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Chiral Pyrophosphoric Acid Catalysts for the *para*-Selective and Eanantioselective Aza-Friedel–Crafts Reaction of Phenols

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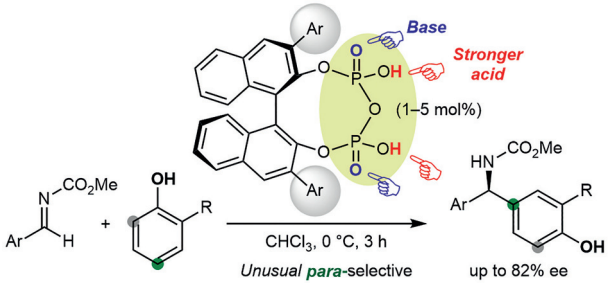
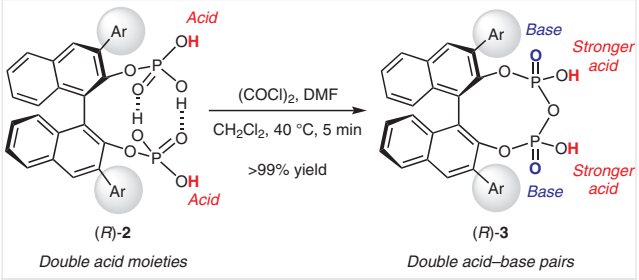


Received: 27.06.2018
Accepted after revision: 24.07.2018
Published online: 22.08.2018
DOI: 10.1055/s-0037-1610250; Art ID: ss-2018-e0435-fa

Abstract Chiral BINOL-derived pyrophosphoric acid catalysts were developed and used for the regio- and enantioselective aza-Friedel–Crafts reaction of phenols with aldimines. *ortho*/*para*-Directing phenols could react at the *para*-position selectively with moderate to good enantioselectivities. Moreover, the gram-scale transformation of a product into the key intermediate for the antifungal agent (*R*)-bifonazole was demonstrated.

Key words Brønsted acid, phosphoric acid, pyrophosphoric acid, organocatalyst, aza-Friedel–Crafts reaction, phenol, regio-selectivity

Pyrophosphoric acid ($H_4P_2O_7$) is a dehydrative condensate of phosphoric acid (H_3PO_4) and is frequently provided in vivo as magnesium(II), calcium(II), and alkali metal(I) pyrophosphates from adenosine triphosphate (ATP).[1] Remarkably, pyrophosphoric acid ($pK_{a1}(H_2O)$ = 0.91, $pK_{a2}(H_2O)$ = 2.10) is a stronger acid than phosphoric acid [$pK_{a1}(H_2O)$ = 2.16, $pK_{a2}(H_2O)$ = 7.21].[2] Indeed, even pK_{a2} of pyrophosphoric acid is lower than pK_{a1} of phosphoric acid. Despite its potential as a strong diprotic acid motif for new chiral organocatalysts, to the best of our knowledge, a chiral pyrophosphoric acid has not yet been developed for asymmetric catalysis. In this regard, chiral BINOL (1,1′-bi-2-naphthol)-derived phosphoric acids **1** have been shown to be highly practical and powerful catalysts for a variety of asymmetric reactions.[3,4] Moreover, several BINOL-derived bis(phosphoric acid)s have recently been developed by Gong,[5] Momiyama/Terada,[6] and our group.[7] In particular, our recent chiral bis(phosphoric acid)s (*R*)-**2**[7] were highly effective for the enantioselective aza-Friedel–Crafts (aza-FC) reaction of 2-methoxyfuran[8] with α-ketimino esters. During the course of our previous study, we found that dehydrative condensation of (*R*)-**2** successfully provided the corresponding (*R*)-**3** (Scheme 1).[7] Fortunately, since chiral pyrophosphoric acids (*R*)-**3** are not very sensitive to moisture, we envisioned that a suitable catalytic system could make the best use of the possible double acid-base cooperative function of novel (*R*)-**3**.

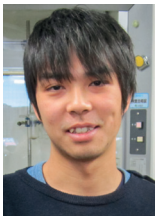


Scheme 1 Preparation of chiral pyrophosphoric acids (*R*)-**3**

In this study, we have developed a regio- and enantioselective aza-FC reaction[9] of phenols **5**[10,11] with aldimines **4** through the use of chiral BINOL-derived pyrophosphoric acids (*R*)-**3** (Scheme 2a). In this reaction, the catalyst should control both the regio-selectivity of **5** (i.e., *para*- and *ortho*-control of **5** leading to **6** and **7**, respectively) and the enantioface-selectivity of **4**.

Although simple phenols have an *ortho*/*para*-orientation,[12] *ortho*-addition is often preferred, particularly for basic carbonyl compounds due to the inherent directing properties of acidic phenols,[10] as seen in the traditional Betti reaction[13] between phenols, aldehydes, and amines (Scheme 2b). Therefore, the *para*-selective catalytic asymmetric FC reaction of phenols has been very limited.[11] Moreover, in spite of the interesting remote regio-control by the asymmetric catalytic system, there has been no previous report on the reason or strategy for the prioritization of *para*-selectivity.[11] In this context, we were interested in the remote

Biographical Sketches



Haruka Okamoto was born in Aichi, Japan, in 1989. He received his BS (2012) and MS (2014) degrees from Nagoya University under the supervision of Prof. Kazuaki Ishihara. Since 2017, he is working at Mitsui Chemicals Agro, Inc. as a researcher and his current research area includes the field of manufacturing technology of agricultural chemicals.

Kohei Toh was born in Fukuoka, Japan, in 1995. He received his BS (2018) degree from Nagoya University under the supervision of Prof. Kazuaki Ishihara. He is currently a Master course student in Ishihara's group.

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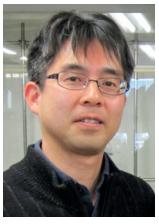
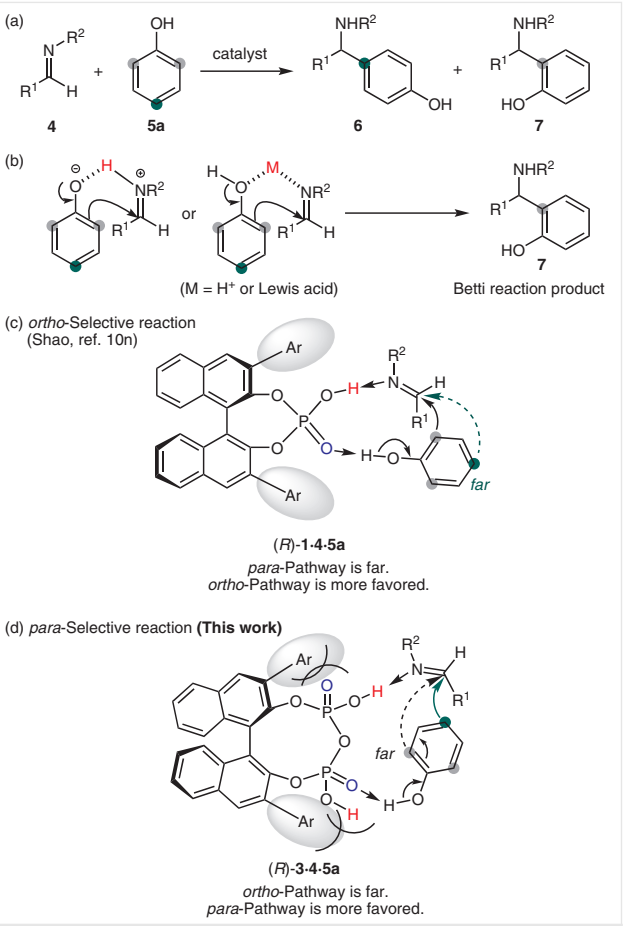
Akira Sakakura was born in Mie, Japan, in 1970, and received his Ph.D. from Nagoya University in 2000 under the direction of Prof. Yoshihiro Hayakawa. After postdoctoral studies with Prof. Shizuaki Murata at Nagoya University for nine months beginning in 2000, he joined Prof. Hideo Kigoshi's group at the University of Tsukuba as an assistant professor in 2001. In 2003, he joined Prof. Ishihara's group at Nagoya University as an associate professor. He was appointed professor at Okayama University in 2012. His research interests include development of efficient methods for synthesis of bioactive natural products and design of asymmetric catalysts based on acid-base combination chemistry.



Manabu Hatano was born in Tokyo, Japan, in 1975, and received his Ph.D. from the Tokyo Institute of Technology in 2003 under the direction of Prof. Koichi Mikami. He was a JSPS Fellow under the Japanese Junior Scientists Program from 2000 to 2003. In 2003, he joined Ishihara's group at Nagoya University as an assistant professor, and became associate professor in 2007. His research interests include the development of asymmetric catalysis based on new design of acid–base cooperative catalysts and supramolecular catalysts.

Kazuaki Ishihara was born in Aichi, Japan, in 1963, and received his Ph.D. from Nagoya University in 1991 under the direction of Prof. Hisashi Yamamoto. He had the opportunity to work under the direction of Prof. Clayton H. Heathcock at the University of California, Berkeley, as a visiting graduate student for three months in 1988. He was a JSPS Fellow under the Japanese Junior Scientists Program from 1989 to 1991. After he completed his postdoctoral studies with Prof. E. J. Corey at Harvard University (15 months beginning in 1991), he returned to Japan and joined Yamamoto's group at Nagoya University as an assistant professor in 1992, and became associate professor in 1997. In 2002, he was appointed to his current position as a full professor at Nagoya University. His research interests include asymmetric catalysis, biomimetic catalysis induced by artificial enzymes, dehydrative condensation catalysis toward green and sustainable chemistry, acid-base combination chemistry, and designer supramolecular acid-base combined catalysts.

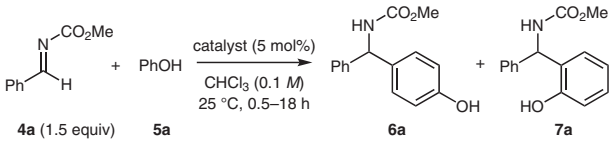


Scheme 2 Strategy for the regio- and enantioselective aza-Friedel–Crafts reaction of phenols with aldimines

control of *para*-selectivity of **5** with aldimines **4** in the presence of the novel catalysts (*R*)-**3**. We cannot completely deny that two P(=O)OH sites in (*R*)-**3** might act independently and activate **4** and **5**. However, unlike a reaction using (*R*)-**1**, which can promote the *ortho*-addition of **5** to **4** (Scheme 2c),[14] a reaction through the single P(=O)OH site of (*R*)-**3** might be geometrically disfavored due to the steric hindrance of the 3,3′-moieties of (*R*)-**3**, and we strongly envisioned that **4** and **5** would be activated respectively on either site of the P(=O)OH moieties (Scheme 2d). Overall, with the use of (*R*)-**3**, normally difficult *para*-addition of **5** to **4** might be exclusive, since the *ortho*-positions of **5** would be far from the imino-carbon of **4**.

