Electronic Supplementary Information

Macrocyclization via Remote *meta*-Selective C–H Olefination Using a Practical Indolyl Template

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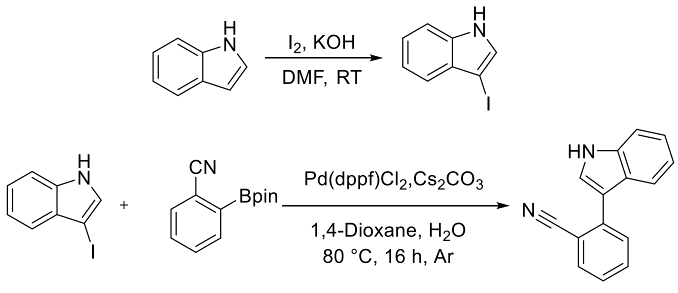
1 General Information

Unless otherwise noted, all solvents and chemicals were commercially available and used directly without further purification. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60 F254. Visualization was carried out with UV light. Preparative TLC was performed on 1.0 mm silica gel (Analtech). Columns for flash chromatography (FC) contained silica gel (32-63μ, Dynamic Adsorbents, Inc.). The melting points were measured with Tektronix X4 microscopic melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on Bruker AV 400 instrument (400 MHz). Chemical shifts were quoted in parts per million (ppm) referenced to 0.00 ppm for tetramethyl silane. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, m = multiplet, br = broad. Coupling constants, *J*, were reported in Hertz unit (Hz). ^{13}C NMR spectra were recorded on Bruker AV 400 instrument (100 MHz) and were fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet peak at 77.0 ppm of chloroform d and the center line of a septet peak at 40.0 ppm of d_6-DMSO. High resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight). For the *in situ* IR kinetic experiments, the reaction spectra were recorded using a React IR 15 from Mettler-Toledo AutoChem fitted with a Silicon-tipped probe.

2 Synthesis and Screening of Templates

2.1 Synthesis of Templates

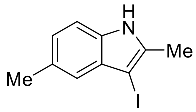


DT_1

General procedure. According to the previously described procedure,[1] 3-iodoindoles were generally prepared from the corresponding unsubstituted indoles: KOH (6.0 g, 106.9 mmol) was added to a solution of indole (5.0 g, 42.7 mmol) in DMF at room temperature. The resulted mixture was stirred for 15 mins and then a solution of I_2 (10.8 g, 42.7 mmol) dissolved in DMF (30 mL) was added by syringe. The reaction mixture was stirred at room temperature for another 4 h. After completion of reaction, the mixture was poured into the cooled (0 ^{o}C) *aq.* Na_2SO_3 (500 mL, 0.1%) to give an orange precipitate. After filtration and dry in air, light orange solid (9.5 g) was obtained in 91.6% yield.

Template **DT_1** was synthesized via an analogous Suzuki coupling reaction described by Russell and co-workers:[2] To a solution of *o*-CN-PhBpin (4.2 g, 18.3 mmol) in 1,4-dioxane (40 mL) was added the above crude 3-iodoindole (2.5 g, 10.3 mmol), Pd(dppf)Cl_2 (0.75 g, 1.0 mmol), and a solution of Cs_2CO_3 (8.4 g, 25.7 mmol) in H_2O (4 mL) at room temperature in turn. The reaction mixture was stirred at 80 ^{o}C for 16 h under argon. The solution was quenched with saturated NH_4Cl (*aq.*) (80 mL) and then diluted with ethyl acetate (100 mL). The organic layer was separated and the aqueous layer extracted with ethyl acetate repeatedly (2 x 60 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulted residue was purified by silica gel column chromatography (eluent: petroleum ether (60 ^{o}C–90^{o}C) /ethyl acetate= 20/1) to provide the **DT_1** (1.7 g, 75.7 %). In a similar manner, templates **DT_2**, **DT_3**, **DT_4**, and **DT_5** were successfully prepared from the starting 3-iodoindoles and ArBpin in good to excellent yields.

3-Iodoindole, 2-methyl-3-iodoindole, and 5-methyl-3-iodoindole are known compounds. The characteristic data for 2,5-dimethyl-3-iodoindole were listed as following:



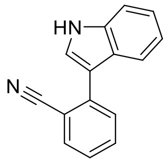
3-iodo-2,5-dimethyl-1*H*-indole

Yield: 92%. Light orange solid, R_f = 0.61 (petroleum ether (60 °C–90 °C)/ethyl acetate = 20 : 1, V/V). m.p.: 134 – 135 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.13 (s, 1H), 7.08 (d, *J* = 8.2 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 2.45 (s, 3H), 2.39 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 136.32, 134.11, 130.93, 129.90, 123.81, 119.92, 110.29, 58.47, 21.38, 14.36.

HR-MS (ESI) m/z calcd for $C_{10}H_{10}INNa^+$ [M+Na$^+$] 293.9750, found 293.9753.



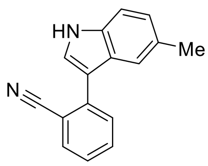
2-(1*H*-indol-3-yl)benzonitrile (DT$_1$)

Yield: 76%. White solid, R_f = 0.51 (petroleum ether (60 °C–90 °C)/ethyl acetate = 8 : 1, V/V). m.p.: 105 – 106 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.83 – 7.75 (m, 3H), 7.69 (d, *J* = 2.7 Hz, 1H), 7.66 (td, *J* = 7.7, 1.5 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.37 (td, *J* = 7.6, 1.3 Hz, 1H), 7.31 – 7.25 (m, 1H), 7.22 (td, *J* = 7.5, 7.0, 1.1 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 138.98, 136.25, 134.00, 132.74, 129.96, 126.22, 125.83, 124.43, 122.90, 120.81, 119.59, 119.25, 113.92, 111.68, 110.90.

HR-MS (ESI) m/z calcd for $C_{15}H_{10}N_2Na^+$ [M+Na$^+$] 241.0736, found 241.0732.



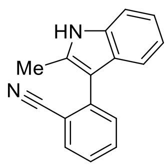
2-(5-methyl-1*H*-indol-3-yl)benzonitrile (DT$_2$)

Yield: 80%. Gray solid, R_f = 0.42 (petroleum ether (60 °C–90 °C)/ethyl acetate = 10 : 1, V/V). m.p.: 112 – 113 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.81 – 7.74 (m, 2H), 7.68 – 7.61 (m, 2H), 7.54 (s, 1H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 1H), 2.46 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 139.22, 134.60, 133.99, 132.73, 130.18, 129.97, 126.09, 126.07, 124.61, 124.49, 119.67, 118.81, 113.37, 111.37, 110.82, 21.65.

HR-MS (ESI) m/z calcd for $C_{16}H_{12}N_2Na^+$ [M+Na$^+$] 255.0893, found 255.0898.



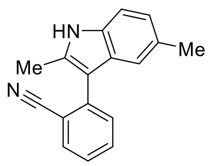
2-(2-methyl-1*H*-indol-3-yl)benzonitrile (DT$_3$)

Yield: 85%. White solid, R_f = 0.47 (petroleum ether (60 °C–90 °C)/ethyl acetate = 9 : 1, V/V). m.p.: 135 – 136 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.67 – 7.57 (m, 2H), 7.46 – 7.38 (m, 2H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.18 – 7.09 (m, 2H), 2.39 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 139.62, 135.27, 133.62, 133.43, 132.58, 131.81, 127.80, 126.74, 121.95, 120.25, 119.26, 118.31, 113.25, 111.38, 110.66, 12.96.

HR-MS (ESI) m/z calcd for $C_{16}H_{12}N_2Na^+$ [M+Na$^+$] 255.0893, found 255.0895.



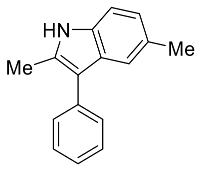
2-(2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (DT$_4$)

Yield: 82%. White solid, R_f = 0.44 (petroleum ether (60 °C–90 °C)/ethyl acetate = 8 : 1, V/V). m.p.: 158 – 159 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.76 (d, *J* = 7.8 Hz, 1H), 7.66 – 7.56 (m, 2H), 7.38 (td, *J* = 7.5, 1.4 Hz, 1H), 7.21 (s, 1H), 7.16 (d, *J* = 8.2 Hz, 1H), 6.97 (d, *J* = 8.2 Hz, 1H), 2.40 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 139.78, 133.69, 133.52, 133.32, 132.49, 131.77, 129.41, 127.96, 126.56, 123.34, 119.24, 117.89, 113.13, 110.84, 110.29, 21.51, 12.88.

HR-MS (ESI) m/z calcd for $C_{17}H_{14}N_2Na^+$ [M+Na$^+$] 269.1049, found 269.1046.



2,5-dimethyl-3-phenyl-1*H*-indole (DT_5)

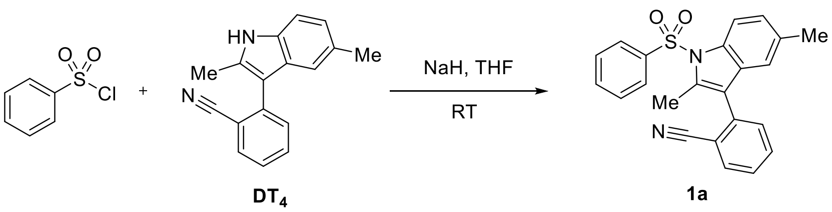
Yield: 70%. Red oil, R_f = 0.50 (petroleum ether (60 °C–90 °C)/ethyl acetate = 10 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.51 – 7.43 (m, 5H), 7.29 (td, *J* = 7.2, 1.6 Hz, 1H), 7.18 (d, *J* = 8.3 Hz, 1H), 6.98 (d, *J* = 8.0 Hz, 1H), 2.44 (s, 3H), 2.42 (s, 3H).

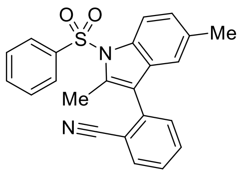
^{13}C NMR (100 MHz, $CDCl_3$) δ 135.64, 133.54, 131.58, 129.49, 129.25, 128.51, 128.11, 125.75, 123.03, 118.53, 114.12, 110.01, 21.59, 12.57.

HR-MS (ESI) m/z calcd for $C_{16}H_{15}NNa^+$ [M+Na^+] 244.1097, found 244.1095.

2.2 Synthesis of Substrates



General procedure.[3] To a solution of **DT_4** (200.00 mg, 0.81 mmol) in THF (15 mL) was added sodium hydride (dispersed in mineral oil, 60% wt, 97.6 mg, 2.44 mmol) under ice bath (0 °C). The resulted mixture was stirred for 15 mins and then benzenesulfonyl chloride (286.81 mg, 1.62 mmol) was added to the reaction mixture with stirring. After that, the mixture was gradually warmed up to room temperature and stirred overnight. After completion of reaction, the reaction was quenched with water (40 mL) and the mixture was then diluted with ethyl acetate (30 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 x 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulted residue was purified by silica gel column chromatography (eluent: petroleum ether (60 °C–90 °C) /ethyl acetate= 40/1) to give the **1a** (258 mg, 82.2%). In a similar manner, arylsulfonate substrates (**1b–1u**) were also prepared in good to excellent yields.



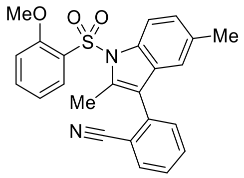
2-(2,5-dimethyl-1-(phenylsulfonyl)-1*H*-indol-3-yl)benzonitrile (1a)

Yield: 90%. White solid, R_f = 0.42 (hexane/ethyl acetate = 8 : 1, V/V). m.p.: 116 – 117 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.5 Hz, 1H), 7.83 – 7.77 (m, 3H), 7.69 (t, *J* = 7.7, 1H), 7.55 – 7.47 (m, 3H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.12 (d, *J* = 7.7 Hz, 1H), 6.96 (s, 1H), 2.57 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 138.72, 137.12, 135.46, 134.43, 133.73, 133.65, 133.33, 132.70, 131.58, 129.64, 129.36, 128.17, 126.40, 126.11, 119.48, 118.67, 117.94, 114.42, 114.19, 21.25, 14.26.

HR-MS (ESI) m/z calcd for $C_{23}H_{18}N_2NaO_2S^+$ [M+Na^+] 409.0981, found 409.0978.



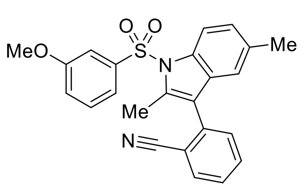
2-(1-((2-methoxyphenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (1b)

Yield: 82%. Yellow solid, R_f = 0.25 (hexane/ethyl acetate = 8 : 1, V/V). m.p.: 146 – 147 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.85 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.69 (td, *J* = 7.7, 1.4 Hz, 1H), 7.55 – 7.46 (m, 3H), 7.10 – 7.04 (m, 2H), 6.96 (s, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 3.56 (s, 3H), 2.46 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.64, 137.73, 136.25, 135.84, 134.75, 133.36, 132.74, 132.67, 131.92, 130.39, 128.91, 127.96, 126.93, 125.42, 120.08, 118.39, 118.03, 117.34, 114.25, 114.14, 112.68, 56.08, 21.25, 13.49.

HR-MS (ESI) m/z calcd for $C_{24}H_{20}N_2NaO_3S^+$ [M+Na^+] 439.1087, found 439.1083.



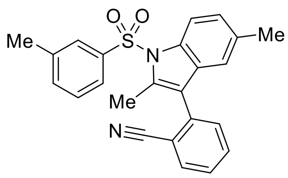
2-(1-((3-methoxyphenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (1c)

Yield: 91%. Yellow oil, R_f = 0.55 (hexane/ethyl acetate = 10 : 1, V/V).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.07 (d, *J* = 8.5 Hz, 1H), 7.78 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.68 (td, *J* = 7.7, 1.4 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.38 – 7.29 (m, 3H), 7.12 (d, *J* = 8.6 Hz, 1H), 7.05 – 7.00 (m, 1H), 6.98 (s, 1H), 3.76 (s, 3H), 2.57 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 159.92, 139.81, 137.11, 135.44, 134.42, 133.66, 133.36, 132.75, 131.65, 130.51, 129.64, 128.21, 126.10, 120.28, 119.38, 118.75, 118.57, 117.96, 114.40, 114.15, 111.03, 55.67, 21.28, 14.29.

HR-MS (ESI) m/z calcd for $C_{24}H_{20}N_2NaO_3S^+$ [M+Na$^+$] 439.1087, found 439.1084.



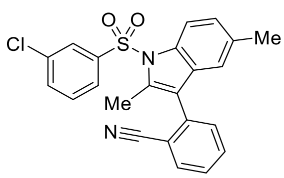
2-(2,5-dimethyl-1-(m-tolylsulfonyl)-1*H*-indol-3-yl)benzonitrile (1d)

Yield: 90%. White solid, R_f = 0.61 (hexane/ethyl acetate =10 : 1, V/V). m.p.: 124 – 125 °C.

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.05 (d, *J* = 8.5 Hz, 1H), 7.79 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.69 (td, *J* = 7.7, 1.4 Hz, 1H), 7.61 (s, 2H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.33 – 7.29 (m, 2H), 7.12 (d, *J* = 8.5 Hz, 1H), 6.98 (s, 1H), 2.58 (s, 3H), 2.35 (s, 3H), 2.34 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 139.83, 138.65, 137.20, 135.49, 134.64, 134.40, 133.53, 133.32, 132.69, 131.60, 129.57, 129.15, 128.13, 126.59, 126.03, 123.63, 119.27, 118.62, 117.96, 114.38, 114.22, 21.29, 21.24, 14.28.

HR-MS (ESI) m/z calcd for $C_{24}H_{20}N_2NaO_2S^+$ [M+Na$^+$] 423.1138, found 423.1134.



2-(1-((3-chlorophenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (1e)

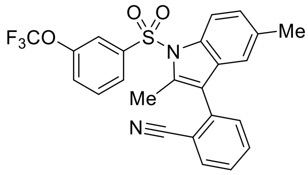
Yield: 79%. Yellow solid, R_f = 0.32 (hexane/ethyl acetate = 10 : 1, V/V). m.p.: 132 – 133 °C.

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.03 (d, *J* = 8.5 Hz, 1H), 7.86 (t, *J* = 2.0 Hz, 1H), 7.82 – 7.78 (m, 1H), 7.70 (t, *J* = 7.0 Hz, 1H), 7.62 (d, *J* = 6.6 Hz, 1H), 7.50 (q, *J* = 9.0, 8.0 Hz, 3H), 7.36 (t, *J* = 8.0

Hz, 1H), 7.14 (d, J = 8.6 Hz, 1H), 6.98 (s, 1H), 2.57 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.12, 136.86, 135.37, 135.29, 134.24, 133.99, 133.94, 133.32, 132.75, 131.50, 130.85, 129.71, 128.29, 126.50, 126.36, 124.51, 119.97, 118.84, 117.93, 114.34, 114.15, 21.25, 14.35.

HR-MS (ESI) m/z calcd for $C_{23}H_{17}ClN_2NaO_2S^+$ [M+Na$^+$] 443.0591, found 443.0593.



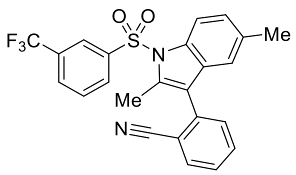
2-(2,5-dimethyl-1-((3-(trifluoromethoxy)phenyl)sulfonyl)-1*H*-indol-3-yl)benzonitrile (1f)

Yield: 80%. Yellow solid, R_f = 0.19 (hexane/ethyl acetate = 6 : 1, V/V). m.p.: 79 – 80 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.5 Hz, 1H), 7.80 (d, J = 7.9 Hz, 1H), 7.74 (s, 1H), 7.71 (td, J = 7.7, 1.4 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.55 – 7.44 (m, 3H), 7.36 (d, J = 7.1 Hz, 1H), 7.15 (d, J = 8.5 Hz, 1H), 6.97 (s, 1H), 2.56 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.13, 140.35, 136.87, 135.32, 134.33, 134.14, 133.34, 132.76, 131.49, 131.37, 129.83, 128.34, 126.43, 126.00, 124.59, 121.50, 120.28, 119.22, 118.89, 117.87, 114.42, 114.23, 21.24, 14.29.

HR-MS (ESI) m/z calcd for $C_{24}H_{17}F_3N_2NaO_3S^+$ [M+Na$^+$] 493.0804, found 493.0801.



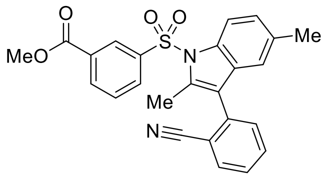
2-(2,5-dimethyl-1-((3-(trifluoromethyl)phenyl)sulfonyl)-1*H*-indol-3-yl)benzonitrile (1g)

Yield: 85%. Yellow oil, R_f = 0.49 (hexane/ethyl acetate = 10 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 8.04 (d, J = 8.5 Hz, 1H), 7.86 (d, J = 8.2 Hz, 1H), 7.82 – 7.75 (m, 2H), 7.71 (td, J = 7.7, 1.4 Hz, 1H), 7.57 (t, J = 7.9 Hz, 1H), 7.54 – 7.48 (m, 2H), 7.15 (d, J = 8.6 Hz, 1H), 6.97 (s, 1H), 2.58 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 139.61, 136.80, 135.30, 134.24 (d, J_{C-F}= 5.3 Hz), 133.32, 132.80, 131.76 (d, J_{C-F}= 33.4 Hz), 131.46, 130.55, 130.42 (q, J_{C-F}= 3.6 Hz), 129.83, 129.56, 128.38, 126.48, 124.30, 123.65 (q, J_{C-F}= 4.0 Hz), 121.59, 120.36, 118.93, 117.90, 114.38, 114.20, 21.25, 14.38.

HR-MS (ESI) m/z calcd for $C_{24}H_{17}F_3N_2NaO_2S^+$ [M+Na$^+$] 477.0855, found 477.0858.



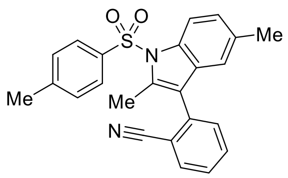
Methyl 3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)benzoate (1h)

Yield: 82%. Yellow oil, R_f = 0.25 (hexane/ethyl acetate = 10 : 1, V/V).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.55 (s, 1H), 8.18 (d, *J* = 6.3 Hz, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 6.5 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.53 – 7.47 (m, 3H), 7.14 (d, *J* = 8.5 Hz, 1H), 6.96 (s, 1H), 3.93 (s, 3H), 2.58 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 165.15, 139.22, 136.94, 135.36, 134.56, 134.29, 133.95, 133.34, 132.74, 131.54, 131.44, 130.25, 129.94, 129.75, 128.28, 127.68, 126.34, 119.97, 118.83, 117.88, 114.44, 114.20, 52.65, 21.25, 14.37.

HR-MS (ESI) m/z calcd for $C_{25}H_{20}N_2NaO_4S^+$ [M+Na$^+$] 467.1036, found 467.1039.



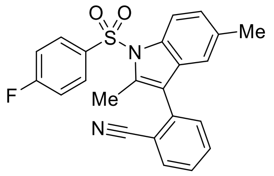
2-(2,5-dimethyl-1-tosyl-1*H*-indol-3-yl)benzonitrile (1i)

Yield: 94%. Yellow oil, R_f = 0.46 (hexane/ethyl acetate = 10 : 1, V/V).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.05 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.72 – 7.65 (m, 3H), 7.52 – 7.46 (m, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.5 Hz, 1H), 6.97 (s, 1H), 2.58 (s, 3H), 2.34 (s, 3H), 2.31 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 144.82, 137.22, 135.84, 135.52, 134.41, 133.53, 133.36, 132.74, 131.64, 129.98, 129.64, 128.17, 126.51, 126.03, 119.31, 118.66, 118.04, 114.45, 114.19, 21.57, 21.28, 14.33.

HR-MS (ESI) m/z calcd for $C_{24}H_{20}N_2NaO_2S^+$ [M+Na$^+$] 423.1138, found 423.1139.



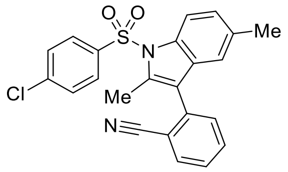
2-(1-((4-fluorophenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (1j)

Yield: 68%. Yellow solid, R_f = 0.26 (hexane/ethyl acetate = 10 : 1, V/V). m.p.: 134 – 135 °C.

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.03 (d, *J* = 8.5 Hz, 1H), 7.85 – 7.79 (m, 3H), 7.70 (t, *J* = 7.6 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 2H), 7.10 (q, *J* = 8.4 Hz, 3H), 6.97 (s, 1H), 2.58 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 165.62 (d, J_{C-F}= 255.1 Hz), 136.99, 135.44, 134.53 (d, J_{C-F} = 3.1 Hz), 134.35, 133.93, 133.35, 132.79, 131.52, 129.81, 129.35 (d, J_{C-F}= 9.7 Hz), 128.30, 126.27, 119.98, 118.81, 118.03, 116.87, 116.64, 114.44, 114.19, 21.27, 14.41.

HR-MS (ESI) m/z calcd for $C_{23}H_{17}FN_2NaO_2S^+$ [M+Na$^+$] 427.0887, found 427.0890.



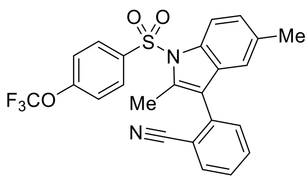
2-(1-((4-chlorophenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (1k)

Yield: 66%. Yellow solid, R_f = 0.54 (hexane/ethyl acetate = 8 : 1, V/V). m.p.: 118 – 119 °C.

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.01 (d, *J* = 8.5 Hz, 1H), 7.80 (d, *J* = 6.7 Hz, 1H), 7.75 – 7.67 (m, 3H), 7.51 (t, *J* = 7.9 Hz, 2H), 7.39 (d, *J* = 8.7 Hz, 2H), 7.12 (d, *J* = 8.5 Hz, 1H), 6.97 (s, 1H), 2.57 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 140.39, 136.94, 136.89, 135.45, 134.31, 134.01, 133.36, 132.81, 131.52, 129.82, 129.73, 128.33, 127.91, 126.32, 120.09, 118.86, 118.05, 114.42, 114.19, 21.28, 14.43.

HR-MS (ESI) m/z calcd for $C_{23}H_{17}ClN_2NaO_2S^+$ [M+Na$^+$] 443.0591, found 443.0590.



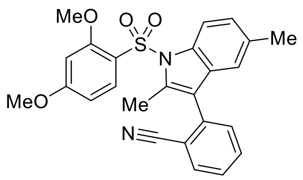
2-(2,5-dimethyl-1-((4-(trifluoromethoxy)phenyl)sulfonyl)-1*H*-indol-3-yl)benzonitrile (1l)

Yield: 76%. Yellow oil, R_f = 0.69 (petroleum ether (60 ºC–90 ºC)/ethyl acetate = 10 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.5 Hz, 1H), 7.88 – 7.83 (m, 2H), 7.81 (dd, J = 8.1, 1.4 Hz, 1H), 7.71 (td, J = 7.7, 1.4 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.26 – 7.22 (m, 2H), 7.14 (d, J = 8.6 Hz, 1H), 6.99 (s, 1H), 2.58 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 152.82 (d, $J_{C\text{-}F}$ = 2.0 Hz), 136.89, 136.65, 135.41, 134.33, 134.05, 133.32, 132.78, 131.48, 129.82, 128.70, 128.33, 126.36, 121.39, 121.01, 120.15, 118.87, 118.00, 114.41, 114.21, 21.25, 14.41.

HR-MS (ESI) m/z calcd for $C_{24}H_{17}F_3N_2NaO_3S^+$ [M+Na$^+$] 493.0804, found 493.0801.



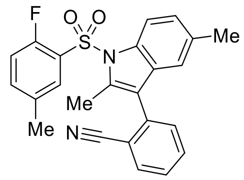
2-(1-((2,4-dimethoxyphenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (1m)

Yield: 84%. Orange oil, R_f = 0.21 (hexane/ethyl acetate = 3 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.9 Hz, 1H), 7.83 (d, J = 8.5 Hz, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.68 (t, J = 7.7 Hz, 1H), 7.48 (t, J = 8.7 Hz, 2H), 7.05 (d, J = 10.3 Hz, 1H), 6.95 (s, 1H), 6.55 (d, J = 8.9 Hz, 1H), 6.34 (s, 1H), 3.81 (s, 3H), 3.54 (s, 3H), 2.47 (s, 3H), 2.34 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.77, 159.28, 137.87, 136.35, 134.60, 133.35, 132.70, 132.48, 132.26, 131.96, 128.92, 127.89, 125.26, 119.22, 118.33, 118.09, 117.03, 114.20, 114.15, 104.65, 99.30, 56.08, 55.72, 21.24, 13.49.

HR-MS (ESI) m/z calcd for $C_{25}H_{22}N_2NaO_4S^+$ [M+Na$^+$] 469.1192, found 469.1194.



2-(1-((2-fluoro-5-methylphenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (1n)

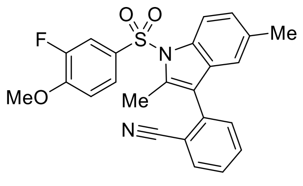
Yield: 83%. Yellow solid, R_f = 0.35 (hexane/ethyl acetate = 6 : 1, V/V). m.p.: 137 – 138 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.6 Hz, 1H), 7.81 (d, J = 7.6 Hz, 1H), 7.70 (t, J = 8.0 Hz, 2H), 7.55 – 7.48 (m, 2H), 7.35 – 7.30 (m, 1H), 7.10 (d, J = 8.5 Hz, 1H), 7.04 – 6.96 (m, 2H), 2.53

(s, 3H), 2.37 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 157.58 (d, J_{C-F}= 282.4 Hz), 137.23, 136.69 (d, J_{C-F}= 8.1 Hz), 136.02, 134.60 (d, J_{C-F}= 4.2 Hz), 134.03, 133.44 (d, J_{C-F}= 3.2 Hz), 132.71, 131.79, 129.61, 129.31, 128.15, 126.45 (d, J_{C-F}= 13.9 Hz), 125.84, 118.72, 118.53, 117.82, 117.51, 117.30, 114.18 (d, J_{C-F}= 2.3 Hz), 106.77, 21.27, 20.67, 13.87.

HR-MS (ESI) m/z calcd for $C_{24}H_{19}FN_2NaO_2S^+$ [M+Na$^+$] 441.1043, found 441.1047.



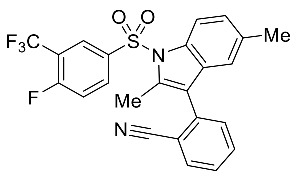
2-(1-((3-fluoro-4-methoxyphenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (1o)

Yield: 72%. Yellow oil, R_f = 0.22 (hexane/ethyl acetate = 5 : 1, V/V).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.03 (d, J = 8.5 Hz, 1H), 7.80 (d, J = 7.9 Hz, 1H), 7.70 (td, J = 7.7, 1.3 Hz, 1H), 7.59 – 7.53 (m, 2H), 7.54 – 7.48 (m, 2H), 7.13 (d, J = 8.6 Hz, 1H), 6.97 (s, 1H), 6.94 (t, J = 8.4 Hz, 1H), 3.86 (s, 3H), 2.57 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 152.28 (d, J_{C-F}= 10.4 Hz), 151.42 (d, J_{C-F}= 250.9 Hz), 137.05, 135.39, 134.29, 133.82, 133.35 (d, J_{C-F}= 17.0 Hz), 132.78 (d, J_{C-F}= 14.4 Hz), 131.56 (d, J_{C-F}= 13.9 Hz), 130.26 (d, J_{C-F}= 5.6 Hz), 129.74, 128.24 (d, J_{C-F}= 18.0 Hz), 126.23 (d, J_{C-F}= 5.5 Hz), 123.96 (d, J_{C-F}= 16.0 Hz), 119.75, 118.76, 118.05, 114.76 (t, J_{C-F}= 19.5 Hz), 114.42 (d, J_{C-F}= 14.0 Hz), 114.15, 113.24 (d, J_{C-F}= 2.6 Hz), 56.39 (d, J_{C-F}= 2.5 Hz), 21.28, 14.40 (d, J_{C-F}= 6.8 Hz).

HR-MS (ESI) m/z calcd for $C_{24}H_{19}FN_2NaO_3S^+$ [M+Na$^+$] 457.0993, found 457.0990.



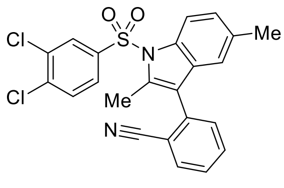
2-(1-((4-fluoro-3-(trifluoromethyl)phenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (1p)

Yield: 62%. Yellow solid, R_f = 0.38 (hexane/ethyl acetate = 8 : 1, V/V). m.p.: 151 – 152 °C.

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.17 (d, J = 6.4 Hz, 1H), 8.02 (d, J = 8.5 Hz, 1H), 7.92 – 7.86 (m, 1H), 7.81 (d, J = 7.8 Hz, 1H), 7.72 (td, J = 7.7, 1.5 Hz, 1H), 7.56 – 7.49 (m, 2H), 7.27 – 7.21 (m, 1H), 7.16 (d, J = 8.5 Hz, 1H), 6.98 (s, 1H), 2.57 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.56 (d, J_{C-F}= 265.1 Hz), 136.71, 135.29, 134.93 (d, J_{C-F}= 3.9 Hz), 134.46, 134.23, 133.28, 132.82, 132.64, 132.54, 131.37, 129.98, 128.46, 126.61, 120.80, 119.02, 118.99, 118.77, 117.93, 114.42, 114.23, 21.25, 14.48.

HR-MS (ESI) m/z calcd for $C_{24}H_{16}F_4N_2NaO_2S^+$ [M+Na$^+$] 495.0761, found 495.0764.



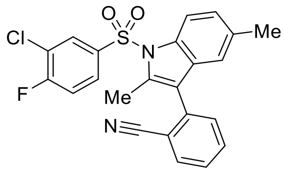
2-(1-((3,4-dichlorophenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (1q)

Yield: 74%. White solid, R_f = 0.62 (hexane/ethyl acetate = 5 : 1, V/V). m.p.: 150 – 151 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.5 Hz, 1H), 7.95 (d, J = 2.1 Hz, 1H), 7.81 (d, J = 7.7 Hz, 1H), 7.71 (t, J = 6.9 Hz, 1H), 7.57 – 7.46 (m, 4H), 7.15 (d, J = 8.7 Hz, 1H), 6.98 (s, 1H), 2.57 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 138.83, 137.97, 136.78, 135.32, 134.27, 134.18, 133.93, 133.35, 132.82, 131.67, 131.46, 129.87, 128.40, 126.53, 125.45, 120.44, 118.99, 118.01, 114.38, 114.20, 21.28, 14.48.

HR-MS (ESI) m/z calcd for $C_{23}H_{16}Cl_2N_2NaO_2S^+$ [M+Na$^+$] 477.0202, found 477.0204.



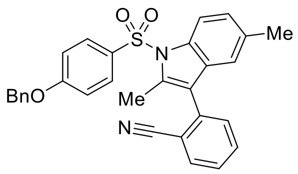
2-(1-((3-chloro-4-fluorophenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (1r)

Yield: 85%. White oil, R_f = 0.40 (hexane/ethyl acetate = 7 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.5 Hz, 1H), 7.94 (dd, J = 6.5, 2.4 Hz, 1H), 7.81 (d, J = 7.4 Hz, 1H), 7.74 – 7.68 (m, 1H), 7.67 – 7.61 (m, 1H), 7.52 (t, J = 7.5 Hz, 2H), 7.20 – 7.13 (m, 2H), 6.98 (s, 1H), 2.57 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.21 (d, J_{C-F}= 257.2 Hz), 136.81, 135.37, 135.32, 134.23, 133.33, 132.82, 131.45, 129.88, 129.51, 128.39, 127.07 (d, J_{C-F}= 8.9 Hz), 126.50, 122.79, 122.60, 120.40, 118.96, 118.04 (d, $J_{C\text{-}F}$= 7.4 Hz), 117.85, 114.39, 114.21, 21.28, 14.48.

HR-MS (ESI) m/z calcd for $C_{23}H_{16}ClFN_2NaO_2S^+$ [M+Na$^+$] 461.0497, found 461.0499.



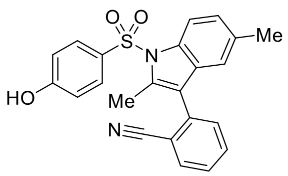
2-(1-((4-(benzyloxy)phenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (1s)

Yield: 87%. White solid, R_f = 0.49 (hexane/ethyl acetate = 5 : 1, V/V). m.p.: 129 – 130 °C.

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.05 (d, *J* = 8.5 Hz, 1H), 7.80 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.76 (d, *J* = 8.9 Hz, 2H), 7.69 (td, *J* = 7.7, 1.4 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.40 – 7.30 (m, 5H), 7.12 (d, *J* = 8.5 Hz, 1H), 6.98 – 6.93 (m, 3H), 5.02 (s, 2H), 2.58 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 162.84, 137.29, 135.65, 135.49, 134.39, 133.48, 133.34, 132.68, 131.64, 130.57, 129.64, 128.77, 128.71, 128.37, 128.10, 127.55, 126.00, 119.24, 118.61, 118.03, 115.33, 114.44, 114.21, 70.37, 21.27, 14.32.

HR-MS (ESI) m/z calcd for $C_{30}H_{24}N_2NaO_3S^+$ [M+Na$^+$] 515.1400, found 515.1403.



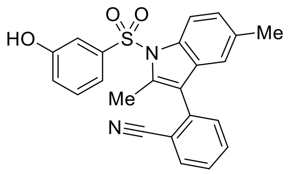
2-(1-((4-hydroxyphenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (1t)

Yield: 72%. Yellow solid, R_f = 0.21 (hexane/ethyl acetate = 2 : 1, V/V). m.p.: 113 – 114 °C.

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.16 (d, J = 8.5 Hz, 1H), 7.79 (d, J = 7.7 Hz, 1H), 7.72 (t, J = 7.7 Hz, 1H), 7.51 (t, J = 7.5 Hz, 2H), 7.39 (d, J = 8.5 Hz, 2H), 7.29 (d, J = 8.5 Hz, 1H), 6.97 (s, 2H), 6.30 (d, J = 8.5 Hz, 2H), 2.57 (s, 3H), 2.38 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 161.09, 137.79, 135.44, 134.27, 133.91, 133.38, 133.30, 131.70, 129.72, 129.16, 128.69, 128.34, 126.26, 119.16, 118.59, 117.98, 115.81, 114.63, 113.40, 21.28, 14.14.

HR-MS (ESI) m/z calcd for $C_{23}H_{18}N_2NaO_3S^+$ [M+Na$^+$] 425.0930, found 425.0935.



2-(1-((3-hydroxyphenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (1u)

Yield: 90%. White solid, R_f = 0.38 (hexane/ethyl acetate = 5 : 1, V/V). m.p.: 136 – 137 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.5 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.78 (td, *J* = 7.7, 1.3 Hz, 1H), 7.61 – 7.54 (m, 2H), 7.51 (d, *J* = 8.1 Hz, 1H), 7.29 (t, *J* = 8.0 Hz, 1H), 7.06 (d, *J* = 8.6 Hz, 1H), 6.97 – 6.93 (m, 2H), 6.92 (s, 1H), 6.83 (t, *J* = 2.1 Hz, 1H), 2.62 (s, 3H), 2.31 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 158.34, 140.06, 138.89, 137.26, 135.53, 135.08, 134.62, 134.32, 132.67, 131.32, 130.89, 129.63, 127.48, 122.83, 121.30, 119.59, 119.39, 119.23, 115.71, 114.57, 112.45, 22.31, 15.46.

HR-MS (ESI) m/z calcd for $C_{23}H_{18}N_2NaO_3S^+$ [M+Na$^+$] 425.0930, found 425.0933.

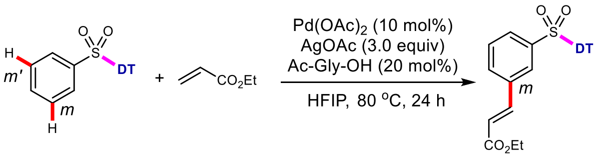
2.3 Screening of Templates

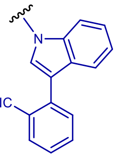
Based on the previous procedures for palladium-catalyzed *meta*-C–H olefination reactions,[4,5] the directing of templates **DT$_1$–DT$_5$** in this reaction was evaluated.

To a 15-mL Schlenk tube equipped with a Teflon cap was charged with $PhSO_2$-**DT** (0.1 mmol, 1.0 equiv), $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 10 mol%), Ac-Gly-OH (2.34 mg, 0.02 mmol, 20 mol%), AgOAc (0.3 mmol, 3.0 equiv) in turn. Hexafluoro-2-propanol (HFIP, 1.0 mL) was added to the mixture via a syringe, followed by ethyl acrylate (2.0 equiv). The reaction tube was then capped and stirred at room temperature for 15 minutes. The tube was then placed onto a preheated (80 °C) heating block. The reaction was stirred for 24 h and cooled to room temperature. The reaction mixture was diluted with EtOAc (5 mL) and filtered through a short pad of Celite. The filtrate was concentrated *in vacuo*, and the residue was purified by flash column chromatography (silica gel) or preparative thin layer chromatography using petroleum ether (60 °C–90 °C)/EtOAc as the eluent to provide the olefinated products.

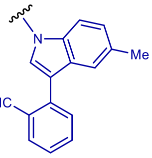
The results for the different directing templates were reported in the Table S1.

Table S1. Evaluation of directing template for *meta*-C–H functionalization of arylsulfonates.

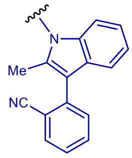




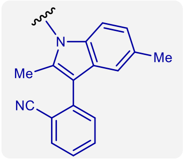
DT$_1$, 52%
mono:di = 2.3:1
meta:others > 20:1



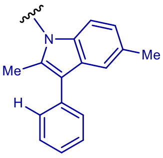
DT$_2$, 56%
mono:di = 2.5:1
meta:others > 20:1



DT$_3$, 68%
mono:di = 1.5:1
meta:others > 20:1



DT$_4$, 94%
mono:di = 1:1
meta:others > 20:1

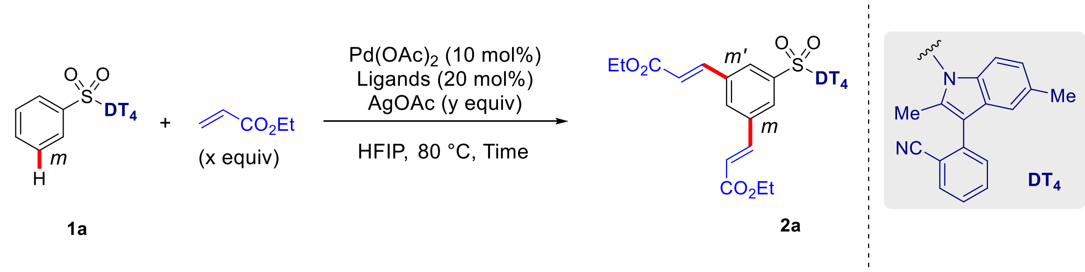


DT$_5$, n.d.
messy products
conversion <30%

3 Pd-Catalyzed *meta*-C–H Olefination of Aryl Sulfonic Acids

3.1 Optimization of Reaction Conditions

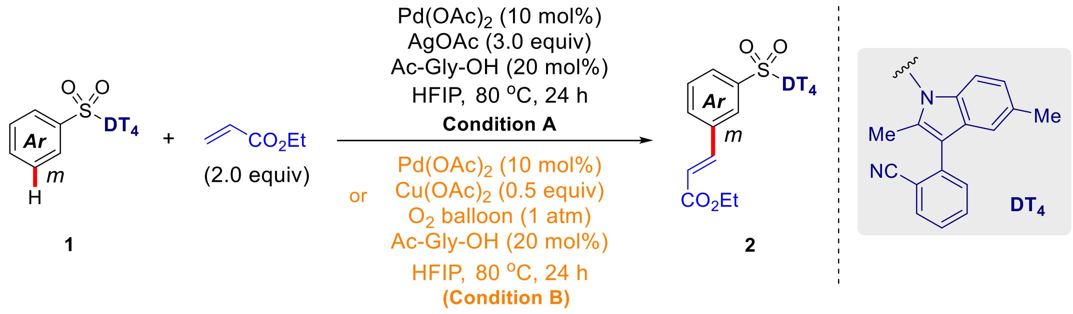
Table S2. Condition screening for *meta*-C–H olefination of aryl sulfonic acids[a]



Entry	Ligands	Ethyl acrylate (eq.)	AgOAc (eq.)	Time (h)	Ratio (mono:di)	Yield (%)
1	***N*-Ac-Gly-OH**	**2.0**	**3.0**	**24**	**1:1**	**94**
2	*N*-Ac-Val-OH	2.0	3.0	24	1:1.2	55
3	*N*-Ac-Ala-OH	2.0	3.0	24	1:2	46
4	*N*-Ac-Leu-OH	2.0	3.0	24	1.3:1	33
5	*N*-Boc-Gly-OH	2.0	3.0	24	1.1:1	46
6	*N*-Boc-Val-OH	2.0	3.0	24	1:1	22
7	*N*-Boc-Phe-OH	2.0	3.0	24	1.5:1	38
8	*N*-For-Gly-OH	2.0	3.0	24	1:1.4	65
9	Gly-OH	2.0	3.0	24	1.2:1	42
10	without ligand	2.0	3.0	24	n.d.	<30
11	*N*-Ac-Gly-OH	1.5	3.0	24	1.3:1	90
12	*N*-Ac-Gly-OH	1.2	3.0	24	1:2	40
13	*N*-Ac-Gly-OH	1.0	3.0	24	1:2.2	28
14	*N*-Ac-Gly-OH	1.5	2.0	24	1:2.5	60
15	*N*-Ac-Gly-OH	1.5	1.5	24	1:1.7	64
16	*N*-Ac-Gly-OH	1.5	3.0	12	1:1	80
17	***N*-Ac-Gly-OH**	**1.5**	**3.0**	**6**	**1.4:1**	**92**
18	*N*-Ac-Gly-OH	1.5	3.0	2	1.3:1	84

[a]Reaction conditions: **1a** (0.1 mmol), ethyl acrylate (x eq.), $Pd(OAc)_2$ (10 mol%), Ligands (20 mol%), AgOAc (y equiv), reaction time (h). Yield and ratio of mono- and di-products were determined by ^1H NMR analysis of the crude products with $Cl_2CHCHCl_2$ as an internal standard. N.d.: not detected.

3.2 Scope of Aryl Sulfonic Acids.

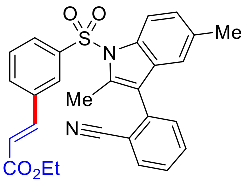


General procedure for *meta*-C–H olefination.

Condition A: To a 15-mL Schlenk sealed tube equipped with a Teflon cap was charged with $ArSO_2$-$\mathbf{DT_4}$ **1** (0.1 mmol, 1.0 equiv), $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 10 mol%), Ac-Gly-OH (2.3 mg, 0.02 mmol, 20 mol%), AgOAc (0.3 mmol, 3.0 equiv) in turn. Hexafluoro-2-propanol (HFIP, 1.5 mL) was added to the mixture along the inside wall of the tube via a syringe, followed by ethyl acrylate (21.74 μL, 0.2mmol, 2.0 equiv). The reaction tube was then capped and stirred at room temperature for 15 minutes. The tube was then placed onto a preheated (80 °C) heating block. The reaction was stirred for 24 h and cooled to room temperature.

Condition B: To a 15-mL Schlenk sealed tube equipped with a Teflon cap was charged with $ArSO_2$-$\mathbf{DT_4}$ **1** (0.1 mmol, 1.0 equiv), $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 10 mol%), Ac-Gly-OH (2.3 mg, 0.02 mmol, 20 mol%), $Cu(OAc)_2$ (9.1 mg, 0.05 mmol, 0.5 equiv) in turn. Hexafluoro-2-propanol (HFIP, 1.5 mL) was added to the mixture along the inside wall of the tube via a syringe, followed by ethyl acrylate (21.74 μL, 0.2mmol, 2.0 equiv). The reaction tube was capped, then evacuated briefly under vacuum and charged with O_2 (1 atm, balloon, × 3). The tube was stirred at room temperature for 15 minutes, and then placed onto a preheated (80 °C) heating block. The reaction was stirred for 24 h and cooled to room temperature.

Work up: The crude reaction mixture was diluted with EtOAc (5 mL) and filtered through a short pad of Celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography (silica gel) or preparative thin layer chromatography using petroleum ether (60 °C–90 °C)/EtOAc as the eluent to provide the olefinated products **2**. Isolated yields for compounds **2** were reported in Scheme 2. of Main Text. The characterization data of new compounds are shown below:



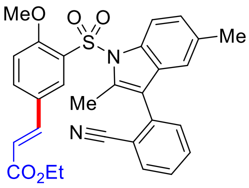
Ethyl (*E*)-3-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenyl)acrylate (2a)

Yellow oil, R_f = 0.45 (hexane/ethyl acetate = 7 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.5 Hz, 1H), 7.95 (s, 1H), 7.80 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.75 (dt, *J* = 8.1, 1.3 Hz, 1H), 7.70 (td, *J* = 7.7, 1.4 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 16.0 Hz, 1H), 7.51 (ddd, *J* = 8.1, 6.2, 1.4 Hz, 2H), 7.45 (t, *J* = 7.9 Hz, 1H), 7.14 (dd, *J* = 8.6, 1.8 Hz, 1H), 6.97 (s, 1H), 6.43 (d, *J* = 16.1 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.59 (s, 3H), 2.35 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.25, 142.11, 139.60, 137.00, 135.91, 135.44, 134.35, 133.92, 133.30, 132.72, 132.47, 131.52, 130.13, 129.74, 128.25, 127.49, 126.31, 125.77, 121.05, 119.88, 118.81, 117.91, 114.38, 114.26, 60.82, 21.25, 14.40, 14.28.

HR-MS (ESI) m/z calcd for $C_{28}H_{24}N_2NaO_4S^+$ [M+Na$^+$] 507.1349, found 507.1346.



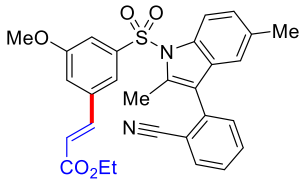
Ethyl (*E*)-3-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-4-methoxyphenyl)acrylate (2b)

Yellow solid, R_f = 0.34 (hexane/ethyl acetate = 10 : 1, V/V). m.p.: 169 – 170 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 2.2 Hz, 1H), 7.83 (d, *J* = 8.5 Hz, 1H), 7.79 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.73 – 7.63 (m, 3H), 7.53 – 7.46 (m, 2H), 7.08 (dd, *J* = 8.6, 1.7 Hz, 1H), 6.96 (s, 1H), 6.90 (d, *J* = 8.7 Hz, 1H), 6.41 (d, *J* = 16.0 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.57 (s, 3H), 2.44 (s, 3H), 2.35 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.64, 158.68, 142.12, 137.60, 136.03, 134.98, 134.74, 133.34, 132.90, 132.78, 131.86, 130.05, 129.01, 128.06, 127.60, 126.94, 125.60, 118.51, 118.48, 117.98, 117.75, 114.22, 114.16, 113.20, 60.67, 56.45, 21.24, 14.33, 13.50.

HR-MS (ESI) m/z calcd for $C_{29}H_{26}N_2NaO_5S^+$ [M+Na$^+$] 537.1455, found 537.1451.



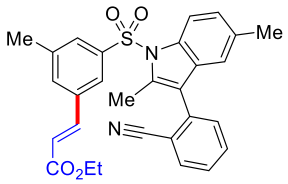
Ethyl (*E*)-3-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-5-methoxyphenyl)acrylate (2c)

Yellow oil, R_f = 0.43 (hexane/ethyl acetate = 8 : 1, V/V).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.04 (d, *J* = 8.5 Hz, 1H), 7.79 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.70 (td, *J* = 7.7, 1.4 Hz, 1H), 7.57 (d, *J* = 16.0 Hz, 1H), 7.53-7.48 (m, 3H), 7.27 (s, 1H), 7.17 – 7.13 (m, 2H), 6.99 (s, 1H), 6.39 (d, *J* = 16.0 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 3.78 (s, 3H), 2.59 (s, 3H), 2.36 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 166.26, 160.34, 142.21, 140.55, 137.14, 136.99, 135.36, 134.27, 133.87, 133.31, 132.72, 131.57, 129.67, 128.23, 126.25, 121.15, 119.67, 118.85, 118.77, 118.14, 117.90, 114.30, 114.20, 112.24, 60.83, 55.87, 21.27, 14.43, 14.28.

HR-MS (ESI) m/z calcd for $C_{29}H_{26}N_2NaO_5S^+$ [M+Na$^+$] 537.1455, found 537.1453.



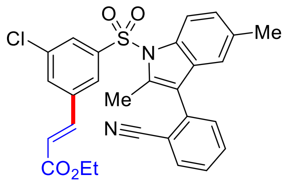
Ethyl (*E*)-3-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-5-methylphenyl)acrylate (2d)

White solid, R_f = 0.40 (hexane/ethyl acetate = 7 : 1, V/V). m.p.: 122 – 123 ^{o}C.

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.02 (d, *J* = 8.5 Hz, 1H), 7.80 (d, *J* = 7.7 Hz, 1H), 7.77 (s, 1H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.59 (d, *J* = 16.0 Hz, 1H), 7.55 (s, 1H), 7.54-7.48 (m, 2H), 7.46 (s, 1H), 7.13 (d, *J* = 7.9 Hz, 1H), 6.99 (s, 1H), 6.41 (d, *J* = 16.0 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.60 (s, 3H), 2.35 (s, 6H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 166.35, 142.35, 140.75, 139.43, 137.04, 135.65, 135.44, 134.23, 133.77, 133.42, 133.28, 132.70, 131.52, 129.63, 128.20, 127.84, 126.22, 123.19, 120.71, 119.63, 118.75, 117.96, 114.29, 114.25, 60.77, 21.26, 14.47, 14.28.

HR-MS (ESI) m/z calcd for $C_{29}H_{26}N_2NaO_4S^+$ [M+Na$^+$] 521.1505, found 521.1501.



