Advanced Synthesis & Catalysis

Supporting Information

Supporting Information

Expedient Iodocyclization Approach Toward Polysubstituted 3*H*-Benzo[*e*]indoles

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General experimental details

Solvents were purified and dried according to usual techniques prior to use.[1] All other reagents were obtained commercially. Purification of the compounds was performed by column chromatography using silica gel 60 H (40–63 μm particle size, 230–400 mesh. Elution was carried out with hexane or EtOAc:hexane mixtures. All new compounds gave single spots on TLC plates run in different solvent systems (hexane or EtOAc:hexane). Chromatographic spots were detected by exposure to 254 nm UV light, as well as by treatment with iodine or with an acid solution of vanillin.

The melting points are reported uncorrected. IR spectra were recorded as thin films held between NaCl cells or as solid dispersions in KBr disks. The wavelength scale was calibrated with a 0.05 mm thick polystyrene film, employing the absorption band at 1601 cm^{-1}. The ^1H NMR spectra were acquired in $CDCl_3$ (δ_H = 7.27 ppm; δ_C = 77.0 ppm), at 200 or 400 MHz. Chemical shifts are reported in parts per million in the δ scale and *J*-values are given in Hertz. Signals are reported as follows: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), ddd (doublet of doublet of doublets), and m (multiplet). The low resolution mass spectra were obtained from a GC-MS instrument. Fragments are described with regards to their *m/z* ratios, in terms of relative intensity (%) of their signals.

Synthesis and characterization

Synthesis of precursors

2-Bromo-4,5-dimethoxybenzaldehyde.[2] A stirred solution of 3,4-dimethoxy benzaldehyde (3.98 g, 24mmol) in MeOH (40mL) was treated dropwise with Br_2 (1.32mL, 26 mmol) during 30 min., and the system was left to react at room temperature for a further period of 1 hour. Then, the solvent was removed under reduced pressure, the solid was filtered and the solid residue was successively washed with cold water and petroleum ether, affording the title compound (5.7 g, 98 %), as a yellowish solid. ^1H NMR (400 MHz, $CDCl_3$) δ 10.18 (s, 1H), 7.41 (s, 1H), 7.05 (s, 1H), 3.96 (s, 3H), 3.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.6, 154.4, 148.8, 126.5, 120.3, 115.4, 110.4, 56.4, 56.1.

(*E*)-4-Chlorocinnamic acid.[3,4] A solution of 4-chlorobenzaldehyde (5.6 g, 40mmol) and malonic acid (9.15 g, 88 mmol) in pyridine (18 mL) was treated with piperidine (0.7 mL) and stirred under reflux for 5 h. After completion of the reaction, the system was cooled in an ice-bath and treated with a cold HCl solution (2 N, 350 mL). The precipitate was filtered and dried under vacuum, affording the title compound (7.20 g, 99%), as a white solid, mp. 248–252ºC (Lit.[4] 249–251ºC).

2.3-Dibromo-3-(4-chlorophenyl)propionic acid.[5] A stirred solution of *trans*-cinnamic acid (4.55g, 25 mmol) in AcOH (30 mL) was cooled to 0ºC and treated dropwise with Br_2 (1.52 mL, 30 mmol) during 30 min. Stirring continued for additional 3 h at room temperature, when water (250 mL) was admitted into the reaction. Stirring continued for a few minutes and then the solids were filtered through a Büchner funnel, successively washing with water and cold petroleum ether. The title product (8.24 g, 97%) was obtained as a beige solid, mp. 193–195ºC (Lit.[5] 194–195ºC).

(*Z*)-1-Chloro-4-(2-bromovinyl)benzene.[6] A solution of 2,3-dibromo-3-(4-chloro phenyl) propionic acid (3.39 g, 10 mmol) in DMF (20 mL) was treated with Et_3N (1.46 mL, 10.5 mmol) under microwave irradiation (1 min., 500 W). The system was cooled to room temperature and the products were extracted with EtOAc (3 × 100 mL). The organic phase was washed with water and brine, and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue purified by chromatography on silica gel, eluting with hexane, furnishing the title product (2.05 g, 95%), as a colorless oil, slightly contaminated with the *cis* isomer. MS (*m/z*, rel. int., %) 220 ($[M+4]^+$, 19), 218 ($[M+2]^+$, 74), 137 (M^+, 100), 102 (77), 75 (51).

1-Chloro-4-ethynylbenzene.[4] 18-Crown-6 (300 mg) was added to a stirred solution of (*Z*)-1-chloro-4-(2-bromovinyl)benzene (2.15 g, 10 mmol) in cyclopentane (30 mL). The solution was cooled to 0ºC and treated portion wise with ^{t}BuOK (1.34 g, 12 mmol), stirring at this temperature for additional 30 minutes. Then, the system was further stirred for 30 min. at room temperature and 1 h at 40ºC. After completion of the reaction, the system was brought to room temperature and the reaction passed through a chromatographic column, eluting with petroleum ether. The product (1.26 g, 93%) was obtained as a white solid, mp. 45–45.5ºC (Lit.[4] 45–46ºC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.6, 2H), 7.29 (d, *J* = 8.6, 2H), 3.10 (s, 3H).

Synthesis of the 2(2-aryl-/2-alkyl- ethynyl)benzaldehydes

$Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (1 mol%) and the appropriate acetylene (12 mmol) were successively added to a stirred mixture of Et_3N (30 mL) and the corresponding 2-bromobenzaldehyde (10 mmol), under argon. The resulting mixture was heated at 50 °C for 2–5 h. After the reaction was completed, it was extracted with EtOAc (3 × 100 mL). The combined extracts were successively washed with water and brine, dried over $MgSO_4$ and filtered. The solvent was evaporated under reduced pressure and the residue was purified via column chromatography on silica gel, eluting with EtOAc:hexane (2:98).

2-(Phenylethynyl)benzaldehyde (3a).[7] Yellow oil.^{1}H NMR (400 MHz, $CDCl_3$) δ 10.64 (s, 1H), 7.93 (dd, *J* = 0.82, 7.79 1H), 7.62 (dd, *J* = 0.7 and 7.7, 1H), 7.57–753 (m, 3H), 7.42 (t, *J* = 7.4, 1H), 7.38–7.35 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ191.5, 135.8, 133.6, 133.1, 131.6, 128.9, 128.5, 128.4, 127.2, 126.7, 122.2, 96.2, 84.8.MS (*m/z*, rel. int., %) 206 (M^+, 100), 178 (42), 176 (41), 152 (32), 111 (2), 101 (4), 88 (22), 77 (9).

2-(*p*-Tolylethynyl)benzaldehyde(3b).[8] Yellow solid. Mp. 46–47ºC (Lit.[8b] 48ºC). ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.65 (s, 1H), 7.94 (d, *J* = 7.8, 1H), 7.65–7.53 (m, 2H), 7.47–7.40 (m, 3H), 7.25–7.17 (m, 2H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.6, 139.3, 135.9, 133.6, 133.1, 131.6, 129.2, 128.3, 127.2, 127.1, 119.3, 96.6, 84.3, 21.5. MS (*m/z*, rel. int., %) 220 (M^+, 100), 191 (52), 165 (18), 94 (13), 88 (3), 77 (2).

2-(*m*-Tolylethynyl)benzaldehyde (3c).[9] Yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.60 (s, 1H), 7.92 (d, *J* = 7.8, 1H), 7.60 (d, *J* = 7.7, 1H), 7.54 (td, *J* = 1.3 and 7.3, 1H), 7.41 (t, *J* = 7.3, 1H), 7.37 – 7.34 (m, 2H), 7.26 – 7.22 (m, 1H), 7.18–7.16 (m, 1H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.6, 138.2, 135.8, 133.7, 133.1, 132.2, 129.9, 128.7, 128.4, 128.3, 127.2, 126.9, 122.1, 96.5, 84.5, 21.1.

2-((4-Chlorophenyl)ethynyl)benzaldehyde (3d).[8a,10] Beige solid. Mp. 91–93ºC (Lit.[10] 83–89ºC). ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.61 (s, 1H), 7.94 (d, *J* = 7.6, 1H), 7.64–7.56 (m, 2H), 7.50–7.44 (m, 3H), 7.36 (d, *J* = 8.4 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 191.4, 135.8, 135.1, 133.7, 133.2, 132.8, 129.0, 128.8, 127.4, 126.3, 120.8, 95.0, 85.8. MS (*m/z*, rel. int., %) 242 ($[M+2]^+$, 31), 240 (94), 205 (100), 177 (53), 176 (81), 88(34).

2-((2-Chlorophenyl)ethynyl)benzaldehyde (3e).[11] Yellowish solid, mp. 64–65ºC (Lit.[11] 65–67ºC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.72 (s, 1H), 7.98–7.85 (m, 1H), 7.69–7.67 (m, 1H), 7.61–7.57 (m, 2H), 7.49–7.44 (m, 2H), 7.33–7.25 (m, 2H).^{13}C NMR (50 MHz, $CDCl_3$) δ 191.8, 136.2, 136.0, 133.7, 133.3, 130.0, 129.4, 128.9, 127.1, 126.6, 126.4, 122.4, 92.9, 89.9. MS (*m/z*, rel. int., %) 242 ($[M+2]^+$, 4), 240 (12), 205 (100), 88 (78).

5-Fluoro-2-(phenylethynyl)benzaldehyde (3f).[12] Pale yellow solid. Mp. 53–54ºC (Lit.[12b] 51–52ºC). ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.59 (d, *J* = 3.2, 1H), 7.67–7.53 (m, 4H), 7.40–7.34 (m, 3H), 7.33–7.25 (m, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 190.4, 162.3 (d, *J* = 252.7), 137.7 (d, *J* = 6.8), 135.2 (d, *J* = 7.6), 131.6, 129.1, 128.5, 122.9 (d, *J* = 3.3), 122.0, 121.3 (d, *J* = 22.7), 113.6 (d, *J* = 23.0), 95.9, 83.7.

5-Methoxy-2-(phenylethynyl)benzaldehyde (3g).[13] Yellow solid. Mp. 80–83ºC (Lit.[13] 79–81ºC). ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.60 (s, 1H); 7.56–7.52 (m, 3H), 7.42 (d, *J* = 2.7, 1H), 7.37–7.35 (m, 3H), 7.13 (dd, *J* = 2.8 and 8.5, 1H), 3.86 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 191.5, 159.7, 137.2, 134.5, 131.4, 128.7, 128.4, 122.6, 121.6, 119.5, 109.8, 94.8, 84.8, 55.5.

4,5-Dimethoxy-2-(phenylethynyl)benzaldehyde (3h).[12,14] Deep yellow solid. Mp. 139–143ºC (Lit.[14] 138–140ºC). ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.50 (s, 1H), 7.58–7.53 (m, 2H), 7.43–7.37 (m, 3H), 7.26 (s, 1H), 7.06 (s, 1H), 4.00 (s, 3H), 3.96 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 190.4, 153.7, 149.8, 131.5, 130.2, 128.8, 128.5, 122.5, 121.5, 114.3, 108.3, 94.9, 84.8, 56.3, 56.1. MS (*m/z*, rel. int., %) 266 (M^+, 87), 251 (56), 195 (79), 165 (61), 152

(100), 126 (28), 102 (37), 77 (23), 63 (33).

2-(hex-1-yn-1-yl)benzaldehyde (3i).[12] Yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.54 (s, 1H), 7.88 (d, *J* = 7.5, 1H), 7.52–7.49 (m, 2H), 7.44–7.33 (m, 1H), 2.49 (t, *J* = 6.8, 2H), 1.72–1.40 (m, 4H), 0.96 (t, *J* = 7.0, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 192.2, 135.9, 133.6, 133.2, 127.9, 127.7, 126.8, 98.1, 30.5, 22.0, 19.2, 13.5. MS (*m/z*, rel. int., %) 186 (M^+, 6), 157 (22), 144 (97), 128 (35), 115 (100), 102, (11), 89 (22), 77 (9), 63 (18).

Synthesis of the 1,2,3,4-tetrasubstituted pyrroles[15]

Benzylamine (10 mmol) and ethyl acetoacetate (10 mmol), were successively added to a mixture of $NiCl_2.6H_2O$ (10 mol%) in $MeNO_2$ (10 mL), magnetically stirred at room temperature. After ~10 minutes, formation of a precipitate was observed and the corresponding aldehyde (10 mmol) was added. The open system was heated at 80ºC for 6–12 h. After the reaction was completed, the system was cooled to room temperature and the products were extracted with EtOAc (3 × 100 mL), the organic phase was washed with water and brine, and dried over anhydrous $MgSO_4$ and filtered. The solvent was evaporated under reduced pressure and the residue was purified via column chromatography on silica gel, eluting with EtOAc:hexane (5:95).

Ethyl 1-benzyl-2-methyl-4-(2-(phenylethynyl)phenyl)-1*H*-pyrrole-3-carboxylate (2a). Yelow oil. Yield: 47%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 1.2 and 7.3, 1H), 7.35–7.30 (m, 3H), 7.26 (dd, *J* = 1.2 and 7.2, 1H), 7.23–7.19 (m, 4H), 7.18–7.13 (m, 3H), 6.96 – 6.94 (m, 2H), 6.57 (s, 1H), 4.95 (s, 2H), 4.05 (q, *J* = 7.1, 2H), 2.45 (s, 3H), 0.97 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 138.7, 136.8, 135.5, 131.6, 131.3, 129.7, 128.6, 128.0, 127.6, 127.5, 127.4, 126.1, 126.0, 124.1, 123.5, 123.2, 120.7, 112.3, 91.2, 89.8, 59.1, 50.2, 13.6, 11,0. IR (film, υ) 3401, 3060, 3029, 2978, 2900, 2215, 1693 cm^{-1}. MS (*m/z*, rel. int., %) 419 (M^+, 21), 346 (18), 254 (10), 228 (3), 226 (6), 91 (100), 77 (2), 65 (14). HRMS (ESI, *m/z*) calcd. for $C_{25}H_{29}NO_2$ ($[M+H]^+$): 420.1964; Found: 420.1933.

Ethyl 1-benzyl-2-methyl-4-(2-(*p*-tolylethynyl)phenyl)-1*H*-pyrrole-3-carboxylate

(2b). White solid. Mp. 119–120ºC. Yield: 41%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.3, 1H), 7.32–7.31 (m, 1H), 7.28–7.21 (m, 7H), 7.05 (d, *J* = 7.9, 2H), 7.03–7.01 (m, 2H), 6.64 (s, 1H), 5.06 (s, 2H), 4.06 (q, *J* = 7.1, 2H), 2.48 (s, 3H), 2.32 (s, 3H), 0.98 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 138.7, 137.8, 136.9, 135.7, 131.7, 131.4, 129.8, 128.9, 128.8, 127.6, 127.4, 126.3, 126.1, 124.3, 123.5, 120.8, 120.6, 112.4, 91.5, 89.1, 59.3, 50.4, 21.4, 13.8, 11.2. IR (KBr, υ) 3403, 3085–3028, 2978, 2868, 2213, 1694 cm^{-1}. MS (*m/z*, rel. int., %) 433 (M^+, 35), 258 (42), 268 (19), 225 (12), 105 (5), 91 (100), 65 (13). Anal. Calc. for $C_{30}H_{27}NO_2$C, 83.11; H, 6.28; N, 3.23. Found C, 83.41; H, 6.40; N, 3.24.

Ethyl 1-benzyl-2-methyl-4-(2-(*m*-tolylethynyl)phenyl)-1*H*-pyrrole-3-carboxylate (2c). Pale yellow solid. Mp. 136–138ºC. Yield: 40%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 1.3 and 7.5, 1H), 7.31–7.31 (dd, *J* = 1.3 and 7.4, 1H), 7.27–7.18 (m, 3H), 7.16–7.13 (m, 4H), 7.13–7.09 (m, 1H), 7.04–7.02 (m, 1H), 6.98–6.96 (m, 2H), 6.59 (s, 1H), 4.98 (s, 2H), 4.05 (q, *J* = 7.1, 2H), 2.46 (s, 3H), 2.23 (s, 3H), 0.97 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 138.8, 137.5, 136.8, 135.5, 132.0, 131.5, 129.7, 128.6, 128.5, 128.4, 127.9, 127.4, 126.1, 126.0, 124.2, 123.4, 120.8, 112.4, 91.5, 89.4, 59.1, 50.2, 21.0, 13.6, 11.0. IR (KBr, υ) 3425, 3055, 3032, 2978, 2924, 2206 cm^{-1}. MS (*m/z*, rel. int., %) 433 (M^+, 48), 360 (50), 356 (45), 268 (20), 91 (100), 65 (11). HRMS (ESI, *m/z*) calcd. for $C_{30}H_{27}NO_2$ ($[M+H]^+$): 434.2120; Found: 434.2118.

Ethyl 1-benzyl-4-(2-((4-chlorophenyl)ethynyl)phenyl)-2-methyl-1*H*-pyrrole-3-carboxylate (2d). Yellow oil. Yield: 40%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.5, 1H), 7.31 (d, 7.5, 1H), 7.27–7.21 (m, 4H), 7.19–7.15 (m, 5H), 6.97–6.95 (m, 2H), 6.57 (s, 1H), 4.95 (s, 2H), 4.04 (q, *J* = 7.1, 2H), 2.45 (s, 3H), 0.96 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 138.8, 136.7, 135.4, 133.5, 132.4, 131.4, 129.6, 128.5, 128.2, 127.6, 127.4, 126.1, 125.9, 124.0, 122.8, 122.0, 120.6, 112.3, 90.8, 90.0, 59.0, 50.1, 13.5, 10.9. IR(film, υ) 3425, 3062, 3031, 2978, 2893, 2214, 1689 cm^{-1}. HRMS (ESI, *m/z*) calcd. for $C_{29}H_{24}ClNO_2$ ($[M+Na]^+$): 476.1393; Found: 476.1382.

Ethyl 1-benzyl-4-(2-((2-chlorophenyl)ethynyl)phenyl)-2-methyl-1*H*-pyrrole-3-carboxylate (2e). Yellow oil**.** Yield: 38%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60–7.58 (m, 1H), 7.37–7.29 (m, 4H), 7.28–7.22 (m, 2H), 7.21–7.18 (m, 2H), 7.17–7.10 (m, 2H), 7.04–7.01 (m, 2H), 6.68 (s, 1H), 5.05 (s, 2H), 4.05 (q, *J* = 7.1, 2H), 2.47 (s, 3H), 0.99 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 139.0, 136.9, 135.8, 135.6, 133.3, 132.0, 130.1, 129.0, 128.7, 128.6, 127.8, 127.5, 126.3, 126.2, 126.1, 124.1, 123.7, 123.1, 121.0, 112.4, 95.0, 88.0, 59.1, 50.4, 13.7, 11.2. IR (film, υ) 3371, 3063, 3024, 2978, 2924, 2214, 1689 cm^{-1}. HRMS (ESI, *m/z*) calcd. for $C_{29}H_{24}ClNO_2$($[M+Na]^+$): 476.1393; Found: 476.1388.

Ethyl 1-benzyl-4-(5-fluoro-2-(phenylethynyl)phenyl)-2-methyl-1*H*-pyrrole-3-carboxylate (2f). Yellow oil. Yield: 35%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51–7.47 (m, 1H), 7.34–7.31 (m, 2H), 7.25–7.22 (m, 3H), 7.21–7.18 (m, 3H), 7.06–7.03 (m, 1H), 7.01–6.99 (m, 2H), 6.93 (td, *J*= 2.7 and 8.4, 1H), 6.65 (s, 1H), 5.04 (s, 2H), 4.08 (q, *J* = 7.1, 2H), 2.48 (s, 3H), 1.02 (t, *J* = 7.1, 3H). IR (film, υ) 3396, 3064, 3032, 2977, 2850, 2217, 1701 cm^{-1}. MS (*m/z*, rel. int., %) 437 (M^+, 39), 364 (29), 360 (28), 91 (100), 65 (11). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 161.8 (d, *J* = 248.5), 141.1 (d, *J* = 8.9), 136.6, 135.9, 133.2 (d, *J* = 8.6), 131.3, 128.8, 128.1, 127.7, 127.6, 126.2, 123.5, 123.2 (d, *J* = 1.9), 121.0, 119.5 (d, *J* = 3.0), 116.9 (d, *J* = 22.0), 113.1 (d, *J* = 21.8), 112.2, 90.9, 88.8, 59.3, 50.4, 13.7, 11.1. Anal. Calcd. for $C_{29}H_{24}FNO_2$ C, 79.61; H, 5.53; N, 3.20. Found C, 79.19; H, 5.59; N, 3.11.

Ethyl 1-benzyl-4-(5-methoxy-2-(phenylethynyl)phenyl)-2-methyl-1*H*-pyrrole-3-carboxylate (2g). Yellow oil. Yield: 32%.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.5, 1H), 7.33–7.30 (m, 2H), 7.22–7.15 (m, 6H), 7.00–6.97 (m, 2H), 6.88 (d, *J* = 2.6, 1H), 6.77 (dd, *J* = 2.7 and 8.5, 1H), 6.61 (s, 1H), 4.99 (s, 2H), 4.07 (q, *J* = 7.1, 2H), 3.76 (s, 3H), 2.46 (s, 3H), 1.00 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 158.9, 140.4, 136.8, 135.5, 132.9, 131.2, 128.6, 127.9, 127.4, 127.2, 126.2, 124.1, 124.0, 120.8, 115.8, 115.4, 112.4, 111.9, 90.0, 89.9, 59.1, 55.1, 50.3, 13.7, 11.0. IR (film, υ) 3379, 3062, 3032, 2978, 2931, 2214, 1697 cm^{-1}. MS (*m/z*, rel. int., %) 449 (M^+, 59), 376 (54), 284 (11), 91 (100), 77 (2). Anal. Calcd. for $C_{30}H_{27}NO_3$ C, 80.15; H, 6.05; N, 3.12. Found C, 79.39; H, 6.37; N, 3.20.

