

Catalytic Asymmetric Epoxidation of Enones Using La–BINOL–Triphenylarsine Oxide Complex: Structural Determination of the Asymmetric Catalyst

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Abstract: The catalytic asymmetric epoxidation of enones using the La–BINOL–Ph₃As=O complex generated from La(O-*i*-Pr)₃, BINOL, and Ph₃As=O in a ratio of 1:1:1 is described herein. Using 1–5 mol % of the asymmetric catalyst, a variety of enones, including a dienone and a *cis*-enone, were found to be epoxidized in a reasonable reaction time, providing the corresponding epoxy ketones in up to 99% yield and with more than 99% ee. The possible structure of the actual asymmetric catalyst has been clarified by various methods, including X-ray crystal structure analysis. This is the first X-ray analysis of an alkali-metal free lanthanoid–BINOL complex. Although La(binaphthoxide)₂(Ph₃As=O)₂ (**7**) was observed as the major complex in the complexes' solution, generated from La(O-*i*-Pr)₃, BINOL, and Ph₃As=O in a ratio of 1:1:1, the possible active species turned out to be the La–BINOL–Ph₃As=O complex in a ratio of 1:1:1. A probable reaction mechanism of the catalytic asymmetric epoxidation of enones is also proposed, suggesting that preferential formation of a heterochiral complex is the reason for asymmetric amplification. Moreover, the interesting role of La(O-*i*-Pr)₃ for accelerating the epoxidations while maintaining high ee's is discussed.

Introduction

Asymmetric epoxidation of olefins is one of the most important functional group manipulations in organic synthesis¹ due to the fact that enantiomerically enriched epoxides can be converted into various useful optically active synthetic intermediates. In 1980, Sharpless et al. reported the stoichiometric asymmetric epoxidation of allylic alcohols,^{2a} a method which was later improved to a catalytic version by the addition of molecular sieves.^{2b} Catalytic asymmetric epoxidations of unfunctionalized olefins using salen–manganese complexes have been reported independently by Jacobsen et al.,^{3a} Katsuki et al.,^{3b} and Mukaiyama et al.^{3c} Moreover, asymmetric epoxidations of a wide range of olefins using optically active dioxiranes⁴ and hydroperoxide⁵ have been developed recently. Since the initial report by Juliá and co-workers,⁶ catalytic asymmetric epoxidation of α,β -unsaturated ketones has been studied using several

other methodologies such as asymmetric ligand–metal catalysis,⁷ asymmetric phase transfer catalysis,⁸ and polyamino acid catalysis.^{6,9} A few years ago, we reported a general catalytic asymmetric epoxidation of enones using alkali-metal free lanthanoid–BINOL complexes.¹⁰ These complexes were prepared from Ln(O-*i*-Pr)₃ and BINOL in a ratio of 1:1, providing the corresponding products in up to 95% yield and up to 94% ee. We speculated that this asymmetric induction might be induced by the multifunctionality of the asymmetric catalysts, where activation of both substrates (enone and peroxide) as well as control of their position is realized at the same time.

Despite excellent yields and enantiomeric excesses (ee's), this catalytic process is still unsatisfactory in terms of its rather low reactivity. Thus, we decided to overcome the drawback of our catalytic asymmetric epoxidation by tuning the reaction conditions. It is known that addition of triphenylphosphine oxide (Ph₃P=O) is effective for the enhancing the rate while maintain-

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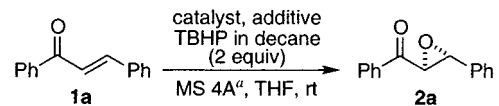
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Table 1. Catalytic Asymmetric Epoxidation of Chalcone **1a** to Epoxy Ketone **2a** Using the La–BINOL Complex


entry	catalyst (mol %)	additives (mol %)	time (min)	yield (%)	ee (%)
1	La(O- <i>i</i> -Pr) ₃ (10)		480	90	
2	La-(<i>R</i>)-BINOL (1:1) (10)		90	92	71
3	La-(<i>R</i>)-BINOL (1:1) (10)	Ph ₃ P=O (40)	30	98	97
4	La-(<i>R</i>)-BINOL (1:1) (10)	Ph ₃ P=O (30)	30	97	97
5	La-(<i>R</i>)-BINOL (1:1) (10)	Ph ₃ P=O (20)	30	94	95
6	La-(<i>R</i>)-BINOL (1:1) (10)	Ph ₃ P=O (10)	30	93	94
7	La-(<i>R</i>)-BINOL (1:1) (10)	Ph ₃ As=O (40)	60	92	85
8	La-(<i>R</i>)-BINOL (1:1) (10)	Ph ₃ As=O (30)	30	92	93
9	La-(<i>R</i>)-BINOL (1:1) (10)	Ph ₃ As=O (20)	30	96	95
10	La-(<i>R</i>)-BINOL (1:1) (10)	Ph ₃ As=O (10)	3	95	97
11	La(O- <i>i</i> -Pr) ₃ (10)	Ph ₃ As=O (10)	480	64	

^a MS 4A was not dried (1000 mg/mmol).

ing high ee's.^{10d} However, addition of 3–6 equiv of Ph₃P=O to the La–BINOL complex is needed to enhance the reaction rate, and we became interested in finding new additives which might be more effective in terms of atom economy. Moreover, we hoped to determine the structure of an alkali-metal free lanthanoid–BINOL complex unequivocally by X-ray of the complex with the new additive. The structure of the alkali-metal free lanthanoid–BINOL complex had not been clarified, mainly due to the specific feature of lanthanoid metals.¹¹ In this article, we report a catalytic asymmetric epoxidation of enones using a novel multifunctional asymmetric catalyst, the La–BINOL–triphenylarsine oxide (Ph₃As=O) complex. This catalyst system exhibits much higher activity and selectivity compared to those of Ln–BINOL complexes, affording optically active epoxy ketones with broad generality in up to 99% yield and more than 99% ee. Furthermore, we report the first example of X-ray analysis of an alkali-metal free lanthanoid–BINOL–Ph₃As=O complex as well as a possible reaction mechanism of the catalytic asymmetric epoxidation of enones.

