Pushing the Limits of Steric Demand Around a Biaryl Axis: Synthesis of Tetra-*Ortho*-Substituted Biaryl Naphthalenes

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Supporting Information

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General

All oxygen and moisture-sensitive manipulations were carried out under an inert atmosphere using either standard Schlenk techniques or a glove box.

THF, Et_2O, toluene, and pentane were purified by passing through a neutral alumina column under argon. Anhydrous benzene, 1,2-dichloroethane, acetonitrile, and hexane were purchased from Aldrich and used as received. All other reagents were purchased (Aldrich, TCI, Alfa Aesar, or Acros) and used as received. 2-methyl-1-indenone[1] and 2-isopropyl-1-indenone[2] were prepared according to known procedures.

Thin layer chromatography and preparatory chromatography were performed on Silicycle glass backed plates with UV indicator. Column chromatography was performed on Silicycle silica gel P60.

^{1}H NMR spectra were recorded on a Varian Unity/Inova 300 or Varian Unity/Inova 600 spectrometer. ^{13}C NMR spectra were recorded on a Varian Unity/Inova 300 or Varian Unity/Inova 500 spectrometer. All spectra were referenced to their respective solvents: $CDCl_3$ 7.27 ppm, and CD_2Cl_2 5.32 ppm. Gas chromatography was performed on an Agilent 6850 Series II GC with an auto loader using ChemStation.

IR spectra were recorded on a Nicolet Magna 550 FT-IR instrument with OMNIC software.

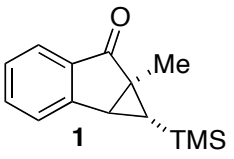
High-resolution mass spectroscopy data were obtained at the Mass Spectroscopy Facilities and Services Core of the Environmental Health Sciences Center at Oregon State University. Financial support for this facility has been furnished in part by the National Institute of Environmental Health Sciences, NIH (P30 ES00210).

X-ray Crystallography. X-ray diffraction intensities for **2c (liu48)** and **7d (liu66)** were collected at 173(2) K on a Bruker Apex CCD diffractometer using MoKα radiation λ= 0.71073 Å. Space groups were determined based on systematic absences (**liu66**) and intensity statistics (**liu48**). Absorption corrections in both cases were applied by SADABS. Structures were solved by direct methods and Fourier techniques and refined on F^2 using full matrix least-squares procedures. All non-H atoms were refined with anisotropic thermal parameters. H atoms in **liu48** were found from the F-map and refined with isotropic thermal parameters. H atoms in **liu66** were refined in calculated positions in a rigid group model. There are two symmetrically independent molecules in **liu66**. One of terminal –$CHMe_2$ groups is disordered over two positions in a ratio of 1:1. All crystals of **liu66** are thin plates and provide very weak X-ray diffraction reflections at high angles and as a result the value of R_{int} for the collected data is relatively high, 0.0934. Diffraction intensity data for **liu66** were collected up to $2\theta_{max}$=56.00 degree, but only reflections with 2θ less 48.00 degree were used in the final refinement. All calculations were performed by the Bruker SHELXTL (v. 6.10) package.

(1) The synthesis of 2-methyl indenone was adapted from a procedure used by Clive et al., see: Clive, D. L. J.; Yu, M.; Sannigrahi, M. *J. Org. Chem.* **2004**, *69*, 4116-4125.

(2) Malosh, C. F.; Ready, J. M. *J. Am. Chem. Soc.* **2004**, *126*, 10240-10241.

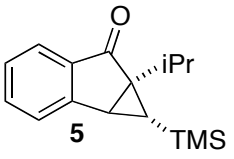
Synthesis of Silylcyclopropyl Indanones 1 and 5



1

Compound 1 [1072849-07-0]. 2-methyl-1-indenone (1.90 g, 13.1 mmol) and palladium acetate (289 mg, 1.31 mmol) were added to an oven-dried flask under nitrogen. Anhydrous benzene (100 mL) was added followed by dropwise addition of $TMSCHN_2$ (20.0 mL, 39.0 mmol, 2.0 M in diethyl ether). The evolution of N_2 gas is apparent and the solution turned black. The reaction mixture was allowed to stir at room temperature for 16 h. At the conclusion of the reaction, the reaction mixture was filtered through a plug of Celite, and the solvent removed under reduced pressure. The crude material was subjected to column chromatography (Hex:Et_2O = 9:1), and **1** was isolated as a light yellow solid (2.50 g, 84 % yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.13 (s, 9H), 0.85 (d, J = 4.8 Hz, 1H), 1.58 (s, 3H), 2.65 (d, J = 4.8 Hz, 1H), 7.21-7.45 (m, 3H), 7.64 (d, J = 8.1 Hz, 1H).

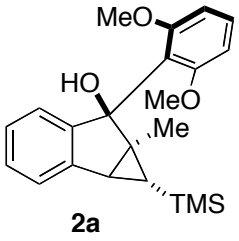


5

Compound 5. The procedure for the preparation of **1** has been used for the synthesis of **5** employing 2-isopropyl-1-indenone (762 mg, 4.40 mmol), palladium acetate (98 mg, 0.44 mmol), 44.0 mL benzene, and $TMSCHN_2$ (6.50 mL, 13.1 mmol, 2.0 M in diethyl ether). The reaction was run at 50 ^oC for 3h. Compound **5** was isolated as a pale yellow solid (872 mg, 76 % yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.14 (s, 9H), 0.82 (d, J = 5.1 Hz, 1H), 1.14 (d, J = 6.6 Hz, 3H), 1.51 (d, J = 6.6 Hz, 3H), 1.78 (septet, J = 7.2 Hz, 1H), 2.51 (d, J = 4.8 Hz, 1H), 7.18-7.43 (m, 3H), 7.60 (d, J = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ –0.3, 20.3, 20.5, 29.4, 30.9, 47.1, 47.5, 123.3, 124.8, 126.1, 133.2, 134.6, 156.3, 204.4. IR (Neat): 1715 s, (carbonyl). HRMS (EI) calcd for $C_{16}H_{22}OSi$ (M+) 258.1440 found 258.1434

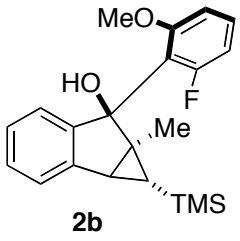
Nucleophillic Addition to 1 (Table 1):



2a

Compound 2a (Entry 1) [1072849-18-3]. An oven-dried flask was charged with 50.0 mL anhydrous Et_2O and *m*-dimethoxybenzene (750 mg, 5.42 mmol). *n*-BuLi (2.0 mL, 5.0 mmol, 2.5 M in hexanes) was added dropwise, and the reaction was allowed to stir for 24h. The ether was removed under reduced pressure to yield a white solid. Anhydrous THF was added (15.0 mL) and the reaction was cooled to –78 ^oC. Indanone **1** (500 mg, 2.17 mmol) in THF (5.0 mL) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 24h. At the conclusion of the reaction, 10 mL of NH_4Cl (saturated, aqueous) was added followed by 100 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to column chromatography (Hex:Ether = 3:1). Compound **2a** was isolated as a white solid (596 mg, 75% yield). A second run had a yield of 64%.

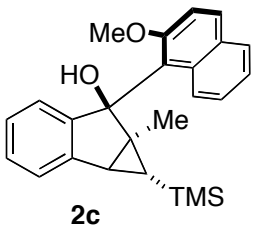
^1H NMR (300 MHz, $CDCl_3$): d 0.13 (s, 9H), 0.55 (d, J = 5.1 Hz, 1H), 1.10 (s, 3H), 2.27 (d, J = 5.4 Hz, 1H), 3.09 (s, 3H), 4.01 (s, 3H), 6.45 (s, 1H), 6.51 (d, J = 8.1 Hz, 1H), 6.71 (d, J = 8.4 Hz, 1H), 7.00-7.08 (m, 3H), 7.16-7.24 (m, 2H).