We initially examined the reaction of phenol **5a** with aldimine **4a** through the use of achiral Brønsted acid catalysts (5 mol%) in chloroform (0.1 *M* based on **5a**) at 25 °C (Table 1). As a result, carboxylic acid catalysts, which are more or less acidic than phosphoric acids, gave **6a** and **7a** in low yields under such mild conditions (Table 1, entries 1, 2, 4, 5, and 7). Although much more acidic sulfonic acids greatly promoted the conversion of **5a**, many unknown polar by-products were obtained due to overreaction/decomposition via **4a** and/or **5a** (entries 8 and 9).[15] In contrast, phosphoric acids, which have not only an acid function (POH) but also a conjugate base function (P=O), did not give any by-products, although the catalytic activity was moderate, and meaningful regio-selectivity (i.e., **6a** vs **7a**) was not observed (entries 3 and 6). Overall, we found that phosphoric acids with the bifunctional acid-base moieties would be suitable for promoting the present reaction efficiently without side reactions.

Table 1 Screening of Achiral Brønsted Acid Catalysts[a]



Entry	Catalyst	pK_a in H_2O	Reaction time (h)	Conversion (%) of **5a**	Yield (%) of **6a**	Yield (%) of **7a**
1	$MeCO_2H$	4.76	18	0	0	0
2	CH_2BrCO_2H	2.86	18	0	0	0
3	**$PhOP(=O)(OH)_2$**	1.42	18	**40**	**25**	**15**
4	CHF_2CO_2H	1.24	18	0	0	0
5	CCl_3CO_2H	0.65	18	16	2	14
6	**$(PhO)_2P(=O)OH$**	0.26	18	**24**	**15**	**9**
7	CF_3CO_2H	0.26	18	8	6	2
8	*p*-$MeC_6H_4SO_3H$	–1.34	0.5	>99	45	11
9	CF_3SO_3H	–13.0	0.5	>99	53	7

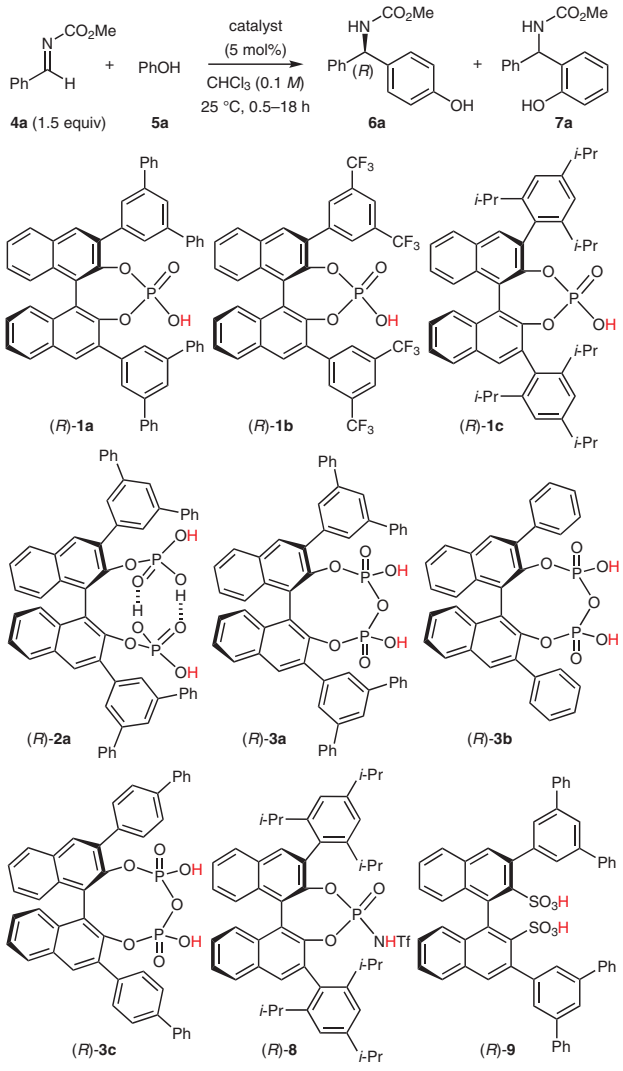
[a] The reactions were carried out with catalyst (5 mol%), **4a** (1.5 equiv), and **5a** (1 equiv) in $CHCl_3$ (0.1 *M* based on **5a**) at 25 °C.

Next, we examined the use of chiral phosphoric acids (*R*)-**1a–c**, chiral bis(phosphoric acid) (*R*)-**2a**, and chiral pyrophosphoric acids (*R*)-**3a–c** (Table 2). As a result, although catalysts (*R*)-**1a** and (*R*)-**1b** promoted the reaction, the desired **6a** was obtained in low yields with low enantioselectivities, along with undesired **7a** (Table 2, entries 1 and 2). The reaction did not proceed with the use of highly regarded chiral phosphoric acid (*R*)-**1c** (TRIP),[16] which would be less acidic and sterically more hindered than (*R*)-**1a** and (*R*)-**1b** (entry 3). Moreover, catalyst (*R*)-**2a**,[7] which has stronger acidity and much weaker basicity than (*R*)-**1a**, showed lower catalytic activity than (*R*)-**1a** (entry 4). In sharp contrast, as a novel stronger acid catalyst with a conjugate base function, chiral pyrophosphoric acid (*R*)-**3a** dramatically facilitated the reaction, and **6a** was obtained in 82% yield with 52% ee within 30 minutes (entry 5).

As entry 5 in Table 2 shows, the catalyst (*R*)-**3a** provided at that time **7a** in only 1% yield. The substituent effect at the 3,3′-positions of the binaphthyl backbone was important, and sterically less hindered (*R*)-**3b** and (*R*)-**3c** showed much lower catalytic activity than (*R*)-**3a** (Table 2, entries 6 and 7). Moreover, much stronger Brønsted acids, such as chiral phosphoramide (*R*)-**8**[17] and chiral disulfonic acid (*R*)-**9**[18] also facilitated the reaction and the substrates were consumed within 30 minutes (entries 8 and 9). However, the enantiocontrol was hardly achieved and many unknown polar by-products were generated. The tendency of the results in Table 2 was mostly similar to that with achiral catalysts in Table 1; the sterically-optimized chiral catalysts should have both appropriate acid and base functions to promote the desired reaction.[19]

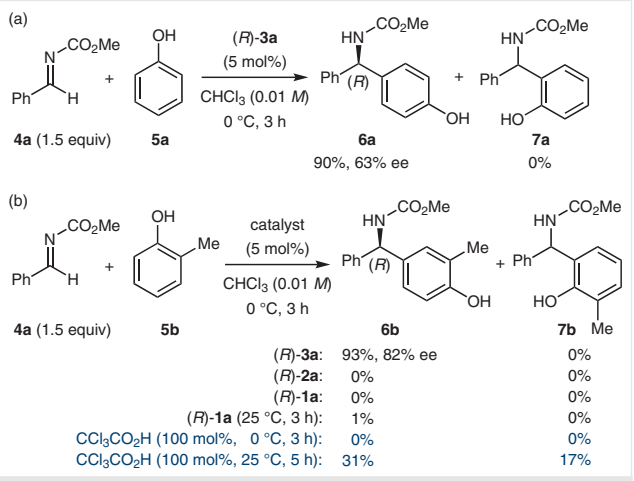
After further optimization of the reaction conditions,[20–22] a reaction in diluted chloroform (0.01 *M* based on **5a**) at lower temperature (0 °C) improved both the yield and enantioselectivity of **6a** up to 63% ee (Scheme 3a). Interestingly, the enantioselectivity was greatly improved when *o*-cresol (**5b**) was used instead of phenol (**5a**), and *para*-adduct **6b** was obtained as a sole product in 93% yield with 82% ee without the generation of *ortho*-adduct **7b** (Scheme 3b). Notably, (*R*)-**3a** was detected almost intact in the resulting reaction mixture,[23] and recovered as (*R*)-**2a** through silica gel column chromatography. In contrast, (*R*)-**1a** and (*R*)-**2a** were not effective at that time, and the reaction hardly proceeded under the same reaction conditions or even at 25 °C (Scheme 3b). Moreover, as another control experiment, 100 mol% of trichloroacetic acid as an achiral catalyst also could not promote the reaction at 0 °C, and ultimately promoted the reaction at 25 °C. However, a meaningful regio-selectivity for **6b** and **7b** was not observed as expected. Therefore, the observed *para*-selective reactions with (*R*)-**3a** did not depend on *ortho*-substituted phenol **5b**.

Table 2 Screening of Chiral Brønsted Acid Catalysts[a]



Entry	Catalyst	Reaction time (h)	Yield (%) of **6a**	ee (%) of **6a**	Yield (%) of **7a**	ee (%) of **7a**
1	(*R*)-**1a**	3	40	0	12	0
2	(*R*)-**1b**	3	16	4	7	7
3	(*R*)-**1c**	18	0	–	0	–
4	(*R*)-**2a**	3	15	23	10	0
5	(*R*)-**3a**	**0.5**	**82**	**52**	**1**	–
6	(*R*)-**3b**	0.5	41	4	0	–
7[b]	(*R*)-**3c**	0.5	4	–3	0	–
8	(*R*)-**8**	0.5	50	3	26	11
9	(*R*)-**9**	0.5	61	2	12	10

[a] The reactions were carried out with catalyst (5 mol%), **4a** (1.5 equiv), and **5a** (1 equiv, 0.20 mmol) in $CHCl_3$ (0.1 *M* based on **5a**) at 25 °C.
[b] (*S*)-**6a** was obtained with 3% ee.

