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# Enantioselective Ring Opening of *meso*-Epoxides by Aromatic Amines Catalyzed by Lanthanide Iodo Binaphtholates

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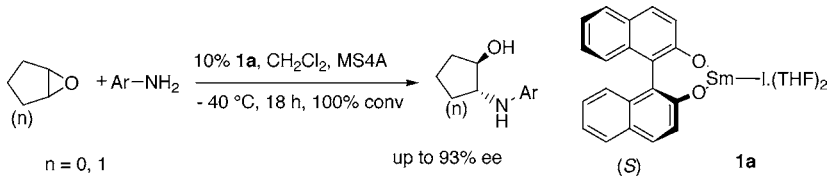
## ABSTRACT




**Lanthanide iodo binaphtholates are efficient enantioselective catalysts for the ring opening of *meso*-epoxides by various aromatic amines. The study of the influence of temperature on the ring opening of cyclohexene oxide by *o*-anisidine catalyzed by the samarium complex shows an isoinversion effect with the maximum enantiomeric excess at −40 °C. Reactions of aniline, *o*-anisidine, or *p*-anisidine with five- or six-membered ring epoxides at this temperature allow the preparation of *β*-amino alcohols with enantiomeric excesses up to 93%.**

Enantiopure *β*-amino alcohols are highly important molecules both as building blocks for biologically active compounds[1] and for their applications as chiral auxiliaries or ligands in numerous enantioselective reactions.[2] The enantioselective, catalyzed ring opening of epoxides with amines affords an easy route to asymmetric *β*-amino alcohols, but, up to now, this process has been scarcely studied.[3] Catalytic enantioselective ring opening of epoxides has been the focus of recent studies[4] and studies using silylated derivatives[5] or various nucleophiles leading to the formation of C−O, C−S, or C−C bonds.[6] Enantioselective ring opening of epoxides by aliphatic amines using binaphthol and titanium has been described, but this catalytic system is efficient for eight-membered ring epoxides with ketal groups only.[3a] Recently, aminolytic kinetic resolution of aromatic epoxides with

(1) Rogers, G. A.; Parsons, S. M.; Anderson, D. C.; Nilsson, L. M.; Bahr, B.A; Kornreich, W. D.; Kaufman, R; Jacobs, R. S.; Kirtman, B. *J. Med. Chem.* **1989**, *32*, 1217.

(2) (a) Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49. (b) Nugent, W. A.; Licini, G.; Boncio, M.; Bortolini, O.; Finn, M. G.; McCleland, B. W. *Pure Appl. Chem.* **1998**, *70*, 1041.

(3) (a) Sagawa, S.; Abe, H.; Hase, Y.; Inaba, T. *J. Org. Chem.* **1999**, *64*, 4962. (b) Sekine, A.; Oshima, T.; Shibasaki, M. *Tetrahedron* **2002**, *58*, 75. (c) Bartoli, G.; Bosco, M.; Carlone, A.; Locatelli, M.; Massaccesi, M.; Melchiorre P.; Sambri, L. *Org. Lett.* **2004**, *6*, 2173. (d) Bartoli, G.; Bosco, M.; Carlone, A.; Locatelli, M.; Melchiorre P.; Sambri, L. *Org. Lett.* **2004**, *6*, 3973. (e) Schneider, C.; Sreekanth, A. R.; Mai, E. *Angew. Chem., Int. Ed.* **2004**, *43*, 5691.

(4) (a) Hodgson, D. M.; Gibbs, A. R.; Lee, G. P. *Tetrahedron* **1996**, *52*, 14631. (b) Willis, C. M. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1765.

(5) For ring opening by silyl azide, see: (a) Nugent, W. A. *J. Am. Chem. Soc.* **1992**, *114*, 2765. (b) Nugent, W. A.; Harlow, R. L. *J. Am. Chem. Soc.* **1994**, *116*, 6142. (c) McCleland, B. W.; Nugent, W. A.; Finn, M. G. *J. Org. Chem.* **1998**, *63*, 6656. (d) Martinez, L. E.; Leighton, J. L.; Carsten, D. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5897. (e) Hansen, K. B.; Leighton, J. L.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1996**, *118*, 10924. For ring opening by trimethyl silyl cyanide, see: (f) Shimizu, K. D.; Cole, B. M.; Krueger, C. A.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **1997**, *36*, 1704. (g) Zhu, C.; Yuan, F.; Gu, W.; Pan, Y. *Chem. Commun.* **2003**, 692.

