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Enantioselective synthesis of oxiranes by the reactions of dimethylsulfonium methylide and aromatic aldehydes and ketones in the presence of chiral micelles

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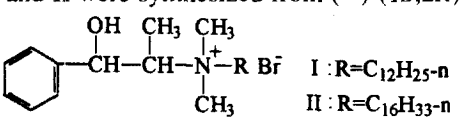
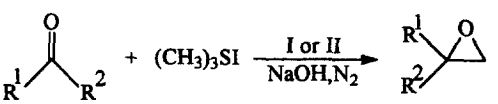
Abstract: Within chiral micelles formed from chiral surfactants *N*-dodecyl-*N,N*-dimethyl ephedrine bromide I and *N*-hexadecyl-*N,N*-dimethyl ephedrine bromide II, a series of optically active products was obtained by the reactions of dimethylsulfonium methylide and aromatic aldehydes, ketones. The highest ee was up to 57.2%. Meanwhile, we have found that the asymmetric induction depends on a number of factors, such as the alkyl chain length of surfactant, reaction temperature, reaction time and the concentration of base in aqueous micellar solution. © 1997 Elsevier Science Ltd

Goldberg[1] first reported the reduction of prochiral ketones in an aqueous micellar solution of (+)-(*R*)-dodecyl-*N,N*-dimethyl-α-phenylethylammonium bromide to give chiral alcohols, but the enantiomeric excess was only 1.7%. Recently we have utilized chiral micelles as an asymmetric environment in the reaction of many types of prochiral substrates such as the synthesis of α-aminoarylacetic acids, reduction of prochiral ketones and oxidation of prochiral sulfides.[2]

It is well-known that oxiranes, especially homochiral oxiranes, are important in biology, hence enantioselective oxirane synthesis by means of chiral reagents is very important, for instance, the Sharpless reaction.[3] Our group have previously reported optically active oxirane synthesis in chiral micelles formed from chiral surfactants, such as epoxidation of chalcones and optically active α,β-epoxyketones by Darzens condensation.[4] It has been reported that oxiranes were synthesized enantioselectively by means of dimethylsulfonium methylide and chiral phase-transfer catalysts.[5] Here we wish to report the formation of optically active oxiranes in chiral micellar systems. Two homochiral quaternary ammonium salts I and II were synthesized from (−)-(1*S*,2*R*)-ephedrine for our work.[6]



The micelles which were produced by certain compositions of surfactants I, II and water provided the asymmetric microenvironments for enantioselective oxirane synthesis by the reaction of dimethylsulfonium methylide and aromatic aldehydes, ketones (Scheme 1). The results are shown in Table 1.



Scheme 1.

The results shown in Table 1 clearly demonstrate that stereoselectivity was achieved in all chiral micelles employed. On the other hand, it is shown in Table 1 that the micelle formed from the surfactant with longer alkyl chain II provided better enantioselectivity than the shorter chain analogue I. Evidently,

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Table 1. The reactions of aromatic aldehydes and ketones and dimethylsulfonium methylide in chiral micelles[a)]

Entry	Surfactant[b)]	R^1	R^2	Yield (%)	$[\alpha]^{25}{}_{D}$ [c)]	e.e.%[d)]	Absolute Configuration[e)]
1	I	Ph	H	61	2.8	42.2	R
2	II	Ph	H	59	3.8	57.2	R
3	I	$PhCH_2$	H	49	-3.8	23.3	S
4	II	$PhCH_2$	H	40	-4.2	25.8	S
5	I	Ph	CH_3	39	-0.71	21.7	S
6	II	Ph	CH_3	52	-0.76	23.2	S

a) Reaction temperature is 38°C, C_{NaOH}=50%.
b) Concentration of chiral surfactants are 0.0268 M.
c) Acetone is used as solvent for 1–2, ether for 3–4 and ethanol for 5–6.
d) Obtained from $[\alpha]_D^{25}/[\alpha]_{D.max}^{25}$. $[\alpha]_{D.max}^{25}$ are cited from the literature.[5,7]
e) Absolute configurations depend on the literature.[5,7]

Table 2. The influence of reaction temperature[a,b)]

Temperature (℃)	Yield (%)	$[\alpha]^{25}{}_{D}$	e.e.%
20	49.9	1.2	18.1
30	56.0	2.7	40.7
40	45.2	3.7	55.7
50	52.1	3.0	45.2

a) Surfactant is II and substrate is benzaldehyde.
b) Reaction time is 48 h.

Table 3. The influence of reaction time[a,b)]

Reaction Time (hr)	Yield (%)	$[\alpha]^{25}{}_{D}$	e.e.%
24	20	0.34	5.1
36	40	2.3	34.6
48	59	3.8	57.2
60	45	3.8	57.2

a) Surfactant is II and substrate is benzaldehyde.
b) Reaction temperature is 38°C.

these results can be attributable to hydrophobic–lipophilic interactions between the substrate and the micelle. The binding of the substrate by the chiral micelle is a dynamic process, the micelle and their monomeric surfactants are also in a dynamic equilibrium. Therefore increasing the alkyl chain length in surfactants of chiral micelles, the better enantioselectivity would be obtained. This was identical with the results of our previous reports.[2,4]

From Table 2, it is clear that temperature does not influence the chemical yield, but does significantly affect the enantiomeric excess. At about 40°C, the ee was at a maximum.

