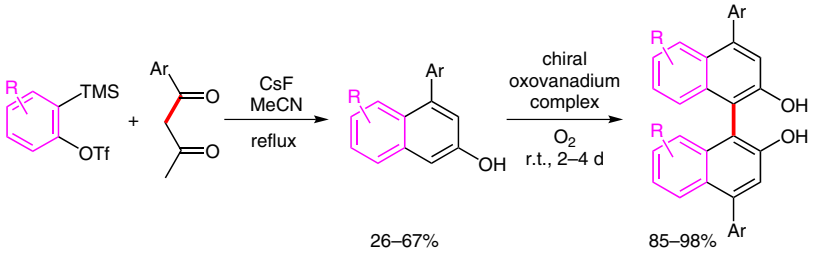
Synthesis K. Okuma et al. Special Topic

Enantioselective Synthesis of 4,4′-Biaryl-BINOLs from Arynes and β-Diketones

Kentaro Okuma*
Kenta Horigami
Noriyoshi Nagahora
Kosei Shioji

Department of Chemistry, Fukuoka University, Jonan-ku, Fukuoka 814-0180, Japan
kokuma@fukuoka-u.ac.jp



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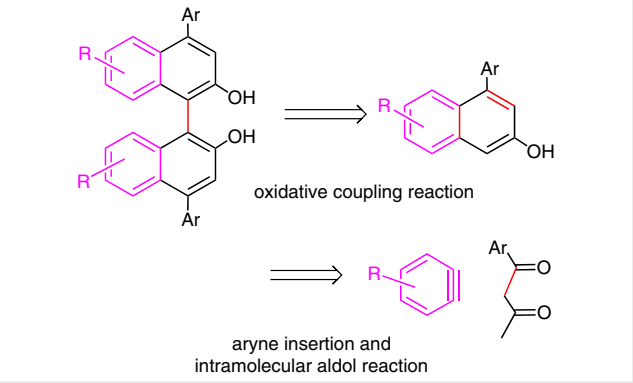
Abstract The reaction of 2-(trimethylsilyl)phenyl triflate with aroylacetones in the presence of CsF gave the corresponding 4-aryl-2-naphthols. Substituted triflates also reacted with aroylacetones to afford 4-aryl-2-naphthols regioselectively. The enantioselective oxidation of 4-aryl-2-naphthols with a chiral tridentate oxovanadium(IV) complex furnished the corresponding 4,4′-biaryl-1,1′-binaphthols in good yields.

Key words aryne, β-diketone, carbon–carbon bond insertion, 4-aryl-2-naphthol, BINOL

Arynes have received considerable attention over the last decades because of the important role they play as intermediates.[1] The chemistry of arynes has shown extensive progress because of the development of the benzyne precursor, 2-(trimethylsilyl)phenyl triflate (**1a**), which forms benzyne under very mild conditions.[2] Arynes are extremely electron-poor reactive intermediates that exhibit a highly electrophilic character; even neutral nucleophiles can easily add to arynes to produce zwitterions that act as key intermediates in the subsequent transformation to yield a variety of benzoannulated compounds.[3] Stoltz et al. and Yoshida et al. reported that the reaction of **1a** with β-keto esters or β-diketones provided ortho-substituted benzoyl compounds via carbon–carbon single bond insertion,[4] which has opened the door to carbon–carbon single bond cleavage reactions using an aryne intermediate. Naphthalene derivatives are commonly found in many organic materials, such as natural products, pharmaceuticals, agrochemicals, and functional organic materials, and are useful synthetic building blocks.[5] Whereas the synthesis of 4-substituted 2-naphthols is generally difficult,[6] the synthesis of 4-aryl-2-naphthols is relatively unknown. Reported examples include the Friedel–Crafts reaction,[7] the rhodium-catalyzed ring closure of diazoacetate,[8] and the palladium-catalyzed direct arylation of naphthyl carbamate.[9] All these reactions, however, generally require many steps. To do away with tedious procedures, we designed the synthesis of 4-aryl-2-naphthols from β-diketones and benzyne by using carbon–carbon single bond cleavage and carbon–carbon binding reactions.[10] We herein describe the full details of the synthesis of 4-aryl-2-naphthols and enantiomerically pure 4,4′-biaryl-1,1′-binaphthols (4,4′-biaryl-BINOLs) from triflate **1** and β-diketones (Scheme 1).

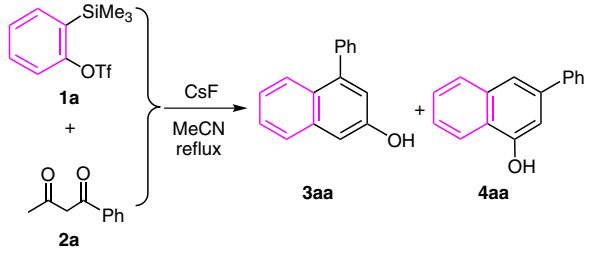


Scheme 1 Retrosynthetic analysis of 4,4′-biaryl-BINOLs

We first attempted to perform the reaction of 2-(trimethylsilyl)phenyl triflate (**1a**) with benzoylacetone (**2a**) in the presence of CsF. Treatment of benzoylacetone (**2a**) with triflate **1a** in the presence of CsF in refluxing MeCN resulted in the formation of 4-phenyl-2-naphthol (**3aa**) and 3-phenyl-1-naphthol (**4aa**) in 52–58% and 9–12% yields, respectively (Table 1, entries 1 and 2). When the reaction was carried out by using 1.6 equivalents of triflate **1a**, 2-naphthol **3aa** and 1-naphthol **4aa** were isolated in

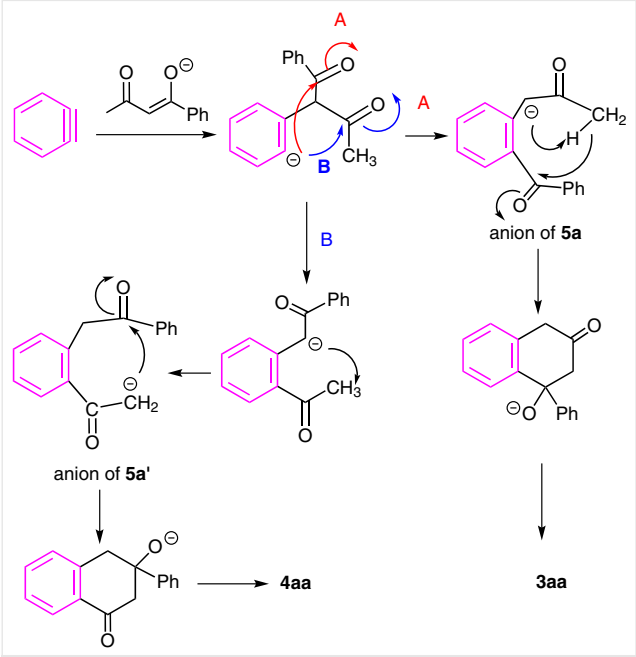
53% and 10% yield, respectively (entry 3). Use of excess **1a** resulted in low yields of the naphthols due to the formation of inseparable side products (entry 4).

