$R = 0.0719$ (for 4529 reflections $I > 2\sigma(I)$), $wR(F^2) = 0.2142$ for all 9201 unique reflections ($R_{int} = 0.1101$, $R_\sigma = 0.1214$), $S = 0.962$, min./max. residual electron density $= -0.24/0.32$ e Å^{-3}, $\sigma_{C-C} = 0.006$ Å. Crystallographic data of this structure (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-119100. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[14] The reference plane of **1** is defined by the four bridging methin carbon atoms.

A Catalytic Enantioselective Electron Transfer Reaction: Titanocene-Catalyzed Enantioselective Formation of Radicals from *meso*-Epoxides[**]

Andreas Gansäuer,[*] Thorsten Lauterbach,
Harald Bluhm, and Mathias Noltemeyer

In this communication we wish to disclose our results on the use of enantiomerically pure titanocene complexes in the opening of *meso*-epoxides based on our recently developed [Cp_2TiCl_2]-catalyzed reductive opening of epoxides[1] and pinacol couplings.[2, 3] The resulting transformation is to the best of our knowledge the first example of a transition metal catalyzed enantioselective formation of radicals.[4] Our reaction, in which the crucial β-titanoxy radical intermediate is generated selectively, is conceptually different from the enantioselective opening of *meso*-epoxides by an S_N2 reaction, where the path of the incoming nucleophile has to be controlled. The essential characteristics of a useful catalyst in the enantioselective opening of a *meso*-epoxide are depicted in Figure 1.

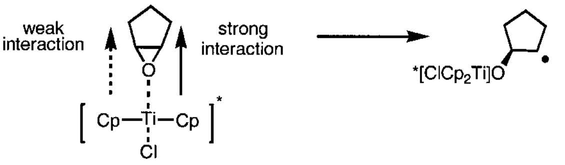
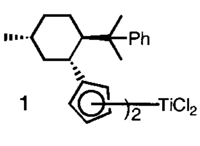


Figure 1. Steric requirements for selective epoxide opening.

To achieve high enantioselectivity the catalyst should allow for distinctly differing interactions of the ligand with the enantiotopic substituents of the epoxide. To implement rationally designed catalysis the catalyst's chiral pocket must be tailored to allow for recognition of structural elements of the substrate distant from the epoxy group. Efficient chirality transfer to the periphery of the complex is thus essential for successful catalysis. Inspection of the extensive literature on titanocene complexes[5] suggested that complexes with ligands derived from terpenes are suitable. After consideration of molecular models we decided to use **1**[6] because its methyl groups seemed to shield the chlorine atoms bound to titanium. The crystal structure of **1**, determined by us for the first time, confirmed our assumptions nicely (Figure 2).



1

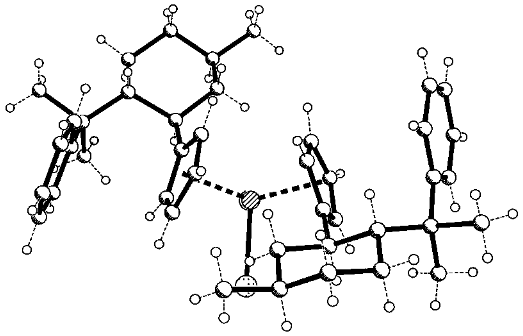
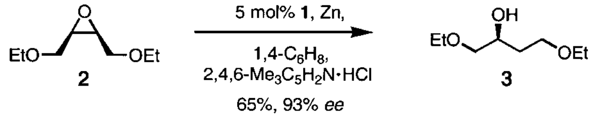


Figure 2. X-ray crystal structure of **1**.

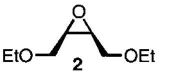
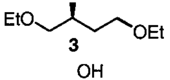
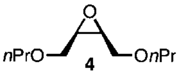
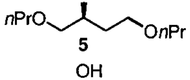
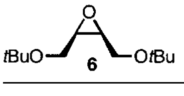
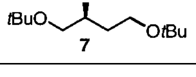
We used epoxides derived from (Z)-butenediol dialkyl ethers as substrates for optimizing the reaction conditions. The absolute configuration of the products was established as S by comparison with samples derived from (S)-malic acid. The reaction conditions are summarized in Scheme 1 and the results in Table 1.



Scheme 1. Optimized conditions for the enantioselective reductive opening with 5 mol% of **1**.

