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ASYMMETRIC RING-OPENING OF CYCLOHEXENE OXIDE WITH VARIOUS THIOLS CATALYZED BY ZINC Lg-TARTRATE

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Optically active trans-2-(arylthio or alkylthio)-cyclohexanols are prepared by the asymmetric ring-opening of cyclohexene oxide with various arylthiols or alkylthiols in 52 - 85% ee by the use of zinc Lg-tartrate as a heterogeneous chiral Lewis acid catalyst.

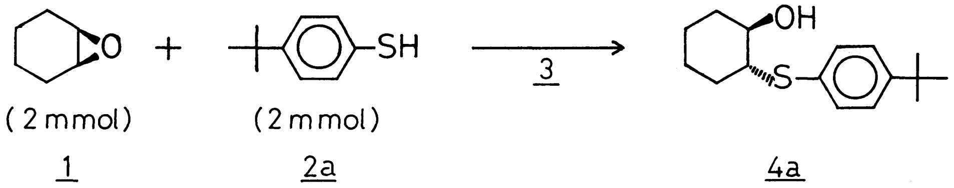
Asymmetric synthesis starting from meso-compounds has been recognized as one of the useful methods for the synthesis of optically active compounds. A number of biological$^{1)}$ or chemical$^{2)}$ methods have been reported in this category, and we also reported an asymmetric synthesis of bicyclic lactones from meso-1,2-dicarboxylic acids,$^{3)}$ asymmetric acylations of meso-1,2-diols$^{4)}$ and prochiral glycerols.$^{5)}$ Recently, M. Asami reported an asymmetric transformation of cyclohexene oxide, a meso-compound, into optically active 2-cyclohexen-1-ol in 92% ee by using chiral lithium amide.$^{6)}$ In this communication, we wish to describe an asymmetric ring-opening of cyclohexene oxide with various thiols by the use of zinc Lg-tartrate as a heterogeneous chiral Lewis acid catalyst.

At first, we screened various chiral catalysts for the ring cleavage of cyclohexene oxide (1) with p-t-butylphenylthiol (2a) and found that zinc Lg-tartrate (3) gave optically active trans-2-(p-t-butylphenylthio)cyclohexanol (4a).$^{7)}$ Then, we examined the reaction parameters such as solvent, concentration, temperature, and amount of catalyst. These results are summarized in Table 1.

The following conditions (entry 11) gave the best result. In a CH_2Cl_2 (5 ml) solution of 1 (2 mmol) and 2a (2 mmol) was suspended 3 (0.2 mmol) which was easily prepared from zinc chloride and pottasium Lg-tartrate in water and dried at 120 °C / 1 mmHg for 5 h.$^{8)}$ This heterogeneous mixture was stirred at 25 °C for 5 d. After filtration of 3, the filtrate was concentrated and purified by silica-gel column chromatography (hexane / ethyl acetate = 10 / 1) to give 4a in 96% yield ($[\alpha]_D^{23}$ -29.8°(c 5.00, CH_2Cl_2), 52% ee). Furthermore, there was no change in the catalytic activity of 3 after recovery by filtration.

The results shown in Table 1 can be noted as follows; since the catalytic activity of 3 was decreased by the tight coordination of polar solvent such as DMF to 3, only a small amout of 4a was formed (entry 19). On the other hand, by the use of low polar solvent such as cyclohexane, poor optical yield (entry 2) was observed probably because the coordination of the formed alcohol (4a) to 3

Table 1. Asymmetric ring-opening of cyclohexene oxide (1) with p-t-butylphenylthiol (2a) catalyzed by zinc Lg-tartrate (3)