2b

Compound 2b (Entry 2). An oven-dried flask was charged with 2.0 mL anhydrous THF and *m*-fluoroanisole (219 mg, 1.74 mmol). The reaction was cooled to –78 ^oC, and *n*-BuLi (0.66 mL, 1.7 mmol, 2.5 M in hexanes) was added dropwise. The reaction was allowed to stir for 2 hours at –78 °C. Subsequently, indanone **1** (200 mg, 0.870 mmol) in THF (2.4 mL) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 24h. At the conclusion of the reaction, 5 mL of NH_4Cl (saturated, aqueous) was added followed by 20 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to column chromatography (Hex:Ether = 3:1). Compound **2b** was isolated as a light yellow oil (229 mg, 73% yield). A second run had a yield of 68%.

^1H NMR (300 MHz, $CDCl_3$): δ 0.12 (s, 9H), 0.52 (d, J = 5.1 Hz, 1H), 1.13 (s, 3H), 2.31 (d, J = 4.8 Hz, 1H), 4.06 (s, 3H), 6.15 (s, 1H), 6.59 (dd, J = 8.1,1.8 Hz, 1H) 6.84 (d, J = 8.7 Hz, 1H) 7.07-7.28 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ -0.3, 15.7, 28.2, 35.2, 36.8, 56.8, 88.3, 107.7, 110.0, 110.3, 121.9, 125.3, 125.6, 127.2, 128.5, 128.7, 147.7 (d, $^1J_{CF}$ = 82 Hz), 158.4, 161.7. IR (Neat): 3501 s, (alcohol). HRMS (EI) calcd for $C_{21}H_{25}O_2FSi$ (M+) 356.1608 found 356.1599



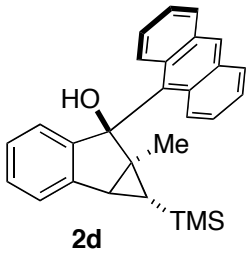
2c

Compound 2c (Entry 3). An oven-dried flask was charged with 2.0 mL anhydrous Et_2O and 1-bromo-2-methoxynaphthalene (412 mg, 1.74 mmol). *n*-BuLi (0.66 mL, 1.7 mmol, 2.5 M in hexanes) was added dropwise at room temperature, and the reaction was allowed to stir for 15 minutes. The reaction was cooled to –78 ^oC, and indanone **1** (200 mg, 0.870 mmol) in Et_2O (2.4 mL) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 24h. At the

conclusion of the reaction, 5 mL of NH_4Cl (saturated, aqueous) was added followed by 20 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to column chromatography (Hex:Ether = 3:1). Compound **2c** was isolated as a white solid (236 mg, 70% yield). A second run had a yield of 63%. Crystals suitable for diffraction were obtained by slow evaporation of the solvent of a concentrated solution of **2c** in dichloromethane at –20 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.17 (s, 9H), 1.03 (d, J = 5.4 Hz, 1H), 1.12 (s, 3H), 2.48 (d, J = 5.1 Hz, 1H), 4.16 (s, 3H), 6.72 (s, 1H), 6.81 (d, J = 7.2 Hz, 1H) 6.97-7.41 (m, 7H) 7.72 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 8.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ –0.3, 16.6, 28.3, 36.1, 38.7, 57.3, 89.8, 114.1, 122.7, 123.2, 125.2, 126.0, 126.2, 126.4, 126.5, 127.5, 128.1, 129.9, 130.1, 132.4, 147.4, 149.9, 155.2. IR (Neat): 3487 s, (alcohol). HRMS (EI) calcd for $C_{25}H_{28}O_2Si$ (M+) 388.1859 found 388.1853

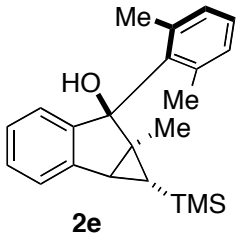
Compound 2d (Entry 4). An oven-dried flask was charged with 2.0 mL anhydrous Et_2O and 9-bromoanthracene (447 mg, 1.74 mmol). *n*-BuLi (0.66 mL, 1.7 mmol, 2.5 M in hexanes) was added dropwise at room temperature, and the reaction was allowed to stir for 15 minutes. The reaction was cooled to –78 ^{o}C, and indanone **1** (200 mg, 0.870 mmol) in Et_2O (2.4 mL) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 24h. At the conclusion of the reaction, 5 mL of NH_4Cl (saturated, aqueous) was added followed by 20 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to column chromatography (Hex:Ether = 3:1). Compound **2d** was isolated as an off-white solid (246 mg, 69% yield). A second run had a yield of 71%.



2d

^{1}H NMR (300 MHz, $CDCl_3$): δ –0.17 (s, 9H), 1.04 (d, J = 5.3 Hz, 1H), 1.90 (s, 3H), 2.40 (d, J = 4.8 Hz, 1H), 2.42 (s, 1H), 6.99-7.51 (m, 10H), 7.99 (d, J = 27 Hz, 2H), 9.85 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ –0.5, 16.9, 26.8, 34.8, 42.7, 89.9, 123.8, 124.2, 126.0, 128.4, 129.3, 130.0, 130.4, 136.1, 144.2, 151.2, the remaining 10 carbon signals appear as broad peaks. IR (Neat): 3543 s, (alcohol).

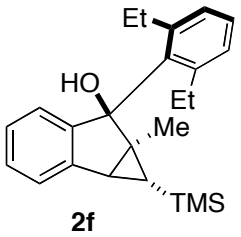
Compound 2e (Entry 5). An oven-dried flask was charged with 2.0 mL anhydrous Et_2O and 1-bromo-2,6-dimethylbenzene (321 mg, 1.74 mmol). *n*-BuLi (0.66 mL, 1.7 mmol, 2.5 M in hexanes) was added dropwise at room temperature, and the reaction was allowed to stir for 15 minutes. The reaction was cooled to –78 ^{o}C, and indanone **1** (200 mg, 0.870 mmol) in Et_2O (2.35 mL) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 24h. At the conclusion of the reaction, 5 mL of NH_4Cl (saturated, aqueous) was added followed by 20 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to column chromatography (Hex:Ether = 3:1). Compound **2e** was isolated as an oil (208 mg, 71% yield). A second run had a yield of 64%.



2e

^{1}H NMR (300 MHz, $CDCl_3$): δ –0.01 (s, 9H), 0.56 (d, J = 5.1 Hz, 1H), 1.65 (s, 3H), 1.68 (s, 3H), 1.91 (s, 1H), 2.88 (s, 3H), 6.91-7.31 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$): δ –0.4, 16.0, 16.1, 25.7, 26.3, 26.6, 42.5, 88.8, 123.5, 125.5, 125.8, 126.2, 128.1, 130.8, 131.5, 135.3, 139.4, 139.7, 144.9, 150.2. IR (Neat): 3535 s, (alcohol). HRMS (EI) calcd for $C_{22}H_{28}OSi$ (M+) 336.1909 found 336.1899

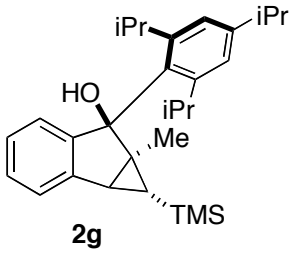
Compound 2f (Entry 6). An oven-dried flask was charged with 2.0 mL anhydrous Et_2O and 1-bromo-2,6-diethylbenzene (241 mg, 1.13 mmol). The reaction was cooled to –78 °C, and *t*-BuLi (1.3 mL, 2.3 mmol, 1.7 M in pentane) was added dropwise. The reaction was allowed to stir for 2 hours at –78 °C. Subsequently, the reaction was warmed to ambient temperature for 30 minutes before it was cooled to –78 °C again. Indanone **1** (200 mg, 0.870 mmol) in Et_2O (2.4 mL) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 24h. At the conclusion of the reaction, 5 mL of NH_4Cl (saturated, aqueous) was added followed by 20 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to column chromatography (Hex:Ether = 9:1). Compound **2f** was isolated as a clear oil (224 mg, 71% yield). A second run had a yield of 63%.



