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Chiral Ligand Control in Enantioselective Reduction of Ketones by SmI_2 for Ketyl Radical Addition to Olefins

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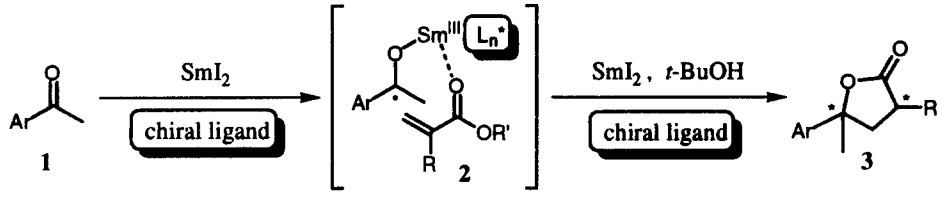
Abstract: *Samarium(II) diiodide-mediated reductive coupling of ketones with α,β-unsaturated esters is shown to afford enantioselectively γ-butyrolactones by the addition of 2,2'-bis(diphenylphosphinyl)-1,1'-binaphthyl (BINAPO) as a chiral ligand.*

Because of the great potential of samarium(II) diiodide (SmI_2) in organic synthesis,[1] so much attention has currently been focused on the stereochemically controlled reduction of ketones for addition reaction to olefins via SmI_2-promoted radical process.[2] However, there has been no report, to our knowledge, concerning chiral ligand control in enantioselective inter- or intra-molecular ketyl radical addition reaction to olefin which has, therefore, remained as a challenging problem.[3] Reported herein is the first example of chiral ligand control in enantioselective intermolecular addition reactions of ketyl radicals to olefins mediated by SmI_2 and a chiral phosphine oxide ligand (Scheme 1).[4]

Scheme 1



A typical experimental procedure is as follows: To a solution of acetophenone (0.20 mmol), methyl acrylate (0.20 mmol), and *t*-butyl alcohol (0.40 mmol) in anhydrous THF (2.0 mL) was added a 0.05 M solution of SmI_2 in THF (8 mL, 0.4 mmol) in the presence of a chiral ligand (0.4 mmol) at -78 °C under an argon atmosphere. SmI_2 was rapidly consumed as indicated by the dissipation of its characteristic deep purple color. After stirring for 20 min at that temperature, the solution was warmed to room temperature. The reaction mixture was then quenched with saturated $NaHCO_3$. Standard workup followed by silica gel chromatography afforded the ketyl-olefin coupling product, γ-butyrolactone along with the homo-coupling by-product with the ketone of its own at the *p*-position in about 15% yield[5] (Table 1).

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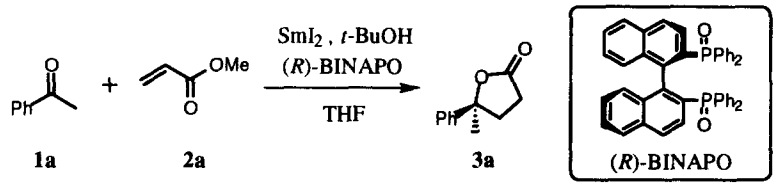


1a 2a 3a

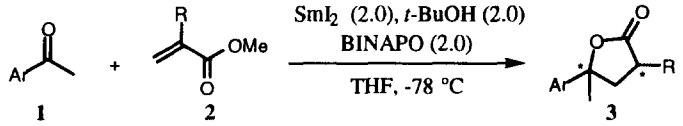
Table 1. Reductive coupling of **1a** with **2a** mediated by SmI_2 with (*R*)-BINAPO.

entry	SmI_2 (eq.)	BINAPO (eq.)	temp. (°C)	% yield[a]	% ee[b]	config.[c]
1	2.0	2.0	-78	46	67	*S*
2	2.0	2.0	-105	26	74	*S*
3	4.0	4.0	-78	39	65	*S*
4	2.5	1.0	-78	71	26	*S*

[a] Isolated yield. [b] Determined by chiral capillary GC analysis (CP-Cyclodextrin-B-2,3,6,-M-19). [c] Assigned by optical rotation. See Ref. 10.

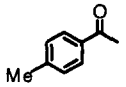
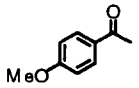
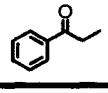
Amongst chiral ligands including diphenylethylenediamine-derived diphenylphosphinamide, 2,2'-bis(diphenylphosphinyl)-1,1'-binaphthyl, BINAPO is found to be the best ligand in this type of reduction with SmI_2.[6] In the presence of BINAPO, a reasonably short reaction time (10 min) is attained upto 1 equiv to 2 equiv of BINAPO to SmI_2.[7] At lower temperature (-105 °C), higher enantioselectivity (74% ee) was obtained, however, along with low chemical yield of the ketyl-olefin coupling product (entry 2). At least, 1 equiv of BINAPO to SmI_2 is necessary to give a reasonably high level of enantioselectivity. Otherwise, SmI_2 without any chiral ligand is involved in the reduction to give low % ee (entry 4).