Table 1 Reaction of Triflate **1a** with β-Diketone **2a**



Entry	**1a** (equiv)	Time (h)	Product **3aa**	Yield (%) of **4aa**
1	1.0	3.0	52	9
2	1.2	6.0	58	12
3	1.6	3.0	53	10
4	2.0	6.0	48	8

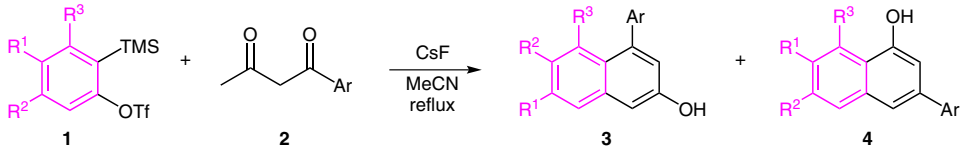
The reaction was surmised to proceed as follows: fluoride-induced enolate anion attacks benzyne to give a zwitterion, and this in turn reacts with the benzoyl carbon to furnish an enolate anion of **5a** (route A). Another pathway would be that the anion attacks acetyl carbon to give an enolate anion of **5a′** (route B). The obtained enolates react intramolecularly with carbonyl carbon to afford aldol reaction products, and the products are dehydrated and aromatized to give **3aa** and **4aa** (Scheme 2).



Scheme 2 Reaction mechanism

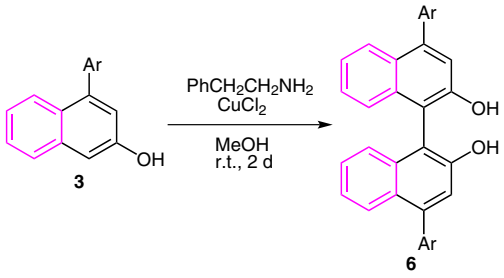
To confirm the reaction mechanism, compound **1a** was treated with **2a** at room temperature for 5 hours to give **5a** in 58% yield. When **5a** was further treated with CsF in refluxing MeCN, 2-naphthol **3aa** was obtained. Thus, the anion of **5a** would be the intermediate for the formation of **3aa** (Scheme 3).

Table 2 Synthesis of Aryl-Substituted Naphthols



Entry	**1a**	R^1	R^2	R^3	**2**	Ar	**3**	Yield (%)	**4**	Yield (%)
1	**1a**	H	H	H	**2a**	Ph	**3aa**	58	**4aa**	12
2	**1a**	H	H	H	**2b**	4-MeC_6H_4	**3ab**	37	**4ab**	25
3	**1a**	H	H	H	**2c**	4-ClC_6H_4	**3ac**	65	**4ac**	15
4	**1a**	H	H	H	**2d**	4-$O_2NC_6H_4$	**3ad**	67	**4ad**	0
5	**1a**	H	H	H	**2e**	1-naphthyl	**3ae**	44	**4ae**	31
6	**1a**	H	H	H	**2f**	2-thienyl	**3af**	30	**4af**	25
7	**1b**	OCH_2O		H	**2c**	4-ClC_6H_4	**3bc**	33	**4bc**	11
8	**1c**	H	H	OMe	**2c**	4-ClC_6H_4	**3cc**	26	**4cc**	13
9	**1d**	Me	Me	H	**2c**	4-ClC_6H_4	**3dc**	30	**4dc**	20

Table 3 Synthesis of 4,4′-Biaryl-BINOLS **6**



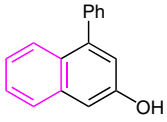
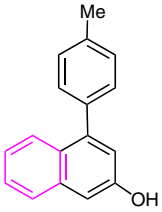
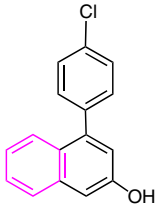
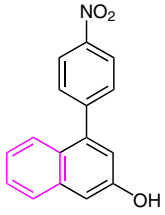
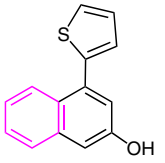
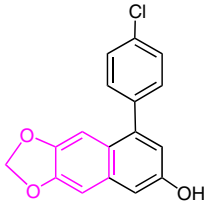
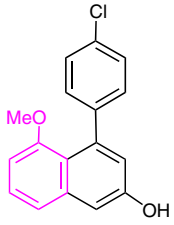
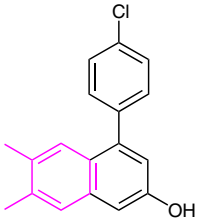
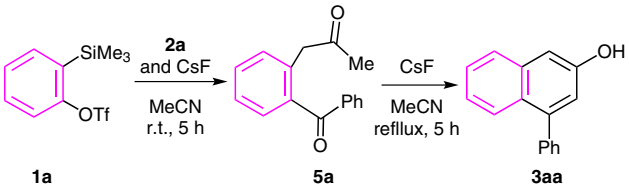
3		6	Yield (%)
3aa		**6a**	75
3ab		**6b**	80
3ac		**6c**	76
3ad		**6d**	65
3af		**6e**	72
3bc		**6f**	70

Table 3 (continued)

3		6	Yield (%)
3cc		**6g**	72
3dc		**6h**	73

After determining the optimum conditions (1.2 equiv of **1**, reflux in MeCN), substituted 2-arylnaphthols **3** were synthesized from substituted triflates **1b**–**d** and aroylacetones **2b**–**f** in the presence of CsF. Treatment of triflate **1a** with 4-chlorobenzoylacetone (**2c**) in the presence of CsF gave the corresponding 4-(4-chlorophenyl)-2-naphthol (**3ac**) and 3-(4-chlorophenyl)-1-naphthol (**4ac**) in 65% and 15% yield, respectively (Table 2, entry 3). In the presence of an electron-donating group in the aryl group of the substrate **2b**, the reaction afforded also the 1-naphthol **4ab** in moderate yield (entry 2). Substrates **2** substituted with electron-withdrawing groups at the para position of the aryl group afforded 2-naphthols **3** in comparatively high yields (entries 3, 4, 7, and 8). In particular, the nitro substituent afforded only 2-naphthol **3ad** (entry 4). When 1-(1-naphthyl)butane-1,3-dione (**2e**) and 1-(2-thienyl)butane-1,3-dione (**2f**) were used as substrates, corresponding 4-(1-naphthyl)-2-naphthol (**3ae**) and 4-(2-thienyl)-2-naphthol (**3af**) were obtained in moderate yields (entries 5 and 6). Thus, naphthols **3** and **4** were synthesized in one pot starting from easily available substituted aroylacetones **2** and benzyne precursor **1**.

