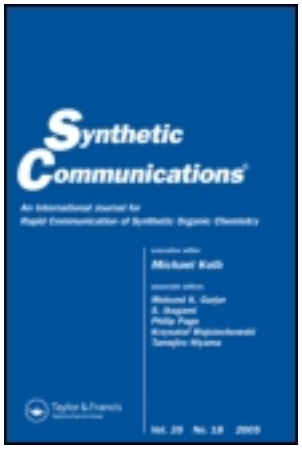

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Synthesis of Planar Chiral [2.2]Paracyclophanyl Imidazo[1,5-a]pyridinium Salts for the Rhodium-Catalyzed Asymmetric Arylation

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SYNTHESIS OF PLANAR CHIRAL [2.2]PARACYCLOPHANYL IMIDAZO[1,5-*a*] PYRIDINIUM SALTS FOR THE RHODIUM-CATALYZED ASYMMETRIC ARYLATION

Dengxia Wang, Yudao Ma, Fuyan He, Wenzeng Duan, Lei Zhao, and Chun Song

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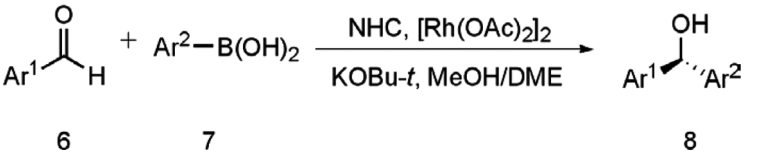
GRAPHICAL ABSTRACT



Abstract *Several novel flexibility-restricted imidazo[1,5-*a*]pyridinium triflates (abbreviated as imidazolium salts) were synthesized from (4*S*$_p$,13*R*$_p$)-(−)-4-amino-13-bromo[2.2] paracyclophane and pyridylaldehyde. These imidazolium salts can be used as nitrogen-containing heterocyclic carbene precursors in asymmetric catalysis and here they are applied in the Rh-catalyzed asymmetric 1,2-addition of arylboronic acids to aldehydes. After optimizing the catalytic situations and testing a series of substrates, moderate enantioselectivity and good yield were obtained.*

Keywords Aldehyde; asymmetric arylation; N-heterocyclic carbene; [2.2]paracyclophane; planar chirality

INTRODUCTION

N-Heterocyclic carbenes (NHCs) have emerged during the past two decades as a new type of stable compound,[1,2] and they have become indispensable ligands in many kinds of transition-metal catalysis.[3–15] The stabilizing properties of NHCs, expressed by the strong metal–carbene bond and slow dissociation rate, are the key factors in most of the reactions using NHC complexes as catalysts.[16] The structure of NHC is easily modified by changing the substitutuents on the carbene precursor, allowing the design of new ligands with different geometries.[17–20] Much work has been devoted to the design and development of carbene compounds with new structures to tune their steric and electronic properties and also to their application in organometallic catalysis and organocatalysis.[21–25]

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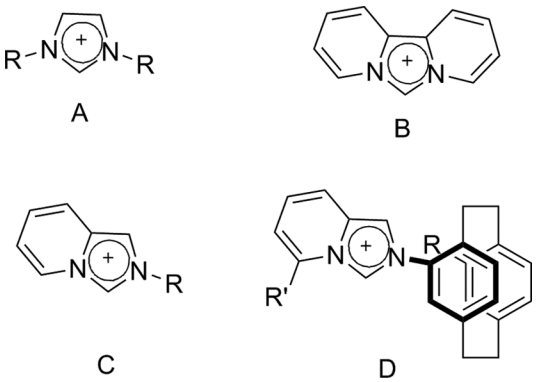
Chiral diarylmethanols are important intermediates for the synthesis of biologically and pharmaceutically active compounds.[26–32] The Rh-catalyzed addition of arylboronic acid derivatives to aldehydes for the synthesis of optically active diarylmethanols deserves particular mention for its high efficiency and wide tolerance toward polar substitutuents in the substrate.[4,33–37] However, examples of using chiral N-heterocyclic carbenes in ligand-catalyzed asymmetric arylation of aldehydes are rare.[38] Developing new chiral N-heterocyclic carbene ligands and efficient catalytic systems for the asymmetric 1,2-addition of organoboronic acid to aldehydes is an important synthetic goal.

The backbone structure of [2.2]paracyclophane and the directing effect of its substitutuents make it possible to design chiral ligands of essentially different patterns.[39] Previous [2.2]paracyclophanyl-based ligands included diphosphanes,[40–43] oxazoline–phosphanes,[44–46] imidazoliniums,[38,47–49] oxazoline–alcohols,[50–52] and imine ligands.[53–56] However, tailor-made imidazolium salts bearing bulky [2.2]paracyclophane-substituted combinations have been rarely reported[13,57] and their preparation is still a challenge. The construction of benzannulated derivatives is a very simple strategy to modify Arduengo's original imidazolium (Scheme 1, structure A),[1] as was demonstrated in the bipyridine-derived imidazolium (Scheme 1, structure B),[21,58] and the monopyridine-derived imidazolium (Scheme 1, structure B).[22,25] Herein, we report the synthesis of a new series of NHC precursors, [2.2]paracyclophanyl imidazo[1,5-a]pyridinium (Scheme 1, structure D), which combines imidazo[1,5-*a*]pyridine and [2.2]paracyclophane. Then, these NHC precursors were used as ligands for the rhodium-NHC-catalyzed asymmetric 1,2-addition of arylboronic acids to aldehydes.

