ORGANIC LETTERS

2004
Vol. 6, No. 9
1429−1431

Development of a Recyclable Fluorous Chiral Phase-Transfer Catalyst: Application to the Catalytic Asymmetric Synthesis of α-Amino Acids

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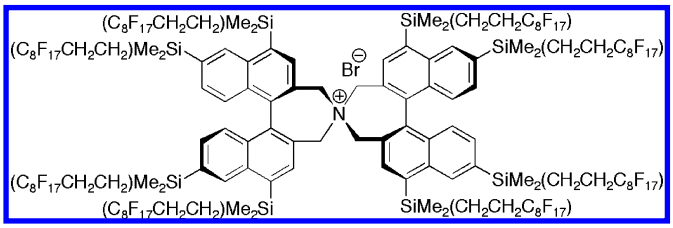
Received February 16, 2004

ABSTRACT



A recyclable fluorous chiral phase-transfer catalyst was synthesized and successfully applied for the catalytic asymmetric synthesis of both natural and unnatural α-amino acids. The reaction involves alkylation of a glycine derivative followed by extractive recovery of the chiral phase-transfer catalyst using fluorous solvent.

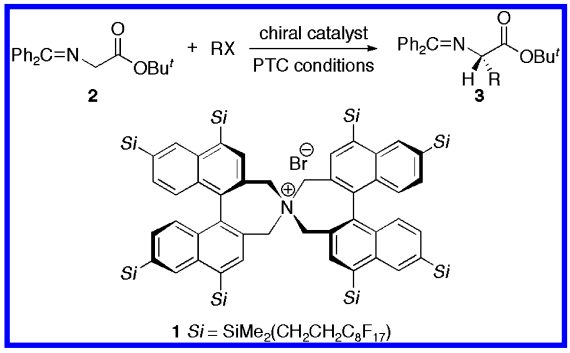
The development of chiral phase-transfer catalysts for the synthesis of optically active natural and unnatural α-amino acids by the enantioselective alkylation of prochiral protected glycine derivatives is one of the recent exciting topics in synthetic organic chemistry,[1] and hence several efficient catalysts for the system have been developed by our group[2] and others.[3] A further useful advance in the field of such chiral phase-transfer catalysis would involve the design of easily recyclable catalysts. Few examples of polymer-supported chiral phase-transfer catalysts derived from *cinchona* alkaloid have been reported for this purpose;[4] however, unfortunately almost all of these systems seriously reduced the enantioselection of the product compared with that of nonsupported catalyst systems. In this context, we are interested in the development of a fluorous chiral phase-transfer catalyst as a recyclable catalyst, since fluorous phase separation techniques for the recovery of fluorinated catalyst have been found a most useful method in recently advanced catalyst recovery techniques,[5] and some fluorous chiral metal catalysts for this method have been developed.[6,7] Here we wish to report the design and synthesis of easily recyclable fluorous chiral phase-transfer catalyst and their successful use in the asymmetric synthesis of α-amino acid derivatives (Scheme 1). To the best of our knowledge, this is the first example of a recyclable fluorous chiral phase-transfer catalyst.

The design of the fluorous chiral phase-transfer catalyst originated from a series of our recently developed binaphthyl-modified spiro-type catalysts.[2] We focused on the very recently reported symmetrical 4,4′,6,6′-tetra-substituted catalysts[2n] to prepare a highly fluorinated catalyst of type **1**

(1) For reviews, see: (a) O'Donnell, M. J. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Verlag Chemie: New York, 1993; Chapter 8. (b) Shioiri, T. In *Handbook of Phase-Transfer Catalysis*; Sasson, Y., Neumann, R., Eds.; Blackie Academic & Professional: London, 1997; Chapter 14. (c) O'Donnell, M. J. *Phases−The Sachem Phase Transfer Catalysis Review*; Sachem: Austin, TX, 1998; issue 4, p 5. (d) O'Donnell, M. J. *Phases−The Sachem Phase Transfer Catalysis Review*; Sachem: Austin, TX, 1999; issue 5, p 5. (e) Shioiri, T.; Arai, S. In *Stimulating Concepts in Chemistry*; Vogtle, F., Stoddart, J. F., Shibasaki, M., Eds.; Wiley−VCH: Weinheim, 2000; p 123. (f) O'Donnell, M. J. *Aldrichim. Acta* **2001**, *34*, 3. (g) Maruoka, K.; Ooi, T. *Chem. Rev.* **2003**, *103*, 3013.