Ethyl 1-benzyl-4-(4,5-dimethoxy-2-(phenylethynyl)phenyl)-2-methyl-1*H*-pyrrole-3-carboxylate (2h). Yellow oil. Yield: 42%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.32 (m, 2H), 7.25–7.22 (m, 6H), 7.05–7.03 (m, 3H), 6.86 (s, 1H), 6.67 (s, 1H), 5.07 (s, 2H), 4.09 (q, *J* = 7.1, 2H), 3.91 (s, 3H), 3.88 (s, 3H), 2.49 (s, 3H), 1.05 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 148.7, 147.3, 136.9, 135.6, 132.4, 131.3, 128.8, 128.1, 127.6, 127.5, 126.3, 124.1, 123.9, 120.9, 115.2, 114.5, 113.5, 112.5, 90.0, 89.9, 59.2, 56.0, 55.8, 50.5, 13.9, 11.2. IR (film, υ) 3462, 3062, 3029, 2993, 2835, 2203, 1686 cm^{-1}. MS (*m/z*, rel. int., %) 479 (M^+, 51), 407 (19), 406 (56), 402 (19), 249 (9), 189 (3), 91 (100), 77 (2). Anal. Calcd. for $C_{31}H_{29}NO_4$ C, 77.64; H, 6.10; N, 2.92. Found C, 77.61; H, 6.03; N, 2.65.

Ethyl 1-benzyl-4-(2-(hex-1-in-1-yl)phenyl)-2-methyl-1*H*-pyrrole-3-carboxylate (2i). Yellow oil. Yield: 40%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.42–7.37 (m, 1H), 7.31–7.22 (m, 4H), 7.20–7.10 (m, 2H), 7.06–7.02 (m, 2H), 6.58 (s, 1H), 5.02 (s, 2H), 4.05 (q, *J* = 7.1, 2H), 2.44 (s, 3H), 2.26 (t, *J* = 6.7, 2H), 1.50–1.21 (m, 4H), 0.99 (t, *J* = 7.1, 3H), 0.83 (t, *J* = 6.9, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.6, 138.4, 136.9, 135.3, 131.6, 129.5, 128.6, 127.5, 126.6, 126.2, 125.8, 124.3, 124.0, 120.5, 112.3, 92.1, 80.4, 59.0, 50.2, 30.5, 21.6, 19.0, 13.6, 13.5, 10.9. IR (film, υ) 3395, 3062, 3029, 2228, 1702 cm^{-1}. MS (*m/z*, rel. int., %) 399 (M^+, 23), 326 (18), 284 (12), 235 (4), 91 (100), 65 (10), 55 (1). HRMS (ESI, *m/z*) calcd. for $C_{27}H_{29}NO_2$ ($[M+Na]^+$): 422.2096; Found: 476.2101.

Ethyl 1-benzyl-4-(2-((4-fluorophenyl)ethynyl)phenyl)-2-methyl-1H-pyrrole-3-carboxylate (2j). Yellow oil; Yield: 31%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, 7.4, 1H), 7.33-7.17 (m, 8H), 7.01-6.99 (m, 2H), 6.92 (t, 8.5, 2H), 6,61 (s, 1H), 5.03 (s, 2H), 4.05 (q, 7.2, 2H), 2.48 (s, 3H), 0,98 (t, 7.2, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 162.2 (d, 248.9), 138.8, 136.9, 135.6, 133.3 (d, 8.1), 131.5, 129.8, 128.7, 127.7, 127.6, 126.3, 126.1, 124.3, 123.2, 120.7, 119.83 (d, 3.3), 115.32 (d, 22.0), 112.5, 90.2, 89.5, 59.2, 50.41, 13.7, 11.1. MS (*m/z*, rel. int., %): 437 (M^+, 15), 364 (17), 360 (4), 272 (8), 91 (100), 65 (20). HRMS (ESI, *m/z*) calcd. for $C_{29}H_{24}FNO_2$ ($[M+Na]^+$): 460.1689; Found: 460.1723.

Ethyl 2-methyl-1-phenethyl-4-(2-(phenylethynyl)phenyl)-1*H*-pyrrole-3-carboxylate (2k). Yellow oil. Yield: 45%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.2, 1H), 7.41–7.38 (m, 2H), 7.27–7.25 (m, 3H), 7.24–7.22 (m, 2H), 7.21–7.18 (m, 1H), 7.17–7.14 (m, 3H), 6.98 (dd, *J* = 2.4 and 7.2, 2H), 6.45 (s, 1H), 4.04 (q, *J* = 7.1, 2H), 3.99 (t, *J* = 6.8, 2H), 2.93 (t, *J* = 6.8, 2H), 2.35 (s, 3H), 0.96 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 138.9, 137.6, 135.3, 131.7, 131.5, 129.5, 128.7, 128.5, 128.1, 127.7, 127.6, 126.7, 126.0, 124.1, 123.7, 123.4, 119.7, 111.7, 91.1, 89.9, 59.1, 48.1, 37.5, 13.7, 10.8. IR(film, υ) 3410, 3055, 3024, 2978, 2931, 2214, 1698 cm^{-1}. MS (*m/z*, rel. int., %) 433 (M^+, 100), 360 (44), 328 (41), 268 (39), 253 (63), 180 (10), 105 (81), 91 (44), 77 (43). HRMS (ESI, *m/z*) calcd. for $C_{30}H_{27}NO_2$ ($[M+H]^+$): 434.2120; Found: 434.2118.

1-Benzyl-2-methyl-4-(2-(phenylethynyl)phenyl)-1*H*-pyrrole (2l). An alcoholic solution of NaOH (4 % P/V, 40 mL) was added to a stirred solution of compound **2a** (4.195 g, 10.0 mmol) in EtOH (40 mL) and the mixture was heated under reflux for 5 h. The system was cooled in an ice bath and the solution was adjusted to pH 5 with glacial acetic acid. The thus formed precipitate was collected by filtration, affording 1-benzyl-2-methyl-4-(2-(phenylethynyl)phenyl)-1*H*-pyrrole carboxylic acid (3.408 g, 87%), as a beige solid, mp. 204–204.5ºC. MS (*m/z*, rel. int., %) 391 (M^+, 2), 242 (20), 189(8), 111(14), 97(29), 83(31), 57(85), 43(100). IR (KBr, υ) 3432, 3132, 3095, 3027, 2963, 2851, 2215, 1655 cm^{-1}. HRMS (ESI, *m/z*) calcd. for $C_{27}H_{21}NO_2$ ($[M+Na]^+$): 414.1470; Found: 414.1467.

To a stirred solution of the above acid (391 mg, 1.0 mmol) in quinoline (2 mL) was added metallic Cu (0.7 mmol) and the system was heated under reflux for 4 hours. Then, it was cooled with an ice bath and the pH of the solution was adjusted to 4 with 2N HCl. The products were extracted with EtOAc (3 × 10 mL), the organic phase was washed with water, brine and saturated $NaHCO_3$ solution, dried over $MgSO_4$ and filtered. The solvent was evaporated under reduced pressure and the residue was purified via column chromatography on silica gel, eluting with EtOAc:hexane (5:95), affording compound **2k** (236 mg, 68%), as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25–8.22 (m, 1H), 7.82–7.79 (m, 1H), 7.51 (ddd, *J* = 1.3, 6.9 and 8.2, 1H), 7.51 (ddd, *J* = 1.3, 6.9 and 8.2, 1H), 7.26–7.24 (m, 2H), 7.19–7.14 (m, 4H), 7.10–7.06 (m, 3H), 6.99 (s, 1H), 6,37 – 6,34 (m, 2H), 4.95 (s, 2H), 2.35 (s, 3H). HRMS (ESI, *m/z*) calcd. for $C_{26}H_{21}N$ ($[M+H]^+$): 348.1752; Found: 348.1752.

Synthesis of the 3*H*-benzo[*e*]indoles

Solid K_2CO_3 (0.5 mmol) was added to a solution of the pyrrole (0.25 mmol) in CH_2Cl_2 (2 mL) and the system was stirred at room temperature for 10 minutes. Then, it was treated dropwise with a solution of iodine (0.3 mmol) in CH_2Cl_2 (2 mL). After the reaction was completed, the product was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were successively washed with 15% aqueous $Na_2S_2O_3$ (50 mL), water and brine, dried over $MgSO_4$ and filtered. The solvent was evaporated under reduced pressure and the residue was purified via column chromatography on silica gel eluting with EtOAc:hexane (10:90).

Ethyl 3-benzyl-5-iodo-2-methyl-4-phenyl-3*H*-benzo[*e*]indole-1-carboxylate (1a). White solid. Mp. 152–153ºC. Yield: 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79–8.76 (m, 1H), 8.44–8.41 (m, 1H), 7.57 (ddd, *J* = 1.4, 6.8 and 8.2, 1H), 7.51 (ddd, *J* = 1.4, 6.8 and 8.3, 1H), 7.39–7.33 (m, 1H), 7.24–7.19 (m, 2H), 7.14–7.09 (m, 3H), 6.94 (dd, *J* = 1.3 and 8.2, 2H), 6.34 (dd, *J* = 1.9 and 7.5, 2H), 4.73 (s, 2H), 4.53 (q, *J* = 7.1, 2H), 2.46 (s, 3H), 1.47 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5,143.8, 141.4, 137.3, 134.3, 133.3, 131.6, 130.7, 130.1, 128.4, 128.2, 128.1, 127.3, 127.0, 126.1, 125.7, 125.3, 124.9, 122.0, 109.1, 104.3,60.7, 48.2, 14.4, 12.0. IR (KBr, υ) 3363, 3055, 3026, 2978, 2908, 1697 cm^{-1}. MS (*m/z*, rel. int., %) 545 (M^+, 2), 418 (65), 373 (6), 281 (19), 253 (26), 105 (5), 91 (100), 77 (2), 45 (6). Anal. Calcd. for $C_{29}H_{24}INO_2$ C, 63.86; H, 4.44; N, 2.57. Found C, 64.18; H, 4.61; N, 2.35.

Ethyl 3-benzyl-5-iodo-2-methyl-4-(*p*-tolyl)-3*H*-benzo[*e*]indole-1-carboxylate (1b). White solid. Mp. 147–148ºC. Yield: 96%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (dd, *J* = 0.9 and 8.2, 1H), 8.42 (dd, *J* = 0.9 and 8.3, 1H), 7.56 (ddd, *J* = 1.4, 6.8 and 8.3, 1H), 7.51, (ddd, *J* = 1.4, 6.8 and 8.2, 1H), 7.14–7.09 (m, 3H), 7.01 (d, *J* = 7.7, 2H), 6.82 (d, *J* = 7.9, 2H), 6.36–6.34 (m, 2H), 4.75 (s, 2H), 4.52 (q, *J* = 7.1, 2H), 2.45 (s, 3H), 2.38 (s, 3H), 1.46 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 141.3, 140.7, 138.0, 137.4, 134.2, 133.4, 131.8, 130.6, 129.8, 128.7, 128.2, 127.2, 126.9, 126.0, 125.6, 125.2, 124.8, 121.8, 108.9, 104.6, 60.6, 48.1, 21.4, 14.3, 12.0. IR (KBr, υ) 3369, 3061, 3028, 2970, 2920, 1703 cm^{-1}. MS (*m/z*, rel. int., %) 559 (M^+, 100), 487 (2), 432 (1), 386 (12), 268 (15), 91 (57), 65 (7).

Anal. Calcd. for $C_{30}H_{26}INO_2$ C, 64.41; H, 4.68; N, 2.50. Found C, 64.37; H, 4.76; N, 2.39.

Ethyl 3-benzyl-5-iodo-2-methyl-4-(*m*-tolyl)-3*H*-benzo[*e*]indole-1-carboxylate (1c). Yellow solid. Mp. 136–138ºC. Yield: 94%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (dd, *J* = 0.9 and 8.3, 1H), 8.42 (dd, *J* = 0.9 and 8.3, 1H), 7.57 (ddd, *J* = 1.4, 6.9 and 8.3, 1H), 7.51 (ddd, *J* = 1.3, 6.9 and 8.1, 1H), 7.20–7.13 (m, 5H), 6.84 (d, *J* = 6.5, 1H), 6.63 (s, 1H), 6.36 (dd, *J* = 2.8 and 6.4, 2H), 4.77 (d, *J* = 17.9, 1H), 4.68 (d, *J* = 17.9, 1H), 4.53 (q, *J* = 7.1, 2H), 2.45 (s, 3H), 2.04 (s, 3H), 1.47 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 143.5, 141.3, 137.9, 137.5, 134.2, 133.4, 131.6, 130.8, 130.6, 128.8, 128.3, 127.8, 127.2, 127.1, 126.8, 126.0, 125.6, 125.3, 124.7, 121.8, 108.9, 104.1, 60.7, 48.1, 21.1, 14.3, 12.0. IR (KBr, υ) 3378, 3060, 3030, 2925, 2870, 1707 cm^{-1}. MS (*m/z*, rel.int., %) 559 (M^+, 33), 386 (5), 341 (8), 137 (10), 91 (44), 81 (52), 69 (100), 43 (63). HRMS (ESI, *m/z*) calcd. for $C_{30}H_{26}INO_2$ ($[M+Na]^+$): 582.0906; Found: 582.0904.

Ethyl 3-benzyl-4-(4-chlorophenyl)-5-iodo-2-methyl-3*H*-benzo[*e*]indole-1-carboxylate (1d). White solid. Mp. 147–148ºC. Yield: 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78–8.75 (m, 1H), 8.41–8.38 (m, 1H), 7.57 (ddd, *J* = 1.4, 6.8 and 8.3, 1H), 7.51 (ddd, *J* = 1.4, 6.8 and 8.2, 1H), 7.17–7.11 (m, 5H), 6.87–6.84 (m, 2H), 6.38–6.36 (m, 2H), 4.79 (s, 2H), 4.53 (q, *J* = 7.1, 2H), 2.47 (s, 3H), 1.47 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 142.1, 141.4, 137.0, 134.3, 132.0, 131.6, 131.4, 130.6, 128.5, 128.2, 127.4, 127.2, 126.4, 125.9, 125.4, 124.8, 122.2, 109.2, 104.4, 60.8, 48.3, 14.4, 12.0. IR (KBr, υ) 3365, 3108, 3087, 2982, 2873, 1693 cm^{-1}. MS (*m/z*, rel. int., %) 581 ($[M+2]^+$, 17), 579 (44), 453 (10), 253 (8), 149 (21), 91 (100), 69 (22). HRMS (ESI, *m/z*) calcd. for $C_{29}H_{23}ClINO_2$ ($[M+H]^+$): 580.0540; Found: 580.0544.

Ethyl 3-benzyl-4-(2-chlorophenyl)-5-iodo-2-methyl-3*H*-benzo[*e*]indole-1-carboxylate (1e). White solid. Mp. 175–175.5ºC. Yield: 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (dd, *J* = 0.8 and 8.3, 1H), 8.41 (dd, *J* = 0.8 and 8.4, 1H), 7.58 (ddd, *J* = 1.3, 6.8 and 8.3, 1H), 7.51 (ddd, *J*= 1.3, 6.8 and 8.2, 1H), 7.40 (dd, *J*= 0.9 and 8.0, 1H), 7.29 (td, *J* = 1.6 and 7.7,1H), 7.16–7.07 (m, 3H), 6.92 (td, *J* = 1.1 and 7.4, 1H), 6.77 (dd, *J* = 1.5 and 7.6, 1H), 6.38 (d, *J* = 6.7, 2H), 4.95 (d, *J* = 18.0, 1H), 4.76 (d, *J* = 18.0, 1H), 4.54 (q, *J* = 7.1, 2H), 2.49 (s, 3H), 1.47 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 142.1, 141.3, 136.8, 134.7, 134.2, 132.3, 131.1, 130.6, 130.4, 129.8, 129.2, 128.3, 127.4, 127.1, 126.5, 126.4, 125.7, 125.3, 124.8, 122.2, 109.1, 104.3, 60.7, 47.9, 14.4, 12.0. IR (KBr, υ) 3379, 3124, 3024, 2978, 2869, 1697 cm^{-1}. MS (*m/z*, rel.int., %) 581 ($[M+2]^+$, 17), 579 (M^+, 44), 453 (10), 253 (8), 149 (21), 91 (100), 69 (22). HRMS (ESI, *m/z*) calcd. for $C_{29}H_{23}ClINO_2$ ($[M+H]^+$): 580.0540; Found: 580.0530.

Ethyl 3-benzyl-8-fluoro-5-iodo-2-methyl-4-phenyl-3*H*-benzo[*e*]indole-1-carboxylate (1f). Yellow solid. Mp. 161–162ºC. Yield: 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (dd, *J* =2.5 and 11.9, 1H), 8.43 (dd, *J* =5.9 and 9.3, 1H), 7.37–7.33 (m, 1H), 7.25–7.23–(m, 1H), 7.22–7.18 (m, 2H), 7.14–7.09 (m, 3H), 6.93–6.91 (m, 2H), 6.34–6.32 (m, 2H), 4.73 (s, 2H), 4.54 (q, *J* = 7.1, 2H), 2.46 (s, 3H), 1.48 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 160.9 (d, *J* = 245.2), 143.5, 142.0, 137.1, 136.8 (d, *J* = 8.9), 132.6, 131.8, 130.0, 128.3, 128.2, 128.1, 127.9 (d, *J* = 10.0), 127.5, 127.0, 124.8, 121.4 (d, *J* = 4.4), 114.9 (d, *J* = 24.2), 109.5 (d, *J* = 23.8), 108.9, 103.7, 60.8, 48.1, 14.2, 12.1. IR (KBr, υ) 3386, 3105, 3027, 2988, 2869, 1702 cm^{-1}. MS (*m/z*, rel. int., %) 563 (M^+, 100), 436 (1), 363 (8), 345 (17), 272 (13), 91 (82). Anal. Calcd. for $C_{29}H_{23}FINO_2$ C, 61.82; H, 4.11; N, 2.49. Found C, 61.67; H, 4.02; N, 2.41.

3-Benzyl-5-iodo-8-methoxy-2-methyl-4-phenyl-3*H*-benzo[*e*]indole-1-carboxylate (1g). Yellow solid. Mp. 171–171.5ºC. Yield: 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 2.5, 1H), 8.32 (d, *J* = 9.2, 1H), 7.35–7.32 (m, 1H), 7.21–7.17 (m, 2H), 7.16–7.08 (m, 4H), 6.95–6.93 (m, 2H), 6.36–6.34 (m, 2H), 4.72 (s, 2H), 4.5 (q, *J* = 7.1, 2H), 3.99 (s, 3H), 2.44 (s, 3H), 1.45 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 158.1, 143.9, 141.1, 137.4, 135.8, 131.9, 130.8, 130.4, 128.3, 128.1, 128.0, 126.9, 125.7, 124.9, 121.4, 116.9, 109.0, 105.4, 104.0, 60.6, 55.5, 48.1, 14.4, 12.2. IR (KBr, υ) 3437, 3138, 3023, 2997, 2898, 2832, 1690 cm^{-1}. MS (*m/z*, rel. int., %) 575 (M^+, 100), 530 (4), 448 (2), 357 (52), 241 (16), 91 (66), 57 (15). Anal. Calcd. for $C_{30}H_{26}INO_3$ C, 62.62; H, 4.55; N, 2.43. Found C, 62.67; H, 4.58; N, 2.30.

Ethyl 3-benzyl-5-iodo-7,8-dimethoxy-2-methyl-4-phenyl-3*H*-benzo[*e*]indole-1-carboxylate (1h). Yellow solid. Mp. 181–182ºC. Yield: 73%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.82 (s, 1H), 7.35 (t, *J* = 7.6, 1H), 7.20 (t, *J* = 7.2, 2H), 7.14–7.10 (m, 3H), 6.94 (d, *J* = 7.5, 2H), 6.34 (d, *J* = 7.6, 2H), 4.72 (s, 2H), 4.50 (q, *J* = 7.1, 2H), 4.10 (s, 3H), 4.05 (s, 3H), 2.46 (s, 3H), 1.45 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 149.1, 148.8, 144.0, 141.7, 137.4, 131.1, 131.0, 130.3, 128.3, 128.1, 128.0, 126.9, 126.2, 124.9, 122.1, 121.8, 114.3, 108.2, 105.9, 103.0, 60.6, 56.1, 55.8, 48.1, 14.4, 12.4. IR (KBr, υ) 3350, 3150, 3027, 2992, 2902, 2827, 1985, 1738, 1699 cm^{-1}. MS (*m/z*, rel. int., %) 605 (M^+, 13), 432 (1), 387 (7), 261 (3), 149 (12), 91 (11), 69 (100), 55 (21), 43 (25). Anal. Calcd. for $C_{31}H_{28}INO_4$ C, 61.50; H, 4.66; N, 2.31. Found C, 61.34; H, 4.52; N, 2.27.

