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Highly efficient asymmetric amination of β-keto esters catalyzed by chiral quaternary ammonium bromides

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ABSTRACT

A highly efficient asymmetric amination of β-keto esters was achieved under phase transfer conditions using chiral quaternary ammonium bromide as a catalyst. The amination products were obtained in quantitative yields with up to 97% ee. One of the amination products represents a key intermediate for the preparation of aldose reductase inhibitor AS-3201.

Catalytic asymmetric amination, which directly generates a C–N bond with an asymmetric carbon center, is among the simplest methods for the preparation of optically active α-amino acid derivatives.[1] Accordingly, in the past years the catalytic asymmetric amination has attracted extensive attention in academia. Asymmetric α-amination of aldehydes,[2] ketones,[3] α-keto esters,[4] β-keto esters,[4,5] and α-cyano esters[5b,6] has been developed successfully. Among these, the α-amination of β-keto esters is particularly important because it offers a method for the preparation of α-amino acids possessing quaternary carbon centers.[1,4,5] It is also desirable to combine the phase transfer catalysis which has been recognized as a convenient and highly useful synthetic tool in both academia and industry because of numerous advantages (operational simplicity, mild reaction conditions with aqueous media and environmental consciousness, amenability for large scale reactions, etc.) for practical organic synthesis.[7,8] Accordingly, we here wish to report a highly efficient asymmetric amination of β-keto esters by using chiral quaternary ammonium bromides as phase transfer catalysts. We began our study on the asymmetric amination of *tert*-butyl 2-oxo-1-cyclopentanecarboxylate **2a** with diethyl azodicarboxylate in the presence of a catalytic amount (1 mol %) of phase transfer catalysts. A previously utilized spiro-type phase transfer catalyst (*S*)-**1b**[9] gave higher enantioselectivity than non-spiro-type catalyst **1a** (Table 1, entries 1 and 2). The screening of bases by using catalyst (*S*)-**1b** showed that K_2CO_3, Cs_2CO_3, and K_2HPO_4 gave the similar selectivity for the substrate **2a** (entries 2–4). However, when di-*tert*-butyl azodicarboxylate was employed as amination partner, the enantioselectivity was dramatically decreased (entry 5). Among several solvents, toluene, which was often used in our previous study,[8] was also an optimal solvent in this amination system (entries 3, 6, and 7). After screening of aryl groups on catalysts of type (*S*)-**1**, (*S*)-**1c** was found to be the best (entry 8). Finally, the highest enantioselectivity was achieved at low temperature (−40 °C) (entry 10).

With the optimal reaction conditions at hand, we further studied the generality of the asymmetric amination of several β-keto esters under the influence of chiral quaternary ammonium bromide (*S*)-**1c** as shown in Table 2. Five-membered cyclic β-keto esters **2a–f** gave the corresponding amination products in almost quantitative yields with high to excellent enantioselectivity (up

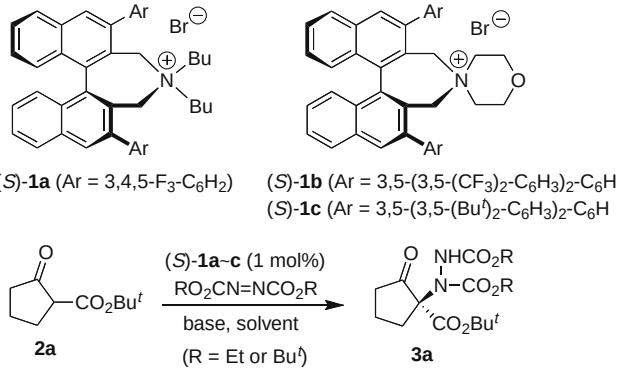

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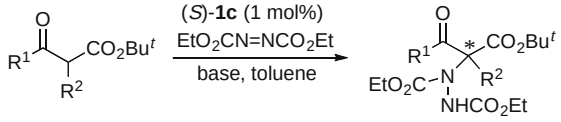
Table 1
Asymmetric amination of β-keto ester **2a** with chiral phase transfer catalyst (*S*)-**1**[a]

