{*}{\text{C}}\text{HMe-NCS} + \text{R}^1{}_2\text{N-S(:O)-NR}^1{}_2 + \text{R}^2\text{SH} \rightarrow$$

$$\text{R}^1{}_2\text{N-}\overset{*}{\text{S}}\text{(:O)-SR}^2 + \text{PhCHMe-C(:S)NR}^1{}_2 \qquad (1)$$

a; R^1=Me, R^2=Pr^n **c**; R^1=Me,R^2=Bu^t
b; R^1=Me, R^2=Bu^n **d**; R^1=piperidin-1-yl, R^2=Bu^t
e; R^1=morpholino, R^2=Bu^t

were in the range 1—4°.†

The relative optical stability‡ of (**2**) enabled us to perfom the nucleophilic reactions at the sulphinyl centre in the Scheme. Reaction of (−)-(**2c**) with $HgCl_2$ gave the optically active sulphinyl chloride (**3**) which, owing to its fast racemization, was used without isolation.§ Treatment of optically active (**3**) with Bu^{t}SH in the presence of K_2CO_3 yielded (+)-(**2c**). In this way (−)-(**2c**) was converted into its enantiomer and the two-reaction sequence represents a new Walden cycle for sulphur involving one retention and one inversion process.

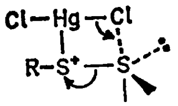


SCHEME

To establish the stereochemistry of the above reactions, the propanolysis of (−)-(**2c**) and (**3**) was investigated. This gave the optically active amidosulphites (−)-(**4**) with the same sign of rotation. As it is reasonable to expect that the propanolyses (c) and (d) should follow the same steric course, the splitting of the sulphur–sulphur bond in (**2**) by $HgCl_2$ (a) should proceed with retention of configuration at the sulphinyl sulphur atom.[4] Hence, reaction (b) as well as (c) and (d), being typical nucleophilic substitutions of the S_N2-*S* type, should involve inversion at sulphur.[5]

Reaction (a) originally performed by Mukaiyama[6] on racemic (**2**) is interesting in that $HgCl_2$ acts simultaneously as an electrophilic catalyst converting sulphenyl sulphur into a better leaving group and as a nucleophilic reagent attacking a sulphinyl sulphur *via* chlorine.

A transition state or intermediate in this displacement which accounts for the retention of configuration is a bipyramidal structure with the entering chlorine atom and departing thiol group occupying axial and equatorial positions, respectively.



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† The optical rotation measurements were carried out in benzene solution on a Perkin-Elmer Model 141 polarimeter with a sensitivity of ± 0·002°.

‡ They are racemized in benzene at 70°, a slightly higher temperature than was required for the racemization of (**1**). Furthermore, in contrast to the spontaneous loss of optical activity by (**1**) in pyridine solution at 25°, racemization of (**2**) takes place at a measurable rate.

§ Pure racemic (**3**) was isolated from the reaction of (±)-(**2c**) and $HgCl_2$ and fully characterized (satisfactory elemental analysis, and n.m.r. and i.r. spectra). The optical rotation of (**3**) has not yet been measured since it gives a turbid solution.

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[4] For other examples of retention at sulphur see: S. Oae, M. Yokoyama, M. Kise, and N. Furukawa, *Tetrahedron Letters*, 1968, 4131; B. W. Christiensen and A. Kjaer, *Chem. Comm.*, 1969, 934; B. W. Christiensen, *ibid.*, 1971, 597.
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[6] T. Mukaiyama, H. Shimizu, and H. Takei, *J. Org. Chem.*, 1967, **32**, 3475.