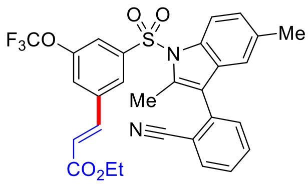
Ethyl (*E*)-3-(3-chloro-5-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenyl)acrylate (2e)

Yellow solid, R_f = 0.52 (hexane/ethyl acetate = 7 : 1, V/V). m.p.: 71 – 72 °C. This compound was obtained as a mixture of isomers (*m*:others = 4:1). The characteristic data for major isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.5 Hz, 1H), 7.97 – 7.68 (m, 4H), 7.64 – 7.60 (m, 1H), 7.60 – 7.49 (m, 3H), 7.19 – 7.13 (m, 1H), 7.00 – 6.97 (m, 1H), 6.44 – 6.37 (m, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.60 – 2.57 (m, 3H), 2.37 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.85, 140.74, 138.33, 137.76, 136.78, 136.12, 135.27, 134.23, 133.27, 132.73, 132.22, 131.44, 129.80, 128.77, 128.34, 127.27, 126.52, 124.74, 123.95, 122.34, 120.28, 118.99, 117.86, 114.29, 60.95, 21.26, 14.49, 14.24.

HR-MS (ESI) m/z calcd for $C_{28}H_{23}ClN_2NaO_4S^+$ [M+Na$^+$] 541.0959, found 541.0955.



Ethyl (*E*)-3-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-5-(trifluoromethoxy)phenyl)acrylate (2f)

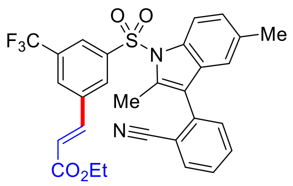
Yellow solid, R_f = 0.37 (hexane/ethyl acetate = 8 : 1, V/V). m.p.: 73 – 74 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.75 (s, 1H), 7.71 (t, *J* = 7.7 Hz, 1H), 7.68 (s, 1H), 7.58 (d, *J* = 16.0 Hz, 1H), 7.55 – 7.47 (m, 3H), 7.17 (d, *J* = 8.5 Hz, 1H), 6.98 (s, 1H), 6.41 (d, *J* = 16.0 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.58 (s, 3H), 2.36 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.77, 149.55, 141.07, 140.63, 138.40, 136.70, 135.24, 134.36, 134.17, 133.26, 132.74, 131.39, 129.88, 128.38, 126.57, 124.17, 123.89, 122.65, 121.43, 120.54,

119.89, 119.02, 117.81, 114.32, 114.26, 61.01, 21.25, 14.48, 14.24.

HR-MS (ESI) m/z calcd for $C_{29}H_{23}F_3N_2NaO_5S^+$ [M+Na$^+$] 591.1172, found 591.1175.



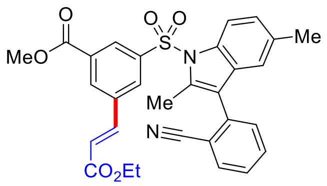
Ethyl (*E*)-3-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-5-(trifluoromethyl)phenyl)acrylate (2g)

Yellow oil, R_f = 0.49 (hexane/ethyl acetate = 10 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 7.95 (s, 1H), 7.89 (s, 1H), 7.79 (d, *J* = 7.2 Hz, 1H), 7.71 (td, *J* = 7.7, 1.4 Hz, 1H), 7.64 (d, *J* = 16.1 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.17 (d, *J* = 8.7 Hz, 1H), 6.99 (s, 1H), 6.45 (d, *J* = 16.1 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.60 (s, 3H), 2.36 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.72, 140.57, 140.49, 137.47, 136.67, 135.25, 134.43, 134.14, 133.24, 132.75, 132.43, 131.37, 129.89, 128.78 (q, $J_{C\text{-}F}$= 3.5 Hz), 128.62, 128.40, 126.61, 124.27 (q, $J_{C\text{-}F}$= 3.8 Hz), 124.00, 122.89, 120.61, 119.07, 117.77, 114.30, 114.28, 61.02, 21.24, 14.54, 14.23.

HR-MS (ESI) m/z calcd for $C_{29}H_{23}F_3N_2NaO_4S^+$ [M+Na$^+$] 575.1223, found 575.1227.



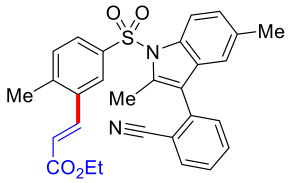
Methyl (*E*)-3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-5-(3-ethoxy-3-oxoprop-1-en-1-yl)benzoate (2h)

Yellow oil, R_f = 0.19 (hexane/ethyl acetate = 8 : 1, V/V). This compound was obtained as a mixture of isomers (*m*:others = 7.6:1). The characteristic data for major isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.32 (s, 1H), 8.05 (d, *J* = 8.5 Hz, 1H), 7.97 (s, 1H), 7.78 (d, *J* = 7.2 Hz, 1H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.64 (d, *J* = 16.0 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 7.16 (d, *J* = 8.5 Hz, 1H), 6.97 (s, 1H), 6.47 (d, *J* = 16.1 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 3H), 2.60 (s, 3H), 2.35 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.98, 164.67, 141.10, 140.06, 136.78, 136.73, 135.29, 134.16, 134.13, 133.27, 132.92, 132.72, 132.24, 131.45, 129.80, 129.36, 128.35, 128.32, 126.48, 122.17, 120.24, 118.95, 117.80, 114.32, 114.24, 60.92, 52.85, 21.25, 14.51, 14.25.

HR-MS (ESI) m/z calcd for $C_{30}H_{26}N_2NaO_6S^+$ [M+Na$^+$] 565.1404, found 565.1408.



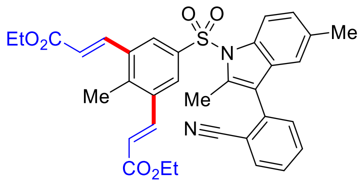
Ethyl (*E*)-3-(5-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-2-methylphenyl)acrylate (2i$_{mono}$)

Yellow oil, R_f = 0.21 (hexane/ethyl acetate = 8 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.5 Hz, 1H), 8.01 (d, J = 2.1 Hz, 1H), 7.85 – 7.77 (m, 2H), 7.70 (td, J = 7.6, 1.4 Hz, 1H), 7.59 (dd, J = 8.1, 2.1 Hz, 1H), 7.51 (t, J = 7.4 Hz, 2H), 7.25 (d, J = 8.0 Hz, 1H), 7.14 (d, J = 8.7 Hz, 1H), 6.97 (s, 1H), 6.34 (d, J = 15.9 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 2.58 (s, 3H), 2.39 (s, 3H), 2.36 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.35, 143.70, 140.14, 137.08, 136.85, 135.46, 134.74, 134.34, 133.78, 133.32, 132.69, 131.99, 131.56, 129.73, 128.19, 126.92, 126.17, 124.50, 122.24, 119.65, 118.75, 117.93, 114.41, 114.21, 60.82, 21.25, 20.03, 14.40, 14.30.

HR-MS (ESI) m/z calcd for $C_{29}H_{26}N_2NaO_4S^+$ [M+Na$^+$] 521.1505, found 521.1502.



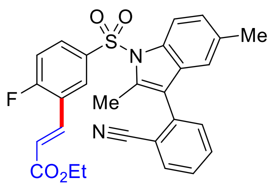
Diethyl 3,3'-(5-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-2-methyl-1,3-phenylene)(2*E*,2'*E*)-diacrylate (2i$_{di}$)

Yellow oil, R_f = 0.12 (hexane/ethyl acetate = 8 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.5 Hz, 1H), 7.89 – 7.82 (m, 4H), 7.77 (d, J = 7.9 Hz, 1H), 7.69 (td, J = 7.7, 1.4 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H), 7.19 (d, J = 8.5 Hz, 1H), 6.98 (s, 1H), 6.22 (d, J = 15.9 Hz, 2H), 4.28 (q, J = 7.1 Hz, 4H), 2.58 (s, 3H), 2.40 (s, 3H), 2.37 (s, 3H), 1.35 (t, J = 7.1 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.09, 142.16, 140.49, 136.90, 136.52, 135.40, 134.32, 134.06, 133.27, 132.66, 131.49, 129.92, 128.22, 126.28, 125.16, 123.60, 119.98, 118.89, 117.71, 114.51, 114.24, 60.88, 21.25, 16.33, 14.54, 14.29.

HR-MS (ESI) m/z calcd for $C_{34}H_{32}N_2NaO_6S^+$ [M+Na$^+$] 619.1873, found 619.1875.



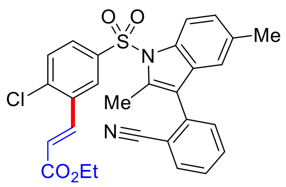
Ethyl (*E*)-3-(5-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-2-fluorophenyl)acrylate (2j)

White solid, R_f = 0.46 (hexane/ethyl acetate = 10 : 1, V/V). m.p.: 61 – 62 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 7.99 (m, 2H), 7.80 (dd, J = 8.2, 1.4 Hz, 1H), 7.75 – 7.64 (m, 3H), 7.55 – 7.49 (m, 2H), 7.18 – 7.11 (m, 2H), 6.97 (s, 1H), 6.53 (d, J = 16.2 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 2.58 (s, 3H), 2.36 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.11, 162.40, 136.86, 135.39, 135.05, 134.25, 134.13, 133.28, 132.76, 131.43, 129.86, 129.70, 129.59, 128.33, 128.04 (d, $J_{C\text{-}F}$= 4.6 Hz), 126.41, 123.90 (d, $J_{C\text{-}F}$= 13.4 Hz), 123.67 (d, $J_{C\text{-}F}$= 6.7 Hz), 120.26, 118.90, 117.95, 117.71, 114.37, 114.21, 60.94, 21.25, 14.53, 14.26.

HR-MS (ESI) m/z calcd for $C_{28}H_{23}FN_2NaO_4S^+$ [M+Na$^+$] 525.1255, found 525.1252.



Ethyl (*E*)-3-(2-chloro-5-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenyl)acrylate (2k)

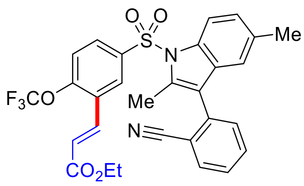
White oil, R_f = 0.36 (hexane/ethyl acetate = 8 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 2.3 Hz, 1H), 8.02 (d, J = 8.6 Hz, 1H), 7.93 (d, J = 16.0

Hz, 1H), 7.80 (d, J = 7.7 Hz, 1H), 7.71 (t, J = 7.7 Hz, 1H), 7.61 (dd, J = 8.5, 2.3 Hz, 1H), 7.52 (t, J = 8.0 Hz, 2H), 7.45 (d, J = 8.5 Hz, 1H), 7.16 (d, J = 8.6 Hz, 1H), 6.98 (s, 1H), 6.41 (d, J = 16.0 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 2.58 (s, 3H), 2.36 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.83, 140.19, 138.37, 137.50, 136.79, 135.40, 134.24, 134.21, 134.12, 133.30, 132.76, 131.52, 131.43, 129.90, 128.34, 127.86, 126.42, 125.66, 123.64, 120.35, 118.95, 117.93, 114.39, 114.18, 61.00, 21.25, 14.53, 14.27.

HR-MS (ESI) m/z calcd for $C_{28}H_{23}ClN_2NaO_4S^+$ [M+Na$^+$] 541.0959, found 541.0962.



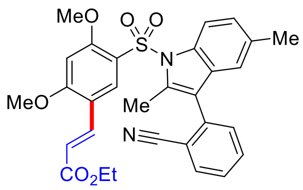
Ethyl (*E*)-3-(5-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-2-(trifluoromethoxy)phenyl)acrylate (2l)

Yellow oil, R_f = 0.50 (hexane/ethyl acetate = 7 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 2.4 Hz, 1H), 8.04 (d, J = 8.5 Hz, 1H), 7.83 – 7.67 (m, 4H), 7.52 (t, J = 7.3 Hz, 2H), 7.31 (d, J = 8.8 Hz, 1H), 7.17 (d, J = 8.5 Hz, 1H), 6.99 (s, 1H), 6.46 (d, J = 16.1 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 2.58 (s, 3H), 2.37 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.79, 150.55, 137.14, 136.79, 135.40, 135.26, 134.33, 134.29, 133.29, 132.76, 131.42, 129.93, 128.85, 128.64, 128.38, 126.70, 126.51, 123.98, 121.37, 120.45, 118.99, 117.89, 114.43, 114.27, 61.02, 21.25, 14.52, 14.25.

HR-MS (ESI) m/z calcd for $C_{29}H_{23}F_3N_2NaO_5S^+$ [M+Na$^+$] 591.1172, found 591.1169.



Ethyl (*E*)-3-(5-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-2,4-dimethoxyphenyl)acrylate (2m)

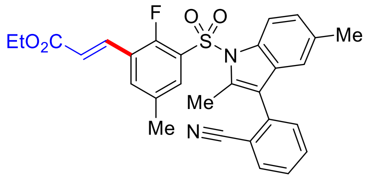
White solid, R_f = 0.43 (hexane/ethyl acetate = 3 : 1, V/V). m.p.: 104 – 105 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.86 (d, J = 16.2 Hz, 1H), 7.82 (d, J = 8.6 Hz, 1H), 7.79

(d, J = 8.0 Hz, 1H), 7.69 (td, J = 7.7, 1.4 Hz, 1H), 7.53 – 7.46 (m, 2H), 7.08 (d, J = 8.6 Hz, 1H), 6.95 (s, 1H), 6.54 (d, J = 16.2 Hz, 1H), 6.31 (s, 1H), 4.28 (q, J = 7.1 Hz, 2H), 3.89 (s, 3H), 3.58 (s, 3H), 2.44 (s, 3H), 2.35 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.28, 163.93, 160.37, 138.04, 137.74, 136.15, 134.60, 133.35, 132.81, 132.69, 131.93, 131.52, 128.98, 128.01, 125.46, 119.16, 118.70, 118.44, 118.12, 117.37, 115.98, 114.15, 114.10, 95.75, 60.52, 56.42, 56.09, 21.27, 14.39, 13.50.

HR-MS (ESI) m/z calcd for $C_{30}H_{28}N_2NaO_6S^+$ [M+Na$^+$] 567.1560, found 567.1565.



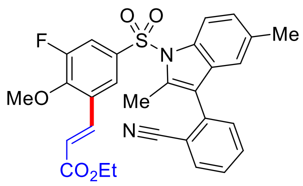
Ethyl (*E*)-3-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-2-fluoro-5-methylphenyl)acrylate (2n)

White oil, R_f = 0.39 (hexane/ethyl acetate = 7 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.5 Hz, 1H), 7.81 (dd, J = 8.1, 1.4 Hz, 1H), 7.71 (ddd, J = 7.8, 6.8, 1.5 Hz, 2H), 7.63 (d, J = 16.2 Hz, 1H), 7.55 – 7.49 (m, 3H), 7.11 (d, J = 8.6 Hz, 1H), 7.00 (s, 1H), 6.46 (d, J = 16.2 Hz, 1H), 4.24 (q, J = 7.1 Hz, 2H), 2.53 (s, 3H), 2.39 (s, 3H), 2.37 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.09, 157.04, 154.43, 137.08, 135.91, 134.98 (d, J_{C-F}= 3.3 Hz), 134.81 (d, J_{C-F}= 3.0 Hz), 134.68 (d, J_{C-F}= 4.3 Hz), 134.01, 133.64, 133.38, 132.71, 131.76, 130.89, 129.34, 128.21, 127.64 (d, J_{C-F}= 14.7 Hz), 126.00, 124.47 (d, J_{C-F}= 11.9 Hz), 122.98 (d, J_{C-F}= 5.9 Hz), 118.84, 117.79, 114.27, 114.14, 60.86, 21.26, 20.75, 14.25, 13.91 (d, J_{C-F}= 2.9 Hz).

HR-MS (ESI) m/z calcd for $C_{29}H_{25}FN_2NaO_4S^+$ [M+Na$^+$] 539.1411, found 539.1415.



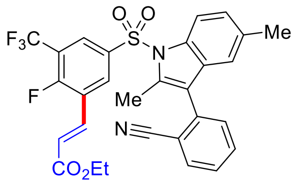
Ethyl (*E*)-3-(5-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-3-fluoro-2-methoxyphenyl)acrylate (2o)

White solid, R_f = 0.38 (hexane/ethyl acetate = 5 : 1, V/V). m.p.: 59 – 60 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.6 Hz, 1H), 7.82 – 7.75 (m, 3H), 7.70 (td, J = 7.7, 1.4 Hz, 1H), 7.54 – 7.45 (m, 3H), 7.17 (d, J = 8.7 Hz, 1H), 6.99 (s, 1H), 6.44 (d, J = 16.2 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 4.03 (d, J = 3.8 Hz, 3H), 2.56 (s, 3H), 2.37 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.38, 155.43, 152.91, 150.43 (d, J_{C-F}= 9.7 Hz), 136.85 (t, J_{C-F}= 3.0 Hz), 135.29, 134.29, 134.11, 133.28, 132.72, 132.64 (d, J_{C-F}= 7.3 Hz), 131.45, 129.88, 129.66 (d, J_{C-F}= 3.6 Hz), 128.29, 126.41, 122.63, 122.02 (d, J_{C-F}= 3.0 Hz), 120.13, 118.89, 117.84, 116.42 (d, J_{C-F}= 23.4 Hz), 114.43, 114.27, 61.58 (d, J_{C-F}= 8.7 Hz), 60.83, 21.26, 14.45, 14.29.

HR-MS (ESI) m/z calcd for $C_{29}H_{25}FN_2NaO_5S^+$ [M+Na$^+$] 555.1360, found 555.1366.



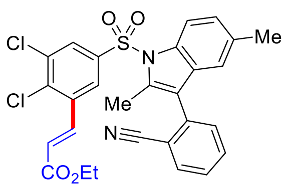
Ethyl (*E*)-3-(5-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-2-fluoro-3-(trifluoromethyl)phenyl)acrylate (2p)

Yellow oil, R_f = 0.35 (hexane/ethyl acetate = 15 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 8.02 (m, 3H), 7.79 (d, J = 7.1 Hz, 1H), 7.71 (td, J = 7.7, 1.4 Hz, 1H), 7.66 (d, J = 16.2 Hz, 1H), 7.52 (t, J = 7.5 Hz, 2H), 7.20 (d, J = 8.7 Hz, 1H), 7.00 (s, 1H), 6.51 (d, J = 16.2 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 2.58 (s, 3H), 2.37 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.61, 136.57, 135.23 (d, J_{C-F}= 3.6 Hz), 134.67, 134.14, 133.45 (d, J_{C-F}= 2.9 Hz), 133.20, 132.78, 131.27, 130.90 (d, J_{C-F}= 4.9 Hz), 130.07, 129.90, 128.47, 126.71, 126.63 (d, J_{C-F}= 5.0 Hz), 126.18, 126.05, 125.46 (d, J_{C-F}= 6.9 Hz), 122.56, 120.98, 119.84, 119.17, 117.75, 114.39, 114.28, 61.15, 21.25, 14.66, 14.22.

HR-MS (ESI) m/z calcd for $C_{29}H_{22}F_4N_2NaO_4S^+$ [M+Na$^+$] 593.1129, found 593.1131.



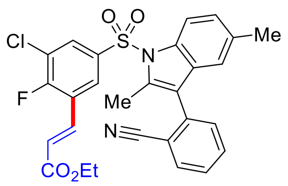
Ethyl (*E*)-3-(2,3-dichloro-5-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenyl)acrylate (2q)

Yellow oil, R_f = 0.37 (hexane/ethyl acetate = 8 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.5 Hz, 1H), 7.91 (d, *J* = 16.0 Hz, 1H), 7.86 (s, 2H), 7.79 (d, *J* = 7.3 Hz, 1H), 7.71 (td, *J* = 7.6, 1.4 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.19 (d, *J* = 8.6 Hz, 1H), 7.00 (s, 1H), 6.33 (d, *J* = 15.9 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.58 (s, 3H), 2.38 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.56, 138.56, 138.49, 137.83, 136.65, 136.51, 135.48, 135.24, 134.48, 134.18, 133.28, 132.74, 131.39, 130.00, 128.40, 128.17, 126.59, 124.81, 123.41, 120.64, 119.11, 117.79, 114.40, 114.27, 61.11, 21.26, 14.59, 14.26.

HR-MS (ESI) m/z calcd for $C_{28}H_{22}Cl_2N_2NaO_4S^+$ [M+Na$^+$] 575.0570, found 575.0574.



Ethyl (*E*)-3-(3-chloro-5-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-2-fluorophenyl)acrylate (2r)

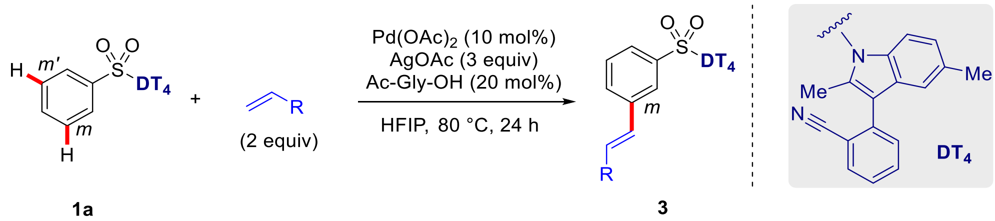
Yellow oil, R_f = 0.40 (hexane/ethyl acetate = 5 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.5 Hz, 1H), 7.87 – 7.77 (m, 3H), 7.71 (td, *J* = 7.7, 1.4 Hz, 1H), 7.64 (d, *J* = 16.2 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.18 (d, *J* = 8.6 Hz, 1H), 7.00 (s, 1H), 6.50 (d, *J* = 16.2 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 2.58 (s, 3H), 2.37 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H).

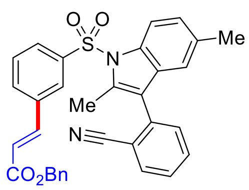
^{13}C NMR (100 MHz, $CDCl_3$) δ 165.80, 160.66, 158.03, 136.69, 135.43 (d, $J_{C\text{-}F}$= 4.5 Hz), 135.25, 134.37 (d, $J_{C\text{-}F}$= 9.8 Hz), 134.13, 133.26, 132.77, 131.37, 129.94, 129.49, 128.40, 126.60, 125.78 (d, $J_{C\text{-}F}$= 4.1 Hz), 125.37 (d, $J_{C\text{-}F}$= 13.1 Hz), 124.83 (d, $J_{C\text{-}F}$= 6.9 Hz), 123.85 (d, $J_{C\text{-}F}$= 19.5 Hz), 120.59, 119.08, 117.87, 114.33, 114.27, 61.08, 21.26, 14.62, 14.24.

HR-MS (ESI) m/z calcd for $C_{28}H_{22}ClFN_2NaO_4S^+$ [M+Na$^+$] 559.0865, found 559.0868.

3.3 Scope of Olefins.



General procedure for *meta*-C–H olefination. To a 15-mL Schlenk sealed tube equipped with a Teflon cap was charged with $PhSO_2$-**DT_4** **1a** (0.1 mmol, 1.0 equiv), $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 10 mol%), Ac-Gly-OH (2.3 mg, 0.02 mmol, 20 mol%), AgOAc (0.3 mmol, 3.0 equiv) in turn. Hexafluoro-2-propanol (HFIP, 1.5 mL) was added to the mixture along the inside wall of the tube via a syringe, followed by olefin (2.0 equiv). The reaction tube was then capped and stirred at room temperature for 15 minutes. The tube was then placed onto a preheated (80 °C) heating block. The reaction was stirred for 24 h and cooled to room temperature. The crude reaction mixture was diluted with EtOAc (5 mL) and filtered through a short pad of Celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography (silica gel) or preparative thin layer chromatography using petroleum ether (60 °C–90 °C)/EtOAc as the eluent to provide the olefinated products **3**. Isolated yields for compounds **3** were reported in Scheme 3. of Main Text. The characterization data of new compounds are shown below:



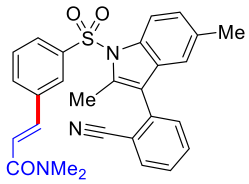
Benzyl (*E*)-3-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenyl)acrylate (3a)

White oil, R_f = 0.28 (hexane/ethyl acetate = 5 : 1, V/V).

^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.5 Hz, 1H), 7.94 (s, 1H), 7.79 (dd, J = 8.1, 1.4 Hz, 1H), 7.75 (d, J = 8.2 Hz, 1H), 7.72 – 7.63 (m, 3H), 7.54 – 7.48 (m, 2H), 7.48 – 7.32 (m, 6H), 7.13 (d, J = 8.5 Hz, 1H), 6.97 (s, 1H), 6.48 (d, J = 16.1 Hz, 1H), 5.25 (s, 2H), 2.58 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.04, 142.68, 139.62, 136.99, 135.81, 135.78, 135.44, 134.33, 133.93, 133.28, 132.71, 132.49, 131.51, 130.14, 129.73, 128.63, 128.35, 128.32, 128.25, 127.61, 126.32, 125.81, 120.66, 119.90, 118.80, 117.90, 114.37, 114.25, 66.63, 21.24, 14.41.

HR-MS (ESI) m/z calcd for $C_{33}H_{26}N_2NaO_4S^+$ [M+Na$^+$] 569.1505, found 569.1508.



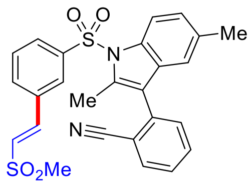
(*E*)-3-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenyl)-*N*,*N*-dimethylacrylamide (3b)

White oil, R_f = 0.23 (hexane/ethyl acetate = 1 : 1, V/V).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.05 (d, *J* = 8.5 Hz, 1H), 7.94 (s, 1H), 7.79 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.75 – 7.67 (m, 2H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 15.5 Hz, 1H), 7.54 – 7.48 (m, 2H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.13 (d, *J* = 8.5 Hz, 1H), 6.98 (s, 1H), 6.86 (d, *J* = 15.5 Hz, 1H), 3.15 (s, 3H), 3.06 (s, 3H), 2.58 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 165.93, 139.83, 139.46, 137.00, 136.88, 135.46, 134.37, 133.84, 133.29, 132.98, 132.72, 131.54, 129.99, 129.69, 128.22, 126.81, 126.23, 124.83, 120.39, 119.74, 118.81, 117.90, 114.37, 114.19, 37.46, 35.99, 21.25, 14.43.

HR-MS (ESI) m/z calcd for $C_{28}H_{25}N_3NaO_3S^+$ [M+Na$^+$] 506.1509, found 506.1513.



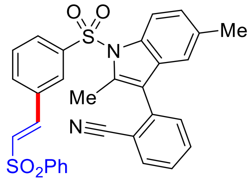
(*E*)-2-(2,5-dimethyl-1-((3-(2-(methylsulfonyl)vinyl)phenyl)sulfonyl)-1*H*-indol-3-yl)benzonitrile (3c)

White solid, R_f = 0.29 (hexane/ethyl acetate = 2 : 1, V/V). m.p.: 108 – 109 ^{o}C.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.96 (d, *J* = 8.6 Hz, 1H), 7.94 (d, *J* = 8.2 Hz, 1H), 7.84 (s, 1H), 7.81 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.72 (td, *J* = 7.7, 1.4 Hz, 1H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.58 – 7.50 (m, 4H), 7.13 (d, *J* = 8.6 Hz, 1H), 7.06 – 6.96 (m, 2H), 3.03 (s, 3H), 2.62 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 141.09, 139.83, 136.92, 135.49, 134.10, 134.07, 133.92, 133.58, 133.26, 132.88, 131.47, 130.21, 129.73, 129.48, 128.77, 128.36, 126.38, 125.39, 120.03, 118.88, 118.04, 114.25, 114.08, 43.04, 21.25, 14.57.

HR-MS (ESI) m/z calcd for $C_{26}H_{22}N_2NaO_4S_2^+$ [M+Na$^+$] 513.0913, found 513.0910.



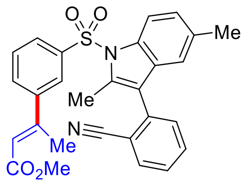
(*E*)-2-(2,5-dimethyl-1-((3-(2-(phenylsulfonyl)vinyl)phenyl)sulfonyl)-1*H*-indol-3-yl)benzonitrile (3d)

White solid, R_f = 0.41 (hexane/ethyl acetate = 3 : 1, V/V). m.p.: 91 – 92 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.92 (m, 3H), 7.86 (s, 1H), 7.81 (t, *J* = 7.3 Hz, 2H), 7.71 (td, *J* = 7.6, 1.4 Hz, 1H), 7.66 – 7.50 (m, 7H), 7.46 (t, *J* = 7.9 Hz, 1H), 7.11 (d, *J* = 8.5 Hz, 1H), 6.97 (s, 1H), 6.91 (d, *J* = 15.5 Hz, 1H), 2.58 (s, 3H), 2.34 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.06, 139.92, 139.71, 136.87, 135.47, 134.17, 134.05, 133.95, 133.65, 133.23, 133.07, 132.79, 131.43, 130.23, 129.74, 129.39, 128.51, 128.32, 127.91, 126.36, 126.04, 120.08, 118.86, 117.91, 114.29, 114.17, 21.25, 14.55.

HR-MS (ESI) m/z calcd for $C_{31}H_{24}N_2NaO_4S_2^+$ [M+Na$^+$] 575.1070, found 575.1073.



Methyl (*E*)-3-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenyl)but-2-enoate (3e)

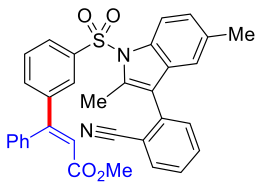
White oil, R_f = 0.32 (hexane/ethyl acetate = 5 : 1, V/V). This compound was obtained as a mixture of *Z/E* isomers (*Z/E* = 1/25). The characteristic data for *E*-isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.5 Hz, 1H), 7.93 (s, 1H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.70 (t, *J* = 7.5 Hz, 2H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 7.43 (t, *J* = 7.9 Hz, 1H), 7.15 (d, *J* = 9.4 Hz, 1H), 6.97 (s, 1H), 6.06 (d, *J* = 1.4 Hz, 1H), 3.76 (s, 3H), 2.57 (s, 3H), 2.50 (d, *J* = 1.3 Hz, 3H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.69, 153.28, 143.35, 139.06, 136.97, 135.41, 134.40, 133.90, 133.32, 132.71, 131.52, 129.87, 129.75, 128.23, 126.47, 126.23, 124.21, 119.82, 118.78, 117.86,

114.45, 114.17, 110.80, 51.34, 21.25, 17.82, 14.37.

HR-MS (ESI) m/z calcd for $C_{28}H_{24}N_2NaO_4S^+$ [M+Na$^+$] 507.1349, found 507.1352.



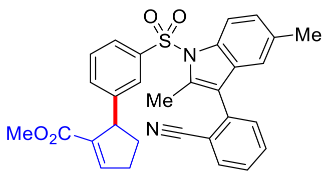
Methyl (*E*)-3-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenyl)-3-phenylacrylate (3f)

White oil, R_f = 0.21 (hexane/ethyl acetate = 5 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.5 Hz, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.76 (s, 1H), 7.75 – 7.67 (m, 2H), 7.54 – 7.42 (m, 3H), 7.41 – 7.31 (m, 4H), 7.12 – 7.08 (m, 3H), 6.96 (s, 1H), 6.29 (s, 1H), 3.62 (s, 3H), 2.50 (s, 3H), 2.37 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.90, 154.43, 142.10, 138.93, 137.48, 136.99, 135.28, 134.29, 133.79, 133.32, 133.23, 132.70, 131.54, 129.73, 129.69, 129.04, 128.66, 128.22, 128.13, 126.87, 126.28, 126.10, 119.79, 118.86, 118.74, 117.84, 114.37, 114.16, 51.47, 21.28, 14.27.

HR-MS (ESI) m/z calcd for $C_{33}H_{26}N_2NaO_4S^+$ [M+Na$^+$] 569.1505, found 569.1501.



Methyl (*R*)-5-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenyl)cyclopent-1-ene-1-carboxylate (3g)

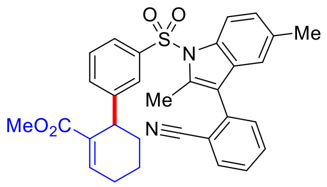
Yellow oil, R_f = 0.22 (hexane/ethyl acetate = 5 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 12.1, 8.5 Hz, 1H), 7.79 (d, *J* = 7.7 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 4.6 Hz, 1H), 7.61-7.54 (m, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.33 (d, *J* = 4.8 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 1H), 7.04 – 6.94 (m, 2H), 4.13 (s, 1H), 3.49 (d, *J* = 27.6 Hz, 3H), 2.54 (d, *J* = 2.2 Hz, 3H), 2.53-2.44 (m, 2H), 2.36 (s, 3H), 1.87 – 1.70 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.64, 146.88, 146.10, 138.84, 138.32, 137.19, 135.47, 134.49, 133.51, 133.34, 132.71, 132.66, 131.69, 129.63, 129.53, 128.11, 126.03, 124.91, 124.21, 119.27,

118.61, 117.89, 114.45, 114.18, 51.36, 49.75, 33.76, 32.16, 21.25, 14.19.

HR-MS (ESI) m/z calcd for $C_{30}H_{26}N_2NaO_4S^+$ [M+Na$^+$] 533.1505, found 533.1506.



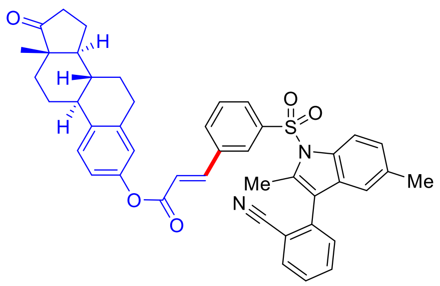
Methyl (*R*)-3'-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-1,4,5,6-tetrahydro-[1,1'-biphenyl]-2-carboxylate (3h)

White oil, R_f = 0.36 (hexane/ethyl acetate = 8 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 17.3, 8.6 Hz, 1H), 7.79 (dd, *J* = 7.9, 5.0 Hz, 1H), 7.68 (td, *J* = 7.7, 1.4 Hz, 1H), 7.66 – 7.54 (m, 2H), 7.53 – 7.45 (m, 2H), 7.36 – 7.32 (m, 2H), 7.30 – 7.23 (m, 1H), 7.12 (dt, *J* = 8.6, 2.3 Hz, 1H), 6.99 – 6.95 (m, 1H), 3.95 – 3.89 (s, 1H), 3.48 (d, *J* = 28.7 Hz, 3H), 2.53 (s, 3H), 2.36 (s, 3H), 2.30 – 2.16 (m, 2H), 1.94 – 1.78 (m, 1H), 1.68 – 1.60 (m, 1H), 1.52 – 1.31 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.93, 146.83, 142.94, 138.53, 137.19, 135.44, 134.51, 133.48, 133.41, 133.35, 132.65, 131.68, 130.64, 129.64, 129.48, 128.11, 126.03, 125.44, 124.04, 119.26, 118.60, 117.90, 114.48, 114.16, 51.54, 39.30, 31.04, 25.72, 21.25, 16.70, 14.16.

HR-MS (ESI) m/z calcd for $C_{31}H_{28}N_2NaO_4S^+$ [M+Na$^+$] 547.1662, found 547.1665.



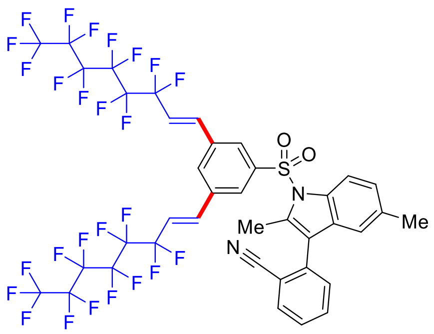
(8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthren-3-yl (*E*)-3-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenyl)acrylate (3i)

White solid, R_f = 0.39 (hexane/ethyl acetate = 4 : 1, V/V). m.p.: 121 – 122 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.5 Hz, 1H), 8.00 (s, 1H), 7.83 – 7.76 (m, 3H), 7.70 (t, *J* = 7.4 Hz, 2H), 7.55 – 7.46 (m, 3H), 7.31 (d, *J* = 8.5 Hz, 1H), 7.15 (d, *J* = 8.5 Hz, 1H), 6.98 (s, 1H), 6.93 (d, J = 8.4 Hz, 1H), 6.90 (s, 1H), 6.61 (d, J = 16.0 Hz, 1H), 2.97 – 2.91 (m, 2H), 2.60 (s, 3H), 2.56 – 2.47 (m, 1H), 2.42 (m, 1H), 2.36 (s, 3H), 2.18 (t, J = 8.9 Hz, 1H), 2.12 – 1.95 (m, 3H), 1.68 – 1.43 (m, 7H), 0.92 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 220.80, 164.96, 148.50, 143.86, 139.64, 138.07, 137.51, 136.92, 135.58, 135.41, 134.30, 133.96, 133.28, 132.75, 131.48, 130.24, 129.74, 128.28, 127.87, 126.45, 126.33, 125.94, 121.53, 120.18, 119.95, 118.82, 118.70, 117.93, 114.36, 114.19, 110.29, 50.42, 47.94, 44.16, 37.99, 35.86, 31.54, 29.42, 26.34, 25.75, 21.59, 21.26, 14.44, 13.83.

HR-MS (ESI) m/z calcd for $C_{44}H_{40}N_2NaO_5S^+$ [M+Na$^+$] 731.2550, found 731.2545.



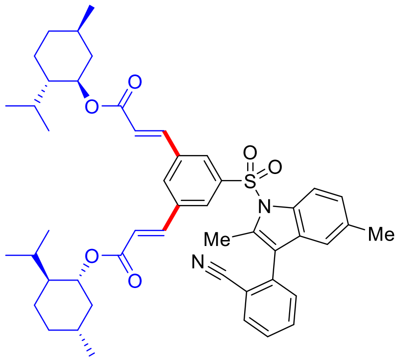
2-(1-((3,5-bis((*E*)-3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)phenyl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (3j)

White solid, R_f = 0.79 (hexane/ethyl acetate = 5 : 1, V/V). m.p.: 114 – 115 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.5 Hz, 1H), 7.85 (s, 2H), 7.81 (d, J = 7.6 Hz, 1H), 7.72 (t, J = 7.7 Hz, 1H), 7.66 (s, 1H), 7.53 (t, J = 8.3 Hz, 2H), 7.19 (d, J = 16.2 Hz, 2H), 7.14 (d, J = 10.6 Hz, 1H), 7.00 (s, 1H), 6.25 (dt, J = 16.1, 11.7 Hz, 2H), 2.63 (s, 3H), 2.34 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.40, 137.21 (d, J_{C-F} = 9.4 Hz), 136.71, 135.87, 135.63, 134.40, 134.19, 133.17, 132.78, 131.27, 130.70, 129.96, 128.41, 126.35 (d, J_{C-F} = 4.9 Hz), 120.62, 118.99, 118.27 (d, J_{C-F} = 23.3 Hz), 117.81, 114.38, 114.24, 21.13, 14.77.

HR-MS (ESI) m/z calcd for $C_{39}H_{20}F_{26}N_2NaO_2S^+$ [M+Na$^+$] 1097.0723, found 1097.0720.



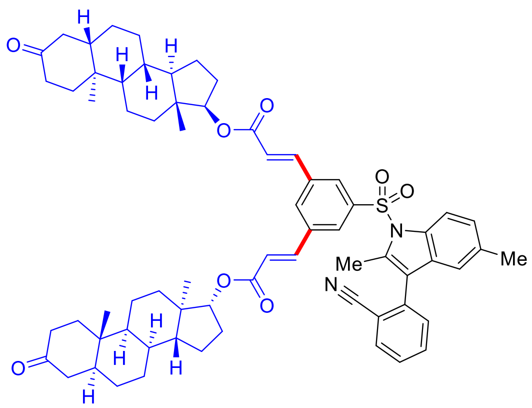
Bis((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl) 3,3'-(5-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-1,3-phenylene)(2*E*,2'*E*)-diacrylate (3k)

Yellow solid, R_f = 0.55 (hexane/ethyl acetate = 6 : 1, V/V). m.p.: 93 – 94 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 10.9, 8.5 Hz, 1H), 7.86 (d, *J* = 8.5 Hz, 2H), 7.78 (s, 2H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.60 (dd, *J* = 16.1, 3.5 Hz, 2H), 7.54 – 7.49 (m, 2H), 7.15 (d, *J* = 8.1 Hz, 1H), 6.99 (s, 1H), 6.44 (dd, *J* = 16.0, 4.6 Hz, 2H), 4.81 (td, *J* = 10.9, 4.4 Hz, 2H), 2.61 (d, *J* = 10.3 Hz, 3H), 2.36 (d, *J* = 2.8 Hz, 3H), 2.10 – 2.03 (m, 2H), 1.91 (ddt, *J* = 13.8, 7.0, 3.6 Hz, 2H), 1.71 (d, *J* = 11.8 Hz, 4H), 1.56 – 1.43 (m, 4H), 1.13 – 1.01 (m, 4H), 0.95 – 0.89 (m, 14H), 0.79 (s, 3H), 0.77 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.62, 141.24, 140.48, 140.32, 136.78, 135.45, 134.24, 134.13, 134.10, 133.22, 132.70, 131.45, 130.85, 129.76, 128.29, 126.58, 126.43, 122.25, 120.09, 118.94, 117.83, 114.29, 74.82, 47.13, 40.91, 34.25, 31.42, 26.28, 23.46, 22.04, 21.25, 20.82, 16.37, 14.62.

HR-MS (ESI) m/z calcd for $C_{49}H_{58}N_2NaO_6S^+$ [M+Na$^+$] 825.3908, found 825.3913.



Bis((5*S*,8*S*,9*S*,10*S*,13*R*,14*R*,17*R*)-10,13-dimethyl-3-oxohexadecahydro-1*H*-cyclopenta[a]phenanthren-17-yl) 3,3'-(5-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)-1,3-phenylene)(2*E*,2'*E*)-diacrylate (3l)

Yellow solid, R_f = 0.15 (hexane/ethyl acetate = 5 : 1, V/V). m.p.: 167 – 168 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.7 Hz, 1H), 7.86 (d, J = 2.1 Hz, 2H), 7.81 – 7.77 (m, 2H), 7.71 (t, J = 7.7 Hz, 1H), 7.59 (d, J = 16.0 Hz, 2H), 7.55 – 7.49 (m, 2H), 7.15 (d, J = 8.6 Hz, 1H), 6.99 (s, 1H), 6.45 (dd, J = 16.0, 1.5 Hz, 2H), 4.76 – 4.69 (m, 2H), 2.61 (d, J = 2.7 Hz, 3H), 2.44 – 2.18 (m, 13H), 2.13 – 2.00 (m, 4H), 1.84 – 1.78 (m, 2H), 1.76 – 1.48 (m, 16H), 1.40 – 1.30 (m, 12H), 1.04 (s, 6H), 0.89 (s, 6H).

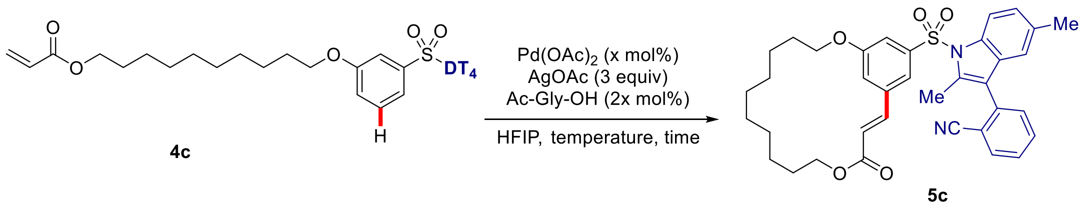
^{13}C NMR (100 MHz, $CDCl_3$) δ 211.92, 166.05, 141.23, 140.43, 136.78, 135.45, 134.20, 134.12, 133.20, 132.73, 131.42, 130.93, 129.75, 128.30, 126.45, 122.08, 120.11, 118.93, 117.86, 114.26, 83.28, 83.26, 53.72, 50.61, 46.61, 44.65, 42.93, 42.91, 38.50, 38.11, 36.87, 35.73, 35.20, 31.23, 28.76, 27.63, 23.60, 21.26, 20.93, 14.60, 12.27, 11.49.

HR-MS (ESI) m/z calcd for $C_{67}H_{78}N_2NaO_8S^+$ [M+Na$^+$] 1093.5371, found 1093.5376.

4 Macrocyclization via Intramolecular *meta*-C–H Olefination

4.1 Optimization of Reaction Conditions

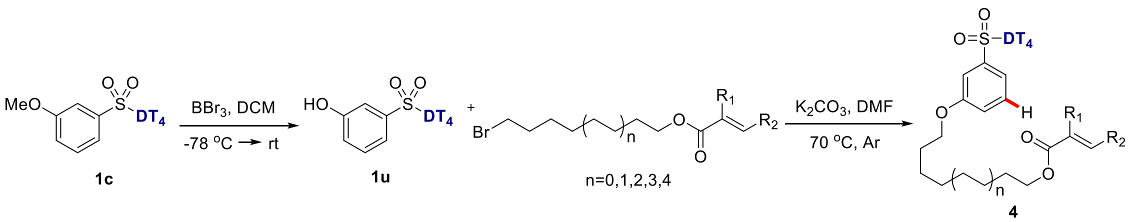
Table S3. Condition screening for Macrocyclization via Intramolecular *meta*-C–H Olefination[a]



entry	time (h)	temperature (°C)	[Pd] amount (mol %)	concentration (mmol/L)	yield (%)
1	0.5	60	10	100	40
2	1.5	60	10	100	52
3	3.0	60	10	100	46
4	6.0	60	10	100	42
5	24	60	10	100	n.d.
6	1.5	70	10	100	trace
7	1.5	80	10	100	n.d.
8	1.5	60	10	50	44
9	1.5	60	10	25	68
10	1.5	60	10	5	58
11	1.5	60	5	25	42
12	1.5	60	2	25	34

[a]Reaction conditions: **4c** (0.05 mmol), $Pd(OAc)_2$ (x mol%), Ac-Gly-OH (2x mol%), oxidant (3 equiv), concentration (mmol/L), temperature (°C), reaction (h), isolated yield.

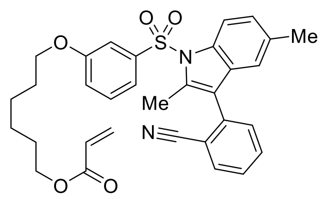
4.2 Synthesis of Macrolactones via Intramolecular *meta*-C–H Olefination



General procedure for preparation of substrates 4. To a solution of **1c** (700 mg, 1.68 mmol) in DCM (20 mL) was added BBr_3 dissolved in DCM (4.2 mL, 4.2 mmol, 1 mol/L), the mixture was stirred overnight from -78 °C to room temperature gradually under argon. After completion of reaction, the reaction was quenched with water (40 mL) and the mixture was then diluted with DCM

(30 mL). The organic layer was separated and the aqueous layer was extracted with DCM (2 x 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulted residue was purified by silica gel column chromatography (eluent: petroleum ether (60 °C–90 °C) /ethyl acetate= 5/1) to give the intermediate **1u** (610 mg, 90.2%).

To a solution of **1u** (200 mg, 0.50 mmol) in DMF (10 mL) was added K_2CO_3 (103 mg, 0.75 mmol) at room temperature under argon. The mixture was stirred for 15 mins and then bromoalkyl acrylate (1.5 equiv) was added to the reaction mixture with stirring overnight at 70 °C. After completion of reaction, the reaction was quenched with water (50 mL) and the mixture was then diluted with ethyl acetate (30 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 x 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulted residue was purified by silica gel column chromatography (eluent: petroleum ether /ethyl acetate= 10/1) to give the desired products **4**. The characterization data of new compounds are shown below:



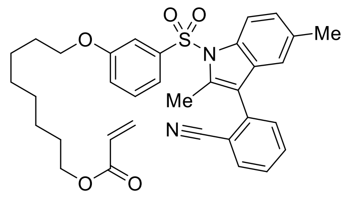
6-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenoxy)hexyl acrylate (4a)

Yield: 91%. White oil, R_f = 0.55 (hexane/ethyl acetate = 10 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.5 Hz, 1H), 7.79 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.68 (td, *J* = 7.7, 1.4 Hz, 1H), 7.52 – 7.47 (m, 2H), 7.37 – 7.27 (m, 3H), 7.12 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.05 – 7.00 (m, 1H), 6.98 (s, 1H), 6.39 (dd, *J* = 17.3, 1.5 Hz, 1H), 6.11 (dd, *J* = 17.3, 10.4 Hz, 1H), 5.80 (dd, *J* = 10.4, 1.5 Hz, 1H), 4.16 (t, *J* = 6.6 Hz, 2H), 3.97 – 3.85 (m, 2H), 2.57 (s, 3H), 2.35 (s, 3H), 1.79 – 1.65 (dt, *J* = 14.1, 7.4 Hz, 4H), 1.52 – 1.39 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.32, 159.39, 139.77, 137.13, 135.45, 134.41, 133.58, 133.35, 132.71, 131.64, 130.55, 130.46, 129.60, 128.59, 128.17, 126.05, 120.81, 119.28, 118.71, 118.39, 117.91, 114.38, 114.16, 111.42, 68.29, 64.50, 28.84, 28.53, 25.69, 25.61, 21.26, 14.26.

HR-MS (ESI) m/z calcd for $C_{32}H_{32}N_2NaO_5S^+$ [M+Na$^+$] 579.1924, found 579.1927.



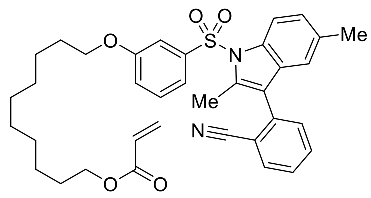
8-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenoxy)octyl acrylate (4b)

Yield: 94%. Yellow oil, R_f = 0.45 (hexane/ethyl acetate = 8 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.36 – 7.28 (m, 3H), 7.13 (d, *J* = 8.6 Hz, 1H), 7.03 (d, *J* = 7.0 Hz, 1H), 6.97 (s, 1H), 6.40 (d, *J* = 17.3 Hz, 1H), 6.12 (dd, *J* = 17.3, 10.4 Hz, 1H), 5.81 (d, *J* = 10.4 Hz, 1H), 4.15 (t, *J* = 6.7 Hz, 2H), 3.96 – 3.85 (m, 2H), 2.57 (s, 3H), 2.36 (s, 3H), 1.70 (dt, *J* = 22.6, 7.0 Hz, 4H), 1.45 – 1.31 (s, 6H), 0.91 – 0.80 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.35, 159.41, 139.76, 137.17, 135.46, 134.42, 133.55, 133.35, 132.66, 131.65, 130.47, 130.44, 129.59, 128.64, 128.13, 126.03, 120.82, 119.23, 118.68, 118.32, 117.90, 114.38, 114.20, 111.43, 68.44, 64.65, 29.19, 29.13, 28.91, 28.59, 25.86, 25.83, 21.26, 14.24.

HR-MS (ESI) m/z calcd for $C_{34}H_{36}N_2NaO_5S^+$ [M+Na$^+$] 607.2237, found 607.2239.



10-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenoxy)decyl acrylate (4c)

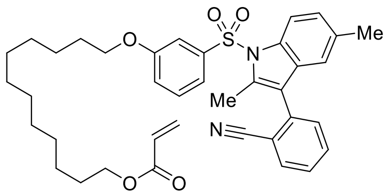
Yield: 88%. White oil, R_f = 0.51 (hexane/ethyl acetate = 9 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 7.7 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.33 – 7.28 (m, 3H), 7.13 (d, *J* = 8.5 Hz, 1H), 7.05 – 7.00 (m, 1H), 6.98 (s, 1H), 6.40 (d, *J* = 17.3 Hz, 1H), 6.12 (dd, *J* = 17.3, 10.4 Hz, 1H), 5.81 (d, *J* = 10.4 Hz, 1H), 4.15 (t, *J* = 6.7 Hz, 2H), 3.90 (q, *J* = 6.1 Hz, 2H), 2.57 (s, 3H), 2.36 (s, 3H), 1.70 (dt, *J* = 22.9, 7.1 Hz, 4H), 1.43 – 1.28 (m, 10H), 0.91 – 0.82 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.38, 159.42, 139.73, 137.16, 135.46, 134.41, 133.56, 133.35, 132.67, 131.65, 130.48, 130.45, 129.58, 128.65, 128.13, 126.04, 120.80, 119.23, 118.68, 118.29,

117.91, 114.38, 114.18, 111.45, 68.50, 64.71, 31.94, 29.43, 29.30, 29.23, 28.94, 28.61, 25.92, 25.89, 21.26, 14.26.

HR-MS (ESI) m/z calcd for $C_{36}H_{40}N_2NaO_5S^+$ [M+Na$^+$] 635.2550, found 635.2555.