Results and Discussion

Catalytic Asymmetric Epoxidation of Enones Using the La–BINOL–Ph₃As=O Complex. Optimization of Reaction Conditions and Scope and Limitations of the Reaction. In an attempt to improve the catalytic asymmetric epoxidation of enones developed in our group^{10a,b} and improved in Inanaga's group,^{10d} we examined the reaction in detail using chalcone (**1a**) as a representative starting material. The results are summarized in Table 1. As previously reported, the catalyst (10 mol %) prepared from La(O-*i*-Pr)₃ and (*R*)-BINOL in a ratio of 1:1 gave the epoxide **2a** in 92% yield and 71% ee (Table 1, entry 2). On the other hand, the conditions developed by Inanaga using 40 mol % of Ph₃P=O gave rise to **2a** in 98% yield and 97% ee in a much shorter reaction time (30 min). However, as shown in entry 6 (Table 1), when the reaction was carried out in the presence of 10 mol % of Ph₃P=O, a slightly less satisfactory result was obtained. We examined the influence of many

additives instead of Ph₃P=O on the catalytic asymmetric epoxidation, which would result in the formation of **2a** more efficiently, even in the presence of 10 mol % of an additive. As a result, we were pleased to find that the addition of Ph₃As=O (10 mol %) produced **2a** in 95% yield and 97% ee in only 3 min. Interestingly, different from the case of Ph₃P=O, the addition of 40 mol % of Ph₃As=O provided a less satisfactory result, giving **2a** in 92% yield and 85% ee (60 min). This difference could be explained by the fact that the Lewis basicity of Ph₃As=O is higher than that of Ph₃P=O.^{12,13} From these results, we concluded that the complex generated from La(O-*i*-Pr)₃, (*R*)-BINOL, and Ph₃As=O in a ratio of 1:1:1 was the most effective asymmetric catalyst for the epoxidation of chalcone (**1a**).

Having developed the novel asymmetric catalyst for the asymmetric epoxidation of chalcone (**1a**), next we sought to explore the generality of this catalytic asymmetric reaction. Table 2 summarizes the use of the asymmetric catalyst generated from La(O-*i*-Pr)₃, (*R*)-BINOL, and Ph₃As=O in a ratio of 1:1:1 for the epoxidation of various substrates. As shown, almost all reactions proceeded to completion in reasonable reaction times when 5 mol % of the new catalyst was used at room temperature. Additionally, a slight improvement was achieved in almost all cases with the exception of enones **1e** and **1i** in terms of yield and ee. Aryl ketone type substrates such as **1a–c** were epoxidized smoothly and afforded the corresponding epoxy ketones in excellent yields and enantiomeric excesses (Table 2, entries 1–4). Particularly, epoxidation of **1a** proceeded quite efficiently, and the reaction was completed in 3 h, even with use of 1 mol % of the catalyst (Table 2, entry 2). This asymmetric catalyst system was also quite effective for alkyl ketone type substrates. In addition to the *tert*-butyl ketone derivative **1d** (Table 2, entry 5), excellent results were obtained also in the case of the enolizable enones **1e–i**¹⁴ (Table 2, entries 6–10), which are generally difficult to epoxidize.¹⁵ In particular, the epoxidation of **1f** proceeded with a big increase in terms of enantioselectivity (>99% ee, >200:1 enantioselectivity) relative to the previous result (94% ee, 32:1 enantioselectivity). Furthermore, we examined the epoxidation of other unique enones. We had already reported the catalytic asymmetric epoxidation of *cis*-enones using the Yb–3-hydroxymethyl–BINOL complex.^{10c} It was found that the La–BINOL–Ph₃As=O complex also catalyzed the transformation of *cis*-enone **3** into *cis*-epoxy ketone **4**, but unfortunately the result was less satisfactory, and **4** was obtained in only 61% yield and 59% ee, together with less than 10% of the corresponding *trans*-epoxy ketone (Scheme 1a). We also tried the epoxidation of dienone **5**. The reaction was completed in 3 h with the use of 5 mol % of the catalyst and gave the product **6** in 95% yield and 96% ee with complete regioselectivity (Scheme 1b).¹⁶ In this way, the new asymmetric catalyst system consisting of La(O-*i*-Pr)₃, BINOL, and Ph₃As=O in a ratio of 1:1:1 was found to have a broad generality for enones, affording the products in excellent yields and more than

(12) Cruickshank, D. W. J. *J. Chem. Soc.* **1961**, 5486.

(13) When **1i** was used as a substrate, the different tendencies between the two additives were more noticeable. For the detailed data, see the Supporting Information.

(14) Epoxy ketone **2i** can be converted into several natural coumarins efficiently. See: Nemoto, T.; Ohshima, T.; Shibasaki, M. *Tetrahedron Lett.* **2000**, *41*, 9569.

(15) A few successful examples using the polyleucine catalyst have been reported. See: Adger, B. M.; Barkley, J. V.; Bergeron, S.; Cappi, M. W.; Flowerdew, B. E.; Jackson, M. P.; McCague, R.; Nugent, T. C.; Roberts, S. M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3501.

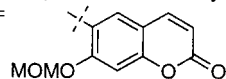
(16) The Yb–BINOL complex also catalyzes this reaction (5 mol % of the catalyst, 2 h, 87% yield, 93% ee). Watanabe, S. Ph.D. Thesis, The University of Tokyo, 1999.

(11) Although several catalytic asymmetric reactions using alkali-metal free lanthanoid–BINOL derivative complexes have been developed, the catalyst structures have not been unequivocally clarified yet. However, partial information has been obtained in some cases, see: (a) Kim, Y.-S.; Matsunaga, S.; Das, J.; Sekine, A.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 6506. (b) Furuno, H.; Hanamoto, T.; Sugimoto, Y.; Inanaga, J. *Org. Lett.* **2000**, *2*, 49. (c) Kobayashi, S.; Ishitani, H.; Araki, M.; Hachiya, I. *Tetrahedron Lett.* **1994**, *35*, 6325. (d) Kobayashi, S.; Araki, M.; Hachiya, I. *J. Org. Chem.* **1994**, *59*, 3758.

