Electronic Supplementary Information

Synthesis of Unsymmetrically Substituted 2,2’-Dihydroxy-1,1’-biaryl Derivatives Using Organic Base-Catalyzed Ferrier-Type Rearrangement as the Key Step

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**General Information:** Infrared spectra were recorded on a JASCO FT/IR-4100 spectrometer. $^1$H NMR spectra were recorded on JEOL JNM-ECS400 (400 MHz) and JEOL JNM-ECA600 (600 MHz) spectrometer. Chemical shifts are reported in ppm from the solvent resonance as the internal and coupling constants (Hz). $^{13}$C NMR spectra were recorded on JEOL JNM-ECS400 (100 MHz) and JEOL JNM-ECA600 (150 MHz) spectrometer with complete proton decoupling. HPLC analysis was performed on a JASCO 2000 Plus system with UV and CD detectors and Daicel chiral stationary phase column Chiralpak IA-3 and AD-3. Mass spectra analysis was performed on a JEOL JMS-T100GC spectrometer, a JEOL JMS-700V spectrometer, and a Waters Xevo QTof-MS spectrometer at the Daiichisankyo Co., Ltd., a Thermo Fischer Scientific Exactive FT-ICR-MS spectrometer at the Graduate School of Engineering, Nagoya University, and a Bruker Daltonics sorariX FT-ICR-MS spectrometer at the Instrumental Analysis Center for Chemistry, Graduate School of Science, Tohoku University. Optical rotations were measured on a JASCO P-1020 digital polarimeter with a sodium lamp and reported as follows; $[\alpha]_D^T\degree C (c = g/100 mL, solvent)$. Analytical thin layer chromatography (TLC) was performed on Merck precoated TLC plates (silica gel 60 GF254, 0.25 mm). Flash column chromatography was performed on silica gel 60N (spherical, neutral, 40-50 μm; Kanto Chemical Co., Inc.).

All reactions were carried out under an argon (Ar) atmosphere in dried glassware.

**Material:** Unless otherwise noted, materials were purchased from Wako Pure Chemical Industries, Ltd., Tokyo Chemical Industry Co., Ltd., Aldrich Inc., and other commercial suppliers were used without purification. Chiral bicyclic guanidine catalyst 3 was prepared according to the literature procedure. Tetrahydrofuran was supplied from Kanto Chemical Co., Inc. as “Dehydrated solvent system”. Other solvents were purchased from commercial suppliers as dehydrated solvents, and used under argon atmosphere.
Experimental Procedure

1. Preparation of \(N, N\)-Dimethylbenzamide 6

To a solution of 2-bromo-6-methoxynaphthalene (8.54 g, 36 mmol) and phthalic anhydride (2.96 g, 20 mmol) in \(\text{CH}_2\text{Cl}_2\) (40 mL) was added \(\text{AlCl}_3\) (4.00 g, 30 mmol) at 0 °C. After the reaction mixture was stirred at room temperature for 1 day, the reaction was quenched by saturated aqueous \(\text{NH}_4\text{Cl}\) (40 mL), and the water layer was extracted with \(\text{CH}_2\text{Cl}_2\) (30 mL × 3). The combined organic layers were added aqueous \(\text{NaOH}\) (3 \(\text{N}\)) until \(\text{pH}\) 10, stirred for 5 min, and extracted with \(\text{Et}_2\text{O}\) (50 mL). The water layer was added \(\text{HCl}\) (12 \(\text{N}\)) until \(\text{pH}\) 1, stirred for 20 min, and extracted with \(\text{CH}_2\text{Cl}_2\) (30 mL × 3). The combined organic layers were washed with brine, dried over \(\text{Na}_2\text{SO}_4\), and concentrated under reduced pressure after filtration. The residue was used for the next step without further purification.

To a mixture of obtained product, \(\text{Zn}\) dust (13.1 g, 200 mmol), and \(\text{CuSO}_4\) (128 mg, 0.8 mmol) was added aqueous \(\text{NH}_3\) (28 %, 100 mL). The reaction mixture was stirred at reflux for 1 day with addition of aqueous \(\text{NH}_3\) (40 mL) every 8 h. After filtration, the solution was added \(\text{HCl}\) (12 \(\text{N}\)) until \(\text{pH}\) 1, and extracted with \(\text{CH}_2\text{Cl}_2\) (30 mL × 3). The combined organic layers were added aqueous \(\text{NaOH}\) (3 \(\text{N}\)) until \(\text{pH}\) 10, stirred for 5 min, and extracted with \(\text{Et}_2\text{O}\) (50 mL). The water layer was added \(\text{HCl}\) (12 \(\text{N}\)) until \(\text{pH}\) 1, stirred for 20 min, and extracted with \(\text{CH}_2\text{Cl}_2\) (40 mL × 3). The combined organic layers were washed with brine, dried over \(\text{Na}_2\text{SO}_4\), and concentrated under reduced pressure after filtration. The residue was used for the next step without further purification.

To a solution of obtained product in \(\text{CH}_2\text{Cl}_2\) (40 mL) was added \(\text{DMF}\) (0.153 ml, 0.2
mmol) and oxalyl chloride (6.86 mL, 80 mmol) at 0 ºC. After the reaction mixture was stirred for 3 h, the mixture was pumped up for 2 h. The residue was added dimethylamine hydrochloride (2.12 g, 26 mmol), CH₂Cl₂ (40 mL), and NEt₃ (7.61 mL, 60 mmol) at 0 ºC. After the reaction mixture was stirred at room temperature overnight, the reaction was quenched by saturated aqueous NH₄Cl (20 mL), and the water layer was extracted with CH₂Cl₂ (20 mL × 3). The combined organic layers were washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure after filtration. The residue was purified by silica gel column chromatography (hexane/AcOEt = 1/1 as the eluent) to give product 6a (4.22 g, 66% yield from phthalic anhydride).

\[ \text{N,N-Dimethylbenzamide} \ 6b, 6c, 6d \]

\[ 6b, 6c, 6d \]

were prepared according to the modified literature procedures.

