metallics **1998**, *17*, 1798 – 1811; h) A. Choplin, F. Quignard, *Coord. Chem. Rev.* **1998**, *180*, 1679 – 1702, and references therein.
[2] a) W. A. Herrmann, B. Cornils, *Angew. Chem.* **1997**, *109*, 1074 – 1095; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1048 – 1067; b) P. Hernan, C. del Pino, E. Ruiz-Hitzky, *Chem. Mater.* **1992**, *4*, 49 – 55; c) S. Wieland, P. Panster, *Catal. Org. React.* **1994**, *62*, 383 – 392.
[3] J. Blum, A. Rosenfeld, N. Polak, O. Israelson, H. Schumann, D. Avnir, *J. Mol. Catal.* **1996**, *107*, 217 – 223.
[4] Homogeneous alkene epoxidation with the Ti^{IV} silsesquioxane complex $[(cy_7Si_7O_{12})Ti(\eta^5\text{-}C_5H_5)]$ as catalyst was reported by Abbenhuis et al.: H. C. L. Abbenhuis, S. Krijnen, R. A. van Santen, *Chem. Commun.* **1997**, 331 – 332.
[5] The partially condensed silsesquioxane $(R_7Si_7O_9)(OR')_3$ was identified as a soluble molecular species: a) F. J. Feher, D. A. Newman, J. F. Walzer, *J. Am. Chem. Soc.* **1989**, *111*, 1741 – 1748; b) F. J. Feher, D. A. Newman, *J. Am. Chem. Soc.* **1990**, *112*, 1931 – 1936; c) F. J. Feher, T. A. Budzichowski, R. L. Blanski, K. J. Weller, J. W. Ziller, *Organometallics* **1991**, *10*, 2526 – 2528.
[6] Detailed syntheses of **2** and **3** will be published elsewhere.
[7] The relative molecular weights and weight distributions of **2** and **3** were determined by gel permeation chromatography (GPC) with a polystyrene standard as reference.
[8] The solution ^{29}Si NMR spectrum of polysiloxane **2** gave four signals at $\delta = -68$, -61, -56, and $+8$, which were assigned as $Si(O_{0.5})_3R$, $Si(O_{0.5})_2R(OTMS)$, $Si(O_{0.5})R(OTMS)_2$, and OTMS, respectively, with a intensity ratio of 6:2:1:3.
[9] a) J. Blümel, *Inorg. Chem.* **1994**, *33*, 5050 – 5056; b) M. R. Buchmeiser, K. Wurst, *J. Am. Chem. Soc.* **1999**, *121*, 11 101 – 11 107, and references therein.
[10] The crystallographic data of $CH_2{=}CH(CH)_9NHP(O)(2\text{-}py)_2$ will be published elsewhere.
[11] G. P. F. van Strijdonck, M. D. K. Boele, P. C. J. Kamer, J. G. de Vries, P. W. N. M. van Leeuwen, *Eur. J. Inorg. Chem.* **1999**, 1073 – 1096.
[12] Recent reviews: a) M. Lautens, W. Klute, W. Tam, *Chem. Rev.* **1996**, *96*, 49 – 92; b) A. Takeda, A. Ohno, I. Kadota, V. Gevorgyan, Y. Yamamoto, *J. Am. Chem. Soc.* **1997**, *119*, 4547 – 4548; c) S. Saito, Y. Yamamoto, *Chem. Rev.* **2000**, *100*, 2901 – 2915.
[13] a) B. E. Mann, P. M. Bailey, P. M. Maitlis, *J. Am. Chem. Soc.* **1975**, *97*, 1275 – 1276; b) P. M. Maitlis, *Acc. Chem. Res.* **1976**, *9*, 93 – 99.

