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Catalytic Asymmetric Ring-Opening Reaction of *meso*-Epoxides with Aryl Selenols and Thiols Catalyzed by a Heterobimetallic Gallium-Titanium-Salen Complex

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Abstract: A chiral heterobimetallic Lewis acid complex has been developed as an efficient catalyst. The enantioselective desymmetrization of *meso*-epoxides with aryl selenols and thiols catalyzed by the heterobimetallic complex has been optimized. The optically active β-arylseleno alcohols and β-hydroxy sulfides were obtained in good yields and high enantioselectivities (up to 97% *ee* and 92% *ee*, respectively). A strong synergistic effect between different Lewis acids was exhibited in the catalytic process.

Keywords: asymmetric catalysis; catalyst design; epoxides; gallium; synthetic methods

Introduction

The design and use of bimetallic complexes for asymmetric catalysis have seen significant progress and is emerging as a rapidly developing area. Inspired by the advantages of enzymes containing two or more active sites, and in the assumption that the potential well-organized spatial arrangement of the bimetallic or multimetallic complex would make the reaction more reactive and selective, chemists have succeeded in developing several kinds of multifunctional catalysts for asymmetric reactions.[1] In the 1990s, Shibasaki and co-workers reported their first investigations using a chiral heterobimetallic complex in asymmetric reactions with good enantioselectivities.[2] Subsequently, they developed a series of bimetallic Lewis acid–Brønsted base, Lewis acid–Lewis acid catalytic systems for use in various asymmetric reactions with excellent results.[3] Recently, several other groups have also reported the successful applications of chiral bi- or multimetallic complexes in asymmetric reactions with high catalytic reactivities and enantioselectivities.[4]

Metal complexes of the salen ligand, classified as a "privileged catalyst", have been widely used in asymmetric reactions over the past several decades. Until now, many efforts have been devoted to developing new catalysts based on the salen framework. Quite recently, Shibasaki and co-workers reported the discovery and utility of a new type of salen complex – the dinucleated Schiff base complex **1** as efficient catalysts in asymmetric aza-Henry reactions and nitroaldol reactions (Figure 1).[5] This N_2O_4 Schiff base selectively incorporated M^1 into the inner N_2O_2 cavity and an oxophilic rare earth metal (M^2), into the outer O_4 cavity. They found that the cooperative function of the two metals was the key factor to achieving high diastereo- and enantioselectivity in the reactions.

The broad applicability of salen ligands makes further developments possible by serving as useful platforms for the discovery of new catalysts.[6b] For traditional metal-salen complexes, the tetradentate motif incorporates a metal into the N_2O_2 cavity to form a "closed" structure (Figure 1, previous work). Thus, many of the applications associated with these catalysts rely upon this arrangement and the predominance of the chelate effect.[6] In some cases, however, metal-salen complexes have been shown to support monometallic or bimetallic formulations of metals with a "open" mode. The fact that the monometallic

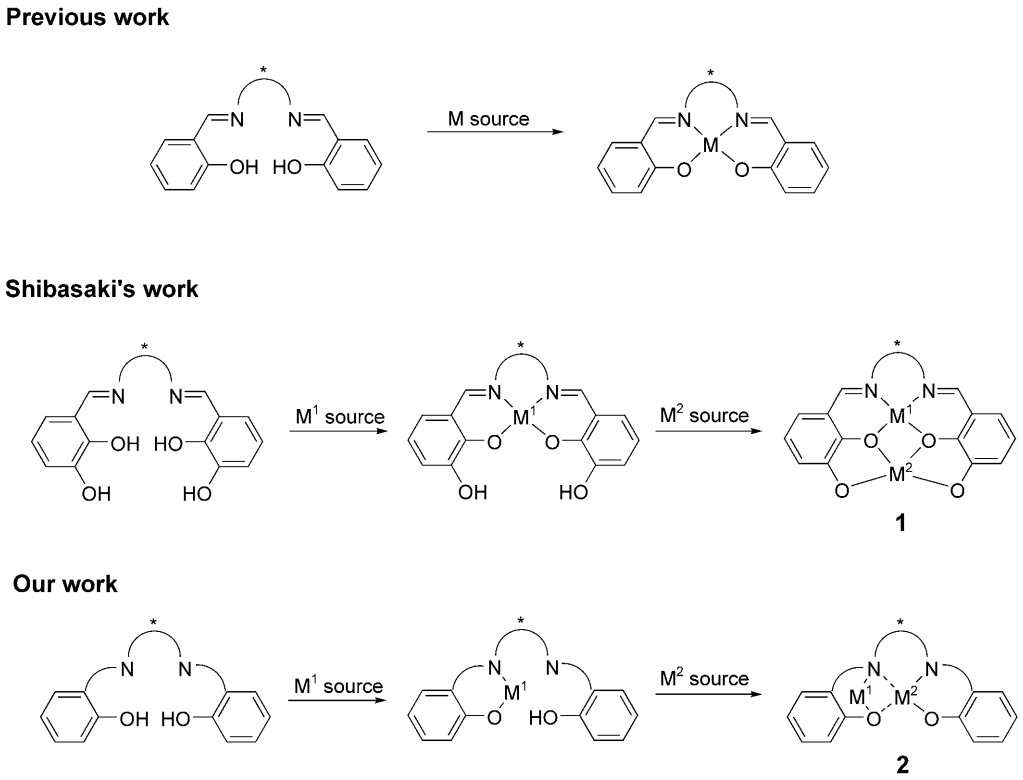


Figure 1. Different metal-ligand complexes.