2. Representative Procedure for the Synthesis of 1a

To a solution of LDA [prepared from n-BuLi (1.6 M solution in hexane, 2.71 mL, 4.4 mmol) and diisopropylamine (0.617 mL, 4.4 mmol) at 0 ºC in THF (8 mL)] was added a solution of N,N-dimethylbenzamide 6a (1.28 g, 4.0 mmol) in THF (8 mL) at -78 ºC. The dark blue solution was stirred for 1 h, and transferred into a solution of propionyl chloride (0.489 mL, 5.6 mmol) in THF (4 mL) at -78 ºC. After the reaction mixture was stirred for 2 h, the reaction was quenched by saturated aqueous NH₄Cl (40 mL), and the water layer was extracted with AcOEt (30 mL × 3). The combined organic layers were washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure after filtration. The residue was passed through shortpass column chromatography.
(hexane/AcOEt = 1/1 as the eluent). The obtained product was used for the next step without further purification.

To a solution of the obtained product in CH$_2$Cl$_2$ (8 mL) was added p-toluenesulfonic acid monohydrate (1.67 g, 8.8 mmol) at 0 °C. After the reaction mixture was stirred at room temperature overnight, the reaction was quenched by saturated aqueous NaHCO$_3$ (50 mL), and the water layer was extracted with CH$_2$Cl$_2$ (30 mL × 3). The combined organic layers were washed with brine, dried over Na$_2$SO$_4$, and concentrated under reduced pressure after filtration. The residue was purified by silica gel column chromatography (hexane/AcOEt = 2/1 as the eluent) to give the product 7 (601 mg, 46% yield from 6a).

To a solution of isochromenone 7 (601 mg, 1.82 mmol) in CH$_2$Cl$_2$ (9 mL) was added DIBAL-H (1.03 M solution in hexane, 1.94 mL) at -78 °C. After the reaction mixture was stirred for 2 h, the reaction was quenched by saturated aqueous NH$_4$Cl (10 mL), and the water layer was extracted with CH$_2$Cl$_2$ (20 mL × 3). The combined organic layers were washed with brine, dried over Na$_2$SO$_4$, added one drop of triethylamine (to avoid self condensation), and concentrated under reduced pressure after filtration. The residue was purified by silica gel column chromatography (hexane/Et$_2$O = 2/1 as the eluent) to give the product 1a (567 mg, 94% yield).

3. Representative Procedure for the TBD Base-Catalyzed Synthesis of 2a

To a sealed tube were added isochromenol 1a (66.4 mg, 0.2 mmol), THF (1 mL), and TBD (2.78 mg, 20 μmol) under an Ar atmosphere. After the reaction mixture was stirred at 100 °C for 12 h, the reaction was quenched by saturated aqueous NH$_4$Cl and
the water layer was extracted with AcOEt (20 mL × 3). The combined organic layers were washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure after filtration. The residue was purified by silica gel column chromatography (hexane/AcOEt = 8/1 as the eluent) to give the product 2a (56.8 mg, 90% yield).

4. Procedure for the Chiral Bicyclic Guanidine Base-Catalyzed Enantioselective Synthesis of 2a

To a solution of isochromenol 1a (33.2 mg, 0.1 mmol) in THF (0.5 mL) was added (S,S)-3 (5.83 mg, 20 µmol) under an Ar atmosphere. After the reaction mixture was stirred at 100 °C for 12 h, the reaction was quenched by saturated aqueous NH₄Cl and the water layer was extracted with AcOEt (20 mL × 3). The combined organic layers were washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure after filtration. The residue was purified by silica gel column chromatography (hexane/AcOEt = 8/1 as the eluent) to give the product 2a (9.4 mg, 30% yield, 12% ee (S)).

5. Procedure for the Demethylation of 2a

To a solution of naphthol 2a (1.16 g, 3.7 mmol) in CH₂Cl₂ (12 mL) was added BBr₃ (2.0 mL, 21 mmol) at 0 °C. After the reaction mixture was stirred for 2 h, the reaction was quenched by water (30 mL), and the water layer was extracted with CH₂Cl₂ (20 mL × 3). The combined organic layers were washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure after filtration. The residue was purified by silica gel column chromatography (hexane/AcOEt = 4/1 as the eluent) to give the product 4 in quantitative yield.
6. Resolution of 4

Resolution of 4 was performed according to the literature procedure.\textsuperscript{7} To a solution of racemic binaphthol derivative 4 (718 mg, 2.4 mmol) in toluene (4 mL) was added (S,S)-5 (507 mg, 2.4 mmol). After the mixture was heated until turning the suspension to be clear, the heated solution was allowed to stand at room temperature. White crystalline solid was collected by filtration, and dissolved in methanol. The solution was added aqueous HCl (1 N) and stirred for 30 min. CH$_2$Cl$_2$ was poured into the reaction mixture to dissolve the precipitate, the organic layer was separated from the water layer, and the water layer was extracted with CH$_2$Cl$_2$. The combined organic layers were washed with brine, dried over Na$_2$SO$_4$, and concentrated under reduced pressure after filtration. The residue was purified by silica gel column chromatography (hexane/AcOEt = 4/1 as the eluent) to give the product (R)-4 (158 mg, 22% yield, 95% ee).

