Chiral Lanthanum(III)-Binaphthyldisulfonate Complexes for Catalytic Enantioselective Strecker Reaction

e 2009 Vol. 11, No. 11 2321–2324

ORGANIC LETTERS

Manabu Hatano, Yasushi Hattori, Yoshiro Furuya, and Kazuaki Ishihara*

Graduate School of Engineering, Nagoya University, Furo-cho, Chikusa, Nagoya 464-8603, Japan

ishihara@cc.nagoya-u.ac.jp

Received April 2, 2009



ABSTRACT

A catalytic enantioselective Strecker reaction catalyzed by novel chiral lanthanum(III)—binaphthyl disulfonate complexes was developed. The key to promoting the reactions was a semistoichiometric amount of AcOH or i-PrCO₂H, which takes advantage of HCN generation in situ. The corresponding cyanation products were obtained in high yields and with high enantioselectivities.

The catalytic enantioselective Strecker reaction is one of the most convenient methods for the synthesis of optically active natural and unnatural α -amino acids.¹ This process usually involves the addition of hydrogen cyanide (HCN) or trimethylsilyl cyanide (TMSCN) to imines, and several chiral

organocatalysts² and metal catalysts³ have recently been developed to achieve a high level of enantioselectivity. In particular, chiral binaphthyl derivatives offer great advantages in the design of both organocatalysts and metal catalysts for the Strecker reaction.^{4,5} In the course of our studies of chiral binaphthyl chemistry, we recently developed chiral 1,1'binaphthyl-2,2'-disulfonic acid (BINSA, **1**) as an organocatalyst for the enantioselective direct Mannich-type reaction.⁶ BINSA, which has an extremely simple structure, should be a highly promising chiral ligand for metal-mediated

For reviews, see: (a) Duthaler, R. O. *Tetrahedron* **1994**, *50*, 1539.
Yet, L. *Angew. Chem., Int. Ed.* **2001**, *40*, 875. (c) Gröger, H. *Chem. Rev.* **2003**, *103*, 2795. (d) Spino, C. *Angew. Chem., Int. Ed.* **2004**, *43*, 1764. (e) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1520. (f) Shibasaki, M.; Kanai, M.; Mita, T. *Org. React.* **2008**, *70*, 1. (g) Connon, S. J. *Angew. Chem., Int. Ed.* **2008**, *47*, 1176.

^{(2) (}a) Iyer, M. S.; Gigstad, K. M.; Namdev, N. D.; Lipton, M. J. Am. Chem. Soc. 1996, 118, 4910. (b) Corey, E. J.; Grogan, M. J. Org. Lett. 1999, 1, 157. (c) Sigman, M. S.; Vachal, P.; Jacobsen, E. N. Angew. Chem., Int. Ed. 2000, 39, 1279. (d) Vachal, P.; Jacobsen, E. N. Org. Lett. 2000, 2, 867. (e) Vachal, P.; Jacobsen, E. N. J. Am. Chem. Soc. 2002, 124, 10012. (f) Huang, J.; Corey, E. J. Org. Lett. 2004, 6, 5027. (g) Huang, X.; Huang, J.; Wen, Y.; Feng, X. Adv. Synth. Catal. 2006, 348, 2579. (h) Herrera, R. P.; Sgarzani, V.; Bernardi, L.; Fini, F.; Pettersen, D.; Ricci, A. J. Org. Chem. 2006, 71, 9869. (i) Huang, J.; Liu, X.; Wen, Y.; Qin, B.; Feng, X. J. Org. Chem. 2007, 72, 204. (j) Negru, M.; Schollmeyer, D.; Kunz, H. Angew. Chem., Int. Ed. 2007, 46, 9339. (k) Wen, Y.; Xiong, Y.; Chang, L.; Huang, J.; Liu, X.; Feng, X. J. Org. Chem. 2007, 72, 7115. (l) Wen, Y.; Gao, B.; Fu, Y.; Dong, S.; Liu, X.; Feng, X. Chem.—Eur. J. 2008, 14, 6789.