"open" complex still contains an uncoordinated NO moiety makes it possible to incorporate another metal (M^2) into the N_2O_2 cavity, resulting in the formation of heterobimetallic complex **2** (Figure 1, our work). In addition, the design of this type of catalyst has also been governed by the hypothetical existence of cooperative effects between the two metal centers under the same chiral template, which may lead to better asymmetric induction in the reaction transition state. Furthermore, as it is well known that even if a small change in the structure of the catalyst may exert a tremendous influence on the catalytic reactivity and selectivity, this also prompted us to explore the applications of the heterobimetallic salen-M^1–M^2 complexes in asymmetric reactions.

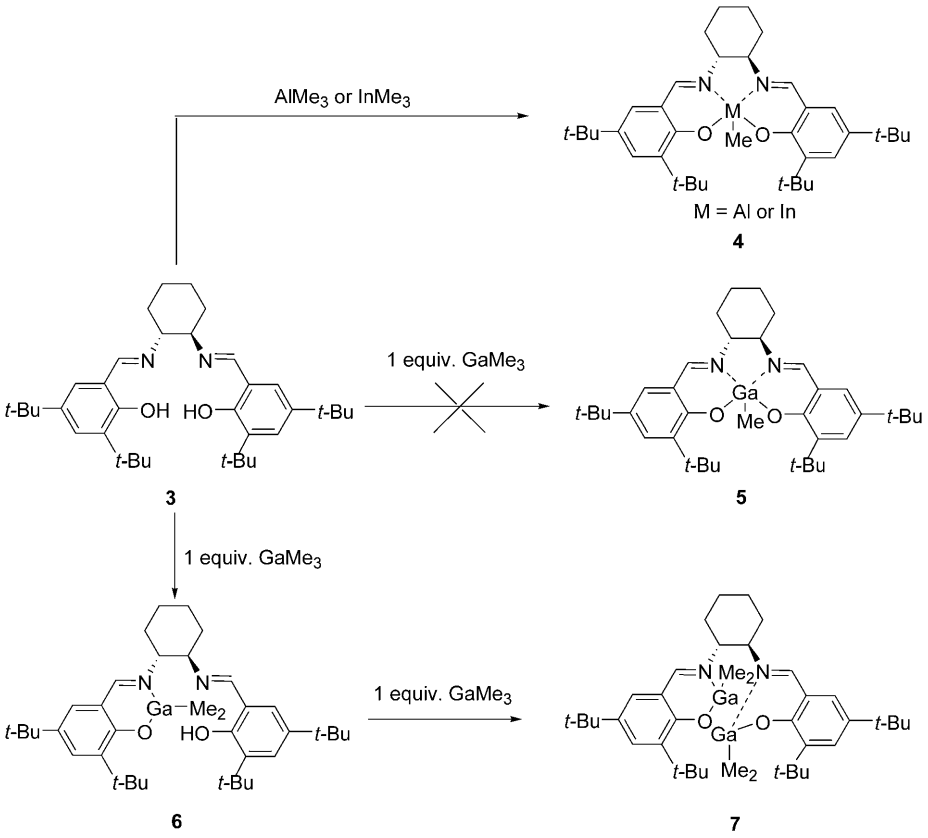
Compared with transition metals, the combination of group 13 elements with chiral salen ligands has attracted less attention in asymmetric reactions, except for salen-Al.[7] In general, group 13-salen complexes can be prepared by combining the ligand with trialkyl group 13 reagents in non-oxygenated solvents.[8] The reaction of $AlMe_3$ with a chiral salen ligand afforded the monometallic chelate salen-AlMe and we found the same situation with indium (Scheme 1). Meanwhile, the metal, Al or In, is coordinated by all of the four heteroatoms of the ligand in a planar arrangement. However, some investigations have reported and what we have discovered, is that gallium readily forms open structures with salen ligands (complex **6**, Scheme 1).[9] The reaction of 1 equivalent of $GaMe_3$ with salen gave the "open" complex **6** not **5**, subsequent reaction with another 1 equivalent of $GaMe_3$ furnished the "open" homobimetallic complex **7** (Scheme 1).

In the present work we report the reaction of monometallic chiral complexes (salen-$GaMe_2$) with another metal source (M^2) to form the heterobimetallic complexes (salen-Ga-M^2) and their applications in the enantioselective ring-opening reactions of *meso*-epoxides with aryl selenols and thiols.