2f

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.02 (s, 9H), 0.42 (d, J = 4.5 Hz, 1H), 0.91 (t, J = 7.5 Hz, 3H), 1.36 (t, J = 7.2 Hz, 3H), 1.62 (s, 3H), 1.81 (s, 1H), 1.82-1.90 (m, 2H), 2.24 (d, J = 4.8 Hz, 1H), 2.84-2.91 (m, 1H), 3.60-3.67 (m, 1H), 7.04-7.32 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$): δ –0.4, 15.4, 17.8, 19.2, 26.6, 29.0, 30.4, 33.9, 41.4, 86.6, 123.3, 124.5, 125.7, 126.5, 127.9, 128.8, 130.1, 138.6, 142.0, 144.4, 146.4, 151.0. IR (Neat): 3591 s, (alcohol). HRMS (EI) calcd for $C_{24}H_{32}OSi$ (M+) 364.2223 found 364.2216

Compound 2g (Entry 7). An oven-dried flask was charged with 2.0 mL anhydrous Et_2O and 1-bromo-2,4,6-triisopropylbenzene (320 mg, 1.13 mmol). The reaction was cooled to –78 °C and *t*-BuLi (1.3 mL, 2.3 mmol, 1.7 M in pentane) was added dropwise. The reaction was allowed to stir for 2 hours at –78 °C. Subsequently, the reaction was warmed to ambient temperature for 30 minutes before it was cooled to –78 °C again. Indanone **1** (200 mg, 0.870 mmol) in Et_2O (2.4 mL) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 24h. At the conclusion of the reaction, 5 mL of NH_4Cl (saturated, aqueous) was added followed by 20 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to column chromatography (Hex:Ether = 9:1). Compound **2g** was isolated as a white solid (302 mg, 80% yield). A second run had a yield of 81%.

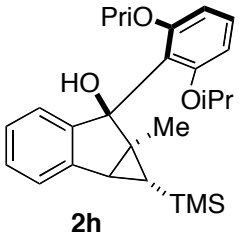


2g

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.05 (s, 9H), 0.54 (d, J = 4.8 Hz, 1H), 0.89-0.92 (m, 6H), 1.26 (d, J = 6.9 Hz, 3H), 1.30 (d, J = 6.9 Hz, 6H), 1.40 (d, J = 3.3 Hz, 3H), 1.67 (s, 3H), 1.80 (s, 1H), 2.09 (septet, J = 6.3 Hz, 1H), 2.21 (d, J = 4.8 Hz, 1H), 2.91 (septet, J = 7.2 Hz, 1H), 4.38 (septet, J =

6.9 Hz, 1H), 6.95-7.29 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ –0.3, 15.6, 23.7, 23.8, 24.0, 24.1 26.0, 26.5, 26.9, 30.6, 30.8, 33.5, 34.3, 40.7, 88.4, 123.0, 124.0, 124.5, 125.5, 127.7, 135.7, 141.2, 143.9, 146.2, 146.7, 151.2, 151.6. IR (Neat): 3425 s, (alcohol). HRMS (EI) calcd for $C_{29}H_{42}OSi$ (M+) 434.3005 found 434.3008

Compound 2h (Entry 8). An oven-dried flask was charged with 10.0 mL anhydrous Et_2O and *m*-diisopropylbenzene (337 mg, 1.74 mmol). *n*-BuLi (2.0 mL, 5.0 mmol, 2.5 M in hexanes) was added dropwise at room temperature, and the reaction was allowed to stir for 24h. The ether was removed under reduced pressure to yield a white solid. Anhydrous THF was added (2.0 mL) and the reaction was cooled to –78 °C. Subsequently, indanone **1** in THF (2.4 mL) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 24h. At the conclusion of the reaction, 5 mL of NH_4Cl (saturated, aqueous) was added followed by 20 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to column chromatography (Hex:Ether = 3:1). Compound **2h** was isolated as a white solid (254 mg, 69% yield). A second run had a yield of 66%.



2h

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.14 (s, 9H), 0.55 (d, J = 6.0 Hz, 3H), 0.61 (d, J = 5.7 Hz 1H), 0.99 (d, J = 6.3 Hz, 3H), 1.13 (s, 3H), 1.47-1.53 (m, 6H), 4.26 (septet, J = 6.0 Hz, 1H), 4.79 (septet, J = 6.3 Hz, 1H), 6.41 (d, J = 8.1 Hz, 1H), 6.64 (d, J = 8.1 Hz, 1H) 6.98-7.18 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ –0.3, 16.2, 19.9, 21.3, 22.0, 22.3, 27.1, 36.1, 37.3, 67.8, 72.3, 89.0, 105.7, 106.6, 121.7, 122.0, 124.7, 125.0, 126.0, 127.8, 148.9, 149.9, 155.8, 156.8. IR (Neat): 3466 s, (alcohol). HRMS (EI) calcd for $C_{26}H_{36}O_2Si$ (M+) 424.2434 found 424.2422

Optimization Survey for the Regioselective Synthesis of 3a (Table 2):

General Procedure: In a glovebox, a vial was charged with compound **2a**, Lewis acid, and the solvent. The reaction vial was immersed into an oil bath at 80 °C for 24 hours. At the conclusion of the reaction, hexadecane as an internal GC standard was added via syringe (25.0 μL, 19.2 mg), and the mixture was filtered through a silica plug with copious ether washing. An aliquot of the resulting solution was subjected to GC analysis. All GC yields (Table 2) have been corrected for response factors. Because the yields that are reported in Table 2 are the average of two runs, the yields that are reported below for a specific experiment may differ from the values presented in the table.

Entry 1: The general procedure was followed, using **2a** (20 mg, 0.054 mmol), 1,2-dichloroethane (0.50 mL), and $Eu(OTf)_3$ (3.2 mg, 0.0054 mmol). GC analysis indicated the formation of the biaryl naphthalenes (**3a** + **4a**) in 70% yield in 73:27 (**3a:4a**) ratio.

Entry 2: The general procedure was followed, using **2a** (20 mg, 0.054 mmol), $Eu(OTf)_3$ (3.2 mg, 0.0054 mmol), and toluene (0.50 mL). GC analysis indicated the formation of the biaryl naphthalenes (**3a** + **4a**) in 81% yield in 92:8 (**3a:4a**) ratio.

Entry 3: The general procedure was followed, using **2a** (20 mg, 0.054 mmol), $Eu(OTf)_3$ (3.2 mg, 0.0054 mmol), and THF (0.50 mL). GC analysis indicated the formation of the biaryl naphthalenes (**3a** + **4a**) in 53% yield in 91:9 (**3a:4a**) ratio.

Entry 4: The general procedure was followed, using **2a** (20 mg, 0.054 mmol), $Eu(OTf)_3$ (3.2 mg, 0.0054 mmol), and DMF (0.50 mL). GC analysis indicated the formation of the biaryl naphthalenes (**3a** + **4a**) in 30% yield in 79:21 (**3a:4a**) ratio.

Entry 5: The general procedure was followed, using **2a** (20 mg, 0.054 mmol), $Eu(OTf)_3$ (3.2 mg, 0.0054 mmol), and *t*-BuOH (0.50 mL). GC analysis indicated the formation of the biaryl naphthalenes (**3a** + **4a**) in 41% yield in 81:19 (**3a:4a**) ratio.

Entry 6: The general procedure was followed, using **2a** (20 mg, 0.054 mmol), $Eu(OTf)_3$ (3.2 mg, 0.0054 mmol), and chlorobenzene (0.50 mL). GC analysis indicated the formation of the biaryl naphthalenes (**3a** + **4a**) in 47% yield in 95:5 (**3a:4a**) ratio.

Entry 7: The general procedure was followed, using **2a** (20 mg, 0.054 mmol), $Eu(OTf)_3$ (3.2 mg, 0.0054 mmol), and 1,3-dichlorobenzene (0.50 mL). GC analysis indicated the formation of the biaryl naphthalenes (**3a** + **4a**) in 48% yield in 93:7 (**3a:4a**) ratio.

Entry 8: The general procedure was followed, using **2a** (20 mg, 0.054 mmol), $Eu(OTf)_3$ (3.2 mg, 0.0054 mmol), and MeCN (0.50 mL). GC analysis indicated the formation of the biaryl naphthalenes (**3a** + **4a**) in 15% yield in 27:73 (**3a:4a**) ratio.