Absolute configuration was determined in accordance with the literature value of the optical rotation.\textsuperscript{8}

Optical rotation of prepared sample 4: $[\alpha]_D^{20.3} = +22.1$ ($c = 1.5$, CDCl$_3$) (95% ee)

Optical rotation of literature value of (R)-4: $[\alpha]_D^{26} = +25$ ($c = 1.5$, CDCl$_3$)

7. Racemization of 4

To a solution of (R)-4 (60.0 mg, 0.2 mmol, 95% ee) in THF (1 mL) was added TBD (2.78 mg, 20 $\mu$mol) under an Ar atmosphere. The reaction mixture was stirred at 100 °C. Enantiomeric excess was dropped as shown in the following Table.

<table>
<thead>
<tr>
<th>time (h)</th>
<th>ee (%)</th>
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<tr>
<td>12</td>
<td>57</td>
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<tr>
<td>24</td>
<td>43</td>
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<td>36</td>
<td>29</td>
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3-Ethyl-4-(2-methoxynaphthalen-1-yl)-1H-isochromen-1-ol (1a): white solid; R<sub>f</sub> = 0.20 (hexane/Et<sub>2</sub>O = 2/1); diastereomeric mixture (ca. 1:1 mixture) <sup>1</sup>H NMR (600 MHz, C<sub>6</sub>D<sub>6</sub>) δ 1.08 (3H, t, J = 7.8 Hz), 1.09 (3H, t, J = 7.8 Hz), 2.07 (2H, q, J = 7.8 Hz), 2.19 (2H, q, J = 7.8 Hz), 3.20 (3H, s), 3.32 (3H, s), 6.22 (1H, s), 6.37 (1H, s), 6.54 (1H, d, J = 7.8 Hz), 6.63 (1H, d, J = 7.8 Hz), 6.82-6.97 (5H, m), 7.04-7.21 (7H, m), 7.68-7.77 (5H, m), 8.10 (1H, d, J = 7.8 Hz); <sup>13</sup>C NMR (150 MHz, C<sub>6</sub>D<sub>6</sub>) δ 11.20, 11.37, 25.61, 25.73, 55.87, 56.09, 93.19, 93.69, 106.39, 113.67, 113.76, 119.51, 119.69, 123.09, 123.11, 124.06, 124.15, 125.40, 125.56, 125.82, 125.89, 126.03, 126.21, 127.12, 127.28, 128.29, 128.36, 128.53, 129.26, 129.82, 129.67, 129.69, 129.74, 129.89, 131.65, 131.95, 134.88, 135.19, 152.76, 152.84, 155.50, 155.52; IR (ATR) 3396, 2971, 2936, 1641, 1507, 1489, 1260, 1246, 1061, 993 cm<sup>-1</sup>; HRMS (ESI) Calcd for C<sub>22</sub>H<sub>19</sub>O<sub>3</sub> (M-): 331.1334, Found 331.1333.

3-Butyl-4-(2-methoxynapthalen-1-yl)-1H-isochromen-1-ol (1b): white solid; R<sub>f</sub> = 0.30 (hexane/Et<sub>2</sub>O = 2/1); diastereomeric mixture (ca. 1:1 mixture) <sup>1</sup>H NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>) δ 0.67 (3H, t, J = 7.6 Hz), 0.67 (3H, t, J = 7.2 Hz), 1.05-1.20 (4H, m), 1.60-1.73 (4H, m), 2.06-2.20 (2H, m), 2.26 (2H, t, J = 7.6 Hz), 3.20 (3H, s), 3.34 (3H, s), 6.23 (1H, s), 6.38 (1H, s), 6.56 (1H, d, J = 7.6 Hz), 6.64 (1H, d, J = 7.6 Hz), 6.85-6.97 (6H, m), 7.04-7.10 (3H, m), 7.16-7.22 (3H, m), 7.69-7.74 (4H, m), 7.78-7.80 (4H, m), 8.09 (1H, d, J = 8.0 Hz); <sup>13</sup>C NMR (100 MHz, C<sub>6</sub>D<sub>6</sub>) δ 13.97, 22.37, 22.53, 28.96, 29.09, 31.80, 32.00, 55.78, 55.91, 93.23, 93.72, 107.01, 107.10, 113.54, 119.49, 119.63, 123.07, 123.13, 124.04, 124.13, 125.35, 125.61, 125.79, 125.89, 126.09, 126.22, 127.07, 127.29, 128.49, 129.30, 129.64, 129.71, 129.84, 131.65, 131.97, 134.87, 135.19, 151.92, 152.09, 155.52; IR (ATR) 3397, 2955, 2929, 1639, 1507, 1489, 1246, 1249, 1060, 984 cm<sup>-1</sup>; HRMS (Cl) Calcd for C<sub>27</sub>H<sub>33</sub>O<sub>3</sub>Si (M+SiMe<sub>3</sub>)<sup>+</sup>: 433.2199, Found 433.2195.
HRMS sample was prepared from mixing 1b and N,O-bis(trimethylsilyl)trifluoroacetamide, before HRMS analysis.