Catalytic Enantioselective Protonation of Lithium Ester Enolates Generated by Conjugate Addition of Arylthiolate to Enoates**

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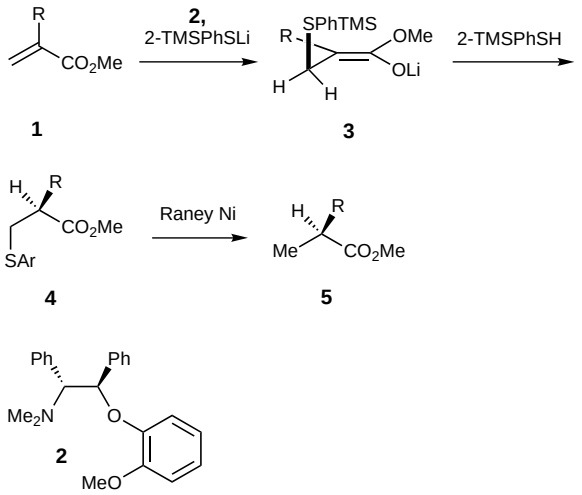
Enantioselective protonation of prochiral enolates represents a most useful advance in recent synthetic chemistry.[1, 2] In particular, catalytic enantioselective protonation has been a challenging target.[3] Generally, such reactions rely on a combination of an excess achiral proton source and a substoichiometric chiral proton source such as imides,[4] phenols,[5] alcohols,[6] amino alcohols,[7] and amines.[8] Prochiral substrates are often metal enolates, generated by the reaction of silyl enol ethers or enol acetates with an excess of an organometallic species. In spite of the recent impressive progress in this field, there have been few approaches that use a catalytic amount of a metal cation for the generation of metal enolates.[9]

We present here the chiral ligand catalyzed enantioselective protonation of a transient lithium ester enolate **3**—generated by a conjugate addition of lithium arylthiolate to propenoates **1** in the presence of the chiral amino diether **2**—to give the 3-arylsulfanyl 2-substituted propanoates **4** with high *ee* values (Scheme 1).[10] Reductive desulfurization of **4**, bearing a chiral



Scheme 1. Catalytic asymmetric addition – protonation and desulfurization. TMS = trimethylsilyl.

center at the C2 position, with Raney nickel completes the catalytic enantioselective protonation to afford the corresponding chiral propanoates **5** in high yield without racemization. The two-step procedure is characterized by an asymmetric protonation of a lithium enolate generated by a catalytic amount of a lithium cation.

The strategy for the catalytic asymmetric protonation is based on our previously developed asymmetric addition of 2-trimethylsilylbenzenethiol (2-TMSPhSH) to enoates, which is controlled by a chiral ligand.[11] The addition of a thiolate to an enoate and protonation of the resulting enolate by a thiol are highly stereoselective procedures and provide the *anti*-protonation product.[12] Furthermore, the attack of the thiolate on the 2-enoate is the rate-determining step of the addition – protonation reaction,[13] and hence protonation of the resulting enolate by thiol is rapid. Consequently, if the protonation of enolate **3** takes place before this species undergoes a conformational change, it probably proceeds in an *anti* manner to the C–S bond to afford **4** with high *ee* values.

The asymmetric addition – protonation is exemplified by the reaction of methyl 2-phenylpropenoate (**1c**, R = Ph) with 1.2 equivalents of 2-trimethylsilylbenzenethiol. The reaction

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was catalyzed by a combination of lithium 2-trimethylsilylbenzenethiolate (1 mol %) and (1*R*,2*R*)-1-dimethylamino-2-(2-methoxyphenoxy)-1,2-diphenylethane (**2**, 1.2 mol %)[14] in toluene/hexane (1/1) at −78 °C for 0.5 h to give methyl 3-(2-trimethylsilylphenylsulfanyl)-2-phenylpropanoate (**4c**, Ar = 2-TMSPh, R = Ph), bearing a chiral center at C2, in quantitative yield (Scheme 1). The enantioselectivity was determined to be 92 % by chiral stationary phase HPLC (Daicel Chiralcel AS) of the protodesilylated phenylsulfanyl ester (Ar = R = Ph), which was obtained quantitatively by treatment of **4c** with trifluoromethanesulfonic acid in toluene at room temperature for 10 min.[15] The absolute configuration of **4c** was determined to be *S* by measurement of the specific rotation of desulfurized methyl 2-phenylpropanoate (**5c**, R = Ph):[16] Desulfurization of **4c** with Raney nickel W-4 in THF/methanol in the presence of acetate buffer at room temperature for 0.5 h gave **5c** in 97 % yield without racemization. The other propenoates **1a**, **b**, **d**–**f** having methyl, benzyl, 1-naphthyl, 2-naphthyl, and 6-methoxy-2-naphthyl groups at C2 were successfully converted into the corresponding chiral propanoates **4a**, **b**, **d**–**f** with good to high *ee* values (Table 1). The absolute configuration of **4a** was determined by protodesilylation and subsequent $LiAlH_4$ reduction to the *S* alcohol.[17] For the other products the absolute configurations were determined by measurement of the specific rotations of **5b**,[18] **5d**,[19] **5e**,[19] and **5f**.[20]