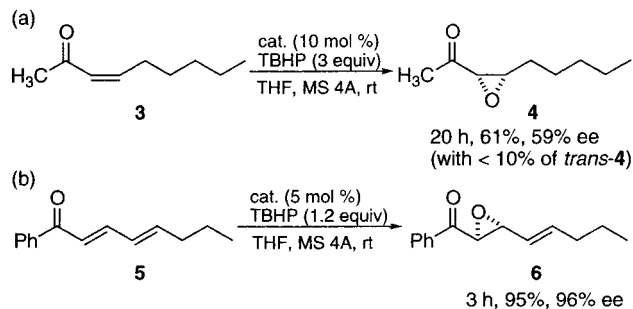
Table 2. Catalytic Asymmetric Epoxidation of Various Enones **1a–i**

			$\text{R}_1-\text{C}(=\text{O})-\text{CH}=\text{CH}-\text{R}_2 \xrightarrow[\text{MS 4A}^d, \text{THF, rt}]{\text{(R)-Ln catalyst (5 mol \%)} \\ \text{TBHP in decane (1.2 equiv)}} \text{R}_1-\text{C}(=\text{O})-\text{CH}(\text{O})-\text{CH}(\text{R}_2)$											
entry	enones	products	La-(R)-BINOL-Ph ₃ As=O complex			Ln-(R)-BINOL complex ^b			Yb-(R)-BINOL (2:3) complex ^c			La-(R)-BINOL-Ph ₃ P=O complex ^d		
			time (h)	yield (%)	ee (%)	time (h)	yield (%)	ee (%)	time (h)	yield (%)	ee (%)	time (h)	yield (%)	ee (%)
1		1a 2a	0.25	99	96	7	93	91	1	99	81	0.5	99	96
2 ^e		1a 2a	3	97	89	44	95	89	—	—	—	—	—	—
3 ^f		1b 2b	4	91	95	20	85	85	—	—	—	—	—	—
4		1c 2c	1.5	95	94	7	95	94	—	—	—	1	89	93
5		1d 2d	7	94	98	—	—	—	—	—	—	—	—	—
6		1e 2e	8	72 (91) ^g	95	159 ^h	55 ^h	88 ^h	48	82	93	12	67	96
7		1f 2f	6	92	>99	96	83	94	13	92	94	6	92	93
8		1g 2g	1.5	98	92	118 ^h	91 ^h	88 ^h	—	—	—	1	92	87
9		1h 2h	1.5	89	95	67 ^h	71 ^h	91 ^h	—	—	—	—	—	—
10 ^{i, k}		1i 2i	2 (5) ^j	94 (90) ^j	96 (93) ^j	15	88	83	48	65	85	2.5 (4) ^j	98 (91) ^j	97 (95) ^j

^a MS 4A was not dried (1000 mg/mmol). ^b Reference 10a. ^c Reference 10b. ^d Reference 10d. ^e 1 mol % of the catalyst was used. ^f Ar = *o*-MOMO-C₆H₄. ^g Conversion yield. ^h 8 mol % of the catalyst was used. ⁱ 25 mol % of the catalyst was used. ^j 10 mol % of the catalyst was used. ^k Ar =



Scheme 1. Catalytic Asymmetric Epoxidation of *cis*-Enone **3** (a) and Dienone **5** (b) Using the La-(R)-BINOL-Ph₃As=O Complex



99% ee, even at room temperature.¹⁷ It is obvious that reactions which proceed at room temperature have significant practical advantages compared to those that require low temperature for the induction of higher selectivity. Additionally, the simple chiral ligand, unmodified BINOL, makes this process more accessible.

Structural Determination of the La-BINOL-Ph₃As=O Complex. In contrast to some successful examples of structural

(17) Epoxidations of **1a** and **1f** using 5 mol % of the Yb-(R)-BINOL-Ph₃As=O complex gave less satisfactory results, producing the corresponding epoxy ketones **2a** (1 h, 97%, 94% ee) and **2f** (10 h, 85%, 94% ee), respectively.

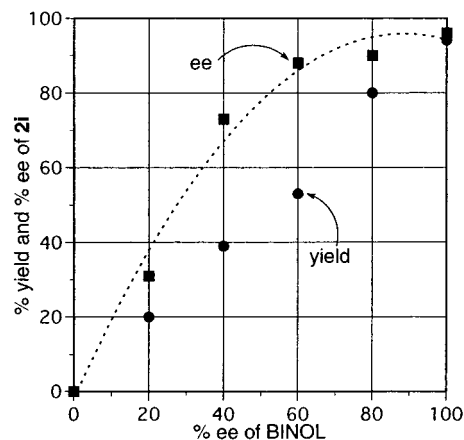


Figure 1. Nonlinear relationship between the enantiomeric purities of the product **2i** and BINOL.

determination of lanthanoid asymmetric catalysts,¹⁸ little is known about the structure of alkali-metal free Ln-BINOL complexes.¹¹ First we made attempts to clarify their structures using NMR analysis. However, the ¹³C NMR spectrum of the La-BINOL complex in THF was quite obscure. Additionally, asymmetric amplification was observed in the epoxidation. Thus,

(18) Sasai, H.; Suzuki, T.; Itoh, N.; Tanaka, K.; Date, T.; Okamura, K.; Shibasaki, M. *J. Am. Chem. Soc.* **1993**, *115*, 10372.