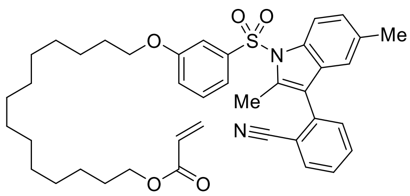
12-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenoxy)dodecyl acrylate (4d)

Yield: 92%. Yellow oil, R_f = 0.44 (hexane/ethyl acetate = 8 : 1, V/V).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.06 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 7.0 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.3 Hz, 2H), 7.34 – 7.27 (m, 3H), 7.12 (d, *J* = 8.6 Hz, 1H), 7.05 – 7.01 (m, 1H), 6.98 (s, 1H), 6.40 (d, *J* = 17.3 Hz, 1H), 6.12 (dd, *J* = 17.3, 10.4 Hz, 1H), 5.81 (d, *J* = 10.3 Hz, 1H), 4.15 (t, *J* = 6.7 Hz, 2H), 3.95 – 3.86 (m, 2H), 2.57 (s, 3H), 2.36 (s, 3H), 1.76 – 1.63 (m, 4H), 1.41 – 1.26 (m, 16H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 166.36, 159.43, 139.75, 137.17, 135.46, 134.43, 133.55, 133.34, 132.66, 131.65, 130.43, 129.59, 128.67, 128.13, 126.03, 120.80, 119.23, 118.68, 118.28, 117.90, 114.39, 114.20, 111.47, 68.53, 64.72, 29.54, 29.52, 29.51, 29.33, 29.25, 28.95, 28.62, 25.93, 25.90, 21.26, 14.24.

HR-MS (ESI) m/z calcd for $C_{38}H_{44}N_2NaO_5S^+$ [M+Na$^+$] 663.2863, found 663.2866.



14-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenoxy)tetradecyl acrylate (4e)

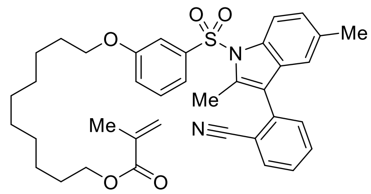
Yield: 86%. Yellow oil, R_f = 0.39 (hexane/ethyl acetate = 10 : 1, V/V).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.06 (d, *J* = 8.5 Hz, 1H), 7.79 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.69 (td, *J* = 7.7, 1.4 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.34 – 7.28 (m, 3H), 7.12 (d, *J* = 8.6 Hz, 1H), 7.03 (dt, *J* =

6.6, 2.5 Hz, 1H), 6.98 (s, 1H), 6.40 (dd, *J* = 17.3, 1.5 Hz, 1H), 6.12 (dd, *J* = 17.3, 10.4 Hz, 1H), 5.81 (dd, *J* = 10.4, 1.5 Hz, 1H), 4.15 (t, *J* = 6.8 Hz, 2H), 3.95– 3.84 (m, 2H), 2.57 (s, 3H), 2.36 (s, 3H), 1.76 – 1.62 (m, 4H), 1.44 – 1.26 (m, 20H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.38, 159.43, 139.73, 137.16, 135.47, 134.42, 133.56, 133.36, 132.68, 131.66, 130.46, 129.59, 128.67, 128.14, 126.04, 120.81, 119.24, 118.69, 118.28, 117.92, 114.39, 114.19, 111.47, 68.53, 64.75, 29.65, 29.61, 29.59, 29.56, 29.54, 29.36, 29.28, 28.96, 28.63, 25.95, 25.92, 21.28, 14.27.

HR-MS (ESI) m/z calcd for $C_{40}H_{48}N_2NaO_5S^+$ [M+Na$^+$] 691.3176, found 691.3178.



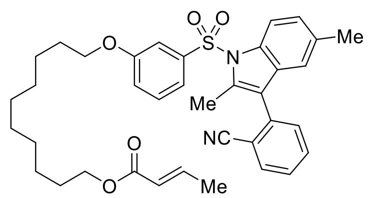
10-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenoxy)decyl methacrylate (4f)

Yield: 80%. Yellow oil, R_f = 0.45 (hexane/ethyl acetate = 8 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.5 Hz, 1H), 7.78 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.68 (td, *J* = 7.7, 1.4 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.35 – 7.27 (m, 3H), 7.12 (d, *J* = 8.6 Hz, 1H), 7.02 (dt, *J* = 7.6, 2.4 Hz, 1H), 6.98 (s, 1H), 6.10 (s, 1H), 5.56 – 5.52 (m, 1H), 4.14 (t, *J* = 6.7 Hz, 2H), 3.95 – 3.84 (m, 2H), 2.57 (s, 3H), 2.35 (s, 3H), 1.94 (s, 3H), 1.70 (ddd, *J* = 20.7, 8.2, 6.4 Hz, 4H), 1.43 – 1.29 (m, 12H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.56, 159.43, 139.73, 137.12, 136.56, 135.45, 134.41, 133.56, 133.35, 132.71, 131.65, 130.46, 129.60, 128.17, 126.05, 125.19, 120.78, 119.26, 118.71, 118.29, 117.93, 114.38, 114.16, 111.47, 68.50, 64.83, 29.73, 29.45, 29.32, 29.25, 28.95, 28.62, 25.99, 25.91, 21.28, 18.37, 14.29.

HR-MS (ESI) m/z calcd for $C_{37}H_{42}N_2NaO_5S^+$ [M+Na$^+$] 649.2707, found 649.2711.



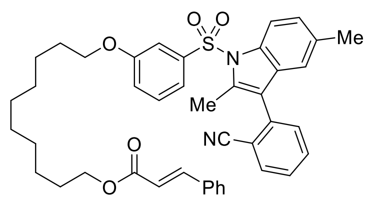
10-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenoxy)decyl (*E*)-but-2-enoate (4g)

Yield: 95%. White oil, R_f = 0.38 (hexane/ethyl acetate = 8 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 7.7 Hz, 1H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.33 – 7.27 (m, 3H), 7.13 (d, *J* = 8.6 Hz, 1H), 7.05 – 7.01 (m, 1H), 7.00 – 6.92 (m, 2H), 5.85 (d, *J* = 15.6 Hz, 1H), 4.11 (t, *J* = 6.7 Hz, 2H), 3.95 – 3.86 (m, 2H), 2.57 (s, 3H), 2.36 (s, 3H), 1.87 (d, *J* = 6.9 Hz, 3H), 1.68 (dt, *J* = 31.5, 7.2 Hz, 4H), 1.41 – 1.29 (m, 12H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.71, 159.43, 144.42, 139.74, 137.17, 135.47, 134.42, 133.56, 133.35, 132.67, 131.66, 130.45, 129.59, 128.14, 126.04, 122.83, 120.81, 119.23, 118.69, 118.30, 117.91, 114.39, 114.19, 111.46, 68.51, 64.33, 29.45, 29.31, 29.26, 28.95, 28.70, 25.96, 25.90, 21.28, 17.98, 14.27.

HR-MS (ESI) m/z calcd for $C_{37}H_{42}N_2NaO_5S^+$ [M+Na$^+$] 649.2707, found 649.2709.



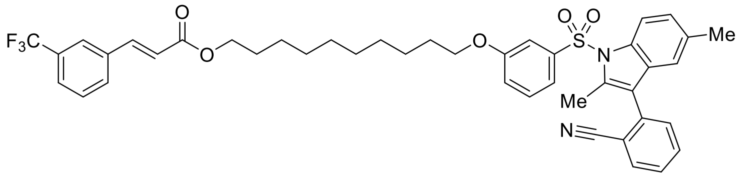
10-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenoxy)decyl cinnamate (4h)

Yield: 87%. Yellow oil, R_f = 0.36 (hexane/ethyl acetate = 6 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.6 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.72 – 7.64 (m, 2H), 7.54 – 7.47 (m, 4H), 7.41 – 7.35 (m, 3H), 7.34 – 7.28 (d, *J* = 7.4 Hz, 3H), 7.12 (d, *J* = 8.6 Hz, 1H), 7.02 (d, *J* = 7.1 Hz, 1H), 6.97 (s, 1H), 6.44 (d, *J* = 16.0 Hz, 1H), 4.20 (t, *J* = 6.7 Hz, 2H), 3.94 – 3.85 (m, 2H), 2.56 (s, 3H), 2.35 (s, 3H), 1.71 (q, *J* = 7.2 Hz, 4H), 1.43 – 1.30 (m, 12H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.11, 159.43, 144.58, 139.75, 137.17, 135.46, 134.48, 134.43, 133.55, 133.35, 132.66, 131.65, 130.45, 130.24, 129.59, 128.89, 128.13, 128.06, 126.04, 120.81, 119.23, 118.68, 118.31, 117.90, 114.39, 114.20, 111.47, 68.51, 64.72, 29.45, 29.31, 29.27, 28.95, 28.74, 25.98, 25.90, 21.26, 14.25.

HR-MS (ESI) m/z calcd for $C_{42}H_{44}N_2NaO_5S^+$ [M+Na$^+$] 711.2863, found 711.2866.



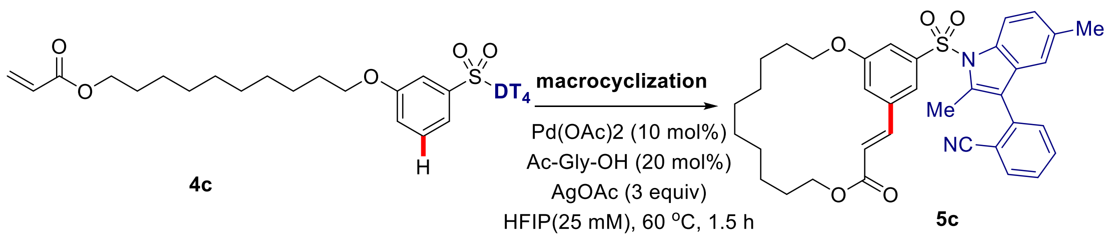
10-(3-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenoxy)decyl (*E*)-3-(3-(trifluoromethyl)phenyl)acrylate (4i)

Yield: 92%. White oil, R_f = 0.30 (hexane/ethyl acetate = 7 : 1, V/V).

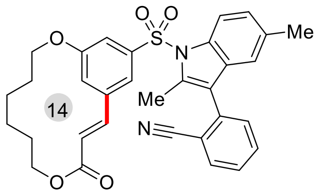
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.5 Hz, 1H), 7.81 – 7.75 (m, 2H), 7.73 – 7.66 (m, 3H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.47 (m, 3H), 7.35 – 7.27 (m, 3H), 7.12 (d, *J* = 8.5 Hz, 1H), 7.02 (dt, *J* = 7.0, 2.3 Hz, 1H), 6.98 (s, 1H), 6.51 (d, *J* = 16.0 Hz, 1H), 4.22 (t, *J* = 6.7 Hz, 2H), 3.95 – 3.84 (m, 2H), 2.57 (s, 3H), 2.35 (s, 3H), 1.77 – 1.66 (m, 4H), 1.45 – 1.30 (m, 12H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.54, 159.40, 142.72, 139.71, 137.13, 135.44, 135.24, 134.39, 133.54, 133.33, 132.66, 131.60 (d, J_{C-F} = 5.9 Hz), 131.07, 130.44, 129.57, 129.45, 128.12, 126.60 (q, J_{C-F} = 4.0 Hz), 126.02, 125.13, 124.54 (q, J_{C-F} = 3.8 Hz), 122.43, 120.77, 120.26, 119.22, 118.67, 118.28, 117.90, 114.36, 114.16, 111.44, 68.47, 64.96, 29.44, 29.30, 29.25, 28.93, 28.68, 25.95, 25.89, 21.25, 14.25.

HR-MS (ESI) m/z calcd for $C_{43}H_{43}F_3N_2NaO_5S^+$ [M+Na$^+$] 779.2737, found 779.2738.



General procedure for synthesis of macrolactones via intramolecular *meta*-C–H olefination. To a 15-mL Schlenk sealed tube equipped with a Teflon cap was charged with **4c** (30.6 mg, 0.05 mmol, 1.0 equiv), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 10 mol%), Ac-Gly-OH (1.2 mg, 0.01 mmol, 20 mol%), AgOAc (25.0 mg, 0.15 mmol, 3.0 equiv) in turn. Hexafluoro-2-propanol (HFIP, 2 mL) was then added to the mixture along the inside wall of the tube via a syringe as follows. The reaction tube was then capped and then placed onto a preheated (60 °C) heating block. The reaction was stirred for 1.5 h and cooled to room temperature. The crude reaction mixture was diluted with EtOAc (5 mL) and filtered through a short pad of Celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by preparative thin layer chromatography (eluent: hexane/ethyl acetate= 8/1) to provide the olefinated products **5c** (20.8 mg, 68%). Isolatedyields for compounds **5** were reported in the Scheme 4 of main text. The characterization data of new compounds are shown below:



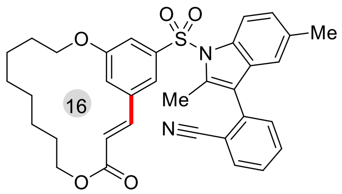
(*E*)-2-(2,5-dimethyl-1-((10-oxo-2,9-dioxa-1(1,3)-benzenacyclododecaphan-11-en-1^5-yl)sulfonyl)-1*H*-indol-3-yl)benzonitrile (5a)

White oil, R_f = 0.44 (hexane/ethyl acetate = 8 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.6 Hz, 1H), 7.80 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.70 (td, *J* = 7.7, 1.4 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 2H), 7.34 (s, 1H), 7.19 (s, 1H), 7.15 – 7.09 (m, 2H), 6.97 (d, *J* = 12.7 Hz, 2H), 5.97 (d, *J* = 12.5 Hz, 1H), 4.24 (t, *J* = 5.7 Hz, 2H), 4.06 – 3.97 (m, 2H), 2.59 (s, 3H), 2.35 (s, 3H), 1.40 – 1.22 (m, 8H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.44, 158.77, 139.47, 138.79, 138.52, 137.03, 135.58, 134.27, 133.75, 133.35, 132.74, 131.56, 129.66, 128.23, 126.17, 123.50, 122.63, 119.65, 118.75, 118.56, 118.01, 114.42, 114.38, 114.16, 69.61, 64.33, 27.33, 26.74, 24.29, 24.08, 21.26, 14.50.

HR-MS (ESI) m/z calcd for $C_{32}H_{30}N_2NaO_5S^+$ [M+Na$^+$] 577.1768, found 577.1772.



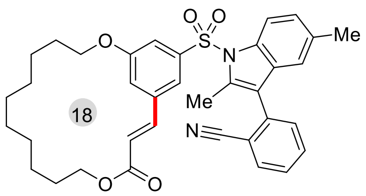
(*E*)-2-(2,5-dimethyl-1-((12-oxo-2,11-dioxa-1(1,3)-benzenacyclotetradecaphan-13-en-1^5-yl)sulfonyl)-1*H*-indol-3-yl)benzonitrile (5b)

White oil, R_f = 0.50 (hexane/ethyl acetate = 8 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.6 Hz, 1H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.70 (t, *J* = 7.9 Hz, 1H), 7.54 – 7.48 (dt, *J* = 7.5, 3.6 Hz, 2H), 7.27 (s, 1H), 7.18 (s, 1H), 7.12 (d, *J* = 8.7 Hz, 1H), 7.07 (s, 1H), 6.99 (s, 1H), 6.94 (d, *J* = 12.3 Hz, 1H), 5.99 (d, *J* = 12.4 Hz, 1H), 4.10 (t, *J* = 5.9 Hz, 2H), 3.97 (q, J = 5.5 Hz, 2H), 2.60 (s, 3H), 2.35 (s, 3H), 1.73 – 1.68 (m, 2H), 1.45 – 1.36 (m, 2H), 1.32 – 1.24 (m, 4H), 1.20 (t, J = 7.4 Hz, 2H), 1.07 – 0.97 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.23, 158.34, 139.59, 139.36, 138.63, 137.06, 135.52, 134.22, 133.70, 133.37, 132.71, 131.60, 129.59, 128.19, 126.15, 123.28, 121.62, 119.42, 118.76, 118.43, 117.97, 114.30, 114.16, 111.14, 67.81, 64.52, 27.80, 26.18, 26.04, 25.93, 23.99, 22.69, 21.27, 14.48.

HR-MS (ESI) m/z calcd for $C_{34}H_{34}N_2NaO_5S^+$ [M+Na$^+$] 605.2081, found 605.2084.



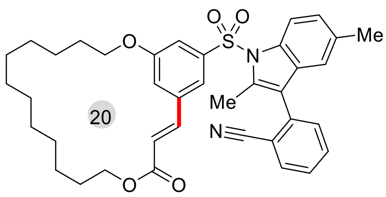
(*E*)-2-(2,5-dimethyl-1-((14-oxo-2,13-dioxa-1(1,3)-benzenacyclohexadecaphan-15-en-1^5-yl)sulfonyl)-1*H*-indol-3-yl)benzonitrile (5c)

Yellow oil, R_f = 0.38 (hexane/ethyl acetate = 8 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.6 Hz, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.69 (t, J = 7.6 Hz, 1H), 7.58 – 7.47 (m, 3H), 7.41 (s, 1H), 7.37 (s, 1H), 7.15 (d, J = 8.6 Hz, 1H), 7.11 (s, 1H), 6.98 (s, 1H), 6.37 (d, J = 16.1 Hz, 1H), 4.22 (t, J = 5.2 Hz, 2H), 4.15 (t, J = 8.3 Hz, 2H), 2.56 (s, 3H), 2.36 (s, 3H), 1.78 – 1.69 (m, 4H), 1.56 – 1.44 (m, 6H), 1.42 – 1.34 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.69, 158.97, 142.36, 141.05, 137.16, 137.03, 135.29, 134.27, 133.79, 133.32, 132.69, 131.58, 129.60, 128.20, 126.31, 121.52, 119.55, 118.79, 117.87, 117.56, 116.74, 115.49, 114.31, 114.26, 67.58, 66.59, 30.36, 29.74, 29.63, 28.70, 28.57, 26.40, 25.53, 24.61, 21.28, 14.32.

HR-MS (ESI) m/z calcd for $C_{36}H_{38}N_2NaO_5S^+$ [M+Na$^+$] 633.2394, found 633.2399.



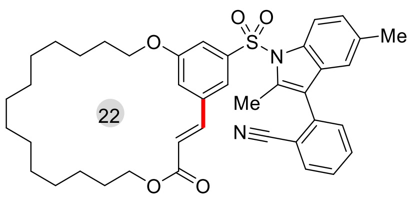
(*E*)-2-(2,5-dimethyl-1-((16-oxo-2,15-dioxa-1(1,3)-benzenacyclooctadecaphan-17-en-1^5-yl)sulfonyl)-1*H*-indol-3-yl)benzonitrile (5d)

White oil, R_f = 0.33 (hexane/ethyl acetate = 10 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.5 Hz, 1H), 7.79 (dd, J = 8.1, 1.4 Hz, 1H), 7.69 (td, J = 7.7, 1.4 Hz, 1H), 7.57 – 7.47 (m, 3H), 7.44 (s, 1H), 7.37 (t, J = 2.0 Hz, 1H), 7.15 (d, J = 8.6 Hz, 1H), 7.09 (s, 1H), 6.98 (s, 1H), 6.35 (d, J = 16.0 Hz, 1H), 4.21 (dd, J = 6.1, 4.3 Hz, 2H), 4.13 (t, J = 7.8 Hz, 2H), 2.57 (s, 3H), 2.36 (s, 3H), 1.69 (dt, J = 10.6, 7.1 Hz, 4H), 1.52 – 1.45 (m, 2H), 1.43 – 1.28 (m, 14H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.92, 159.32, 142.23, 140.93, 137.18, 137.04, 135.31, 134.28, 133.79, 133.30, 132.66, 131.58, 129.61, 128.18, 126.30, 121.17, 119.56, 118.78, 117.84, 117.59, 117.31, 116.32, 114.31, 114.28, 68.77, 65.41, 29.66, 29.34, 28.86, 28.71, 28.43, 28.28, 27.37, 26.88, 26.05, 24.88, 21.26, 14.32.

HR-MS (ESI) m/z calcd for $C_{38}H_{42}N_2NaO_5S^+$ [M+Na$^+$] 661.2707, found 661.2708.



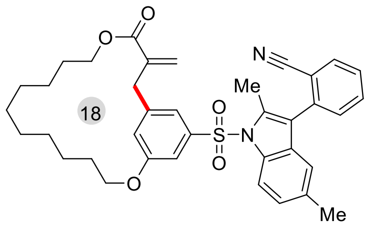
(*E*)-2-(2,5-dimethyl-1-((18-oxo-2,17-dioxa-1(1,3)-benzenacycloicosaphan-19-en-1^5-yl)sulfonyl)-1*H*-indol-3-yl)benzonitrile (5e)

Yellow oil, R_f = 0.45 (hexane/ethyl acetate = 10 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.6 Hz, 1H), 7.79 (d, J = 8.6 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.57 – 7.48 (m, 3H), 7.46 (s, 1H), 7.30 (s, 1H), 7.17 – 7.11 (m, 2H), 6.99 (s, 1H), 6.36 (d, J = 16.0 Hz, 1H), 4.23 (t, J = 5.3 Hz, 2H), 4.08 – 4.00 (m, 2H), 2.59 (s, 3H), 2.36 (s, 3H), 1.78 – 1.64 (m, 4H), 1.49 – 1.23 (m, 20H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.01, 159.66, 142.07, 140.68, 137.08, 137.00, 135.35, 134.23, 133.81, 133.30, 132.66, 131.57, 129.63, 128.19, 126.26, 121.23, 119.58, 119.08, 118.81, 117.96, 117.87, 114.27, 114.23, 113.73, 69.22, 65.15, 29.84, 29.74, 29.71, 28.99, 28.88, 28.48, 28.02, 27.83, 27.39, 26.06, 25.62, 21.26, 14.41.

HR-MS (ESI) m/z calcd for $C_{40}H_{46}N_2NaO_5S^+$ [M+Na$^+$] 689.3020, found 689.3023.



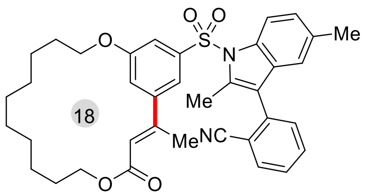
2-(2,5-dimethyl-1-((15-methylene-14-oxo-2,13-dioxa-1(1,3)-benzenacyclohexadecaphane-1^5-yl)sulfonyl)-1*H*-indol-3-yl)benzonitrile (5f)

Yellow oil, R_f = 0.38 (hexane/ethyl acetate = 8 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.5 Hz, 1H), 7.80 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.70 (td, *J* = 7.7, 1.4 Hz, 1H), 7.53 – 7.48 (m, 2H), 7.18 (s, 1H), 7.14 (t, *J* = 2.2 Hz, 1H), 7.11 (dd, *J* = 8.6, 1.7 Hz, 1H), 6.98 (s, 1H), 6.90 – 6.87 (m, 1H), 6.30 (d, *J* = 1.5 Hz, 1H), 5.68 (d, *J* = 1.4 Hz, 1H), 4.06 – 3.94 (m, 4H), 3.60 (s, 2H), 2.59 (s, 3H), 2.35 (s, 3H), 1.73 – 1.66 (m, 2H), 1.48 – 1.39 (m, 2H), 1.34 – 1.25 (m, 4H), 1.22 – 0.96 (m, 8H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.37, 159.23, 142.89, 139.55, 138.28, 137.17, 135.51, 134.23, 133.47, 133.34, 132.65, 131.67, 129.49, 128.34, 128.09, 126.00, 121.24, 119.13, 118.62, 118.24, 117.94, 114.29, 114.13, 108.60, 67.32, 64.60, 38.03, 28.42, 27.69, 27.38, 27.22, 27.09, 26.25, 25.21, 23.42, 21.26, 14.37.

HR-MS (ESI) m/z calcd for $C_{37}H_{40}N_2NaO_5S^+$ [M+Na$^+$] 647.2550, found 647.2554.



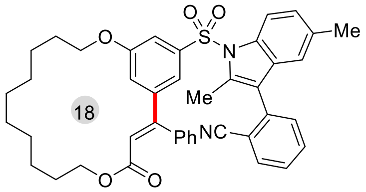
(*E*)-2-(2,5-dimethyl-1-((16-methyl-14-oxo-2,13-dioxa-1(1,3)-benzenacyclohexadecaphan-15-en-1^5-yl)sulfonyl)-1*H*-indol-3-yl)benzonitrile (5g)

Yellow oil, R_f = 0.43 (hexane/ethyl acetate = 10 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.6 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.69 (td, *J* = 7.7, 1.4 Hz, 1H), 7.52 – 7.47 (m, 2H), 7.43 (t, *J* = 1.6 Hz, 1H), 7.33 (t, *J* = 2.0 Hz, 1H), 7.15 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.12 – 7.09 (m, 1H), 6.98 (s, 1H), 6.08 (d, *J* = 1.5 Hz, 1H), 4.21 – 4.11 (m, 4H), 2.55 (s, 3H), 2.49 (d, *J* = 1.3 Hz, 3H), 2.37 (s, 3H), 1.77 – 1.68 (m, 4H), 1.52 – 1.32 (m, 12H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.01, 158.78, 153.66, 144.42, 140.55, 137.06, 135.25, 134.38, 133.72, 133.34, 132.64, 131.61, 129.61, 128.15, 126.20, 119.43, 118.76, 118.72, 117.79, 116.98, 115.90, 114.40, 114.37, 114.23, 67.98, 65.90, 29.86, 28.94, 28.84, 28.75, 28.26, 26.80, 26.29, 24.79, 21.26, 17.00, 14.24.

HR-MS (ESI) m/z calcd for $C_{37}H_{40}N_2NaO_5S^+$ [M+Na$^+$] 647.2550, found 647.2555.



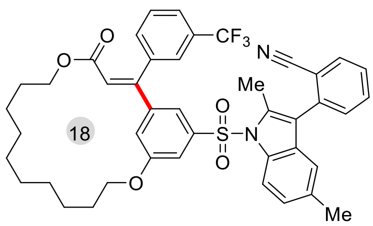
(*E*)-2-(2,5-dimethyl-1-((14-oxo-16-phenyl-2,13-dioxa-1(1,3)-benzenacyclohexadecaphan-15-en-1^5-yl)sulfonyl)-1*H*-indol-3-yl)benzonitrile (5h)

Yellow oil, R_f = 0.35 (hexane/ethyl acetate = 10 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.6 Hz, 1H), 7.79 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.69 (td, *J* = 7.7, 1.4 Hz, 1H), 7.51 (td, *J* = 7.7, 1.2 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.32 – 7.27 (m, 3H), 7.15 – 7.08 (m, 2H), 7.01 (dd, *J* = 8.7, 1.7 Hz, 1H), 6.92 (s, 1H), 6.86 (t, *J* = 1.6 Hz, 1H), 6.28 (s, 1H), 4.24 – 4.18 (m, 2H), 4.15 – 4.06 (m, 2H), 2.38 (s, 3H), 2.36 (s, 3H), 1.80 (dt, *J* = 10.9, 6.6 Hz, 2H), 1.66 (s, 2H), 1.50 – 1.34 (m, 12H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.78, 158.91, 155.81, 143.71, 140.28, 137.14, 136.53, 134.99, 134.18, 133.47, 133.36, 132.61, 131.68, 129.41, 128.83, 128.13, 127.96, 126.26, 119.41, 119.28, 118.64, 118.52, 117.75, 117.21, 114.99, 114.18, 68.12, 66.05, 29.86, 29.02, 28.88, 28.78, 28.13, 26.84, 26.43, 24.83, 21.30, 13.89.

HR-MS (ESI) m/z calcd for $C_{42}H_{42}N_2NaO_5S^+$ [M+Na$^+$] 709.2707, found 709.2710.



(*E*)-2-(2,5-dimethyl-1-((14-oxo-16-(3-(trifluoromethyl)phenyl)-2,13-dioxa-1(1,3)-benzenacyclohexadecaphan-15-en-1^5-yl)sulfonyl)-1*H*-indol-3-yl)benzonitrile (5i)

White oil, R_f = 0.42 (hexane/ethyl acetate = 7 : 1, V/V).

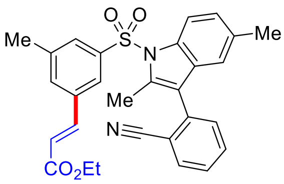
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.6 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.68 (td, *J* = 7.7, 1.4 Hz, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.50 (td, *J* = 7.7, 1.3 Hz, 1H), 7.46 – 7.35 (m, 4H), 7.32 – 7.27 (m, 2H), 6.99 (dd, *J* = 8.6, 1.8 Hz, 1H), 6.91 (s, 1H), 6.71 (s, 1H), 6.34 (s, 1H), 4.25 – 4.18 (m, 2H), 4.14 – 4.04 (m, 2H), 2.37 (s, 3H), 2.32 (s, 3H), 1.80 (dq, *J* = 12.4, 6.2 Hz, 2H), 1.66 (s, 2H), 1.51 – 1.34 (m, 12H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.37, 159.07, 154.08, 142.94, 140.66, 137.28, 137.00, 134.88, 134.28, 133.60, 133.29, 132.78, 132.64, 131.53, 130.44, 130.11, 129.42, 128.43, 128.17, 126.28 (d, $J_{C\text{-}F}$= 3.6 Hz), 126.23, 125.43 (d, $J_{C\text{-}F}$= 3.9 Hz), 119.70, 119.44, 118.76, 118.65, 117.74, 117.53, 114.86, 114.20, 114.08, 68.12, 66.30, 29.88, 29.00, 28.89, 28.81, 28.14, 26.82, 26.35, 24.82, 21.24, 13.81.

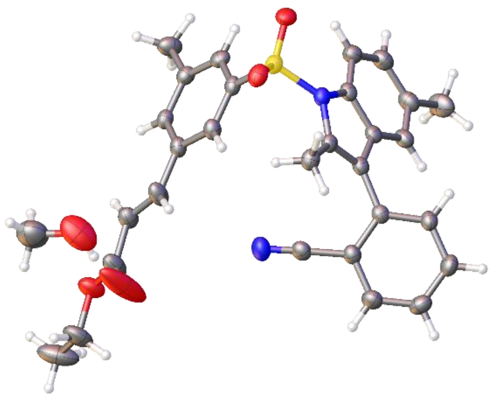
HR-MS (ESI) m/z calcd for $C_{43}H_{41}F_3N_2NaO_5S^+$ [M+Na$^+$] 777.2580, found 777.2586.

5 Crystal Data for Compound 2d

The single crystals of compound **2d** suitable for X-ray diffraction analysis were obtained by recrystallization in methanol. Crystallographic parameters for compound **2d** is available free of charge from the Cambridge Crystallographic Data Centre (CCDC) (www.ccdc.cam.ac.uk/data_request/cif) under **CCDC** 2142546.



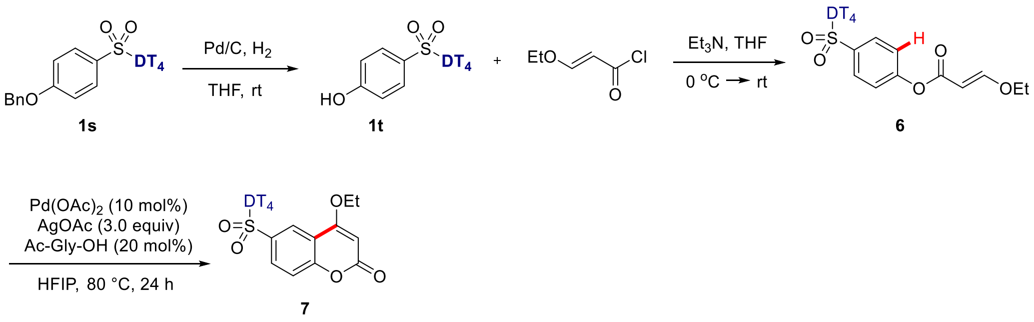
2d



Crystal data for compound **2d**: $C_{29.5}H_{28}N_2O_{4.5}S$, Monoclinic, $P2_1/c$, a = 21.8311 (11) Å, b = 8.2255 (4) Å, c = 29.1754 (14) Å, α = γ = 90°, β = 93.759 (4)°, Mo *K*α radiation, λ = 0.71073 Å, μ = 0.164 mm^{-1}. V = 5227.8 (4) $Å^3$, Z = 8, F(000) = 2168

6 Synthetic Utility of *meta*-C–H Functionalization.

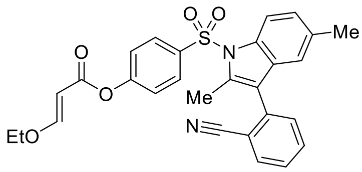
6.1 Synthesis of Coumarins via Intramolecular *meta*-C–H Olefination



General procedure for synthesis of coumarins via *meta*-C–H olefination. To a solution of **1s** (500 mg, 1.02 mmol) in THF (15 mL) was added 10% Pd/C (50 mg), the mixture was stirred for 24 h at room temperature under 1 atm of hydrogen pressure. The crude reaction mixture was filtered through a short pad of celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography (silica gel) using petroleum ether (60 °C–90°C)/EtOAc = 5 : 1 as the eluent to provide the white products **1t** (294 mg, 72%).

To a solution of **1t** (200 mg, 0.5 mmol) in THF (10 mL) was added triethylamine (101 mg, 1.0 mmol) under ice bath (0 °C). The mixture was stirred for 15 mins and then 3-Ethoxyacryloyl chloride (1.2 equiv) was added to the reaction mixture with stirring. After completion of reaction, the reaction was quenched with water (40 mL) and the mixture was then diluted with ethyl acetate (30 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 x 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulted residue was purified by silica gel column chromatography (eluent: petroleum ether /ethyl acetate= 5/1) to give the desired product **6** (230 mg, 92%).

To a 15-mL Schlenk sealed tube equipped with a Teflon cap was charged with **6** (0.1 mmol, 1.0 equiv), $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 10 mol%), Ac-Gly-OH (2.3 mg, 0.02 mmol, 20 mol%), AgOAc (0.3 mmol, 3.0 equiv) in turn. Hexafluoro-2-propanol (HFIP, 1.5 mL) was then added to the mixture along the inside wall of the tube via a syringe as follows. The reaction tube was then capped and stirred at room temperature for 15 minutes. The tube was then placed onto a preheated (80 °C) heating block. The reaction was stirred for 24 h and cooled to room temperature. The crude reaction mixture was diluted with EtOAc (5 mL) and filtered through a short pad of Celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by preparative thin layer chromatography using hexane/ ethyl acetate as the eluent to provide the olefinated products **7** (22.9 mg, 46%). The characterization data of new compounds are shown below:



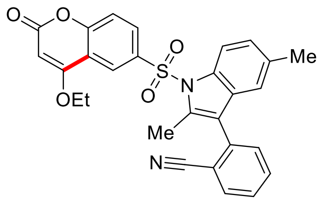
4-((3-(2-cyanophenyl)-2,5-dimethyl-1*H*-indol-1-yl)sulfonyl)phenyl (*E*)-3-ethoxyacrylate (6)

White oil, R_f = 0.39 (hexane/ethyl acetate = 5 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.5 Hz, 1H), 7.85 – 7.79 (m, 3H), 7.75 – 7.67 (m, 2H), 7.53 – 7.48 (m, 2H), 7.23 – 7.18 (m, 2H), 7.12 (d, *J* = 8.6 Hz, 1H), 6.97 (s, 1H), 5.31 (d, *J* = 12.6 Hz, 1H), 3.98 (q, *J* = 7.1 Hz, 2H), 2.57 (s, 3H), 2.35 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.18, 164.83, 154.93, 137.11, 135.40, 134.36, 133.73, 133.32, 132.69, 131.62, 129.70, 128.17, 128.09, 126.20, 122.72, 119.60, 118.75, 117.97, 114.40, 114.22, 95.11, 67.49, 21.25, 14.41, 14.32.

HR-MS (ESI) m/z calcd for $C_{28}H_{24}N_2NaO_5S^+$ [M+Na^+] 523.1298, found 523.1300.



2-(1-((4-ethoxy-2-oxo-2*H*-chromen-6-yl)sulfonyl)-2,5-dimethyl-1*H*-indol-3-yl)benzonitrile (7)

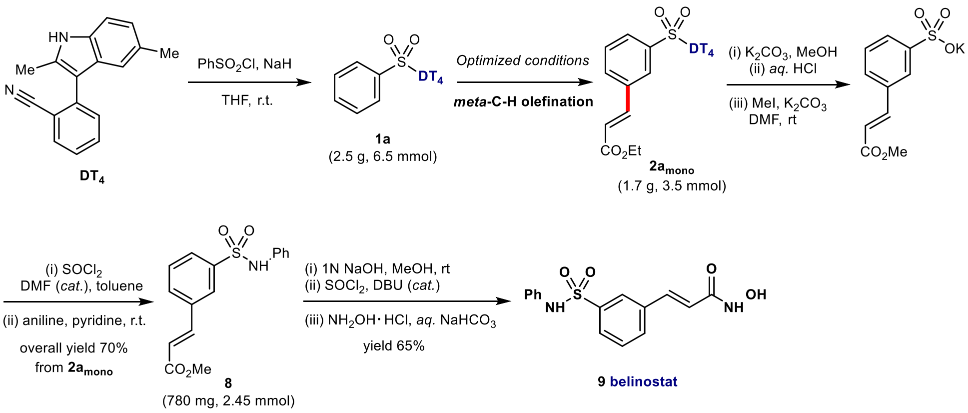
Yellow oil, R_f = 0.31 (hexane/ethyl acetate =10 : 1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 2.4 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.83 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.79 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.70 (td, *J* = 7.7, 1.4 Hz, 1H), 7.54 – 7.48 (m, 2H), 7.30 (d, *J* = 8.8 Hz, 1H), 7.15 (d, *J* = 8.6 Hz, 1H), 6.97 (s, 1H), 5.67 (s, 1H), 4.19 (q, *J* = 7.0 Hz, 2H), 2.57 (s, 3H), 2.36 (s, 3H), 1.54 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.27, 161.43, 156.19, 136.85, 135.34, 134.35, 134.23, 134.07, 133.33, 132.74, 131.48, 129.87, 129.69, 128.32, 126.32, 122.78, 120.16, 118.91, 118.39, 117.85, 116.30, 114.44, 114.20, 91.43, 65.75, 21.26, 14.39, 14.00.

HR-MS (ESI) m/z calcd for $C_{28}H_{22}N_2NaO_5S^+$ [M+Na^+] 521.1142, found 521.1148.

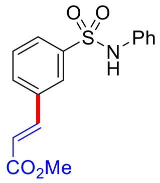
6.2 Synthesis of HDAC-inhibitory Belinostat



Compound **1a** (2.5 g, 6.5 mmol) was prepared from $PhSO_2Cl$ in 90% yield according the abovementioned procedure, which was subsequently subjected to *meta*-C-H olefination using the optimized conditions ($Pd(OAc)_2$ (10 mol%), ethyl acrylate (1.5 eq), AgOAc (3 eq), Ac-Gly-OH (20 mol%), HFIP, 80 °C, 6 h). The olefinated product **2a$_{mono}$** was obtained in 54% yield (1.7 g, 3.5 mmol), together with the corresponding diolefinated product **2a$_{di}$** in 38% yield.

To a solution of above product **2a$_{mono}$** (1.7 g, 3.5 mmol) in methanol (50 ml) was added K_2CO_3 (0.97 g, 7.0 mmol, 2.0 equiv), the reaction mixture was then stirred at 70 °C overnight. The solvent was removed in vacuo and the mixture was partitioned between water (50 mL) and ethyl acetate (50 mL). The water layer was adjusted to pH 2–3 with 1 M HCl (*aq.*), and water then removed in vacuo. Next, to a solution of the resulted residue in DMF (20 mL) was added K_2CO_3 (1.45 g, 10.5 mmol, 3.0 equiv) and MeI (0.44 mL, 7 mmol, 2.0 equiv) dropwise at room temperature. The reaction mixture was stirred overnight at room temperature. After that, the volatile solvent was removed in vacuo to give the crude intermediated salt, which was directly used in next reaction without further purification.

Subsequently, the chlorination and amidation procedure described by Helgea and coworker[7] was adopted, and the intermediate **8** afforded in an overall yield of 70% (780 mg, 2.45 mmol) from **2a$_{mono}$**. And then, hydroxamic acid moiety was successfully incorporated to provide the target drug belinostat in an isolated yield of 65% from compound **8**. Finally, belinostat **9** was synthesized in a five-step sequence with an overall yield of 22% from the inexpensively readily available $PhSO_2Cl$.



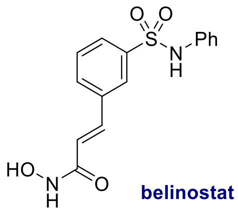
Methyl (*E*)-3-(3-(*N*-phenylsulfamoyl)phenyl)acrylate (8)

Yellow solid, R_f = 0.21 (hexane/ ethyl acetate = 4 :1, V/V). m.p.: 144 – 145 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.66 – 7.58 (m, 2H), 7.45 (t, J = 7.8 Hz, 1H), 7.31 (s, 1H), 7.23 (d, J = 7.2 Hz, 2H), 7.11 (d, J = 8.6 Hz, 3H), 6.42 (d, J = 16.0 Hz, 1H), 3.81 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.89, 142.62, 139.98, 136.16, 135.51, 132.24, 129.70, 129.45, 128.40, 126.35, 125.80, 121.99, 120.28, 52.01.

HR-MS (ESI) m/z calcd for $C_{16}H_{15}NNaO_4S^+$ [M+Na$^+$] 340.0614 found 340.0617.



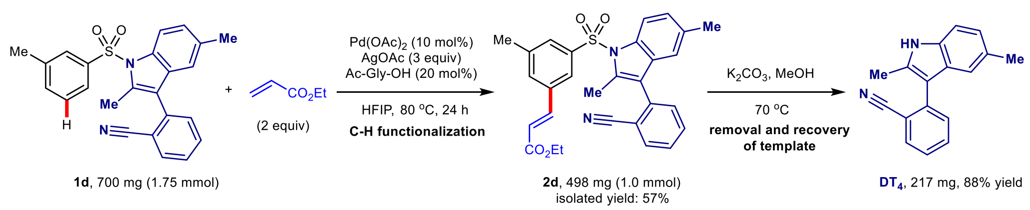
(*E*)-*N*-hydroxy-3-(3-(*N*-phenylsulfamoyl)phenyl)acrylamide (9)

Light orange solid, m.p.: 172 – 173 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.75−10.42 (m, 2H), 9.15 (s, 1H), 7.92 (s, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.71 (d, J = 7.8 Hz, 1H), 7.56 (d, J = 7.8 Hz, 1H),7.47 (d, J = 15.8 Hz, 1H), 7.24 (m, 2H), 7.10−7.01 (m, 3H), 6.51 (d, J = 15.8 Hz, 1H).

HR-MS (ESI) m/z calcd for $C_{15}H_{14}N_2NaO_4S^+$ [M+Na$^+$] 341.0566 found 341.0569.

6.3 Scale-up Reaction, Removal and Recovery of Template

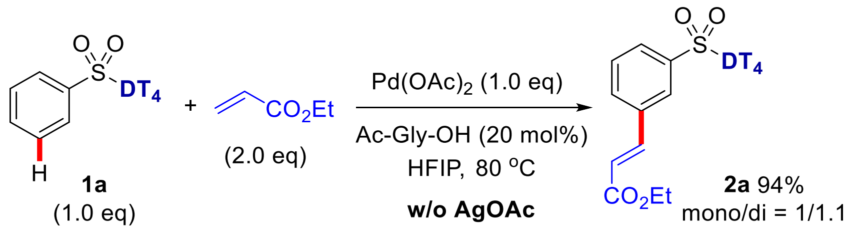


To a solution of **1d** (700 mg, 1.75 mmol) in HFIP (25 mL) was added $Pd(OAc)_2$ (39.3 mg, 0.175 mmol, 10 mol%), Ac-Gly-OH (41.0 mg, 0.35 mmol, 20 mol%), AgOAc (5.25 mmol, 3.0 equiv) in turn. The resulted mixture was stirred at room temperature for 15 mins. Then, ethyl acrylate (0.38 mL, 3.5 mmol, 2.0 equiv) was added dropwise by syringe. The reaction mixture was then stirred at 80 °C for 24 h. After cooled to room temperature, the mixture was filtered through a short pad of Celite, and the filtrate was concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography (eluent: petroleum ether (60 °C–90 °C) /ethyl acetate = 10/1) to provide the white solid **2d** (498 mg, 57%).

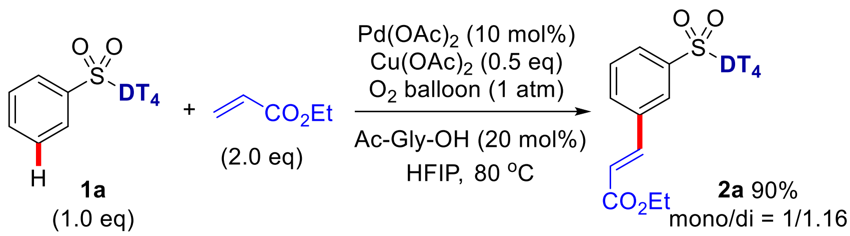
The previously described procedure[6] was adopted for removal of template **DT$_4$**: To a solution of above product **2d** (498 mg, 1.0 mmol) in methanol (15 ml) was added K_2CO_3 (276 mg, 2.0 mmol), the reaction mixture was then stirred at 70 °C overnight. After completion of reaction, the mixture was cooled to room temperature and concentrated under reduced pressure. Then the residue was partitioned between ethyl acetate (30 mL) and water (30 mL). The organic layer was separated off and the aqueous layer was extracted with ethyl acetate twice times (2 × 20 mL). The organic phase was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The resulted residue was purified by silica gel column chromatography (eluent: petroleum ether (60 °C–90 °C)/ethyl acetate = 20/1) to provide the white solid **DT$_4$** (217 mg, 88%).

7 Mechanistic Study

7.1 Pd-Catalyzed *meta*-C–H Olefination under the Variable Conditions

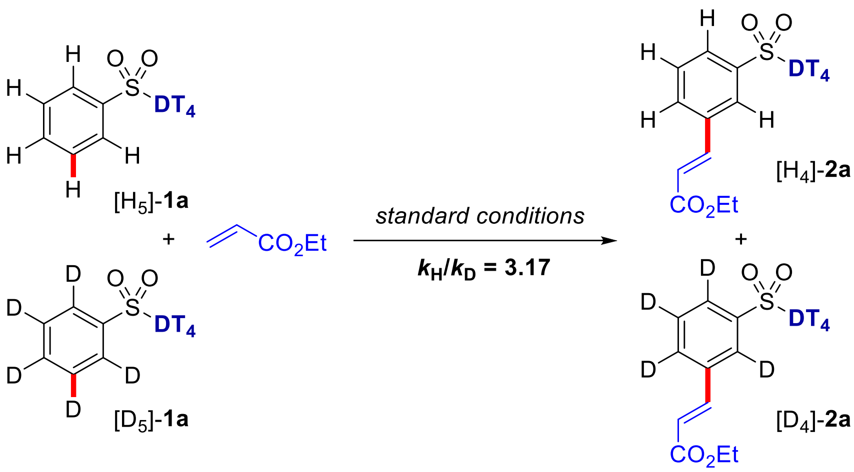


General procedure for *meta*-C-H olefination without silver acetate. To a 15-mL Schlenk sealed tube equipped with a Teflon cap was charged with **1a** (38.65 mg, 0.1 mmol), $Pd(OAc)_2$ (22.45 mg, 0.1 mmol, 1.0 equiv), Ac-Gly-OH (2.34 mg, 0.02 mmol, 20 mol%) in turn. Hexafluoro-2-propanol (HFIP, 1.5 mL) was added to the mixture along the inside wall of the tube via a syringe, followed by ethyl acrylate (21.74 µL, 0.2mmol). The reaction tube was then capped and stirred at room temperature for 15 minutes. The tube was then placed onto a preheated (80 °C) heating block. The reaction was stirred for 24 h and cooled to room temperature. The crude reaction mixture was diluted with EtOAc (5 mL) and filtered through a short pad of Celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by preparative thin layer chromatography using petroleum ether (60 °C–90 °C)/EtOAc = 10 : 1 as the eluent to provide the olefinated products **2a** (yield = 94%, mono : di = 1 : 1.1).



General procedure for *meta*-C-H olefination using catalytic $Cu(OAc)_2$ and O_2 as the oxidants. To a 15-mL Schlenk sealed tube equipped with a Teflon cap was charged with **1a** (38.65 mg, 0.1 mmol), $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 10 mol%), Ac-Gly-OH (2.3 mg, 0.02 mmol, 20 mol%), $Cu(OAc)_2$ (9.1 mg, 0.05 mmol, 0.5 equiv) in turn. Hexafluoro-2-propanol (HFIP, 1.5 mL) was added to the mixture along the inside wall of the tube via a syringe, followed by ethyl acrylate (21.74 µL, 0.2mmol). The reaction tube was capped, then evacuated briefly under vacuum and charged with O_2 (1 atm, balloon, × 3). The tube was stirred at room temperature for 15 minutes, and then placed onto a preheated (80 °C) heating block. The reaction was stirred for 24 h and cooled to room temperature. The crude reaction mixture was diluted with EtOAc (5 mL) and filtered through a short pad of Celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by preparative thin layer chromatography using petroleum ether (60 ºC–90 ºC)/EtOAc = 10 : 1 as the eluent to provide the olefinated products **2a** (yield = 90%, mono : di = 1 : 1.16).

7.2 Kinetic Isotope Effect Experiment



General procedure for kinetic isotope effect experiment. To a 15-mL Schlenk sealed tube equipped with a Teflon cap was charged with [H_5]-**1a** (19.32 mg, 0.05 mmol), [D_5]-**1a** (19.58 mg, 0.05 mmol), $Pd(OAc)_2$ (2.3 mg, 0.01 mmol), Ac-Gly-OH (2.34 mg, 0.02 mmol), AgOAc (50.07 mg, 0.3 mmol) in turn. Hexafluoro-2-propanol (HFIP, 1.5 mL) was added to the mixture along the inside wall of the tube via a syringe, followed by ethyl acrylate (21.74 μL, 0.2mmol). The reaction tube was then capped and stirred at room temperature for 15 minutes. The tube was then placed onto a preheated (80 ºC) heating block. The reaction was stirred for 0.5 h and cooled to room temperature. The crude reaction mixture was diluted with EtOAc (5 mL) and filtered through a short pad of Celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by preparative thin layer chromatography using petroleum ether (60 ºC–90 ºC)/EtOAc = 10 : 1 as the eluent to provide the olefinated products [H_4/D_4]-**2a** and analyzed for its isotopic distribution. The KIE value for the *meta*-C–H olefination reaction was measured to be $\boldsymbol{k_H/k_D = 3.17}$ by ^{1}H NMR analysis of the products.

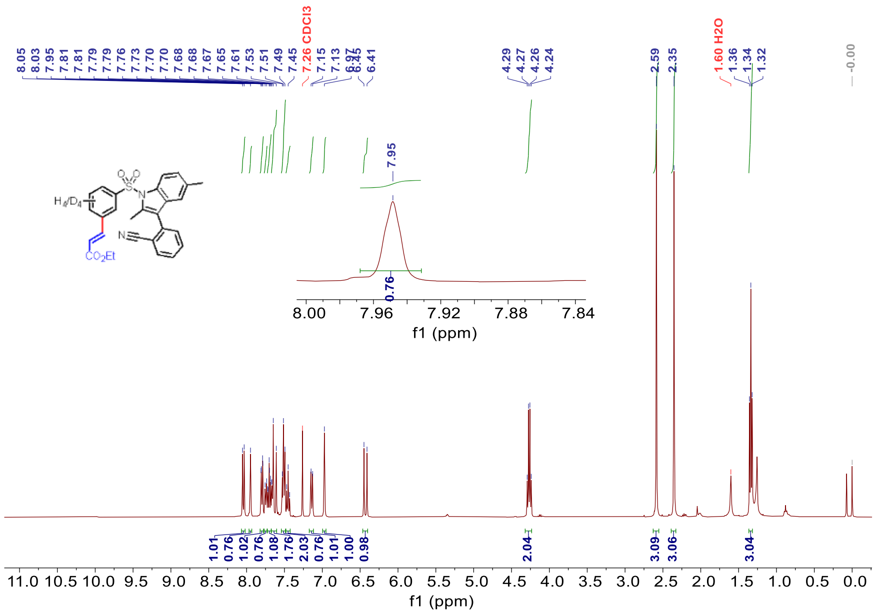
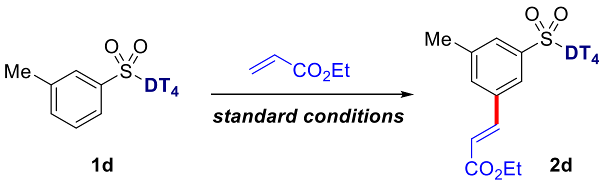


Fig. S1 ^{1}H NMR spectra of [H_4/D_4]-**2a**

7.3 Kinetic Studies on the Reaction Orders



General procedure for order measurements. To a 15-mL Schlenk sealed tube equipped with a Teflon cap was charged with **1d,** $Pd(OAc)_2$ (1.12 mg, 0.005 mmol), Ac-Gly-OH (1.17 mg, 0.01 mmol), AgOAc (25.04 mg, 0.15 mmol) in turn. Hexafluoro-2-propanol (HFIP, 1 mL) was added to the mixture along the inside wall of the tube via a syringe, followed by ethyl acrylate. The reaction tube was then capped and placed onto a preheated (80 ^{o}C) heating block. The reaction was stirred for a definite amount of time and cooled to room temperature. The crude reaction mixture was diluted with EtOAc (5 mL) and filtered through a short pad of Celite. The filtrate was concentrated *in vacuo*, diluted with 0.5 mL $CDCl_3$, and equivalent amount of $C_2H_2Cl_4$ was added to the reaction mixture. All yields were determined by ^{1}H NMR analysis using $C_2H_2Cl_4$ as an internal standard.

