

Structure and Chiral Recognition Ability of *endo*-3-Benzamidonorborn-5-ene-2-carboxylic Acid

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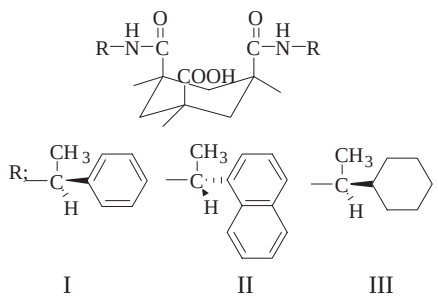
The absolute configuration of *endo*-3-benzamidonorborn-5-ene-2-carboxylic acid was determined by X-ray single crystal analysis of the diastereomeric salt with *cis*-2-(benzylamino)cyclohexylmethanol. It was demonstrated that the CH–π interaction between the vinylic hydrogen atom of the acid and the aromatic ring of the amine worked as an additional interaction for the stabilization of the structure formed by the hydrogen bond network. The chiral recognition ability was studied using a ^{1}H NMR titration technique and the intermolecular interactions were discussed based on the results of its saturated counterpart, *endo*-3-benzamidonorbornane-2-carboxylic acid.

Three Kemp's acid diamides (I–III, Scheme 1) were synthesized and their chiral recognition ability for several chiral amines was reported.[1,2] High recognition ability was observed for Kemp's acid diamides I and II, derived from 1-phenylethylamine and 1-(1-naphthyl)ethylamine, respectively, while III, derived from 1-(cyclohexyl)ethylamine, showed very poor discrimination ability. In addition, I and II were useful as ^{1}H NMR shift reagents for optical purity determination for some chiral amines.[2] These studies demonstrated that the substituents affect the discrimination ability in the order: naphthyl > phenyl > cyclohexyl group. This finding suggested that shielding and anisotropy effects as well as π–π interactions of the aromatic structures are important factors. Although I and II became good solvating agents,[2] they could not be used for optical resolution due to their poor crystallinity.

In order to elucidate more information on the relationship between chiral discrimination and optical resolution abilities, we chose *endo*-3-benzamidonorborn-5-ene-2-carboxylic acid (**1**) and *endo*-3-benzamidonorbornane-2-carboxylic acid (**2**) for further investigation. The former was resolved by preferential crystallization and a diastereomeric salt formation method,[3] but the structural features were not fully investigated. Their basic framework was rigid, due to the bicyclic structure, and the functional groups were located on one side of the molecule, possessing similar structural characteristics to those of I–III.



Scheme 1.

Herein, we report a new optical resolution method of **1**. The absolute configuration was determined to study the favorable structural features as an optical resolving agent. The chiral amine recognition ability in solution of **1** and **2** were discussed, based on a structural comparison and the ^{1}H NMR titration behavior toward several chiral amines.

Results and Discussion

Preparation of Chiral *endo*-3-Benzamidonorborn-5-ene-2-carboxylic Acid (1) and *endo*-3-Benzamidonorbornane-2-carboxylic Acid (2). Racemic compound **1** was easily synthesized in three steps according to the previously reported method;[3b] ammonolysis of 5-norbornene-2-*endo*,3-*endo*-dicarboxylic anhydride prepared from cyclopentadiene and maleic anhydride, Hoffmann reaction, and then Schotten–Baumann reaction to achieve a total yield of 56% (Scheme 3).

Optical resolution of **1** by preferential crystallization using benzylamine was reported.[3] More conveniently, the diastereomeric salt formation method was also developed using ephedrine,[3] but use of this material is legally limited in Japan. Accordingly, we screened new amines **3**–**7** (Scheme 2) and their derivatives for a diastereomeric salt formation method and succeeded in obtaining optically pure **1*** by using **3**, which has been used for resolution of several chiral acids.[4–9] Other amines **4**–**7** yielded no crystals from the diastereomeric salts with **1**.

In order to obtain a new chiral acid and to investigate the structure versus optical resolution ability relationship, we tried to prepare optically pure **2***. However, optical resolution of racemic **2** was unsuccessful using several chiral amines including **3**–**7**, so that **2*** was prepared by hydrogenation of **1***. The difference of the crystallinity between **1**–**3** and **2**–**3** salts suggested that a small structural difference, that is a double bond in **1** versus a single one in **2**, was important for crystallization.

