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ENANTIOFACE DIFFERENTIATING ASYMMETRIC REACTION BY p-TOLYLSULFINYLCARBANION

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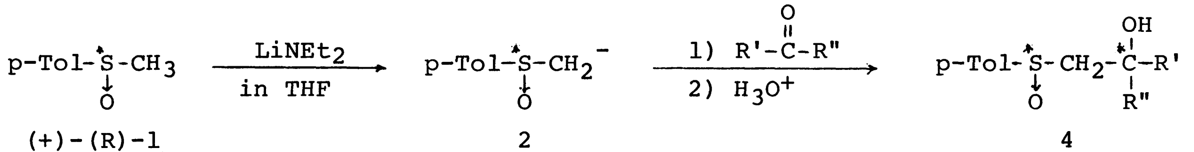
The enantioface differentiating reaction by p-tolylsulfinylcarbanion(**2**), derived from (+)-(R)-methyl p-tolyl sulfoxide(**1**), toward unsymmetrical ketones(**3**) is described. The carbanion(**2**) readily reacts with **3** to produce a mixture of (R_SR_C)- and (R_SS_C)-β-hydroxy sulfoxides (**4**). The ratio of the diastereoisomers in **4** and the absolute configuration of the predominant diastereoisomer were determined with the aid of NMR and the specific rotation of alcohol(**6**) which was prepared by desulfurization of **4**.

Recently, we reported two types of asymmetric inductions by chiral sulfinyl group. The one is enantiomer differentiating reaction1) by optically active sulfinic esters.2) The other is diastereoface differentiating reaction1) by chiral sulfinyl compounds.3) In this communication, we wish to report an enantioface differentiating reaction1) toward unsymmetrical ketones by p-tolylsulfinylcarbanion(**2**) developed by Tsuchihashi et al.4)



$$\underset{\downarrow\atop O}{\text{p-Tol-}\overset{*}{S}\text{-CH}_3} \xrightarrow[\text{in THF}]{\text{LiNEt}_2} \underset{\downarrow\atop O}{\text{p-Tol-}\overset{*}{S}\text{-CH}_2^-} \xrightarrow[\text{2) H}_3\text{O}^+]{\text{1) R'-}\overset{O}{\overset{\|}{C}}\text{-R''}} \text{p-Tol-}\underset{\downarrow\atop O}{\overset{*}{S}}\text{-CH}_2\text{-}\overset{OH}{\underset{R''}{\overset{*|}{C}}}\text{-R'}$$

(+)-(R)-**1** **2** **4**

In a typical reaction, a solution of 0.40 g(2.59 mmol) of (+)-(R)-methyl p-tolyl sulfoxide(**1**)($[\alpha]_D$ +143°(acetone)) in 10 ml of dry tetrahydrofuran was added dropwise to a solution of lithium diethylamide(prepared from 0.33 ml of diethylamine and 2 ml of a 0.1 g/ml solution of n-butyllithium in n-hexane) in 15 ml of dry tetrahydrofuran at 0°C under nitrogen. After 30 minutes, acetophenone(3d)(0.32 g, 2.70 mmol) was added with vigorous stirring. When addition was complete, stirring was continued for 1 hour and 5 ml of a saturated solution of ammonium chloride was added followed by 30 ml of water. The mixture was extracted with chloroform(3 x 30 ml). The combined extracts were washed with brine and dried over anhydrous magnesium sulfate. After evaporation of the solvent under reduced pressure, acetophenone remaining in the residue was removed under a highly diminished pressure, giving a diastereomeric mixture of β-hydroxy sulfoxides(4d) in a 99% yield.

The ratio of the diastereoisomers in 4d was supported by the NMR spectrum which exhibited resonances at δ 1.6 and δ 1.9 due to two kinds of diastereotropic methyl groups. By integration of the respective signals, the per cent ratio of the diastereoisomers was found to be 33 : 67.

The reaction was conducted using some other unsymmetrical ketones(3a-h). The results are summarized in Table 1.

