

Supplementary Information

A General Approach to Triphenylenes and Azatriphenylenes: Total Synthesis of Dehydrotylophorine and Tylophorine

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1. Synthetic Procedures and Analytical Data

Representative procedure for compounds 6-17: Compound **5** (5-10 mg) and the corresponding alkyne (10 eq.) or nitrile (10 eq.) were added to a flame dried microwave vial and dissolved in toluene (500 μ L). To this solution either CpCo(CO)₂ or Ni(CO)₂(PPh₃)₂ (10 mol%) were added and the vial was irradiated at 300 W for 4-20 minutes in a CEM Discover microwave synthesizer. The reaction was concentrated and purified by silica gel flash chromatography, eluting with 0-100% hexanes/EtOAc.

2-Butyltriphenylene (6): ¹H NMR (300 MHz, CDCl₃) δ 8.69-8.61 (m, 4H), 8.57 (d, J = 8.1 Hz, 1H), 8.45 (s, 1H), 7.67-7.63 (m, 4H), 7.50 (dd, J = 8.1 Hz, 1H), 2.88 (t, J = 7.5 Hz, 2H), 1.77 (p, J = 7.5 Hz, 2H), 1.46 (s, J = 7.5 Hz, 2H), 0.99 (t, J = 7.5 Hz, 3H); ¹³C NMR (300 MHz, CDCl₃) δ 142.1, 130.1, 130.0, 129.9, 129.6, 128.2, 127.9, 127.3, 127.2, 126.9, 123.5, 123.4, 123.3, 122.9, 36.2, 34.0, 22.7, 14.2; MS (EI) calcd for C₂₂H₂₀ M⁺ 284, found 284.ⁱ

2-(Triphenylen-7-yl)pyridine (7): ¹H NMR (300 MHz, CDCl₃) δ 9.39 (s, 1H), 8.89-8.82 (m, 2H), 8.76 (d, J = 8.7 Hz, 1H), 8.72-8.67 (m, 3H), 8.27 (dd, J = 8.5, 1.9 Hz, 1H), 7.99 (d, J = 8.1 Hz, 1H), 7.88 (td, 7.6, 1.5 Hz, 1H), 7.73-7.66 (m, 4H), 7.34 (dd, J = 7.3, 4.9 Hz, 1H); ¹³C NMR (300 MHz, CDCl₃) δ 156.4, 148.5, 138.9, 135.7, 131.1, 130.5, 130.2, 129.9, 129.5, 128.0, 127.8, 127.7, 127.6, 125.7, 124.3, 124.1, 123.9, 123.6, 123.5, 122.9, 122.7, 121.8; HRMS (ESI⁺) calcd for C₂₃H₁₆N (M+H)⁺ 306.1277, found 306.1278.

tert-Butyl (triphenylen-7-yl)methylcarbamate (8): ¹H NMR (300 MHz, CDCl₃) δ 8.66-8.61 (m, 5H), 8.55 (s, 1H), 7.69-7.64 (m, 4H), 7.59 (d, J = 7.5 Hz, 1H), 4.58 (d, J = 4.5 Hz, 2H), 1.51 (s, 9H); ¹³C NMR (300 MHz, CDCl₃) δ 156.2, 137.9, 130.2, 130.1, 129.9, 129.8, 129.7, 129.2, 127.5, 127.4, 127.3, 126.8, 123.9, 123.5, 122.3, 79.9, 45.2, 28.7; HRMS (ESI⁺) calcd for C₂₄H₂₃NO₂ (M+H)⁺ 357.1729, found 357.1724.

(Triphenylen-7-yl)methanol (9): ¹H NMR (300 MHz, CDCl₃) δ 8.69-8.61 (m, 6H), 7.68-7.63 (m, 5H), 4.95 (s, 2H), 1.75 (s, 1H); ¹³C NMR (300 MHz, CDCl₃) δ 139.9, 130.1, 130.0, 129.9, 129.5, 127.6, 127.4, 126.3, 123.9, 123.5, 121.7, 65.8; HRMS (ESI⁺) calcd for C₁₉H₁₄O (M+H)⁺ 258.10447, found 258.1037.