(6) For ring opening by thiols or phenols, see: (a) Iida, T.; Yamamoto, N.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1997**, *119*, 4783. (b) Matsunaga, S.; Das, J.; Roels, J.; Vogl, E. M.; Yamamoto, N.; Iida, T.; Yamaguchi, K.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 2252. (c) Iida, T.; Yamamoto, N.; Mastunaga, S.; Woo, H. G.; Shibasaki, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 2223. (d) Vogl, E. M.; Matsunaga, S.; Kanai, M.; Iida, T.; Shibasaki, M. *Tetrahedron Lett.* **1998**, *39*, 7917. For ring opening by acids: (e) Jacobsen, E. N. *Tetrahedron Lett.* **1997**, *38*, 773. For ring opening by indoles, see: (f) Bandini, M.; Cozzi, P. G.; Melchiorre, P.; Umani-Ronchi, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 84.

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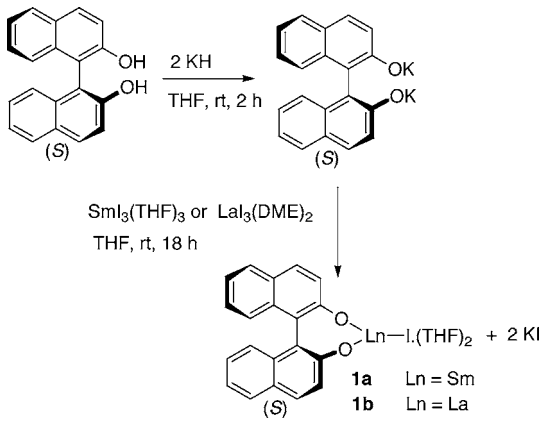
aromatic amines and carbamates catalyzed by chromium salen complexes has been reported as an efficient synthesis of *anti*-$\beta$-amino alcohols with high enantiomeric purity.[3c,d]

Enantioselective reactions catalyzed by lanthanides are now the concern of increasing interest,[7] but after the first reports on the catalytic activity of lanthanide chlorides, cyanides, or triflates for opening of epoxides,[8] only scarce examples of asymmetric ring opening of epoxides catalyzed by lanthanides have been published. Jacobsen has performed with high enantioselectivity the opening of *meso*-epoxides by trimethylsilyl cyanide catalyzed by ytterbium chloride coordinated with pybox.[9] Several lanthanide catalysts for enantioselective aminolysis of epoxides have been reported. Wu has prepared $\beta$-amino alcohols using samarium trichloride as a catalyst and realized asymmetric reactions by preparing in situ the catalysts from (*R*)-binaphthol and lanthanide chlorides with low enantiomeric excesses.[10] Ytterbium triflate in the presence of (*R*)-binaphthol and diphenyl benzylamine afforded higher enantiomeric excesses in the same reaction.[11] Shibasaki has studied an in situ-prepared catalytic system based on Pr(O-*i*Pr)$_3$, (*R*)-BINOL, and $Ph_3P{=}O$, which performed ring opening of cyclic epoxides by *o*-anisidine with up to 65% ee.[3b] The method was applied to the formal synthesis of 4-demethoxydaunomycin. Recently, the use of scandium triflate coordinated with chiral bipyridine ligand was reported for the catalysis of enantioselective opening of *meso*-epoxides by alcohols and amines with higher enantiomeric excess in reactions involving alcohols.[3e]

Our previous studies investigated the activity of samarium diiodide as an efficient Lewis acid catalyst for a wide range of reactions such as Mukaiyama aldol reactions, Diels−Alder reactions, or tandem Mukaiyama Michael−aldol reactions.[12] We also found that in the presence of catalytic amounts of samarium diiodide, epoxides react with various nucleophiles such as trimethylsilyl azide, trimethylsilyl cyanide, and amines leading to the corresponding opening products under mild conditions.[13] Recently, we reported the transformation of cyclic *meso*-epoxides in $\beta$-amino alcohols by aromatic amines.[13b] We checked that samarium diiodide as well as other lanthanide iodides display higher activities than chlorides or bromides.[12a] With the aim to develop asymmetric catalysts based on lanthanides, we have prepared lanthanide iodo binaphtholates, which are active catalysts for Diels−Alder reactions, albeit with low enantioselectivities.[14] These

**Scheme 1**




complexes afforded high enantiomeric excesses for an iminoaldol reaction involving glyoxylic imine.[15] Herein, we present our results concerning ring opening of *meso*-epoxides by aromatic amines catalyzed by lanthanide iodo binaphtholates that allows the preparation of highly enantiomerically enriched $\beta$-amino alcohols.

