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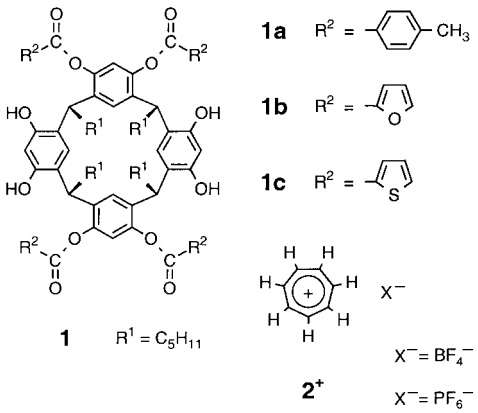
Guest-Controlled Formation of a Hydrogen-Bonded Molecular Capsule**

Alexander Shivanyuk,* Erich F. Paulus,* and Volker Böhmer*

Several concave, self-complementary molecules[1] have been shown to form self-assembled dimeric capsules held together by multiple hydrogen bonds in which various guests can be reversibly entrapped. The encapsulation of a suitable guest is usually necessary for the dimerization, since an empty or incompletely filled cavity would be thermodynamically disadvantageous.[2] Herein we describe a novel type of dimeric hydrogen-bonded molecular capsules whose formation can be strictly controlled by the amount of guest available for the encapsulation.

C_{2v}-symmetrical tetraesters **1** are easily prepared by regioselective acylation of resorcarenes with various acid chlorides.[3] These molecules contain four phenolic hydroxy groups and four ester carbonyl groups as potential hydrogen-bond donors and acceptors and should be able, according to molecular models, to dimerize through eight CO···HO hydrogen bonds forming a closed π-basic cavity. The tropylium cation $\mathbf{2}^+$ as π acceptor was considered to be an appropriate guest and template for such an assembly.



^{1}H NMR spectra of tetraesters **1a–c** ($CDCl_3$, 293 K) are sharp and contain one triplet for the methine protons of the bridges and four singlets for the protons of the resorcinol rings[4] (Figure 1a). Surprisingly, in the case of **1a** and **1b** the proton exchange between hydroxy groups and water (always present in traces) occurs with such a rate that no signals are observed for the corresponding protons. This indicates that the hydroxy groups are not involved in strong CO···HO hydrogen bonds, but are available for the solvation by water in $CDCl_3$.

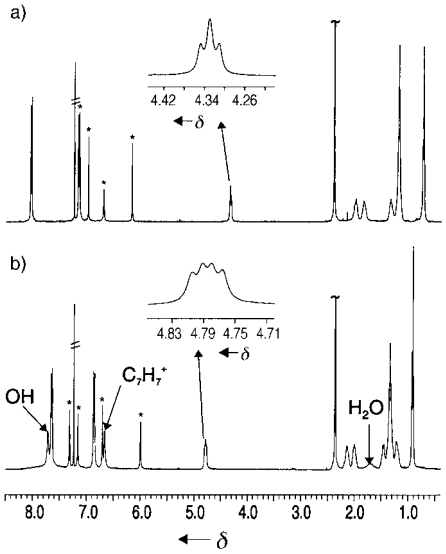


Figure 1. ^{1}H NMR spectra (400 MHz, $CDCl_3$, 293 K, $c(\mathbf{1a}) = 10^{-2}$ M) of: a) tetraester **1a**; b) (**1a**$C_7H_7^+$**1a**)PF_6^-. The signals for the protons of resorcinol rings are marked with an asterisk.

Compounds **1** solubilize tropylium salts $\mathbf{2}^+X^-$ in CH_2Cl_2 or $CHCl_3$. The intensive orange-red color of such solutions ($\lambda_{max} = 463$ nm, CH_2Cl_2) is caused by the formation of charge-transfer complexes with $C_7H_7^+$.[5] The complexation with $C_7H_7^+PF_6^-$ also drastically changes the ^{1}H NMR spectra of resorcarenes **1a–c** ($CDCl_3$, 293 K). Especially remarkable is the down field shift for the signal of the bridges ($\Delta\delta = 0.45$) and the change of its multiplicity (Figure 1b).[6] Furthermore, the proton exchange between hydroxy groups of **1a**,**b** and water becomes slow on the NMR time scale, suggesting the formation of strong hydrogen bonds.

