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Study of the Lewis acid-promoted rearrangement of 2-aryl-2,3-epoxy acylates

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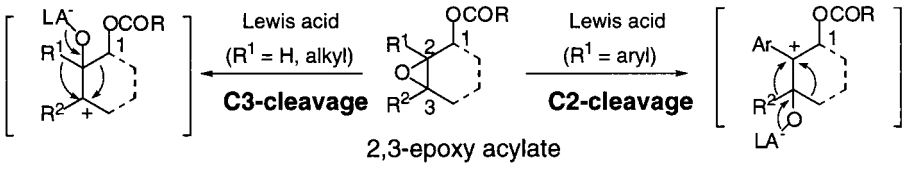
Abstract—The reaction of 2-aryl-2,3-epoxy acylates with Lewis acids was examined in detail. Cyclic 2-aryl-2,3-epoxy acylates afforded the rearranged products via the C2-carbocation intermediates obtained by the C2-cleavage of the oxirane rings. On the other hand, acyclic 2-aryl-2,3-epoxy acylates gave the rearranged products via the phenonium ion intermediates obtained by the C3-cleavage of the oxirane rings. The method was also applied to the synthesis of the optically active benzylic quaternary carbon center.

1. Introduction

The rearrangement of epoxides is one of the well known carbon skeleton constructions and a very useful method for the synthesis of carbonyl compounds.[1] In the rearrangement reactions of epoxides, the control of the regio- and stereochemistries is very important in order to make them more useful. Many techniques have been developed so far. In these cases, neighboring groups such as hydroxyl, its alkyl or silyl ether,[2a] phenyl,[2b] vinyl,[2c] silyl,[2d] and carbonyl groups[2e] can often help to control the regio- and stereochemistries.

Recently, we reported the Lewis acid-catalyzed rearrangement of 2,3-epoxy acylates with alkyl substituents in the C2- and C3-positions. Although the acyloxy group is recognized as one of the most popular functional groups causing neighboring group participation, we succeeded in controlling the regiochemistry of the Lewis acid-catalyzed rearrangement of alkyl substituted 2,3-epoxy acylates via the C3-cleavage of oxiranes by diversifying the bulkiness and electron-withdrawing nature of the acyloxy group (Eq. (1)).[3] On the other hand, in our synthesis of fredericamycin A, which has the 2-aryl substituted 2,3-epoxy acylate moiety, the rearrangement proceeded via the C2-cleavage of the oxirane ring.[4] Therefore, aryl and acyloxyalkyl groups showed the opposite nature for the cleavage of the oxirane ring. We then examined the Lewis acid-catalyzed reactions of various cyclic 2-aryl-2,3-epoxy acylates which were recently communicated. In these cases, every rearrangement reaction proceeded via the C2-cleavage of the oxirane ring and it proved that the carbocation stabilizing ability of the aryl group is stronger than the electron withdrawing nature of the acyloxyalkyl group (Eq. (2)).[5] We now examined the reactions of the acyclic 2-aryl-2,3-epoxy acylates and suprisingly found that the rearrangement proceeds via the C3-cleavage of the oxirane ring (Eq. (3)). In this paper, we present the full details of the study concerning the rearrangement of the 2-aryl-2,3-epoxy acylates in both cyclic and acyclic systems.



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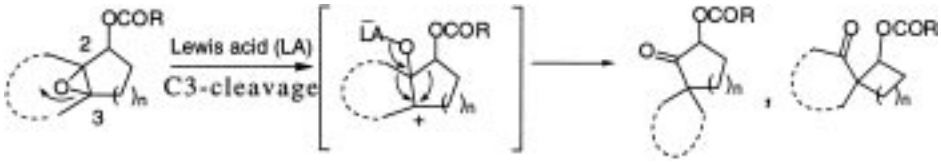

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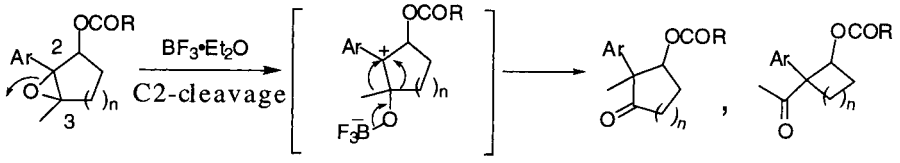

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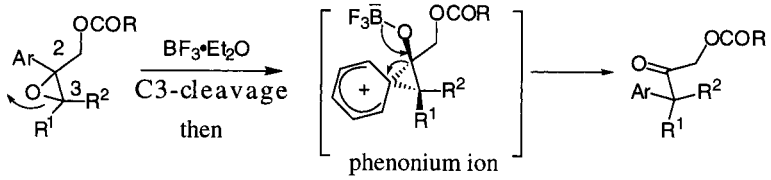


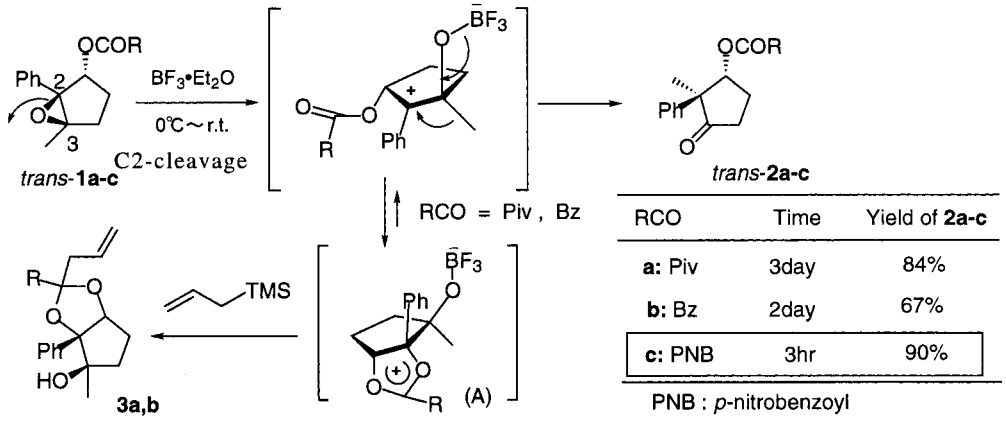
(3)

2. Results and discussion

2.1. The rearrangement of the epoxy acylates[6] in cyclic system

2.1.1. The epoxy acylates[6] with phenyl group. For the reaction of the five-membered epoxy acylates, the *trans*-epoxy acylates (*trans*-**1a**–**c**) afforded high yields of the corresponding rearrangement products (*trans*-**2a**–**c**) via the C2-cleavage of the oxirane ring by $BF_3{\cdot}Et_2O$ treatment.[7] The reactivity, however, depended on the acyloxy group. That is, the benzoyloxy and pivaloyloxy compounds required longer reaction times than that of the *p*-nitrobenzoyloxy compound. During the reactions, the formation of the intermediates was observed using TLC for *trans*-**1a**,**b**. The structures of the intermediates were found to be the dioxenium cations (A) by trapping them using allyltrimethylsilane leading to the allylates **3a**,**b**. The intermediates (A) might be formed by neighboring group participation of the acyloxy groups. The *p*-nitrobenzoate, *trans*-**1c**, did not show such a reaction. The difference between these tendencies must depend on the electron-withdrawing strength, because the *p*-nitrobenzoyl group has a very strong electron-withdrawing nature and does not show any neighboring group participation (Scheme 1). Effect of Lewis acid was also examined using **1c** as a substrate and $BF_3{\cdot}Et_2O$ proved to be the most effective Lewis acid (Table 1).