Results and Discussion

The enantioselective desymmetrization of *meso*-epoxides with nucleophiles has proven to be a valuable tool for the straightforward synthesis of enantiomerically highly enriched 1,2-difunctionalized organic compounds.[10] Although ring-opening reactions of *meso*-epoxides with different nucleophiles have been described,[11] up to now, only a few reports have been concerned with the use of thiols as nucleophiles[12] and much less with selenols.[13]

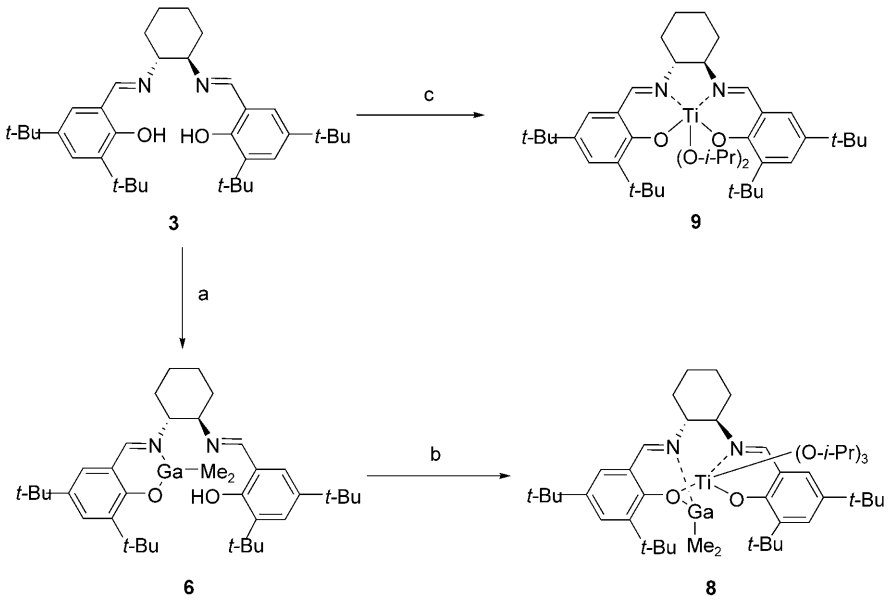
Our preliminary experiments showed that 5 mol% of Ga-Ti-salen complex effectively catalyzed the selenolysis of various *meso*-epoxides in excellent yields and enantioselectivities.[13a] Herein, we wish to report our further investigations on the optimizations of var-



Scheme 1. Reactions of salen ligand with different trimethyl group 13 reagents.

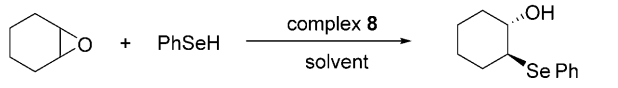
ious reaction parameters in the ring-opening reactions with aryl selenols and thiols.

In order to avoid solubility problems, we firstly investigated salen(*t*-Bu)-**3** which possesses *tert*-butyl groups at two positions on the phenol rings in the ring-opening reactions. As shown in Scheme 2, treatment of **3** with one equivalent of $GaMe_3$ provided monometallic "open" complex **6**. Subsequent reaction



Scheme 2. *Reagents and conditions:* a) $GaMe_3$, hexane, 0–25 °C, 4 h; b) Ti(O-*i*-Pr)$_4$ (1 equiv.), hexane, 0 °C, 1 h; c) Ti(O-*i*-Pr)$_4$, hexane, 0 °C, 1 h.

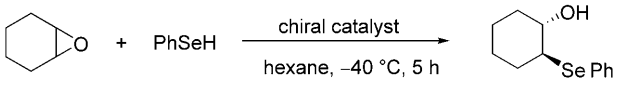
Table 1. Asymmetric ring-opening of cyclohexene oxide with selenophenol.[a]



Entry	Amount [mol%]	Solvent	Temp. [°C]	Time [h]	Yield [%][b]	*ee* [%][c]
1	10	Et_2O	20	2	96	69
2	10	CH_2Cl_2	20	2	90	35
3	10	toluene	20	2	93	83
4	10	hexane	20	2	96	85
5	10	hexane	0	3	96	90
6	10	hexane	−20	5	94	95
7	10	hexane	−40	5	94	97
8	10	hexane	−78	5	83	91
9	5	hexane	−40	5	93	97
10	2	hexane	−40	5	92	95
11	1	hexane	−40	5	85	92
12	0.5	hexane	−40	5	62	89
13[d]	5	Hexane	−40	5	92	94

[a] Unless otherwise noted, all reactions were conducted under the following conditions: cyclohexene oxide (1.0 mmol), PhSeH (1.1 mmol), catalyst **8** (10 mol%), solvent (3 mL).
[b] Isolated yields.
[c] Determined by HPLC with a Daicel Chiralcel OD-H column.
[d] 4 Å molecular sieves were added as additives.

Table 2. Asymmetric ring-opening of cyclohexene oxide with selenophenol.[a]



Entry	Catalyst	Yield [%][b]	*ee* [%][c]
1	**3**+$GaMe_3$ (**6**)	75	32
2	**3**+2 equivalent $GaMe_3$ (**7**)	75	35
3	**3**+Ti(O-*i*-Pr)$_4$ (**9**)	85	59
4	**3**+$GaMe_3$+Ti(O-*i*-Pr)$_4$ (1:1:0.5)	85	50
5	**3**+$GaMe_3$+Ti(O-*i*-Pr)$_4$ (1:1:2)	93	80
6	**3**+$GaMe_3$+Ti(O-*i*-Pr)$_4$ (1:1:3)	94	76

[a] *Reaction conditions:* cyclohexene oxide (1.0 mmol), PhSeH (1.1 mmol), catalyst (5 mol%), hexane (3 mL).
[b] Isolated yields.
[c] Determined by HPLC with a Daicel Chiralcel OD-H column.

with one equivalent of Ti(O-*i*-Pr)$_4$ gave the heterobimetallic complex **8** (Scheme 2), which was directly used as chiral catalyst in the reaction.

