

## Novel Cerium(III)–(*R*)-BNP Complex as a Storable Chiral Lewis Acid Catalyst for the Enantioselective Hetero-Diels–Alder Reaction

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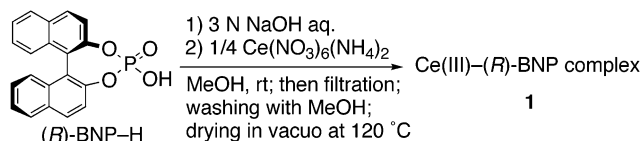
(Received April 14, 2003; CL-030316)

A novel Ce(III)–(*R*)-BNP complex was conveniently prepared from CAN and (*R*)-BNP–Na, then successfully used as a homogeneous catalyst for the asymmetric hetero-Diels–Alder reaction affording, after acidic work-up, 6-substituted 5,6-dihydro-4*H*-pyran-4-one derivatives with high enantioselectivities (up to 94% ee). A mechanistically interesting positive nonlinear effect was also observed.

While utilization of chiral rare earth metal complexes as Lewis acid catalysts for various asymmetric reactions has currently received much attention,<sup>1</sup> the central metal ions of such complexes are rather limited to scandium, yttrium, or the heavier lanthanides like ytterbium because of their stronger Lewis acidities compared with the lighter lanthanides. Also, there have been no reports that structurally defined chiral cerium complexes functioned as an effective Lewis acid catalyst though cerium is one of the most economical rare earth elements.<sup>2</sup> Recently, we demonstrated that some of the Ln[(*R*)-BNP]<sub>3</sub> complexes (Ln = La–Lu, Y, and Sc; BNP = 1,1'-binaphthyl-2,2'-diyl phosphate) prepared from LnCl<sub>3</sub> and (*R*)-BNP–Na effectively catalyzed the asymmetric hetero-Diels–Alder reaction of aldehydes **2** with the Danishefsky's diene **3** at room temperature.<sup>3,4</sup> In the above reaction, the Yb[(*R*)-BNP]<sub>3</sub> complex was found to be the most effective, having a 70% ee (77% yield) for the reaction of benzaldehyde (**2a**). When 2,6-lutidine was used as an additive, the reaction proceeded under homogeneous conditions, improving both the optical and chemical yields,<sup>3b</sup> and a remarkably high asymmetric amplification was also observed in the reaction.<sup>3c</sup> On the other hand, the corresponding Ce[(*R*)-BNP]<sub>3</sub> complex turned out to be the least effective for the same transformation (5% ee, 40% yield). The low catalytic activity of the Ce(III) complex prompted us to examine the corresponding Ce(IV) complex because it can be a stronger Lewis acid by having a capacity of four chiral ligands. Therefore, we tried to prepare a chiral Ce(IV) complex from ammonium cerium(IV) nitrate (CAN) and (*R*)-BNP–Na. Unfortunately, the Ce(IV) complex could not be produced but the corresponding Ce(III) complex **1** was generated (Scheme 1).<sup>5</sup> We further found that **1** works as an effective homogeneous catalyst for the hetero-Diels–Alder reaction.

The Ce/P ratio of **1** was analyzed to be ca. 1:3.2 using an inductively coupled plasma (ICP) mass spectrometer, which suggests the formation of Ce(III) species. The electron spectroscopy for chemical analysis (ESCA) study of **1** also supported the trivalent cerium structure, and it was finally confirmed based on its magnetic susceptibility measurement.<sup>5</sup>

Using various aldehydes **2**, the complex **1**-catalyzed asymmetric hetero-Diels–Alder reaction was carried out at room



Scheme 1. Preparation of the Ce–(*R*)-BNP complex **1**.

temperature.<sup>6</sup> The results are summarized in Table 1. All reactions proceeded under homogeneous conditions and, in the case of the aromatic aldehydes (**2a–i**), generally high enantioselectivities (80–94% ee) were obtained. The high performance of the catalyst **1** clearly indicates that the structure of **1** is different from that of the Ce[(*R*)-BNP]<sub>3</sub> complex previously prepared from CeCl<sub>3</sub>. It should be noted that the catalyst **1** is very stable with respect to maintaining its original activity even after two years (Entry 8). The relatively low ee observed in the reaction of an aliphatic aldehyde (**2j**) suggests the importance of some  $\pi$ – $\pi$  interaction between the aromatic ring of the aldehydes and that of the catalyst in the transition state.

Figure 1 shows the linear and the positive nonlinear effects observed during the reaction of 4-ethylbenzaldehyde (**2c**) with **3**.<sup>1a,8</sup> For example, when the optically impure catalyst prepared by mixing the Ce–(*R*)-BNP and the Ce–(*S*)-BNP complexes in

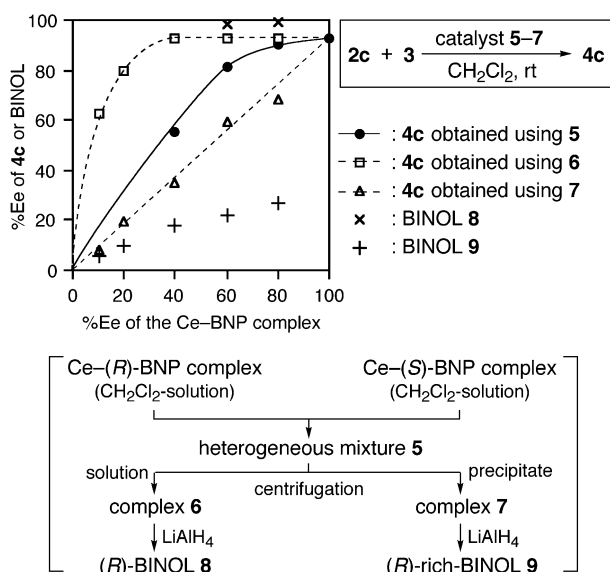
Table 1. The Ce(III)–(*R*)-BNP-catalyzed asymmetric hetero-Diels–Alder reaction of **2** with **3**

