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Oxidation Catalysis of Nb(salan) Complexes: Asymmetric Epoxidation of Allylic Alcohols Using Aqueous Hydrogen Peroxide as an Oxidant

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Abstract: Several optically active Nb(salan) complexes were synthesized, and their oxidation catalysis was examined. A dimeric μ-oxo Nb(salan) complex that was prepared from Nb(O*i*Pr)$_5$ and a salan ligand was found to catalyze the asymmetric epoxidation of allylic alcohols using a urea−hydrogen peroxide adduct as an oxidant with good enantioselectivity. However, subsequent studies of the time course of this epoxidation and of the relationship between the ee of the ligand and the ee of the product indicated that the μ-oxo dimer dissociates into a monomeric species prior to epoxidation. Moreover, monomeric Nb(salan) complexes prepared in situ from Nb(O*i*Pr)$_5$ and salan ligands followed by water treatment were found to catalyze the epoxidation of allylic alcohols better using aqueous hydrogen peroxide in $CHCl_3$/brine or toluene/brine solution with high enantioselectivity ranging from 83 to 95% ee, except for the reaction of cinnamyl alcohol that showed a moderate ee of 74%. This is the first example of the highly enantioselective epoxidation of allylic alcohols using aqueous hydrogen peroxide as an oxidant.

1. Introduction

A number of synthesis methods have been reported to date and used for various organic syntheses. With resource conservation and waste reduction in mind, selectivity and atom efficiency are two important criteria for choosing a method for efficient synthesis from among many methods.

Chiral epoxy alcohols are versatile building blocks for organic synthesis, and asymmetric epoxidation of readily available allylic alcohols is the most straightforward method of synthesis.[1] In 1980, Sharpless and Katsuki reported a highly enantioselective, practical epoxidation of allylic alcohols using a titanium/tartrate/*t*-butyl hydroperoxide system.[2] Later, a catalytic version of this reaction was achieved by adding molecular sieves to the system.[3] Subsequently, Basset and co-workers developed an enantioselective epoxidation using a heterogeneous silica-supported tantalum/tartrate complex as the catalyst.[4] Another approach to the epoxidation, pioneered by Sharpless, is the method using a vanadium/hydroxamic acid complex as the catalyst.[5] Later, Yamamoto and other groups improved the catalysis of the vanadium catalyst by introducing a bulky hydroxamic acid ligand that prevents the formation of a catalytically inactive multihydroxamic acid-coordinating vanadium complex.[6] In 2005, Malkov et al. reported a method for the epoxidation using a vanadium/hydroxamic acid/*t*-butyl hydroperoxide system in water, with moderate to good enantioselectivity.[7] Moreover, Yamamoto and co-workers made a breakthrough in this type of epoxidation by introducing a unique bis-hydroxamic acid ligand.[8] The scope of the reaction using the vanadium-bis-hydroxamic acid complex is very wide: it can be applied not only to allylic alcohols but also to homoallylic alcohols with high enantioselectivity.[8b,9] The reactions described above satisfy the first criterion of selectivity, but they require the use of an

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alkyl hydroperoxide as the oxidant. Still, the second criterion of ecological sustainability is a challenging issue to address.

The ecological sustainability of oxidation primarily depends on the oxidant used.[10,11] The use of an oxidant that has a high active oxygen content and generates a small and innocuous coproduct such as water after oxygen-atom transfer is essential for green oxidation. In light of this, asymmetric epoxidation using hydrogen peroxide, in particular, aqueous hydrogen peroxide, that is safe and cheap and generates water as a coproduct is a topic of current interest.[10] Although several highly enantioselective methods for epoxidation using aqueous hydrogen peroxide at room temperature have been reported,[12] no method for the epoxidation of allylic alcohols with it has been achieved. We have recently revealed that Ti(salalen)[13,14] and Ti(salan)[13,15] complexes are excellent catalysts for the asymmetric epoxidation of simple olefins using aqueous hydrogen peroxide. These reactions have been proposed to proceed via a peroxo Ti species that is activated by hydrogen bonding with the adjacent amino proton. Different from simple olefins, allylic alcohols can precoordinate with a metal ion, and an (allylalkoxo)(peroxo) metal species is likely to be a possible intermediate for the epoxidation using hydrogen peroxide as an oxidant. Because salalen or the salan ligand is divalent and quadridentate, a metal−(salalen) or metal−(salan) complex was considered to show the asymmetric catalysis of the epoxidation of allylic alcohols, when the valency of the metal ion is five or greater and the corresponding salalen or salan complex can adopt heptacoordination such as in a pentagonal bipyramidal configuration. The titanium ion is tetravalent, and its salalen and salan complexes generally adopt an octahedral configuration. Indeed, these complexes scarcely or poorly catalyze the epoxidation of allylic alcohols with low enantioselectivity.[16] In contrast to the titanium complexes, zirconium− and hafnium−(salen) complexes have been reported to adopt a pentagonal bipyramidal configuration.[17] We expected that metal ions of the second and third transition-metal series in group V would also form a complex with a pentagonal bipyramidal configuration. Hence, we were intrigued by the asymmetric epoxidation catalysis of Nb− or Ta−(salan) or Nb− or Ta−(salalen) complexes.[18,19] In this article, we describe the preparation of Nb− and Ta−(salan) complexes and their asymmetric catalysis of the epoxidation of allylic alcohols with the urea−hydrogen peroxide adduct (UHP)[20] or with aqueous hydrogen peroxide.

2. Results and Discussion

2.1. Preparation of μ-Oxo−Nb(salan) Complexes. Mixing Nb(O*i*Pr)$_5$ and ligand **1** in dichloromethane immediately provided an unstable monomeric Nb(salan)(O*i*Pr)$_3$ complex, **2**,[21] that was slowly converted to a μ-oxo−Nb(O)(salan) dimer complex, **3**, under ambient conditions over a period of 7−10 days (Scheme 1). The preparation of **2** and **3** was traced by ^{1}H NMR and MS analysis. Monomeric complex **2** decomposed during chromatographic analysis and could not be purified completely. However, complex **3** was purified using silica gel column chromatography and was used for the following

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(16) Titanium(salan) complexes scarcely catalyzed the epoxidation of *trans*- and *cis*-2-hexen-1-ols whereas a titanium(salalen) complex that is an excellent catalyst for the epoxidation of isolated olefins (ref 14b) catalyzed the epoxidation of allylic alcohols, albeit sluggishly and with only modest enantioselectivity: the epoxidation of *cis*-2-hexene-1-ol at room temperature for 24 h gave the corresponding epoxy alcohol of 20% ee in 30% yield.

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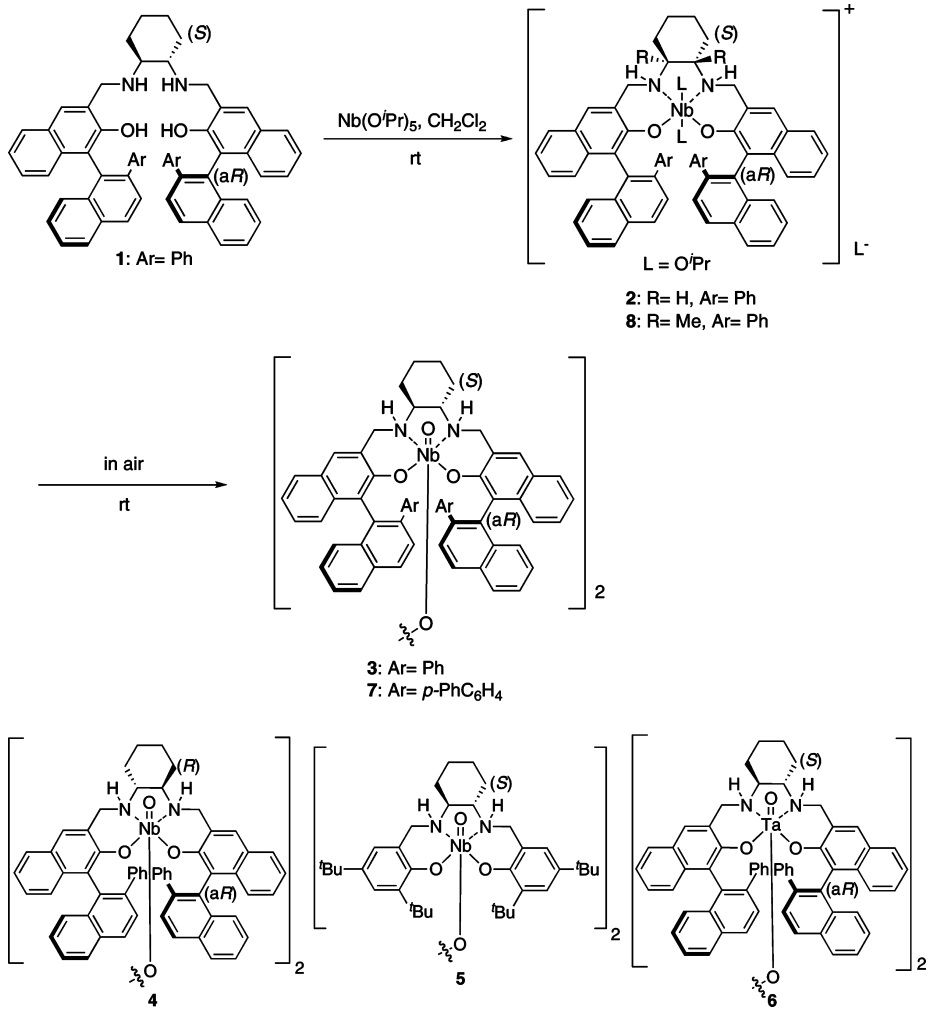
(21) The crude mixture was submitted to MS analysis. **2**: ESI$^+$-TOFMS. Calcd for $[(C_{60}H_{48}N_2O_2)(C_3H_7O)_2Nb]^+$: m/z = 1039.3768. Found: m/z = 1039.3738.

