Aryl Amidation Routes to Dihydropyrrolo[3,2-e]indoles and pyrrolo[3,2-

f]tetrahydroquinolines: The Total Synthesis of the (+/-) CC-1065 CPI Subunit.

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General Experimental

Melting points are reported uncorrected. Infrared spectra were recorded as thin films on NaCl plates. ¹H spectra were obtained at either 400 MHz or 600 MHz (100 MHz or 150 MHz for ¹³C). Spectra recorded in CDCl₃ were referenced to residual CHCl₃ at 7.26 ppm for ¹H or 77.0 ppm for ¹³C. The multiplicities of the ¹H signal are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dt = doublet of triplets, ad = apparent doublet, at = apparent triplet, br = broad. High resolution mass spectra (HRMS) were obtained at an ionizing voltage of 70 eV. All solvents were purified via a solvent purification system. High pressure reactions were performed in a high-pressure generator. Palladium (0) dibenzylideneacetone, and Xantphos were kept in a dessicator under an argon atmosphere between uses. Reactions were checked for completion by TLC (silica gel 0.25mm, 60 F₂₅₄). Flash chromatography was performed using silica (230-400 mesh).

p-aminophenol (12). Nitrophenol 11 was prepared using the two-step procedure of Otten *et al.*¹² To 1.24 g of NiCl₂H₂O (4.1 mmol) in 250 ml of methanol and 150 ml of THF was added nitrophenol 11 (10.0 g, 41.0 mmol). The resulting mixture was stirred at ambient temperature until the nickel (II) was dissolved, at which point, the reaction mixture was cooled to -20°C. Once at this temperature, sodium borohydride (9.31 g, 245 mmol) of was added, portion-wise. Approximately 15 minutes after the final addition of borohydride, the reaction was deemed complete and the mixture was filtered over celite, and the residue was washed with THF. The resulting liquid was concentrated *in-vacuo* and the resulting solid was taken up in ethyl acetate and washed with brine twice, dried over MgSO₄, and filtered. The resulting organic phase was concentrated via rotary evaporation to yield crude aniline **12** as a black powder. m.p. = 134

(dec.); ¹H NMR (400 MHz, CDCl₃) δ = 7.45-7.30 (m, 5H), 6.62 (d, J = 8.4, 1H), 6.46 (d, J = 2.8, 1H), 6.30 (dd, J = 8.4, 2.8 Hz, 1H), 5.02 (s, 1H), 2.20 (s, 1H); Note that due to the instability of this compound, the crude aniline was used immediately in the following reaction.

N-Tosylated *p*-aminophenol (13). Aniline 12 (2.68g, 12 mmol) was added to a solution of 75 ml of 1:2 CH₂Cl₂:pyridine. To this solution was then added tosyl chloride (2.42 g, 13 mmol) of in three increments over five minutes. The reaction mixture was then allowed to stir at room temperature for four hours, at which point it was concentrated *in vacuo*. The residue was then taken up in ethyl acetate, and washed with dilute H₂SO₄. After re-extraction, the organic layers were dried, evaporated *in vacuo* and then taken up in 1:6 ethyl acetate: hexanes and heated briefly to leave, upon recrystallization, 3.79 g (84%) of **13** as a slightly pink powder. m.p. = 190-192°C; ¹H NMR (400 MHz, d6-DMSO) δ = 9.43 (s, 1H), 9.10 (s, 1H), 7.43 (d, J = 8.0, 2H), 7.30 (m, 3H), 7.18 (d, J = 7.2, 2H), 7.13 (d, J = 8.0, 2H), 6.96 (d, J = 9.2, 1H), 6.26 (m, 2H), 4.72 (s, 2H), 2.27 (s, 3H); ¹³C NMR (100 MHz, d6-DMSO) δ = 157.5, 153.5, 142.5, 138.2, 136.8, 129.1, 128.4, 127.5, 127.0, 126.7, 116.3, 106.5, 101.3, 69.3, 21.2; IR (thin film) v = 3409, 3225, 1652, 1618, 1508, 1458, 1335, 1157 cm⁻¹; MS *m*/z (relative intensity) 369 (20, M⁺⁺), 278 (13), 214.1 (49, loss of toluenesulfonyl), 155 (29), 91 (100); HRMS calc'd for C₂₀H₁₉NO₄S = 369.1035, found: 369.1039.