Entry 9: The general procedure was followed, using **2a** (20 mg, 0.054 mmol), $Sm(OTf)_3$ (3.2 mg, 0.0054 mmol), and toluene (0.50 mL). GC analysis indicated the formation of the biaryl naphthalenes (**3a** + **4a**) in 78% yield in 80:20 (**3a:4a**) ratio.

Entry 10: The general procedure was followed, using **2a** (20 mg, 0.054 mmol), $Er(OTf)_3$ (3.2 mg, 0.0054 mmol), and toluene (0.50 mL). GC analysis indicated the formation of the biaryl naphthalenes (**3a** + **4a**) in 80% yield in 82:18 (**3a:4a**) ratio.

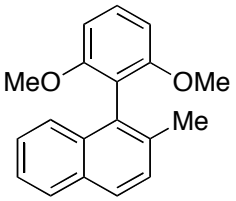
Entry 11: The general procedure was followed, using **2a** (20 mg, 0.054 mmol), $SnCl_4$ (1.4 mg, 0.0054 mmol), and toluene (0.50 mL). GC analysis indicated the formation of the biaryl naphthalenes (**3a** + **4a**) in 31% yield in 40:60 (**3a:4a**) ratio.

Entry 12: The general procedure was followed, using **2a** (20 mg, 0.054 mmol), $BF_3 \bullet Et_2O$ (0.8 mg, 0.0054 mmol), and toluene (0.50 mL). GC analysis indicated the formation of the biaryl naphthalenes (**3a** + **4a**) in 30% yield in 39:61 (**3a:4a**) ratio.

Rearrangement of 2 under Optimized Conditions (Table 3):

General Procedure: In a glovebox, a vial was charged with **3**, toluene, and 10% $Eu(OTf)_3$. The vessel was sealed and stirred at 80 °C for 24 h. The reaction was cooled to ambient temperature, and the mixture was filtered through a silica plug with copious ether washings. The solvents were removed under reduced pressure, and the crude material was subjected to preparatory thin-layer chromatography using 9:1 hexanes:ether as the eluent.

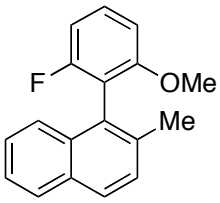
Compound 3a [1072849-22-9] (Entry 1). The general procedure was applied using **2a** (191 mg, 0.520 mmol), toluene (5.3 mL), and $Eu(OTf)_3$ (32 mg, 0.053 mmol). The biaryl product was isolated as mixture of **3a** and **4a** (106 mg, 74% yield, in 93:7 (**3a:4a)** ratio). A second run had a yield of 68%.



3a

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.24 (s, 3H), 3.67 (s, 6H), 6.76 (m, 2H), 7.28-7.49 (m, 5H), 7.85 (m, 2H).

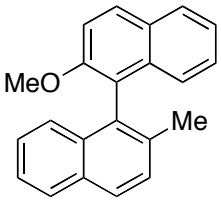
Compound 3b (Entry 2). The general procedure was applied using **2b** (181 mg, 0.516 mmol), toluene (5.2 mL), and $Eu(OTf)_3$ (31 mg, 0.052 mmol). The product **3b** was isolated as a white solid (56 mg, 41% yield, >95:5 regioselectivity). A second run had a yield of 44%.



3b

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.28 (s, 3H), 3.70 (s, 3H), 6.89 (d, J = 9.0 Hz, 2H), 7.37-7.49 (m, 5H), 7.86 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.3, 56.0, 106.6 106.7, 108.2 (d, J_{CF} = 23 Hz), 124.7, 125.2, 125.9, 127.9, 128.0, 128.4, 129.3, 129.5, 131.9, 132.6, 134.9, 158.8 (d, J_{CF} = 30 Hz), 162.3. HRMS (EI) calcd for $C_{18}H_{15}OF_2$ (M+) 364.2223 found 364.2216

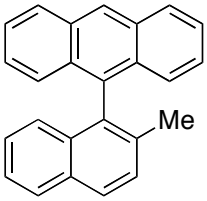
Compound 3c [106909-87-9] (Entry 3). The general procedure was applied using **2c** (233 mg, 0.600 mmol), toluene (5.2 mL), and $Eu(OTf)_3$ (36 mg, 0.059 mmol). The product **3c** was isolated as a fluffy white solid (110 mg, 61% yield, >95:5 regioselectivity). A second run had a yield of 64%.



3c

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.13 (s, 3H), 3.79 (s, 3H), 7.03 (d, J = 9.0 Hz, 1H), 7.15-7.56 (m, 7H), 7.91 (m, 3H), 8.02 (d, J = 9 Hz, 1H).

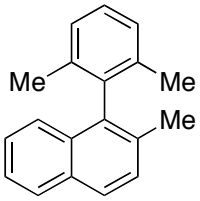
Compound 3d [191791-93-2] (Entry 4). The general procedure was applied using **2d** (250 mg, 0.610 mmol), toluene (6.1 mL), and $Eu(OTf)_3$ (37 mg, 0.061 mmol). The product **3d** was isolated as an off-color solid (107 mg, 55% yield, >95:5 regioselectivity). A Second run had a yield of 55%.



3d

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.01 (s, 3H), 6.90 (d, J = 8.4 Hz, 1H), 7.12-7.62 (m, 9H), 8.00 (dd, J = 3, 12 Hz, 1H), 8.14 (d, J = 9 Hz, 1H), 8.63 (s, 1H).

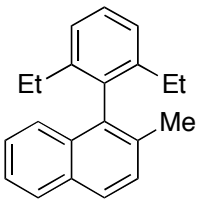
Compound 3e [814254-89-2] (Entry 5). The general procedure was applied using **2e** (171 mg, 0.508 mmol), toluene (5.1 mL), and $Eu(OTf)_3$ (30 mg, 0.051 mmol). The product **3e** was isolated as an off-color oil (96 mg, 77% yield, >95:5 regioselectivity). A second run had a yield of 81%.



3e

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.87 (s, 6H), 2.16 (s, 3H), 7.18-7.50 (m, 7H), 7.81-7.91 (m, 2H).

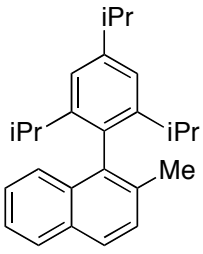
Compound 3f [1157867-56-5] (Entry 6). The general procedure was applied using **2f** (250 mg, 0.690 mmol), toluene (6.9 mL), and $Eu(OTf)_3$ (41 mg, 0.069 mmol). The product **3f** was isolated as a light yellow oil (141 mg, 75% yield, >95:5 regioselectivity). A second run had a yield of 80%.



3f

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.06 (m, 6H), 2.17 (m, 7H), 7.25-7.53 (m, 7H), 7.86-7.94 (m, 2H).

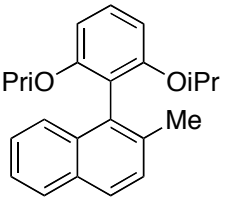
Compound 3g (Entry 7). The general was applied using **2g** (279 mg, 0.642 mmol), toluene (6.5 mL), and $Eu(OTf)_3$ (39 mg, 0.064 mmol). The product **3g** was isolated as an off-color solid (192 mg, 87% yield, >95:5 regioselectivity). A second run had a yield of 85%.



3g

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.01 (d, J = 6.9 Hz, 6H), 1.20 (d, J = 6.6 Hz, 6H), 1.50 (d, J = 6.9 Hz, 6H), 2.30 (s, 3H), 2.40 (septet, J = 6.6 Hz, 2H), 3.14 (septet, J = 6.9 Hz, 1H), 7.28 (s, 2H), 7.41-7.56 (m, 4H), 7.90 (d, J = 8.7 Hz, 1H), 7.95 (d, J = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.8, 24.1, 24.7, 30.5, 34.2, 121.0, 122.0, 124.3, 124.7, 125.4, 126.5, 126.7, 127.7, 128.4, 131.9 133.0, 133.9, 136.0, 136.5, 146.8, 148.1.