We formerly reported the preparation of ytterbium, samarium, and lanthanum iodo binaphtholate by reaction of the binaphthol potassium salt (obtained from KH and binaphthol) with the corresponding lanthanide triiodides (Scheme 1). By this method, precipitation of potassium iodide facilitates the metathesis reaction leading to lanthanide iodo binaphtholates. Samarium and lanthanum complexes furnished higher enantiomeric excesses than ytterbium for Diels−Alder reactions.[14] For iminoaldolization reactions catalyzed by samarium iodo binaphtholate, careful optimization of the reaction conditions was necessary to obtain high enantioselectivity.[15] We thus carried out some preliminary experiments to test the ring opening of epoxides with amines and studied first the activity of samarium iodobinaphthoxide **1a** in dichloromethane at room temperature with molecular sieves in the reaction of cyclohexene oxide **2a** with aniline using 10% catalyst.[16] When aniline was added to the catalyst before the epoxide, $\beta$-amino alcohol was isolated with 20% enantiomeric excess, while a racemic product was obtained for the reverse order of addition of substrates. The presence of aniline has been shown to have a dramatic influence on asymmetric induction in the imino aldol reaction, which could be explained by a modification of the structure of the catalyst by the amine ligand.[15] Introduction of amine prior to epoxide could produce the same effect for aminolysis of epoxides. We then compared samarium and lanthanum iodobinaphthoxides **1a** and **1b** for the ring opening of cyclohexene oxide **2a** by several amines at room temperature (Scheme 2). Results are collected in Table 1.

(7) (a) Aspinall, H. C. *Chem. Rev.* **2002**, 1807. (b) Shibazaki, M.; Yoshikawa. N. *Chem. Rev.* **2002**, 2187. (c) Kobayashi, S.; Sugiura, M.; Kitagawa, H.; Lam, W. L. *Chem. Rev.* **2002**, 2227.

(8) Vougioukas, A. E.; Kagan, H. B. *Tetrahedron Lett.* **1987**, *28*, 6065.

(9) Schaus, S. E.; Jacobsen, E. N. *Org. Lett.* **2000**, *2*, 1001.

(10) Fu, X. L.; Wu, S. H. *Synth. Commun.* **1997**, *27*, 1677−1683.

(11) Hou, X. L.; Wu, J.; Dai, L. X.; Xia, L. J.; Tang, M. H. *Tetrahedron: Asymmetry* **1998**, *9*, 1747.

(12) (a) Collin, J.; Giuseppone, N.; Van de Weghe, P. *Coord. Chem. Rev.* **1998**, *178*−*180*, 117. (b) Giuseppone, N.; Van de Wèghe, P.; Mellah, M.; Collin, J. *Tetrahedron* **1998**, *54*, 13129. (c) Van de Weghe, P.; Collin, J. *Tetrahedron Lett.* **1994**, *35*, 2545. (d) Giuseppone, N.; Collin, J. *Tetrahedron* **2001**, *57*, 8989. (e) Jaber, N.; Assié, M.; Fiaud, J.-C.; Collin, J. *Tetrahedron* **2004**, *60*, 3075. (f) Gil, R.; Eternot, M.; Guillerez, M.-G.; Collin, J. *Tetrahedron* **2004**, *60*, 3085.

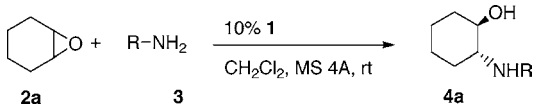
(13) (a) Van de Weghe, P.; Collin, J. *Tetrahedron Lett.* **1995**, *36*, 1649. (b) Carrée, F.; Gil, R.; Collin, J. *Tetrahedron Lett.* **2004**, *45*, 7749.