TBDPS protected hexa-2,4-diene-1,6-diol (14a). The diene diol precursor to compounds 14a and 14b was obtained as per the procedure of Roush *et. al.*¹⁵ To 1.01 g (8.76 mmol) of this diene diol precursor and imidazole (1.79 g, 26.3 mmol) of in 10 ml of dry DMF was added TBDPSCl (5.30 g, 19.3 mmol). After stirring for 48h at ambient temperature, the reaction mixture was diluted with 10 ml of diethyl ether and washed three times with 100 ml of water, followed by

brine. The organic phase was then washed with brine, dried over MgSO₄, and filtered. After concentration, the crude residue was purified by flash chromatography (5% ethyl ether in hexanes) to give 4.60 g (88% yield) of white, crystalline solid **14a**. m.p. = 62-64 °C; ¹H NMR (400 MHz, CDCl₃) δ = 7.74-7.71 (m, 8H), 7.45-7.39 (m, 12H), 6.38-6.28 (m, 2H), 5.81-5.75 (m, 2H), 4.28 (d, J = 4.4, 4H), 1.11 (s, 18H); ¹³C NMR (100 MHz, CDCl₃) δ = 135.5, 133.7, 131.7, 129.6, 129.3, 127.6, 64.1, 26.8, 19.2; IR (thin film) v = 2932, 2858, 1473, 1429, 1114, 822 cm⁻¹ HRMS calc'd for C₃₈H₄₆O₂Si₂ = 590.3036; found: 590.3025.

MOM protected hexa-2,4-diene-1,6-diol (14b) To 1.01 g (8.8 mmol) of the diene diol precursor (refer to preparation of **14a**) and diisopropylethylamine (4.58 ml, 26.3 mmol) of in 25 ml of dry dichloromethane and 25 ml of dry THF at 0°C was added MOMCl (1.33 ml, 17.5 mmol). After stirring for 20 h at ambient temperature, the reaction mixture was diluted with 50 ml of diethyl ether and washed three times with 100 ml of water, followed by brine. The organic phase was then washed with brine, dried over MgSO₄, and filtered. After concentration, the crude residue was purified by flash chromatography (5 - 20% ethyl acetate in hexanes) to give 1.75 g (98% yield) of clear yellow oil **14b**. ¹H NMR (400 MHz, CDCl₃) δ = 6.26-6.18 (m, 2H), 5.76-5.66 (m, 2H), 4.57 (s, 4H), 4.03 (d, J = 5.6, 4H), 3.30 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ = 131.7, 129.4, 95.3, 67.1, 55.0; IR (thin film) v = 2952, 2885, 1451, 1149, 1044cm⁻¹. HRMS calc'd for C₁₀H₁₈O₄ = 202.1205; found: 202.1198.

Triflated dihydronaphthol (16a). The dihydronaphthol **15a** (60 mg, 0.062 mmol) was dissolved in 1.5 ml dry THF at 0°C and added by cannula to a vigorously stirred suspension of washed (NaH 2.8 mg, 0.094 mmol) in 1.0 ml THF at 0°C. N-phenyltriflamide (27 mg, 0.075 mmol) was then dissolved in 1.0 ml of THF at 0°C and added by cannula to the reaction mixture.