3-Isobutyl-4-(2-methoxynaphthalen-1-yl)-1H-isochromen-1-ol (1c): white solid; Rf = 0.15 (hexane/Et2O = 4/1); diastereomeric mixture (ca. 1:1 mixture) \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)) \(\delta\) 0.76 (3H, d, \(J = 6.8\) Hz), 0.79 (3H, d, \(J = 6.4\) Hz), 0.84 (3H, d, \(J = 6.8\) Hz), 0.86 (3H, d, \(J = 6.4\) Hz), 1.97 (1H, dd, \(J = 14.0, 8.8\) Hz), 2.14-2.19 (2H, m), 2.23-2.34 (3H, m), 3.21 (3H, s), 3.34 (3H, s), 6.25 (1H, s), 6.39 (1H, s), 6.56 (1H, d, \(J = 7.6\) Hz), 6.63 (1H, d, \(J = 8.0\) Hz), 6.84-6.97 (6H, m), 7.04-7.11 (3H, m), 7.16-7.24 (3H, m), 7.69-7.74 (4H, m), 7.78-7.81 (1H, m), 8.09 (1H, d, \(J = 8.8\) Hz); \(^{13}\)C NMR (100 MHz, C\(_6\)D\(_6\)) \(\delta\) 21.99, 22.57, 22.82, 23.06, 26.53, 26.57, 41.08, 41.26, 55.76, 93.20, 93.66, 107.82, 107.89, 113.33, 113.50, 119.46, 119.53, 123.12, 123.21, 124.02, 124.09, 125.36, 125.63, 125.76, 125.90, 126.24, 126.28, 127.00, 127.29, 128.41, 128.53, 129.29, 129.32, 129.56, 129.61, 129.69, 129.79, 131.63, 131.96, 134.79, 135.14, 151.35, 151.57, 155.48, 155.56; IR (ATR) 3392, 2953, 1637, 1508, 1463, 1266, 1250, 1060, 985 cm\(^{-1}\); HRMS (CI) Calcd for C\(_{27}\)H\(_{33}\)O\(_3\)Si (M+SiMe\(_3\))\(^+\) 433.2199, Found 433.2184. HRMS sample was prepared from mixing 1c and N,O-bis(trimethylsilyl)trifluoroacetamide, before HRMS analysis.

3-(Methoxymethyl)-4-(2-methoxynaphthalen-1-yl)-1H-isochromen-1-ol (1d): white solid; Rf = 0.20 (hexane/AcOEt = 2/1); diastereomeric mixture (ca. 1:1 mixture) \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)) \(\delta\) 3.05 (3H, s), 3.10 (3H, s), 3.17 (3H, s), 3.26 (3H, s), 3.82 (1H, d, \(J = 12.4\) Hz), 3.99 (1H, d, \(J = 12.4\) Hz), 4.01 (1H, d, \(J = 12.4\) Hz), 4.26 (1H, d, \(J = 12.4\) Hz), 6.30 (1H, s), 6.41 (1H, s), 6.57 (1H, d, \(J = 8.0\) Hz), 6.64 (1H, d, \(J = 8.0\) Hz), 6.80-6.88 (2H, m), 6.92-6.97 (4H, m), 7.00 (1H, d, \(J = 8.8\) Hz), 7.07 (2H, t, \(J = 8.0\) Hz), 7.12-7.21 (3H, m), 7.67-7.73 (5H, m), 8.09-8.11 (1H, m); \(^{13}\)C NMR (100 MHz, C\(_6\)D\(_6\)) \(\delta\)
55.91, 56.21, 57.45, 57.60, 69.78, 69.87, 93.44, 93.69, 110.80, 110.93, 113.41, 113.94, 118.32, 118.47, 123.56, 123.70, 124.12, 124.20, 125.29, 125.87, 126.06, 126.45, 126.88, 127.08, 127.33, 127.41, 128.53, 129.12, 129.17, 129.50, 129.71, 129.75, 129.99, 130.05, 131.29, 131.47, 135.01, 135.10, 147.27, 147.49, 155.56, 155.73; IR (ATR) 3372, 2937, 1591, 1508, 1460, 1267, 1249, 1090, 979 cm\(^{-1}\); HRMS (ESI) Calcd for C\(_{22}\)H\(_{19}\)O\(_4\) (M\(^-\)) 347.1283, Found 347.1285.

![Image](4-(2-Methoxynaphthalen-1-yl)-3-((methylthio)methyl)-1H-isochromen-1-ol (1e): white solid; \(R_f = 0.40\) (hexane/AcOEt = 2/1); diastereomeric mixture (ca. 1:1 mixture) \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)) \(\delta\) 1.75 (3H, s), 1.90 (3H, s), 3.03 (1H, d, \(J = 14.0\) Hz), 3.09 (1H, d, \(J = 14.0\) Hz), 3.19 (3H, s), 3.28-3.29 (5H, m), 6.21 (1H, s), 6.33 (1H, s), 6.55 (1H, d, \(J = 8.0\) Hz), 6.60 (1H, d, \(J = 7.2\) Hz), 6.81-6.88 (2H, m), 7.02-7.07 (2H, m), 7.11-7.22 (4H, m), 7.66-7.74 (5H, m), 8.00-8.04 (1H, m); \(^{13}\)C NMR (100 MHz, C\(_6\)D\(_6\)) \(\delta\) 15.49, 15.65, 34.89, 35.20, 55.78, 55.87, 93.31, 93.69, 108.99, 109.37, 113.45, 113.48, 118.41, 123.36, 123.56, 124.13, 125.58, 125.65, 125.87, 126.42, 126.49, 126.71, 127.17, 127.47, 127.75, 128.44, 128.53, 128.98, 129.23, 129.27, 129.53, 129.68, 130.02, 130.07, 131.42, 131.73, 134.67, 135.02, 147.79, 148.05, 155.33, 155.670; IR (ATR) 3394, 2918, 1621, 1508, 1460, 1267, 1249, 1090, 979 cm\(^{-1}\); HRMS (ESI) Calcd for C\(_{22}\)H\(_{16}\)O\(_4\)S (M\(^-\)) 363.1055, Found 363.1052.