Table S4. Kinetic Studies to Determine the Reaction Order

Entry	**1d** (mmol)	Ethyl Acrylate (mmol)	$Pd(OAc)_2$ (mmol)	Ac-Gly-OH (mmol)	AgOAc (mmol)	HFIP (mL)
1	0.1	0.1	10 mol%	20 mol%	0.3	1
2	0.05	0.1	10 mol%	20 mol%	0.3	1
3	0.025	0.1	10 mol%	20 mol%	0.3	1
4	0.0125	0.1	10 mol%	20 mol%	0.3	1
5	0.05	0.2	10 mol%	20 mol%	0.3	1
6	0.05	0.3	10 mol%	20 mol%	0.3	1
7	0.05	0.4	10 mol%	20 mol%	0.3	1

Determination of order with respect to substrate:[8] **Comparing Entry 1, Entry 2, Entry 3 and Entry 4**

Entry 1: 0.1 mmol

$x_1 = 0.6606$, $y_1 = 0.0920$

$x_2 = 5.1251$, $y_2 = 0.0752$

$dx = x_2 - x_1 = (5.1251 - 0.6606) = 4.4645$

$dy = y_2 - y_1 = (0.0752 - 0.0920) = -0.0168$

$R_1 = dy/dx = -0.0168/4.4645 = -0.0038$

Entry 2: 0.05 mmol

$X_1 = 1.7057$, $Y_1 = 0.0459$

$X_2 = 5.4894$, $Y_2 = 0.0400$

$Dx = X_2 - X_1 = (5.4894 - 1.7057) = 3.7837$

$Dy = Y_2 - Y_1 = (0.0400 - 0.0459) = -0.0059$

$R_2 = Dy/Dx = -0.0059/3.7837 = -0.0016$

Entry 3: 0.025 mmol

$x_1' = 0.8108$, $y_1' = 0.0238$

$x_2' = 7.3173$, $y_2' = 0.0189$

$dx' = x_2' - x_1' = (7.3173 - 0.8108) = 6.5065$

$dy' = y_2' - y_1' = (0.0189 - 0.0238) = -0.0049$

$R_3 = dy'/dx' = -0.0049/6.5065 = -0.00075$

Entry 4: 0.0125 mmol

X_1' = 0.8588, Y_1' = 0.0122

X_2' = 4.4504, Y_2' = 0.0110

Dx' = X_2' - X_1' = (4.4504 - 0.8588) = 3.5916

Dy' = Y_2' - Y_1' = (0.0110 - 0.0122) = -0.0012

R_4 = Dy'/Dx' = -0.0012/3.5916 = -0.00033

We know

Rate = dy/dx= k[substrate]^a[olefin]^b

Now, R_1/R_2 ={dy/dx}$_{entry1}$/{DY/DX}$_{entry2}$ = {k[substrate]$^a_{entry1}$ [olefin]$^b_{entry1}$}/{k[substrate]$^a_{entry2}$ [olefin]$^b_{entry2}$}

At t=0; [olefin] $_{entry1}$= [olefin] $_{entry2}$

⇨R_1/R_2 = [substrate] $^a_{entry1}$/[substrate] $^a_{entry2}$

⇨-0.0038/-0.0016= [substrate] $^a_{entry1}$/[substrate] $^a_{entry2}$

⇨2.38 = [substrate] $^a_{entry1}$/[substrate] $^a_{entry2}$

At t=0; [substrate] $^a_{entry1}$/[substrate] $^a_{entry2}$ = [0.1/0.05]^a = 2^a

So, 2.38 = 2^a

log(2.38) = alog(2)

0.3766 = a*0.3010

So, a = 1.25

R_2/R_3 ={Dy/Dx}$_{entry2}$/{dy'/dx'}$_{entry3}$ = {k[substrate]$^a_{entry2}$ [olefin]$^b_{entry2}$}/{k[substrate]$^a_{entry3}$ [olefin]$^b_{entry3}$}

At t=0; [olefin] $_{entry2}$= [olefin] $_{entry3}$

⇨R_2/R_3 = [substrate] $^a_{entry2}$/[substrate] $^a_{entry3}$

⇨-0.0016/-0.00075= [substrate] $^a_{entry2}$/[substrate] $^a_{entry3}$

⇨2.13 = [substrate] $^a_{entry2}$/[substrate] $^a_{entry3}$

At t=0; [substrate] $^a_{entry2}$/[substrate] $^a_{entry3}$ = [0.05/0.025]^a = 2^a

So, 2.13 = 2^a

log(2.13) = alog(2)

0.3284 = a*0.3010

So, a = 1.09

$R_3/R_4 = \{dy'/dx'\}_{entry3}/\{Dy'/Dx'\}_{entry4} = \{k[substrate]^a_{entry3}\ [olefin]^b_{entry3}\}/\{k[substrate]^a_{entry4}\ [olefin]^b_{entry4}\}$

At t=0; $[olefin]_{entry3} = [olefin]_{entry4}$

⇨ $R_3/R_4 = [substrate]^a_{entry3}/[substrate]^a_{entry4}$

⇨ $-0.00075/-0.00033 = [substrate]^a_{entry3}/[substrate]^a_{entry4}$

⇨ $2.27 = [substrate]^a_{entry3}/[substrate]^a_{entry4}$

At t=0; $[substrate]^a_{entry3}/[substrate]^a_{entry4} = [0.025/0.0125]^a = 2^a$

So, $2.27 = 2^a$

$\log(2.27) = a\log(2)$

$0.3560 = a*0.3010$

So, a = 1.18

Which indicates that the reaction rate with respect to substrate is **one**, and the C–H activation step is evidently the rate-limiting step in the overall reactions.

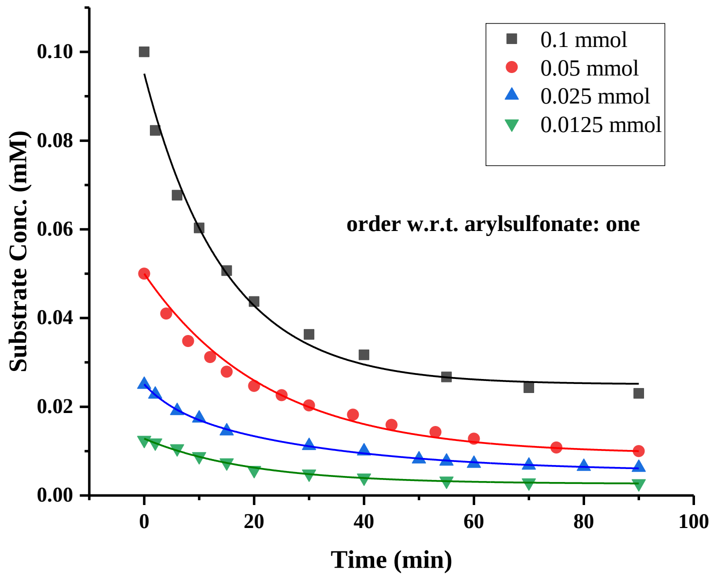


Fig. S2 Order determination with respect to substrate.

Determination of order with respect to olefin: Comparing Entry 2, Entry 5, Entry 6 and

Entry 7

From Entry 2 we have seen that

$R_2 = Dy/Dx = -0.0059/3.7837 = -0.0016$

From Entry 5 :

$x_1'' = 1.1891$, $y_1'' = 0.0455$

$x_2'' = 3.6516$, $y_2''= 0.0415$

$dx'' = x_2'' - x_1'' = (3.6516 – 1.1891) = 2.4625$

$dy'' = y_2'' - y_1'' = (0.0415 - 0.0455) = -0.004$

$R_5 = dy''/dx'' = -0.004/2.4625 = -0.0016$

From Entry 6 :

$X_1'' = 1.5515$, $Y_1'' = 0.0463$

$X_2'' = 4.8648$, $Y_2''= 0.0409$

$Dx'' = X_2'' - X_1'' = (4.8648 – 1.5515) = 3.3133$

$Dy'' = Y_2'' - Y_1'' = (0.0409 - 0.0463) = -0.0054$

$R_6 = Dy''/Dx'' = -0.0054/3.3133 = -0.0016$

From Entry 7 :

$x_1''' = 1.2122$, $y_1''' = 0.0471$

$x_2''' = 4.9649$, $y_2''' = 0.0410$

$dx''' = x_2''' - x_1''' = (4.9649 – 1.2122) = 3.7527$

$dy''' = y_2''' - y_1''' = (0.0410 - 0.0471) = -0.0061$

$R_7 = dy'''/dx''' = -0.0061/3.7527 = -0.0016$

So slope of Entry 2, Entry 5, Entry 6 and Entry 7 is same following the same route to calculate the order with respect to olefin;

Rate = $dy/dx= k[substrate]^a[olefin]^b$

Now, $R_5/R_2 =\{dy''/dx''\}_{entry5}/\{Dy/Dx\}_{entry2} = \{k[substrate]^a_{entry5}\ [olefin]^b_{entry5}\}/\{k[substrate]^a_{entry2}\ [olefin]^b_{entry2}\}$

At t=0; $[substrate]_{entry5}= [substrate]_{entry2}$

⇨ $R_5/R_2 = [olefin]^b_{entry5}/[olefin]^b_{entry2}$

⇨ $-0.0016/-0.0016= [olefin]^b_{entry5}/[olefin]^b_{entry2}$

⇨ $1 = [olefin]^b_{entry5}/[olefin]^b_{entry2}$

At t=0; $[olefin]^b_{entry5}/[olefin]^b_{entry2} = 2^b$

So, $1 = 2^b$

log(1) = blog(2)

0 = b*0.3010

So, b = 0

R_6/R_2 ={Dy''/Dx''}$_{entry6}$/{Dy/Dx}$_{entry2}$ = $\{k[substrate]^a_{entry6}\ [olefin]^b_{entry6}\}/\{k[substrate]^a_{entry2}\ [olefin]^b_{entry2}\}$

At t=0; $[substrate]_{entry6} = [substrate]_{entry2}$

⇨ $R_6/R_2 = [olefin]^b_{entry6}/[olefin]^b_{entry2}$

⇨ -0.0016/-0.0016= $[olefin]^b_{entry6}/[olefin]^b_{entry2}$

⇨ $1 = [olefin]^b_{entry6}/[olefin]^b_{entry2}$

At t=0; $[olefin]^b_{entry6}/[olefin]^b_{entry2} = 3^b$

So, $1 = 3^b$

log(1) = blog(3)

0 = b*0.4771

So, b = 0

R_7/R_2 ={dy'''/dx'''}$_{entry7}$/{Dy/Dx}$_{entry2}$ = $\{k[substrate]^a_{entry7}\ [olefin]^b_{entry7}\}/\{k[substrate]^a_{entry2}\ [olefin]^b_{entry2}\}$

At t=0; $[substrate]_{entry7} = [substrate]_{entry2}$

⇨ $R_7/R_2 = [olefin]^b_{entry7}/[olefin]^b_{entry2}$

⇨ -0.0016/-0.0016= $[olefin]^b_{entry7}/[olefin]^b_{entry2}$

⇨ $1 = [olefin]^b_{entry7}/[olefin]^b_{entry2}$

At t=0; $[olefin]^b_{entry7}/[olefin]^b_{entry2} = 4^b$

So, $1 = 4^b$

log(1) = blog(4)

0 = b*0.6021

So, b = 0

Which indicates that the reaction rate with respect to olefin is **zero**, i.e. the rate is independent on the amount of olefin.

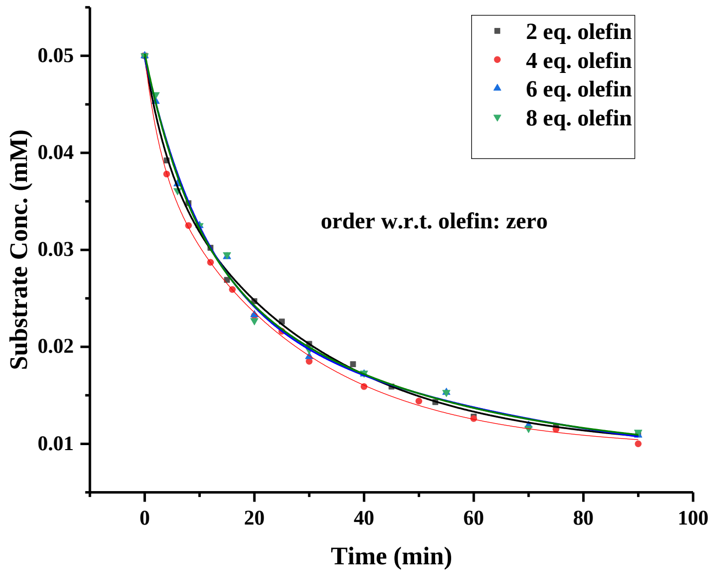
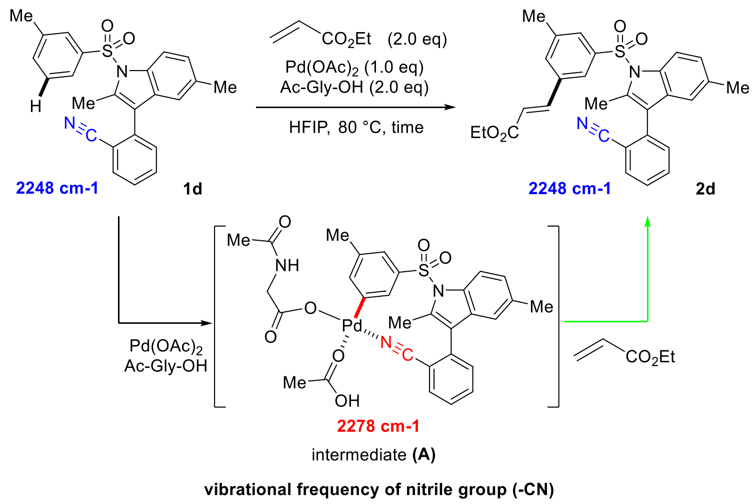


Fig. S3 Order determination with respect to olefin.

7.4 *In situ* FTIR experiments



Ceneral procedure for *in situ* FTIR experiments. Initially, the IR probe was inserted to a 15-mL two necked Schlenk sealed tube to subtract the air background, followed by 3 mL HFIP was charged to the reaction vessel, in order to subtract the solvent background. And then, aryl sulfonate **1d** (400.5 mg, 1 mmol), whose absorbance is at peak 2248 cm^{-1}, was added to the HFIP in the tube. When its absorbance intensity value tended to stabilized, $Pd(OAc)_2$ (224.5 mg, 1 mmol, 1.0 equiv) and Ac-Gly-OH (234.2 mg, 2 mmol, 2.0 equiv) were then added to the mixture at 1074 s, aryl sulfonate **1d** was consumed promptly and a new intermediate (**A**) generated (absorbance at peak 2278 cm^{-1}) during no more than 30 minutes. Subsequently, after the introduction of ethyl acrylate (0.22 mL, 2 mmol, 2.0 equiv) at 2649s, the absorbance at peak 2278 cm^{-1} subsided instantly, accompanied by the rapid formation of C–H olefination products **2d** (also absorbance peak at 2248 cm^{-1}).

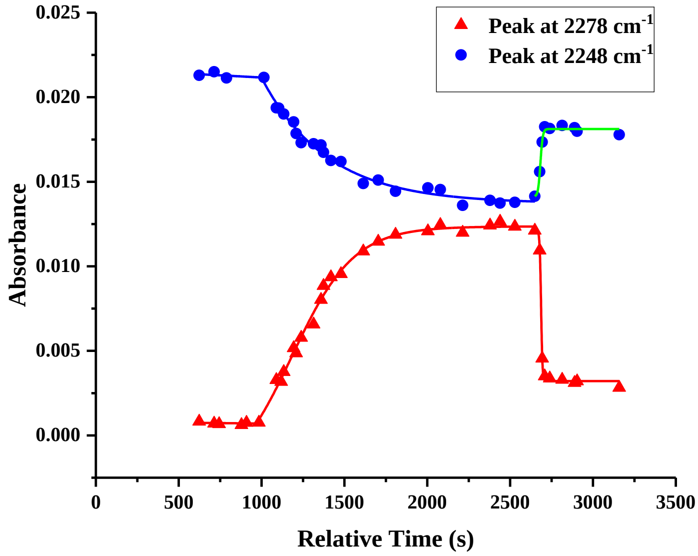
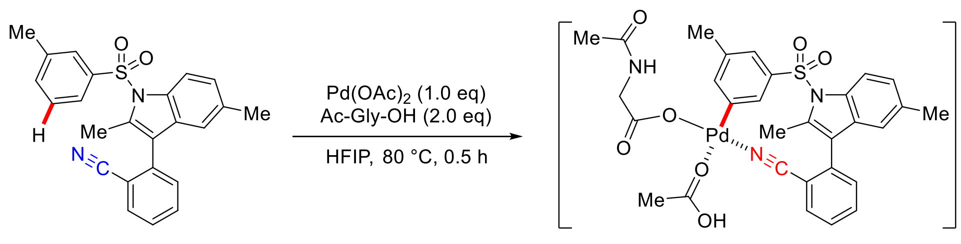


Fig. S4 *In situ* IR reaction kinetic profiles

7.5 ESI-MS analysis



General procedure for synthesis of intermediate (A). To a 15-mL Schlenk sealed tube equipped with a Teflon cap was charged with **1d** (40.05 mg, 0.1 mmol), $Pd(OAc)_2$ (22.45 mg, 0.1 mmol), Ac-Gly-OH (23.42 mg, 0.2 mmol) in turn. Hexafluoro-2-propanol (HFIP, 1.5 mL) was added to the mixture along the inside wall of the tube via a syringe. The reaction tube was then capped and placed onto a preheated (80 °C) heating block. The reaction was stirred for 0.5 h and cooled to room temperature. The crude reaction mixture was diluted with EtOAc (5 mL) and filtered through a short pad of Celite. The filtrate was concentrated in vacuo, and the resulting residue was then recorded the ESI-MS.

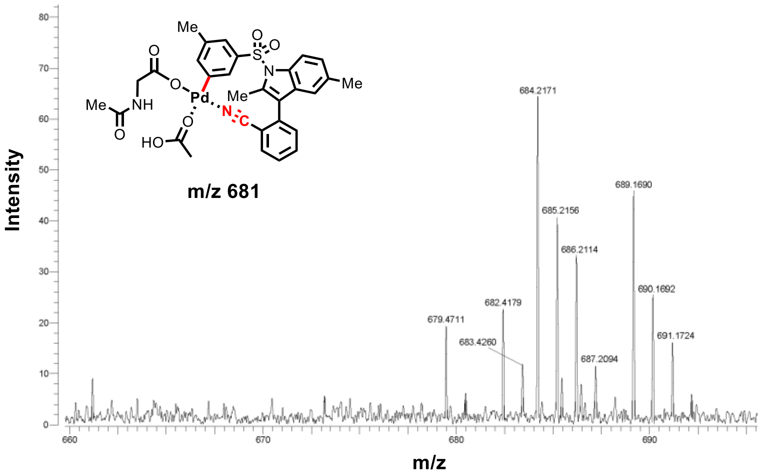
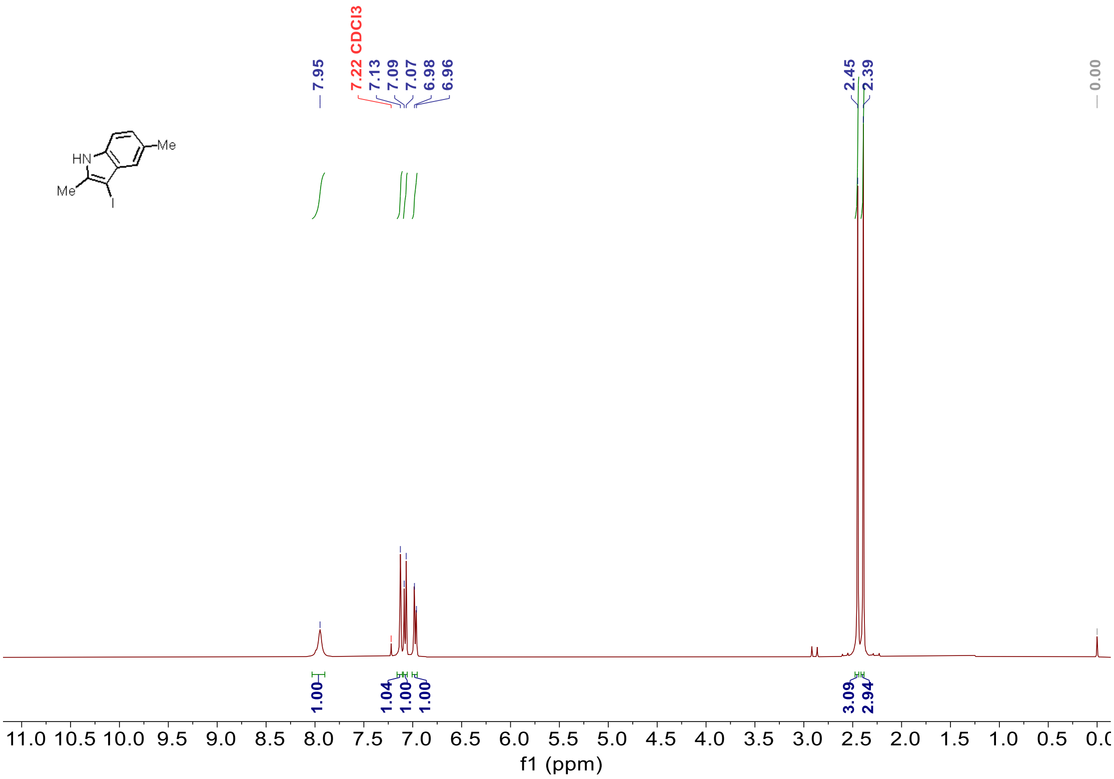


Fig. S5 ESI-MS analysis to detect the **PdL$_n$-arene** complex with substrate **1d**

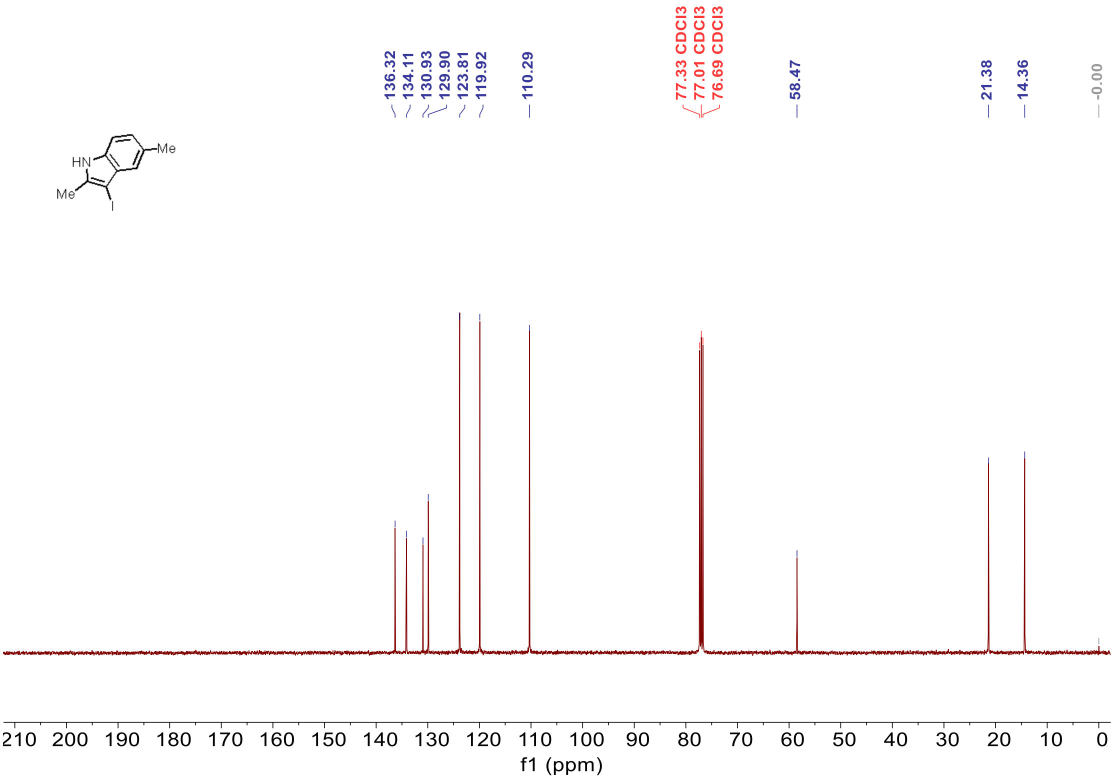
8 Reference

1. A. Mandal, S. M. Mandal, S. Jana, S. S. Bag, A. K. Das, A. Basak, *Tetrahedron*. **2018**, *74*, 3543.
2. M. G. N. Russell, R. W. Carling, L. J. Street, D. J. Hallett, S. Goodacre, E. Mezzogori, M. Reader, S. M. Cook, F. A. Bromidge, R. Newman, A. J. Smith, K. A. Wafford, G. R. Marshall, D. S. Reynolds, R. Dias, P. Ferris, J. Stanley, R. Lincoln, S. J. Tye, W. F. A. Sheppard, B. Sohal, A. Pike, M. Dominguez, J. R. Atack, J. L. Castro, *J. Med. Chem*. **2006**, *49*, 1235.
3. X. Zhou, Y. Luo, L. Kong, Y. Xu, G. Zheng, Y. Lan, X. Li, *ACS Catalysis*. **2017**, *7*, 7296.
4. G. Li, Y. Yan, P. Zhang, X. Xu, Z. Jin, *ACS Catalysis*. **2021**, *11*, 10460.
5. J. Xu, J. Chen, F. Gao, S. Xie, X. Xu, Z. Jin, J.-Q. Yu, *J. Am. Chem. Soc*. **2019**, *141*, 1903.
6. T. C. Leboho, J. P. Michael, W. A. L. van Otterlo, S. F. van Vuuren, C. B. de Koning, *Bioorg Med Chem Lett*, **2009**, *19*, 4948.
7. H. A. Reisch, P. Leeming, P. S. Raje, *PCT Int. Appl.* **2009**, WO2009040517.
8. U. Dutta, A. Modak, B. Bhaskararao, M. Bera, S. Bag, A. Mondal, D. W. Lupton, R. B. Sunoj, D. Maiti, *ACS Catal.* **2017**, *7*, 3162.

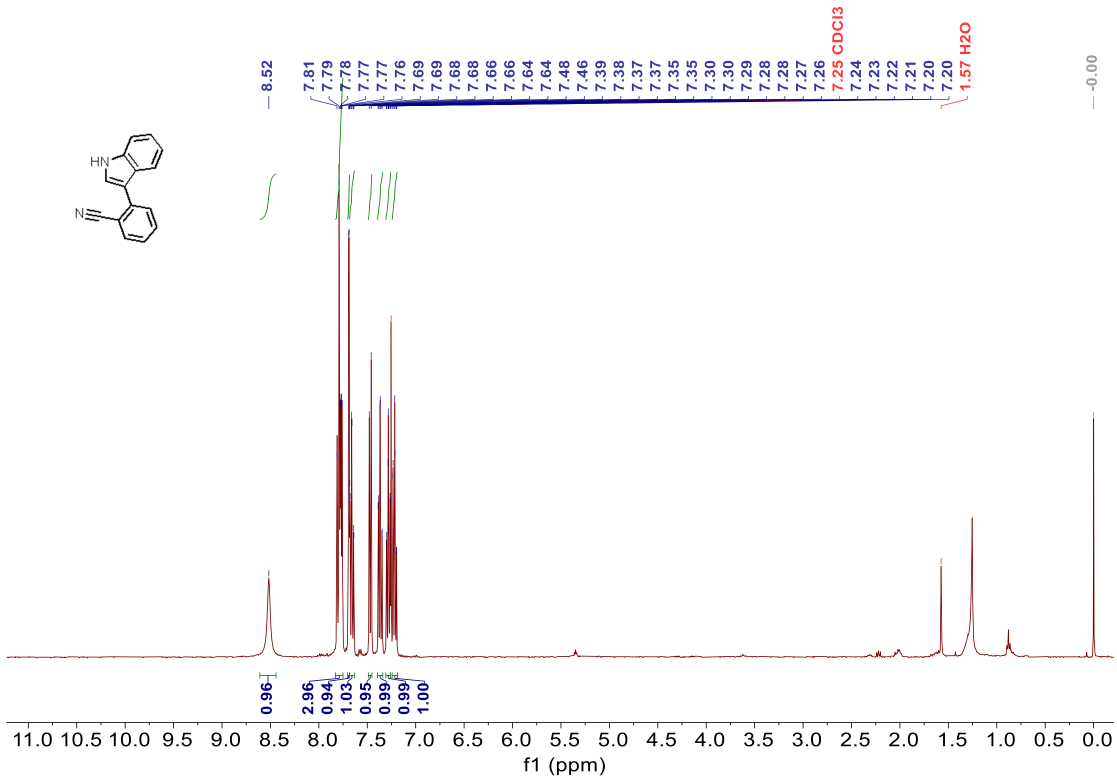
NMR Spectra Data for All New Compounds



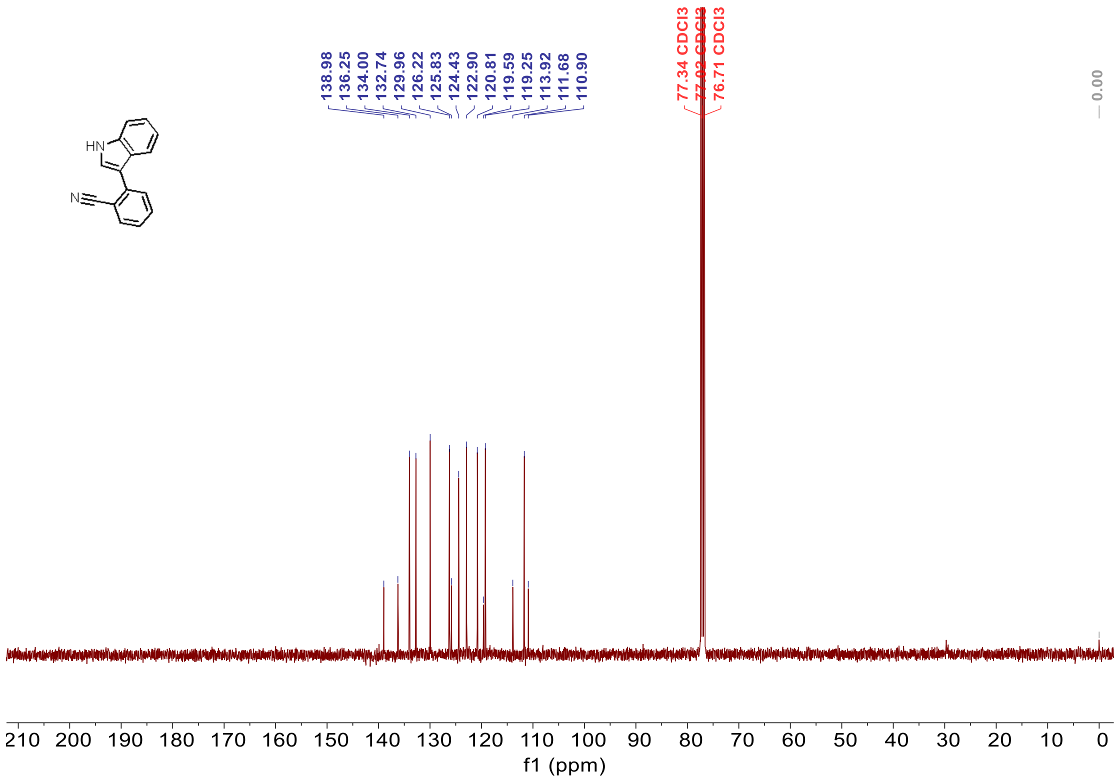
[1]H NMR spectra of **3-iodo-2,5-dimethyl-1H-indole**



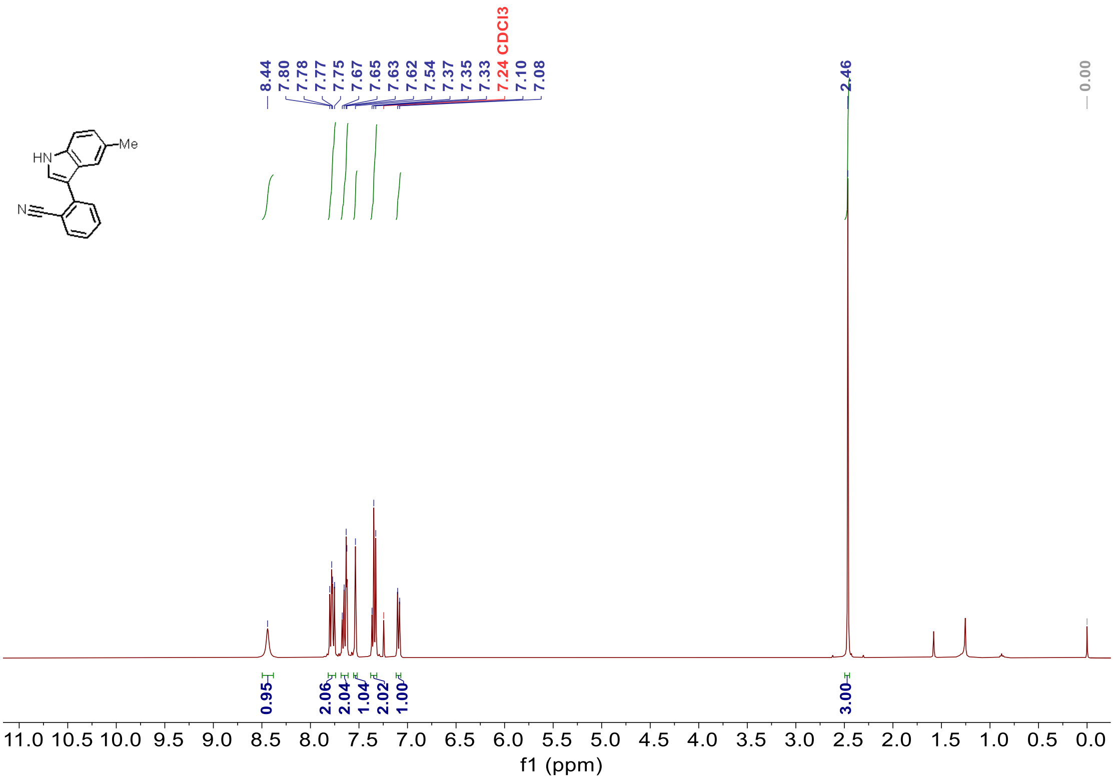
[13]C NMR spectra of **3-iodo-2,5-dimethyl-1H-indole**



