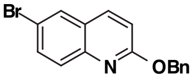
Chiral Discrimination in Hydrogen-Bonded [7]-Helicenes

Elisa Murguly, Robert McDonald and Neil R. Branda*

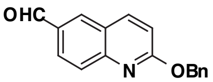
Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada, T6g 2G2

Experimental

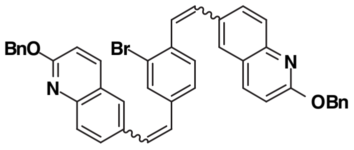
All solvents (Caledon) were used as received except THF that was distilled prior to use. Solvents for NMR analysis (Cambridge Isotope Laboratories) were used as received. ^{1}H NMR characterizations were performed on a Varian Inova-300 instrument, working at 299.96 MHz or on a Varian Inova-500 instrument, working at 499.92 MHz. Chemical shifts (δ) are reported in parts per million relative to tetramethylsilane using the residual solvent peak as a reference standard. Coupling constants (*J*) are reported in hertz. FT-IR measurements were preformed using a Nicolet Magna-IR 750. High resolution mass spectrometry measurements were preformed using Kratos MS-50 with an electron impact sourc, while low resolution mass spectrometry measurements were preformed using an Agilent Technologies 1100 MSD with an electrospray source.



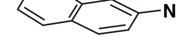
2-Benzoxy-6-bromoquinoline (2a) A suspension of 6-bromoquin-2-ol (2.71 g, 12 mmol), silver carbonate (7.00 g, 25 mmol) and benzyl bromide (2.69 g, 16 mmol), in chloroform, was stirred in the dark for 48 hours. The silver salts were filtered off and the filtrate was purified by normal phase chromatography over silica gel (9:1 Hex/EtOAc) to afford 3.0 g (79%) of a pure white solid: mp 79-80°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, *J* = 9 Hz, 1H), 7.85 (d, *J* = 2 Hz, 1H), 7.71 (s, 1H), 7.68 (d, *J* = 2 Hz, 1H), 7.50 (m, 2H), 7.35 (m, 3H), 6.95 (d, *J* = 9 Hz, 1H), 5.51 (s, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 162.12, 145.26, 137.83, 137.09, 132.79, 129.55, 129.06, 128.55, 128.36, 128.04, 126.45, 117.33, 114.32, 67.92; FT-IR (microscope) 3030, 2938, 2876, 1612, 1598, 1299; MS (ES) *m/z* calcd for $C_{16}H_{12}NOBr$ 315, found 316.0 $(M + H)^+$.



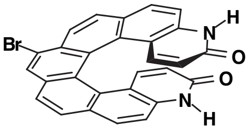
2-Benzoxy-6-bromoquinolinecarboxaldehyde (2b) A solution of *n*-BuLi, in hexanes, (1.4 mL, 3.5 mmol) was added dropwise to a solution of **(2a)** (842 mg, 2.7 mmol), in dry THF (35 mL) at –78°C. After 1 hour, dry DMF (0.27 mL, 3.5 mmol) was added and the mixture was allowed to stir at –78°C for 45 min and then allowed to warm to room temperature. The reaction was quenched with NH_4Cl (50 mL), extracted with ether (3 x 30 mL), dried over $MgSO_4$ and evaporated to dryness. Purification by normal phase chromatography over silica gel (16:1 hexane/EtOAc) afforded 290 mg (42%) of the product as a white solid. ^{1}H NMR (300MHz, $CDCl_3$) δ 10.11 (s, 1H), 8.21 (d, *J* = 2 Hz, 1H), 8.11 (d, *J* = 8.7 Hz, 2H), 7.94 (d, *J* = 8.7 Hz, 1H), 7.49 (m, 2H), 7.34 (m, 3H), 7.03 (d, *J* = 8.7 Hz, 1H), 5.57 (s, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 191.48, 163.85, 150.27, 139.86, 136.80, 132.70, 132.54, 128.60, 128.44, 128.18, 127.70, 124.66, 114.68, 68.26; FT-IR (microscope) 3039, 2893, 1734, 1689, 1621; MS (ES) *m/z* calcd for $C_{17}H_{13}NO_2$ 263, found 264.0 $(M + H)^+$.