(14) Collin, J.; Carrée, F.; Giuseppone, N.; Santos, I. *J. Mol. Catal.* **2003**, *200/1*−*2*, 185.

(15) Jaber, N.; Carrée, F.; Fiaud, J. C.; Collin, J. *Tetrahedron: Asymmetry* **2003**, *14*, 2067.

(16) During studies of Diels−Alder reactions, we observed that the presence of molecular sieves allowed improvement of the conversion without modification of the enantiomeric excess, and all our subsequent catalytic experiments have been performed with 4 Å molecular sieves.

**Scheme 2**




The reaction of cyclohexene oxide with aniline led to *β*-amino alcohol **4a-1** with total conversion, and the enantiomeric excess was higher with lanthanum complex **1b** than with samarium complex **1a** (entries 1 and 2). Reactions of cyclohexene oxide with *o*-anisidine gave the same enantiomeric excess for **4a-2** with both complexes (entries 3 and 4). The samarium complex was more enantioselective in the reaction of cyclohexene oxide with *p*-anisidine (entries 5 and 6). Reaction of cyclohexene oxide with benzylamine catalyzed by samarium complex allowed isolation of the corresponding amino alcohol in good yield but as an almost racemic product.

**Table 1.** Aminolysis of Epoxides Catalyzed by Samarium and Lanthanum Complexes **1** at Room Temperature

| entry | catalyst | epoxide | amine | product[a] | yield (%)[b] | ee (%)[c] |
|---|---|---|---|---|---|---|
| 1 | **1a** | **2a** | aniline | **4a-1** | 55 | 20 |
| 2 | **1b** | **2a** | aniline | **4a-1** | 90 | 40 |
| 3 | **1a** | **2a** | *o*-anisidine | **4a-2** | 70 | 52 |
| 4 | **1b** | **2a** | *o*-anisidine | **4a-2** | 85 | 52 |
| 5 | **1a** | **2a** | *p*-anisidine | **4a-3** | 55 | 58 |
| 6 | **1b** | **2a** | *p*-anisidine | **4a-3** | 80 | 51 |
| 7 | **1a** | **2a** | benzylamine | **4a-4** | 60 | 6 |

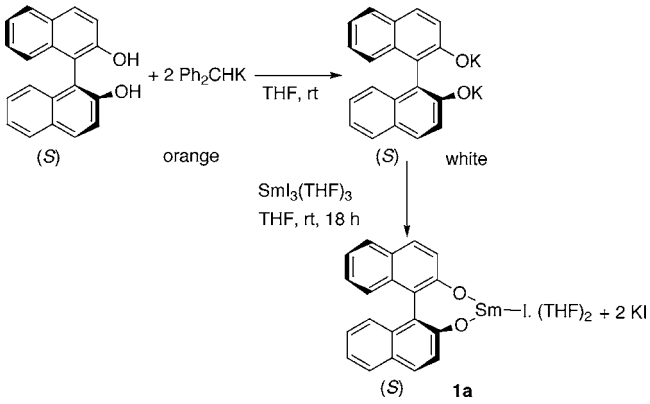
[a] Absolute configuration of the major enantiomer (1*R*,2*R*) was assigned by comparison of the rotation values in the literature or by analogy. [b] Reaction time was 18 h; yield of isolated product (100% conversion). [c] Determined by HPLC (see Supporting Information).

The highest enantiomeric excess (58%) has so far been obtained with samarium iodobinaphthoxide **1a**, and the further studies have been realized with this catalyst. The synthesis of catalyst **1a** was improved by a different method of preparation for the binaphthol potassium salt (since the binaphthol potassium salt is insoluble in THF, excess potassium hydride must be avoided), involving the use of potassium diphenyl methide. This derivative is isolated as an orange powder, and its preparation has been reported in the literature.[17] Replacement of the potassium source allows adjustment of the stoichiometry, which is indicated by a change of color from orange to white at the end of the formation of potassium bis binaphthoxide (Scheme 3). Complex **1a** is then obtained by reaction of potassium bisbinaphthoxide with samarium triiodide.[14]

We next examined the influence of temperature on selectivity for aminolysis of cyclohexene oxide by *o*-anisidine catalyzed by complex **1a**. The results are indicated in Table

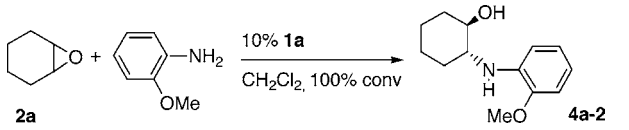
(17) Tjaden, E. B.; Casty, G. L.; Stryker, J. M. *J. Am. Chem. Soc.* **1993**, *115*, 9814.