ⁱ Due to the absence of any heteroatoms, this compound could not be ionized by ESI and thus no HRMS could be obtained.

4-(Triphenylen-7-yl)butanenitrile (10): ^1H NMR (300 MHz, CDCl_3) δ 8.66-8.59 (m, 5H), 8.46 (d, $J = 1.2$ Hz, 1H), 7.70-7.64 (m, 4H), 7.50 (dd, $J = 8.4, 1.2$ Hz, 1H), 3.06 (t, $J = 6.9$ Hz, 2H), 2.41 (t, $J = 6.9$ Hz, 2H), 2.15 (p, $J = 6.9$ Hz, 2H); ^{13}C NMR (300 MHz, CDCl_3) δ 138.8, 130.23, 130.2, 129.8, 129.7, 128.6, 127.8, 127.6, 127.5, 127.4, 127.3, 124.0, 123.6, 123.5, 123.4, 123.3, 123.2, 119.7, 34.9, 27.2, 16.7; HRMS (ESI^+) calcd for $\text{C}_{22}\text{H}_{17}\text{N}$ ($\text{M}+\text{H}$) $^+$ 295.1361, found 295.13631.

2,3-Bis(methoxymethyl)triphenylene (11): ^1H NMR (300 MHz, CDCl_3) δ 8.72-8.66 (m, 6H), 7.68-7.64 (m, 4H), 4.78 (s, 4H), 3.51 (s, 6H); ^{13}C NMR (300 MHz, CDCl_3) δ 135.4, 130.1, 129.8, 129.4, 127.4, 123.7, 123.6, 123.5, 72.8, 58.6; HRMS (ESI^+) calcd for $\text{C}_{22}\text{H}_{20}\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 316.14633, found 316.1456.

3-Methyl-2-azatriphenylene (12): ^1H NMR (300 MHz, CDCl_3) δ 9.83 (s, 1H), 8.70-8.60 (m, 4H), 8.26 (s, 1H), 7.81-7.67 (m, 4H), 2.84 (s, 3H); ^{13}C NMR (300 MHz, CDCl_3) δ 155.1, 146.2, 136.0, 131.6, 129.8, 129.5, 128.4, 128.0, 127.9, 127.7, 123.9, 123.7, 123.6, 122.6, 115.5, 24.6; HRMS (ESI^+) calcd for $\text{C}_{18}\text{H}_{14}\text{N}$ ($\text{M}+\text{H}$) $^+$ 244.1120, found 244.1121.

3-Ethyl-2-azatriphenylene (13): ^1H NMR (300 MHz, CDCl_3) δ 9.86 (s, 1H), 8.71-8.61 (m, 4H), 8.24 (s, 1H), 7.79-7.67 (m, 4H), 3.10 (q, $J = 7.5, 2\text{H}$), 1.48 (t, $J = 7.5, 3\text{H}$); ^{13}C NMR (300 MHz, CDCl_3) δ 160.1, 146.1, 136.3, 131.7, 129.8, 129.6, 128.4, 128.1, 127.9, 127.8, 127.7, 124.0, 123.7, 123.6, 122.8, 122.6, 114.4, 31.4, 14.4; HRMS (ESI^+) calcd for $\text{C}_{19}\text{H}_{16}\text{N}$ ($\text{M}+\text{H}$) $^+$ 258.1277, found 258.1278.

3-Vinyl-2-azatriphenylene (14): ^1H NMR (300 MHz, CDCl_3) δ 9.90 (s, 1H), 8.72-8.63 (m, 4H), 8.36 (s, 1H), 7.81-7.68 (m, 4H), 7.08 (dd, $J = 17.4, 10.8$ Hz, 1H), 6.51 (d, $J = 17.4$ Hz, 1H), 5.64 (d, $J = 10.8, 1\text{H}$); ^{13}C NMR (300 MHz, CDCl_3) δ 152.7, 147.0, 137.0, 135.9, 131.7, 130.1, 129.5, 128.5, 128.1, 127.9, 127.7, 123.9, 123.8, 123.7, 123.6, 122.8, 118.3, 114.4; HRMS (ESI^+) calcd for $\text{C}_{19}\text{H}_{14}\text{N}$ ($\text{M}+\text{H}$) $^+$ 256.1120, found 256.1121.

