Synthetic Method for 2,2'-Disubstituted Fluorinated Binaphthyl Derivatives and Application as Chiral Source in Design of Chiral Mono-Phosphoric Acid Catalyst

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ABSTRACT A practical synthetic method for 2,2'-disubstituted fluorinated binaphthyl derivatives was achieved using magnesium bis(2,2,6,6-tetramethylpiperamide) [$Mg(TMP)_2$], prepared from LiTMP (2 equiv) and $MgBr_2$ (1 equiv), which allows for access to a variety of fluorinated binaphthyl compounds. The utility of the fluorinated binaphthyl backbone was evaluated in F_{10}BINOL derived chiral mono-phosphoric acid (*R*)-**19** as the chiral Brønsted acid catalyst. The catalyst (*R*)-**19** performs exceptionally well in the catalytic enantioselective imino-ene reaction, demonstrating the potential of a fluorinated binaphthyl framework. *Chirality 00:000–000, 2015.* © 2015 Wiley Periodicals, Inc.

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The axially chiral 1,1'-binaphthyl framework has been known as the broadly applicable chiral sources in the design of chiral molecular catalysts.[1] Among varieties of reported catalysts to date, the optically active 1,1'-bi-2-naphthol (BINOL)-derived chiral Brønsted acids have been recently recognized as useful chiral catalysts in catalytic asymmetric synthesis.[2–9] Dicarboxylic acids,[10,11] phosphoric acids[12–17] and their analogs,[18–21] disulfonic acids,[22–24] and disulfonimides[25–28] with a binaphthyl backbone are representatives. The acidic functionalization at the 2,2'-position and the modifications at the 3,3'-position are general strategies to realize suitable catalyst activity and asymmetric reaction space.

Fluorinated binaphthyls have been attractive motifs of 1,1'-binaphthyl framework, since their properties of steric and electronic alterations would lead to considerable changes in catalyst activity and asymmetric environment. In this regard, Yudin and co-workers reported optically active F_4- and F_8BINOL, which are fluorinated at the 5, 6, 7, 8 position or 5,5', 6,6', 7,7', 8,8' positions of the back aryl rings, respectively.[29,30] Piers and co-workers developed synthesis and resolution of 2,2'-dihydroxy-3,3',4,4',5,5',6,6',7,7',8,8'-dodecafluoro-1,1'-binaphthyl (F_{12}BINOL).[31] Due to the higher electron-withdrawing nature of fluoroaryls,[32] it has been expected that a fluorinated binaphthyl backbone would greatly enhance the acidity at the 2,2'-position that would lead to improving the efficiency in the chiral Brønsted acid catalysis.[33,34] Although the utilities of a fluorinated binaphthyl scaffold has been indicated in the design of chiral molecular catalysts,[35,36] the practical synthetic method and systematic studies on 2,2'- and 3,3'-substitution have not been fully established, due to synthetic difficulties, unlike for the general binaphthyl backbone. Herein, we report the practical synthetic method for fluorinated binaphthyl compounds and its application as chiral mono-phosphoric acid catalyst in the catalytic asymmetric imino-ene reaction.[37–40]

EXPERIMENTAL

Instruments and Materials

^{1}H NMR spectra were recorded on a JEOL ECA-600 (600 MHz) and a JEOL ECA-400 (400 MHz) spectrometer at ambient temperature. Chemical shifts are reported in ppm, with solvent resonance employed as internal standard; $CDCl_3$ (7.26 ppm), C_6D_6 (7.16 ppm), and acetone-d_6 (2.06 ppm). ^{13}C NMR spectra were recorded on a JEOL ECA-600 (151 Hz) and a JEOL ECA-400 (101 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from the solvent resonance as the internal standard; $CDCl_3$ (77.0 ppm), C_6D_6 (128.0 ppm), and acetone-d_6 (206.7 ppm, 29.9 ppm). ^{19}F NMR spectra were recorded on a JEOL ECA-600 (565 MHz) and JEOL ECA-400 (376 MHz). Chemical shifts are reported in ppm from the C_6F_6 (−162 ppm) resonance as the external standard. ^{31}P NMR spectra were recorded on a JEOL ECA-600 (243 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from the $(PhO)_3PO$ (−17.8 ppm) resonance as the external standard. Infrared spectra were recorded on a Jasco FT/IR-4100 spectrometer. Optical rotations were measured on a Jasco P-1020 digital polarimeter with a sodium lamp and reported as follows; $[\alpha]_D^{T^\circ C}$ (c = g/100 mL, solvent, % enantiomeric excess [*ee*]). The enantioselectivies were determined by ultrahigh- or high-performance liquid chromatography (UHPLC or HPLC), which was performed on a Jasco X-LC-3000 system or a Jasco HPLC-2000 system with UV detectors. High-resolution mass spectra analysis was performed on a Bruker Daltonics solariX 9.4 T spectrometer at the Research and Analytical Center for Giant Molecules, Graduate School of Science, Tohoku University.

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Materials and Methods

CH_2Cl_2, toluene and tetrahydrofuran (THF) were supplied from Kanto Chemical (Tokyo, Japan) as "Dehydrated solvent system." Other solvents were dried over activated MS 4Å and used under nitrogen atmosphere. Reagents were purchased from commercial suppliers and used without further purification. All reactions were carried out in flame-dried glassware with magnetic stirring under nitrogen atmosphere. Analytical thin-layer chromatography (TLC) was performed on Merck (Darmstadt, Germany) precoated TLC plates (silica gel 60 GF 254, 0.25 mm). Purification of reaction products was carried out by flash column chromatography using silica gel 60 (spherical, neutral, 100–210 μm; KANTO Chemical), silica gel 60 (230–400 mesh; E. Merck), and DIOL silica gel (45–75 μm; Fuji Silysia Chemical, Japan). NH silica gel (45–75 μm; Fuji Silysia Chemical).

Syntheses

Preparation of magnesium bis(2,2,6,6-tetramethyl piperamide) [Mg(TMP)$_2$][41,42]. A flame-dried 100-mL three-necked round-bottomed flask equipped with a reflux condenser, a Teflon-coated magnetic stirring bar, a rubber septum, and an inlet adapter with three-way stopcock was charged with Mg turning (273 mg, 11.3 mmol). The flask was evacuated under heating then backfilled with nitrogen. After THF (11.3 mL) was added to the flask, the reaction mixture was heated at reflux, and 1,2-dibromoethane (969 μL, 11.3 mmol) was added dropwise at reflux. The resulting suspension was stirred at reflux for 45 min. In another 100-mL two-necked round-bottomed flask equipped with a Teflon-coated magnetic stirring bar, a rubber septum, and an inlet adapter with three-way stopcock was charged with 2,2,6,6-tetramethylpiperidine (3.80 mL, 22.5 mmol) and THF (11.3 mL). The solution was cooled to −78°C. To the solution was added *n*-BuLi (1.51 M in *n*-hexane, 14.9 mL, 22.5 mmol) dropwise at −78°C. The resulting suspension was stirred at −78°C for 10 min and warmed at 0°C for 30 min. The resulting pale yellow solution was transferred to the $MgBr_2$-THF solution via cannula, and the reaction mixture was stirred for an additional 2 h to afford a pale yellow solution of $Mg(TMP)_2$ (0.27 M in THF).

3,3',4,4',5,5',6,6',7,7',8,8'-Dodecafluoro-[1,1'-binaphthalene]-2,2'-dicarbaldehyde (2). To an ice bath-cooled solution of $Mg(TMP)_2$ (0.27 M in THF, 5.6 mL, 1.5 mmol, 3.0 equiv.) was added the 3,3',4,4',5,5',6,6',7,7',8,8'-dodecafluoro-1,1'-binaphthalene (**1**)[31] (235 mg, 0.5 mmol, 1.0 equiv.) at 0°C. After being stirred for 2 h, the reaction mixture was transferred to the THF (2.5 mL) solution of DMF (387 μL, 5 mmol, 10 equiv.) by cannula at 0°C and the resulting solution was stirred for a further 2 h at the same temperature. After the reaction mixture was warmed to room temperature, the reaction was quenched with 1 M HCl aq. (~10 mL) and extracted with Et_2O (~15 mL × 2). The combined Et_2O extracts were washed with brine (~10 mL), dried over Na_2SO_4, and concentrated under reduced pressure after filtration to give a brown solid. The residual crude was purified by silica gel column chromatography (0–5% EtOAc in hexane as an eluent) to give the product 3,3',4,4',5,5',6,6',7,7',8,8'-dodecafluoro-[1,1'-binaphthalene]-2,2'-dicarbaldehyde (**2**) (201 mg, 0.39 mmol, 77% yield) as a yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ 10.23 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 185.8 (d, J = 9 Hz), 148.8 (dd, J = 257 Hz, 13 Hz), 144.5 (dm, J = 264 Hz, 2 peaks were overlapped), 141.6 (dm, J = 256 Hz), 140.9 (dt, J = 259 Hz, 16 Hz), 139.6 (dt, J = 257 Hz, 16 Hz), 130.3, 123.7, 116.7, 114.3. ^{19}F NMR (565 MHz, $CDCl_3$): δ −137.0 (t, J = 16.7 Hz, 2F), −141.0 (dd, J = 63.2 Hz, 17.9 Hz, 2F), −143.7 (dtm, J = 64.4 Hz, 16.7 Hz, 2F), −148.3 (m, 2F), −149.1 (t, J = 19.1 Hz, 2F), −153.3 (t, J = 19.1 Hz, 2F). HRMS (ESI-): calcd. for $C_{22}H_2F_{12}O_2$, [M+I]-: 652.8913; found: 652.8913. IR (neat, cm^{-1}): 2891, 1710, 1662, 1642, 1582, 1528, 1495, 1390, 1276, 1256, 1178, 1114, 1078, 1046, 1008, 991, 910, 851. mp: 156-160°C.

3,3',4,4',5,5',6,6',7,7',8,8'-Dodecafluoro-[1,1'-binaphthalene]-2,2'-dimethanol (3). To an ice bath cooled MeOH (7.4 mL) solution of 3,3',4,4',5,5',6,6',7,7',8,8'-dodecafluoro-[1,1'-binaphthalene]-2,2'-dicarbaldehyde (**2**) (389 mg, 0.74 mmol, 1.0 equiv.) was added $NaBH_4$ (62 mg, 1.63 mmol, 2.2 equiv.) at 0°C. After being stirred for 15 min, the reaction mixture was quenched with 1 M HCl aq. (~10 mL) and extracted with Et_2O (~15 mL × 2). The combined Et_2O extracts were washed with brine (~15 mL), dried over Na_2SO_4 and concentrated under reduced pressure after filtration. The residual crude was purified by silica gel column chromatography (0–10% EtOAc in hexane as an eluent) to give the product 3,3',4,4',5,5',6,6',7,7',8,8'-dodecafluoro-[1,1'-binaphthalene]-2,2'-dimethanol (**3**) (345 mg, 0.65 mmol, 88% yield) as a white solid. ^{1}H NMR (600 MHz, acetone-d_6): δ 4.88 (bs), 4.59 (d, J = 12.4 Hz), 4.16 (dd, J = 12.0 Hz, 1.4 Hz). ^{13}C NMR (151 MHz, acetone-d_6): δ 148.0 (dd, J = 251 Hz, 11 Hz), 144.0 (dd, J = 260 Hz, 16 Hz), 143.6 (dm, J = 256 Hz), 141.4 (dm, J = 256 Hz), 139.3 (dm, J = 252 Hz, 4 peaks were overlapped), 131.9 (d, J = 15 Hz), 127.5, 117.1, 111.6 (t, J = 10 Hz), 55.0. ^{19}F NMR (565 MHz, acetone-d_6): δ −140.8 (t, J = 16.7 Hz, 2F), −142.8 (d, J = 14.3 Hz, 2F), −145.5 (dd, J = 64.4 Hz, 16.7 Hz, 2F), −148.3 (dtd, J = 64.4 Hz, 16.7 Hz, 4.8 Hz, 2F), −157.4 (t, J = 17.9 Hz, 2F), −158.5 (tm, J = 15.5 Hz). HRMS (ESI+): calcd. for $C_{22}H_6F_{12}O_2$, [M+Na]+: 553.0068; found: 553.0068. IR (neat, cm^{-1}): 3286, 2956, 2902, 1663, 1646, 1591, 1528, 1496, 1410, 1253, 1179, 1113, 1086, 1037, 995. mp: 232°C.