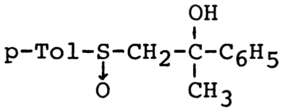
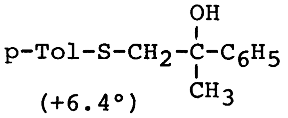
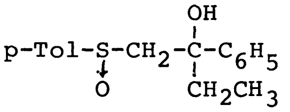
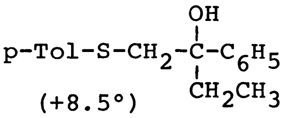
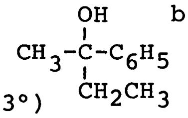
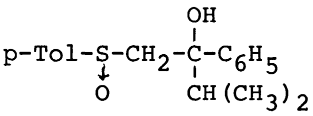
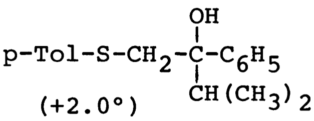
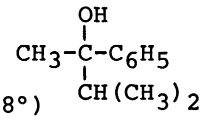
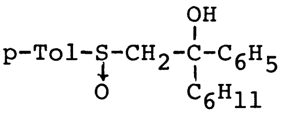
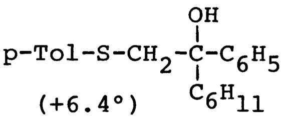
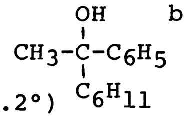
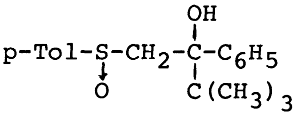
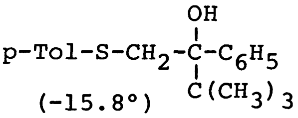
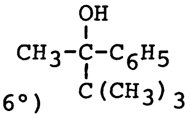
Table 1. Diastereomer ratio of product obtained by enantioface differentiating reaction with p-tolylsulfinylcarbanion(2)

Ketones		β-Hydroxy sulfoxides[a)]	Diastereomer ratio of 4 [b)] Major : Minor[c)]
(3a)	CH_3-CO-CH_2CH_3	4a	50 : 50 (50 : 50)[d)]
(3b)	CH_3-CO-CH$(CH_3)_2$	4b	51 : 49 (52 : 48)[d)]
(3c)	CH_3-CO-C$(CH_3)_3$	4c	53 : 47 (55 : 45)[e)]
(3d)	C_6H_5-CO-CH_3	4d	67 : 33 (75 : 25)[d)]
(3e)	C_6H_5-CO-CH_2CH_3	4e	58 : 42 (75 : 25)[e)]
(3f)	C_6H_5-CO-CH$(CH_3)_2$	4f	60 : 40 (73 : 27)[e)]
(3g)	C_6H_5-CO-C_6H_{11}	4g	59 : 41 (72 : 28)[e)]
(3h)	C_6H_5-CO-C$(CH_3)_3$	4h	70 : 30 (77 : 23)[e)]

a) β-Hydroxy sulfoxides were obtained almost quantitatively.
b) Measured by NMR analysis.
c) Values in parentheses show the results of the reaction run at -78°C.
d) Based on the integration of methyl signals.
e) Based on the integration of methylene signals.

When the β-hydroxy sulfoxide(4e)(290 mg, 1 mmol)(obtained by the reaction run at -78°C) was treated with W-4 type Raney nickel(prepared from 2 g of alloy, 45% nickel) in ethanol at room temperature for 5 hours, the corresponding dextrorotatory

Table 2. Optically active β-hydroxy sulfides(5) and alcohols(6) derived from β-hydroxy sulfoxides(4)

Diastereomeric mixture of β-hydroxy sulfoxides[a]	β-Hydroxy sulfides ($[\alpha]_D$ in acetone)	Alcohols ($[\alpha]_D$ in acetone)
(4d)  $\text{p-Tol-}\underset{\underset{\text{O}}{\downarrow}}{\text{S}}\text{-CH}_2\text{-}\overset{\text{OH}}{\underset{\text{CH}_3}{\text{C}}}\text{-C}_6\text{H}_5$	(5d)  $\text{p-Tol-S-CH}_2\text{-}\overset{\text{OH}}{\underset{\text{CH}_3}{\text{C}}}\text{-C}_6\text{H}_5$ (+6.4°)	
(4e)  $\text{p-Tol-}\underset{\underset{\text{O}}{\downarrow}}{\text{S}}\text{-CH}_2\text{-}\overset{\text{OH}}{\underset{\text{CH}_2\text{CH}_3}{\text{C}}}\text{-C}_6\text{H}_5$	(5e)  $\text{p-Tol-S-CH}_2\text{-}\overset{\text{OH}}{\underset{\text{CH}_2\text{CH}_3}{\text{C}}}\text{-C}_6\text{H}_5$ (+8.5°)	(6e)  $\text{CH}_3\text{-}\overset{\text{OH}}{\underset{\text{CH}_2\text{CH}_3}{\text{C}}}\text{-C}_6\text{H}_5$ (+5.3°) [b]
(4f)  $\text{p-Tol-}\underset{\underset{\text{O}}{\downarrow}}{\text{S}}\text{-CH}_2\text{-}\overset{\text{OH}}{\underset{\text{CH(CH}_3)_2}{\text{C}}}\text{-C}_6\text{H}_5$	(5f)  $\text{p-Tol-S-CH}_2\text{-}\overset{\text{OH}}{\underset{\text{CH(CH}_3)_2}{\text{C}}}\text{-C}_6\text{H}_5$ (+2.0°)	(6f)  $\text{CH}_3\text{-}\overset{\text{OH}}{\underset{\text{CH(CH}_3)_2}{\text{C}}}\text{-C}_6\text{H}_5$ (+3.8°)
(4g)  $\text{p-Tol-}\underset{\underset{\text{O}}{\downarrow}}{\text{S}}\text{-CH}_2\text{-}\overset{\text{OH}}{\underset{\text{C}_6\text{H}_{11}}{\text{C}}}\text{-C}_6\text{H}_5$	(5g)  $\text{p-Tol-S-CH}_2\text{-}\overset{\text{OH}}{\underset{\text{C}_6\text{H}_{11}}{\text{C}}}\text{-C}_6\text{H}_5$ (+6.4°)	(6g)  $\text{CH}_3\text{-}\overset{\text{OH}}{\underset{\text{C}_6\text{H}_{11}}{\text{C}}}\text{-C}_6\text{H}_5$ (+15.2°) [b]
(4h)  $\text{p-Tol-}\underset{\underset{\text{O}}{\downarrow}}{\text{S}}\text{-CH}_2\text{-}\overset{\text{OH}}{\underset{\text{C(CH}_3)_3}{\text{C}}}\text{-C}_6\text{H}_5$	(5h)  $\text{p-Tol-S-CH}_2\text{-}\overset{\text{OH}}{\underset{\text{C(CH}_3)_3}{\text{C}}}\text{-C}_6\text{H}_5$ (-15.8°)	(6h)  $\text{CH}_3\text{-}\overset{\text{OH}}{\underset{\text{C(CH}_3)_3}{\text{C}}}\text{-C}_6\text{H}_5$ (+3.6°)