The tendency observed in the *trans*-epoxy acylate systems was also obtained with the *cis*-epoxy acylates (*cis*-**1a**–**c**). Thus, *cis*-epoxy pivalate (*cis*-**1a**) and *cis*-epoxy benzoate (*cis*-**1b**) rearranged to give the corresponding 3-oxo-acylates (*cis*-**2a** and *cis*-**2b**) in low yields accompanied with orthoesters **4a**,**b** formed by neighboring group participation followed by the attack of the oxygen atom to the resulting dioxenium cations (B). *p*-Nitrobenzoate (*cis*-**1c**) was also produced *cis*-**2c** in moderate yield, but the by-product was the enone **5**, not the orthoester. The formation of **5** was rationalized as follows. The carbocation is formed first via the C2-cleavage of the oxirane ring, then 1,2-hydride migration and 1,5-acyl migration followed by β-elimination. The change in the *p*-nitrobenzoyl group to



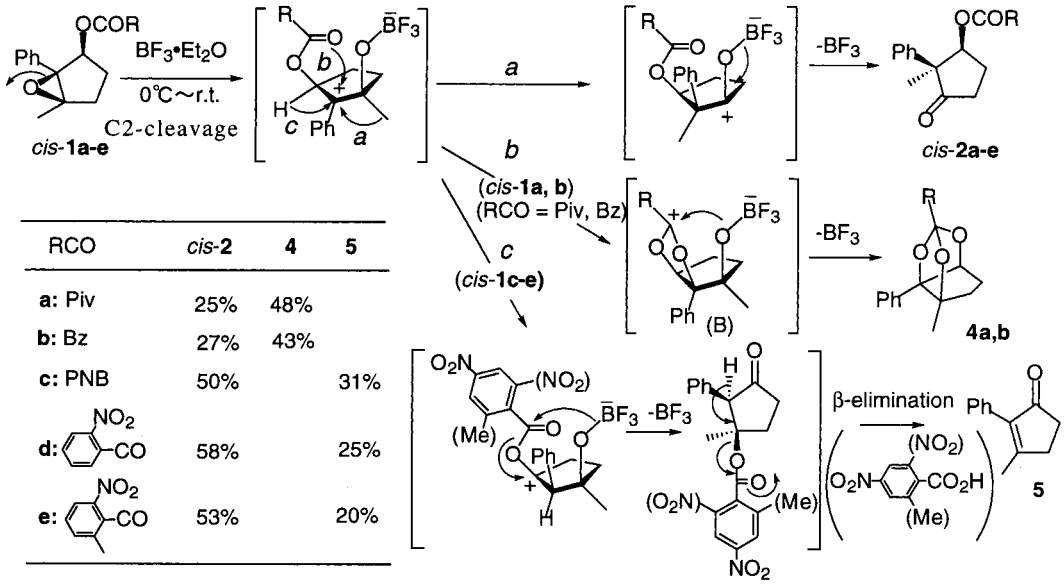
RCO	Time	Yield of **2a-c**
a: Piv	3day	84%
b: Bz	2day	67%
c: PNB	3hr	90%

PNB : *p*-nitrobenzoyl

Scheme 1.

Table 1. Effect of Lewis acid on rearrangement of **1c** in CH_2Cl_2

Lewis acid	Time (h)	Yield of **2c**
$BF_3{\cdot}Et_2O$	3	90%
$SnCl_4$	4	82%
TMSOTf	1	Trace
$TiCl_4$	1	Trace

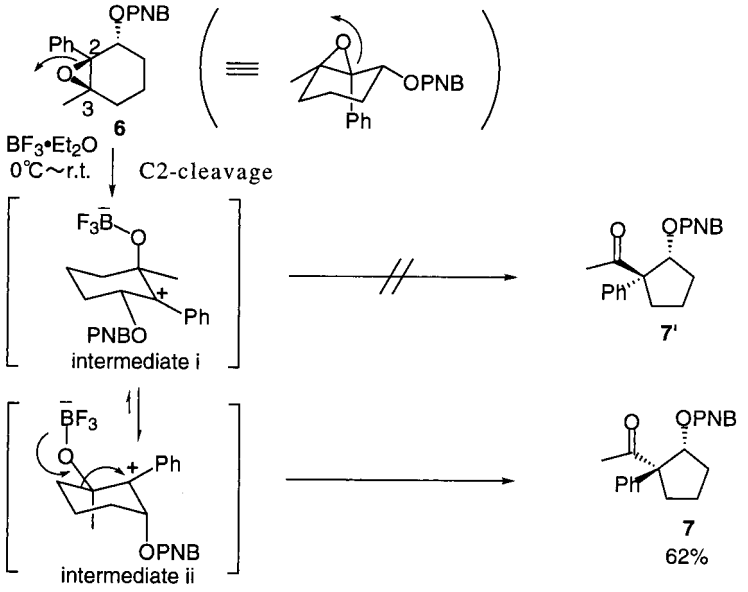


Scheme 2.

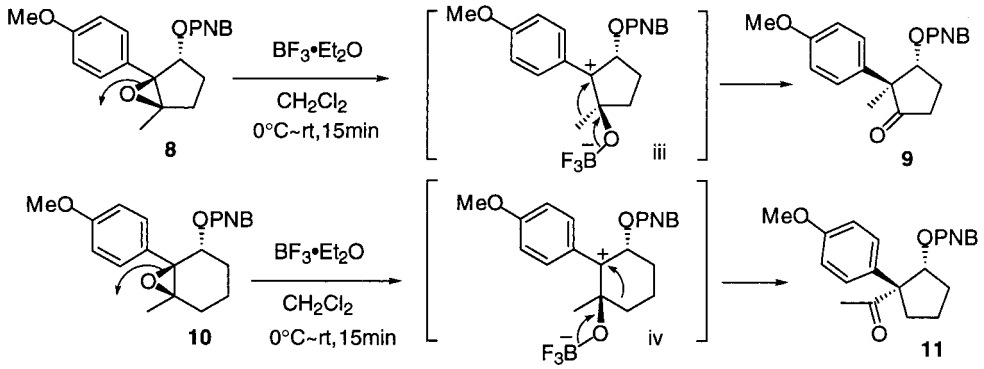
2-nitrobenzoyl (*cis*-**1d**) or 2-methyl-6-nitrobenzoyl (*cis*-**1e**) does not have much of an effect. Thus, the Lewis acid-catalyzed reactions of the *cis*- and *trans*-2-phenyl-2,3-epoxy acylates proceeded via the C2-cleavage of the oxirane ring (Scheme 2).

Rearrangement via the C2-cleavage of the oxirane ring was also observed in the six-membered ring. That is, 2-phenyl *trans*-epoxy *p*-nitrobenzoate **6** afforded the ring-contracted five-membered product **7** via the C2-cleavage of the oxirane ring followed by ring-methylene unit rearrangement. The structure of **7** was unambiguously determined by X-ray analysis. The configuration of the quaternary carbon center of **7** proved to be opposite to the configuration predicted by the concerted rearrangement. Quite recently, Neef et al. reported that it is very difficult to predict the configuration of the quaternary carbon center produced by the rearrangement via benzylic cation intermediates, because the benzylic group prolongs the lifetime of the cation and the rearrangement proceeds in a non-concerted way.[8] However, we rationalized that our result must be due to the more stable conformation of the cation intermediate ii than the intermediate i first formed by cleavage of the oxirane ring due to the long life of the cation. In fact, the PM3 calculation shows that intermediate ii is 3.2 kcal/mol more stable than intermediate i (Scheme 3).

2.1.2. The epoxy acylates[6] with *p*-methoxyphenyl group. The stabilization ability of the benzylic cation by the *p*-methoxyphenyl group is usually recognized as being much stronger than that of the phenyl group. We then tried the reactions of the 2,3-epoxy acylates with the *p*-methoxyphenyl group at the C2-position (Scheme 4). As expected, the reactions of **8** and **10** proceeded very smoothly



Scheme 3.