Table 1. Asymmetric addition–protonation of methyl 2-substituted propenoates **1** and subsequent desulfurization of **4** to provide **5** (Scheme 1).

Entry	Propenoate	*T* [°C]	*t* [h]	**4**[a]		**5**[b]	
				yield [%]	*ee* [%]	yield [%]	*ee* [%]
1	**1a** (R = Me)	−60	16	99	75[c]		
2	**1b** (R = $PhCH_2$)	−60	16	99	60[c]	94	59
3	**1c** (R = Ph)	−78	0.5	99	92	97	92
4	**1d** (R = 1-naphthyl)	−78	0.5	99	88	95	87
5	**1e** (R = 2-naphthyl)	−78	0.5	93	91	96	90
6	**1f** (R = 6-MeO-2-naphthyl)	−78	0.5	99	90[c]	99	99[d]

[a] The reaction was carried out with 2-TMSPhSH (1.2 equiv), 2-TMSPhSLi (1 mol %), **2** (1.2 mol %), and **1** (1 mmol) in toluene/hexane (3 mL, 1/1) unless otherwise noted. The *ee* values of **4a**, **b**, **d**–**f** were determined by chiral stationary phase HPLC using Daicel Chiralcel AD. [b] The absolute configuration and the *ee* values were determined from the specific rotation of **5**. [c] The reaction was carried out using 2-TMSPhSLi (8 mol %) and **2** (10 mol %). [d] Enantiomerically enriched **4f** (Ar = Ph), obtained by protodesilylation and recrystallization in 82 % yield and with 99 % *ee*, was desulfurized to **5f**.

The synthesis of a pharmaceutical agent demonstrates the utility of the present asymmetric protonation reaction. Compound **5f**, an intermediate on the way to the antiinflammatory agent naproxen, was successfully synthesized in 80 % overall yield and with 99 % *ee* from **1f** through enantioenrichment by recrystallization of **4f** (Ar = Ph, 91 % *ee*), which was obtained quantitatively by protodesilylation (Table 1, entry 6).

The reactions of **1c**–**f** bearing aryl substituents at C2 proceeded to completion within 0.5 h at −78 °C, while those of **1a** and **1b** bearing alkyl groups required higher temperatures and longer reaction times. The aryl substituents proved to be more advantageous than alkyl substituents in terms of enantioselectivity as well.

The sense of the asymmetric protonation was the same in all reactions examined, regardless of whether an α-alkyl or aryl substituent was present. The absolute configurations are those expected based on enantiofacial differentiating attack of arylthiolate with **1** to give **3**, controlled by the chiral ligand **2**, and subsequent *anti* protonation.

The asymmetric protonation was highly dependent on the substituent of the benzenethiol. In the presence of 8 mol % of lithium benzenethiolate and 10 mol % of **2** in toluene, the reaction of three equivalents of benzenethiol with **1a** (R = Me) at −60 °C was quite sluggish. In contrast, at −20 °C the reaction was completed within 3 h to give the corresponding product (*S*)-**4a** (Ar = Ph) with 37 % *ee* and in 94 % yield.

The amount of 2-TMS-benzenethiol had little affect on the selectivity. The reaction of **1c** (R = Ph) with 1.2, 3, and 9 equivalents of the thiol in the presence of 2-TMSPhSLi (8 mol %) and **2** (10 mol %) at −78 °C for 0.5 h afforded **4c** in quantitative yield and with 92–93 % *ee*. The dose-independent effects on both enantioselectivity and reactivity imply that the present enantioselective protonation is quite fast, probably due to rapid electrophilic trapping of the transient lithium enolate **3**.[21]

The characteristic features of the present asymmetric protonation are the use of a catalytic amount of a lithium cation as well as a chiral ligand, and the absence of any chiral proton source. The chiral ligand **2** can be recovered quantitatively for reuse.