[*] Dr. A. Shivanyuk, Dr. V. Böhmer
Fachbereich Chemie und Pharmazie
Abteilung Lehramt Chemie der Universität
Duesbergweg 10–14, D-55099 Mainz (Germany)
Fax: (+49) 6131-395-419.
E-mail: shiva@mail.uni-mainz.de
vboehmer@mail.uni-mainz.de
Dr. E. F. Paulus
Hoechst Marion Roussel
D-65926 Frankfurt/Main (Germany)
E-mail: erich.paulus@hmrag.com

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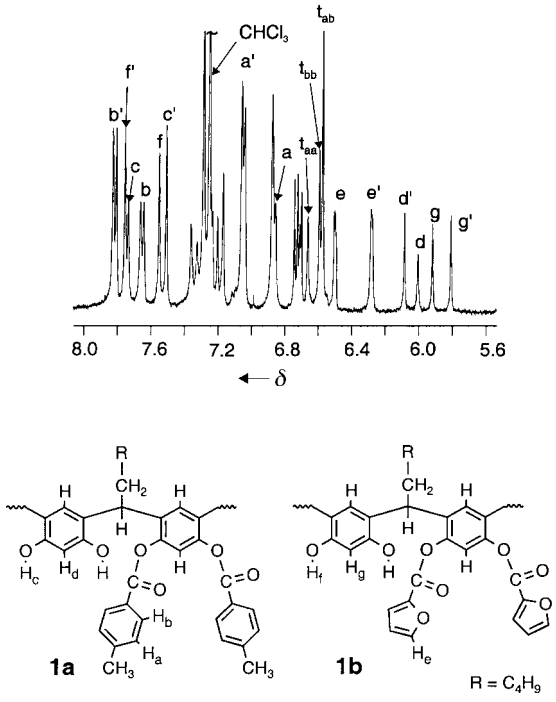
Combination of COSY, ^{13}C DEPT, and ^{1}H-^{13}C correlation NMR techniques enables an unambiguous assignment of the resonances of the complexed $C_7H_7^+$ ion (Figure 1b). Its ^{1}H NMR singlet appears at $\delta = 6.66$, 6.58, and 6.53 in the complexes with **1a**, **1b**, and **1c**, respectively, strongly shifted upfield ($\Delta\delta \approx -2.6$) due to the shielding by the resorcarene aryl rings.[7] Integration shows that two molecules of resorcarene **1** complex one tropylium cation.[8]

All these data are in agreement with the encapsulation of the $C_7H_7^+$ ion in the π-basic cavity of the hydrogen-bonded resorcarene dimers. No changes were observed in the ^{1}H NMR spectra of **1** upon addition of benzene or toluene as potentially space-filling guests for $\mathbf{1}_2$, suggesting that host–guest interactions play an important role in the formation of $(\mathbf{1}\,C_7H_7^+\mathbf{1})X^-$.

The ^{1}H NMR spectrum of the mixture $(\mathbf{1a}\,C_7H_7^+\mathbf{1a})PF_6^-$ and $(\mathbf{1b}\,C_7H_7^+\mathbf{1b})PF_6^-$ exhibits a double set of sharp signals for each resorcarene along with three signals for the protons of $C_7H_7^+$ (Figure 2). This pattern can be interpreted by the



$$(\mathbf{1a}\ 2^+\mathbf{1a})\ PF_6^- \ +\ (\mathbf{1b}\ 2^+\mathbf{1b})\ PF_6^- \rightleftharpoons 2\ (\mathbf{1a}\ 2^+\mathbf{1b})\ PF_6^-$$

Figure 2. Section of the ^{1}H NMR spectrum of the mixture $(\mathbf{1a}\,C_7H_7^+\mathbf{1a})PF_6^-$ and $(\mathbf{1b}\,C_7H_7^+\mathbf{1b})PF_6^-$. The signals of the heterodimer $(\mathbf{1a}\,C_7H_7^+\mathbf{1b})PF_6^-$ are marked with a dash. The singlets of the tropylium cation encapsulated in the dimers of **1a**, **1b**, and in the heterodimer are labeled with t_{aa}, t_{bb}, and t_{ab}, respectively.

formation of the kinetically stable hetero-associate $(\mathbf{1a}\,C_7H_7^+\mathbf{1b})PF_6^-$ in a more or less statistical ratio. Accordingly, the ROESY spectrum shows intensive exchange cross peaks between the resolved signals of the homo- and heteroassociates.

The high thermodynamic stability of $(\mathbf{1c}\,C_7H_7^+\mathbf{1c})BF_4^-$ in CH_2Cl_2 is demonstrated by the fact that the absorbance of the charge-transfer band is proportional to the concentration, ($c = 0.35 - 5.5$ mM, $\varepsilon_{463} = 398\ M^{-1}cm^{-1}$). This proves that no dissociation of the complex occurs upon dilution.