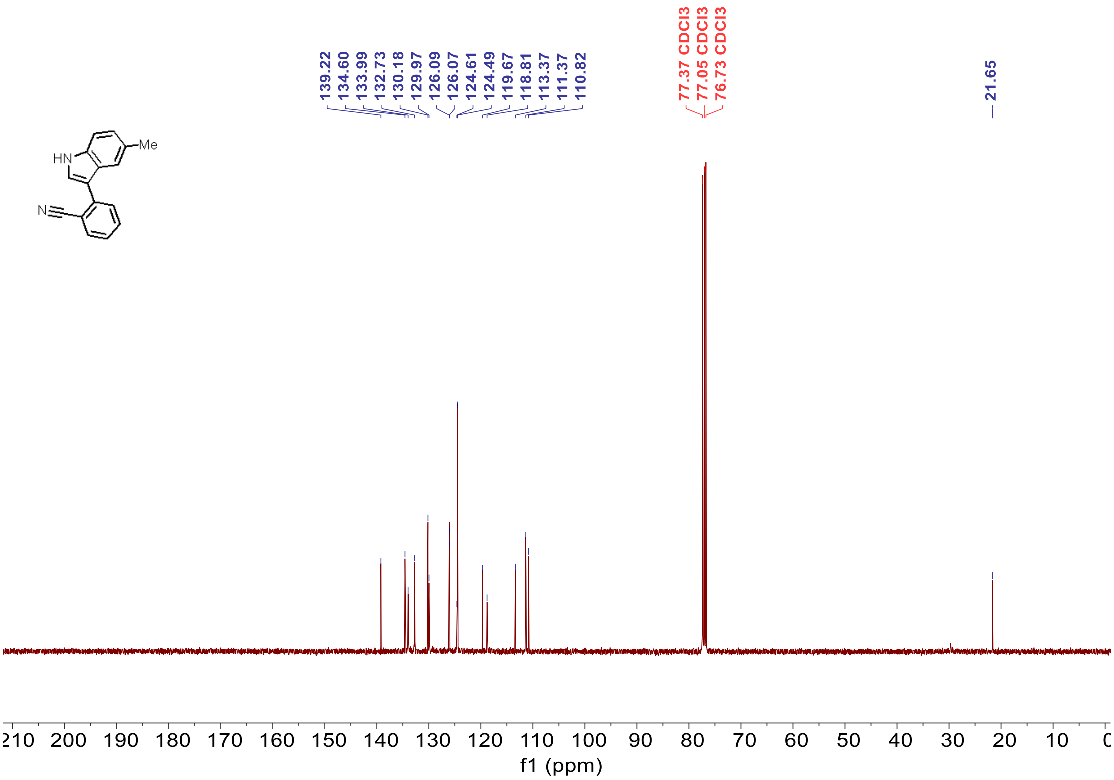
[1]H NMR spectra of **DT$_1$**



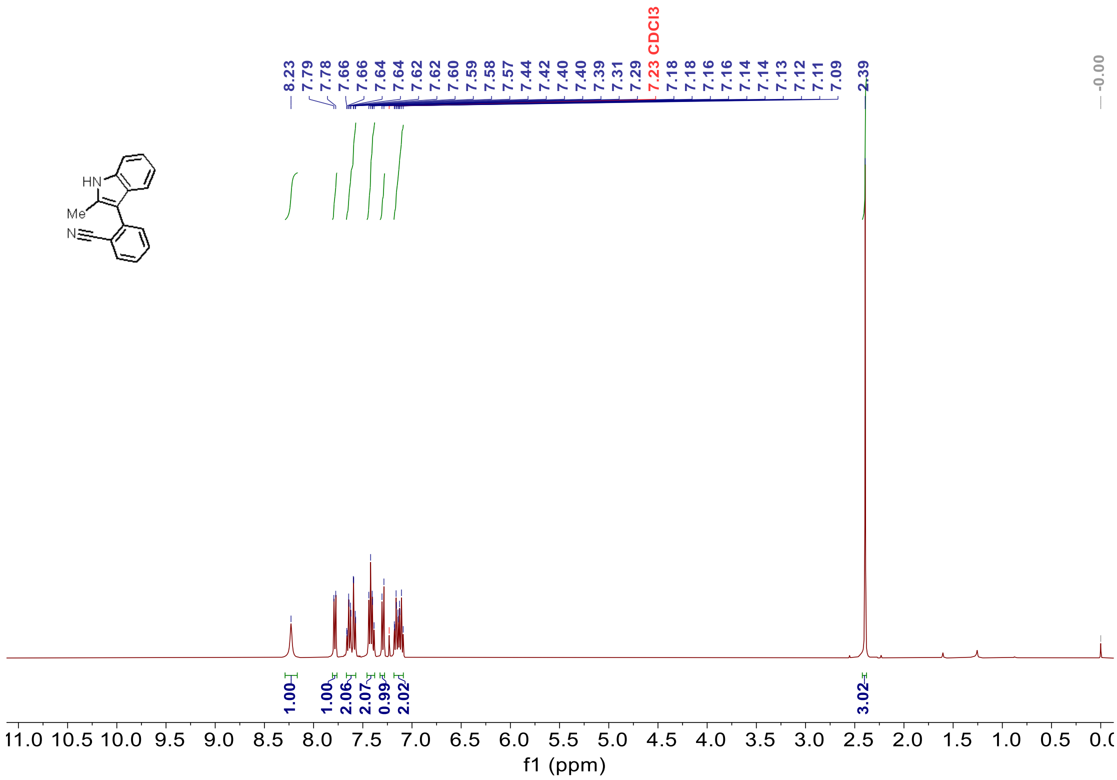
[13]C NMR spectra of **DT$_1$**



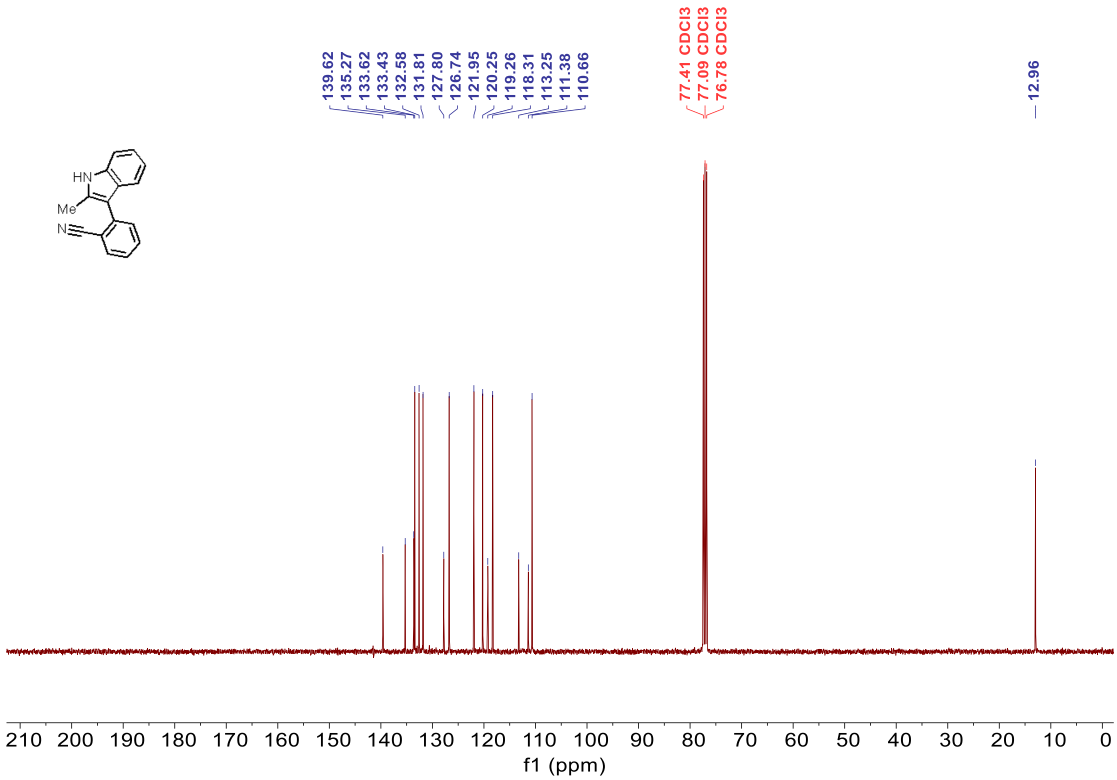
^{1}H NMR spectra of **DT$_2$**



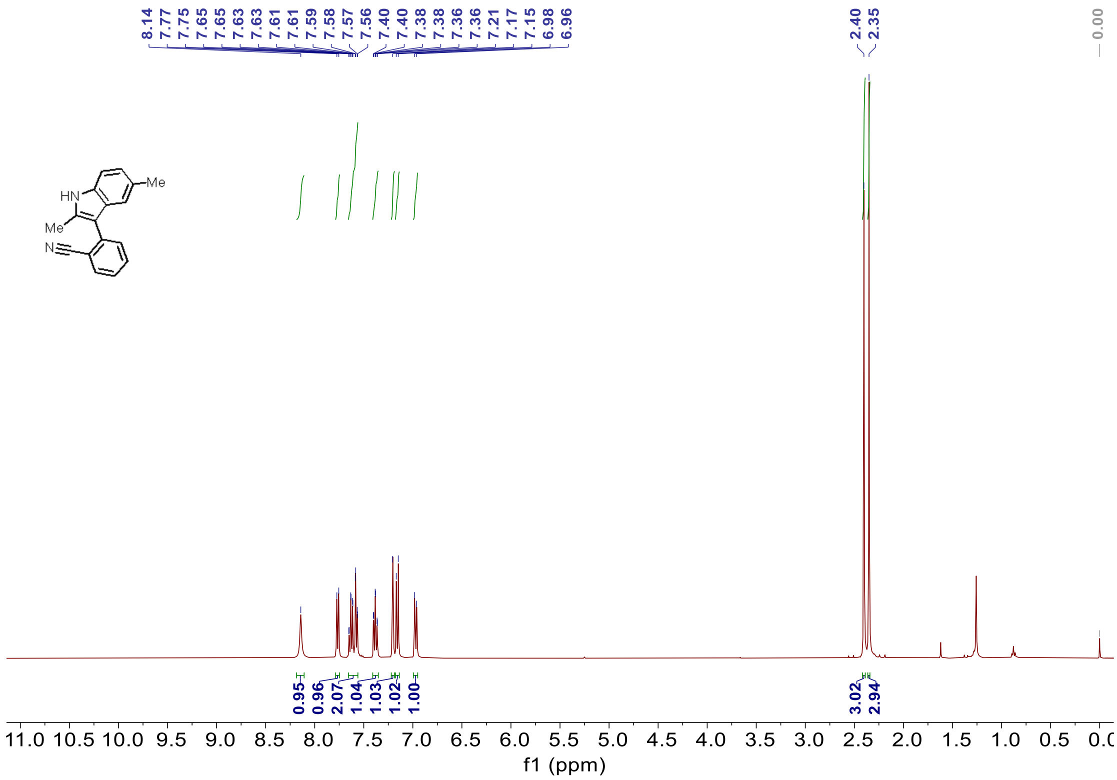
^{13}C NMR spectra of **DT$_2$**



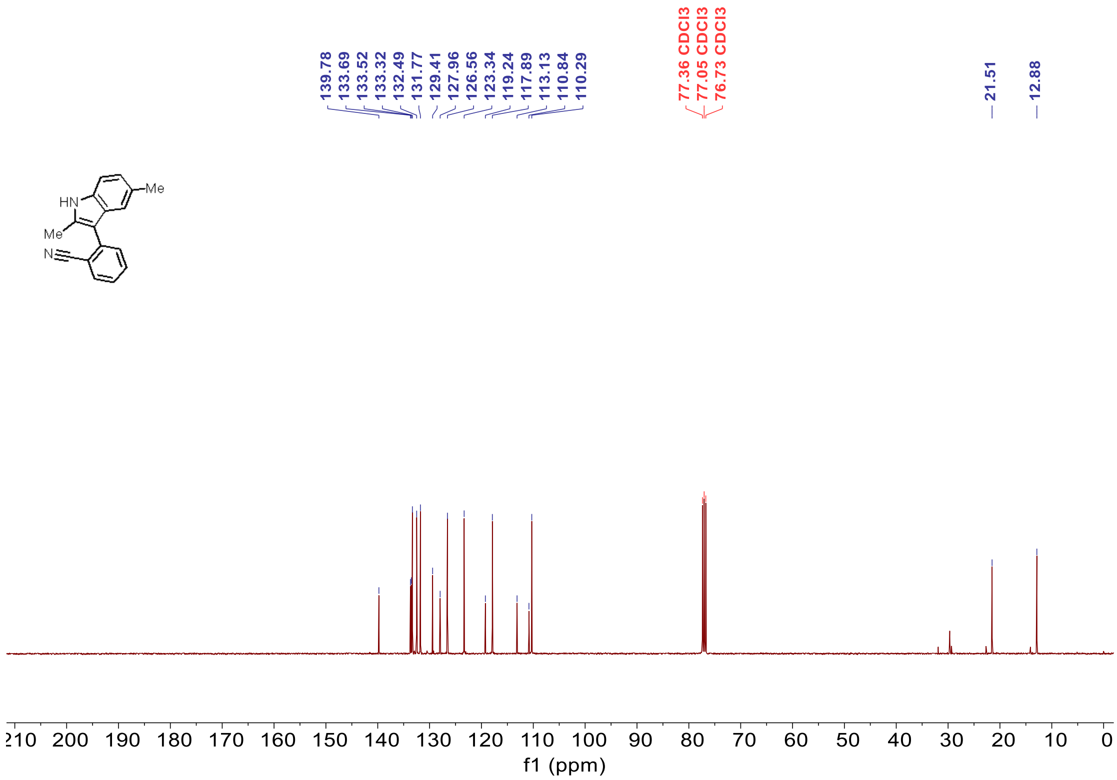
^{1}H NMR spectra of **DT$_3$**



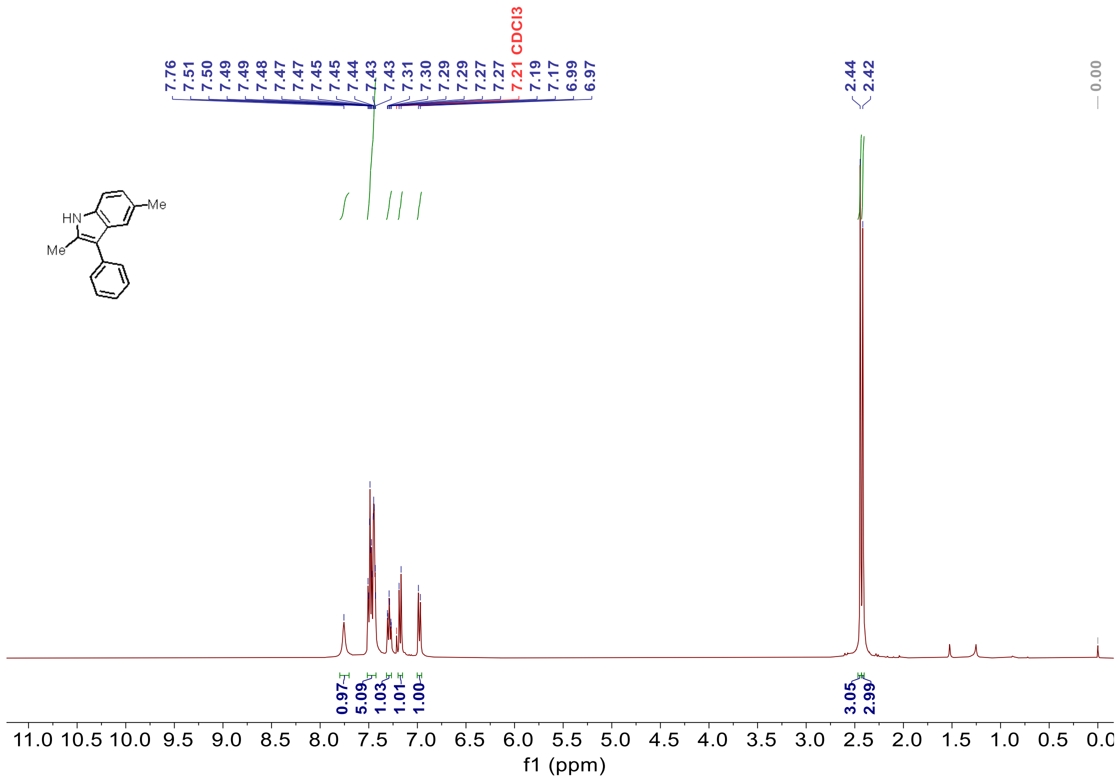
^{13}C NMR spectra of **DT$_3$**



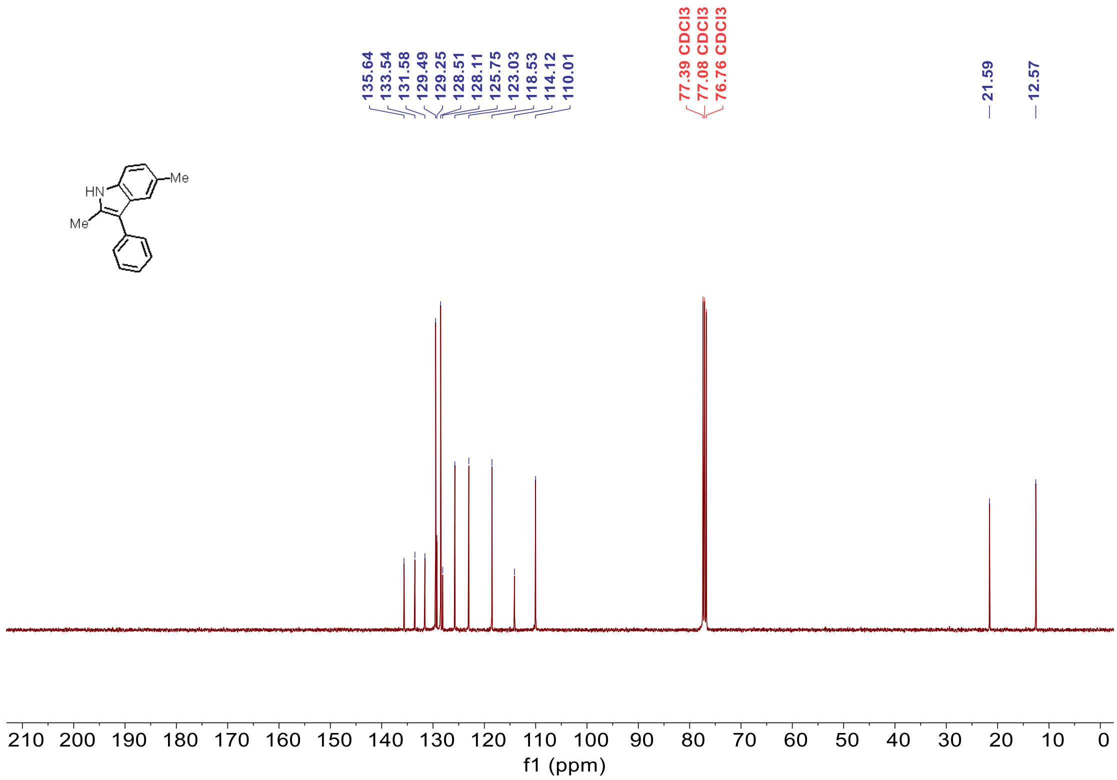
[1]H NMR spectra of **DT$_4$**



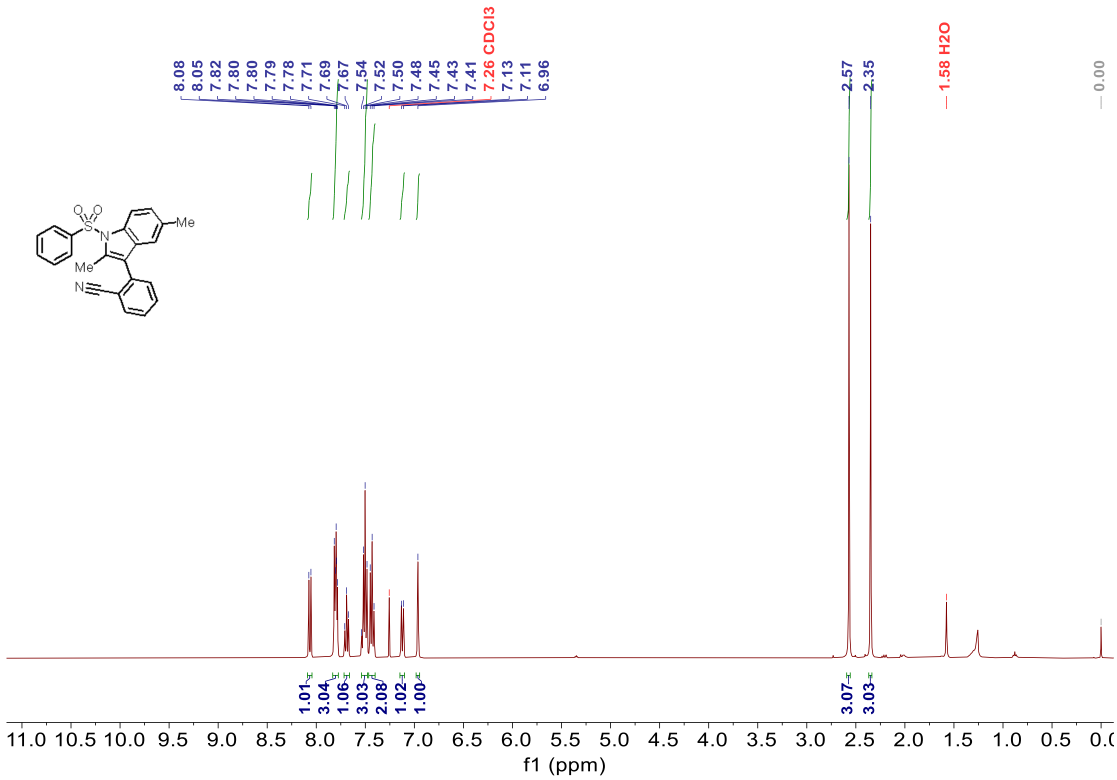
[13]C NMR spectra of **DT$_4$**



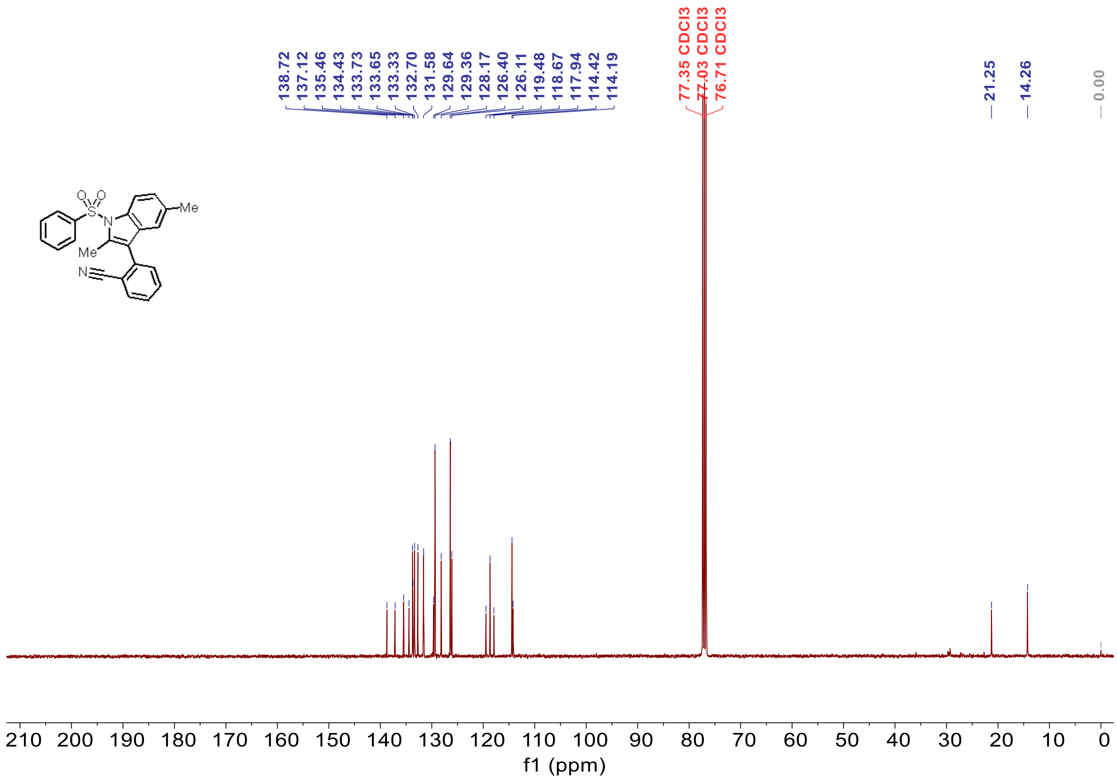
[1]H NMR spectra of **DT$_5$**



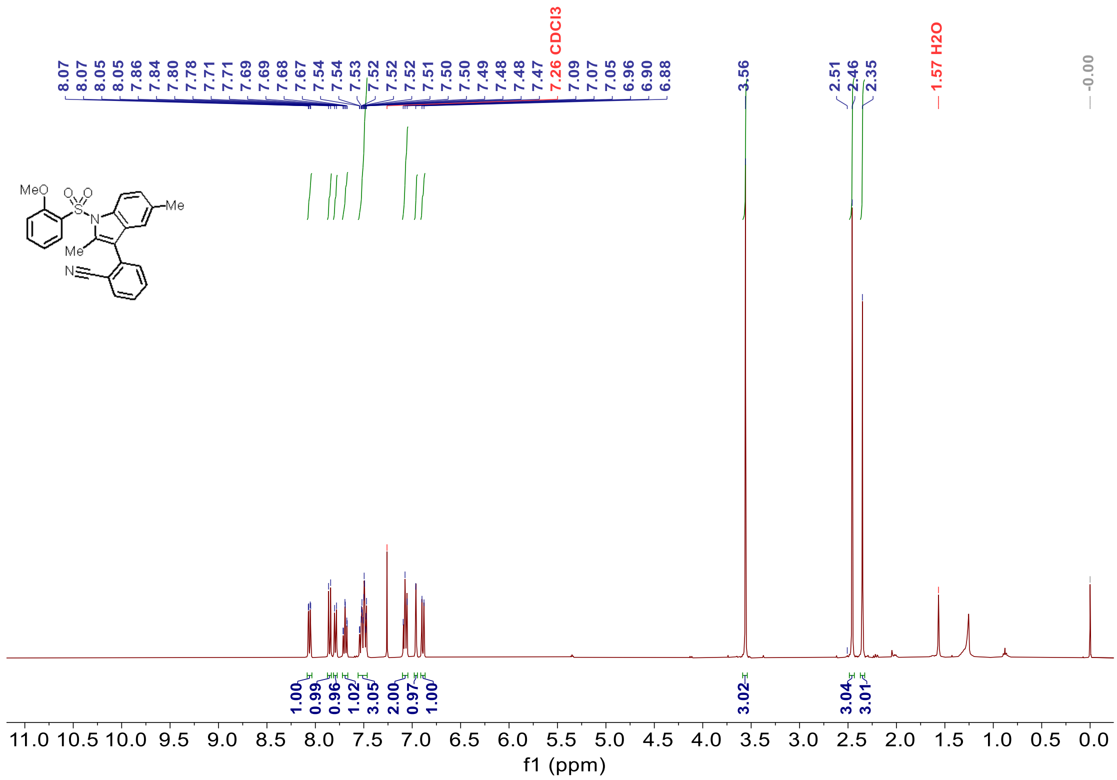
[13]C NMR spectra of **DT$_5$**



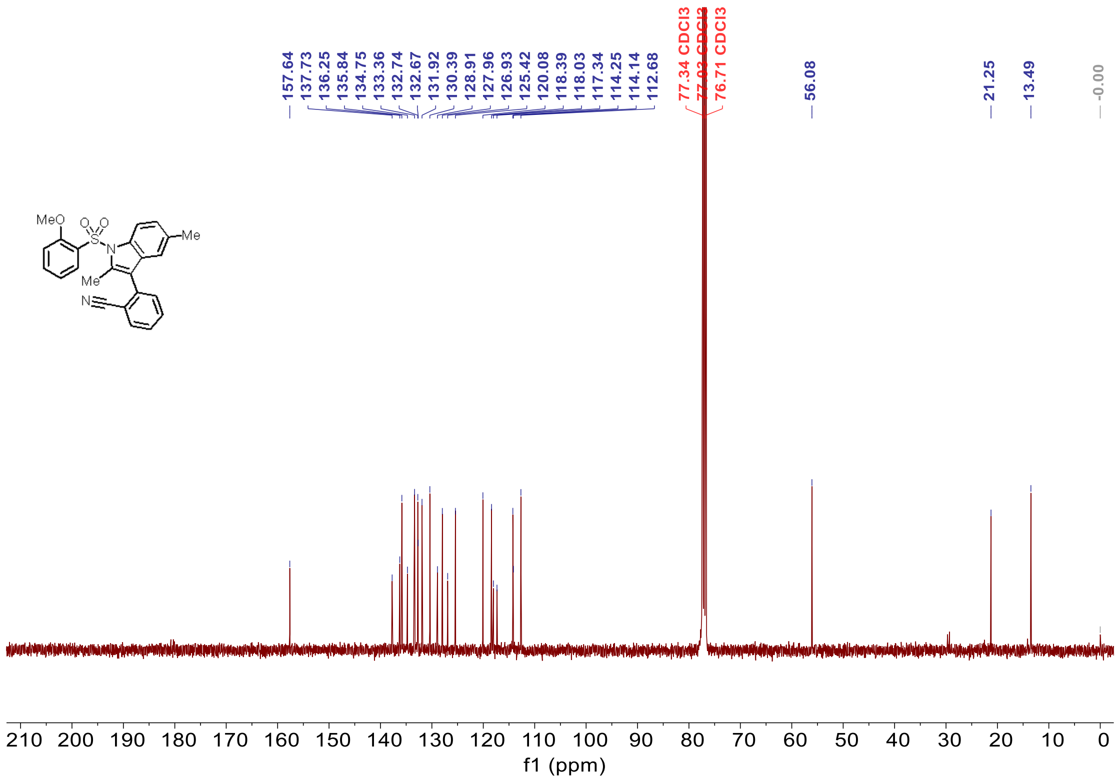
^{1}H NMR spectra of **1a**



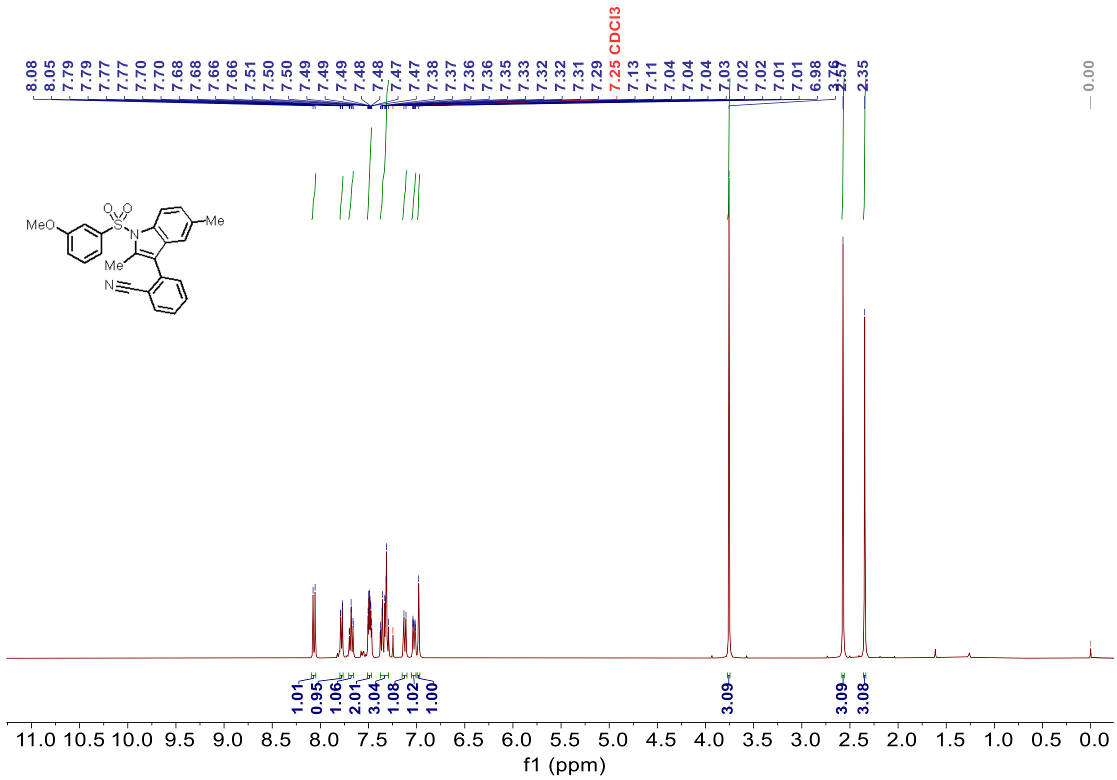
^{13}C NMR spectra of **1a**



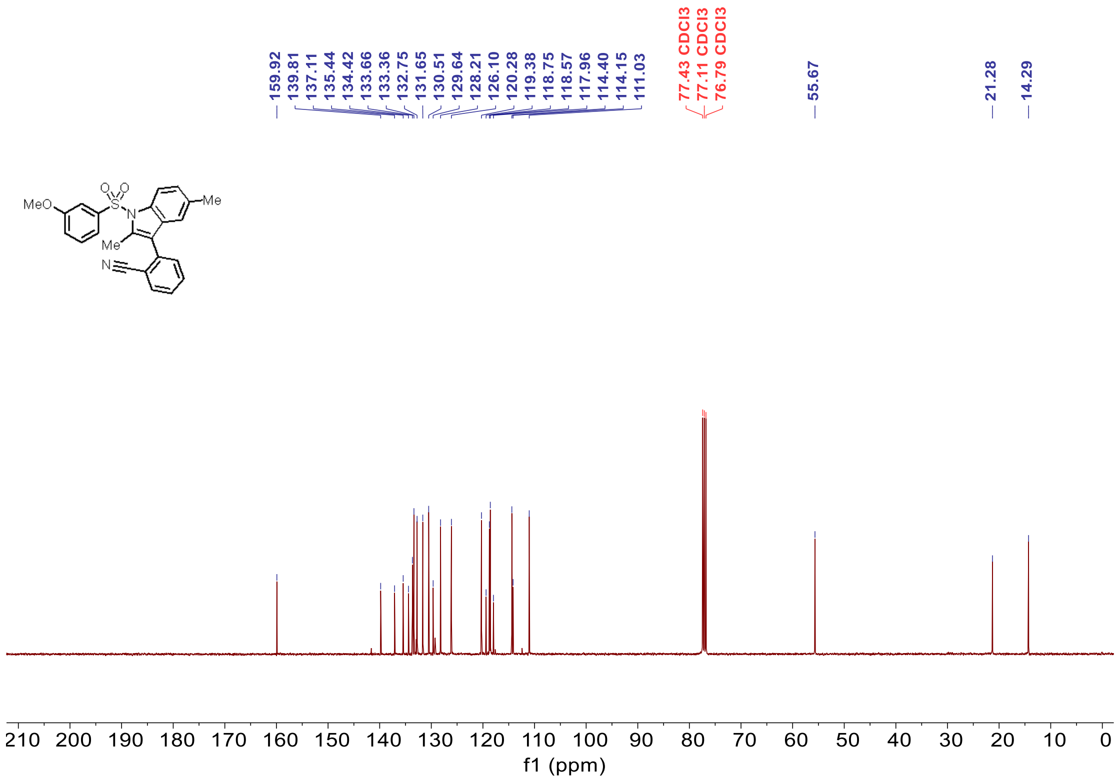
^{1}H NMR spectra of **1b**



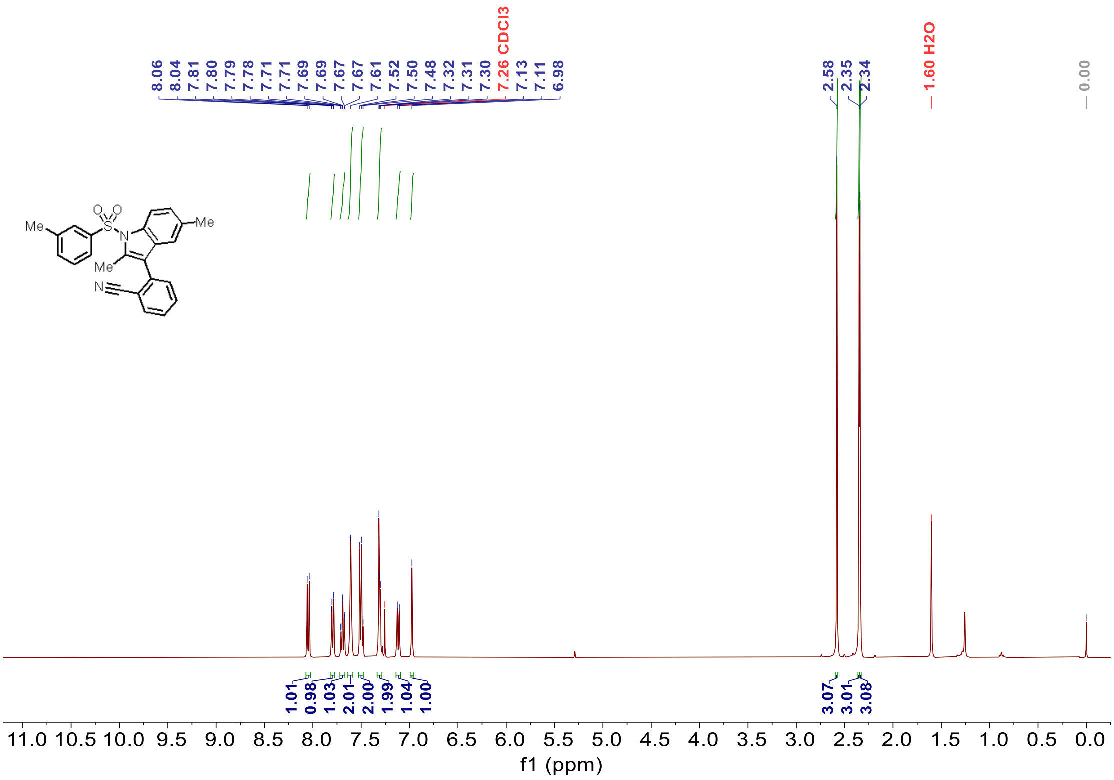
^{13}C NMR spectra of **1b**



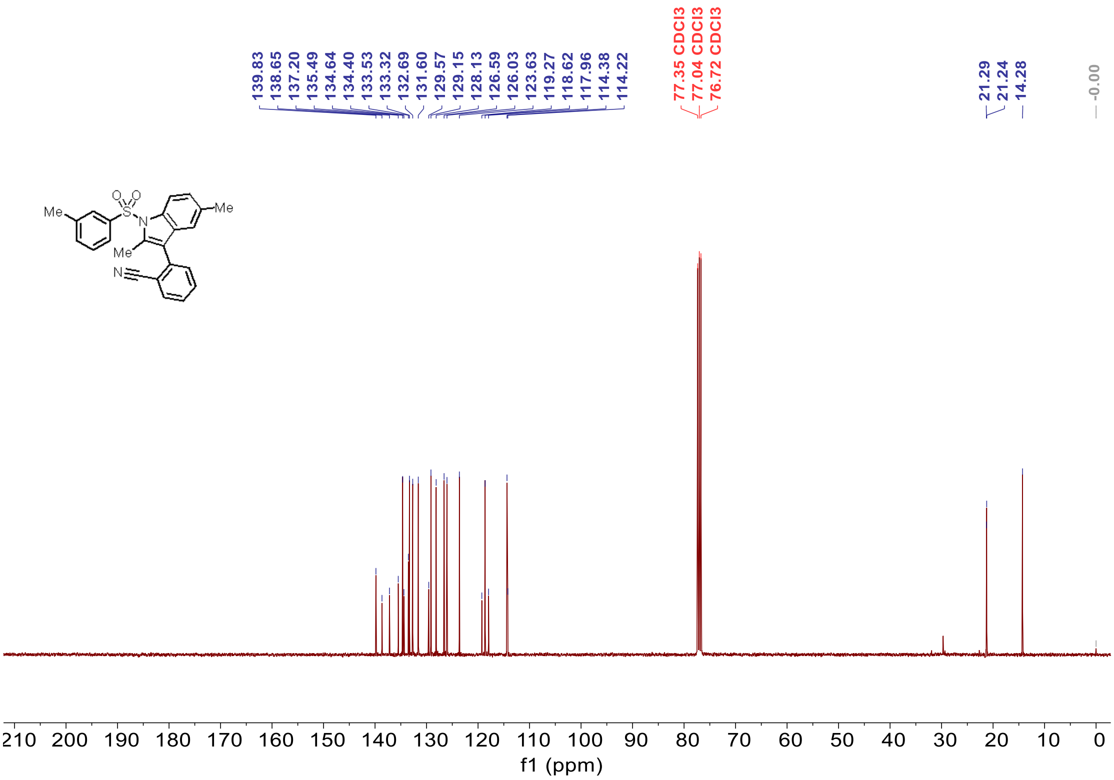
^{1}H NMR spectra of **1c**



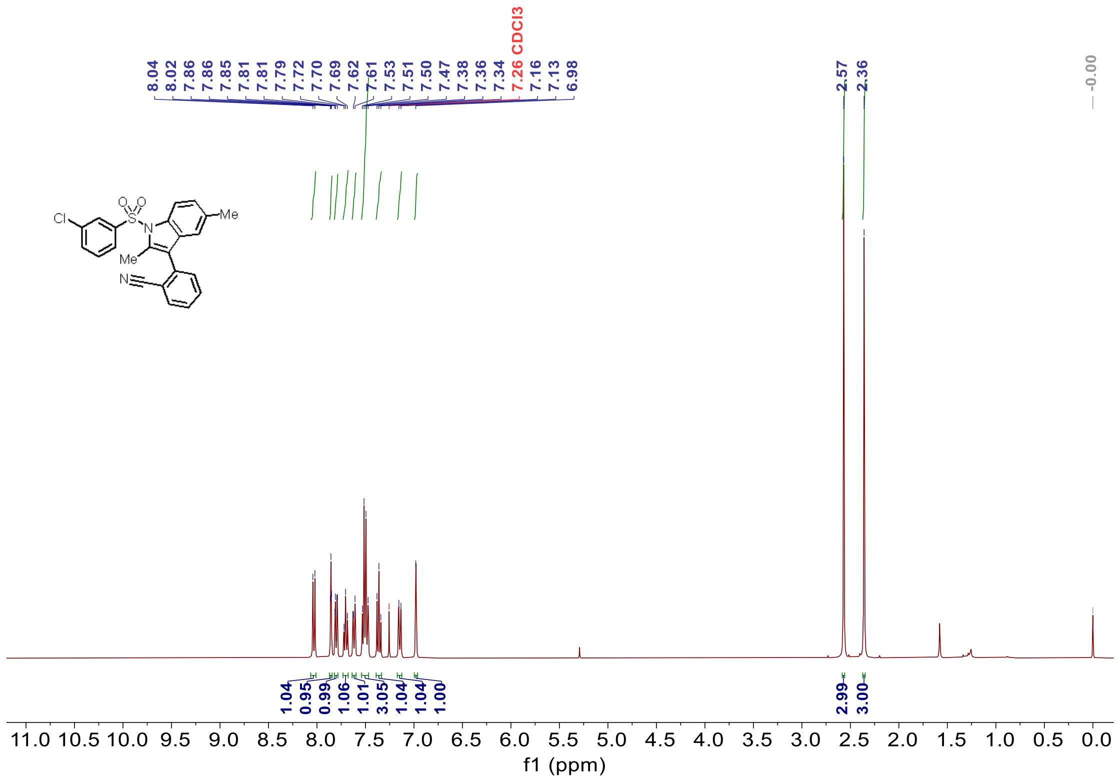
^{13}C NMR spectra of **1c**



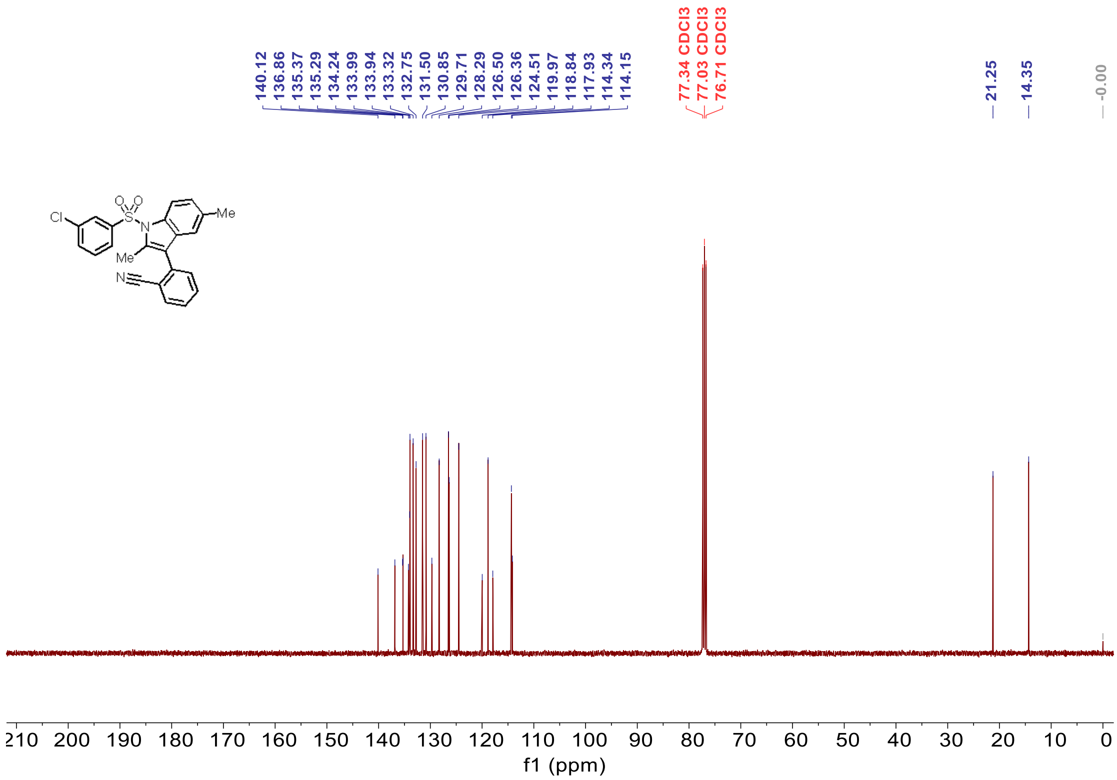
[1]H NMR spectra of **1d**



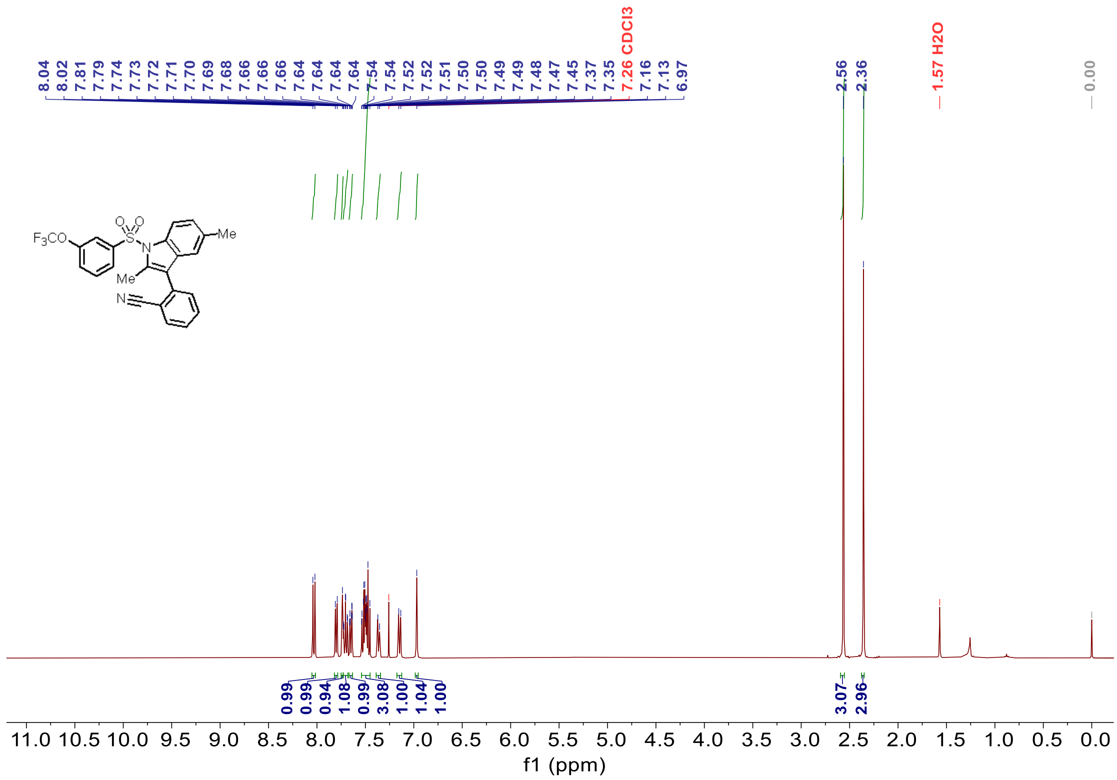
[13]C NMR spectra of **1d**



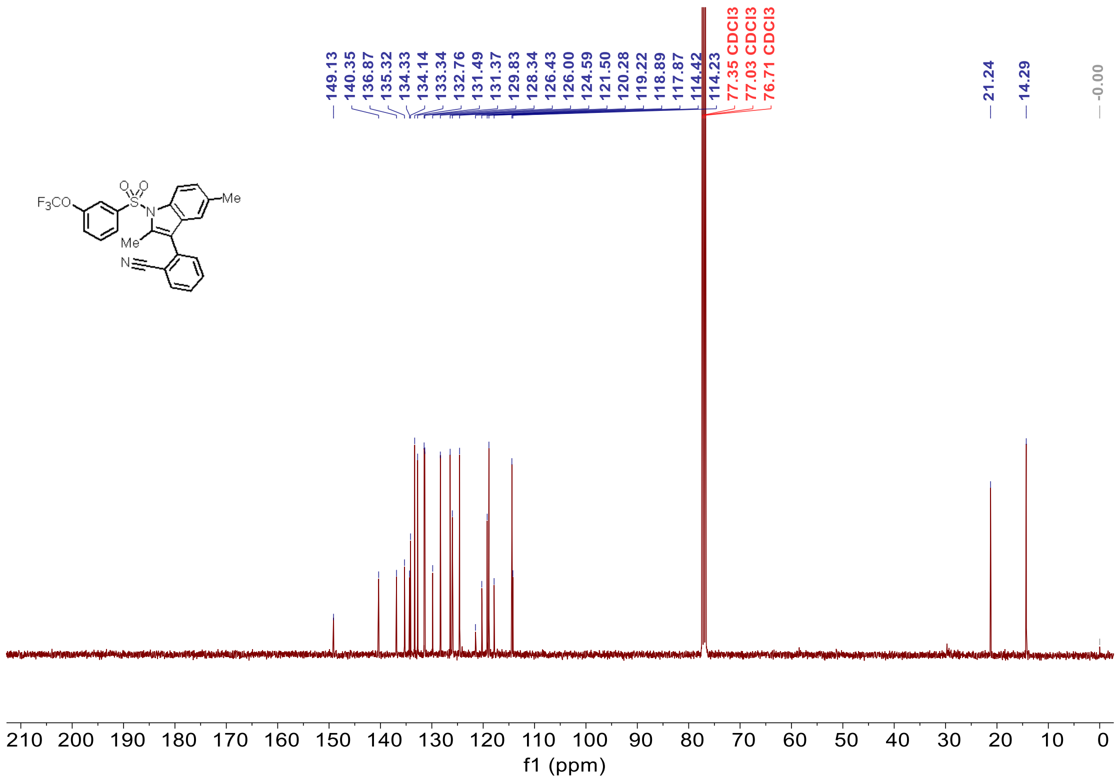
[1]H NMR spectra of **1e**



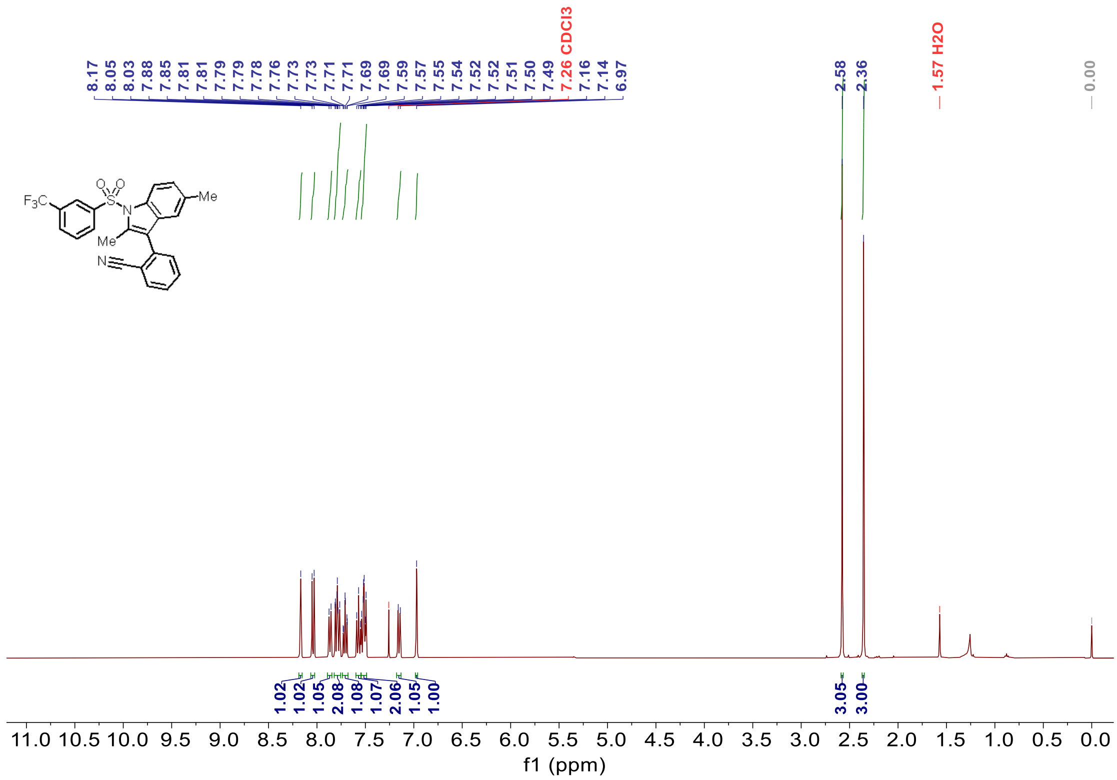
[13]C NMR spectra of **1e**



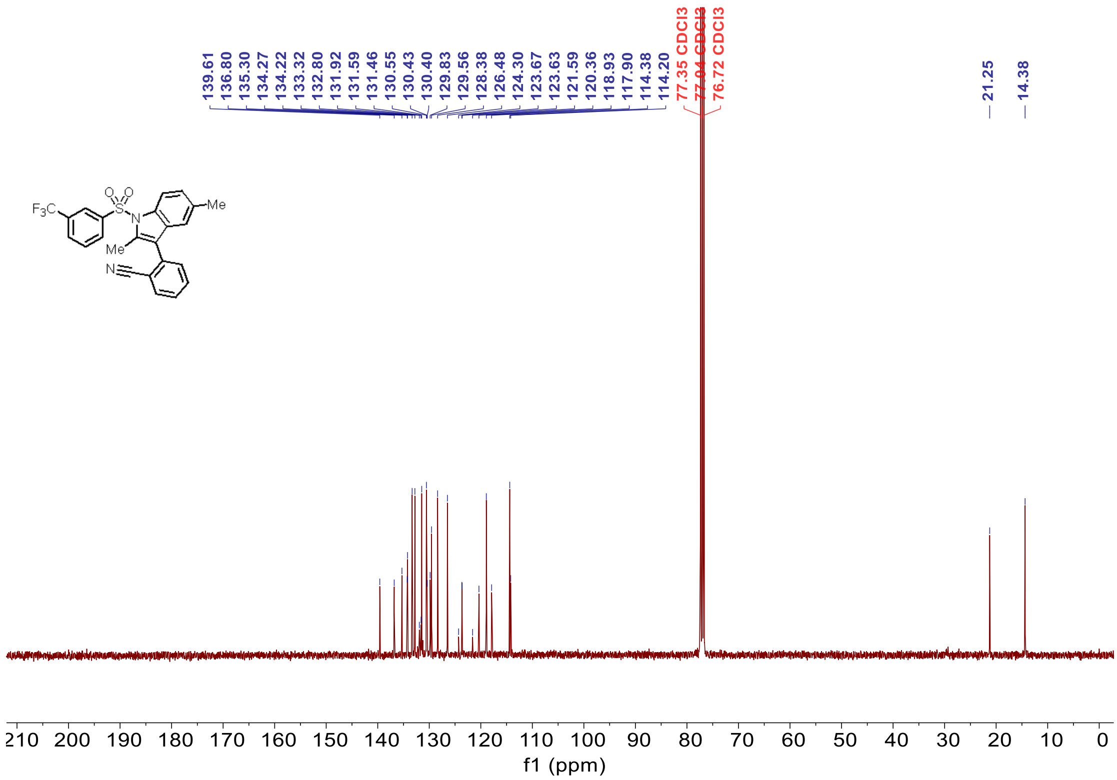
^{1}H NMR spectra of **1f**