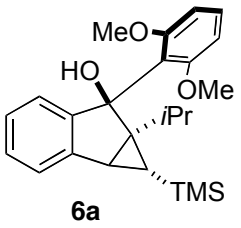
Compound 3h (Entry 8). The general procedure was applied using **2h** (152 mg, 0.360 mmol), toluene (3.6 mL), and $Eu(OTf)_3$ (22 mg, 0.036 mmol). The product **3h** was isolated as a light yellow oil (97 mg, 81% yield, >95:5 regioselectivity). A second run had a yield of 77%.



3h

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (d, J = 6.0 Hz, 6H), 1.03 (d, J = 6.3 Hz, 6H), 2.26 (s, 3H), 4.26 (septet, J = 6.3 Hz, 2H), 6.73 (d, J = 8.1 Hz, 2H), 7.27-7.44 (m, 5H), 7.77 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.4, 21.9, 22.0, 70.7, 107.9, 120.0, 124.0, 124.9, 126.1, 126.5, 127.5, 128.3, 128.5, 131.6, 131.7, 133.0, 134.3, 157.0. HRMS (EI) calcd for $C_{23}H_{26}O_2$ (M+) 334.1933 found 334.1932

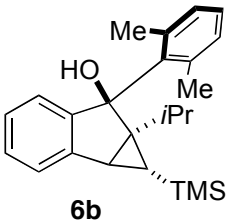
Nucleophillic Addition to 5 (Scheme 2)



6a

Compound 6a. An oven-dried flask was charged with 10.0 mL anhydrous Et_2O and *m*-dimethoxybenzene (267 mg, 1.93 mmol). *n*-BuLi (0.73 mL, 1.8 mmol, 2.5 M in hexanes) was added dropwise at room temperature, and the reaction was allowed to stir for 24h. The ether was then removed under reduced pressure to yield a white solid. Anhydrous THF was added (4.0 mL) and the reaction mixture was cooled to –78 ^oC. Indanone **5** (250 mg, 0.967 mmol) in THF (1.0 mL) was added dropwise at –78 °C. The reaction was allowed to warm to ambient temperature and stirred for 24h. At the conclusion of the reaction, 5 mL of NH_4Cl (saturated, aqueous) was added followed by 20 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to column chromatography (Hex:Ether = 3:1). Compound **6a** was isolated as a clear oil (46 mg, 12% yield). A second run had a yield of 15%.

^1H NMR (300 MHz, $CDCl_3$): δ 0.14 (s, 9H), 0.47 (d, J = 5.4 Hz, 1H), 0.72 (d, J = 6.9 Hz, 3H), 1.02 (d, J = 7.2 Hz, 3H), 1.70 (septet, J = 6.9 Hz, 1H), 2.38 (d, J = 5.4 Hz, 1H), 3.04 (s, 3H), 4.02 (s, 3H), 6.41 (d, J = 9.6 Hz, 1H), 6.60 (s, 1H), 6.69 (d, J = 9.3 Hz, 1H), 6.85-7.28 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.5, 20.0, 20.2, 30.1, 31.3, 34.8, 48.6, 55.0, 56.8, 89.0, 105.7, 106.8, 120.3, 122.7, 123.7, 124.8, 126.1, 128.4, 150.1, 150.6, 158.1, 158.7. IR (Neat) 3495 m, (alcohol).

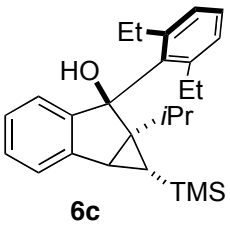


6b

Compound 6b. An oven-dried flask was charged with 3.0 mL anhydrous Et_2O and 1-bromo-2,6-dimethylbenzene (279 mg, 1.51 mmol). The reaction mixture was cooled to –78 ^oC, and *t*-BuLi (1.8 mL, 3.0 mmol, 1.7 M in hexanes) was added dropwise. The reaction was allowed to stir for 2 hours at –78 °C. Subsequently, the reaction was allowed to warm to ambient temperature for 30 minutes. The reaction mixture was cooled to –78 ^oC before indanone **5** (300 mg, 1.16 mmol) in Et_2O (3.0 mL) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 24h. At the conclusion of the reaction, 5 mL of NH_4Cl (saturated, aqueous) was added followed by 20 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to column chromatography (Hex:Ether = 6:1). Compound **6b** was isolated as a viscous oil (249 mg, 59% yield). A second run had a yield of 54%.

^1H NMR (300 MHz, $CDCl_3$): δ 0.09 (s, 9H), 0.62 (d, J = 5.7 Hz, 1H), 0.98 (d, J = 7.5 Hz, 3H), 1.11 (d, J = 7.2 Hz, 3H), 1.77 (s, 3H), 1.77 (s, 1H), 2.40 (d, J = 5.7 Hz, 1H), 2.94 (s, 3H), 3.10 (septet, J = 7.2 Hz, 1H), 6.95-7.32 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.6, 21.0, 23.4, 25.3, 26.6, 26.8, 27.6, 32.0, 53.7, 90.9, 122.9, 125.2, 125.4, 126.3, 128.0, 131.1, 131.7, 135.4, 139.7, 139.9, 145.3, 150.2. IR (Neat) 3534 m, (alcohol). HRMS (EI) calcd for $C_{24}H_{32}OSi$ (M+) 364.2223 found 364.2213

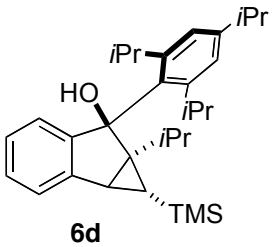
Compound 6c. An oven-dried flask was charged with 3.0 mL anhydrous Et_2O and 1-bromo-2,6-diethylbenzene (321 mg, 1.51 mmol). The reaction was cooled to –78 ^oC. *t*-BuLi (1.8 mL, 3.0 mmol, 1.7 M in pentane) was added dropwise at –78°C, and the reaction was allowed to stir for 2 hours. Subsequently, the reaction was allowed to warm to ambient temperature for 30 minutes. The reaction mixture was cooled to –78 ^oC before indanone **5** (300 mg, 1.16 mmol) in Et_2O (3.0 mL) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 24h At the conclusion of the reaction, 5 mL of NH_4Cl (saturated, aqueous) was added followed by 20 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to column chromatography (Hex:Ether = 9:1). Compound **6c** was isolated as an off color oil (226 mg, 50% yield). A second run had a yield of 46%.



6c

^1H NMR (300 MHz, $CDCl_3$): δ 0.10 (s, 9H), 0.50 (d, J = 5.4 Hz, 1H), 0.93 (t, J = 7.5 Hz, 3H), 1.01 (d, J = 7.2 Hz, 3H), 1.14 (d, J = 6.9, 3H), 1.41 (t, J = 6.9 Hz, 3H), 1.72 (s, 1H), 1.94 (m, 2H), 2.40 (d, J = 6 Hz, 1H), 2.74 (m, 2H), 3.91 (m, 1H), 7.07-7.32 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.6, 18.0, 19.3, 20.8, 23.1, 27.5, 29.6, 32.2, 32.4, 90.8, 122.8, 124.1, 125.5, 127.1, 127.9, 129.2, 130.6, 138.8, 142.1, 144.5, 146.7, 151.2. IR (Neat) 3594 m, (alcohol). HRMS (EI) calcd for $C_{26}H_{36}OSi$ (M+) 392.2536 found 392.2525.

Compound 6d. An oven-dried flask was charged with 3.0 mL anhydrous Et_2O and 1-bromo-2,4,6-triisopropylbenzene (427 mg, 1.51 mmol). The reaction mixture was cooled to –78 ^oC, and *t*-BuLi (1.8 mL, 3.0 mmol, 1.7 M in pentane) was added dropwise. The reaction was allowed to stir for 2 hours. Subsequently, the reaction was allowed to warm to ambient temperature for 30 minutes. The reaction mixture was cooled to –78 ^oC before indanone **5** (300 mg, 1.16 mmol) in Et_2O (2.8 mL) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 24h. At the conclusion of the reaction, 5 mL of NH_4Cl (saturated, aqueous) was added followed by 20 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to column chromatography (Hex:Ether = 9:1). Compound **6d** was isolated as a white solid (76 mg, 14% yield). A second run had a yield of 12%.