Axially dissymmetric 1,1′-binaphthol (BINOL) and its derivatives are important chiral auxiliaries in asymmetric catalyses.[11] Although many substituted BINOLs have ap-

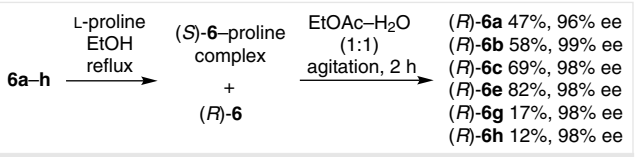


Scheme 3 Reaction of **5a** with CsF

peared in the literature, the synthesis of 4,4′-biaryl-BINOLs **6** remains a very difficult task. Until the publication of our preliminary communication,[10] 4,4′-biaryl-BINOLs **6** had been synthesized by bromination of the alkyl ethers of BINOL followed by the Suzuki–Miyaura coupling reaction and dehalogenation.[12] We synthesized the 4,4′-biaryl-BINOLs **6** according to the method described by Brussee et al.[13] When 2-naphthol **3aa** was treated with copper(II) chloride and phenethylamine in ethanol at room temperature for 2 days, 4,4′-biphenyl-BINOL (**6a**) was obtained in 75% yield. Other reactions were carried out in a similar manner (Table 3).

Next, the enantioselective synthesis of 4,4′-biaryl-BINOLs **6** was tried by adopting the method of Chen et al.,[14] who used a chiral tridentate oxovanadium(IV) catalyst for the enantioselective synthesis of BINOLs. Treatment of 2-naphthol **3aa** with tridentate oxovanadium catalyst in the presence of oxygen gave the corresponding BINOL **6a** in 85% yield with 65% ee (Table 4).

The yields of the reported synthesis of enantiomerically pure BINOLs by simple recrystallization were low.[14] Therefore, a BINOL-proline complex was prepared to separate enantiomerically pure isomers.[15] Treatment of BINOL **6a** with proline gave the corresponding 1:1 complex that was easily separated by filtration. The filtrate was washed with water and extracted with ethyl acetate to afford enantiomerically pure (*R*)-4,4′-biphenyl-BINOL [(*R*)-**6a**] (ee >96%) in 47% yield. Other enantiomerically pure BINOLs were synthesized in a similar manner (Scheme 4).



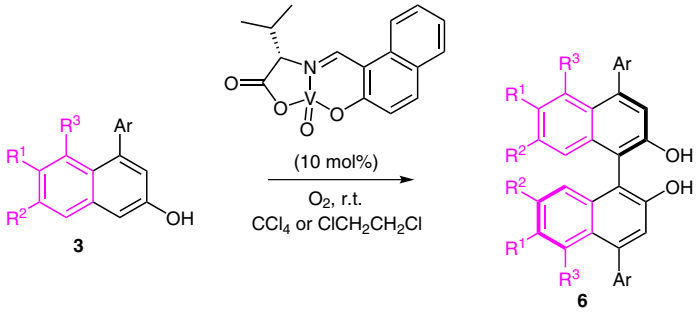
Scheme 4 Synthesis of enantiomerically pure **6**

The results clearly suggest that enantiomerically pure 4,4′-biaryl-BINOLs **6** could be obtained in short-step operations via three C–C bond cleavage and C–C bond forming reactions: aryne insertion, intramolecular aldol condensation, and oxidative coupling reaction.

In summary, we have accomplished the synthesis of 4-aryl-substituted naphthols **3** from aryne precursors and aroylacetones in one pot. Oxidative coupling of the naphthols **3** by using a chiral tridentate oxovanadium(IV) complex afforded substituted 4,4′-biaryl-BINOLs **6** in excellent yields. This method is expected to pave the way for the construction of new four carbon–carbon bonds in short-step operations and the efficient synthesis of various 4,4′-biaryl-BINOLs **6** in moderate yields.

All chemicals were obtained from commercial suppliers and used without further purification. Analytical TLC was carried out on precoated plates (Merck silica gel 60, F254), and flash column chromatography was performed with silica gel (Merck, 70–230 mesh). NMR spectra (^{1}H at 400 MHz; ^{13}C at 100 MHz) were recorded in $CDCl_3$, and chemical shifts are expressed in ppm relative to internal TMS for ^{1}H and ^{13}C NMR. Melting points are uncorrected.

Table 4 Enantioselective Synthesis of 4,4′-Biaryl-BINOLs **6**



Entry	**3**	R^1	R^2	R^3	Ar	Time (d)	Product	Yield (%)	ee (%)
1	**3aa**	H	H	H	Ph	2	**6a**	85	65
2	**3ab**	H	H	H	4-MeC_6H_4	4	**6b**	90	74
3	**3ac**	H	H	H	4-ClC_6H_4	4	**6c**	95	71
4	**3af**	H	H	H	2-thienyl	3	**6e**	98	80
5	**3cc**	OMe	OMe	H	4-ClC_6H_4	3	**6g**	97	56
6	**3dc**	Me	Me	H	4-ClC_6H_4	2	**6h**	98	23

Reaction of 2-(Trimethylsilyl)phenyl Triflates 1 with Aroylacetones 2; 4-Aryl-2-naphthols 3 and 3-Aryl-1-naphthols 4; General Procedure

To a suspension of aroylacetone **2** (10 mmol) and CsF (5.5 g, 36 mmol) in MeCN (15 mL) was added a solution of triflate **1** (12 mmol) in MeCN (15 mL). After refluxing for 6 h, the reaction mixture was poured into H_2O (15 mL). The resulting suspension was extracted with CH_2Cl_2 (3 × 10 mL), dried (Na_2SO_4), filtered, and evaporated to give colorless oil, which was chromatographed over silica gel, eluting with hexane–EtOAc (3:1), to give **3** and **4** (Table 2).

4-Phenyl-2-naphthol (3aa)[6a]

Yield: 1.3 g (5.8 mmol, 58%); pale yellow oily crystals.

^{1}H NMR ($CDCl_3$): δ = 7.79 (d, *J* = 8.4 Hz, 1 H_{Ar}), 7.74 (d, *J* = 8.0 Hz, 1 H_{Ar}), 7.49–7.41 (m, 6 H_{Ar}), 7.27 (t, *J* = 7.6 Hz, 1 H_{Ar}), 7.18 (s, 1 H_{Ar}), 7.07 (s, 1 H_{Ar}), 5.02 (br s, 1 H, OH).