![Image](3-Ethyl-4-(2,6-dimethoxynaphthalen-5-yl)-1H-isochromen-1-ol (1f): white solid; \(R_f = 0.25\) (hexane/Et\(_2\)O = 1/1); diastereomeric mixture (ca. 1:1 mixture) \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)) \(\delta\) 1.11 (6H, t, \(J = 7.6\) Hz), 2.11 (2H, q, \(J = 7.6\) Hz), 2.23 (2H, q, \(J = 7.6\) Hz), 3.21 (3H, s), 3.36 (3H, s), 3.40 (3H, s), 3.44 (3H, s), 6.20 (1H, s), 6.36 (1H, s), 6.61 (1H, d, \(J = 8.0\) Hz), 6.70 (1H, d, \(J = 7.6\) Hz), 6.87 (1H, td, \(J = 7.6, 1.6\) Hz), 6.89-6.96 (4H, m), 7.02-7.07 (2H, m), 7.11-7.22 (4H, m), 7.66-7.74 (5H, m), 8.00-8.04 (1H, m); \(^{13}\)C NMR (100 MHz, C\(_6\)D\(_6\)) \(\delta\) 15.49, 15.65, 34.89, 35.20, 55.78, 55.87, 93.31, 93.69, 108.99, 109.37, 113.45, 113.48, 118.41, 123.36, 123.56, 124.13, 125.58, 125.65, 125.87, 126.42, 126.49, 126.71, 127.17, 127.47, 127.75, 128.44, 128.53, 128.98, 129.23, 129.27, 129.53, 129.68, 130.02, 130.07, 131.42, 131.73, 134.67, 135.02, 147.79, 148.05, 155.33, 155.670; IR (ATR) 3394, 2918, 1621, 1508, 1267, 1250, 1061, 979 cm\(^{-1}\); HRMS (ESI) Calcd for C\(_{22}\)H\(_{16}\)O\(_3\)S (M\(^-\)) 363.1055, Found 363.1052.
7.01 (1H, d, J = 8.8 Hz), 7.04-7.12 (6H, m), 7.64 (1H, d, J = 8.8 Hz), 7.65 (1H, d, J = 8.8 Hz), 7.69 (1H, d, J = 8.8 Hz); 13C NMR (100 MHz, C6D6) δ 11.23, 11.40, 25.64, 25.77, 54.77, 54.85, 56.07, 56.26, 93.20, 93.70, 106.34, 106.40, 106.55, 114.39, 114.42, 119.94, 120.02, 120.14, 120.32, 123.13, 123.19, 125.38, 125.79, 125.88, 126.22, 127.30, 128.59, 129.22, 129.25, 129.77, 130.32, 130.60, 130.67, 130.89, 131.74, 132.06, 152.71, 152.83, 154.05, 154.10, 156.88, 157.00; IR (ATR) 3400, 2969, 2937, 1596, 1506, 1338, 1251, 993 cm⁻¹; HRMS (ESI) Calcd for C23H21O4 (M⁻) 361.1440, Found 361.1432.

3-Ethyl-4-(2,7-dimethoxynaphthalen-8-yl)-1H-isochromen-1-ol (1g): white solid; Rf = 0.25 (hexane/AcOEt = 2/1); diastereomeric mixture (ca. 1:1 mixture) ¹H NMR (400 MHz, C₆D₆) δ 1.11 (3H, t, J = 7.6 Hz), 1.15 (3H, t, J = 7.6 Hz), 2.17 (2H, q, J = 7.6 Hz), 2.23 (2H, q, J = 7.6 Hz), 3.18 (6H, m), 3.36 (3H, s), 3.43 (3H, s), 6.19 (1H, s), 6.37 (1H, s), 6.69 (1H, d, J = 7.2 Hz), 6.78 (1H, d, J = 8.0 Hz), 6.84 (1H, d, J = 8.4 Hz), 6.89 (1H, td, J = 7.6, 1.6 Hz), 6.91-6.99 (4H, m), 7.05-7.09 (2H, m), 7.14-7.18 (2H, m), 7.20 (1H, s), 7.48 (1H, s), 7.59 (1H, d, J = 8.8 Hz), 7.61 (1H, d, J = 8.8 Hz), 7.64 (1H, d, J = 8.8 Hz), 7.69 (1H, d, J = 8.8 Hz); ¹³C NMR (100 MHz, C₆D₆) δ 11.33, 11.41, 25.65, 25.70, 54.62, 54.84, 55.75, 55.95, 93.19, 93.74, 103.03, 104.00, 106.82, 107.35, 110.79, 110.85, 117.41, 117.59, 118.44, 118.59, 123.07, 123.14, 125.18, 125.37, 125.46, 125.63, 125.88, 126.31, 128.71, 129.32, 129.41, 129.46, 129.77, 129.98, 130.15, 131.50, 131.85, 136.33, 136.76, 152.48, 152.72, 156.15, 159.14, 159.55; IR (ATR) 3418, 2969, 2937, 1624, 1509, 1492, 1259, 1222, 1056, 1036 cm⁻¹; HRMS (Cl) Calcd for C₂₆H₃₁O₄Si (M⁺+SiMe₃)⁺ 435.1992, Found 435.1984. HRMS sample was prepared from mixing 1g and N,O-bis(trimethylsilyl)trifluoroacetamide, before HRMS analysis.
3-Ethyl-4-(2-methoxy-4,6-dimethylphenyl)-1H-isochromen-1-ol (1h): white solid; Rf = 0.25 (hexane/Et2O = 2/1); diastereomeric mixture (ca. 1:1 mixture) 1H NMR (400 MHz, C6D6) δ 1.18 (6H, t, J = 7.2 Hz), 2.11-2.12 (6H, m), 2.18 (2H, q, J = 7.2 Hz), 2.23-2.29 (8H, m), 3.07 (3H, s), 3.24 (3H, s), 6.16 (1H, s), 6.29 (1H, s), 6.38 (1H, s), 6.48 (1H, s), 6.69 (1H, s), 6.71 (1H, s), 6.78 (1H, d, J = 8.8 Hz), 6.81 (1H, d, J = 8.0 Hz), 6.94-7.07 (6H, m); 13C NMR (100 MHz, C6D6) δ 11.16, 11.31, 19.58, 19.95, 21.66, 25.27, 25.50, 55.01, 55.21, 93.04, 93.61, 107.42, 107.61, 109.40, 109.58, 122.12, 122.38, 122.62, 123.47, 123.64, 125.43, 125.82, 126.19, 128.80, 129.20, 129.22, 130.00, 131.23, 131.63, 138.14, 138.23, 139.42, 139.87, 150.48, 156.01; IR (ATR) 3406, 2967, 2934, 1643, 1608, 1574, 1462, 1311, 1094, 993 cm\(^{-1}\); HRMS (CI) Calcd for C23H31O3Si (M+SiMe\(_3\))\(^+\) 383.2043, Found 383.2040. HRMS sample was prepared from mixing 1h and N,O-bis(trimethylsilyl)trifluoroacetamide, before HRMS analysis.