^{(3) (}a) Sigman, M. S.; Jacobsen, E. N. J. Am. Chem. Soc. 1998, 120, 4901. (b) Sigman, M. S.; Jacobsen, E. N. J. Am. Chem. Soc. 1998, 120, 5315. (c) Krueger, C. A.; Kuntz, K. W.; Dzierba, C. D.; Wirschun, W. G.; Gleason, J. D.; Snapper, M. L.; Hoveyda, A. H. J. Am. Chem. Soc. 1999, 121, 4284. (d) Porter, J. R.; Wirschun, W. G.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. J. Am. Chem. Soc. 1999, 121, 4284. (d) Porter, J. R.; Wirschun, W. G.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. J. Am. Chem. Soc. 2000, 122, 2657. (e) Masumoto, S.; Usuda, H.; Suzuki, M.; Kanai, M.; Shibasaki, M. J. Am. Chem. Soc. 2003, 125, 5634. (f) Kato, N.; Suzuki, M.; Kanai, M.; Shibasaki, M. Tetrahedron Lett. 2004, 45, 3147. (g) Banphavichit, V.; Mansawat, W.; Bhanthumnavin, W.; Vilaivan, T. Tetrahedron 2004, 60, 10559. (h) Blacker, J.; Clutterbuck, L. A.; Crampton, M. R.; Grosjean, C.; North, M. Tetrahedron: Asymmetry 2006, 17, 1449. (i) Nakamura, S.; Nakashima, H.; Sugimoto, H.; Shibata, N.; Toru, T. Tetrahedron Lett. 2006, 47, 7599. (j) Wang, J.; Hu, X.; Jiang, J.; Gou, S.; Huang, X.; Liu, X.; Feng, X. Angew. Chem., Int. Ed. 2007, 46, 8468. (k) Chen, Y.-J.; Chen, C. Tetrahedron: Asymmetry 2008, 19, 2201.

enantioselective catalyses. First, the bidentate electronwithdrawing sulfonate groups should effectively activate the metal center after metal complexation (eq 1). Second, high enantioselectivity may be induced even without any 3,3'modification of the 1,1'-binaphthyl skeleton, since the $-SO_3H$ substituents of BINSA are sterically more demanding than other 2,2'-substituents of 1,1'-binaphthyl such as -OHand $-CO_2H$. In this paper, we describe the catalytic enantioselective Strecker reaction of aldimines with the use of novel chiral lanthanum(III)-1,1'-binaphthyl 2,2'-disulfonate complexes, which is the first catalysis with **1**-metal complexes.



First, we examined the metal tuning for 1 (10-15 mol %) in the reaction of aldimine **2a** with TMSCN (1.5 equiv) at -20 °C for 20 h (Table 1).⁷ Monovalent, divalent, and

Table 1. 1-M(III)X₃-Catalyzed Strecker Reaction of 2a with TMSCN^{*a*}

| | Ph N Ph H (1.5 2a | 1 (0 MSCN (III)) 5 equiv) solven | ⊢15 mol %) X ₃ (10 mol %) t, –20 °C, 20 I | Ph HN P T Ph (S) CN 3a | 'n |
|--------|----------------------------|--|--|--------------------------------------|--------|
| entry | M(III)X ₃ | 1 (mol %) | solvent | yield (%) | ee (%) |
| 1 | $Sc(Oi-Pr)_3$ | 15 | toluene | 56 | 18 |
| 2 | $Y(Oi-Pr)_3$ | 15 | toluene | 28 | 0 |
| 3 | $La(Oi-Pr)_3$ | 15 | toluene | 34 | 54 |
| 4 | $Pr(Oi-Pr)_3$ | 15 | toluene | 24 | 46 |
| 5 | $Nd(Oi-Pr)_3$ | 15 | toluene | 29 | 49 |
| 6 | $Sm(Oi-Pr)_3$ | 15 | toluene | 35 | 34 |
| 7 | $Dy(Oi-Pr)_3$ | 15 | toluene | 6 | 20 |
| 8 | $Er(Oi-Pr)_3$ | 15 | toluene | 12 | 10 |
| 9 | $Yb(Oi-Pr)_3$ | 15 | toluene | 29 | 10 |
| 10 | $La(Oi-Pr)_3$ | 15 | EtCN | 27 | 55 |
| 11 | $La(OPh)_3$ | 15 | EtCN | 38 | 57 |
| 12 | La(OPh)3 | 10 | EtCN | 22 | 65 |
| 13^b | | 10 | EtCN | 26 | 13 |
| 14^c | $La(OPh)_3$ | 0 | EtCN | 16 | |
| 15^d | $La(OPh)_{3} \\$ | 0 | EtCN | 9 | 0 |