Not only is the enantioselectivity of the electron transfer high (96.5:3.5), but **1** also constituted the catalytically most active complex amongst a series of titanocene complexes. The

Table 1. Enantioselective reduction of *meso*-epoxides in the presence of 5 mol% of **1** (0.1 M in THF, 60 h).

Substrate	Product	Yield [%]	(S):(R)[a]
 **2**	 **3**	65	96.5:3.5
 **4**	 **5**	61	96:4
 **6**	 **7**	60	87.5:13.5

[a] Determined by gas chromatography on chiral phases.

---

[*] Dr. A. Gansäuer, T. Lauterbach, H. Bluhm
Institut für Organische Chemie und Biochemie der Universität
Albertstrasse 21, D-79104 Freiburg (Germany)
Fax: (+49)761-203-6100
E-mail: agansaeu@organik.chemie.uni-freiburg.de
Dr. M. Noltemeyer
Institut für Anorganische Chemie der Universität Göttingen (Germany)

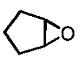
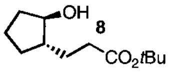
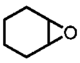
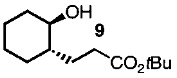
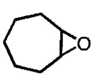
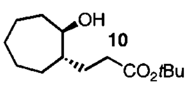
[**] Financial support by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the BASF AG is gratefully acknowledged. We thank Prof. R. Brückner for constant and generous support of our work.

reason for the high selectivity of epoxide opening with **1** seems to stem from its striking structural feature, the almost perfect coplanarity of the benzene rings and the cyclopentadienyl rings, presumably due to π stacking. This interaction seems to lock the ligands in a conformation necessary for highly selective binding of the substrate. The methyl groups of the terpene moiety point towards the homotopic binding sites of the supposed catalytically active titanium(III) complex.[7] These binding sites should be located close to the Cl atoms of the almost C_2-symmetrical titanium (IV) complex, by comparison with other titanocene(III) and titanocene(IV) complexes.[8] Therefore, **1** meets all requirements we believed to be necessary for a succesful catalyst.

Our anticipated mechanism is supported by the reduced enantioselectivity of the opening of **6**. In the case of the *n*-alkyl ethers **2** and **4** the selectivity was similar and high. However, in the case of **6** both *tert*-butyl groups made a rather strong contact with the chiral pocket of **1**, resulting in dimished steric differentiation.

An interesting and demanding problem is the use of bicyclic epoxides in enantio- and diastereoselective C–C bond forming reactions by addition of the β-titanoxy radical to *tert*-butyl acrylate. The results of our investigation are summarized in Table 2. With increasing ring size the enantioselectivity of the epoxide opening increases and reaches synthetically useful levels for the six- and seven-membered rings. This indicates a better fit of the larger substrates in the chiral pocket of the catalyst. The diastereoselectivity of the C–C bond forming steps[9] was higher than with $[Cp_2TiCl_2]$ as catalyst[3b,c] (**8**: 86:14 vs. 97.5:2.5; **9**: 60:40 vs. 81:19; **10**: 70:30 vs. 87:13) or with stoichiometric amounts of reagent.[10]

Table 2. Enantioselective C–C bond forming reactions in the presence of 5 mol% of **1** (0.1 M in THF, 48 h).

Substrate	Product	Yield [%]	(*R*,*S*):(*S*,*R*)[a]
	 **8**	68	87:13[b]
	 **9**	61	91:9[c]
	 **10**	65	91:9[d]

[a] Determined by gas chromatography on chiral phases. [b] *trans*:*cis* > 97:3. [c] *trans*:*cis* = 81:19, same *ee* value for the two diastereoisomers. [d] *trans*:*cis* = 87:13.

In summary we have demonstrated for the first time that the catalytic opening of *meso*-epoxides by electron transfer can be performed with high enantioselectivity and high diastereoselectivity with **1** as rationally designed catalyst.

Received: April 23, 1999 [Z13306IE]
German version: *Angew. Chem.* **1999**, *111*, 3112–3114

Keywords: enantioselectivity · epoxides · homogeneous catalysis · radical reactions · titanium

[1] a) A. Gansäuer, M. Pierobon, H. Bluhm, *Angew. Chem.* **1998**, *110*, 107; *Angew. Chem. Int. Ed.* **1998**, *35*, 101; b) A. Gansäuer, H. Bluhm, *Chem. Commun.* **1998**, 2143; c) A. Gansäuer, H. Bluhm, M. Pierobon, *J. Am. Chem. Soc.* **1998**, *120*, 12849.