3-Phenyl-1-naphthol (4aa)

Yield: 0.26 g (1.2 mmol, 12%); colorless crystals; mp 92–93 °C (Lit.[16] mp 97–98 °C)

^{1}H NMR ($CDCl_3$): δ = 8.19 (d, *J* = 8.4 Hz, 1 H_{Ar}), 7.87 (d, *J* = 6.8 Hz, 1 H_{Ar}), 7.70–7.67 (m, 3 H_{Ar}), 7.55–7.46 (m, 4 H_{Ar}), 7.39 (t, *J* = 7.6 Hz, 1 H_{Ar}), 7.09 (s, 1 H_{Ar}), 5.47 (br s, 1 H, OH).

4-(4-Methylphenyl)-2-naphthol (3ab)

Yield: 0.87 g (0.37 mmol, 37%); pale brown oily crystals.

^{1}H NMR ($CDCl_3$): δ = 7.81 (d, *J* = 8.4 Hz, 1 H_{Ar}), 7.74 (d, *J* = 8.0 Hz, 1 H_{Ar}), 7.42 (t, *J* = 7.6 Hz, 1 H_{Ar}), 7.37 (d, *J* = 8.0 Hz, 2 H_{Ar}), 7.30–7.24 (m, 3 H_{Ar}), 7.16 (s, 1 H_{Ar}), 7.04 (s, 1 H_{Ar}), 4.94 (br s, 1 H, OH), 2.46 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 152.9, 142.7, 137.5, 137.4, 135.5, 130.0, 129.3, 127.7, 127.1, 126.7, 126.4, 123.9, 118.9, 103.3, 21.51.

HRMS: *m*/*z* [M$^+$] calcd for $C_{17}H_{15}O$: 234.1044; found: 234.1048.

3-(4-Methylphenyl)-1-naphthol (4ab)

Yield: 0.59 g (0.25 mmol, 25%); colorless crystals; mp 148–149 °C (Lit.[17] mp 145–146 °C).

^{1}H NMR ($CDCl_3$): δ = 8.19 (d, *J* = 8.8 Hz, 1 H_{Ar}), 7.86 (d, *J* = 8.4 Hz, 1 H_{Ar}), 7.65 (s, 1 H_{Ar}), 7.59 (d, *J* = 8.0 Hz, 2 H_{Ar}), 7.54–7.47 (m, 2 H_{Ar}), 7.29 (d, *J* = 8.0 Hz, 2 H_{Ar}), 7.08 (s, 1 H_{Ar}), 5.40 (br s, 1 H, OH), 2.43 (s, 3 H, CH_3).

4-(4-Chlorophenyl)-2-naphthol (3ac)

Yield: 1.65 g (0.65 mmol, 65%); colorless crystals; mp 84–85 °C.

^{1}H NMR ($CDCl_3$): δ = 7.74 (d, *J* = 8.4 Hz, 2 H_{Ar}), 7.47–7.39 (m, 5 H_{Ar}), 7.29 (t, *J* = 8.0 Hz, 1 H_{Ar}), 7.19 (s, 1 H_{Ar}), 7.04 (s, 1 H_{Ar}), 5.19 (br s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 152.9, 141.3, 138.7, 135.4, 133.8, 132.6, 131.4, 128.8, 127.1, 126.9, 125.9, 124.2, 119.0, 109.76.

HRMS: *m*/*z* [M$^+$] calcd for $C_{17}H_{14}ClO_2$: 254.0498; found: 254.0490.

3-(4-Chlorophenyl)-1-naphthol (4ac)

Yield: 0.38 g (1.5 mmol, 15%); colorless crystals; mp 159–160 °C (Lit.[17] mp 160–161 °C).

^{1}H NMR ($CDCl_3$): δ = 8.18 (d, *J* = 8.8 Hz, 1 H_{Ar}), 7.86 (d, *J* = 8.0 Hz, 1 H_{Ar}), 7.61–7.48 (m, 5 H_{Ar}), 7.43 (d, *J* = 8.8 Hz, 2 H_{Ar}), 7.02 (s, 1 H_{Ar}), 5.45 (br s, 1 H, OH).

4-(4-Nitrophenyl)-2-naphthol (3ad)

Yield: 0.59 g (0.67 mmol, 67%); yellow crystals; mp 192–193 °C.

^{1}H NMR ($CDCl_3$): δ = 8.36 (d, *J* = 8.8 Hz, 2H, H_{Ar}), 7.77(d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.67 (t, *J* = 8.8 Hz, 3H, H_{Ar}), 7.48 (t, *J* = 8.0 Hz, 1H, H_{Ar}), 7.32 (t, *J* = 8.0 Hz, 1H, H_{Ar}), 7.25 (s, 1H, H_{Ar}), 7.08 (s, 1H, H_{Ar}), 5.13 (br s, 1H, OH).

^{13}C NMR ($CDCl_3$): δ = 153.0, 147.7, 147.3, 140.2, 135.6, 131.2, 127.4, 127.3, 126.9, 125.5, 124.8, 124.0, 119.2, 110.8.

HRMS: *m*/*z* [M$^+$] calcd for $C_{16}H_{11}NO_3$: 265.0739; found: 265.0731.

4-(1-Naphthyl)-2-naphthol (3ae)

Yield: 1.2 g (4.4 mmol, 44%); colorless crystals; mp 158–160 °C.

^{1}H NMR ($CDCl_3$): δ = 7.94 (d, *J* = 8.4 Hz, 1 H_{Ar}) 7.93 (d, *J* = 8.0 Hz, 1 H_{Ar}), 7.76 (d, *J* = 8.0 Hz, 1 H_{Ar}), 7.53 (t, *J* = 8.4 Hz, 1 H_{Ar}), 7.49–7.39 (m, 4 H_{Ar}), 7.31–7.25 (m, 3 H_{Ar}), 7.14–7.10 (m, 2 H_{Ar}), 5.10 (br s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 152.8, 140.9, 137.9, 135.0, 133.6, 132.8, 128.7, 128.3, 128.2, 127.8, 126.8, 126.7, 126.7, 126.6, 126.2, 126.0, 125.5, 123.9, 119.8, 109.6.

HRMS: *m*/*z* [M$^+$] calcd for $C_{20}H_{14}O$: 270.1044; found: 270.1055.

3-(1-Naphthyl)-1-naphthol (4ae)

Yield: 0.84 g (3.1 mmol, 31%); reddish oil.[17]

^{1}H NMR ($CDCl_3$): δ = 8.29–8.26 (m, 1 H_{Ar}), 7.98 (d, *J* = 8.4 Hz, 1 H_{Ar}) 7.94 (d, *J* = 8.0 Hz, 1 H_{Ar}), 7.90 (d, *J* = 8.0 Hz, 1 H_{Ar}), 7.88–7.86 (m, 1 H_{Ar}), 7.57–7.48 (m, 6 H_{Ar}), 7.43 (t, *J* = 8.4 Hz, 1 H_{Ar}), 6.94 (s, 1 H_{Ar}), 5.48 (br s, 1 H, OH).

