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# Rational Design of CH/$\pi$ Interaction Sites in a Basic Resolving Agent

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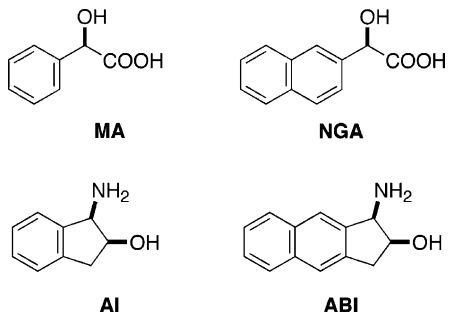
A novel synthetic basic resolving agent, *cis*-1-aminobenz[*f*]indan-2-ol (**ABI**), was rationally designed by introducing effective CH/$\pi$ interaction sites to *cis*-1-aminoindan-2-ol (**AI**), whose chiral recognition ability has been reported from our laboratory. **ABI** was applicable to a wide variety of racemic arylalkanoic acids and showed moderate to excellent chiral recognition ability, which was obviously higher than that of **AI**. The fundamental and important role of CH/$\pi$ interactions, such as tunable CH($sp^2$)/$\pi$ and CH($sp^3$)/$\pi$ interactions, in the chiral recognition by **ABI** was revealed by X-ray crystallographic study.

## Introduction

Crystals can offer a suitable environment for chiral recognition phenomena, since the movement of molecules in crystals is highly prevented to achieve three-dimensionally dissymmetric fixation. From this point of view, the sole crystallization of one of a pair of diastereomeric salts (diastereomeric salt formation) is very fascinating for the recognition of the chirality of racemates. In the diastereomeric salt formation, an enantiopure acidic or basic reagent (resolving agent) is essential, and natural products, their derivatives, and synthetic mandelic acid and 1-phenylethylamine are currently used as resolving agents. However, the number of basic resolving agents, which are widely applied in diastereomeric salt formation, is limited, compared with that of acidic resolving agents; basic resolving agents frequently used are 1-phenylethylamine, amino acid esters, and alkaloids. Moreover, these resolving agents are not necessarily applicable for the chiral recognition of given target racemates. Therefore, the development of a new synthetic basic resolving agent, which can be applicable to a wide variety of racemates, is highly desired.

We have recently reported that enantiopure *cis*-1-aminoindan-2-ol (**AI**) showed recognition ability with a variety of racemic arylalkanoic acids.[1] However, the chiral recognition ability was insufficient; a structural modification of **AI** was considered to be one attractive way to improve the chiral recognition ability of **AI**. On the other hand, we have also demonstrated that enantiopure 2-naphthylglycolic acid (NGA), designed on the basis of the structural characteristics and chiral recognition mechanism of enantiopure mandelic acid (MA) in diastereomeric salt formation, could recognize the chirality of a variety of racemic arylalkylamines and that its chiral recognition ability, higher than that of MA, was supposed to arise from effective CH/$\pi$ interactions in the corresponding less-soluble diastereomeric salts.[2] Although CH/$\pi$ interaction is generally considered to be very weak, compared with other nonbonding interactions such as hydrogen-bonding interaction and coordination interaction,[3] CH/$\pi$ interaction has been attracting much attention in recent years, owing to its remarkable role for the determination of molecular arrangement in crystals.[4] These facts strongly suggest that the introduction of CH/$\pi$ interaction site(s) to a known resolving agent is very attractive for the development of an efficient

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[‡] Department of Integrated Biosciences, Graduate School of Frontier Sciences.

(1) Kinbara, K.; Kobayashi, Y.; Saigo, K. *J. Chem. Soc., Perkin Trans. 2* **2000**, 111.

(2) (a) Kinbara, K.; Harada, Y.; Saigo, K. *J. Chem. Soc., Perkin Trans. 2* **2000**, 1339. (b) Kinbara, K.; Harada, Y.; Saigo, K. *Tetrahedron: Asymmetry* **1998**, *9*, 2219.

(3) Nishio, M.; Hirota, M.; Umezawa, Y. *The CH/π interaction. Evidence, Nature and Consequences*; Wiley−VCH: New York, 1998.

(4) (a) Matsumoto, A.; Kunisue, T.; Nagahama, S.; Matsumoto, A.; Sada, K.; Inoue, K.; Tanaka, T.; Miyata, M. *Mol. Cryst. Liq. Cryst.* **2003**, *390*, 11. (b) Thuery, P.; Jeong, T. G.; Yamato, T. *Supramol. Chem.* **2003**, *15* (5), 359. (c) Suezawa, H.; Yoshida, T.; Umezawa, Y.; Tsuboyama, S.; Nishio, M. *Eur. J. Inorg. Chem.* **2002**, *12*, 3148. (d) Abe, H.; Miyamura, K. *Inorg. Chim. Acta* **2000**, *298*, 90. (e) Umezawa, Y.; Tsuboyama, S.; Takahashi, H.; Uzawa, J.; Nishio, M. *Tetrahedron* **1999**, *55*, 10047.

