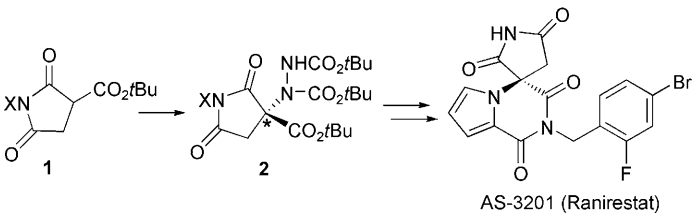
Phase-Transfer Catalysis

DOI: 10.1002/ange.200804140

Binaphthyl-Modified Quaternary Phosphonium Salts as Chiral Phase-Transfer Catalysts: Asymmetric Amination of β-Keto Esters**

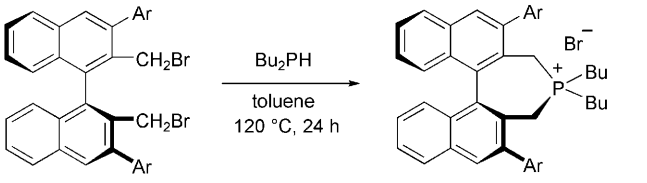
*Rongjun He, Xisheng Wang, Takuya Hashimoto, and Keiji Maruoka**

In contrast to the broad synthetic utility of chiral quaternary tetraalkylammonium salts in asymmetric phase-transfer catalysis,[1,2] chiral quaternary tetraalkylphosphonium salts have not been regarded as reliable phase-transfer catalysts due to facile formation of the corresponding ylides (Wittig reagents) under basic conditions.[3] Indeed, catalytic asymmetric synthesis utilizing chiral quaternary tetraalkylphosphonium salts as phase-transfer catalysts remains poorly studied, and only a few special examples have been reported so far with limited success.[4] In this context, we are interested in using certain chiral quaternary phosphonium salts in asymmetric phase-transfer catalysis. Here we report their application in asymmetric amination of β-keto esters.[5,6] Such an asymmetric transformation of cyclic five-membered β-keto ester **1** is valuable for preparing key intermediate **2** for asymmetric synthesis of aldose reductase inhibitor AS-3201 (Ranirestat), as shown in Scheme 1.[7]



Scheme 1. Synthesis of Ranirestat from β-keto ester **1**.

We employed a binaphthyl structure as a basic chiral unit and first prepared C_2-symmetric chiral quaternary tetraalkylphosphonium bromide (*S*)-**3a** from axially chiral dibromide (*S*)-**4a** (Scheme 2). Asymmetric phase-transfer amination of *tert*-butyl 1-oxo-2-indanecarboxylate (**5**) with 1 mol% of (*S*)-**3a** and di-*tert*-butyl azodicarboxylate (1.2 equiv) in toluene under basic conditions (K_2CO_3 or K_2HPO_4) at 0°C resulted in moderate induction (0–64% *ee*) and a quantitative yield of **6** (Table 1, entries 1 and 2). Replacing the phenyl group of

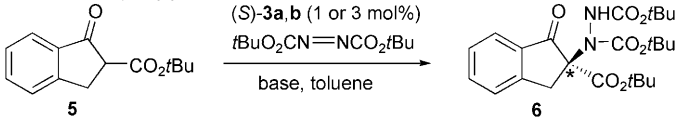


Scheme 2. Synthesis of chiral quaternary tetraalkylphosphonium bromides from axially chiral dibromides.

catalyst (*S*)-**3a** by a 3,5-bis(trifluoromethyl)phenyl group as in (*S*)-**3b** brought a moderate increase in enantiomeric excess (Table 1, entries 3–6), and use of an excess of K_2HPO_4 further enhanced the enantioselectivity (Table 1, entry 7). An enantiomeric excess of more than 90% *ee* was finally attained by using 3 mol% of catalyst (*S*)-**3b** (Table 1, entries 9 and 10).

With the optimal reaction conditions at hand, we studied the generality of the asymmetric amination of several five-

Table 1: Asymmetric amination of β-keto ester **5** with chiral phase transfer catalyst (*S*)-**3**.[a]



Entry	Catalyst (mol%)	Base (equiv)	Conditions [°C, h]	Yield [%][b]	*ee* [%][c]
1	(*S*)-**3a** (1)	K_2CO_3 (1)	0, 0.5	99	0
2	(*S*)-**3a** (1)	K_2HPO_4 (1)	0, 24	99	64
3	(*S*)-**3b** (1)	K_2CO_3 (1)	0, 0.5	99	7
4	(*S*)-**3b** (1)	K_2CO_3 (1)	−20, 0.5	99	−20
5	(*S*)-**3b** (1)	K_2HPO_4 (1)	0, 20	80	70
6	(*S*)-**3b** (1)	K_2HPO_4 (1)	−20, 40	86	73
7	(*S*)-**3b** (1)	K_2HPO_4 (5)	−20, 16	99	87
8	(*S*)-**3b** (1)	K_2HPO_4 (5)	−40, 24	99	68
9	(*S*)-**3b** (3)	K_2HPO_4 (1)	−20, 14	99	91
10	(*S*)-**3b** (3)	K_2HPO_4 (5)	−20, 10	99	90