Run	substrate	BF_3•Et_2O	product
1	**8**	1.0eq.	97%
2	"	0.1eq.	93%
3	**10**	1.0eq.	94%
4	"	0.1eq.	93%

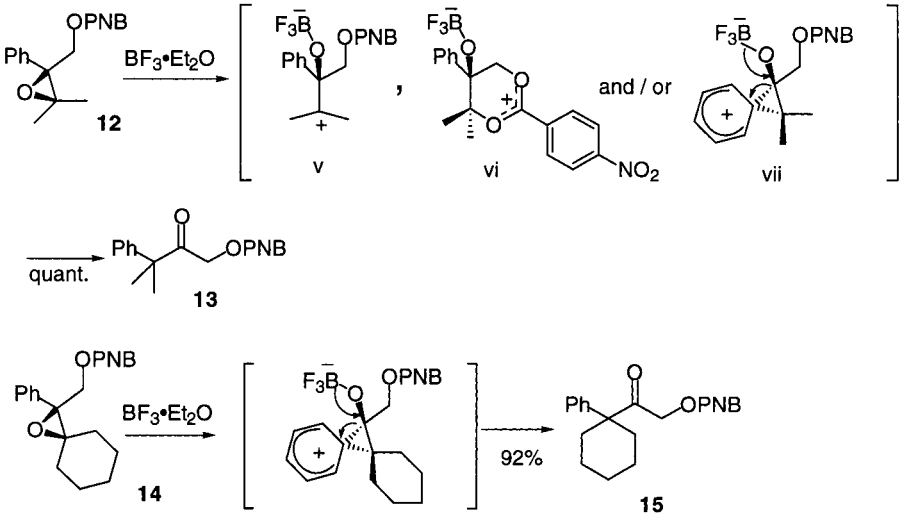
Scheme 4.

to give the rearranged products **9** and **11**, respectively (Runs 1 and 3). The reaction times were very short, and the yields were very high by just using BF_3·Et_2O. The effect of the *p*-methoxyphenyl group was clarified in the catalytic version. That is, the reactivity of the epoxides was examined using 0.1 equiv. of BF_3·Et_2O. The reaction times and the yields of the rearranged products from the 2,3-epoxy acylates with the *p*-methoxyphenyl group **8**, **10** are the same as those obtained using 1 equiv. of BF_3·Et_2O (Runs 2 and 4).[9]

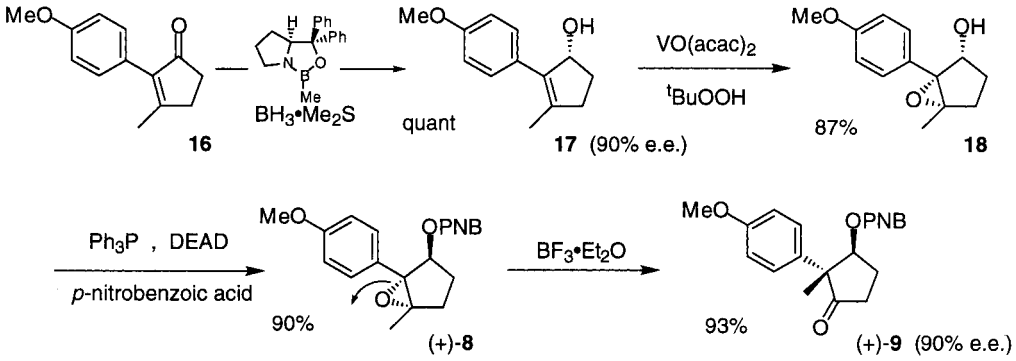
2.2. The rearrangement of the epoxy acylates[6] in an acyclic system

As mentioned above, we found that the rearrangements of the 2-aryl-2,3-epoxy acylates in the cyclic system proceeded via the C2-cleavage of the oxirane rings due to the stronger carbocation stabilizing ability of the aryl groups in comparison with the C2-carbocation destabilization ability of the acyloxy group.

However, the results obtained by the reaction of the 2-aryl-2,3-epoxy acylates in an acyclic system are completely different from those in the cyclic systems (Scheme 5). First, we examined 3,3-dimethyl epoxy *p*-nitrobenzoate **12**. In this case, to our surprise, **13** afforded the phenyl migrated product **13** in a quantitative yield through the C3-cleavage of the oxirane ring. We rationalized the formation of **13** as follows. Although there are three possible cationic intermediates v, vi, and vii to give **13**, the C3-cation intermediate v is unfavorable in this case because we already recognize that in more conformationary fixed cyclic



Scheme 5.



Scheme 6.

compounds, the formation of the C3-cation intermediates cannot be observed. Therefore, we think that **13** was obtained via a neighboring group, like the ester and phenyl group participation. (The dioxenium ion (vi) formation by neighboring participation of the ester group is not clear for *p*-nitrobenzoate compounds. We can't see any product which exemplifies the formation of vi on TLC though such a product from the reaction of the intermediate and water on TLC was observed in the case of benzoate in place of *p*-nitrobenzoate.) The formation of the phenonium ion intermediate (vii) is well recognized in the rearrangement reaction of the phenyl group. The difference in the results between the cyclic and acyclic systems must be due to the flexibility of the starting epoxides. In the acyclic system, the structure of the starting material is more flexible. The phenyl group can work as a good β-cation stabilizer by forming a phenonium ion. The same reaction was also observed for the cyclohexyl epoxy *p*-nitrobenzoate **14**. That is, the treatment of **14** with $BF_3{\cdot}Et_2O$ afforded **15** in 92% yield.

2.3. Application to the construction of a chiral benzylic quaternary carbon center in an optically active form

Rearrangement reactions are usually divided into two categories. One is a concerted rearrangement and the other is a stepwise rearrangement depending on the lifetime of the cation intermediates. The stepwise rearrangement sometimes loses stereoselectivity. Although our reaction is a stepwise reaction, the rearrangement proceeds in a diastereoselective manner as mentioned above. We then applied our method to the asymmetric synthesis of benzylic quaternary carbon centers.

The reduction of the enone **16** by Corey's method[10] afforded the (*R*)-allyl alcohol **17** in 90% ee. The ee value of **17** was determined by HPLC analysis. Epoxidation of **17** with *t*-BuOOH/$VO(acac)_2$[11] stereoselectively gave the epoxy alcohol **18** in 87% yield. The Mitsunobu reaction[12] of **18** with *p*-nitrobenzoic acid gave the *trans*-epoxy *p*-nitrobenzoate (+)-**8** in 90% yield. The reactions proceeded without losing chiral integrity during the conversions of **17** to (+)-**8**. The treatment of epoxy *p*-nitrobenzoates (+)-**8** with $BF_3{\cdot}Et_2O$ afforded the optically active product (+)-**9** with the same ee values as the starting epoxy acylates. This experiment showed that the reaction stereospecifically proceeded during the rearrangements (Scheme 6).

3. Conclusion

As mentioned above, the rearrangements of the 2-aryl-2,3-epoxy acylate systems are governed by the flexibility of the conformations of the intermediates. Aryl groups in these systems intrinsically work as neighboring group participating functions to cause the C3-cleavage of the oxirane rings because the acyloxy groups also assist in the cleavage of the oxirane rings at the C3-positions. However, when the conformations of the intermediates are fixed like cyclic systems and neighboring group participation is difficult, aryl groups work as benzylic cation (C2-carbocation) stabilizing groups and their aptitudes are stronger than the C2-carbocation destabilizing aptitudes of the acyloxy groups. The method was also applied to the asymmetric construction of benzylic quaternary carbon centers found in many natural products.

4. Experimental

All melting points are uncorrected. The NMR spectra were measured using 270 and 300 MHz spectrometers with $CDCl_3$ as the solvent and $SiMe_4$ as the internal standard. Infrared (IR) absorption spectra were recorded as a KBr pellet. All solvents were distilled and dried according to standard procedures.