4-(2-Thienyl)-2-naphthol (3af)

Yield: 0.68 g (3.0 mmol, 30%); colorless crystals; mp 65–66 °C (Lit.[18] mp 67 °C).

^{1}H NMR ($CDCl_3$): δ = 8.12 (d, *J* = 8.4 Hz, 1 H_{Ar}), 7.73 (d, *J* = 8.4 Hz, 1 H_{Ar}), 7.47–7.43 (m, 2 H_{Ar}), 7.34 (s, *J* = 7.6 Hz, 1 H_{Ar}), 7.26 (s, 1 H_{Ar}), 7.21 (s, 1 H_{Ar}), 7.19–7.17 (m, 2 H_{Ar}) 5.03 (br s, 1 H, OH).

3-(4-Thienyl)-1-naphthol (4af)

Yield: 0.57 g (0.25 mmol, 25%): colorless crystals; mp 115–116 °C (Lit.[17] mp 115–116 °C).

^{1}H NMR ($CDCl_3$): δ = 8.15 (d, *J* = 8.4 Hz, 1 H), 7.82 (d, *J* = 8.0 Hz, 1 H_{Ar}), 7.68 (s, 1 H_{Ar}), 7.52–7.44 (m, 2 H_{Ar}), 7.38 (d, *J* = 3.6 Hz, 1 H_{Ar}), 7.31 (d, *J* = 5.2 Hz, 1 H_{Ar}), 7.12–7.10 (m, 2 H_{Ar}), 5.63 (br s, 1 H, OH).

4-(4-Chlorophenyl)-6,7-methylenedioxy-2-naphthol (3bc)

Yield: 0.99 g (3.3 mmol, 33%); colorless crystals; mp 139–140 °C.

^{1}H NMR ($CDCl_3$): δ = 7.43 (d, *J* = 8.4 Hz, 2 H_{Ar}), 7.40 (d, *J* = 8.4 Hz, 2 H_{Ar}), 7.05 (s, 1 H_{Ar}), 7.01 (s, 2 H_{Ar}), 6.86 (s, 1 H_{Ar}), 5.98 (s, 2 H, OCH_2O), 5.08 (br s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 152.0, 148.2, 146.7, 140.1, 139.1, 133.6, 132.5, 131.1, 128.7, 123.7, 116.7, 110.0, 103.1, 102.3, 101.18.

HRMS: *m*/*z* [M$^+$] calcd for $C_{17}H_{11}ClO_3$: 298.0397; found: 298.0391.

3-(4-Chlorophenyl)-6,7-methylenedioxy-1-naphthol (4bc)

Yield: 0.33 g (1.1 mmol, 11%); colorless crystals; mp 234–236 °C.

^{1}H NMR ($CDCl_3$): δ = 7.56 (d, *J* = 8.4 Hz, 2 H_{Ar}), 7.45 (s, 1 H_{Ar}), 7.43 (s, 1 H_{Ar}), 7.41 (d, *J* = 8.4 Hz, 2 H_{Ar}), 7.13 (s, 1 H_{Ar}), 6.91 (s, 1 H_{Ar}), 6.06 (s, 2 H, OCH_2O), 5.22 (br s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 151.5, 148.7, 147.7, 139.6, 136.5, 133.5, 132.5, 129.1, 128.5, 120.3, 118.2, 107.3, 104.2, 101.3, 98.7.

HRMS: *m*/*z* [M⁺] calcd for $C_{17}H_{11}ClO_3$: 298.0397; found: 298.0404.

4-(4-Chlorophenyl)-5-methoxy-2-naphthol (3cc)

Yield: 0.74 g (2.6 mmol, 26%); colorless crystals; mp 112–114 °C.

^{1}H NMR ($CDCl_3$): δ = 7.38–7.34 (m, 2 H_{Ar}), 7.31 (d, *J* = 8.4 Hz, 2 H_{Ar}), 7.22 (d, *J* = 8.4 Hz, 2 H_{Ar}), 7.12 (s, 1 H_{Ar}), 6.83 (s, 1 H_{Ar}), 6.65 (d, *J* = 7.2 Hz, 1 H_{Ar}), 5.29 (br s, 1 H, OH), 3.49 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 156.9, 152.6, 143.3, 140.1, 137.4, 132.0, 130.0, 127.1, 126.9, 120.5, 120.1, 119.0, 109.9, 104.3, 55.1.

HRMS: *m*/*z* [M⁺] calcd for $C_{17}H_{13}ClO_2$: 284.0604; found: 284.0614.

3-(4-Chlorophenyl)-8-methoxy-1-naphthol (4cc)

Yield: 0.37 g (1.3 mmol, 13%), yellow crystals; mp 151–153 °C.

^{1}H NMR ($CDCl_3$): δ = 9.37 (br s, 1 H, OH), 7.62 (d, *J* = 8.4 Hz, 2 H_{Ar}), 7.48 (s, 1 H_{Ar}), 7.47–7.41 (m, 3 H_{Ar}), 7.33 (t, *J* = 8.4 Hz, 1 H_{Ar}), 7.12 (s, 1 H_{Ar}), 6.78 (d, *J* = 7.6 Hz, 1 H_{Ar}), 4.07 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 156.2, 155.1, 139.3, 139.2, 137.1, 133.7, 129.0, 128.6, 126.4, 122.3, 116.9, 114.5, 109.5, 104.3, 56.3.

HRMS: *m*/*z* [M⁺] calcd for $C_{17}H_{13}ClO_2$: 284.0604; found: 284.0613.

4-(4-Chlorophenyl)-6,7-dimethyl-2-naphthol (3dc)

Yield: 0.85 g (3.0 mmol, 30%); colorless crystals; mp 125–127 °C.

^{1}H NMR ($CDCl_3$): δ = 7.49 (s, 1 H_{Ar}), 7.46 (d, *J* = 8.4 Hz, 2 H_{Ar}), 7.45 (s, 1 H_{Ar}), 7.40 (d, *J* = 8.4 Hz, 2 H_{Ar}), 7.08 (s, 1 H_{Ar}), 6.92 (s, 1 H_{Ar}), 5.01 (br s, 1 H, OH), 2.34 (s, 3 H, CH_3), 2.31 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 152.1, 140.2, 139.0, 136.6, 134.2, 133.7, 133.5, 131.2, 128.6, 126.7, 126.1, 125.2, 117.9, 108.9, 20.3, 20.2.

HRMS: *m*/*z* [M⁺] calcd for $C_{18}H_{15}ClO$: 282.0811; found: 282.0821.

3-(4-Chlorophenyl)-6,7-dimethyl-1-naphthol (4dc)

Yield: 0.57 g (2.0 mmol, 20%); colorless crystals; mp 179–180 °C.