Experimental Section

Typical procedure (Table 1, entry 3): To a solution of 2-trimethylsilylbenzenethiol (2.18 g, 12 mmol) in toluene/hexane (1/1, 26 mL) was added BuLi (0.063 mL, 0.1 mmol, hexane) followed by a solution of **2** (42 mg, 0.12 mmol) in toluene/hexane (1/1, 1 mL) at 0 °C. After the mixture had been stirred for 0.5 h at room temperature, a solution of **1c** (R = Ph, 1.62 g, 10 mmol) in toluene/hexane (1/1, 3 mL) was added at −78 °C. The mixture was stirred for 0.5 h at −78 °C, and quenched with water. The aqueous layer was extracted with toluene. The combined organic layers were washed with 10 % aq KOH and brine, and then dried over Na_2SO_4. Concentration followed by column chromatography on silica gel (benzene, then benzene/acetone (2/1)) gave (*S*)-**4c** (Ar = 2-TMSPh, R = Ph; 3.44 g, 99 %) as colorless cubes and recovered **2** (42 mg, 99 %).

(*S*)-**4c**: M.p. 82–83 °C; $[\alpha]_D^{25} = +49.2$ ($c = 1.17$, $CHCl_3$); ^1H NMR ($CDCl_3$, 270 MHz): $\delta = 0.32$ (s, 9H), 3.24 (dd, $J = 5.3$, 13.2 Hz, 1H), 3.62 (dd, $J = 9.9$, 13.2 Hz, 1H), 3.68 (s, 3H), 3.87 (dd, $J = 5.3$, 9.9 Hz, 1H), 7.16–7.41 (m, 8H), 7.45 (dd, $J = 1.7$, 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz): $\delta = -0.05$, 38.2, 51.2, 52.1, 125.8, 127.6, 127.8, 128.8, 129.7, 135.0, 137.7, 142.0, 172.8; IR (nujol): $\tilde{\nu} = 1735\ cm^{-1}$; MS: *m*/*z*: 344 [$M^+$]; elemental analysis calcd for $C_{19}H_{24}O_2SSi$: C 66.23, H 7.02; found: C 66.16, H, 7.09.

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[1] Reviews on enantioselective protonation: a) C. Fehr, *Angew. Chem.* **1996**, *108*, 2726–2748; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2566–2587; b) A. Yanagisawa, K. Ishihara, H. Yamamoto, *Synlett* **1997**, 411–420.

[2] Recent publications on stoichiometric asymmetric protonation: a) Y. Nakamura, S. Takeuchi, Y. Ohgo, M. Yamaoka, A. Yoshida, K. Mikami, *Tetrahedron Lett.* **1997**, *38*, 2709–2712; b) H. Kosugi, K.

Hoshino, H. Uda, *Tetrahedron Lett.* **1997**, *38*, 6861 – 6864; c) J. Martin, M.-C. Lasne, J.-C. Plaquevent, L. Duhamel, *Tetrahedron Lett.* **1997**, *38*, 7181 – 7182; d) H. Kosugi, M. Abe, R. Hatsuda, H. Uda, M. Kato, *Chem. Commun*. **1997**, 1857 – 1858; e) T. Takahashi, N. Nakao, T. Koizumi, *Tetrahedron: Asymmetry* **1997**, *8*, 3293 – 3308; f) G. Asensio, P. A. Aleman, L. R. Domingo, M. Medio-Simón, *Tetrahedron Lett.* **1998**, *39*, 3277 – 3280; g) G. Asensio, P. Alemán, A. Cuenca, J. Gil, M. Medio-Simón, *Tetrahedron: Asymmetry* **1998**, *9*, 4073 – 4078; h) H. Fujihara, K. Tomioka, *J. Chem. Soc. Perkin Trans. 1* **1999**, 2377 – 2381; i) Y. Nakamura, S. Takeuchi, Y. Ohgo, D. P. Curran, *Tetrahedron* **2000**, *56*, 351 – 356.