In contrast to other self-assembled molecular capsules,[9] the degree of dimerization of **1** can be controlled by the amount of tropylium salt. If less than 0.5 equivalents of $C_7H_7^+X^-$ (per equivalent **1**) are solubilized the corresponding amounts of $(\mathbf{1}\,C_7H_7^+\mathbf{1})X^-$ and free **1** are observed.[10] At the ratios $\mathbf{1}$:$(\mathbf{1}\,C_7H_7^+\mathbf{1})X^-$ of 3.0, 1.0, 0.33 the exchange of **1** between the monomer and dimer is slow on the ^{1}H NMR time scale (200 MHz, $CDCl_3$, 293 K) although a slight broadening of the signals takes place.[11] The addition of CD_3CN (10–20%) to this solution causes the collapse of the signals so that one set of broad resonances is detected for the resorcarene protons. This is obviously caused by hydrogen bonding between hydroxy groups of **1** and acetonitrile molecules.

Exactly one equivalent of **1c** can be solubilized per equivalent of $C_7H_7^+BF_4^-$ in CD_3CN at 293 K resulting in the formation of a colored ($\lambda_{max} = 475$ nm) charge-transfer complex. However, the absorbance is not proportional to the concentration in this case ($c(\mathbf{1c}) = c(\mathbf{2}^+) = 0.35 - 5.5$ mM), evidently due to the dissociation of the weaker complex. If larger amounts of **1c** are dissolved by heating, the excess of resorcarene crystallizes again upon cooling, suggesting a 1:1 stoichiometry for the complexation in acetonitrile. NMR dilution experiments show that the complex formed is not kinetically stable at 293 K. In this case the signal of $C_7H_7^+$ undergoes only a relatively small upfield shift ($\Delta\delta = -0.22$ at $c(\mathbf{1c}) = c(\mathbf{2}^+) = 10^{-2}$ M).[12]

Thus the high (thermodynamic and kinetic) stability of $(\mathbf{1}\,C_7H_7^+\mathbf{1})X^-$ in $CDCl_3$ arises from the cooperation of eight CO···HO hydrogen bonds *and* the tropylium-resorcinol interactions.

Structural details were obtained from a single-crystal X-ray analysis.[13] In fact, two molecules of **1c** form in the crystalline state a dimer through eight intermolecular CO···HO hydrogen bonds (O–O distances 2.76–2.86 Å) (Figure 3). One tropylium cation is encapsulated in the cavity formed in this way and forms angles of 54.8° and 55.0° with the reference planes[14] of A and B, respectively. In addition two clefts are created by the pendant pentyl chains. One of them (molecule A) is occupied by a BF_4^- ion ($C_7H_7^+ - B1 = 7.72$ Å), while the other one hosts a hexane molecule. This entrapment of the BF_4^- ion between the pentyl chains of resorcarene A leads to the asymmetric location of the tropylium cation in the cavity. The distances of the center of $C_7H_7^+$ from the centers of the reference planes of A and B are 4.13 and 4.89 Å, respectively.

One unsubstituted resorcinol ring of molecule A (C122 to C127) and one diacylated resorcinol ring of molecule B (C215 to C220) are arranged around the tropylium cation in a sandwichlike manner (Figure 4). The distance of the center of $C_7H_7^+$ from the plane of the quasi-parallel resorcinol ring C122 to C127 (dihedral angle 5.4°) was found to be 3.57 Å, which is suitable for charge transfer, while the same values for the less π-basic diacylated ring C215 to C220 (23.0°, 5.62 Å) do not suggest any strong interactions. On the other hand the distances between all the carbon atoms of $C_7H_7^+$ and the planes of the other six resorcinol rings are in accordance with the formation of CH···π bonds (Figure 4).

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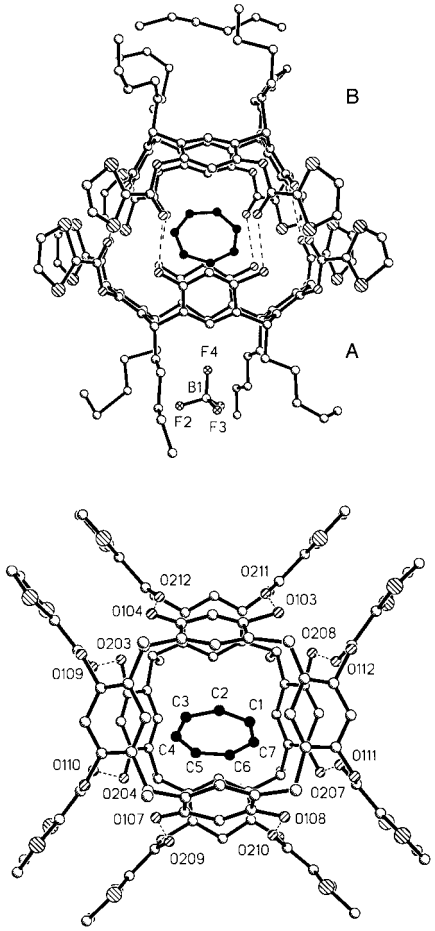

