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Preliminary communication

Asymmetric ring-opening of cyclohexene oxide with trimethylsilyl azide in the presence of titanium isopropoxide / chiral ligand

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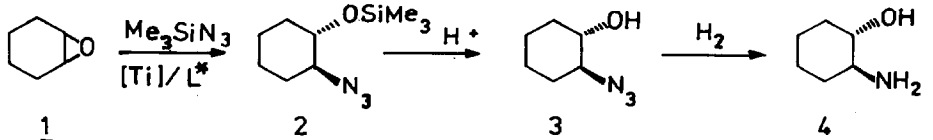
Abstract

trans-2-Azidocyclohexanol of enantiomeric excess up to 24% is obtained in the ring opening of cyclohexene oxide by use of trimethylsilyl azide in the presence of stoechiometric amount of titanium tetraisopropoxide and chiral diols or aminoalcohols.

A wide variety of highly stereoselective asymmetric reactions has been reported by many research groups [1]. Most of those reactions are diastereo or enantioface-differentiating reactions. Although highly selective transformations of enantiotopic groups in *meso*-compounds are well-known in enzymatic process [2], only a few enantioselective chemical approaches have been reported [3–5]. Highly stereoselective transformation of cyclohexene oxide to (*S*)-2-cyclohexene-1-ol using chiral lithium amides has been reported [4], as well as the asymmetric ring-opening of cyclohexene oxide with various thiols by the use of zinc (2*R*,3*R*)-tartrate as a heterogeneous chiral Lewis acid catalyst [5].

In a recent paper [6], Yamashita reported the asymmetric ring-opening of symmetrical oxiranes with trimethylsilyl azide catalysed by zinc or cupric (2*R*,3*R*)-tartrate. In this communication, we describe the asymmetric ring-opening of cyclohexene oxide with the system trimethylsilyl azide/titanium tetraisopropoxide in the presence of a chiral ligand L *.



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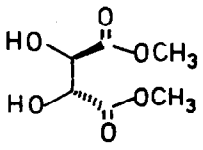

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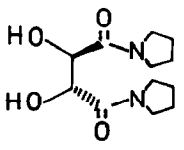

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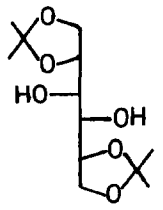

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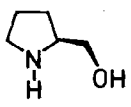

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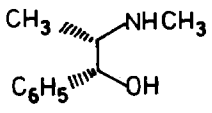

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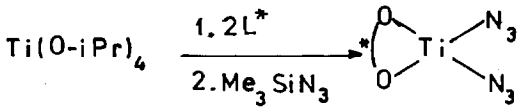
The reaction between cyclohexene oxide **1** and trimethylsilyl azide in the presence of a catalytic amount of titanium tetraisopropoxide and chiral diols or amino alcohols carried out by the procedure previously described [7,8]. It was found that optically active *trans-O*-trimethylsilyl-2-azidocyclohexanol (**2**) was obtained in high chemical yield, but unfortunately in very low optical yield (entries 1–4,10 and 13 in Table 1).

We thus examined the reaction of cyclohexene oxide **1** with increasing amounts of the complex $Ti(N_3)_2(L^*)$ prepared in situ from titanium tetraisopropoxide, two equivalents of L^*, and two equivalents of trimethylsilyl azide [9 *] (eq. 1). Using methyl (2*R*,3*R*)-tartrate **5** as ligand L^*, we found that increasing the amount of



(1)

complex increased the enantiomeric excess, values up to 24% being reached when the complex was used in stoechiometric amount (entry 6). Owing to some problems in careful separation of the chiral ligand from the azido alcohol formed, chemical yields were moderate (27–35%). Lowering the temperature of the reaction had practically no influence on the enantioselectivity (entry 7). Tartramide (**6**) gave a lower enantioselectivity (e.e. up to 7%) but higher chemical yield (entry 8). Di-*O*-isopropylidene-1,2; 5,6-D-mannitol (**7**), a chiral-1,2-diol, gave low enantioselectivity (entry 9). It is noteworthy that the absolute configuration of the azido alcohol obtained using methyl (2*R*,3*R*)-tartrate (**5**) as inducer is opposite to that obtained by Yamashita [6] using the same inducer.

* A reference number with an asterisk indicates a note in the list of references.

Table 1

Asymmetric ring-opening of cyclohexene oxide **1**

Entry	Ligand L*	1/L*/[Ti]	T (°)	**2**		**3**		e.e.% (conf.) [a]
				Yield (%)	$[\alpha]_D^{20}$ [b]	Yield (%)	$[\alpha]_D^{20}$ [b]	
1	**5**	50/2/1	25	79	+0.98	65	−1.9	6.5 (1*R*,2*R*)
2	**5**	25/2/1	25	67	−1.38	70	+1.61	5.5 (1*S*,2*S*)
3	**5**	10/2/1	25	30	−0.35	53	+0.8	2.7 (1*S*,2*S*)
4	**5**	5/2/1	25	–	–	62	+0.31	1.1 (1*S*,2*S*)
5	**5**	2/2/1	25	–	–	21	+2.46	8.5 (1*S*,2*S*)
6	**5**	1/2/1	25			27	+6.98	24.0 (1*S*,2*S*)
7	**5**	1/2/1	−20			35	+5.7	19.7 (1*S*,2*S*)
8	**6**	1/2/1	25			71	+2.07	7.0 (1*S*,2*S*)
9	**7**	1/2/1	25			18	−0.88	3.0 (1*R*,2*R*)
10	**8**	50/2/1	25	85	0.34	80	−0.72	3.5 (1*R*,2*R*)
11	**8**	1/2/1	25	–	–	67	−1.73	6.0 (1*R*,2*R*)
12	**8**	1/2/1	−50			48	−0.6	2.0 (1*R*,2*R*)
13	**9**	50/2/1	25	85	0.00	–	–	0.0
14	**9**	1/2/1	25			69	−1.36	4.7 (1*R*,2*R*)
15	**9**	1/2/1	−50			95	−4.97	17.0 (1*R*,2*R*)