3-Phenyl-2-azatriphenylene (15): ^1H NMR (300 MHz, CDCl_3) δ 10.04 (s, 1H), 8.82 (s, 1H), 8.78-8.65 (m, 4 H), 8.23 (d, $J = 7.2$ Hz, 2H), 7.80-7.72 (m, 4 H), 7.58 (t, $J = 7.2$ Hz, 2H), 7.49 (t, $J = 7.2, 1\text{H}$); ^{13}C NMR (300 MHz, CDCl_3) δ 154.3, 146.8, 139.6, 136.2, 131.7, 130.1, 129.6, 129.2, 129.1, 128.3, 128.2, 128.1, 127.9, 127.7, 127.3, 123.9, 123.7, 123.6, 123.5, 122.8, 113.1; HRMS (ESI^+) calcd for $\text{C}_{23}\text{H}_{16}\text{N}$ ($\text{M}+\text{H}$) $^+$ 306.1277, found 306.1276.

3-(Azatriphen-3-yl)propan-1-ol (16): ^1H NMR (300 MHz, CDCl_3) δ 9.82 (s, 1H), 8.65-8.59 (m, 4H), 8.26 (s, 1H), 7.76-7.67 (m, 4H), 3.81 (t, $J = 6.7$ Hz, 2H), 3.23 (t, $J = 6.7$ Hz, 2H), 2.14 (p, $J = 6.7$ Hz, 2H); ^{13}C NMR (300 MHz, CDCl_3) δ 158.0, 145.8, 136.5, 131.8, 129.9, 129.8, 128.2, 127.8, 127.5, 124.1, 123.7, 123.67, 123.66, 115.7, 62.5, 53.6, 35.4, 32.2; HRMS (ESI^+) calcd for $\text{C}_{20}\text{H}_{17}\text{NO}$ ($\text{M}+\text{H}$) $^+$ 287.1310, found 287.1308.

Propyl-2-(azatriphen-3-yl)acetate (17): ^1H NMR (300 MHz, CDCl_3) δ 9.90 (s, 1H), 8.73-8.62 (m, 4H), 8.42 (s, 1H), 7.78-7.68 (m, 4H), 4.25 (q, $J = 7.2$ Hz, 2H), 4.12 (s, 2H), 1.30 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (300 MHz, CDCl_3) δ 171.0, 151.0, 146.5, 136.1, 131.6, 129.9, 129.6, 128.2, 128.0, 127.7, 127.4, 124.0, 123.6, 123.4, 122.7, 116.6, 61.4, 43.9, 14.4; HRMS (ESI^+) calcd for $\text{C}_{21}\text{H}_{18}\text{NO}_2$ ($\text{M}+\text{H}$) $^+$ 316.1332, found 316.1331.