3,3',4,4',5,5',6,6',7,7',8,8'-Dodecafluoro-[1,1'-binaphthalene]-2,2'-dicarboxylic acid (4). 3,3',4,4',5,5',6,6',7,7',8,8'-Dodecafluoro-[1,1'-binaphthalene]-2,2'-dicarbaldehyde (**2**) (53 mg, 0.1 mmol, 1.0 equiv.), $NaClO_2$ (81 mg, 0.9 mmol, 9.0 equiv.) and NaH_2PO_4 (54 mg, 0.45 mmol, 4.5 equiv.) was dissolved in the mixed solution of THF (125 μL), *t*BuOH (300 μL) and H_2O (60 μL). To the resulting mixture was added 2-methyl-2-butene (106 μL,1.0 mmol, 10.0 equiv.) dropwise. After being stirred for 3 h, the reaction mixture was quenched with water (~10 mL) and extracted with Et_2O (~10 mL × 2). The organic layer was extracted with 0.4 M NaOH aq. (10 mL × 3). The combined aqueous extracts were acidified with 6 M HCl aq. (5 mL) and extract with Et_2O (10 mL × 3). The combined Et_2O extracts were washed with brine (~10 mL), dried over Na_2SO_4 and concentrated under reduced pressure after filtration to give the crude product (90% yield). The residual crude was dissolved in CH_2Cl_2 (3 mL) and purified by filtration to give the product 3,3',4,4',5,5',6,6',7,7',8,8'-dodecafluoro-[1,1'-binaphthalene]-2,2'-dicarboxylic acid (**4**) (30 mg, 0.06 mmol, 60% yield) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.16 (br, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 162.5, 144.5 (dd, J = 254 Hz, 13 Hz), 144.3 (dm, J = 259 Hz), 143.9 (dm, J = 255 Hz), 141.3 (dm, J = 263 Hz), 140.1 (dt, J = 254 Hz, 15 Hz), 139.5 (dm, J = 253 Hz), 127.1, 126.2 (d, J = 17 Hz), 117.5, 111.9 (t, J = 11 Hz). ^{19}F NMR (565 MHz, $CDCl_3$): δ −140.6 (t, J = 15.5 Hz, 2F), −141.4 (m, 2F), −143.6 (dd, J = 63.2, 17.9 Hz, 2F), −147.5 (dtm, J = 64.4 Hz, 16.1 Hz, 2F), −154.8 (t, J = 16.7 Hz, 2F), −157.1 (tm, J = 16.7 Hz, 2F). HRMS

(ESI-): calcd. for $C_{22}H_2F_{12}O_4$, [M-H]-: 556.9689; found: 556.9688. IR (neat, cm^{-1}): 2985, 2870, 1723, 1666, 1647, 1531, 1497, 1458, 1434, 1388, 1286, 1252, 1228, 1180, 1156, 1112, 1083, 999, 976, 919. mp: Due to the decomposition of titled compound at 285-287°C, mp could not be determined.

3,4,5,6,7,8-Hexafluoro-2-naphthalen-2-ol (8). To an ice bath-cooled solution of $Mg(TMP)_2$ (0.27 M in THF, 225 mL, 60.8 mmol, 1.5 equiv.) was added a THF (40 mL) solution of F_6naphthalene (**7**) (9.56 g, 40.5 mmol, 1.0 equiv.) at 0°C. The reaction mixture was stirred for 1 h. To the reaction mixture was added an ice bath-cooled $B(OMe)_3$ (22.6 mL, 202 mmol, 5 equiv.), then the resulting solution was warmed to room temperature. The reaction mixture was quenched with 1 M HCl aq. (~300 mL) and extracted with Et_2O (~200 mL × 2). The combined Et_2O extracts were washed with 1 M HCl aq. (~100 mL × 2), brine (~50 mL), dried over Na_2SO_4, and concentrated under reduced pressure after filtration to give a brown solid. The brown solid was dissolved in THF (100 mL). H_2O_2 (30% aqueous solution, 50 mL, 10 equiv.) was added dropwise to the solution. After being stirred for 30 min, brine (100 mL) was added to the reaction mixture. The resulting mixture was extracted with Et_2O (~150 mL × 3) and the combined Et_2O extracts were washed with brine (100 mL), dried over Na_2SO_4, and concentrated under reduced pressure after filtration. The residual crude oil was dissolved in Et_2O (~150 mL). The resulting Et_2O was extracted with 0.4 M NaOH aq. (100 mL × 3). The combined aqueous extracts were acidified with 6 M HCl aq. (50 mL) and extract with Et_2O (150 mL × 3). The combined Et_2O extracts were washed with brine (~50 mL), dried over Na_2SO_4, and concentrated under reduced pressure after filtration to give Et_2O complex of 3,4,5,6,7,8-hexafluoro-2-naphalene-2-ol (**8**) (10.2 g, 40.5 mmol on crude) as a light brown solid. Analytical data were reported as 3,4,5,6,7,8-hexafluoro-2-2naphthalene-2-ol (**8**) diethylether complex. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.34 (bs, 1H), 7.18 (d, J = 7.8 Hz, 1H), 3.80 (q, J = 7.2 Hz, 2 H), 1.36 (t, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 146.1 (d, J = 13 Hz), 144.8 (dm, J = 262 Hz), 141.1 (dm, J = 257 Hz), 140.8 (dm, J = 253 Hz), 140.7 (dd, J = 249 Hz, 13 Hz), 138.1 (dt, J = 254 Hz, 15 Hz), 137.3 (dt, J = 251 Hz, 15 Hz), 116.8 (d, J = 16 Hz), 105,74 (t, J = 9 Hz), 100.0, 66.4, 14.4. ^{19}F NMR (565 MHz, $CDCl_3$): δ –143.2 (dd, J = 51.1 Hz, 16.1 Hz, 1F), −148.3 (dtd, J = 51.2 Hz, 16.4 Hz, 5.1 Hz, 1F), −145.0 (t, J = 16.7 Hz, 1F), −157.5 (m, 1F), −158.2 (tm, J = 16.9 Hz, 1F), −161.1 (td, J = 18.4 Hz, 3.6 Hz, 1F). HRMS (APCI+): calcd. for $C_{10}H_2F_6O$ [M]+: 252.0004; found: 252.0004. IR (neat, cm^{-1}): 3240, 1650, 1463, 1398, 1373, 1293, 1191, 1071, 989. mp: 45–48°C.

1-Bromo-3,4,5,6,7,8-hexafluoro-2-naphthalen-2-ol. To a H_2O (120 mL) solution of KBr (12.1 g, 101 mmol, 2.5 equiv.) was added Br_2 (2.3 mL, 44.5 mmol, 1.1 equiv.). To the resulting solution were further added THF (120 mL) and a THF (120 mL) solution of 3,4,5,6,7,8-hexafluoro-2-naphthalene-2-ol (10.2 g, 40.5 mmol on crude, 1.0 equiv) in this order. The reaction mixture was quenched with sat. Na_2SO_3 aq. (~100 mL), acidified with 1 M HCl aq. (~200 mL), and extracted with Et_2O (~150 mL × 3). The combined Et_2O extracts were washed with brine (100 mL), dried over Na_2SO_4, and concentrated under reduced pressure after filtration to give 1-bromo-3,4,5,6,7,8-hexafluoro-2-naphthalen-2-ol as a brown solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.43 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 144.4 (dm, J = 254 Hz), 144.1 (d, J = 13.0 Hz), 141.8 (dm, J = 260 Hz), 141.4 (dm, J = 255 Hz), 140.1 (dd, J = 254 Hz, 16 Hz), 139.3 (dd, J = 253 Hz, 15 Hz), 137.7 (dt, J = 253 Hz, 15 Hz), 115.0, 107.3, 95.3. ^{19}F NMR (565 MHz, $CDCl_3$): δ –141.3 (m, 1F), −142.2 (m, 1F), −145.3 (dm, J = 68.3 Hz, 1F), −151.7 (m, 1F), −153.9 (m, 1F), −157.5 (m, 1F). HRMS (ESI-): calcd. for $C_{10}H_{Br}F_6O$ [M-H]-: 328.9042; found: 328.9041. IR (neat, cm^{-1}): 3404, 1654, 1529, 1465, 1448, 1389, 1313, 1249, 1194, 1084, 998, 832. mp: 101–103°C.

1-Bromo-3,4,5,6,7,8-hexafluoro-2-methoxynaphthalene (9). To a DMF (120 mL) suspension of 1-bromo-3,4,5,6,7,8-hexafluoronaphthalen-2-ol (13.4 g, 40.5 mmol on crude, 1.0 equiv.) and K_2CO_3 (8.4 g, 61 mmol, 1.5 equiv.) was added MeI (3.8 mL, 61 mmol, 1.5 equiv.). The black mixture was stirred for 12 h. The resulting mixture was quenched with H_2O (~200 mL) and extracted with ethyl acetate and hexane 10:1 (~150 mL × 3). The combined organic extracts were washed with sat. Na_2SO_3 aq. (~100 mL), H_2O (150 mL × 2), brine (~150 mL), and dried over Na_2SO_4. The residual crude was purified by silica gel column chromatography using hexane to give the product 1-bromo-2-methoxy-3,4,5,6,7,8-hexafluoronaphthalene (**9**) (12.4 g, 35.9 mmol, 89% yield from 1,2,3,4,5,6-hexafluoronaphthalene (**7**)) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.08 (d, J = 1.8 Hz, 3H).^{13}C NMR (151 MHz, $CDCl_3$): δ 147.6 (d, J = 13 Hz), 144.3 (dm, J = 266 Hz), 143.2 (dd, J = 256 Hz, 13 Hz), 142.5 (dm, J = 270 Hz), 141.0 (dm, J = 259 Hz), 139.8 (dt, J = 254 Hz,16 Hz), 138.4 (dt, J = 256 Hz, 15 Hz), 115.4 (d, J = 7 Hz), 109.2 (t, J = 9 Hz), 104.0, 61.8 (d, J = 6 Hz). ^{19}F NMR (565 MHz, $CDCl_3$): δ –139.0 (tm, J = 16.4 Hz, 1F), −141.5 (ddt, J = 68.9 Hz, 16.4 Hz, 4.52 Hz, 1F), −145.8 (dtm, J = 18.5 Hz, 4.6 Hz, 1F), −148.7 (m, 1F), −154.4 (tm, J = 16.9 Hz, 1F), −156.0 (t, J = 18.9 Hz, 1F). HRMS (ACPI+): calcd. for $C_{10}H_3BrF_6O$ [M]+: 343.9266; found: 343.9266. IR (neat, cm^{-1}): 1665, 1644, 1522, 1467, 1407, 1375, 1205, 1177, 1085, 998, 950, 837. mp: 52–53°C.