^{*a*} Prior to the reaction, each catalyst was prepared in situ from 1 and MX₃ in the solvent at 60 °C for 1 h. ^{*b*} In the absence of MX₃. ^{*c*} Reaction time was 20 h. ^{*d*} 10 mol % of (*R*)-BINOL was used in place of 1.

tetravalent MX_n precursors, such as AgOAc, CuOAc, Cu(OAc)₂, Cu(OMe)₂, Pd(OAc)₂, Ti(O-*i*-Pr)₄, Zr(O-*t*-Bu)₄, Hf(O-*t*-Bu)₄, etc., were not effective, and the corresponding product (**3a**) was obtained in low yields with low enantioselectivities (<20% ee). Interestingly, however, we found that trivalent precursors improved both the yields and the enantioselectivities. In particular, La(O-*i*-Pr)₃ and early lanthanide complexes showed moderate enantioselectivities (entries 3-5), while Sc(O-*i*-Pr)₃, Y(O-*i*-Pr)₃, and late lanthanide complexes showed lower enantioselectivities (entries 1, 2, 7-9).^{8,9} When more polar EtCN was used in place of toluene, the solubility of the heterogeneous catalysts was slightly improved to give the same enantioselectivity (entry 10). La(OPh)₃ was found to be most effective among the La(III) precursors (LaX) examined (entry 11).¹⁰ Moreover, the enantioselectivity was improved to 65% ee when the ratio of **1** to La(OPh)₃ was optimized as 1:1. As expected, the activities of **1** without La(OPh)₃ (entry 13) and of La(OPh)₃ without **1** (entry 14) were low. A poor result was also observed when La(OPh)₃ and (*R*)-BINOL were used (entry 15).

Further optimization was examined by adding protic compounds, since the actual cyanide source has been previously shown to be HCN rather than TMSCN.^{3c,d,h,4c,e,i} The addition of protic compounds such as H₂O and PhOH improved the yields of **3a** (Table 2, entries 2 and 3).

Table 2. Effect of Protic Additives^a

| 2a | + TMSCN — (1.5 equiv) | 1 (10 mol %), La(OPh) ₃ (10 mol %) additive (0–150 mol %) EtCN, −20 °C, 20 h | | | | (<i>S</i>)- 3a | |
|----------------|------------------------------------|---|-----------|-------|-------------------------------------|-------------------------|-----------|
| entry | additive (mol %) | yield (%) | ee (%) | entry | additive (mol %) | yield (%) | ee (%) |
| 1 | | 22 | 65 | 7 | <i>i</i> -PrCO ₂ H (70) | 88 | 74 |
| $\overline{2}$ | H ₂ O (50) | 46 | 65 | 8 | $i-\Pr CO_2 H (100)$ | 89 | 73 |
| 3 | PhOH (50) | 42 | 53 | 9 | <i>i</i> -PrCO ₂ H (150) | 69 | 23 |
| 4 | AcOH (50) | 98 | 84 | 10 | $HCO_{2}H(50)$ | 46 | 49 |
| 5 | <i>i</i> -PrCO ₂ H (30) | 58 | 64 | 11 | $CF_{3}CO_{2}H(50)$ | 34 | 38 |
| 6 | i-PrCO ₂ H (50) | 86 | 84 | 12 | t-BuCO ₂ H (50) | 62 | 73 |

^{*a*} Prior to the reaction, each catalyst was prepared in situ from **1** and La(OPh)₃ in EtCN at 60 °C for 1 h. Then, **2a**, the additive, and TMSCN were poured into the heterogeneous suspension at -20 °C.