4.1. Synthesis of the starting epoxides (cf. Scheme 6)

4.1.1. Synthesis of (±)-*trans*-epoxy acylates in Scheme 1. *trans*-5-Methyl-1-phenyl-6-oxabicyclo[3.1.0]hex-2-yl 2,2-dimethylpropanoate (*trans*-1a). DIBAH (*n*-hexane solu. 7.5 mL, 7.05 mmol) was added dropwise to a solution of the enone, 3-methyl-2-phenyl-2-cyclopenten-1-one,[13] (1.01 g, 5.86 mmol) in CH_2Cl_2 (30 mL) at 0°C under N_2 and the resulting mixture was stirred for 20 min at the same temperature. The reaction mixture was quenched by the addition of MeOH and then extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo to give the crude allyl alcohol. A solution of *t*-BuOOH (60% solu., dried over Na_2SO_4, 2.10 g, 15.8 mmol) in benzene (10 mL) was added dropwise to a solution of a cat. amount of $VO(acac)_2$ and the above crude allyl alcohol in benzene (20 mL) at rt under N_2. The mixture was stirred for 1.5 h. Sat. aq. $Na_2S_2O_3$ was then added to the mixture. The resulting solution was extracted with AcOEt. The organic layer was washed with brine, dried over

Na_2SO_4, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography using hexane–AcOEt (9/1) as the eluent to give the *cis*-epoxy alcohol (1.04 g, 93% in 2 steps). Pivalic acid (449 mg, 4.40 mmol) and Ph_3P (1.12 g, 4.26 mmol) were added to a solution of the above *cis*-epoxy alcohol (405 mg, 2.13 mmol) in toluene (10 mL) at 0°C under N_2. Diethyl azadicarboxylate (toluene solu., 1.90 mL, 4.36 mmol) was added dropwise to the resulting solution. The mixture was stirred overnight, then treated with sat. aq. $NaHCO_3$. The resulting solution was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography using hexane–AcOEt (9/1) as the eluent to give *trans*-**1a** (524 mg, 90%). Colorless oil; IR (KBr) 1732, 1279, 1151 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12 (s, 9H), 1.31 (s, 3H), 1.57–1.65 (m, 1H), 1.92–2.07 (m, 3H), 5.34 (d, 1H, J=5.2 Hz), 7.29–7.43 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 16.1, 27.0, 28.3, 30.7, 38.7, 70.0, 70.8, 77.6, 127.8, 128.0, 128.6, 133.6, 177.2; HRMS (FAB) Calcd for $C_{17}H_{23}O_3$ (M^++H): 275.1647. Found: 275.1647.

4.1.2. *trans*-5-Methyl-1-phenyl-6-oxabicyclo[3.1.0]hex-2-yl benzoate (*trans*-1b). In the same procedure for *trans*-**1a**, *trans*-**1b** (489 mg, 60%) was obtained from the *cis*-epoxy alcohol (525 mg, 2.76 mmol), benzoic acid (867 mg, 7.10 mmol), Ph_3P (1.81 g, 6.91 mmol), diethyl azadicarboxylate (toluene solu., 3.0 mL, 6.89 mmol), and toluene (10 mL). Colorless needles; mp 69–72°C (hexane–EtOAc); IR (KBr) 1723, 1271, 1113 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.81–1.84 (m, 1H), 2.05–2.14 (m, 3H), 5.63 (d, 1H, J=4.9 Hz), 7.25–7.31 (m, 3H), 7.42–7.59 (m, 5H), 7.99 (d, 2H, J= 8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 15.9, 28.3, 30.7, 70.2, 70.7, 78.5, 128.0, 128.2, 128.3, 129.4, 130.2, 132.9, 133.6, 165.3; Anal. Calcd for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16. Found: C, 77.43; H, 6.21.

4.1.3. *trans*-5-Methyl-1-phenyl-6-oxabicyclo[3.1.0]hex-2-yl 4-nitrobenzoate (*trans*-1c). In the same procedure for *trans*-**1a**, *trans*-**1c** (519 mg, 72%) was obtained from the *cis*-epoxy alcohol (406 mg, 2.13 mmol), *p*-nitrobenzoic acid (709 mg, 4.24 mmol), Ph_3P (1.12 g, 4.25 mmol), diethyl azadicarboxylate (toluene solu., 1.90 mL, 4.36 mmol), and toluene (10 mL). Yellowish crystals; mp 98–100°C (hexane–EtOAc); IR (KBr) 1728, 1532, 1271, 1177, 1117 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (s, 3H), 1.84–1.87 (m, 1H), 2.08–2.19 (m, 3H), 5.65 (d, 1H, J=5.1 Hz), 7.27–7.44 (m, 5H), 8.12 (d, 2H, J=9.0 Hz), 8.28 (d, 2H, J=9.0 Hz); ^{13}C NMR ($CDCl_3$) δ 16.0, 28.2, 30.7, 70.2, 70.6, 79.5, 123.6, 128.1, 128.2, 128.3, 130.5, 133.2, 135.5, 150.5, 163.5; Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 66.98; H, 5.19; N, 4.12.

4.2. Synthesis of (±)-*cis*-epoxy acylates in Scheme 2

4.2.1. *cis*-5-Methyl-1-phenyl-6-oxabicyclo[3.1.0]hex-2-yl 2,2-dimethylpropanoate (*cis*-1a). Pivaloyl chloride (390 μL, 3.17 mmol) was added dropwise to a solution of the *cis*-epoxy alcohol (the same one used in the synthesis of **1a**, 403 mg, 2.12 mmol) in pyridine (5.0 mL) at 0°C under N_2. The mixture was stirred for 3 h at rt, then treated with H_2O. The resulting solution was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography using hexane–AcOEt (7/1) as the eluent to give *cis*-**1a** (575 mg, 99%). Colorless crystals mp 69–71°C (hexane–EtOAc); IR (KBr) 1728, 1283, 1161 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (s, 9H), 1.21 (s, 3H), 1.40–1.57 (m, 1H), 1.75–1.87 (m, 1H), 2.04–2.21 (m, 2H), 5.67 (t, 1H, J=8.1 Hz), 7.26–7.37 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 15.3, 24.5, 26.9, 30.5, 38.6, 68.1, 71.2, 75.9, 126.8, 127.6, 128.0, 133.7, 178.4; Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.28; H, 8.05.

4.2.2. *cis*-5-Methyl-1-phenyl-6-oxabicyclo[3.1.0]hex-2-yl benzoate (*cis*-1b). In the same procedure for *cis*-**1a**, *cis*-**1b** (763 mg, 98%) was obtained from the *cis*-epoxy alcohol (503 mg, 2.64 mmol), benzoyl chloride (460 μL, 3.96 mmol), and pyridine (5.0 mL). Colorless crystals; mp 74–80°C (hexane–AcOEt); IR (KBr) 1717, 1451, 1271, 1120, 1099 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (s, 3H), 1.59–1.67 (m, 1H), 1.83–1.91 (m, 1H), 2.19–2.32 (m, 2H), 5.94 (t, 1H, J= 8.1 Hz), 7.28–7.52 (m, 8H), 7.96 (dd, 2H, J=8.5, 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 15.3, 24.9, 30.5, 68.3, 71.1, 76.9, 126.8, 127.7, 128.1, 128.2, 129.7, 129.8, 132.9, 133.7, 166.3; Anal. Calcd for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16. Found: C, 77.29; H, 6.18.

4.2.3. *cis*-5-Methyl-1-phenyl-6-oxabicyclo[3.1.0]hex-2-yl 4-nitrobenzoate (*cis*-1c). In the same procedure for *cis*-**1a**, *cis*-**1c** (633 mg, 88%) was obtained from the *cis*-epoxy alcohol (404 mg, 2.12 mmol), *p*-nitrobenzoyl chloride (593 mg, 3.20 mmol), and pyridine (5.0 mL). Colorless oil; IR (KBr) 1728, 1537, 1273, 1123, 1101 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (s, 3H), 1.60–1.73 (m, 1H), 1.85–1.97 (m, 1H), 2.21–2.38 (m, 2H), 5.95 (t, 1H, J=8.0 Hz), 7.28–7.44 (m, 5H), 8.11 (d, 2H, J=8.9 Hz), 8.21 (d, 2H, J=8.9 Hz); ^{13}C NMR ($CDCl_3$) δ 15.2, 24.9, 30.5, 68.6, 70.9, 78.1, 123.3, 126.7, 127.9, 128.3, 130.7, 133.3, 135.1, 150.4, 164.4; HRMS (FAB) Calcd for $C_{19}H_{18}NO_5$ (M^++H): 340.1185. Found: 340.1183.

4.2.4. *cis*-5-Methyl-1-phenyl-6-oxabicyclo[3.1.0]hex-2-yl 2-nitrobenzoate (*cis*-1d). In the same procedure for *cis*-**1a**, *cis*-**1d** (178.5 mg, 99%) was obtained from the *cis*-epoxy alcohol (101.2 mg, 0.532 mmol), *o*-nitrobenzoyl chloride (100 μL, 0.757 mmol), and pyridine–CH_2Cl_2 (1:1, 2.0 mL). Colorless crystals; mp 76–78°C (hexane–AcOEt); IR (KBr) 1732, 1539, 1352, 1289, 1132, 1075 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (s, 3H), 1.60–1.93 (m, 2H), 2.20–2.39 (m, 2H), 5.97 (t, 1H, J=7.9 Hz), 7.30–7.59 (m, 8H), 7.84–7.87 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 15.2, 24.4, 30.5, 68.8, 70.8, 78.4, 123.8, 126.8, 127.5, 127.9, 128.3, 129.6, 131.6, 132.8, 133.3, 147.7, 165.3; Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 67.35; H, 5.16; N, 4.15.