Ethyl 3-benzyl-4-butyl-5-iodo-2-methyl-3*H*-benzo[*e*]indole-1-carboxylate (1i). White solid. Mp. 148–148.5ºC. Yield: 61%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57–8.53 (m, 1H), 8.42–8.38 (m, 1H), 7.49–7.43 (m, 2H), 7.31–7.23 (m, 3H), 6.85 (d, *J* = 6.8, 2H), 5.56 (s, 2H), 4.51 (q, *J* = 7.1, 2H), 3.15 (t, *J* = 7.9, 2H), 2.55 (s, 3H), 1.77–1.57 (m, 2H), 1.47–1.40 (m, 5H), 0.95 (t, *J* = 7.2, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 140.6, 137.4, 134.0, 131.8, 131.2, 131.1, 129.1, 127.5, 126.5, 125.4, 125.3, 124.9, 122.1, 109.2, 105.1, 60.7, 49.0, 38.7, 32.9, 22.6, 14.3, 13.8, 12.0. IR (KBr, υ) 3439, 3046, 3024, 2979, 2870, 1981, 1820, 1690 cm^{-1}. MS (*m/z*, rel. int., %) 525 (M^+, 41), 480 (2), 398 (2), 352 (17), 283 (12), 137 (10), 91 (72), 81 (59), 69 (100), 57 (27), 43 (28). Anal. Calcd. for $C_{27}H_{28}INO_2$ C, 61.72; H, 5.37; N, 2.67. Found C, 61.74; H, 5.32; N, 2.72.

Ethyl 3-benzyl-4-(4-fluorophenyl)-5-iodo-2-methyl-3*H*-benzo[*e*]indole-1-carboxylate (1j). White solid. Mp. 154–155ºC. Yield: 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (dd, *J* = 0.8 and 8.2, 1H), 8.40 (dd, *J* = 0.9 and 8.4, 1H), 7.49 – 7.59 (m, 2H), 7.14 – 7.10 (m, 3H), 6.88 – 6.87 (m, 4H), 6.37 – 6.35 (m, 2H), 4.77 (s, 2H), 4.53 (q, *J* = 7.1, 2H), 2.47 (s, 3H), 1.46 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 162.5 (d, *J* = 247.9), 141.3, 139.6 (d, *J* = 3.5), 137.0, 134.3, 132.1, 131.8 (d, *J* = 8.1), 130.6, 128.4, 127.3, 127.1, 126.2, 125.8, 125.3, 124.7, 122.0, 115.0 (d, *J* = 21.4), 114.9, 109.1, 104.9, 60.7, 48.1, 14.3, 12.0. MS (*m/z*, rel. int., %): 563 (M^+, 8), 262 (19), 183 (21), 108 (18), 91 (32), 69 (100), 41 (70). HRMS (ESI, *m/z*) calcd. for $C_{29}H_{23}FINO_2$ ($[M+Na]^+$): 586.0655; Found: 586.0663.

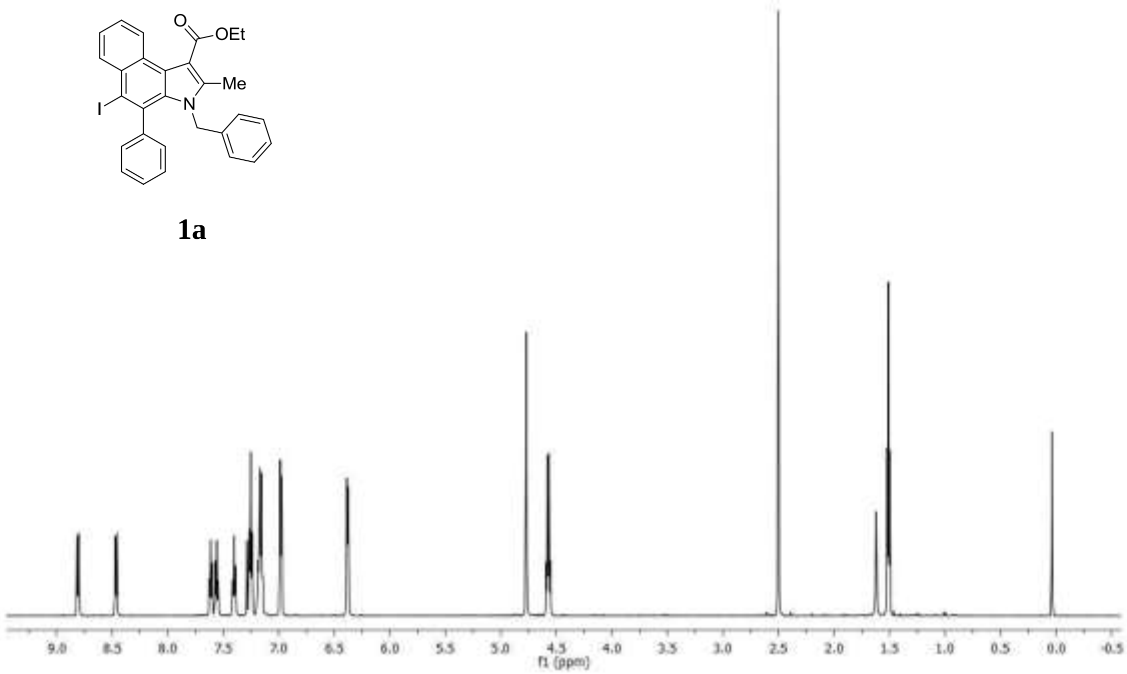
Ethyl 5-iodo-2-methyl-3-phenylethynyl-4-phenyl-3*H*-benzo[*e*]indole-1-carboxylate (1k). White solid. Mp. 120–121ºC. Yield: 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70–8.67 (m, 1H), 8.45–8.43 (m, 1H), 7.56–7.48 (m, 5H), 7.40–7.38 (m, 2H), 7.18–7.16 (m, 3H), 6.71–6.99 (m, 2H), 4.51 (q, *J* = 7.1, 2H), 3.69 (t, *J* = 8.1, 2H), 2.56 (t, *J* = 8.1, 2H), 2.47 (s, 3H), 1.46 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 144.6, 140.8, 137.4, 134.3, 133.0, 131.0, 130.6, 130.5, 128.7, 128.6, 128.4, 128.4, 127.1, 126.7, 126.1, 125.7, 125.2, 122.1, 109.0, 104.4, 60.7, 45.9, 37.0, 14.4, 12.1. IR (KBr, υ) 3367, 3053, 3017, 2973, 2923, 1955, 1803, 1697 cm^{-1}. MS (*m/z*, rel. int., %) 559 (M^+, 30), 558 (100), 421 (86), 311 (23), 268 (31), 201 (3), 105 (41), 101 (2), 77 (23), 69 (55), 45 (15), 43 (41). Anal. Calcd. for $C_{30}H_{26}INO_2$ C, 64.41; H, 4.68; N, 2.50. Found C, 64.52; H, 4.59; N, 2.38.

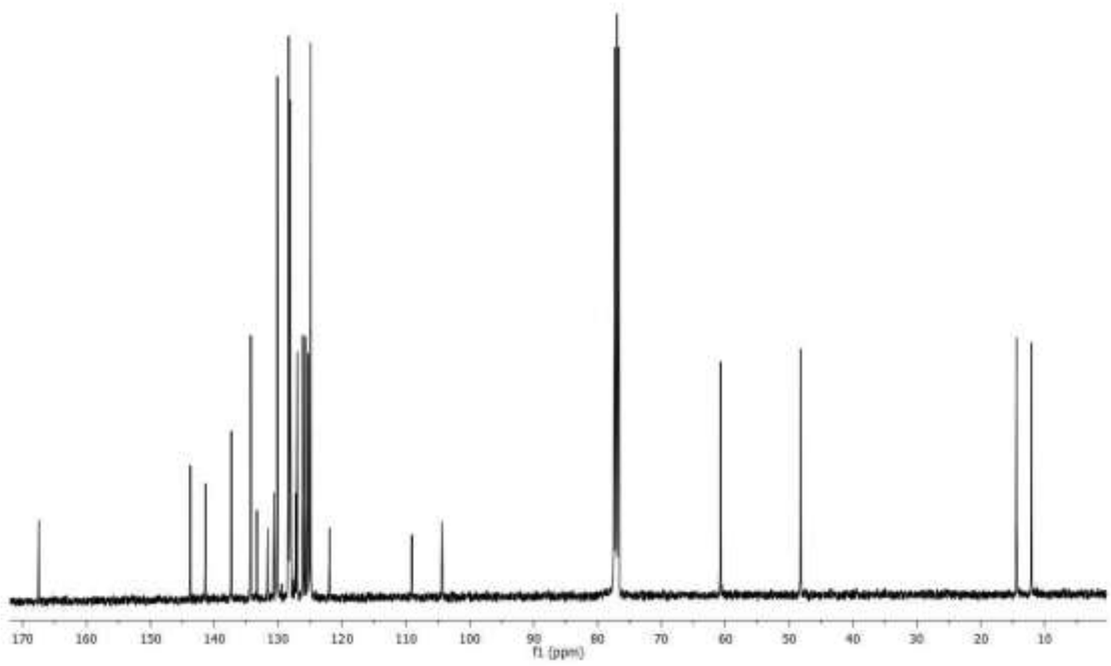
3-Benzyl-5-iodo-2-methyl-4-phenyl-3*H*-benzo[*e*]indole (1l). White solid. Mp. 171–172ºC. Yield: 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36–8.34 (m, 1H), 8.21–8.19 (m, 1H), 7.57–7.53 (m, 1H), 7.47 (ddd, *J* = 1.2, 6.9 and 8.2, 1H), 7.36 – 7.32 (m, 1H), 7.20 (t, *J* = 7.6, 2H), 7.10–7.06 (m, 3H), 6.98–6.95 (m, 3H), 6.32–6.30 (m, 2H), 4.66 (s, 2H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 138.6, 137.0, 133.9, 133.8, 131.6, 130.1, 129.7, 128.2, 128.0, 127.9, 127.4, 126.7, 126.0, 125.1, 125.0, 124.9, 123.0, 100.6, 100.5, 47.7, 13.0. IR (KBr, υ) 3445, 3076, 3026, 2936, 2865, 1972, 1835 cm^{-1}. MS (*m/z*, rel. int., %) 473 (M^+, 100), 346 (4), 268 (19), 254 (52), 91 (59), 65 (6). Anal. Calcd. for $C_{26}H_{20}IN$ C, 65.97; H, 4.26; N, 2.96. Found C, 66.20; H, 4.31; N, 2.91.

Ethyl 3-benzyl-2-methyl-4-phenyl-3*H*-benzo[*e*]indole-1-carboxylate (1'a). Yellow solid. Mp. 132–133ºC. Yield: 41%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91–8.89 (m, 1H), 7.82–7.79 (m, 1H), 7.54 (ddd, *J*= 1.4, 6.8 and 8.4, 1H), 7.43 (ddd, *J* = 1.2, 6.8 and 8.0, 1H), 7.35, (s, 1H), 7.31–7.27 (m, 1H), 7.19–7.15 (m, 2H), 7.12–7.06 (m, 5H), 6.39–6.37 (m, 2H), 4.97 (s, 2H), 4.53 (q, *J* = 7.1, 2H),2.52 (s, 3H), 1.47 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 141.1, 139.8, 137.2, 131.2, 129.6, 129.4, 128.3, 128.2, 127.7, 127.6, 127.3, 127.0, 126.9, 126.5, 125.4, 125.1, 125.0, 124.1, 121.4, 109.1, 60.4, 48.2, 14.4, 12.0. IR (KBr, υ) 3378, 3058, 3025, 2980, 2850, 1958, 1799, 1690 cm^{-1}. MS (*m/z*, rel. int., %) 563 (M^+, 100), 436 (1), 363 (8), 345 (17), 272 (13), 91 (82). Anal. Calcd. for $C_{29}H_{25}NO_2$ C, 83.03; H, 6.01; N, 3.34. Found C, 82.98; H, 5.78; N, 3.27.

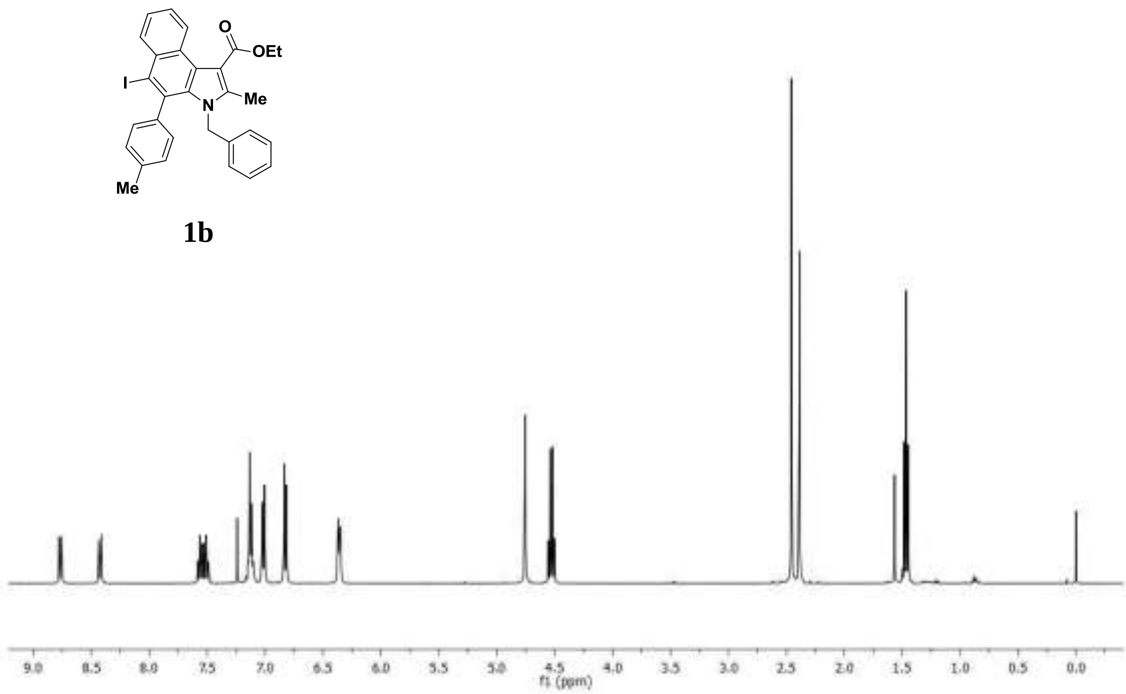
Example of functionalization of an iodocyclized product

Ethyl 11-benzyl-12-methyl-5,6-diphenyl-11*H*-benzo[*e*]naphtho[*2,1-g*]indole-13-carboxylate (6a).[16] Diphenylacetylene (89mg,0.5mmol), $Pd(OAc)_2$ (5 mg, 5mol%), NaOAc (41 mg, 0.5 mmol) and LiCl (10 mg, 0.25 mmol) were successively added to a stirred solution of **1a** (139 mg, 0.25 mmol) in DMF (1 mL). The system was heated at 100ºC for 24 h. After the reaction was completed, the system was cooled to room temperature and the products were extracted with EtOAc (3 × 10 mL), the organic phase was washed with water and brine. The extract was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified via column chromatography on silica gel, eluting with hexane. The product (145 mg, 98%) was obtained as a yellow solid. Mp. 236–236.5ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 – 8.71 (m, 1H), 8.35–8.33 (m, 1H), 7.69–7.64 (m, 3H), 7.47–7.38 (m, 3H), 7.35–7.31 (m, 2H), 7.22–7.17 (m, 2H), 7.07–7.06 (m, 4H), 7.01–6.90 (m, 5H), 6.27 (d, *J* = 7.2, 2H), 5.71 (d, *J* = 15.6, 1H), 5.36 (d, *J* = 15.6, 1H), 4.54–4.51 (m, 2H), 2.67 (s, 3H), 1.48 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 143.6, 143.1, 139.5, 137.4, 136.4, 136.0, 132.5, 131.8, 131.5, 130.8, 130.5, 129.6, 128.8, 128.3, 128.1, 128.0, 127.5, 127.3, 126.9, 126.8, 126.6, 126.3, 126.1, 126.0, 125.9, 125.5, 125.0, 124.7, 123.1, 121.8, 121.5, 111.9, 60.5, 51.6, 14.4, 13.1. MS (*m/z*, rel. int., %) 595 (M^+, 17), 458 (10), 419 (23), 254 (14), 149 (13), 105 (100), 91 (84), 77 (45). HRMS (ESI, *m/z*) calcd. for $C_{43}H_{33}NO_2$($[M+H]^+$): 596.2590; Found: 596.2583.

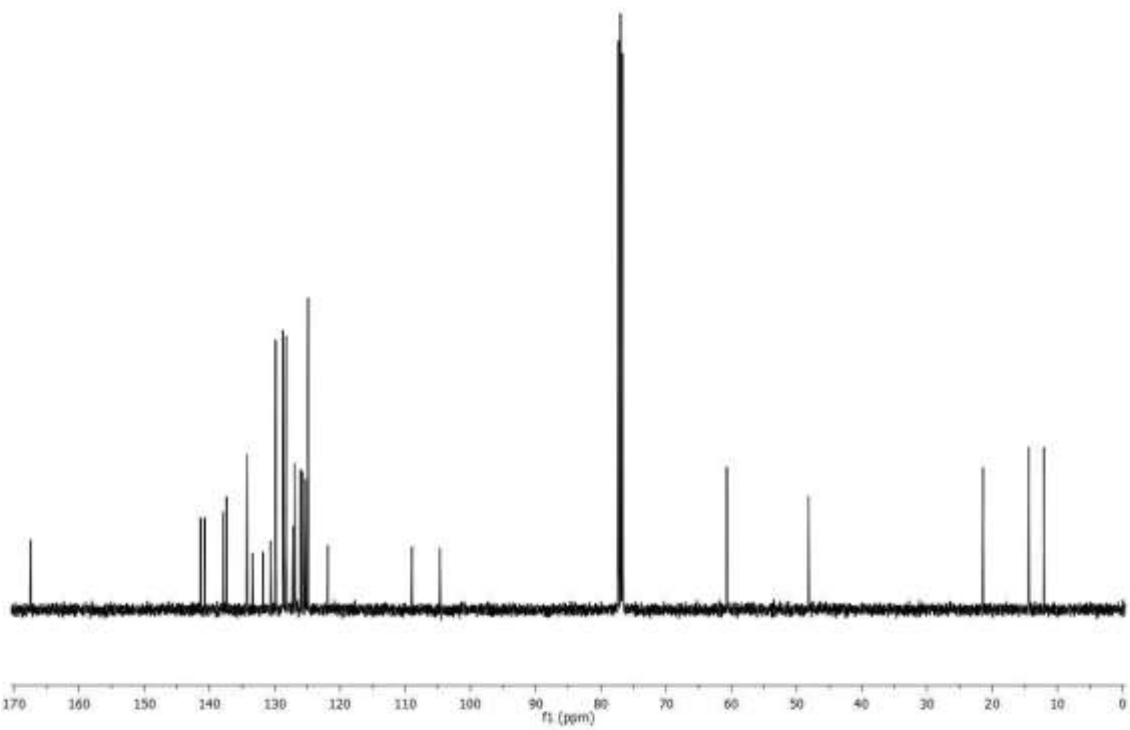




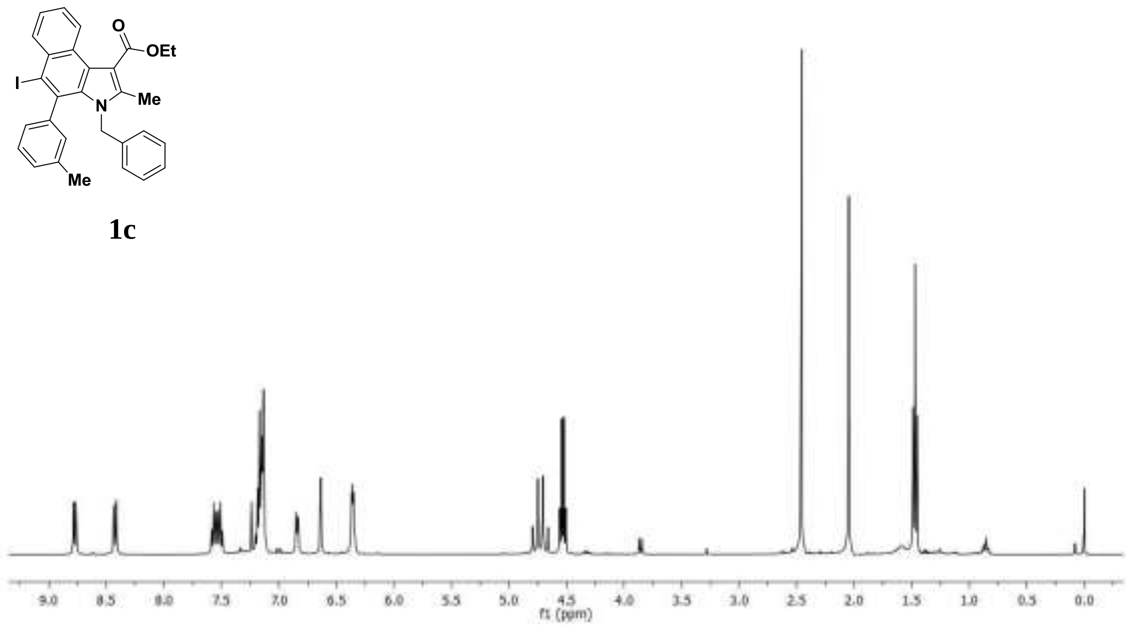
[1]H NMR (top) and [13]C NMR (bottom) spectra of Compound **1a**.