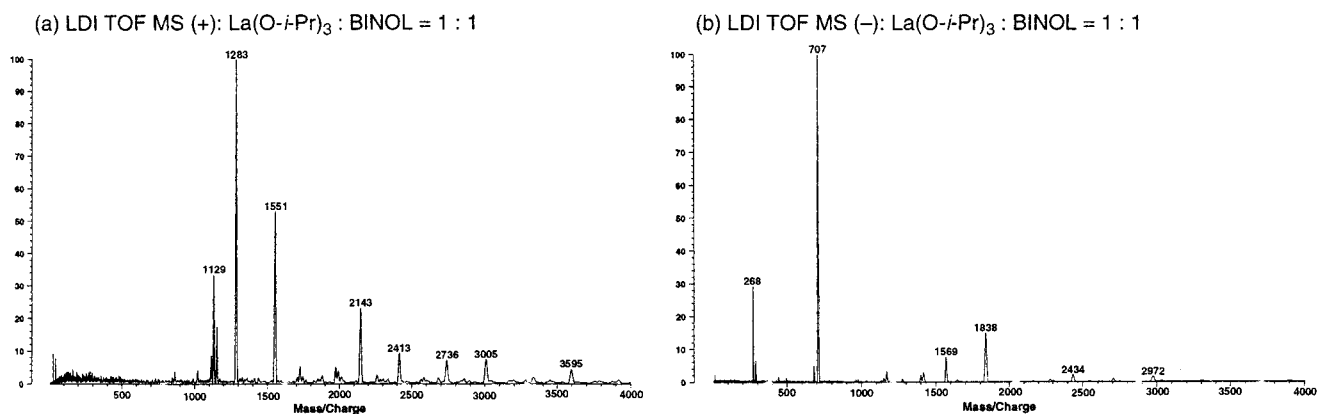


Figure 2. LDI TOF MS spectra of a complexes' solution generated from $\text{La}(\text{O-}i\text{-Pr})_3$ and BINOL in a ratio of 1:1: (a) positive mode and (b) negative mode.

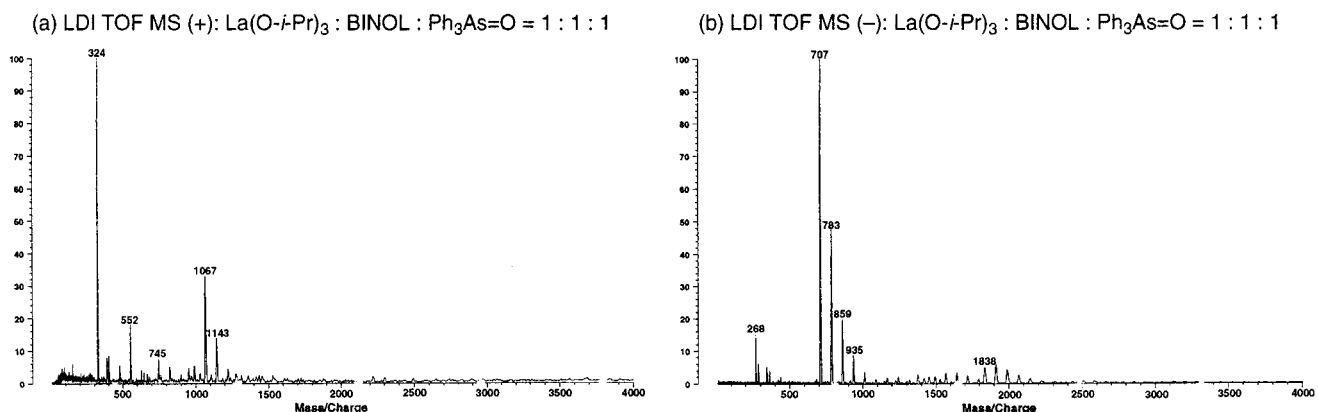


Figure 3. LDI TOF MS spectra of a complexes' solution generated from $\text{La}(\text{O-}i\text{-Pr})_3$, BINOL, and $\text{Ph}_3\text{As}=\text{O}$ in a ratio of 1:1:1: (a) positive mode and (b) negative mode.

we concluded that the optically active lanthanoid complex should exist as an oligomer.

It is well known that oxygen ligands such as $\text{Ph}_3\text{As}=\text{O}$ and $\text{Ph}_3\text{P}=\text{O}$ have a high affinity to lanthanoid metals.¹⁹ Thus, we expected that the newly developed asymmetric catalyst, the La -BINOL- $\text{Ph}_3\text{As}=\text{O}$ complex, would have a different structure, leading to the structural determination of the complex. Our investigation started with a comparison with the information that had been already obtained from the La -BINOL complex. First we measured the ^{13}C NMR spectrum of the La -BINOL- $\text{Ph}_3\text{As}=\text{O}$ (1:1:1) complex in THF. The obtained spectrum, however, was similar to that of the La -BINOL complex. Next, we examined if asymmetric amplification might be observed in the epoxidation using the La -BINOL- $\text{Ph}_3\text{As}=\text{O}$ complex. We investigated the reaction using enone **1i**,²⁰ and a positive nonlinear effect was observed, as shown in Figure 1. Moreover, it was of interest that a decrease in the reactivity was observed when BINOL with low enantiomeric excess was used. In particular, when (*rac*)-BINOL was used, no product could be obtained.²¹ Unfortunately, at this stage, these results appeared to suggest that the chiral lanthanoid complex would have an oligomeric structure even in the presence of $\text{Ph}_3\text{As}=\text{O}$. Laser

(19) Cotton, F. A.; Wilkinson, G.; Murillo, C. A.; Bochmann, M. *Advanced Inorganic Chemistry*, 6th ed.; John Wiley & Sons: New York, 1999; p 1108.

(20) The reactions were carried out using 25 mol % of the catalyst at room temperature and quenched after 6 h, except for the reaction using optically pure (*R*)-BINOL (2 h). For detailed data, see the Supporting Information.