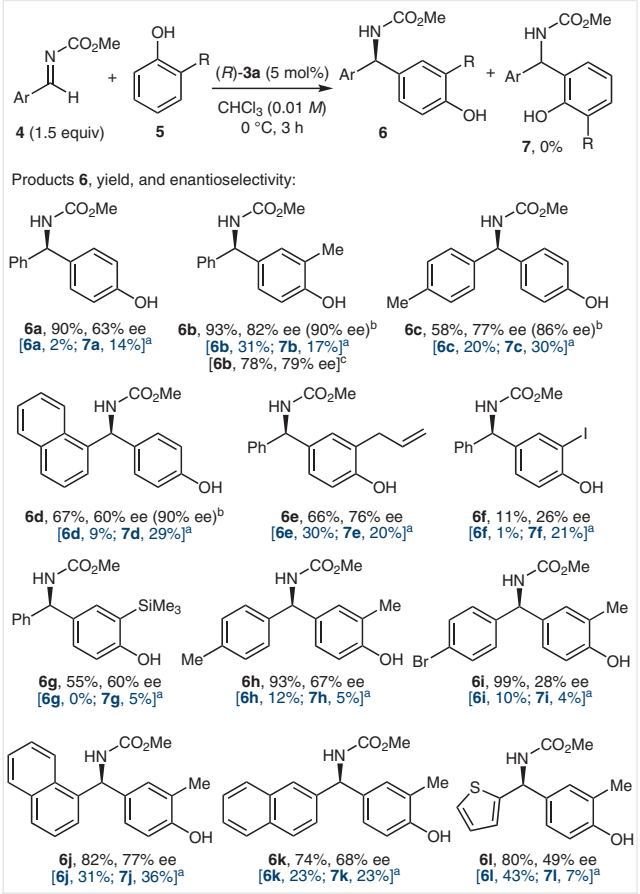


Scheme 3 Further optimization of the reaction conditions and the *para*-selective reaction with *o*-cresol **5b**

With the optimized reaction conditions in hand, we next examined the scope of phenols **5** with aldimines **4** (Scheme 4). As a result, not only phenyl-, but also *p*-tolyl- and 1-naphthylaldimines were used, and the corresponding *para*-adducts **6c** and **6d** were exclusively obtained with 77% ee and 60% ee, respectively. Moreover, *o*-cresol (**5b**) and 2-allylphenol reacted with **4a**, and **6b** and **6e** were obtained with 82% ee and 76% ee, respectively.

The amount of catalyst (*R*)-**3a** could be reduced to 1 mol%, and **6b** was then obtained in 78% yield with 79% ee. Unfortunately, 2-iodophenol gave **6f** in low yield with low enantioselectivity (26% ee). In contrast, bulky *o*-(trimethylsilyl)phenol was tolerable, and **6g** was obtained with moderate enantioselectivity (60% ee). Moreover, other aryl aldimines were also examined with the use of *o*-cresol (**5b**). As a result, *p*-tolyl, 1-naphthyl, and 2-naphthyl substrates could be used, and good enantioselectivities (67–77% ee) were observed in the corresponding *para*-adducts **6h**, **6j**, and **6k**. On the other hand, 4-bromophenyl and 2-thienyl moieties decreased the enantioselectivities (see **6i** and **6l**). Some products in Scheme 4 were crystalline, and a single recrystallization effectively increased the enantiopurity (see superscript footnote b for **6b**, **6c**, and **6d**).[24] Overall, the observed enantioselectivities in Scheme 4 were not excellent and further improvements are needed. However, it should be noted that *ortho*-adducts **7** were not obtained in any of the cases examined with (*R*)-**3a** in Scheme 4 (also see superscript footnote a in Scheme 4 for the results with CCl_3CO_2H (100%) at 25 °C for 5 h),[25] and this might be a pioneering result for the normally difficult *para*-selective aza-FC reaction of phenols.[11]

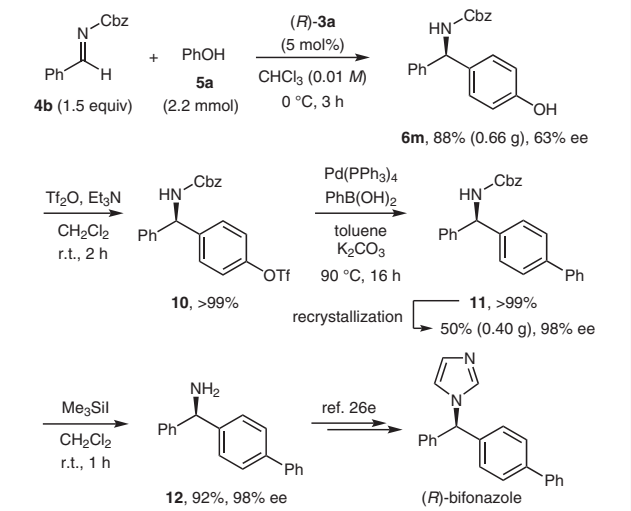
To demonstrate the synthetic utility of the present catalytic system, we performed a formal total synthesis of (*R*)-bifonazole, which is a well-established antifungal agent for superficial mycoses (Scheme 5).[26,27]



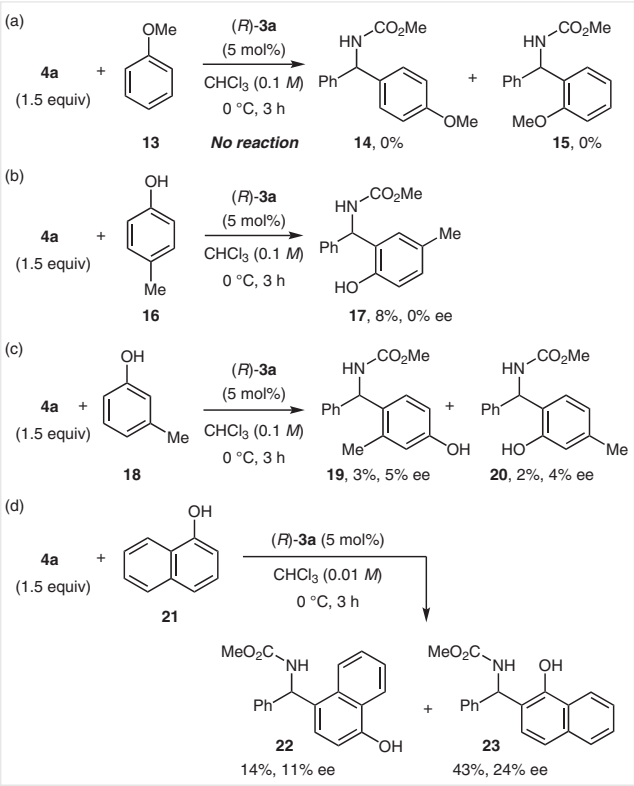
Scheme 4 Scope of substrates in the regio- and enantioselective aza-FC reaction of phenols. *Reagents and conditions:* (*R*)-**3a** (5 mol%), **4** (1.5 equiv), and **5** (1 equiv, 0.20 mmol) in $CHCl_3$ (0.01 *M* based on **5**) at 0 °C for 3 h. [a] Data in square brackets are the results with the use of CCl_3CO_2H (100 mol%) at 25 °C for 5 h. [b] Results after recrystallization. [c] 1 mol% of (*R*)-**3a** was used.

Fortunately, more stable NCbz aldimine **4b** in place of less stable NCO_2Me aldimine **4a** could be used in a scalable aza-FC reaction of **5a** (2.2 mmol), and the corresponding **6m** was obtained in 88% yield (0.66 g), although the enantioselectivity was still moderate (63% ee).[22] Treatment of **6m** with trifluoromethanesulfonic anhydride (Tf_2O) gave **10**, which was used in Suzuki–Miyaura coupling with $PhB(OH)_2$ to give **11** quantitatively. Recrystallization of **11** improved the optical purity to 98% ee. Finally, after deprotection of the NCbz moiety with the use of trimethylsilyl iodide, the desired key compound **12**[26e] was obtained in 92% yield.

To consider the reaction mechanism, particularly the *para*-selectivity of phenols, several control experiments were performed. When anisole (**13**), instead of unsubstituted phenol (**5a**), was used with **4a**, the reaction did not proceed (Scheme 6a). This result suggests that the deprotonation process of phenol might be necessary to promote the reaction.



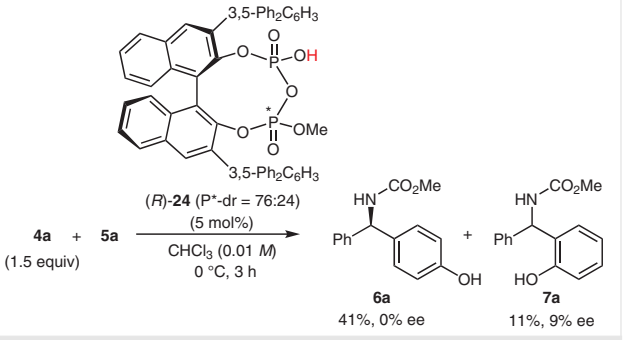
Scheme 5 Transformation toward (*R*)-bifonazole



Scheme 6 Control experiments with other phenols and naphthols

Moreover, when *p*-cresol (**16**) was used, the corresponding *ortho*-adduct **17** was obtained in only 8% yield with 0% ee (Scheme 6b). This result strongly suggests that *para*-selective activation might occur in our reaction system. Moreover, we also examined the reaction with *m*-cresol (**18**) (Scheme 6c). As a result, both *para*-adduct **19** and *ortho*-adduct **20** were obtained in very low yields. Moreover, the enantioselectivity of *para*-adduct **19** was low (5% ee), and thus *meta*-substituted phenols would not be suitable in the present reaction system, probably because the *para*-addition reaction is preferred due to steric reasons. Next, we examined whether or not 1-naphthol (**21**) could be used for the *para*-selective reaction (Scheme 6d). As a result, the reaction proceeded preferentially at the 2-position (i.e., *ortho*-position) of **21**, and compound **23** was obtained in 43% yield with 24% ee. However, 4(*para*)-adduct **22** was barely obtained in 14% yield with 11% ee, even though 1-naphthol (**21**) is strongly conjugated between the 1- and 2-positions and the 2(*ortho*)-adduct would usually be dominant.[28] Although the enantioselectivity of **22** was still low at this stage, *para*-addition-induced catalyst (*R*)-**3a** might show some resistance such as in the normally *ortho*-addition of 1-naphthol (**21**).

