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HIGHLY ENANTIOSELECTIVE ADDITION OF (S)-LITHIOMETHYL 1-NAPHTHYL SULFOXIDE TO KETONES

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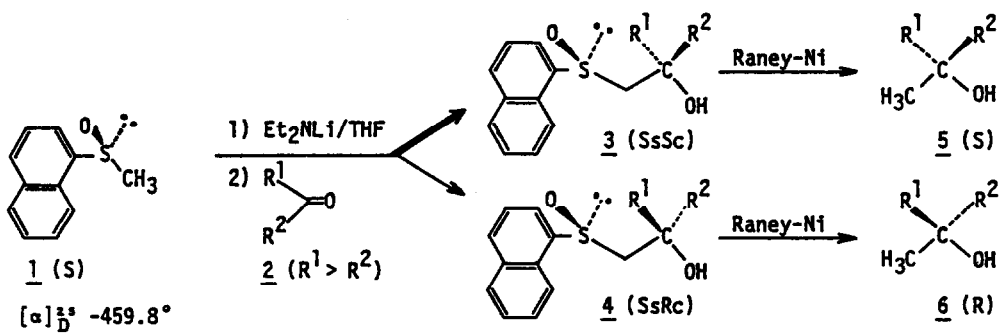
Summary: The anion of (S)-(-)-methyl 1-naphthyl sulfoxide reacts enantioselectively with alkyl phenyl ketones to give (SsSc)-β-hydroxysulfoxides with diastereomeric excess (de) up to 100 %. Optically pure (S)-tertiary alcohols are prepared by desulfurization of the corresponding diastereomers.

Chiral sulfoxides have been widely used as a chiral auxiliary for asymmetric synthesis.[1] Especially, the asymmetric reduction of ß-ketosulfoxides derived from (R)-(+)-methyl p-tolyl sulfoxide was achieved in a highly diastereoselectivity to be controlled by the chelated species with zinc cation.[2,3] However, the nucleophilic addition of the chiral α-p-tolylsulfinylcarbanion to various carbonyl compounds proceeded with a low enantioselectivity.[4] In contrast with the reaction exemplified above, the addition of the sulfinylcarbanion towards the C=N bond of imines was a highly enantioselective process.[5,6]

Solladié et al.[7] reported that the addition of (R)-lithiomethyl sulfoxide to benzaldehyde, on changing the substituents of methylsulfinyl group from p-tolyl to p-pyridyl and 1-naphthyl groups, increased in 60 and 18% enantioselectivities, respectively. However, no enantioselective addition of 1-naphthylsulfinylcarbanion was carried out with aromatic ketones.

In this paper, we report a highly enantioselective addition of the anion of (S)-(-)-methyl 1-naphthyl sulfoxide 1 to aromatic ketones, and the successful application to the preparation of optically pure tertiary alcohols.

The general procedure for the addition of the lithium carbanion of 1 to various ketones 2 was as follows (scheme 1). Optically pure sulfoxide 1 [8-10] (0.38 g, 2 mmol) in



Scheme 1

tetrahydrofuran (THF, 5 ml) was added dropwise to a solution of lithium diethylamide[11] (ca. 2.5 mmol) in THF (10 ml) at 0°C under nitrogen. To the cooled solution was added 2 (2.1 mmol) directly at -40°C, and the reaction mixture was stirred at -40°C for 2 h. The reaction was quenched with saturated aqueous ammonium chloride (50 ml). The organic layer was separated off and the aqueous layer was extracted with dichloromethane. The combined organic layers were washed with brine, dried, and evaporated in vacuo to give the diastereomeric mixtures 3 and 4 of ß-hydroxysulfoxides in 96-98% chemical yields. The total yields of the diastereomers and the diastereomeric ratios were determined by HPLC analysis on a silica gel (Zorbax SIL, 4.6 x 250 mm) using CH_2Cl_2-AcOEt (98:2) as a eluent.