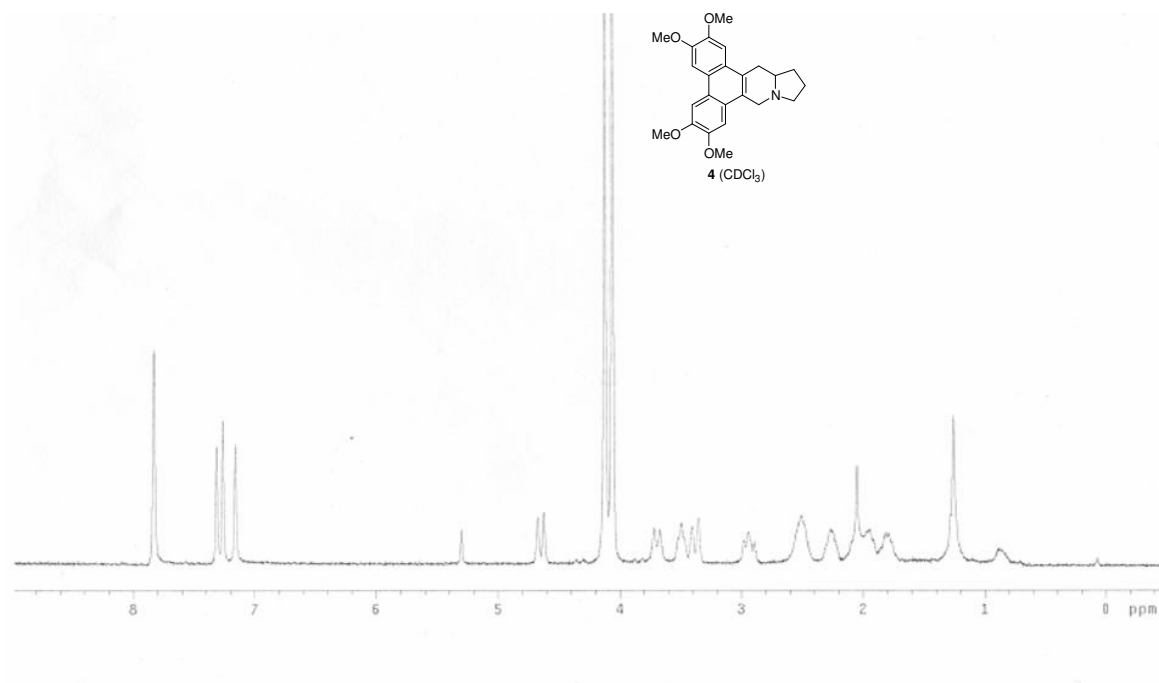
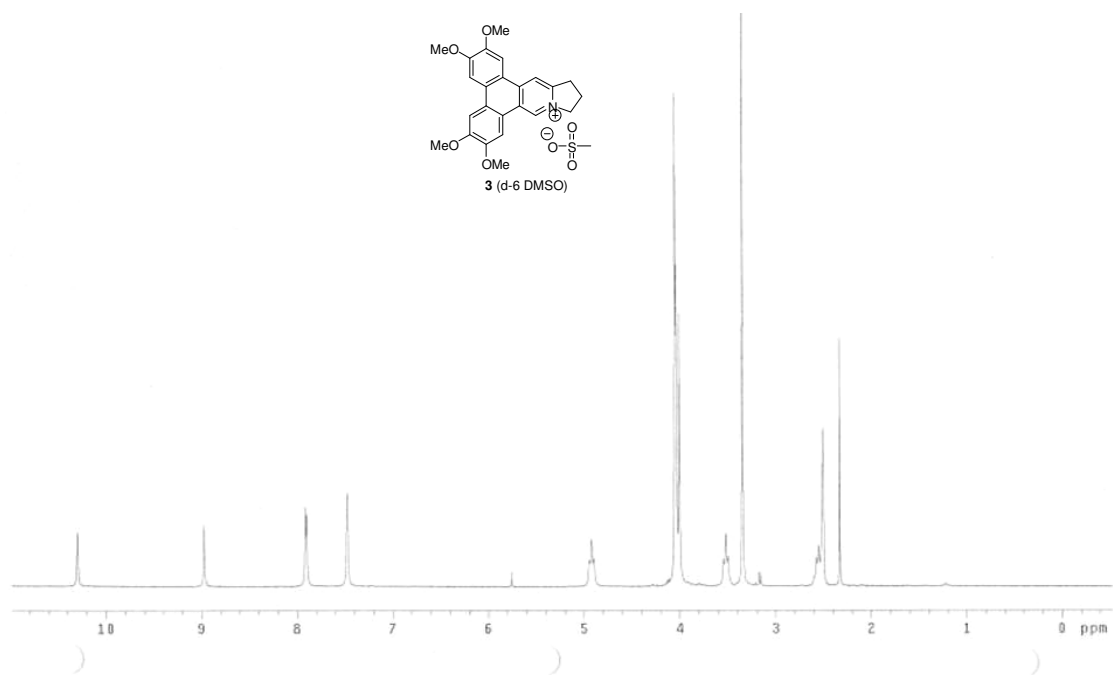
4,5,4',5'-Tetramethoxydiphenyl-2,2'-dicarbaldehyde (20): *t*-BuLi (1.2 M in hexanes, 1.03 mL, 1.24 mmol) was added dropwise over 30 min to a solution of **19** (145 mg, 0.276 mmol) in THF (13 mL) at -78°C . The solution was stirred at -78°C for 3 h before DMF (427 μL , 5.52 mmol) was added and the reaction mixture was allowed to warm to room temperature over 3.5 h. The reaction was quenched with H_2O (15 mL) and extracted with DCM (2×30 mL). The organic layers were combined, washed with H_2O (20 mL) and brine (20 mL), dried over Na_2SO_4 , filtered and concentrated to dryness. The residue was purified by flash silica gel chromatography, eluting with hexanes/EtOAc (3:2) to give **20** (76.4 mg, 84%) as a light yellow solid. ^1H NMR (300 MHz, CDCl_3) δ 9.66 (s, 2H), 7.55 (s, 2H), 6.79 (s, 2H), 4.00 (s, 6H), 3.95 (s, 6H); ^{13}C NMR (300 MHz, CDCl_3) δ 190.0, 153.4, 149.6, 136.3, 113.9, 108.8, 56.6, 56.4; HRMS (ESI⁺) calcd for $\text{C}_{18}\text{H}_{19}\text{O}_6$ (M+H)⁺ 331.1176, found 331.1172.