The mixture was allowed to warm to room temperature and was stirred for a total of 5 hours before quenching with water. The quenched mixture was extracted with ethyl acetate and the aqueous phase was then re-extracted three times. Combined extracts were dried and concentrated *in vacuo* to leave 0.067 g (99%) of pale yellow oil **16a**. ¹H NMR (400 MHz, CDCl₃) $\delta = 8.24$ (s, 1H), 7.57 (d, J = 8.0, 2H), 7.43 (d, J = 7.6, 2H), 7.39 (d, J = 7.6, 2H), 7.33-7.14 (m, 14H), 7.02-6.90 (m, 7H), 6.84 (t, J = 7.6, 1H), 6.73 (t, J = 7.6, 1H), 6.18 (dd, J = 10.0, 5.2, 1H), 5.67 (dd, J = 10.0, 5.2, 1H), 4.71 (d, J = 12.4, 1H), 4.61 (d, J = 12.4, 1H), 4.24 (m, 1H), 3.72 (m, 2H), 3.49 (dd, J = 9.2, 4.8, 1H), 2.73 (t, J = 10.0, 1H), 2.41 (t, J = 10.0, 1H), 2.23 (s, 3H), 0.89 (s, 9H), 0.84 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) $\delta = 153.2$, 145.8, 142.7, 138.6, 135.5, 135.4 (2C), 135.1, 133.1, 132.9, 131.5, 131.1, 130.5, 129.9, 129.7, 139.6, 129.5, 129.4, 128.8, 128.5, 128.0, 127.8, 127.5 (2C), 127.3, 127.1, 125.1, 125.0, 122.1 [(trifluoromethanesulfonate CF₃) q, J = 279.0], 105.0, 70.4, 70.2, 69.3, 39.1, 38.4, 26.7, 26.5, 21.5, 19.0, 18.9; IR (thin film) v = 3234, 2932, 2859, 1614, 1471, 1408 cm⁻¹; TOF MS ES+ calc'd for C₅₉H₆₂F₃NO₈S₂Si₂ = 1089.3408; found: 1089.3408.

Triflated dihydronaphthol (16b). Dihydronaphthol **15b** (0.510 g, 0.896 mmol) was dissolved in 15 ml dry THF at 0°C and added by cannula to a vigorously stirred suspension of washed NaH (32 mg, 1.34 mmol) in 20.0 ml THF at 0°C. N-phenyltriflamide (39 mg, 1.10 mmol) was then dissolved in 15.0 ml of THF at 0°C and added by cannula to the reaction mixture. The mixture was allowed to warm to room temperature and was stirred for a total of 40 minutes before quenching with saturated ammonium chloride. The quenched mixture was extracted with ethyl acetate and the aqueous phase was then re-extracted three times. Combined extracts were dried and concentrated *in vacuo* to leave 0.620 g (98%) of pale yellow oil **16b**. ¹H NMR (400 MHz, CDCl₃) δ = 7.94 (s, 1H), 7.60 (d, J = 8.4, 2H), 7.33-7.30 (m, 3H), 7.22-7.19 (m, 2H), 7.09 (d, J = 8.4, 2H), 6.77 (s, 1H), 6.12 (dd, J = 10.0, 5.2, 1H), 5.92 (dd, J = 10.0, 5.6, 1H), 4.81 (d, J = 12.0, 1H), 4.67 (d, J = 12.0, 1H), 4.61-4.55 (AB, δ_A = 4.60, δ_B = 4.56, J_{AB} = 6.8, 2H), 4.54-4.51 (AB, δ_A = 4.54, δ_B = 4.52, J_{AB} = 6.8, 2H), 4.24-4.18 (m, 1H), 3.88-3.82 (m, 1H), 3.76 (dd, J = 9.2, 4.8, 1H), 3.67 (dd, J = 9.2, 4.8, 1H), 3.51 (dd, J = 17.6, 8.8, 2H), 3.25 (s, 3H), 3.20 (s, 3H), 2.35 (s, 3H) ; ¹³C NMR (100 MHz, CDCl₃) δ = 153.7, 146.0, 143.1, 139.2, 138.0, 135.3, 129.6, 129.1, 128.5, 128.3, 128.1, 127.2, 126.9, 126.6, 126.4, 124.8, 121.9, 118.3 [(trifluoromethanesulfonate CF₃) q, J = 317.5], 105.0, 96.0, 72.6, 70.9, 70.8, 55.4, 55.0, 37.1, 36.2, 21.5; IR (thin film) v = 2928, 2885, 1437, 1215, 1038 cm⁻¹; HRMS calc'd for C₃₁H₃₄F₃NO₁₀S₂ = 701.1576; found: 701.1567.

