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KINETIC RESOLUTION OF RACEMIC SULPHILIMINES BY ENANTIOSELECTIVE REDUCTION WITH ARENETHIOLS CATALYZED BY CHIRAL AMINES

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Summary: *S*-Methyl-*S*-*p*-tolyl- and *S*-ethyl-*S*-*p*-tolyl-*N*-tosylsulphilimine can be obtained in optically active form by enantioselective reduction of their racemic mixture with arenethiols catalyzed by chiral amines.

Optically active sulphur derivatives are widely used as synthons for various kinds of chiral compounds and, therefore, many efforts have been devoted to the preparation of a number of chiral sulphur units.[1]

In previous papers[2] we shoved that sulphilimines (**1**) can be easily reduced to the corresponding sulphides by arenethiols in alcoholic solvents:

$$\underset{\textbf{1}}{Ar^1(R)SNSO_2Ar^2} + 2\ Ar^3SH \longrightarrow Ar^1SR + Ar^3SSAr^3 + Ar^2SO_2NH_2$$

This reaction, however, does not occur in non-polar non-protic solvents unless catalyzed by amines. We have found now that, if chiral amines are used as catalysts, the reaction of *S*-methyl-*S*-*p*-tolyl- (**1a**) and *S*-ethyl-*S*-*p*-tolyl-*N*-tosylsulphilimine (**1b**) with a deficiency of arenethiols in various non-polar non-protic solvents proceeds with chiral discrimination and an enantiomeric enrichment (ee) of up to 80% is observed in the unreacted substrate. Some preliminary results are collected in the Table.

The reactions were carried out under argon in the temperature range 40° to 0°. Equimolar amounts (1.6 mmol) of racemic substrate and chiral amine, dissolved in 100 ml of solvent and added of the calculated deficiency of benzenethiol (**2**) or 2,4,6-trimethylbenzenethiol (**3**), were allowed to stand in a thermostatic bath. The completion of the reaction was determined by titration of the thiol with mercury(II) perchlorate.[3] The unreacted sulphilimine was isolated, purified by column chromatography, and the optical activity measured in acetone. The ee's of **1a** were evaluated in the usual way on the basis of the highest reported $[\alpha]$ value: $[\alpha]^{25}_{546}$ (c 1.36, acetone) -326° for S optically pure **1a**.[4] The ee of the recovered **1b** was determined by ^{1}H NMR spectroscopy in the presence of the chiral shift reagent Eu(tfc)$_3$.

Table

Kinetic Resolution of Sulphilimines **1a** and **1b** in Various Solvents and at Different Temperatures

Substr.	Thiol	Catalyst*	Solv.,Temp.(°C),Time(h)	Recovd.**1** (%)	$[\alpha]^{25}_{546}$	e.e.
1a	2	Qu	Toluene,25°,96	13	+ 70.2	21.5
1a	3	Qu	Toluene,25°,96	9.5	+166.3	51.0
1a	3	Qu	Toluene,25°,24	30	+ 98.3	30.2
1a	3	Qu	Toluene,25°,24	43	+ 57.9	17.8
1a	3	Qu	Toluene, 0°,96	41	+ 81.7	25.0
1a	3	Qu	Toluene,40°,72	9.9	+129.4	39.7
1a	3	Br	Toluene,25°,96	11	+ 33.0	10.1
1a	3	PEA	Toluene,25°,120	14.6	+ 8.1	2.5
1a	3	Qu	Chloroform,25°,96	43	+ 2.3	0.7
1a	3	Qu	THF,25°,72	16	+203.2	62.3
1a	3	Qu	THF,25°,120	4.5	+266.6	81.8
1a	3	Qu	Dioxane,25°,120	16	+128.6	39.4
1b	3	Qu	THF,25°,240	23	+218.8	65.6

* Qu = (-)-quinine; Br = (-)-brucine; PEA = (+)-1-phenylethylamine.

The data collected in the Table show that the absolute configuration of unreacted **1a** appears to be independent of the kinds of solvents and catalysts tested. Conversely, the trend observed for the ee values indicates that several factors (such as the nature of the solvent, of the chiral amine, and of the thiol together with the reaction temperature and the conversion percentage) have a large influence on the enantioselectivity of the studied reduction reactions.

On the basis of the obtained results and taking also into account that the starting sulphilimines can be easily prepared from the corresponding sulphides and chloramine T,[5] we think that the studied reaction represents a good alternative to other methods[4] used for the preparation of optically active sulphilimines.

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