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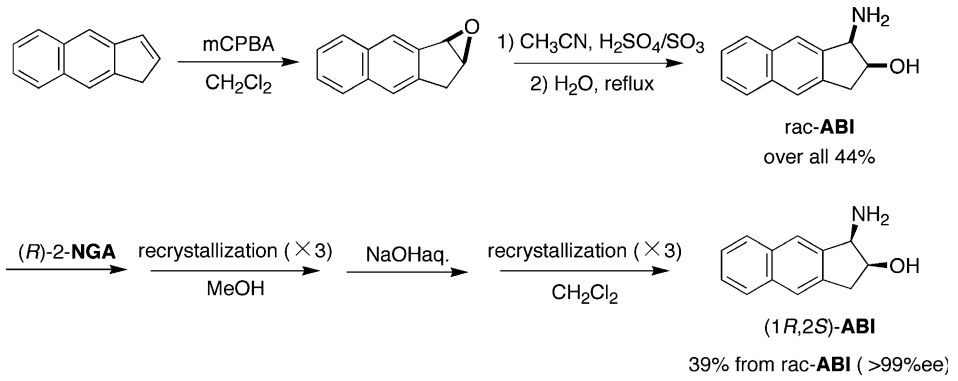
**SCHEME 1. Synthesis of Enantiopure ABI**



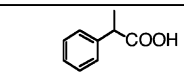
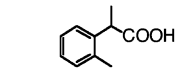
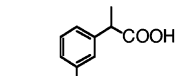
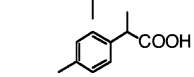
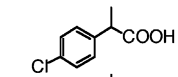
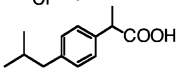
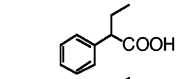
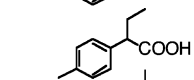
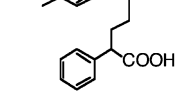
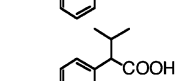
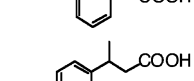
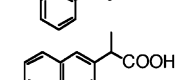
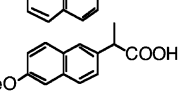

resolving agent. Thus, we rationally designed a novel basic resolving agent, *cis*-1-aminobenz[*f*]indan-2-ol (**ABI**), upon replacing the phenyl group of **AI** by a naphthyl group with an expectation that the naphthyl group would highly contribute to the realization of effective CH/π interactions in less-soluble diastereomeric salt crystals. In this paper, we report the synthesis and chiral recognition ability of enantiopure **ABI** and the chiral recognition mechanism for racemic arylalkanoic acids.

## Results and Discussion

**Preparation of (1*R*,2*S*)-1-Aminobenz[*f*]indan-2-ol (ABI).** Racemic *cis*-1-aminobenz[*f*]indan-2-ol (*rac*-**ABI**) was prepared by a procedure similar to that for the synthesis of racemic *cis*-1-aminoindan-2-ol.[5] The starting material, benz[*f*]indene, could be obtained in 64% total yield via five steps from commercially available 2-formylbenzoic acid.[6] The epoxidation of benz[*f*]indene, followed by the Ritter-type reaction, yielded *rac*-**ABI** in 44% total yield as shown in Scheme 1. The enantioseparation of *rac*-**ABI** was achieved in methanol by use of (*R*)-2-naphthylglycolic acid[2] as a resolving agent. Recrystallization of the crude less-soluble diastereomeric salt from methanol three times gave the diastereopure salt. Treatment of the salt with aqueous sodium hydroxide afforded the crude product, which was purified by recrystallization from chloroform to give (1*R*,2*S*)-1-aminobenz[*f*]indan-2-ol (**ABI**) in 39% overall yield.

**Chiral Recognition Ability of ABI for Arylalkanoic Acids**. At first, we tried the enantioseparation of various arylalkanoic acids by using **ABI** as a resolving agent in order to investigate the chiral recognition ability of **ABI**. The enantioseparations were performed under almost the same conditions: the diastereomeric salt was allowed to crystallize from ethanol/water at a constant temperature (30 °C), and the ratio and amount of the mixed solvent were adjusted so as to control the yield of the precipitated salt to be as close as possible to a range of 50−80%. No recrystallization was performed. The results are summarized in Table 1.

**TABLE 1. Chiral Recognition Ability of ABI for Arylalkanoic Acids**

| entry | racemic acid | | yield (%) | ee (%) | Absolute configuration | efficiency[a, b] |
|---|---|---|---|---|---|---|
| 1 |  | **1a** | 61 | 91 | *S* | 0.56 (0.62) |
| 2 |  | **1b** | 68 | 85 | *S* | 0.58 (0.20) |
| 3 |  | **1c** | 61 | 92 | *S* | 0.56 (0.54) |
| 4 |  | **1d** | 64 | 83 | *S* | 0.53 (0.20) |
| 5 |  | **1e** | 81 | 85 | —[c] | 0.69 (—[d]) |
| 6 |  | **1f** | 64 | 75 | *S* | 0.48 (0.06) |
| 7 |  | **1g** | 70 | 68 | *R* | 0.48 (0.37) |
| 8 |  | **1h** | 72 | 83 | *S* | 0.60 (0.56) |
| 9 |  | **1i** | 59 | 48 | *R* | 0.28 (0.35) |
| 10 |  | **1j** | 59 | 75 | *R* | 0.44 (0.39) |
| 11 |  | **2** | 83 | 54 | *S* | 0.45 (0) |
| 12 |  | **3a** | 53 | 55 | *S* | 0.29 (—[d]) |
| 13 |  | **3b** | 75 | 20 | *S* | 0.15 (—[d]) |

[a] Product yield of the diastereomeric salt and the ee of the liberated acid. [b] Values in parentheses are the resolution efficiencies when **AI** was used in place of **ABI**. [c] Not determined [d] Not crystallized.