5-trifloxyindole (17a). The dihydronaphthalene **16a** (0.271 g, 0.249 mmol) was suspended in a mixture of THF (20 ml) and H₂O (10 ml). A crystal of osmium tetraoxide (~ 2 mg) was added and the mixture was stirred for 30 minutes, giving a black solution, after which NMO (0.044 g, 0.373 mmol) was added. The solution was stirred until the starting material was consumed by TLC (~ 5.0 h), at which point Na₂S₂O₃ (0.376 g, 2.983 mmol) was added and the mixture stirred for a further 30 minutes. The mixture was extracted with ethyl acetate and the aqueous phase was then re-extracted. Combined extracts were dried and concentrated *in vacuo* to leave the crude diol. The crude diol was used without further purification, and was suspended in 10 ml CH₂Cl₂. This suspension was added dropwise, via cannula, to a vigorously stirred mixture of NaIO₄/SiO₂ (2.80 g, 0.68 mmol/g loading) in 10 ml of CH₂Cl₂. The mixture was stirred for one hour, filtered and concentrated to yield the crude dialdehyde, which was taken up in dry THF. Catalytic H₂SO₄ was added to the solution and the mixture was stirred under argon until

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complete consumption of the starting material was indicated by TLC (~24 hours). The mixture was diluted with 20 ml dichloromethane and washed with 20 ml of saturated NaHCO₃. Aqueous washes were re-extracted 3 times with 10 ml dichloromethane, combined with the original extract, dried and preabsorbed with 3 g SiO₂ in vacuo. This crude, silica supported indole was then purified by FCC (elution with a gradient of 2 - 10% ethyl acetate in hexanes) to yield 0.214 g (78% over 3 steps) of pure **17a** as a white powder. m.p. 126-128 °C; ¹H NMR (600 MHz, $CDCl_3$) $\delta = 9.85$ (s, 1H), 7.73 (d, J = 6.6, 2H), 7.61 (d, J = 8.4, 2H), 7.54 (s, 1H), 7.48-7.24 (m, 1) 13H), 7.31-7.24 (m, 6H), 7.17 (d, J = 8.4, 2H), 7.10 (d, J = 8.4, 2H) 7.06 (t, J = 8.4, 2H), 6.72 (s, 1H), 5.20 (m, 1H), 5.04 (m, 1H), 5.04-4.98 (AB, $\delta_A = 5.03$, $\delta_B = 4.99$, $J_{AB} = 12.0$, 2H), 4.73 (d, J = 12.6, 1H), 4.46 (dd, J = 10.2, 6.0, 1H), 3.86 (t, J = 10.2, 1H), 2.36 (s, 3H), 1.02 (s, 9H), 0.80 (s, 9H): ¹³C NMR (100 MHz, CDCl₃) δ = 198.9, 145.8, 144.4 (2C), 136.9, 135.7, 135.6, 135.4, 135.2, 135.1, 132.9, 132.8, 132.7, 130.4, 130.0, 129.7, 129.5, 128.6, 128.5, 127.9 (2C), 127.7 (2C),127.0, 124.2, 123.7, 119.5, 111.6 [(CF₃) q, J = 365.1] 100.8, 71.1, 62.6, 58.5, 53.8, 26.8, 26.5, 21.6, 19.1, 18.9; IR (thin film) v = 2932, 2859, 1734, 1617, 1428, 1218, 1113 cm⁻¹; m/zcalc'd for $C_{59}H_{60}F_3NO_9S_2Si_2 = 1103.3200$; TOF MS ES⁺ found: 1103.3200.