^{1}H NMR ($CDCl_3$): δ = 7.90 (s, 1 H_{Ar}), 7.60 (s, 1 H_{Ar}), 7.58 (d, *J* = 8.4 Hz, 2 H_{Ar}), 7.50 (s, 1 H_{Ar}), 7.41 (d, *J* = 8.4 Hz, 2 H_{Ar}), 6.94 (s, 1 H_{Ar}), 5.30 (br s, 1 H, OH), 2.46 (s, 3 H, CH_3), 2.44 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 151.4, 139.8, 137.0, 136.8, 135.6, 134.1, 133.4, 129.05, 128.6, 127.9, 122.5, 121.0, 118.0, 107.4, 20.5, 20.3.

HRMS: *m*/*z* [M⁺] calcd for $C_{18}H_{15}ClO$: 282.0811; found: 282.0831.

Reaction of 1a with 2a in the Presence of CsF at Room Temperature; 1-(2-Benzoylpenyl)acetone (5a)

Triflate **1a** (0.36 g, 1.2 mmol) in MeCN (5 mL) was added to a mixture of **2a** (0.16 g, 1.0 mmol) and CsF (0.55 g, 3.6 mmol) in MeCN (5 mL). After stirring for 5 h at r.t., the reaction mixture was poured into H_2O and extracted with CH_2Cl_2 (3 × 5 mL). The combined extracts were dried (Na_2SO_4), filtered, and evaporated to give a pale yellow oil, which was chromatographed over silica gel, eluting with hexane–EtOAc (5:1), to afford **5a**[4b] a colorless oil; yield: 0.13 g (0.55 mmol, 58%).

^{1}H NMR ($CDCl_3$): δ = 2.29 (s, 3 H, CH_3), 2.58 (s, 3 H, CH_3), 4.02 (s, 2 H, CH_2), 7.18 (d, *J* = 7.6 Hz, 1 H_{Ar}), 7.38 (t, *J* = 7.6 Hz, 1 H_{Ar}), 7.45 (t, *J* = 7.6 Hz, 1 H_{Ar}), 7.97 (d, *J* = 7.6 Hz, 1 H_{Ar}).

Reaction of 5a with CsF in Refluxing MeCN; 4-Phenyl-2-naphthol (3aa)

A mixture of **5a** (0.12 g, 0.50 mmol) and CsF (0.15 g, 1.0 mmol) in MeCN (5 mL) was refluxed for 5 h, and the reaction mixture was poured into H_2O and extracted with CH_2Cl_2 (3 × 3 mL). The combined extracts were dried (Na_2SO_4), filtered, and evaporated to give almost pure 4-phenyl-2-naphthol (**3aa**); yield: 0.088 g (0.40 mmol, 80%).

Synthesis of BINOLs by Copper-Amine Complex Catalyzed Oxidation; General Procedure

To a solution of **6** (0.2 mmol) in EtOH was added $CuCl_2$ (5 mg, 0.4 mmol) and phenethylamine (194 mg, 1.6 mmol). After stirring in an O_2 atmosphere for 2 days, the reaction mixture was added to a solution of aq HCl (0.5 mL) in MeOH (5 mL). The resulting suspension was extracted with CH_2Cl_2 (3 × 3 mL), dried (Na_2SO_4), filtered, and evaporated to give colorless crystals, which were chromatographed over silica gel, eluting with hexane–CH_2Cl_2 (1:1), to afford BINOL **6**.

4,4′-Biphenyl-1,1′-BINOL (6a)

Yield: 0.033 g (0.075 mmol, 75%); colorless crystals; mp 145–146 °C (Lit.[10b] mp 147–148 °C).

^{1}H NMR ($CDCl_3$): δ = 7.96–7.94 (m, 2 H_{Ar}), 7.62 (d, *J* = 8.0 Hz, 4 H_{Ar}), 7.56 (t, *J* = 7.2 Hz, 4 H_{Ar}), 7.50 (t, *J* = 7.2 Hz, 2 H_{Ar}), 7.38 (s, 2 H_{Ar}), 7.36–7.31 (m, 6 H_{Ar}), 5.16 (br s, 2 H, OH)

4,4′-Bis(4-methylphenyl)-1,1′-BINOL (6b)

Yield: 0.037 g (0.080 mmol, 80%); colorless crystals; mp 230–231 °C (Lit.[19] mp 224–225 °C).

^{1}H NMR ($CDCl_3$): δ = 8.00–7.97 (m, 2 H_{Ar}), 7.52 (d, *J* = 8.0 Hz, 4 H_{Ar}), 7.38 (d, *J* = 7.6 Hz, 6 H_{Ar}), 7.36–7.30 (m, 6 H_{Ar}), 5.15 (br s, 2 H, OH), 2.51 (s, 6 H, CH_3)

4,4′-Bis(4-chlorolphenyl)-1,1′-BINOL (6c)

Yield: 0.039 g (0.076 mmol, 76%); colorless crystals; mp 263–265 °C.

^{1}H NMR ($CDCl_3$): δ = 7.90–7.88 (m, 2 H_{Ar}), 7.55 (m, 8 H_{Ar}), 7.38–7.30 (m, 8 H_{Ar}), 5.12 (br s, 2 H, OH).

^{13}C NMR ($CDCl_3$): δ = 152.3, 142.7, 138.4, 134.1, 131.4, 128.8, 127.9, 127.7, 126.6, 124.5, 118.8, 110.9.

Anal. Calcd for $C_{32}H_{20}Cl_2O_2$ + ½ H_2O: C, 74.43; H, 4.10. Found: C, 74.29; H, 4.19.

4,4′-Bis(4-nitrophenyl)-1,1′-BINOL (6d)

Yield: 0.035 g (0.065 mmol, 65%): yellow crystals; mp 275 °C (dec.).

^{1}H NMR ($CDCl_3$): δ = 7.84–7.79 (m, 8 H_{Ar}), 7.42–7.32 (m, 8 H_{Ar}), 5.21 (br s, 2 H, OH).

^{13}C NMR ($CDCl_3$): δ = 152.28, 147.8, 146.8, 141.7, 134.1, 131.1, 128.2, 127.6, 126.3, 125.2, 125.0, 124.0, 119.1, 111.71.

Anal. Calcd for $C_{32}H_{20}N_2O_6$ + 2 H_2O: C, 68.08; H, 4.28; N, 4.96. Found: C, 68.00; H, 4.41; N, 4.94.

4,4′-Bi(2-thienyl)-1,1′-BINOL (6e)

Yield: 0.032 g (0.072 mmol, 72%); colorless crystals; mp 166–168 °C.