Figure 3. Structure of $(\mathbf{1c}\,C_7H_7^+\mathbf{1c})BF_4^-$ in the crystal. Sulfur atoms of the thiophene rings are disordered over two positions. Side view (top): Hydrogen bonds are shown as dotted lines; the carbon atoms of the encapsulated tropylium cation are darkened for clarity. Top view of a resorcarene (bottom): The pentyl chains, the BF_4^- ion, and the hexane molecule are omitted for clarity; the hydrogen-bonded oxygen atoms are labeled; distances [Å]: O103–O211 2.81, O104–O212 2.81, O107–O209 2.86, O108–O210 2.79, O203–O109 2.79, O204–O110 2.76, O207–O111 2.80, O208–O112 2.79.

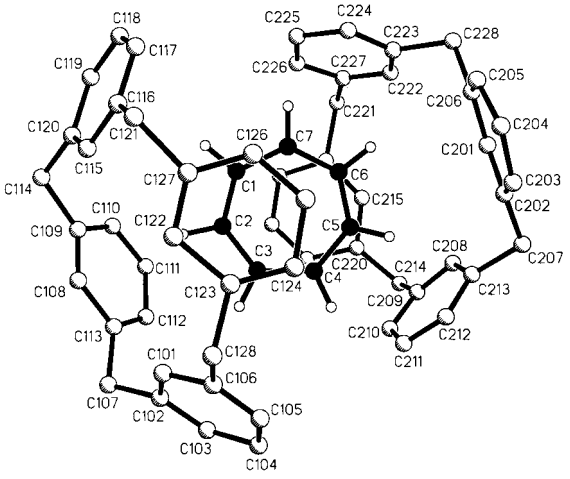

Figure 4. The location of $C_7H_7^+$ between the molecules A and B. Only the parts, which are important for the host–guest interactions are shown; the shortest distances [Å] between carbon atoms of the tropylium cation and the planes of the aryl rings are: C1–(C115–C120) 3.47, C2–(C108–C113) 3.35, C3–(C101–C106) 3.43, C4–(C208–C213) 3.15, C5–(C208–C213) 3.31, C6–(C201–C206) 3.61, C7–(C222–C227) 3.27.

In conclusion, C_{2v}-symmetrical resorcarenes **1** represent a novel class of self-complementary molecules capable of reversible dimerization controlled by the encapsulation of tropylium cations. It could be unambiguously shown that neither the host–guest interaction alone nor the interaction of the two self-complementary molecules **1** through hydrogen bonds is sufficient by itself to form $(\mathbf{1}\,C_7H_7^+\mathbf{1})X^-$. Only the cooperative action of both factors leads to the quantitative formation of the 2:1 host–guest complex. Due to charge transfer the self-assembly of $(\mathbf{1}\,C_7H_7^+\mathbf{1})X^-$ is accompanied by a well-pronounced optical response which is unprecedented so far for molecular capsules.

