Asymmetric Synthesis of Sulphinic Esters with the Sulphur Atom as a Sole Chirality Centre

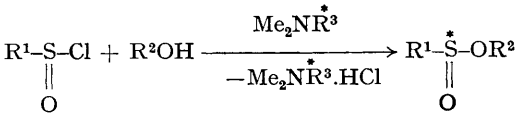
By Marian Mikołajczyk* and Józef Drabowicz

(*Centre of Molecular and Macromolecular Sciences, Polish Academy of Sciences, Department of Organic Sulphur Compounds, 90—924 Łódz 40, Żwirki 36, Poland*)

Summary The reaction of sulphinyl chlorides with achiral alcohols in the presence of optically-active tertiary amines has been found, by means of ^{1}H n.m.r. spectroscopy using a chiral europium complex, to give optically-active sulphinates with optical purity up to 45%.

Optically-active sulphinates are important key intermediates widely applied in the synthesis and configurational correlations of other classes of chiral sulphur compounds.[1] Most optically-active sulphinates have been obtained by the asymmetric reaction of racemic sulphinyl chlorides with optically-active alcohols affording a mixture of diastereomeric esters in unequal amounts.[2] However, syntheses of optically-active sulphinates, $R^1S(O)OR^2$ (**1**), with the sulphur atom as a sole chirality centre are relatively few in number[3–5] and for the most part of limited applicability. The synthetic utility of the transesterification of menthyl sulphinates[3] and the asymmetric oxidation of sulphenates[4] to give (**1**) is limited by the low stereoselectivity (1—2%).

We now report a new and general asymmetric synthesis of optically-active sulphinates (**1**) by the reaction of sulphinyl chlorides with achiral alcohols in the presence of optically-active tertiary amines as asymmetric reagents [equation (1)]. The condensation was carried out at *ca.* −70° by adding a mixture of alcohol and optically-active amine to a solution of sulphinyl chloride in ether; work-up gave compounds (**1**).



$$\underset{\underset{\displaystyle O}{\|}}{R^1\text{–}S\text{–}Cl} + R^2OH \xrightarrow[-Me_2\overset{*}{N}R^3.HCl]{Me_2N\overset{*}{R}^3} R^1\text{–}\underset{\underset{\displaystyle O}{\|}}{\overset{*}{S}}\text{–}OR^2 \qquad (1)$$

(**1**)

* Optically active.

Me_2NR = (+)- or (−)-*NN*-dimethyl-α-phenylethylamine, (−)-*NN*-dimethylmenthylamine, or (+)-*NN*-dimethyldehydroabietylamine.

In the Table some representative examples of the optically-active alkyl alkanesulphinates (**1a**—**h**) and alkyl arenesulphinates (**1i**—**o**) obtained by the above asymmetric reaction are given.

Optical purity and absolute configuration of sulphinates (**1**) was determined chemically by means of their stereospecific conversion into known sulphoxides ("Andersen synthesis").[6] In some cases (**1c**, **1d**, **1f**, **1i**, **1l**) the enantiomeric content and optical purity was estimated using chiral tris-[3-(trifluoromethylhydroxymethylene)-(+)-camphorato]europium (TFMC-Eu) (**2**).[7] In contrast to the work of Nozaki *et al.*[8] who were not able to observe the difference between the enantiomeric methyl signals of the

TABLE

Asymmetric synthesis of alkyl-, alkane-, and arene-sulphinates (**1**)

(**1**)	R^1	R^2	Amine[a,b]	$[\alpha]_{589}$ (c)[d,f]	Optical purity/ %	Absolute configuration
a	Me	Pr^n	(+)-A	−26·92 (5·45)	19·3	*S*
b	Me	Bu^n	(+)-A	−18·95 (1·93)	14·3	*S*
c	Me	Bu^t	(−)-A	−15·80 (3·24)	9·2 (11·1)	*S*
d	Me	Np[c]	(+)-A	−22·12 (4·93)	14·1 (16·4)	*S*
e	Et	Pr^n	(−)-A	+38·20 (6·03)	23·9	*R*
f	Pr^n	Me	(−)-A	+23·80 (1·89)	14·1 (19·1)	*R*
g	Pr^i	Pr^n	(−)-A	+37·10 (2·05)	29·2	*R*
h	$PhCH_2$	Pr^n	(−)-A	+28·80 (3·23)	21·0	*R*
i	Ph	Me	(−)-B	+23·90 (2·28)	8·9 (12·6)	*R*
j	Ph	Pr^n	(−)-B	+23·40 (6·26)	13·8	*R*
k	Ph	Pr^n	(+)-C	+20·06 (2·94)	11·8	*R*
l	p-MeC_6H_4	Me	(−)-B	+45·23 (3·23)	20·6 (21·0)	*R*
m	p-MeC_6H_4	Et	(−)-B	+91·80 (3·36)	43·6	*R*
n	p-MeC_6H_4	Et	(+)-C	+20·66 (3·65)	9·8	*R*
o	p-MeC_6H_4	Pr^n	(+)-C	+23·10 (3·93)	12·1	*R*