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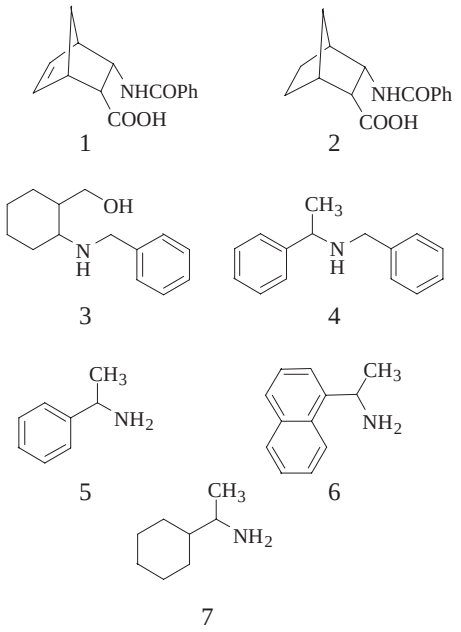
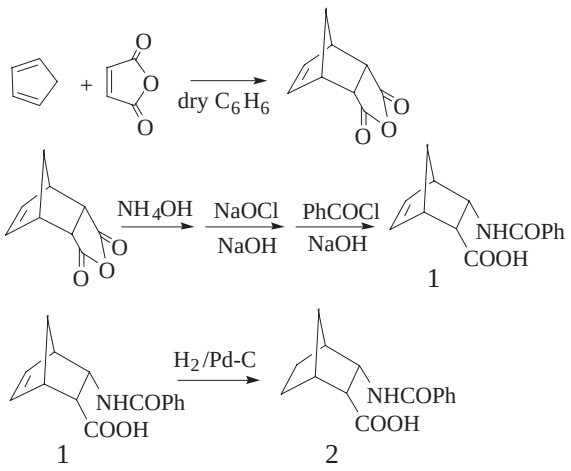


Scheme 2.

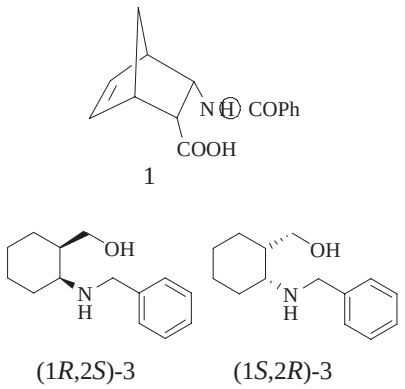


Scheme 3. Synthesis of **1** and **2**.

Determination of Optical Purity and Absolute Configuration. The optical purity of **1** and **2** was determined by HPLC analysis of their methyl esters using a chiral column (CHIRALCEL OJ, Daicel Chemical Industries, Ltd., Japan) with 2-propanol/hexane ratio of 5/95 and 15/85 as a mobile phase, respectively, at a flow rate of 0.5 $cm^3\ min^{-1}$. The retention times of the two enantiomers of **1** were 26.3 and 32.1 min, and were 13.2 and 16.7 min for those of **2**.

The less-soluble salt of (−)-**1** and (1*R*,2*S*)-**3** (Scheme 4) was recrystallized from ethyl acetate and the molecular structure was determined by single crystal X-ray analysis.[10] Selected experimental parameters and crystal data are summarized in Table 1. According to the result shown in Fig. 1, the absolute configuration was determined as (1*R*,2*S*,3*R*,4*S*)-**1**. If one compares with the HPLC data, one can identify the enantiomer eluted at a retention time of 26.3 min as (−)-(1*R*,2*S*,3*R*,4*S*)-**1**; therefore, that at 32.1 min was (+)-(1*S*,2*R*,3*S*,4*R*)-**1**.

Previously we reported that hydrogen bond networks form



Scheme 4.