As can be seen from Table 1, **ABI** showed good to excellent chiral recognition ability for 2-phenylalkanoic acids. The chiral recognition ability of **ABI** was generally higher than that of (1*S*,2*R*)-1-aminoindan-2-ol (**AI**), as we expected.[7] Especially, the resolution efficiencies for 2-phenylalkanoic acids having a substituent on the phenyl group were remarkably improved by using **ABI**

(5) (a) Larrow, F.; Roberts, E.; Verhoeven, R. T.; Ryan, K. M.; Senanayake, C. H.; Reider, P. J.; Jacobsen, E. N. *Org. Synth.* **1999**, *76*, 46. (b) Senanayake, C. H.; Michele, L. M.; Liu, J.; Fredenburgh, L. E.; Ryan, K. M.; Roberts, F. E.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J. *Tetrahedron Lett.* **1995**, *36*, 7615. (c) Hijfte, L. V.; Little, D. R.; Petersen, J. L.; Moeller, K. D. *J. Org. Chem.* **1987**, *52*, 4647.

(6) Sujit, K.; Ghorai, K. S.; Harza, K. N.; Mal, D. *Tetrahedron Lett.* **1998**, *39*, 689.

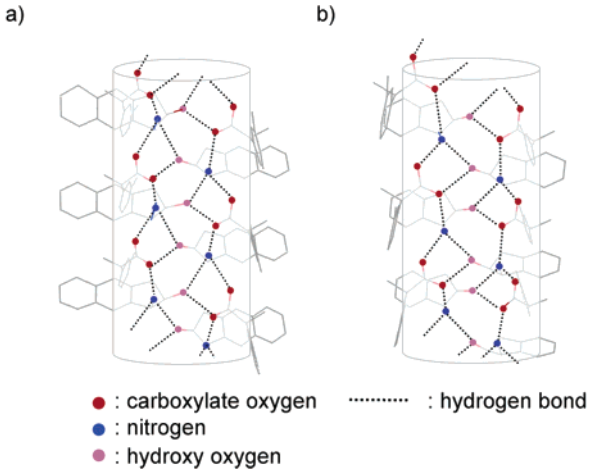



**FIGURE 1.** Hydrogen-bonding networks constructed in (a) **ABI·1c** and (b) **AI·1c** salt crystals.

in the place of **AI** (entries 2 and 4−6). Moreover, **ABI** could recognize the chirality of some arylalkanoic acids, for which **AI** showed no chiral recognition ability (entries 11−13).

**Structural Characteristics of the Less-Soluble ABI Salt Crystals. ABI** showed obviously higher chiral recognition ability than did **AI** for some of arylalkanoic acids we examined. This result strongly suggests that **ABI** would be able to stabilize the less-soluble salts more efficiently than does **AI** by additional CH/$\pi$ interaction-(s) between **ABI** molecules and/or between the **ABI** molecule and the acid molecule, which would arise from the enlarged aromatic part of **ABI** (the naphthyl group in place of the phenyl group of **AI**), as was expected. To clarify the role of the enlarged aromatic part for the stabilization of the less-soluble salts, we next carried out X-ray crystallographic analyses of the less-soluble **ABI** salts and compared their crystal structures with those of the corresponding **AI** salts.

As a typical example for the comparison, we selected a pair of the less-soluble salts of 2-(3-methylphenyl)-propionic acid (**1c**) with **ABI** and **AI**.[8] In both less-soluble **ABI·1c** and **AI·1c** salt[9] crystals, a one-dimensional, helical columnar hydrogen-bonding network ($2_1$ column) is commonly constructed from the ammonium cations, the carboxylate anions, and the hydroxy groups, as shown in Figure 1. Moreover, the molecular arrangements in the $2_1$ columns, which should be determined not only by the pattern of the $2_1$ columns but also by the molecular shapes of the amine and carboxylic acid components, are almost identical so that the packing modes of the $2_1$ columns in the crystals are also very similar to each other. As a result, the hydrogen-bond distances in the $2_1$ columns in the **ABI** and **AI** salt crystals are very similar: the N···O distances are 2.69−2.83 and 2.69−2.87 Å, and the O···O distances are 2.66 and 2.62 Å in the **ABI** and **AI** salt crystals, respectively, strongly indicating that the hydrogen-bonding networks would contribute in a similar manner for the stabilization of the salt crystals.