RESULTS AND DISCUSSION

Synthesis of N-[(4S_p,13R_p)-13-R-4-[2.2]Paracyclophanyl]-imidazo[1,5-*a*]pyridinium Triflates [5a–e]

A range of substituted pyridine-derived NHC precursors was synthesized from pyridine carboxaldehydes **3** and sterically hindered 4-amino-[2.2]paracyclophane

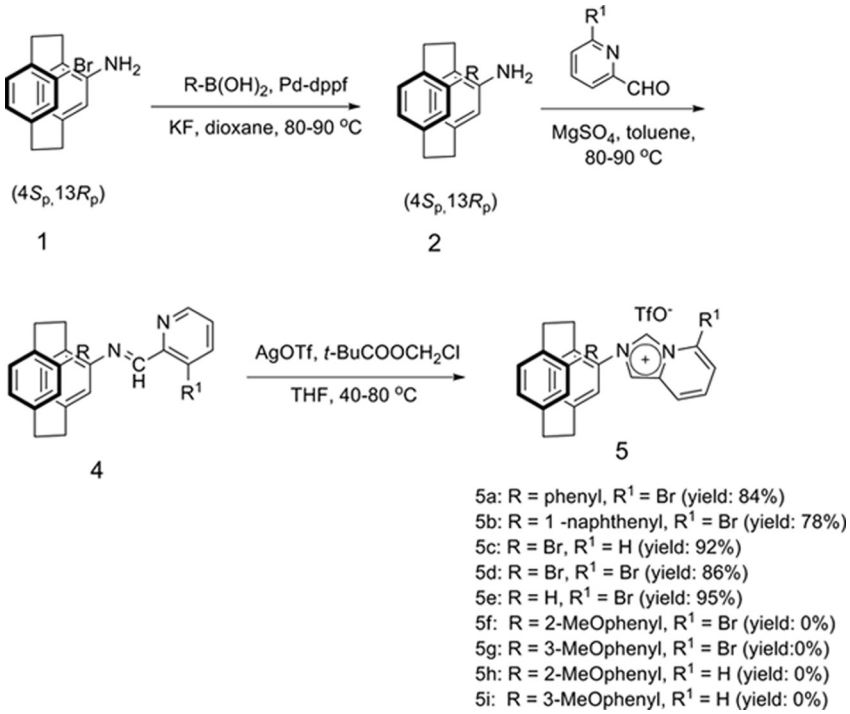


Scheme 1. Representative N-heterocyclic carbene precursors.

derivative **2**, which was prepared by Suzuki–Miyaura coupling reaction from ($4S_p$,$13R_p$)-4-amino-13-bromo[2.2]paracyclophane and arylboronic compounds.[39] The condensation of 4-amino[2.2]paracyclophane derivative **2** and pyridine carboxaldehyde **3** in toluene afforded the corresponding imine **4** in excellent yield (Scheme 2).[25] Then, treatment of pyridine imines **4** with a reagent formed from equal amounts of AgOTf and chloromethyl pivalate in tetrahydrofuran (THF) resulted in the formation of the desired imidazolium triflates **5a**–**e** in good yields (Scheme 2).[18] However, imidazolium triflates **5f**–**g** could not be prepared from **4f**–**g**, although we changed the reaction conditions, such as temperature and solvents. Their lack of reactivity may be ascribed to the steric hindrance of the R′ group at the 6-position of the pyridinyl group.

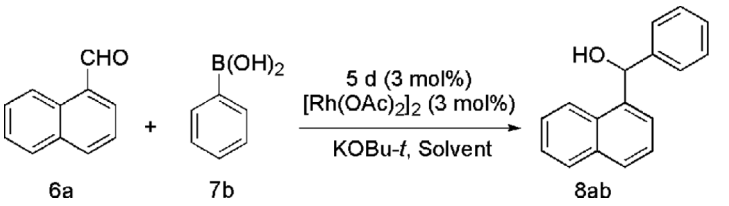
Catalytic Addition of Arylboronic Acids to Aromatic Aldehydes

Imidazolium salts **5a**–**e** were used as precursors for Rh-NHC complexes and applied in the catalytic asymmetric addition of arylboronic acids to aromatic aldehydes (Table 1). To develop an effective Rh-NHC catalysis for the reaction, several experimental variables were investigated. Foremost among the factors that can influence the rate and enantioselectivity of the reaction are the solvents and catalysts. Therefore, a systematic study of these two variables was performed. The 1,2-addition of phenylboronic acid to 1-naphthaldehyde with a catalyst generated in situ from imidazolium salt **5d** (3 mol%) and $[Rh(OAc)_2]_2$ (3 mol%) in the presence of KOBu-*t*



Scheme 2. Synthesis of imidazolium triflates **5**.

Table 1. Solvent effect on the arylation[a]



Entry	Solvent	Yield (%)[b]	*ee* (%)[c]
1	CH_3CN/DME (5:1)	12	
2	Pyridine	0	
3	DMF	0	
4	$MeOCH_2CH_2OH$/DME (5:1)	62	16 (R)
5	MeOH/DME (1:1)	98	17 (R)
6	MeOH/DME (5:1)	92	20 (R)

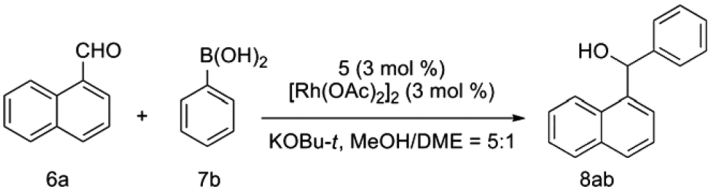
[a]Reaction conditions: $[Rh(OAc)_2]_2$ (3 mol%), **5d** (3 mol%), KOBu-*t* (1 eq), arylboronic acids (2 eq), N_2, 80 °C, 2 h.
[b]Isolated yield.
[c]Determined by chiral HPLC (CHIRALPAK IA Columns) analysis.