Entry	R	Catalyst	Base	Solvent	Condition (°C, min)	Yield[b] (%)	ee[c] (%)
1	Et	(*S*)-**1a**	33% aq K_2CO_3	Toluene	0, 5	99	74
2	Et	(*S*)-**1b**	33% aq K_2CO_3	Toluene	0, 5	99	89
3	Et	(*S*)-**1b**	66% aq Cs_2CO_3	Toluene	0, 5	99	89
4	Et	(*S*)-**1b**	50% aq K_2HPO_4	Toluene	0, 5	99	86
5	Bu^t	(*S*)-**1b**	66% aq Cs_2CO_3	Toluene	0, 5	99	52
6	Et	(*S*)-**1b**	66% aq Cs_2CO_3	Ether	0, 5	99	85
7	Et	(*S*)-**1b**	66% aq Cs_2CO_3	THF	0, 5	99	10
8	Et	(*S*)-**1c**	33% aq K_2CO_3	Toluene	0, 5	99	92
9	Et	(*S*)-**1c**	33% aq K_2CO_3	Toluene	−20, 5	99	95
10	Et	(*S*)-**1c**	33% aq K_2CO_3	Toluene	−40, 5	99	97

[a] Unless otherwise specified, the reaction was carried out with 1.2 equiv of azodicarboxylate in the presence of 1 mol % of (*S*)-**1** and base in toluene under the given reaction conditions.
[b] Isolated yield.
[c] Enantiopurity of the products was determined by HPLC analysis using a chiral column [DAICEL Chiralcel OD–H or AD–H] with hexane-isopropanol or hexane-ethanol as solvent.

to 97% ee). The electronic effect on the aromatic moiety in *tert*-butyl indanecarboxylate **2b** was found to be not so sensitive on the enantioselectivity (entries 1–6). It is noteworthy that optically active amination product **3g** derived from β-keto ester **2g** is a key intermediate for aldose reductase inhibitor AS-3201 (Scheme 1).[10] In contrast, six-membered cyclic β-keto esters **2h–i** required much longer reaction time due to the lower reactivity, and gave slightly lower enantioselectivity (entries 8 and 9).

Table 2
Asymmetric amination of β-keto esters **2** with chiral phase transfer catalyst (*S*)-**1c**[a]



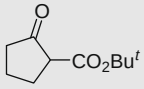
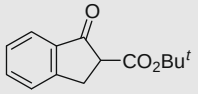
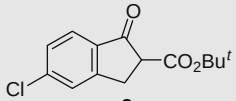
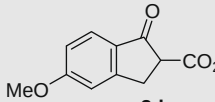
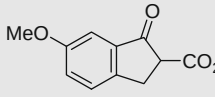
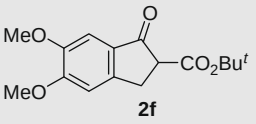
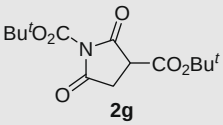
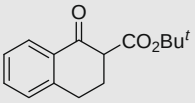
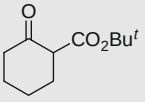
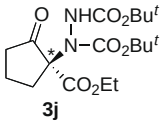
Entry	Substrate	Base	Condition (°C, min)	Yield[b] (%)	ee[c] (%)
1	 **2a**	33% aq K_2CO_3	−40, 5	99	97
2	 **2b**	50% aq K_2HPO_4	−40, 5	99	95
3	 **2c**	50% aq K_2HPO_4	−40, 5	99	93
4	 **2d**	50% aq K_2HPO_4	−40, 5	99	92
5	 **2e**	50% aq K_2HPO_4	−40, 5	99	94

Table 2 (*continued*)

Entry	Substrate	Base	Condition (°C, min)	Yield[b] (%)	ee[c] (%)
6	 **2f**	33% aq K_2CO_3	−40, 5	99	90
7[d]	 **2g**	50% aq K_2HPO_4	0, 420	95–99[e]	88
8	 **2h**	33% aq K_2CO_3	−40, 120	95–99[e]	76
9	 **2i**	66% aq Cs_2CO_3	−40, 120	95–99[e]	83

[a] Unless otherwise specified, the reaction was carried out with 1.2 equiv of diethyl azodicarboxylate in the presence of 1 mol % of (*S*)-**1c** and base in toluene under the given reaction conditions.
[b] Isolated yield.
[c] Enantiopurity of the products was determined by HPLC analysis using a chiral column [DAICEL Chiralcel OD–H or AD–H] with hexane-isopropanol or hexane-ethanol as solvent.
[d] Use of 1.2 equiv of di-*tert*-butyl azodicarboxylate as electrophile.
[e] The yield is slightly variable depending on the stirring efficiency.