5-trifloxyindole (17b). The dihydronaphthalene **16b** (0.925 g, 1.24 mmol) was suspended in a mixture of THF (20 ml) and H₂O (10 ml). A crystal of osmium tetraoxide (~ 2 mg) was added, followed by 2,6-lutidine (0.456 ml, 3.91 mmol)¹⁸ and the mixture was stirred for 30 minutes, giving a black solution, after which NMO (0.460 g, 3.91 mmol) was added. The solution was stirred until the starting material was consumed by TLC (~ 3.5 h), at which point Na₂S₂O₃ (0.376g, 2.983 mmol) was added and the mixture stirred for a further 30 minutes. The mixture was extracted with ethyl acetate and the aqueous phase was then re-extracted. Combined extracts were dried and concentrated *in vacuo* to leave the crude diol. The crude diol was used

without further purification, and was suspended in 15 ml CH₂Cl₂. This suspension was added dropwise, via cannula, to a vigorously stirred mixture of NaIO₄/SiO₂ (2.73 g, 0.68 mmol/g loading) in 10 ml of CH_2Cl_2 . The mixture was stirred for two and a half hours, filtered and concentrated to yield the crude dialdehyde, which was taken up in dry THF. Triethylamine (1.04 ml, 7.44 mmol), followed by 0.385 ml (4.95 mmol) of mesyl chloride were then added to the solution and the mixture was stirred under argon for 20 minutes. The reaction mixture was then washed with 5% HCl and extracted with ethyl acetate. Aqueous washes were re-extracted 3 times with 10 ml of ethyl acetate, combined with the original extract, dried and preabsorbed with SiO₂ in vacuo. This crude, silica supported indole was then purified by FCC (elution with isocratic 30% ethyl acetate in hexanes) to yield 0.790 g (86% over 3 steps) of **17b** as a clear oil. ¹H NMR (400 MHz, CDCl₃) δ = 9.81 (s, 1H), 8.03 (s, 1H), 7.49 (d, J = 8.0, 2H), 7.38-7.34 (m, 3H), 7.24-7.21 (m, 2H), 7.14 (d, J = 8.0, 2H), 6.71 (s, 1H), 5.03-4.95 (AB, $\delta_A = 5.01$, $\delta_B = 4.97$, $J_{AB} = 12.4, 2H$), 4.86 (d, J = 12.4, 1H), 4.73-4.65 (m, 4H), 4.61-4.56 (AB, $\delta_A = 4.60, \delta_B = 4.57$, $J_{AB} = 6.4, 2H$, 4.31-4.27 (dd, J = 10.0, 6.4, 1H), 3.94-3.90 (dd, J = 10.0, 6.4, 1H), 3.40 (s, 1H), 3.23 (s, 1H), 2.38 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ = 198.5, 146.0, 144.6, 144.4, 136.6, 134.8, 132.5, 131.6, 129.5, 128.6, 127.9, 127.2, 124.6, 118.1 [(trifluoromethanesulfonate CF₃) q, J = 317.9], 116.2, 113.4, 101.3, 96.4, 95.0, 71.1, 65.7, 61.0, 55.8, 55.2, 51.5, 21.6; IR (thin film) $v = 2926, 1701, 1610, 1507, 1420, 1175, 1139 \text{ cm}^{-1}$; HRMS calc'd for $C_{31}H_{32}F_{3}NO_{11}S_{2} =$ 715.1369; found: 715.1362.

Indole-4-ethylcarbonate (**18a**). To compound **17a** (0.185 g, 0.167 mmol) in 2 ml of dry methanol and 2 ml of dry THF was added sodium borohydride (0.006 g, 0.184 mmol) at 0°C and the resulting reaction mixture was stirred for 20 minutes. After this time the reaction was quenched with saturated aqueous ammonium chloride and the mixture was partitioned with ethyl