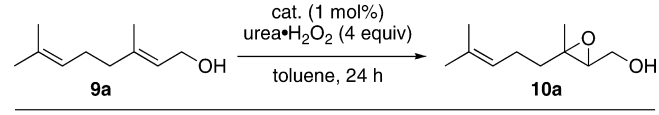
Scheme 1. Preparation of μ-Oxo−Nb(salan) and Ta(salan) Complexes



epoxidation. Other dimeric Nb− and Ta−(salan) complexes (**4**−**7**) were synthesized during the same procedure.

2.2. Asymmetric Epoxidation of Allylic Alcohols with μ-Oxo−Nb(salan) Complexes and UHP. It is known that most polyoxo−metal complexes show epoxidation catalysis.[22] Thus, we were intrigued with the catalysis of dimeric complexes **3**−**7**, and we examined the epoxidation of geraniol in the presence of 4 equiv of UHP at 20 °C in toluene (Table 1). Although the epoxidation using **3** was slow, it had the best results (68% ee, 24%) in terms of enantioselectivity and yield, though both were still moderate (entry 1). The reaction with complex **4** was slower and less selective (entry 2). Complex **5** did not show epoxidation catalysis (entry 3). The reaction with Ta complex **6** that carries the same ligand as **3** was slower and less selective than that with **3** (entry 4). On the basis of these results, we optimized the reaction temperature for the epoxidation with complex **3**, and it was found that a good enantioselectivity of 81% ee and acceptable chemical yields were obtained at 40 °C (entry 5). The effect of solvent was also investigated at 40 °C, and toluene was proven to be the solvent of choice in terms of enantioselectivity and yield (entries 5 and 7−10). The epoxide was obtained in a good yield when 2 mol % of **3** was used (entry 11). The epoxidation using **7** as the catalyst, which bears the ligand with the same configuration as **3** and gave a single crystal

Table 1. Asymmetric Epoxidation of Geraniol with Dimeric Nb− and Ta−(salan) Complexes as the Catalyst[a]



entry	cat.	solvent	T (°C)	yields (%)	ee (%)[b]
1	**3**	toluene	20	24	68
2	**4**	toluene	20	10	−42
3	**5**	toluene	20	N.R.[c]	
4	**6**	toluene	20	13	42
5	**3**	toluene	40	61	81
6	**3**	toluene	60	32	67
7	**3**	CH_2Cl_2	40	22	68
8	**3**	THF	40	<5	
9	**3**	AcOEt	40	10	56
10	**3**	MeOH	40	40	rac
11[d]	**3**	toluene	40	83	81 (2*S*, 3*S*)
12	**7**	toluene	40	58	79 (2*S*, 3*S*)

[a] The reaction was carried out on a 0.5 mmol scale with catalyst (1 mol %) and UHP (4 equiv), unless otherwise mentioned. [b] Determined by HPLC analysis on a chiral phase (Daicel Chiralpak OB-H) after benzoylation. [c] No reaction. [d] Run with 2 mol % of **3**.

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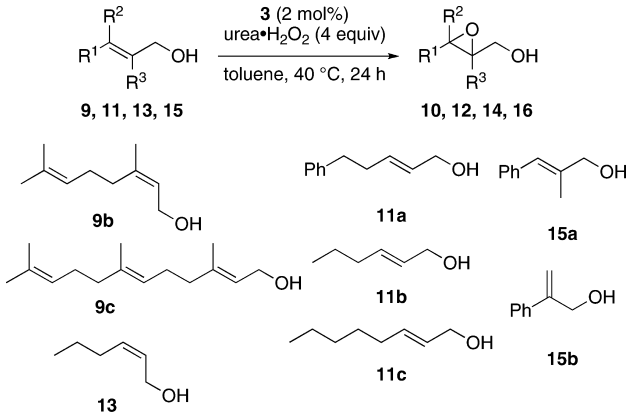
Table 2. Asymmetric Epoxidation of Various Allylic Alcohols with **3** as the Catalyst[a]



entry	substrate	yield (%)	ee (%)[b]	config[c]
1	**9b**	66	80[d]	2*S*, 3*R*
2	**9c**	72	80[d]	2*S*, 3*S*
3	**11a**	83	79	2*S*, 3*S*
4	**11b**	78	80[d]	2*S*, 3*S*
5	**11c**	81	79[d]	2*S*, 3*S*
6	**13**	79	83[d]	2*S*, 3*R*
7	**15a**	86	72	2*S*, 3*S*
8	**15b**	83	68	2*S*

[a] The reaction was carried out on a 0.5 mmol scale with **2** (2 mol %) and UHP (4 equiv) at 40 °C. [b] Determined by HPLC analysis on a chiral phase. [c] Determined by comparison of the chiroptical data with the literature value. [d] Determined by HPLC analysis on a chiral phase after conversion to the corresponding benzoate.

suitable for X-ray analysis, provided the epoxide with 79% ee (entry 12). A μ-oxo−Nb complex bearing the corresponding (a*R*,*S*,*S*,a*R*)-salalen ligand (dehydrogenated **1**) was also prepared in the same manner[23] and was used as the catalyst in the epoxidation with UHP. However, its catalytic activity was poor.

Under optimized conditions, the epoxidation of various allylic alcohols was examined (Table 2). The epoxidation of di- and trisubstituted olefins proceeded with a similarly good level of enantioselectivity to that of geraniol, irrespective of their geometry (entries 1−6). However, the presence of a geminal substituent diminished the enantioselectivity to some extent (entries 7 and 8). It is noteworthy that the present epoxidation is stereospecific. The oxidation with aqueous hydrogen peroxide, which is a cheaper and easier-to-handle oxidant, was also examined at 40 °C, but it was found to be inferior to the reaction with UHP in terms of enantioselectivity and yield. For example, the epoxidation of geraniol gave the epoxide at 40% ee in 38% yield.

2.3. Asymmetric Epoxidation of Allylic Alcohols with Aqueous Hydrogen Peroxide. In situ-prepared **2** was also used as the catalyst in the epoxidation of geraniol using UHP in toluene at 40 °C for 24 h. The reaction gave the corresponding epoxide with inferior enantioselectivity (74% ee) in 42% yield. Although complex **2** is converted to **3**, this result suggests that a Nb(salan) complex other than dimeric **3** could catalyze this epoxidation. However, in situ-prepared **8**,[24] which has a dimethylcyclohexane unit in the salan ligand and cannot be converted into the corresponding μ-oxo dimer due to steric hindrance, did not catalyze the epoxidation of allylic alcohols. In a continuing study, however, we encountered two meaningful observations. It was found that in situ-prepared **2** showed epoxidation catalysis, even after it was treated with water for 30 min, albeit with inferior enantioselectivity and yield. The epoxidation of geraniol with this pretreated catalyst in the presence of UHP gave the corresponding epoxide of 60% ee in 43% yield. The MS analysis of the pretreated complex indicated the formation of a (HO)Nb(O)(salan) complex.[25] Another finding was that the oxidation with pretreated catalyst has no induction period whereas the reaction with **3** does have an induction period (Figure 1). X-ray analysis of μ-oxo−Nb(salan) complex **7** indicated that the oxygen atoms of the two Nb═O bonds form hydrogen-bond pairs with the amino protons of the salan ligand on the other Nb ion, and this hydrogen-bond pair stabilizes the dimeric structure of the Nb(salan) complex (vide infra). We inferred that the induction period represents the time necessary for the cleavage of the hydrogen bond pair and an activated species for the epoxidation is formed via a monomeric Nb═O species. Thus, we expected that an in situ-prepared and -pretreated complex could be a better catalyst for the epoxidation of allylic alcohol using hydrogen peroxide under aqueous conditions.

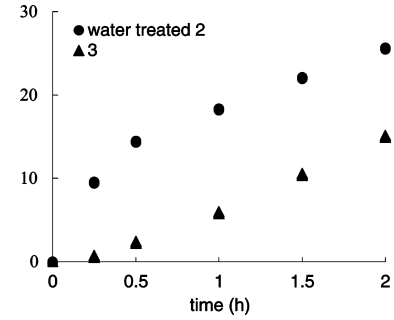


Figure 1. Initial reaction rates of the epoxidation of *trans*-2-hexene-1-ol using pretreated **2** or **3** as a catalyst in the presence of UHP.