was examined in different solvents at 80 °C for 2 h (Table 1). The results showed that the solvent had a great impact on both the yield and the enantioselectivity of this catalyzed addition reaction. The rapid rate and good enantioselectivity of the addition in MeOH/DME (5:1) (Table 1, entry 6) compared to other solvents clearly identified it as the solvent of choice for this transformation. Next, various precatalysts, such as $[Rh(nbd)Cl]_2$, $[Rh(COD)Cl]_2$, $RhCl_3 \cdot xH_2O$, and $[Ru(p\text{-cymene})Cl_2]_2$ were subjected to the same reaction, but none of them exhibited any catalytic activity. Then we tested different bases, such as NaOH, K_2CO_3, and Cs_2CO_3, in place of KOBu-*t*, but none of these bases improved the yield or enantiomeric excess. Finally, we investigated the effect of the amount of the catalyst on this reaction. The catalytic activity decreased significantly when the catalyst loading was reduced to 1.0 mol%.

Based on these results, we chose MeOH/DME (5:1) as the solvent system, KOBu-*t* as the base, and $[Rh(OAc)_2]_2$ (3 mol%) as the precatalyst. Other imidazolium salts **5a, 5b, 5c,** and **5e** were screened in the phenylation of 1-naphthaldehyde (Table 2), which showed that all the Rh-NHC complexes prepared by combining $[Rh(OAc)_2]_2$ with the corresponding imidazolium salts could afford the desired diarylmethanol in good yield and moderate enantioselectivity (Table 2, entries 1, 3, 4 and 5). Among them, imidazolium salt **5d** gave the best enantioselectivity. The lowest *ee* (Table 2, entry 2), obtained using imidazolium salt **5b,** may be explained by too much congestion around the ligand, preventing complete complexation of the ligand to the rhodium center. The ligand screening revealed that ligand substitution can greatly affect the enantioselectivity.

The optimized catalyst system was tested in the asymmetric arylation of aldehydes with different steric and electronic properties (Table 3). The system was compatible with a wide variety of functional groups on both reaction partners, and in most cases, the reaction could proceed with notable efficiency (up to 98% isolated yield) with

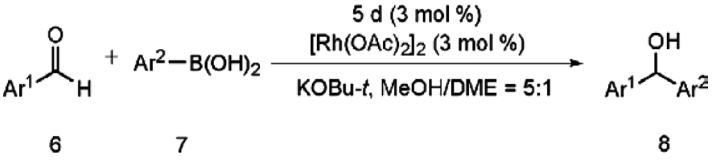
Table 2. Evaluation of ligand effects[a]



Entry	Ligand	Yield (%)[b]	*ee* (%)[c]
1	**5a**	89	14.5 (R)
2	**5b**	45	0.8 (S)
3	**5c**	76	16 (R)
4	**5d**	92	20 (R)
5	**5e**	87	18 (R)

[a]Reaction conditions: $[Rh(OAc)_2]_2$ (3 mol%), ligand **5** (3 mol%), KOBu-*t* (1 eq), arylboronic acids (2 eq), N_2, MeOH/DME (5:1), reflux, 2 h.
[b]Isolated yield.
[c]Determined by chiral HPLC (CHIRALPAK IA Columns) analysis.

Table 3. Evaluation of different reaction partners[a]



Entry	Ar^1	Ar^2	Yield (%)[b]	*ee* (%)[c]
1	1-naphthyl (6a)	Phenyl (7b)	92 (8ab)	20 (R)
2	1-naphthyl (6a)	2-Methoxyphenyl (7c)	98 (8ac)	27 (−)
3	1-naphthyl (6a)	3-Methoxyphenyl (7d)	60 (8ad)	57 (+)
4	Phenyl (6b)	1-naphthyl (7a)	69 (8ba)	16 (S)
5	2,4,6-trimethylphenyl (6c)	1-naphthyl (7a)	65 (8ca)	30 (−)
6	4-chlorophenyl (6d)	Phenyl (7b)	43 (8db)	17 (S)
7	4-chlorophenyl (6d)	2-MethoxyPhenyl (7b)	57 (8dc)	12 (−)
8	4-chlorophenyl (6d)	3-Methoxyphenyl (7d)	62 (8dd)	22 (R)
9	4-chlorophenyl (6d)	1-naphthyl (7a)	88 (8da)	13 (R)
10	2-Methoxyphenyl (6e)	Phenyl (7b)	37 (8eb)	24 (R)
11	2-Methoxyphenyl (6e)	1-naphthyl (7a)	76 (8ea)	10 (+)
12	4-(methoxylcarbonyl)phenyl (6f)	1-naphthyl (7a)	79 (8fa)	18 (+)
13	4-(methoxylcarbonyl)phenyl (6f)	Phenyl (7b)	93 (8fb)	45 (−)
14	4-(methoxylcarbonyl)phenyl (6f)	2-Methoxyphenyl (7c)	97 (8 fc)	22 (−)
15	4-(methoxylcarbonyl)phenyl (6f)	3-Methoxyphenyl (7d)	85 (8fd)	32 (+)

[a]Reaction conditions: $[Rh(OAc)_2]_2$ (3 mol%), ligand **5d** (3 mol%), KOBu-*t* (1 eq), arylboronic acids (2 eq), N_2, MeOH/DME (5:1), reflux, 2 h.
[b]Isolated yield.
[c]Determined by chiral HPLC (CHIRALPAK IA Columns) analysis.

a catalyst generated in situ from the same amount of imidazolium salt **5d** (3 mol%) and $[Rh(OAc)_2]_2$ (3 mol%). The substitution of the substrate has an important effect on the enantioselectivity of the catalytic reaction. Aromatic aldehydes or arylboronic acids bearing meta-substituents afforded chiral diarylmethanols with greater enantiomeric excess than those bearing *ortho*-substituents (Table 3, entries 2 and 3, 7 and 8, and 14 and 15). An interesting feature of this methodology is that in most cases both enantiomers of a given diarylmethanol can be easily prepared with the same chiral ligand, just by appropriate choice of the reaction partners—the arylboronic acid and aldehyde.