In the **ABI** and **AI** salt crystals there are other interactions, which stabilize the crystals. The packing motifs of the $2_1$ columns viewed down from the column axis are displayed in Figure 2. In the crystals, there exist CH/$\pi$ interactions, which can be classified into two types: (1) intracolumnar CH/$\pi$ interaction in the $2_1$ column and (2) intercolumnar CH/$\pi$ interaction between the $2_1$ columns. According to the definition, CH/$\pi$ interaction should be discussed on the basis of the distance between a $\pi$-plane and a H atom facing the $\pi$-plane.[3] On the other hand, an essential factor contributing to stabilization energy is known to be determinable on the basis of the distance between a $\pi$-plane and a C atom facing the $\pi$-plane.[10] In the present X-ray analyses, the C···$\pi$-plane distances could be determined, although the H atoms could not be precisely positioned. Therefore, we used the C···$\pi$-plane distances to explain the role of the CH/$\pi$ interactions.[11]

**Intracolumnar CH/$\pi$ Interaction in the ABI and AI Salt Crystals.** The helical columnar hydrogen-bonding network ($2_1$ column) makes the arrangement of the amine and carboxylic acid molecules helical along the $2_1$ column to realize CH($sp^3$)/$\pi$ interaction between the methyl group attached at the chiral center of the carboxylic acid **1c** and the $\pi$-plane of **ABI** or **AI** (Figure 2), indicating that this CH($sp^3$)/$\pi$ interaction plays a very important role in the chiral recognition. The C···$\pi$-plane distance for the CH($sp^3$)/$\pi$ interaction is 3.96 Å in the **ABI** salt crystal, which is the same as that in the **AI** salt crystal (Figure 3). These facts indicate that the $\pi$-planes of **ABI** and **AI** directly recognize the chirality of **1c** and that the intracolumnar CH($sp^3$)/$\pi$ interactions in the **ABI** and **AI** salt crystals similarly contribute to the stabilization of the respective salt crystals.

**Intercolumnar CH/$\pi$ Interaction in the ABI and AI Salt Crystals.** In the **ABI** and **AI** salt crystals, there are two kinds of CH/$\pi$ interactions between the $2_1$ columns other than van der Waals interaction as attractive nonbonding interactions; CH($sp^3$)/$\pi$ interaction between the methyl group at the 3-position of the phenyl group of **1c** and the phenyl group of **1c** located in the neighboring column, and T-shaped CH($sp^2$)/$\pi$ interaction between the aromatic rings of two molecules of **ABI** or **AI** in the neighboring columns (Figure 2). The CH($sp^3$)/$\pi$ interaction would be exceptional for **1c**, since such CH-($sp^3$)/$\pi$ interaction cannot be found in the other less-soluble **ABI** and **AI** salt crystals we examined. This CH($sp^3$)/$\pi$ interaction is fundamentally similar in the **ABI** and **AI** salt crystals, although the C···$\pi$-plane distances and the orientations of the two interacting **1c** molecules are a little different (Figure 4).

(7) We used (1*R*,2*S*)-1-aminobenz[*f*]indan-2-ol (**ABI**) and compared its chiral recognition ability with that of (1*S*,2*R*)-1-aminoindan-2-ol (**AI**); their absolute configurations are inverse to each other. Consequently, the less-soluble diastereomeric salts with **ABI** and **AI** consist of the amino alcohol and the antipodes of the arylalkanoic acids, respectively.

(8) Cambridge Crystallographic Data Centre, ref CCDC-140008, contains the supplementary crystallographic data for (1*S*,2*R*)-1-aminoindan-2-ol·(*R*)-2-(3-methylphenyl)propionic acid (**AI·1c**) salt.[1] These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html.

(9) The less-soluble salts are **ABI**·(*S*)-**1c** and **AI**·(*R*)-**1c**.

(10) Tsuzuki, S.; Honda, K.; Uchimaru, T.; Mikami, M.; Tanabe, K. *J. Am. Chem. Soc.* **2000**, *122*, *15*, 3746.

(11) We defined CH/$\pi$ interactions as those with a C···$\pi$-plane distance less than 4.1 Å, according to the intermolecular interaction potentials of benzene−methane complexes estimated with ab initio molecular orbital calculations.[10]