[a] Determined by transformation into amino-alcohol **4** whose optical rotation is known; $[\alpha]_D^{20}$ +48.5 (*c* 1.0, MeOH) for (1*S*,2*S*)-*trans*-2-aminocyclohexanol and confirmed for entry 6 by ^{19}F NMR measurement of the MTPA ester of azido-alcohol **3**. [b] *c* 10, $CHCl_3$.

We also examined chiral amino alcohols as inducers. (*S*)-Prolinol (**8**) gave low enantioselectivity when used in catalytic or stoechiometric amount, even at low temperature (entries 10–12), but ephedrine (**9**) gave an enantiomeric excess of up to 17% at −50 °C with 95% chemical yield when used stoechiometrically (entry 15).

The absolute configuration of **2** or **3** was confirmed by conversion of **2** to the desilylated **3** in aqueous acidic methanol; the azidocyclohexanol (**3**) was then catalytically hydrogenated with 10% Pd–C in ethanol to give optically active *trans*-β-aminocyclohexanol (**4**) whose configuration and absolute rotation are known [10]. The enantiomeric excess of the azido alcohol (**3**) was determined by transformation to the β-aminoalcohol (**4**) (a sample of **3** of $[\alpha]_D^{20}$ +6.66 (*c* 10, $CHCl_3$) gave a sample of **4** of $[\alpha]_D^{20}$ +11.07 (*c* 10, CH_3OH) corresponding to 23% e.e.) and by ^{19}F NMR measurement of the MTPA ester of azidoalcohol (**3**).

In spite of the modest optical yields obtained, the procedure described could be a useful new strategy for obtaining chiral *trans*-β-amino alcohol by asymmetric ring-opening of *meso*-epoxides using titanium tetraisopropoxide/chiral ligand. Further studies are now in progress aimed at improvement of chemical and optical yields, and for making the catalytic reaction more enantioselective.

References

1 J.D. Morrison, Asymmetric Synthesis; Academic Press, New-York, 1983, Vol. 1–5.

2 For example: I.J. Jakovac, H.B. Goodbrand, K.P. Lok and J.B. Jones, J. Am. Chem. Soc., 104 (1982) 4659; M. Kurihara, K. Kamiyama, S. Kobayashi and M. Ohno, Tetrahedron Lett., 26 (1985) 5831; K. Laumen and M. Schneider, ibid., 26 (1985) 2073 and ref. cited therein.

3 (a) N. Cohen, Acc. Chem. Res., 9 (1976) 412; (b) K. Osakada, M. Obana, T. Ikariya, M. Saburi and S. Yoshikawa, Tetrahedron Lett., 22 (1981) 4297; (c) S. Hanessian, D. Delorme, S. Beaudoin and Y.

Leblanc, J. Am. Chem. Soc., 106 (1984) 5754; (d) N.S. Simpkins, J. Chem. Soc., Chem. Commun., (1986) 88; (e) R. Shirai, M. Tanaka and K. Koga, J. Am. Chem. Soc., 108 (1986) 543; (f) Y. Naruse and H. Yamamoto, Tetrahedron Lett., 27 (1986) 1363.

4 (a) J.K. Whitesell and S.W. Feldman, J. Org. Chem., 45 (1980) 755; (b) J.I. Ichikawa, M. Asami and T. Mukayama, Chem. Lett. (1984) 949; (c) T. Mukayama, H. Yamashita and M. Asami, Chem. Lett. (1983) 385; (d) M. Asami, ibid., (1984) 829; (e) M. Asami, Tetrahedron Lett., 26 (1985) 5803; (f) M. Asami and H. Kirihara, Chem. Lett. (1987) 389.

5 H. Yamashita and T. Mukayama, Chem. Lett., (1985) 1643.

6 H. Yamashita, Chem. Lett., (1987) 525.

7 C. Blandy, R. Choukroun and D. Gervais, Tetrahedron Lett., 24 (1983) 4189.

8 M. Emziane and D. Sinou, Tetrahedron Lett., 27 (1986) 4423.

9 A typical procedure: A homogeneous solution of 40.8 mmol of L * and 20.4 mmol of $Ti(O\text{-}i\text{-}Pr)_4$ in 14 ml of tetrahydrofuran was stirred under argon during 1 h. The solvent and the liberated isopropanol were evaporated under vacuum, the oil obtained dissolved in 10 ml of tetrahydrofuran and stirred during 2 days with 40.8 mmol of trimethylsilyl azide. Then epoxy-1,2-cyclohexane was added at the desired temperature and the solution was stirred during 2 days. After evaporation of the tetrahydrofuran and hydrolysis of the residue with 5 ml of water, the solution is stirred during 2 hours with 100 ml of dichloromethane. After filtration and evaporation of the solvent, the azido-alcohol is obtained by chromatography (silica gel 60, 35–70 μ; eluent: ethyl acetate/hexane, 2/3).

10 L.E. Overman and S. Sugai, J. Org. Chem., 50 (1985) 4154.