Enantioselective intermolecular radical additions to olefins controlled by BINAPO as a chiral ligand can be applied to a variety of aromatic methylketones particularly with *p*-substituents to retard the homo-coupling reaction to give a high enantioselectivity along with a moderate level of diastereoselectivity (Table 2).[8]



1 2 3

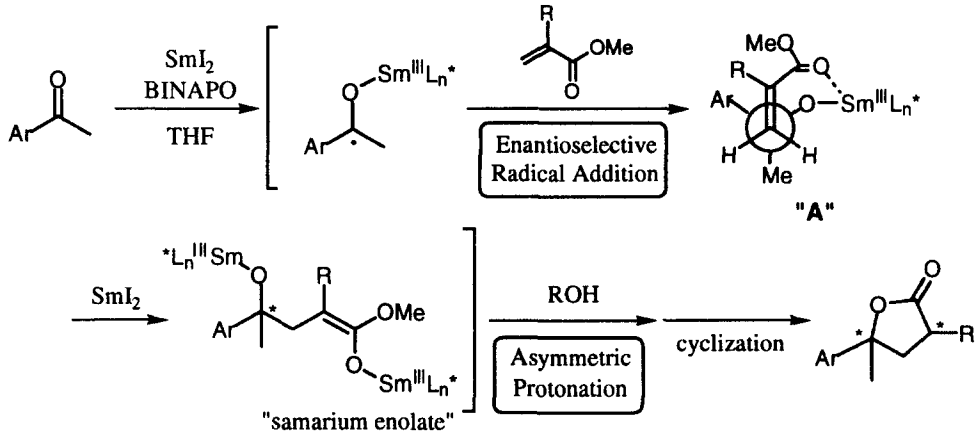
Table 2. Enantioselective ketyl-olefin coupling reactions mediated by SmI_2 with (*R*)-BINAPO.

entry	**1**	**R**	% yield[a]	*cis* : *trans*[b]	% ee (*cis*/*trans*)[c]
1		H	46	–	67
2		Me	42	66 : 34	89/55
3		(Me	16	32 : 68	62/60)[d]
4		H	58	–	62[e]
5		Me	46	51 : 49	77/–[f]
6		H	57	–	57[e]
7		(H	18	–	63[e])

[a] Isolated yield. [b] Determined by ^1H NMR analysis. [c] Determined by chiral capillary GC analysis (CP-chirasil-DEX CB). [d] The reaction was carried out using (*R*)-2-methoxy-1-phenylethanol as a proton source instead of *t*-BuOH. [e] Determined by chiral HPLC analysis (DAICEL CHIRALCEL AS). [f] Not determined.

Although the stereoconfiguration of ketyl intermediates is not well established, the mechanism of enantioselective reductive coupling of aromatic ketones with α,β-unsaturated esters can be exemplified as shown in Scheme 2. The ketylsamarium intermediates can be trapped by α,β-unsaturated esters through medium ring cyclic chelate (**A**)[9] to form new carbon-carbon bonds. Indeed, the formation of (*cis*)-γ-butyrolactone (36% ee) was observed in the coupling reaction of the known system of methyl crotonate and cyclohexyl carboaldehyde through the medium ring cyclic chelate (**A**) even in the presence of the sterically demanding BINAPO. Asymmetric protonation of the resultant samarium enolate takes place to control the second stereogenic center of the α-substituted γ-butyrolactone by the assistance of BINAPO ligated to the samarium enolate. In fact, changeover of *cis-/trans*-diastereoselectivity was observed by changing from *t*-BuOH to mandelate-derived (*R*)-2-methoxy-1-phenylethanol as a proton source.

Scheme 2



In summary, we have disclosed herein the first example of chiral ligand control in enantioselective samarium(II) diiodide-mediated reductive coupling of ketones with α,β-unsaturated esters to give enantioselectively γ-butyrolactones by the addition of BINAPO as a chiral ligand.