Using the *in situ* prepared complex **8** (10 mol%) as catalyst, we initially tested the asymmetric ring-opening of cyclohexene oxide with selenophenol as a model reaction in different solvents at 20 °C. From the summarized results (Table 1) we found that the solvents toluene and hexane gave the ring-opening products in good yields and high enantioselectivities (Table 1, entries 3 and 4), while diethyl ether displayed good reactivity but moderate selectivity (entries 1). The use of CH_2Cl_2 led to good yield but a very low *ee* value. Among the solvents tested, hexane was proven to be the best one in terms of yield and selectivity. A variation of the reaction temperature from 20 to −40 °C caused a significant increase in the enantioselectivity (up to 97%, entry 7), but a slight decrease was observed when the reaction was carried out at −78 °C (entry 8). Using hexane as solvent, different catalyst loadings were then investigated at −40 °C. The results showed there was no significant change in reactivity and selectivity when the catalyst loading was decreased to 5 mol% (entry 9). The reactions still showed good results even with 2 mol% catalyst loading (entry 10), and 1 mol% still provided the product in 92% *ee* and 85% yield (entry 11). However, further decreasing the catalyst loading to 0.5 mol% resulted in a moderate yield and a slight lower enantioselectivity (89% *ee*) (entry 12). However, the addition of 4 Å molecular sieves did not gave any positive effect (entry 13). So we chose 5 mol% catalyst loading, hexane as solvent and −40 °C as preferred reaction temperature for further optimization.

For comparison, the mono- and homobigallium catalysts **6**, **7** and monotitanium complex **9** have also been investigated under the above optimized reaction conditions. However, we found that when **6** and **7** were used, moderate yields and low selectivities were obtained. In particular, **6** and **7** displayed similar reactivity and selectivity (Table 2, entries 1 and 2). The use of cyclic titanium complex **9** provided high yield but moderate selectivity (entry 3). The molar ratio of Ga/Ti/**3** was also critical for the selectivity. Changing the molar ratio of $GaMe_3$/Ti(O-*i*-Pr)$_4$ to either higher or lower avlues resulted in a decreased enantioselectivity. Meanwhile, changing the ratio of $GaMe_3$/Ti(O-*i*-Pr)$_4$ to 1:0.5 gave a much lower enantioselectivity. So this optimization demonstrated that the combination of Ga-Ti-salen heterobimetallic complex in a ratio of 1:1:1 was essential for the high enantioselectivity.

The selection of the chiral ligand is an important factor in the asymmetric reaction. A suitable chiral ligand would offer an optimal chiral environment in the asymmetric induction process. Under the optimized reaction conditions (5 mol% catalyst loading, −40 °C, hexane as solvent), we initiated the optimization by investigating the steric and electron effects of the substituents on the phenyl ring of the salen ligands (Figure 2).[14] All chiral complexes were used with *in situ* formation. The results revealed that the bulky *ortho*-substitution on the phenyl ring of the

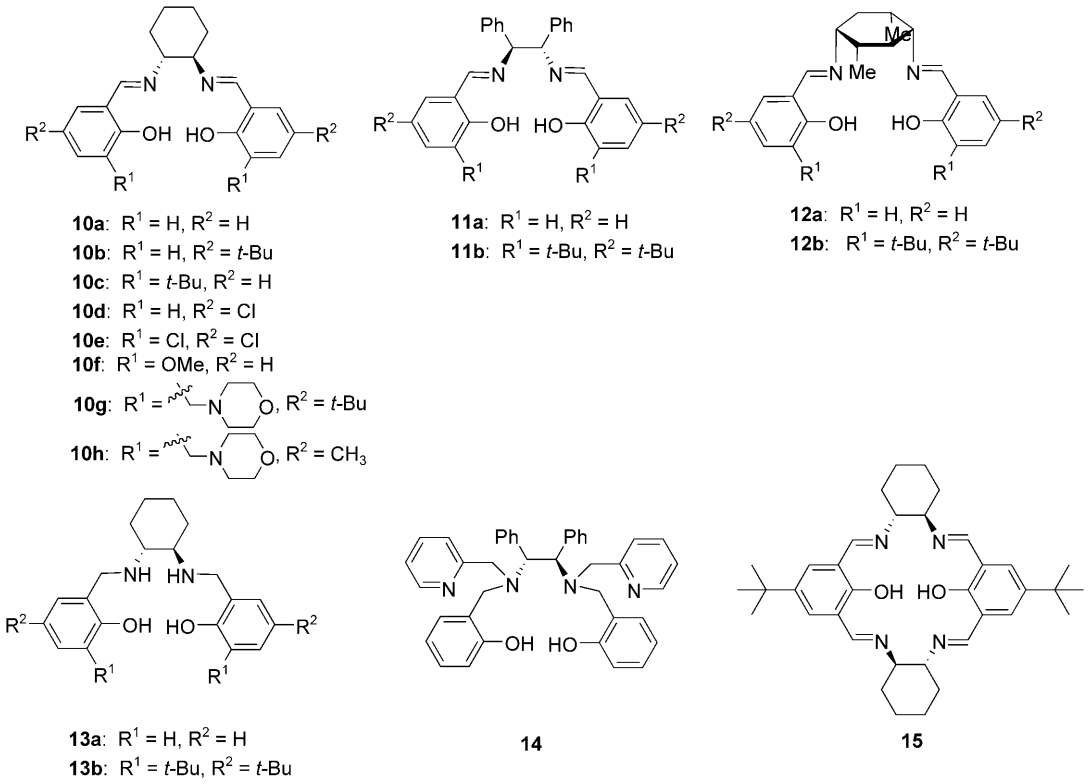
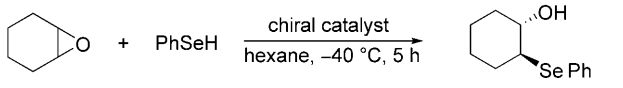


Figure 2. List of chiral ligands investigated in the ring-opening reaction.