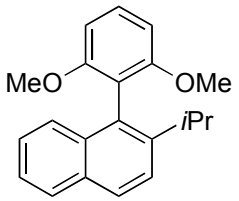
6d

^1H NMR (300 MHz, $CDCl_3$): δ 0.12 (s, 9H), 0.57 (d, J = 5.7 Hz, 1H), 0.84 (d, J = 6.3 Hz, 3H), 0.99 (d, J = 7.2 Hz, 6H), 1.09 (d, J = 6.9 Hz, 3H), 1.19-1.37 (m, 12H), 1.61 (s, 1H), 2.17 (septet, J = 6.9 Hz, 1H), 2.37 (d, J = 5.7 Hz, 1H), 2.90 (septet, J = 6.9 Hz, 1H), 3.11 (m, 1H), 4.41 (septet, J = 6.6 Hz, 1H), 6.96-7.28 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.8, 21.3, 23.7, 23.8, 24.1, 24.3, 24.9 (2 peaks), 26.7, 27.9, 31.1, 31.6, 31.8, 33.4, 52.7, 85.3, 91.0, 122.6, 123.2, 124.1, 125.4, 127.7, 135.6, 144.0, 146.1, 146.8, 151.3, 151.8 IR (Neat) 3302 s, (alcohol).

Rearrangement of 6 under Optimized Conditions (Table 4):

General Procedure: In a glovebox, a vial was charged with **6**, toluene, and 10% $Eu(OTf)_3$. The vessel was sealed and stirred at 80 °C for 24 h. The reaction was cooled to ambient temperature, and trifluoroacetic acid was added. The reaction mixture was stirred for one hour before it was filtered through a silica plug with copious ether washings. The solvents were removed under reduced pressure, and the crude material was subjected to preparatory thin-layer chromatography using 9:1 hexanes:ether as the eluent.

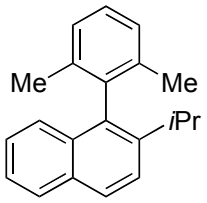
Compound 7a (Entry 1). The general procedure was applied using **6a** (40 mg, 0.010 mmol), toluene (1.0 mL), and $Eu(OTf)_3$ (6.0 mg, 0.0010 mmol). The product **7b** was isolated as an oil (20 mg, 65% yield, >95:5 regioselectivity). A second run had a yield of 60%.



7a

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.20 (d, J = 7.2 Hz, 6H), 2.83 (septet, J = 6.9 Hz, 1H), 3.64 (s, 6H), 6.75 (d, J = 8.4 Hz, 2H), 7.28-7.46 (m, 4H), 7.58 (d, J = 9 Hz, 1H), 7.83-7.91 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.5, 31.1, 55.7, 103.9, 116.2, 123.6, 124.6, 125.3, 125.5, 125.9, 127.8, 128.2, 129.0, 131.9, 132.8, 144.5, 158.5. HRMS (EI) calcd for $C_{21}H_{22}O_2$ (M+) 306.1619 found 306.1617

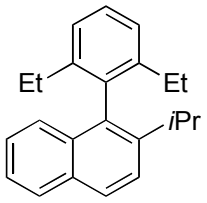
Compound 7b (Entry 2). The general procedure was applied using **6b** (169 mg, 0.464 mmol), toluene (5.0 mL), and $Eu(OTf)_3$ (30 mg, 0.046 mmol). The product **7b** was isolated as an off-color oil (89 mg, 70% yield, >95:5 regioselectivity). A second run had a yield of 75%.



7b

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.24 (d, J = 6.9 Hz, 6H), 1.91 (s, 6H), 2.78 (septet, J = 6.9 Hz, 1H), 7.18-7.48 (m, 6H), 7.62 (d, J = 8.7 Hz, 1H), 7.88-7.94 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.3, 23.7, 30.5, 124.0, 125.0, 125.5, 126.0, 127.1, 127.4, 127.7, 127.9, 131.9, 132.2, 134.8, 137.2, 138.3, 143.0. HRMS (EI) calcd for $C_{21}H_{22}$ (M+) 274.1722 found 274.1724.

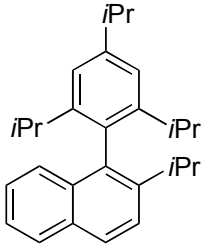
Compound 7c (Entry 3). The general procedure was applied using **6c** (218 mg, 0.555 mmol), toluene (5.6 mL), and $Eu(OTf)_3$ (33 mg, 0.056 mmol). The product **7c** was isolated as a light yellow oil (122 mg, 73% yield, >95:5 regioselectivity). A second run had a yield of 72%.



7c

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.02 (t, J = 7.5 Hz, 6H), 1.24 (d, J = 7.2 Hz, 6H), 2.12-2.36 (m, 4H), 2.79 (septet, J = 6.9 Hz, 1H), 7.24-7.51 (m, 6H), 7.64 (d, J = 8.7 Hz, 1H), 7.89-7.96 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.6, 23.6, 26.1, 30.4, 123.9, 124.9, 125.1, 125.4, 125.5, 126.5, 127.5, 127.7, 132.0, 132.7, 134.4, 137.1, 142.7, 143.2. HRMS (EI) calcd for $C_{23}H_{26}$ (M+) 302.2035 found 302.2038.

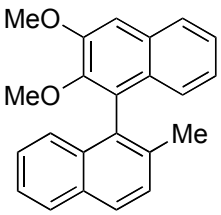
Compound 7d (Entry 4). The general procedure was applied using **6d** (50 mg, 0.011 mmol), toluene (1.1 mL), and $Eu(OTf)_3$ (6.5 mg, 0.0011 mmol). The product **7d** was isolated as an off-color oil (29 mg, 73% yield, >95:5 regioselectivity). A second run had a yield of 78%. Crystals suitable for diffraction were obtained by slow evaporation of the solvent of a concentrated solution of **7d** in dichloromethane at –20 °C.



7d

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.83 (d, J = 6.6 Hz, 6H), 1.12 (d, J = 6.9 Hz, 6H), 1.22 (d, J = 6.6 Hz, 6H), 1.39 (d, J = 6.6 Hz, 6H), 2.35 (hep, J = 6.6 Hz, 2H), 2.87 (hep, J = 7.2 Hz, 1H), 3.03 (hep, J = 6.9 Hz, 1H), 7.14-7.29 (m, 4H), 7.39 (t, J = 6.9 Hz, 1H), 7.57 (d, J = 9 Hz, 1H), 7.82-7.90 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.8, 23.9, 24.1, 25.3, 30.1, 30.3 30.4, 34.1, 120.9, 123.7, 124.9, 125.0, 127.4, 127.5, 127.7, 132.0, 132.7, 133.5, 134.6, 143.8, 147.3, 147.9. HRMS (EI) calcd for $C_{28}H_{36}$ (M+) 372.2817 found 372.2809.

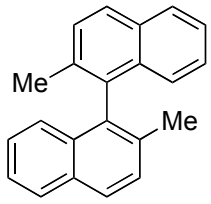
Biaryl Naphthalene Synthesis without Isolation of Intermediates (Table 5):



9a

Compound 9a (Entry 1). An oven-dried flask was charged with 2.0 mL anhydrous Et_2O and 1-bromo-2,3-dimethoxynaphthalene (232 mg, 0.868 mmol). *n*-BuLi (0.330 mL, 0.868 mmol, 2.5 M in hexanes) was added dropwise at room temperature, and the reaction was allowed to stir for 15 minutes. The reaction was then cooled to –78 ^oC, and indanone **1** (200 mg, 0.870 mmol) in Et_2O (2.4 mL) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 24h. At the conclusion of the reaction, 5 mL of NH_4Cl (saturated, aqueous) was added followed by 20 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to a silica plug (Hex:Ether = 3:1). This crude material (221 mg, 0.530 mmol) was subjected to the optimized rearrangement procedure (Table 3) using toluene (5.3 mL), and $Eu(OTf)_3$ (32 mg, 0.053 mmol). The product **9a** was isolated as a white solid (176 mg, 62% yield from indanone **1**). A second run had a yield of 60%.