Table 1. Crystal Data and Experimental Conditions for (1*R*,2*S*,3*R*,4*S*)-**1** and (1*R*,2*S*)-**3**

Empirical formula	$C_{29}H_{36}N_2O_4$
Formula weight	476.61
Crystal system	Monoclinic
Space group	$P2_1$
a/Å	6.3370(9)
b/Å	22.553(2)
c/Å	9.433(1)
β/°	105.740(6)
V/Å^3	1297.5(2)
Z	2
D_{cald}/g cm^{-3}	1.220
μ(Cu Kα)/mm^{-1}	6.47
No. of measured reflections	2759
No. of independent reflections	2529
R_{int}	0.019

in a diastereomeric salt and that van der Waals interactions play a significant role in stabilizing the crystal structures.[8,9] In the present case, **1** and **3** form columns along the *b*-axis and the acids and amines line up, respectively, in the same direction but facing the opposite side in each column, as seen in Fig. 1B. One oxygen atom of a carboxyl group forms two hydrogen bonds with an amino group and a hydroxy group of another amine in the same *ac* plane (Fig. 1A). The distance between the vinylic H atom of **1** and the aromatic ring of **3** was 2.977 Å, which suggests a CH–π interaction[11] (dotted line), as separately shown in Fig. 2. These two kinds of interactions seem to make the firm network in the *ac* plane, probably leading to the good crystallinity of the salt. On the other hand, the C–H bond angle of the corresponding sp^3 carbon in the norbornane moiety of **2** does not seem to allow the same CH–π interaction, judging from the CPK model examination.

Chiral Amine Recognition of 1. The chiral amine recognition ability of **1*** and **2*** in solution was investigated for five chiral amines **3**–**7** using a ^{1}H NMR titration method. The chemical shifts of **1*** and **2*** were observed after mixing with (*R*)- or (*S*)-amine in $CDCl_3$ at room temperature. As the structures of the two diastereomeric salts differ from each other, that is, the compounds are different, the corresponding protons of **1*** or **2*** are placed in different magnetic environments and the chemical shift change can be observed.

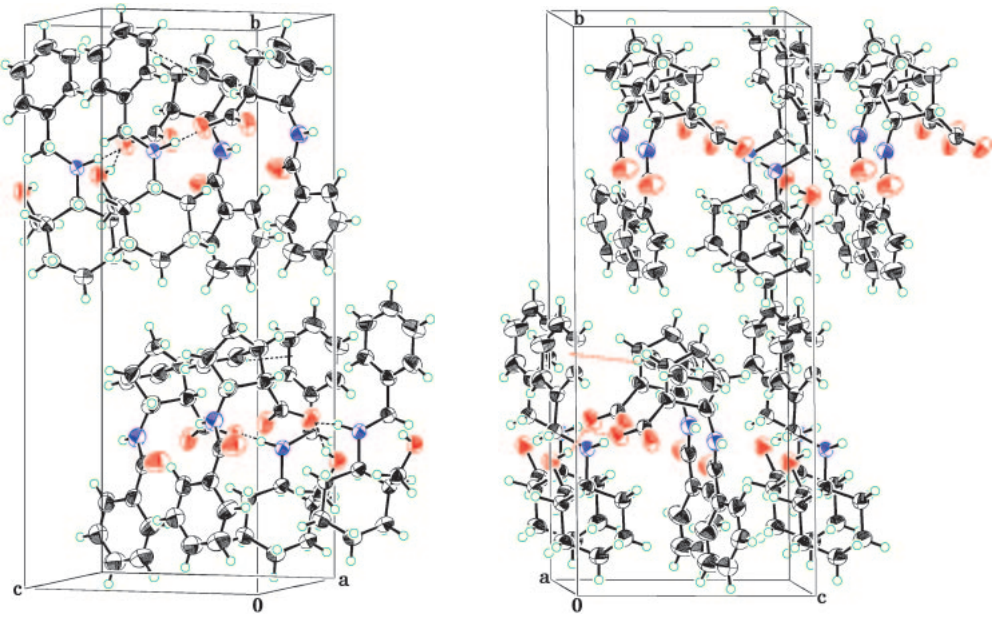


Fig. 1. Crystal packing of (1*R*,2*S*,3*R*,4*S*)-**1** and (1*R*,2*S*)-**3**.

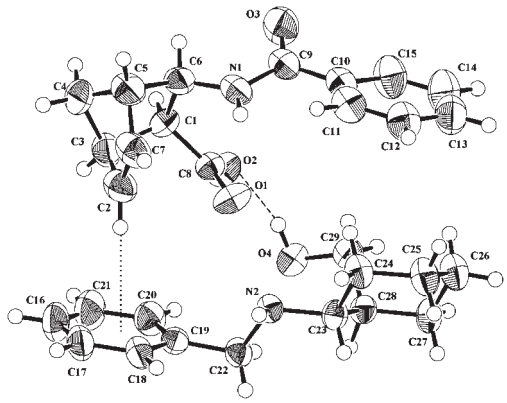


Fig. 2. ORTEP drawing of (1*R*,2*S*,3*R*,4*S*)-**1** and (1*R*,2*S*)-**3** with the hydrogen bonds (dashed line) and the CH–π interaction (dotted line).