4.2.5. *cis*-5-Methyl-1-phenyl-6-oxabicyclo[3.1.0]hex-2-yl 2-methyl-6-nitrobenzoate (*cis*-1e). In the same procedure for *cis*-**1a**, *cis*-**1e** (76.9 mg, 40%) was obtained from the *cis*-epoxy alcohol (104.0 mg, 0.547 mmol), 2-methyl-4-nitrobenzoyl chloride (204 mg, 1.02 mmol), and pyridine–CH_2Cl_2 (1:1, 4.0 mL). Light yellowish crystals; mp 143–145°C (hexane–AcOEt); IR (KBr) 1738, 1538, 1271, 1121, 1076 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (s, 3H), 1.71–1.93 (m, 2H), 1.98 (s, 3H), 2.21–2.40 (m, 2H), 6.13 (t, 1H,

J=8.1 Hz), 7.30–7.47 (m, 7H), 7.91–7.95 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 15.2, 18.4, 24.1, 30.6, 69.0, 71.0, 77.7, 121.6, 126.9, 127.9, 128.3, 129.4, 129.5, 133.2, 135.9, 137.3, 145.6, 166.4; Anal. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.79; H, 5.48; N, 3.95.

4.3. Synthesis of (±)-*trans*-6-methyl-1-phenyl-7-oxabicyclo[4.1.0]hept-2-yl 4-nitrobenzoate (6) in Scheme 3

DIBAH (*n*-hexane solu. 1.40 mL, 1.33 mmol) was added dropwise to a solution of 3-methyl-2-phenyl-2-cyclohexen-1-one[14] (202 mg, 1.08 mmol) in CH_2Cl_2 (11 mL) at 0°C under N_2 and the resulting mixture was stirred for 20 min at the same temperature. The reaction mixture was quenched by addition of MeOH and extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo to give the crude allyl alcohol. A solution of *tert*-BuOOH (68% solu., dried over $MgSO_4$, 430 mg, 3.24 mmol) in benzene (3.0 mL) was added dropwise to a solution of cat. amount of $VO(acac)_2$ and the above crude allyl alcohol in benzene (7.0 mL) at rt under N_2. The mixture was stirred for 1.5 h. Sat. aq. $Na_2S_2O_3$ was added to the mixture. The resulting solution was extracted with AcOEt. The organic layer was washed with water and brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography using hexane–AcOEt (2/1) as the eluent to give the *cis*-epoxy alcohol (209 mg, 94% in 2 steps). *p*-Nitrobenzoic acid (341 mg, 2.04 mmol) and Ph_3P (536 mg, 2.04 mmol) were added to a solution of the above *cis*-epoxy alcohol (209 mg, 1.02 mmol) in toluene (10 mL) at 0°C under N_2. Diethyl azadicarboxylate (toluene solu., 890 μL, 2.04 mmol) was added dropwise to the resulting solution. The mixture was stirred for 2.5 h, then treated with sat. aq. $NaHCO_3$. The resulting solution was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography using hexane–AcOEt (9/1) as the eluent to give *trans*-epoxy *p*-nitrobenzoate **6** (327 mg, 90%). Colorless crystals; mp 123–124°C (hexane–AcOEt); IR (KBr) 1728, 1530, 1271 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.10 (s, 3H), 1.57–1.73 (m, 3H), 1.93–2.16 (m, 3H), 5.51 (t, 1H, J=5.3 Hz), 7.18–7.36 (m, 5H), 7.98 (d, 2H, J=8.5 Hz), 8.22 (d, H, J=8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 15.9, 22.1, 26.5, 29.6, 64.2, 66.6, 73.0, 123.3, 127.6, 127.7, 127.8, 130.4, 135.4, 136.6, 150.3, 163.2; Anal. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.87; H, 5.49; N, 3.92.

4.4. Synthesis of (±)-epoxy *p*-nitrobenzoates in Scheme 4

4.4.1. *trans*-5-Methyl-1-[4-(methyloxy)phenyl]-6-oxabicyclo[3.1.0]hex-2-yl 4-nitrobenzoate (8). In the same procedure for *trans*-**1a**, **8** was obtained. Reduction of 3-methyl-2-[4-(methyloxy)phenyl]-2-cyclopenten-1-one (257 mg, 1.27 mmol) with DIBAH (1.60 mL, 1.52 mmol) in CH_2Cl_2 (10 mL) gave the allyl alcohol (247 mg, 95%). *cis*-Epoxy alcohol (266 mg, quant.) was obtained from the allyl alcohol (247 mg, 1.21 mmol), $VO(acac)_2$, *tert*-BuOOH (68%, 480 mg, 3.62 mmol), and benzene (7–3 mL). Epoxy *p*-nitrobenzoate **8** (420 mg, 94%) was obtained from epoxy alcohol (266 mg, 1.21 mmol), Ph_3P (638 mg, 2.43 mmol), *p*-nitrobenzoic acid (411 mg, 2.46 mmol), diethyl azadicarboxylate (toluene solu., 1.05 mL, 2.41 mmol), and toluene (10 mL). Colorless needles; mp 105–107°C (hexane–AcOEt); IR (KBr) 1728, 1526, 1271, 1250, 1117, 1103 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.36 (s, 3H), 1.81–2.16 (m, 4H), 3.77 (s, 3H), 5.62 (d, 1H, J=4.9 Hz), 6.83 (dd, 2H, J=6.8, 1.8 Hz), 7.33 (dd, 2H, J=6.8, 1.8 Hz), 8.12 (d, 2H, J=7.0 Hz), 8.29 (d, 2H, J=7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 16.0, 28.1, 30.7, 55.2, 70.1, 70.4, 79.6, 113.6, 123.6, 125.2, 129.4, 130.6, 135.6, 150.5, 159.4, 163.6; Anal. Calcd for $C_{20}H_{19}NO_6$: C, 65.03; H, 5.18; N, 3.79. Found: C, 64.81; H, 5.26; N, 3.76.

4.4.2. *trans*-6-Methyl-1-[4-(methyloxy)phenyl]-7-oxabicyclo[4.1.0]hept-2-yl 4-nitrobenzoate (10). In the same procedure for **6**, **10** was prepared. Reduction of 3-methyl-2-[4-(methyloxy)phenyl]-2-cyclohexen-1-one (704 mg, 3.25 mmol) with DIBAH (4.15 mL, 3.91 mmol) in CH_2Cl_2 (33 mL) gave the allyl alcohol (692 mg, 98%). Epoxy alcohol (682 mg, 94%) was obtained from the allyl alcohol (674 mg, 3.09 mmol), $VO(acac)_2$ (cat. amount), *tert*-BuOOH (1.50 g, 11.3 mmol), and benzene (10–4 mL). Epoxy *p*-nitrobenzoate **10** (513 mg, 90%) was obtained from epoxy alcohol (351 mg, 1.49 mmol), Ph_3P (862 mg, 3.29 mmol), *p*-nitrobenzoic acid (550 mg, 3.29 mmol), diethyl azadicarboxylate (toluene solu., 1.50 mL, 3.45 mmol), and toluene (15 mL). Colorless crystals; mp 85–88°C (hexane–AcOEt); IR (KBr) 1728, 1538, 1273, 1119, 1102 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.10 (s, 3H), 1.60–1.72 (m, 3H), 1.92–2.16 (m, 3H), 3.71 (s, 3H), 5.50 (t, 1H, J=5.0 Hz), 6.76 (d, 2H, J=8.5 Hz), 7.25 (d, 2H, J=8.5 Hz), 8.02 (d, 2H, J=8.8 Hz), 8.23 (d, 2H, J=8.8 Hz); ^{13}C NMR ($CDCl_3$) δ 15.9, 22.1, 26.4, 29.6, 55.1, 64.4, 66.2, 73.3, 113.2, 123.4, 128.7, 128.8, 130.4, 135.5, 150.3, 158.9, 163.3; Anal. Calcd for $C_{21}H_{21}NO_6$: C, 65.79; H, 5.52; N, 3.65. Found: C, 65.74; H, 5.59; N, 3.63.