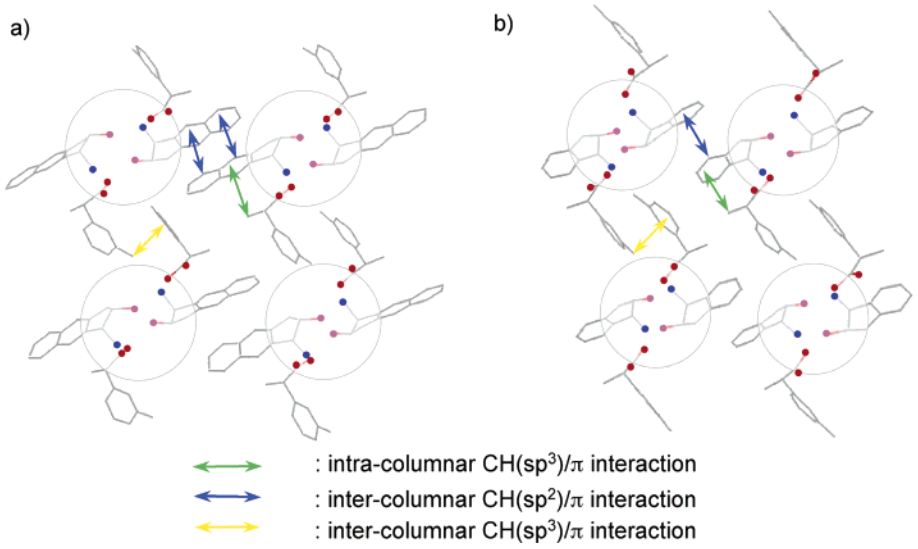



**FIGURE 2.** Crystal structures viewed down from the *b* axis for (a) **ABI·1c** and (b) **AI·1c** salt crystals.

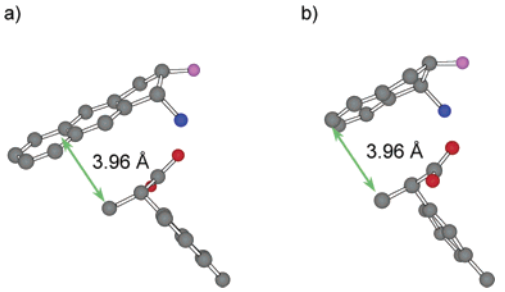



**FIGURE 3.** Intracolumnar CH(sp$^3$)/$\pi$ interactions in (a) **ABI·1c** and (b) **AI·1c** salt crystals.

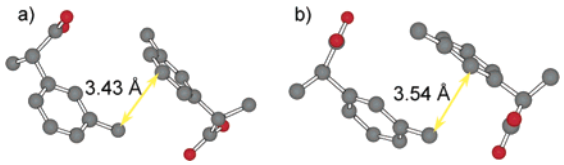



**FIGURE 4.** Intercolumnar CH(sp$^3$)/$\pi$ interactions in (a) **ABI·1c** and (b) **AI·1c** salt crystals.

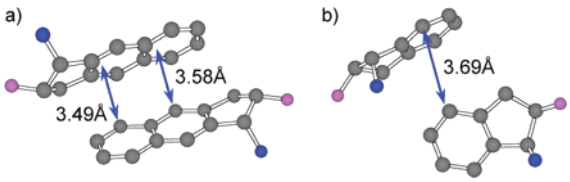



**FIGURE 5.** Intercolumnar CH(sp$^2$)/$\pi$ interactions in (a) **ABI·1c** and (b) **AI·1c** salt crystals.

In contrast, the T-shaped CH(sp$^2$)/$\pi$ interactions in the **ABI** and **AI** salt crystals are quite different from each other; in the **ABI** salt crystal there are two short contacts, while only one short contact exists in the **AI** salt crystal (Figure 5). This means that the T-shaped double CH(sp$^2$)/$\pi$ interaction in the **ABI** salt crystal is obviously stronger than the T-shaped single CH(sp$^2$)/$\pi$ interaction in the **AI** salt crystal and that the **ABI** salt crystal is stabilized more effectively than the **AI** salt crystal by the intercolumnar T-shaped CH(sp$^2$)/$\pi$ interaction. This difference in the magnitude of the intercolumnar T-shaped CH(sp$^2$)/$\pi$ interactions between the **ABI** and **AI** salt crystals would cause the difference in chiral recognition ability between **ABI** and **AI**.

**Wide Applicability of ABI to the Chiral Recognition of (4-Substituted Aryl)alkanoic Acids.** Thus, in **ABI·1c** and **AI·1c** salt crystals, one-dimensional helical hydrogen-bonding columns ($2_1$ columns) aggregate by CH/$\pi$ interactions and van der Waals interaction to give the corresponding three-dimensional crystals. The most outstanding characteristic of the **ABI** salt crystal, which cannot be observed in the **AI** salt crystal, is the T-shaped double CH(sp$^2$)/$\pi$ interaction, probably leading to higher crystallinity of **ABI** salts and better chiral recognition ability of **ABI**. This structural feature of the **ABI** salt crystal strongly suggests that the T-shaped CH(sp$^2$)/$\pi$ interaction would have flexibility to a considerable extent; in the other less-soluble **ABI** salt crystals, the T-contacted naphthyl groups of **ABI** molecules would be able to slide, depending on the molecular arrangement of **ABI** and the carboxylic acid component in the $2_1$ column, with maintaining T-shaped double or at least single CH(sp$^2$)/$\pi$ interaction. Such a slide would be unexpectable in **AI** salt crystals. To verify this consideration, we investigated the crystal structure of the less-soluble salt of **ABI** with 2-(4-isobutylphenyl)propionic acid (ibuprofen, **1f**), which has a long substituent at the 4-position of the phenyl group.

The unit cell lengths of **ABI·1f** salt crystal are significantly altered, compared with those of **ABI·1c** salt crystal; the *c* axis is elongated due to the long isobutyl group in **1f**, while the *a* axis is shortened due to the slide of the T-contacted naphthyl groups (Figure 6a). As a result, a new pattern of CH/$\pi$ interaction appears between the naphthyl groups; there exists CH(sp$^3$)/$\pi$ interaction between the methylene of the five-membered ring of **ABI** and the $\pi$-plane of **ABI** in the neighboring $2_1$ column as well as T-shaped single CH(sp$^2$)/$\pi$ interaction between them (Figure 6b). The crystal structures of **ABI·1c** and **ABI·1f** clearly demonstrate that the naphthyl group of **ABI** plays an important role for its wide applicability in chiral recognition.