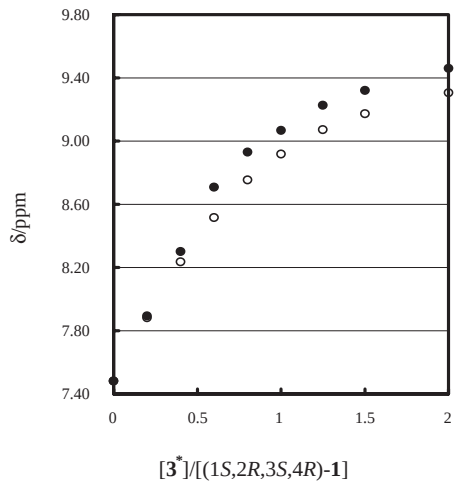


Fig. 3. ^{1}H NMR titration curves of amide protons of (1*S*,2*R*,3*S*,4*R*)-**1** with **3***, optically pure **3**, in $CDCl_3$ at room temperature. Solid symbols represent (1*S*,2*R*,3*S*,4*R*)-**1** + (1*R*,2*S*)-**3** and open symbols represent (1*S*,2*R*,3*S*,4*R*)-**1** + (1*S*,2*R*)-**3**. See Scheme 4 for the structures.

The NMR spectra of (1*S*,2*R*,3*S*,4*R*)-**1** with each enantiomer of **3** showed a large chemical shift change $\Delta\delta$ for the amide proton of **1** and as much as 0.16 ppm of $\Delta\Delta\delta$ (the chemical shift difference between (1*S*,2*R*,3*S*,4*R*)-**1** + (1*R*,2*S*)-**3** and (1*S*,2*R*,3*S*,4*R*)-**1** + (1*S*,2*R*)-**3**), as shown in Fig. 3. The downfield shift may be due to the decrease of intramolecular H-bonding with the carboxyl group, which forms the intermolecular H-bonding with the hydroxy group of **3** (Figs. 1 and 2). The titration of (1*S*,2*R*,3*S*,4*R*)-**1** with other amines also showed large $\Delta\delta$, but less diastereomeric difference, $|\Delta\Delta\delta|$, as summarized in Table 2. Especially, 1-(cyclohexyl)ethylamine **7** gave the smallest $|\Delta\Delta\delta|$ (0.017 ppm) in spite of having a large $\Delta\delta$.

In our previous work,[2] we demonstrated that the diastereomeric difference was large for amines having aromatic rings. The present results also demonstrated the same effect of the aromatic structure from the order of the $|\Delta\Delta\delta|$ value; 1-(1-naphthyl)ethylamine **6** > 1-phenylethylamine **5** > 1-(cyclohexyl)-ethylamine **7**. The salt formation constants, K_a, for (1*S*,2*R*,3*S*,4*R*)-**1** and **3**–**7** were calculated from the titration curves of the chemical shifts of the amide protons using a non-linear least-square fitting method.[2a] The ratio $K_a(R)/K_a(S)$ suggests the enantiomer discrimination ability toward the chiral amine; this became largest for **3**, while for **7** it became unity, as expected from the very small $|\Delta\Delta\delta|$. The interaction strength between carboxyl groups and amine groups is expected to be almost the same in any case. The results, therefore, mean that additional weak interactions, such as van der Waals interaction, π–π interaction, and CH–π interaction, act as important factors of structure fitting in chiral recognition. The NMR titration data in the aromatic proton region indicate that

Table 2. Chemical Shift ($\Delta\delta$) and Diastereomeric Difference ($|\Delta\Delta\delta|$) of Amide Proton of (1*S*,2*R*,3*S*,4*R*)-**1** and Salt Formation Constant (K_a)

	Amine	$\Delta\delta$/ppm	$\lvert\Delta\Delta\delta\rvert$/ppm	K_a	$K_a(R)/K_a(S)$
3	1*S*,2*R*	1.977	0.155	120	1.20
	1*R*,2*S*	1.822		100	
4	*R*	1.505	0.087	40	1.11
	S	1.592		36	
5	*R*	1.657	0.088	210	0.70
	S	1.569		300	
6	*R*	1.658	0.098	120	0.71
	S	1.560		170	
7	*R*	1.907	0.017	1000	1.00
	S	1.890		1000	