1-(2-Methoxynaphthalen-1-yl)-3-methylnaphthalen-2-ol (2a): white solid; Rf = 0.35 (hexane/AcOEt = 4/1); HPLC analysis Chiralpak AD-3 (hexane/i-PrOH = 95/5, 1.0 mL/min, 254 nm, 30 °C); 8.0 (major), 23.5 min; 12% ee (S); 1H NMR (400 MHz, CDCl\(_3\)) δ 2.51 (3H, s), 3.80 (3H, s), 4.96 (1H, s), 6.97 (1H, d, J = 8.0 Hz), 7.13-7.17 (2H, m), 7.25-7.29 (2H, m), 7.36 (1H, td, J = 7.6, 1.2 Hz), 7.49 (1H, d, J = 9.2 Hz), 7.73 (1H, s), 7.78 (1H, d, J = 8.4 Hz), 7.90 (1H, d, J = 8.0 Hz), 8.05 (1H, d, J = 9.2 Hz); 13C NMR (100 MHz, CDCl\(_3\)) δ 17.07, 56.65, 113.78, 114.37, 115.56, 123.12, 124.13, 124.55, 124.93, 125.36, 126.52, 127.28, 127.31, 128.10, 129.05, 129.25, 129.41, 130.99, 132.50, 134.06, 150.48, 156.01; IR (ATR) 3530, 3057, 2934, 2839, 1620, 1592, 1507, 1266, 1249, 1205, 1077 cm\(^{-1}\); HRMS (CI) Calcd for C\(_{22}\)H\(_{19}\)O\(_2\) (M+H)\(^+\) 315.1385, Found 315.1389.

cf. 86% ee (R): [α]\(_D\)\(^{22,4}\) = -25.5 (c = 0.75, CHCl\(_3\)).

1H NMR (400 MHz, CDCl\(_3\)) δ 2.51 (3H, s), 3.80 (3H, s), 4.96 (1H, s), 6.97 (1H, d, J = 8.0 Hz), 7.13-7.17 (2H, m), 7.25-7.29 (2H, m), 7.36 (1H, td, J = 7.6, 1.2 Hz), 7.49 (1H, d, J = 9.2 Hz), 7.73 (1H, s), 7.78 (1H, d, J = 8.4 Hz), 7.90 (1H, d, J = 8.0 Hz), 8.05 (1H, d, J = 9.2 Hz); 13C NMR (100 MHz, CDCl\(_3\)) δ 17.07, 56.65, 113.78, 114.37, 115.56, 123.12, 124.13, 124.55, 124.93, 125.36, 126.52, 127.28, 127.31, 128.10, 129.05, 129.25, 129.41, 130.99, 132.50, 134.06, 150.48, 156.01; IR (ATR) 3530, 3057, 2934, 2839, 1620, 1592, 1507, 1266, 1249, 1205, 1077 cm\(^{-1}\); HRMS (CI) Calcd for C\(_{22}\)H\(_{19}\)O\(_2\) (M+H)\(^+\) 315.1385, Found 315.1389.

cf. 86% ee (R): [α]\(_D\)\(^{22,4}\) = -25.5 (c = 0.75, CHCl\(_3\)).
1-(2-Methoxynaphthalen-1-yl)-3-propynaphthalen-2-ol (2b): white solid; R\text{f} = 0.70 (hexane/AcOEt = 2/1); \text{\textsuperscript{1}}H NMR (400 MHz, CDCl\textsubscript{3}) \delta 1.04 (3H, t, J = 7.6 Hz), 1.81 (2H, m), 2.85 (2H, m), 3.80 (3H, s), 4.94 (1H, s), 6.97 (1H, d, J = 7.6 Hz), 7.13-7.16 (2H, m), 7.25-7.29 (2H, m), 7.36 (1H, t, J = 7.6 Hz), 7.48 (1H, d, J = 8.8 Hz), 7.72 (1H, s), 7.80 (1H, d, J = 8.0 Hz), 7.89 (1H, d, J = 8.4 Hz), 8.05 (1H, d, J = 8.4 Hz); \text{\textsuperscript{13}}C NMR (100 MHz, CDCl\textsubscript{3}) \delta 14.12, 22.84, 32.93, 56.65, 113.85, 114.52, 115.67, 123.07, 124.11, 124.51, 124.92, 125.38, 127.26, 127.38, 128.10, 128.43, 129.02, 129.42, 130.89, 130.97, 132.39, 134.08, 150.27, 156.03; IR (ATR) 3532, 2958, 2932, 1592, 1507, 1266, 1249, 1203 cm\textsuperscript{-1}; HRMS (CI) Caled for C\textsubscript{24}H\textsubscript{23}O\textsubscript{2} (M+H)+ 343.1698, Found 343.1693.