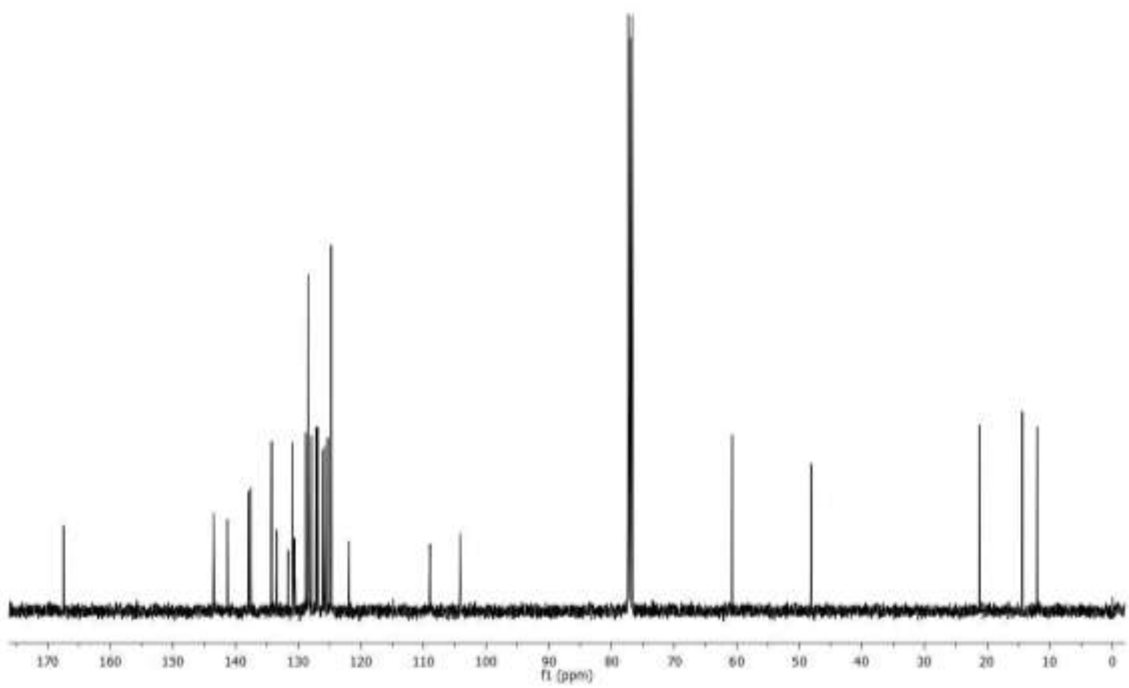
1b



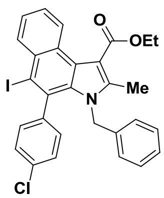
^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **1b**.



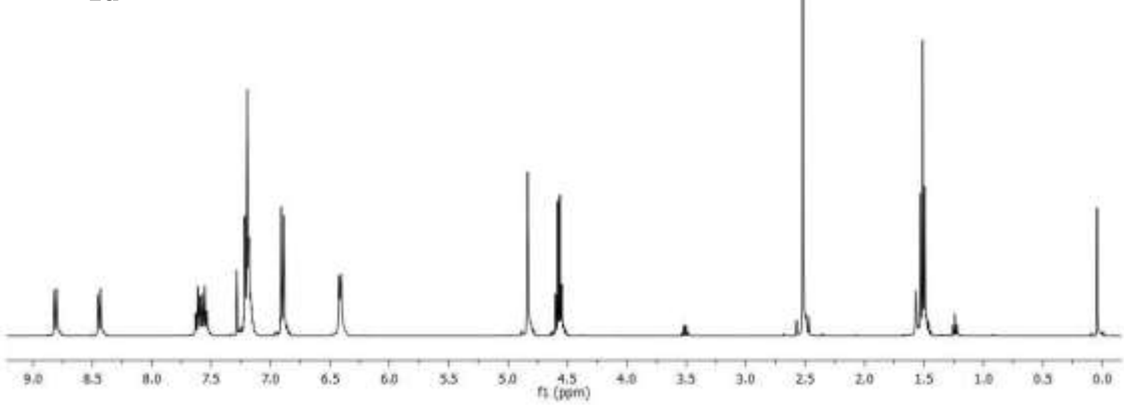
1c

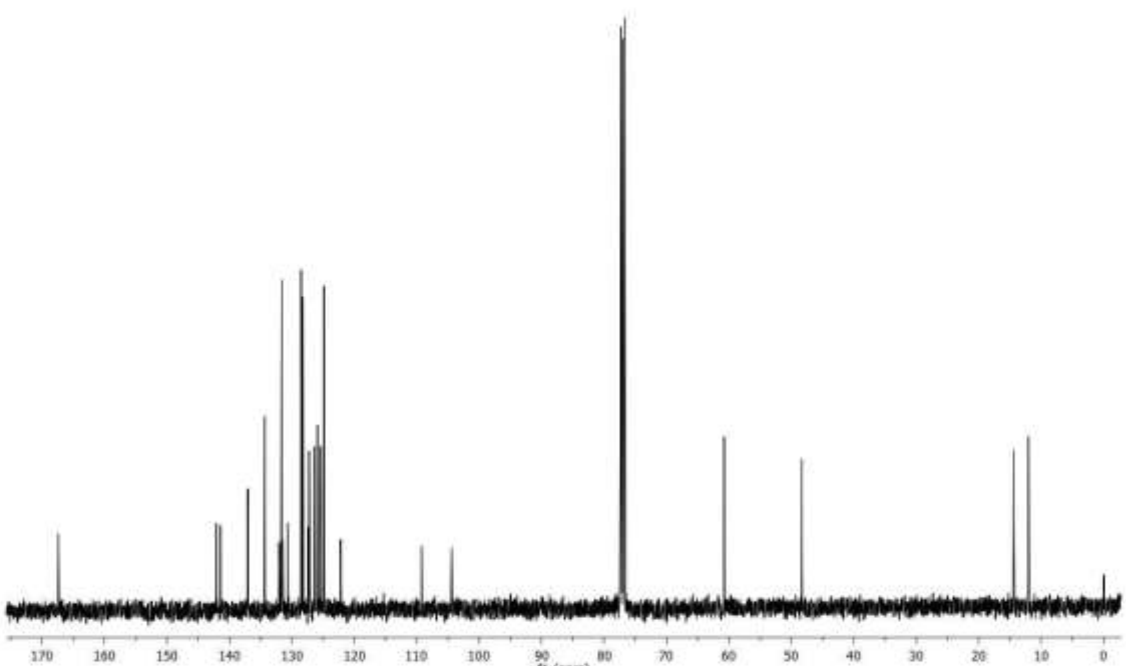


[1]H NMR (top) and [13]C NMR (bottom) spectra of Compound **1c**.

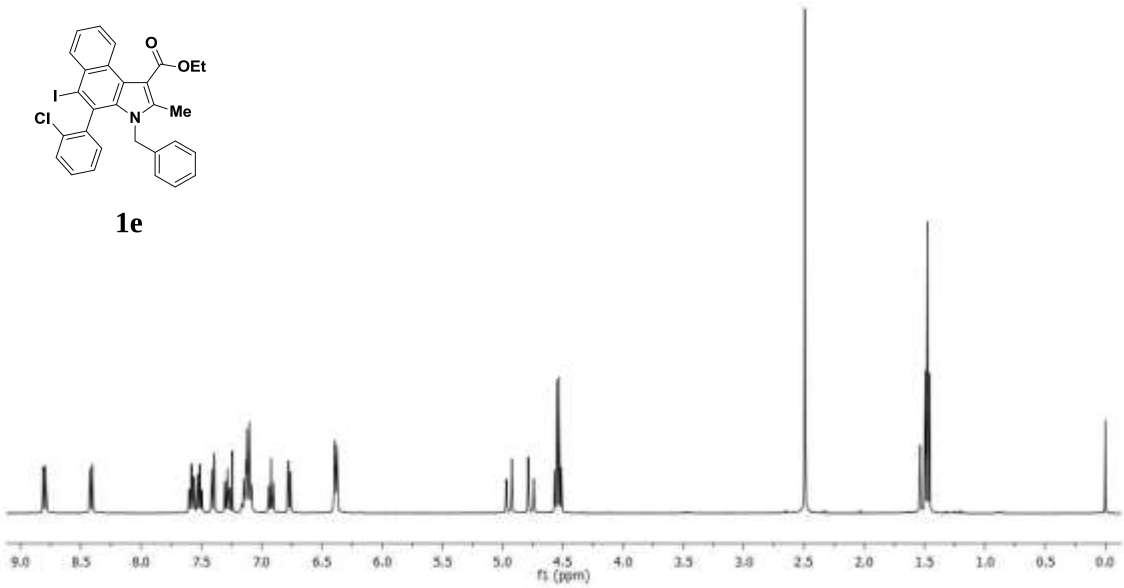


1d

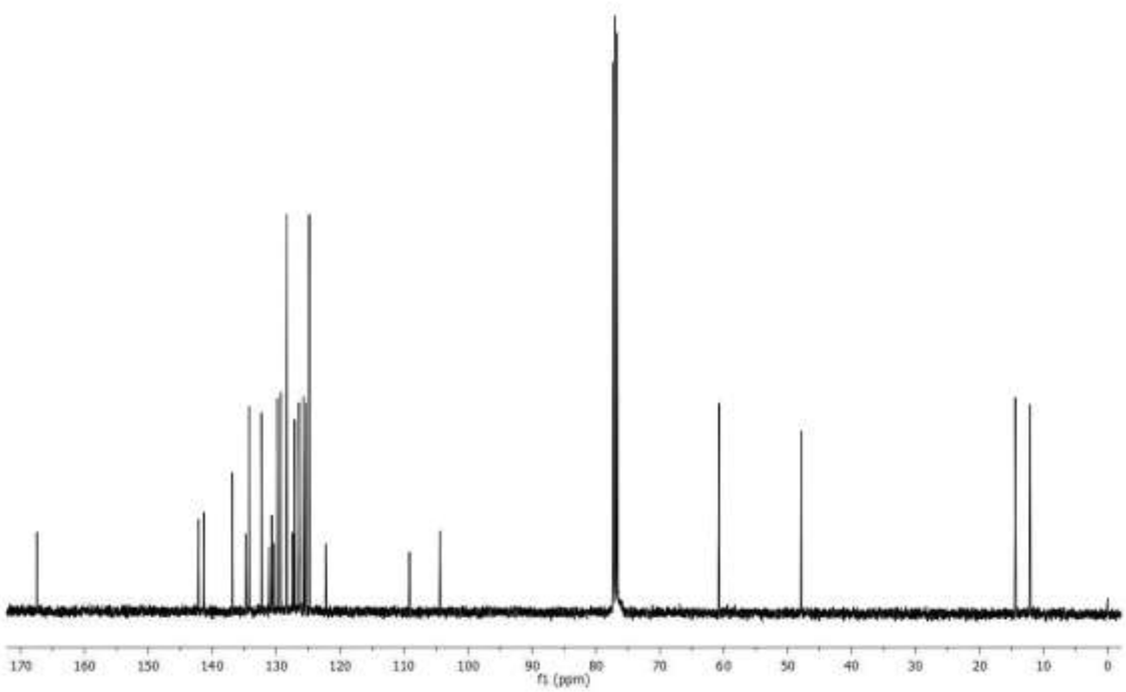




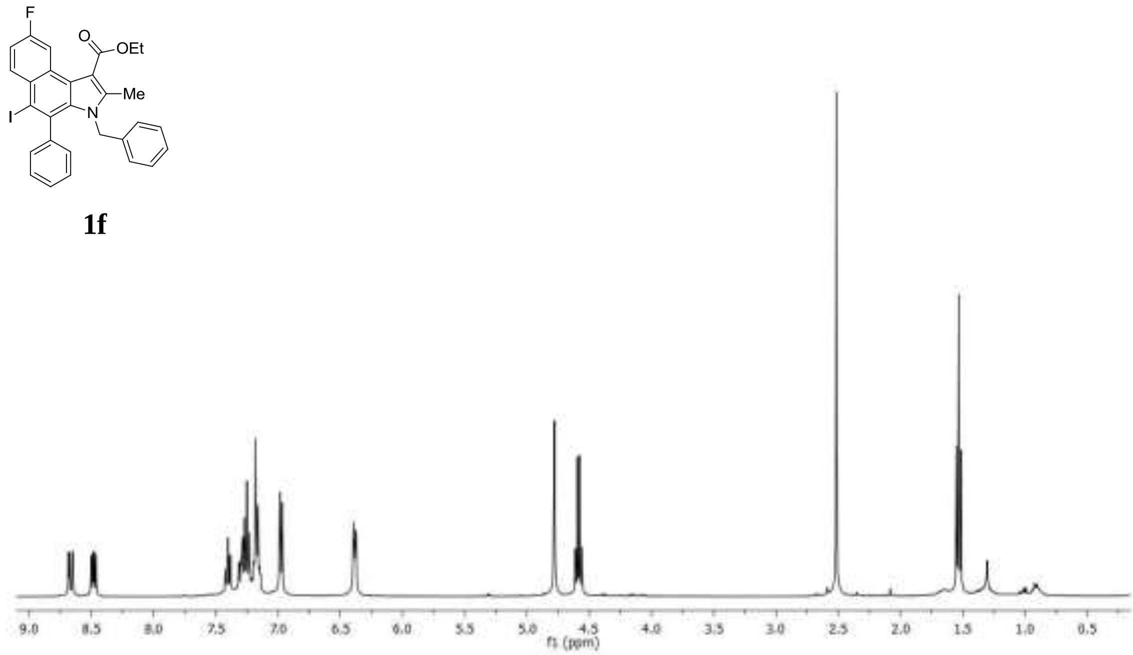
^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **1d**.



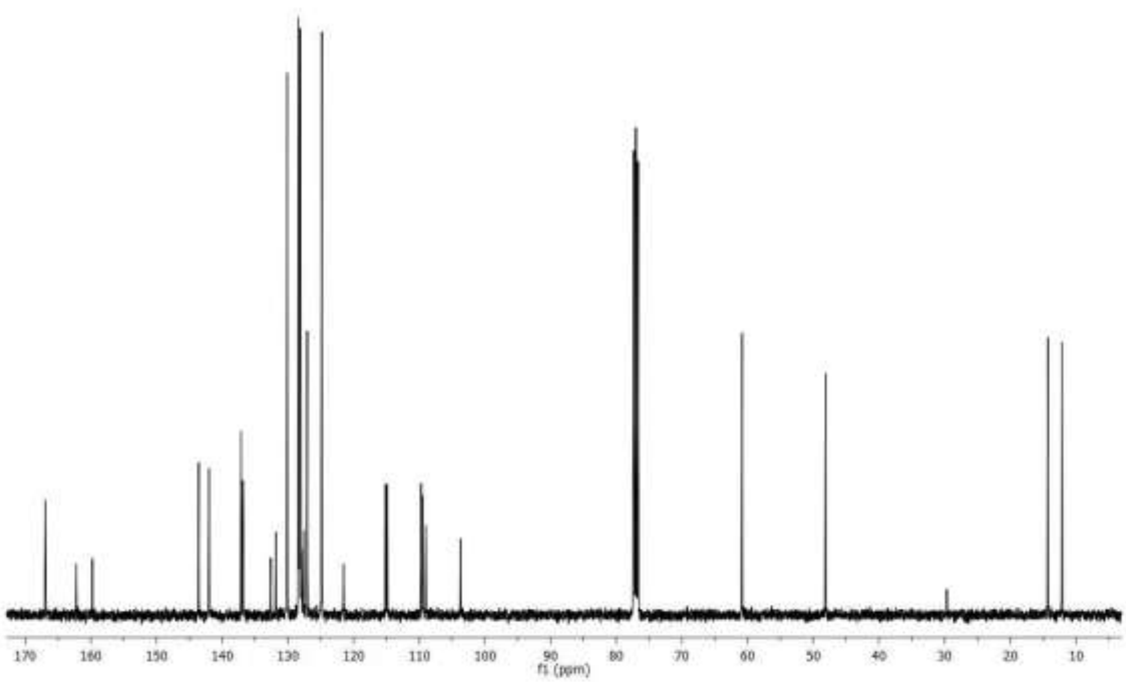
1e



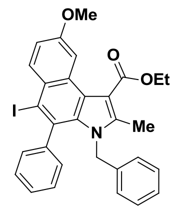
^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **1e**.



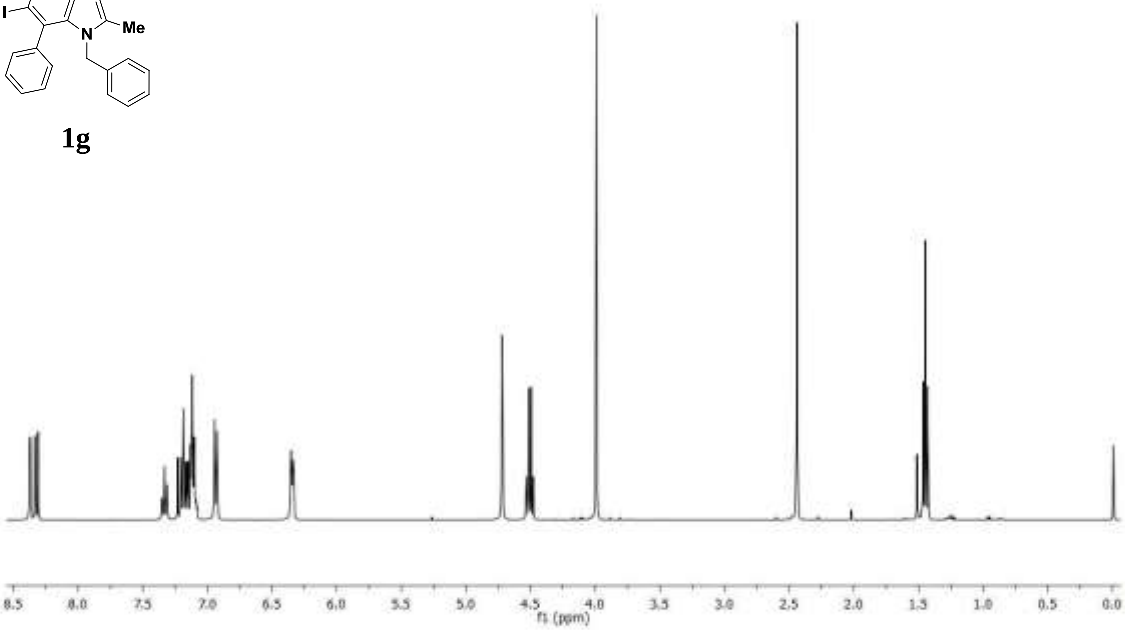
1f

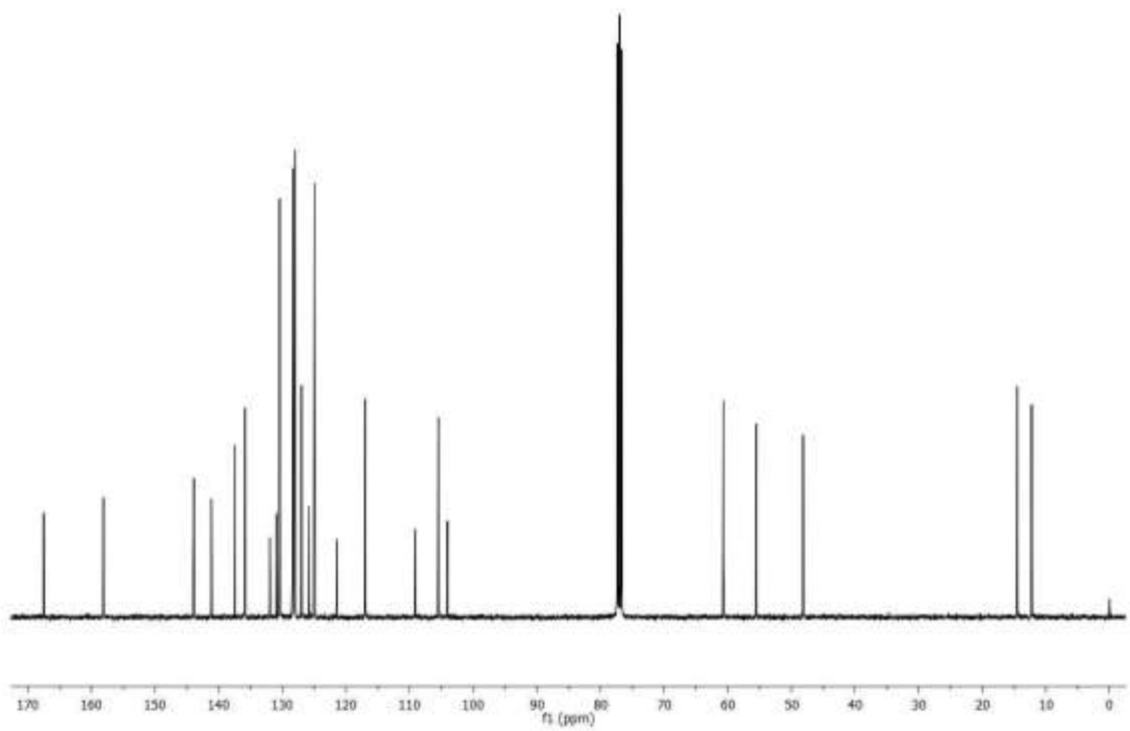


^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **1f**.