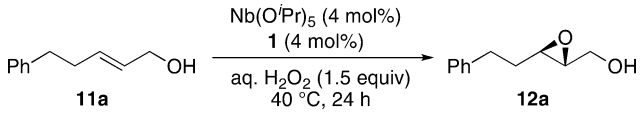
In the communication of our preliminary study,[20] we described that complex **3** is the catalyst for epoxidation and that it is decomposed by water. With these new results, however, we suspected that water dissociates only the μ-oxo Nb(salan) dimer into a monomeric Nb(salan) complex and that hydrogen peroxide might be mainly responsible for the decomposition of the catalyst. Hydrogen peroxide has a high coordination ability and nucleophilicity, and many metal complexes degrade more rapidly in its presence. Therefore, we expected that the epoxidation using aqueous hydrogen peroxide would be realized in aqueous media with the pretreated catalyst prepared from **1** if the accumulation of hydrogen peroxide can be avoided. To explore this possibility, we examined the reaction of 5-phenyl-2-pentenol using 30% aqueous hydrogen peroxide at 40 °C (Table 3). As expected, epoxidation proceeded with better enantioselectivity and yield when aqueous hydrogen peroxide was added dropwise rather than all at once (cf. entries 1 and 3). Moreover, the reaction in toluene/brine was found to give a further-improved yield and enantioselectivity, which were comparable to those obtained with a **3**/UHP system (cf., entry 2 and Table 2, entry 3).

(23) (a*R*,*S*,*S*,a*R*)-μ-oxo-Nb(salalen) dimer complex: ESI$^+$-TOFMS. Calcd for $[(C_{60}H_{46}N_2O_2)(O)Nb-O-Nb(O)(C_{60}H_{46}N_2O_2)+Na]^+$: m/z = 1910.5022. Found: m/z = 1910.5019.

(24) The crude mixture was submitted for MS analysis. **8**: ESI$^+$-TOFMS. Calcd for $[(C_{62}H_{52}N_2O_2)(C_3H_7O)_2Nb]^+$: m/z = 1067.4081. Found: m/z = 1067.4061.

(25) (HO)Nb(O)(salan) complex: ESI$^+$-TOFMS. Calcd For $[(C_{60}H_{48}N_2O_2)Nb(OH)(O)+Na]^+$: m/z = 977.2648. Found: m/z = 977.2624.

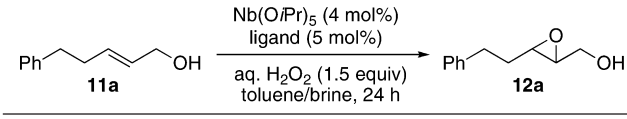
Table 3. Asymmetric Epoxidation of 5-Phenyl-2-pentenol with Aqueous Hydrogen Peroxide[a]



entry	solvent	yield (%)	ee (%)[b]
1[c]	toluene	53	58
2[c]	toluene/brine	74	80
3[d]	toluene	43	36
4[d]	toluene/H_2O	48	58
5[d]	toluene/brine	21	72

[a] The reactions were carried out on a 0.5 mmol scale with 30% H_2O_2(aq) (1.5 equiv) in the presence of the catalyst that was prepared in situ from Nb(O^{i}Pr)$_5$ (4 mol %) and **1** (4 mol %) and pretreated with water. [b] Determined by HPLC analysis using a chiral stationary phase column (Daicel Chiralpak OD-H). [c] H_2O_2(aq) was added dropwise every 2 h in seven batches. [d] H_2O_2(aq) was added all at once.

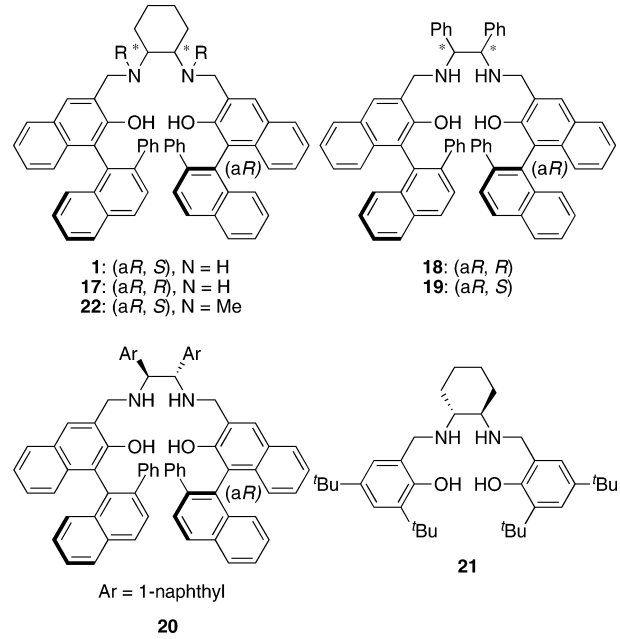
Table 4. Optimization of the Asymmetric Epoxidation of Allylic Alcohols[a]



entry	temp (°C)	ligand	yield (%)	ee (%)[b]	config[c]
1[d]	40	**1**	74	80	2*S*, 3*S*
2	40	**1**	80	81	2*S*, 3*S*
3[e]	40	**1**	82	81	2*S*, 3*S*
4[f]	40	**1**	71	81	2*S*, 3*S*
5	20	**1**	28	75	2*S*, 3*S*
6	60	**1**	55	80	2*S*, 3*S*
7	40	**17**	31	48	2*R*, 3*R*
8	40	**18**	46	52	2*R*, 3*R*
9	40	**19**	72	87	2*S*, 3*S*
10[g]	40	**19**	76[h]	91	2*S*, 3*S*
11[g]	40	**20**	81[h]	92	2*S*, 3*S*
12	40	**21**	N.R.[i]		
13	40	**22**	N.R.[i]		

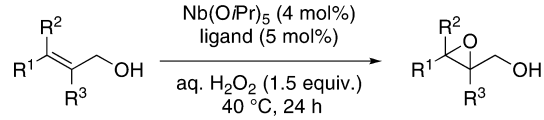
[a] The reactions were carried out in toluene/brine on a 0.5 mmol scale with 30% H_2O_2(aq) (1.5 equiv) in the presence of the catalyst that was prepared in situ from Nb(OiPr)$_5$ (4 mol %) and the ligand (5 mol %) and pretreated with water. H_2O_2(aq) (1.5 equiv) was added in a dropwise manner, unless otherwise mentioned. [b] Determined by HPLC analysis using a chiral stationary phase column (Daicel Chiralpak OD-H). [c] Determined by comparison of the chiroptical data with literature values. [d] Run with 4 mol % of the ligand. [e] Run with 6 mol % of the ligand. [f] Nb(OEt)$_5$ was used as the metal source. [g] The reaction was carried out in chloroform/brine. [h] The reaction mixture was treated with $NaBH_4$ before isolation of the product. [i] No reaction occurred.

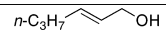
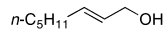
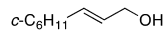
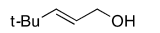
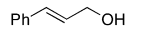
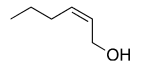
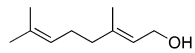
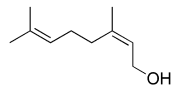
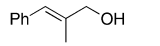
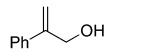
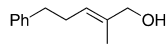
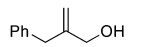
Under these conditions, we further optimized the reaction in terms of the metal/ligand ratio, reaction temperature, and ligand structure (Table 4). The amount of ligand loading had little effect on the yield and enantioselectivity (entries 1−3). Nb(OiPr)$_5$ did not catalyze the epoxidation in the absence of the salan ligand. The reaction with the catalyst prepared from Nb(OEt)$_5$ showed an equal enantioselectivity to that with the catalyst prepared from Nb(OiPr)$_5$, albeit in a slightly reduced yield (entry 4). This indicates that the Nb(salan) complex does not carry the alkoxide ligand at the transition state for the epoxidation. The yield was diminished at both lowered and raised temperatures, though good enantioselectivity was obtained at 60 °C (entries 5 and 6). The reaction with (a*R*,*R*)-salan ligand **17** was less selective, and the sense of asymmetric induction by it was opposite to that by (a*R*,*S*)-**1** (entry 7). Under the same conditions, we examined the catalysis of niobium complexes bearing the salan ligands derived from the 1,2-diphenylethylenediamines (entries 8 and 9). It was again observed that (a*R*,*R*)-salan ligand **18** was less efficient than (a*R*,*S*)-ligand **19**. Moreover, ligand **19** showed better asymmetric induction than **1** (entry 9). Thus, we surveyed the reaction using **19** in several solvents and found that a better enantioselectivity was obtained in chloroform/brine (entry 10). Eventually, high enantioselectivity of 92% ee was obtained with ligand **20** bearing 1-naphthyl groups at the diamine subunit (entry 11). It is of note that a complex of ligand **21** that does not possess a binaphthyl subunit did not catalyze the epoxidation (entry 12). It is also noteworthy that *N*,*N*′-dimethylated ligand **22** did not catalyze the epoxidation (entry 13).