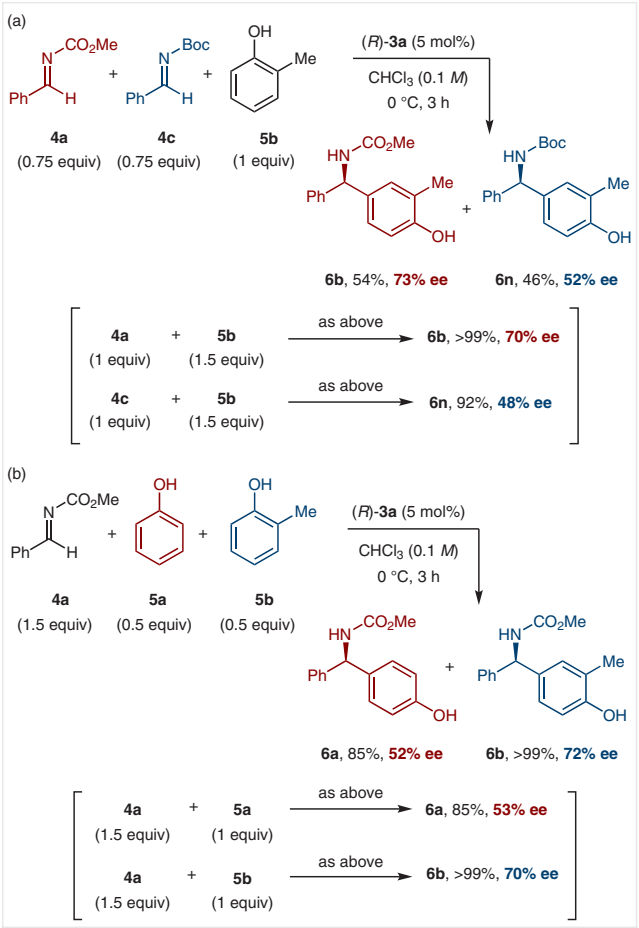
To elucidate the function of the Brønsted acid parts of (*R*)-**3a**, (*R*)-**24** was used as a catalyst, which was prepared from (*R*)-**3a** by Me-protecting one of the P(=O)OH moieties (Scheme 7). Catalyst (*R*)-**24** was used as an inseparable diastereomeric mixture based on the chiral P center (dr = 76:24). As a result, the reaction of **5a** with **4a** proceeded, and **6a** (41% yield with 0% ee) and **7a** (11% yield with 9% ee) were obtained. Neither regio-selectivity nor enantioselectivity was effectively induced. Therefore, the double P(=O)OH moieties in (*R*)-**3a** should be essential for successful activation of the aldimine and phenol.



Scheme 7 Role of two P(=O)OH moieties of the catalysts

As expected in Scheme 2d, we considered an activation model. To support the consideration that aldimine **4** and phenol **5** might be activated independently by two acid-base moieties of (*R*)-**3a**, preliminary competition experiments were performed with either two different aldimines or phenols (Scheme 8). If a more complicated activation mechanism with the two acid-base moieties of (*R*)-**3a** is involved, the enantioselectivity of the products might be affected by the interaction among the competitive substrates. First, we examined a reaction with the use of two different aldimines **4a** and **4c** (Scheme 8a). As a result, the corresponding products **6b** and **6n** were obtained with almost the same enantioselectivities as in the case with each alone. Next, a reaction with the use of two different phenols **5a**

and **5b** was examined (Scheme 8b). As a result, the corresponding products **6a** and **6b** were obtained with almost the same enantioselectivities as in the case with each alone.



Scheme 8 Control experiments with competitive substrates

Overall, a possible activation mechanism might involve a (*R*)-**3a**:**4**:**5** ratio of 1:1:1, as shown in Scheme 2d, and (*R*)-**3a**·**4**$_2$·**5**, (*R*)-**3a**·**4**·**5**$_2$, (*R*)-**3a**·**4**$_2$·**5**$_2$, or more complicated species might be unlikely.

Based on the above experimental results, Figure 1 shows a possible transition state through the use of (*R*)-**3a**·**4**·**5** as a working model. Due to the steric constraints of bulky aryl substituents at the 3,3′-positions, each aldimine **4a** and phenol **5** might be activated independently at two different P(=*O*)O*H* sites of (*R*)-**3a**. Phenol **5** would be deprotonated by a Brønsted base moiety (P=*O*) at one site, whereas aldimine **4a** would coordinate to the Brønsted acid center (PO*H*) at the other site. To avoid significant steric constraint due to the catalyst, the aryl moiety of **4a** might be oriented inward.

Thus, a *para*-selective reaction pathway might be suitable, since the *para*-position of **5** would be close to the imino-carbon of **4a**, while the *ortho*-position of **5** would be far from the imino-carbon of **4a**. As a result, *si*-face attack of **5**

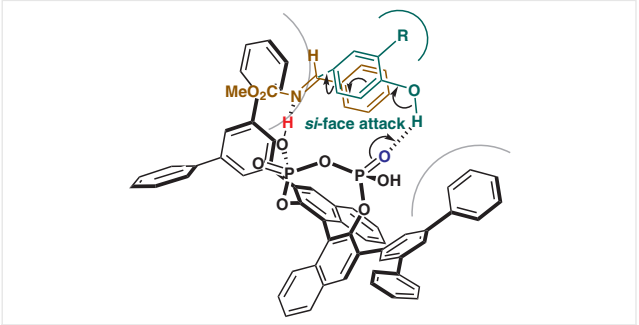


Figure 1 A possible transition state

to **4a** might proceed, and the corresponding (*R*)-isomer **6** might be provided with high regio-selectivity and moderate to good enantioselectivities. Some *ortho*-substituted phenols, which offered higher enantioselectivities than unsubstituted phenol (**5a**), might help to provide the favored transition state, since the *ortho*-substituent would direct outward, as shown in Figure 1. Moreover, an electrostatic π–π stacking interaction between **4** and **5** cannot be ruled out, where a not very bulky but electron-donating *ortho*-substituent on phenol might be effective, as shown in Scheme 4.

In summary, we have developed chiral BINOL-derived pyrophosphoric acid catalysts for the first time, which were effective for the *para*-selective and enantioselective aza-Friedel–Crafts reaction of phenols to aldimines. Since phenols have an *ortho*/*para*-orientation, exclusive *para*-addition is difficult and geometric remote control would be needed through the use of designer chiral catalysts. With the use of the present chiral pyrophosphoric acid catalysts, both aldimines and phenols would be activated cooperatively, and phenols could react at a *para*-position with moderate to good enantioselectivities. Moreover, transformation of a product into (*R*)-bifonazole was demonstrated on an enlarged scale. This is the first example of chiral pyrophosphoric acid catalysts, and the further application to asymmetric reactions is underway.

^{1}H NMR spectra were recorded on a JEOL ECS400 (400 MHz) spectrometer at ambient temperature, unless otherwise noted. Data were recorded as follows: chemical shift in ppm from internal TMS on the δ scale, multiplicity (standard abbreviations), coupling constant (Hz), integration, and assignment. ^{13}C NMR spectra were recorded on a JEOL ECS400 (100 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard ($CDCl_3$ at 77.10 ppm). ^{19}F NMR spectra were recorded on a JEOL ECS-400 (376 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the external standard ($CFCl_3$ at 0 ppm). ^{31}P NMR spectra were recorded on a JEOL ECS-400 (161 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the external standard (H_3PO_4 at 0 ppm). High-resolution mass spectral analyses (HRMS) were per-

formed at Chemical Instrument Center, Nagoya University (JEOL JMS-700 (FAB), JEOL JMS-T100GCV (EI), Bruker Daltonics micrOTOF-QII (ESI)). IR spectra were recorded on a JASCO FT/IR 460 plus spectrometer. High-performance liquid chromatography (HPLC) analysis was conducted using Shimadzu LC-10 AD coupled diode array-detector SPD-M20A and chiral column of Daicel CHIRALCEL OD-H, OD-3 and CHIRALPAK AS-3, IA-3, IC-3. Optical rotations were measured on Rudolph Autopol IV digital polarimeter. X-ray analysis was performed by Rigaku PILATUS-200K. The products were purified by column chromatography on silica gel (Kanto Chemical Co., Inc. 37560). In experiments that required anhydrous solvents such as $CHCl_3$ were distilled in prior to use. Aldimines **4** were known compounds and were prepared based on the literature procedure.[29] Phenols are commercially available, although 2-(trimethylsilyl)phenol was prepared from 2-bromophenol based on the literature procedure.[30]

Chiral 1,1′-Binaphthyl-2,2′-pyrophosphoric Acids (*R*)-3; General Procedure (Table 2)

To a solution of chiral bis(phosphoric acid) (*R*)-**2**[7] (0.010 mmol) in CH_2Cl_2 (0.2 mL) was added one drop of DMF. Oxalyl chloride (3.0 μL, 0.035 mmol) was added at r.t., and the reaction mixture was warmed to 40 °C. The mixture was stirred at 40 °C for 5 min. After the mixture was allowed to cool to r.t., toluene (2 mL) was added. The volatiles were removed in vacuo, and the desired pyrophosphoric acid (*R*)-**3** was obtained, which was used for the catalysis without further purification. A small amount of DMF and CH_2Cl_2 were usually involved.

(*R*)-3,3′-Di(3,5-terphenyl)-1,1′-binaphthyl-2,2′-pyrophosphoric Acid [(*R*)-3a]

Pale yellow solid; yield: 8.8 mg (99%), $[\alpha]_D^{23}$ +60.0 (*c* 1.00, THF).

IR (KBr): 3444, 2929, 1655, 1498, 1402, 1239, 1191, 1088, 1029 cm^{-1}.

^1H NMR (THF-d_8, 400 MHz): δ = 4.00–5.00 (br, 2 H), 7.12 (d, *J* = 8.2 Hz, 2 H), 7.26–7.35 (m, 6 H), 7.37–7.50 (m, 10 H), 7.75–8.10 (m, 16 H), 8.31 (s, 2 H).

^{13}C NMR (THF-d_8, 100 MHz): δ = 125.6 (2 C), 126.0 (2 C), 126.3 (2 C), 126.8 (2 C), 127.9 (2 C), 128.0 (4 C), 128.2 (8 C), 128.3 (4 C), 129.1 (2 C), 129.5 (8 C), 132.5 (2 C), 132.7 (2 C), 134.2 (2 C), 135.4 (2 C), 140.5 (2 C), 142.3 (4 C), 142.5 (4 C), 146.5 (2 C).

^{31}P NMR (THF-d_8, 160 MHz): δ = –21.2.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{56}H_{37}O_7P_2$: 883.2009; found: 883.2008.

(*R*)-3,3′-Diphenyl-1,1′-binaphthyl-2,2′-pyrophosphoric Acid [(*R*)-3b]

Pale yellow solid; yield: 5.8 mg (99%); $[\alpha]_D^{26}$ +219.5 (*c* 1.00, THF).

IR (KBr): 3421, 3058, 1496, 1457, 1420, 1246, 1193, 993 cm^{-1}.