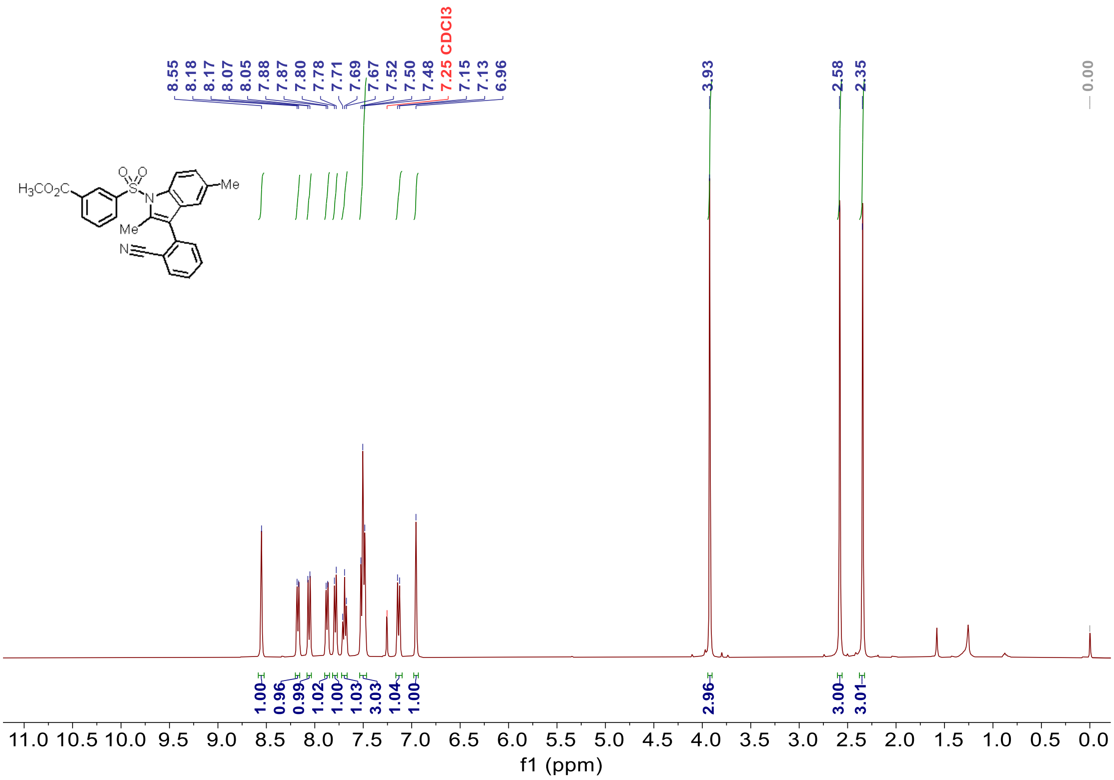
^{13}C NMR spectra of **1f**



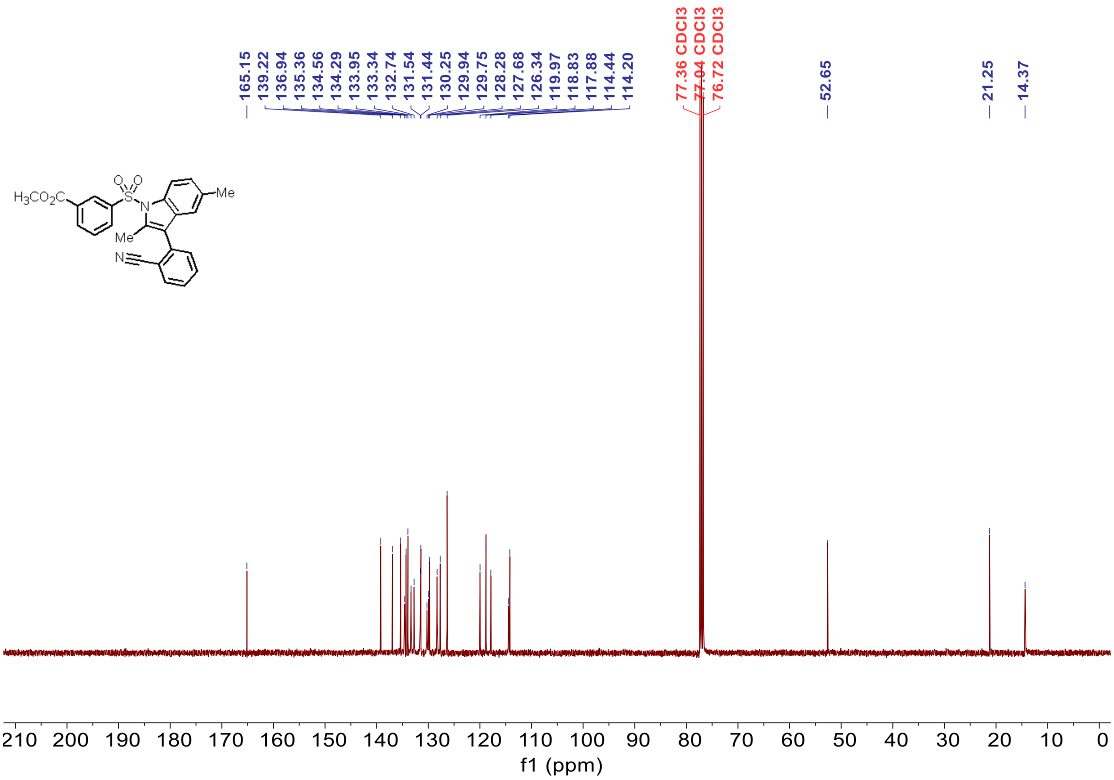
^{1}H NMR spectra of **1g**



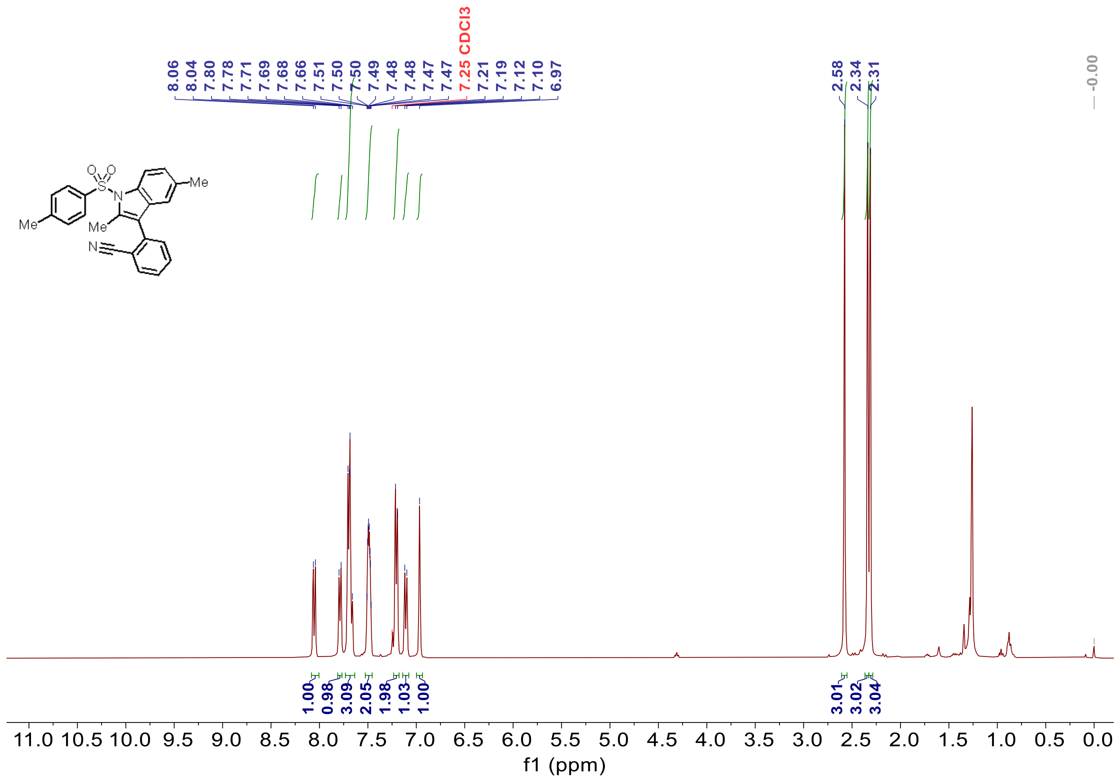
^{13}C NMR spectra of **1g**



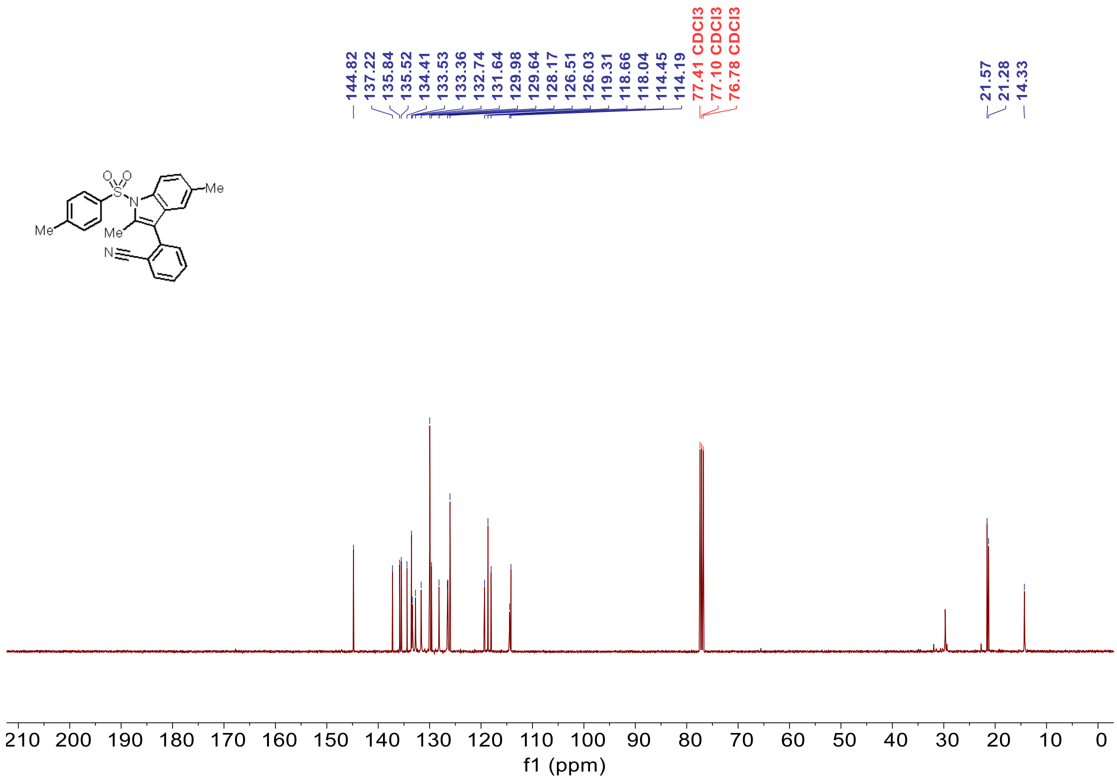
^{1}H NMR spectra of **1h**



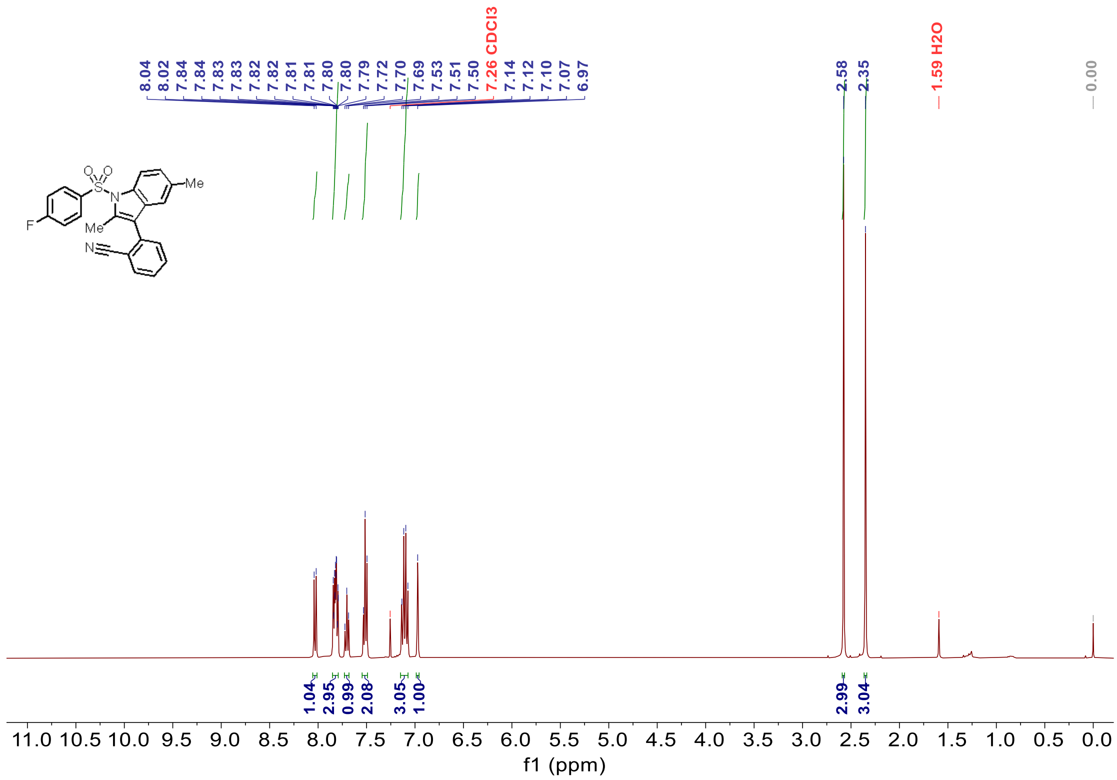
^{13}C NMR spectra of **1h**



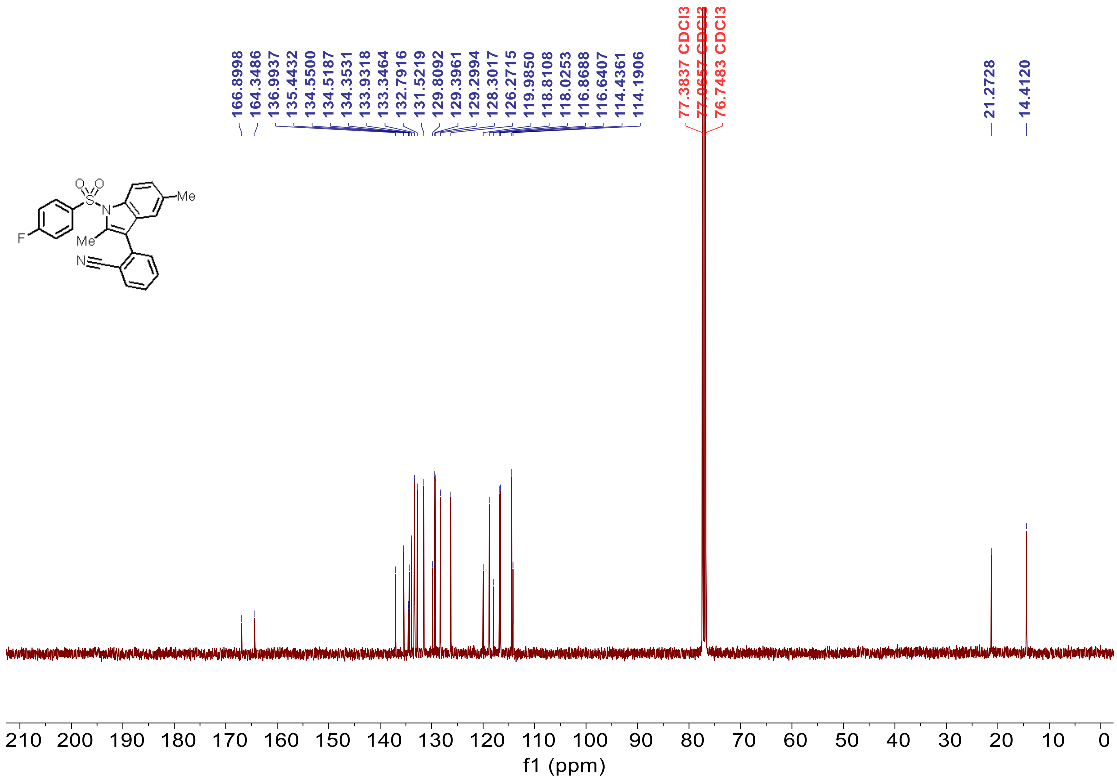
^{1}H NMR spectra of **1i**



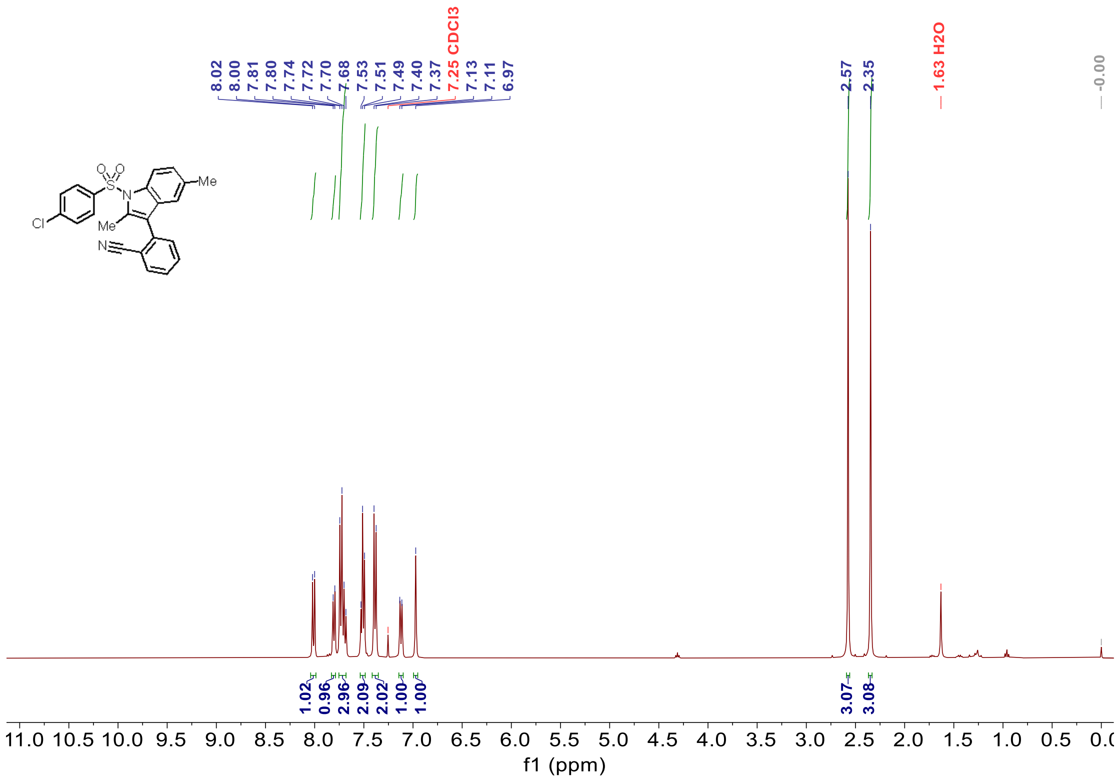
^{13}C NMR spectra of **1i**



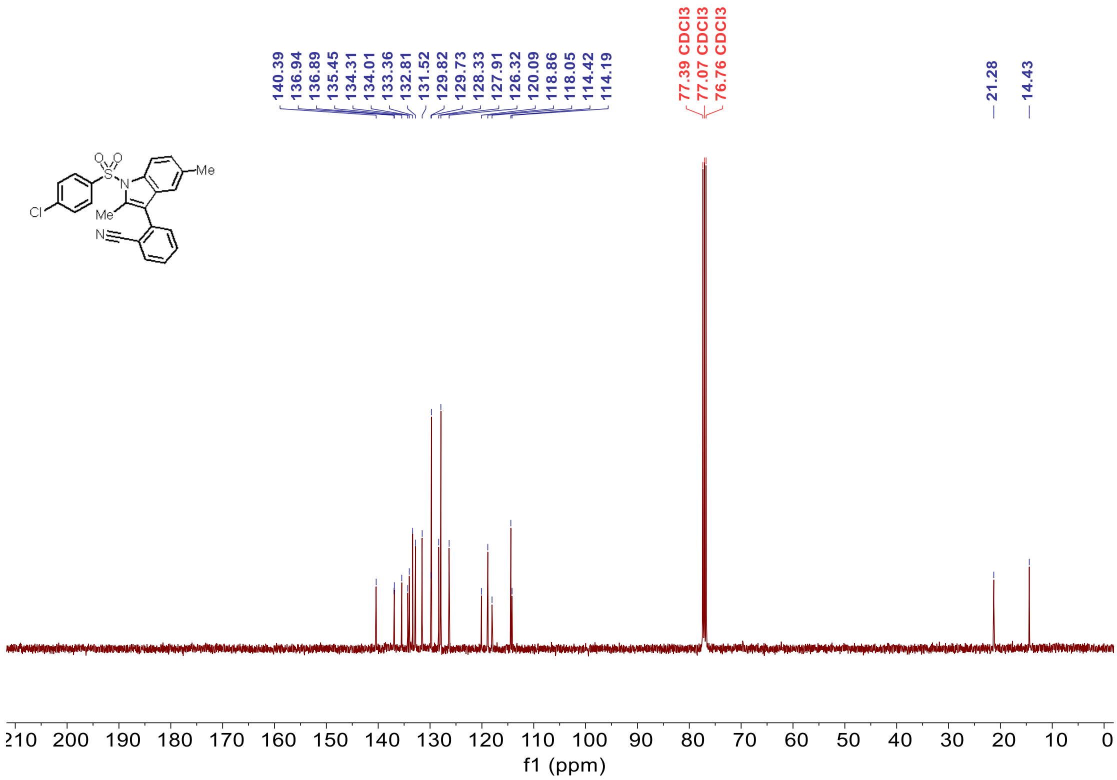
[1]H NMR spectra of **1j**



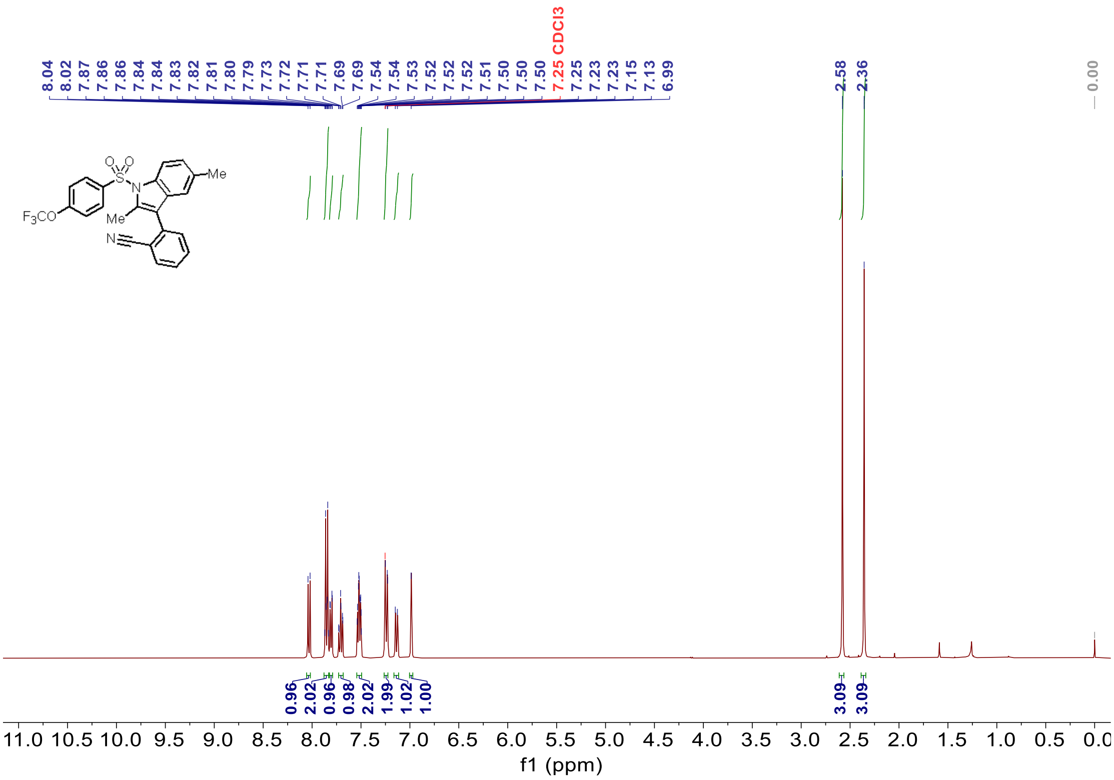
[13]C NMR spectra of **1j**



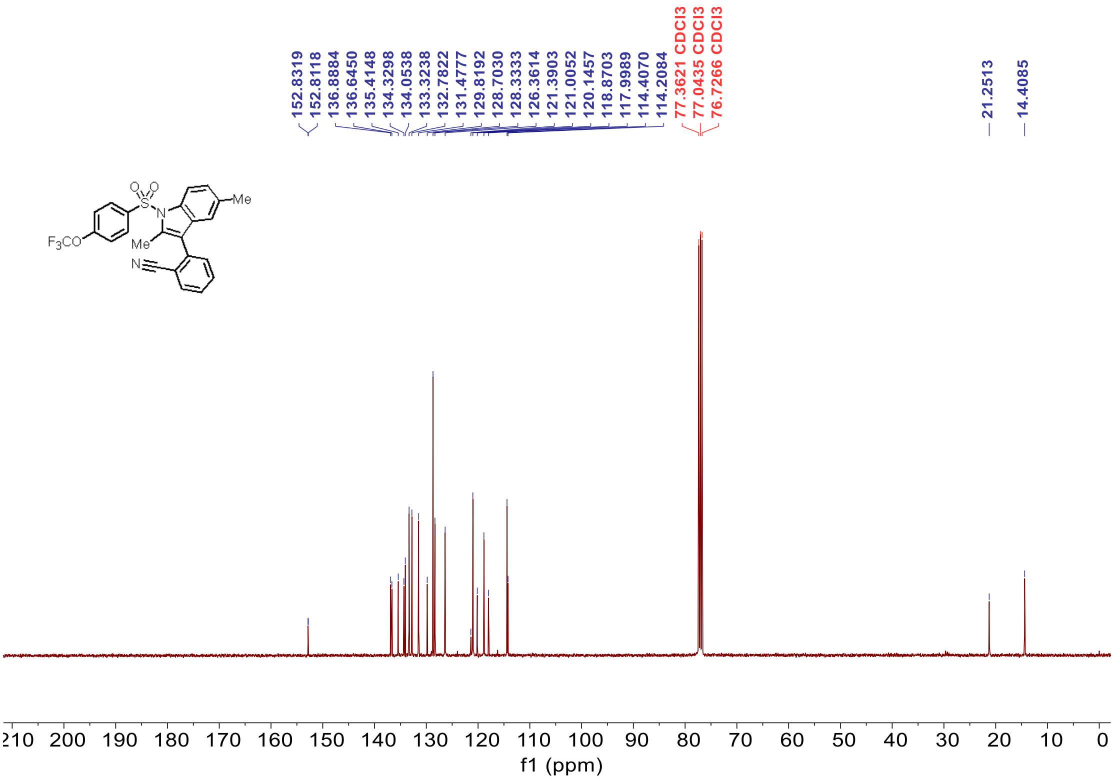
^{1}H NMR spectra of **1k**



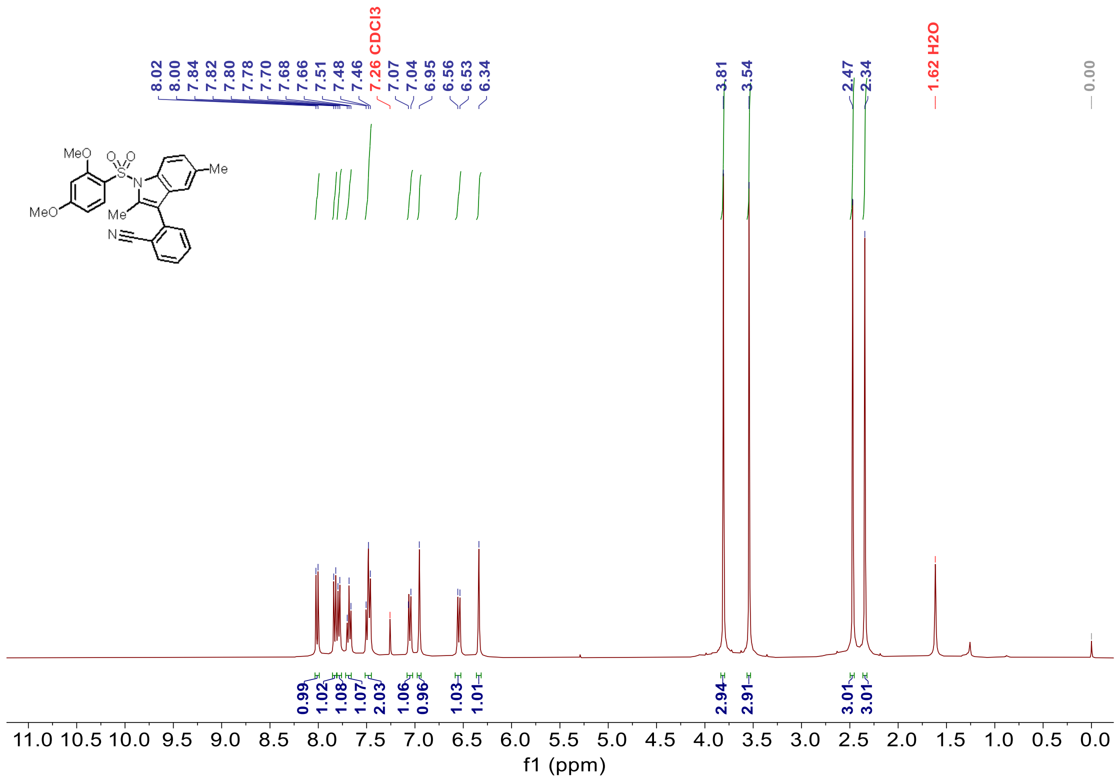
^{13}C NMR spectra of **1k**



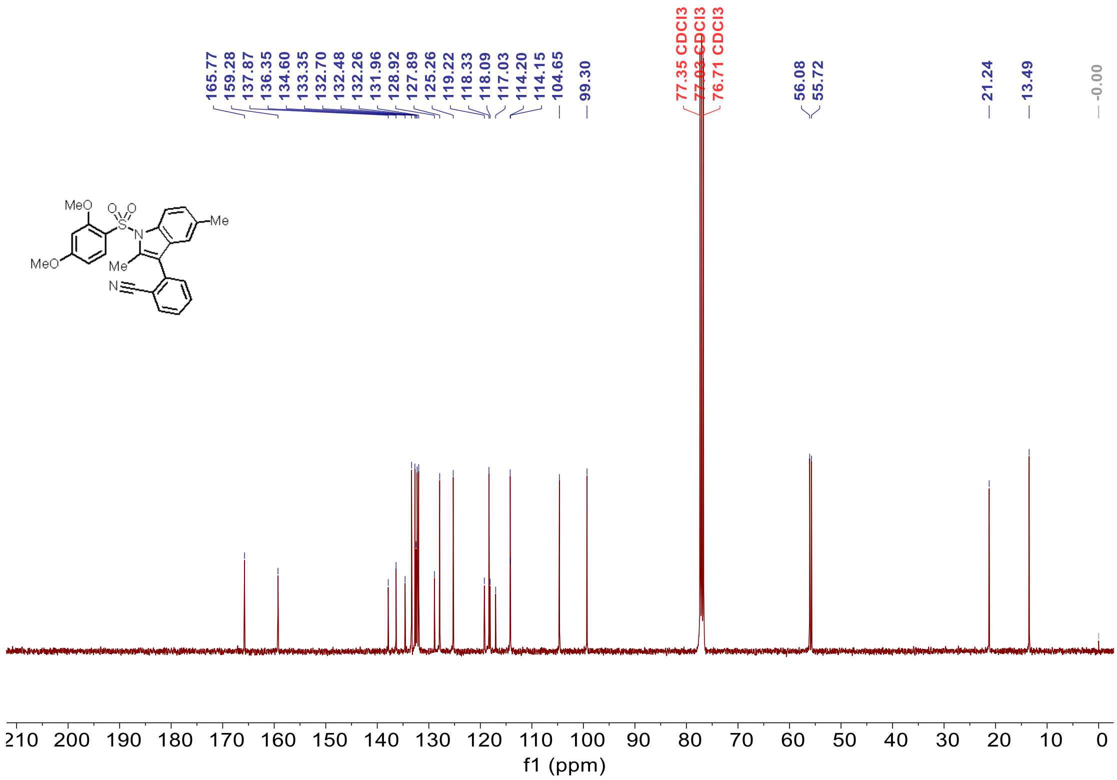
^{1}H NMR spectra of **1l**



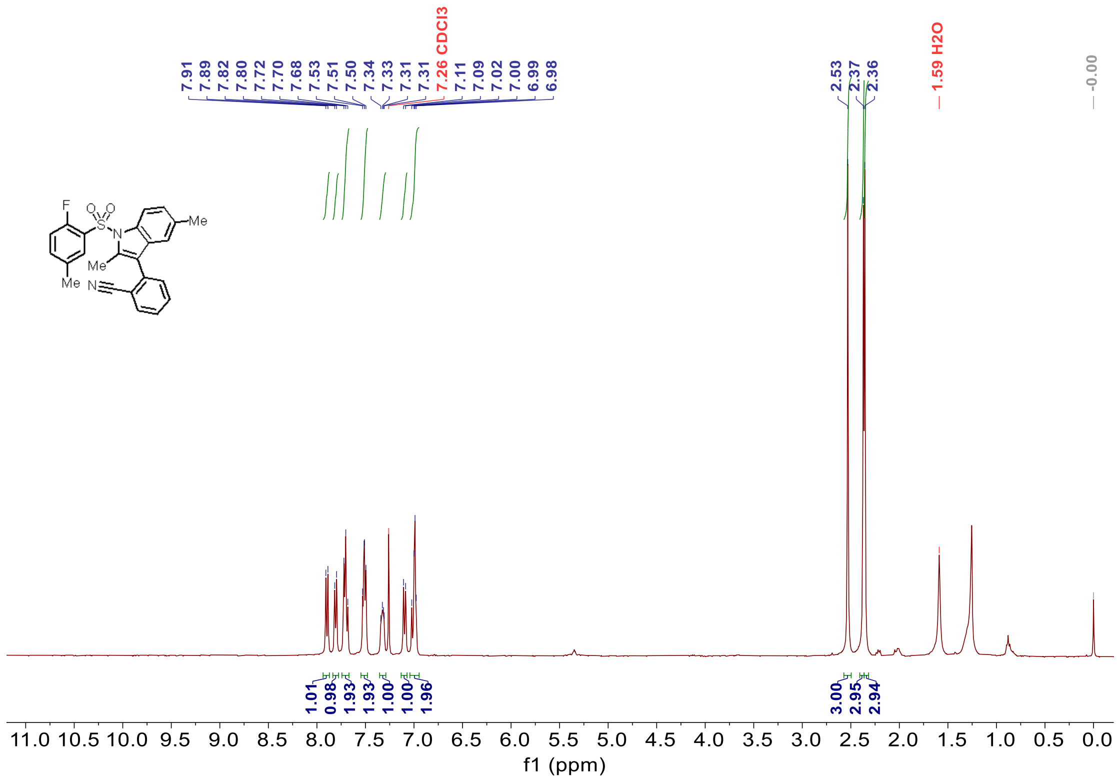
^{13}C NMR spectra of **1l**



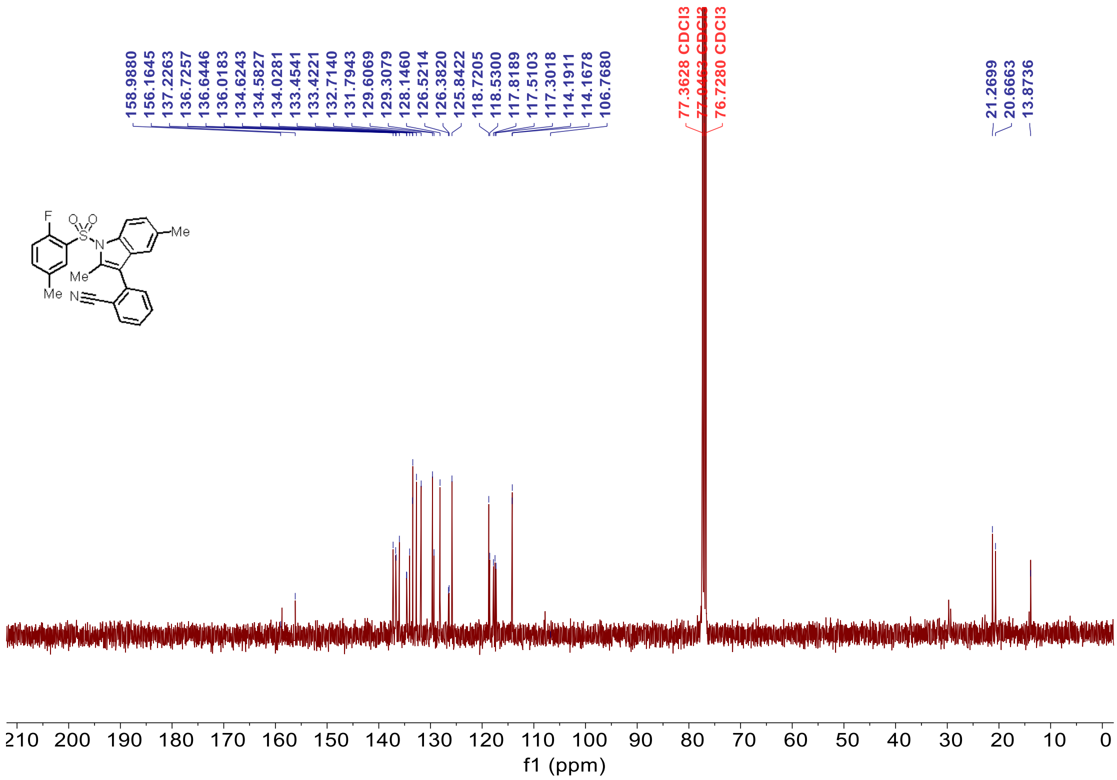
^{1}H NMR spectra of **1m**



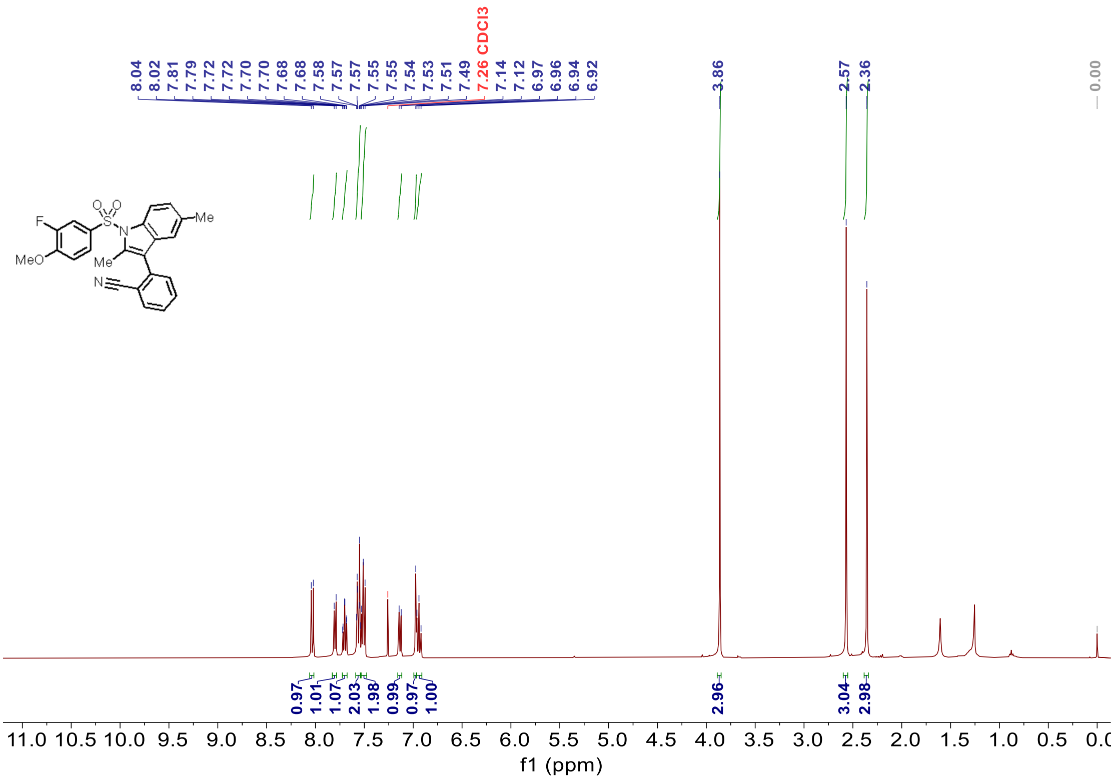
^{13}C NMR spectra of **1m**



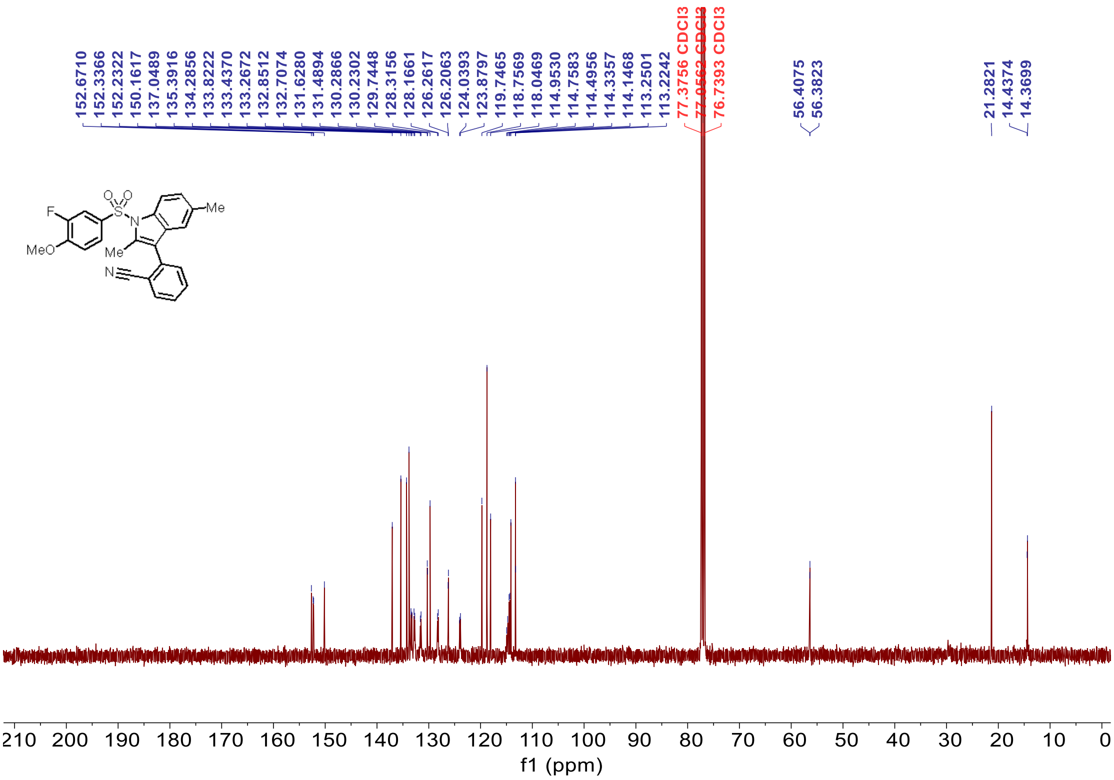
^{1}H NMR spectra of **1n**



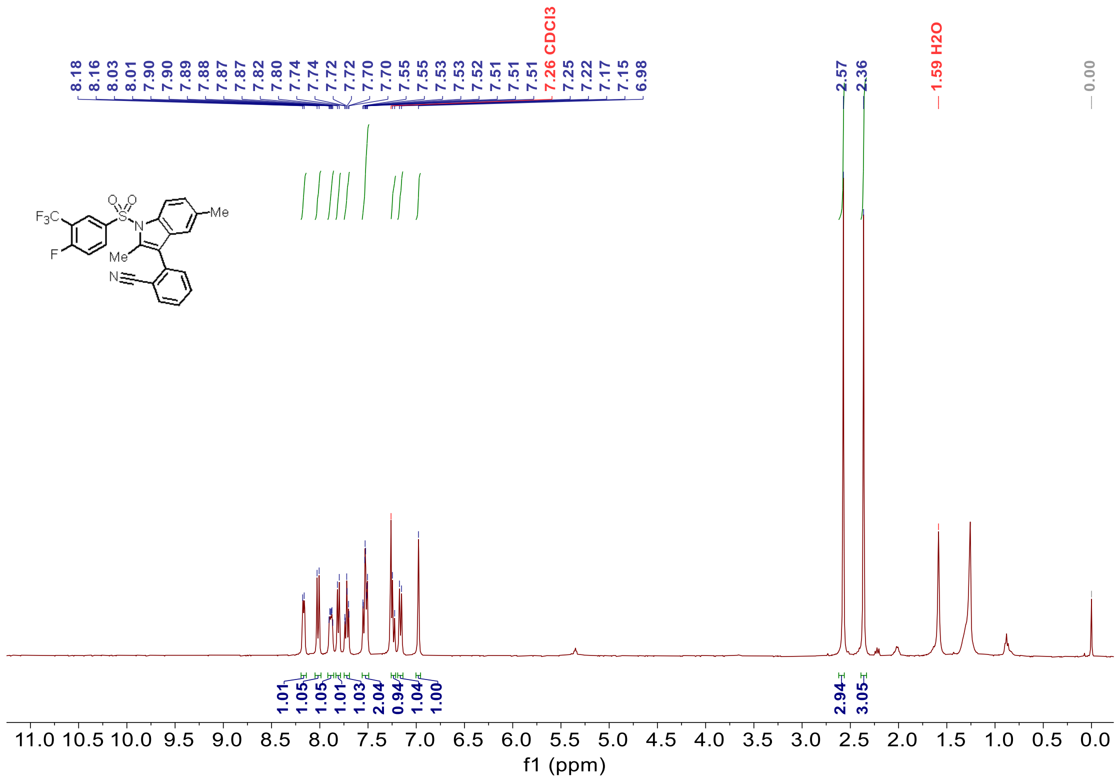
^{13}C NMR spectra of **1n**



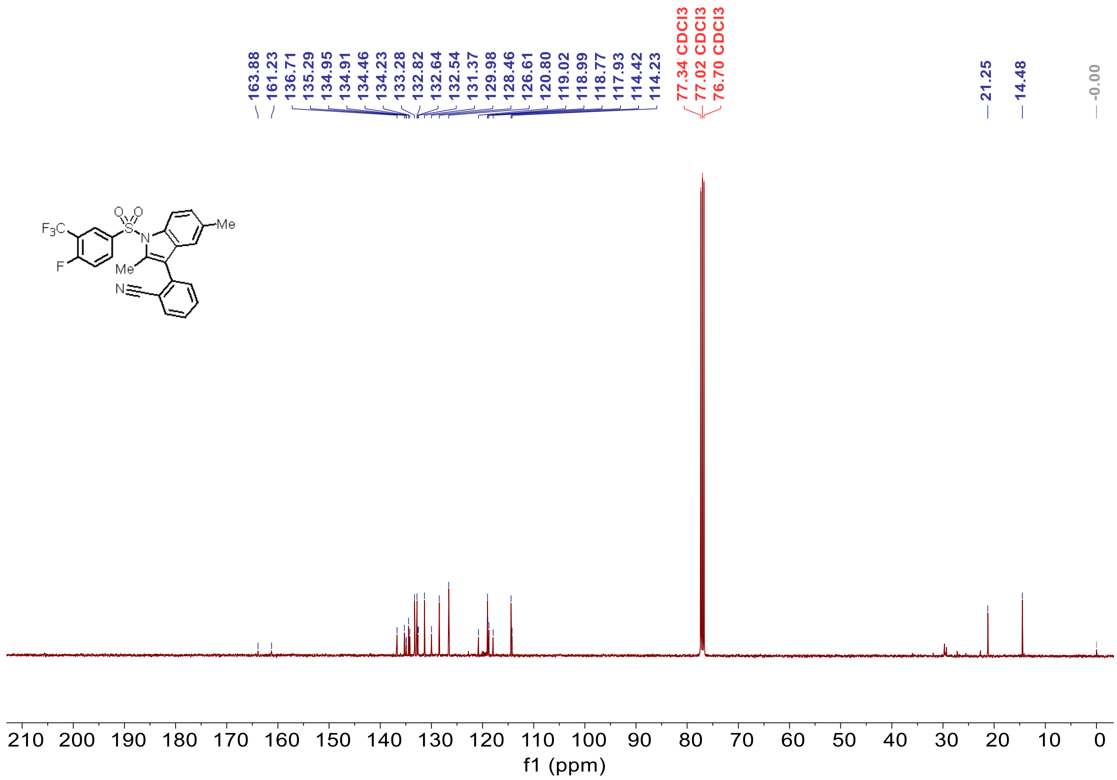
^{1}H NMR spectra of **1o**



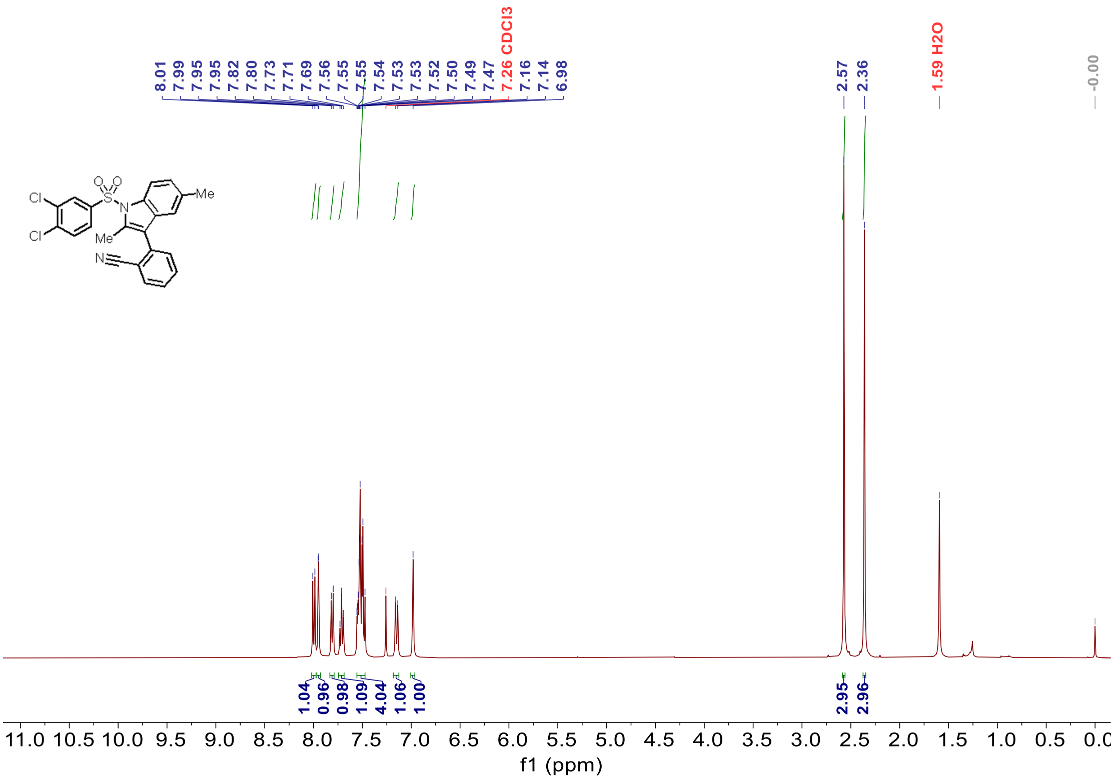
^{13}C NMR spectra of **1o**



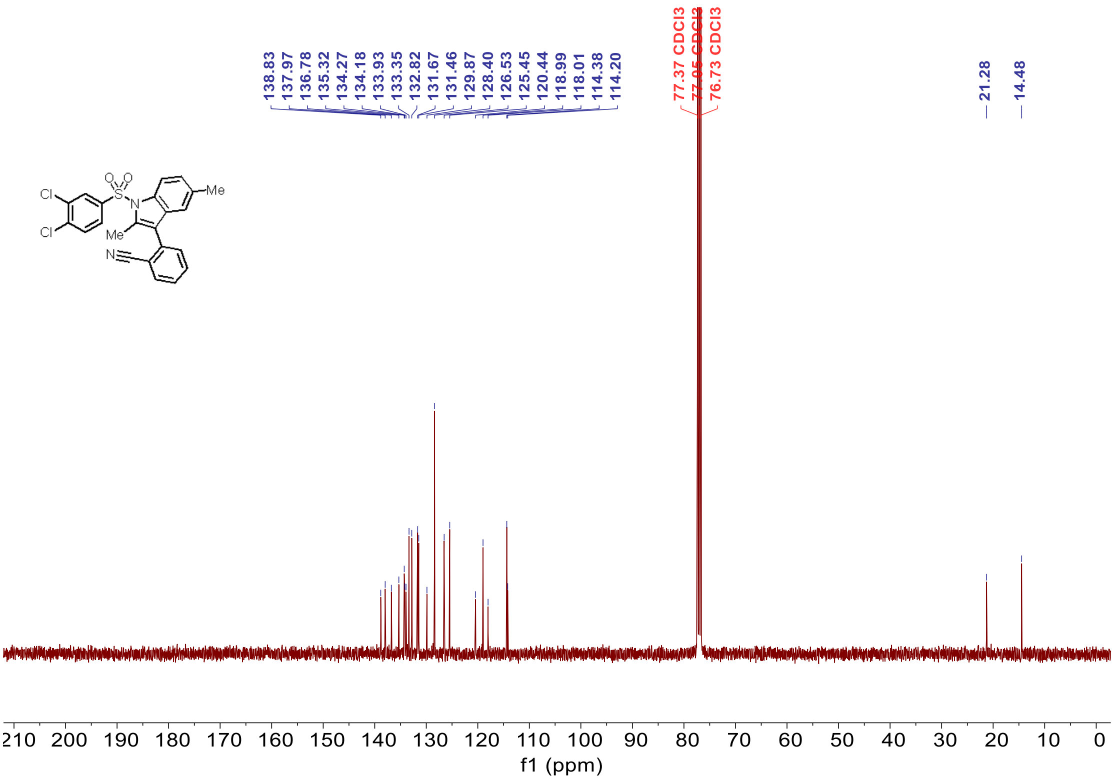
^{1}H NMR spectra of **1p**



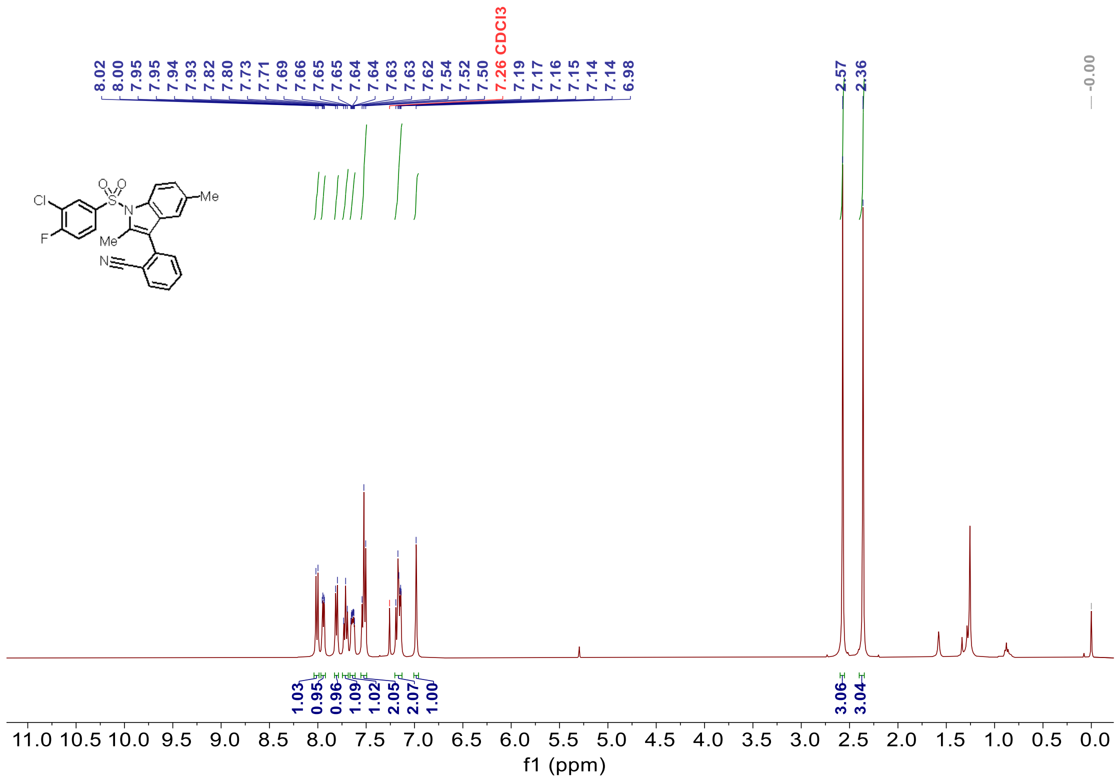
^{13}C NMR spectra of **1p**



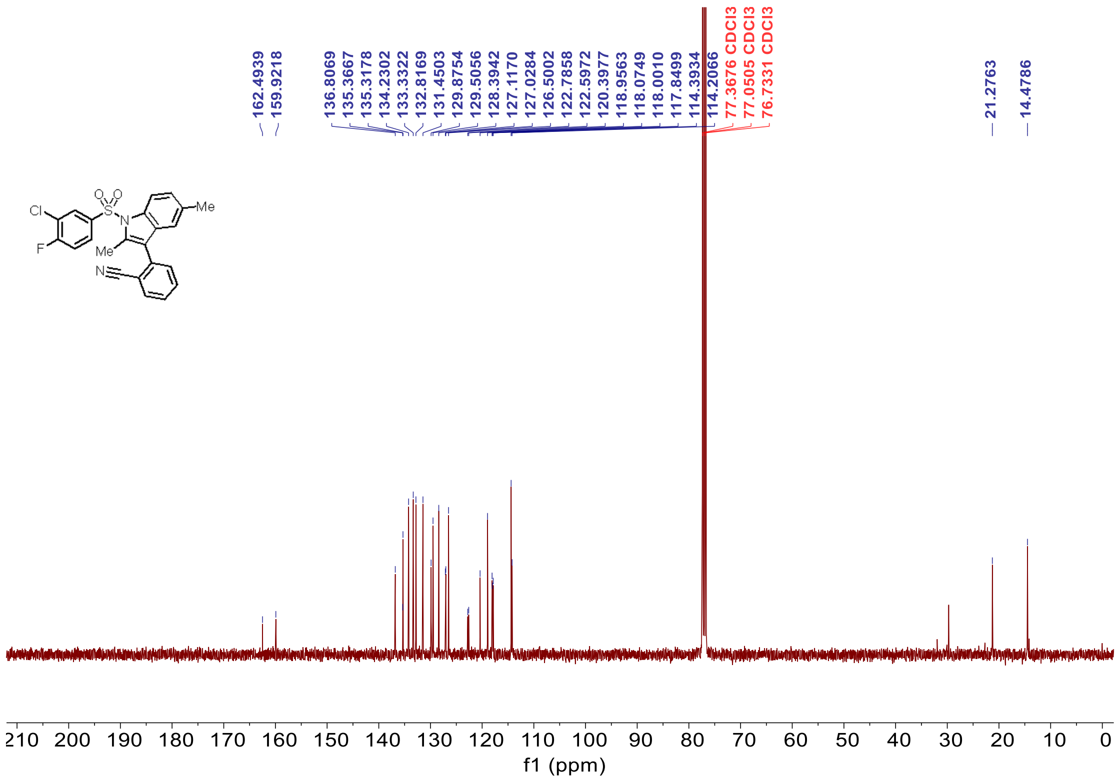