acetate. The aqueous layer was re-extracted three times with ethyl acetate and the combined organic layers were washed with brine and dried over MgSO₄ before being concentrated in vacuo to yield the crude alcohol which was used without purification for carbonate formation. This crude alcohol was dissolved in 2 ml of pyridine and 2 ml of dry dichloromethane at 0°C under an argon atmosphere. Methyl chloroformate (0.015 ml, 0.201 mmol) was then added drop-wise to this reaction mixture, which was stirred and allowed to reach room temperature overnight. After this time period, the solvents were removed by rotary-evaporation and the remaining residue was taken up in 10 ml ethyl acetate and extracted thrice with 10 ml of 5% HCl, followed by a sodium bicarbonate wash to neutralize the organic phase. The organic phase was then washed with brine and dried over MgSO₄ before being concentrated in vacuo to yield 0.188 g (96 % yield) of white semi-solid **18a**. ¹H NMR (400 MHz, CDCl₃) δ = 7.75 (d, J = 6.8, 2H), 7.66 (m, 3H), 7.48-7.20 (m, 21H), 7.14-7.07 (AB, $\delta_A = 7.11$, $\delta_B = 7.10$, $J_{AB} = 7.8$, 4H), 6.59 (s, 1H), 5.14 (d, J = 12.4, 1H), 5.00-4.92 (AB, $\delta_A = 4.97$, $\delta_B = 4.95$, $J_{AB} = 12.4$, 2H), 4.86 (d, J = 12.4, 1H), 4.58 (t, J = 12.4, 1H), 4.58 (t, J = 12.4, 1H) 10.0, 1H), 4.48-4.41 (m, 1H), 4.28-4.20 (m, 1H), 3.99 (t, J = 6.4, 1H), 3.82-3.74 (m, 1H), 3.60 (s, 3H), 2.35 (s, 3H), 1.08 (s, 9H), 0.81 (s, 9H); 13 C NMR (100 MHz, CDCl₃) δ = 155.4, 145.1, 144.6, 144.2, 137.1, 135.6, 135.4, 135.3, 135.2, 133.2 (2C), 132.9, 132.7, 132.6, 129.8, 129.6, 129.5, 129.4, 128.6, 128.4, 127.8, 127.7, 127.6, 127.5, 127.0, 124.1, 123.4, 120.5, 116.6, 101.3, 71.0, 67.3, 64.3, 59.6, 54.5, 41.4, 26.8, 26.5, 21.5, 19.2, 18.9; IR (thin film) v = 2958, 2932, 2859, 1757, 1424, 1271, 1175 cm⁻¹; HRMS calc'd for $C_{61}H_{64}F_3NO_{11}S_2Si_2 = 1163.3411$; found: 1163.3413.

Indole-4-ethylcarbonate (18b). To compound **17b** (0.200 g, 0.278 mmol) in 4 ml of dry methanol and 4 ml of dry THF was added 0.010 g (0.305 mmol) of sodium borohydride at 0°C and the resulting reaction mixture was stirred for 20 minutes. After this time the reaction was

quenched with saturated aqueous ammonium chloride and the mixture was partitioned with ethyl acetate. The aqueous layer was re-extracted three times with ethyl acetate and the combined organic layers were washed with brine and dried over MgSO₄ before being concentrated in vacuo to yield the crude alcohol which was used without purification for carbonate formation. This crude alcohol was dissolved in 5 ml of pyridine and 5 ml of dry dichloromethane at 0°C under an argon atmosphere, and methyl chloroformate (0.024 ml, 0.308 mmol) was added drop-wise to this reaction mixture, which was stirred and allowed to reach room temperature overnight. After this time period, the solvents were removed by rotary-evaporation and the remaining residue was taken up in 10 ml ethyl acetate and extracted thrice with 10 ml of 5% HCl, followed by a sodium bicarbonate wash to neutralize the organic phase. The organic phase was then washed with brine and dried over MgSO₄ before being concentrated with SiO₂ in vacuo to yield solid supported indole carbonate which was then subjected to column chromatography (100 ml each of 10%, 20%, and 30% ethyl acetate in hexanes). Evaporation of the resulting pure fractions yielded 0.104 g (52 % yield) of white foam **18b**. ¹H NMR (400 MHz, CDCl₃) δ = 7.99 (s, 1H), 7.49 (d, J = 8.0, 2H), 7.40-7.32 (m, 3H), 7.24-7.20 (m, 2H), 7.13 (d, J = 8.0, 2H), 6.34 (s, 1H), 4.96 (s, 2H), 4.81 (s, 2H), 4.73 (s, 2H), 4.66-4.61 (dd, J = 10.6, 7.2, 1H), 4.55 (s, 2H), 4.50 (dd, J = 10.6, 6.4, 1H), 4.19 (dt, J = 7.2, 6.6, 1H), 3.93-3.82 (m, 2H), 3.72 (s, 3H), 3.44 (s, 3H), 3.22 (s, 3H), 2.37 (s, 3H); 13 C NMR (100 MHz, CDCl₃) δ = 155.5, 145.3, 144.8, 144.4, 136.8, 135.0, 132.2, 131.2, 129.5, 128.6, 128.5, 127.9, 127.2, 124.4, 116.7, 116.5, 101.6, 96.2, 95.2, 71.0, 67.7, 67.5, 61.8, 55.6, 55.1, 54.7, 39.0, 21.5; IR (thin film) v = 2956, 1759, 1754, 1613, 1216, 1139, 1039 cm^{-1} ; HRMS calc'd for $C_{33}H_{36}F_3NO_{13}S_2 = 775.1580$; found: 775.1601.