[a] A = *NN*-Dimethyl-α-phenylethylamine, B = *NN*-dimethylmenthylamine, C = *NN*-dimethyldihydroabietylamine. [b] (−)-A, $[\alpha]_{589} = -45·00°$ (5·38, ethanol, 90% of optical purity), (+)-(A), $[\alpha]_{589} = +36·90°$ (4·32, ethanol, 81% of optical purity), (−)-(B), $[\alpha]_{589} = -63·12°$ (1·73, methanol, 100% of optical purity), (+)-(C), $[\alpha]_{589} = +39·50°$ (3·30, ethanol, 100% of optical purity). [c] Np = neopentyl. [d] All rotations were measured on a Perkin-Elmer Photopolarimeter 141 and refer to solvent ethanol. [e] Calculations based on: $[\alpha]_{589} = -139·02°$ (ethanol) for (*R*)-$MePr^nSO$ sulphoxide,[9] $[\alpha]_{589} = -54·53°$ (ethanol) for (*R*)-$MePr^iSO$,[10] $[\alpha]_{589} = -106·80°$ (ethanol) for (*R*)-$MePhCH_2SO$,[9] $[\alpha]_{589} = +176·5°$ (ethanol) for (*R*)-Et(*p*-tol)SO,[10] $[\alpha]_{589} = +148·02°$ (ethanol) for (*R*)-Me(*p*-tol)SO[9], and $[\alpha]_{589} = +147·0°$ (ethanol) for (*R*)-MePhSO.[10] [f] Optical activities have been corrected for the optical purity of the amine used. [g] Values of the optical purity determined by ^1H-n.m.r. spectroscopy are given in parentheses.

racemic methyl *p*-toluenesulphinate (**1l**) in the presence of chiral tris-[3-(t-butylhydroxymethylene)-(+)-camphorato]-europium, the use of TFCM-Eu (**2**) leads to quite sufficient separation of the enantiomeric protons in sulphinates (**1**).

The optical purity of the sulphinates (**1**) formed, strongly depends on the reaction temperature and also to some extent on the structure of all the reaction components as shown in the Table. For instance, whereas the reaction of methylsulphinyl chloride with n-propanol in the presence of (+)-A at −60° gave (**1a**) which had 19·3% of optical purity, at −12° it resulted in the formation of (**1a**) having 6·2% of optical purity only. The order of the reagents addition and the use of other solvents instead of ether (light petroleum, toluene, methylene chloride) has practically no influence on the extent of the asymmetric induction.

It is worthwhile to mention that the extent of asymmetric induction in the sulphinate synthesis reported here is comparable with that observed in the reaction of sulphinyl chlorides with optically-active alcohols.[2] However, in our case the chiral inducing amine is very easily recovered as the hydrochloride and sulphinates (**1**) contain only one chirality centre on the sulphur atom.

(*Received, 22nd April* 1974; *Com.* 450.)

---

[1] P. H. Laur, in 'Sulfur in Organic and Inorganic Chemistry', ed. A. Senning, Marcel Dekker, New York, vol. 3, pp. 181—222.

[2] I. D. Morrison and H. S. Mosher, 'Asymmetric Organic Reactions,' Prentice-Hall, Englewood Cliffs, New Jersey, 1971, pp. 362—365.

[3] H. Phillips, *J. Chem. Soc.*, 1925, 2552.

[4] L. Sagramora, P. Koch, A. Garbesi, and A. Fava, *Chem. Comm.*, 1967, 985; E. Ciuffarin, M. Isola, and A. Fava, *J. Amer. Chem. Soc.*, 1968, **90**, 3594.

[5] M. Mikołajczyk and J. Drabowicz, *Tetrahedron Letters*, 1972, 2379.

[6] K. K. Andersen, *Internat. J. Sulfur Chemistry*, 1971, **6**, 69.

[7] A. F. Cockerill, G. L. O. Davies, R. C. Harden, and D. M. Rackham, *Chem. Rev.*, 1973, **6**, 553.

[8] H. Nozaki, K. Yoshino, K. Oshima, and Y. Yamamoto, *Bull. Soc. Chem. Japan.*, 1972, **45**, 3495.

[9] M. Mikołajczyk and J. Drabowicz, unpublished results.

[10] Ref. 1, p. 186.