3,3',4,4',5,5',6,6',7,7',8,8'-Dodecafluoro-2,2'-dimethoxy-1,1'-binaphthyl (10). An anhydrous DMF (22 mL) suspension of 1-bromo-2-methoxy-3,4,5,6,7,8-hexafluoronaphthlene (**9**) (12.4 g, 36.0 mmol, 2.0 equiv.) and freshly activated copper powder (23 g, 360 mmol, 20 equiv.) was heated at 155°C. After being stirred for 30 min, the reaction mixture was concentrated under reduced pressure. The residual mixture was diluted with EtOAc (50 mL) after cooled to room temperature. The resulting suspension was passed via a pad of silica gel and washed with EtOAc (200 mL). The filtrate was concentrated under reduced pressure to give a yellow solid. The solid was recrystallized from hot hexane to give the product 3,3',4,4',5,5',6,6',7,7',8,8'- dodecafluoro-2,2'-bis(methoxy)-1,1'-binaphthyl (**10**) (8.9 g, 16.7 mmol, 93% yield) as a white crystal. ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.80 (d, J = 2.1 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 146.9 (d, J = 10 Hz), 145.4 (dm, J = 250 Hz), 143.3 (dd, J = 254 Hz, 13 Hz), 142.6 (dm, J = 256 Hz), 141.6 (dm, J = 256 Hz), 139.3 (dt, J = 253 Hz, 16 Hz), 138.1 (dt, J = 253 Hz, 16 Hz), 116.9, 116.0, 108.4 (t, J = 9 Hz), 61.8 (d, J = 7 Hz). ^{19}F NMR (565 MHz, $CDCl_3$): δ –140.2 (dd, J = 62.1 Hz, 16.4 Hz, 2F), −143.6 (t, J = 16.4 Hz, 2F), −145.7 (dtd, J = 63.0 Hz, 16.4 Hz, 5.2 Hz, 2F), −150.4 (bs, 2F), −155.4 (t, J = 18.1 Hz, 2F), −157.1 (t, J = 19.0 Hz, 2F). HRMS (ACPI+): calcd. for $C_{22}H_6F_{12}O_2$ [M]+: 530.0171; found: 530.0170. IR (neat, cm^{-1}): 2953, 2930, 2852, 1666, 1643, 1522, 1495, 1461, 1404, 1376, 1279, 1254, 1205, 1174,

1111, 1077, 991, 954, 825. HPLC: DAICEL CHIRALCEL OD-3 4.6 × 250 mm, *n*-hexane 1.0 mL/min, 30°C, 254 nm, 6.4 min (minor) 7.3 min (minor), 99% ee. $[\alpha]_D^{25}$ -12.2 (c = 0.52, CH_2Cl_2, 99% ee) mp: 174–176°C. Activation of copper powder: To a suspension of copper (27.6 g, 431 mmol, 1.0 equiv.) in acetone (100 mL) was added iodine (1.8 g, 14.4 mmol, 0.03 equiv.) at room temperature. The suspension was stirred until the iodine color disappeared. To the mixture was added 12 M HCl aq. (100 mL). The mixture was filtered and washed with acetone (100 mL). The solid was dried in a desiccator under reduced atmosphere for 12 h.

3,3',4,4',5,5',6,6',7,7',8,8'-Dodecafluoro-1,1'-binaphthyl-2,2'-diol (F_{12}BINOL, 5)[31]. To a CH_2Cl_2 (50 mL) solution of 3,3',4,4', 5,5',6,6',7,7',8,8'-dodecafluoro-2,2'-bis(methoxy)-1,1'-binaphthyl (**10**) (6.6 g, 12.5 mmol, 1.0 equiv.) was added BBr_3 (4.7 mL, 50 mmol, 4.0 equiv.) and the resulting mixture was stirred at 40°C for 12 h. After being cooled at −78°C, the resulting solution was carefully diluted with EtOH. The reaction mixture was quenched with H_2O and extracted with CH_2Cl_2 (50 mL × 3). The combined CH_2Cl_2 extracts were washed with brine (50 mL), passed via a pad of silica gel. The filtrate was concentrated under reduced pressure to give a gray solid. The residual crude solid was dissolved with Et_2O (50 mL). The organic layer was extracted with 0.4 M NaOH aq. (30 mL × 3). The combined aqueous extracts were acidified with 6 M HCl aq. (10 mL) and extracted with Et_2O (30 mL × 3). The combined Et_2O extracts were washed with brine (~50 mL), dried over Na_2SO_4, and concentrated under reduced pressure after filtration to give 2,2'-dihydroxy-3,3',4,4',5,5',6,6',7,7',8,8'-dodecafluoro-1,1'-binaphthyl (F_{12}BINOL, **5**) as a white solid. F_{12}BINOL **5** was recrystallized from hot Et_2O to give a colorless crystal of F_{12}BINOL·nEt_2O complex. The coordinated Et_2O was removed at 60°C in vacuo for 12 h (6.1 g, 11.7 mmol, 94% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.56 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 144.8 (dm, J = 263 Hz), 143.4 (d, J = 13 Hz), 142.6 (dm, J = 250 Hz), 141.8 (dm, J = 260 Hz), 139.5 (dm, J = 260 Hz, 2 peaks were overlapped), 137.6 (dt, J = 260 Hz, 14 Hz), 116.5, 108.3, 106.9 (m). ^{19}F NMR (565 MHz, $CDCl_3$): δ −140.2 (dd, J = 62.1 Hz, 19.0 Hz, 2F), −145.5 ~ −145.8 (m, 4F), −155.0 (tm, J = 19.0 Hz, 2F), −157.0 (dm, J = 17.3 Hz, 2F), −158.3 (td, J = 19.0 Hz, 3.5 Hz, 2F). HRMS (ESI-): calcd. for $C_{20}H_2F_{12}O_2$ [M-H]-: 500.9790; found: 500.9789. IR (neat, cm^{-1}): 3674, 3577, 3396, 1652, 1530, 1456, 1393, 1350, 1288, 1230, 1191, 1115, 1077, 992, 910. mp: 184–186°C.

1-Bromo-3,4,5,6,7,8-hexafluoro-2-naphthaldehyde (12). To an acetone-dry ice bath-cooled solution of $Mg(TMP)_2$ (0.27 M in THF, 13.3 mL, 3.6 mmol, 1.2 equiv.) was added a THF (3 mL) solution of 8-bromo-1,2,3,4,5,6-hexafluoro naphthalene (945 mg, 3 mmol, 1.0 equiv.) at −78°C. After being stirred for 2 h, DMF (1.2 mL, 15 mmol, 5.0 equiv.) was added. After being stirred for 4 h, the reaction mixture was quenched with conc. HCl (~2 mL) and warmed to room temperature. The resulting mixture was extracted with Et_2O (~15 mL × 2). The combined Et_2O extracts were washed with brine (~15 mL), dried over Na_2SO_4, and concentrated under reduced pressure after filtration. The residual crude was purified by silica gel column chromatography (0–5% EtOAc in hexane as an eluent) to give the 1-bromo-3,4,5,6,7,8-hexafluoro-2-naphthaldehyde (**12**) as a brown solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ 10.43, (d, J = 1.0 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 187.9 (s), 145.6 (dd, J = 246 Hz, 13 Hz), 144.3 (dm, J = 251 Hz), 143.9 (dm, J = 259 Hz), 141.1 (dm, J = 263 Hz), 140.8 (dt, J = 260 Hz, 16 Hz), 140.3 (dt, J = 256 Hz,16 Hz), 127.2 (d, J = 12 Hz), 116.2 (s), 114.4 (m, 2 peaks were overlapped). ^{19}F NMR (565 MHz, $CDCl_3$): δ −153.3 (tt, J = 17.9 Hz, 6.0 Hz, 1F), −141.2 (ddm, J = 69.1 Hz, 16.7 Hz, 1F), −142.8 (m, 1F), −143.7 (dtm, J = 66.8 Hz, 16.7 Hz, 1F), −148.9 (tm, J = 20.3 Hz, 1F), −153.7 (tm, J = 18.9 Hz, 1F). HRMS (ESI+): calcd. for $C_{11}HBrF_6O$, [M]+: 341.9109; found: 341.9110. IR (neat, cm^{-1}): 3387, 2885, 1702, 1660, 1637, 1580, 1526, 1489, 1396, 1368, 1335, 1257, 1193, 1165, 1086, 999, 845, 806. mp: 68°C.

(1-Bromo-3,4,5,6,7,8-hexafluoronaphthalen-2-yl)methanol (13). To an ice bath-cooled THF (15 mL) and MeOH (15 mL) solution of 1-bromo-3,4,5,6,7,8-hexafluoro-2-naphthaldehyde (**12**) was added $NaBH_4$ (136 mg, 3.6 mmol, 1.2 equiv.) at 0°C. After being stirred for 15 min, the reaction mixture was quenched with 1 M HCl aq. (~5 mL) and extracted with Et_2O (~15 mL × 2). The combined Et_2O extracts were washed with brine (~15 mL), dried over Na_2SO_4, and concentrated under reduced pressure after filtration. The residual crude was purified by silica gel column chromatography (0-10% EtOAc in hexane as an eluent) to give the product (1-bromo-3,4,5,6,7,8-hexafluoronaphthalen-2-yl)methanol (**13**) (558 mg, 1.4 mmol, 46% yield in 2 steps) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.07 (dd, J = 7.2Hz, 2.8 Hz, 2H), 2.31 (t, J = 7.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 146.5 (dd, J = 254Hz, 12 Hz), 143.5 (dm, J = 254 Hz), 143.4 (dm, J = 256 Hz), 141.0 (dm, J = 257 Hz), 139.9 (dt, J = 254 Hz, 15 Hz), 139.5 (dt, J = 259Hz, 15 Hz), 132.6 (d, J = 17 Hz), 116.5 (m), 112.8 (m), 59.0 (d, J = 3 Hz). ^{19}F NMR (565 MHz, $CDCl_3$): δ −137.2 (tt, J = 16.7 Hz, 4.8Hz, 1F), −137.8 (dm, J = 11.9 Hz, 1F), −142.6 (ddt, J = 69.1Hz, 16.7Hz, 4.8 Hz, 1F), −144.9 (dm, J = 70.3 Hz, 1F), −152.9 (tm, J = 19.1 Hz, 1F), −153.7 (m, 1F). HRMS (ACPI+): calcd. for $C_{11}H_3BrF_6O$, [M]+: 343.9266; found: 343.9266. IR (neat, cm^{-1}): 3258, 2960, 2925, 2856, 1730, 1664, 1643, 1581, 1526, 1494, 1401, 1248, 1167, 996. mp: 122–125°C.

1-Bromo-2-((1-bromo-3,4,5,6,7,8-hexafluoronaphthalen-2-yl) methoxy)-3,4,5,6,7,8-hexafluoronaphthalene (14a). To a THF (4 mL) solution of (1-bromo-3,4,5,6,7,8-hexafluoro naphthalen-2-yl)methanol (**13**) (146 mg, 0.42 mmol, 1.0 equiv.), 1-bromo-3,4,5,6,7,8-hexafluoronaphthalen-2-ol (140 g, 0.42 mmol, 1.0 equiv.), and PPh_3 (134 mg, 0.51 mmol, 1.2 equiv.) was added DIAD (270 μL, 0.51 mmol, 1.2 equiv.) at 0°C. The reaction mixture was stirred at 0°C for 1 h. The resulting suspension was concentrated under reduced pressure. The residual crude was dissolved in MeOH (5 mL) and purified by filtration to give the product 1-bromo-2-((1-bromo-3,4,5,6,7,8- hexafluoronaphthalen-2-yl)methoxy)-3,4,5,6,7,8-hexafluoro naphthalene (**14a**) (238 mg, 0.36 mmol, 85% yield) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.71 (d, J = 2.8 Hz, 2H). ^{13}C NMR could not be measured due to low solubility in any solvent. ^{19}F NMR (565 MHz, $CDCl_3$): δ −135.8 (m, 1F), −135.9 (tm, J = 15.5 Hz, 1F), −138.2 (t, J = 16.7 Hz, 1F), −140.4 (ddm, J = 68.0 Hz, 17.9 Hz, 1F), −142.2 (ddm, J = 69.1 Hz, 16.7 Hz, 1F), −144.6 (dtm, J = 69.1 Hz, 17.9 Hz, 1F), −145.0 (dtm, J = 69.1 Hz, 16.7 Hz, 1F), −147.0 (m, 1F), −151.6 (t, J = 17.9 Hz, 1F), −153.1 (tm, J = 17.9 Hz, 1F), −153.4 (tm, J = 17.9 Hz, 1F), −154.6 (t,

J = 17.9 Hz, 1F). HRMS (APCI+): calcd. for $C_{21}H_3Br_2F_{12}O$, [M]+: 655.8275; found: 655.8275. IR (neat, cm^{-1}): 1667, 1647, 1527, 1507, 1496, 1472, 1458, 1439, 1412, 1375, 1339, 1249, 1187, 1084, 1025, 1000, 942, 836, 820. mp: 210°C. Anal. calcd. for $C_{21}H_3Br_2F_{12}O$: C, 38.33; H, 0.31; Br, 24.29; F, 34.65. found: C, 38.05; H, 0.43; Br, 24.25; F, 34.46.