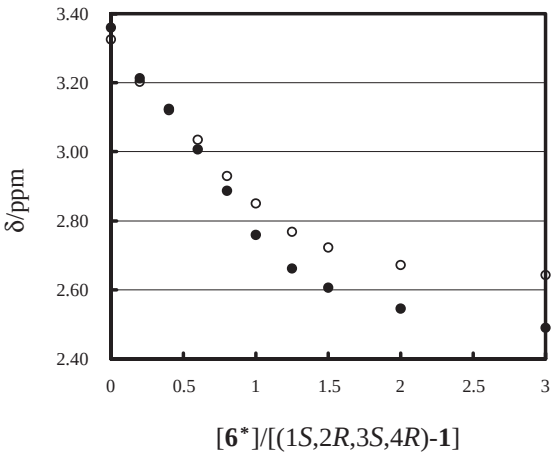
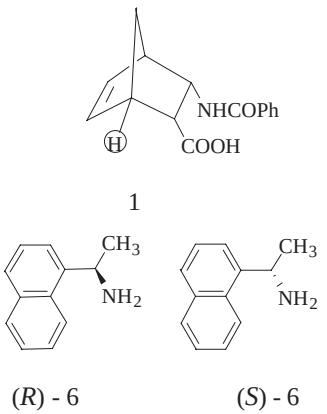


Fig. 4. ^{1}H NMR titration curves of methine protons of (1*S*,2*R*,3*S*,4*R*)-**1** with **6***, optically pure **6**, in $CDCl_3$ at room temperature. Solid symbols represent data for (1*S*, 2*R*,3*S*,4*R*)-**1** + (*R*)-**6**. Open symbols represent data for (1*S*,2*R*,3*S*,4*R*)-**1** + (*S*)-**6**. See Scheme 5 for the structures.



Scheme 5.

the chiral recognition ability increases as the aromatic feature of the amines increases, which suggests that the π–π interaction should be the major factor.

Comparison of Recognition Ability between 1 and 2. Similar diastereomeric differences in the ^{1}H NMR were also observed for the other protons of (1*S*,2*R*,3*S*,4*R*)-**1**. Figure 4, for example, shows the titration results of the methine proton of (1*S*,2*R*,3*S*,4*R*)-**1** with (*R*)- and (*S*)-**6** (Scheme 5). The upfield shift could be the result of the ring current effects because of larger shift for **6** (0.87 and 0.68 ppm for (*R*)- and (*S*)-isomer, respectively, as seen in Fig. 4) than for **5** (0.61 and 0.46 ppm for (*R*)- and (*S*)-isomer, respectively. Not shown.), although the structure of **1**–**6** is not elucidated. These results are summarized in Table 3. Similar to the results for the amide proton described above, the order of the substituent effect for chiral recognition of α-chiral primary amines was naphthyl > phenyl > cyclohexyl.

Almost the same results were seen for (1*R*,2*S*,3*R*,4*S*)-**2**. The results for each enantiomeric amine are summarized for the methine proton in Table 4. If we compared the results of Tables 3 and 4, we find that both $|\Delta\Delta\delta|$ values and

Table 3. Chemical Shift ($\Delta\delta$) and Diastereomeric Difference ($|\Delta\Delta\delta|$) of Methine Proton of (1*S*,2*R*,3*S*,4*R*)-**1** and Salt Formation Constant (K_a)

	Amine	$\Delta\delta$/ppm	$\lvert\Delta\Delta\delta\rvert$/ppm	K_a	$K_a(R)/K_a(S)$
3	1*S*,2*R*	0.124	0.016	150	2.14
	1*R*,2*S*	0.108		70	
4	*R*	0.102	0.001	110	1.10
	S	0.103		100	
5	*R*	0.610	0.147	400	0.66
	S	0.463		600	
6	*R*	0.870	0.186	200	0.66
	S	0.684		300	
7	*R*	0.219	0.006	1000	0.77
	S	0.225		1300	

Table 4. Chemical Shift ($\Delta\delta$) and Diastereomeric Difference ($|\Delta\Delta\delta|$) of Methine Proton of (1*R*,2*S*,3*R*,4*S*)-**2** and Salt Formation Constant (K_a)