4.5. Synthesis of acyclic epoxy *p*-nitrobenzoates in Scheme 5

4.5.1. (3,3-Dimethyl-2-phenyloxiran-2-yl)methyl 4-nitrobenzoate (12). Light yellowish crystals; IR (KBr) 1732, 1532, 1273, 1118 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.07 (s, 3H), 1.60 (s, 3H), 4.57 (d, 1H, J=11.9 Hz), 4.97 (d, 1H, J=11.9 Hz), 7.29–7.40 (m, 5H), 8.00 (d, 2H, J=9.0 Hz), 8.22 (d, 2H, J=9.0 Hz); ^{13}C NMR ($CDCl_3$) δ 20.5, 21.8, 63.7, 66.7, 68.1, 123.4, 126.7, 127.6, 128.1, 130.5, 135.0, 137.2, 150.4, 164.1; Anal. Calcd for $C_{18}H_{17}NO_5$: C, 66.05; H, 5.23; N, 4.28. Found: C, 65.99; H, 5.23; N, 4.27.

4.5.2. (2-Phenyl-1-oxaspiro[2.5]oct-2-yl)methyl 4-nitrobenzoate (14). Light yellowish crystals; IR (KBr) 1730, 1529, 1273 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.19–1.88 (m, 10H), 4.59 (d, 1H, J=11.9 Hz), 4.98 (d, 1H, J=11.9 Hz), 7.28–7.42 (m, 5H), 7.99 (d, 2H, J=8.9 Hz), 8.22 (d, 2H, J=8.9 Hz); ^{13}C NMR ($CDCl_3$) δ 24.5, 25.4, 25.5, 30.8, 31.6, 67.6, 68.0, 68.3, 123.5, 126.8, 127.6, 128.2, 130.6, 135.1, 137.1, 150.5, 164.3; Anal. Calcd for $C_{21}H_{21}NO_5$: C, 68.65; H, 5.76; N, 3.81. Found: C, 68.74; H, 5.77; N, 3.81.

4.6. Lewis acid treatment of the epoxides

4.6.1. General procedure of the reaction of epoxy acylates and Lewis acid. Lewis acid (0.3 mmol) was

Reactions in Scheme 1

Entry	Substrate	Lewis acid	CH_2Cl_2 (mL)	Product yield
1	*trans*-**1a** 108.9 mg (0.397 mmol)	$BF_3{\cdot}Et_2O$ 50 μL (0.407 mmol)	4.0	*trans*-**2a** 91.1 mg (84%)
2	*trans*-**1b** 95.4 mg (0.324 mmol)	$BF_3{\cdot}Et_2O$ 40 μL (0.325 mmol)	3.2	*trans*-**2b** 64.1 mg (67%)
3	*trans*-**1c** 101.3 mg (0.299 mmol)	$BF_3{\cdot}Et_2O$ 40 μL (0.325 mmol)	3.0	*trans*-**2c** 91.2 mg (90%)

added dropwise to a solution of epoxy acylate (0.3 mmol) in CH_2Cl_2 (3 mL) at 0°C under N_2 and the resulting mixture was stirred at 0°C or rt. After completion of the reaction (TLC check), sat. aq. $NaHCO_3$ was added to the mixture. The resulting solution was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography using hexane–AcOEt as the eluent.

4.6.2. *trans*-2-Methyl-3-oxo-2-phenylcyclopentyl 2,2-dimethylpropanoate (*trans*-2a). Colorless oil; IR (KBr) 1748, 1732, 1283, 1146 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (s, 9H), 1.35 (s, 3H), 1.92–2.14 (m, 2H), 2.40–2.48 (m, 2H), 5.75 (t, 1H, J=3.5 Hz), 7.24–7.36 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 19.4, 25.1, 27.0, 34.4, 38.9, 58.0, 79.1, 126.2, 127.2, 128.9, 140.5, 177.5, 217.7; HRMS (FAB) Calcd for $C_{17}H_{23}O_3$ (M^++H): 275.1647. Found: 275.1674.

4.6.3. *trans*-2-Methyl-3-oxo-2-phenylcyclopentyl benzoate (*trans*-2b). Colorless oil; IR (KBr) 1748, 1722, 1273, 1111 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (s, 3H), 2.18–2.23 (m, 2H), 2.49–2.59 (m, 2H), 6.05 (t, 1H, J=3.7 Hz), 7.28–7.62 (m, 8H), 8.03 (d, 2H, J=7.6 Hz); ^{13}C NMR ($CDCl_3$) δ 19.7, 25.2, 34.5, 58.3, 80.0, 126.2, 127.3, 128.5, 129.0, 129.5, 129.7, 133.3, 140.4, 165.7, 217.7; HRMS (FAB) Calcd for $C_{19}H_{19}O_3$ (M^++H): 295.1334. Found: 295.1344.

4.6.4. *trans*-2-Methyl-3-oxo-2-phenylcyclopentyl 4-nitrobenzoate (*trans*-2c). Light yellowish crystals; mp 119–121°C (hexane–EtOAc); IR (KBr) 1748, 1728, 1532, 1273, 1117, 1103 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (s, 3H), 2.17–2.30 (m, 2H), 2.52–2.60 (m, 2H), 6.08 (t, 1H, J=3.6 Hz), 7.29–7.40 (m, 5H), 8.20 (d, 2H, J=9.0 Hz), 8.31 (d, 2H, J=9.0 Hz); ^{13}C NMR ($CDCl_3$) δ 19.6, 25.2, 34.4, 58.3, 81.2, 123.7, 126.2, 127.6, 129.2, 130.7, 135.0, 140.0, 150.7, 163.9, 217.1; Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 67.01; H, 5.12; N, 4.09.

4.6.5. *cis*-2-Methyl-3-oxo-2-phenylcyclopentyl 2,2-dimethylpropanoate (*cis*-2a). Colorless needles; mp 129–133°C (hexane–AcOEt); IR (KBr) 1738, 1717, 1285, 1167 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.84 (s, 9H), 1.48 (s, 3H), 2.03–2.11 (m, 1H), 2.31–2.42 (m, 1H), 2.56–2.62 (m, 2H), 5.43 (dd, 1H, J=4.3, 2.1 Hz), 7.19–7.30 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 23.2, 25.8, 26.6, 35.8, 38.5, 56.7, 79.6, 126.7, 127.6, 128.0, 138.8, 177.1, 217.9; Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.27; H, 8.04.

4.6.6. 1-(1,1-Dimethylethyl)-3-methyl-6-phenyl-2,7,8-trioxatricyclo[3.2.1.03,6]octane (4a). Colorless crystals; mp 56–59°C (hexane–AcOEt); IR (KBr) 1489, 1455, 1402, 1163, 1063 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (s, 3H), 1.26 (s, 9H), 1.82–1.93 (m, 1H), 2.17–2.25 (m, 3H), 4.21 (dd, 1H, J=2.1, 1.8 Hz), 7.25–7.42 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 19.8, 25.4, 28.5, 32.8, 33.0, 82.9, 88.8, 94.0, 122.3, 125.4, 128.1, 128.5, 133.4; Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.28; H, 8.04.

4.6.7. *cis*-2-Methyl-3-oxo-2-phenylcyclopentyl benzoate (*cis*-2b). Colorless crystals; mp 101–102°C (hexane–AcOEt)); IR (KBr) 1748, 1717, 1279, 1113 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.56 (s, 3H), 2.24–2.29 (m, 1H), 2.45–2.72 (m, 3H), 5.62 (t, 1H, J=4.0 Hz), 7.14–7.50 (m, 8H), 7.65 (dd, 2H, J=8.5, 1.4 Hz); ^{13}C NMR ($CDCl_3$) δ 22.8 25.8, 35.8, 57.1, 80.6, 127.0, 127.8, 128.1, 128.2, 129.4, 129.8, 133.0, 138.7, 165.5, 217.9.