1,2,5,6,7,8,9,10,11,12,13,14-Dodecafluoro-4*H*-benzo[*f*] naphtha[2,1-*c*]chromene (15a). An anhydrous DMF (4 mL) suspension of 1-bromo-2-((1-bromo-3,4,5,6,7,8-hexafluoronaphthalen-2-yl)methoxy)-3,4,5,6,7,8-hexafluoronaphthalene (**14a**) (526 mg, 0.8 mmol, 1.0 equiv.) and freshly activated copper powder (508 mg, 8 mmol, 10 equiv.) was heated at 150°C. After being stirred for 2.5 h, the reaction mixture was filtered via a pad of Celite. The filtrate was dissolved in Et_2O (15 mL) and washed with 1 M HCl aq. (~10 mL × 3) and brine (~10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure after filtration to give 1,2,5,6,7,8,9,10,11,12,13,14-dodecafluoro-4*H*-benzo[*f*]naphtha [2,1-*c*]chromene (**15a**) as a white solid. ^{1}H NMR (600 MHz, acetone-d_6): δ 5.93 (d, J = 13.8 Hz, 1H), 5.15 (d, J = 13.8 Hz, 1H). ^{13}C NMR (151 MHz, acetone-d_6): δ 148.8 (d, J = 13 Hz), 145.0 (dm, J = 269 Hz), 143.6 (dm, J = 254 Hz, 3 peaks were overlapped), 143.2 (dm, J = 257 Hz), 141.8 (dm, J = 260 Hz), 141.6 (dm, J = 250 Hz), 140.4 (dd, J = 251 Hz, 15 Hz), 138.9 (dm, J = 260 Hz, 3 peaks were overlapped), 137.8 (dt, J = 250 Hz, 16 Hz), 127.9 (d, J = 17 Hz), 120, 116.2 (m), 115.9 (m), 113.1, 112.0 (m), 107.2 (m), 65.0. ^{19}F NMR (565 MHz, acetone-d_6): δ –137.7 (m, 1F), –139.0 (m, 1F), –141.2 (dd, J = 66.8 Hz, 16.7 Hz, 1F), –145.3 (dd, J = 68.0 Hz, 17.9 Hz, 1F), –146.7 (m, 1F), –147.7 (dtm, J = 66.8 Hz, 15.5 Hz, 1F), –147.9 (dtm, J = 66.8 Hz, 15.5 Hz, 1F), –157.7 (t, J = 19.1 Hz, 1F), –157.8 (m, 1F), –158.3 (tm, J = 16.7 Hz, 1F), –158.4 (tm, J = 17.9 Hz, 1F), –160.5 (t, J = 19.1 Hz, 1F). HRMS (ESI-): calcd. for $C_{21}H_2F_{12}O$, [M+I]-: 624.8964; found: 624.8963. IR (neat, cm^{-1}): 1668, 1645, 1532, 1500, 1457, 1438, 1410, 1380, 1345, 1248, 1172, 1118, 1090, 1077, 1026, 1009, 988, 972, 898, 853. mp: 220–222°C.

2'-(Bromomethyl)-3,3',4,4',5,5',6,6',7,7',8,8'-dodecafluoro-[1,1'-binaphthalen]-2-ol (16a)[43]. To a CH_2Cl_2 (2.4 mL) solution of 1,2,5,6,7,8,9,10,11,12,13,14-dodecafluoro-4*H*-benzo[*f*] naphtha [2,1-*c*]chromene (**15a**) was added BBr_3 (227 μL, 2.4 mmol, 3.0 equiv.) and the resulting mixture was stirred at 40°C for 18 h. After being cooled at –78°C, the resulting solution was carefully diluted with EtOH. The reaction mixture was quenched with H_2O and extracted with CH_2Cl_2 (~10 mL × 2). The combined CH_2Cl_2 extracts were washed with brine (~10 mL), dried over Na_2SO_4, and concentrated under reduced pressure after filtration. The residual crude was purified by silica gel column chromatography (0–15% EtOAc in hexane as an eluent) to give the product 2'-(bromomethyl)-3,3',4,4',5,5',6,6',7,7',8,8'-dodecafluoro-[1,1'-binaphthalen]-2-ol (**16a**) (339 mg, 0.58 mmol, 73% yield in 2 steps) as a brown oil. ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.97 (bs, 1H), 4.27 (dd, J = 10.5 Hz, 1.5 Hz, 1H), 4.15 (dd, J = 10.5 Hz, 2.2 Hz, 1H). ^{13}C NMR (151 MHz, acetone-d_6): δ 146.6 (dd, J = 251 Hz, 12 Hz), 145.2 (dm, J = 251 Hz), 145.2 (d, J = 14 Hz), 144.0 (dm, J = 249 Hz), 143.5 (dm, J = 244 Hz), 142.4 (dm, J = 246 Hz), 141.6 (dm, J = 251 Hz), 141.5 (dm, J = 255 Hz), 140.8 (dm, J = 248 Hz), 139.4 (dm, J = 251 Hz, 3 peaks were overlapped), 137.3 (dt, J = 250 Hz, 14 Hz), 129.4 (d, J = 14 Hz), 126.4, 117.2 (m), 116.4 (m), 112.0 (tm, J = 9 Hz), 110.8, 106.3 (m), 22.2. ^{19}F NMR (565 MHz, $CDCl_3$): δ –139.3 (m, 1F), –139.5 (dd, J = 62.0 Hz, 19.1 Hz, 1F), –141.5 (dd, J = 63.2 Hz, 17.9 Hz, 1F), –142.9 (t, J = 16.7 Hz, 1F), –143.0 (t, J = 15.5 Hz, 1F), –145.0 (dtm, J = 62.0 Hz, 16.1 Hz, 1F), –145.3 (dtm, J = 62.0 Hz, 16.1 Hz, 1F), –153.5 (t, J = 17.9 Hz, 1F), –154.3 (tm, J = 15.5 Hz, 1F), –154.9 (tm, J = 17.9 Hz, 1F), –156.3 (m, 1F), –157.7 (t, J = 19.1 Hz, 1F). HRMS (ESI-): calcd. for $C_{21}H_2BrF_{12}O$, [M-H]-: 576.9103; found: 576.9103. IR (neat, cm^{-1}): 3578, 1647, 1527, 1495, 1458, 1388, 1185, 1114, 1075, 1022, 994, 927, 869, 820.

1-Bromo-2-(((1-bromonaphthalen-2-yl)oxy)methyl)-3,4,5,6,7,8-hexafluoronaphthalene (14b). To a THF (37 mL) solution of (1-bromo-3,4,5,6,7,8-hexafluoronaphthalen-2-yl) methanol (**13**) (1.3 g, 3.7 mmol, 1.0 equiv.), 1-bromonaphthalen-2-ol (990 mg, 4.4 mmol, 1.2 equiv.) and PPh_3 (1.2 g, 4.4 mmol, 1.2 equiv.) was added DIAD (953 μL, 4.4 mmol, 1.2 equiv.). The reaction mixture was stirred for 1 h. The resulting suspension was concentrated under reduced pressure. The residual crude was dissolved in MeOH (20 mL) and purified by filtration to give the product 1-bromo-2-(((1-bromonaphthalen-2-yl)oxy)methyl)-3,4,5,6,7,8-hexafluoronaphthalene (**14b**) (1.7 g, 3.1 mmol, 83% yield) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.23 (d, J = 8.6 Hz, 1H), 7.85 (d, J = 8.9 Hz, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.59 (tm, J = 7.7 Hz, 1H), 7.45 (tm, J = 7.5 Hz, 1H), 7.44 (d, J = 8.9 Hz, 1H), 5.61 (d, J = 2.8 Hz, 2H). ^{13}C NMR could not be measured due to low solubility in any solvent. ^{19}F NMR (565 MHz, $CDCl_3$): δ –136.2 (m, 1F), –136.4 (tm, J = 16.7 Hz, 1F), –142.6 (ddm, J = 69.1 Hz, 16.7 Hz, 1F), –144.9 (dtm, J = 69.1 Hz, 17.6 Hz, 1F), –152.4 (t, J = 17.9 Hz, 1F), –153.6 (tm, J = 19.1 Hz, 1F). HRMS (APCI+): calcd. for $C_{21}H_8Br_2F_6O$, [M]+: 547.8841; found: 547.8841. IR (neat, cm^{-1}): 2924, 2854, 1748, 1715, 1698, 1667, 1647, 1625, 1594, 1559, 1544, 1527, 1507, 1496, 1458, 1421, 1375, 1348, 1339, 1261, 1252, 1240, 1181, 1045, 1025, 998, 906, 824. mp: 238°C. Anal. calcd. for $C_{21}H_8Br_2F_6O$: C, 45.85; H, 1.47; Br, 29.05; F, 20.72. found: C, 46.00; H, 1.47; Br, 29.12; F, 20.69.

5,6,7,8,9,10-Hexafluoro-4*H*-benzo[*f*]naphtha[2,1-*c*]chromene (15b). An anhydrous DMF (30 mL) suspension of 1-bromo-2-(((1-bromonaphthalen-2-yl)oxy)methyl)-3,4,5,6,7,8-hexafluoro naphthalene (**14b**) (3.3 g, 6 mmol, 1.0 equiv.) and freshly activated copper powder (3.8 g, 60 mmol, 10 equiv.) was heated at 150°C. After being stirred for 2.5 h, the reaction mixture was filtered via a pad of Celite. The filtrate was dissolved in Et_2O (~50 mL) and washed with 1 M HCl aq. (~50 mL × 3) and brine (~50 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure after filtration to give 5,6,7,8,9,10-hexafluoro-4*H*-benzo[*f*] naphtha[2,1-*c*]chromene (**15b**) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.86 (m, 2H), 7.41 (m, 2H), 7.34 (m, 2H), 5.59 (d, J = 13.8 Hz, 1H), 4.74 (d, J = 13.8 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 155.1, 150.0 (d, J = 12 Hz), 142.8 (dm, J = 259 Hz), 142.5 (dm, J = 253 Hz), 141.2 (dm, J = 259 Hz), 139.2 (dm, J = 257 Hz, 2 peaks were overlapped), 131.7 (d, J = 7 Hz), 131.4, 129.8, 128.7, 128.6 (d, J = 17 Hz), 126.9, 124.5, 122.8 (d, J = 6 Hz), 122.1, 117.9, 117.6, 114.7 (d, J = 13 Hz), 112.2 (m), 63.9. ^{19}F NMR (565 MHz, $CDCl_3$): δ –128.7 (t, J = 16.7 Hz, 1F), –144.7 (dd, J = 62.0 Hz, 19.1 Hz, 1F), –145.5 (d, J = 19.1 Hz, 1F), –146.0 (dtm, J = 62.0 Hz, 15.5 Hz, 1F), –155.5 (t, J = 19.1 Hz, 1F), –156.4 (tm, J = 19.1 Hz, 1F). HRMS (ESI-): calcd. for $C_{21}H_8F_6O$, [M+H]+:

391.0552; found: 391.0552. IR (neat, cm^{-1}): 1667, 1640, 1598, 1567, 1500, 1416, 1376, 1247, 1226, 1168, 1099, 1018, 1003, 981, 935, 867. mp: 197°C.

