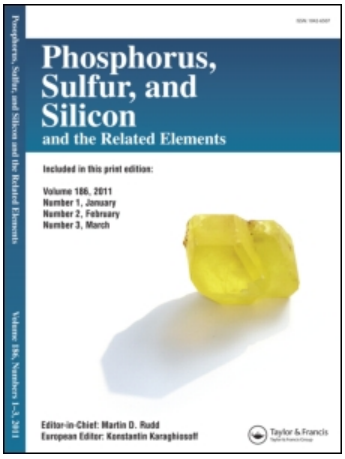

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A NEW ASYMMETRIC SYNTHESIS OF CHIRAL *t*-BUTYL *t*-BUTANETHIOSULPHINATE[1]

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Thermal decomposition of di-*t*-butyl sulphoxide (**3**) in the presence of chiral amines has been found to give chiral *t*-butyl *t*-butanethiosulphinate (**1**). Optical purities of **1** were in the range between 1 and 26%.

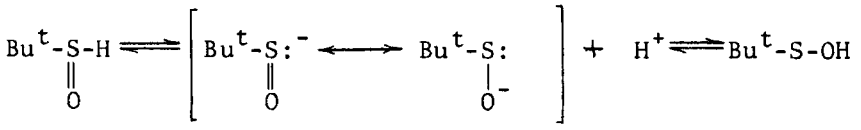
Chiral thiosulphinate S-esters, which possess a labile S(O)S-grouping, are interesting model compounds for studies of nucleophilic substitution at sulphinyl sulphur and may serve as starting materials for the synthesis of other classes of chiral sulphinyl compounds.[2] However, the major factor limiting the wider use of chiral thiosulphinates in stereochemical studies is their difficult accessibility. In contrast to chiral sulphinates,[2b] the synthetic approaches to simple chiral thiosulphinates with sulphur as a sole centre of chirality are relatively few in number, and for the most part their applicability is limited.

Chiral aromatic thiosulphinates were first prepared[3] by asymmetric oxidation of diaryl disulphides with (+)-percamphoric acid. Apart from the fact that the optical purities of diaryl thiosulphinates prepared in this way were very low (up to 3%), the method failed in the syntheses of chiral diaryl thiosulphinates which are chemically not very stable compounds.[4] Simple, optically stable alkane- or arenethiosulphinates containing the *t*-butyl group—a factor that increased their chemical and optical stability—have been obtained in our laboratory by partial optical resolution of racemates *via* β-cyclodextrin inclusion complexes.[5] More conveniently, they may be prepared by the asymmetric condensation of racemic sulphinyl chlorides with achiral thiols in the presence of optically active tertiary amines.[6] However, both the optical resolution and the asymmetric condensation afford chiral thiosulphinates with optical purities below 15%. Very recently, Davis *et al.*[7] reported asymmetric oxidation of di-*p*-tolyl and di-*t*-butyl disulphide using chiral 2-sulphonyloxaziridine affording the corresponding thiosulphinates with the optical purity values 2.1 and 13.8% ee, respectively.

In the present paper we report a new asymmetric synthesis of chiral *t*-butyl *t*-butanethiosulphinate (**1**) which is based on the asymmetric dehydration of *t*-butane-sulphenic acid (**2**) in the presence of optically active amines.

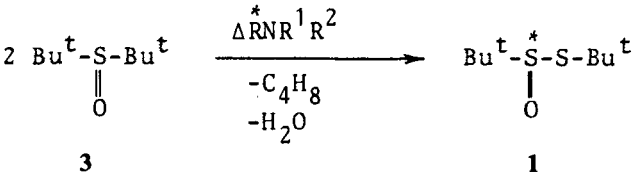
The most characteristic property of di-*t*-butyl sulphoxide (**3**) is its thermal decomposition to *t*-butanesulphenic acid (**2**) which then undergoes ready conversion to thiosulphinate **1**.[8] It is interesting to note that sulphenic acid **2** exists in two tautomeric forms **2A** and **2B**. The form **2B** containing divalent sulphur is achiral.