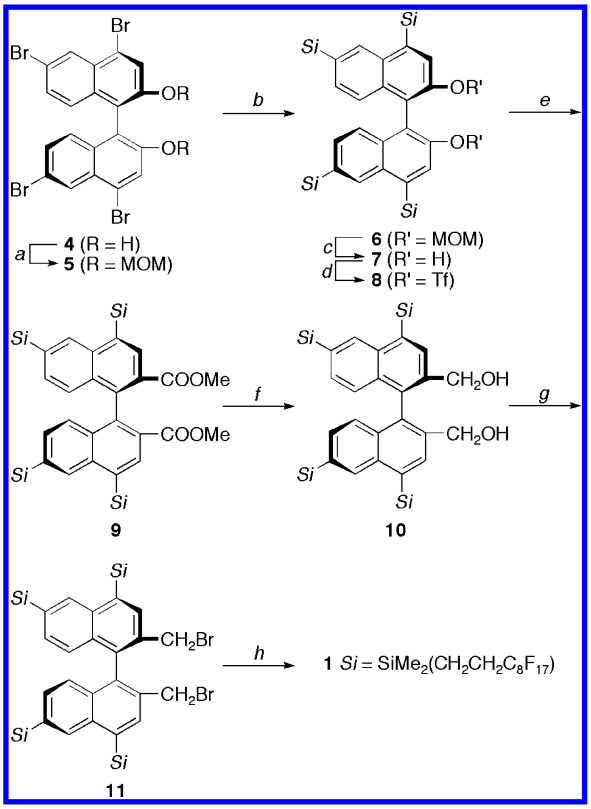
10.1021/ol049724w CCC: $27.50
Published on Web 04/03/2004

Scheme 1. Catalytic Asymmetric Synthesis of α-Amino Acids



with high efficiency. For introduction of several fluoroalkyl chains on the 4,4′,6,6′ positions of catalyst **1**, we used commercially available $C_8F_{17}CH_2CH_2SiMe_2Cl$. The requisite catalyst **1** can be prepared from the known (*R*)-4,4′6,6′-tetrabromobinaphthol **4**[8] as outlined in Scheme 2.

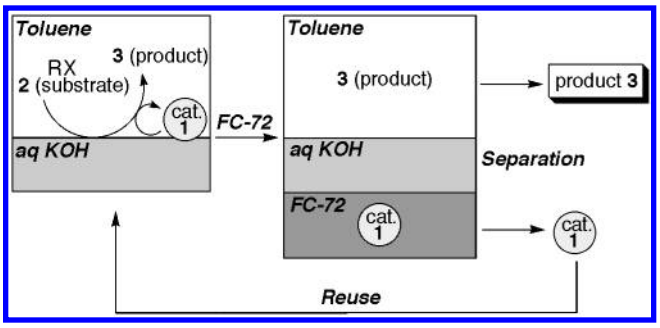
Scheme 2. Synthesis of Fluorous Chiral Phase-Transfer Catalyst **1**[a]



[a] Conditions: (a) MOMCl, NaH, THF, 0 °C to rt, 99%; (b) ^{t}BuLi, THF, −78 °C, then $C_8F_{17}CH_2CH_2SiMe_2Cl$, −78 °C to rt, 78%; (c) TsOH, CH_2Cl_2/MeOH, 50 °C, 92%; (d) Tf_2O, NEt_3, CH_2Cl_2, 0 °C, 64%; (e) CO, $Pd(OAc)_2$, DPPP, $^i Pr_2NEt$, MeOH/DMSO, 100 °C, 15 atm, 80%; (f) $LiAlH_4$, THF, 0 °C to rt, 95%; (g) CBr_4, PPh_3, THF, 0 °C to rt, 95%; (h) 28% aq NH_3, CH_3CN, reflux, 90%.