CONCLUSIONS

A new type of planar-chiral NHC precursor, 2*H*-imidazo[1,5-*a*]pyridin-4-ium triflate, has been synthesized in good yield from 4-amino-13-bromo[2.2]paracyclophane and pyridylaldehyde. Their application in rhodium-catalyzed asymmetric 1,2-additions of arylboronic acids to aromatic aldehydes has been demonstrated. The system was shown to be widely compatible with many functional groups in both reaction partners and the enantiomeric excess of the corresponding diarylmethanols reached 57%. Future investigations are in progress, aiming at modification of the [2.2]paracyclophane-based NHC ligands to improve the catalytic performance in terms of activity and enantioselectivity.

EXPERIMENTAL

All nonaqueous reactions were carried out in flame-dried glassware under a slight positive pressure of nitrogen. THF, dioxane, dimethoxyethane (DME), and toluene were dried by sodium benzophenone ketyl and distilled under nitrogen before use. CH_2Cl_2 was dried by P_2O_5 and distilled under nitrogen before use. Other commercially available solvents were used without further purification. Commercially available reagents were used without further purification unless otherwise noted. ($4S_p$,$13R_p$)-4-Amino-13-bromo[2.2]paracyclophane **1** and ($4S_p$,$13R_p$)-4-amino-12-aryl-[2.2]paracyclophane **2** were prepared according to the literature procedures.[49] Pyridylaldehyde **3** was purchased from J&K Chemical Ltd. Reactions were magnetically stirred and monitored by thin-layer chromatography (TLC) on silica-gel 0.25-mm precoated plates. All thin-layer chromatography (TLC) plates were visualized by ultraviolet (UV) fluorescence quenching. Yields refer to chromatographically and spectroscopically pure material unless otherwise noted. Melting points were recorded on a melting-point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a 300-MHz spectrometer. Chemical shifts were reported as δ values in parts per million (ppm) and were referenced to residual solvent signals: $CDCl_3$ (H 7.26 ppm and C 77.0 ppm) and dimethylsulfoxide (DMSO-d_6) (H 2.50 and C 39.5) using tetramethylsilane (TMS) as an internal standard. Data are reported as [δ shift] ([s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet]). The electropray ionization–mass spectrometry (ESI-MS) spectra were recorded on a mass spectrometer. Optical rotations were measured on a polarimeter with a wavelength of 589 nm: the concentration "*c*" has units of g/100 mL unless otherwise noted. Enantiomeric and diastereomeric analyses were determined by chiral high-performance liquid chromatography (HPLC) (Chiralpak IA column).

General Procedure for the Synthesis of Planar Chiral (4,13)-Disubstituted [2.2]Paracyclophanyl Imidazo[1,5-*a*]pyridinium Triflate 5a–e

4-Amino-[2.2]paracyclophane derivative **1** or **2** (1 mmol) and pyridylaldehyde **3** (1.1 mmol) were dissolved in dry toluene (4 mL), and anhydrous $MgSO_4$ (240 mg, 2 mmol) was added as dehydration agent. The resulting mixture was heated to 90 °C for 30–60 min. After filtration of $MgSO_4$, evaporation of the solvent in vacuo, and crystallization from EtOH, imine **4** was obtained as a yellow solid (yield >90%).

To a suspension of AgOTf (308 mg, 1.2 mmol) in THF (2 mL), chloromethyl pivalate (170 μL, 1.2 mmol) was added and the resulting suspension was stirred in a sealed tube in the dark at 40 °C for 1 h. Then imine **4** (0.9 mmol) was added to the tube. The resulting mixture was stirred at 40–80 °C for 5–6 h. After the suspension was cooled to room temperature, the solvent was removed in vacuum. The resulting oil was chromatographed on silica gel (2.5 × 20 cm, CH_2Cl_2/MeOH = 50:1 to 10:1), and the pure product was isolated. The resulting foam was crystallized from EtOH to give imidazolium triflate **5** as colorless crystals.

Imidazolium triflate 5a. Compound **4a**: 95.5% yield. Compound **5a**: 84% yield. Mp: 229–231 °C (decomp), $R_f = 0.45$ (CH_2Cl_2/MeOH = 10:1); $[\alpha]_D^{20} = +113.9$ (*c* 0.13, DMSO); ^{1}H NMR (300 MHz, DMSO, rt): δ 10.10 (s, 1 H), 8.54 (d, $J = 1.5$ Hz, Hz, 1 H), 7.80 (d, $J = 9.0$ Hz, 1 H), 7.67 (d, $J = 7.2$ Hz, 1 H), 7.47 (s, 1 H), 7.36 (d, $J = 6.3$ Hz, 2 H), 7.22 (dd, $J = 9.3$ Hz, $J = 7.2$ Hz, 1 H), 7.11–6.98 (m, 6 H), 6.89 (d, $J = 7.8$ Hz, 1 H), 6.77 (d, $J = 7.8$ Hz, 1 H), 3.15–3.35 (m, 8 H); ^{13}C NMR (75 MHz, DMSO, rt): δ 142.7, 140.0, 139.5 139.2, 138.2, 136.9, 136.5, 135.9, 134.1, 132.8, 132.1, 131.1, 131.0, 128.8, 128.5, 127.4, 126.5, 126.0, 125.4, 123.1, 121.1 (q, $J = 319$ Hz), 118.1, 116.7, 112.6, 34.9, 34.6, 34.4, 34.3. HRMS (ESI): calcd for $C_{29}H_{24}BrN_2$ $(M–OTf)^+$ 479.1123; found 479.1118.