[a] Unless otherwise specified, the reaction was carried out with 1.2 equiv of di-*tert*-butyl azodicarboxylate in the presence of 1–3 mol% of (*S*)-**3** and base in toluene under the given reaction conditions. [b] Yield of isolated product. [c] Enantiopurity of the products was determined by HPLC analysis on a chiral column (DAICEL Chiralcel OD-H or AD-H) with hexane/2-propanol or hexane/ethanol as solvent.

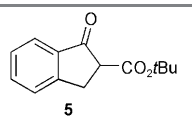
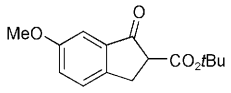
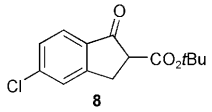
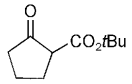
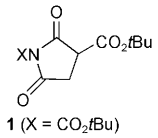
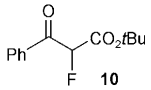
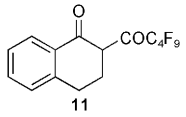
[*] Dr. R. He, X. Wang, T. Hashimoto, Prof. Dr. K. Maruoka
Department of Chemistry
Graduate School of Science
Kyoto University
Sakyo, Kyoto, 606-8502, (Japan)
Fax: (+81) 75-753-4041
E-mail: maruoka@kuchem.kyoto-u.ac.jp

[**] This work was supported by a Grant-in-Aid for Scientific Research on Priority Areas "Advanced Molecular Transformation of Carbon Resources" from the Ministry of Education, Culture, Sports, Science and Technology (Japan).

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.200804140.

membered cyclic β-keto esters under the influence of chiral quaternary tetraalkylphosphonium bromide (*S*)-**3b** (Table 2). The enantioselectivity was found to be relatively insensitive to the electronic effects of substituents on the aromatic ring of

Table 2: Asymmetric amination of β-keto esters and a β-diketone with chiral phase-transfer catalyst (*S*)-**3b**.[a]

Entry	Substrate	Base (equiv)	Conditions [°C, h]	Yield [%][b]	*ee* [%][c]
1	 **5**	K_2HPO_4 (1)	−20, 14	99	91
2	 **7**	K_2HPO_4 (5)	−40, 70	97	90
3		K_2CO_3 (1)	−40, 5	99	77
4	 **8**	K_2HPO_4 (1)	−20, 22	99	89
5	 **9**	K_2HPO_4 (1)	−20, 40	42	83
6		K_2HPO_4 (5)	−20, 10	99	85
7		K_2HPO_4 (5)	−40, 16	99	95
8		K_2CO_3 (1)	−20, 2	99	90
9		K_2CO_3 (1)	−40, 2	99	92
10	 **1** (X = CO_2tBu)	K_2HPO_4 (1)	−20, 40	99	92
11		K_2HPO_4 (5)	−20, 18	99	90
12	 **10**	K_2HPO_4 (5)	−20, 84[d]	99	73
13	 **11**	K_2HPO_4 (5)	−20, 84[e]	55	87
14		K_2HPO_4 (5)	−20, 96[d]	75	88

[a] Unless otherwise specified, the reaction was carried out with 1.2 equiv of di-*tert*-butyl azodicarboxylate in the presence of 3 mol% of (*S*)-**3b** and base in toluene under the given reaction conditions. [b] Yield of isolated product. [c] Enantiopurity of the products was determined by HPLC analysis on a chiral column (DAICEL Chiralcel OD-H or AD-H) with hexane/2-propanol or hexane/ethanol as solvent. [d] 5 mol% of (*S*)-**3b** and 10 equiv of azodicarboxylate were used. [e] 5 equiv of azodicarboxylate were used.

tert-butyl indanecarboxylate **5** (Table 2, entries 1–4). In general, use of K_2CO_3 lowered the enantioselectivity. Notably, optically active amination product **2** (X = CO_2tBu) derived from β-keto ester **1** (X = CO_2tBu) is a key intermediate for aldose reductase inhibitor AS-3201 (Table 2, entries 10 and 11).[7] Asymmetric amination of functionalized acyclic β-keto ester **10** and six-membered cyclic β-diketone **11** appears feasible (Table 2, entries 12–14).