^1H NMR (THF-d_8, 400 MHz): δ = 6.60–7.20 (br, 2 H), 7.10 (d, *J* = 8.2 Hz, 2 H), 7.26–7.34 (m, 4 H), 7.38 (t, *J* = 7.3 Hz, 4 H), 7.46 (t, *J* = 7.3 Hz, 2 H), 7.67 (d, *J* = 7.3 Hz, 4 H), 8.00 (d, *J* = 8.2 Hz, 2 H), 8.10 (s, 2 H).

^{13}C NMR (THF-d_8, 100 MHz): δ = 125.9 (2 C), 126.2 (2 C), 126.8 (2 C), 127.7 (2 C), 127.8 (2 C), 128.7 (4 C), 129.1 (2 C), 130.4 (4 C), 132.2 (2 C), 132.7 (2 C), 133.9 (2 C), 135.8 (2 C), 139.4 (2 C), 146.3 (2 C).

^{31}P NMR (THF-d_8, 160 MHz): δ = –20.8.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{32}H_{21}O_7P_2$: 579.0768; found: 579.0757.

(*R*)-3,3-Di(4-biphenyl)-1,1′-binaphthyl-2,2′-pyrophosphoric Acid [(*R*)-3c]

Pale yellow solid; yield: 7.3 mg (99%); $[\alpha]_D^{30}$ +112.0 (*c* 1.00, THF).

IR (KBr): 3408, 3056, 2930, 1656, 1488, 1428, 1396, 1246, 1194, 1104, cm^{-1}.

^1H NMR (THF-d_8, 400 MHz): δ = 7.13 (br, 2 H), 7.28–7.35 (m, 4 H), 7.37–7.52 (m, 6 H), 7.60–7.82 (m, 12 H), 8.01 (m, 2 H), 8.15 (s, 2 H) (Two P–OH moieties were not clearly observed.).

^{13}C NMR (THF-d_8, 100 MHz): δ = 125.9 (2 C), 126.4 (2 C), 126.8 (2 C), 127.2 (4 C), 127.7 (4 C), 127.8 (2 C), 127.9 (2 C), 129.1 (2 C), 129.5 (4 C), 130.9 (4 C), 132.1 (2 C), 132.7 (2 C), 134.0 (2 C), 135.4 (2 C), 138.6 (2 C), 140.3 (2 C), 141.7 (2 C), 146.3 (2 C).

^{31}P NMR (THF-d_8, 160 MHz): δ = –20.2.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{44}H_{29}O_7P_2$: 731.1383; found: 731.1380.

Catalytic Enantioselective Aza-Friedel–Crafts Reaction of Phenols 5 with Aldimines 4; General Procedure (Scheme 4)

To a well-dried round-bottomed flask (50 mL) containing (*R*)-**3a** (8.8 mg, 0.010 mmol), which was prepared in situ in advance, were added $CHCl_3$ (18 mL) and aldimine **4** (0.30 mmol) under a N_2 atmosphere. The solution was cooled to 0 °C, and then a solution of phenol **5** (0.20 mmol) in $CHCl_3$ (2 mL) was added. The resultant mixture was stirred at 0 °C for 3 h. To quench the reaction, Et_3N (0.20 mL, 1.44 mmol) was added at 0 °C and the mixture was stirred for 5 min. Brine (10 mL) was poured into the reaction mixture, and the product was extracted with EtOAc (2 × 10 mL). The combined extracts were washed with brine (10 mL) and dried (Na_2SO_4). The organic phase was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 5:1 to 3:1) to give the desired product **6**. Hydrolyzed catalyst (*R*)-**2a** [partially, some metal salts of (*R*)-**2a**] could be recovered through the same silica gel column chromatography (eluent: $CHCl_3$/MeOH = 3:1) almost quantitatively. If the catalyst was to be reused for another reaction, further purification with washing by aq 1 *M* HCl was necessary. The enantiomeric purity of **6** was determined by HPLC analysis.

Methyl (*R*)-[(4-Hydroxyphenyl)(phenyl)methyl]carbamate (6a)

Colorless oil; yield: 46.4 mg (90%); $[\alpha]_D^{27}$ –16.0 (*c* 1.00, $CHCl_3$, 63% ee).

IR (neat): 3326, 1698, 1508, 1456, 1362, 1233, 1038 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 3.69 (s, 3 H), 5.32 (br, 1 H), 5.74 (br, 1 H), 5.89 (br, 1 H), 6.73 (d, *J* = 8.7 Hz, 2 H), 7.05 (d, *J* = 7.3 Hz, 2 H), 7.20–7.28 (m, 3 H), 7.21–7.34 (t, *J* = 7.3 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 52.6, 58.4, 115.6 (2 C), 127.2 (2 C), 127.5, 128.6 (2 C), 128.7 (2 C), 133.3, 141.8, 155.5, 156.7.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{15}NO_3Na$: 280.0950; found: 280.0944.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALCEL OD-H, *n*-hexane/*i*-PrOH = 4:1, 210 nm, flow rate = 0.6 mL/min, t_R = 21.7 min (minor, *S*) and 25.9 min (major, *R*).

Methyl [(2-Hydroxyphenyl)(phenyl)methyl]carbamate (7a)

Colorless oil; yield: 7.7 mg (15%, Table 1, entry 3).

IR (neat): 3407, 1696, 1600, 1519, 1457, 1348, 1267, 1025 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 3.72 (s, 3 H), 5.84 (br, 1 H), 6.17 (br, 1 H), 6.83–6.88 (m, 2 H), 6.99 (br, 1 H), 7.07 (br, 1 H), 7.15 (td, *J* = 7.8, 1.4 Hz, 1 H), 7.23–7.34 (m, 5 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 52.8, 54.8, 116.8, 120.4, 126.8 (2 C), 127.3, 128.5 (2 C), 128.8, 129.1 (2 C), 140.8, 154.2, 157.6.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{15}NO_3Na$: 280.0950; found: 280.0942.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALCEL OD-H, *n*-hexane/*i*-PrOH = 4:1, 210 nm, flow rate = 0.6 mL/min, t_R = 10.9 min and 60.5 min.

Methyl (*R*)-[(4-Hydroxy-3-methylphenyl)(phenyl)methyl]carbamate (6b)

Colorless solid; yield: 50.5 mg (93%); mp 119–123 °C; $[\alpha]_D^{21}$ –23.6 (*c* 1.00, $CHCl_3$, 82% ee).

IR (KBr): 3394, 2924, 1699, 1509, 1267, 1118, 1039 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.21 (s, 3 H), 3.69 (s, 3 H), 4.76 (s, 1 H), 5.25 (br, 1 H), 5.87 (br, 1 H), 6.70 (d, *J* = 8.2 Hz, 1 H), 6.92 (d, *J* = 8.2 Hz, 1 H), 6.99 (s, 1 H), 7.23–7.28 (m, 3 H), 7.32 (t, *J* = 6.9 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 16.0, 52.5, 58.4, 115.0, 124.4, 125.9, 127.2 (2 C), 127.4, 128.6 (2 C), 129.9, 133.3, 142.0, 153.7, 156.6.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{17}NO_3Na$: 294.1106; found: 294.1105.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALCEL OD-H, *n*-hexane/*i*-PrOH = 4:1, 254 nm, flow rate = 0.6 mL/min, t_R = 17.8 min (minor, *S*) and 25.9 min (major, *R*).

Methyl [(2-Hydroxy-3-methylphenyl)(phenyl)methyl]carbamate (7b)

Colorless oil; yield: 9.5 mg (17%, Scheme 3b).

IR (neat): 3410, 1703, 1518, 1468, 1345, 1266, 1193, 1028 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.26 (s, 3 H), 3.72 (s, 3 H), 5.72 (br, 1 H), 6.20 (d, *J* = 8.2 Hz, 1 H), 6.60 (br, 1 H), 6.78 (t, *J* = 7.8 Hz, 1 H), 6.86 (d, *J* = 8.2 Hz, 1 H), 7.08 (d, *J* = 8.2 Hz, 1 H), 7.25–7.38 (m, 5 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 16.1, 52.8, 54.7, 120.6, 125.6, 126.8 (2 C), 126.9, 127.5, 128.3, 128.7 (2 C), 130.6, 140.7, 152.6, 157.7.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{17}NO_3Na$: 294.1106; found: 294.1108.

Methyl (*R*)-(4-Hydroxyphenyl)(*p*-tolyl)methylcarbamate (6c)

Colorless solid; yield: 31.8 mg (58%); mp 133–137 °C; $[\alpha]_D^{25}$ –5.1 (*c* 0.87, $CHCl_3$, 77% ee).

IR (KBr): 3361, 1664, 1542, 1512, 1439, 1266, 1039 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.33 (s, 3 H), 3.69 (s, 3 H), 4.92 (s, 1 H), 5.22 (br, 1 H), 5.86 (br, 1 H), 6.76 (dt, *J* = 8.7, 2.7 Hz, 2 H) 7.07–7.15 (m, 6 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.2, 52.6, 58.2, 115.6 (2 C), 127.2 (2 C), 128.6 (2 C), 129.4 (2 C), 133.5, 137.3, 139.0, 155.4, 156.6.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{17}NO_3Na$: 294.1101; found: 294.1105.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALPAK IA-3, *n*-hexane/*i*-PrOH = 4:1, 210 nm, flow rate = 1.0 mL/min, t_R = 8.8 min (major, *R*) and 11.5 min (minor, *S*).

Methyl (*S*)-[(4-Hydroxyphenyl)(naphthalen-1-yl)methyl]carbamate (6d)

Colorless solid; yield: 41.3 mg (67%); mp 208–222 °C; $[\alpha]_D^{26}$ –26.8 (*c* 1.00, MeOH, 60% ee).

IR (KBr): 3398, 3349, 1697, 1515, 1448, 1263, 1225, 1191, 1174, 1056 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz, 40 °C): δ = 3.56 (s, 3 H), 6.50 (d, *J* = 9.2 Hz, 1 H), 6.68 (d, *J* = 8.7 Hz, 2 H), 7.07 (d, *J* = 8.3 Hz, 2 H), 7.45 (t, *J* = 7.3 Hz, 1 H), 7.48–7.51 (m, 3 H), 7.84 (d, *J* = 7.8 Hz, 1 H), 7.93 (m, 1 H), 8.00 (m, 1 H), 8.13 (br, 1 H), 9.28 (br, 1 H).

^{13}C NMR (DMSO-d_6, 100 MHz, 40 °C): δ = 51.3, 54.2, 115.0 (2 C), 123.4, 124.3, 125.2, 125.4, 126.1, 127.4, 128.5, 128.7 (2 C), 130.4, 132.1, 133.3, 138.4, 155.9, 156.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{17}NO_3Na$: 330.1101; found: 330.1093.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALCEL ID-3, *n*-hexane/*i*-PrOH = 4:1, 284 nm, flow rate = 0.5 mL/min, t_R = 24.4 min (major, *S*) and 29.3 min (minor, *R*).