Fortunately, we found that 50 mol % of AcOH or *i*-PrCO₂H significantly improved the catalytic activity, and **3a** was obtained with 84% ee in good yields (entries 4 and 6). The amount of *i*-PrCO₂H was also important, and less or more than 50 mol % of *i*-PrCO₂H decreased the catalytic activity (entries 5–9). Other carboxylic acids such as HCO₂H, CF₃CO₂H, and *t*-BuCO₂H gave less improvement than AcOH or *i*-PrCO₂H (entries 10–12).

^{(4) (}a) Ishitani, H.; Komiyama, S.; Kobayashi, S. Angew. Chem., Int. Ed. 1998, 37, 3186. (b) Byrne, J. J.; Chavarot, M.; Chavant, P.-Y.; Vallée, Y. Tetrahedron Lett. 2000, 41, 873. (c) Takamura, M.; Hamashima, Y.; Usuda, H.; Kanai, M.; Shibasaki, M. Angew. Chem., Int. Ed. 2000, 39, 1650. (d) Chavarot, M.; Byrne, J. J.; Chavant, P. Y.; Vallée, Y. Tetrahedron: Asymmetry 2001, 12, 1147. (e) Nogami, H.; Matsunaga, S.; Kanai, M.; Shibasaki, M. Tetrahedron Lett. 2001, 42, 279. (f) Rueping, M.; Sugiono, E.; Azap, C. Angew. Chem., Int. Ed. 2006, 45, 2617. (g) Ooi, T.; Uematsu, Y.; Maruoka, K. J. Am. Chem. Soc. 2006, 128, 2548. (h) Ooi, T.; Uematsu, Y.; Hujimoto, J.; Fukumoto, K.; Maruoka, K. Tetrahedron Lett. 2007, 48, 1337. (i) Hou, Z.; Wang, J.; Liu, X.; Feng, X. Chem.–Eur. J. 2008, 14, 4484.

⁽⁵⁾ Our preliminary reports of catalytic enantioselective trimethylsilylcyanation of aldehydes and ketones with BINOL derivatives: (a) Hatano, M.; Ikeno, T.; Miyamoto, T.; Ishihara, K. J. Am. Chem. Soc. **2005**, 127, 10776. (b) Hatano, M.; Ikeno, T.; Matsumura, T.; Torii, S.; Ishihara, K. Adv. Synth. Catal. **2008**, 350, 1776.

A direct comparison with HCN was also examined (eq 2). The reaction proceeded smoothly when 3 equiv of HCN was used, and **3a** was obtained in 86% yield with 56% ee. Although the enantioselectivity was not as high as under the conditions using TMSCN (Table 2, entry 1), these results strongly suggest that HCN is a key reagent in this reaction.

Next, we examined the scope of the aldimine substrates in the presence of 10 mol % each of 1 and La(OPh)₃, *i*-PrCO₂H or AcOH (50 mol %), and TMSCN (1.5 equiv) in EtCN at -20 °C (Table 3). For *N*-protection, a CHPh₂ group

Table 3. 1-La(OPh)₃-Catalyzed Strecker Reaction^a

| Ph N Ph H TMSCN R H (1.5 equiv) 2 | | 1 (10 mol %) La(OPh) ₃ (10 mol %) <i>i</i> ·PrCO ₂ H (50 mol %) EtCN, -20 °C | | Ph HN Ph R CN 3 |
|---|--|---|-------------------------------|--|
| entry | R | $\begin{array}{c} \text{reaction} \\ \text{time}^{b}\left(\mathbf{h}\right) \end{array}$ | yield ^b (%) | $ee^{b,c}$ (%) |
| $\frac{1}{2}$ | Ph 4-ClC∉H₄ | 20 [20] 20 [24] | 86 [98] 92 [78] | 84 (S) [84 (S)] 88 (S) [88 (S)] |
| 3 | $4-\text{MeOC}_6\text{H}_4$ $3.4-\text{OCH}_9\text{OC}_6\text{H}_9$ | 20 [16] | 97 [97] 95 [96] | 90 (S) [85 (S)] 86 [74] |
| 5 | 3-furyl | 20 [20] | 99 [96] 97 [92] | 86 [80] |
| 67 | 3-thienyl | 86 [96] 24 [20] | 97 [83] 97 [96] | 92 (<i>R</i>) [76 (<i>R</i>)] 83 [84] |
| 8 9 10 | 2-Naph PhCH=CH PhC≡C | 96 [20] 86 [72] 92 [96] | 64 [28] 97 [99] 68 [79] | $\begin{array}{l} 92 \ (S) \ [85 \ (S)] \\ 80 \ (S) \ [64 \ (S)] \\ 52 \ [66] \end{array}$ |
| 11 | <i>t</i> -Bu | 20 [48] | 99 [98] | 41(S)[33(S)] |