(21) The results which were obtained for the reactions quenched after 6 h indicate that quenching the reactions after 2 h should lead to a negative nonlinear relationship.

desorption/ionization time-of-flight mass spectrometry (LDI TOF MS) is often utilized for a structural analysis of organo-metallic complexes, and previously we succeeded in obtaining analyzable spectra of several lanthanoid complexes such as $\text{LnM}_3\text{tris}(\text{binaphthoxide})$ complex.^{18,22} It has also been found that analyzable spectra can be obtained even in the case of alkali-metal free Ln -BINOL complexes ($\text{Ln} = \text{La}$ or Yb).²³ The spectra of the complexes' solution generated from $\text{La}(\text{O-}i\text{-Pr})_3$ and BINOL in a ratio of 1:1 are shown in Figure 2, and some peaks a molecular weight of the order of thousands are observed in both the positive and negative modes. Likewise, spectra of the complexes' solution generated from $\text{La}(\text{O-}i\text{-Pr})_3$, BINOL, and $\text{Ph}_3\text{As}=\text{O}$ in a ratio of 1:1:1 are shown in Figure 3. In contrast to our expectation mentioned above, we could find only some small peaks which represent oligomers, and only one analyzable peak each was detected in the positive and negative modes.²⁴ The peak observed in the positive mode (MW 1067) corresponds to the molecular weight of the cationic complex described in Figure 4a, and the peak observed in negative mode (MW 707) corresponds to the molecular weight of the anionic complex described in Figure 4b. These data suggested that the monomeric $\text{La}(\text{binaphthoxide})_2(\text{Ph}_3\text{As}=\text{O})_2$ complex (**7**) (Figure 4c) would be the major component in the solution generated from $\text{La}(\text{O-}i\text{-Pr})_3$, BINOL, and $\text{Ph}_3\text{As}=\text{O}$ in a ratio of 1:1:1, and these results appeared to support our expectation that the

(22) Yoshikawa, N.; Yamada, M. A. Y.; Das, J.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1999**, *121*, 4168.

(23) Watanabe, S. Ph.D. Thesis, The University of Tokyo, 1999.

(24) In the presence of $\text{Ph}_3\text{As}=\text{O}$, unknown peaks were observed every 76 units of molecular weight from the base peaks (1067 and 707), respectively.

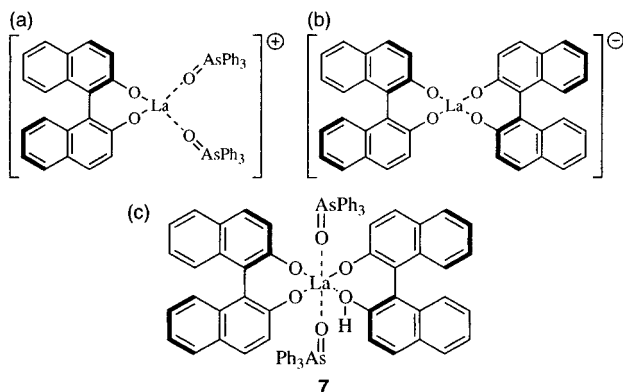


Figure 4. Structures corresponding to the molecular weight observed in positive mode (a) and negative mode (b) of LDI TOF MS and (c) the possible structure of the major complex in a complexes' solution generated from La(O-*i*-Pr)₃, (*R*)-BINOL, and Ph₃As=O in a ratio of 1:1:1.

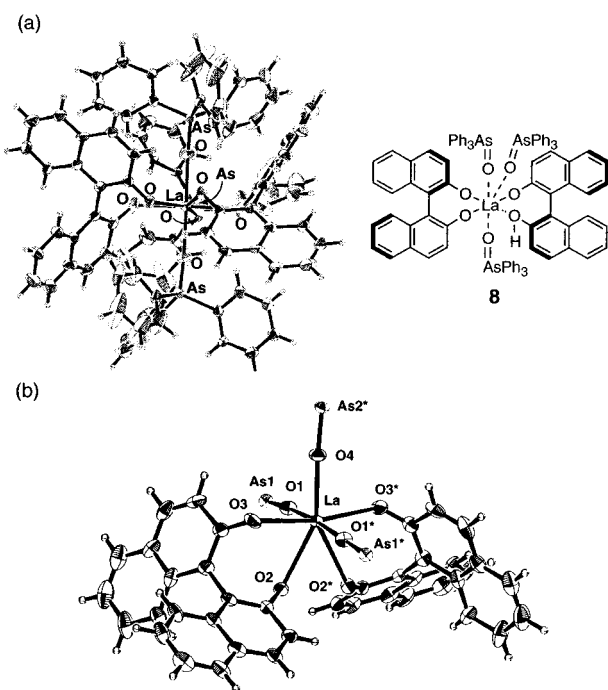


Figure 5. X-ray structure of La(binaphthoxide)₂(Ph₃As=O)₃ **8** (a). Triphenyl moieties of the triphenylarsine oxides are omitted for clarity (b). Selected bond lengths (Å): La–O(1), 2.365(5); La–O(1*), 2.365(5); La–O(2), 2.684(6); La–O(2*), 2.684(6); La–O(3), 2.437(5); La–O(3*), 2.437(5); La–O4, 2.391(8).

stable complex is formed by coordination of Ph₃As=O to the lanthanum metal. At this stage we expected that the complex stabilized by the coordination of Ph₃As=O could crystallize, and after several attempts we were pleased to get X-ray-grade crystal from the complexes' solution generated from La(O-*i*-Pr)₃, BINOL, and Ph₃As=O in a ratio of 1:1:3, containing an excess amount of Ph₃As=O relative to the best ratio for the asymmetric epoxidation. The X-ray crystal structure analysis is shown in Figure 5. The crystal structure turned out to be La(binaphthoxide)₂(Ph₃As=O)₃ (**8**) (Figure 5a) with a pentagonal bipyramidal structure (Figure 5b). To the best of our knowledge, this is the first X-ray crystal structure analysis of an alkali-metal free lanthanoid–BINOL complex. Considering the distance between the La atom and the oxygen atoms of Ph₃As=O, it can be expected that the ligands should coordinate strongly and contribute to the stability of the active species.

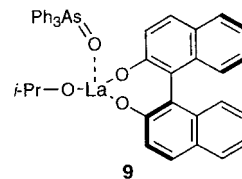


Figure 6. Speculated active species in a complexes' solution generated from La(O-*i*-Pr)₃, (*R*)-BINOL, and Ph₃As=O in a ratio of 1:1:1.