On the basis of these results, we examined the epoxidation of various allylic alcohols using ligand **1**, **19**, or **20** in a mixed solvent, toluene/brine or chloroform/brine, under otherwise optimized conditions, and the best results obtained are shown in Table 5. High enantioselectivity greater than 91% ee and acceptable yields were obtained in the epoxidation of *E*-alkyl-substituted allylic alcohols using **20** as the ligand (Table 5, entries 1−4). The resulting epoxy alcohols were partially oxidized under the conditions of the corresponding epoxy aldehydes (10−20%), and the reaction mixture was treated with $NaBH_4$ before isolating the products. It should be noted that the oxidation of the aldehydes occurred in an enantiomer-differentiating manner, albeit with low selectivity, and that the enantiomeric excesses of whole epoxides were slightly better than for the epoxides isolated without $NaBH_4$ treatment. The reaction of cinnamyl alcohol was moderately enantioselective, and the competitive OH oxidation giving the cinnam aldehyde was observed (entry 5). As opposed to the epoxidation of *E*-allylic alcohols, that of *cis*-2-hexenol was best carried out in toluene/brine with a high enantioselectivity (85% ee) by using **1** as a ligand (entry 6). The reactions of trisubstituted substrates, geraniol and nerol, were also better carried out by the catalyst obtained from **1** (entries 7 and 8). However, the epoxidation of geminally substituted allylic alcohols using ligands **1**, **19**, or **20** did not show good enantioselectivity higher than 80% ee. To our delight, high enantioselectivity greater than 83% ee was obtained by using **18** as a ligand, albeit with moderate yields due to the competitive OH oxidation (entries 9−12). The use

Table 5. Asymmetric Epoxidation of Various Allylic Alcohols[a]



entry	substrate		ligand	solvent	yield (%)[b]	ee (%)[c]	Config.[d]
1		**11b**	**20**	$CHCl_3$/brine	57	91[e]	2*S*, 3*S*
2		**11c**	**20**	$CHCl_3$/brine	79	93[e]	2*S*, 3*S*
3		**11d**	**20**	$CHCl_3$/brine	82	93[e]	2*S*, 3*S*
4		**11e**	**20**	$CHCl_3$/brine	52	95[e]	2*S*, 3*S*
5		**11f**	**20**	$CHCl_3$/brine	61	74	2*S*, 3*S*
6		**13**	**1**	toluene/brine	52[f]	85[e]	2*S*, 3*R*
7		**9a**	**1**	$CHCl_3$/brine	82	84[e]	2*S*, 3*S*
8		**9b**	**1**	$CHCl_3$/brine	76	83[e]	2*S*, 3*R*
9		**15a**	**18**	C_6H_5F /brine	40	83	2*R*, 3*R*
10		**15b**	**18**	toluene/brine	43[f]	85	2*R*
11[g]		**15c**	**18**	C_6H_5F/brine	64	90	-
12		**15d**	**18**	toluene/brine	52[f]	90	2*R*

[a] The reactions were carried out on a 0.5 mmol scale in the presence of the catalyst that was prepared in situ from Nb(O*i*Pr)$_5$ (4 mol %) and ligand (5 mol %) and pretreated with water. 30% aqueous H_2O_2 (1.5 equiv.) was added in a dropwise manner, unless otherwise mentioned. [b] Yield after treatment of the reaction mixture with $NaBH_4$, unless otherwise mentioned. [c] Determined by HPLC analysis using a chiral stationary phase column. [d] Determined by comparison of the chiroptical data with the literature values. [e] Determined by HPLC analysis after conversion into the corresponding benzoate. [f] Yield without $NaBH_4$ reduction. [g] Run with 8 mol % of Nb(O*i*Pr)$_5$ and 9 mol % of the ligand.

of fluorobenzene/brine as a solvent slightly improved the yields in some reactions (entries 9 and 11). The undesired OH oxidation is likely to be accelerated by the presence of aryl and geminal substituents.

It is of note that high enantioselectivity greater than 83% ee in the epoxidation of allylic alcohols using 30% aqueous hydrogen peroxide was achieved with an appropriate Nb(salan) complex as a catalyst, except for the epoxidation of cinnamyl alcohol, though the yields of some reactions were moderate because of competitive OH oxidation.

2.4. X-ray Analysis of *μ*-Oxo−Nb(salan) Complex 7 and Mechanistic Consideration of the Present Epoxidation. Complex **7** showed almost identical oxidation catalysis to that of complex **3**, and it gave a single crystal from dichloromethane and ether (2: 1) (vide supra). The X-ray analysis determined its structure unambiguously (Figure 2):[26] complex **7** was an approximately C_2-symmetric *μ*-oxo dimer. Both Nb(salan) units of **7** adopted a distorted octahedral configuration, and the chirality of the niobium-bound amine nitrogen atoms was *R*. It is noteworthy that the Nb(1)−O(4) distance is 1.744 Å, a dimension appropriate for a double bond. It is also noted that the Nb(1)−O(1) bond

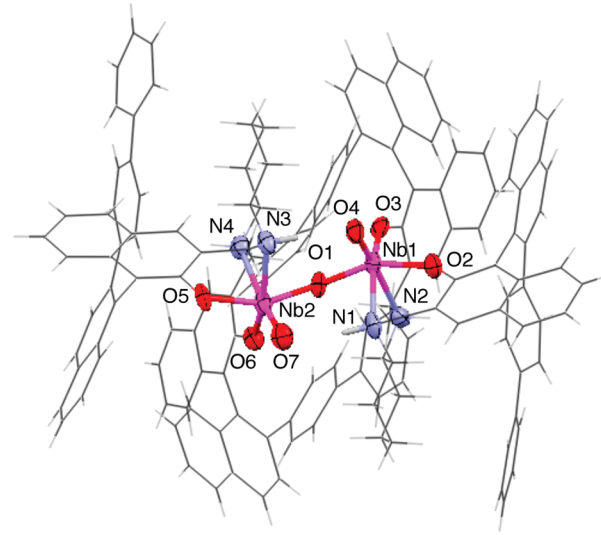


Figure 2. X-ray structure of *μ*-oxo−Nb(salan) complex **7**.

is slightly shorter than the Nb(1)−O(2) and Nb(1)−O(3) bonds. Moreover, the N(3)−O(4) and N(1)−O(7) distances are as short as 2.824 and 2.902 Å, respectively, indicating the presence of hydrogen bonding between the oxo oxygen and amino hydrogen atoms.

(26) CCDC-677278 contains the supplementary crystallographic data for this article. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

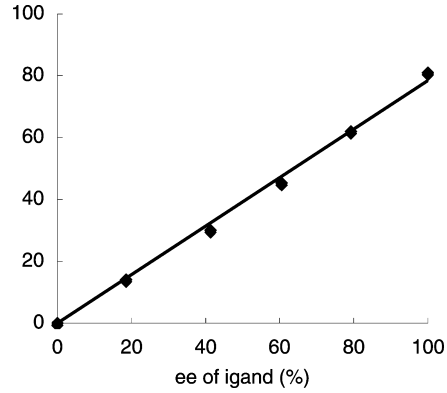
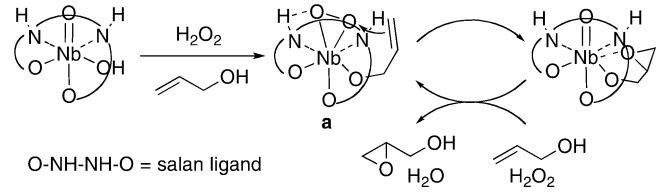


Figure 3. Correlation between ee's of ligand **1** and the product in the epoxidation of 5-phenyl-2-pentenol.

The epoxidation with a pretreated catalyst has no induction period whereas the reaction with **3** does have an induction period (Figure 1) and the pretreated catalyst was suggested to be a (HO)Nb(O)(salan) complex by MS analysis. Taking into consideration the X-ray structure, the induction period represents the necessary time for cleaving the hydrogen bond pairing between the N═O bond and the amino protons as described above. Because these results suggested that a genuine catalyst is a monomeric (hydroxo)(oxo)niobium species, we examined the relationship between the ee of ligand **1** and the ee of the product.[27] In accord with the suggestion, a linear relationship ($R^2 = 0.9962$) between them was observed in the epoxidation of 5-phenyl-2-pentenol (Figure 3).

It is known that oxo metal species gives the corresponding peroxo metal species upon hydrogen peroxide treatment,[28] and it seemed likely that pretreated complex **2** was converted to the corresponding peroxo species under the present conditions. Moreover, Nb complexes of salan ligands that have an amino proton underwent epoxidation catalysis whereas the complex of *N*,*N*′-dimethylated salan ligand **22** did not (Table 4, entry 13). The same phenomenon has been observed in the epoxidation using the Ti(salalen) or Ti(salan) complex as a catalyst.[13−15] These results suggest that the resultant Nb peroxo species could be further activated by hydrogen bond formation between the oxygen atom of the peroxo species and the amine proton.[29] However, the fact that water-treated **2** and **3** do not catalyze the epoxidation of a simple olefin such as 1,2-dihydronaphthalene suggests that the precoordination of allylic alcohol is essential for this epoxidation. On the basis of these results, we propose monomeric peroxo niobium species **a** with heptacoordination as a possible intermediate for the epoxidation using the pretreated niobium−salan complex as a catalyst (Scheme 2).