4.6.8. 3-Methyl-1,6-diphenyl-2,7,8-trioxatricyclo[3.2.1.03,6]-octane (4b). Colorless oil; IR (KBr) 1453, 1387, 1317, 1078, 1053 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.11 (s, 3H), 1.97–2.04 (m, 1H), 2.30–2.45 (m, 3H), 4.45 (d, 1H, J=4.3 Hz),

Reactions in Scheme 2

Entry	Substrate	Lewis acid	CH_2Cl_2 (mL)	Product yield
1	*cis*-**1a** 103.1 mg (0.376 mmol)	$BF_3{\cdot}Et_2O$ 50 μL (0.407 mmol)	3.8	*cis*-**2a** 25.7 mg (25%) **4a** 49.4 mg (48%)
2	*cis*-**1b** 103.3 mg (0.351 mmol)	$BF_3{\cdot}Et_2O$ 45 μL (0.366 mmol)	3.5	*cis*-**2b** 28.1 mg (27%) **4b** 45.2 mg (43%)
3	*cis*-**1c** 103.9 mg (0.306 mmol)	$BF_3{\cdot}Et_2O$ 40 μL (0.326 mmol)	3.0	*cis*-**2c** 51.5 mg (50%) **5** 16.5 mg (31%)
4	*cis*-**1d** 93.6 mg (0.276 mmol)	$BF_3{\cdot}Et_2O$ 35 μL (0.285 mmol)	2.8	*cis*-**2d** 53.9 mg (58%) **5** 11.9 mg (25%)
5	*cis*-**1e** 58.2 mg (0.165 mmol)	$BF_3{\cdot}Et_2O$ 20 μL (0.163 mmol)	1.7	*cis*-**2e** 30.6 mg (53%) **5** 5.6 mg (20%)

Reactions in Scheme 4

Entry	Substrate	Lewis acid	CH_2Cl_2 (mL)	Product yield
1	**8** 101.1 mg (0.273 mmol)	$BF_3{\cdot}Et_2O$ 35 μL (0.285 mmol)	2.8	**9** 97.9 mg (97%)
2	**8** 42.6 mg (0.115 mmol)	$BF_3{\cdot}Et_2O$ 2 μL (0.016 mmol)	1.2	**9** 39.6 mg (93%)
3	**10** 91.4 mg (0.238 mmol)	$BF_3{\cdot}Et_2O$ 30 μL (0.244 mmol)	2.4	**11** 87.6 mg (94%)
4	**10** 58.4 mg (0.152 mmol)	$BF_3{\cdot}Et_2O$ 2 μL (0.016 mmol)	1.5	**11** 54.1 mg (93%)

7.34–7.45 (m, 8H), 7.79–7.83 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 20.2, 28.3, 33.1, 83.5, 89.8, 95.1, 117.0, 125.3, 127.0, 128.2, 128.4, 128.6, 130.1, 131.2, 132.7; HRMS (FAB) Calcd for $C_{19}H_{19}O_3$ (M^++H): 295.1334. Found: 295.1325.

4.6.9. *cis*-2-Methyl-3-oxo-2-phenylcyclopentyl 4-nitrobenzoate (*cis*-2c). Light yellowish needles; mp 125–127°C (hexane–AcOEt); IR (KBr) 1748, 1725, 1531, 1277, 1116, 1103 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.59 (s, 3H), 2.27–2.33 (m, 1H), 2.50–2.74 (m, 3H), 5.66 (dd, 1H, *J*=4.6, 2.7 Hz), 7.16–7.32 (m, 5H), 7.75 (d, 2H, *J*=8.9 Hz), 8.15 (d, 2H, *J*=8.9 Hz); ^{13}C NMR ($CDCl_3$) δ 22.7, 25.7, 35.8, 57.2, 81.7, 123.3, 127.1, 127.6, 128.2, 130.4, 135.1, 138.4, 150.4, 163.5, 217.4; Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 67.18; H, 5.12; N, 4.09.

4.6.10. 3-Methyl-2-phenylcyclopent-2-en-1-one (5). Colorless oil; IR (KBr) 1696, 1379, 1134 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.19 (s, 3H), 2.54–2.67 (m, 4H), 7.27–7.44 (m, 5H).

4.6.11. *cis*-2-Methyl-3-oxo-2-phenylcyclopentyl 2-nitrobenzoate (*cis*-2d). Colorless oil; IR (KBr) 1738, 1732, 1538, 1352, 1288, 1129, 1075 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.56 (s, 3H), 2.37–2.68 (m, 4H), 5.74 (dd, 1H, *J*=4.3, 2.1 Hz), 6.77 (dd, 1H, *J*=7.6, 1.8 Hz), 7.23–7.37 (m, 5H), 7.45–7.56 (m, 2H), 7.87 (d, 1H, *J*=7.9 Hz); ^{13}C NMR ($CDCl_3$) δ 22.8, 25.2, 35.7, 57.1, 81.9, 123.8, 126.9, 127.9, 128.1, 129.2, 131.4, 132.9, 138.5, 164.2, 217.5; HRMS (FAB) Calcd for $C_{19}H_{18}NO_5$ (M^++H): 340.1185. Found: 340.1204.

4.6.12. *cis*-2-Methyl-3-oxo-2-phenylcyclopentyl 2-methyl-6-nitrobenzoate (*cis*-2e). Colorless needles; mp 146–149°C (hexane–AcOEt); IR (KBr) 1740, 1725, 1545, 1285, 1273, 1116 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.55 (s, 3H), 1.63 (s, 3H), 2.46–2.62 (m, 4H), 5.71 (dd, 1H, *J*=2.9, 1.8 Hz), 7.19–7.41 (m, 7H), 7.91 (dd, 1H, *J*=7.3, 2.2 Hz); ^{13}C NMR ($CDCl_3$) δ 18.1, 23.0, 24.7, 35.4, 55.6, 82.4, 121.6, 127.0, 127.9, 128.1, 128.9, 129.7, 135.9, 137.7, 138.6, 145.8, 165.2, 217.1; Anal. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.88; H, 5.50; N, 3.98.

Reactions in Scheme 3

4.6.13. *trans*-2-Acetyl-2-phenylcyclopentyl 4-nitrobenzoate (7). **7** (49.8 mg, 62%) was obtained from **6** (80.9 mg, 0.229 mmol), $BF_3{\cdot}Et_2O$ (30 mL, 0.244 mmol), and CH_2Cl_2 (2.3 mL). Colorless crystals; mp 149–151°C (hexane–AcOEt); IR (KBr) 1725, 1715, 1530, 1277 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.57–1.62 (m, 1H), 1.86–1.98 (m, 2H), 1.91 (s, 3H), 2.20–2.37 (m, 2H), 2.71–2.83 (m, 1H), 6.17 (d, 1H, *J*=5.2 Hz), 7.30–7.43 (m, 5H), 8.14 (d, 2H, *J*=9.1 Hz), 8.30 (d, 2H, *J*=9.1 Hz); ^{13}C NMR ($CDCl_3$) δ 20.6, 27.3, 31.6, 33.2, 68.5, 81.2, 123.7, 126.3, 127.7, 129.2, 130.7, 135.3, 138.8, 150.7, 163.9, 205.7; Anal. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.97; H, 5.39; N, 3.98.

4.6.14. *trans*-2-Methyl-2-[4-(methyloxy)phenyl]-3-oxocyclopentyl 4-nitrobenzoate (9). Yellowish crystals; mp 167–169°C (hexane–AcOEt); IR (KBr) 1746, 1723, 1520, 1277, 1253, 1117, 1105 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.41 (s, 3H), 2.17–2.59 (m, 4H), 3.80 (s, 3H), 6.05 (t, 1H, *J*=3.5 Hz), 6.90 (d, 2H, *J*=9.0 Hz), 7.22 (d, 2H, *J*=9.0 Hz), 8.19 (d, 2H, *J*=9.0 Hz), 8.31 (d, 2H, *J*=9.0 Hz); ^{13}C NMR ($CDCl_3$) δ 19.7, 25.2, 34.4, 55.3, 57.7, 81.3, 114.6, 123.7, 127.4, 130.8, 131.8, 135.2, 150.8, 158.9, 164.0, 217.2; Anal. Calcd for $C_{20}H_{19}NO_6$: C, 65.03; H, 5.18; N, 3.79. Found: C, 64.89; H, 5.22; N, 3.83.