Schiff base part was necessary for high enantioselectivity (Table 3, entries 3 and 5 *vs.* the others). However, the utilization of Kozlowski's modular bifunctional salen ligands,[15] which contain both Lewis acid and Lewis base activating groups, did not improve but rather decreased the reactivity and selectivity (entries 7 and 8). Secondly, we attempted to change the chiral backbone from cyclohexane-1,2-diamine to 1,2-diphenylethane-1,2-diamine and 2,5-dimethylcyclohexane-1,4-diamine,[16] but these changes did not make any improvements either on reactivity or on selectivity. Next, we chose salan [*N*,*N*′-alkylbis(salicylamine)] ligands as chiral sources. Compared with salen, salan ligands have increased basicity due to 2 N–H groups and a more flexible framework, these properties make possible the salan ligand and the metal atom binding in a non-planar arrangement which afforded superior asymmetric induction to metal-salen in several reactions.[17] However, the heterobimetallic complex Ga-Ti-**13** gave inferior selectivity and inverse configuration compared with the corresponding salen ligands (entries 13 and 14). A further modification towards an increase of the ligand's coordination sites[18] was performed, in the expectation that this hexadentate chiral ligand (**14**) could coordinate more easily with two metals to afford favorable stereochemical control in the asymmetric induction process. It turned out, however, that Ga-Ti-**14** gave poor results (entry 15). The last modification of the ligand structure was the change to the macrocycle Schiff-base ligand (**15**),[19] with the expectation that this multidentate N_4O_2-coordination compartment could bind the two metals in a planar mode. Unfortunately, the enantioselectivity obtained was still far from satisfying (entry 16). The optimization of the ligand structure revealed that ligand **3** remained the best one when combined with Ga and Ti species in this ring-opening reaction.

As the chiral complex Ga-Ti-**3** worked very well in the enantioselective ring-opening reaction of *meso*-epoxides with selenophenol, a further investigation on the combination of $GaMe_3$-**3** with different Lewis acids was performed. All reactions were conducted with 5 mol% chiral complexes in hexane at −40 °C. The results are summarized in Table 4. From the results we can see that the combination of Ga-$TiCl_4$-**3** caused a slight decrease in enantioselectivity (entry 1). Compared with Ti(O-*i*-Pr)$_4$, the use of the relatively weaker Lewis acid VO(O-*i*-Pr)$_3$ led to both lower reactivity and selectivity (entry 2). Similar phenomena were observed with $CrCl_3$ and $Cu(OAc)_2$ (entries 3 and 4). Also, the introduction of another trimethyl group 13 reagent, $AlMe_3$ or $InMe_3$, gave moderate reactivity but pretty low selectivity (entries 5 and 6). Screening of two rare earth metals indicated that both of them gave poor reactivities and low selectivities (entries 7 and 8). Inspection of different Lewis acids revealed that Ti(O-*i*-Pr)$_4$ was the best

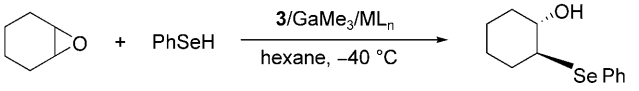
Table 3. Optimization of ligands in the ring-opening reaction.[a]



Entry	Ligand	Yield[b] [%]	*ee*[c] [%]	Configuration[d]
1	**10a**	85	32	(1*S*,2*S*)
2	**10b**	84	39	(1*S*,2*S*)
3	**10c**	93	72	(1*S*,2*S*)
4	**10d**	78	12	(1*S*,2*S*)
5	**10e**	73	55	(1*S*,2*S*)
6	**10f**	82	23	(1*S*,2*S*)
7	**10g**	81	36	(1*S*,2*S*)
8	**10h**	83	8	(1*S*,2*S*)
9	**11a**	92	47	(1*R*,2*R*)
10	**11b**	73	55	(1*R*,2*R*)
11	**12a**	64	28	(1*S*,2*S*)
12	**12b**	76	46	(1*S*,2*S*)
13	**13a**	83	30	(1*R*,2*R*)
14	**13b**	87	66	(1*R*,2*R*)
15	**14**	65	25	(1*R*,2*R*)
16	**15**	86	72	(1*S*,2*S*)

[a] *Reaction conditions:* cyclohexene oxide (1.0 mmol), PhSeH (1.1 mmol), catalyst (5 mol%), hexane (3 mL), −40 °C, 5 h.
[b] Isolated yields.
[c] Determined by HPLC with a Daicel Chiralcel OD-H column.
[d] Absolute configurations of the major products were assigned by comparison of CD spectroscopy with that of sulfur anologue with known absolute configuration.