Scheme 2. Plausible Mechanism for the Epoxidation Using Pretreated Complex **2** as a Catalyst



3. Conclusions

We found a unique asymmetric catalysis of epoxidation of allylic alcohols using hydrogen peroxide by niobium−salan complexes. We first discovered that μ-oxo [Nb(salan)]$_2$ complex **3** serves as a catalyst for the asymmetric epoxidation of allylic alcohols with a urea−hydrogen peroxide adduct. On the basis of the analysis of the time course of the epoxidation, we also discovered that in situ-prepared Nb(salan) complexes catalyze the epoxidation of allylic alcohols using aqueous hydrogen peroxide in aqueous media. It is of note that the latter method does not require the troublesome purification of the catalyst and allows easy ligand tuning. Eventually, we could achieve highly enantioselective epoxidation of allylic alcohols using aqueous hydrogen peroxide. To the best of our knowledge, this is the first report on the asymmetric epoxidation of allylic alcohols using hydrogen peroxide as an oxidant and on the asymmetric catalysis of a niobium complex in aqueous media. This study will open a new avenue toward a sustainable system for asymmetric oxidation.

4. Experimental Section

4.1. General. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-AL400 spectrometer at 400 and 100 MHz, respectively. All chemical shifts were recorded in δ relative to tetramethylsilane (TMS). Melting points were measured with a Büchi melting-point B-545 apparatus and were uncorrected. Infrared spectra were obtained via a KBr disk or a thin film using a KBr plate on a Shimadzu FTIR-8400 spectrophotometer, and only diagnostic absorptions are listed below. Optical rotation was measured with a Jasco P-1020 polarimeter. TOFMS(ESI$^+$) spectra were obtained from Bruker Daltonics micrOTOF-KS1focus spectrometer. Enantiomeric excesses were determined by HPLC analysis using a Shimadzu LC-10AT-VP equipped with a column packed with an appropriate optically active material, as described below. TLC analysis was performed on silica gel 60 F_{254}-coated glass plates (Merck). Visualization was accomplished via irradiation with 254 nm UV light or spraying a 12-molybdo(VI)phosphoric acid ethanol solution as the developing agent. Water was deionized by using an Advantec PWR-500.

4.2. Synthesis of Salan Ligands. According to our previous report,[30] salan ligands **1**, **17**−**19**, **20**, and **22** were synthesized.

4.2.1. Ligand 18. Slightly yellow powder. IR (KBr): 3053, 3024, 2851, 1624, 1583, 1495, 1433, 1352, 1315, 1250, 1109, 1026, 862, 821, 748, 698 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 10.9 (bs, 2H), 8.02 (d, 2H, J = 8.3 Hz), 7.96 (d, 2H, J = 8.1 Hz), 7.65 (d, 2H, J = 8.5 Hz), 7.52 (d, 2H, J = 7.6 Hz), 7.45−7.36 (m, 4H), 7.31−7.17 (m, 14H), 7.16−7.06 (m, 4H), 7.03−6.92 (m, 8H), 6.84−6.76 (m, 4H), 4.02−3.91 (m, 4H), 3.62 (d, 2H, J = 13.7 Hz), 2.14 (bs, 2H). ^{13}C NMR ($CDCl_3$): δ 153.4, 141.9, 140.3, 137.3, 133.7, 132.9, 132.8, 131.6, 128.5, 128.3, 128.2, 128.1, 127.9, 127.8, 127.5, 127.2, 127.1, 126.2, 126.1, 125.8, 125.5, 124.6, 123.4, 122.7, 119.3, 65.3, 49.9. Anal. Calcd for $C_{68}H_{52}N_2O_2 + {}^1/_2H_2O$: C, 87.06; H, 5.69; N, 2.99. Found: C, 87.21; H, 5.65; N, 2.95. ESI$^+$-TOFMS. Calcd for $[C_{68}H_{52}N_2O_2+Na]^+$: m/z = 951.3921. Found: m/z = 951.3925.

4.2.2. Ligand 19. Slightly yellow powder. IR (KBr): 3053, 3026, 2849, 1624, 1597, 1495, 1431, 1354, 1319, 1252, 1204, 1111, 1026,

(27) (a) Puchot, C.; Samuel, O.; Dunach, E.; Zhao, S.; Agami, C.; Kagan, H. B. *J. Am. Chem. Soc.* **1986**, *108*, 2353–2357. (b) Kagan, H. B. *Adv. Synth. Catal.* **2001**, *343*, 227–233. (c) Kitamura, M.; Suga, S.; Oka, H.; Noyori, R. *J. Am. Chem. Soc.* **1998**, *120*, 9800–9809.
(28) Bayot, D.; Devillers, M. *Coord. Chem. Rev.* **2006**, *250*, 2610–2626.
(29) (a) Somma, F.; Canton, P.; Strukul, G. *J. Catal.* **2005**, *229*, 490–498. (b) Ruddy, D. A.; Tilley, T. D. *J. Am. Chem. Soc.* **2008**, *130*, 11088–11096.
(30) (a) Egami, H.; Katsuki, T. *J. Am. Chem. Soc.* **2007**, *129*, 8940–8941. (b) Tashiro, T.; Mori, K. *Tetrahedron: Asymmetry* **2005**, *16*, 1801–1806.

939, 862, 822, 748, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ 10.31 (bs, 2H), 8.00 (d, 2H, $J = 8.3$ Hz), 7.92 (d, 2H, $J = 8.1$ Hz), 7.68−7.61 (m, 4H), 7.40 (t, 2H, $J = 6.9$ Hz), 7.31−7.01 (m, 26H), 6.94 (t, 2H, $J = 7.3$ Hz), 6.67 (d, 4H, $J = 6.6$ Hz), 4.02 (d, 2H, $J = 13.5$ Hz), 3.55 (d, 2H, $J = 13.5$ Hz), 3.44 (s, 2H), 1.76 (bs, 2H). ^{13}C NMR ($CDCl_3$): δ 153.0, 142.6, 139.5, 136.7, 134.5, 132.9, 132.8, 131.2, 128.9, 128.3, 128.0, 127.8, 127.7, 127.5, 127.4, 127.1, 126.6, 126.2, 126.1, 125.5, 125.0, 124.4, 122.7, 119.1,65.1, 49.9. Anal. Calcd for $C_{68}H_{52}N_2O_2$: C, 87.90; H, 5.64; N, 3.01. Found: C, 87.62; H, 5.72; N, 2.95.

4.2.3. Ligand 20. Yellow powder. IR (KBr): 3530, 3051, 2922, 2851, 1624, 1597, 1507, 1433, 1254, 1111, 1028, 941, 858, 764, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.99 (d, 2H, $J = 8.3$ Hz), 7.90 (d, 2H, $J = 8.3$ Hz), 7.68−7.60 (m, 4H), 7.51−6.77 (m, 38H), 4.48 (bs, 2H), 3.99 (d, 2H, $J = 13.8$ Hz), 3.33 (d, 2H, $J = 13.8$ Hz). ^{13}C NMR ($CDCl_3$): δ 153.0, 143.0, 139.4, 134.8, 134.3, 133.1, 133.0, 132.9, 131.7, 131.2, 129.2, 128.7, 128.4, 128.3, 128.0, 127.9, 127.8, 127.5, 127.3, 127.1, 126.7, 126.4, 126.2, 126.1, 125.5, 125.4, 125.3, 125.0, 124.4, 124.2, 123.0, 122.6, 118.8, 58.7, 49.7. ESI^+-TOFMS. Calcd for $[C_{76}H_{56}N_2O_2+H]^+$: $m/z = 1029.4415$. Found: $m/z = 1029.4412$.