Imidazolium triflate 5b. Compound **4b**: 92% yield. Compound **5b**: 78% yield. Mp: 146–148 °C (decomp), $R_f = 0.44$ (CH_2Cl_2/MeOH = 10:1); $[\alpha]_D^{20} = +69.9$ (*c* 0.39, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 8.98 (s, 1 H), 8.28 (s, 1 H), 7.83 (d, $J = 9.3$ Hz, 1 H), 7.76 (d, $J = 8.4$ Hz, 2 H), 7.54 (d, $J = 8.1$ Hz, 1 H), 7.49 (s, 1 H), 7.39–7.23 (m, 5 H), 7.08–7.03 (m, 1 H), 6.91–6.78 (m, 6 H), 3.33–3.14 (m, 6 H), 2.91–2.87 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 143.7, 140.5, 138.0, 137.7, 137.6, 137.2, 135.7, 135.0, 133.8, 133.1, 132.6, 132.5, 132.0, 131.6, 130.5, 128.5, 128.4, 127.1, 126.5, 126.0, 125.7, 125.4, 124.2, 124.1, 122.7, 121.0 (q, $J = 318$ Hz), 118.2, 116.8, 111.7, 35.1, 34.9, 34.6, 33.2. HRMS (ESI): calcd. for $C_{33}H_{26}BrN_2$ $(M–OTf)^+$ 529.1279; found 529.1266.

Imidazolium triflate 5c. Compound **4c**: 97.2% yield. Compound **5c**: 92% yield. Mp: 215–217 °C (decomp), $R_f = 0.47$ (CH_2Cl_2/MeOH = 10:1); $[\alpha]_D^{20} = +83.7$ (*c* 0.47, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 10.57 (s, 1 H), 8.84 (d, $J = 7.2$ Hz, Hz, 1 H), 7.77 (s, 1 H), 7.67 (d, $J = 9.3$ Hz, 1 H), 7.33 (s, 1 H), 7.25–7.20 (m, 1 H), 7.12–7.04 (m, 2 H), 6.78–6.65 (m, 4 H), 3.50–2.80 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 142.8, 142.6, 138.0, 137.5, 136.4, 136.1, 135.5, 134.1, 131.6, 131.5, 129.6, 126.4, 125.3, 125.2, 124.5, 124.4, 120.7 (q, $J = 319$ Hz), 118.3, 114.3, 36.9, 34.8, 34.2, 28.6. HRMS (ESI): calcd. for $C_{23}H_{20}BrN_2$ $(M–OTf)^+$ 403.0810; found 403.0816.

Imidazolium triflate 5d. Compound **4d**: 93.4% yield. Compound **5d**: 86% yield. Mp: 208–211 °C (decomp), $R_f = 0.42$ (CH_2Cl_2/MeOH = 10:1); $[\alpha]_D^{20} = +62.1$ (*c* 0.12, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 9.82 (s, 1 H), 8.43 (d, $J = 1.2$ Hz, Hz, 1 H), 7.84 (d, $J = 9.3$ Hz, 1 H), 7.41 (s, 1 H), 7.32 (d, $J = 6.9$ Hz, 1 H), 7.10 (dd, $J = 9.3$ Hz, $J = 7.2$ Hz, 1 H), 6.97 (s, 1 H), 6.69–6.63 (m, 3 H), 6.48 (d, $J = 7.8$ Hz, 1 H), 3.46–3.08 (m, 6 H), 2.92–2.78 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 142.7, 137.8, 137.4, 136.5, 136.1, 135.4, 133.9, 131.8, 131.5, 130.8, 126.3, 126.1, 125.2, 124.7, 124.5, 122.6, 120.9 (q, $J = 319$ Hz), 118.3, 117.7, 112.5, 36.9, 34.5, 34.1, 28.6. HRMS (ESI): calcd. for $C_{23}H_{19}Br_2N_2$ $(M–OTf)^+$ 480.9909; found .480.9918.

Imidazolium triflate 5e. Compound **4e**: 96.0% yield. Compound **5e**: 95% yield. Mp: 214–215 °C (decomp), $R_f = 0.47$ (CH_2Cl_2/MeOH 10:1); $[\alpha]_D^{20} = -26.7$ (*c* 2.21, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 9.36 (s, 1 H), 8.68 (s, 1 H), 8.11 (d, $J = 9.0$ Hz, 1 H), 7.42 (d, $J = 7.2$ Hz, 1 H), 7.26–7.18 (m, 1 H), 7.04 (s, 1 H), 6.87 (d, $J = 7.8$ Hz, 1 H), 6.72–6.63 (m, 3 H), 6.55 (d, $J = 7.8$ Hz, 1 H), 6.50–6.47 (d, $J = 8.1$ Hz, 1 H), 3.42–2.89 (m, 7 H), 2.74–2.71 (m, 1 H); ^{13}C NMR (300 MHz, $CDCl_3$, rt): δ 144.0, 140.3, 138.4, 137.4, 136.2, 133.9, 133.4, 132.8, 132.5, 132.3, 128.6, 127.3, 125.1, 124.6, 123.0, 119.1, 116.8, 35.0, 34.8, 34.5, 31.9. HRMS (ESI): $C_{23}H_{20}BrN_2$ $(M–OTf)^+$ 403.0810; found 403.0796.