Entry	R	2/4	Yield/% <sup>a</sup>	Ee/% <sup>b,c</sup>
1	Ph	<b>2a/4a</b>	91	80
2	4-MePh	<b>2b/4b</b>	96	88
3	4-EtPh	<b>2c/4c</b>	95	93
4	4- <i>i</i> -BuPh	<b>2d/4d</b>	61	93
5	4- <i>t</i> -BuPh	<b>2e/4e</b>	75	94
6	4-Biphenyl	<b>2f/4f</b>	46	93
7	4-FPh	<b>2g/4g</b>	91	85
8 <sup>d</sup>	4-ClPh	<b>2h/4h</b>	93	88
9	4-BrPh	<b>2i/4i</b>	80	92
10	<i>n</i> -Pr	<b>2j/4j</b>	36	61

<sup>a</sup>Isolated yield. <sup>b</sup>Determined by the HPLC analysis using chiral column (Daicel CHIRALCEL OD for **4a–e,g–i** or CHIRALPAK AD for **4f,j**). <sup>c</sup>The absolute configuration of **4a** was determined to be *R* by comparison with the sign of the optical rotation in the literature,<sup>7</sup> and these of **4b–i** and **4j** were tentatively assigned to be *R* and *S*, respectively, based on the retention times on the HPLC analyses and the optical rotations. <sup>d</sup>The catalyst **1** stored for two years was used.

9:1 (80% ee) and 4:1 (60% ee) ratios was used, ee's of 90% and 81% for **4c** were produced, respectively. These reactions proceeded under heterogeneous conditions because the mixing of the (*R*)- and (*S*)-catalysts produced precipitates, the amounts of which were dependent on their mixing ratios. Therefore, the precipitate of the heterogeneous mixture **5** was separated by centrifugation, and both the soluble complex **6**<sup>9</sup> and the insoluble complex **7**<sup>9</sup> were independently used for the reaction. As anticipated from our previous finding on the Yb(BNP)<sub>3</sub>-catalyzed reaction,<sup>3c</sup> the soluble complex **6** showed a high asymmetric amplification. Unexpectedly, however, the insoluble complex **7** exhibited considerable activity and brought about an almost linear relationship. More interestingly, the (*R*)-rich-BINOLs **9** obtained from **7** by the LiAlH<sub>4</sub> reduction showed uniformly lower ee values than those of the products obtained using catalyst **7**, whereas the reduction of complex **6** afforded the almost enantiopure (*R*)-BINOL **8**. These behaviors are much different from those previously observed ones with the optically impure Yb[(*R*)-BNP]<sub>3</sub>-2,6-lutidine system.<sup>3c</sup> We do not have a clear explanation for these phenomena at the moment but rapid exchange of the chiral ligands of **7** must occur in order to realize such a new-type asymmetric amplification. The existence of a small amount of nitrate ion derived from CAN seems to play an important role in such a ligand exchange reaction and also in increasing the solubility of the catalyst. Actually, when the previously prepared Ce[(*R*)-BNP]<sub>3</sub> was used in the presence of nitrate ions for the reaction of **2a** with **3**, the reaction mixture became clear and the enantioselectivity increased from 5% ee to 73% ee (with NH<sub>4</sub>NO<sub>3</sub>) and 68% ee (with NaNO<sub>3</sub>).

In conclusion, we succeeded for the first time, in developing a chiral storable cerium(III) complex **1** that can work as an efficient Lewis acid catalyst and found a new type of asymmetric amplification for the **1**-catalyzed hetero-Diels-Alder reaction. Further investigations on the precise structure of the complex and mechanism of the asymmetric amplification are now in progress.



**Figure 1.** The relation between optical purities of the catalyst and ee's of the reaction product.

This work was supported by a Grant-in-Aid for Scientific Research on Priority Areas from the Ministry of Education, Culture, Sports, Science and Technology, Japan, the Japan Society for the Promotion of Science, and also by the Kyushu University P&P Programs 'Green Chemistry' (to J.I.). We are grateful to Professor H. Kanno of National Defense Academy in Japan, and Mr. S. Watanabe of Shimadzu Corporation, Japan for the measurement of Raman spectrum and the ESCA of **1**, respectively. Special thanks are due to Tosoh Analysis and Research Center, Japan for providing us with the ICP data.

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- Data of **1**: [ $\alpha$ ]<sub>D</sub><sup>16</sup> -490.8 (c 1.00, CHCl<sub>3</sub>). Anal. calcd for C<sub>60</sub>H<sub>36</sub>CeO<sub>12</sub>P<sub>3</sub>·3H<sub>2</sub>O·0.5NaNO<sub>3</sub>: C, 56.37; H, 3.31; N, 0.55. Found: C, 56.24; H, 3.50; N, 0.39. ICP spectrometry analysis: Ce, 10; P, 7.0 (calculated data for the composition ratio, Ce/P 1:3.2). Effective magnetic moment (rt):  $\mu_{\text{eff}}$ , 2.35  $\mu_{\text{B}}$ .
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