Methyl (*R*)-[(3-Allyl-4-hydroxyphenyl)(phenyl)methyl]carbamate (6e)

Colorless oil; yield: 39.2 mg (66%); $[\alpha]_D^{27}$ –29.9 (*c* 1.00, $CHCl_3$, 76% ee).

IR (neat): 3326, 2923, 2855, 1698, 1267 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.36 (d, *J* = 6.4 Hz, 2 H), 3.69 (s, 3 H), 5.08–5.20 (m, 2 H), 5.30 (br, 1 H), 5.40 (br, 1 H), 5.89 (d, *J* = 7.3 Hz, 1 H), 5.96 (m, 1 H), 6.71 (d, *J* = 8.2 Hz, 1 H), 6.93 (d, *J* = 8.2 Hz, 1 H), 6.97 (s, 1 H), 7.22–7.27 (m, 3 H), 7.30–7.34 (m, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 35.3, 52.5, 58.4, 116.0, 116.7, 125.7, 126.8, 127.2 (2 C), 127.5, 128.7 (2 C), 129.5, 134.0, 136.3, 142.0, 153.7, 156.4.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{19}NO_3Na$: 320.12657; found: 320.1257.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALCEL OD-H, *n*-hexane/*i*-PrOH = 4:1, 230 nm, flow rate = 0.6 mL/min, t_R = 13.3 min (minor, *S*) and 23.8 min (major, *R*).

Methyl (*R*)-[(4-Hydroxy-3-iodophenyl)(phenyl)methyl]carbamate (6f)

Colorless oil; yield: 8.5 mg (11%); $[\alpha]_D^{25}$ –10.3 (*c* 1.00, $CHCl_3$, 26% ee).

IR (neat): 3305, 2919, 1691, 1268, 1225, 1040 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.70 (s, 3 H), 5.24 (br, 1 H), 5.42 (s, 1 H), 5.87 (br, 1 H), 6.91 (d, *J* = 8.7 Hz, 1 H), 7.10 (dd, *J* = 8.2, 1.8 Hz, 1 H), 7.21 (d, *J* = 6.9 Hz, 2 H), 7.27–7.38 (m, 3 H), 7.54 (d, *J* = 2.3 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 52.6, 57.7, 85.8, 115.1, 127.3 (2 C), 127.8, 128.9 (2 C), 129.2, 135.4, 137.0, 141.2, 154.4, 156.3.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{14}INO_3Na$: 405.9916; found: 405.9906.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALCEL OD-H, *n*-hexane/*i*-PrOH = 4:1, 210 nm, flow rate = 0.6 mL/min, t_R = 16.9 min (minor, *S*) and 46.8 min (major, *R*).

Methyl (*R*)-{[4-Hydroxy-3-(trimethylsilyl)phenyl](phenyl)methyl}carbamate (6g)

Colorless oil; yield: 36.2 mg (55%); $[\alpha]_D^{25}$ –22.8 (*c* 1.00, $CHCl_3$, 60% ee).

IR (neat): 3335, 2953, 1699, 1508, 1405, 1243, 1074 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.26 (s, 9 H), 3.69 (s, 3 H), 5.19 (br, 1 H), 5.28 (br, 1 H), 5.90 (br, 1 H), 6.57 (d, *J* = 8.2 Hz, 1 H), 6.99 (br, 1 H), 7.20 (s, 1 H), 7.22–7.28 (m, 3 H), 7.32 (t, *J* = 7.8 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = –1.0 (3 C), 52.5, 58.6, 114.6, 125.8, 127.1 (2 C), 127.4, 128.6 (2 C), 129.7, 133.0, 134.4, 142.0, 156.5, 160.2.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{23}NO_3SiNa$: 352.1345; found: 352.1335.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALCEL OD-H, *n*-hexane/*i*-PrOH = 4:1, 210 nm, flow rate = 0.6 mL/min, t_R = 7.5 min (minor, *S*) and 10.0 min (major, *R*).

Methyl (*R*)-[(4-Hydroxy-3-methylphenyl)(*p*-tolyl)methyl]carbamate (6h)

Colorless oil; yield: 53.0 mg (93%); $[\alpha]_D^{27}$ –8.0 (*c* 1.00, $CHCl_3$, 67% ee).

IR (neat): 3334, 2921, 1697, 1511, 1268, 1117, 1039 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.20 (s, 3 H), 2.32 (s, 3 H), 3.68 (s, 3 H), 4.90 (br, 1 H), 5.23 (br, 1 H), 5.83 (br, 1 H), 6.68 (d, *J* = 8.2 Hz, 1 H), 6.91 (d, *J* = 7.8 Hz, 1 H), 6.98 (s, 1 H), 7.12 (s, 4 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 16.0, 21.1, 52.4, 58.2, 115.0, 124.3, 125.8, 127.1 (2 C), 129.3 (2 C), 129.9, 133.7, 137.1, 139.1, 153.5, 156.5.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{19}NO_3Na$: 308.1257; found: 308.1261.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALCEL OD-H, *n*-hexane/*i*-PrOH = 4:1, 280 nm, flow rate = 0.6 mL/min, t_R = 16.3 min (major, *R*) and 19.8 min (minor, *S*).

Methyl (*R*)-[(4-Bromophenyl)(4-hydroxy-3-methylphenyl)methyl]carbamate (6i)

Colorless oil; yield: 70.0 mg (99%); $[\alpha]_D^{23}$ –2.8 (*c* 1.00, $CHCl_3$, 28% ee).

IR (neat): 3327, 2922, 1697, 1511, 1266, 1118, 1071, 1039, 1011 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.19 (s, 3 H), 3.69 (s, 3 H), 5.22 (m, 2 H), 5.80 (br, 1 H), 6.65 (d, *J* = 8.2 Hz, 1 H), 6.85 (d, *J* = 7.8 Hz, 1 H), 6.93 (s, 1 H), 7.12 (d, *J* = 8.2 Hz, 2 H), 7.44 (d, *J* = 8.7 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 16.0, 52.6, 58.0, 115.1, 121.3, 124.6, 126.0, 128.8 (2 C), 130.0, 131.7 (2 C), 132.8, 141.1, 153.8, 156.5.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{16}BrNO_3Na$: 372.0206; found: 372.0197.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALPAK AS-3, *n*-hexane/*i*-PrOH = 3:1, 230 nm, flow rate = 1.0 mL/min, t_R = 9.8 min (minor, *S*) and 11.0 min (major, *R*).

Methyl (*S*)-[(4-Hydroxy-3-methylphenyl)(naphthalen-1-yl)methyl]carbamate (6j)

Colorless oil; yield: 52.7 mg (82%); $[\alpha]_D^{26}$ –7.6 (*c* 1.00, $CHCl_3$, 77% ee).

IR (neat): 3335, 2975, 1698, 1508, 1260, 1118 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.19 (s, 3 H), 3.70 (s, 3 H), 4.86 (d, *J* = 9.6 Hz, 1 H), 5.31 (d, *J* = 8.2 Hz, 1 H), 6.62 (br, 1 H), 6.68 (d, *J* = 8.2 Hz, 1 H), 6.93 (br, 1 H), 7.04 (s, 1 H), 7.33 (m, 1 H), 7.41–7.48 (m, 3 H), 7.80 (d, *J* = 8.2 Hz, 1 H), 7.87 (m, 1 H), 7.97 (br, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 16.0, 52.6, 55.3, 115.0, 123.8, 124.4, 124.9, 125.3, 125.8, 125.9, 126.5, 128.4, 128.8, 130.0, 131.0, 133.0, 134.0, 137.4, 153.6, 156.4.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{19}NO_3Na$: 344.1263; found: 344.1263.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALCEL OD-H, *n*-hexane/*i*-PrOH = 4:1, 230 nm, flow rate = 0.6 mL/min, t_R = 21.7 min (minor, *R*) and 32.0 min (major, *S*).

Methyl (*R*)-[(4-Hydroxy-3-methylphenyl)(naphthalen-2-yl)methyl]carbamate (6k)

Colorless oil; yield: 47.7 mg (74%); $[\alpha]_D^{25}$ –28.6 (*c* 1.00, $CHCl_3$, 68% ee).

IR (neat): 3330, 1696, 1508, 1265, 1114, 1040 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.18 (s, 3 H), 3.71 (s, 3 H), 5.22 (s, 1 H), 5.37 (br, 1 H), 6.03 (br, 1 H), 6.66 (d, *J* = 8.2 Hz, 1 H), 6.90 (d, *J* = 7.8 Hz, 1 H), 7.00 (s, 1 H), 7.31 (d, *J* = 8.7 Hz, 1 H), 7.43–7.52 (m, 2 H), 7.71 (s, 1 H), 7.75–7.83 (m, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 15.9, 52.5, 58.5, 115.1, 124.4, 125.5 (2 C), 126.0, 126.1, 126.3, 127.7, 128.1, 128.5, 130.2, 132.7, 133.3, 133.5, 139.4, 153.6, 156.5.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{19}NO_3Na$: 344.1263; found: 344.1257.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALCEL OD-H, *n*-hexane/*i*-PrOH = 4:1, 254 nm, flow rate = 0.6 mL/min, t_R = 20.2 min (major, *R*) and 29.3 min (minor, *S*).

Methyl (*S*)-[(4-Hydroxy-3-methylphenyl)(thiophen-2-yl)methyl]carbamate (6l)

Colorless solid; yield: 44.5 mg (80%); mp 42–45 °C; $[\alpha]_D^{25}$ –9.6 (*c* 1.00, $CHCl_3$, 49% ee).

IR (KBr): 3398, 2918, 1509, 1256, 1118, 1044 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.23 (s, 3 H), 3.70 (s, 3 H), 5.02 (s, 1 H), 5.36 (br, 1 H), 6.06 (br, 1 H), 6.72 (d, *J* = 8.2 Hz, 1 H), 6.81 (dm, *J* = 3.7 Hz, 1 H), 6.93 (dd, *J* = 5.3, 3.7 Hz, 1 H), 7.02 (d, *J* = 8.2 Hz, 1 H), 7.08 (br, 1 H), 7.22 (dd, *J* = 5.3, 1.4 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 16.0, 52.5, 54.6, 115.1, 124.3, 125.2, 125.6, 125.7, 126.9, 129.7, 133.4, 146.5, 153.8, 156.2.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{15}NO_3SNa$: 300.0670; found: 300.0666.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALCEL OD-H, *n*-hexane/*i*-PrOH = 4:1, 230 nm, flow rate = 0.6 mL/min, t_R = 15.4 min (minor, *R*) and 18.6 min (major, *S*).