4.3. Synthesis of μ-Oxo−Nb(salan) Complexes. 4.3.1. Complex 3. To the CH_2Cl_2 solution of salan ligand **1** (450 mg, 0.54 mmol) was added $Nb(OiPr)_5$ (210 mg, 0.54 mmol) under a nitrogen atmosphere, and the solution immediately changed to a light-yellow color. After the mixture was stirred for 1 h, it was exposed to air. The composition was monitored by ^1H NMR analysis. When monomer complex **2** was completely converted, the solvent was removed and **3** was purified with silica gel chromatography (CH_2Cl_2/MeOH = 100/1) to give 362.2 mg or a 72% yield. Light-yellow crystals. IR (KBr): 3250, 3051, 2932, 2860, 1622, 1595, 1495, 1448, 1423, 1354, 1256, 1113, 953, 883, 748, 698, 663 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.78 (d, 2H, $J = 8.5$ Hz), 7.74 (d, 2H, $J = 8.3$ Hz), 7.61 (t, 4H, $J = 8.4$ Hz), 7.58−7.48 (m, 6H), 7.45−7.05 (m, 20H), 6.99 (d, 2H, $J = 8.5$ Hz), 6.94−6.83 (m, 10H), 6.82−6.71 (m, 10H), 6.67−6.61 (m, 2H), 6.58−6.50 (m, 6H), 5.00−4.93 (m, 2H), 4.76 (d, 2H, $J = 14.6$ Hz), 4.09−4.01 (m, 2H), 3.83−3.72 (m, 2H), 3.56 (d, 2H, $J = 10.7$ Hz), 2.52−2.40 (m, 2H), 1.73−0.93 (m, 10H), 0.45−0.25 (m, 6H), −0.12− −0.26 (m, 2H), −0.30 to −0.46 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 156.1, 154.2, 142.7, 141.3, 138.8, 136.8, 136.3, 134.4, 133.5, 133.0, 132.0, 131.9, 131.8, 131.4, 129.1, 128.4, 127.9, 127.5, 127.3, 127.1, 126.9, 126.5, 126.2, 125.9, 125.7, 125.4, 125.3, 124.5, 122.9, 122.4, 120.6, 119.5, 59.4, 59.3, 51.9, 48.8, 28.7, 27.4, 24.2, 23.8. Anal. Calcd for $C_{120}H_{96}N_4Nb_2O_7 + H_2O$: C, 75.46; H, 5.17; N, 2.93. Found: C, 75.41; H, 5.24; N, 2.89%. ESI^+-TOFMS. Calcd for $[C_{120}H_{96}N_4Nb_2O_7+H]^+$: $m/z = 1892.5512$. Found: $m/z = 1892.5524$.

4.3.2. Complex 4. Light-yellow crystals. IR (KBr): 2949, 2864, 1593, 1445, 1423, 1352, 1252, 1113, 881, 698 cm^{-1}. ^1H NMR ($CDCl_3$): δ 18.06−7.97 (m, 2H), 7.85−7.76 (m, 2H), 7.74−6.30 (m, 56H), 5.96−5.85 (m, 4H), 4.92−4.80 (m, 2H), 4.55−4.36 (m, 4H), 3.78−3.66 (m, 2H), 2.64−2.47 (m, 4H), 2.26−2.14 (m, 2H), 1.95−1.75 (m, 4H) 1.40−0.76 (m, 14H). ^{13}C NMR ($CDCl_3$): δ 155.9, 155.6, 141.8, 140.9, 140.8, 140.4, 134.7, 133.2, 133.1, 133.0, 132.9, 132.8, 131.9, 128.8, 128.5, 128.2, 128.1, 127.7, 127.5, 127.4, 127.0, 126.9, 126.7, 126.5, 125.8, 125.7, 125.6, 125.5, 125.3, 125.2, 125.1, 125.0, 124.8, 124.1, 122.9, 122.7, 122.3, 121.7, 120.6, 61.7, 60.9, 52.4, 51.5, 32.2, 28.1, 25.0, 24.8. ESI^+-TOFMS. Calcd for $[C_{120}H_{96}N_4Nb_2O_7 + K]^+$: $m/z = 1930.5071$. Found: $m/z = 1930.5074$.

4.3.3. Complex 5. Slightly yellow crystals. IR (KBr): 2953, 2866, 1474, 1442, 1242, 1165, 1128, 881, 843, 708, 544 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.32−7.24 (m, 2H), 7.20−7.16 (m, 2H), 6.89−6.84 (m, 2H), 6.71−6.66 (m, 2H), 4.87 (d, 2H, $J = 14.3$), 4.11 (d, 2H, $J = 14.3$), 3.96−3.85 (m, 2H), 3.51 (d, 2H, $J = 12.0$), 3.33−3.20 (m, 2H), 2.42−2.12 (m, 6H), 1.85−0.88 (m, 86H), 0.80−0.64 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 156.8, 155.8, 141.6, 140.0, 136.7, 136.5, 124.4, 124.2, 123.5, 123.1, 121.2, 60.0, 59.8, 52.0, 49.0, 35.4, 35.1, 34.3, 34.2, 31.8, 31.7, 31.1, 30.7, 30.0, 28.2, 24.8, 24.1. ESI^+-TOFMS. Calcd for $[C_{72}H_{112}N_4Nb_2O_7+H]^+$: $m/z = 1331.6731$. Found: $m/z = 1331.6729$.

4.3.4. Complex 6. Light-yellow crystals. IR (KBr): 3242, 3051, 2934, 2858, 1622, 1595, 1495, 1448, 1425, 1354, 1256, 1113, 955, 862, 746, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.80−7.73 (m, 4H), 7.66−7.48 (m, 10H), 7.43−7.05 (m, 20H), 7.03−6.68 (m, 24H), 6.60−6.49 (m, 6H), 4.96−4.91 (m, 2H), 4,81 (d, 2H, $J = 14.6$ Hz), 4.13−4.05 (m, 2H), 3.91−3.81 (m, 2H), 3.64−3.56 (m, 2H), 2.53−2.41 (m, 2H), 1.86−1.09 (m, 8H), 1.04−0.89 (m, 2H), 0.55−0.28 (m, 6H), −0.10 to −0.23 (m, 2H), −0.30 to −0.44 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 155.2, 154.0, 142.9, 141.5, 139.0, 136.9, 136.6, 134.7, 133.7, 133.1, 132.1, 132.0, 131.5, 129.3, 128.5, 128.2, 128.1, 127.7, 127.5, 127.3, 127.1, 126.9, 126.8, 126.3, 126.1, 126.0, 125.9, 125.8, 125.5, 125.2, 125.0, 123.2, 122.7, 122.1, 120.5, 59.8, 51.8, 48.9, 29.1, 27.5, 24.5, 24.1. ESI^+-TOFMS. Calcd for $[C_{120}H_{96}N_4Ta_2O_7+H]^+$: $m/z = 2068.6345$. Found: $m/z = 2068.6352$.

4.3.5. Complex 7. Light-yellow crystals. IR (KBr): 3248, 3051, 2932, 2858, 1620, 1595, 1489, 1448, 1421, 1352, 1254, 1111, 953, 816, 748 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.77 (d, 2H, $J = 8.1$ Hz), 7.71 (d, 2H, $J = 8.3$ Hz), 7.66 (d, 2H, $J = 8.1$ Hz), 7.60−7.52 (m, 6H), 7.47−7.00 (m, 48H), 6.98−6.92 (m, 4H), 6.91−6.84 (m, 4H), 6.80 (d, 4H, $J = 8.3$ Hz), 6.72 (d, 4H, $J = 8.3$ Hz), 6.58−6.50 (m, 4H), 4.93−4.78 (m, 4H), 4.16−4.06 (m, 2H), 3.85−3.73 (m, 2H), 3.57−3.50 (m, 2H), 2.44−2.31 (m, 2H), 1.74−1.64 (m, 2H), 1.42−1.30 (m, 2H), 1.20−1.06 (m, 4H), 0.69−0.24 (m, 8H), −0.30 to −0.54 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 156.4, 154.4, 141.7, 140.4, 139.5, 139.2, 138.6, 138.3, 137.2, 136.6, 136.5, 134.8, 133.7, 133.2, 132.2, 132.1, 131.9, 131.7, 129.6, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 127.7, 127.5, 127.3, 127.2, 127.1, 126.8, 126.7, 126.6, 126.5, 126.4, 126.2, 126.1, 125.8, 125.7, 125.6, 125.5, 124.7, 124.4, 123.2, 122.6, 121.1, 119.8, 59.7, 59.3, 52.1, 49.4, 29.0, 27.5, 24.4, 23.7. Anal. Calcd for $C_{144}H_{112}N_4Nb_2O_7$: C, 78.75; H, 5.14; N, 2.55. Found: C, 78.64; H, 5.23; N, 2.52.

4.4. Asymmetric Epoxidation of Allylic Alcohols with Hydrogen Peroxide. 4.4.1. μ-Oxo−Nb(salan) 3-Catalyzed Epoxidation of Allylic Alcohols. The μ-Oxo−Nb(salan) complex (**3**, 18.9 mg, 2 mol %) and allylic alcohol (0.5 mmol) were dissolved in toluene, and the mixture was raised to 40 °C. Hydrogen peroxide in the form of a urea adduct (194 mg, 4 equiv) was added all at once. After the mixture was stirred for 24 h, it was diluted with brine and EtOAc. The organic phase was separated and passed through anhydrous Na_2SO_4. The crude mixture was purified with silica gel chromatography (hexane/EtOAc = 9/1). The ee value was determined by HPLC analysis on a chiral stationary phase column. When it was necessary to convert to the corresponding benzoate, triethylamine (1.2 equiv) and benzoyl chloride (1.2 equiv) were added to the CH_2Cl_2 solution of epoxy alcohol and the mixture was stirred for 1 h, followed by purification with silica gel chromatography (pentane/Et_2O = 19/1).