**Scheme 3**




2. We found that variation of the enantiomeric excesses was not monotonic with the temperature. The enantiomeric excess increased first when the temperature was decreased to reach a maximum value of 91% at −40 °C. Reactions performed at lower temperatures gave lower asymmetric inductions. Such variations of enantioselectivity have been already described.[18] The Eyring plot for this reaction is represented in Figure 1 and shows a nonlinear behavior, consisting of two linear regions intersecting at the inversion temperature ($T_{inv}$). This intersection corresponds to a value of −39 °C in Figure 1.

**Table 2.** Influence of Temperature on Enantiomeric Excess




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| $T$ (°C) | 20 | 0 | −20 | −40 | −50 | −60 | −80 |
| $t$ (h) | 18 | 18 | 18 | 48 | 48 | 48 | 72 |
| ee (%) | 52 | 66 | 83 | 91 | 90 | 82 | 68 |

Inversion temperatures can be explained by a reaction pathway with at least two enantioselective steps weighted differentially according to the temperature. Cainelli proposed $T_{inv}$ as the temperature value for the interconversion betweeen two different solvation clusters behaving as two different molecules.[18e,f] In the aminolysis of epoxides catalyzed by samarium iodo binaphtholate, the inversion temperature could be explained similarly. Several catalytic species with variable numbers of THF molecules and/or amines coordinated can

(18) (a) Buschmann, H.; Scharf, H. D.; Hoffman, N.; Esser, P. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 477. (b) Heller, D.; Buschmann, H.; Scharf, H. D. *Angew. Chem., Int. Ed.* **1996**, *35*, 1852. (c) Heller, D.; Buschmann, H.; Neumann, H. *J. Chem. Soc., Perkin Trans. 2* **1999**, 175. (d) Gypser, A.; Norrby, P. O. *J. Chem. Soc., Perkin Trans. 2* **1997**, 939. (e) Cainelli, G.; Giacomini, D.; Galetti, P. *Chem. Commun.* **1999**, 567. (f) Cainelli, G.; Galetti, P.; Giacomini, D.; Orioli, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 523. (g) Pardigon, O.; Tenaglia, A.; Buono, G. *J. Mol. Catal. A* **2003**, *196*, 157. (h) Hénin, F.; Letinois, S.; Muzart, J.; *Tetrahedron: Asymmetry* **2000**, *11*, 2037. (i) Göbel, T.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1329.

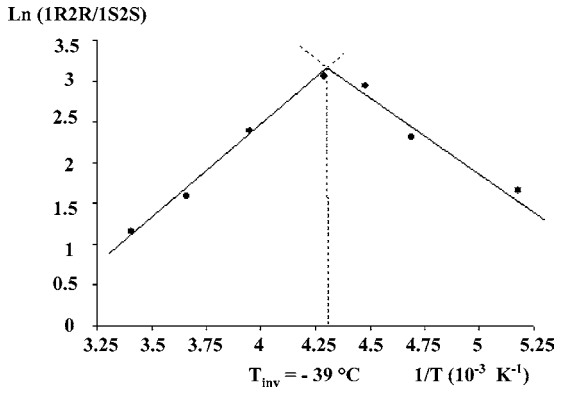
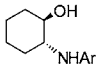
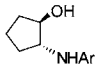
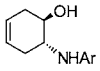
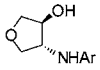



**Figure 1.** Eyring plot for aminolysis of cyclohexene oxide with *o*-anisidine catalyzed by samarium complex **1a**.

be envisaged. Further studies, especially those concerning the structure of active species involved in enantioselective catalysis, are necessary to understand the inversion phenomenon.