Entry	Solvent	(ml)a)	Temp/°C	Time/d	3 (mol%)	Yield/%b)	ee/%c)
1	None		25	5	10	45d)	5.9
2	Cyclohexane	5	25	5	10	96	29
3	Benzene	5	25	5	10	95	40
4	CCl_4	5	25	5	10	91	34
5	$CHCl_3$	5	25	5	10	96	44
6	CH_2Cl_2	2.5	25	5	10	96	48
7	CH_2Cl_2	5	0	7	10	72	46
8	CH_2Cl_2	5	25	5	0	5	—e)
9	CH_2Cl_2	5	25	14	1	98	50
10	CH_2Cl_2	5	25	7	5	98	52
11	CH_2Cl_2	5	25	5	10	96	52
12	CH_2Cl_2	5	25	3	20	98	51
13	CH_2Cl_2	5	reflux	0.5	10	70	35
14	CH_2Cl_2	10	25	5	10	96	50
15	CH_2Cl_2	20	25	5	10	87	49
16	AcOEt	5	25	5	10	98	51
17	THF	5	25	5	10	96	36
18	EtOEt	5	25	5	10	98	45
19	DMF	5	25	5	10	6	—e)
20	MeOH	5	25	5	10	95	6.5

a) Solvents were dried over molecular sieves 4A.
b) Isolated yield after silica-gel column chromatography.
c) Enantiomeric excess was determined by ^{19}F NMR measurement of the MTPA ester of 4a.
d) A significant amount of polymerized product was formed.
e) Not measured.

interferes with the asymmetric interaction between substrates (1 and 2a) and catalyst (3). This interference was clearly shown by the very low optical purity of 4a on the reaction in methanol (entry 20) or without solvent (entry 1). Assuming from these explanations, moderately polar solvents such as CH_2Cl_2 and

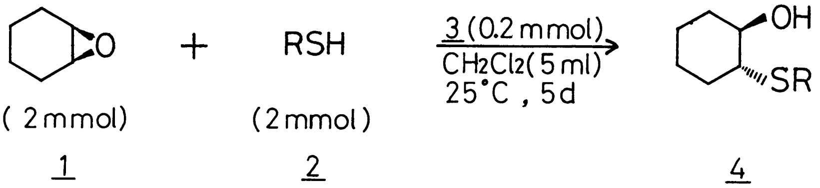
AcOEt would give good optical yields by the solvation of 4a not to interfere with the asymmetric interaction (entries 11, 16).

Concerning the reaction temperature, 25 °C would be required for the efficient solvation of 4a (entries 7, 11, 13). In the cases of low concentration (entries 14, 15) and a small amount of 3 (entry 9), the slight decrease of optical purities of 4a may be explainable in consideration of the reaction between 1 and 2a proceeded without participation of 3 (entry 8) because of the very low population of the heterogeneous catalyst (3).

Next, we examined the effect of the substituents of thiols under the best reaction conditions. The results are summarized in Table 2. Among various thiols screened, alkyl thiols gave higher optical purities of the corresponding products but slower reaction rates than aryl thiols. It is noteworthy that n-butylthiol gave the highest optical yield. These results show that the acidity and the bulkiness of thiol play important roles in the induction of good optical yield and the acceleration of reaction rate.

In order to know the absolute configuration, 4a was transformed into (R)-(+)-2-cyclohexen-1-ol (6)[9] as shown in the following Scheme 1. This result indicates that the absolute configuration of (-)-4a is (1R, 2R).

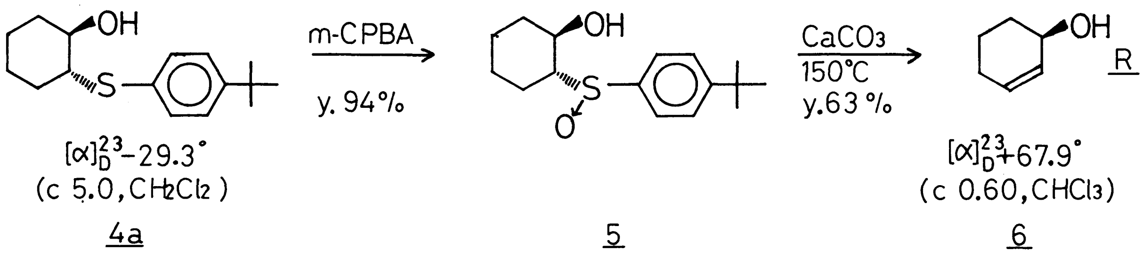
Table 2. Asymmetric ring-opening of cyclohexene oxide (1) with various thiols catalyzed by zinc Lg-tartrate (3)