^{1}H NMR ($CDCl_3$): δ = 8.29 (d, *J* = 7.6 Hz, 2 H_{Ar}), 7.52–7.51 (m, 4 H_{Ar}), 7.42–7.34 (m, 6 H_{Ar}), 7.31–7.29 (m, 6 H_{Ar}), 5.10 (br s, 2 H, OH).

^{13}C NMR ($CDCl_3$): δ = 152.1, 140.9, 136.4, 134.2, 128.3, 128.1, 127.9, 127.6, 124.8, 119.9, 111.3.

Anal. Calcd for $C_{28}H_{18}O_2S_2$: C, 74.64; H, 4.03. Found: C, 74.82; H, 4.22.

4,4′-Bis(4-chlorophenyl)-6,7,6′,7′-bi(methylenedioxy)-1,1′-BINOL (6f)

Yield: 0.041 g (0.070 mmol, 70%); colorless crystals; mp >300 °C.

^{1}H NMR (DMSO-d_6): δ = 9.25 (br s, 2 H, OH), 7.62 (d, J = 8.4 Hz, 4 H_{Ar}), 7.57 (d, J = 8.4 Hz, 4 H_{Ar}), 7.07 (s, 2 H_{Ar}), 6.97 (s, 2 H_{Ar}), 6.36 (s, 2 H_{Ar}), 5.99 (s, 2 H, OCH_2O), 5.96 (s, 2 H, OCH_2O).

^{13}C NMR (DMSO-d_6): δ = 151.6, 147.6, 145.4, 139.3, 138.0, 132.3, 131.6, 131.3, 128.6, 121.9, 117.2, 116.1, 101.4, 101.1, 101.03.

Anal. Calcd for $C_{34}H_{20}Cl_2O_6$ + ½ H_2O: C, 67.56; H, 3.50. Found: C, 67.72; H, 3.68.

4,4′-Bis(4-chlorophenyl)-5,5′-dimethoxy-1,1′-BINOL (6g)

Yield: 0.041 g (0.072 mmol, 72%); colorless crystals; mp 178–180 °C.

^{1}H NMR ($CDCl_3$): δ = 7.40–7.32 (m, 8 H_{Ar}), 7.28–7.24 (m, 4 H_{Ar}), 6.88 (d, J = 8.4 Hz, 2 H_{Ar}), 6.67 (d, J = 7.2 Hz, 2 H_{Ar}), 5.05 (br s, 2 H, OH), 3.54 (s, 6 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 157.4, 152.1, 143.4, 141.6, 136.1, 132.2, 129.9, 128.2, 127.1, 120.4, 119.5, 117.5, 111.3, 104.8, 55.2.

Anal. Calcd for $C_{34}H_{24}Cl_2O_2$ + H_2O: C, 69.75; H, 4.48. Found: C, 69.58; H, 4.70.

4,4′-Bis(4-chlorophenyl)-6,6′,7,7′-tetramethyl-1,1′-BINOL (6h)

Yield: 0.041 g (0.073 mmol, 73%); colorless crystals; mp 282–284 °C.

^{1}H NMR ($CDCl_3$): δ = 7.62 (s, 2 H_{Ar}), 7.58–7.54 (m, 8 H_{Ar}), 7.24 (s, 2 H_{Ar}), 7.08 (s, 2 H_{Ar}), 5.00 (br s, 2 H, OH), 2.32 (s, 6 H, CH_3), 2.23 (s, 6 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 151.6, 141.6, 138.9, 137.7, 134.1, 133.8, 132.8,131.4, 128.8, 126.7, 126.1, 124.4, 117.9, 110.4, 20.4, 20,2.

Anal. Calcd for $C_{36}H_{28}Cl_2O_2$: C, 76.73; H, 5.01. Found: C, 76.69; H, 5.15.

Enantioselective Synthesis of BINOL 6a; Typical Procedure

To a solution of 4-phenyl-2-naphthol (**3aa**; 0.22 g, 1.0 mmol) in CCl_4 (15 mL) was added naphthoaldehyde-valine vanadium oxide complex (0.033 g, 0.10 mmol), and O_2 was applied for 10 min. After stirring for 2 days at r.t., the reaction mixture was evaporated to give brown oily crystals, which were chromatographed over silica gel, eluting with CH_2Cl_2, to afford (*R*)-BINOL (*R*)-**6a** as colorless crystals; mp 135–139 °C; yield: 0.18 g (0.43 mmol, 85%).

HPLC: Chiralcel AD-H, hexane–*i*-PrOH (60:40), temp 27 °C, flow rate, 1.2 mL/min, λ = 254 nm; t_R (major) = 27.4 min, t_R (minor) = 76.7 min; ee 65%.

(*R*)-BINOL (*R*)-6b

Yield: 0.83 g (1.78 mmol, 90%); colorless crystals; mp 236–238 °C.

HPLC: Chiralcel AD-H, hexane–*i*-PrOH (60:40), temp 27 °C, flow rate, 1.1 mL/min, λ = 254 nm; t_R (minor) = 17.4 min, t_R (major) = 33.2 min; ee 74%.

(*R*)-BINOL (*R*)-6c

Yield: 0.41 g (0.81 mmol, 95%); colorless crystals; mp 268–270 °C.

HPLC: Chiralcel AD-H, hexane–*i*-PrOH (40:60), temp 27 °C, flow rate, 1.5 mL/min, λ = 254 nm; t_R (major) = 24.2 min, t_R (minor) = 30.0 min; ee 71%.

(*R*)-BINOL (*R*)-6e

Yield: 0.72 g (1.6 mmol, 98%); colorless crystals; mp 161–162 °C.

HPLC: Chiralcel AD-H, hexane–*i*-PrOH (50:50), temp 27 °C, flow rate: 1.1 mL/min, λ = 254 nm; t_R (minor) = 30.6 min, t_R (major) = 55.1 min; ee 80%.

(*R*)-BINOL (*R*)-6g

Yield: 0.60 g (1.1 mmol, 97%); colorless crystals; mp 151–153 °C.

HPLC: Chiralcel AD-H, hexane–*i*-PrOH (40:60), temp 27 °C, flow rate: 1.1 mL/min, λ = 254 nm; t_R (minor) = 17.4 min, t_R (major) = 33.2 min; ee 56%.

(*R*)-BINOL (*R*)-6h

Yield: 0.67 g (1.2 mmol, 98%); yellow crystals; mp 274–275 °C.

HPLC: Chiralcel AD-H, hexane–*i*-PrOH (40:60), temp 27 °C, flow rate: 1.1. mL/min, λ = 254 nm; t_R (major) = 6.18 min, t_R (minor) = 7.4 min; ee 23%.