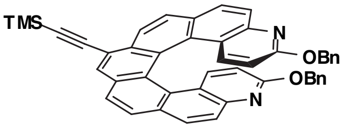
Bis-stilbene 4b. *n*-Butyllithium in hexanes (0.67 mL, 2.5M, 1.7 mmol) was added under argon dropwise to 10 mL of cold (-78°C) dry ethanol. After it had been warmed to room temperature and stirred until homogeneous, the solution was transferred by cannula to a slurry of 200 mg of 2-benzoxy-6-quinolinecarboxaldehyde **2** (0.8 mmol) and 363 mg of (2-bromo-1,4-phenylene)bis(methylene)bis(triphenylphosphonium) dibromide **3b** (0.4 mmol) in 20 mL of dry EtOH under argon. After the mixture was stirred overnight, the *trans, trans* product was filtered off (20 mg, 8%) and the filtrate was evaporated to dryness, redissolved in $CHCl_3$, washed with water (2 x 10 mL), brine (2 x 10 mL), dried over $MgSO_4$ and evaporated to dryness. Purification by normal phase chromatography over silica gel (3:1 Hex/EtOAc) afforded 184 mg (72%) of pure product as a yellow solid, as a mixture of isomers (overall yield of 79%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.7 Hz, 1H), 7.98 (d, *J* = 8.7 Hz, 1H), 7.87–7.17 (m, 23H), 7.10 (d, *J* = 16.2 Hz, 1H), 6.96 (d, *J* = 8.7 Hz, 1H), 5.54, (s, 4H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 162.16, 146.60, 146.58, 142.60, 142.56, 140.10, 140.08, 138.90, 138.84, 138.32, 137.28, 136.00, 133.09, 132.87, 131.06, 131.00, 130.73, 130.62, 129.55, 129.40, 128.55, 128.37, 128.00, 127.88, 127.83, 127.64, 127.34, 127.11, 126.84, 126.61, 126.29, 126.21, 125.67, 125.42, 124.68, 123.89, 120.11, 113.80, 67.85; FT-IR (microscope) 3063, 3032, 2930, 2885, 1724, 1600, 1277; MS (EI) *m/z* calcd for $C_{42}H_{31}N_2O_2Br$ 676.15485, found 676.15413 $(M)^+$.



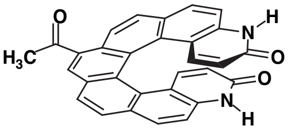
[7]-helicene 5b. A solution of bis-stilbene **4b** (120 mg, 0.178 mmol) and iodine (90 mg, 0.355mmol) in 600 mL of dry benzene was degassed with argon for 1/2 h. Propylene oxide (5 mL) was added, and the solution was irradiated for 12 h. After irradiation, the solution was evaporated to dryness and purified by normal phase chromatography over silica gel (9:1 Hex/EtOAc) to afford 112 mg (63% yield) of a pure yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) ∂ 8.380 (d, *J* = 8.7 Hz, 1H), 8.295 (s, 1H), 7.976 (d, *J* = 8.7 Hz, 1H), 7.923 (d, *J* = 8.7 Hz, 1H), 7.890 (d, *J* = 8.4 Hz, 2H), 7.804 (d, *J* = 8.4 Hz, 2H), 7.696 (d, *J* = 8.7 Hz, 1H), 7.676 (d, *J* = 8.7 Hz, 1H), 7.402 (m, 8H), 7.102 (d, *J* = 8.7 Hz, 2H), 5.904 (d, *J* = 9 Hz, 2H), 5.367 (d, *J* = 12.3 Hz, 2H), 5.303 (d, *J* = 12.3 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) ∂ 161.20, 137.43, 134.65, 134.38, 132.40, 132.31, 130.48, 129.92, 129.53, 129.32, 128.51, 128.40, 127.96, 127.82, 127.63, 126.54, 125.24, 125.20, 124.90, 109.36, 102.42, 67.38; FT-IR (microscope) 3062, 3029, 2944, 1608, 1593, 1268; MS (EI) *m/z* calcd for $C_{42}H_{27}N_2O_2Br$ 672.12354, found 672.11916 $(M)^+$.



[7]-helicene 1b. A solution of protected [7]-helicene **5b** (131 mg, 0.3 mmol), in TFA (5 mL), was stirred at room temperature for 12 h, evaporated to dryness, redissolved in $CHCl_3$, washed with $NaHCO_3$ (2 x 6 mL), brine (2 x 6 mL), dried over $MgSO_4$ to afford 128 mg (98% yield) of a pure yellow solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 13.45 (s, 2H), 8.52 (s, 1H), 8.38 (d, *J* = 8.7 Hz, 1H), 8.13 (d, *J* = 8.7 Hz, 2H), 8.08 (d, *J* = 8.7 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 1H), 6.80 (d, *J* = 9.6 Hz, 1H), 6.79 (d, *J* = 9.6 Hz, 1H), 5.63, (d, *J* = 9.9 Hz, 2H); ^{13}C NMR (500 MHz, THF-d_8) δ163.03, 162.97, 140.04, 139.87, 136.55, 136.37, 133.82, 132.27, 132.09, 131.84, 131.84, 131.77, 129.82, 129.47, 129.44, 127.69, 127.69, 127.55, 126.87, 125.33, 124.73, 124.54, 122.65, 118.79, 118.71, 118.58, 115.43, 115.27; FT-IR (CH_2Cl_2 cast) 3052, 2923, 1652, 1455, 1122, 667; MS (ES) *m/z* 491.1, 982.1; MS (EI) *m/z* calcd for $C_{28}H_{15}N_2O_2Br$ 492.02963, found 492.02954 $(M)^+$.