3-Isopropyl-1-(2-methoxynaphthalen-1-yl)naphthalen-2-ol (2c): white solid; R\text{f} = 0.70 (hexane/AcOEt = 2/1); \text{\textsuperscript{1}}H NMR (400 MHz, CDCl\textsubscript{3}) \delta 1.40 (6H, t, J = 7.6 Hz), 3.49 (1H, m), 3.80 (3H, s), 4.98 (1H, s), 6.96 (1H, d, J = 8.0 Hz), 7.13-7.17 (2H, m), 7.25-7.29 (2H, m), 7.36 (1H, t, J = 7.6 Hz), 7.48 (1H, d, J = 9.2 Hz), 7.77 (1H, s), 7.82 (1H, d, J = 8.4 Hz), 7.89 (1H, d, J = 8.4 Hz), 8.05 (1H, d, J = 9.2 Hz); \text{\textsuperscript{13}}C NMR (100 MHz, CDCl\textsubscript{3}) \delta 22.56, 22.80, 27.80, 56.66, 113.88, 114.59, 115.73, 123.06, 124.13, 124.42, 124.94, 125.01, 125.44, 127.28, 127.73, 128.11, 129.08, 129.45, 131.00, 132.14, 134.09, 136.80, 149.77, 156.09; IR (ATR) 3531, 2960, 2934, 1592, 1507, 1265, 1249, 1146 cm\textsuperscript{-1}; HRMS (CI) Caled for C\textsubscript{24}H\textsubscript{23}O\textsubscript{2} (M+H)+ 343.1698, Found 343.1694.

3-Methoxy-1-(2-methoxynaphthalen-1-yl)naphthalen-2-ol (2d): white solid; R\text{f} = 0.40 (hexane/AcOEt = 2/1); \text{\textsuperscript{1}}H NMR (400 MHz, CDCl\textsubscript{3}) \delta 3.79 (3H, s), 4.09 (3H, s), 5.77 (1H, s), 7.04 (1H, d, J = 8.4 Hz), 7.12 (1H, td, J = 6.8, 0.8 Hz), 7.18 (1H, d, J = 8.4 Hz), 7.22-7.35 (4H, m), 7.47 (1H, d, J = 8.8 Hz), 7.77 (1H, d, J = 7.6 Hz), 7.87 (1H, d, J = 8.0 Hz), 8.01 (1H, d, J = 8.8 Hz); \text{\textsuperscript{13}}C NMR (100 MHz, CDCl\textsubscript{3}) \delta 55.84, 56.85, 105.75, 114.05, 116.05, 117.58, 123.71, 123.82, 124.23, 124.80, 125.07, 126.64, 126.76, 128.01,
128.96, 129.26, 130.08, 143.30, 147.30, 155.23; IR (ATR) 3526, 2939, 2837, 1594, 1462, 1428, 1266, 1248 cm⁻¹; HRMS (CI) Calcd for C₂₂H₁₉O₃ (M+H)⁺ 331.1334, Found 331.1326.

1-(2-Methoxynaphthalen-1-yl)-3-(methylthio)naphthalen-2-ol (2e): white solid; R f = 0.55 (hexane/AcOEt = 2/1); ¹H NMR (400 MHz, CDCl₃) δ 2.58 (3H, s), 3.80 (3H, s), 5.81 (1H, s), 7.02 (1H, d, J = 8.8 Hz), 7.14 (1H, d, J = 8.4 Hz), 7.18 (1H, t, J = 8.0 Hz), 7.24-7.37 (3H, m), 7.48 (1H, d, J = 8.8 Hz), 7.80 (1H, d, J = 7.6 Hz), 7.86 (1H, s), 7.89 (1H, d, J = 8.4 Hz), 8.04 (1H, d, J = 9.2 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 16.86, 56.67, 113.77, 115.23, 116.21, 123.73, 123.98, 124.86, 126.07, 126.28, 127.08, 127.19, 127.97, 128.10, 129.23, 129.31, 130.73, 132.75, 133.77, 149.09, 155.58; IR (ATR) 3524, 3389, 2935, 2838, 1592, 1508, 1264, 1248, 1147 cm⁻¹; HRMS (CI) Calcd for C₂₂H₁₉O₂S (M+H)⁺ 347.1106, Found 347.1107.

1-(2,6-Dimethoxynaphthalen-5-yl)-3-methylnaphthalen-2-ol (2f): white solid; R f = 0.25 (hexane/AcOEt = 2/1); ¹H NMR (400 MHz, CDCl₃) δ 2.50 (3H, s), 3.77 (3H, s), 3.91 (1H, s), 4.98 (1H, s), 6.93-6.98 (2H, m), 7.06 (1H, d, J = 9.2 Hz), 7.15 (1H, dd, J = 8.4, 6.8 Hz), 7.20 (1H, d, J = 2.8 Hz), 7.27 (1H, dd, J = 8.0, 6.8 Hz), 7.45 (1H, d, J = 9.2 Hz), 7.72 (1H, s), 7.77 (1H, d, J = 8.0 Hz), 7.94 (1H, d, J = 8.8 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 17.06, 55.32, 56.85, 106.10, 114.46, 114.58, 116.06, 120.00, 123.11, 124.56, 125.36, 126.52, 126.62, 127.30, 129.02, 129.24, 129.38, 129.50, 130.45, 132.49, 150.45, 154.47, 156.46; IR (ATR) 3533, 2935, 2837, 1595, 1506, 1251, 1078 cm⁻¹; HRMS (ESI) Calcd for C₂₃H₂₀O₃Na (M+Na)⁺ 363.1305, Found 363.1303.

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1-(2,7-Dimethoxynaphthalen-8-yl)-3-methylnaphthalen-2-ol (2g): white solid; \(R_f = 0.40\) (hexane/AcOEt = 2/1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 2.51 (3H, s), 3.47 (3H, s), 3.77 (3H, s), 5.03 (1H, s), 6.42 (1H, d, \(J = 2.0\) Hz), 7.02 (2H, dd, \(J = 8.8, 2.4\) Hz), 7.16 (1H, td, \(J = 8.0, 1.2\) Hz), 7.24-7.31 (2H, m), 7.71 (1H, s), 7.77 (1H, d, \(J = 8.0\) Hz), 7.78 (1H, d, \(J = 9.2\) Hz), 7.95 (1H, d, \(J = 9.2\) Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 17.07, 54.97, 56.43, 103.34, 110.96, 114.37, 114.48, 116.60, 123.05, 124.58, 124.86, 125.27, 126.45, 127.25, 129.07, 129.21, 129.68, 130.60, 132.26, 135.50, 150.39, 156.60, 158.77; IR (ATR) 3526, 2937, 2838, 1623, 1509, 1264, 1223 cm\(^{-1}\); HRMS (CI) Calcd for C\(_{23}\)H\(_{21}\)O\(_3\) (M+H\(^+\)) 345.1491, Found 345.1497.