We then performed various enantioselective aminolysis reactions in the conditions optimized for the preparation of amino alcohol **4a-2**, i.e., temperature of −40 °C, and samarium iodo binaphtholate **1a** as a catalyst, as indicated in Table 3. Three epoxides have been examined, six- and five-membered ring epoxides **2a** and **2b**, respectively, and cyclohexene monoxide **2c**, along with three aromatic amines, aniline, *ortho*-anisidine, and *para*-anisidine. In all cases, a total conversion was observed after one night at −40 °C. Good to high asymmetric inductions were observed with enantiomeric excesses up to 93%. It is noteworthy that the determination of the inversion temperature for one aminolysis reaction has allowed the achievment of high enantioselectivity in other reactions performed at the same temperature. We examined also the reaction of 2,5-dihydrofuran oxide **2d** with *o*-anisidine under the same conditions. Interestingly, we observed the formation of amino alcohol **4d-2**, albeit with reduced activity and enantioselectivity. Lewis base groups do not inhibit catalytic activity, and optimization of this reaction is under study. Acyclic substrates are less reactive, and samarium iodo binaphtholate catalyzes aminolysis of *cis*-stilbene oxide by *o*-anisidine at room temperature to give the corresponding amino alcohol after 24 h with very low enantiomeric excess. Samarium iodo binaphtholate appears to be more active and more enantioselective than the catalysts formerly described in similar reactions. For aminolysis reactions catalyzed by ytterbium triflate in the presence of binol, an enantiomeric excess of 80% was obtained only for the reaction leading to amino alcohol **4a-1**,[11] and the ring

**Table 3.** Enantioselective Aminolysis of Epoxides Catalyzed by Samarium Complex **1a** at −40 °C

| entry | epoxide | $ArNH_2$ | product[a] | yield %[b] | ee%[c] |
|---|---|---|---|---|---|
| | | |  | | |
| 1 | **2a** | aniline | **4a-1** | 79 | 91 |
| 2 | **2a** | *o*-anisidine | **4a-2** | 85 | 91 |
| 3 | **2a** | *p*-anisidine | **4a-3** | 82 | 85 |
| | | |  | | |
| 4 | **2b** | aniline | **4b-1** | 76 | 76 |
| 5 | **2b** | *o*-anisidine | **4b-2** | 80 | 93 |
| 6 | **2b** | *p*-anisidine | **4b-3** | 79 | 93 |
| | | |  | | |
| 7 | **2c** | aniline | **4c-1** | 68 | 83 |
| 8 | **2c** | *o*-anisidine | **4c-2** | 75 | 92 |
| 9 | **2c** | *p*-anisidine | **4c-3** | 79 | 92 |
| | | |  | | |
| 10 | **2d** | *o*-anisidine | **4d-2** | 12[d] | 47 |

[a] Absolute configuration of the major enantiomer (1*R*,2*R*) was assigned by comparison of the rotation values in the literature or by analogy. [b] Yield of isolated product (100% conversion). [c] Determined by HPLC (see Supporting Information). [d] Conversion = 15% (at room temperature, 40% conversion after 18 h, 30% isolated yield, 43% ee) .

opening of cyclic epoxides by *p*-anisidine catalyzed by the system $Pr(O\text{-}iPr)_3$, (*R*)-BINOL, and $Ph_3P{=}O$ has been performed in toluene at 50 °C with lower enantiomeric excesses.[3b] Since the deprotection of nitrogen substituted by *ortho*- and *para*-methoxy phenyl groups has been described in the literature,[19] the amino alcohols that we have isolated with high enantiomeric excesses in reactions involving *ortho*-anisidine and *para*-anisidine can be useful for the preparation of ligands or chiral synthons.

In conclusion, we have found that samarium iodobinaphthoxide catalyzes enantioselective aminolysis of cyclic *meso*-epoxides, producing $\beta$-amino alcohols with high enantiomeric excesses. We are currently extending the scope of enantioselective epoxide ring-opening reactions and studying their synthetic applications.

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**Supporting Information Available:** Experimental procedures, full characterization, and copies of $^{13}C$ NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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(19) (a) Kobayashi, S.; Ishitani, H.; Ueno, M. *J. Am. Chem. Soc.* **1998**, *120*, 431. (b) Porter, J. R.; Traverse, J. F.; Hoveyda, A. H.; Snapper, M. L. *J. Am. Chem. Soc.* **2001**, *123*, 984.