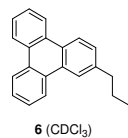
4,5,4',5'-Tetramethoxy-2,2'-diethynyldiphenyl (21): CBr_4 (261 mg, 0.787 mmol), PPh_3 (206 mg, 0.787 mmol), and Zn dust (51 mg, 0.787 mmol) were dissolved in DCM (3 mL) and stirred for 24 h at room temperature. The mixture was cooled to 0°C and **20** (26 mg, 0.0787 mmol) was added in 850 μL DCM and allowed to warm to room temperature until the reaction was complete as indicated by TLC (hexanes/EtOAc, 3:2). The mixture was filtered and concentrated to dryness for purification by flash silica gel chromatography, eluting with hexanes/EtOAc (3:2) to give a light yellow solid. *n*-BuLi (2.5 M in hexanes, 74 μL , 0.935 mmol) was added dropwise to a solution of the intermediate yellow solid (20 mg, 0.0311 mmol) in THF (1.5 mL) at -78°C and allowed to stir for 1h. The reaction was quenched with sat. NH_4Cl (2 mL) and extracted with DCM (2×4 mL). The organic layers were washed with H_2O (5 mL) and brine (5 mL), dried over Na_2SO_4 , filtered and concentrated to dryness. The residue was purified by flash silica gel chromatography, eluting with hexanes/EtOAc (3:2) to give **21** (9.7 mg, 96%) as a pale yellow solid. ^1H NMR (300 MHz, CDCl_3) δ 7.07 (s, 2H), 6.99 (s, 2H), 3.92 (s, 6H), 3.89 (s, 6H), 2.94 (s, 2H); ^{13}C NMR (300 MHz, CDCl_3) δ 149.1, 148.1, 136.7, 115.5, 113.8, 113.4, 83.4, 78.8, 56.2; HRMS (ESI⁺) calcd for $\text{C}_{20}\text{H}_{18}\text{O}_4$ (M+H)⁺ 322.1205, found 322.1203.

Dehydrotylophorine (3): Compounds **21** (8.2 mg, 0.025 mmol) and **22** (41.5 μL , 0.254 mmol) were added to a flame dried microwave vial and dissolved in toluene (500 μL). To this solution $\text{CpCo}(\text{CO})_2$ (10 mol %) was added and the vial was irradiated at 300 W for 20 min in a CEM Discover microwave synthesizer. H_2O (2 mL) and DCM (2 mL) were added to the reaction vial, extracted, and the H_2O layer was separated. The H_2O layer was washed DCM (4×2 mL), and the H_2O layer was concentrated to dryness to give 9.4 mg (78%) of **3** as a bright yellow solid.