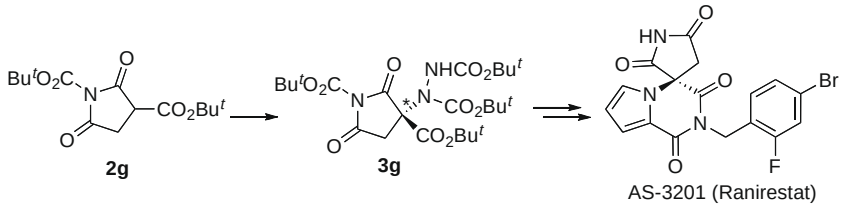
The absolute configuration of the amination product **3j**, which was prepared by asymmetric amination of ethyl 2-oxo-1-cyclopentanecarboxylate with di-*tert*-butyl azodicarboxylate in the presence of 1 mol % of (*S*)-**1c**,[11] was firmly determined to be *S* by comparison of the optical rotation value of the reported compound.[5h]



3j

In conclusion, we have developed a highly efficient and enantioselective amination of β-keto esters using chiral quaternary ammonium bromides as phase transfer catalysts. The reaction afforded products with up to 97% ee and quantitative yield. One of the amination products is the key intermediate for the preparation of aldose reductase inhibitor AS-3201 (Ranirestat).[10]

Typical experimental procedure for asymmetric amination of β-keto esters: A mixture of substrate **2b** (34.8 mg, 0.15 mmol), (*S*)-**1c** (2.0 mg, 1 mol %), and 50% aq K_2HPO_4 (0.5 mL) in toluene (2 mL) was cooled to −40 °C, to which was added diethyl azodicarboxylate (40% in toluene, 0.082 mL, 0.18 mmol) dropwise. The mixture was stirred vigorously at the same temperature for 5 min, quenched with saturated NH_4Cl solution (10 mL), extracted with diethyl ether (10 mL × 3), dried over Na_2SO_4 and concentrated. Purification of the residue by column chromatography on silica gel with hexane-ethyl acetate (5:1) as eluent afforded **3b** as colorless oil (61.0 mg, 99% yield, 95% ee). The product was identified by NMR spectroscopy. The enantiomeric excess of the product was determined by chiral HPLC using a chiral column [Daicel Chiralpak OD–H, hexane/isopropanol = 10:1, flow



Scheme 1. Synthesis of Ranirestat from β-keto ester **2g**.

rate = 1.0 mL/min, λ = 254 nm, retention time: 8.2 min (minor) and 11.1 min (major)].