^1H NMR (300 MHz, $CDCl_3$): δ 2.17 (s, 3H), 3.51 (s, 3H), 4.09 (s, 3H), 6.96-7.54 (m, 8H), 7.83 (d, J = 8.1 Hz, 1H), 7.91 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.4, 55.6, 60.3, 106.8, 124.1, 124.7, 125.3, 125.5, 125.9, 126.6, 127.6, 127.8, 128.4, 128.6, 128.8, 131.3, 131.8, 131.9, 133.2, 134.9, 146.9, 152.3, one aromatic carbon is not observed.



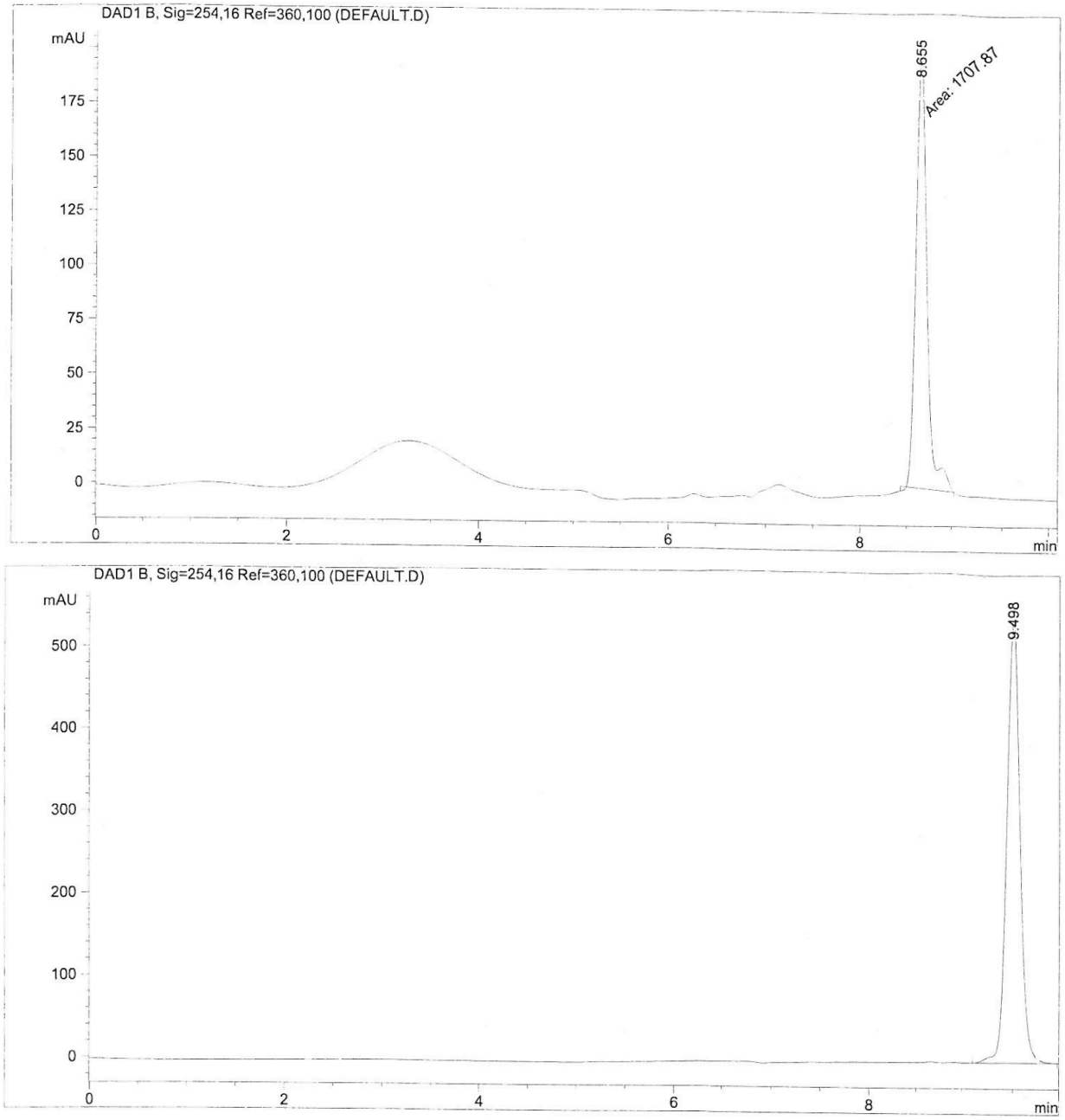
9b

Compound 9b [32854-84-7] (Entry 2). An oven-dried flask was charged with 2.0 mL anhydrous Et_2O and 1-bromo-2-methylnaphthalene (384 mg, 1.74 mmol). *n*-BuLi (0.660 mL, 1.65 mmol, 2.5 M in hexanes) was added dropwise, and the reaction was allowed to stir for 15 minutes. The reaction was then cooled to –78 ^oC, and indanone **1** (200 mg, 0.870 mmol) in Et_2O (2.4 mL) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 24h. At the conclusion of the reaction, 5 mL of NH_4Cl (saturated, aqueous) was added followed by 20 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to a silica plug (Hex:Ether = 3:1). The crude material (278 mg, 0.746 mmol) was subjected to the optimized rearrangement procedure (Table 3) with toluene (7.5 mL), and $Eu(OTf)_3$ (45 mg, 0.075 mmol). The product **9b** was isolated as a light yellow solid (164 mg, 67% yield from indanone **1**). A second run had a yield of 62%.

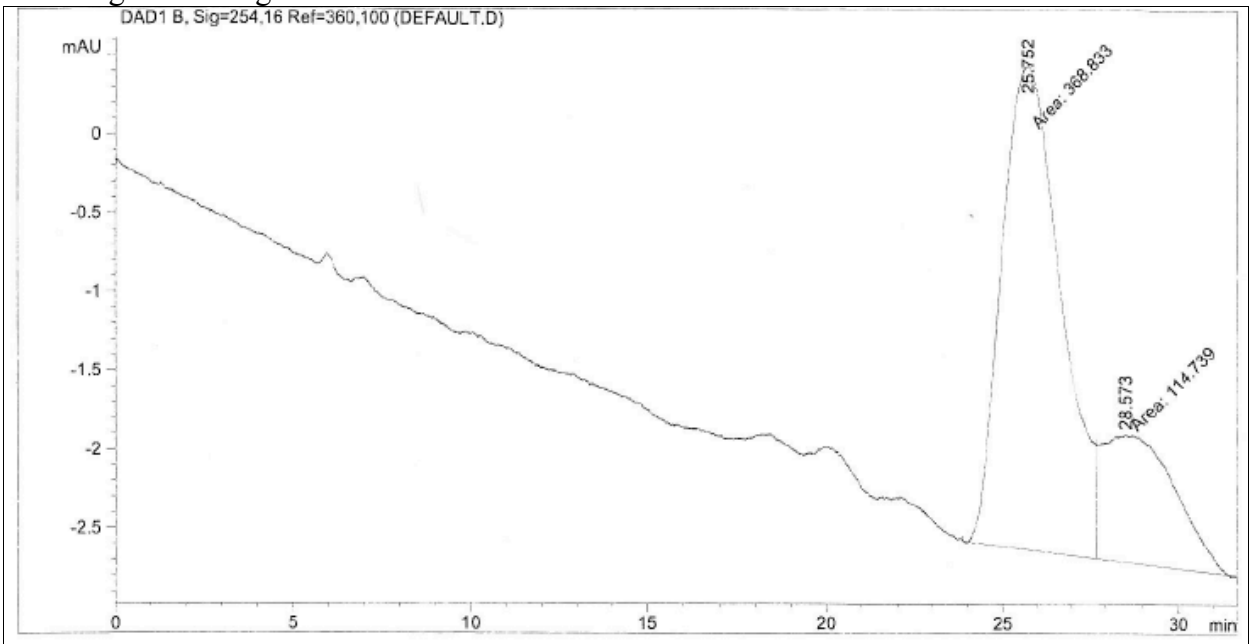
^1H NMR (300 MHz, $CDCl_3$): δ 2.09 (s, 6H), 7.14 (d, J = 8.4 Hz, 2H), 7.25 (m, 2H), 7.41-7.57 (m, 4H), 7.94 (m, 4H).