The absolute structure of catalyst (*S*)-**3b** was unambiguously confirmed by X-ray crystallographic analysis (Figure 1).[8] The absolute configuration of amination product

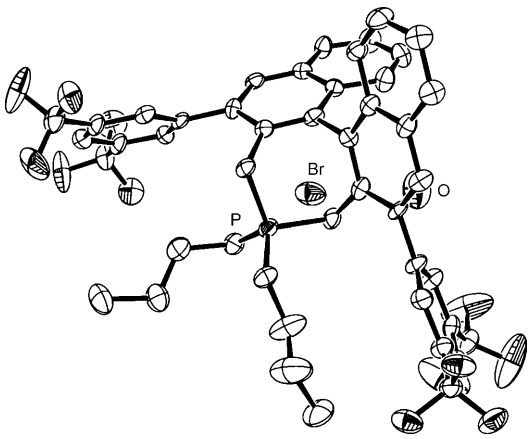
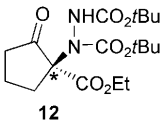


Figure 1. ORTEP diagram of catalyst (*S*)-**3b**.

12, which was prepared by asymmetric amination of ethyl 2-oxo-1-cyclopentanecarboxylate with di-*tert*-butyl azodicarboxylate in the presence of 3 mol% of (*S*)-**3b**,[9] was firmly determined to be *S* by comparison with the optical rotation of the reported compound.[10]


12

In conclusion, we have designed a new chiral quaternary tetraalkylphosphonium bromide as phase-transfer catalyst for asymmetric amination of cyclic β-keto esters and β-diketones. To the best of our knowledge, this is the first successful use of a chiral quaternary tetraalkylphosphonium bromide as phase-transfer catalyst in asymmetric synthesis.

Received: August 22, 2008
Published online: October 31, 2008

Keywords: amination · asymmetric synthesis · phase-transfer catalysis · phosphonium salts · synthetic methods

[1] a) E. V. Dehmlow, S. S. Dehmlow, *Phase Transfer Catalysis*, 3rd ed., VCH, Weinheim, **1993**; b) C. M. Starks, C. L. Liotta, M. Halpern, *Phase-Transfer Catalysis*, Chapman & Hall, New York, **1994**; c) Y. Sasson, R. Neumann, *Handbook of Phase-Transfer Catalysis*, Blackie Academic & Professional, London, **1997**; d) M. E. Halpern, *Phase-Transfer Catalysis* (ACS Symposium Series 659), American Chemical Society, Washington, DC, **1997**.

[2] For representative reviews on asymmetric phase-transfer catalysis, see: a) M. J. O'Donnell in *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), Verlag Chemie, New York, **1993**, chap. 8; b) T. Shioiri in *Handbook of Phase-Transfer Catalysis* (Eds.: Y. Sasson, R. Neumann), Blackie Academic & Professional, London, **1997**, chap. 14; c) M. J. O'Donnell, *Phases—The Sachem Phase Transfer Catalysis Review* **1998**, issue 4, p. 5; d) M. J. O'Donnell, *Phases—The Sachem Phase Transfer Catalysis Review* **1999**, issue 5, p. 5; e) A. Nelson, *Angew. Chem.* **1999**, *111*, 1685; *Angew. Chem. Int. Ed.* **1999**, *38*, 1583; f) T. Shioiri, S. Arai in *Stimulating Concepts in Chemistry* (Eds.: F. Vogtle, J. F.

Stoddart, M. Shibasaki), Wiley-VCH, Weinheim, **2000**, p. 123; g) M. J. O'Donnell in *Catalytic Asymmetric Synthesis*, 2nd ed. (Ed.: I. Ojima), Wiley-VCH, New York, **2000**, chap. 10; h) M. J. O'Donnell, *Aldrichimica Acta* **2001**, *34*, 3; i) K. Maruoka, T. Ooi, *Chem. Rev.* **2003**, *103*, 3013; j) M. J. O'Donnell, *Acc. Chem. Res.* **2004**, *37*, 506; k) B. Lygo, B. I. Andrews, *Acc. Chem. Res.* **2004**, *37*, 518; l) J. Vachon, J. Lacour, *Chimia* **2006**, *60*, 266; m) T. Ooi, K. Maruoka, *Angew. Chem.* **2007**, *119*, 4300; *Angew. Chem. Int. Ed.* **2007**, *46*, 4222; n) T. Hashimoto, K. Maruoka, *Chem. Rev.* **2007**, *107*, 5656.

[3] a) S. Yonemori, Y. Hayashi, S. Kumai, A. Wada, *Nippon Kagaku Kaishi* **1991**, *8*, 1146; b) *Phase-Transfer Catalysis: Fundamentals, Applications, and Industrial Perspectives* (Eds.: C. M. Starks, C. L. Liotta, M. Halpern), Chapman & Hall, New York, **1994**, p. 132.