Table 4. Optimization of Lewis acid in the ring-opening reaction.[a]



Entry	ML_n	Yield [%][b]	*ee* [%][c]	Configuration[d]
1	$TiCl_4$	93	88	(1*S*,2*S*)
2	$VO(O\text{-}i\text{-}Pr)_3$	66	34	(1*S*,2*S*)
3	$CrCl_3$	84	15	(1*S*,2*S*)
4	$Cu(OAc)_2$	63	36	(1*S*,2*S*)
5	$AlMe_3$	75	28	(1*S*,2*S*)
6	$InMe_3$	78	43	(1*S*,2*S*)
7	$Yb(OTf)_3$	62	52	(1*S*,2*S*)
8	$Sm(OTf)_3$	56	37	(1*S*,2*S*)

[a] *Reaction conditions:* cyclohexene oxide (1.0 mmol), PhSeH (1.1 mmol), catalyst (5 mol%), *n*-hexane (3 mL), −40 °C, 5 h.
[b] Isolated yields.
[c] Determined by HPLC with a Daicel Chiralcel OD-H column.
[d] Absolute configurations of the major products were assigned by comparison of CD spectroscopy with that of sulfur anologue with known absolute configuration.

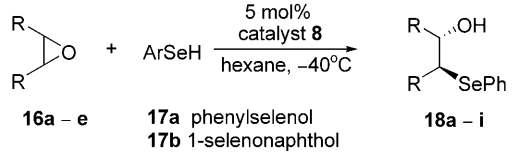
Lewis acid when combined with Ga species and **3** under the same reaction conditions.

Under the optimized reaction conditions, asymmetric ring-openings of a variety of *meso*-epoxides with selenophenol and 1-selenonaphthol were investigated. The results are summarized in Table 5. It can be seen that all reactions proceeded smoothly to afford the β-arylseleno alcohols in high yields for both cyclic and acyclic *meso*-epoxides. In general, the cyclic epoxides gave the ring-opening products in better selectivities than the acyclic ones when reacted with the same selenol (entries 1, 3 and 9 *vs.* 5 and 7). When reacted with the same epoxide substrate, selenophenol gave better enantioselectivity than 1-selenonaphthol in all of the cases (entries 1, 3, 5, 7 *vs.* 2, 4, 6, 8. respectively).

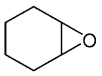
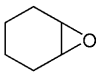
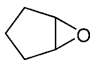
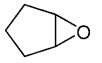
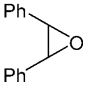
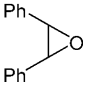
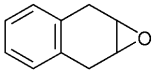
Based on the results obtained when aryl selenols were utilized in the ring-opening reaction, we next studied the use of thiols as nucleophiles for further investigations. For comparison, complexes **6**, **7** and Ga-Ti-**13b** were also examined in the reaction. Choosing cyclohexene oxide as substrate and thiophenol as nucleophile, the reaction conditions were firstly optimized and the results are summarized in Table 6. Among the solvents investigated, hexane was proved to be the best one in terms of reactivity and selectivity. A variation of the reaction temperature from 0 to −20 °C caused a significant increase in the *ee* value (Table 6, entry 5), but a slight decrease was observed when the reaction was carried out at −40 °C (entry 6). Further investigation revealed that there was no significant change when the amount of **8** was decreased to 5 mol% (entry 7). The reaction still showed good reactivity and selectivity even with only 2 mol% catalyst loading (entry 8). However, the monometallic complex **6** and homobimetallic complex **7** gave both low selectivities and moderate reactivities (entries 9 and 10). When Ga-Ti-**13b** was utilized in the reaction, the product was obtained in moderate reactivity and selectivity in the (*R*,*R*) configuration (entry 11).

Under the optimized reaction conditions (5 mol% complex **8**, −20 °C, hexane as solvent), we next investigated the scope of a variety of *meso*-epoxides and different thiols in the reaction. As shown in Table 7, the results revealed that most of reactions proceeded smoothly to furnish the corresponding β-hydroxy sulfides in high yields and moderate to high enantiomeric excesses (65–92% *ee*), except for epoxide **16f**. We also found that cyclic *meso*-epoxides provided the corresponding products with better enantioselectivity than acyclic ones under the same reaction conditions. Unfortunately, for the more sterically hindered epoxide **16f**, the reaction proceeded very sluggishly, affording the ring-opening product in low yield and moderate *ee* value even with a longer reaction time (entries 12). Cyclooctene oxide **16g**, which had been found to entirely unrecative with thiophenol catalyzed

Table 5. Asymmetric addition of ArSeH to *meso*-epoxides catalyzed by **8**.[a]



16a – e **17a** phenylselenol **17b** 1-selenonaphthol **18a – i**

Entry		Epoxide	Ar	Product	Yield[b] [%]	*ee*[c] [%]	Configuration[d]
1	**16a**		**17a**	**18a**	94	97	(1*S*,2*S*)
2	**16a**		**17b**	**18b**	93	78	(1*S*,2*S*)
3	**16b**		**17a**	**18c**	85	94	(1*S*,2*S*)
4	**16b**		**17b**	**18d**	80	70	(1*S*,2*S*)
5	**16c**		**17a**	**18e**	70	72	–
6	**16c**		**17b**	**18f**	70	55	–
7	**16d**		**17a**	**18g**	87	87	–
8	**16d**		**17b**	**18h**	73	75	–
9	**16e**		**17a**	**18i**	92	90	–