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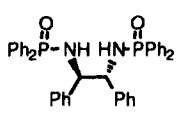
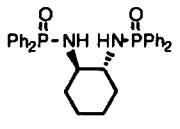
References and Notes:

1. Reviews: (a) Kagan, H. B.; Namy, J. L. *Tetrahedron* **1986**, *42*, 6573-6614. (b) Inanaga, J. *J. Synth. Org. Chem., Jpn.* **1989**, *47*, 200-211. (c) Kagan, H. B. *New J. Chem.* **1990**, *14*, 453-460. (d) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307-338.
2. For SmI_2-promoted diastereoselective ketyl-olefin coupling reactions, see: (a) Inanaga, J.; Ujikawa, O.; Handa, Y.; Otsubo, K.; Yamaguchi, M. *J. Alloys Compd.* **1993**, *192*, 197-199. (b) Kawatsura, M.; Matsuda, F.; Shirahama, H. *J. Org. Chem.* **1994**, *59*, 6900-6901. (c) Molander, G. A.; McWilliams, J. C.; Noll, B. C. *J. Am. Chem. Soc.* **1997**, *119*, 1265-1276. (d) Fukuzawa, S.; Seki, K.; Tatsuzawa, M.; Mutoh, K. *J. Am. Chem. Soc.* **1997**, *119*, 1482-1483. (e) Taniguchi, N.; Uemura, M. *Tetrahedron Lett.* **1997**, *38*, 7199-7202.

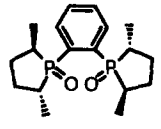
3. For enantioselective radical reactions, see: (a) Murakata, M.; Tsutsui, H.; Hoshino, O. *J. Chem. Soc. Chem. Commun.* **1995**, 481-482. (b) Urabe, H.; Yamashita, K.; Suzuki, K.; Kobayashi, K.; Sato, F. *J. Org. Chem.* **1995**, *60*, 3576-3577. (c) Wu, J. H.; Radinov, R.; Porter, N. A. *J. Am. Chem. Soc.* **1995**, *117*, 11029-11030. (d) Sibi, M. P.; Ji, J. *J. Am. Chem. Soc.* **1996**, *118*, 9200-9201. (e) Nishida, M.; Hayashi, H.; Nishida, A.; Kawahara, N. *Chem. Commun.* **1996**, 579-580. (f) Nanni, d.; Curran, D. P. *Tetrahedron: Asymmetry.* **1996**, *7*, 2417-2422. (g) Blumenstein, M.; Schwarzkopf, K.; Metzger, J. O. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 235-236. (h) Sibi, M.P.; Ji, J. *J. Org. Chem.* **1997**, *62*, 3800-3801. (i) Porter, N. A.; Wu, J. H.; Zhang, G.; Reed, A. D. *J. Org. Chem.* **1997**, *62*, 6702-6703. (j) Murakata, M.; Jono, T.; Mizuno, Y.; Hoshino, O. *J. Am. Chem. Soc.* **1997**, *119*, 11713-11714 and references cited therein.
4. Profs. Kagan and Inanaga independently examined a similar reaction by using prolinol-derived phosphoramide and sparteine as chiral ligands, respectively. We are grateful to them for the private communications. Inanaga, J. "*New Development of Studies on Rere Earth Complexes*", General Steering Committee Ed., Daitoinsatsu, Osaka, 1997; pp 263-274.
5. (a) Shiue, J. -S.; Lin, C. -C.; Fang, J. -M. *Tetrahedron Lett.* **1993**, *34*, 335-338. (b) Shiue, J. -S.; Lin, M. -H.; Fang, J. -M. *J. Org. Chem.* **1997**, *62*, 4643-4649.
6. Enantioselective reductive coupling of 4'-methoxyacetophenone with methyl acrylate mediated by chiral ligands and SmI_2.



33% (5% ee)



27% (0% ee)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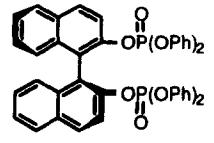
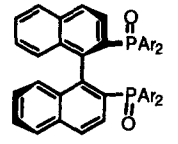


54% (18% ee)



34% (45% ee)

Ar = 3,5-dimethylphenyl

(2,2'-bis[bis(3,5-dimethylphenyl)phosphino]-1,1'-binaphthyl: Mashima, K.; Matsumura, Y.; Kusano, K.; Kumobayashi, H.; Sayo, N.; Hori, Y.; Ishizaki, T.; Akutagawa, S.; Takaya, H. *J. Chem. Soc. Chem. Commun.* **1991**, 609-610.)
7. Precipitate was formed upon mixing SmI_2 and BINAPO in 1:2 ratio.
8. Propiophenone provides very low chemical yield presumably because of the steric hindrance around the radical center (entry 7).
9. Inanaga has already proposed such a cyclic chelate model for the formation of a (*cis*)-γ-butyrolactone from methyl crotonate and cyclohexylcarboaldehyde. Furthermore, he reported the 1:1 ratio of *trans*-/*cis*-diastereomers in the presence of large excess of HMPA to break such a cyclic chelate (**A**). (a) Otsubo, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 5763. (b) Handa, Y.; Otsubo, K.; Inanaga, J.; Yamaguchi, M. *Kidorui*, **1988**, 120.
10. Albinati, A.; Bravo, P.; Ganazzoli, F.; Resnati, G.; Viani, F. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1405.