2'-(Bromomethyl)-3',4',5',6',7',8'-hexafluoro-[1,1'-binaphthale n]-2-ol (16b)[43]. To a CH_2Cl_2 (18 mL) solution of 5,6,7,8,9,10-hexafluoro-4*H*-benzo[*f*]naphtha[2,1-*c*] chromene (**15b**) was added BBr_3 (1.7 mL, 18 mmol, 3.0 equiv.), and the resulting solution was stirred at 40°C for 18 h. After being cooled at −78°C, the resulting solution was carefully diluted with EtOH. The reaction mixture was quenched with H_2O and extracted with CH_2Cl_2 (~50 mL × 2). The combined CH_2Cl_2 extracts were washed with brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure after filtration. The residual crude was purified by silica gel column chromatography (0-15% EtOAc in hexane as an eluent) to give the product 2'-(bromomethyl)-3',4',5',6',7',8'-hexafluoro-[1,1'-binaphthalen]-2-ol (**16b**) (2.37 g, 5.0 mmol, 84% yield in two steps) as a white solid. ^{1}H NMR (600 MHz, acetone-d_6): δ 8.72 (bs, 1H), 7.95 (d, J = 8.9 Hz, 1H), 7.85 (d, J = 7.6 Hz, 1H), 7.37 (d, J = 8.9 Hz, 1H), 7.26 (ddd, J = 7.9 Hz, 7.0 Hz, 1.2 Hz, 1H), 7.22 (ddd, J = 8.3 Hz, 6.9 Hz, 1.4 Hz, 1H), 4.35 (ddd, J = 45.2 Hz, 10.5 Hz, 1.5 Hz, 2H). ^{13}C NMR (151 MHz, acetone-d_6): δ 152.3 (d, J = 3 Hz), 147.2 (dd, J = 251 Hz, 12 Hz), 143.8 (dm, J = 254 Hz), 143.7 (dm, J = 254 Hz), 141.3 (dm, J = 254 Hz), 139.3 (dt, J = 253 Hz, 16 Hz), 139.1 (dt, J = 250 Hz, 16 Hz), 133.7 (d, J = 3 Hz), 130.8, 129.9 (d, J = 13 Hz), 128.6 (2 peaks were overlapped), 128.3, 127.0, 123.7, 123.3, 118.0, 117.8 (d, J = 6 Hz), 115.2 (d, J = 3 Hz), 112.4 (t, J = 9 Hz), 22.6. ^{19}F NMR (565 MHz, acetone-d_6): δ −140.5 (d, J = 14.3 Hz, 1F), −142.4 (t, J = 16.7 Hz, 1F), −146.2 (dd, J = 62.0 Hz, 16.7 Hz, 1F), −148.2 (dtm, J = 64.4 Hz, 16.7 Hz, 1F), −156.9 (t, J = 19.1 Hz, 1F), −158.6 (tm, J = 16.7 Hz, 1F). HRMS (ESI+): calcd. for $C_{21}H_9BrF_6O$, [M+Na]+: 492.9633; found: 492.9633. IR (neat, cm^{-1}): 3423, 3060, 2958, 2925, 2854, 1663, 1646, 1626, 1590, 1495, 1468, 1436, 1410, 1386, 1270, 1251, 1220, 1188, 1174, 1145, 1132, 1098, 1042, 1023, 987, 955, 903, 851, 814. mp: 132–135°C.

(*R*)-3,3',4,4',5,5',6,6',7,7',8,8'-Dodecafluoro-1,1'-binaphthyl-2,2'-diol ((*R*)-5). The optical resolution of the titled compound was performed in accordance with procedure of that of BINOL.[44,45] An acetonitrile (55 mL) suspension of F_{12}BINOL ((±)-**5**) (7.0 g, 13.9 mmol, 2.0 equiv.) and *N*-benzylcinchonidinium chloride (**17**) (3.3 g, 7.6 mmol, 1.1 equiv.) was heated at 80°C and stirred for 4 h. The mixture was stirred at room temperature for 12 h and then cooled to 0°C. The mixture stood for 2 h. The mixture was filtered and washed with Et_2O. The solid was recrystallized from MeOH. The crystal was dissolved in Et_2O (150 mL) and 6 M HCl aq. (100 mL). After being stirred for 60 min, the mixture was extracted with Et_2O (~100 mL × 3). The organic layer was extracted with 0.4 M NaOH aq. (~50 mL × 3). The combined aqueous extracts were acidified with 6 M HCl aq. (50 mL) and extracted with Et_2O (~100 mL × 3). The combined Et_2O extracts were washed with brine (~100 mL), dried over Na_2SO_4, and concentrated under reduced pressure after filtration. The residual oil was dried at 60°C in vacuo to give (*R*)-2,2'-dihydroxy-3,3',4,4',5,5',6,6',7,7',8,8'-dodecafluoro-1,1'-binaphthyl ((*R*)-F_{12}BINOL, **5**) as a white solid (2.7 g, 5.4 mmol, 77% yield, 99% *ee*). Enantiomeric ratio was determined based on Piers' procedure.[31] $[\alpha]_D^{25}$ −28.6 (c = 0.61, CH_2Cl_2, 99% *ee*).

(*R*)-4,4',5,5',6,6',7,7',8,8'-Decafluoro-3,3'-diphenyl-1,1'-bi-2-naphthol ((*R*)-18)[46]. To a mixture of $PdCl_2(PCy_3)_2$ (42 mg, 0.56 mmol, 5 mol%) and (*R*)-F_{12}BINOL **5** (568 mg, 1.13 mmol, 1.0 equiv.) under argon atmosphere was added a THF solution of PhMgBr (1.0 M, 6.8 mL, 6.8 mmol, 6.0 equiv.) at −78°C in THF (1 mL). After evacuated and refilled with argon twice, the reaction mixture was warmed to 60°C and stirred for 36 h. After the resulting mixture was cooled to room temperature, 6 M HCl aq. (~5 mL) was added. The resulting mixture was extracted with Et_2O (20 mL × 3), and the combined Et_2O extracts were washed with 1 M HCl aq. (10 mL × 2) and brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure after filtration. The residual crude was purified by silica gel column chromatography (0-10% acetone in hexane as an eluent) to give the product (*R*)-4,4',5,5',6,6',7,7',8,8'-decafluoro-3,3'-diphenyl-1,1'-bi-2-naphthol, ((*R*)-$C_6H_5F_{10}$BINOL **18**) (544.2 mg, 0.88 mmol, 78%) as a brown solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.5~7.6 (m, 10H), 5.51 (bs, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 140.1 (dt, J = 253 Hz, 16 Hz), 137.0 (dt, J = 250 Hz, 16 Hz), 130.3~130.7 (m), 129.4~129.8 (m), 128.6, 120.4 (bs), 118.3 (d, J = 17 Hz), 107.2 (bs), 106.9 (t, J = 11 Hz). ^{19}F NMR (565 MHz, $CDCl_3$): δ −115.0 (d, J = 74.0 Hz, 1F), −144.4 (dt, J = 74.0 Hz, 16.9 Hz, 1F), −146.7 (t, J = 16.2 Hz, 1F), −155.1 (t, J = 16.8 Hz, 1F), −160.7 (t, J = 19.0 Hz, 1F). HRMS (ESI-): calcd. for $C_{32}H_{12}F_{10}O_2$ [M-H]-: 617.0605; found: 617.0604. IR (neat cm^{-1}): 3530, 1669, 1630, 1602, 1519, 1495, 1411, 1384, 1350, 1275, 1227, 1162, 1091, 1017, 942. HPLC: DAICEL CHIRALPAK AD-3 4.6 × 250 mm, *n*-hexane:2-PrOH 90:10 1.0 mL/min, 30°C, 254 nm, 6.8 min (minor) 8.1 min (minor), 99% *ee*. $[\alpha]_D^{25}$ +22.57 (c = 0.20, CH_2Cl_2, 99% ee). mp: Due to the decomposition of titled compound at 110°C, mp could not be determined.

(*R*)-$C_6H_5F_{10}$BINOL-derived phosphoric acid (*R*)-19. To a pyridine (3.5 mL) solution of (*R*)-$C_6H_5F_{10}$BINOL **18** (570 mg, 0.9 mmol, 1.0 equiv.) was added $POCl_3$ (164 μL, 1.8 mmol, 2.0 equiv.) at 0°C. The reaction mixture was warmed to room temperature. After being stirred for 12 h, the resulting mixture was quenched H_2O (3 mL) at 0°C, acidified with 12 M HCl aq. (5 mL), and extracted with Et_2O (10 mL × 3). The combined Et_2O extracts were washed with 6 M HCl aq. (10 mL × 2) and brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure after filtration. The residual crude was purified by Silica gel 60 extra pure (Cat. No. 107754 Merck KgaA) column chromatography (10–50% Et_2O in hexane as an eluent) to give chiral phosphoric acid (*R*)-**19** as a brown solid (224 mg, 0.48 mmol, 54%). ^{1}H NMR (600 MHz, $CDCl_3$): δ7.73 (bs, 1H), 7.39 (bd, J = 6.9 Hz, 4H), 7.26 (bs, 6H). ^{13}C NMR (151 MHz, C_6D_6): δ 154.9 (d, J = 262 Hz), 145.4, 142.6 (dm, J = 262 Hz), 142.1 (dm, J = 263 Hz), 140.2 (dm, J = 261 Hz), 138.5 (dm, J = 259 Hz), 130.6, 128.9, 128.7, 128.5, 122.0 (d, J = 17 Hz), 119.8 (m), 114.8, 109.5 (m). ^{19}F NMR (565 MHz, C_6D_6): δ −111.3 (d, J = 78.6 Hz, 2F), −140.8 (bs, 2F), −142.3 (d, J = 77.9 Hz, 2F), −155.9 (t, J = 18.5 Hz, 2F), −155.8 (t, J = 18.5 Hz, 2F). ^{31}P NMR (243 MHz, $CDCl_3$): 2.50 (s). HRMS (ESI-): calcd. for $C_{32}H_{11}F_{11}O_4P$ [M-H]-: 679.0163; found: 679.0161. IR (neat, cm^{-1}): 3383, 1664, 1618, 1523, 1479, 1379, 1208, 1094, 1017, 873. $[\alpha]_D^{25}$ −78.04 (c = 0.85, CH_2Cl_2, 99% ee). mp: Due to the decomposition of titled compound at 340°C, mp could not be determined.