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[4] A decrease of the temperature to 217 K results in the broadening and splitting of the ^{1}H NMR spectrum of **1a** ($CDCl_3$, 500 MHz) most probably due to a restricted conformational flexibility of the resorcarene skeleton (two C_{2v}-symmetrical boat conformations).
[5] See for example: M. Lämsä, J. Pursiainen, K. Rissanen, J. Huuskonen, *Acta. Chem. Scand.* **1998**, *52*, 563–570.
[6] Dynamic ^{1}H NMR spectroscopy shows that complexation with tropylium rigidifies the conformation of **1a.**
[7] Although $C_7H_7^+BF_4^-$ and $C_7H_7^+PF_6^-$ are very sparingly soluble in $CDCl_3$ a singlet at $\delta = 9.18$ can be found for the tropylium cation comparable to the value of $\delta = 9.23$ in CD_3CN.[5]
[8] In order to ensure complete complexation the solid/liquid extraction of $C_7H_7^+BF_6^-$ or $C_7H_7^+PF_6^-$ was carried out for 6–8 h assisted by mechanical stirring.
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[10] The degree of dimerization of tetrahydroxy cavitands could be controlled by the amount of base used for the deprotonation of the hydroxy groups to form the dianion, while an appropriate space-filling guest (pyrazine) was available in excess: R. G. Chapman, G. Olovsson, J. Trotter, J. C. Sherman, *J. Am. Chem. Soc.* **1998**, *120*, 6252- 6260.
[11] A signal for the free tropylium cation is not observed.
[12] A similar effect has been observed in the case of 1:1 charge-transfer complexation between $C_7H_7^+BF_4^-$ and dibenzo[24]crown-8 in CD_3CN ($K_{ass} = 10.2 \pm 0.3\,M^{-1}$).[5] Unfortunately, the low solubility of resorcarenes **1** in acetonitrile prevented the accurate determination of K_{ass} with $C_7H_7^+X^-$.
[13] Crystallographic data: Intensively red crystals were obtained by slow evaporation of a solution of $(\mathbf{1c}\,C_7H_7^+\mathbf{1c})BF_4^-$ in CH_2Cl_2/hexane. They were sealed in a Lindemann glass capillary containing some mother liquor. Measurement at 21 °C by a Siemens four-circle diffractometer with CCD, Siemens rotating anode, (50 kV, 120 mA), $Mo_{K\alpha}$ radiation (graphite monochromator, $\lambda = 0.7107$ Å). Lorentz, polarization, and empirical absorption corrections. Direct methods (G. M. Sheldrick, *Acta Crystallogr. Sect. A* **1990**, *46*, 467), refinement with full matrix for every resorcarene molecule in the asymmetric unit versus F^2 (G. M. Sheldrick, SHELXL-93, Universität Göttingen). $2(C_{68}H_{72}O_{12}S_4)\cdot C_7H_7\cdot BF_4\cdot C_6H_{14}$, $M_w = 2683.10$, crystal size $0.24 \times 0.15 \times 0.08$ mm^3, monoclinic, Cc, $a = 23.299(4)$, $b = 26.802(4)$, $c = 23.218(3)$ Å, $\beta = 92.05(1)^\circ$, $Z = 4$, $V = 14489$ Å^3, $\rho_{calcd} = 1.230$ g cm^{-3}, $2\Theta_{max} = 36.0^\circ$, $\mu = 0.20$ mm^{-1}, 1701 parameters, 2210 restraints,

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$R = 0.0719$ (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.

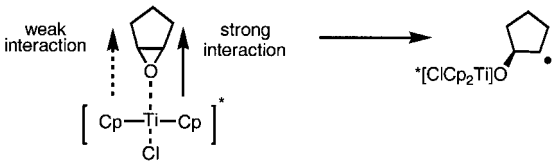
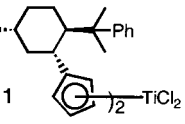


Figure 1. Steric requirements for selective epoxide opening.

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).



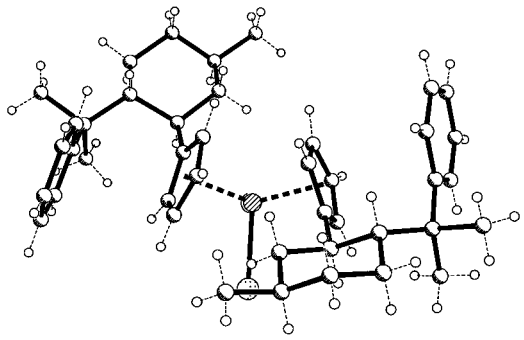
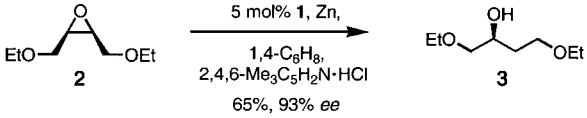


Figure 2. X-ray crystal structure of **1**.

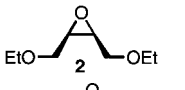
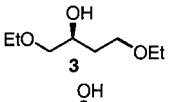
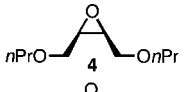
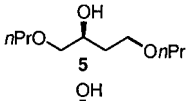
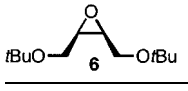
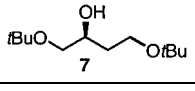
We used epoxides derived from (*Z*)-butenediol dialkyl ethers as substrates for optimizing the reaction conditions. The absolute configuration of the products was established as *S* by comparison with samples derived from (*S*)-malic acid. The reaction conditions are summarized in Scheme 1 and the results 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** (0.1M in THF, 60 h).

Substrate	Product	Yield [%]	(*S*):(*R*)[a]
		65	96.5:3.5
		61	96:4
		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)

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