Large Scale Synthesis of Benzyl (*R*)-[(4-Hydroxyphenyl)(phenyl)methyl]carbamate (6m) (Scheme 5)

To a well-dried round-bottomed flask (500 mL) containing (*R*)-**3a** (99.4 mg, 0.113 mmol), which was prepared in situ in advance, were added $CHCl_3$ (200 mL) and aldimine **4b** (810 mg, 3.39 mmol) under a N_2 atmosphere. The solution was cooled to 0 °C, and then a solution of phenol (**5a**; 213 mg, 2.26 mmol) in $CHCl_3$ (23 mL) was added. The resultant mixture was stirred at 0 °C for 3 h. To quench the reaction, Et_3N (0.20 mL, 1.44 mmol) was added at 0 °C and the mixture was stirred for 5 min. Brine (100 mL) was poured into the mixture, and the product was extracted with EtOAc (2 × 100 mL). The combined extracts were washed with brine (100 mL) and dried (Na_2SO_4). The organic phase was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 5:1 to 3:1) to give the desired product **6m** (663 mg, 88%) as a colorless oil. Hydrolyzed catalyst (*R*)-**2a** [partially, some metal salts of (*R*)-**2a**] could be recovered through the same silica gel column chromatography (eluent: $CHCl_3$/MeOH = 3:1) almost quantitatively. The enantiomeric purity of **6m** was determined by HPLC analysis; colorless oil; yield: 663 mg (88%); $[\alpha]_D^{27}$ –13.6 (*c* 1.00, $CHCl_3$, 63% ee).

IR (neat): 3321, 1696, 1661, 1517, 1356, 1297, 1265, 1237, 1041 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.11 (s, 2 H), 5.41 (br, 1 H) 5.80 (br, 1 H), 5.90 (br, 1 H), 6.66–6.72 (m, 2 H), 7.03 (d, *J* = 7.3 Hz, 2 H), 7.21–7.34 (m, 10 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 58.5, 67.3, 115.6 (2 C), 127.2 (2 C), 127.5, 128.3/128.5/128.6 (9 C), 133.2, 136.1, 141.7, 155.5, 156.0.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{19}NO_3Na$: 356.1263; found: 356.1261.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALPAK IC-3, *n*-hexane/*i*-PrOH = 85:15, 230 nm, flow rate = 1.0 mL/min, t_R = 14.1 min (minor, *S*), 20.9 min (major, *R*).

(*R*)-4-({[(Benzyloxy)carbonyl]amino}(phenyl)methyl)phenyl Trifluoromethanesulfonate (10)

To a solution of **6m** (663 mg, 1.99 mmol, 62% ee) and Et_3N (0.70 mL, 4.98 mmol) in CH_2Cl_2 (5 mL) was added trifluoromethanesulfonic anhydride (721 µL, 4.38 mmol) at 0 °C under a N_2 atmosphere. The mixture was stirred at r.t. for 2 h. The resulting mixture was diluted with EtOAc (10 mL) and brine (10 mL). The product was extracted with EtOAc (2 × 20 mL), the combined organic layers were washed with brine and dried (Na_2SO_4). The organic phase was concentrated under reduced pressure to give compound **10** (930 mg, >99%) as a colorless solid. This crude product was used in the next step without further purification; yield: 930 mg (>99%); mp 112–114 °C; $[\alpha]_D^{26}$ +18.4 (*c* 1.00, $CHCl_3$, 62% ee).

IR (KBr): 3315, 3033, 1696, 1499, 1424, 1140, 1040 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.11 (s, 2 H), 5.41 (br, 1 H), 6.00 (br, 1 H), 7.19–7.24 (m, 4 H), 7.28–7.37 (m, 10 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 58.3, 67.3, 118.7 (q, $J_{C,F}$ = 319 Hz), 121.5 (2 C), 127.4 (2 C), 128.1, 128.3 (3 C), 128.6 (2 C), 129.0 (2 C), 129.1 (2 C), 136.1, 140.6, 142.3, 148.7, 155.6.

^{19}F NMR ($CDCl_3$, 376 MHz): δ = –72.7.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{18}F_3NO_5SNa$: 488.0755; found: 488.0755.

Benzyl (*R*)-[1,1′-Biphenyl-4-yl(phenyl)methyl]carbamate (11)

To a solution of compound **10** (containing impurities from the previous step, 1.99 mmol) in toluene (40 mL) were added phenylboronic acid (388 mg, 3.2 mmol), K_2CO_3 (340 mg, 2.46 mmol), and $Pd(PPh_3)_4$ (236 mg, 0.20 mmol). The mixture was heated to 90 °C, and stirred at that temperature for 16 h. The resulting mixture was diluted with EtOAc (20 mL) and aq 1.0 M HCl. The product was extracted with EtOAc (2 × 20 mL), the combined organic layers were washed with brine (20 mL), and dried (Na_2SO_4). The organic phase was concentrated under reduced pressure, and the crude product was purified by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 5:1 to 3:1) to give **11** (783 mg, >99%) as a colorless solid. Recrystallization from *n*-hexane/Et_2O improved the optical purity to 98% ee (400 mg, 50% recovery). The enantiomeric purity of **11** was determined by HPLC analysis; colorless solid; yield: 783 mg (>99%); mp 109–116 °C; $[\alpha]_D^{25}$ –5.7 (*c* 1.00, $CHCl_3$, 98% ee).

IR (KBr): 3322, 3031, 1686, 1519, 1489, 1231, 1134, 1040 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.13 (s, 2 H), 5.43 (br, 1 H), 6.03 (br, 1 H), 7.25–7.40 (m, 13 H), 7.43 (t, *J* = 7.3 Hz, 2 H), 7.52–7.59 (m, 4 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 58.7, 67.0, 127.1 (2 C), 127.3 (2 C), 127.4 (4 C), 127.6, 127.7 (2 C), 128.2 (2 C), 128.5 (2 C), 128.7 (2 C), 128.8 (2 C), 136.3, 140.4, 140.6, 140.7, 141.6, 155.7.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{23}NO_2Na$: 416.1626; found: 416.1626.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 4:1, 280 nm, flow rate = 1.0 mL/min, t_R = 12.9 min (minor, *S*) and 14.7 min (major, *R*).

(*R*)-1,1′-Biphenyl-4-yl(phenyl)methanamine (12)

To a solution of **11** (55.9 mg, 0.14 mmol) in CH_2Cl_2 (0.56 mL) was added trimethylsilyl iodide (74 µL, 0.52 mmol) at r.t. under a N_2 atmosphere. The mixture was stirred at r.t. for 1 h and then quenched with MeOH (5 mL). Volatiles were removed in vacuo, and the resulting residue was dissolved in 30% aq AcOH and washed with Et_2O (5 mL). The aqueous layer was then neutralized with 1 *M* aq NaOH, and extracted with EtOAc (2 × 10 mL). The combined extracts were washed with brine and dried (Na_2SO_4). The organic phase was concentrated under reduced pressure to give **12** (33.4 mg, 92%) as a colorless solid. The enantiomeric purity of **12** was determined by chiral HPLC analysis (98% ee); yield: 33.4 mg (92%); mp 69–74 °C; $[\alpha]_D^{26}$ +19.6 (*c* 1.00, $CHCl_3$, 98% ee) {Lit.[31b] $[\alpha]_D^{22}$ +8.9 (*c* 2.45, $CHCl_3$, 66% ee)}.

IR, ^{1}H NMR, ^{13}C NMR, and HRMS data were consistent with previously reported values.[31]

IR (KBr): 3378, 3027, 2922, 2850, 1598, 1487, 1448, 1417, 1213, 1147 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.80 (br, 2 H), 5.27 (s, 1 H), 7.23 (m, 1 H), 7.30–7.36 (m, 3 H), 7.39–7.50 (m, 6 H), 7.52–7.58 (m, 4 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 59.6, 127.0 (2 C), 127.1 (4 C), 127.2 (2 C), 127.3 (2 C), 128.6 (2 C), 128.8 (2 C), 140.0, 140.9, 144.7, 145.5.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{19}H_{17}N$: 259.1361; found: 259.1369.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALCEL OD-H, *n*-hexane/*i*-PrOH/Et_2NH = 10:1:0.1, 254 nm, flow rate = 1.0 mL/min, t_R = 35.0 min (major, *R*) and 40.1 min (minor, *S*) [Lit.[31b] HPLC analysis (66% ee): Daicel CHIRALCEL OD-H, *n*-hexane/*i*-PrOH/Et_2NH = 100:10:0.1, 254 nm, 1.0 mL/min, t_R = 25.9 min (major, *R*) and 28.2 min (minor, *S*)].

Methyl [(2-Hydroxy-5-methylphenyl)(phenyl)methyl]carbamate (17)

Colorless solid; yield: 4.5 mg (8%); mp 148–152 °C.

IR (KBr): 3421, 3322, 2958, 1689, 1509, 1450, 1334, 1274, 1238, 1121, 1038 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.23 (s, 3 H), 3.71 (s, 3 H), 5.89 (br, 1 H), 6.11 (br, 1 H), 6.61 (br, 1 H), 6.73 (d, *J* = 8.2 Hz, 1 H), 6.89 (s, 1 H), 6.95 (dd, *J* = 8.0, 1.8 Hz, 1 H), 7.22–7.34 (m, 5 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 20.6, 52.7, 55.4, 116.5, 126.7 (2 C), 127.1, 127.4, 128.4 (2 C), 129.4 (2 C), 129.5, 141.2, 151.8, 157.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{17}NO_3Na$: 294.1101; found: 294.1091.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALCEL OD-3, *n*-hexane/*i*-PrOH = 9:1, 230 nm, flow rate = 1.0 mL/min, t_R = 12.2 min and 17.4 min.

Methyl [(4-Hydroxy-2-methylphenyl)(phenyl)methyl]carbamate (19)

Colorless oil; yield: 1.6 mg (3%).