Table 1. Enantioselective Addition of (S)-Lithiomethyl 1-Naphthyl Sulfoxide to Ketones[a)]

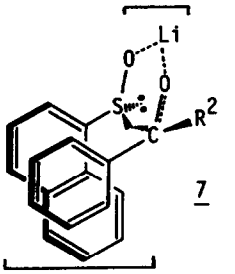
Ketone	R^1COR^2		ß-Hydroxysulfoxide[b)]		Tertiary Alcohol 5[c)]
2	R^1	R^2	3(SsSc) : 4(SsRc)	(% de)[d)]	$[\alpha]_D^{25}$ / ° (c 1.0, solvent)	% ee (Config.)
a	Ph	Me	100 : 0	(100)		
b	Ph	Et	100 : 0	(100)	-16.1 (EtOH)	100(S)[e)]
c	Ph	Pr	100 : 0	(100)	-6.6 (acetone)	100(S)[e)]
d	Ph	Bu	100 : 0	(100)	-10.2 (acetone)	100(S)[e)]
e	Ph	Pr^i	72 : 28	(44)		
f	Ph	Bu^i	76 : 24	(52)		
g	Ph	Bu^t	75 : 25	(50)		
h	Ph	Hexyl	80 : 20	(60)		
i	Et	Me	53 : 47	(6)		

a) The reaction was carried out in a THF solution at -40°C for 2 h. b) In 96-98% yields. c) In 80-85% yields. d) Determined by HPLC. e) C. R. Johnson and C. J. Stark, Jr., *J. Org. Chem.*, 47, 1193(1982).

As shown in Table 1, the presence of a 1-naphthyl substituent instead of a p-tolyl[4,7] on a chiral sulfoxide group increased drastically the asymmetric induction for the nucleophilic addition of the α-sulfinylcarbanion towards aromatic ketones. The perfect enantiofacial selectivity was achieved when the sulfinylcarbanion reacted with the ketone $RCOC_6H_5$ having linear alkyl substituents, R, such as methyl through n-butyl groups. However, there is a trend of decreasing stereoselectivity with increasing size of the alkyl substituent of 2. The stereoselectivity dropped from 100 to 50% de in going from n-butyl to isopropyl, isobutyl, t-butyl, and n-hexyl substituents, R, on 2. Especially, the reaction of 1 to aliphatic ketone such as 2-butanone proceeded in a very poor stereoselection (6% de). To determine the absolute configurations of ß-carbon of the predominant products, the three optically pure diastereomers were desulfurized with Raney-Ni[4] to give the corresponding (S)-tertiary alcohols 5b-d in 100% enantiomeric excess (ee), indicating that all the diastereoisomers were (SsSc)-ß-hydroxysulfoxides 3b-d (scheme 1).

These results show that the stereoselectivity for the asymmetric addition reaction may be influenced by electronic and steric factors namely, naphthyl-phenyl interaction in the six-membered cyclic transition state[12] chelated with lithium cation as depicted in 7. Pirkle et al.[13] found that the HPLC separation of the enantiomers of various sulfoxides was achieved by a column packed with the chiral 3,5-dinitrobenzoyl derivative using as the π-acidic site, resulting in the π-basicity of the aromatic portion of methyl 1-naphthyl sulfoxide being greater than those of phenyl and p-tolyl sulfoxides.

Chelated interaction



7

π-π interaction

The observed (SsSc)-configuration of the products coincides with the transition state model 7 predicted on the assumption that there is a π-π charge transfer interaction between the naphthyl group of 1 acted as the π-basic site and the phenyl group of 2 as the π-acidic site so that the transition state with aromatic rings in juxtaposition would be favorable. Furthermore it gives another support to the transition state 7 that the stereoselectivity for the addition of 1 to 2-butanone extremely decreased because the π-π interaction depending upon the orientation of the flat, π-electron faces of two aromatic rings would be not generated between 1 and 2-butanone. The interaction of two aromatic moieties to be face to face as in 7 is also observed for the asymmetric reduction of trifluoromethyl phenyl ketone with (S)-chiral Grignard reagent having both phenyl and trifluoromethyl groups to give (R)-alcohol.[14] On the other hand, the drop in stereoselectivity for the reaction of 1 with the ketones 2e-h having a somewhat bulky alkyl substituents would be associated with a non- or low coplanarity[15] of the phenyl ring and the carbonyl group of these ketones, that is, a decrease in the coplanarity of 2 may be reducing the π-π interaction between 1 and 2 as in 7.