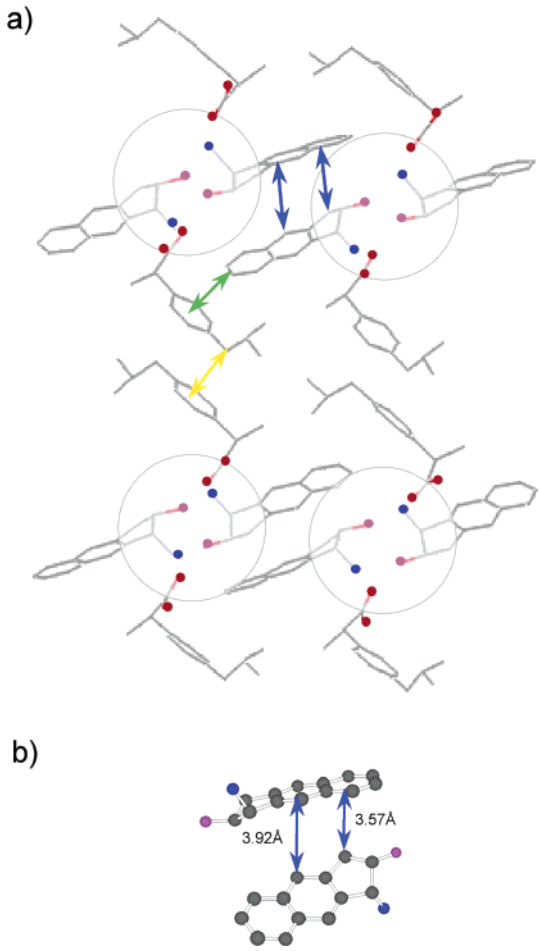



**FIGURE 6.** (a) Crystal structure of **ABI·1f**, viewed down from the *b* axis, and (b) intercolumnar CH(sp$^2$)/$\pi$ interaction in the crystal.

**Applicability of ABI to the Chiral Recognition of 3-Phenylbutyric Acid (2).** The chiral recognition of $\beta$-chiral carboxylic acids and amines is usually difficult by diastereomeric salt formation, since their chiral centers are located far from the chiral center of a resolving agent across a carboxylic acid/amine hydrogen-bonding site. Thus, **AI** showed no chiral recognition ability at all to 3-phenylbutyric acid (**2**). In contrast, **ABI** showed a moderate chiral recognition ability to **2**. This difference in chiral recognition ability between **ABI** and **AI** could be explained on the basis of the X-ray crystallographic analyses of **ABI·2** and **AI·2** salt crystals.

**AI·2** salt crystal consists of hydrogen-bonding columns having inversion centers (i-columns); the column includes both enantiomers of **2** alternatively. On the other hand, **ABI** salt crystal still consists of $2_1$ columns and subsequently includes single enantiomers of 2 (Figure 7a). As shown in Figure 7b, both α-methylene and $\gamma$-methyl of **2** contact with the $\pi$-plane of **ABI** by CH(sp$^3$)/$\pi$ interactions. It is noteworthy that the α-methylene group shortly contacts with the $\pi$-plane, where the C$\cdots\pi$-plane distance is 3.58 Å. These CH(sp$^3$)/$\pi$ interactions would fix the relative geometry of **ABI** and **2** to contribute to the recognition of the chirality of **2**.

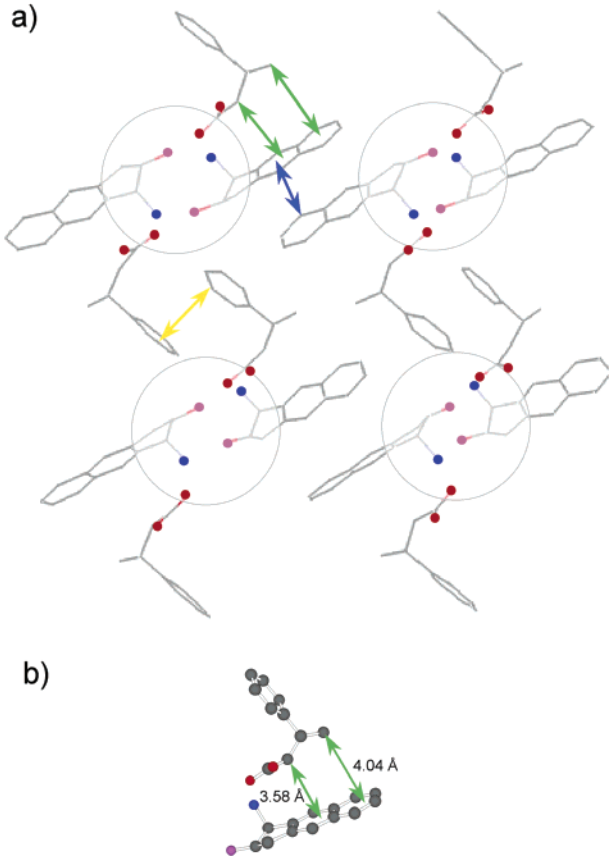



**FIGURE 7.** (a) Crystal structure of **ABI·2**, viewed down from the *b* axis, and (b) intercolumnar CH(sp$^3$)/$\pi$ interaction in the crystal.[12]