General Procedure for the Solvent Effect on the Arylation (Table 1)

$[Rh(OAc)_2]_2$ (3.3 mg, 7.5×10^{-3} mmol, 3 mol%) was weighted into a flame-dried tube equipped with a condenser under an argon atmosphere. The solvent (1.0 mL) was added and the suspension was stirred at room temperature for 5 min. Then, NHC precursor **5d** (4.8 mg, 7.5×10^{-3} mmol, 3 mol%), phenylboronic acid (61.0 mg, 0.50 mmol), KOBu-*t* (28.0 mg, 0.25 mmol, 1 eq), and 1-naphthaldehyde (34.0 mg, 0.25 mmol) were successively added. The resulting mixture was stirred at 80 °C for 3 h. The reaction mixture was concentrated under reduced pressure, and the residue was purified by chromatography (ethyl acetate / hexane), yielding the desired secondary alcohol as a yellowish oil, which crystallized upon standing at low temperature (~4 °C in the refrigerator).

General Procedure for the Evaluation of Ligand Effects (Table 2)

$[Rh(OAc)_2]_2$ (3.3 mg, 7.5×10^{-3} mmol, 3 mol%) was weighted in a flame-dried tube equipped with a condenser under an argon atmosphere. MeOH/DME (5:1) (1.0 mL) was added, and the suspension was stirred at room temperature for 5 min. Then, NHC precursor **5** (7.5×10^{-3} mmol, 3 mol%), phenylboronic acid (61.0 mg, 0.50 mmol), KOBu-*t* (28.0 mg, 0.25 mmol), and 1-naphthaldehyde (34.0 mg, 0.25 mmol) were successively added. The resulting mixture was stirred at reflux for 3 h. The reaction mixture was concentrated under reduced pressure, and the residue was purified by chromatography (ethyl acetate / hexane), yielding the desired secondary alcohol as a slightly yellow oil, which crystallized upon standing at low temperature (~4 °C in the refrigerator).

General Procedure for the Evaluation of Different Reaction Partners (Table 3)

$[Rh(OAc)_2]_2$ (3.3 mg, 7.5×10^{-3} mmol, 3 mol%) was weighted into a flame-dried tube equipped with a condenser under an argon atmosphere. MeOH/DME (5:1) (1.0 mL) was added, and the suspension was stirred at room temperature for 5 min. Then, NHC ligand precursor **5d** (4.8 mg, 7.5×10^{-3} mmol, 3 mol%) arylboronic acid (0.50 mmol), KOBu-*t* (28.0 mg, 0.25 mmol), and aryl aldehyde (0.25 mmol) were successively added. The resulting mixture was stirred at reflux for 3 h. The reaction mixture was concentrated under reduced pressure, and the residue was purified by preparative thin, layer chromatography (ethyl acetate / hexane), yielding the desired secondary alcohol as a yellowish oil, which crystallized upon standing at low temperature (~4 °C in the refrigerator).

(1-Naphthyl)phenylmethanol (8ab and 8ba)

***R*-(+)-8ab.** Yield 92%; $[\alpha]_D^{20} = +5.5$ (*c* 0.5, $CHCl_3$) with 20% *ee*. The *ee* value was determined by HPLC analysis using a chiral column (Chiralpak IA column, n-hexane/chloroform = 3:1, flow 1.0 mL/min, detection at 254 nm), retention times 18.8 min (minor) and 20.1 min (major).

***S*-(–)-8ba.** Yield 69%; $[\alpha]_D^{20} = -4.2$ (*c* 0.5, $CHCl_3$) with 16% *ee*. The *ee* value was determined by HPLC analysis using a chiral column (Chiralpak IA column, *n*-hexane/chloroform = 3:1, flow 1.0 mL/min, detection at 254 nm), retention times 18.7 min (major) and 20.0 min (minor).

^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 8.03 (d, $J = 3.3$ Hz, 1 H), 8.01–7.80 (m, 2 H), 7.64 (d, $J = 6.9$ Hz, 1 H), 7.50–7.35 (m, 5 H) 7.34–7.24 (m, 3 H), 6.53 (s, 1 H), 2.35 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 143.1, 138.7, 133.9, 130.7, 128.8, 128.6, 128.5, 127.7, 127.06, 126.1, 125.6, 125.3, 124.6, 123.9, 73.6. HRMS (ESI): calcd. for $C_{17}H_{13}$ $(M–OH)^+$ 217.1017; found 217.1022.

(1-Naphthyl) (2-methoxyphenyl)methanol (8ac and 8ea)

(–)-8ac. Yield 98%; $[\alpha]_D^{20} = -14.7$ (*c* 0.6, $CHCl_3$) with 27% *ee*; The *ee* value was determined by HPLC analysis using a chiral column (Chiralpak IA column, *n*-hexane/chloroform = 3:1, flow 1.0 mL/min, detection at 254 nm), retention times 15.6 min (minor) and 18.3 min (major).

(+)-8ea. Yield 76%; $[\alpha]_D^{20} = +4.9$ (*c* 0.6, $CHCl_3$) with 10% ee; The ee value was determined by HPLC analysis using a chiral column (Chiralpak IA column, *n*-hexane/chloroform = 3:1, flow 1.0 mL/min, detection at 254 nm), retention times 13.7 min (major) and 14.7 min (minor).

^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 8.00 (d, $J = 7.8$ Hz 1 H), 7.86–7.78 (m, 2 H), 7.65 (d, $J = 7.2$ Hz, 1 H), 7.50–7.38 (m, 3 H) 7.28–7.23 (m, 1 H), 6.96–6.78 (m, 4 H), 3.89 (s, 3 H), 3.05 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 156.9, 138.0, 133.7, 131.3, 131.0, 129.0, 128.6, 128.4, 125.9, 125.5, 125.4, 124.3, 124.2, 120.8, 110.5, 101.1, 72.6, 68.4, 55.5. HRMS (ESI): calcd. for $C_{18}H_{15}O$ $(M–OH)^+$ 247.1123; found 247.1116.