^{*a*} Prior to the reaction, the catalyst was prepared in situ from 1 and La(OPh)₃ in EtCN at 60 °C for 1 h. Then, 2, *i*-PrCO₂H, and TMSCN were poured into the heterogeneous suspension at -20 °C. ^{*b*} Data in brackets are the result when AcOH was used in place of *i*-PrCO₂H. ^{*c*} Absolute configurations are shown in parentheses.

gave the best result (Supporting Information).^{2a,b,j,3c,d,g} The reactions of aromatic and heteroaromatic aldimines bearing electron-withdrawing and electron-donating groups proceeded in high yields with moderate to high enantioselectivities (entries 1–8). In particular, 4-MeOC₆H₄-CH=NCHPh₂ and 2-thienylCH=NCHPh₂ gave each of the products with over 90% ee in high yields (entries 3 and 6). α,β -Unsaturated aldimines gave the corresponding products with moderate to good enantioselectivities (entries 9 and 10), although aliphatic aldimine gave poor enantioselectivity (entry 11).

Finally, we examined the mechanistic aspects. Based on the observation of a positive nonlinear effect between **1** and **3a** (Figure 1), the structure of enantiomerically pure La(III) catalysts in situ might involve a mixture of monomeric and





oligomeric complexes. However, ESI-MS analysis of the catalyst, which was prepared in situ from La(OPh)₃ (1 equiv) and **1** (1 equiv) in AcOH (5 equiv) and MeCN, suggested the dominant generation of monomeric La(III) complexes, $[Ar^*(SO_3)_2La(MeCN)_n]^+$ (Ar*(SO₃H)₂ = **1**, n = 1-4). The observed species may be derived from a parent complex $[Ar^*(SO_3)_2La(OAc)(MeCN)_n]^+$,¹¹ since the pK_a value of HCN is smaller than that of AcOH.¹² Although further investigation is necessary to obtain a clear understanding, postulated catalytic cycles are shown in Figure 2 as a working model. Acidic R'CO₂H (R' = Me or *i*-Pr) provides a counteranion for La(III) and generates HCN via proton-

(11) The possibility of the complexes, $[Ar^*(SO_3)_2La(CN)(MeCN)_n]^+$, cannot be denied.

⁽⁶⁾ Hatano, M.; Maki, T.; Moriyama, K.; Arinobe, M.; Ishihara, K. J. Am. Chem. Soc. 2008, 130, 16858.

⁽⁷⁾ Solubility of the corresponding complexes was low, and the reaction conditions were heterogeneous.

⁽⁸⁾ Shibasaki's pioneering work and a review with La(III) catalysts: (a) Sasai, H.; Suzuki, T.; Arai, S.; Arai, T.; Shibasaki, M J. Am. Chem. Soc. 1992, 114, 4418. (b) Shibasaki, M.; Yoshikawa, N. Chem. Rev. 2002, 102, 2187. Recent work: (c) Kato, N.; Mita, T.; Kanai, M.; Therrien, B.; Kawano, M.; Yamaguchi, K.; Danjo, H.; Sei, Y.; Sato, A.; Furusho, S.; Shibasaki, M. J. Am. Chem. Soc. 2006, 128, 6768. (d) Tosaki, S.; Hara, K.; Gnanadesikan, V.; Morimoto, H.; Harada, S.; Sugita, M.; Yamagiwa, N.; Matsunaga, S.; Shibasaki, M. J. Am. Chem. Soc. 2006, 128, 11776. (e) Morimoto, H.; Lu, G.; Aoyama, N.; Matsunaga, S.; Shibasaki, M. J. Am. Chem. Soc. 2007, 129, 9588. (f) Handa, S.; Nagawa, K.; Sohtome, Y.; Matsunaga, S.; Shibasaki, M. Angew. Chem., Int. Ed. 2008, 47, 3230. (g) Lu, G.; Morimoto, H.; Matsunaga, S.; Shibasaki, M. Angew. Chem., Int. Ed. 2008, 47, 6847. (h) Sone, T.; Yamaguchi, A.; Matsunaga, S.; Shibasaki, M. J. Am. Chem. Soc. 2008, 130, 10078.