Since the anion derived from **2** is also achiral and exists in equilibrium between **2A** and **2B**, it is quite reasonable to assume that sulphenic acid **2** is effectively achiral.



2A **2B**

However, the interaction of sulphenic acid **2** with chiral amines should lead to hydrogen bonded chiral species (or salts) which could undergo condensation in an asymmetric way to give chiral thiosulphinate **1**. Consequently, it was conceivable that decomposition of di-*t*-butyl sulphoxide (**3**) in the presence of optically active amines should afford optically active thiosulphinate **1**. This was found to be the case.



3 **1**

* denotes a chiral, optically active centre

Generally, the reaction was carried out by heating equimolar amounts of di-*t*-butyl sulphoxide (**3**) and optically active amine in boiling benzene. After complete decomposition of sulphoxide **3** (TLC control), optically active thiosulphinate **1** was isolated in the usual manner and purified by preparative thin layer chromatography. The optical rotations and purities of **1** obtained in this way are given in Table I.

An inspection of the results in Table I shows that the reaction investigated afforded optically active thiosulphinate **1** in all cases. The optical purity of **1** was in the range between 1 to 26%. It should be pointed out that the highest value of optical purity observed for **1** is much better than those obtained by any other known method. Another advantage of the asymmetric synthesis presented here is the use of easily available optically active amines which may be recovered after completion of the reaction.

Comparison of the rotation values of chiral **1** obtained indicates the complexity of the stereochemical course of the asymmetric reaction. For example, the decomposition of sulphoxide **3** in the presence of (+)-quinidine and (−)-cinchonidine, which have the enantiomeric relationship at C_8 and C_9, leads to the same (+)-enantiomer of thiosulphinate **1**. The data in Table I show also that there is a pronounced relation between the optical purity of **1** and the structure of the chiral amine used as an asymmetric reagent.

Thus, a substantial increase in optical purity is observed on going from primary to tertiary chiral amines. Similarly, the presence of an hydroxyl group in the molecule of chiral amine causes an increase in the optical purity of **1** formed (compare the

TABLE I

Asymmetric synthesis of chiral *t*-butyl *t*-butanethiosulphinate (**1**)

No.	Amine	Thiosulphinate **1**	
		$[\alpha]_D$	Optical purity [%][a]
1	(+)-*N*,*N*-Dimethyl-α-methylbenzylamine	+8.4	5.4
2	(+)-α-Methylbenzylamine	+1.5	0.97
3	(−)-*N*,*N*-Dimethylmyrtanylamine	−3.88	2.5
4	(−)-Myrtanylamine	−0.26	0.16
5	L(−)-*N*,*N*-Dimethylamphetamine	−1.17	0.75
6	L(−)-*N*-Methylamphetamine	−0.7	0.45
7	L(−)-Amphetamine	−0.2	0.13
8	L(−)-Ephedrine	−9.4	6.07
9	(+)-Quinine	−36.6	25.6
10	(+)-Quinidine	+5.45	3.52
11	(−)-Cinchonidine	+20.5	13.2
12	(−)-Sparteine[b]	+29.46	17.0

[a]Calculated based on the value $[\alpha]_D$ 154.6° determined by NMR technique[5] for optically pure **1**.
[b]Sparteine used in this experiment was 30.2% optically pure; the values of optical rotation and optical purity of **1** obtained in the presence of sparteine are corrected to 100% of its optical purity.

results with (−)-*N*-methyl amphetamine and (−)-ephedrine). In accord with this, the best results were obtained with alkaloids such as quinine and cinchonidine.

Finally, we would like to note that our attempts to prepare other simple chiral thiosulphinates by the method presented above were unsuccessful since the thiosulphinates undergo further decomposition under the reaction conditions.