	Amine	$\Delta\delta$/ppm	$\lvert\Delta\Delta\delta\rvert$/ppm	K_a	$K_a(R)/K_a(S)$
3	1*S*,2*R*	0.086	0.015	110	0.846
	1*R*,2*S*	0.101		130	
4	*R*	0.137	0.016	50	1.67
	S	0.121		30	
5	*R*	0.507	0.178	900	0.82
	S	0.685		1100	
6	*R*	0.805	0.198	800	0.72
	S	1.003		1100	
7	*R*	0.253	0.007	3000	1.00
	S	0.260		3000	

$K_a(R)/K_a(S)$ demonstrate that the chiral recognition ability of **2*** for α-chiral primary amines was almost the same as that of **1*** in solution, in spite of the large difference of crystallinity of the salts with **3**. If one considers the optical resolution abilitiy of **1*** and the structural flexibility of the salt in solution, one will conclude that the CH–π interaction shown in Fig. 2 acts as a supporting interaction with an enantiomer of **3** in the crystallization.

In conclusion, a new diastereomeric salt formation method was developed for the resolution of *endo*-3-benzamidonorborn-5-ene-2-carboxylic acid (**1**) using *cis*-2-(benzylamino)cyclohexylmethanol. The absolute configuration of the diastereomeric complex was also determined. The corresponding saturated acid **2** prepared by hydrogenation of **1** did not crystallize with the various chiral amines studied. The less hindered olefin structure of **1** was favorable for good crystallinity due to the CH–π interactions which reinforce the crystal packing formed by a hydrogen bonding network; this resulted in the optical resolution ability. Although **2** was not applicable as a resolving agent, both **1*** and **2*** showed good chiral recognition with increasing discrimination ability for aromatic amines, which showed that the π–π interaction acts as an important factor in chiral recognition.

Experimental

General. ^{1}H NMR spectra were recordered on a Bruker AM-300 (300 MHz) spectrometer. IR spectra were measured on a JASCO FT/IR-400 spectrometer using KBr pellets. Optical rotations were measured on a JASCO DIP-370 polarimeter. High performance liquid chromatography was performed by a JASCO PU 980 intelligent HPLC system. Melting points were determined with a MEL-TEMP instrument.

cis-2-(Benzylamino)cyclohexylmethanol was prepared by a literature method;[12] 1-phenylethylamine, 1-(1-naphthyl)ethylamine, and *N*-benzylmethylbenzylamine were kindly supplied by Yamakawa Chemical Ind. Co., Ltd. 1-(cyclohexyl)ethylamine was obtained from Aldrich Chem. Co., and was used as received.

X-ray Analysis. The three-dimensional X-ray measurements were made on a Enraf-Nonius CAD4 diffractometer with graphite-monochromated Cu Kα radiation ($\lambda = 1.54178$ Å). The data were collected at a temperature of -42 ± 1 °C using the ω scan technique to a maximum 2θ value of 139.7°. The structure was solved by direct methods (SIR92) and expanded using Fourier techniques (DIRDIF94). The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. All calculations were performed using the teXan crystallographic software package of Molecular Structure Corporation.

Synthesis of *endo*-3-Benzamidonorborn-5-ene-2-carboxylic Acid (1). According to the literature,[3] 5-norbornene-2-*endo*,3-*endo*-dicarboxylic anhydride (6.01 g, 36.7 mmol) prepared from cyclopentadiene and maleic anhydride gave **1** (5.30 g, 20.6 mmol) in 56% after decoloration by active carbon and recrystallization from 99% EtOH.

Optical Resolution of *endo*-3-Benzamidonorborn-5-ene-2-carboxylic Acid (1). Racemic **1** (2.18 g, 8.48 mmol) and *cis*-(1*S*,2*R*)-(−)-**3** (1.86 g, 8.48 mmol) was dissolved in 2-PrOH (10 mL) to give the salt. After the solvent was removed, the remaining solid was recrystallized from AcOEt 3 times to yield the less-soluble salt of (1*R*,2*S*,3*R*,4*S*)-(−)-**1** and *cis*-(1*S*,2*R*)-(−)-**3** (1.31 g, 2.75 mmol, 32%); $[\alpha]_D^{26} = -90.3°$, $[\alpha]_{435}^{25} = -192.9°$ (*c* 0.5, 99% EtOH). The absolute configuration was determined by X-ray analysis, as mentioned in the next paragraph. The less-soluble salt was liberated by 1 M NaOH and *cis*-(1*S*,2*R*)-(−)-**3** was recovered by extraction with benzene. The aqueous layer was treated with 4 M HCl to get optically pure (1*R*,2*S*,3*R*,4*S*)-(−)-**1** (0.667 g, 2.59 mmol, 30%); $[\alpha]_D^{28} = -112.3°$, $[\alpha]_{435}^{25} = -251.7°$ (*c* 0.5, 99% MeOH). mp 178–180 °C.