⁽⁹⁾ Reviews of asymmetric catalyses with chiral lanthanide complexes: (a) Kobayashi, S. *Synlett* **1994**, 689. (b) Aspinall, H. C. *Chem. Rev.* **2002**, *102*, 1807. (c) Molander, G. A.; Romero, A. C. *Chem. Rev.* **2002**, *102*, 2161. (d) Shibasaki, M.; Yokikawa, N. *Chem. Rev.* **2002**, *102*, 2187. (e) Inanaga, J.; Furuno, H.; Hayano, T. *Chem. Rev.* **2002**, *102*, 2211. (f) Kobayashi, S.; Sugiura, M.; Kitagawa, H.; Lam, H. W.-L. *Chem. Rev.* **2002**, *102*, 2227. (g) Mikami, K.; Terada, M.; Matsuzawa, H. *Angew. Chem., Int. Ed.* **2002**, *41*, 3554.

⁽¹⁰⁾ La₂(CO₃)₃, La(OTs)₃, and La(NO₃)₃·6H₂O showed low catalytic activity with poor enantioselectivity. Moreover, other La(OAr)₃ complexes (Ar = Ph, 3,5-xylyl, mesityl, 2,6-Ph₂C₆H₃) did not affect the enantioselectivity of **3**.

⁽¹²⁾ pK_a of HCN is 12.9 in DMSO and 9.1 in H₂O. The pK_a of AcOH is 12.3 in DMSO and 4.75 in H₂O: Taft, R. W.; Bordwell, F. G. Acc. Chem. Res. **1988**, 21, 456.

⁽¹³⁾ For the full generation of HCN (1.5 equiv) in situ, a ratio of $R'CO_2H$ (0.5 equiv) and TMSCN (1.5 equiv) is disputable. PhOH (0.3 equiv) released via ligand exchange and adventitious water also may be involved as protone sources. Moreover, it is notable that the equiliblium among a product, TMSCN, PhOTMS, HCN, and PhOH has been proposed by Shibasaki et al. in ref 4c.





exchange reactions.¹³ First, a possible active EtCN-solvate catalyst [Ar*(SO₃)₂La(OCOR')(EtCN)_n] (**4**) would be generated in situ from the mixture of **1**, La(OPh)₃, R'CO₂H, and TMSCN, and then aldimine **2** would be continuously activated at the La(III) center. HCN is then added to **2**,¹⁴ and the catalyst would be regenerated and the product (**3**) is released. In the transition states, the *re*-face attack, which leads to (*S*)-products, should be favored without conspicuous steric repulsion between the substrate and the ligand (Figure 3).

In summary, we have developed a catalytic enantioselective Strecker reaction catalyzed by chiral lanthanum(III)-

(14) Simón, L.; Goodman, J. M. J. Am. Chem. Soc. 2009, 131, 4070.



Figure 3. Possible transition states.

binaphthyldisulfonate complexes. The key to promoting the reactions was a semistoichiometric amount of AcOH or *i*-PrCO₂H, which takes advantage of HCN generation in situ. Further applications of 1-metal salts to other catalytic enantioselective reactions are now underway.

Acknowledgment. Financial support for this project was provided by JSPS, KAKENHI (20245022), Grant-in-Aid for Young Scientists B of MEXT (19750072 and 21750094), the G-COE Program of MEXT, Toray Science Foundation, and Shorai Foundation for Science and Technology.

Supporting Information Available: Experimental procedures and spectral data, as well as copies of NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

OL900680F