[3] Enantioselective protonation by catalytic antibodies: a) I. Fujii, R. A. Lerner, K. D. Janda, *J. Am. Chem. Soc.* **1991**, *113*, 8528 – 8259; b) J.-L. Reymond, J.-L. Reber, R. A. Lerner, *Angew. Chem.* **1994**, *106*, 485 – 486; *Angew. Chem. Int. Ed. Engl*. **1994**, *33*, 475 – 477.

[4] a) A. Yanagisawa, T. Kikuchi, T. Watanabe, T. Kuribayashi, H. Yamamoto, *Synlett* **1995**, 372 – 374; b) A. Yanagisawa, T. Watanabe, T. Kikuchi, H. Yamamoto, *J. Org. Chem.* **2000**, *65*, 2979 – 2983.

[5] K. Ishihara, S. Nakamura, M. Kaneeda, H. Yamamoto, *J. Am. Chem. Soc*. **1996**, *118*, 12854 – 12855.

[6] Y. Nakamura, S. Takeuchi, A. Ohira, Y. Ohgo, *Tetrahedron Lett*. **1996**, *37*, 2805 – 2808.

[7] J. Muzart, F. Hénin, S. J. Aboulhoda, *Tetrahedron: Asymmetry* **1997**, *8*, 381 – 389.

[8] a) P. Riviere, K. Koga, *Tetrahedron Lett*. **1997**, *38*, 7589 – 7592; b) E. Vedejs, A. W. Kruger, *J. Org. Chem*. **1998**, *63*, 2792 – 2793; c) E. Vedejs, A. W. Kruger, N. Lee, S. T. Sakata, M. Stec, E. Suna, *J. Am. Chem. Soc.* **2000**, *122*, 4602 – 4607; d) Y. Yamashita, Y. Emura, K. Odashima, K. Koga, *Tetrahedron Lett.* **2000**, *41*, 209 – 213.

[9] For the use of transient enolates or enols in catalytic asymmetric protonation, see: a) H. Pracejus, F.-W. Wilcke, K. Hanemann, *J. Prakt. Chem.* **1977**, *319*, 219 – 229; b) N. Kobayashi, K. Iwai, *Polym. J.* **1981**, *13*, 263 – 271; c) A. Kumar, R. V. Salunkhe, R. A. Rane, S. Y. Dike, *J. Chem. Soc. Chem. Commun*. **1991**, 485 – 486; d) F. Toda, K. Tanaka, J. Sato, *Tetrahedron: Asymmetry* **1993**, *4*, 1771 – 1774; e) C. Fehr, I. Stempf, J. Galindo, *Angew. Chem.* **1993**, *105*, 1093 – 1095; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1044 – 1046.

[10] For the use of chiral binaphthol derivatives as a chiral proton source, see: a) E. Emori, T. Arai, H. Sasai, M. Shibasaki, *J. Am. Chem. Soc.* **1998**, *120*, 4043 – 4044; b) E. Emori, T. Iida, M. Shibasaki, *J. Org. Chem.* **1999**, *64*, 5318 – 5320.

[11] K. Nishimura, M. Ono, Y. Nagaoka, K. Tomioka, *J. Am. Chem. Soc.* **1997**, *119*, 12974 – 12975.

[12] a) U. Schmidt, E. Öhler, *Angew. Chem.* **1976**, *88*, 54; *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 42; b) J. Keniya, A. A. Natu, V. N. Gogte, *Chem. Ind.* **1986**, 243; c) J. R. Mohrig, S. S. Fu, R. W. King, R. Warnet, G. Gustafson, *J. Am. Chem. Soc.* **1990**, *112*, 3665 – 3667; d) O. Miyata, T. Shinada, I. Ninomiya, T. Naito, T. Date, K. Okamura, S. Inagaki, *J. Org. Chem*. **1991**, *56*, 6556 – 6564; e) Y. Kita, N. Shibata, T. Miki, Y. Takemura, O. Tamura, *Chem. Pharm. Bull.* **1992**, *40*, 12 – 20; f) J. R. Mohrig, R. E. Rosenberg, J. W. Apostol, M. Bastienaansen, J. W. Evans, S. J. Franklin, C. D. Frisbie, S. S. Fu, M. L. Hamm, C. B. Hirose, D. A. Hunstad, T. L. James, R. W. King, C. J. Larson, H. A. Latham, D. A. Owen, K. A. Stein, R. Warnet, *J. Am. Chem. Soc.* **1997**, *119*, 479 – 486.