The more-soluble salt was also liberated to give (1*S*,2*R*,3*S*,4*R*)-(+)-rich-**1**, which was then resolved with *cis*-(1*R*,2*S*)-(+)-**3** in the same way to obtain optically pure (1*S*,2*R*,3*S*,4*R*)-(+)-**1** (0.542 g, 2.11 mmol, 25%). $[\alpha]_D^{21} = +110.5°$, $[\alpha]_{435}^{25} = +246.6°$ (*c* 0.5, 99% MeOH).

Synthesis of *endo*-3-Benzamidonorbornane-2-carboxylic Acid (2). Racemic **1** (1.95 g, 7.59 mmol) was dissolved in 1 M NaOH (23 mL) and then distilled water (17 mL) was added. The mixture was hydrogenated over 5% Pd–charcoal (150 mg) at room temperature with 1 atm of H_2 for about 21 h. Then 2 M HCl was added to the solution till pH became 2 to obtain a white solid. The crude product was filtered and recrystallized from 99% EtOH to give colorless needles of **2** (1.56 g, 6.02 mmol, 79%). mp 230–232 °C; ^{1}H NMR ($CDCl_3$) δ 8.70 (d, $J = 6.6$ Hz, 1H), 7.87 (m, 2H), 7.85 (m, 4H), 4.45 (m, 1H), 3.05 (dd, $J = 10.7$, 3.7 Hz, 1H), 2.70 (s, 1H), 2.60 (s, 1H), 1.49 (m, 2H), 1.45 (m, 4H). IR (cm^{-1}) 3321, 2958, 1698, 1627, 1538, 1487, 1208, 720, 695. Found: C, 69.52; H, 6.59; N, 5.36%. Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40%.

Synthesis of (1*S*,2*S*,3*R*,4*R*)-(−)-*endo*-3-Benzamidonorbornane-2-carboxylic Acid, (1*S*,2*S*,3*R*,4*R*)-(−)-2. Optically pure (1*S*,2*S*,3*R*,4*R*)-(−)-**2** was prepared by hydrogenating (1*R*,2*S*,3*R*,4*S*)-(−)-**1** as mentioned above; $[\alpha]_D^{25} = -49.4°$, $[\alpha]_{435}^{25} = -106.2°$ (*c* 0.5, 99% MeOH). mp 194–195 °C.

**Synthesis of (1*R*,2*R*,3*S*,4*S*)-(+)-*endo*-3-Benzamidonorbor-

nane-2-carboxylic Acid, (1*R*,2*R*,3*S*,4*S*)-(+)-2. Optically pure (1*R*,2*R*,3*S*,4*S*)-(+)-**2** was also prepared in the same way by hydrogenating (1*S*,2*R*,3*S*,4*R*)-(+)-**1**; $[\alpha]_D^{25} = +48.2^\circ$, $[\alpha]_{435}^{25} = +100.8^\circ$ (*c* 0.5, 99% MeOH). mp 197–200 °C.

Determination of Optical Purity. Carboxylic acid **1** (48.0 mg, 0.187 mmol) was dissolved in MeOH (5 mL) and refluxed with a catalytic amount of concd and H_2SO_4 for about 5 h. Distilled water (10 mL) was added and the mixture was concentrated to remove all MeOH. Then the residue was extracted with Et_2O (10 mL) for 3 times to obtain the methyl ester of **1** (46.0 mg, 0.170 mmol, 91%). ^{1}H NMR ($CDCl_3$) δ 7.76 (s, 1H), 7.72 (s, 1H), 7.44 (m, 4H), 6.28 (m, 2H), 4.94 (dd, $J = 17.1$, 8.8, 3.4 Hz, 1H), 3.65 (s, 3H), 3.27 (m, 3H), 1.52 (q, $J = 8.8$ Hz, 2H).