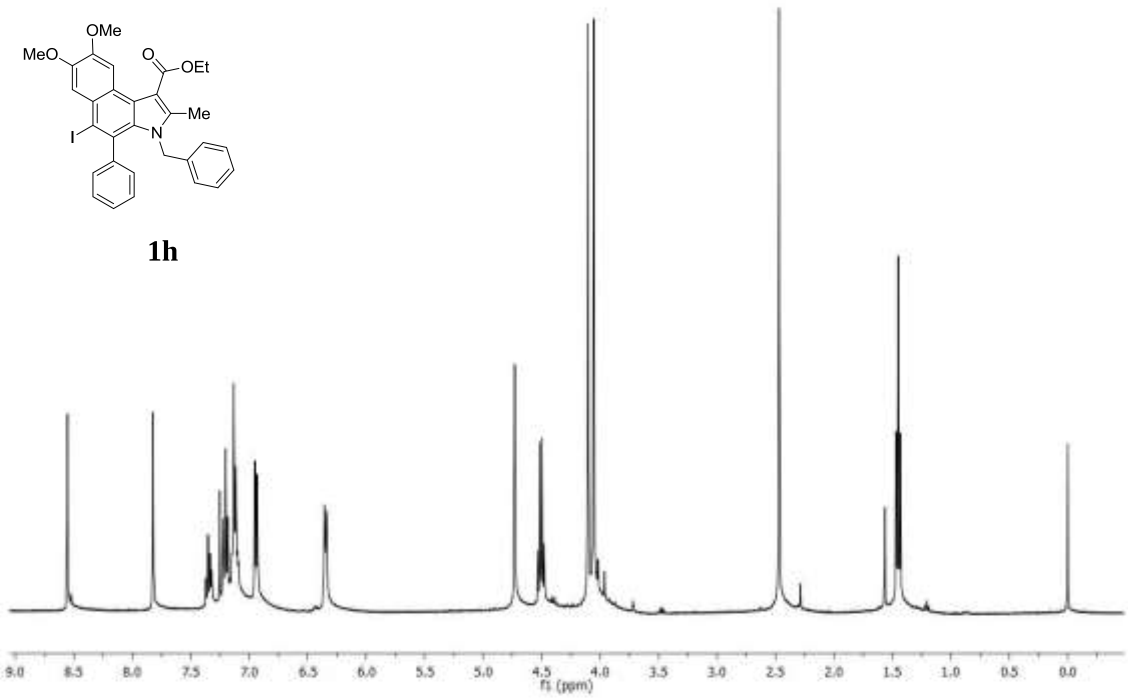


1g

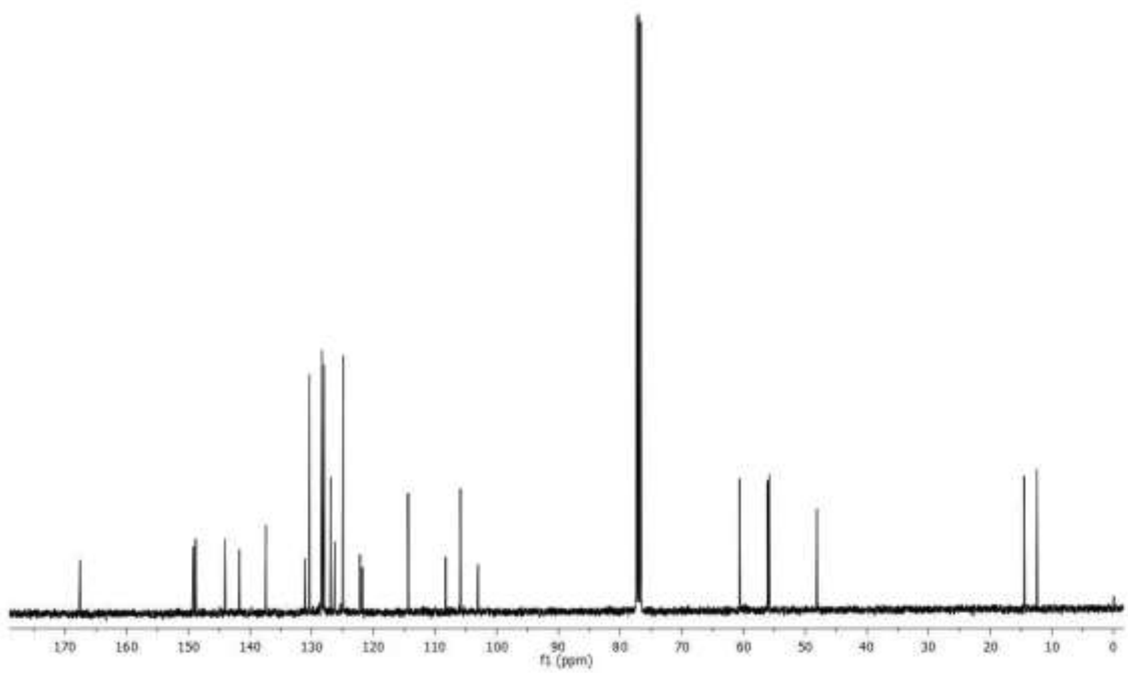




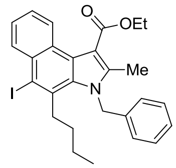
^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **1g**.



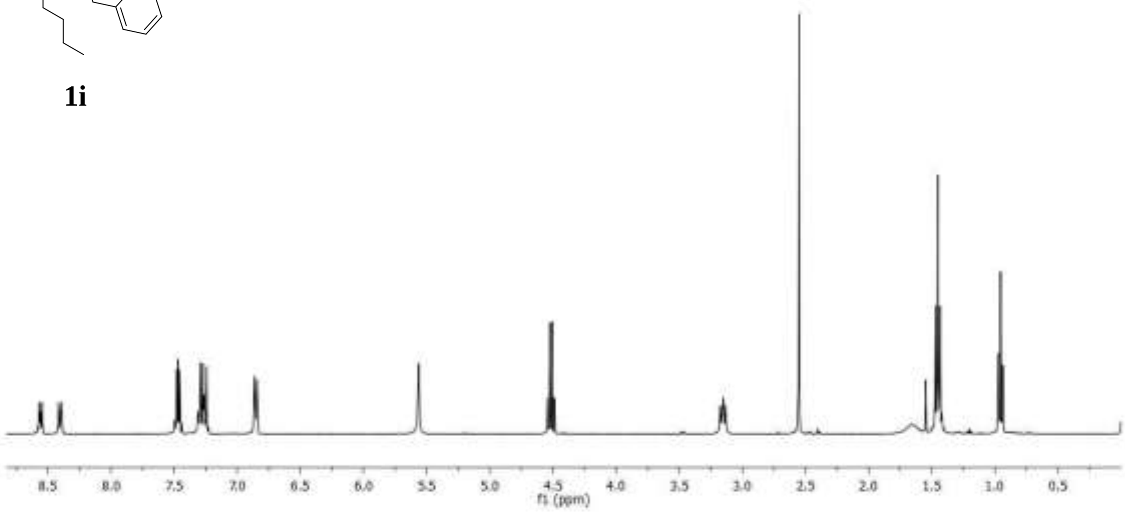
1h

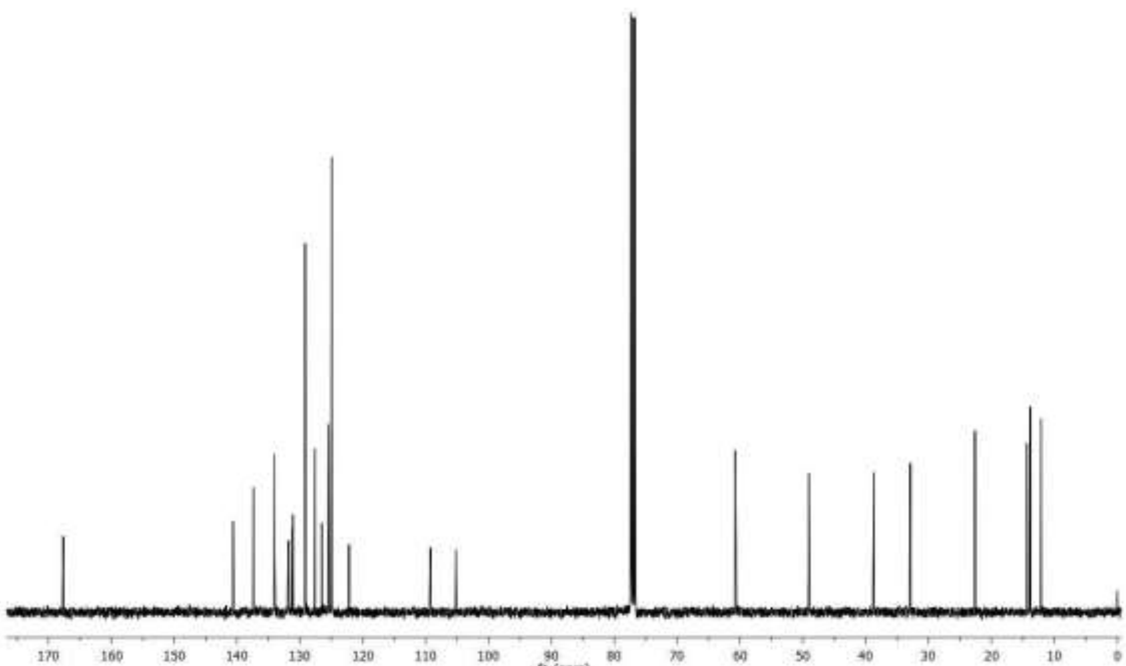


^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **1h**.

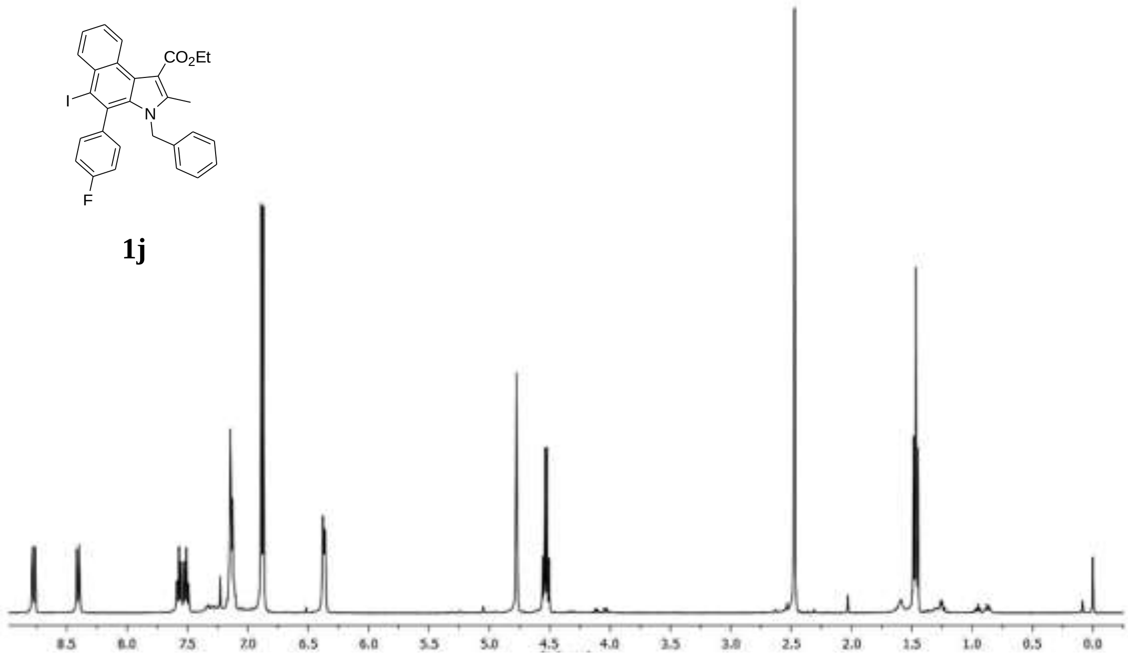


1i

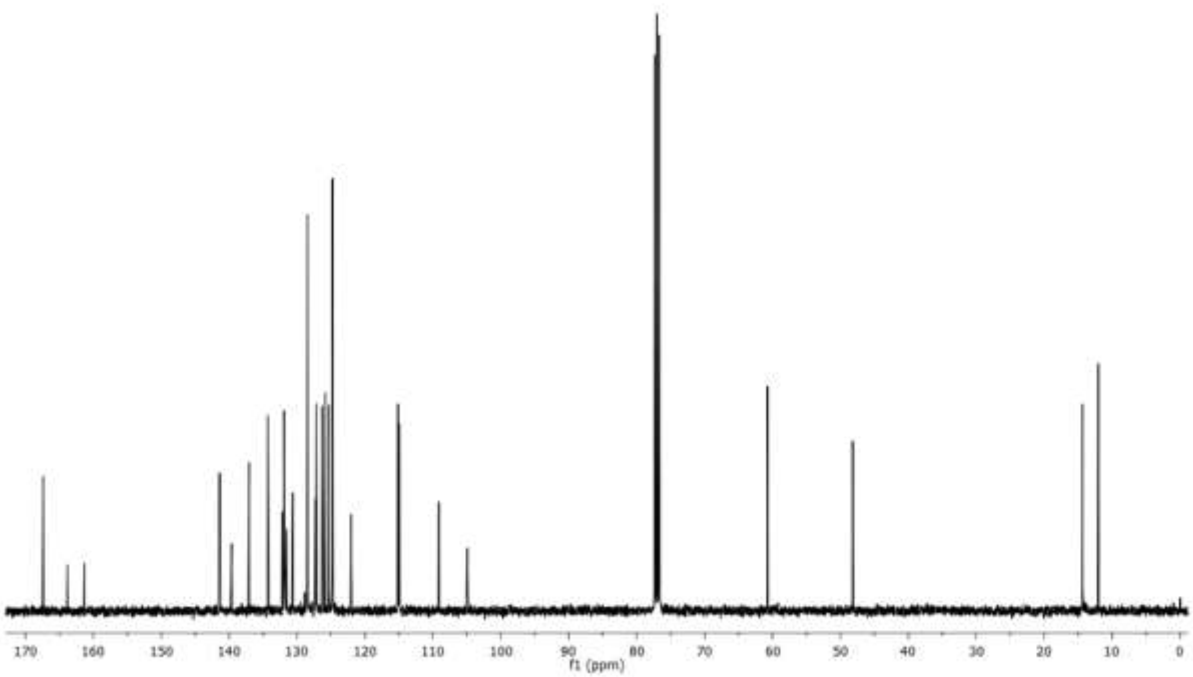




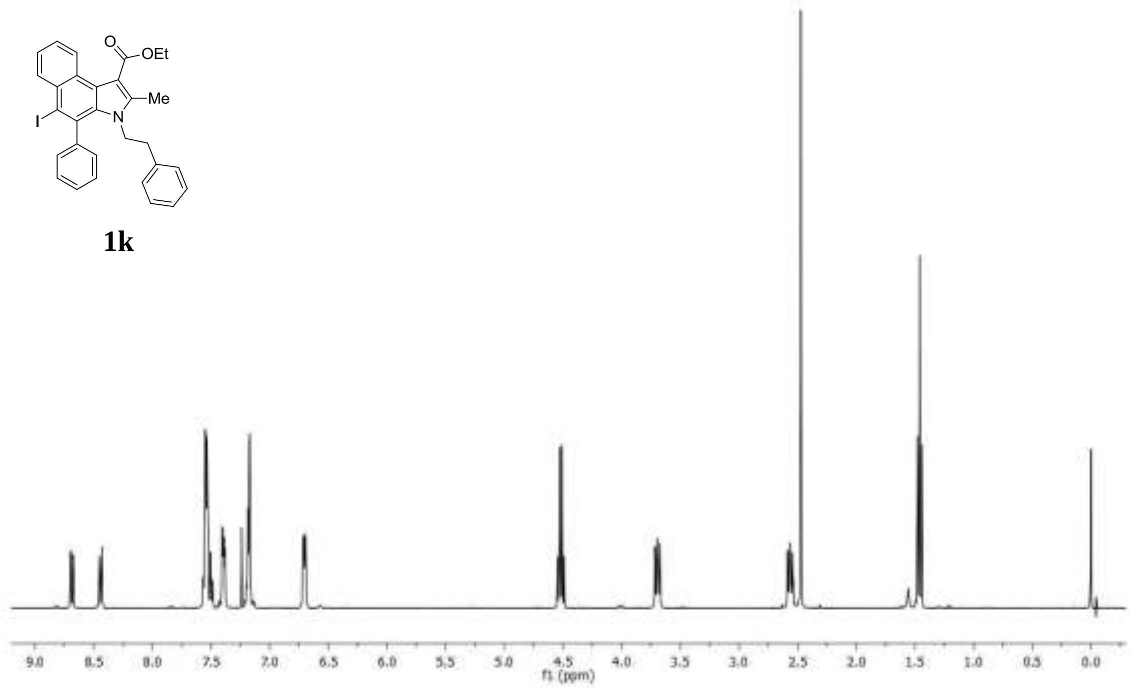
[1]H NMR (top) and [13]C NMR (bottom) spectra of Compound **1i**.



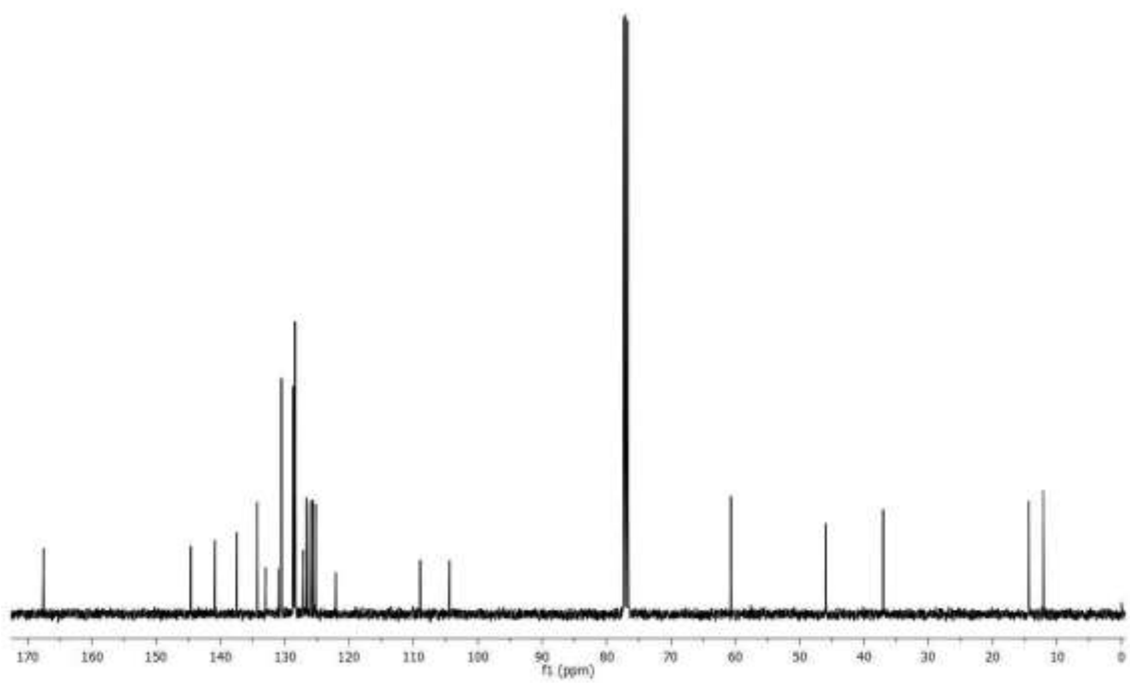
1j



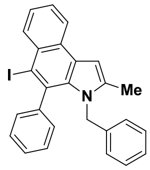
[1]H NMR (top) and [13]C NMR (bottom) spectra of Compound **1j**.