(1-Naphthyl) (3-methoxyphenyl)methanol 8ad

(+)-**8ad**: Yield 60%; $[\alpha]_D^{20} = +34$ (*c* 0.4, $CHCl_3$) with 57% *ee*; The *ee* value was determined by HPLC analysis using a chiral column (Chiralpak IA column, *n*-hexane/chloroform = 3:1, flow 1.0 mL/min, detection at 254 nm), retention times 29.8 min (minor) and 32.3 min (major). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 8.06–8.03 (m, 1 H), 7.86–7.78 (m, 2 H), 7.60 (d, $J = 7.2$ Hz, 1 H), 7.48–7.40 (m, 3 H), 7.25–7.20 (m, 1 H), 6.98–6.98 (m, 1 H), 6.80 (d, $J = 8.1$ Hz, 1 H), 6.49 (s, 1 H), 3.75 (s, 3 H), 2.36 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 159.8, 144.8, 138.7, 133.9, 130.7, 129.5, 128.8, 128.5, 126.2, 125.6, 125.3, 124.7, 123.9, 119.4, 113.0, 112.7, 73.5, 55.2. HRMS (ESI): calcd. for $C_{18}H_{15}O$ $(M–OH)^+$ 247.1123; found 247.1118.

(2-Methoxyphenyl)phenylmethanol (8eb)

R-(+)-**8eb**: 95% yield; $[\alpha]_D^{20} = +9.3$ (*c* 0.4, $CHCl_3$) with 24% *ee*; The *ee* value was determined by HPLC analysis using a chiral column (Chiralpak IA column, *n*-hexane/chloroform = 3:1, flow 1.0 mL/min, detection at 254 nm), retention times 13.2 min (minor) and 14.1 min (major). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 7.39–7.26 (m, 7 H), 6.95–6.85 (m, 2 H), 6.04 (d, $J = 4.5$ Hz, 1 H), 3.78 (s, 3 H), 3.05 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 156.7, 143.3, 132.0, 128.7, 128.1, 127.8, 127.1, 126.6, 120.8, 110.8, 72.1, 55.4. HRMS (ESI): calcd. for $C_{14}H_{13}O$ $(M–OH)^+$ 197.0966; found 197.0960.

(4-Chlorophenyl)(1-naphthyl)methanol (8da)

R-(–)-**8da**: 88% yield; $[\alpha]_D^{20} = -10.2$ (*c* 07, $CHCl_3$) with 13% *ee*. The *ee* value was determined by HPLC analysis using a chiral column (Chiralpak IA column, *n*-hexane/chloroform = 3:1, flow 1.0 mL/min, detection at 254 nm); retention times 23.8 min (major) and 25.1 min (minor).

^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 7.95–7.76 (m, 3 H), 7.51–7.20 (m, 8 H), 6.37 (s, 1 H), 2.56 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 141.6, 138.4, 134.0, 133.3, 130.6, 128.8, 128.7, 128.6, 128.3, 126.3, 125.7, 125.3, 124.8, 123.8, 73.0. HRMS (ESI): calcd for $C_{17}H_{12}Cl$ $(M–OH)^+$ 251.0628, found 251.0622.

(4-Chlorophenyl) (2-methoxyphenyl)methanol (8dc)

(–)-**8dc**: 57% yield; $[\alpha]_D^{20} = -4.5$ (*c* 0.7, $CHCl_3$) with 12% *ee*. The *ee* value was determined by HPLC analysis using a chiral column (Chiralpak IA column, *n*-hexane/chloroform = 3:1, flow 1.0 mL/min, detection at 254 nm), retention times 15.1 min (major) and 15.9 min (minor). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 7.32–7.19 (m, 6 H), 6.96–6.85 (m, 2 H), 6.00 (s, 1 H), 3.79 (s, 3 H), 3.03 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 156.6, 141.9, 132.8, 131.5, 128.9, 128.2, 127.9, 127.7, 120.9, 110.8, 71.6, 55.4. HRMS (ESI): calcd. for $C_{14}H_{12}ClO$ $(M–OH)^+$ 231.0577; found 231.0573.

(4-Chlorophenyl) (3-methoxyphenyl)methanol (8dd)

R-(–)-**8dd**: 62% yield; $[\alpha]_D^{20} = -1.6$ (*c* 1.2, $CHCl_3$) with 22% *ee*. The *ee* value was determined by HPLC analysis using a chiral column (Chiralpak IA column, *n*-hexane/chloroform = 3:1, flow 1.0 mL/min, detection at 254 nm), retention times 33.1 min (major) and 36.1 min (minor). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 7.33–7.21 (m, 5 H), 6.91–6.79 (m, 3 H), 5.76 (s, 1 H), 3.77 (s, 3 H), 2.27 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 159.8, 145.0, 142.1, 133.3, 129.6, 127.8, 118.8, 113.1, 112.1, 75.5, 55.2. HRMS (ESI): calcd for $C_{14}H_{12}ClO$ $(M–OH)^+$ 231.0577, found 231.0579.

(4-Chlorophenyl) Phenylmethanol (8db)

S-(–)-**8db**: 43% yield; $[\alpha]_D^{20} = +5.7$ (*c* 0.36, $CHCl_3$) with 24% *ee*. The *ee* value was determined by HPLC analysis using a chiral column (Chiralpak IA column, *n*-hexane/chloroform = 3:1, flow 1.0 mL/min, detection at 254 nm), retention times 19.6 min (minor) and 23.4 min (major). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 7.35–7.25 (m, 9 H), 5.81 (s, 1 H), 2.23 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 143.4, 142.2, 133.3, 128.7, 128.6, 127.9, 127.86, 126.5, 75.6. HRMS (ESI): calcd. for $C_{13}H_{12}ClO$ $(M + H)^+$ 219.0532; found 219.0249.