## Conclusion

We rationally designed a novel basic resolving agent, (1*R*,2*S*)-1-aminobenz[*f*]indan-2-ol (**ABI**) on the basis of the difference in chiral recognition ability between mandelic acid (MA) and 2-naphthylglycolic acid (NGA). **ABI** showed a moderate to excellent chiral recognition ability for a wide variety of arylalkanoic acids, such as unsubstituted/substituted 2-phenyl- and 2-(2-naphthyl)alkanoic acids and 3-phenylalkanoic acid. The chiral recognition ability of **ABI** was generally higher than that of (1*S*,2*R*)-1-aminoindan-2-ol (**AI**), which was selected as a model for the design; only the replacement of the phenyl group in the indane skeleton by a naphthyl group contributed to the obvious improvement of the chiral recognition ability. X-ray crystallographic study revealed that the higher and wider chiral recognition ability of **ABI** than that of **AI** arose from effective and tunable CH(sp$^2$)/$\pi$ and CH(sp$^3$)/$\pi$ interactions, for which the naphthyl group of **ABI** plays a very important role.

## Experimental Section

**1,2-Epoxybenz[*f*]indene.** To a suspension of sodium hydrogencarbonate (13.6 g, 0.162 mol) and 3-chloroperbenzoic acid (14.6 g, 0.087 mol) in dichloromethane (200 mL), cooled with an ice bath, was added dropwise a solution of benz[*f*]-indene[6] in dichloromethane (400 mL) at 0 °C under Ar

(12) The salt crystal contains single enantiomers of **2** and **ABI**. This means that the actually deposited crystals consist of **ABI**·(*S*)-**2** and **ABI**·(*R*)-**2** as the major and minor diastereomeric salts, respectively.

atmosphere. The suspension was stirred at room temperature for 4 h, and saturated aqueous $NaCO_3$ (400 mL) was added dropwise to the reaction mixture at 0 °C. After being separated from the organic layer, the aqueous layer was extracted with $CH_2Cl_2$ (5 × 300 mL). The combined organic layer and extracts were successively washed with saturated aqueous $NaCO_3$ (3 × 300 mL) and saturated aqueous NaCl (300 mL), dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure to give crude 1,2-epoxybenz[*f*]indene as a pale yellow solid mass (15.90 g, 87 mmol, quant.): mp 148−150 °C; IR (KBr) 3450, 3060, 1420, 830, 490, 470 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 3.14 (1H, d, $J$ = 18.0 Hz), 3.37 (1H, d, $J$ = 18.0 Hz), 4.21 (1H, t, $J$ = 2.7 Hz), 4.41 (1H, d, $J$ = 2.7 Hz), 7.26−7.95 (6H, m).

1,2-Epoxybenz[*f*]indene thus obtained was used in the next reaction without further purification.

**Racemic *cis*-1-Aminobenz[*f*]indan-2-ol (*rac*-ABI).** To dry $CH_3CN$ (200 mL), vigorously stirred with a mechanical stirrer, were successively added fuming sulfuric acid (20 mL) at −10 °C in a period of 1 h and a solution of 1,2-epoxybenz-[*f*]indene (9.76 g, 54 mmol) in dry dichloromethane (160 mL) at −10 °C in a period of 1 h, and the reaction mixture was stirred for 2 h at room temperature. Then, to the solution was added dropwise water (1 L), and the mixture was stirred for 1 h at room temperature. After the organic solvents were evaporated under reduced pressure, ethanol (1 L) was added to the mixture, and the solution was stirred at 100 °C for 50 h. After removal of ethanol, the solution was cooled to room temperature and extracted with $CH_2Cl_2$ (200 mL). The pH of the aqueous solution, cooled with an ice bath, was adjusted at about 13 with 12.5 M aqueous NaOH, and the alkaline solution was extracted with $CH_2Cl_2$ (5 × 400 mL). The combined extracts were dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure to give crude *rac*-**ABI** as a white solid mass. Recrystallization from ethyl acetate gave pure *rac*-**ABI** (4.73 g, 24 mmol, 44%): decomp 169 °C; IR (KBr) 3350, 3270, 3170, 3050, 2970, 2940, 2890, 1580, 1420, 1340, 1260, 1160 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 1.78 (2H, s), 3.09−3.26 (2H, m), 4.20−4.50 (2H, m), 7.28 (1H, s), 7.82 (6H, m).

**(1*R*,2*S*)-1-Amino-benz[*f*]indan-2-ol (ABI).** A solution of *rac*-**ABI** (2.06 g, 10.3 mmol) and (*R*)-2-naphthylglycolic acid[2] (1.23 g, 6.1 mmol) in MeOH (420 mL) was gently refluxed for 1 h, slowly cooled to 30 °C, and kept at 30 °C for 12 h. The deposited solid was collected by filtration and recrystallized three times from MeOH to give diastereopure salt (0.81 g, 2 mmol, 39%) as a white powder. To the diastereopure salt thus obtained was added 3 M aqueous NaOH (250 mL), and the mixture was stirred for 1 h and extracted with $CH_2Cl_2$ (5 × 150 mL). The combined extracts were dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure to give a solid mass, which was recrystallized from chloroform to afford enantiopure **ABI** as a white solid (0.39 g, 2 mmol, quant): decomp 169 °C; $[\alpha]_D$ = 89° (*c* 0.2, $CHCl_3$); IR (KBr) 3350, 3270, 3150, 3070, 2970, 2930, 2870, 2800, 1580, 1420, 1340, 1260, 1160; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 1.78 (2H, s), 3.09−3.26 (2H, m), 4.20−4.50 (2H, m), 7.28 (1H, s), 7.82 (6H, m). Anal. Calcd for $C_{13}H_{13}NO\cdot{}^1/_4H_2O$: C, 76.63; H, 6.68; N, 6.87. Found: C, 76.46; H, 6.47; N, 6.89.