^{1}H NMR spectra of **1q**



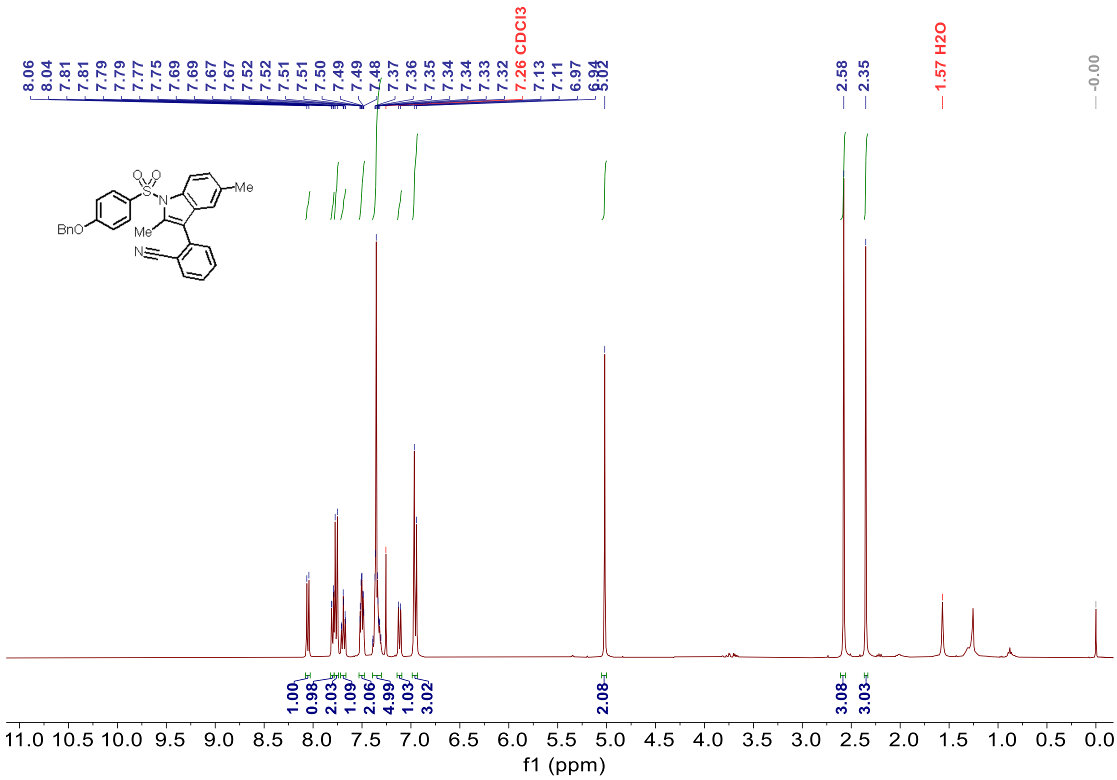
^{13}C NMR spectra of **1q**



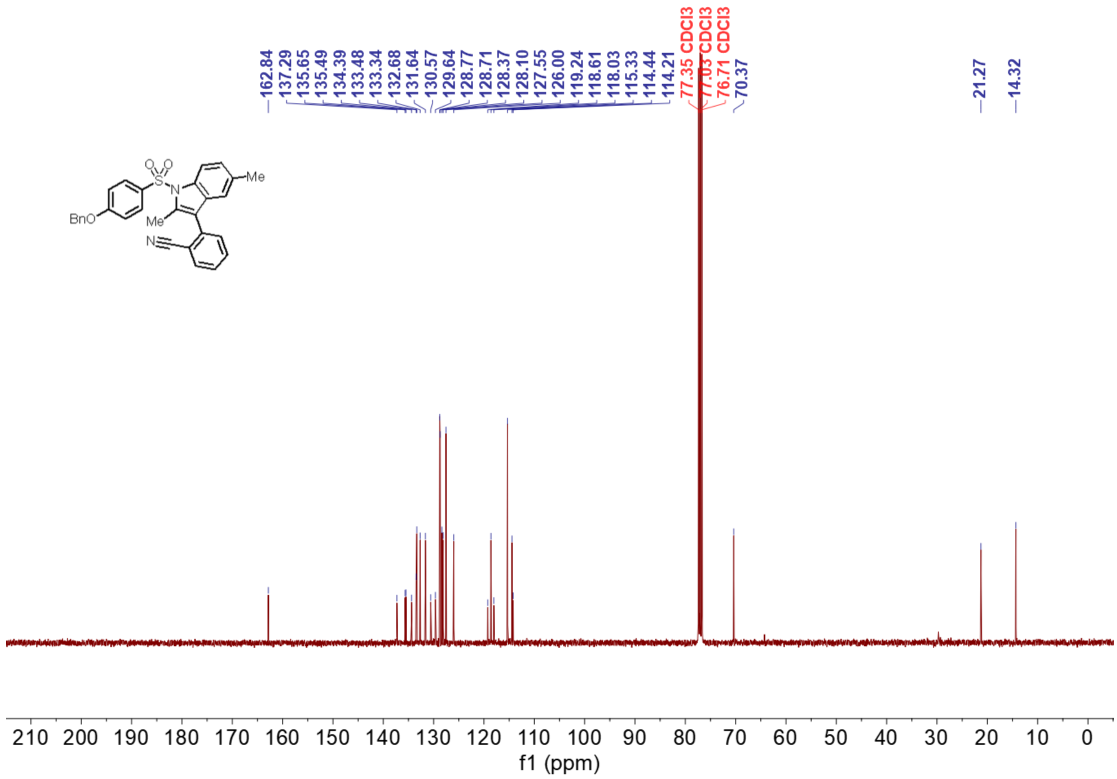
^1H NMR spectra of **1r**



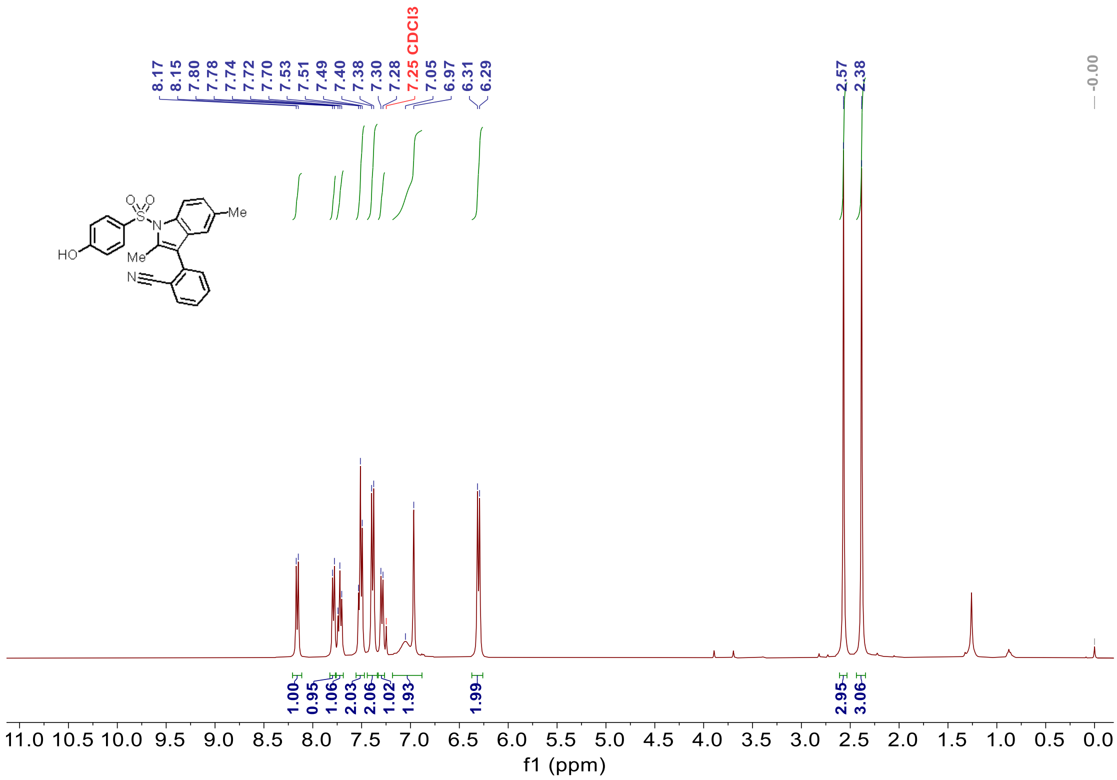
^{13}C NMR spectra of **1r**



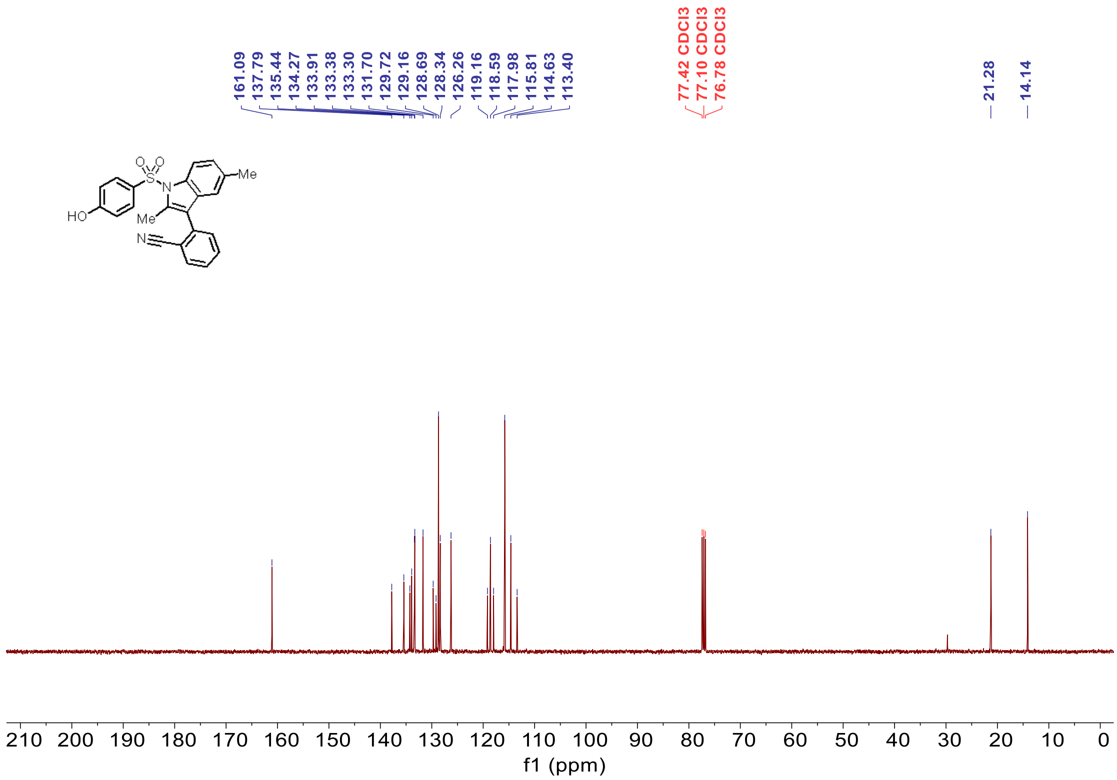
^{1}H NMR spectra of **1s**



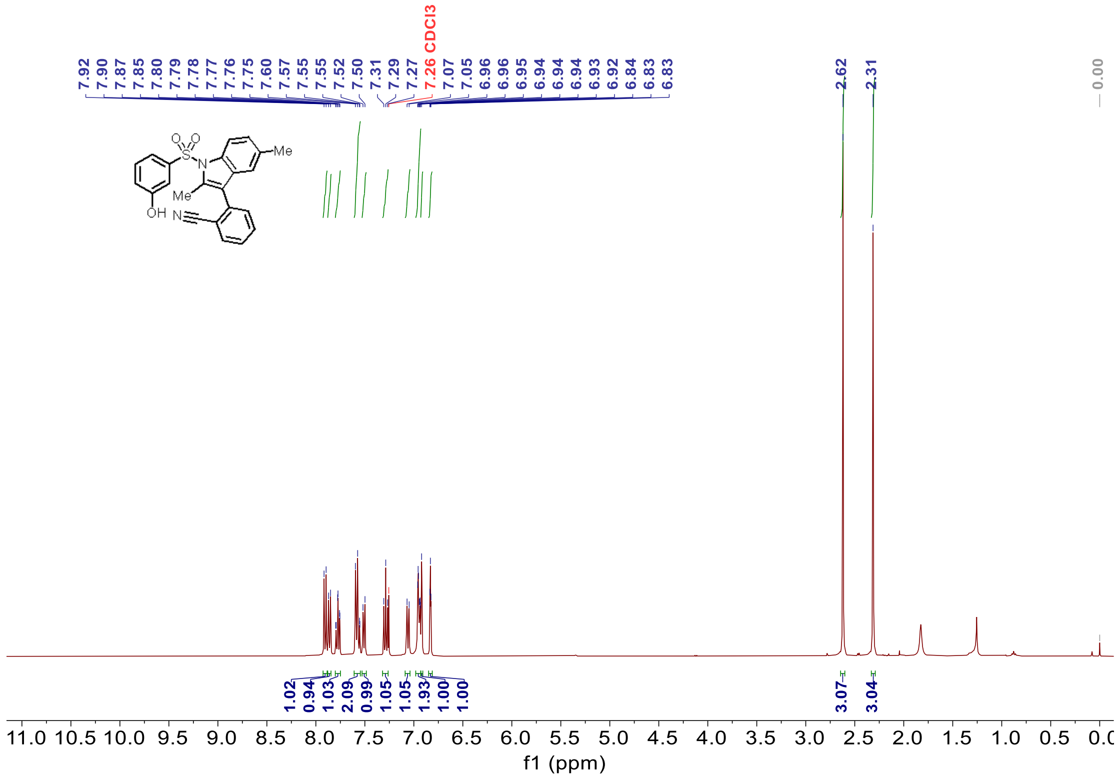
^{13}C NMR spectra of **1s**



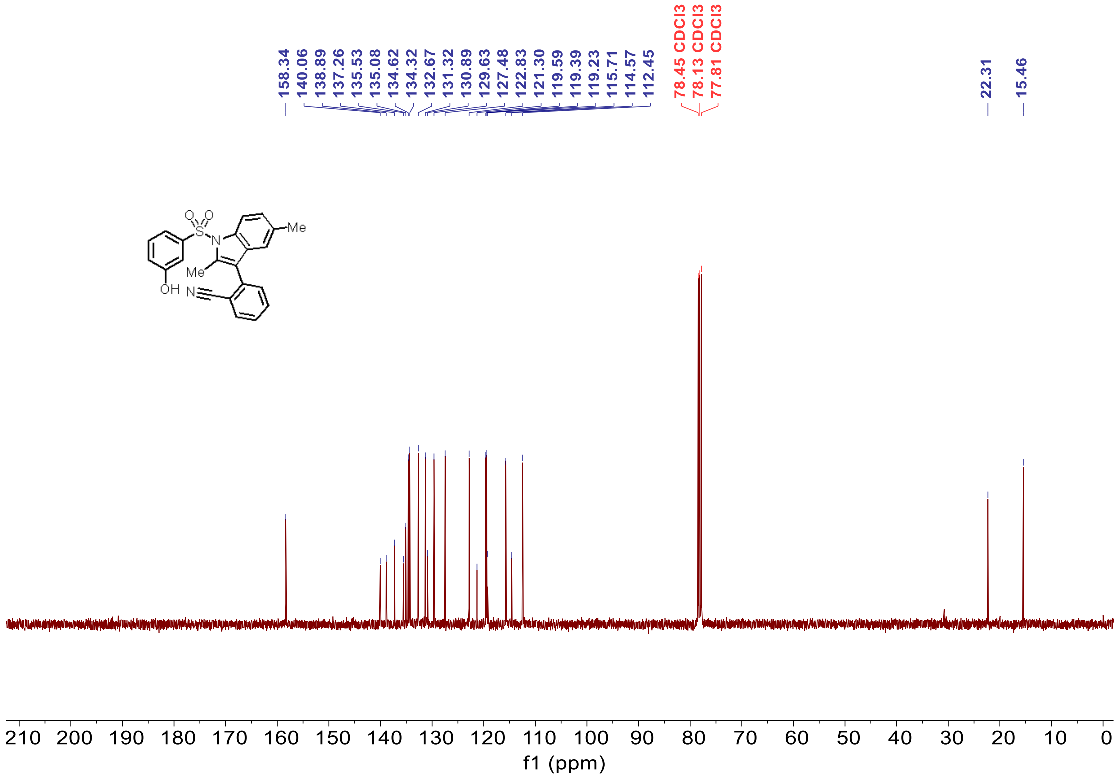
^{1}H NMR spectra of **1t**



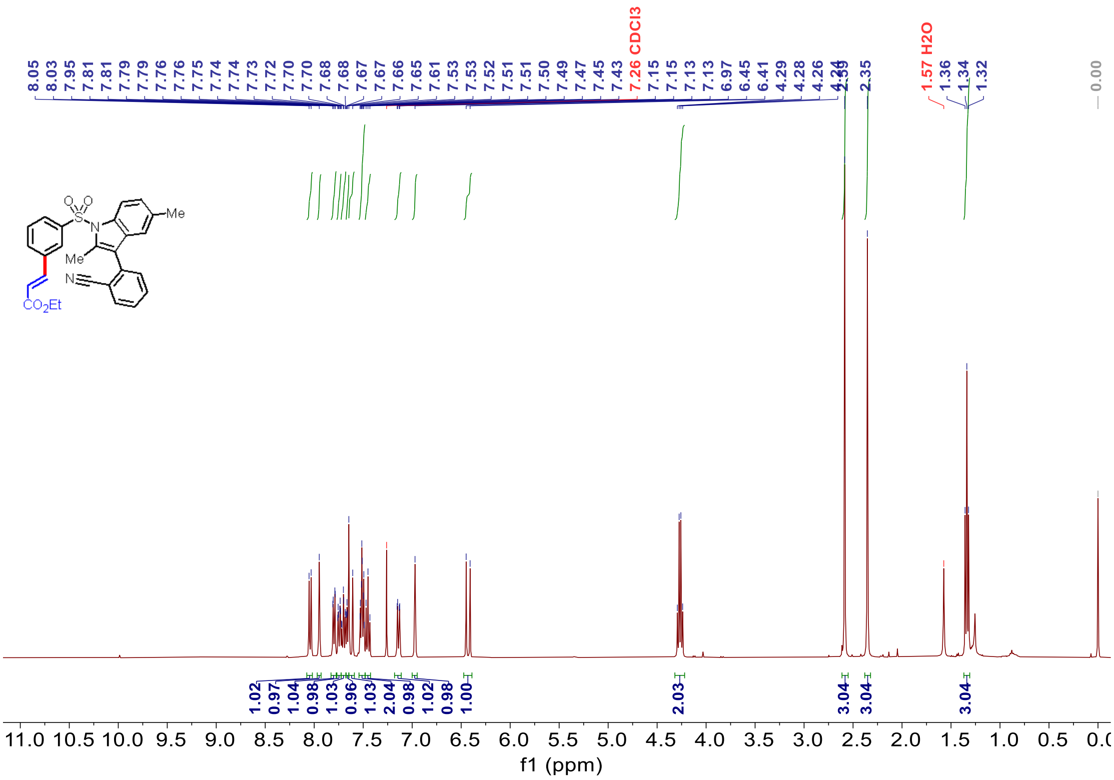
^{13}C NMR spectra of **1t**



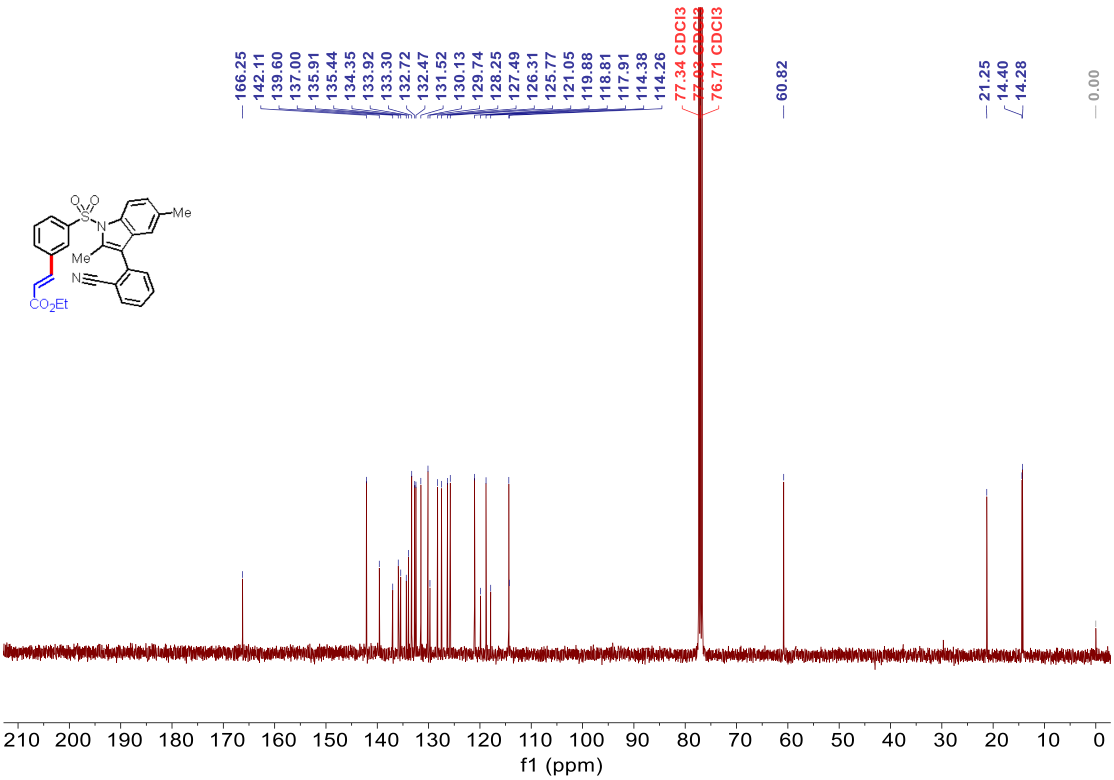
^{1}H NMR spectra of **1u**



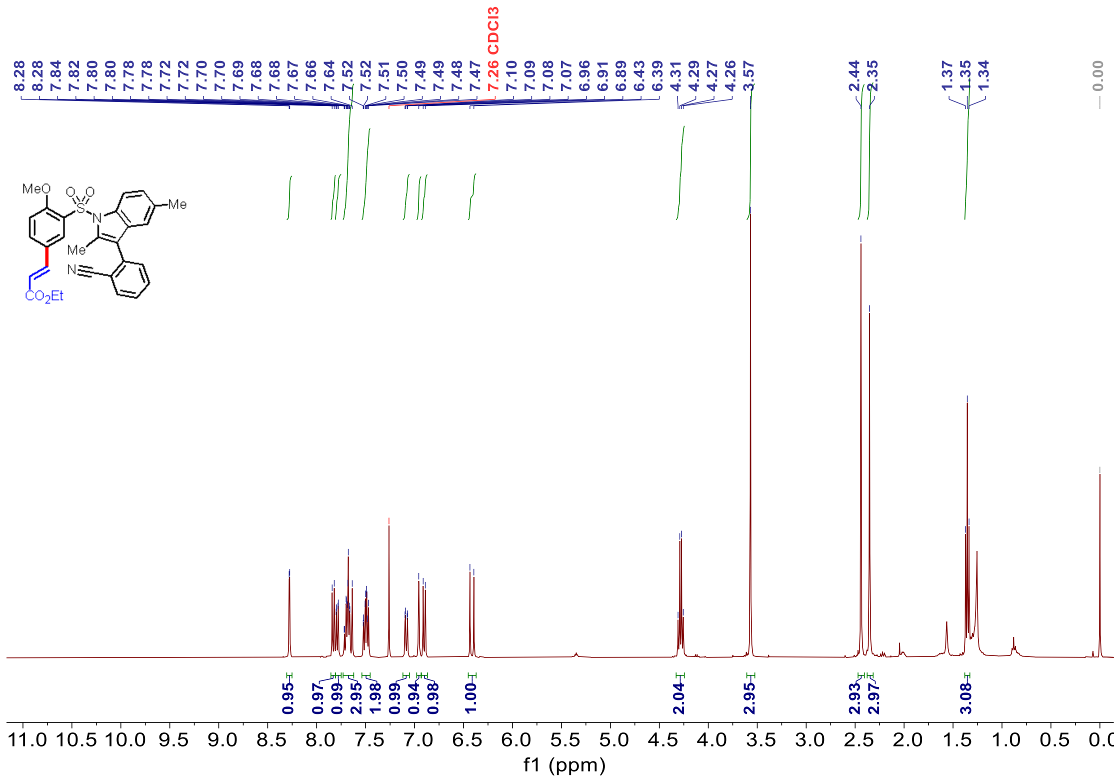
^{13}C NMR spectra of **1u**



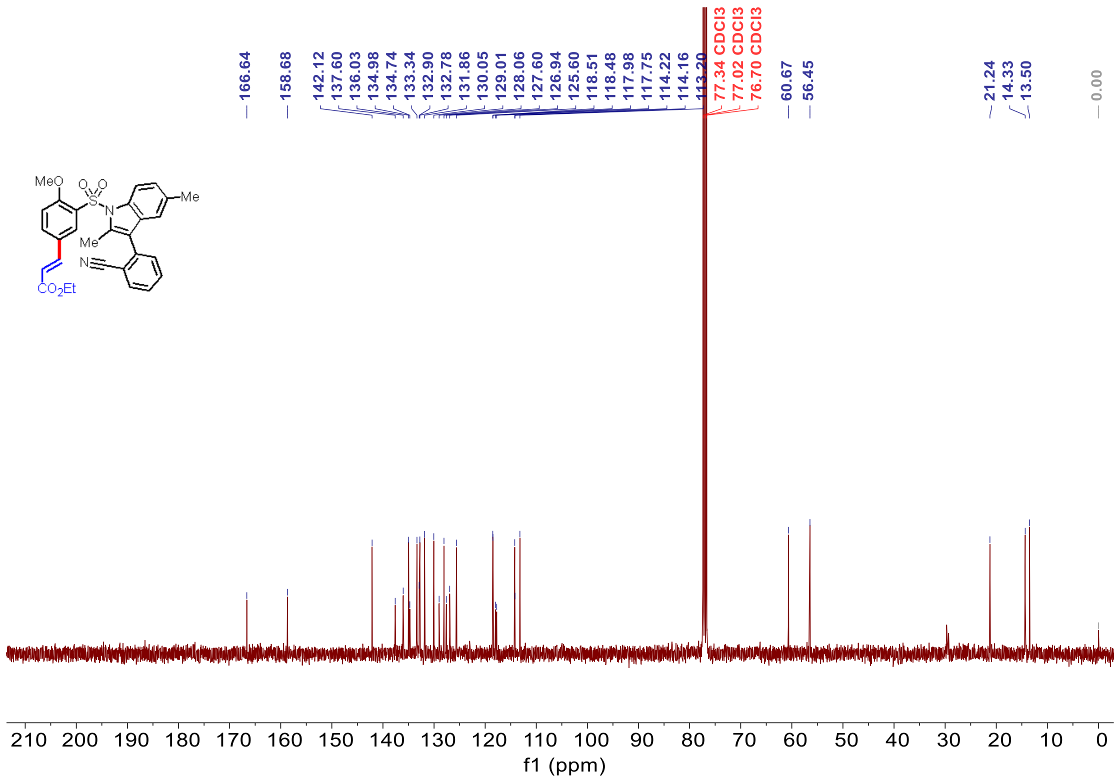
^{1}H NMR spectra of **2a**



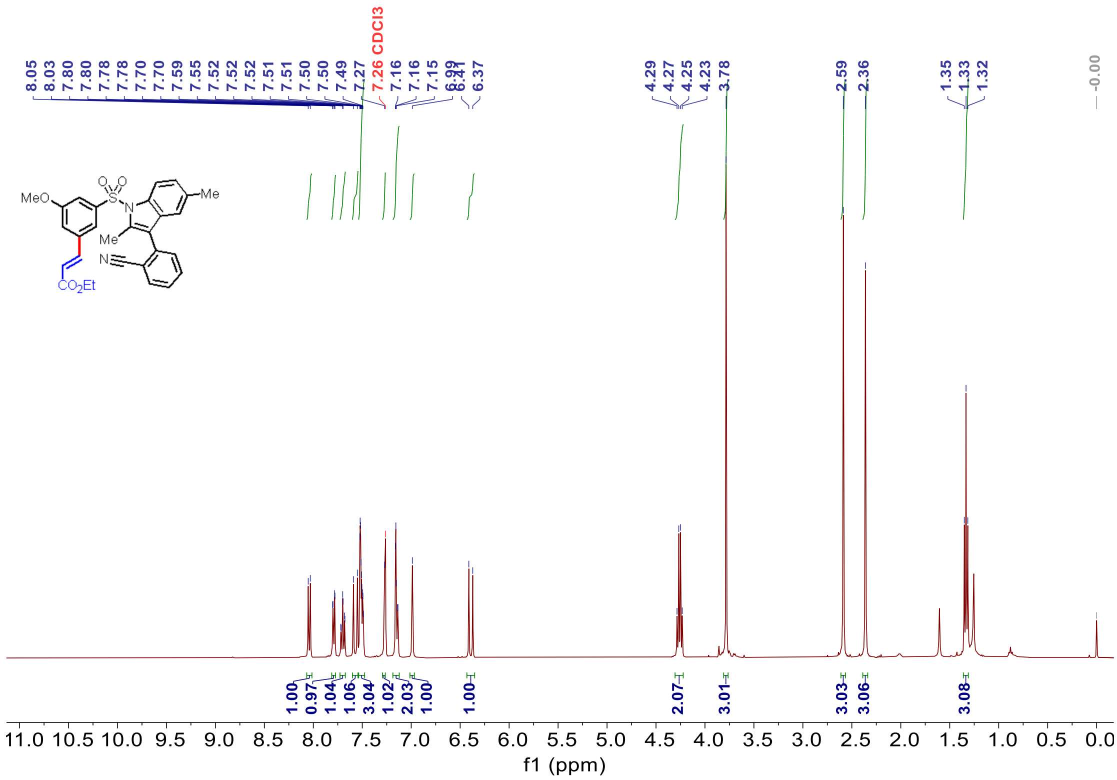
^{13}C NMR spectra of **2a**



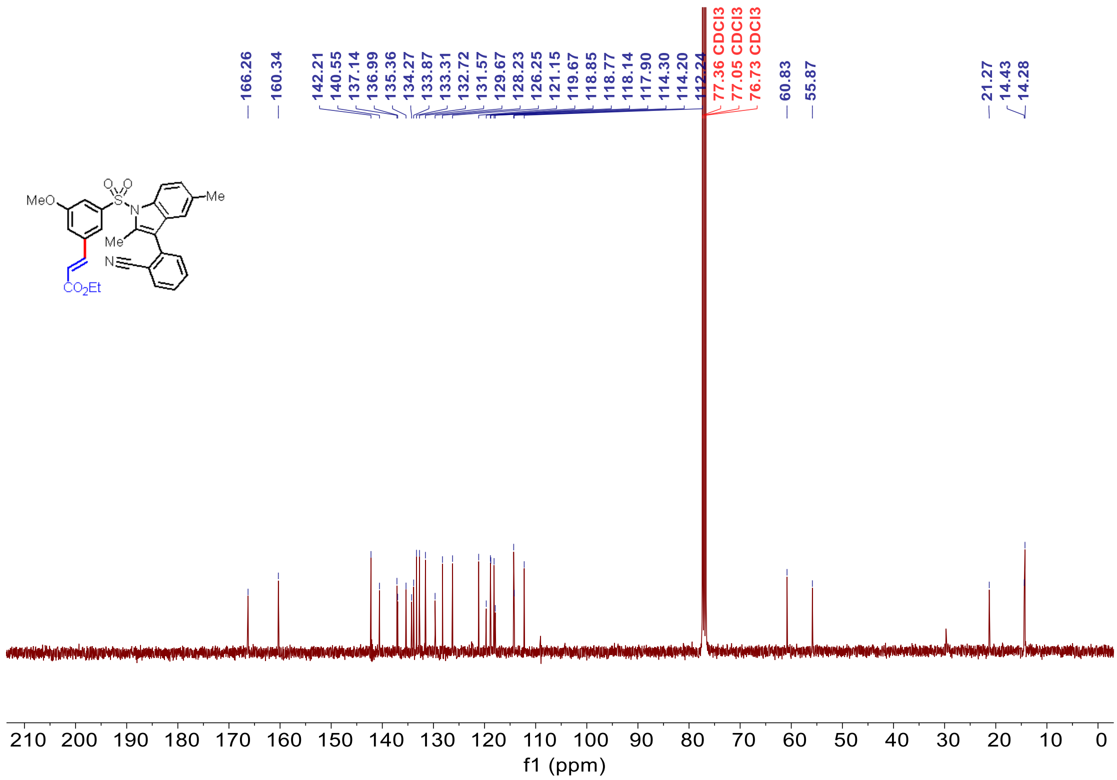
^{1}H NMR spectra of **2b**



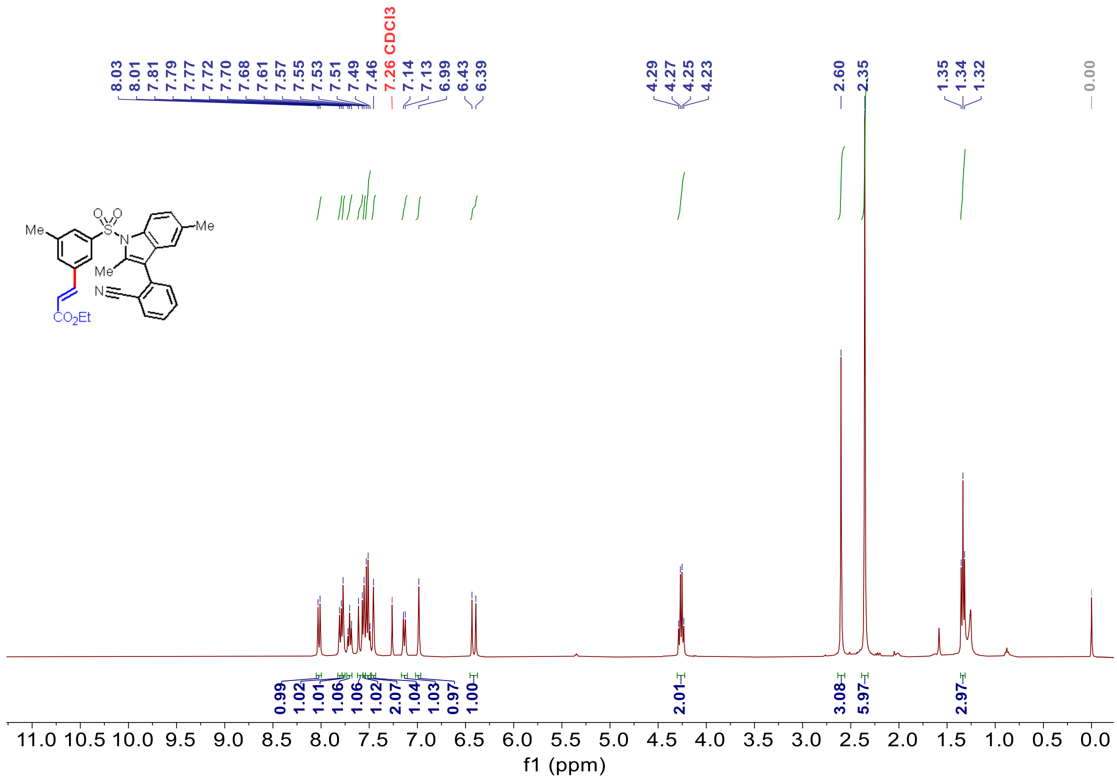
^{13}C NMR spectra of **2b**



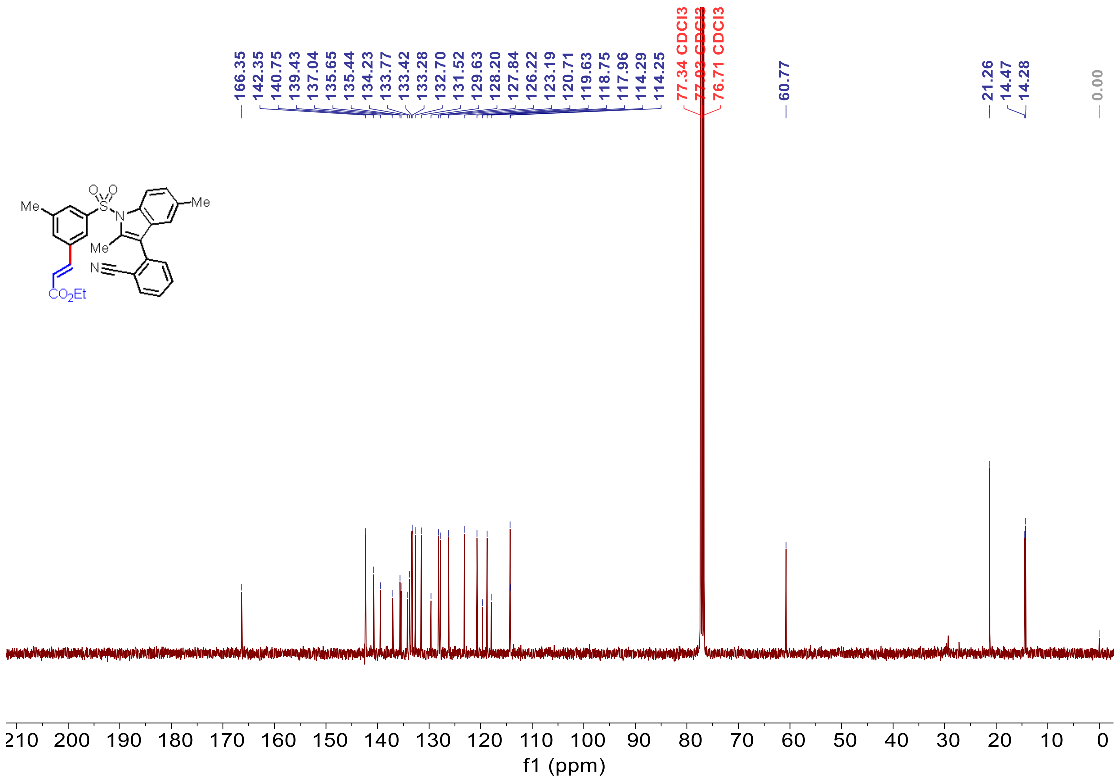
^{1}H NMR spectra of **2c**



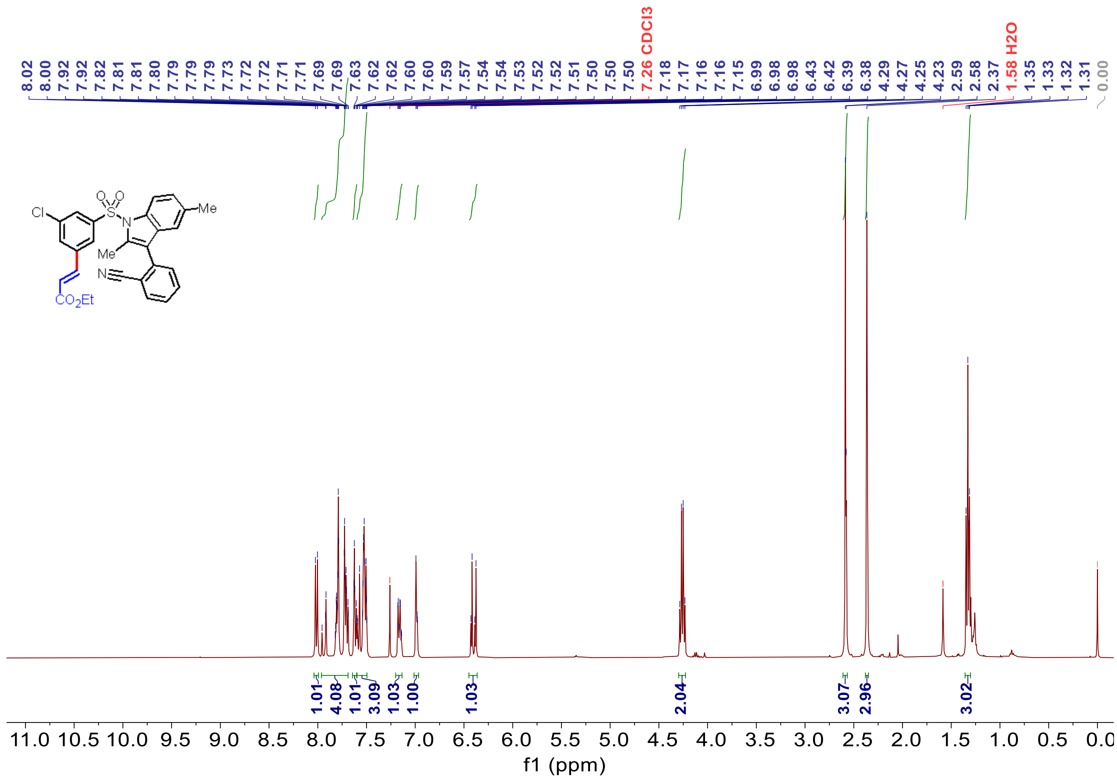
^{13}C NMR spectra of **2c**



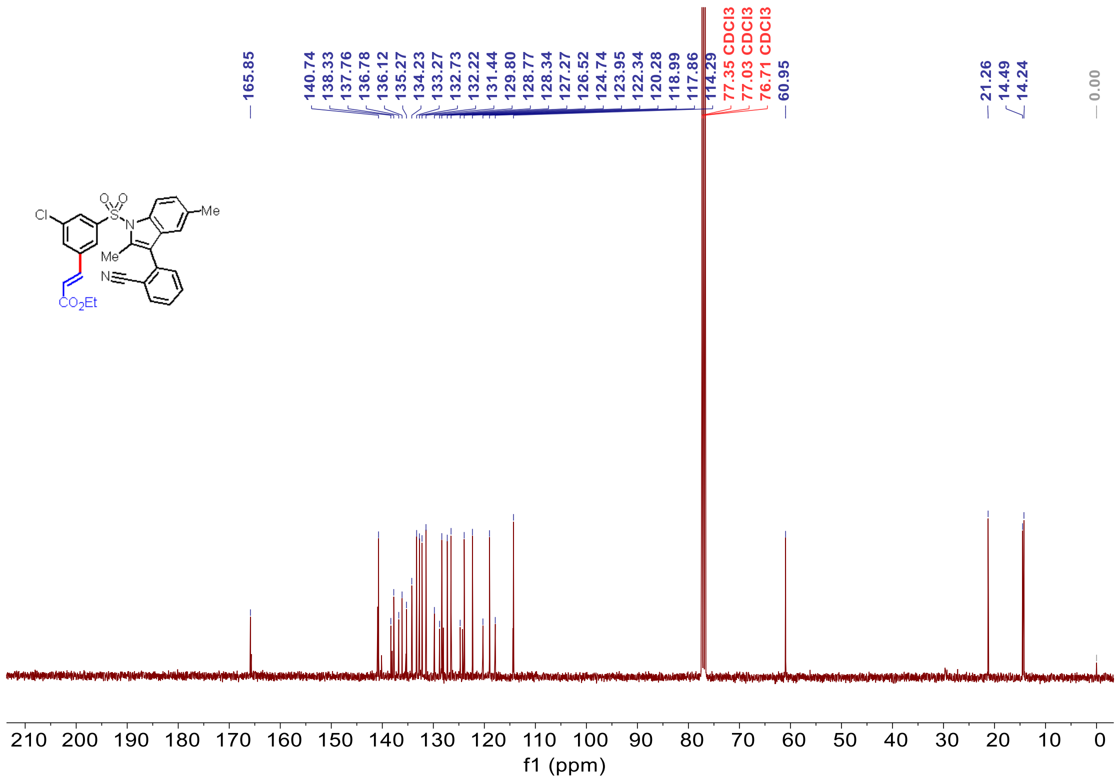
^{1}H NMR spectra of **2d**



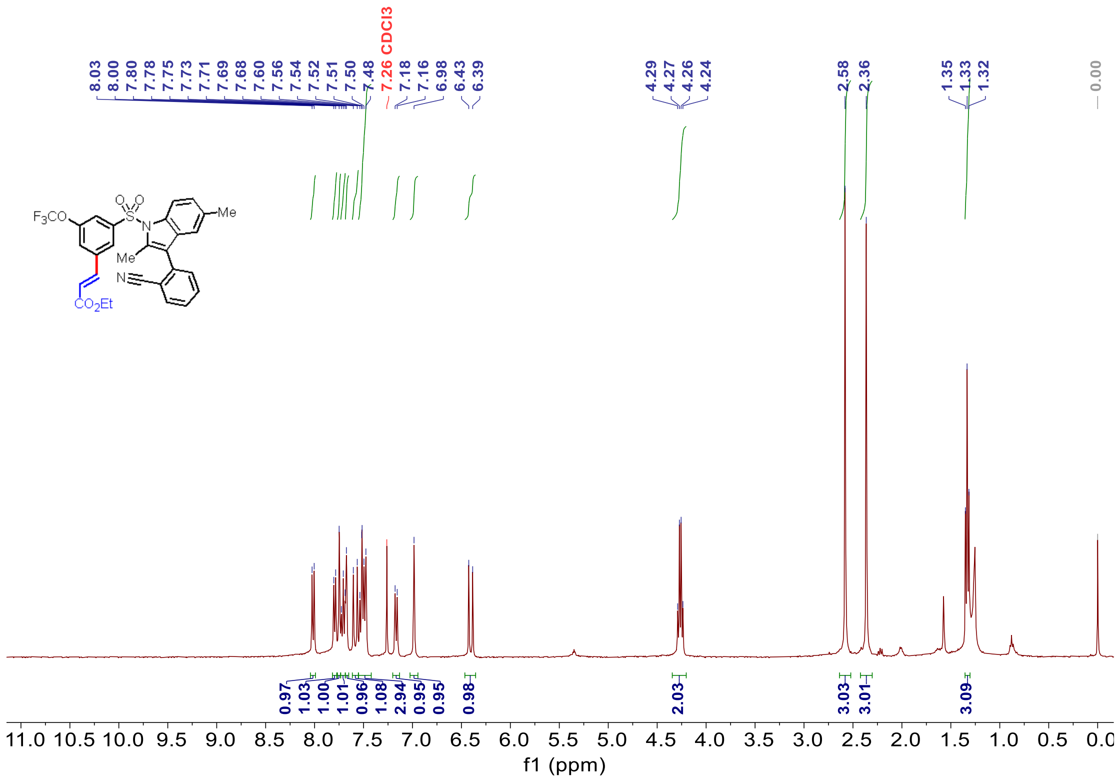
^{13}C NMR spectra of **2d**



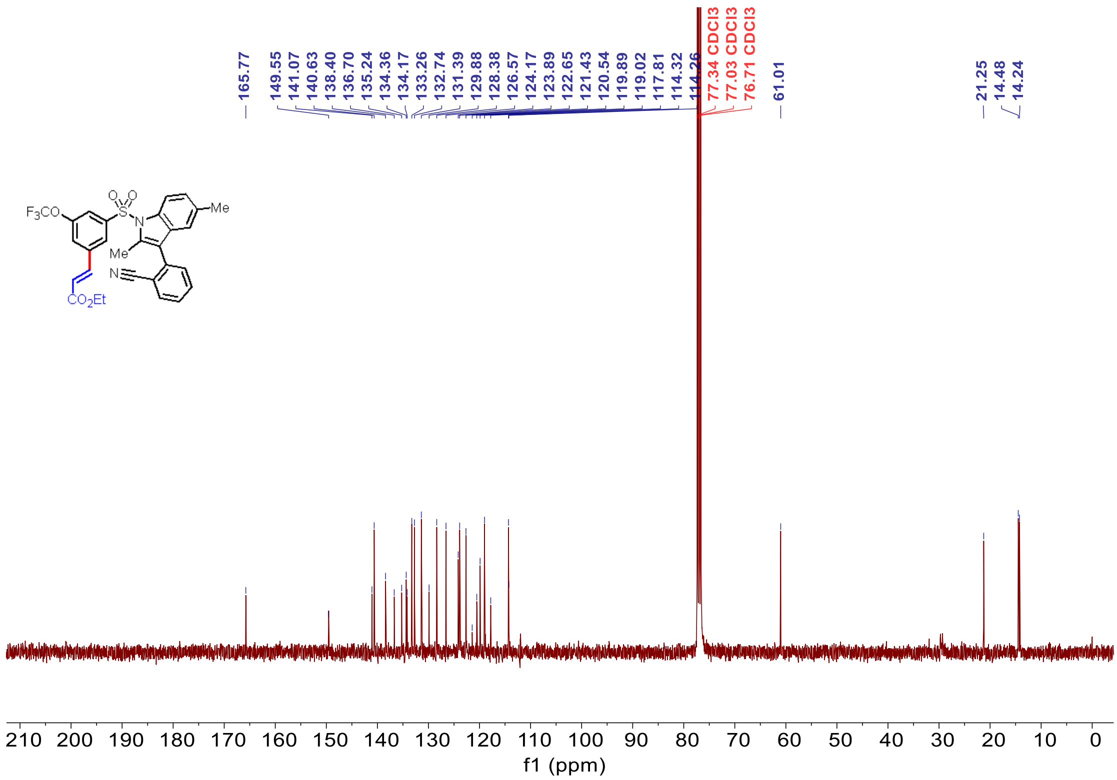
^{1}H NMR spectra of **2e**



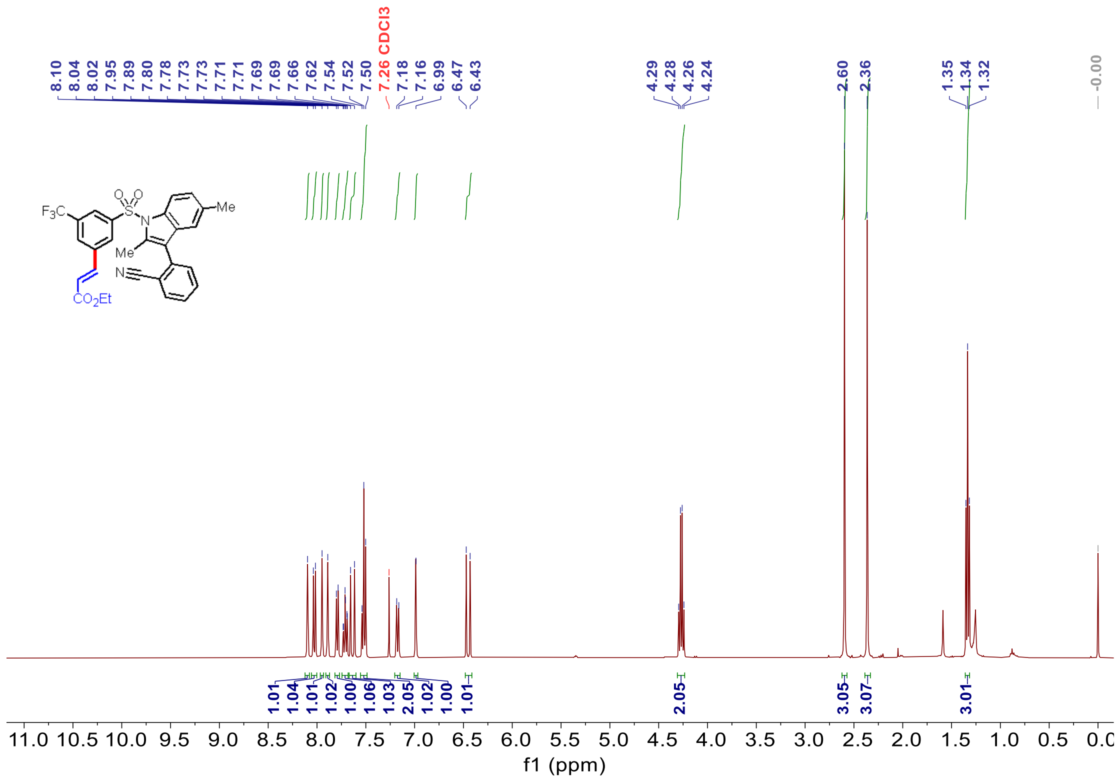
^{13}C NMR spectra of **2e**



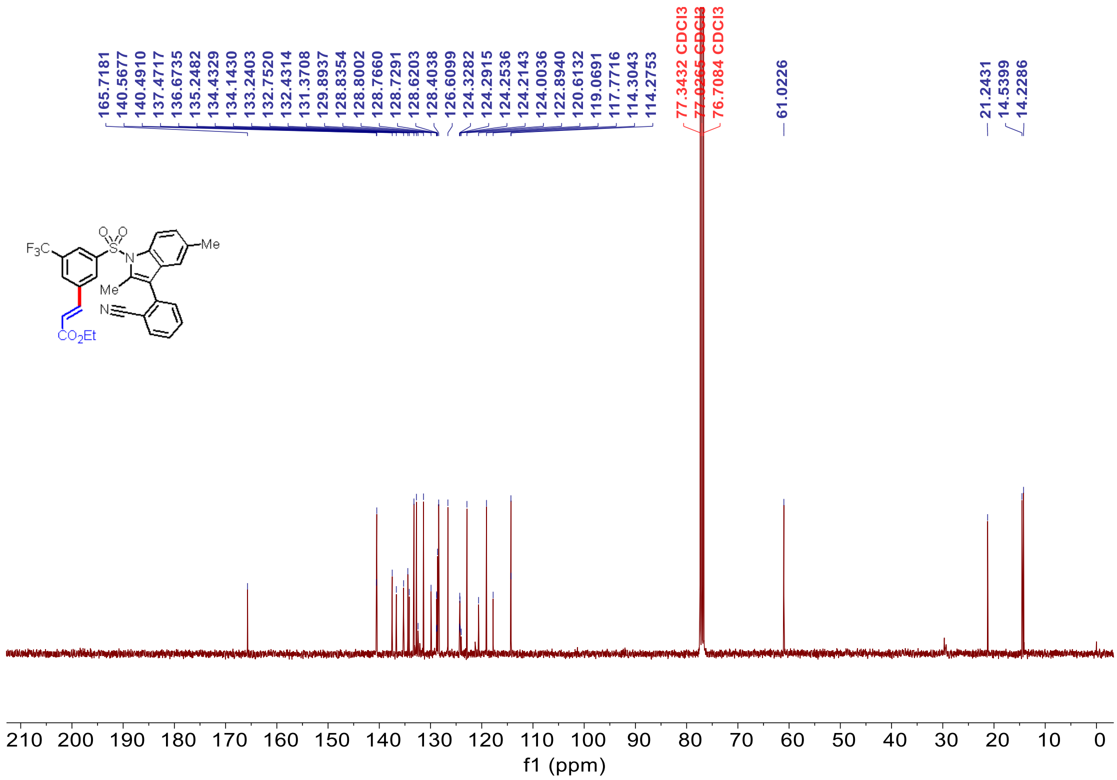
^{1}H NMR spectra of **2f**



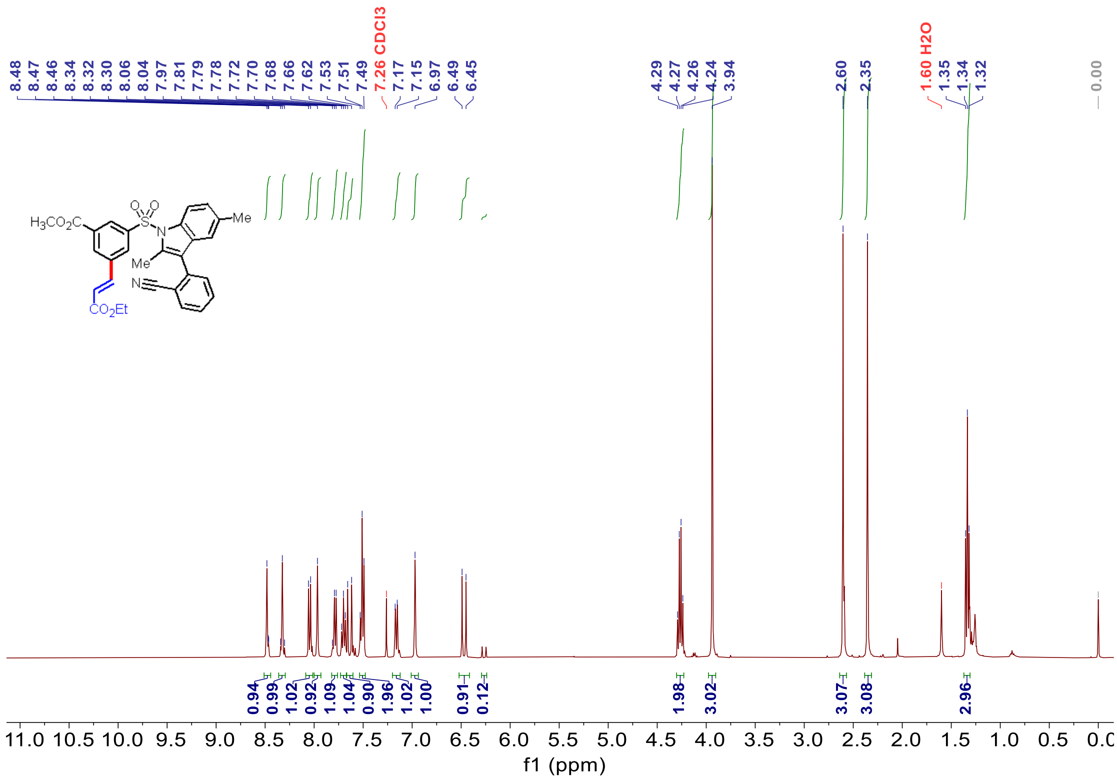
^{13}C NMR spectra of **2f**