Enantiomerically Pure 1,1′-Biaryl-BINOL 6c; Typical Procedure

A solution of 4,4′-bis(4-chlorophenyl)-BINOL (**6c**; 0.41 g, 0.81 mmol) in EtOH (22 mL) was added to a solution of L-proline (0.026 g, 0.23 mmol) in EtOH (10 mL) at r.t. After refluxing for 3 h, the reaction mixture was cooled to r.t. The resulting crystals were filtered, and the filtrate was agitated for 2 h and evaporated to give a colorless solid. The solid was added to H_2O (5 mL), extracted with EtOAc (3 × 5 mL), dried (Na_2SO_4), filtered, and evaporated to give the enantiomerically pure (*R*)-4,4′-bi(4-chlorophenyl)-BINOL [(*R*)-**6c**] as colorless crystals; mp 268–270 °C; yield: 0.28 g (0.56 mmol, 69%); $[\alpha]_D^{20}$ +79.2 (*c* = 1.00, THF); ee >98% .

Other reactions were carried out in a similar manner.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1380452.

References

(1) (a) Hoffman, R. W. *Dehydrobenzene and Cycloalkynes*; Academic Press: New York, **1967**. (b) Kessar, S. V. In *Comprehensive Organic Synthesis*; Vol. 4; Trost, B. M.; Fleming, I., Eds.; Pergamon: Oxford, **1991**, 483–515. (c) Hart, H. In *The Chemistry of Triple-Bonded Functional Groups, Supplement C2*; Patai, S., Ed.; Wiley: Chichester, **1994**, Chap. 18. (d) Wentrup, C. *Aust. J. Chem.* **2010**, *63*, 979. (e) Kitamura, T. *Aust. J. Chem.* **2010**, *63*, 987.

(2) Himeshima, Y.; Sonoda, T.; Kobayashi, H. *Chem. Lett.* **1983**, 1211.

(3) (a) Okuma, K.; Okada, A.; Koga, Y.; Yokomori, Y. *J. Am. Chem. Soc.* **2001**, *123*, 7166. (b) Yoshida, H.; Shirakawa, E.; Honda, Y.; Hiyama, T. *Angew. Chem. Int. Ed.* **2002**, *41*, 3247. (c) Yoshida, H.; Fukushima, H.; Ohshita, J.; Kunai, A. *J. Am. Chem. Soc.* **2006**, *128*, 11040. (d) Gilmore, C. D.; Allan, K. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2008**, *130*, 1558.

(4) (a) Tamber, U. K.; Stoltz, B. M. *J. Am. Chem. Soc.* **2005**, *127*, 5340. (b) Yoshida, H.; Watanabe, M.; Ohshita, J.; Kunai, A. *Chem. Commun.* **2005**, 3292.

(5) (a) Kilian, P.; Knight, F.; Fergus, R.; Woollins, J. D. *Chem. Eur. J.* **2011**, *17*, 2302. (b) Simon, S.; Petrasek, J. *Plant Sci.* **2011**, *180*, 454. (c) Cai, Y. S.; Guo, Y. W.; Krohn, K. *Nat. Prod. Rep.* **2010**, *27*, 1840. (d) Qian, X.; Xiao, Y.; Xu, Y.; Guo, X.; Qian, J.; Zhu, W. *Chem. Commun.* **2010**, *46*, 6418.

(6) (a) Jin, T.; Yamamoto, Y. *Org. Lett.* **2007**, *9*, 5259. (b) Rupard, J. H.; Paulis, T. D.; Janowsky, A.; Smith, H. E. *J. Med. Chem.* **1989**, *32*, 2261. (c) Zhangm, X.; Sarkar, S.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 236. (d) Nishii, Y.; Tanabe, Y. *Tetrahedron Lett.* **1995**, *36*, 8803.
(7) (a) Kim, H. Y.; Oh, K. *Org. Lett.* **2014**, *16*, 5934. (b) Koptyug, V. A.; Andreeva, T. P. *Z. Org. Khim.* **1971**, *7*, 2398; *Chem. Abstr.* **1972**, *76*, 140286.
(8) Karady, S.; Amato, J. S.; Reamer, R. A.; Weinstock, L. M. *Tetrahedron Lett.* **1996**, *37*, 8277.
(9) Zhang, J.; Liu, Q.; Liu, X.; Zhang, S.; Jiang, P.; Wang, Y.; Luo, S.; Li, Y.; Wang, Q. *Chem. Commun.* **2015**, *51*, 1297.
(10) (a) Okuma, K.; Itoyama, R.; Sou, A.; Nagahora, N.; Shioji, K. *Chem. Commun.* **2012**, *48*, 11145. (b) Recently, Wieting et al. reported the synthesis of BINOL **6a** by using our method: Wieting, J. M.; Fisher, T. J.; Schafer, A. G.; Visaco, M. D.; Gallucci, J. C.; Mattson, A. E. *Eur. J. Org. Chem.* **2015**, 525.
(11) (a) Mikami, K.; Shimizu, M. *Chem. Rev.* **1992**, *92*, 1021. (b) *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer-Verlag: Berlin, **1999**. (c) Bolm, C.; Hildebrand, J. P.; Muniz, K.; Hermanns, N. *Angew. Chem. Int. Ed.* **2001**, *40*, 3285. (d) Irie, R.; Masutani, K.; Katsuki, T. *Synlett* **2000**, 1433. (e) Tashiro, A.; Mitsuishi, A.; Irie, R.; Katsuki, T. *Synlett* **2003**, 1868.
(12) (a) Rauniyar, V.; Hall, D. G. *Synthesis* **2007**, 3421. (b) Ma, L.; Mihalcik, D. J.; Lin, W. *J. Am. Chem. Soc.* **2009**, *131*, 4610. (c) Hashimoto, T.; Tanaka, Y.; Maruoka, K. *Tetrahedron: Asymmetry* **2003**, *14*, 1599.
(13) Brussee, J.; Groenendijk, J. L. G.; te Koppele, J. M.; Jansen, A. C. A. *Tetrahedron* **1985**, *41*, 3313.
(14) Hon, S.-W.; Li, C.-H.; Kuo, J.-H.; Barahate, N. B.; Liu, Y.-H.; Wang, Y.; Chen, C.-T. *Org. Lett.* **2001**, *3*, 869.
(15) Hu, X.; Shan, Z.; Chang, Q. *Tetrahedron: Asymmetry* **2012**, *23*, 1327.
(16) Redic, R.; Schuster, G. B. *J. Photochem. Photobiol. A* **2006**, *179*, 66.
(17) Lou, Z.; Zhang, S.; Chen, C.; Pang, X.; Li, M.; Wen, L. *Adv. Synth. Catal.* **2014**, *356*, 153.
(18) Frigoli, M.; Moustrou, C.; Samat, A.; Gugliemetti, R. *Eur. J. Org. Chem.* **2003**, 2799.
(19) Chow, H. F.; Wan, C. W. *J. Org. Chem.* **2001**, *66*, 5042.