The optical purity of the methyl ester was determined by HPLC (2-PrOH/hexane = 5/95) using CHIRALCEL OJ (Daicel Chem. Ind., Ltd). The retention times of the enantiomers of methyl ester of **1** were 26.3 and 32.1 min, respectively, at a flow rate of 0.5 $cm^3\,min^{-1}$.

Carboxylic acid **2** was treated in the same way to obtain the methyl ester (80%). ^{1}H NMR ($CDCl_3$) δ 8.70 (s, 1H), 7.86 (m, 2H), 7.47 (m, 4H), 4.47 (m, 1H), 3.71 (s, 3H), 3.03 (dd, $J =$ 10.9, 4.4 Hz, 1H), 1.45 (m, 6H).

The optical purity was also determined by HPLC (2-PrOH/hexane = 15/85) using the same chiral column. The retention times of the enantiomers of methyl ester of **2** were 13.2 and 16.7 min, respectively, at a flow rate of 0.5 $cm^3\,min^{-1}$.

NMR measurement. NMR titration was performed using a mixture of **1** and a certain amount of chiral amine in $CDCl_3$ (500 μL) at room temperature.

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References

1 a) D. S. Kemp and K. S. Petrakis, *J. Org. Chem.*, **46**, 5140 (1981). b) B. W. Baldwin, T. Hirose, Z.-H. Wang, T. Uchimaru, and A. Yliniemelä, *Chem. Lett.*, **1996**, 415. c) Z.-H. Wang, T. Hirose, B. W. Baldwin, and Y.-Y. Yang, *Chem. Commun.*, **1997**, 297.

2 a) T. Hirose, K. Naito, H. Shitara, H. Nohira, and B. W. Baldwin, *Tetrahedron: Asymmetry*, **12**, 375 (2001). b) T. Hirose, K. Naito, M. Nakahara, H. Shitara, Y. Aoki, H. Nohira, and B. W. Baldwin, *J. Inclusion Phenom. Macrocyclic Chem.*, **43**, 87 (2002).

3 K. Saigo, Y. Okuda, S. Wakabayashi, T. Hoshiko, and H. Nohira, *Chem. Lett.*, **1981**, 857.

4 H. Shitara, Y. Aoki, T. Hirose, and H. Nohira, *Chem. Lett.*, **1998**, 261.

5 Y. Aoki and H. Nohira, *Chem. Lett.*, **1993**, 113.

6 Y. Aoki and H. Nohira, *Liq. Cryst.*, **18**, 197 (1995).

7 H. Shitara, Y. Aoki, T. Hirose, and H. Nohira, *Bull. Chem. Soc. Jpn.*, **73**, 259 (2000).

8 K. Sakai, Y. Hashimoto, K. Kinbara, K. Saigo, H. Murakami, and H. Nohira, *Bull. Chem. Soc. Jpn.*, **66**, 3414 (1993).

9 K. Kinbara, K. Sakai, Y. Hashimoto, H. Nohira, and K. Saigo, *J. Chem. Soc., Perkin Trans. 2*, **1996**, 2615.

10 CCDC 232063 contains the supplementary crystallographic data. These data can be obtained free of charge via the Internet at http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk) upon quoting the full journal citation.

11 a) M. Nishio and M Hirota, *Tetrahedron*, **45**, 7201 (1989). b) M. Nishio, Y. Umezawa, M. Hirota, and Y. Takeuchi, *Tetrahedron*, **51**, 8665 (1995). c) Y. Umezawa, S. Tsuboyama, K. Honda, J. Uzawa, and M. Nishio, *Bull. Chem. Soc. Jpn.*, **71**, 1207 (1998). d) Y. Umezawa, S. Tsuboyama, H. Takahashi, J. Uzawa, and M. Nishio, *Tetrahedron*, **55**, 10047 (1999). e) H. Takahashi, S. Tsuboyama, Y. Umezawa, K. Honda, and M. Nishio, *Tetrahedron*, **56**, 6185 (2000). f) T. Obata, T. Shimo, M. Yasutake, T. Shinmyozu, M. Kawaminami, R. Yoshida, and K. Somekawa, *Tetrahedron*, **57**, 1531 (2001).

12 J. Nishikawa, T. Ishizaki, F. Nakayama, H. Kawa, K. Saigo, and H. Nohira, *Nippon Kagaku Kaishi*, **1979**, 754.