Sodium (*R*)-F_{12}BINOL phosphate. *Preparation of $BnOPOCl_2$ solution*: To a toluene (1.0 mL) solution of $POCl_3$ (93 μL, 1.0 mmol, 1.0 equiv.) was added dropwise a toluene (1.0 mL) solution of NEt_3 (139 μL, 1.0 mmol, 1.0 equiv.) and BnOH (103 μL, 1.0 mmol, 1.0 equiv.) at 0°C, and the reaction mixture was stirred for 6 h. *Preparation of solution of sodium F_{12}binaphtholate*: To a THF (1 mL) suspension of NaH (90 mg 60% in oil, 2.2 mmol, 2.2 equiv.) was added a THF (1.0 mL) solution of (*R*)-F_{12}BINOL **5** (502 mg, 1.0 mmol, 1.0 equiv.) at 0°C, and the resulting solution was stirred for 2 h. *Synthesis of sodium (R)-F_{12}BINOL phosphate*: To a toluene solution of $BnOPOCl_2$ was added the THF solution of sodium F_{12}binaphtholate. After being stirred for 12 h, the mixture was passed via a pad of Celite and the filtrate was evaporated. The residual oil was dissolved in acetone (1.0 mL), and NaI (150 mg, 1.0 mmol, 1.0 equiv.) was added. After being stirred for 30 min, organic solvent was evacuated and residual crude mixture was purified by silica-gel column chromatography (10~80% acetone in CH_2Cl_2 as an eluent) to give a product as sodium (*R*)-F_{12}BINOL phosphate (400 mg, 0.69 mmol, 69% yield). ^{13}C NMR (151 MHz, acetone-d_6): δ 146.0~137.0 (m), 116.4, 108.6. 19F NMR (565 MHz, acetone-d_6: δ −141.5 (t, J = 15.5 Hz, 2F), −142.7 (dd, J = 65.6 Hz, 16.0 Hz, 2F), 147.9 (dm, J = 65.6 Hz, 2F), −152.4 (m, 2F), −157.9 (m, 2F), −159.5 (m, 2F). ^{31}P NMR (243 MHz, acetone-d_6): δ 4.81(s). HRMS (ESI-): calcd. for $C_{20}F_{12}O_4PNa$ [M-Na]-: 562.9348; found: 562.9346. IR (neat, cm^{-1}): 1701, 1667, 1529, 1500, 1481, 1431,1384, 129, 1187, 1112, 1080, 993, 838. $[\alpha]_D^{25}$ -113.7 (c = 1.1, CH_2Cl_2, 99% ee). mp: Due to the decomposition of titled compound at 130°C, mp could not be determined.

(*R*)-F_{12}BINOL-derived phosphoric acid (*R*)-20. To a CH_2Cl_2 solution (2.0 mL) of sodium (*R*)-F_{12}BINOL phosphate (56 mg, 0.1 mmol, 1.0 equiv.) was added Amberlyst 15 hydrogen form (100 mg). After being stirred for 30 min, the resulting suspension was filtered and the filtrate was evaporated to give a product as F_{12}BINOL-derived phosphoric acid (*R*)-**20** (51 mg, 0.09 mmol, 94% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 11.39 (bs). ^{13}C NMR (151 MHz, $CDCl_3$): δ 147.0-137.0 (m), 116.2, 115.4, 109.7. ^{19}F NMR (565 MHz, acetone-d_6): δ −140.05 (dd, J = 66.6 Hz, 15.5 Hz, 2F), −140.6 (t, J = 15.5 Hz, 2F), −147.0 (dt, J = 66.0 Hz, 14.2 Hz, 2F), −153.3 (m, 2F), −156.3 (m, 2F), −157.6 (t, J = 19.0 Hz, 2F). ^{31}P NMR (243 MHz, $CDCl_3$): δ 2.25 (s). HRMS (ESI-): calcd. for $C_{20}HF_{12}O_4P$ [M-H]-: 562.9348; found: 562.9346. IR (neat, cm^{-1}): 3383, 1664, 1618, 1523, 1479, 1379, 1208, 1094, 1017, 873. $[\alpha]_D^{25}$ -132.30 (c = 0.44, CH_2Cl_2, 99% ee). mp: Due to the decomposition of titled compound at 160°C, mp could not be determined.

General Procedure for (R)-$C_6H_5F_{10}$BINOL Phosphoric Acid Catalyzed Imino-Ene Reaction

To a toluene (1.0 mL) solution of α-methylene tetralin (**24**) (29 mg, 0.2 mmol, 1.0 equiv.) and F_{10}BINOL phosphoric acid (*R*)-**19** (3.4 mg, 0.005 mmol, 2.5 mol%) was added *N*-Fmoc imine **23** (65.5 mg, 0.2 mmol, 1.0 equiv.) at 40°C. After being stirred for 10 min, the solution was diluted with CH_2Cl_2 (2 mL), and the diluted solution was directly subjected onto silica gel column for purification. The mixture was purified by silica-gel column chromatography eluted with 10% EtOAc in hexane to give a product (9*H*-fluoren-9-yl)methyl-1,3-diphenylbut-3-enylcarbamate (**25**) (92 mg, 0.194 mmol, 97% yield, 80% *ee* (*R*)).

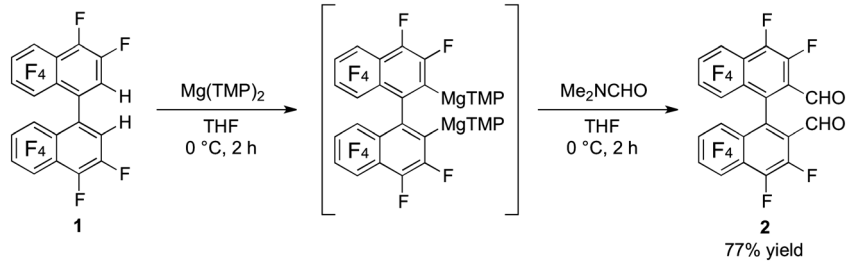
(*R*)-(9*H*-Fluoren-9-yl)methyl-2-(3,4-dihydronaphthalen-1-yl)-1-phenylethyl carbamate (25). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.8-7.0 (m, 17H), 5.76 (bs, 1H), 5.2-4.7 (m, 2H), 4.4-3.9 (m, 3H), 3.0-2.5 (m, 4H), 2.17 (bs, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 155.8, 144.1, 142.6, 141.4, 136.9, 134.2, 132.8, 128.7, 128.2, 127.9, 127.8, 127.5, 127.14, 127.13, 126.8, 126.4, 125.2, 122.7, 120.1, 66.7, 54.2, 47.4, 40.8, 28.4, 23.2. HRMS (ESI+): calcd. for $C_{31}H_{27}NO_2$[M+Na]+: 494.2091; found: 494.2090. IR (neat, cm^{-1}): 3408, 3327, 3063, 2936, 2882, 2829, 1704, 1508, 1450, 1330, 1246, 1130, 1033. UHPLC: DAICEL CHIRALPAK IB-3 2.1 × 150 mm, *n*-hexane:2-PrOH = 90:10, 0.5 mL/min, 40°C, 266 nm, 3.44 min (major) 7.85 (minor), 80% ee. $[\alpha]_D^{25}$ +10.2 (c = 0.81, CH_2Cl_2, 80% ee). mp: 141°C.

RESULTS AND DISCUSSION

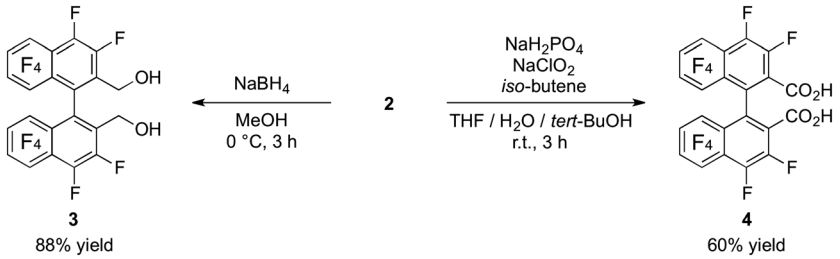
Syntheses of 2,2'-Functionalized F_{12}Binaphthyl Derivatives

The 3,3',4,4',5,5',6,6',7,7',8,8'-dodecafluoro-1,1'-binaphthalene (F_{12}binaphthalene, **1**) was readily prepared from commercially available octafluoronaphthalene based on a reported procedure.[31] In the pioneering work by Piers and co-workers,[31] selective functionalization at the 2,2'-position of **1** was achieved by the deprotonation using the poorly reducing, non-nucleophilic base lithium 2,2,6,6-tetramethylpiperidine (LiTMP) in the presence of tributyltin chloride as an electrophile. The labile fluoroaryllithium compound rapidly undergoes stannylation reaction at low temperature such as −78°C. In this context, we chose $Mg(TMP)_2$ as base.[41,42,47–50] We expected that since $Mg(TMP)_2$ has been known as a thermally stable base, its magnesiation strategy for fluoroaryls may open up to the reactions of thermally robust fluoroaryl amido Grignard reagents with a variety of electrophiles.[51,52]

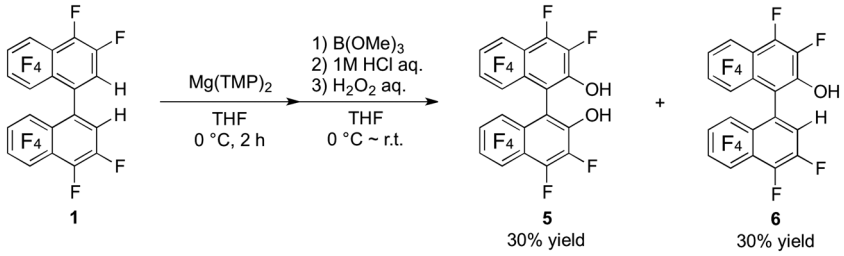
At first, we examined the magnesiation of **1** via the treatment of $Mg(TMP)_2$ in formylation reaction using *N*,*N*-dimethylformamide (DMF) as an electrophile (Scheme 1). We found that the magnesiation of **1** readily proceeded at 0°C followed by the reaction with DMF to give the



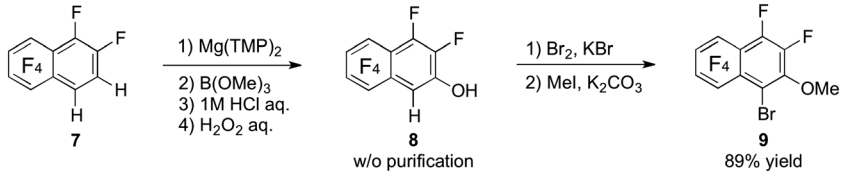
Scheme 1. Magnesiation of F_{12}binaphthalene **1** with $Mg(TMP)_2$[a] followed by the reaction with *N*,*N*-dimethylformamide. [a]$Mg(TMP)_2$ was prepared from LiTMP (2 equiv) and $MgBr_2$ (1 equiv).



Scheme 2. Derivatizations of F_{12}binaphthalene-2,2'-dicarbaldehyde **2**.



Scheme 3. Magnesiation of F_{12}binaphthalene **1** with $Mg(TMP)_2$ in borylation reaction.

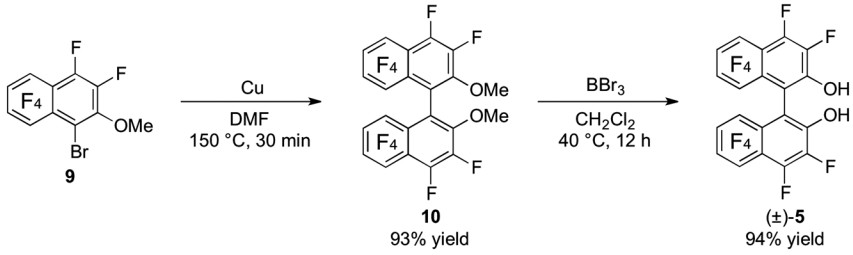


Scheme 4. Magnesiation of F_6naphthalene **7** with $Mg(TMP)_2$ in borylation reaction with trimethyl borate and its derivatization.

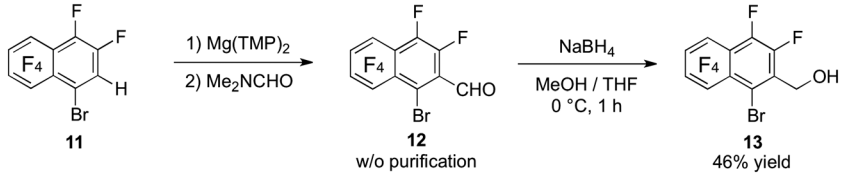
F_{12}binaphthalene-2,2'-dicarbaldehyde **2** in good yield. Compound **2** could be used to install acidic functionalities at the 2,2'-positions (Scheme 2). For instance, treatment with $NaBH_4$ in MeOH led to F_{12}binaphthalene-2,2'-dimethanol **3** in high yield. The Pinnick oxidation of **2** gave F_{12}binaphthalene-2,2'-dicarboxylic acid **4** in moderate yield.