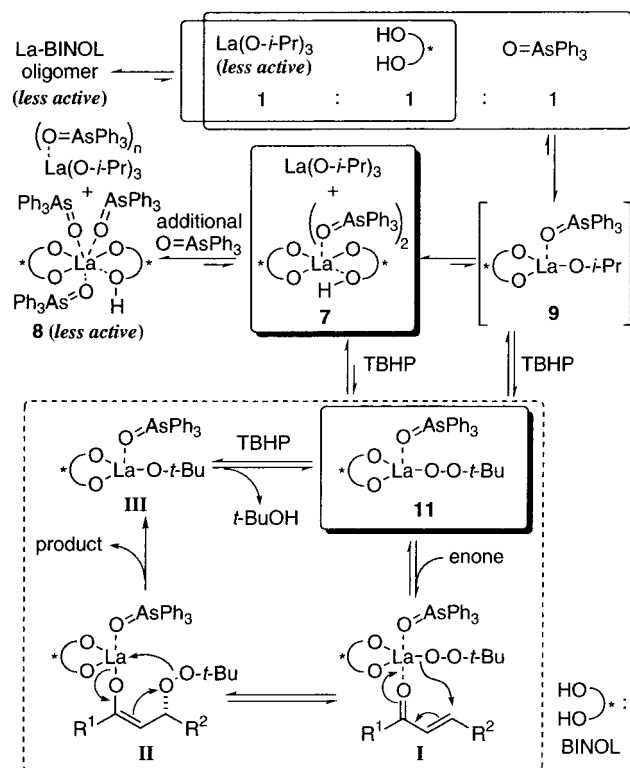
Table 3. Catalytic Asymmetric Epoxidation of **1a** to Epoxy Ketone **2a** Using La–(*R*)-BINOL–Ph₃As=O Complexes

entry	La(O- <i>i</i> -Pr) ₃ (x mol %) (<i>R</i>)-BINOL (y mol %) Ph ₃ As=O (z mol %)			time (min)	yield (%)	ee (%)
	La(O- <i>i</i> -Pr) ₃ (x mol %)	(<i>R</i>)-BINOL (y mol %)	Ph ₃ As=O (z mol %)			
1	10	20	10	72	95	96
2	10	20	20	72	93	92
3	10	20	30	90	92	95
4	10	10	10	3	95	97

^a MS 4A was not dried (1000 mg/mmol).

Furthermore, the X-ray crystal structure strongly suggests that the lanthanum complex should exist not as an oligomeric species, but as a monomeric species in the solution. In conclusion, our speculation that **7** would be the major component in the solution generated from La(O-*i*-Pr)₃, BINOL, and Ph₃As=O in a ratio of 1:1:1 should be reasonable. In striking contrast to the case of Ph₃As=O, no X-ray-grade crystals were obtained in the presence of Ph₃P=O.

Effect of Excess La(O-*i*-Pr)₃ on the La(binaphthoxide)₂(Ph₃As=O)₂ Complex. At first, the results shown in Table 1 encouraged us to speculate that La–BINOL–Ph₃As=O complex **9** (Figure 6) should exist in the complexes' solution generated from La(O-*i*-Pr)₃, BINOL, and Ph₃As=O in a ratio of 1:1:1 and might function as the most effective species. However, the major component in the complexes' solution turned out to be **7**. Moreover, the crystal prepared from the complexes' solution generated from La(O-*i*-Pr)₃, BINOL, and Ph₃As=O in a ratio of 1:1:3 proved to be **8** by X-ray crystal structure analysis. These facts again made us question if the ratio of the three components used (La–BINOL–Ph₃As=O = 1:1:1) was the best one. To solve this problem, we carried out detailed investigations on the ratio of the three components. At first we examined the effect of the amount of Ph₃As=O relative to La–BINOL complex obtained in a ratio of 1:2. The results are shown in Table 3 (entries 1–3). For all conditions, a lower reactivity than under the best conditions (entry 4) was observed, with the ee values remaining unchanged in all cases. Table 4 summarizes the results obtained by changing the ratio of La(O-*i*-Pr)₃ and BINOL. During these investigations, the relative amount of Ph₃As=O to that of BINOL was kept constant because of the fact that the ratio 1:1:1 was apparently superior to the other ratio using more than 1 equiv of Ph₃As=O to BINOL (see Table 1). As a result, an increase in the yield was observed proportional to a decrease in the ratio of BINOL relative to La(O-*i*-Pr)₃. In contrast, no change was observed with respect to the enantiomeric excess, except for the result in entry 1. Moreover, we carried out the epoxidation of **1d** using La–BINOL–Ph₃As=O complex generated in a ratio of 1:1:0.5. As a result, a decrease in the reactivity was observed when less than 1 equiv of Ph₃As=O was used (Scheme 2). All these results supported our conclusion that the La–BINOL–Ph₃As=O complex generated in a ratio of 1:1:1 should be the best one

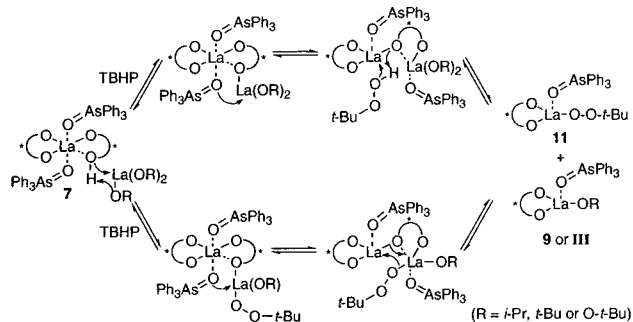
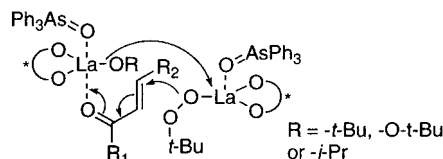
Scheme 4. Proposed Mechanism for the Epoxidation of Enones Catalyzed by the La-(*R*)-BINOL-Ph₃As=O Complex

the actual catalyst. Thus, we can now conclude that the use of La(O-*i*-Pr)₃, BINOL, and Ph₃As=O in a ratio of 1:1:1 gives rise to the best catalytic system in the present asymmetric epoxidation. In addition, it can be expected that the existence of an excess of La(O-*i*-Pr)₃ should cause a very fast equilibrium to be reached between the complexes in the solution generated from La(O-*i*-Pr)₃, BINOL, and Ph₃As=O in a ratio of 1:1:1. This may also be the reason for the ¹³C NMR result mentioned above.