	R	Yield/%[a]	$[\alpha]_D^{23}$ °(c 5.0, CH_2Cl_2)	ee/%[b]
4b	Phenyl	96	-45.2 °	61
4c	2-Methylphenyl	93	-58.2 °	64
4d	3-Methylphenyl	95	-42.8 °	62
4e	4-Methylphenyl	96	-45.0 °	68
4f	4-Chlorophenyl	94	-41.4 °	65
4g	Benzyl	88	-34.4 °	77
4h	n-Butyl	82	-44.7 °	85
4i	Cyclohexyl	29	-46.4 °	79
4j	t-Butyl	trace		

a) Isolated yield after silica-gel column chromatography. All products gave satisfactory NMR and IR spectra.

b) Enantiomeric excess was determined by ^{19}F NMR measurement of its MTPA ester. Only the MTPA ester of 4i was measured in the presence of $Eu(fod)_3$.



Scheme 1.

It should be noted that asymmetric ring-opening of cyclohexene oxide, a meso-compound, with various thiols gave good optical yields by using a catalytic amount of zinc Lg-tartrate. This method has several advantages over the conventional methods in the stability and the easiness of recovery of the catalyst, zinc Lg-tartrate, and the easy control of the reaction conditions. Further applications of this catalyst to the asymmetric ring-opening reactions using the other epoxides and nucleophiles are now under way to elucidate the detailed mechanism of enantiotopos differentiation.

References

1) I. J. Jakovac, H. B. Goodbrand, K. P. Lok, and J. B. Jones, J. Am. Chem. Soc., 104, 4659 (1982); K. Laumen and M. Schneider, Tetrahedron Lett., 1985, 2073 and references cited therein.

2) E. Fujita, Y. Nagao, K. Seno, S. Takao, M. Miyasaka, M. Kimura, and W. H. Watson, J. Chem. Soc., Parkin Trans. 1, 1981, 914; Y. Nagao, T. Ikeda, M. Yagi, E. Fujita, and M. Shiro, J. Am. Chem. Soc., 104, 2079 (1982); K. Osakada, M. Obana, T. Ikariya, M. Saburi, and S. Yoshikawa, Tetrahedron Lett., 1981, 4297; T. Fujisawa, M. Watanabe, and T. Sato, Chem. Lett., 1984, 2055.

3) T. Mukaiyama, H. Yamashita, and M. Asami, Chem. Lett., 1983, 385.

4) T. Mukaiyama, I. Tomioka, and M. Shimizu, Chem. Lett., 1984, 49.

5) J. Ichikawa, M. Asami, and T. Mukaiyama, Chem. Lett., 1984, 949.

6) M. Asami, Chem. Lett., 1984, 829.

7) The cis and trans authentic samples were prepared according to the following literatures; R. L. Crumbie, B. S. Deol, J. E. Nemorin, and D. D. Ridley, Aust. J. Chem., 31, 1965 (1978); G. H. Posner, D. Z. Rogers, C. M. Kinzig, and G. M. Gurria, Tetrahedron Lett., 1975, 3597.

8) G. Spacu and P. Viochescu, Z. Anorg. Allg. Chem., 227, 129 (1936); F. Heckele, Oster. Ch.-Ztg., 31, 28 (1928).

9) R. K. Hill and J. W. Morgan, J. Org. Chem., 33 927 (1968); S. Yamada, N. Takamura, and T. Mizoguchi, Chem. Pharm. Bull., 23, 2539 (1975).

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