[13] a) B. Dmuchovsky, B. D. Vineyard, F. B. Zienty, *J. Am. Chem. Soc.* **1964**, *86*, 2874 – 2877; b) H. Hiemstra, H. Wynberg, *J. Am. Chem. Soc*. **1981**, *103*, 417 – 430.

[14] K. Tomioka, M. Okuda, K. Nishimura, S. Manabe, M. Kanai, Y. Nagaoka, K. Koga, *Tetrahedron Lett.* **1998**, *39*, 2141 – 2144.

[15] Direct HPLC analysis of **4c** (Ar = 2-TMSPh, R = Ph) sometimes did not afford a clear base line separation. The protodesilylated product (Ar = R = Ph) gave a base line separation that was adequate for determining the *ee* value.

[16] a) W. A. Bonner, J. A. Zderic, *J. Am. Chem. Soc.* **1956**, *78*, 3218 – 3221; b) H. Pracejus, *Liebigs Ann. Chem*. **1960**, *634*, 9 – 22.

[17] R. Baker, M. J. O'Mahony, C. J. Swain, *J. Chem. Soc. Perkin Trans. 1* **1987**, 1623 – 1633.

[18] M. Kobayashi, K. Koga, S. Yamada, *Chem. Pharm. Bull*. **1972**, *20*, 1898 – 1905.

[19] R. Menicagli, O. Piccolo, L. Lardicci, M. L. Wis, *Tetrahedron* **1979**, *35*, 1301 – 1306.

[20] a) O. Piccolo, F. Spreafico, G. Visentin, *J. Org. Chem*. **1987**, *52*, 10 – 14; b) I. T. Harrison, B. Lewis, P. Nelson, W. Rooks, A. Roszkowski, A. Tomolonis, J. H. Fried, *J. Med. Chem*. **1970**, *13*, 203 – 205.

[21] Since the lithium atom of the transient enolate **3** is complexed with the chiral amino diether ligand **2**, one can speculate that the enantioselective protonation takes place under the control of the ligand. However, the attempted protonation of a lithium enolate, generated from TMS enol ether and methyllithium in the presence of a stoichiometric amount of **2**, with 2-TMS-benzenethiol gave rather poor selectivity.

Synthesis of Nanophase Iron Oxide in Lumazine Synthase Capsids**

Wayne Shenton, Stephen Mann,* Helmut Cölfen, Adelbert Bacher,* and Markus Fischer

The ability to control the crystallization of inorganic materials at the nanometer length scale has prompted the use of self-assembled "nanoreactors" such as surfactant[1] and block copolymer[2] micelles, liquid crystalline mesophases,[3] and porous two-dimensional protein crystals.[4] In general, these systems consist of spatially confined environments that are topologically distinct and comprise nucleation sites which direct the growth of the inorganic phase. A biological archetype of this strategy is the protein ferritin, in which iron oxide nanoparticles are synthesized within an 8-nm-diameter hollow polypeptide cage.[5] It has previously been shown that this bio-nanoreactor can be used to produce a number of dispersed protein – inorganic nanocomposites[6–8] that have potential applications in medical imaging[9] and neutron capture therapy.[10] The utilization of other biomolecular systems analogous to ferritin could have important implications for the development of a general class of self-assembled bioinorganic materials with designed functionality and biocompatibility. For example, viral capsids have been recently used to synthesize inorganic-based nanoparticles.[11] Herein we describe a new type of bio-nanoreactor based on the enzyme lumazine synthase which can be utilized for the biomimetic synthesis of iron oxide nanoparticles, even though there is no evidence for such a function in vivo.

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