Proposed Mechanism of the Catalytic Asymmetric Epoxidation of Enones Using the La-BINOL-Ph₃As=O Complex. On the basis of the assumed most active catalyst, we propose the reaction mechanism shown in Scheme 4. The 1:2:2 complex **7** (precatalyst),²⁹ which is the major component in the solution generated from La(O-*i*-Pr)₃, BINOL, and Ph₃As=O in a ratio of 1:1:1, reacts with an excess of La(O-*i*-Pr)₃ and TBHP to afford the 1:1:1 complex **11** (active catalyst) in the reaction medium.³⁰ However, if an excess amount

(29) The possibility that La(binaphthoxide)₂(Ph₃As=O) complex might be the efficient active precatalyst to **11** cannot be excluded because (+)-LDI TOF MS data showed that a small amount of La(binaphthoxide)₂(Ph₃As=O) complex existed in the reaction medium.

(30) Following is the proposed mechanism for the transformation of **7** to **11**.

**Scheme 5.** Reaction Mechanism with Several La Complexes Participating

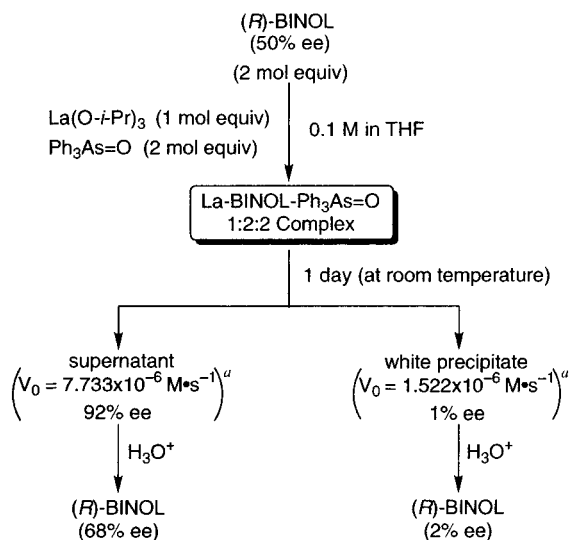
of Ph₃As=O exists in the reaction medium, less active species **8** is formed in part, leading to a decrease in the reactivity. Activation of the enone by coordination to the lanthanum metal of **11** followed by Michael addition of lanthanum peroxide, which should be on the same metal (transition state **I**), affords chiral lanthanum enolate intermediate **II**. Subsequent formation of the epoxy ketone followed by dissociation from the lanthanum complex gives the lanthanum *tert*-butoxide complex **III**. Finally, the reaction of **III** with TBHP regenerates the active catalyst **11**. In the proposed mechanism, we showed only one lanthanum complex, activating both enone and TBHP. However, unfortunately, we cannot completely exclude a mechanism in which several lanthanum complexes participate at the moment. Another possible reaction mechanism is outlined in Scheme 5. The enone is activated by one active complex, and at the same time, lanthanum peroxide, which is the other active complex, attacks the enone. To confirm whether a mechanism catalyzed by one complex is more plausible or not, we carried out kinetic studies. Unfortunately, we were not able to obtain clear results. However, as a result of our investigations on the influence of other solvents, it was found that the ee's of the products did not depend on the polarity of the reaction medium.³¹ These results seem to support a mechanism catalyzed by one complex.

As mentioned above (Figure 1), we observed asymmetric amplification in the present epoxidation. Moreover, the reaction did not proceed well when (*rac*)-BINOL was used. We believe that these results can be explained as follows. The complexes' solution generated from La(O-*i*-Pr)₃, (*rac*)-BINOL and Ph₃As=O in a ratio of 1:1:1 provided the same LDI TOF MS spectra as those using optically pure BINOL, indicating that a 1:2:2 complex should be formed as the major complex in the solution. Therefore, we expected that the stability of the La[(*R*)-binaphthoxide][(*S*)-binaphthoxide](Ph₃As=O)₂ complex [(*R,S*)-**7**] might be much higher than that of **7**, leading to the low reactivity and the observed asymmetric amplification.³² To obtain experimental proof which supports our speculation, we carried out the experiments shown in Scheme 6.^{11b} The 1:2:2 complex was prepared from BINOL with 50% ee, and the resulting solution was allowed to stand at room temperature. After 1 day, a white precipitate was observed. Separation followed by hydrolysis of the white precipitate and the supernatant with aqueous HCl gave the corresponding BINOL with 2% and 68% ee, respectively. Moreover, the ratio of BINOL and Ph₃As=O isolated from the white powder and the supernatant was almost 1:1, respectively.³³ From these results, it is obvious that some heterochiral complex, which likely exists as (*R,S*)-**7**, is formed in the solution, having lower solubility than the corresponding homochiral complex (*R,R*)-**7**. Further-

(31) Epoxidations of **1a** using 10 mol % of the La-(*R*)-BINOL-Ph₃As=O complex proceeded similarly in other solvents such as DME (30 min, 94%, 96% ee), benzene (10 min, 93%, 96% ee), and toluene (10 min, 95%, 95% ee).

(32) At first, we examined crystallization of the heterochiral complex (*R,S*)-**7** extensively. However, a crystal for X-ray analysis could not be obtained.

(33) For the detailed experimental data for Scheme 6, see the Supporting Information.