TMS-[7]-helicene 5c. A solution of protected [7]-helicene **5b** (42 mg, 0.06 mmol), in Et_3N/THF (10 + 3 mL), was degassed with argon for 45 minutes. After 45 minutes, TMS-acetylene (70 mg, 0.10 mL, 0.6 mmol) was added and the solution was degassed for another 15 minutes, after which $Pd(PPh_3)_2Cl_2$ (5 mg, 5% mol) and CuI (1 mg, 2.5% mol) were added and the entire mixture was allowed to stir at 90 °C, under argon, for 72 h. The solution was evaporated to dryness, redissolved in $CHCl_3$(15 mL), washed with water (3 x 5 mL), brine (5 mL), dried over $MgSO_4$ and evaporated to dryness. Purification by normal phase chromatography over silica gel (13:1 Hex/EtOAc) afforded 26 mg (60% yield) of a pure yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (d, *J* = 8.4 Hz, 1H), 8.27 (s, 1H), 8.01 (d, *J* = 8.1 Hz, 1H), 7.95 (d, *J* = 9.0 Hz, 1H), 7.91 (m, 4H), 7.69 (d, *J* = 9 Hz, 1H), 7.67 (d, *J* = 9.0 Hz, 1H), 7.35 (m, 8H), 7.19, (d, *J* = 9.3 Hz, 1H), 7.15 (d, *J* = 9.3 Hz, 1H), 5.91 (d, *J* = 9 Hz, 2H), 5.36 (d, *J* = 12.3 Hz, 2H), 5.29 (d, *J* = 12.3 Hz, 2H), 0.40 (s, 9H); ^{13}C NMR (500 MHz, $CDCl_3$) 161.10, 161.04, 146.01, 137.38, 134.65, 134.39, 131.96, 131.88, 131.27, 130.249, 129.83, 129.48, 128.43, 128.04, 127.97, 127.90, 127.88, 127.74, 127.45, 125.85, 124.89, 124.22, 120.97, 120.91, 119.84, 109.20, 109.13, 102.87, 100.553, 67.31, 0.125; FT-IR ($CHCl_3$ cast) 3030, 2956, 2145, 1593, 1521, 1269; MS (EI) *m/z* calcd for $C_{47}H_{36}N_2O_2Si$ 688.25458, found 688.25367 (M)$^+$.



[7]- helicene 1c. A solution of protected TMS- [7]-helicene **5c** (12 mg, 1.74 x 10^{-5} mol), in TFA (6 mL), was stirred at room temperature for 12 h, evaporated to dryness, redissolved in $CHCl_3$, washed with $NaHCO_3$ (2 x 6 mL), brine (2 x 6 mL), dried over $MgSO_4$ to afford 7.5 mg (94% yield) of a pure yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) ∂ 13.700 (s, 2H), 8.874 (d, *J* = 9 Hz, 1H), 8.491 (s, 1H), 7.988 (m, 5H), 7.607 (d, *J* = 9.0 Hz, 1H), 7.590 (d, *J* = 9.0 Hz, 1H), 6.831 (d, *J* = 9.0 Hz, 1H), 6.762 (d, *J* = 9.0 Hz, 1H), 5.735 (dd, *J* = 1.8, 9.3 Hz, 2H), 2.966 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 201.57, 164.13, 138.53, 138.44, 136.61, 136.33, 135.20, 131.10, 130.91, 130.82, 130.45, 129.98, 129.906, 129.26, 128.67, 128.47, 128.37, 128.23, 126.58, 126.50, 126.45, 125.77, 125.11, 123.04, 118.74, 118.31, 117.72, 117.51, 115.11, 30.22; FT-IR ($CHCl_3$ cast) 2922, 2850, 1958, 1652; MS (ES) *m/z* 455.1, 909.3; MS (EI) *m/z* calcd for $C_{30}H_{19}N_2O_3$ 455.13956 found 455.139213 (M)$^+$.

Crystal structure analysis of 1c

$C_{30}H_{18}N_2O_2 \bullet 1/2H_2O$ (M = 463.47); crystal dimensions 0.36 x 0.19 x 0.10 mm, monoclinic, space group *C*2/*c* (No. 15) *a* = 13.4205(13), *b* = 17.6403(15), and *c* = 18.4087(17) Å, β = 94.4865(16)°, *V* = 4344.8(7) Å^3, ρ_{calc} = 1.417 g cm^{-3}, μ = 0.094 mm^{-1}, *T* = -80°C; Bruker P4/RA/SMART 1000 CCD; Mo Kα radiation (λ = 0.71073 Å), scan method ϕ and ω; 12007 data measured; 4451 independent reflections. The crystal structure was solved using direct methods (SHELXS-86) and refined by full-matrix least squares on F^2 (SHELXL-93). All hydrogens were generated in idealized positions according to the sp^2 or sp^3-hybridized geometries of their attached carbon and nitrogen atoms. Final $R_1(F) = 0.0736$ (for 1941 data with $F_0^2 \geq 2\sigma(F_o^2)$), $wR_2(F^2) = 0.2497$ (on all 4451 unique data), and $S = 0.942$ for 325 parameters varied. The largest difference peak and hole in the final difference Fourier map had intensities of 0.840 and –0.283 e Å^{-3}, respectively.