From Table 3 it can be seen that with the increase in reaction time, chemical yield and ee both increased gradually: when the reaction time was up to 48 h (in accordance with Hiyama,[5] the reaction was almost complete and the enantiomeric excess was also maximised.

From Table 4, we could conclude that the reaction starts only in a certain strength of base, because $(CH_3)_3SI$ needs to be transformed to dimethylsulfonium methylide. When the concentration of NaOH was over 50%, the ee of the product reached a maximum.

Experimental

The optical rotations were obtained from a WZZ-1 automatic rotation detector (Shanghai). The ^1H NMR spectra were recorded on a JEOL JUM-PMX 60 SI (60 Mhz) spectrometer using CCl_4 as the solvent and TMS as the internal standard. The IR was recorded on Perkin Elmer 683 spectrometer.

Table 4. The influence of the concentration of base[a)]

NaOH % (aqueous solution)	Yield (%)	$[\alpha]^{25}_D$	e.e.%
23.1	0	0	0
36	57	0.83	12.5
50	59	3.8	57.2
60	50	3.8	57.2

a) Surfactanct is II and substrate is benzaldehyde.

Table 5. IR and ^{1}H NMR of oxiranes synthesized

Entry	IR (KBr) (cm^{-1})	^{1}H NMR		
1	3050 1610 1500 1250 750 690	7.13(5H,s) 2.50(1H,q)	3.58(1H,q)	2.86(1H,q)
3	3050 1600 1500 1250 740 700	7.19(5H,s) 2.71(1H,q)	3.01(1H,m) 2.43(1H,q)	2.80(2H,d)
5	3050 1610 1500 1250 750 690	7.07 (5H,s) 1.55(3H,s)	2.70(1H,d)	2.48(1H,d)

See Mcallan[8] for the synthesis of trimethylsulfonium iodide.

General procedure

To a 50 ml three-necked flask was added 0.536 mmol surfactant I or II and 612 mg (3.00 mmol) $(CH_3)_3SI$, then 8 ml CH_2Cl_2, 50% aqueous sodium hydroxide (10 g NaOH in 10 ml of water), benzaldehyde (283 mg, dissolved in 2 ml CH_2Cl_2) were added at 38°C under nitrogen atmsphere. After 48 h at this temperature the reaction was worked up. The reaction mixture was extracted with ether. The extracts were dried over anhydrous Na_2SO_4. The solvent was evaporated and preparative TLC (silica gel, n-hexane: ether 10:1, R_f 0.5) give a single product, 2-phenyloxirane. The structures of products were all identified by ^{1}H NMR and IR (Table 5).

Acknowledgements

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References

1. Goldberg, S. I., Baba, N., Green, R. L., *J. Am. Chem. Soc.*, **1978**, 100, 6768.
2. (a) Zhang, Y. M., Li, W. X., *Synth. Commun.*, **1988**, 18, 1685. (b) Zhang, Y. M., Fan, W. Q., Lu, P., Wang, W., *Synth. Commun.*, **1988**, 18, 1495. (c) Zhang, Y. M., Fu, C. L., Fan, W. Q., *Chin, J. Chem.*, **1990**, 1, 89.
3. Sharpless, K. B., Katsuki, T., *J. Am. Chem. Soc.*, **1980**, 102, 5974.
4. (a) Zhang, Y. M., Fu, C. L., Lu, P., Fan, W. Q., *Chem. J. Ch. Univ.*, **1989**, 10, 1208. (b) Zhang, Y. M., Fang, X. H., *J. Hangzhou Univ. (Natural Science)*, **1994**, 21(1).
5. Hiyama, T. *J. Am. Chem. Soc.*, **1975**, 97, 1626.
6. The homochiral quaternary ammonium salts I and II were prepared from ephedrine. See: Fan, W. Q., Zhou, Q., Shen, J., Lu, P., Zhang, Y. M., *Acta Chimica Sinica* 45, 287, **1987**, I: m.p. 88–89°C, $[\alpha]^{20}_D$ – 11.4 (ethanol); II: m.p. 112–113°C, $[\alpha]^{20}_D$ – 9.1 (ethanol). The structures of I and II were identified by ^{1}H NMR and IR.
7. (a) Ohta, T., *Tetrahedron Lett.*, **1990**, 31(20), 2895. (b) Tanaka, Y., Jpn. Kokai Tokkyo Koho JP01, 249, 763[89, 249, 763], *Chem. Abs.* 112:118629 (**1990**).
8. (a) Mcallan, D. T., *J. Am. Chem. Soc.*, **1951**, 73, 3627. (b) Heal, H. G., *J. Chem. Soc.*, **1946**, 1126.

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