Acknowledgment

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References and notes

1. For representative reviews on asymmetric α-amination reactions, see: (a) Genet, J.-P.; Creck, C.; Lavergne, D. In *Modern Amination Methods*; Ricci, A., Ed.; Wiley-VCH: Weinheim, 2000. Chapter 3; (b) Greck, C.; Drouillat, B.; Thomassigng, C. *Eur. J. Org. Chem.* **2004**, 1377; (c) Erdik, E. *Tetrahedron* **2004**, *60*, 8742; (d) Janey, J. M. *Angew.Chem., Int. Ed.* **2005**, *44*, 4292; (e) Najera, C.; Sansano, J. M. *Chem. Rev.* **2007**, *107*, 4584.
2. (a) List, B. *J. Am. Chem. Soc.* **2002**, *124*, 5656; (b) Bøgevig, A.; Juhl, K.; Kumaragurubaran, N.; Zhuang, W.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1790; (c) Vogt, H.; Vanderheiden, S.; Bräse, S. *Chem. Commun.* **2003**, 2448; (d) Iwamura, H.; Mathew, S. P.; Blackmond, D. G. *J. Am. Chem. Soc.* **2004**, *126*, 11770.
3. Kumaragurubaran, N.; Juhl, K.; Zhuang, W.; Bøgevig, A.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2002**, *124*, 6254.
4. Juhl, K.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2002**, *124*, 2420.
5. (a) Marigo, M.; Juhl, K.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 1367; (b) Saaby, S.; Bella, M.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 8120; (c) Ma, S.; Jiao, N.; Zheng, Z.; Ma, Z.; Lu, Z.; Ye, L.; Deng, Y.; Chen, G. *Org. Lett.* **2004**, *6*, 2193; (d) Pihko, P. M.; Pohjakallio, A. *Synlett* **2004**, 2115; (e) Foltz, C.; Stecker, B.; Marconi, G.; Bellemin-Laponnaz, S.; Wadepohl, H.; Gabe, L. H. *Chem. Commun.* **2005**, 5115; (f) Xu, X.; Yabuta, T.; Yuan, P.; Takemoto, Y. *Synlett* **2006**, 137; (g) Kang, Y. K.; Kim, D. Y. *Tetrahedron Lett.* **2006**, *47*, 4565; (h) Terada, M.; Nakano, M.; Ube, H. *J. Am. Chem. Soc.* **2006**, *128*, 16044; (i) Huber, D. P.; Stanek, K.; Togni, A. *Tetrahedron: Asymmetry* **2006**, *17*, 685; (j) Comelles, J.; Pericas, A.; Moreno-Manas, M.; Vallribera, A.; Drudis-Sole, G.; Lledos, A.; Parella, T.; Roglans, A.; Garcia-Granda, S.; Roces-Fernandez, L. *J. Org. Chem.* **2007**, *72*, 2077; (k) He, R.; Wang, X.; Hashimoto, T.; Maruoka, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 9466.
6. Liu, X.; Li, H.; Deng, L. *Org. Lett.* **2005**, *7*, 167.
7. (a) Dehmlow, E. V.; Dehmlow, S. S. *Phase Transfer Catalysis*, 3rd ed.; VCH: Weinheim, 1993; (b) Starks, C. M.; Liotta, C. L.; Halpern, M. *Phase-Transfer Catalysis*; Chapman & Hall: New York, 1994; (c) Sasson, Y.; Neumann, R. *Handbook of Phase-Transfer Catalysis*; Blackie Academic & Professional: London, 1997; (d) Halpern, M. E. *Phase-Transfer Catalysis ACS Symposium Series 659*; American Chemical Society: Washington, DC, 1997.
8. For representative reviews on asymmetric phase transfer catalysis, 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* **1998**, 5; (d) O'Donnell, M. J. *Phases-The Sachem Phase Transfer Catalysis Review* **1999**, 5; (e) Nelson, A. *Angew. Chem.* **1999**, *111*, 1685. *Angew. Chem., Int. Ed.* **1999**, *38*, 1583; (f) Shioiri, T.; Arai, S. In *Stimulating Concepts in Chemistry*; Vogtle, F., Stoddart, J. F., Shibasaki, M., Eds.; Wiley-VCH: Weinheim, 2000; p 123; (g) O'Donnell, M. J. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed., 2nd ed.; Wiley-VCH: New York, 2000. Chapter 10; (h) O'Donnell, M. J. *Aldrichimica Acta.* **2001**, *34*, 3; (i) Maruoka, K.; Ooi, T. *Chem. Rev.* **2003**, *103*, 3013; (j) O'Donnell, M. J. *Acc. Chem. Res.* **2004**, *37*, 506; (k) Lygo, B.; Andrews, B. I. *Acc. Chem. Res.* **2004**, *37*, 518; (l) Vachon, J.; Lacour, J. *Chimia* **2006**, *60*, 266; (m) Ooi, T.; Maruoka, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 4222; (n) Hashimoto, T.; Maruoka, K. *Chem. Rev.* **2007**, *107*, 5656; (o) Ooi, T.; Maruoka, K. *Aldrichimica Acta.* **2007**, *40*, 77; (p) Maruoka, K.; Ooi, T.; Kano, T. *Chem. Commun.* **2007**, 1487; (q) Maruoka, K. *Chimia* **2007**, *61*, 263; (r) Maruoka, K. *Org. Proc. Res. Devel.* **2008**, *12*, 679.
9. (a) Wang, X.; Kitamura, M.; Maruoka, K. *J. Am. Chem. Soc.* **2007**, *129*, 1038; (b) Lan, Q.; Wang, X.; Maruoka, K. *Tetrahedron Lett.* **2007**, *48*, 4675.
10. (a) Negoro, T.; Murata, M.; Ueda, S.; Fujitani, B.; Ono, Y.; Kuromiya, A.; Suzuki, K.; Matsumoto, J.-I. *J. Med. Chem.* **1998**, *41*, 4118; (b) Kurono, M.; Fujiwara, I.; Yoshida, K. *Biochemistry* **2001**, *40*, 8216; (c) Bril, V.; Buchanan, R. A. *Diabetes Care* **2004**, *27*, 2369; (d) Kurono, M.; Fujii, A.; Murata, M.; Fujitani, B.; Negoro, T. *Biochem. Pharmacol.* **2006**, *71*, 338; (e) Giannoukakis, N. *Curr. Opin. Invest. Drugs* **2006**, *7*, 916; (f) Mashiko, T.; Hara, K.; Tanaka, D.; Fujiwara, Y.; Kumagai, N.; Shibasaki, M. *J. Am. Chem. Soc.* **2007**, *129*, 11342; (g) Mashiko, T.; Kumagai, N.; Shibasaki, M. *Org. Lett.* **2008**, *10*, 2725.
11. Reaction condition: di-*tert*-butyl azodicarboxylate (1.2 equiv) and 33% aq. K_2CO_3 (0.5 mL) in toluene (2 mL) in the presence of 1 mol % of (*S*)-**1c** in toluene at 0 °C for 1 h (99% yield, 70% ee, $[\alpha]_D^{20}$ +1.94° [*c* 1.00, $CHCl_3$] [Lit[12]: $[\alpha]_D^{32}$ −3.47° (*c* 1.09, $CHCl_3$) (97% ee, *R* enantiomer)]).