A detailed study on the π-π interaction of the two aromatic rings for the addition of sulfinylcarbanion to ketones or imines is now in progress.

References and Notes:

1. For recent reviews see: (a) G. Solladié, *Synthesis*, 185 (1981). (b) *Idem, Pure Appl. Chem.*, 60, 1699 (1988).
2. H. Kosugi, H. Konta, and H. Uda, *J. Chem. Soc., Chem. Commun.*, 211 (1985).
3. G. Solladié, G. Demailly, and C. Greck, *Tetrahedron Lett.*, 26, 435 (1985).
4. N. Kunieda, M. Kinoshita, and J. Nokami, *Chem. Lett.*, 289 (1977).
5. G. Tsuchihashi, S. Iriuchijima, and K. Maniwa, *Tetrahedron Lett.*, 3389 (1973).
6. S. G. Pyne and B. Dikic, *J. Chem. Soc., Chem. Commun.*, 826 (1989).
7. G. Demailly, C. Greck, and G. Solladié, *Tetrahedron Lett.*, 25, 4113 (1984).
8. To obtain the optically pure (S)-(-)-sulfoxide, the crystalline inclusion compound prepared from an aqueous solution of β-cyclodextrin (34.1 g, 30 mmol) with methyl 1-naphthyl sulfide (5.2 g, 29.8 mmol) was suspended and stirred in a water (100 ml)

containing peracetic acid (40% aqueous solution, 5.7 ml, 30 mmol) at 0℃ for 65 h under nitrogen.[9] After the reaction, the 0.1 M aqueous sodium thiosulfate solution was added to decompose the unreacted peracetic acid, and then water was added to dissolve the complex. The aqueous solution was extracted with dichloromethane. The combined dichloromethane extracts were washed with saturated brine, dried, and evaporated in vacuo. The residue was purified by column chromatography on silica gel (Wakogel C-300) using dichloromethane as eluent. It gave (S)-(-)-methyl 1-naphthyl sulfoxide (5.4 g, 28.4 mmol, $[\alpha]_D^{25}$ -372.7° in ethanol) with 81% ee in the yield of 95% without sulfone formation. Recrystallization of the product from diethylether-pentane mixture yielded the sulfoxide (3.8 g, 20 mmol) which had a purity of 100% ee, as confirmed by ^{1}H NMR (270 MHz) with Eu(hfc)$_3$ or by HPLC analysis on a chiral stationary phase (Daicel Chiralcel OB).

For pure (S)-(-)-1 : mp 55-58℃ (lit.[10] 58-65℃); IR(KBr) 1049 (S=O) cm^{-1}; ^{1}H NMR($CDCl_3$, 270 MHz) δ 2.84 (s, 3H, CH_3), 7.56-7.70 (m, 3H, aromatic), 7.91-7.99 (m, 3H, aromatic), 8.18 (dd, 1H, J=7.25, J=1.32 Hz, aromatic); $[\alpha]_D^{25}$ -459.8° (c 0.1, ethanol)[10].

The detailed results for the asymmetric oxidation of the other sulfides by this method[9] will be reported elsewhere.

9. H. Sakuraba, K. Natori, N. Sato, and Y. Tanaka, The 55th Annual Meeting of The Chemical Society of Japan (Fukuoka), Abstract paper II, p. 704 (1987).
10. J. Jacobus and K. Mislow, *J. Am. Chem. Soc.*, 89, 5228 (1967).
11. R. Annunziate, M. Cinqueni, and F. Cozzi, *J. Chem. Soc. Parkin* I, 1687 (1979).
12. N. Kunieda, J. Nokami, and M. Kinoshita, *Chem. Lett.*, 369 (1974).
13. W. H. Pirkle, J. M. Finn, J. L. Schreiner, and B. C. Hamper, *J. Am. Chem. Soc.*, 103, 3964 (1981).
14. J. D. Morrison and H. S. Mosher, " *Asymmetric Organic Reactions* " Prentice-Hall, Inc., Englewood Cliffs, New Jersey, pp 192-193 (1971).
15. G. D. Hedden and W. G. Brown, *J. Am. Chem. Soc.*, 75, 3744 (1953).

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