The chiral efficiency and reusability of the fluorinated phase-transfer catalyst **1** was examined by carrying out

Scheme 3. Recovery of Fluorous Catalyst **1** by Extraction with FC-72



asymmetric alkylation of protected glycine derivative **2**. For example, treatment of **2** with benzyl bromide (1.2 equiv) and 50% aqueous KOH/toluene (1:3 v/v) under the influence of 3 mol % of **1** at 0 °C for 96 h resulted in formation of phenylalanine derivative **3** (R = CH_2Ph) in 82% yield with 90% ee. In the 50% aqueous KOH/toluene biphasic system, catalyst **1** becomes heterogeneous as a result of its low solubility in toluene solvent.[9] Nevertheless, **1** was found to promote the alkylation efficiently and gave the alkylated product **3** with high enantioselectivity.[10] After the reaction, catalyst **1** could be easily recovered by the simple extraction with FC-72[11] as a fluorous solvent (Scheme 3)[12] and could

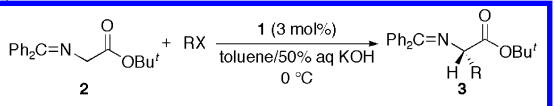
(2) (a) Ooi, T.; Kameda, M.; Maruoka, K. *J. Am. Chem. Soc.* **1999**, *121*, 1, 6519. (b) Ooi, T.; Takeuchi, M.; Kameda, M.; Maruoka, K. *J. Am. Chem. Soc.* **2000**, *122*, 5228. (c) Ooi, T,; Kameda, M.; Tannai, H.; Maruoka, K. *Tetrahedron Lett.* **2000**, *41*, 8339. (d) Ooi, T.; Takeuchi, M.; Maruoka, K. *Synthesis* **2001**, 1716. (e) Maruoka, K. *J. Fluorine Chem.* **2001**, *112*, 95. (f) Ooi, T.; Takeuchi, M.; Ohara, D.; Maruoka, K. *Synlett* **2001**, 1185. (g) Ooi, T.; Uematsu, Y.; Maruoka, K. *Adv. Synth. Catal.* **2002**, *344*, 288. (h) Ooi, T.; Uematsu, Y.; Kameda, M.; Maruoka, K. *Angew. Chem., Int. Ed.* **2002**, *41*, 1551. (i) Ooi, T.; Taniguchi, M.; Kameda, M.; Maruoka, K. *Angew. Chem., Int. Ed.* **2002**, *41*, 4542. (j) Ooi, T.; Tayama, E.; Maruoka, K. *Angew. Chem., Int. Ed.* **2003**, *42*, 579. (k) Ooi, T.; Sakai, T.; Takeuchi, M.; Tayama, E.; Maruoka, K. *Angew. Chem., Int. Ed.* **2003**, *42*, 5868. (l) Ooi, T.; Kubota, Y.; Maruoka, K. *Synlett* **2003**, 1931. (m) Ooi, T.; Kameda, M.; Maruoka, K. *J. Am. Chem. Soc.* **2003**, *125*, 5139. (n) Hashimoto, T.; Tanaka, Y.; Maruoka, K. *Tetrahedron: Asymmetry* **2003**, *14*, 1599. (o) Hashimoto, T.; Maruoka, K. *Tetrahedron Lett.* **2003**, *44*, 3313. (p) Ooi, T.; Uematsu, Y.; Maruoka, K. *Tetrahedron Lett.* **2004**, *45*, 1675.