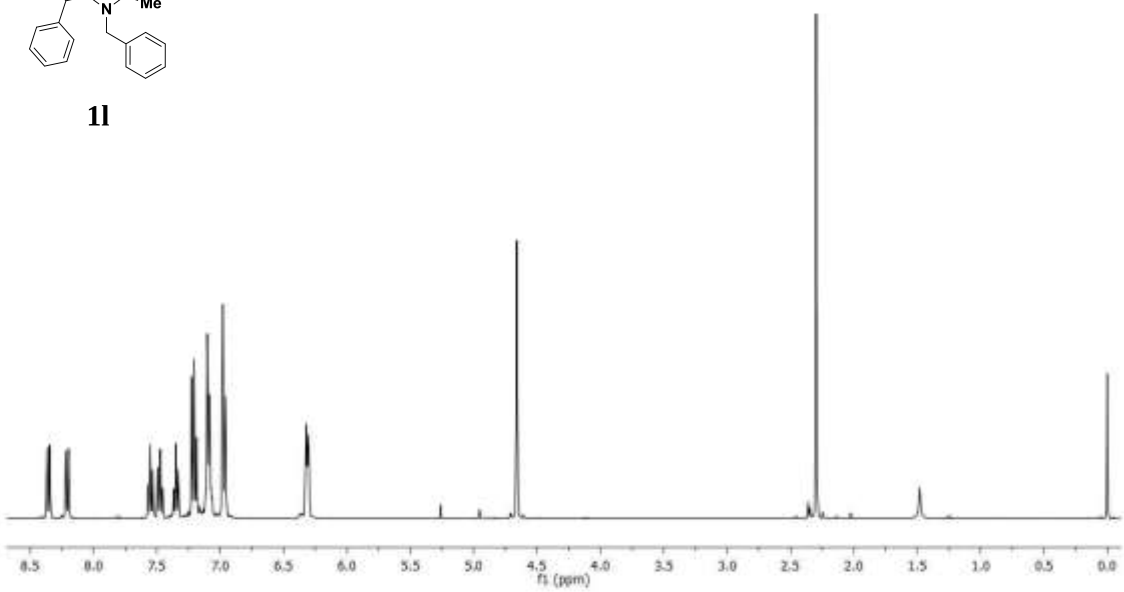
1k

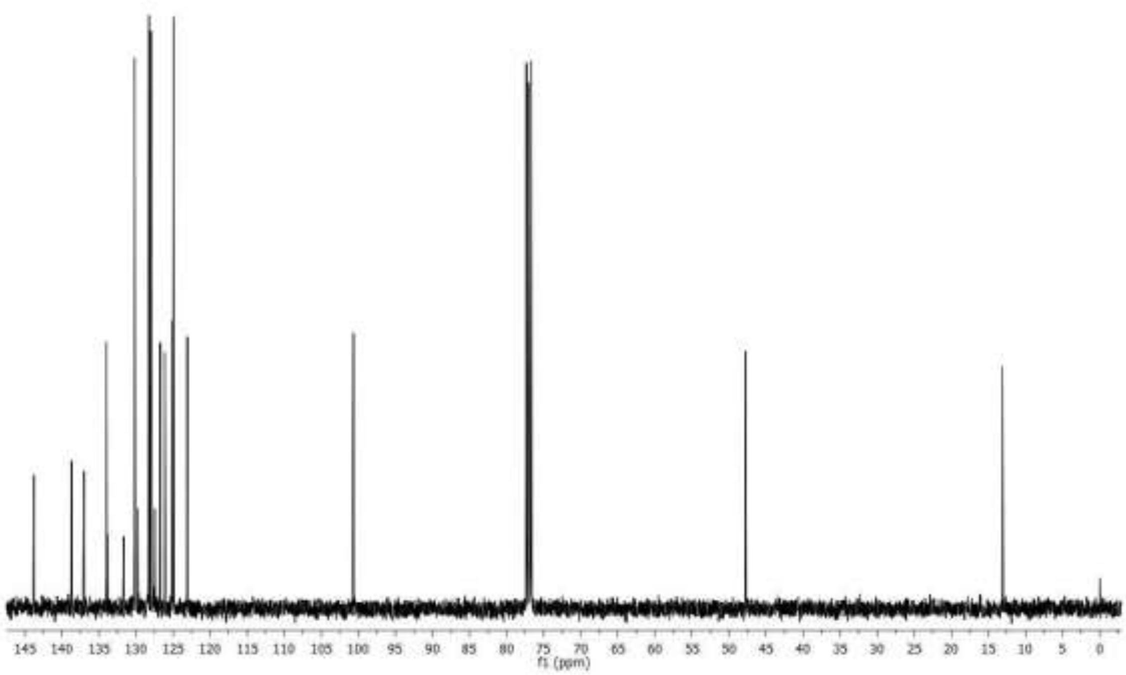


^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **1k**.

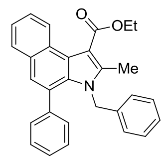


1l

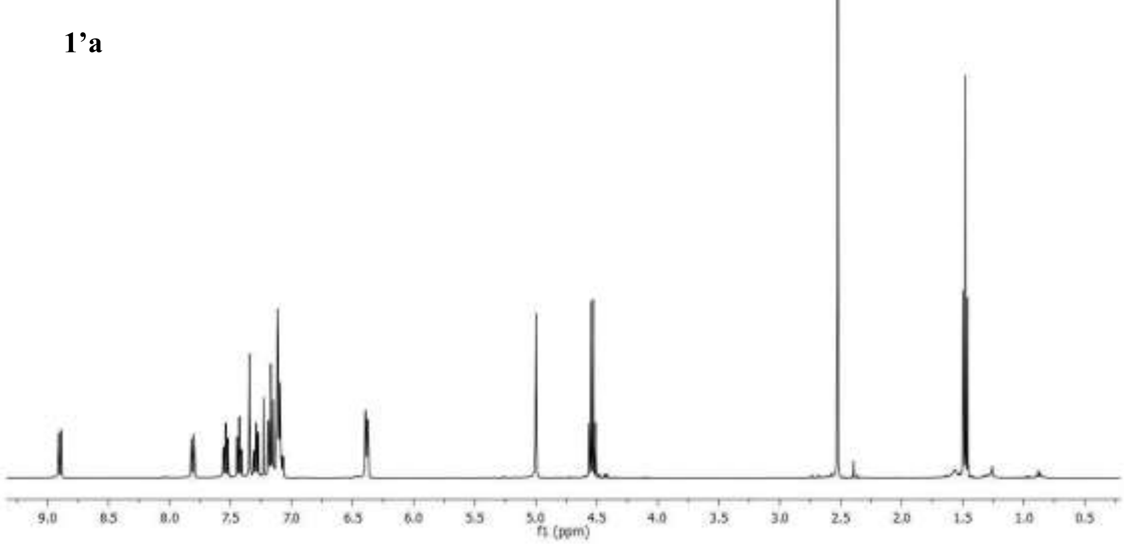


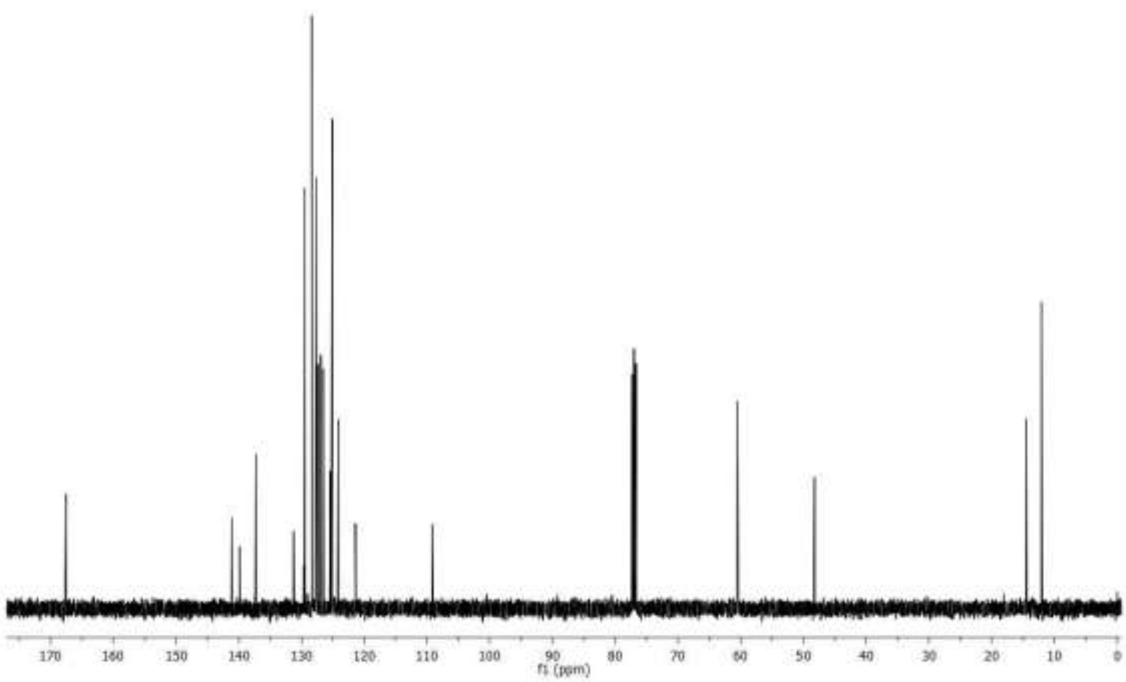


^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **1l**.

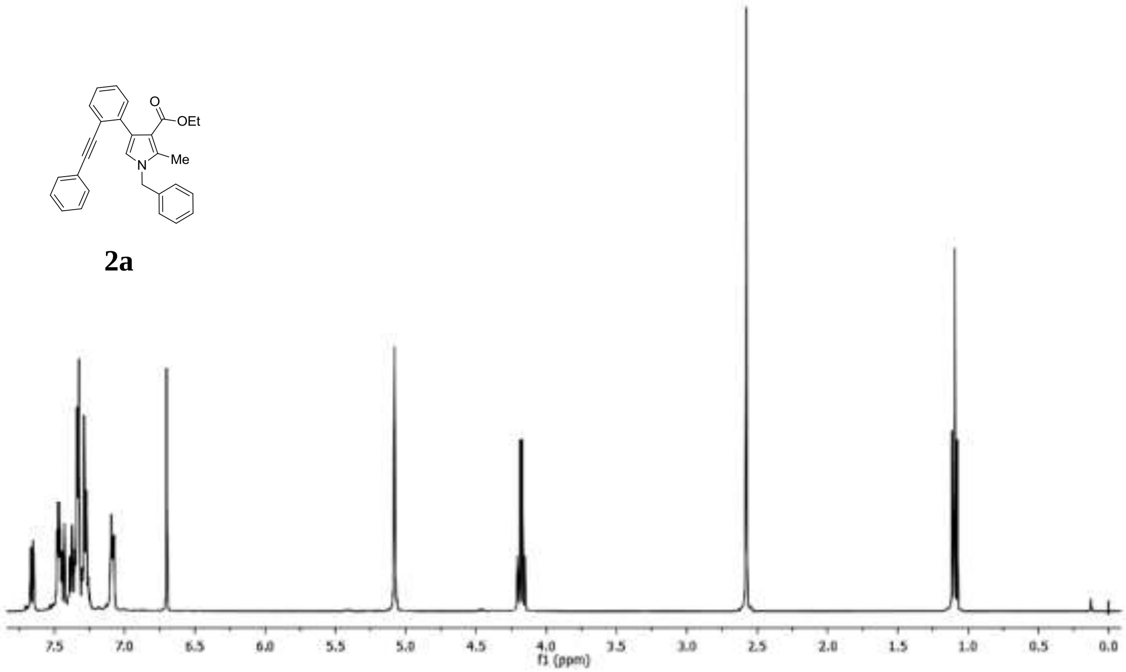


1'a

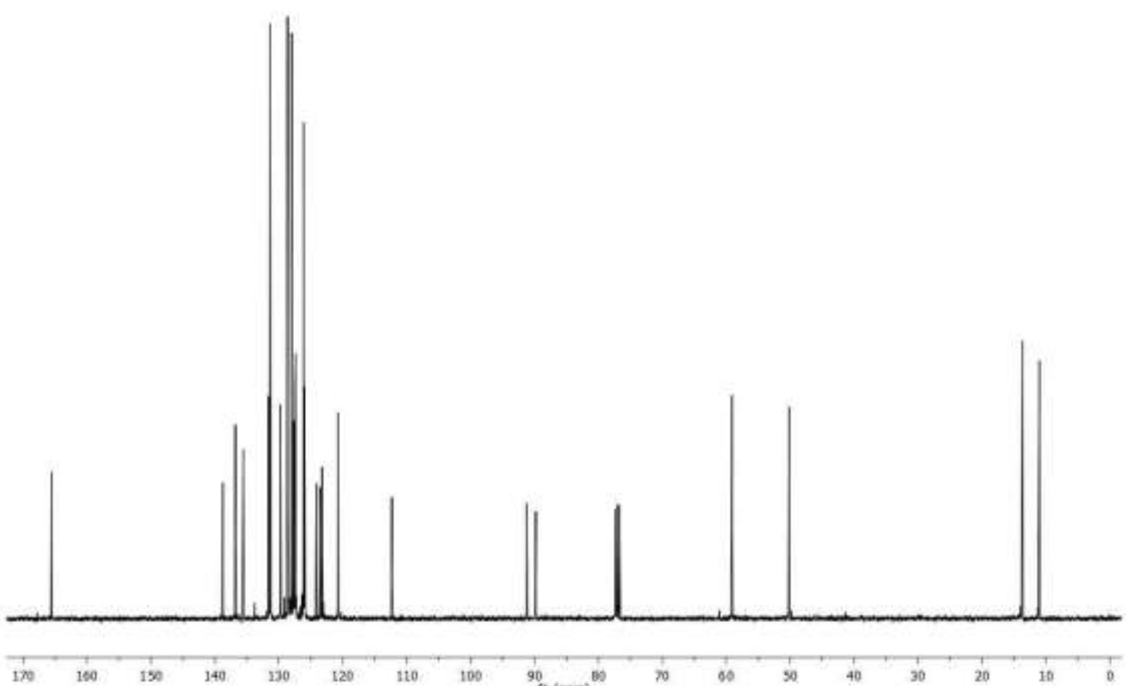




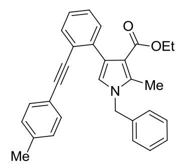
[1]H NMR (top) and [13]C NMR (bottom) spectra of Compound **1'a**.



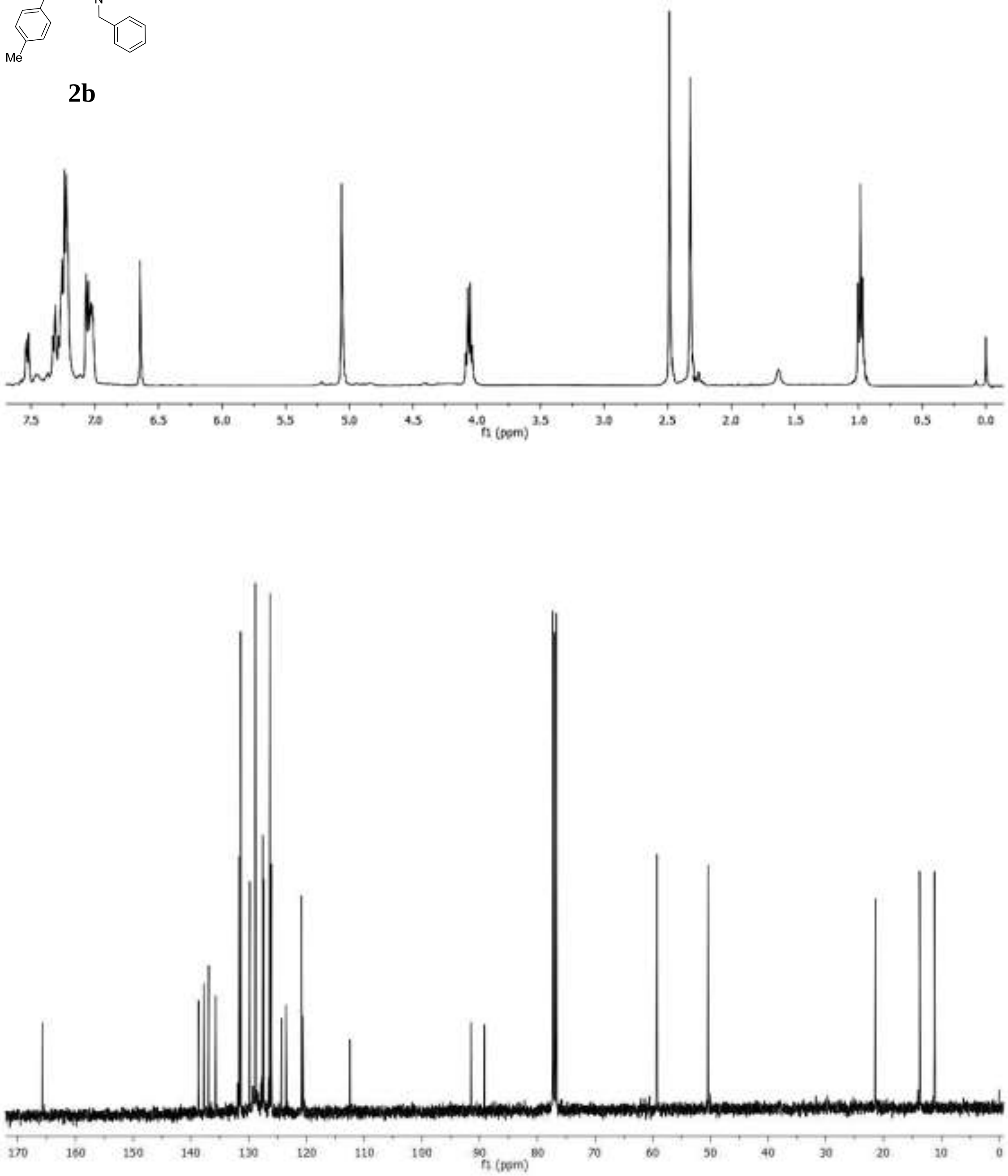
2a



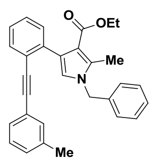
^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **2a**.



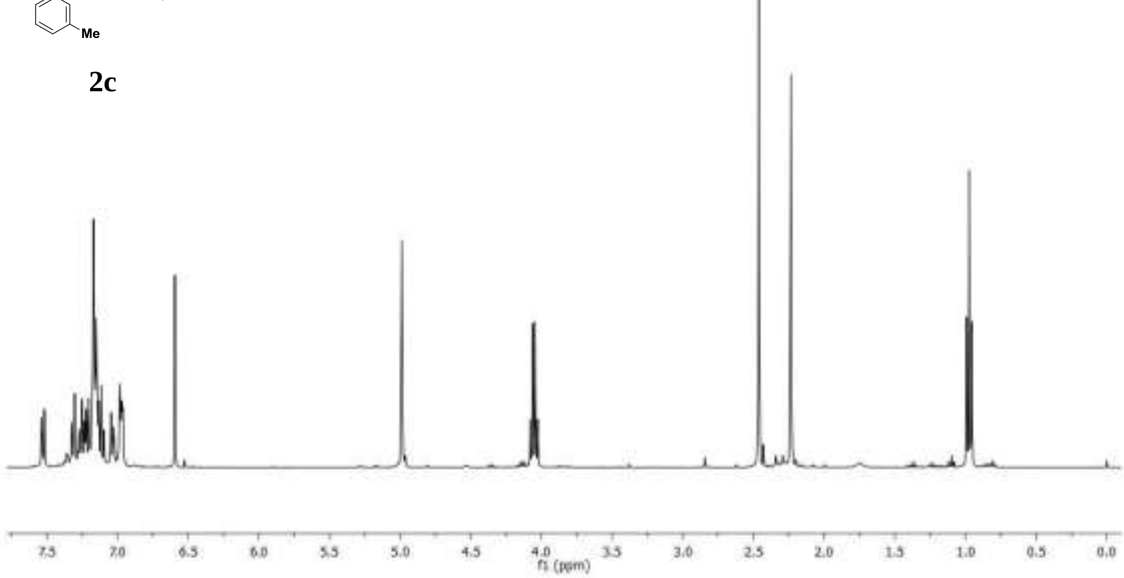
2b

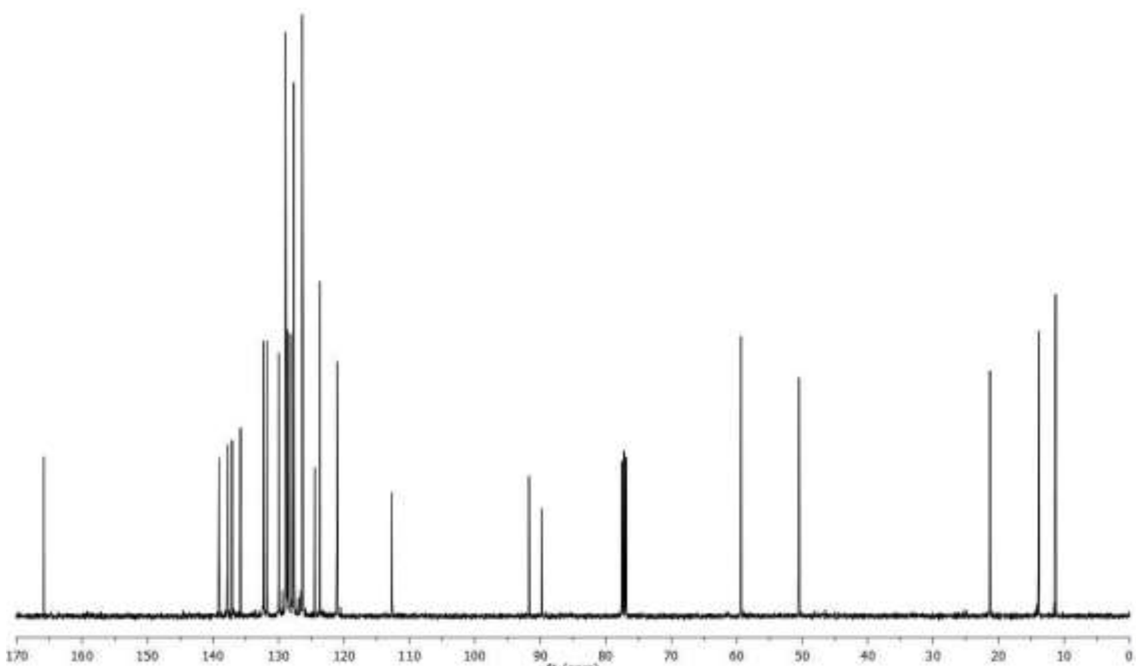


[1]H NMR (top) and [13]C NMR (bottom) spectra of Compound **2b**.