4.6.15. *trans*-2-Acetyl-2-[4-(methyloxy)phenyl]cyclopentyl 4-nitrobenzoate (11). Colorless oil; IR (KBr) 1728, 1722, 1531, 1516, 1277, 1255, 1121, 1105 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.65–2.05 (m, 3H), 1.99 (s, 3H), 2.35–2.54 (m, 3H), 3.74 (s, 3H), 6.19 (d, 1H, *J*=4.9 Hz), 6.84 (d, 2H, *J*=8.3 Hz), 7.22 (d, 2H, *J*=8.3 Hz), 7.71 (d, 2H, *J*=9.2 Hz), 8.12 (d, 2H, *J*=9.2 Hz); ^{13}C NMR ($CDCl_3$) δ 21.3, 24.9, 31.3, 31.5, 55.1, 68.7, 79.6, 114.0, 123.2, 128.5, 129.2, 130.2, 135.8, 150.1, 158.8, 163.6, 207.6; HRMS (FAB) Calcd for $C_{21}H_{22}NO_6$ (M^++H): 384.1448. Found: 384.1450.

4.6.16. (3-Methyl-2-oxo-3-phenylbutyl 4-nitrobenzoate (13). Colorless needles; IR (KBr) 1738, 1716, 1539, 1279, 1128, 1105 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.61 (s, 6H), 4.85 (s, 2H), 7.32–7.44 (m, 5H), 8.20 (d, 2H, *J*=9.0 Hz), 8.28 (d, 2H, *J*=9.0 Hz); ^{13}C NMR ($CDCl_3$) δ 25.3, 50.6, 65.9, 123.5, 126.2, 127.5, 129.1, 131.0, 134.8, 142.5, 150.7, 164.0, 205.0; Anal. Calcd for $C_{18}H_{17}NO_5$: C, 66.05; H, 5.23; N, 4.28. Found: C, 66.17; H, 5.27; N, 4.31.

Reactions in Scheme 5

Entry	Substrate	Lewis acid	CH_2Cl_2 (mL)	Product yield
1	**12** 36.2 mg (0.111 mmol)	$BF_3{\cdot}Et_2O$ 15 μL (0.122 mmol)	1.1	**13** 36.1 mg (quant)
2	**14** 75.1 mg (0.204 mmol)	$BF_3{\cdot}Et_2O$ 25 μL (0.203 mmol)	2.0	**15** 69.4 mg (92%)

4.6.17. 2-Oxo-2-(1-phenylcyclohexyl)ethyl 4-nitrobenzoate (15). Colorless needles IR (KBr) 1738, 1723, 1532, 1275 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25–1.65 (m, 6H), 1.92–2.00 (m, 2H), 2.37–2.42 (m, 2H), 4.85 (s, 2H), 7.28–7.44 (m, 5H), 8.19 (d, 2H, J=9.0 Hz), 8.27 (d, 2H, J=9.0 Hz); ^{13}C NMR ($CDCl_3$) δ 22.8, 25.7, 33.5, 54.7, 66.1, 123.5, 126.6, 127.7, 129.1, 131.0, 134.9, 141.3, 150.6, 164.1, 203.9; Anal. Calcd for $C_{21}H_{21}NO_5$: C, 68.65; H, 5.76; N, 3.81. Found: C, 68.83; H, 5.77; N, 3.81.

Reactions in Scheme 6

4.6.18. (1*R*)-3-Methyl-2-[4-(methyloxy)phenyl]cyclopent-2-en-1-ol (17). $BH_3{\cdot}Me_2S$ (2 M in THF, 400 μL, 0.80 mmol) was added dropwise to a solution of (*S*)-5,5-diphenyl-2-methyl-3,4-propan-1,3,2-oxazaborodine (167 mg, 0.602 mmol) in THF (7.0 mL) at 0°C under N_2. After being stirred for 30min, a solution of 3-methyl-2-phenyl-2-cyclopentan-1-one (100 mg, 0.502 mmol) in THF (8 mL) was added slowly to the resulting mixture. After being stirred for 30 min, MeOH was added to the mixture. The solvent was removed in vacuo. The residue was purified by SiO_2 column chromatography using hexane–AcOEt (3/1) as the eluent to give **17** (103 mg, quant.). Colorless oil; $[\alpha]_D^{20}$=+75.9 (*c* 1.05, $CHCl_3$); IR (KBr) 3400–3200, 1512, 1248 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.75–1.80 (m, 1H), 1.83 (s, 3H), 2.28–2.37 (m, 2H), 2.60–2.68 (m, 1H), 3.82 (s, 3H), 5.11 (brs, 1H), 6.91 (d, 2H, J=8.7 Hz), 7.30 (d, 2H, J=8.7 Hz); HPLC analysis: 90% ee. (CHIRALCEL OD; hexane/iPrOH=95/5; flow rate, 1.0 mL/min).

4.6.19. (1*R*,2*R*,5*S*)-5-Methyl-1-[4-(methyloxy)phenyl]-6-oxabicyclo[3.1.0]hexane-2-ol (18). A solution of *tert*-BuOOH (dried over $MgSO_4$ before use, 68%, 440 mg, 3.32 mmol) in benzene (4 mL) was added dropwise to a solution of **17** (114 mg, 0.558 mmol) and cat. amount of $VO(acac)_2$ in benzene (4 mL) at rt under N_2. After being stirred for 1.5 h at rt, sat. aq. $Na_2S_2O_3$ was added to the mixture. The resulting solution was extracted with AcOEt. Organic layer was washed with water and brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography using hexane–AcOEt (1/1) as the eluent to give **18** (107 mg, 87%). Colorless crystals; $[\alpha]_D^{20}$=−54.2 (*c* 1.01, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.18 (s, 3H), 1.41–1.51 (m, 1H), 1.67–1.79 (m, 1H), 2.03–2.15 (m, 2H), 3.82 (s, 3H), 4.65 (q, 1H, J=8.2 Hz), 6.93 (d, 2H, J=9.0 Hz), 7.33 (d, 2H, J=9.0 Hz).

4.6.20. (+)-(1*R*,2*S*,5*S*)-5-Methyl-1-[4-(methyloxy)phenyl]-6-oxabicyclo[3.1.0]hex-2-yl 4-nitrobenzoate ((+)-8). *p*-Nitrobenzoic acid (162 mg, 0.969 mmol) and Ph_3P (255 mg, 0.972 mmol) were added to a solution of **18** (107 mg, 0.486 mmol) in toluene (5 mL) at 0°C under N_2. Diethyl azadicarboxylate (toluene solu., 420 μL, 0.965 mmol) was added dropwise to the resulting solution. The mixture was stirred for 0.5 h, then treated with sat. aq. $NaHCO_3$. The resulting solution was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography using hexane–AcOEt (6/1) as the eluent to give *trans*-epoxy *p*-nitrobenzoate (+)-**8** (162 mg, 90%). Colorless needles; $[\alpha]_D^{20}$=+2195 (*c* 0.47, $CHCl_3$); HPLC analysis: 90% ee. (CHIRALCEL OD; hexane/iPrOH=98/2; flow rate, 1.0 mL/min).

4.6.21. (+)-(1*S*,2*R*)-2-Methyl-2-[4-(methyloxy)phenyl]-3-oxocyclopentyl 4-nitrobenzoate ((+)-9). (+)-9 (123 mg, 93%) was obtained from (+)-**8** (131.5 mg, 0.355 mmol), $BF_3{\cdot}Et_2O$ (4 μL, 0.032 mmol), CH_2Cl_2 (3.6 mL). Yellowish crystals; $[\alpha]_D^{20}$=+72.6 (*c* 2.53, $CHCl_3$); HPLC analysis: 90% ee. (CHIRALCEL OD; hexane/iPrOH=97/3; flow rate, 1.0 mL/min).

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