1-(2-Methoxy-4,6-dimethylphenyl)-3-methylnaphthalen-2-ol (2h): white solid; \(R_f = 0.35\) (hexane/AcOEt = 8/1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.88 (3H, s), 2.44 (3H, s), 2.47 (3H, s), 3.63 (3H, s), 5.00 (1H, s), 6.75 (1H, s), 6.86 (1H, s), 7.10 (1H, d, \(J = 8.0\) Hz), 7.20-7.28 (2H, m), 7.63 (1H, s) 7.72 (1H, d, \(J = 8.0\) Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 17.01, 19.57, 21.73, 55.74, 109.89, 115.85, 118.29, 122.95, 123.83, 124.06, 125.24, 126.25, 127.30, 128.69, 128.97, 131.94, 139.82, 140.43, 149.70, 158.40; IR (ATR) 3527, 2937, 2838, 1623, 1509, 1264, 1248, 1223 cm\(^{-1}\); HRMS (CI) Calcd for C\(_{20}\)H\(_{21}\)O\(_2\) (M+H\(^+\)) 293.1542, Found 293.1543.

1-(2-Hydroxy-3-methylnaphthalen-1-yl)naphthalen-2-ol (4): white solid; \(R_f = 0.30\) (hexane/AcOEt = 4/1); HPLC analysis Chiralpak IA-3 (hexane/i-PrOH = 90/10, 1.0
mL/min, 254 nm, 30 °C); 11.2, 14.1 min (major); 95% ee (R); [α]D20.3 = +22.1 (c = 1.5, CDCl3); 1H NMR (400 MHz, CDCl3) δ 2.51 (3H, s), 5.03 (1H, s), 5.09 (1H, s), 7.08 (1H, d, J = 8.0 Hz), 7.15 (1H, d, J = 8.0 Hz), 7.22-7.40 (5H, m), 7.81-7.83 (2H, m), 7.90 (1H, d, J = 7.6 Hz), 7.98 (1H, d, J = 8.4 Hz); 13C NMR (100 MHz, CDCl3) δ 16.98, 110.12, 111.09, 117.71, 123.95, 123.97, 124.01, 124.26, 126.42, 127.03, 127.45, 127.57, 128.38, 129.42, 129.46, 130.80, 131.38, 132.09, 133.43, 152.03, 152.77; IR (ATR) 3524, 3491 cm−1; HRMS (ESI) Calcd for C21H16O2Na (M+Na)+ 323.1043, Found 323.1043.

2-((2-Methoxynaphthalen-1-yl)methyl)-N,N-dimethylbenzamide (6a): orange solid; Rf = 0.35 (hexane/AcOEt = 1/1); 1H NMR (400 MHz, CDCl3) δ 2.88 (3H, s), 3.13 (3H, s), 3.89 (3H, s), 4.43 (2H, s), 6.75 (1H, d, J = 7.2 Hz), 7.07 (1H, td, J = 7.6, 1.6 Hz), 7.15 (1H, t, J = 7.2 Hz), 7.20 (1H, dd, J = 7.6, 1.6 Hz), 7.29-7.33 (2H, m), 7.40 (1H, ddd, J = 8.4, 6.8, 1.6 Hz), 7.78-7.83 (2H, m), 7.87 (1H, d, J = 8.8 Hz); 13C NMR (100 MHz, CDCl3) δ 11.53, 25.06, 38.49, 56.46, 109.12, 113.20, 120.34, 123.37, 123.92, 125.56, 125.77, 126.66, 128.21, 128.49, 128.55, 128.69, 129.17, 133.48, 136.39, 137.19, 155.03, 171.54; IR (ATR) 2935, 1631, 1597, 1511, 1394, 1252, 1084 cm−1; HRMS (CI) Calcd for C21H22NO2 (M+H)+ 320.1651, Found 320.1649.

3-Ethyl-4-(2-methoxynaphthalen-1-yl)-1H-isochromen-1-one (7): white solid; Rf = 0.55 (hexane/AcOEt = 2/1); 1H NMR (400 MHz, CDCl3) δ 1.10 (3H, t, J = 7.6 Hz), 2.24 (2H, q, J = 7.6 Hz), 3.84 (3H, s), 6.64-6.67 (1H, m), 7.34-7.46 (6H, m), 7.86-7.89 (1H, m), 8.00 (1H, d, J = 8.8 Hz), 8.36-8.39 (1H, m); 13C NMR (100 MHz, CDCl3) δ 11.53, 25.06, 56.26, 109.12, 113.18, 116.03, 120.34, 123.88, 124.31, 124.36, 127.12, 127.23, 128.21, 129.04, 130.45, 133.71, 134.57, 138.79, 155.19, 157.09, 163.26; IR (ATR) 2977, 2938, 1631, 1597, 1511, 1394, 1252, 1084 cm−1; HRMS (ESI) Calcd for C21H16O2Na (M+Na)+ 323.1043, Found 323.1043.
Calcd for C$_{22}$H$_{28}$O$_3$Na (M+Na)$^+$ 353.1148, Found 353.1147.

References
Electronic Supplementary Material (ESI) for Chemical Communications
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Racemic mixture of 2a

Catalytic reaction: 12% ee (S)

(R)-2a

(S)-2a
Racemic mixture of 4

(R)-4

(S)-4

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