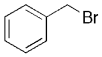
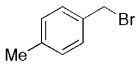
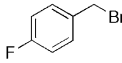
(3) For representative examples, see: (a) O'Donnell, M. J.; Bennett, W. D.; Wu, S. *J. Am. Chem. Soc.* **1989**, *111*, 2353. (b) Corey, E. J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc.* **1997**, *119*, 12414. (c) Lygo, B.; Wainwright, P. G. *Tetrahedron Lett.* **1997**, *38*, 8595. (d) Park, H.-g.; Jeong, B.-S.; Yoo, M.-S.; Lee, J.-H.; Park, M.-k.; Lee, Y.-J.; Kim, M.-J.; Jew, S.-s. *Angew. Chem., Int. Ed.* **2002**, *41*, 3036. (e) Kita, T.; Georgieva, A.; Hashimoto, Y.; Nakata, T.; Nagasawa, K. *Angew. Chem., Int. Ed.* **2002**, *41*, 2832. (f) Shibuguchi, T.; Fukuta, T.; Akachi, Y.; Sekine, A.; Oshima, T.; Shibasaki, M. *Tetrahedron Lett.* **2002**, *43*, 9539. (g) Arai, S.; Tsuji, R.; Nisida, A. *Tetrahedron Lett.* **2002**, *43*, 9535. (h) Jew, S.-s.; Yoo, M.-S.; Jeong, B.-S.; Park, I. Y.; Park, H.-g. *Org. Lett.* **2002**, *4*, 4245. (i) Lygo, B.; Allbutt, B.; James, S. R. *Tetrahedron Lett.* **2003**, *44*, 5629.

(4) (a) Zhengpu, Z.; Yongmer, W.; Zhen, W.; Hodge, P. *React. Funct. Polym.* **1999**, *41*, 37. (b) Chinchilla, R.; Mazón, P.; Nájera, C. *Tetrahedron: Asymmetry* **2000**, *11*, 3277. (c) Thierry, B.; Plaquevent, J.-C.; Cahard, D. *Tetrahedron: Asymmetry* **2001**, *12*, 983. (d) Thierry, B.; Perrard, T.; Audouard, C.; Plaquevent, J.-C.; Cahard, D. *Synthesis* **2001**, 1742. (e) Danelli, T.; Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F.; Tocco, G. *Tetrahedron: Asymmetry* **2003**, *14*, 461. (f) Thierry, B.; Plaquevent, J.-C.; Cahard, D. *Tetrahedron: Asymmetry* **2003**, *14*, 1671.

(5) For reviews, see: (a) Horváth, I. T. *Acc. Chem. Res.* **1998**, *31*, 641. (b) Curran, D. P. *Angew. Chem., Int. Ed.* **1998**, *37*, 1175. (c) Wolf, E. d.; Koten, E. d.; Deelman, B.-J. *Chem. Soc. Rev.* **1999**, *28*, 37. (d) Cavazzini, M.; Montanari, F.; Pozzi, G.; Quici, S. *J. Fluorine Chem.* **1999**, *94*, 183. (e) Fish, R. H. *Chem. Eur. J.* **1999**, *5*, 1677.

Table 1. Chiral Efficiency and Reusability of Fluorous Chiral Catalyst **1**[a]



entry	RX	time (h)	% yield[b]	% ee[c] (config)[d]
1		96	82	90 (*S*)
2[e]		96	79	92 (*S*)
3[f]		96	81	92 (*S*)
4		70	82	92 (*S*)
5		94	93	93 (*S*)
6		140	81	90 (*S*)
7[g]	EtI	10	83	87 (*S*)

[a] Unless otherwise specified, the reaction was carried out with 1.2 equiv of alkyl halide (RX) in the presence of 3 mol % of **1** in 50% aq KOH/toluene (v/v 1:3) at 0 °C under an argon atmosphere. [b] Isolated yield. [c] Enatiopurity of **3** was determined by HPLC analysis of the alkylated imine using a chiral column (DAICEL Chiralcel OD or OD-H) with hexane−2-propanol as solvent. [d] Absolute configuration of **3** was determined by comparison of the HPLC retention time with the authentic sample independently prepared by the reported procedure.[2m] [e] Using the recovered catalyst in entry 1. [f] Using the recovered catalyst in entry 2. [g] 10 equiv each of RX and $CsOH·H_2O$ (as a base), and α,α,α-trifluorotoluene (as a solvent) were used, and the reaction was performed at −20 °C.