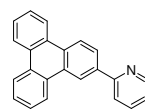
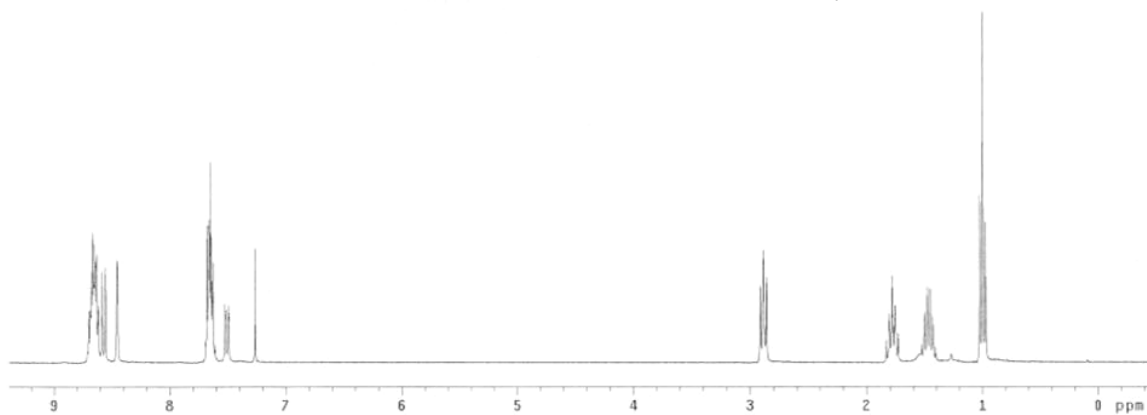
Tylophorine (4): NaBH_4 (1 mg, 0.022 mmol) was added to a solution of **3** (5.7 mg, 0.012 mmol) in 1 mL $\text{H}_2\text{O}/\text{MeOH}$ (1:1). When the bubbling subsided, the reaction was refluxed for 20 min. The reaction was cooled and sat. NH_4Cl (2 mL) was added and extracted with DCM (2×3 mL). The organic layers were dried over Na_2SO_4 , filtered and concentrated to dryness. The residue was purified by flash silica gel chromatography, eluting with 5% MeOH/DCM to give **4** (4.7 mg, 99%) as a yellow solid.

2. ¹H NMR Spectra for Compounds 3-4, 5-17, and 20-21 (300 MHz)

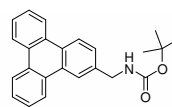
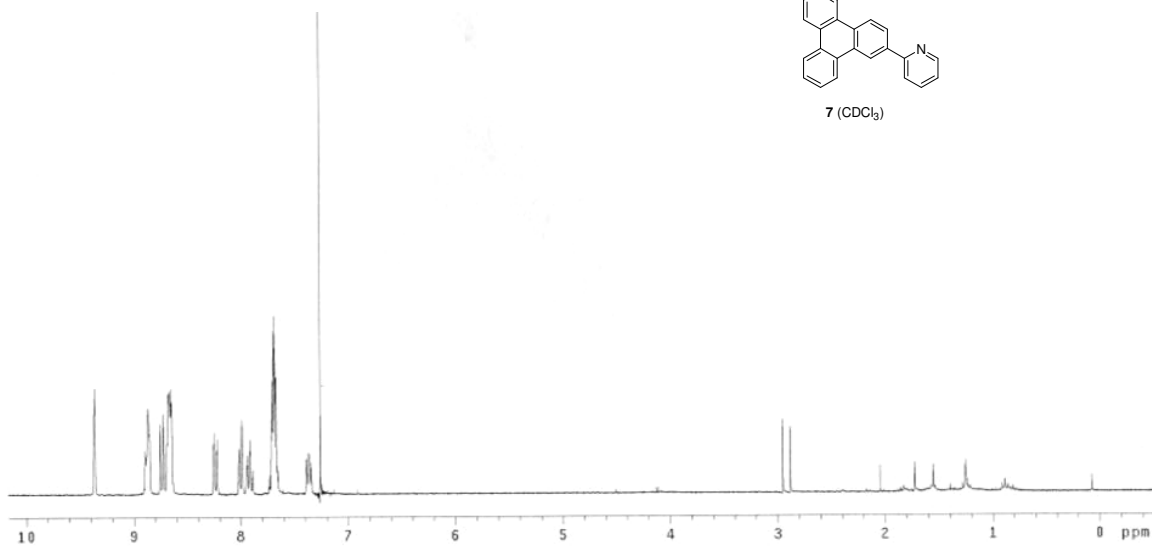




6 (CDCl₃)



7 (CDCl₃)



8 (CDCl₃)