4.4.2. In Situ Method for the Nb(salan)-Catalyzed Asymmetric Epoxidation of Allylic Alcohols. To a $CHCl_3$ solution (1 mL) of salan ligand (5 mol %) was added $Nb(OiPr)_5$ (4 mol %) at room temperature. After stirring for 1 h, substrate (0.5 mmol) and brine (0.5 mL) were added to the mixture. After the reaction mixture was stirred for 30 min at 40 °C, 30% aqueous hydrogen peroxide (1.5 equiv) was dropped into the mixture every 2 h in seven batches. After being stirred for 24 h at 40 °C, the mixture was diluted with ethyl acetate and brine and the two phases were separated. The organic phase was passed through anhydrous Na_2SO_4 and evaporated. The residue was analyzed via chromatography on basic silica gel (pentane/Et_2O = 3/2) to give the product. The ee value was determined by HPLC analysis on a chiral stationary phase column. When it was necessary to convert to the corresponding benzoate, triethylamine (1.2 equiv) and benzoyl chloride (1.2 equiv) were added to the CH_2Cl_2 solution of epoxy alcohol and the mixture was stirred for 1 h, followed by purification with silica gel chromatography (pentane/Et_2O = 19/1).

4.4.2.1. (2*S*,3*S*)-3,7-Dimethyl-2,3-epoxy-6-octenol (10a, Table 5, Entry 7). Colorless oil. 69.6 mg, 82% yield. 84% ee. $[\alpha]^{24}_D$ −4.8 (*c* 2.90, $CHCl_3$), [lit. (2*S*,3*S*)-isomer (91% ee); $[\alpha]^{25}_D$ −5.3 (*c* 3.0, $CHCl_3$)].[3b] IR (neat): 3412, 2966, 2924, 2856, 1643, 1448, 1383,

1223, 1033, 864 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 5.12−5.05 (m, 1H), 3.88−3.79 (m, 1H), 3.73−3.65 (m, 1H), 2.97 (dd, 1H, J = 4.4, 6.8 Hz), 2.13−2.03 (m, 2H), 1.75−1.59 (m, 7H), 1.52−1.43 (m, 1H), 1.30 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 132.0, 123.2, 62.9, 61.5, 61.2, 38.6, 25.8, 23.8, 17.8, 16.9. Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.38; H, 10.59%.

4.4.2.2. (2*S*,3*R*)-3,7-Dimethyl-2,3-epoxy-6-octenol (10b, Table 5, Entry 8). Colorless oil. 64.5 mg, 76% yield. 83% ee. $[\alpha]^{23}_D$ −18.8 (*c* 1.52, $CHCl_3$), [lit. (2*R*, 3*S*)-isomer (99% ee); $[\alpha]^{28}_D$ +13.3 (*c* 1.09, $CHCl_3$)].[30] IR (neat): 3414, 2966, 2924, 2862, 1641, 1448, 1381, 1033, 866 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 5.14−5.06 (m, 1H), 3.88−3.78 (m, 1H), 3.72−3.62 (m, 1H), 2.97 (dd, 1H, J = 4.4, 6.8 Hz), 2.20−2.04 (m, 2H), 1.75−1.60 (m, 7H), 1.54−1.43 (m, 1H), 1.35 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 132.2,123.0, 64.0, 61.4, 61.1, 33.0, 25.6, 24.1, 22.1, 17.6. ESI$^+$-TOFMS. Calcd for $[C_{10}H_{18}O_2$ + Na$]^+$: m/z = 193.1199. Found: m/z = 193.1194.

4.4.2.3. (2*S*,3*S*)-2,3-Epoxy-3,7,11-trimethyl-6,10-dodecadienol (10c, Table 2, Entry 2). Colorless oil. 85.5 mg, 72% yield. 80% ee. $[\alpha]^{24}_D$ − 5.7 (*c* 1.083 $CHCl_3$), [lit. (2*R*, 3*R*)-isomer (96% ee); $[\alpha]^{26}_D$ +6.53 (*c* 4.21, $CHCl_3$)].[31] IR (neat): 3416, 2964, 2922, 2856, 1663, 1448, 1383, 1223, 1105, 1074, 1034, 864 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 5.14−5.05 (m, 2H), 3.88−3.78 (m, 1H), 3.73−3.64 (m 1H), 2.98 (dd, 1H, J = 4.3, 6.7 Hz), 2.14−2.02 (m, 4H), 2.01−1.95 (m, 2H), 1.80 (br, 1H), 1.74−1.57 (m, 10H), 1.52−1.43 (m, 1H), 1.31 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 135.6, 131.3, 124.0, 123.0, 62.9, 61.5, 61.2, 39.7, 38.6, 26.7, 25.8, 23.7, 17.8, 16.9, 16.1. Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.40; H, 11.00.

4.4.2.4. (2*S*,3*S*)-2,3-Epoxy-5-phenylpentanol (12a, Table 4, Entry 11). Colorless oil. 72.1 mg, 81% yield. 92% ee. $[\alpha]^{24}_D$ −45.4 (*c* 1.82, $CHCl_3$), [lit. (2*R*,3*R*)-isomer (97% ee); $[\alpha]^{25}_D$ +42.6 (*c* 2.41, $CHCl_3$)].[32] IR (neat): 3416, 3024, 2926, 2860, 1495, 1452, 1090,1028, 880, 750, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.35−7.15 (m, 5H), 3.84 (ddd, 1H, J = 2.7, 5.4, 12.7 Hz), 3.61−3.53 (m, 1H), 2.99 (ddd, 1H, J = 2.2, 5.9, 5.9 Hz), 2.89−2.69 (m, 3H), 1.98−1.82 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 140.9, 128.3, 128.2, 126.0, 61.6, 58.6, 55.4, 33.4, 32.3. Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.94; H, 7.86.

4.4.2.5. (2*S*,3*S*)-2,3-Epoxyhexanol (12b, Table 5, Entry 1). Colorless oil. 33.3 mg, 57% yield. 91% ee. $[\alpha]^{22}_D$ −47.4 (*c* 0.66, $CHCl_3$), [lit. (2*S*,3*S*)-isomer (94% ee); $[\alpha]^{25}_D$ −46.3 (*c* 3.87, $CHCl_3$)].[3b] IR (neat): 3416, 2961, 2932, 2872, 1464, 1410, 1101, 1067, 1045, 899, 854 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.99−3.85 (m, 1H), 3.70−3.57 (m, 1H), 3.04−2.88 (m, 2H), 1.94−1.83 (m, 1H), 1.62−1.39 (m, 4H), 0.97 (t, 3H, J = 7.3 Hz). ^{13}C NMR ($CDCl_3$): δ 61.7, 58.4, 55.9, 33.7, 19.4, 14.0. ESI$^+$-TOFMS. Calcd for $[C_6H_{12}O_2$ + Na$]^+$: m/z = 139.0730. Found: m/z = 139.0733.

4.4.2.6. (2*S*,3*S*)-2,3-Epoxyoctanol (12c, Table 5, Entry 2). Colorless solid. 56.4 mg, 79% yield. 93% ee. $[\alpha]^{22}_D$ −41.9 (*c* 0.94, $CHCl_3$), [lit. (2*S*,3*S*)-isomer (99% ee); $[\alpha]^{20}_D$ −40.4 (*c* 1.08, $CHCl_3$)].[33] mp 37.2−37.4 °C. IR (KBr): 3280, 3132, 2954, 2928, 2853, 1460, 1375, 1080, 1038, 1007, 989, 878, 714 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.96−3.88 (m, 1H), 3.68−3.59 (m, 1H), 2.99−2.90 (m, 2H), 1.79 (br, 1H), 1.71−1.24 (m, 8H), 0.95−0.84 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 61.7, 58.5, 56.1, 31.7, 31.6, 25.7, 22.7, 14.1. Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.70; H, 11.04.

4.4.2.7. (2*S*,3*S*)-3-Cyclohexyl-2,3-epoxypropanol (12d, Table 5, Entry 3). Colorless oil. 64.4 mg, 82% yield. 93% ee. $[\alpha]^{24}_D$ −31.3 (*c* 1.20, $CHCl_3$), [lit. (2*S*,3*S*)-isomer (92% ee); $[\alpha]^{25}_D$ −23.9 (*c* 7.2, $CHCl_3$)].[34] IR (neat): 3414, 2926, 2853, 1448, 1069, 1047,1018, 974, 881, 864, 756 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.96−3.87 (m, 1H), 3.66−3.56 (m, 1H), 2.98 (ddd, 1H, J = 2.4, 2.4, 4.6 Hz), 2.76 (dd, 1H, J = 2.4, 6.8), 1.90−1.60 (m, 6H), 1.33−1.03 (m, 6H). ^{13}C NMR ($CDCl_3$): δ 61.9, 60.2, 57.3, 39.6, 29.7, 29.0, 26.3, 25.8, 25.6. Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 68.91; H, 10.28.