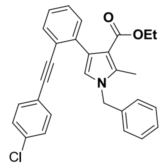


2c

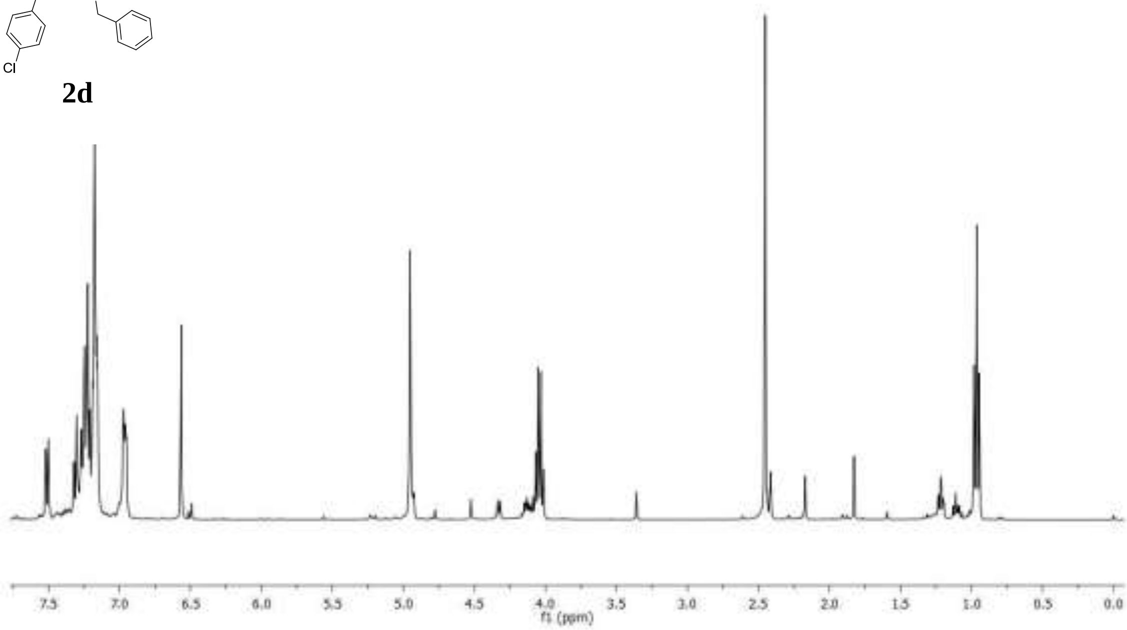


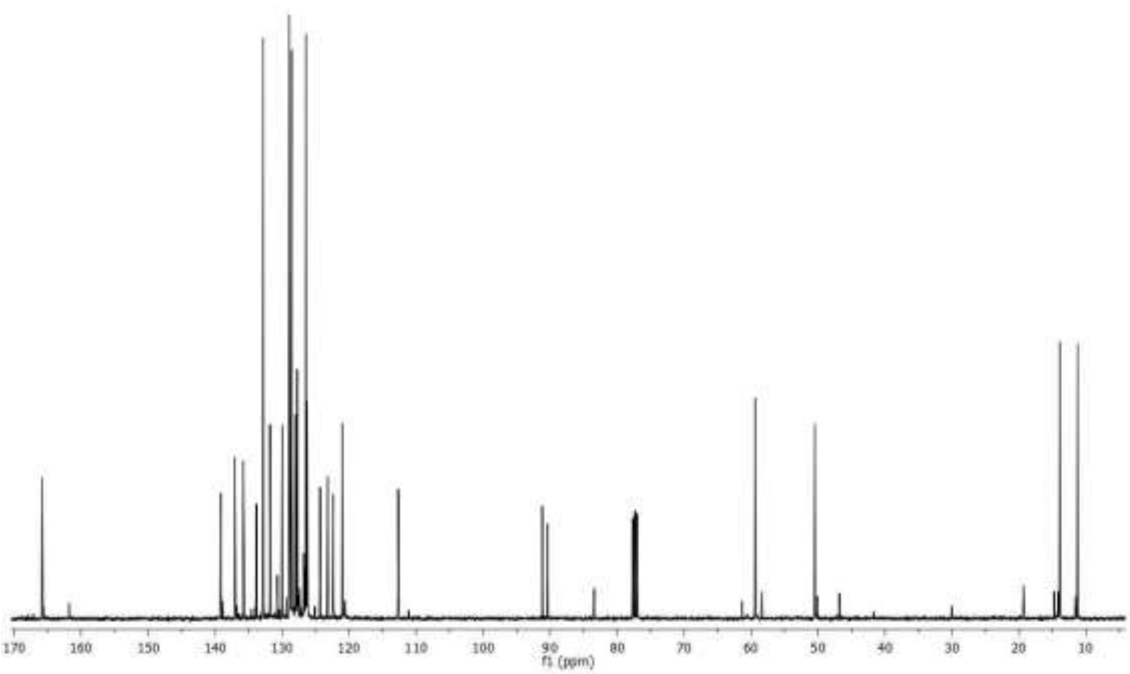


^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **2c**.

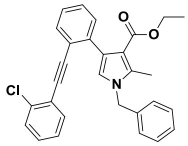


2d

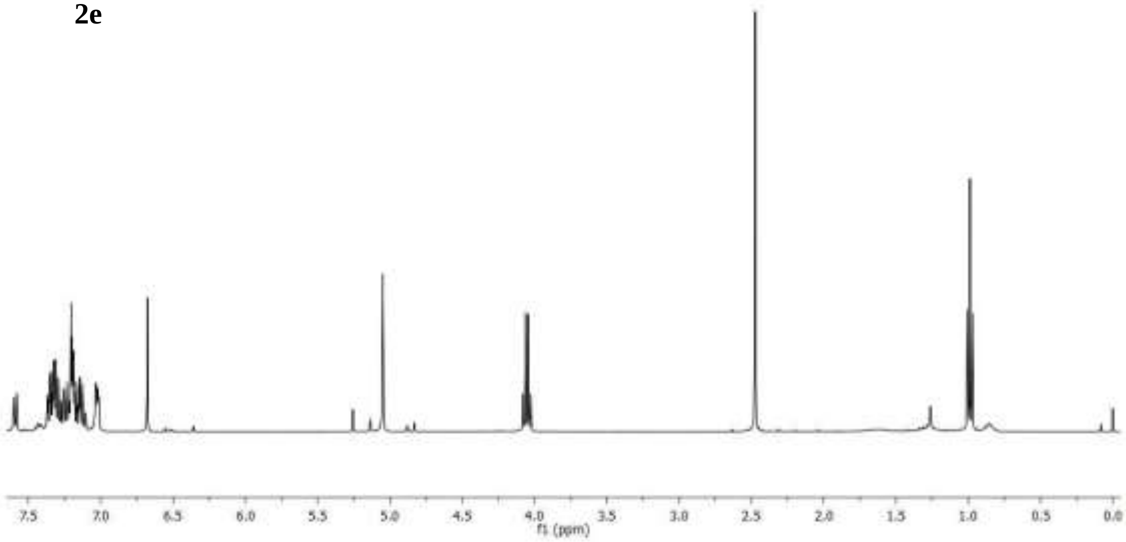


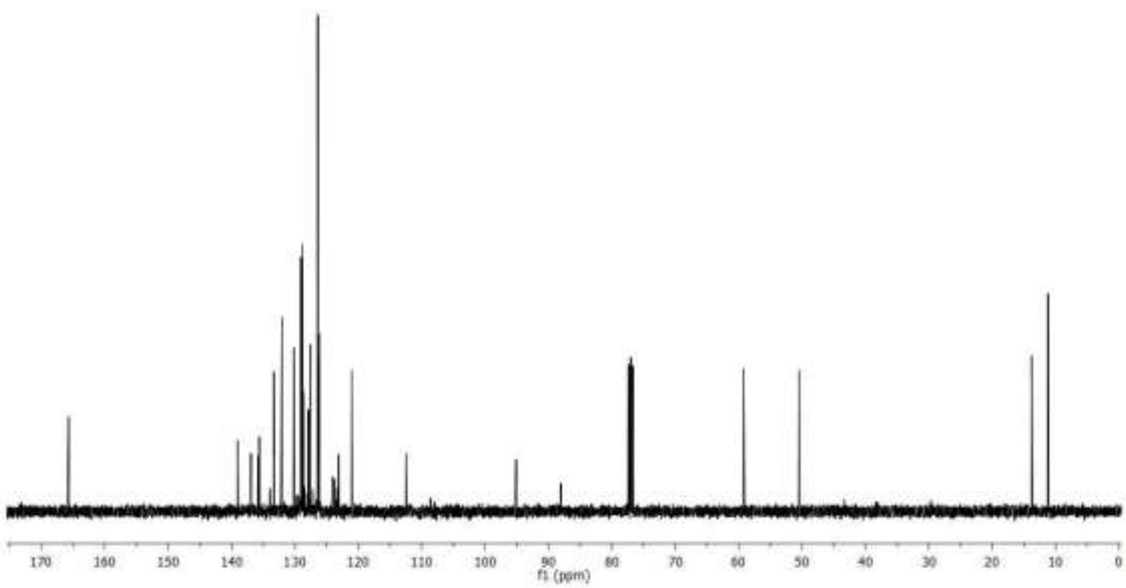


^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **2d**.

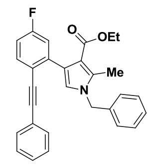


2e

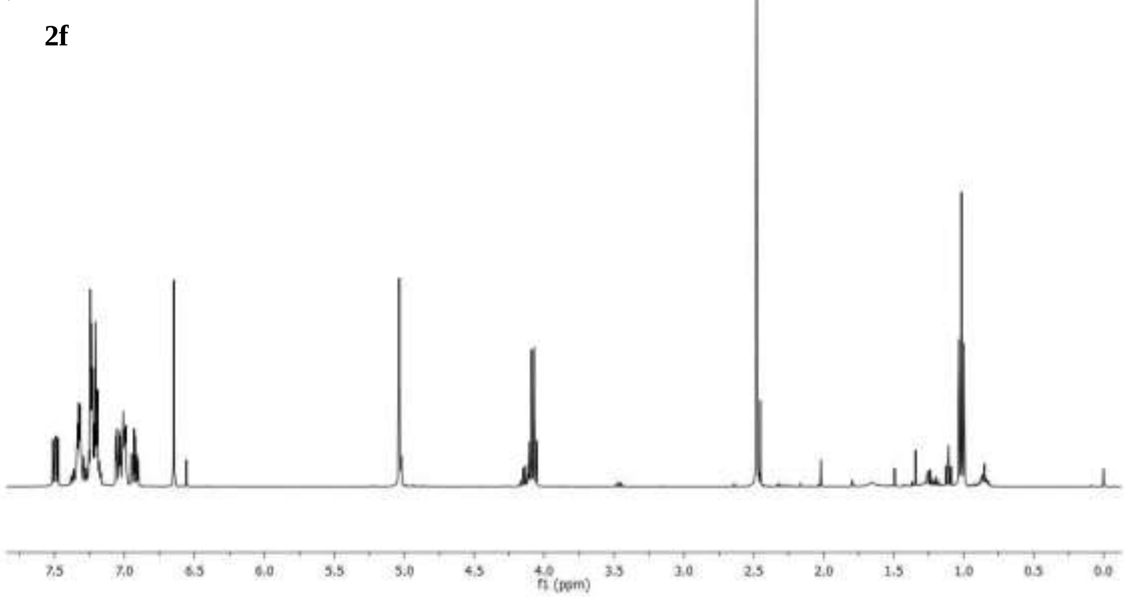


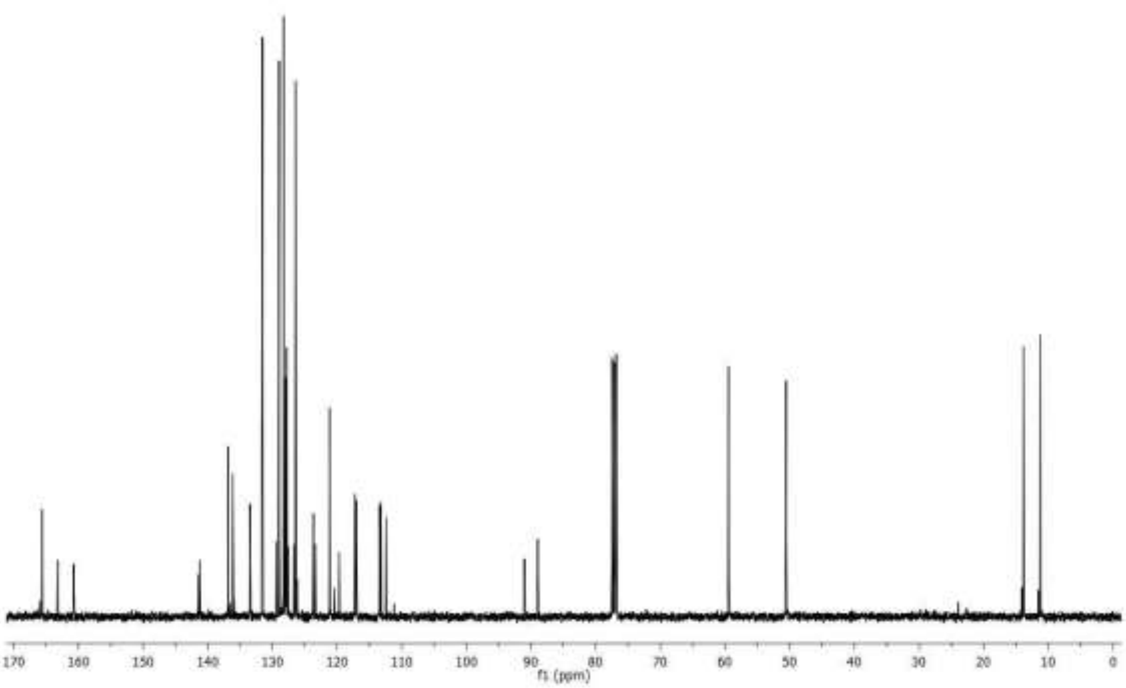


^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **2e**.

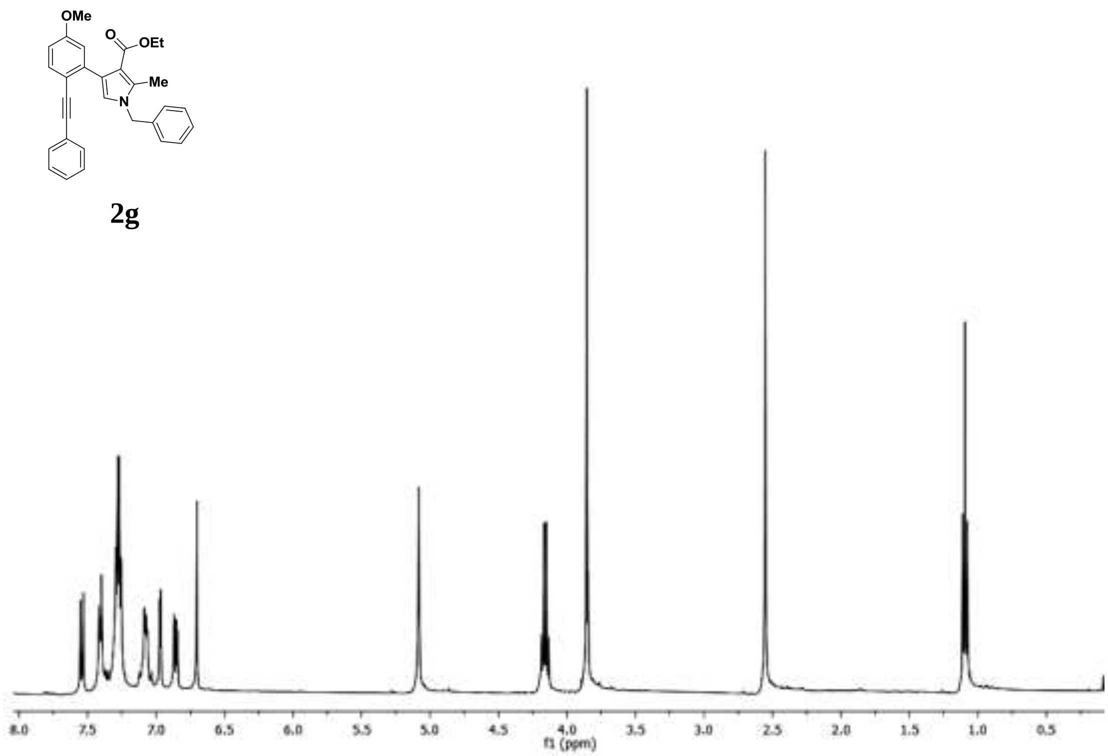


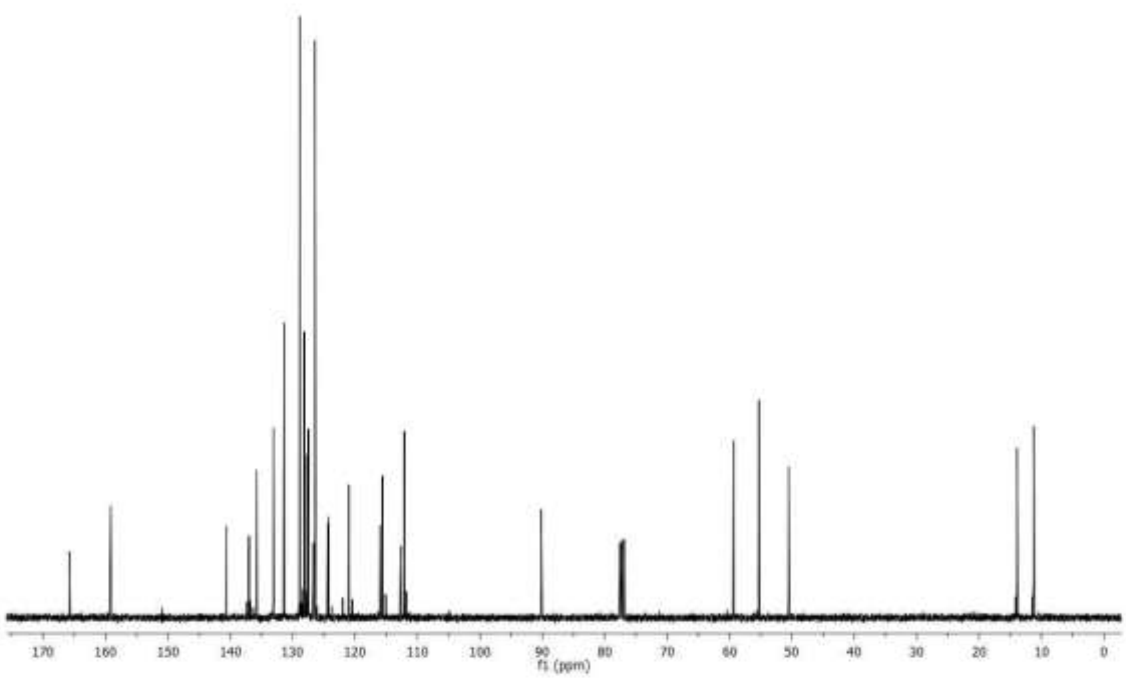
2f



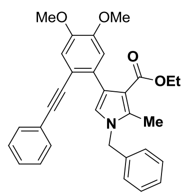


^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **2f**.