Scheme 6. Correlation between Catalytic Activity and Optical Purity of the La-(*R*)-BINOL-Ph₃As=O Complex

^a Epoxidation of **1a** using 6 mol% of the supernatant or using the white precipitate treated with 6 mol% La(O-*i*-Pr)₃. The reactions were carried out at 0 °C, and ee's of the product were determined after completion of the reactions.

more, we carried out the epoxidations of **1a** using the white precipitate and the supernatant in the presence of 1 equiv of La(O-*i*-Pr)₃ as the additive.³⁴ While the reaction using the supernatant gave the product in 92% ee with a moderate initial rate ($7.733 \times 10^{-6} \text{ M s}^{-1}$), the reaction using the white precipitate proceeded more slowly ($1.522 \times 10^{-6} \text{ M s}^{-1}$), affording the product in 1% ee. The results clearly suggested that the transformation of (*R,S*)-**7** to **11** should be much slower, even in the presence of La(O-*i*-Pr)₃, than that of (*R,R*)-**7** due to the low solubility of the heterochiral complex. On the basis of these data, it is difficult to make conclusions about the stability of the La[(*R*)-binaphthoxide][(S)-binaphthoxide](Ph₃As=O)₂ complex [(*R,S*)-**7**]. However, it can be emphasized that preferential formation of the heterochiral complex might be the reason for the asymmetric amplification and the decrease in the reactivity.

Conclusion

We have succeeded in improving catalytic asymmetric epoxidations of enones using the novel asymmetric catalyst, the La-BINOL-Ph₃As=O complex. This catalyst system is quite effective for several *trans*-enones, including a dienone, yielding products in up to 99% yield and more than 99% ee. Moreover, we have carried out detailed investigations on the structural determination of the La-BINOL-Ph₃As=O complex, including the first X-ray crystal structure analysis of an alkali-metal free lanthanoid-BINOL complex. The La-BINOL-Ph₃As=O complex in a ratio of 1:2:2 (**7**) was observed as the major component in the complexes' solution generated from La(O-*i*-Pr)₃, BINOL, and Ph₃As=O in the best ratio (1:1:1). However, the La-BINOL-Ph₃As=O complex generated in a ratio of 1:1:1 (**11**) turned out to be the most active and effective catalyst. Furthermore, preferential formation of the heterochiral complex,

likely La[(*R*)-binaphthoxide][(S)-binaphthoxide](Ph₃As=O)₂, [(*R,S*)-**7**], was found to be the reason for asymmetric amplification. Finally, we have clarified the possible reaction mechanism of the epoxidation on the basis of various experimental results. Further studies are currently underway.

Experimental Section

General Procedure for the Catalytic Asymmetric Epoxidations of Enones Using the La-(*R*)-BINOL-Ph₃As=O Complex. To a mixture of (*R*)-BINOL (7.2 mg, 0.025 mmol), triphenylarsine oxide (8.1 mg, 0.025 mmol), and MS 4A [500 mg; MS 4A was not dried (1000 mg/mmol of starting material)] in dry THF (2.5 mL) was added a solution of La(O-*i*-Pr)₃ (0.125 mL, 0.025 mmol, 0.2 M solution in THF) at room temperature. [La(O-*i*-Pr)₃ was purchased from Kojundo Chemical Laboratory Co., Ltd., 5-1-28, Chiyoda, Sakado-shi, Saitama 350-0214, Japan (fax ++(81)-492-84-1351).] After the mixture was stirred for 1 h at the same temperature, TBHP (0.12 mL, 0.6 mmol, 5 M solution in decane) was added. After the mixture was stirred for 30 min, enone **1f** (73.1 mg, 0.5 mmol) was added directly, and the mixture was stirred at room temperature. After 6 h, the reaction was quenched by addition of 2.5% aqueous citric acid solution (5 mL) at 0 °C and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried over Na₂SO₄. After concentration in vacuo, the residue was purified by flash column chromatography (SiO₂, hexane/ethyl acetate 50:1) to give epoxy ketone **2f** (74.9 mg, 92%, 99.2% ee) as a colorless oil. The IR, ¹H NMR, ¹³C NMR, and mass spectra were identical with those of an authentic sample.^{10a} [α]_D²⁵ +102 (*c* 1.0 CHCl₃). The enantiomeric excess of **2f** was determined by chiral stationary-phase HPLC analysis (Daicel Chiralpak AD, *i*-PrOH/hexane 2/98, flow rate 1.25 mL/min, *t*_R = 10.7 min (3*R*,4*S*)-isomer and 11.9 min (3*S*,4*R*)-isomer, detection at 254 nm).

Preparation of the Crystal of La-bis[(*R*)-binaphthoxide]tris(triphenylarsine oxide) (8**) for X-ray Analysis.** To a stirred mixture of (*R*)-BINOL (28.6 mg, 0.1 mmol) and triphenylarsine oxide (96.6 mg, 0.3 mmol) in THF (0.5 mL) was added a solution of La(O-*i*-Pr)₃ (0.5 mL, 0.1 mmol, 0.2 M solution in THF). After the reaction mixture was stirred for 1 h, the solution was concentrated to 0.125–0.15 M and kept at room temperature under argon. After 24 h, an X-ray-grade crystal of La-bis[(*R*)-binaphthoxide]tris(triphenylarsine oxide) (**8**) was grown.

Data for 8: collected at -100 °C, C₉₈H₈₀O₉As₃La = 1765.37, clear, prism, crystal system trigonal, lattice type primitive, *a* = 17.6048(6) Å, *c* = 26.653(1) Å, *V* = 7153.9(5) Å³, P3₂21,³⁵ *Z* = 3, *D* = 1.229 g/cm³, *R*(*F*) = 0.054, *R*_w(*F*) = 0.082, *GOF* = 1.85. Hydrogen atoms were included but not refined. THF × 1 and H₂O × 1 were incorporated in the crystal. For data collection and solution and refinement of the structure, see the Supporting Information.

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Supporting Information Available: Enantiomeric excess analysis of the epoxy ketones **2a–h**, **4**, and **6**; experimental procedures and spectral and analytical data for all new compounds for the synthetic pathway to **1i**; their ¹H NMR and ¹³C NMR spectra; detailed results of catalytic asymmetric epoxidation of **1i** to **2i** using La-BINOL complexes; general conditions for the kinetic studies and experimental data of Figures 1 and 7 and Scheme 6; and an X-ray crystallographic file (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

JA004201E

(34) The concentration of the 1:2:2 complex in the supernatant was calculated from the ee values of the BINOL contained in the white precipitate and the supernatant, respectively.

(35) The space group is P3₂21 in the case of La-bis[(*S*)-binaphthoxide]tris(triphenylarsine oxide).