a) All of the reactions were run at -78°C.

b) Configurations and specific rotations of these alcohols are reported as follows. (S)-2-Phenyl-2-butanol; $[\alpha]^{27}_D$ -17.7°(neat), (R)-isomer; $[\alpha]^{22}_D$ +17.45°(neat).[5,6] (S)-1-Cyclohexyl-1-phenyl ethanol; $[\alpha]_D$ -20.6°($CHCl_3$).[7]

1-(p-tolylsulfenyl)-2-phenyl-2-butanol(5e)($[\alpha]^{19}_D$ +8.5°(acetone)) was produced in an 89% yield. While, by a similar treatment run at 50°C for 0.5-1 hour, the corresponding alcohol, 2-phenyl-2-butanol(6e)($[\alpha]^{20}_D$ +5.3°(acetone)), was obtained in an 82% yield without the preparation of 5e. Since the specific rotation of (S)-2-phenyl-2-butanol is reported to be $[\alpha]^{27}_D$ -17.7°(neat),[5] the absolute configuration of the predominant diastereoisomer in 4e should be R_SR_C.

In a similar manner as for 4e, treatment of 4g with Raney nickel yielded (R)-rich 1-cyclohexyl-1-phenyl ethanol(6g)($[\alpha]^{20}_D$ +15.2°(acetone)), suggesting that the absolute configuration of the predominant diastereoisomer in 4g is R_SR_C.

Similarly, the desulfurization of 4f and 4h yielded dextrorotatory 2-phenyl-

3-methyl-2-butanol(6f) and 2-phenyl-3,3-dimethyl-2-butanol(6h), respectively. However, no attempt has been made to assign their absolute configurations.

Further investigations are in progress to clarify the stereochemical implications of the reaction.

References and Notes

1) Y. Izumi, Angew. Chem. Int. Ed., 10, 871 (1971); "Chemistry of Asymmetric Reaction", Kagaku Sosetsu, 4, Chem. Soc. Japan Inc., Tokyo (1974).
2) N. Kunieda, J. Nokami, and M. Kinoshita, Chem. Lett., 871 (1973); N. Kunieda, J. Nokami, and M. Kinoshita, Bull. Chem. Soc. Japan, 49, 256 (1976).
3) N. Kunieda, J. Nokami, and M. Kinoshita, Chem. Lett., 369 (1974).
4) G. Tsuchihashi, S. Iriuchijima, and M. Ishibashi, Tetrahedron Lett., 4605 (1972); G. Tsuchihashi, S. Iriuchijima, and K. Maniwa, ibid., 3389 (1973).
5) D.J. Cram and J. Allinger, J. Am. Chem. Soc., 76, 4516 (1954).
6) H.H. Zeiss, ibid., 73, 2391 (1951).
7) T.D. Inch, G.J. Lewis, G.L. Sainsburg, and D.J. Sellers, Tetrahedron Lett., 3657 (1969).

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