Encouraged by the magnesiation of **1** with $Mg(TMP)_2$ in formylation reaction, we examined this method in borylation reaction to synthesize 2,2'-dihydroxy-F_{12}binaphthyl (F_{12}BINOL, **5**). Piers and colleagues reported the synthesis of F_{12}BINOL,[31] in which was the key to synthesizing D_2 symmetric homochiral bromoborane dimer via stannylation of **1**, followed by borylation with BBr_3 at high temperature. We envisioned that F_{12}BINOL **5** could be obtained more efficiently if 2,2'-borylation of **1** proceeded via the magnesiation of **1** with $Mg(TMP)_2$. We examined the direct borylation of **1** with trimethyl borate as an electrophile in THF at 0°C. However, the desired 2,2'-disubstituted compounds **5** was obtained in 30% yield since the 2-monosubstituted compound **6** was generated as an inseparable mixture (Scheme 3).

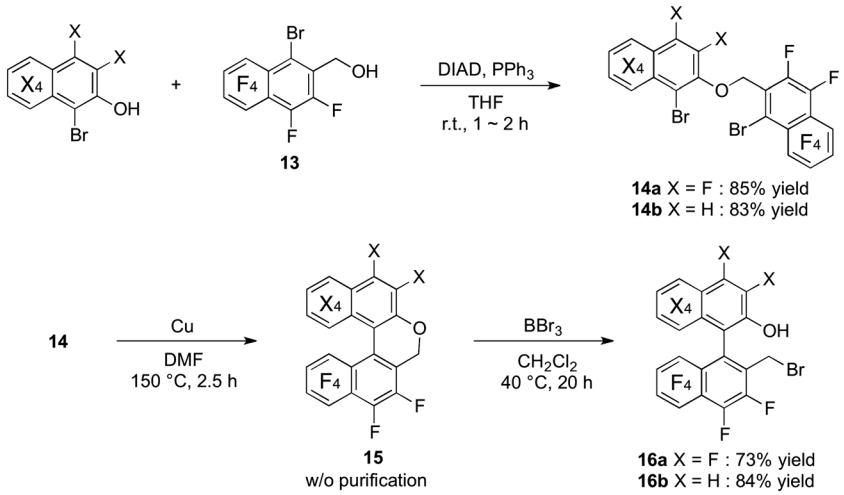
To explore the applicability of $Mg(TMP)_2$, we next examined the magnesiation of **7** and subsequent trapping with trimethyl borate (Scheme 4). Quenching with 1 M HCl aq. followed by the oxidation with aqueous hydrogen peroxide revealed smooth directed borylation, and F_6naphthalene-2-ol **8** was obtained in quantitative yield. To establish the practical method for F_{12}BINOL synthesis, compound **8** was transformed to a 1-bromo-2-methoxy F_6naphthalene **9**. Fortunately, 2-methoxy-F_{12}binaphthyl compound **10** was efficiently synthesized by copper-mediated coupling of **9** in



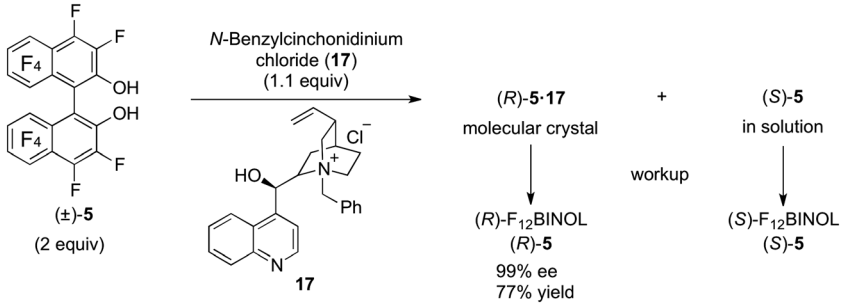
Scheme 5. Synthesis of F_{12}BINOL via Ullman coupling.



Scheme 6. Application of magnesiation using $Mg(TMP)_2$ to synthesize F_6naphthalenyl methanol **13**.



Scheme 7. Synthesis of unsymmetric F_6- and F_{12}binaphthyl compounds **16**.



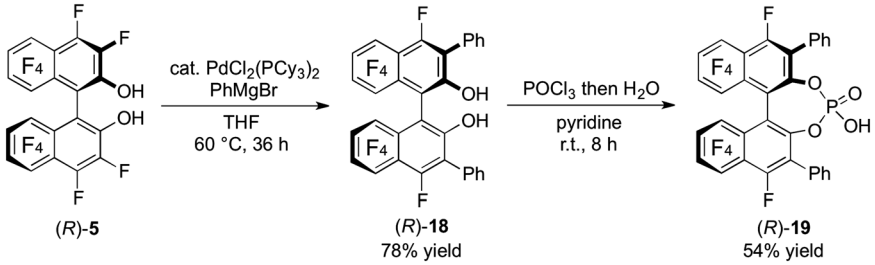
Scheme 8. Optical resolution of F_{12}BINOL.

DMF at 150°C for 30 min in 93% yield, and treatment of **10** with borontribromide in dichloromethane at 40°C for 12 h successfully gave F_{12}BINOL **5** in 94% yield (Scheme 5).

The magnesiation of F_6naphthalene with $Mg(TMP)_2$, followed by derivatization, and copper-mediated coupling realized construction of unsymmetric F_6naphthyl and F_{12}binaphthyl framework (Schemes 6, 7). For instance, the magnesiation of **11** with $Mg(TMP)_2$ in formylation reaction at −78°C for 6 h gave rise to the desired aldehyde **12**. Reduction of **12** with $NaBH_4$ in MeOH/THF at 0°C afforded (1-bromo-3,4,5,6,7,8-hexafluoronaphthalen-2-yl)methanol (**13**), which was used for the synthesis of coupling precursor **14** (Scheme 6). Treatment of **14** with freshly activated copper in DMF at 150°C furnished 5,6,7,8,9,10-hexafluoro-4*H*-benzo[*f*]naphtha[2,1-c]chromene (**15**), which without purification was treated with BBr_3 in CH_2Cl_2 at 40°C for 20 h, producing the 2'-(bromomethyl)-F_{12}-1,1'-binaphthalen-2-ol **16a** in 73% yield and 2'-(bromomethyl)-F_6-1,1'-binaphthalen-2-ol **16b** in 84% yield, respectively (Scheme 7).[43] It should be noted that this type of fluorinated binaphthalen-2-ols were synthesized for the first time that would become potentially useful intermediates in catalyst development of binaphthyl backbone.

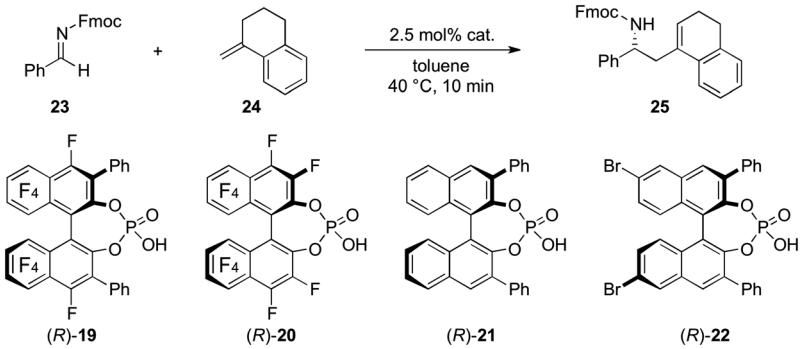
Synthesis of Optically Pure F_{10}BINOL and Its Derivatization to Chiral Mono-Phosphoric Acid

Among varieties of fluorinated binaphthyl compounds, F_{12}BINOL was chosen as one of the representatives for further development (Scheme 8). Optical resolution of F_{12}BINOL (±)-**5** was examined in the usual manner of BINOL.[44,45] Treatment of (±)-**5** with *N*-benzyl cinchonidinium chloride (**17**) in acetonitrile at 80°C for 4 h, at room temperature for 12 h, and then cooled to 0°C for 2 h afforded the solid of the complex of enantiomerically enriched **5** and **17**. After recrystallization from MeOH, followed by manipulation, the optically pure (*R*)-**5** was obtained in 77% yield.



Scheme 9. Synthesis of F_{10}BINOL and its derivatization to chiral mono-phosphoric acid (*R*)-**19**.

TABLE 1. Catalytic enantioselective imino-ene reaction of *N*-Fmoc imine 23 with alkene 24[a]



Entry	Catalyst	Yield (%)[b]	*ee* (%)[c]
1	(*R*)-**19**	97	80
2	(*R*)-**20**	84	19
3	(*R*)-**21**	35	50
4	(*R*)-**22**	43	48

[a]All reactions were performed with *N*-Fmoc imine **23** (0.2 mmol), catalyst (0.005 mmol), and α-methylenetetralin (**24**) (0.2 mmol) in 1 mL of toluene at 40°C for 10 min.
[b]Isolated yield.
[c]Determined by UHPLC analysis (Chiralpak IB-3).

Various aromatic substituents could be installed on the 3,3'-position of (*R*)-**5** to synthesize F_{10}BINOL (Scheme 9). We developed *ortho*-selective cross-coupling of F_{12}BINOL with Grignard reagent.[46] For instance, the reaction of (*R*)-**5** with the THF solution of phenyl magnesium bromide in the presence of 5 mol% $PdCl_2(PCy_3)_2$ in THF at 60°C for 36 h gave rise to the desired coupling product (*R*)-**18** in 78% yield. Furthermore, we transformed (*R*)-**18** to the chiral mono-phosphoric acid (*R*)-**19** in the general manner (Scheme 9).

Catalytic Asymmetric Imino-Ene Reaction Catalyzed by (R)-F_{10}BINOL Derived Chiral Mono-Phosphoric Acid

With the new chiral mono-phosphoric acid (*R*)-**19** in hand, we turned our attention to testing its performance regarding the catalyst activity and enantioselectivity in a catalytic enantioselective transformation. To this end, we assembled (*R*)-**20** with F_{12}binaphthyl, (*R*)-**21** with 3,3'-diphenyl binaphthyl, and (*R*)-**22** with 6,6'-dibromo-3,3'-diphenyl binaphthyl, and these were employed in the catalytic enantioselective imino-ene reaction (Table 1).[37–40] The reaction of *N*-Fmoc Imine **23** with α-methylenetetralin (**24**) in the presence of 2.5 mol% (*R*)-**19** revealed that the reaction proceeded smoothly only for 10 min to give an imino-ene product **25** in excellent yield with good enantioselectivity (entry 1). In contrast, when the reactions were conducted in the presence of (*R*)-**21** and (*R*)-**22**, both the yields and enantioselectivities were not sufficient (entries 3 and 4). We also found that the enantioselectivity showed a strong dependence on the phenyl substituents at the 3,3'-position of F_{10}binaphthyl. When the reaction was conducted in the presence of (*R*)-**20**, the enantioselectivity significantly dropped, although the yield was high (entry 2). These results suggest that F_{10}binaphthyl would be useful and valuable framework in the design of chiral Brønsted acid catalyst.