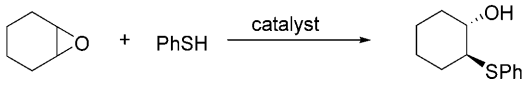
[a] *Reaction conditions:* epoxide (1.0 mmol), ArSeH (1.1 mmol), catalyst (5 mol%), hexane (3 mL), −40 °C, 5 h.
[b] Isolated yields.
[c] Determined by HPLC with a Daicel Chiralcel OD-H column.
[d] Absolute configurations of the major products were assigned by comparison of CD spectroscopy with that of sulfur analogue with known absolute configuration.

by complex **9**, gave the ring-opening product **20m** in moderate yield and 80% *ee* in our case. The addition of 4-chlorothiophenol to epoxide **16h** gave good reactivity and high selectivity (entry 14). The results also revealed that the *para*-chloro- or *para*-methyl-substituted thiophenols gave better reactivity and selectivity than thiophenol. However, benzylthiol (**19d**) displayed lower reactivity and selectivity compared with aryl thiols (entry 15). It is also worth noting that the results represent a considerable improvement comparable to the results catalyzed by complex **9**.[12c]

The X-ray crystal structures of the above mentioned Ga-Ti-salen complexes have never been determined, and this restricted the mechanistic investigations aimed at further improving the catalytic reactivity and enantioselectivity. So it is not easily to identify the active species that contribute to the overall reaction rate. As mentioned in Shibasaki's report on the ring-opening reaction of epoxides with thiols,[2] the heterobimetallic catalyst appears to act as multifunctional catalyst, with a lithium binaphthoxide moiety functioning as a Brønsted base, activating thiol and a gallium metal functioning as a Lewis acid, activating and also controlling the orientation of epoxide, with the result that a high asymmetric induction was realized.

In our case, the current catalyst system has two different Lewis acid centers. Considering that the bimetallic complex salen-Ga_2 (**7**) and the monometallic complex (**6**) gave similar results, we think this probably attributes to the structure characteristic of the complex. So there is probably no cooperative effect between the two gallium atoms. As a result, homobimetallic complex **7** gave similar reactivity and selectivity as the monometallic complex salen-Ga (**6**). The high catalytic activity of Ga-Ti-salen (**8**) can be accounted for by the existence of synergistic cooperation between the two different Lewis acids. Consider-

Table 6. Asymmetric ring-opening of cyclohexene oxide with thiophenol.[a]



Entry	Catalyst	Solvent	Temp. [°C]	Yield [%][b]	*ee* [%][c]	Configuration[d]
1	**8**	hexane	0	96	76	(1*S*,2*S*)
2	**8**	Toluene	0	93	70	(1*S*,2*S*)
3	**8**	Et_2O	0	92	63	(1*S*,2*S*)
4	**8**	CH_2Cl_2	0	90	45	(1*S*,2*S*)
5	**8**	hexane	−20	96	87	(1*S*,2*S*)
6	**8**	hexane	−40	93	86	(1*S*,2*S*)
7[e]	**8**	hexane	−20	95	87	(1*S*,2*S*)
8[f]	**8**	hexane	−20	88	86	(1*S*,2*S*)
9[g]	**6**	hexane	−20	70	22	(1*S*,2*S*)
10[g]	**7**	hexane	−20	72	22	(1*S*,2*S*)
11	**Ga+Ti+13b**	hexane	−20	76	63	(1*R*,2*R*)

[a] Unless otherwise noted, the reactions were carried out under the following conditions: cyclohexene oxide (1 mmol), PhSH (1.2 mmol), catalyst (10 mol%).
[b] Isolated yields.
[c] Determined by HPLC with a Daicel Chiralcel OD-H column.
[d] Absolute configurations of the major enantiomer was assigned by comparison with literature reports.
[e] 5 mol% of **8**.
[f] 2 mol% of **8**.
[g] Reaction time is 4 h.

ing that a fully chelated titanium derivative would be six-coordinate and salen-Ti displaying a "closed" structure, we think it is possible that the reaction of complex **6** with Ti(O-*i*-Pr)$_4$ would favor the formation of a heterobimetallic complex with a partly "closed" structure (Figure 3). And the shorter distance between the two metal centers enables the existence of the synergistic effect between metals Ti and Ga.

Also, it is likely that the harder Lewis acid titanium is apt to coordinate with epoxide (hard Lewis base), while the soft Lewis base nucleophile selenophenol tends to coordinate with the relatively soft gallium (trimethylgallium was also classified as a hard Lewis acid),[20] which directs the attack of the nucleophile to the epoxide (Figure 3). The possible existence of relatively independent coordination modes makes the reaction proceed more effectively and selectively. Also, as mentioned in our previous report, a ^{1}H NMR study showed that the chemical shifts of the dimethylgallium hydrogens of complex **8** appear at a higher field ($\delta = -0.25$ and -0.36 ppm) in comparison with those of complex **6** ($\delta = -0.22$ and -0.31 ppm), which maybe due to the coordination of the oxygen in the isopropoxy group to the gallium, with the result of a change in the bond angle between the Lewis acids and the substrates, which is probably the crucial factor.