Preliminary Studies toward Asymmetric Synthesis

The racemic mixture of precursor **1** was separated by semi-preparatory HPLC using a Chiralcel ODH (98:2 hexanes:isopropanol at 2 mL/min). The HPLC traces of the enantiomers of **1** are shown below.



Optically pure **1 (**35 mg, 0.15 mmol) of was added to a solution of 2-methoxynaphthyllithium in Et_2O (0.21 mmol, 1.5 mL) at –78 °C. The solution was allowed to warm to room temperature and stirred for 24h. At the conclusion of the reaction, 5 mL of NH_4Cl (saturated, aqueous) was added followed by 20 mL ether. The organic phase was washed three times with brine and dried over $MgSO_4$. Solvents were removed under reduced pressure. The resulting crude material was then subjected to rearrangement conditions: $Eu(OTf)_3$ (5.6 mg, 0.093 mmol) in dichloroethane (1.0 mL) at 70 °C for 24h. At the conclusion of the reaction, the mixture was cooled to ambient temperature and filtered through a silica plug with copious ether washings. The solvents were removed under reduced pressure. The crude material was subjected to preparatory thin-layer chromatography using 9:1 hexanes:ether as the eluent to furnish optically enriched **3c** (24 mg, 54% from optically pure indanone **1**). HPLC analysis (Chiracel OT+, hexanes, 1.0 mL/min) indicated an enantiomeric excess of 52%. The HPLC traces of the enantiomerically enriched **3d** and the racemic mixture are shown below. Complete baseline separation was not possible despite a thorough screening of solvent conditions.

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================================================================================
                          Area Percent Report
================================================================================

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Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1  25.752 MF    1.9904  368.83340    3.08846  76.2726
   2  28.573 FM    2.3589  114.73933 8.10689e-1  23.7274

Totals :                   483.57273    3.89915
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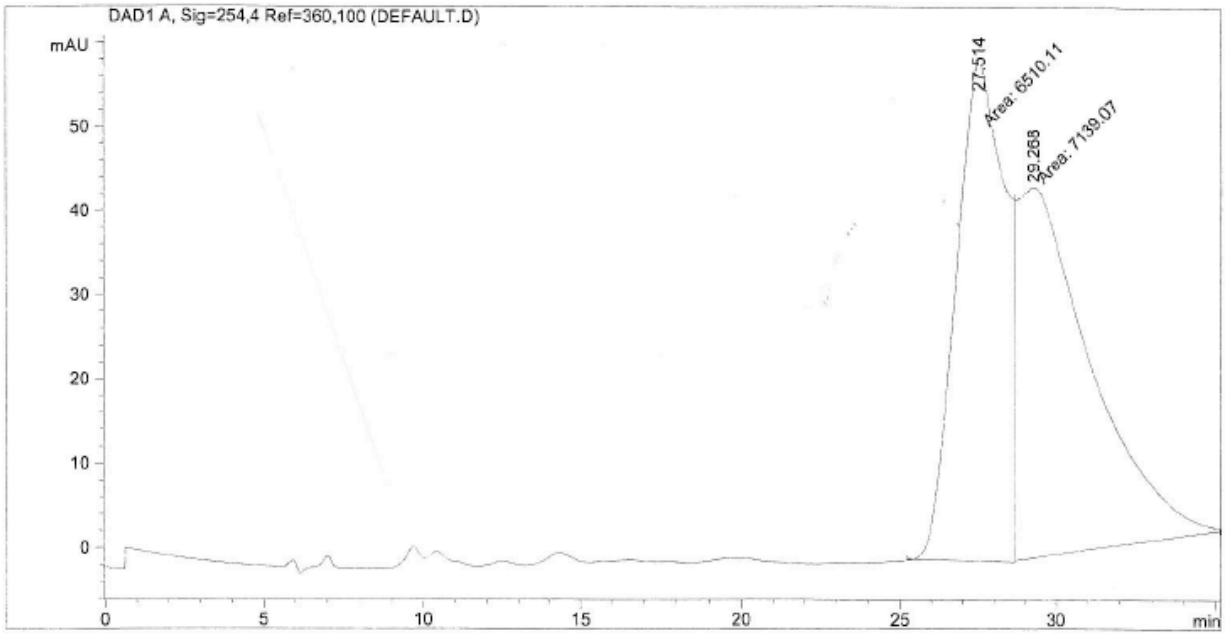


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=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1  27.514 MM    1.8315 6510.10791   59.24355  47.6960
   2  29.268 MM    2.7059 7139.07129   43.97241  52.3040

Totals :                  1.36492e4   103.21596
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Crystal Structure Information for Compound 2c

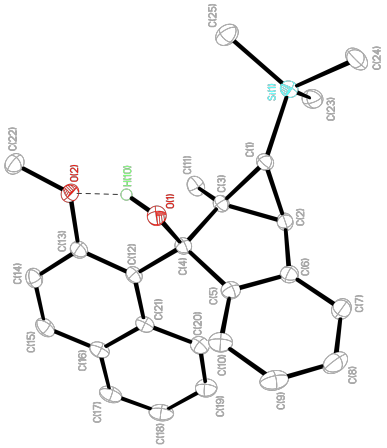

Table 1. Crystal data and structure refinement for liu48 (**2c**).

Identification code	liu48	
Empirical formula	C25 H28 O2 Si	
Formula weight	388.56	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 7.3361(7) Å	α= 77.056(2)°.
	b = 9.8727(9) Å	β= 81.2040(10)°.
	c = 15.9826(15) Å	γ = 74.336(2)°.
Volume	1080.98(18) Å^3	
Z	2	
Density (calculated)	1.194 Mg/m^3	
Absorption coefficient	0.126 mm^{-1}	
F(000)	416	
Crystal size	0.39 x 0.17 x 0.12 mm^3	
Theta range for data collection	2.18 to 27.00°.	
Index ranges	-9<=h<=9, -12<=k<=12, -20<=l<=20	
Reflections collected	12128	
Independent reflections	4706 [R(int) = 0.0151]	
Completeness to theta = 27.00°	99.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9851 and 0.9526	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4706 / 0 / 365	
Goodness-of-fit on F^2	1.055	
Final R indices [I>2sigma(I)]	R1 = 0.0369, wR2 = 0.1016	
R indices (all data)	R1 = 0.0402, wR2 = 0.1052	
Largest diff. peak and hole	0.350 and -0.174 e.Å^{-3}	

Crystal Structure Information for Compound 7d

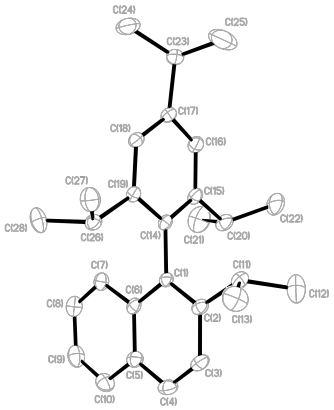

Table 1. Crystal data and structure refinement for liu66 (**7d**).

Identification code	liu66	
Empirical formula	C28 H36	
Formula weight	372.57	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 16.297(4) Å	α= 90°.
	b = 9.649(2) Å	β= 95.118(4)°.
	c = 29.806(7) Å	γ = 90°.
Volume	4668(2) Å^3	
Z	8	
Density (calculated)	1.060 Mg/m^3	
Absorption coefficient	0.059 mm^{-1}	
F(000)	1632	
Crystal size	0.45 x 0.41 x 0.02 mm^3	
Theta range for data collection	1.37 to 24.00°.	
Index ranges	-18<=h<=18, -11<=k<=11, -34<=l<=34	
Reflections collected	38119	
Independent reflections	7311 [R(int) = 0.0934]	
Completeness to theta = 24.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9988 and 0.9739	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7311 / 0 / 511	
Goodness-of-fit on F^2	1.004	
Final R indices [I>2sigma(I)]	R1 = 0.0687, wR2 = 0.1617	
R indices (all data)	R1 = 0.1209, wR2 = 0.2024	
Largest diff. peak and hole	0.343 and -0.218 e.Å^{-3}	