CONCLUSION

In summary, varieties of fluorinated binaphthyl compounds were synthesized using thermally stable Grignard reagents generated by the magnesiation of fluoroaryls with $Mg(TMP)_2$ and subsequent trapping with an appropriate electrophile. We showed that acidic functional groups such as alcohol, naphthol, carboxylic acid, and cyclic phosphoric acid can be installed at the 2,2'-position. Furthermore, aryl substitution of F_{12}BINOL at 3,3'-position was realized by palladium catalyzed *ortho*-selective cross-coupling with Grignard reagent, allowing easy access to F_{10}BINOL. The application of F_{10}BINOL-derived

chiral mono-phosphoric acid as a chiral Brønsted acid catalyst demonstrated the utility of F_{10}binaphthyl framework for catalyst activity and enantioselectivity in catalytic enantioselective imino-ene reaction.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article at the publisher's web site.

LITERATURE CITED

1. Noyori R. Asymmetric catalysis in organic synthesis. Wiley: New York; 1994.
2. Akiyama T. Stronger Brønsted acids. Chem Rev 2007; 107: 5744–5758.
3. Kampen D, Reisinger CM, List B. Chiral Brønsted acids for asymmetric organocatalysis. Top Curr Chem 2010; 291: 395–456.
4. Terada M. Chiral phosphoric acids as versatile catalysts for enantioselective transformations. Synthesis 2010; 12: 1929–1982.
5. Peng FZ, Shao ZH. Asymmetric organocatalytic cascade reactions catalyzed by chiral Brønsted acids. Curr Org Chem 2011; 15: 4144–4160.
6. Hirashima S, Yamamoto H. Development of new chiral Brønsted acid catalysis. J Synth Org Chem Jpn 2013; 71: 1116–1125.
7. Akiyama T. Phosphoric Acid catalyzed reactions of imines. In: Maruoka K editor, Science of synthesis, asymmetric organocatalysis 2, Brønsted base and acid catalysts, and additional topics. Georg Thieme: New York; 2012. p 169–217.
8. Terada M, Momiyama N. Phosphoric acid catalysis of reactions not involving imines. In: Maruoka K, editor. Science of synthesis, asymmetric organocatalysis 2, Brønsted base and acid catalysts, and additional topics. New York: Georg Thieme; 2012; Vol. 2, pp. 219–296.
9. Bhadury PS, Sun Z. Axially chiral Brønsted acid catalyzed transformations of electrophilic imines. Curr Organ Chem 2014; 18: 127–150.
10. Hashimoto T, Maruoka K. Design of axially chiral dicarboxylic acid for asymmetric Mannich reaction of arylaldehyde *N*-boc imines and diazo compounds. J Am Chem Soc 2007; 129: 10054–10055.
11. Hashimoto T, Maruoka K. Development of axially chiral dicarboxylic acid catalyzed asymmetric transformations. J Synth Org Chem Jpn 2013; 71: 472–479.
12. Akiyama T, Itoh J, Yokota K, Fuchibe K. Enantioselective Mannich-type reaction catalyzed by a chiral Brønsted acid. Angew Chem Int Ed 2004; 43: 1566–1568.
13. Uraguchi D, Terada M. Chiral Brønsted acid-catalyzed direct mannich reactions via electrophilic activation. J Am Chem Soc 2004; 126: 5356–5357.
14. Terada M, Kanomata K. Metal-free chiral phosphoric acid or chiral metal phosphate as active catalyst in the activation of *N*-acyl aldimines. Synlett 2011; 1255–1258.
15. Terada M. Binaphthol-derived phosphoric acid as a versatile catalyst for enantioselective carbon-carbon bond forming reactions. Chem Commun 2008; 4097–4112.
16. Akiyama T. Asymmetric C-C bond formation using chiral phosphoric acid. In: Christmann M, Brase S editors, Asymmetric synthesis II. Wiley-VCH: Weinheim; 2012. p 261–266.
17. Parmar D, Sugiono E, Raja S, Rueping M. Complete field guide to asymmetric BINOL-phosphate derived Brønsted acid and metal catalysis: history and classification by mode of activation; Brønsted acidity, hydrogen bonding, ion pairing, and metal phosphates. Chem Rev 2014; 114: 9047–9153.
18. Nakashima D, Yamamoto H. Design of chiral *N*-triflyl phosphoramide as a strong chiral Brønsted acid and its application to asymmetric Diels-Alder reaction. J Am Chem Soc 2006; 128: 9626–9627.
19. Jiao P, Nakashima D, Yamamoto H. Enantioselective 1,3-dipolar cycloaddition of nitrones with ethyl vinyl ether: the difference between Brønsted and Lewis acid catalysis. Angew Chem Int Ed 2008; 47: 2411–2413.
20. Cheon CH, Yamamoto H. Brøsted acid catalyst for the enantioselective protonation reaction. J Am Chem Soc 2008; 130: 9246–9247.
21. Čorić I, List B. Asymmetric spiroacetalization catalysed by confined Brønsted acids. Nature 2012; 483: 315–319.
22. Hatano M, Maki T, Moriyama K, Arinobe M, Ishihara K. Pyridinium 1,1'-binaphthyl-2,2'-disulfonates as highly effective chiral Brønsted acid-base combined salt catalysts for enantioselective Mannich-type reaction. J Am Chem Soc 2008; 130: 16858–16860.
23. Hatano M, Ishihara K. Highly practical BINOL-derived acid-base combined salt catalysts for the asymmetric direct Mannich-type reaction. Synthesis 2010; 3785–3801.
24. Hatano M, Ishihara K. Chiral 1,1'-binaphthyl-2,2'-disulfonic acid (BINSA) and its derivatives for asymmetric catalysis. Asian J Org Chem 2014; 3: 352–365.
25. Garcia-Garcia P, Lay F, Garcia-Garcia P, Rabalakos C, List B. A powerful chiral counteranion motif for asymmetric catalysis. Angew Chem Int Ed 2009; 48: 4363–4366.
26. Ratjen L, Garcia-Garcia P, Lay F, Beck ME, List B. Disulfonimide-catalyzed asymmetric vinylogous and bisvinylogous mukaiyama aldol reactions. Angew Chem Int Ed 2011; 50: 754–758.
27. Wang Q, Leutzsch M, van Gemmeren M, List B. Disulfonimide-catalyzed asymmetric synthesis of β3-amino esters directly from N-boc-amino sulfones. J Am Chem Soc 2013; 135: 15334–15337.
28. van Gemmeren M, Lay F, List B. Asymmetric catalysis using chiral, enantiopure disulfonimides. Aldrichim Acta 2014; 47: 3–13.
29. Yekta S, Krasnova LB, Mariampillai B, Picard CJ, Chen G, Pandiaraju S, Yudin AK. Preparation and catalytic applications of partially fluorinated binaphthol ligands. J Fluorine Chem 2004; 125: 517–525.
30. Yudin AK, Martyn LJP, Pandiaraju S, Zheng J, Lough A. F_8BINOL, an electronically perturbed version of BINOL with remarkable configurational stability. Org Lett 2000; 2: 41–44.
31. Morrison DJ, Riegel SD, Piers WE, Parvez M, McDonald R. 2,2'-Disubstituted F_{12}Binaphthyl derivatives: stannanes, boranes, and (*R*)-F_{12}BINOL. Chem Commun 2006; 2875–2877.
32. Han J, Tao FM. Correlations and predictions of pKa values of fluorophenols and bromophenols using hydrogen-bonded complexes with ammonia. J Phys Chem A 2006; 110: 257–263.
33. Yang C, Xue XS, Jin JL, Li X, Cheng JP. Theoretical study on the acidities of chiral phosphoric acids in dimethyl sulfoxide: hints for organocatalysis. J Org Chem 2013; 78: 7076–7085.
34. Kaupmees K, Tolstoluzhsky N, Raja S, Rueping M, Leito I. On the acidity and reactivity of highly effective chiral Brønsted acid catalysts: establishment of an acidity scale. Angew Chem Int Ed 2013; 52: 11569–11572.
35. Pandiaraju S, Chen G, Lough A, Yudin AK. Generation of highly enantioselective catalysts from the pseudoenatiomeric assembly of BINOL, F_8BINOL, and $Ti(OiPr)_4$. J Am Chem Soc 2001; 123: 3850–3851.
36. Suzuki S, Furuno H, Yokoyama Y, Inanaga J. Asymmetric fluorination of β-keto esters catalyzed by chiral rare earth perfluorinated organophosphates. Tetrahedron Asymmetry 2006; 17: 504–507.
37. Drury WJ III, Ferraris D, Cox C, Young B, Lectka T. A novel synthesis of α-amino acid derivatives through catalytic, enantioselective ene-reactions of α-imino esters. J Am Chem Soc 1998; 120: 11006–11007.
38. Ferraris D, Young BC, Dudding T, Drury WJ III, Ryzhkov L, Taggi AE, Lectka T. Catalytic, enantioselective alkylation of α-imino esters: the synthesis of nonnatural α-amino acid derivatives. J Am Chem Soc 2002; 124: 67–77.
39. Caplan N, Hancock FE, Bulman P, Philip C, Hutchings GJ. Heterogeneous enantioselective catalyzed carbonyl- and imino-ene reactions using copper bis(oxazoline) zeolite Y. Angew Chem Int Ed 2004; 43: 1685–1688.
40. Oliver LH, Puls LA, Tobey SL. Brønsted acid promoted imino-ene reactions. Tetrahedron Lett 2008; 49: 4636–4639.
41. Ooi T, Uematsu Y, Maruoka K. New, improved procedure for the synthesis of structurally diverse *N*-spiro C_2-symmetric chiral quaternary ammonium bromides. J Org Chem 2003; 68: 4576–4578.
42. Noji R, Fujiwara H, Okano K, Tokuyama H. Synthesis of substituted indoline and carbazole by benzyne-mediated cyclization-functionalization. Org Lett 2013; 15: 1946–1949.
43. Campeau LC, Parisien M, Jean A, Fagnou K. Catalytic direct arylation with aryl chlorides, bromides, and iodides: intramolecular studies leading to new intermolecular reactions. J Am Chem Soc 2006; 128: 581–590.

44. Wang Y, Sun J, Ding K. Practical method and novel mechanism for optical resolution of BINOL by molecular complexation with *N*-benzylcinchoninium chloride. Tetrahedron 2000; 56: 4447–4451.
45. Cai D, Hughes DL, Verhoeven TR, Reider PJ. Resolution of 1,1'-bi-2-naphthol. Organ Synth 2004; Coll10: 93.
46. Manabe K, Ishikawa S. Ortho-selective cross-coupling of fluorobenzenes with Grignard reagents: acceleration by electron-donating ortho-directing groups. Synthesis 2008; 2645–2649.
47. Eaton PE, Lee CH, Xiong Y. Magnesium amide bases and amido-Grignards. 1, Ortho magnesiation. J Am Chem Soc 1989; 111: 8016–8018.
48. Eaton PE, Xiong Y, Gilardi R. Systematic substitution on the cubane nucleus. synthesis and properties of 1,3,5-trinitrocubane and 1,3,5,7-tetranitrocuban. J Am Chem Soc 1993; 115: 10195–10202.
49. Henderson KW, Kerr WJ. Bisamides as reagents in synthesis. Chem Eur J 2001; 7: 3430–3437.
50. Haag B, Mosrin M, Ila H, Malakhov V, Knochel P. Regio- and chemoselective metalation of arenes and heteroarenes using hindered metal amide bases. Angew Chem Int Ed 2011; 50: 9794–9824.
51. Morgan MM, Marwitz AJV, Piers WE, Parvez M. Comparative Lewis acidity in fluoroarylboranes: $B(o\text{-}HC_6F_4)_3$, $B(p\text{-}HC_6F_4)_3$, and $B(C_6F_5)_3$. Organometallics 2013; 32: 317–322.
52. Mohr J, Durmaz M, Irran E, Oetreich M. Tris(5,6,7,8-tetrafluoronaphthalen-2-yl)borane, a partially fluorinated boron Lewis acid with fluorination distal to the boron atom. Organometallics 2014; 33: 1108–1111.