Conclusions

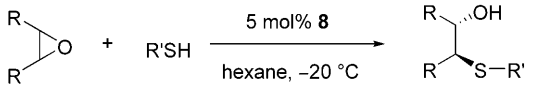
In summary, we have succeeded in developing a highly efficient heterobimetallic catalytic system in the enantioselective ring-opening reactions and a strong synergistic cooperation between the different Lewis acids was exhibited in the catalysis process. The enantioselective ring-opening reaction of *meso*-epoxides with aryl selenols and thiols gave optically active β-arylseleno alcohols and β-hydroxy sulfides in good yields and high enantioselectivities. Further applications of this kind of heterobimetallic catalytic system in other reactions are under study.

Experimental Section

General Procedure for the Asymmetric Ring-Opening of *meso*-Epoxides by Aryl Selenols

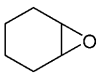
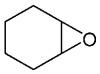
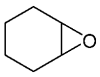
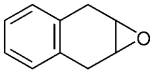
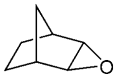
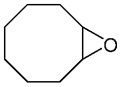
$GaMe_3$ (0.05 mmol, 0.5 M in hexane) was added dropwise to 3 mL of a hexane solution of ligand (*R,R*)-**3** (28 mg, 0.05 mmol) under an argon atmosphere at 0 °C. After the solution had been stirred for 1 h at room temperature, a solution of Ti(O-*i*-Pr)$_4$ (0.05 mmol, 0.2 M in hexane) was then added and stirring was continued for another 1 h to form the Ti-Ga-salen complex. The resulting yellow solution was cooled to −40 °C. The epoxide (1.0 mmol) and aryl selenol (1.2 mmol) were added successively. The mixture was stirred for 5 h at the same temperature before being quenched with a saturated NH_4Cl solution and extracted with ether. The organic phase was dried over Na_2SO_4, and the solvent re-

Table 7. Asymmetric thiolysis of *meso*-epoxides catalyzed by **8**.[a]



16a – h **20a – o**

19a R' = Ph
19b R' = 4-Me-C_6H_4
19c R' = 4-Cl-C_6H_4
19d R' = -CH_2Ph

Entry	Epoxide		R′SH	Product	Yield[b] [%]	ee[c] [%]
1	**16a**		Ph	**20a**	95	84
2	**16a**		4-Me-C_6H_4	**20b**	95	87
3	**16a**		4-Cl-C_6H_4	**20c**	97	92
4	**16b**		Ph	**20d**	96	71
5	**16b**		4-Me-C_6H_4	**20e**	95	82
6	**16c**		Ph	**20f**	91	74
7	**16c**		4-Me-C_6H_4	**20g**	95	84
8	**16c**		4-Cl-C_6H_4	**20h**	90	85
9	**16d**		Ph	**20i**	88	72
10	**16d**		4-Me-C_6H_4	**20j**	92	81
11	**16e**		Ph	**20k**	83	65
12[d]	**16f**		Ph	**20l**	23	53
13[d]	**16g**		Ph	**20m**	50	80
14[d]	**16h**		4-Cl-C_6H_4	**20n**	85	82
15	**16a**		-CH_2Ph	**20o**	74	76

[a] Unless otherwise noted, all reactions were carried out under such conditions: epoxide (1.0 mmol), thiol (1.2 mmol), complex **8** (5 mol%), hexane (3 mL), –20 °C, 1 h.
[b] Isolated yields.
[c] Determined by HPLC with a Daicel Chiralcel OD-H or OB-H column. Absolute configurations of the major enantiomers (1*S*,2*S*) were assigned by comparison of the rotation values in the literature or by analogy.
[d] Reaction was carried out at –20 °C for 24 h.

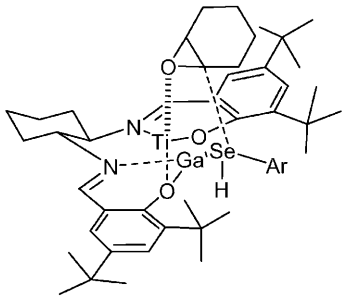


Figure 3. Proposed working model for the catalytic process (other groups are omitted for clarity)

moved. After being separated by preparative silica gel TLC, the β-arylseleno alcohol was obtained.

General Procedure for the Asymmetric Ring-Opening of *meso*-Epoxides by Thiols

$GaMe_3$ (0.05 mmol, 0.5 M in hexane) was added dropwisely to 3 mL of a hexane solution of ligand (*R*,*R*)-**8** (28 mg, 0.05 mmol) under argon at 0 °C. After the solution had been stirred for 1 h at room temperature, a solution of $Ti(O\text{-}i\text{-}Pr)_4$ (0.05 mmol, 0.2 M in hexane) was then added and stirring was continued for another 1 h to form the Ga-Ti-**8** complex. The resulting yellow solution was cooled to −20 °C. Then epoxide (1.0 mmol) and thiol (1.2 mmol) were added successively. The mixture was stirred for 1 h at the same temperature before being quenched with a saturated NH_4Cl solution and extracted with ether. The organic phase was dried over anhydrous sodium sulfate, and the solvent removed. After being separated by preparative silica gel TLC, the β-hydroxy sulfide was obtained and the *ee* value was determined by chiral HPLC with a Daicel Chiralcel OD-H or OB-H column.

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