4.4.2.8. (2*S*,3*S*)-4,4-Dimethyl-2,3-epoxypentanol (12e, Table 5, Entry 4). Colorless oil. 34.1 mg, 52% yield. 95% ee. $[\alpha]^{24}_D$ −20.4 (*c* 1.33, $CHCl_3$), [lit. (2*S*,3*S*)-isomer (95% ee); $[\alpha]^{20}_D$ −20.1 (*c* 1.3, $CHCl_3$)].[34] IR (neat): 3414, 2959, 2870, 1483, 1466, 1366, 1086, 1040, 899 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.91 (ddd, 1H, J = 2.4, 5.4, 12.5 Hz), 3.65−3.57 (m, 1H), 3.06−3.02 (m, 1H), 2.76 (d, 1H, J = 2.4 Hz), 1.78−1.71 (m, 1H), 0.94 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 63.6, 62.1, 55.4, 30.6, 25.9. ESI$^+$-TOFMS. Calcd for $[C_7H_{14}O_2$+Na$]^+$: m/z = 153.0886. Found: m/z = 153.0885.

4.4.2.9. (2*S*,3*S*)-2,3-Epoxy-3-phenylpropanol (12f, Table 5, Entry 5). White solid. 45.7 mg, 61% yield. 74% ee. $[\alpha]^{25}_D$ −38.5 (*c* 1.05, $CHCl_3$), [lit. (2*S*,3*S*)-isomer (>98% ee); $[\alpha]^{25}_D$ −49.6 (*c* 2.4, $CHCl_3$)].[3b] mp 42.7−43.0 °C. IR (KBr): 3381, 3030, 2988, 2924, 2868, 1605, 1497, 1462, 1312, 1290, 1231, 1200, 1070, 1024, 880, 768, 698 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.40−7.23 (m, 5H), 4.05 (ddd,1H, J = 2.2, 5.4, 12.7 Hz), 3.92 (d, 1H, J = 2.2 Hz), 3.80 (ddd, 1H, J = 3.9, 7.6, 12.7 Hz), 3.23 (ddd, 1H, J = 2.2, 2.2, 3.9 Hz), 2.14−2.07 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 136.4, 128.4, 128.2, 125.6, 62.5, 61.2, 55.6. Anal. Calcd for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 72.01; H, 6.74.

4.4.2.10. (2*S*,3*R*)-2,3-Epoxyhexanol (14, Table 5, Entry 6). Colorless oil. 30.0 mg, 52% yield. 85% ee. $[\alpha]^{26}_D$ −5.4 (*c* 1.23, $CHCl_3$), [lit. (2*S*,3*R*)-isomer (63% ee); $[\alpha]_D$ −2.3 (*c* 1.000, $CHCl_3$)].[7a] IR (neat): 3412, 2961, 2934, 2872, 1464, 1381, 1042, 914, 858, 829, 768 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.92−3.82 (m, 1H), 3.73−3.62 (m, 1H), 3.20−3.13 (m, 1H), 3.09−3.01 (m, 1H), 2.14−2.02 (m, 1H), 1.62−1.41 (m, 4H), 1.02−0.95 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 61.0, 57.2, 56.9, 30.0, 20.1, 14.0. ESI$^+$-TOFMS. Calcd for $[C_6H_{12}O_2$+Na$]^+$: m/z = 139,0730. Found: m/z = 139.0734.

4.4.2.11. (2*R*,3*R*)-2,3-Epoxy-2-methyl-3-phenylpropanol (16a, Table 5, Entry 9). Colorless solid. 25.8 mg, 40% yield. 83% ee. $[\alpha]^{25}_D$ +14.3 (*c* 1.00, $CHCl_3$), [lit. (2*S*,3*S*)-isomer (>98% ee), $[\alpha]_D$ −16.9 (*c* 2.00, $CHCl_3$)].[3b] mp 50.9−51.0 °C. IR (KBr): 3420, 3061, 2995, 2970, 2930, 2864, 1497, 1450, 1383, 1234, 1094, 1069, 851, 741, 698 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.41−7.25 (m, 5H), 4.22 (s, 1H), 3.86 (dd, 1H, J = 2.9, 12.2 Hz), 3.76 (dd, 1H, J = 8.4, 12.2 Hz), 1.99 (br, 1H), 1.09 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 135.4, 128.0, 127.4, 126.2, 64.9, 63.7, 60.1, 13.6. Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 72.98; H, 7.30.

4.4.2.12. (2*R*)-2,3-Epoxy-2-phenylpropanol (16b, Table 5, Entry 10). Colorless oil. 32.2 mg, 43% yield. 85% ee. $[\alpha]^{24}_D$ +16.9 (*c* 1.30, EtOH), [lit. (*S*)-isomer (98% ee); $[\alpha]^{25}_D$ −15.8 (*c* 2.53 EtOH)].[35] IR (neat): 3412, 3059, 2922, 1496, 1448, 1385, 1088, 1043, 1024, 760, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.42−7.29 (m, 5H), 4.11 (dd, 1H, J = 2.9, 12.7 Hz), 4.02 (dd, 1H, J = 8.9, 12.7 Hz), 3.28 (d, 1H, J = 5.1 Hz), 2.83 (d, 1H, J = 5.1 Hz) 1.86 (br, 1H). ^{13}C NMR ($CDCl_3$): δ 137.2, 128.4, 128.0, 125.8, 63.1, 60.4, 52. 5. ESI$^+$-TOFMS. Calcd for $[C_9H_{10}O_2$+Na$]^+$: m/z = 173.0573. Found: m/z = 173.0577.

4.4.2.13. (+)-2,3-Epoxy-2-methyl-5-phenylpentanol (16c, Table 5, Entry 11). Colorless oil. 61.6 mg, 64% yield. 90% ee. $[\alpha]^{23}_D$ +29.7 (*c* 1.25, $CHCl_3$). IR (neat): 3416, 3024, 2997, 2926, 2858, 1603, 1495, 1452, 1385, 1072, 1040, 866, 750, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.34−7.26 (m, 2H), 7.25−7.17 (m, 3H), 3.63 (dd, 1H, J = 3.7, 12.2 Hz), 3.51 (dd, 1H, J = 8.3, 12.2 Hz), 3.09 (dd, 1H, J = 6.3, 6.3 Hz), 2.91−2.81 (m, 1H), 2.77−2.67 (m, 1H), 2.02−1.92 (m, 1H), 1.89−1.76 (m, 2H), 1.12 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 140.9, 128.3, 126.0, 65.3, 61.2, 59.6, 32.8, 30.1, 14.2. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.68; H, 8.39.

4.4.2.14. (2*R*)-2,3-Epoxy-2-benzylpropanol (16d, Table 5, Entry 12). Colorless oil. 42.6 mg, 52% yield. 90% ee. $[\alpha]^{23}_D$ +36.1 (*c* 1.03, CH_2Cl_2), [lit. (*S*)-isomer (>98% ee); $[\alpha]_D$ −39 (*c* 2.5,

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CH_2Cl_2)].[36] IR (neat): 3422, 3028, 2922, 2871, 1603, 1495, 1454, 1400, 1051, 972, 912, 876, 804, 758, 702, 605 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.32−7.28 (m, 2H), 7.26−7.21 (m, 3H), 3.76−3.71 (dd, 1H, J = 4.7, 12.4 Hz), 3.61−3.56 (dd, 1H, J = 8.0, 12.4 Hz), 3.09−3.06 (d, 1H J = 14.4 Hz), 2.89−2.87 (d, 1H, J = 4.4 Hz), 2.89−2.85 (d, 1H, J = 14.4 Hz), 2.67−2.66 (d, 1H, J = 4.4 Hz), 1.87−1.84 (dd, 1H, J = 8.0, 4.7). ^{13}C NMR ($CDCl_3$): δ 136.0, 129.5, 128.5, 126.8, 62.7, 60.0, 49.6, 38.2. ESI^+-TOFMS. Calcd for $[C_{10}H_{12}O_2+Na]^+$: m/z = 187.0730. Found: m/z = 187.0732.

4.5. Study of the Correlation between the ee Value of Ligand 1 and the ee Value of Ligand 12a. Ligands **1** and *ent*-**1** were mixed in certain ratios, and the ee's of the mixtures were determined by HPLC analysis on a chiral stationary phase column (Daicel Chiralpak AD-H; hexane/*i*-PrOH = 90/10).

To the toluene solution (1 mL) of each mixed ligand (5 mol %) was added $Nb(OiPr)_5$ (4 mol %) at room temperature. After the mixture was stirred for 1 h, **11a** (0.5 mmol) and brine (0.5 mL) were added. After the mixture was stirred for 30 min at 40 °C, aqueous hydrogen peroxide (1.5 equiv) was added dropwise every 2 h in seven batches. After the mixture was stirred for 24 h at 40 °C, it was diluted with ethyl acetate and brine and the two phases were separated. The organic phase was passed through anhydrous Na_2SO_4 and evaporated. The residue was analyzed via chromatography on basic silica gel (pentane/Et_2O = 3/2) to give the product. The ee value was determined by HPLC analysis on a chiral stationary phase column (Daicel Chiralpak OD-H; hexane/*i*-PrOH = 95/5).

These results were plotted as shown in Figure 3.

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Supporting Information Available: X-ray crystallographic data files in CIF format for complex **7** and HPLC conditions and NMR spectral data for benzoated epoxy alcohols. This material is available free of charge via the Internet at http://pubs.acs.org.

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