EXPERIMENTAL

IR spectra were recorded on a Perkin-Elmer Infracord 237 spectrometer for liquid film. ^{1}H NMR spectra were taken on a Perkin-Elmer R-20 spectrometer in chloroform solution with HMDSO as an internal standard. The optical activity measurements were performed on a Perkin-Elmer 241 MC photopolarimeter. The following optically active amines were used for asymmetric synthesis of **1**: (+)-α-methylbenzylamine $[\alpha]_{589}$ = +37.3° (neat); (+)*N*,*N*-dimethyl-α-methylbenzylamine $[\alpha]_{589}$ = +65.3° (neat); (−)-myrtanylamine $[\alpha]_{589}$ = −30.5° (neat); (−)-*N*,*N*-dimethylmyrtanylamine $[\alpha]_{589}$ = −28.6° (chloroform) (−)-amphetamine $[\alpha]_{589}$ = −37.6° (neat); (−)-*N*-methylamphetamine $[\alpha]_{589}$ = +3.32° (neat); (−)ephedrine $[\alpha]_{589}$ = −5.02° (ethanol) (−)-quinine $[\alpha]_{589}$ = −145.2° (ethanol); (+)-quinidine $[\alpha]_{589}$ = 262.0° (ethanol); (−)-cinchonidine $[\alpha]_{589}$ = −109.2° (ethanol); (−)-sparteine $[\alpha]_{589}$ = −5.9 (benzene). Di-*t*-butyl sulphoxide was prepared according to procedure which has recently been worked up in our laboratory[9] using hydrogen peroxide in the presence of optically active sec-amyl alcohol as catalyst.

Asymmetric Synthesis of t-Butyl t-Butanethiosulphinate (**1**) *General Procedure.* A solution of di-*t*-butyl sulphoxide (**3**) (0.5 g) and an equimolar amount of chiral amine in benzene (10 ml) was heated under reflux for 2–3 hr. The progress of the reaction was followed by TLC (silica gel; benzene–methanol, 10 : 1; iodine vapour as developer). After completion of the reaction, the reaction mixture was cooled and ether (20 ml) and water (15 ml) were added. The organic layer was separated and washed successively with 5% hydrochloric acid solution, 5% sodium bicarbonate solution, water and then dried over anhydrous magnesium sulphate. Evaporation of the solvents gave the crude product in 70–90% yield. Thin layer chromatography of the crude **1** afforded pure (TLC, IR, ^{1}H-NMR assay), optically active *t*-butyl *t*-butanethiosulphinate (**1**) spectroscopic data of which were identical with an authentic sample of **1**;[6] ^{1}H NMR ($CDCl_3$): δ 1.3 (s, 9 H, Bu^{t}SO), 1.5 (s, 9 H, Bu^{t}S); IR (film): 1080 cm^{-1} ($\nu_{S=O}$).

REFERENCES AND NOTES

1. Part XXXI of the series Organosulphur Compounds: Part XXX: J. Drabowicz, B. Bujnicki and M. Mikołajczyk, *J. Org. Chem.*, **47**, 3325 (1982).
2. (a) M. Mikołajczyk and J. Drabowicz, *Topics in Stereochemistry*, Vol. 13, N. L. Allinger, and E. L. Eliel, Eds.; Interscience, New York, 1982, Vol. 13, pp. 333–468; (b) E. Wenschuh, K. Dölling, M. Mikołajczyk and J. Drabowicz, *Z. Chem.*, **20**, 122 (1980).
3. (a) J. L. Kice and G. B. Large, *Tetrahedron Letters*, 3537 (1965); (b) L. Sagramora, P. Koch, A. Garbesi and A. Fava, *Chem. Commun.*, 985 (1967).
4. E. Block and J. O'Connor, *J. Am. Chem. Soc.*, **96**, 3921 (1974); *ibid.*, **96**, 3929 (1974).
5. M. Mikołajczyk and J. Drabowicz, *J. Am. Chem. Soc.*, **100**, 2510 (1978).
6. M. Mikołajczyk and J. Drabowicz, *J. Chem. Soc., Chem. Commun.*, 220 (1976).
7. F. A. Davis, R. H. Jenkins, S. A. Awad, O. D. Stringer, W. H. Watson and J. Galloy, *J. Am. Chem. Soc.*, **104**, 5412 (1982).
8. J. R. Shelton and K. E. Davis, *J. Am. Chem. Soc.*, **89**, 718 (1967).
9. J. Drabowicz, P. Łyzwa and M. Mikołajczyk, sent to *Synthesis*.