The enantiopurity of **ABI** thus obtained was determined by an HPLC analysis (Chiralcel OD; eluent hexane/2-propanol = 9/1; flow rate 1.0 mL/min) of its derivative, N,O-diacetylated **ABI**, which was obtained by the reaction with a large excess amounts of acetic anhydride and pyridine, followed by the usual workup: (1*S*,2*R*)-**ABI** 23 min, (1*R*,2*S*)-**ABI** 30 min; enantiopurity >99%.

**Typical Procedure for Enantioseparation of Arylalkanoic Acids** [Table 1, **entry 1].** A solution of **ABI** (99.2 mg, 0.5 mmol) and racemic 2-phenylpropionic acid (**1a**) (75.8 mg, 0.5 mmol) in EtOH/$H_2O$ (6/4 v/v; 5 mL) was refluxed for 1 h, and the solution was cooled to and kept at 30 °C in a thermostat for 12 h. The deposited crystals were collected by filtration, washed with a small amount of cooled EtOH, and dried in vacuo to give **ABI·1c** salt (53.7 mg, 0.15 mmol, 61%) as white needle crystals. The salt was treated with 1 M aqueous HCl (50 mL), and the aqueous solution was extracted with ether (3 × 50 mL). The combined extracts were dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure to give enantioseparated **1c**, of which the enantiomeric excess (ee) was determined by an HPLC analysis (Chiralcel OJ-R; eluent aqueous $HClO_4$ (pH 2)/$CH_3CN$ = 7/3; flow rate 0.5 mL/min): 91% ee.

The enantioseparations of the other carboxylic acids were performed under almost the same conditions: the diastereomeric salts were allowed to crystallize at 30 °C from ethanol/$H_2O$, of which the ratio and amount were adjusted so as to control the yield of the salts to be as close as possible to a range of 50−80%. The carboxylic acids, except for 2-phenylpropionic acid, 2-(4-isobutylphenyl)propionic acid, and 2-phenylbutyric acid, were converted into their methyl esters by reaction with (trimethylsilyl)diazomethane prior to their HPLC analyses.

**Structure of (1*R*,2*S*)-ABI·(*S*)-1c Salt.** Crystals of the salt belong to the monoclinic space group $P2_1$ with $a$ = 12.112(8) Å, $b$ = 6.291(4) Å, $c$ = 13.038(9) Å, and $\beta$ = 98.248(9)°. $V$ = 983.1(12) Å$^3$, $D_{calcd}$ = 1.228 g cm$^{-3}$, $R_f$ = 0.0590, and $R_w$ = 0.0620.

**Structure of (1*R*,2*S*)-ABI·(*S*)-1f Salt.** Crystals of the salt belong to the monoclinic space group $P2_1$ with $a$ = 10.04(2) Å, $b$ = 6.261(10) Å, $c$ = 17.58(3) Å, and $\beta$ = 95.48(2)°. $V$ = 1100.0-(34) Å$^3$, $D_{calcd}$ = 1.224 g cm$^{-3}$, $R_f$ = 0.0900, and $R_w$ = 0.0890.

**Structure of (1*R*,2*S*)-ABI·(*S*)-2 Salt.** Crystals of the salt belong to the monoclinic space group $P2_1$ with $a$ = 12.81(2) Å, $b$ = 6.099(7) Å, $c$ = 12.650(10) Å, and $\beta$ = 95.28(2)°. $V$ = 984.1-(17) Å$^3$, $D_{calcd}$ = 1.226 g cm$^{-3}$, $R_f$ = 0.0900, and $R_w$ = 0.1390.

**Structure of (1*S*,2*R*)-AI·(*R*)-2 Salt.** Crystals of the salt belong to the triclinic space group $P1$ with $a$ = 11.206(3) Å, $b$ = 13.618(6) Å, $c$ = 5.869(3) Å, $\alpha$ = 97.73(3)°, $\beta$ = 99.51(3)°, and $\gamma$ = 75.43(3)°. $V$ = 850.9(6) Å$^3$, $D_{calcd}$ = 1.223 g cm$^{-3}$, $R_f$ = 0.0510, and $R_w$ = 0.0630.

**Supporting Information Available:** $^1H$ NMR and IR spectra of (1*R*,2*S*)-1-aminobenz[*f*]indan-2-ol (**ABI**) and CIF files for the crystals of (1*R*,2*S*)-**ABI·**(*S*)-**1c**, (1*R*,2*S*)-**ABI·**(*S*)-**1f**, (1*R*,2*S*)-**ABI·**(*S*)-**2**, and (1*S*,2*R*)-**AI·**(*R*)-**2** salts (PDF, CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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