[2] a) A. Gansäuer, D. Bauer, *J. Org. Chem.* **1998**, *63*, 2070; b) A. Gansäuer, D. Bauer, *Eur. J. Org. Chem.* **1998**, 2673.

[3] Review: A. Gansäuer, *Synlett* **1998**, 801.

[4] For some enantioselective radical reactions based on different concepts, see a) J. H. Wu, R. Radinov, N. A. Porter, *J. Am. Chem. Soc.* **1995**, *117*, 11029; b) M. P. Sibi, J. Ji, J. H. Wu, S. Gürtler, N. A. Porter, *J. Am. Chem. Soc.* **1996**, *118*, 9200; c) M. Blumenstein, K. Schwartzkopf, J. O. Metzger, *Angew. Chem.* **1997**, *109*, 245; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 225; K. Mikami, M. Yamaoka, *Tetrahedron Lett.* **1998**, *39*, 4501.

[5] R. L. Halterman in *Metallocenes*, *Vol. 1* (Eds.: A. Togni, R. L. Halterman), WILEY-VCH, Weinheim, **1998**, p. 455.

[6] R. L. Halterman, K. P. C. Vollhardt, *Organometallics* **1988**, *7*, 883.

[7] X-ray crystal structure analysis of $\mathbf{1}\cdot CHCl_3$ ($C_{43}H_{55}Cl_5Ti$): $M_r = 797.0$, orthorhombic, space group $P2_12_12_1$, $a = 1290.76(12)$, $b = 1310.0(2)$, $c = 2517.8(6)$ pm, $V = 4.2572\ nm^3$, $\rho_{calcd} = 1.244\ g\,cm^{-3}$, 3454 independent reflections, $R1 = 0.0473$ for $I > 2\sigma(I)$, $wR2 = 0.1101$ for all data. The structure was solved by direct methods and refined with anisotropic temperature factors for all non-hydrogen atoms; hydrogen atoms were added in idealized positions and included in the refinement. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-118965. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[8] a) M. Bochman in *Comprehensive Organometallic Chemistry II*, *Vol. 4* (Eds.: E. W. Abel, F. G. A. Stone, G. Wilkinson), Pergamon, Oxford, **1995**, pp. 221, 273; b) T. C. McKenzie, R. D. Scanner, J. E. Bercaw, *J. Organomet. Chem.* **1975**, *102*, 457; c) J. W. Pattiasina, H. J. Heeres, F. van Bolhuis, A. Meetsma, J. H. Teuben, A. L. Speek, *Organometallics* **1987**, *6*, 1004.

[9] a) B. Giese, *Angew. Chem.* **1989**, *101*, 993; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 969; b) B. Giese, K. Heuck, H. Lenhardt, *Chem. Ber.* **1984**, *117*, 2132.

[10] a) W. A. Nugent, T. V. RajanBabu, *J. Am. Chem. Soc.* **1988**, *110*, 8561; b) T. V. RajanBabu, W. A. Nugent, *J. Am. Chem. Soc.* **1994**, *116*, 986.

Noncatalytic Organic Synthesis Using Supercritical Water: The Peculiarity Near the Critical Point

Yutaka Ikushima,* Kiyotaka Hatakeda, Osamu Sato, Toshirou Yokoyama, and Masahiko Arai

As industry is interested in moving away from toxic or environmentally damaging solvents, the finding of an ideal replacement medium for conventional nonpolar solvents offers new opportunities in, for example, reaction engineering, environmental science and technology, and materials science. Supercritical water (scH_2O) heated and pressurized

---

[*] Dr. Y. Ikushima, Dr. K. Hatakeda, Dr. O. Sato, Dr. T. Yokoyama
National Industrial Research Institute of Tohoku
4-2-1 Nigatake, Miyagino-ku, Sendai 983-8551 (Japan)
Fax: (+81)22-237-5224
E-mail: ikushima@tniri.go.jp

Dr. M. Arai
Institute for Chemical Reaction Science, Tohoku University
2-1-1 Katahira, Aoba-ku, Sendai 980-8577 (Japan)

1433-7851/99/3819-2910 $ 17.50+.50/0