IR (neat): 3332, 2923, 1695, 1610, 1504, 1453, 1358, 1232, 1097, 1027 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz, 40 °C): δ = 2.24 (s, 3 H), 3.69 (s, 3 H), 5.04 (s, 1 H), 5.18 (br, 1 H), 6.06 (br, 1 H), 6.61 (d, *J* = 7.8 Hz, 1 H), 6.62 (s, 1 H), 6.95 (d, *J* = 7.8 Hz, 1 H), 7.19 (d, *J* = 7.3 Hz, 2 H), 7.25 (t, *J* = 7.3 Hz, 1 H), 7.31 (t, *J* = 7.2 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz, 40 °C): δ = 19.6, 52.5, 55.4, 112.9, 117.7, 127.4 (2 C), 127.5, 128.2, 128.7 (2 C), 132.1, 138.0, 141.5, 155.0, 156.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{17}NO_3Na$: 294.1101; found: 294.1100.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALPAK IC-3, *n*-hexane/*i*-PrOH = 85:15, 210 nm, flow rate = 0.4 mL/min, t_R = 33.8 min (minor) and 37.4 min (major).

Methyl [(2-Hydroxy-4-methylphenyl)(phenyl)methyl]carbamate (20)

Colorless oil; yield: 1.2 mg (2%).

IR (neat): 3319, 1694, 1618, 1516, 1452, 1421, 1347, 1291, 1232, 1120, 1028 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz, 40 °C): δ = 2.28 (s, 3 H), 3.72 (s, 3 H), 5.76 (d, *J* = 9.2 Hz, 1 H), 6.14 (d, *J* = 8.2 Hz, 1 H), 6.54 (br, 1 H), 6.68 (d, *J* = 7.8 Hz, 1 H), 6.69 (s, 1 H), 6.89 (d, *J* = 7.8 Hz, 1 H), 7.26–7.28 (m, 3 H), 7.33 (t, *J* = 7.8 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz, 40 °C): δ = 21.1, 52.8, 54.9, 117.3, 121.1, 124.9, 126.8 (2 C), 127.1, 128.4 (2 C), 128.7, 139.1, 141.2, 154.1, 157.6.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{17}NO_3Na$: 294.1106; found: 294.1116.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALPAK IC-3, *n*-hexane/*i*-PrOH = 4:1, 230 nm, flow rate = 0.4 mL/min, t_R = 18.5 min (major), 23.8 min (minor).

Methyl [(4-Hydroxynaphthalen-1-yl)(phenyl)methyl]carbamate (22)

Colorless solid; Yield: 8.7 mg (14%); mp 212–222 °C; $[\alpha]_D^{25}$ +5.9 (*c* 0,54, $CHCl_3$, 11% ee).

IR (KBr): 3335, 2946, 1699, 1528, 1391, 1339, 1274, 1237, 1053 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 3.56 (s, 3 H), 6.48 (d, *J* = 9.2 Hz, 1 H), 6.79 (d, *J* = 8.2 Hz, 1 H), 7.05 (d, *J* = 7.8 Hz, 1 H), 7.24 (m, 1 H), 7.28–7.34 (m, 4 H), 7.44 (t, *J* = 7.3 Hz, 1 H) 7.50 (t, *J* = 7.2 Hz, 1 H), 7.93 (d, *J* = 8.7 Hz, 1 H), 8.18 (d, *J* = 7.8 Hz, 2 H), 10.1 (s, 1 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 51.3, 54.3, 107.0, 122.6, 123.2, 124.3, 124.8, 125.8, 126.5, 126.9, 127.5 (2 C), 128.1, 128.2 (2 C), 131.9, 142.5, 152.7, 156.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{17}NO_3Na$: 330.1101; found: 330.1100.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALPAK IC-3, *n*-hexane/*i*-PrOH = 9:1, 240 nm, flow rate = 1.0 mL/min, t_R = 23.1 min (minor), 35.4 min (major).

Methyl (*R*)-[(1-Hydroxynaphthalen-2-yl)(phenyl)methyl]carbamate (23)

Colorless solid; yield: 26.6 mg (43%); mp 115–122 °C; $[\alpha]_D^{25}$ –23.3 (*c* 0,98, $CHCl_3$, 24% ee).

IR (KBr): 3313, 3058, 1695, 1511, 1356, 1244, 1189, 1081 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.72 (s, 3 H), 5.78 (br, 1 H), 6.49 (d, *J* = 9.6 Hz, 1 H), 6.93 (d, *J* = 8.2 Hz, 1 H), 7.22–7.40 (m, 6 H), 7.45–7.51 (m, 2 H), 7.73 (d, *J* = 8.2 Hz, 1 H), 8.33 (d, *J* = 7.4 Hz, 1 H) 8.47 (br, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 53.1, 53.2, 120.6, 122.5, 122.9, 125.7, 125.8, 126.2, 126.7, 126.8 (2 C), 127.5, 127.7, 128.8 (2 C), 134.2, 139.5, 150.8, 158.8.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{17}NO_3Na$: 330.1101; found: 330.1107.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALPAK IC-3, *n*-hexane/*i*-PrOH = 9:1, 230 nm, flow rate = 1.0 mL/min, t_R = 12.8 min (major) and 14.7 min (minor).

(*R*)-24

Following the general procedure for (*R*)-**3**, (*R*)-**24** was prepared from the methyl ester of (*R*)-**2a** (9.2 mg 0.010 mmol).[7] (*R*)-**24** was obtained (9.0 mg, 99%) as *P*-diastereomers (76:24; pale yellow solid), which were not separable from each other, and the diastereomeric mixture was used for subsequent analysis and the reaction. A small amount of toluene was used under azeotropic conditions, but a small amount of DMF and CH_2Cl_2 were involved; pale yellow solid; yield: 9.0 mg (99%); $[\alpha]_D^{30}$ +112.0 (*c* 1.00, THF).

IR (KBr): 3408, 3056, 2930, 1656, 1488, 1428, 1396, 1246, 1194, 1104, cm^{-1}.

^{1}H NMR (THF-d_8, 400 MHz): δ = 3.22 (d, $J_{H,P}$ = 11.9 Hz), 7.06–7.27 (m), 7.28–7.65 (m), 7.74–8.16 (m), 8.32 (s), 8.35 (s). Many peaks were overlapped, and two P-OH moieties were not clearly observed.

^{13}C NMR (THF-d_8, 100 MHz): δ = 56.3 (d, $J_{C,P}$ = 5.8 Hz), 125.5, 125.8, 125.9, 126.0, 127.2, 128.1, 128.2, 128.3, 128.4, 128.7, 128.9, 129.2, 129.5, 129.7, 132.6, 132.7, 132.8, 134.0, 134.1, 135.3, 135.4, 135.6, 138.4, 139.5, 140.2, 142.2 (d, $J_{C,P}$ = 6.7 Hz), 142.5 (d, $J_{C,P}$ = 5.8 Hz), 146.2 (d, $J_{C,P}$ = 8.6 Hz), 146.5 (d, $J_{C,P}$ = 10.5 Hz). Many peaks were overlapped.

^{31}P NMR ($CDCl_3$, 160 MHz): δ = –20.8 (d, *J* = 26.0 Hz, minor), –20.6 (d, *J* = 25.8 Hz, major), –20.2 (d, *J* = 26.0 Hz, major), –19.7 (d, *J* = 25.9 Hz, minor).

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{57}H_{39}O_7P_2$: 897.2177; found: 897.2169.

***tert*-Butyl (*R*)-[(4-Hydroxy-3-methylphenyl)(phenyl)methyl]carbamate (6n)**

Colorless oil; yield: 57.6 mg (92%); $[\alpha]_D^{27}$ = –13.6 (*c* 1.00, $CHCl_3$, 48% ee).

IR (neat): 3337, 2977, 1685, 1613, 1508, 1367, 1269, 1164, 1117 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.44 (s, 9 H), 2.18 (s, 3 H), 5.13 (br, 1 H), 5.24 (br, 1 H), 5.80 (br, 1 H), 6.65 (m, 1 H), 6.88 (d, *J* = 7.8 Hz, 1 H), 6.96 (s, 1 H), 7.21–7.27 (m, 3 H), 7.30 (t, *J* = 7.8 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 16.0, 28.5 (3 C), 58.0, 80.0, 115.0, 124.3, 125.8, 127.1 (2 C), 127.2, 128.6 (2 C), 129.9, 133.7, 142.5, 153.5, 155.2.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{23}NO_3Na$: 336.1570; found: 336.1566.

The enantiomeric purity of the product was determined by HPLC analysis: Daicel CHIRALCEL OD-H, *n*-hexane/*i*-PrOH = 4:1, 230 nm, flow rate = 0.6 mL/min, t_R = 25.1 min (minor, *S*) and 30.0 min (major, *R*).

Funding Information

This work was financially supported by JSPS KAKENHI Grant Numbers JP26288046, JP17H03054, and JP15H05810 in Precisely Designed Catalysts with Customized Scaffolding.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1610250.

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(20) A higher concentration (i.e., >0.1 M based on **5** in $CHCl_3$) gave much lower enantioselectivities, whereas a lower concentration gave almost the same enantioselectivity as with the optimal concentration (0.01 M). Moreover, the effect of the reaction temperature (–40, –20, 0, and 25 °C) was also investigated. As a result, 0 °C gave better results in terms of yield and enantioselectivity than the other temperatures.

(21) $CHCl_3$ provided a better yield and enantioselectivity than other low-polarity solvents, such as CH_2Cl_2, 1,2-dichloroethane, toluene, and benzotrifluoride. In contrast, no reaction occurred when polar solvents were used, such as Et_2O, THF, propionitrile, and nitroethane.

(22) Aldimines with other N-protecting groups, such as CO_2t-Bu (Boc), showed lower enantioselectivities (see Scheme 8). Relatively stable N-CO_2CH_2Ph (Cbz) aldimines could be used, but showed slightly lower yields with almost the same enantioselectivities as less stable NCO_2Me aldimines. Moreover, no reaction occurred when NCO_2CH_2 (9-fluorenyl) (Fmoc), NSO_2Ph, NPh, and NBn aldimines were used.

(23) We performed the ^{31}P NMR ($CDCl_3$) analysis after the routine workup with Et_3N. As a result, (R)-**3**·$(Et_3N)_n$ was observed as a sole peak at –19.7 ppm, which strongly suggests that (R)-**3a** was intact during the reaction [cf. ^{31}P NMR ($CDCl_3$) spectra; (R)-**3a**: δ = –20.8; (R)-**2a**: δ = –0.4].

(24) Compounds **6b**, **6c**, and **6d** were subjected to X-ray analysis. See the Supporting Information for details.

(25) As shown in Table 2 and Scheme 3, the catalytic activity of (R)-**1a** was lower than that of (R)-**3a**, and (R)-**1a** did not promote the reactions of **5b** (0.01 M $CHCl_3$) effectively at 0 °C for 3 h. A mixture of the corresponding adducts **6** and **7** was obtained in <5% yield.

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