[4] a) *Phase-Transfer Catalysis: Mechanism and Syntheses* (Ed.: M. E. Halpern, (ACS Symposium Series 659), American Chemical Society, Washington, DC, **1997**; b) K. Manabe, *Tetrahedron Lett.* **1998**, *39*, 5807; c) K. Manabe, *Tetrahedron* **1998**, *54*, 14465; d) M. Koehler, Neue optisch aktive Phosphoniumsalze als Phasentransferkatalysatoren sowie die Verwendung der korrespondierenden Phosphane in der asymmetrischen Katalyse, Ger. Diss. **2003**, D1018-3.

[5] For selected examples of asymmetric amination of β-keto esters, see: a) K. Juhl, K. A. Jørgensen, *J. Am. Chem. Soc.* **2002**, *124*, 2420; b) M. Marigo, K. Juhl, K. A. Jørgensen, *Angew. Chem.* **2003**, *115*, 1405; *Angew. Chem. Int. Ed.* **2003**, *42*, 1367; c) S. Saaby, M. Bella, K. A. Jørgensen, *J. Am. Chem. Soc.* **2004**, *126*, 8120; d) S. Ma, N. Jiao, Z. Zheng, Z. Ma, Z. Lu, L. Ye, Y. Deng, G. Chen, *Org. Lett.* **2004**, *6*, 2193; e) P. M. Pihko, A. Pohjakallio, *Synlett* **2004**, 2115; f) X. Liu, H. Li, L. Deng, *Org. Lett.* **2005**, *7*, 167; g) C. Foltz, B. Stecker, G. Marconi, S. Bellemin-Laponnaz, H. Wadepohl, L. H. Gabe, *Chem. Commun.* **2005**, 5115; h) X. Xu, T. Yabuta, P. Yuan, Y. Takemoto, *Synlett* **2006**, 137; i) Y. K. Kang, D. Y. Kim, *Tetrahedron Lett.* **2006**, *47*, 4565; j) M. Terada, M. Nakano, H. Ube, *J. Am. Chem. Soc.* **2006**, *128*, 16044; k) D. P. Huber, K. Stanek, A. Togni, *Tetrahedron: Asymmetry* **2006**, *17*, 685; l) J. Comelles, A. Pericas, M. Moreno-Manas, A. Vallribera, G. Drudis-Sole, A. Lledos, T. Parella, A. Roglans, S. Garcia-Granda, L. Roces-Fernandez, *J. Org. Chem.* **2007**, *72*, 2077.

[6] For representative reviews on asymmetric α-amination reactions, see: a) J.-P. Genet, C. Creck, D. Lavergne in *Modern Amination Methods* (Ed.: A. Ricci), Wiley-VCH, Weinheim, **2000**, chap. 3; b) C. Greck, B. Drouillat, C. Thomassigng, *Eur. J. Org. Chem.* **2004**, 1377; c) E. Erdik, *Tetrahedron* **2004**, *60*, 8742; d) J. M. Janey, *Angew. Chem.* **2005**, *117*, 4364 – 4372; *Angew. Chem. Int. Ed.* **2005**, *44*, 4292; e) C. Najera, J. M. Sansano, *Chem. Rev.* **2007**, *107*, 4584.

[7] a) T. Negoro, M. Murata, S. Ueda, B. Fujitani, Y. Ono, A. Kuromiya, K. Suzuki, J.-I. Matsumoto, *J. Med. Chem.* **1998**, *41*, 4118; b) M. Kurono, I. Fujiwara, K. Yoshida, *Biochemistry* **2001**, *40*, 8216; c) V. Bril, R. A. Buchanan, *Diabetes Care* **2004**, *27*, 2369; d) M. Kurono, A. Fujii, M. Murata, B. Fujitani, T. Negoro, *Biochem. Pharmacol.* **2006**, *71*, 338; e) N. Giannoukakis, *Curr. Opin. Invest. Drugs* **2006**, *7*, 916; f) T. Mashiko K. Hara, D. Tanaka, Y. Fujiwara, N. Kumagai, M. Shibasaki, *J. Am. Chem. Soc.* **2007**, *129*, 11342; g) T. Mashiko, N. Kumagai, M. Shibasaki, *Org. Lett.* **2008**, *10*, 2725.

[8] CCDC-685327 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[9] Reaction conditions: di-*tert*-butyl azodicarboxylate (1.2 equiv) and K_2HPO_4 (5 equiv) in the presence of 3 mol% of (*S*)-**3b** in toluene at −20 °C for 6 h (99% yield, 73% *ee*).

[10] M. Terada, M. Nakano, H. Ube, *J. Am. Chem. Soc.* **2006**, *128*, 16044.