be utilized for the next run without any loss of reactivity and selectivity (entries 1−3 in Table 1). Other selected examples are also listed in Table 1. The chiral phase-transfer catalysis of **1** found a broad scope, and good to high asymmetric inductions were achieved with not only substituted benzyl bromides but also propargylic bromide (entries 4−6). In the reaction with a simple alkyl halide such as ethyl iodide, excess alkyl halide and $CsOH·H_2O$ were employed to attain sufficient reactivity (entry 7).[2m]

In conclusion, we have developed recyclable fluorous chiral phase-transfer catalyst **1** and applied it to the catalytic asymmetric synthesis of α-amino acids. Further application of this catalyst to other asymmetric transformations is now in progress.

Acknowledgment. This work was supported by the Asahi Glass Foundation and a Grant-in-Aid for Scientific Research (13853003) from the Ministry of Education, Culture, Sports, Science and Technology, Japan. S.S. thanks the Japan Society for the Promotion of Science for Young Scientists for a research fellowship.

Supporting Information Available: Experimental procedures and characterization for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OL049724W

(6) (a) Pozzi, G.; Cinato, F.; Montanari, F.; Quici, S. *Chem. Commun.* **1998**, 877. (b) Pozzi, G.; Cavazzini, M.; Cinato, F.; Montanari, F.; Quici, S. *Eur. J. Org. Chem.* **1999**, 1947. (c) Kleijn, H.; Rijnberg, E.; Jastrzebski, J. T. B. H.; Koten, G. v. *Org. Lett.* **1999**, *1*, 853. (d) Tian, Y.; Chan, K. S. *Tetrahedron Lett.* **2000**, *41*, 8813. (e) Nakamura, Y.; Takeuchi, S.; Ohgo, Y.; Curran, D. P. *Tetrahedron Lett.* **2000**, *41*, 57. (f) Cavazzini, M.; Manfredi, A.; Montanari, F.; Quici, S.; Pozzi, G. *Chem. Commun.* **2000**, 2171. (g) Nakamura, Y.; Takeuchi, S.; Ohgo, Y.; Curran, D. P. *Tetrahedron* **2000**, *56*, 351. (h) Cavazzini, M.; Pozzi, G.; Quici, S.; Maillard, D.; Sinou, D. *Chem. Commun.* **2001**, 1220. (i) Nakamura, Y.; Takeuchi, S.; Okumura, K.; Ohgo, Y. *Tetrahedron* **2001**, *57*, 5565. (j) Maillard, D.; Bayardon, J.; Kurichiparambil, J. D.; Nguefack-Fournier, C.; Sinou, D. *Tetrahedron: Asymmetry* **2002**, *13*, 1449. (k) Cavazzini, M.; Quici, S.; Pozzi, G. *Tetrahedron* **2002**, *58*, 3943. (l) Tian, Y.; Yang, Q. C.; Mak, T. C. W.; Chan, K. S. *Tetrahedron* **2002**, *58*, 3951. (m) Nakamura, Y.; Takeuchi, S.; Okumura, K.; Ohgo, Y.; Curran, D. P. *Tetrahedron* **2002**, *58*, 3963. (n) Maillard, D.; Pozzi, G.; Quici, S.; Sinou, D. *Tetrahedron* **2002**, *58*, 3971.

(7) Fluorous chiral base catalyst derived from *cinchona* alkaloid: Fache, F.; Piva, O. *Tetrahedron Lett.* **2001**, *42*, 5655.

(8) Hu, Q.-S.; Pugh, V.; Sabat, M.; Pu, L. *J. Org. Chem.* **1999**, *64*, 7528.

(9) Catalyst **1** is soluble in CH_2Cl_2, $CHCl_3$, Et_2O, and perfluoro solvents and less soluble in toluene, benzene, hexane, etc.

(10) The reaction in the toluene/50% aqueous KOH/FC-72 (as catalyst phase) triphase system caused a slight decrease of the enantioselectivity in the asymmetric alkylation of **2**.

(11) FC-72 = perfluorohexanes.

(12) In each run, >95% of the catalyst **1** was recovered by the fluorous extraction.