TIPS protected dihydronaphthol (26). To a slurry of NaH (0.303 g, 7.57 mmol) of in 50 ml of dry THF at 0 °C was added via cannula 75 ml of dry THF containing dihydronaphthol **25** (2.203

g, 5.05 mmol). The naphthol was allowed to stir at this temperature for 15 minutes before neat TIPSCI was added to the mixture. The resulting reaction mixture was allowed to warm to room temperature and was then stirred for 15 minutes before quenching with 5% HCl. The biphasic mixture was then diluted with diethyl ether and extracted, followed by another ether extraction of the aqueous phase. The organic extracts were then washed with brine and dried over $MgSO_4$ before being concentrated in vacuo to yield a crude adduct which was then subjected to column chromatography (2% to 14% gradient of ethyl acetate in hexanes, 2% intervals of 250 ml each) to yield 2.93 g (94% yield) of the protected dihydronaphthalene 26 as a white crystalline solid. m.p. = 170-171 °C; ¹H NMR (600 MHz, CDCl₃) δ = 7.44 (d, J = 7.8, 2H), 7.29-7.22 (m, 3H), 7.01 (d, J = 8.4, 2H), 6.98 (d, J = 7.8, 2H), 6.22 (s, 1H), 5.97 (s, 1H), 5.96-5.91 (m, 1H), 5.88-5.83 (m, 1H), 4.47 (d, J = 12.6, 1H), 4.42-4.36 (m, 1H), 4.21 (d, J = 12.6, 1H), 3.30 (d, J = 22.2, 1H), 3.06 (d, J = 22.2, 3H), 2.33 (s, 3H), 1.17 (d, J = 6.6, 3H), 1.00 (m, 21H); 13 C NMR (100 MHz, CDCl₃) $\delta = 153.2, 152.5, 142.7, 142.2, 136.9, 136.5, 131.1, 128.7, 128.3, 127.7, 126.2, 136.9, 136.5, 131.1, 128.7, 128.3, 127.7, 126.2, 136.9, 136.5, 131.1, 128.7, 128.3, 127.7, 126.2, 136.9, 136.5, 131.1, 128.7, 128.3, 127.7, 126.2, 136.9, 136.5, 131.1, 128.7, 128.3, 127.7, 126.2, 136.9, 136.5, 131.1, 128.7, 128.3, 127.7, 126.2, 136.9, 136.5, 131.1, 128.7, 128.3, 127.7, 126.2, 136.9, 136.5, 131.1, 128.7, 128.3, 127.7, 126.2, 136.9, 136.5, 131.1, 128.7, 128.3, 127.7, 126.2, 136.9, 136.5, 131.1, 128.7, 128.3, 127.7, 126.2, 136.9, 136.5, 131.1, 128.7, 128.3, 127.7, 126.2, 136.9, 136.5, 131.1, 128.7, 128.3, 127.7, 126.2, 136.9, 136.5, 131.1, 128.7, 128.3, 127.7, 126.2, 136.9, 136.5, 131.1, 128.7, 128.3, 127.7, 126.2, 136.9, 136.5, 136$ 122.3, 118.7, 114.5, 100.7, 69.9, 30.1, 25.0, 22.5, 21.4, 17.9 (2C), 12.8; IR (thin film) v = 3268, 2943, 1598, 1598, 1327 cm⁻¹; HRMS calc'd for $C_{34}H_{45}NO_4SSi = 591.2839$; found: 591.2833.



































































































S-61