(1-Naphthyl)(2,4,6-trimethylphenyl)methanol (8ca)

(–)-**8ca**: 65% yield; $[\alpha]_D^{20} = -12.4$ (*c* 1.1, $CHCl_3$) with 30% *ee*. The *ee* value was determined by HPLC analysis using a chiral column (Chiralpak IA column, *n*-hexane/chloroform = 3:1, flow 1.0 mL/min, detection at 254 nm), retention times 24.9 min (major) and 26.2 min (minor). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 8.22 (d, $J = 3.3$ Hz, 1 H), 7.89 (d, $J = 5.2$ Hz, 1 H), 7.87 (d, $J = 6.9$ Hz, 1 H), 7.80–7.86 (m, 7 H) 6.53 (s, 1 H), 2.30 (s, 9 H), 2.15 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 137.2, 137.1, 137.06, 135.4, 134.1, 131.5, 130.4, 128.8, 128.5, 126.2, 125.6, 125.1, 125.0, 124.4, 70.9, 21.2, 20.9. HRMS (ESI): calcd. for $C_{20}H_{19}$ $(M–OH)^+$ 259.1487; found 259.1493.

(1-Naphthyl) [4-(methoxylcarbonyl)phenyl] Methanol (8fa)

(+)-**8fa**: 79% yield; $[\alpha]_D^{20} = +11.6$ (c 0.45, CH_2Cl_2) with 18% *ee*. The *ee* value was determined by HPLC analysis using a chiral column (Chiralpak IA column, n-hexane/*i*-propanol = 4:1, flow 1.0 mL/min, detection at 254 nm), retention times 15.7 min (major) and 18.0 min (minor). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 8.04–8.00 (t, 1 H), 7.97 (d, $J = 6.0$ Hz, 2 H), 7.87–7.80 (m, 2 H), 7.53–7.40 (m, 6 H), 6.53 (s, 1 H), 3.87(s, 3 H), 2.55 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 166.9, 148.2, 138.3, 134.1, 130.6, 129.8, 129.3, 128.9, 128.8, 126.8, 126.3, 125.8, 125.3, 125.2, 123.9, 73.5, 52.1. HRMS (ESI): calcd. for $C_{19}H_{15}O_2$ (M-OH)$^+$ 275.1072; found 275.1079.

[4-(Methoxylcarbonyl)phenyl]phenylmethanol (8fb)

(–)-**8fb**: 93% yield; $[\alpha]_D^{20} = -12.2$ (c 0.38, CH_2Cl_2) with 45% *ee*. The *ee* value was determined by HPLC analysis using a chiral column (Chiralpak IA column, n-hexane/*i*-propanol = 4:1, flow 1.0 mL/min, detection at 254 nm), retention times 13.2 min (major) and 14.3 min (minor). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 8.05–7.97 (m, 3 H), 7.98–7.81 (m, 2 H), 7.54–7.40 (m, 6 H), 6.55 (s, 1 H), 3.88 (s, 3 H), 2.50 (d, $J = 3.0$ Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 166.9, 148.1, 138.3, 134.1, 130.6, 129.8, 129.3, 128.9, 126.8, 126.4, 125.8, 125.3, 125.2, 123.9, 73.6, 52.1. HRMS (ESI): calcd. for $C_{15}H_{13}O_2$ $(M\text{-}OH)^+$ 225.0916; found 225.0910.

(2-Methoxyphenyl)[4-(methoxylcarbonyl)phenyl]methanol (8fc)

(–)-**8fc**: 97% yield; $[\alpha]_D^{20} = -9.2$ (c 0.25, CH_2Cl_2) with 22% *ee*. The *ee* value was determined by HPLC analysis using a chiral column (Chiralpak IA column, n-hexane/*i*-propanol = 4:1, flow 1.0 mL/min, detection at 254 nm), retention times 14.7 min (major) and 16.2 min (minor). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 8.00–7.97 (d, 2 H), 7.47 (d, $J = 9.0$ Hz, 2 H), 7.31–7.20 (m, 2 H), 6.97–6.88 (m, 2 H), 6.08 (s, 1 H), 3.90 (s, 3 H), 3.80 (s, 3 H), 3.08 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 156.7, 148.5, 131.4, 129.5, 129.1, 128.9, 127.9, 126.4, 120.9, 110.9, 72.1, 55.4, 52.0. HRMS (ESI): calcd. for $C_{16}H_{15}O_3$ $(M\text{-}OH)^+$ 255.1021; found 255.1010.

(3-Methoxyphenyl)[4-(methoxylcarbonyl)phenyl]methanol (8fd)

(+)-**8fd**: 85% yield; $[\alpha]_D^{20} = +20.1$ (c 0.23, CH_2Cl_2) with 32% *ee*. The *ee* value was determined by HPLC analysis using a chiral column (Chiralpak IA column, n-hexane/*i*-propanol = 4:1, flow 1.0 mL/min, detection at 254 nm), retention times 16.4 min (major) and 20.0 min (minor). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 7.99 (d, $J = 6.0$ Hz, 2 H), 7.46 (d, $J = 6.0$ Hz, 2 H), 7.28–7.22 (m, 1 H), 6.92 (d, $J = 6.0$ Hz, 2 H), 6.83–6.79 (m, 1 H), 5.84 (s, 1 H), 3.89 (s, 3 H), 3.77 (s, 3 H), 2.38 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, rt): δ 166.9, 159.9, 148.5, 144.9, 129.8, 129.7, 129.3, 126.3, 118.9, 113.3, 112.2, 75.8, 55.2, 52.1. HRMS (ESI): calcd. for $C_{16}H_{15}O_3$ $(M\text{-}OH)^+$ 255.1021; found 255.1031.

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