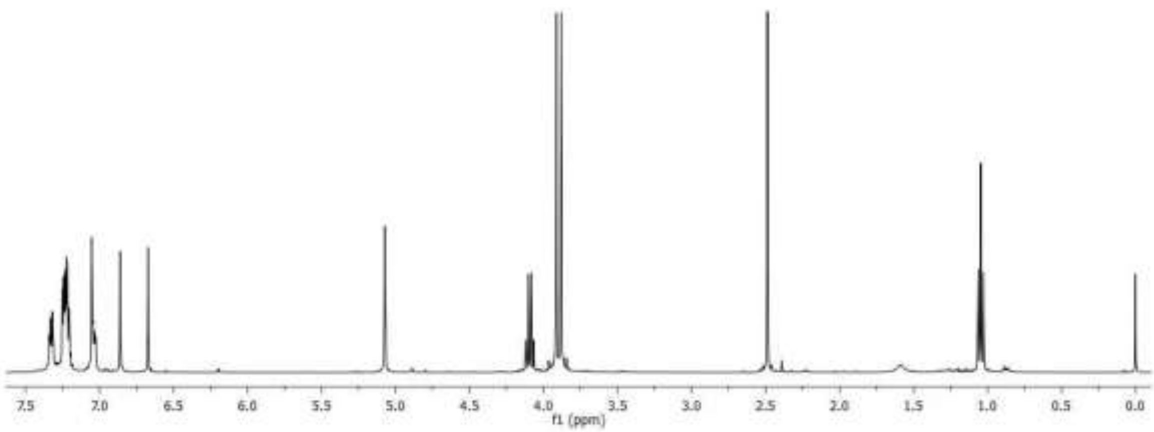


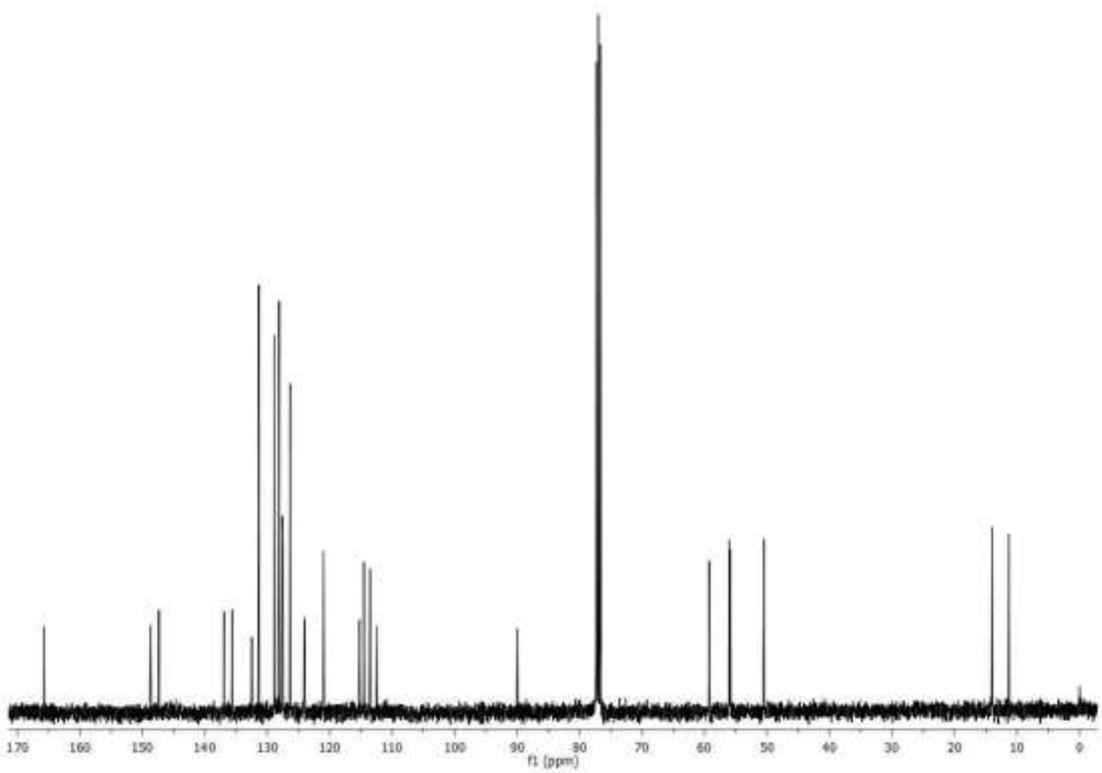


^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **2g**.

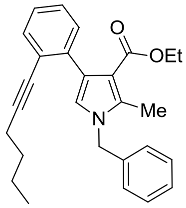


2h

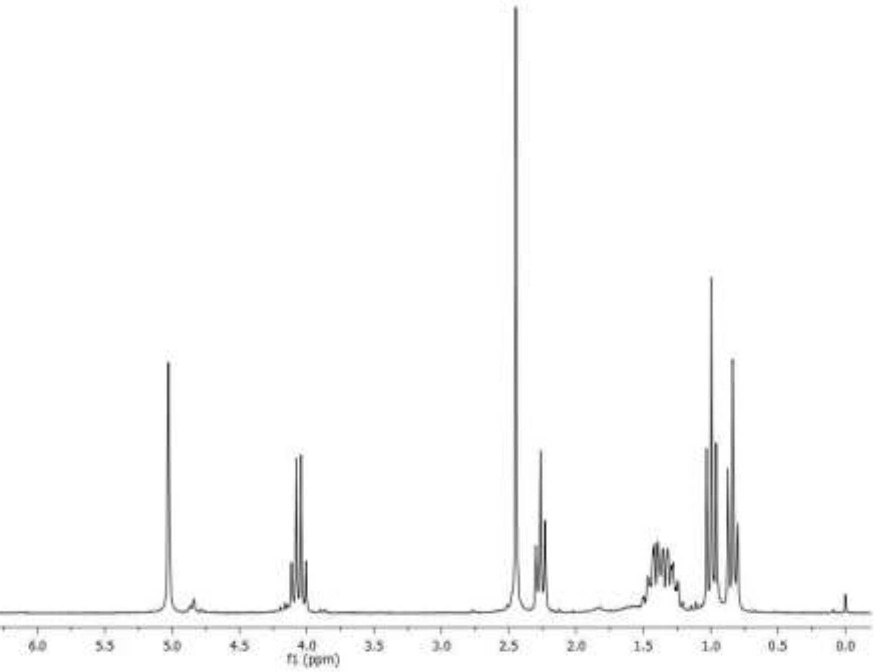


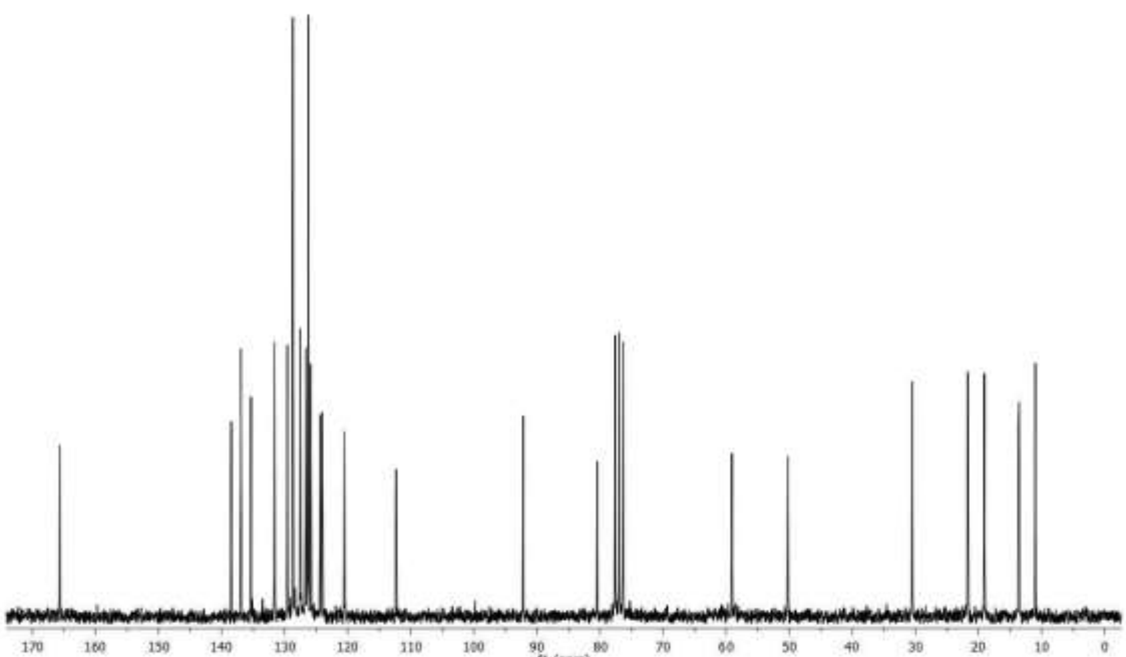


[1]H NMR (top) and [13]C NMR (bottom) spectra of Compound **2h**.

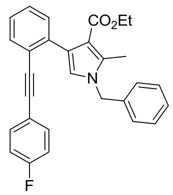


2i

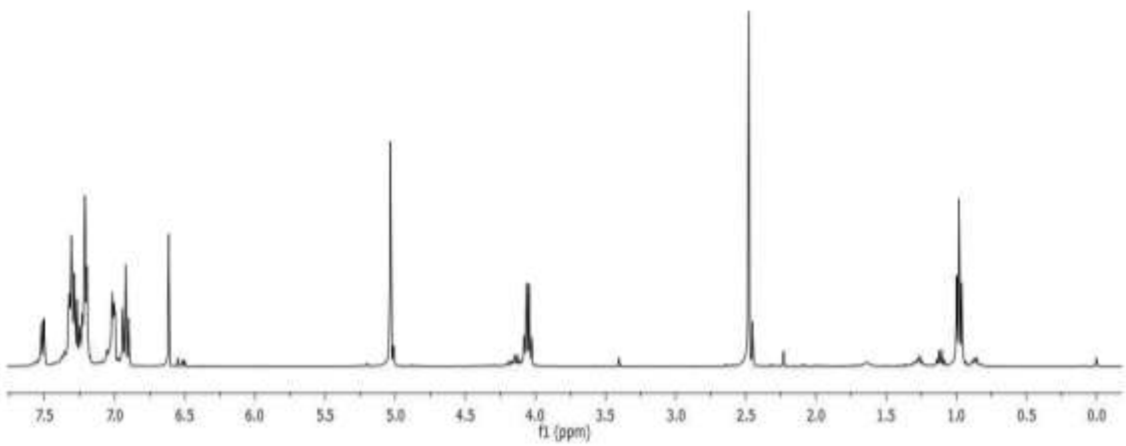


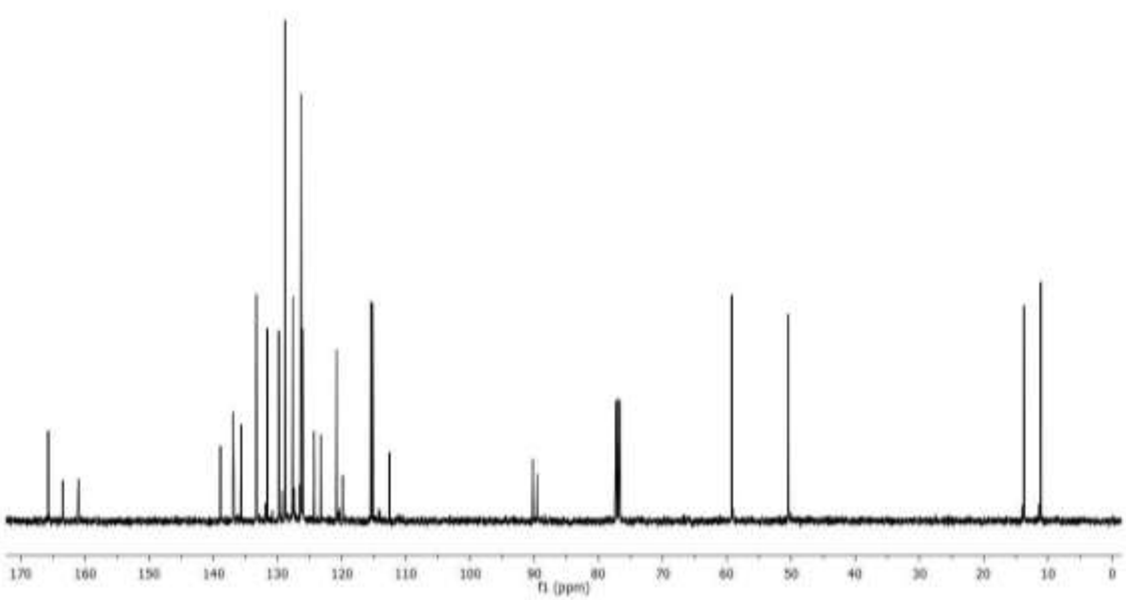


[1]H NMR (top) and [13]C NMR (bottom) spectra of Compound **2i**.

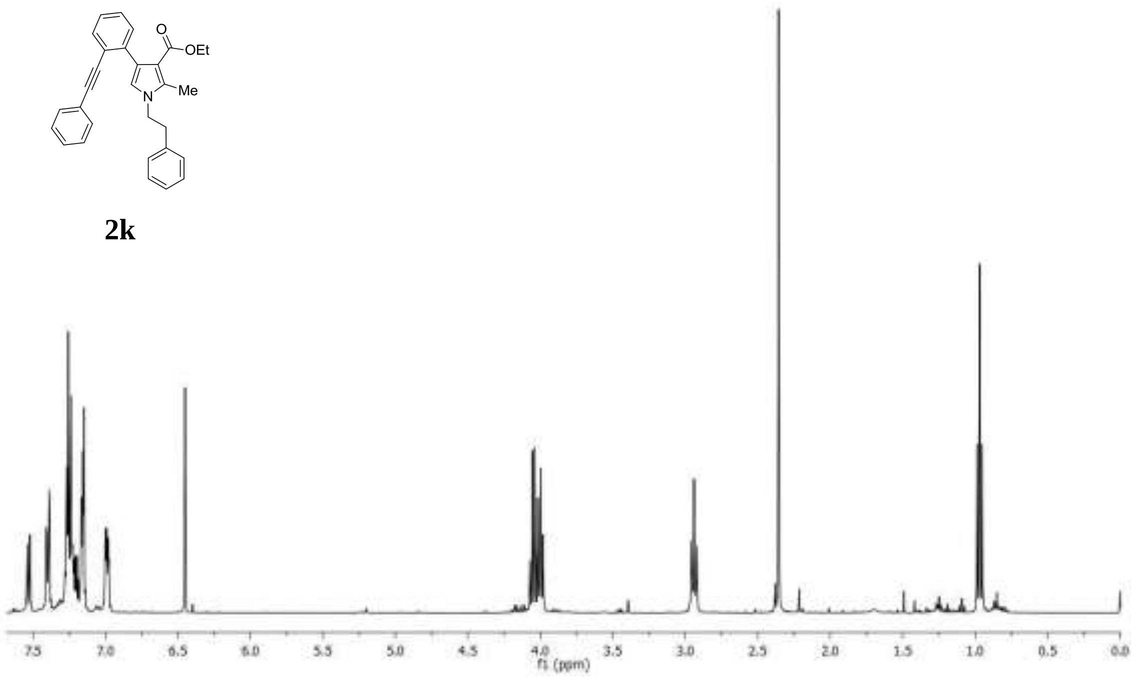


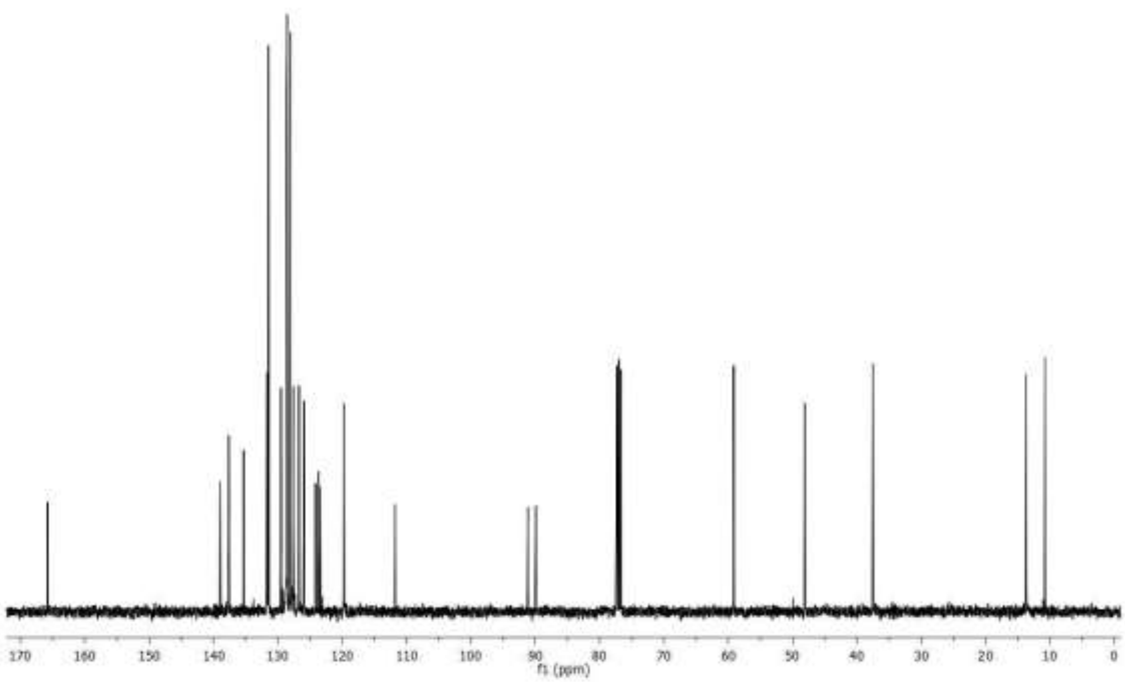
2j



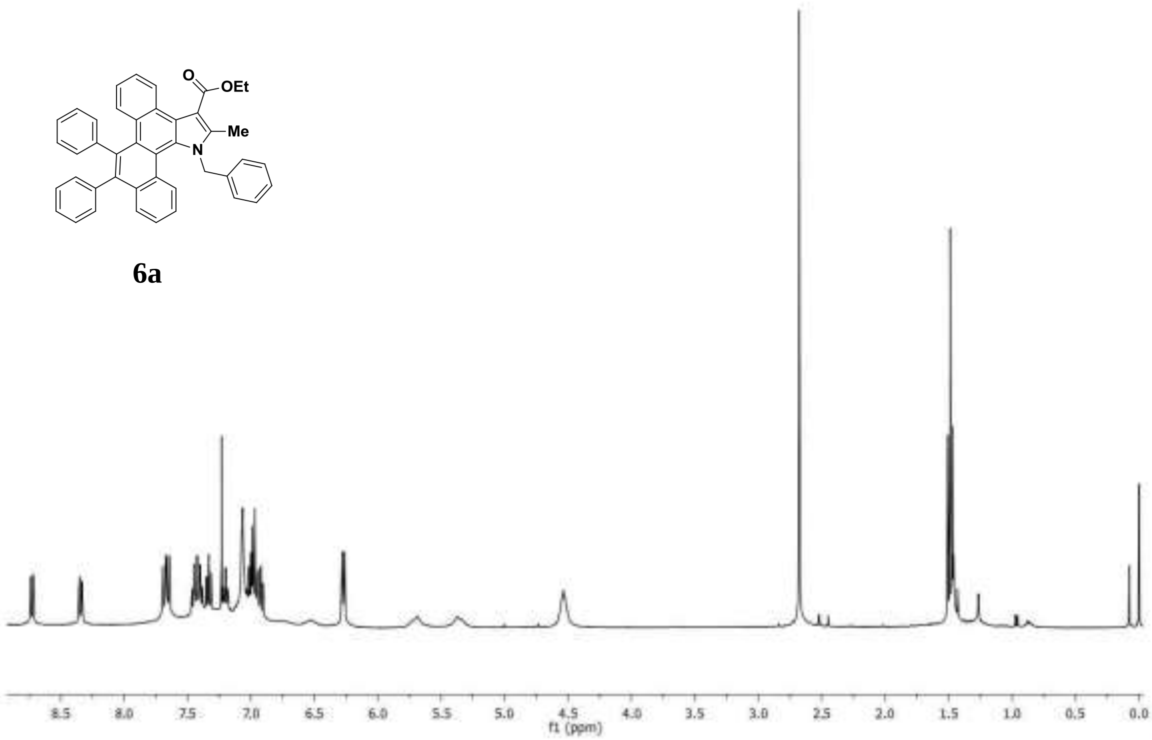


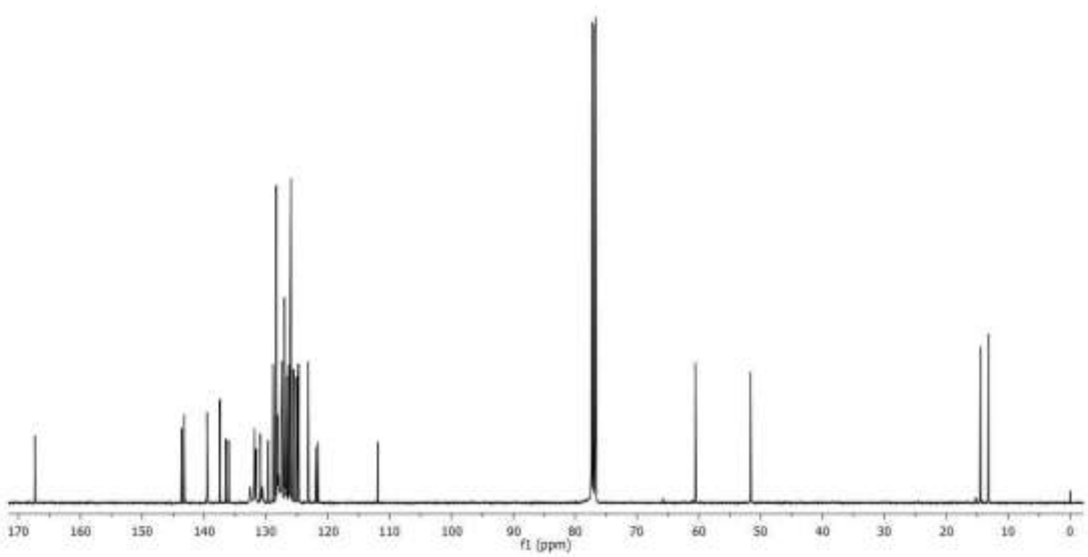
[1]H NMR (top) and [13]C NMR (bottom) spectra of Compound **2j**.





^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **2k**.





^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of Compound **6a**.

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