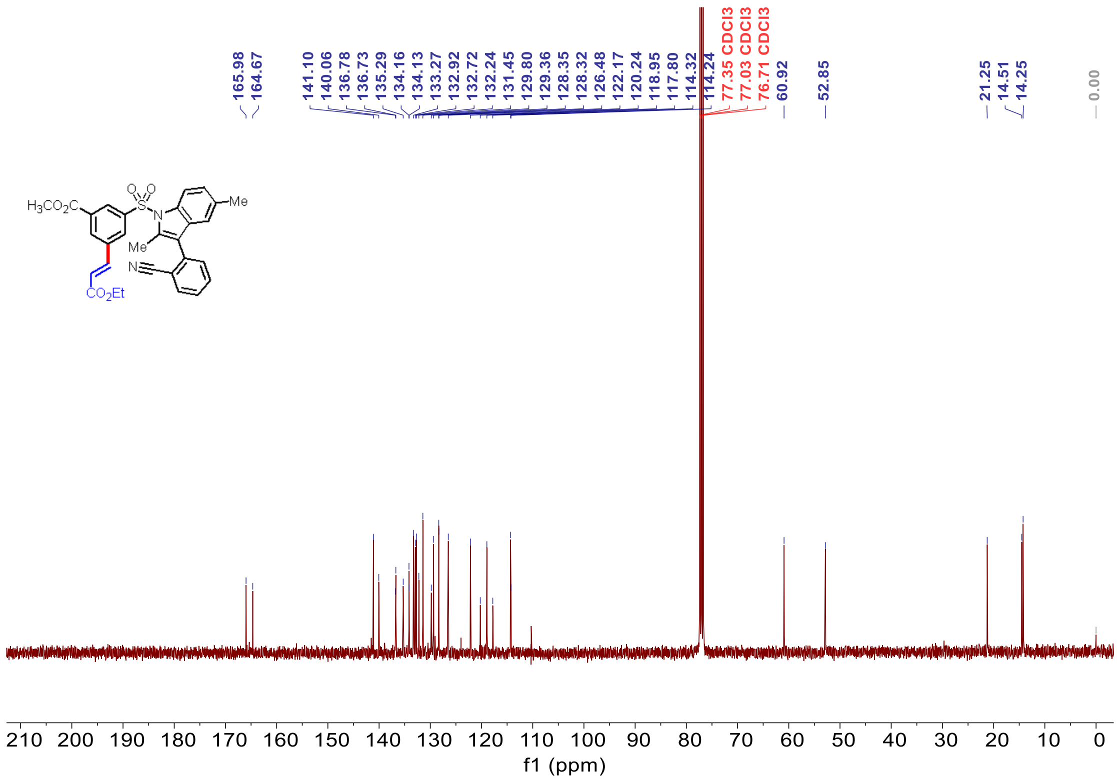
^{1}H NMR spectra of **2g**



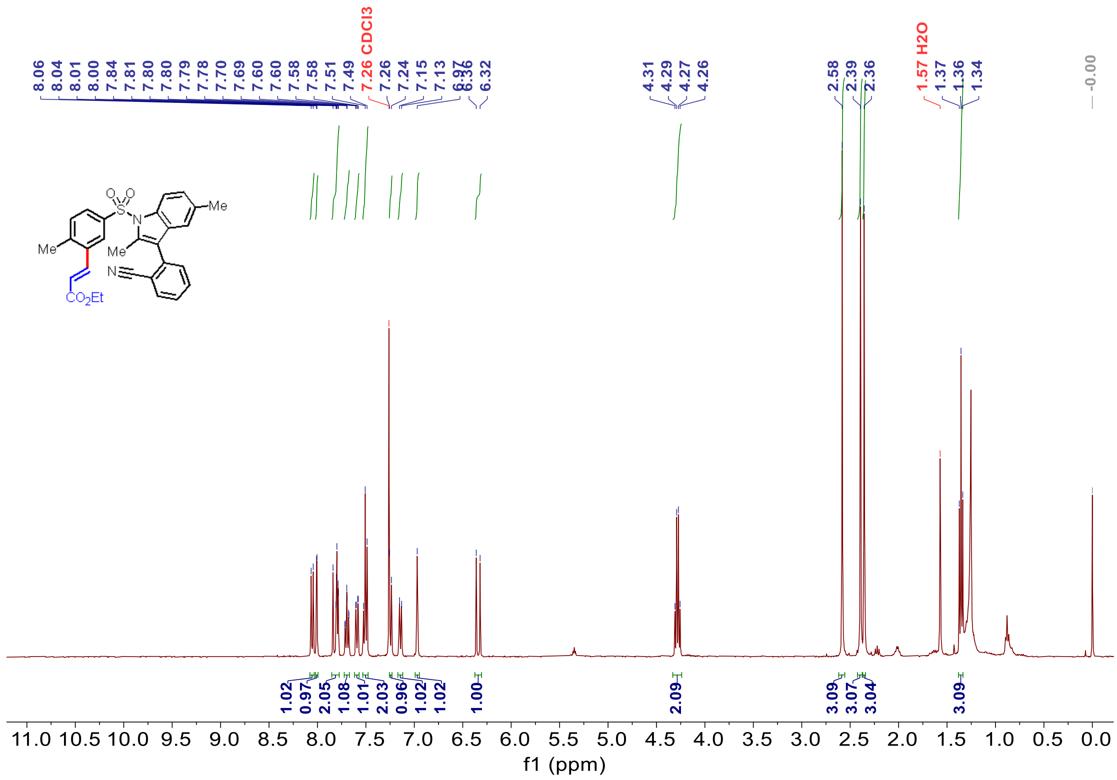
^{13}C NMR spectra of **2g**



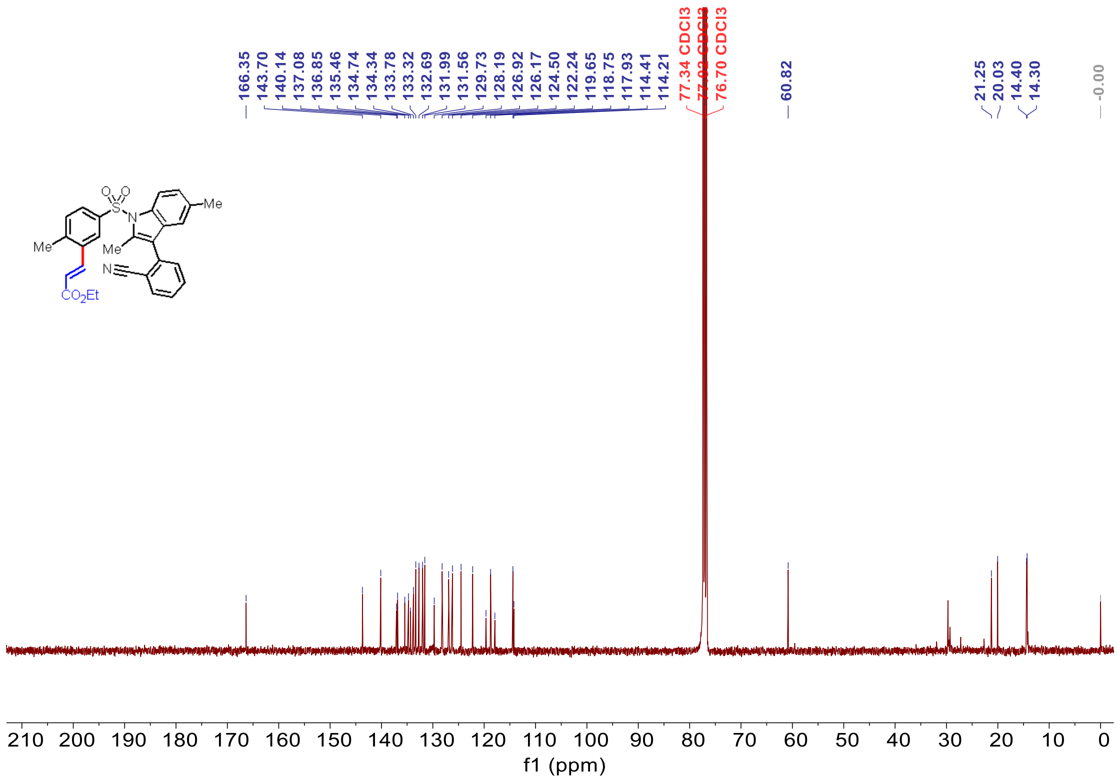
^{1}H NMR spectra of **2h**



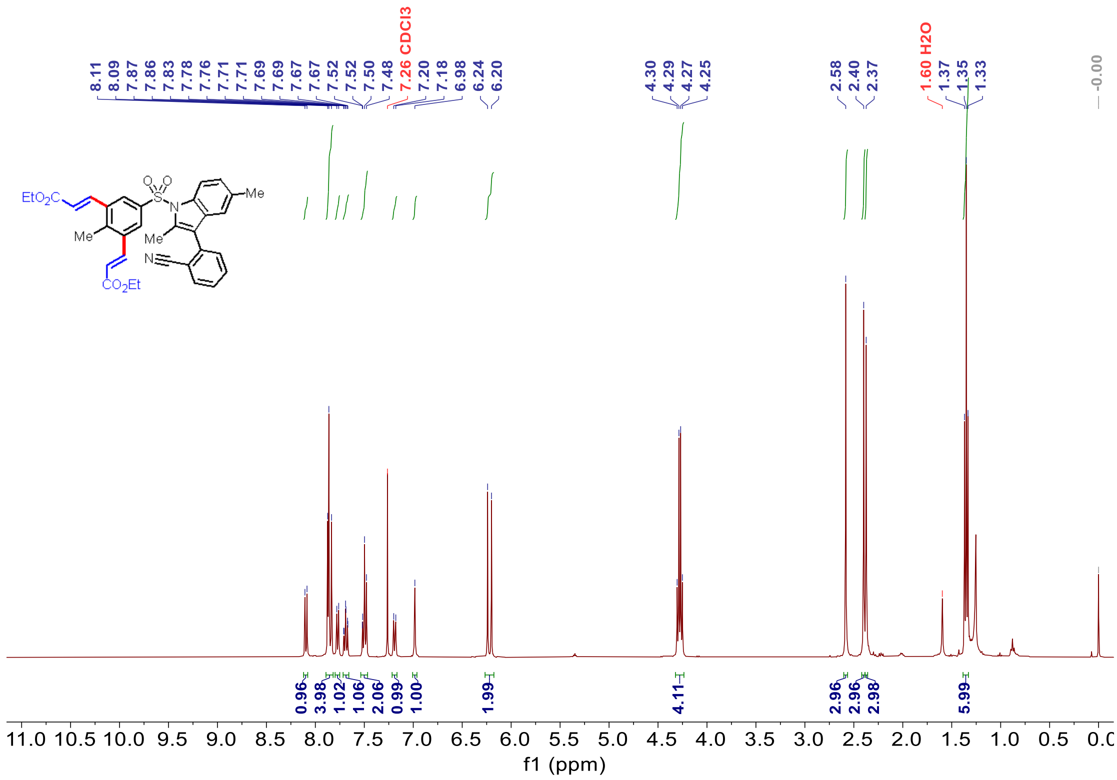
^{13}C NMR spectra of **2h**



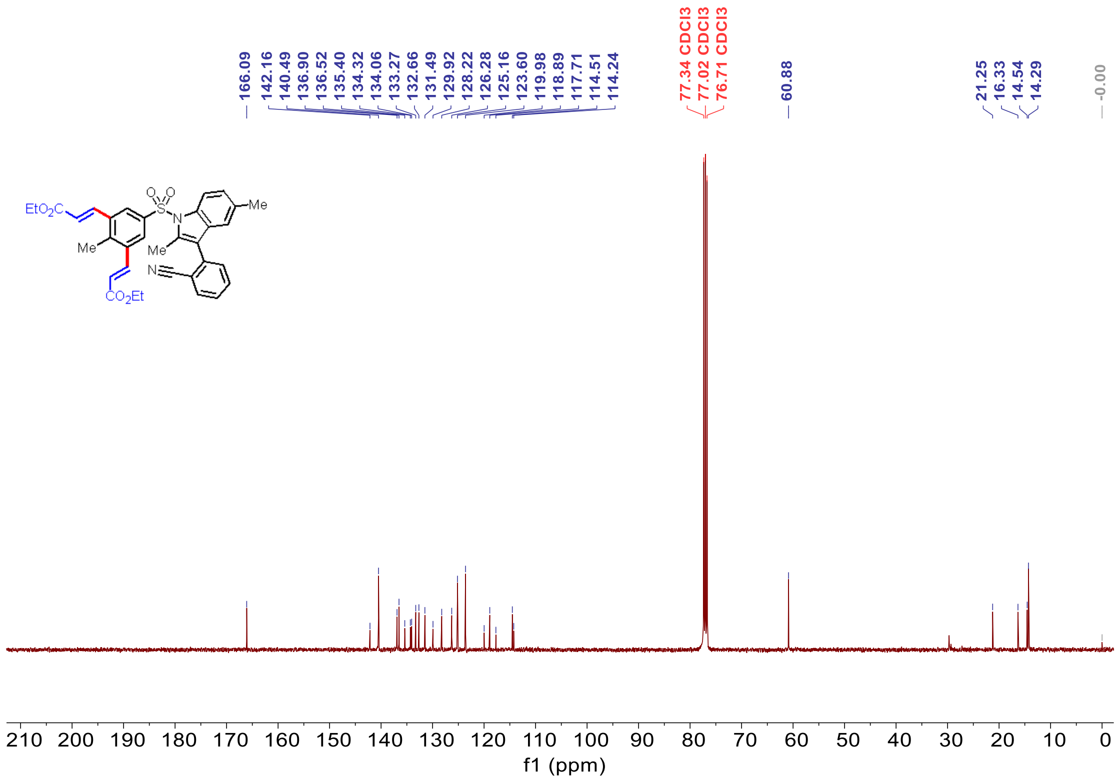
^{1}H NMR spectra of **2i$_{mono}$**



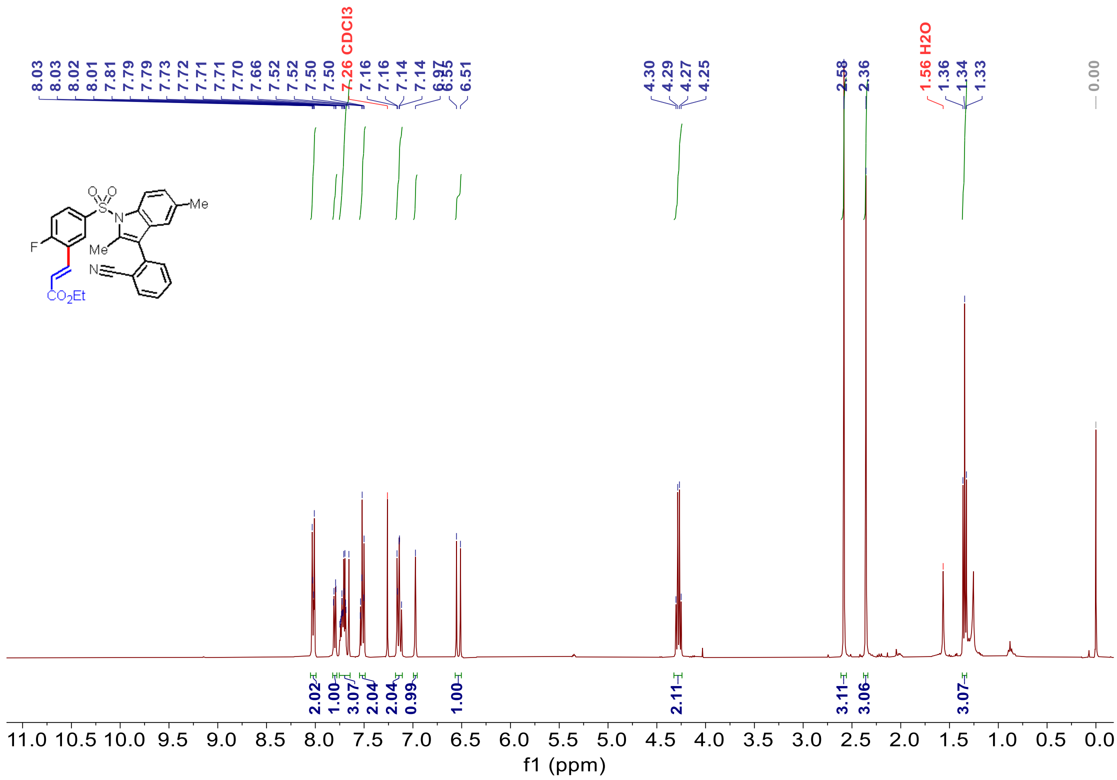
^{13}C NMR spectra of **2i$_{mono}$**



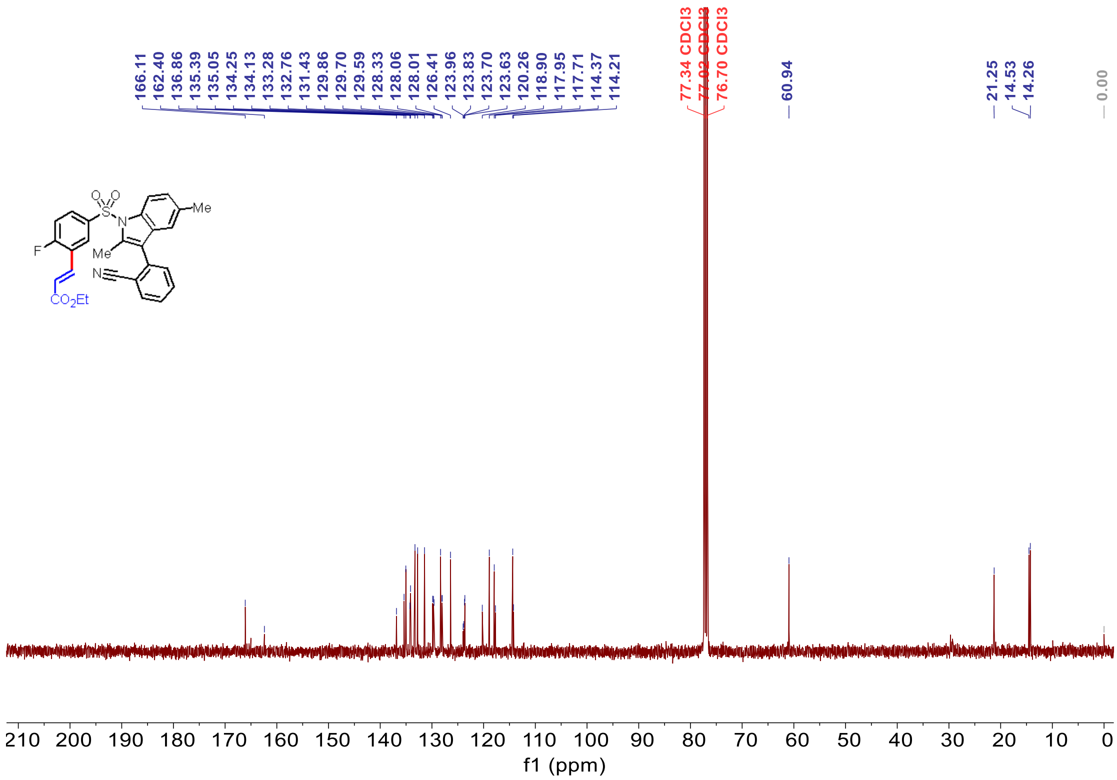
^{1}H NMR spectra of **2i$_{di}$**



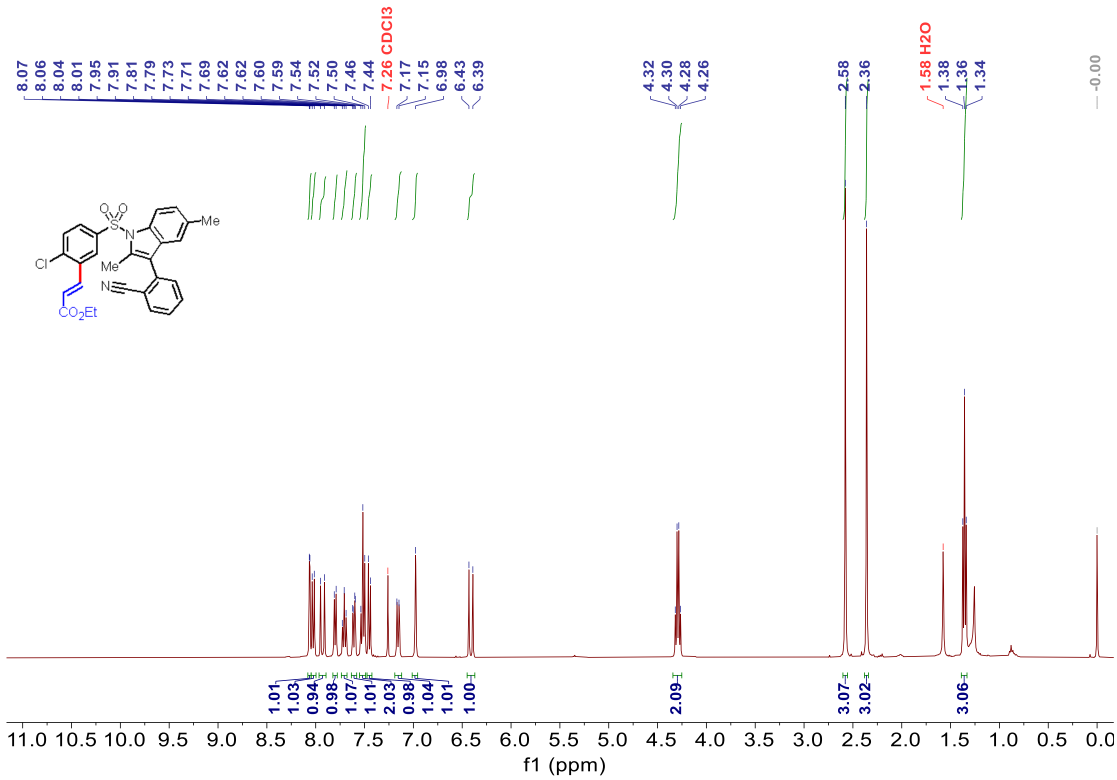
^{13}C NMR spectra of **2i$_{di}$**



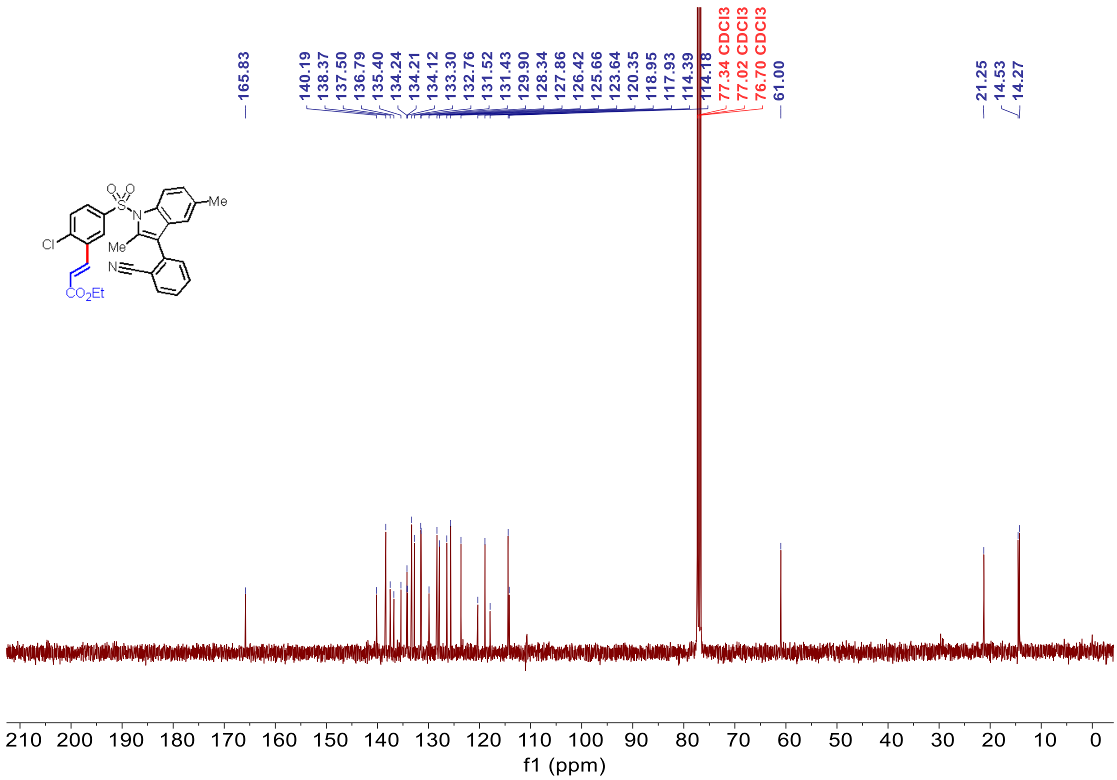
^{1}H NMR spectra of **2j**



^{13}C NMR spectra of **2j**



^{1}H NMR spectra of **2k**



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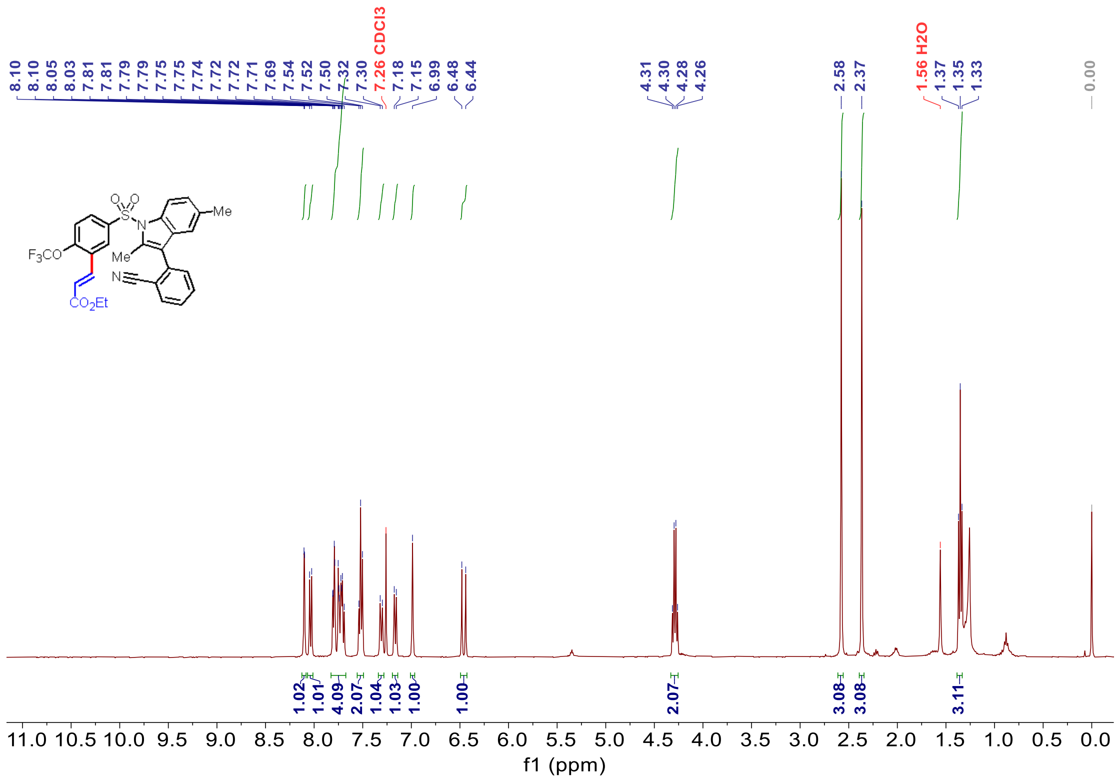

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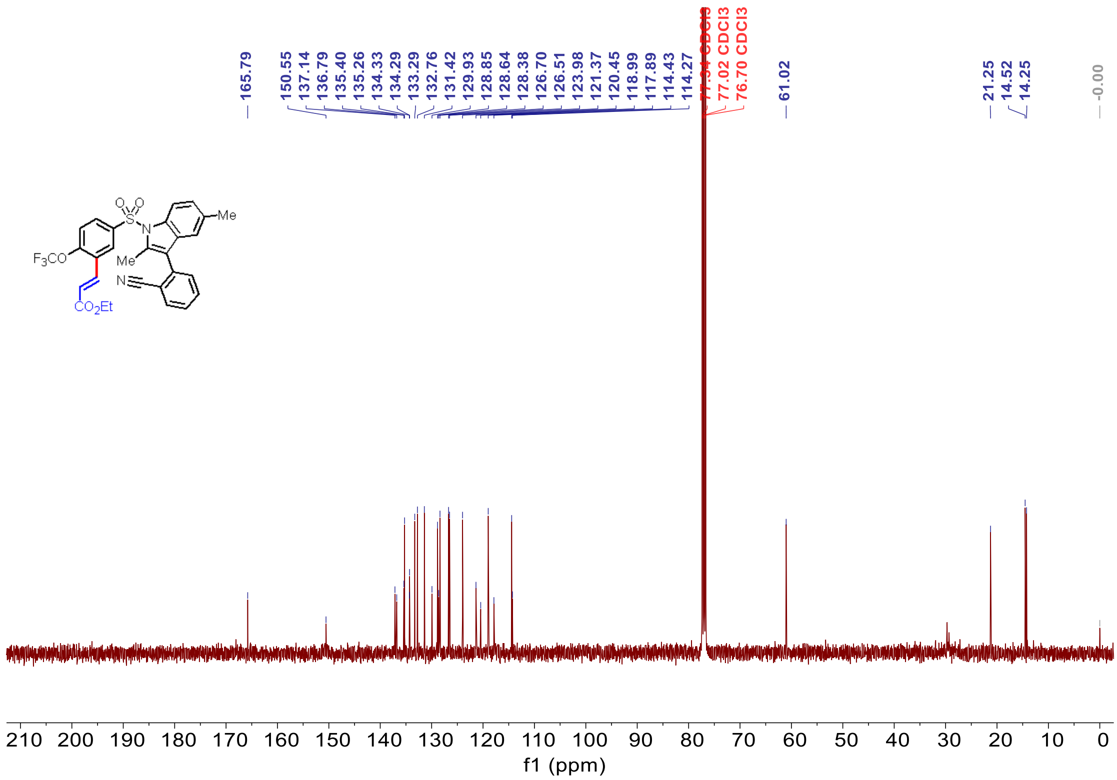

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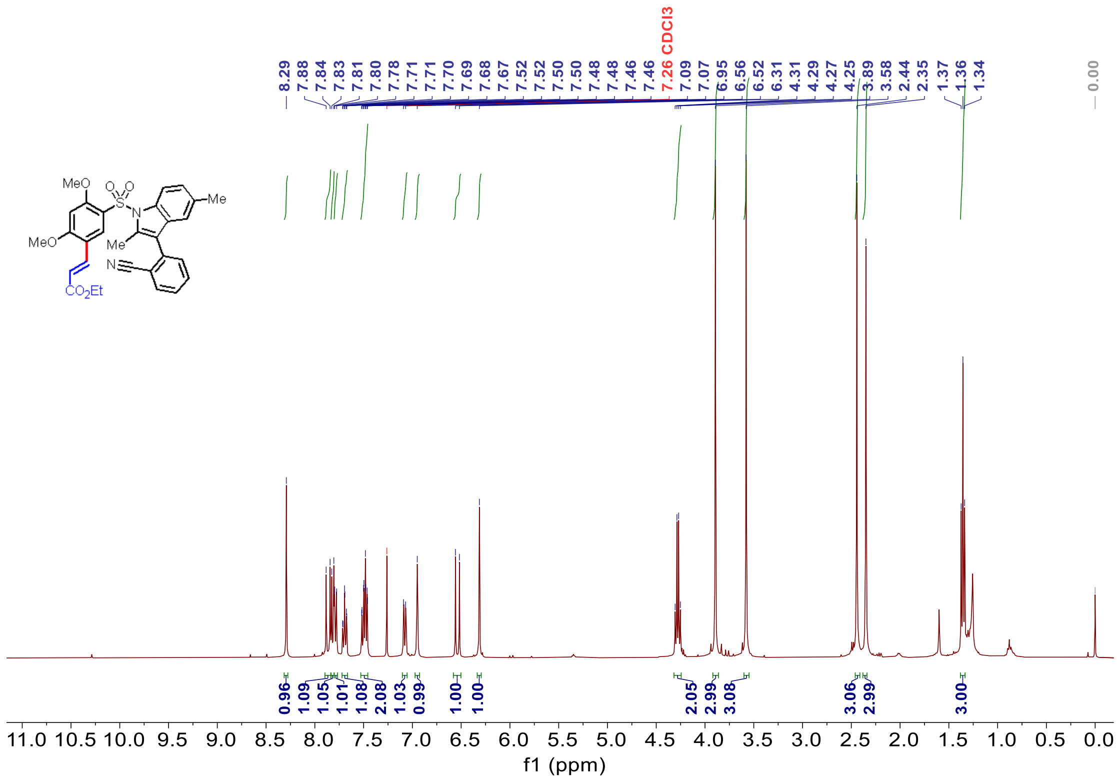
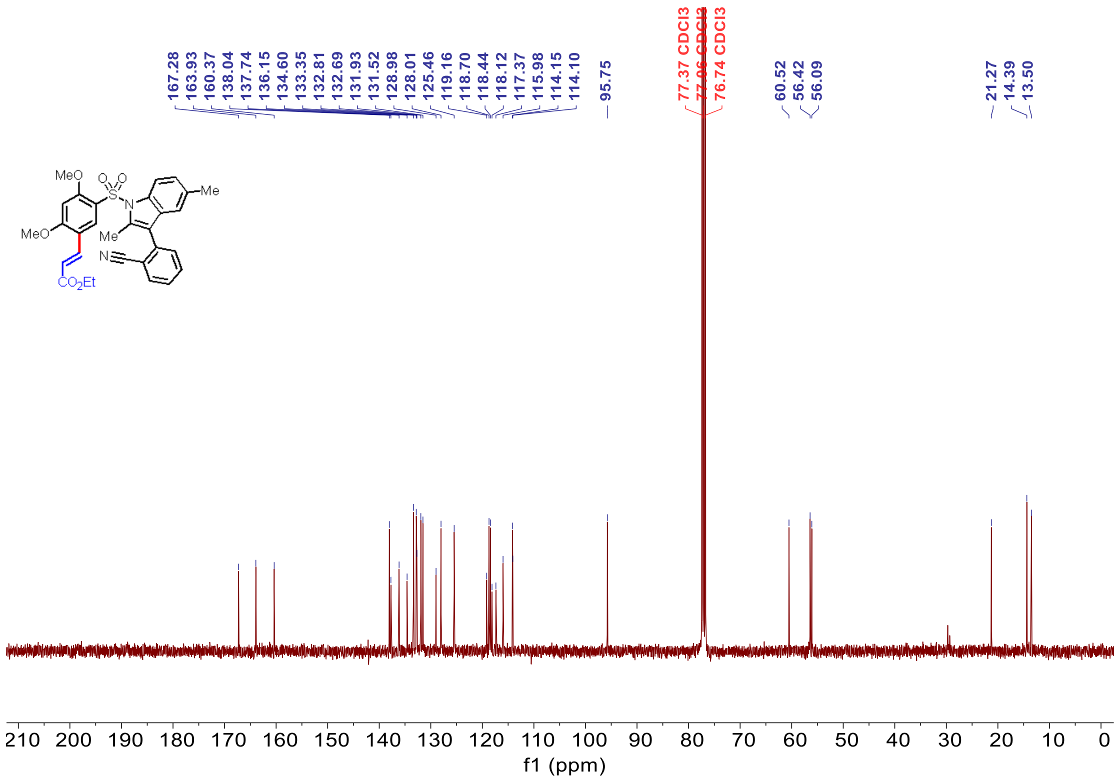
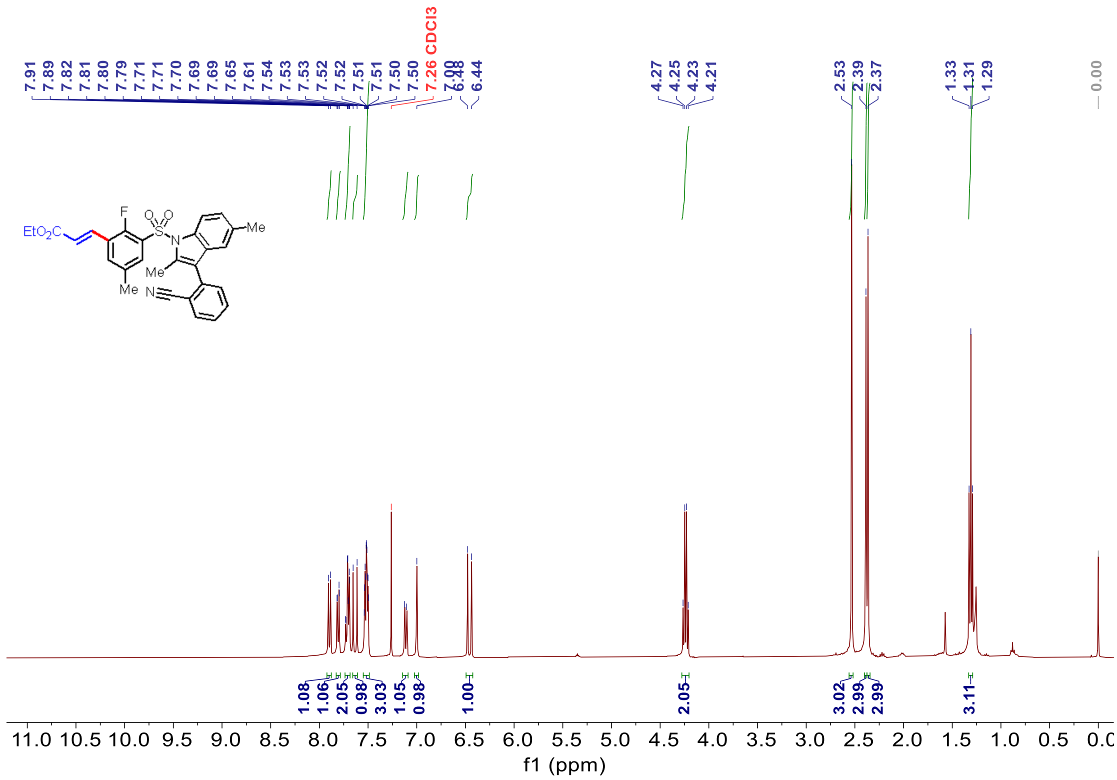


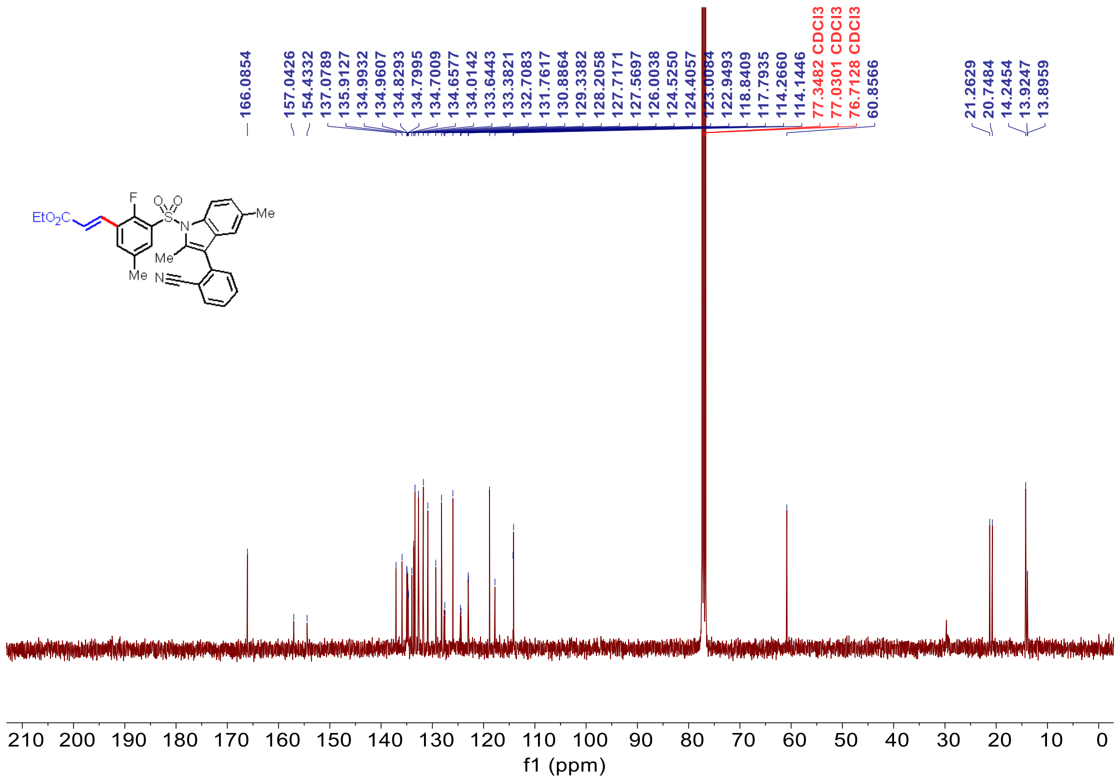
^{1}H NMR spectra of **2m**



^{13}C NMR spectra of **2m**



^{1}H NMR spectra of **2n**



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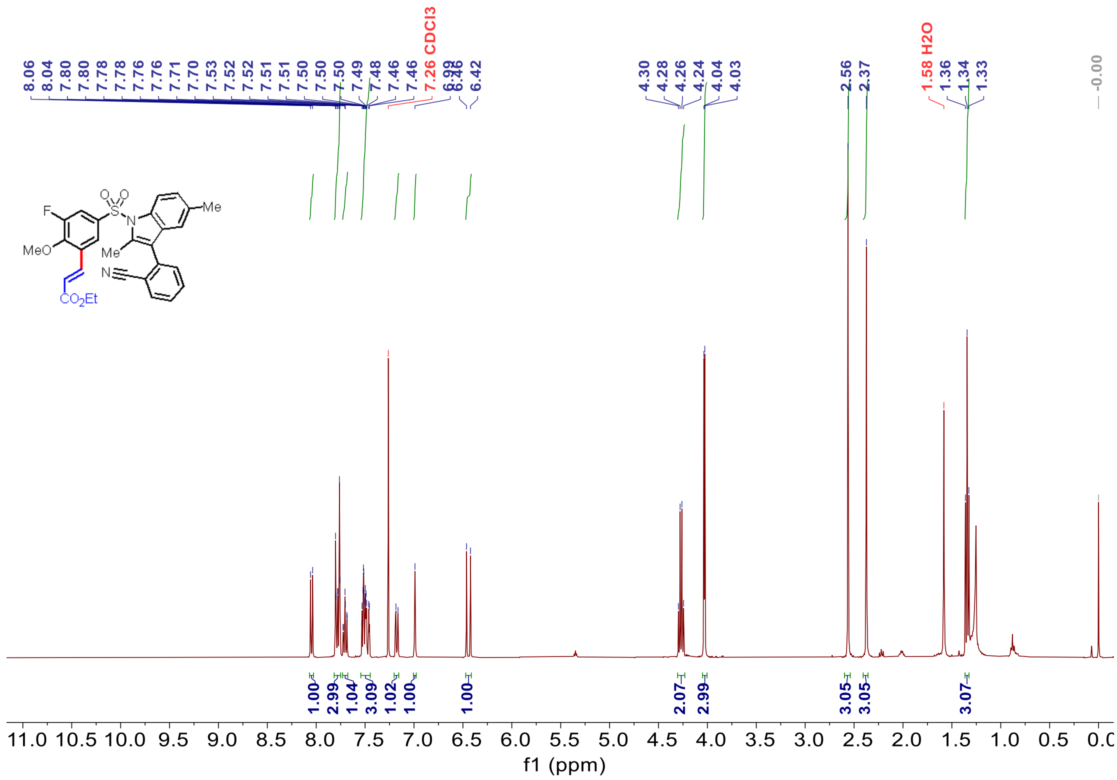
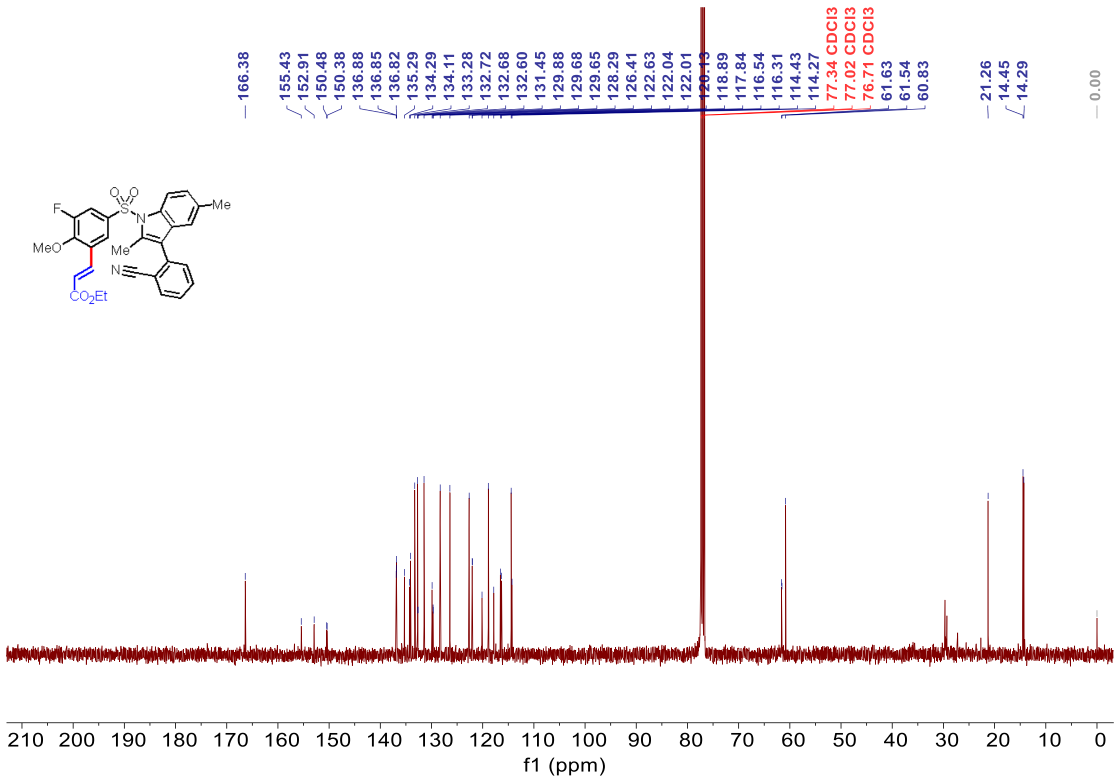


^{1}H NMR spectra of **2o**



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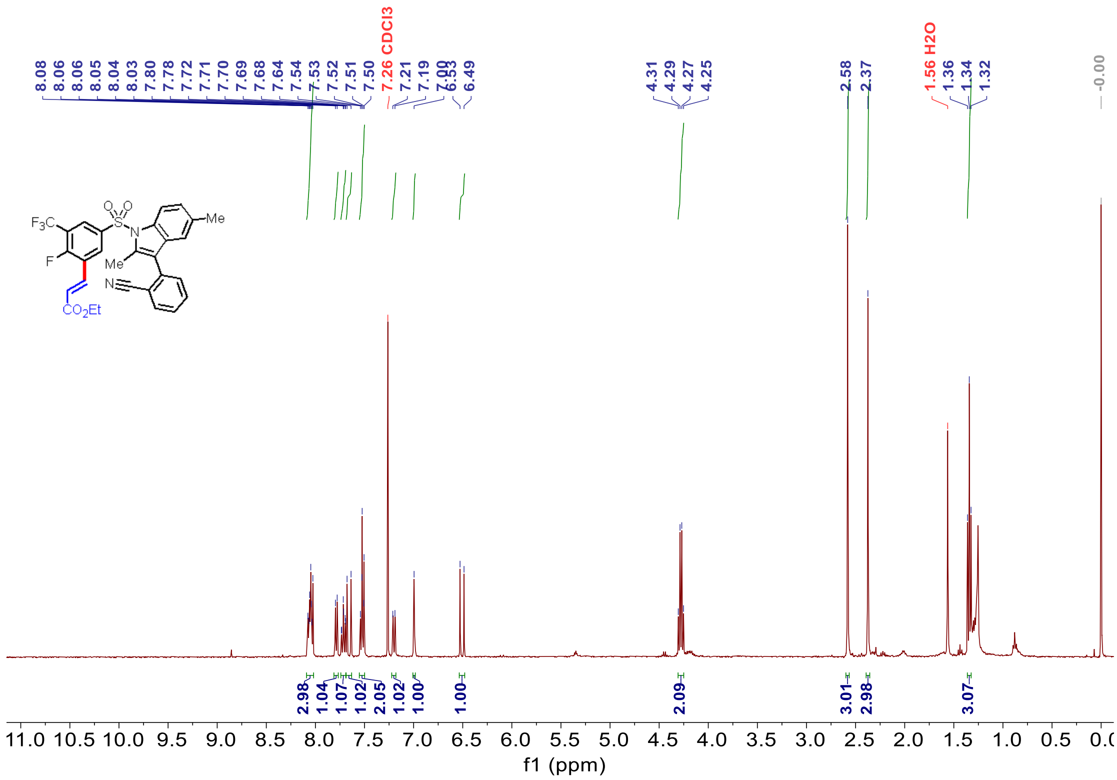
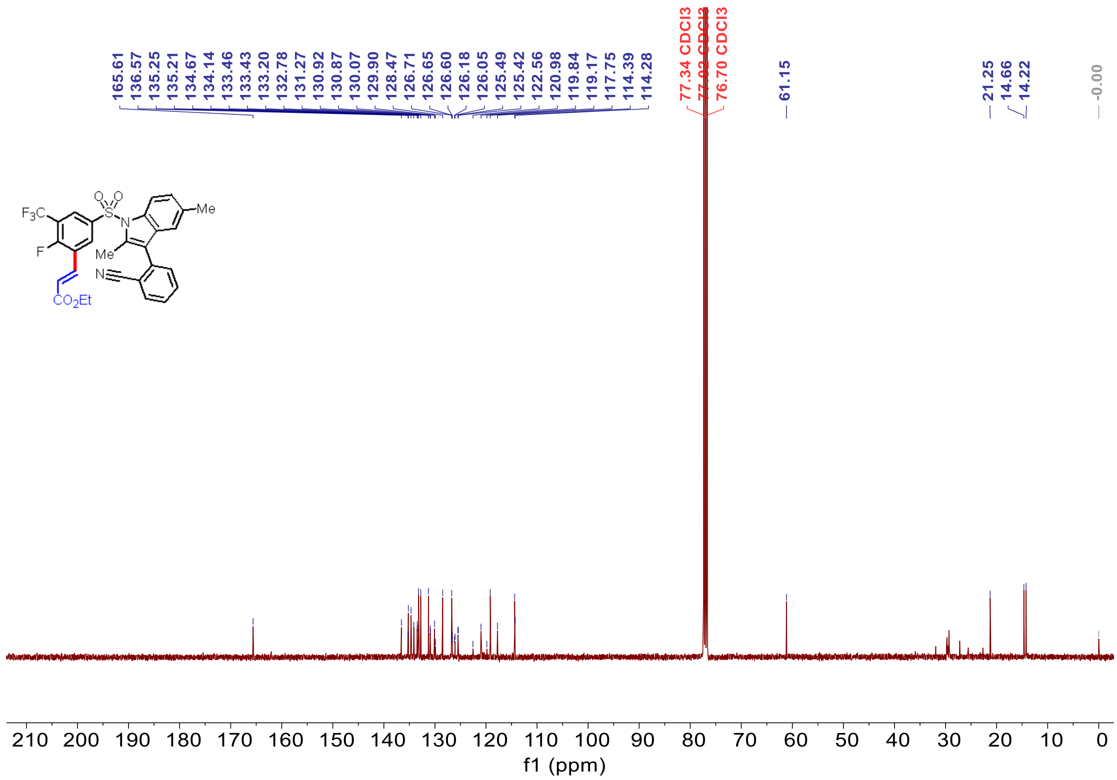
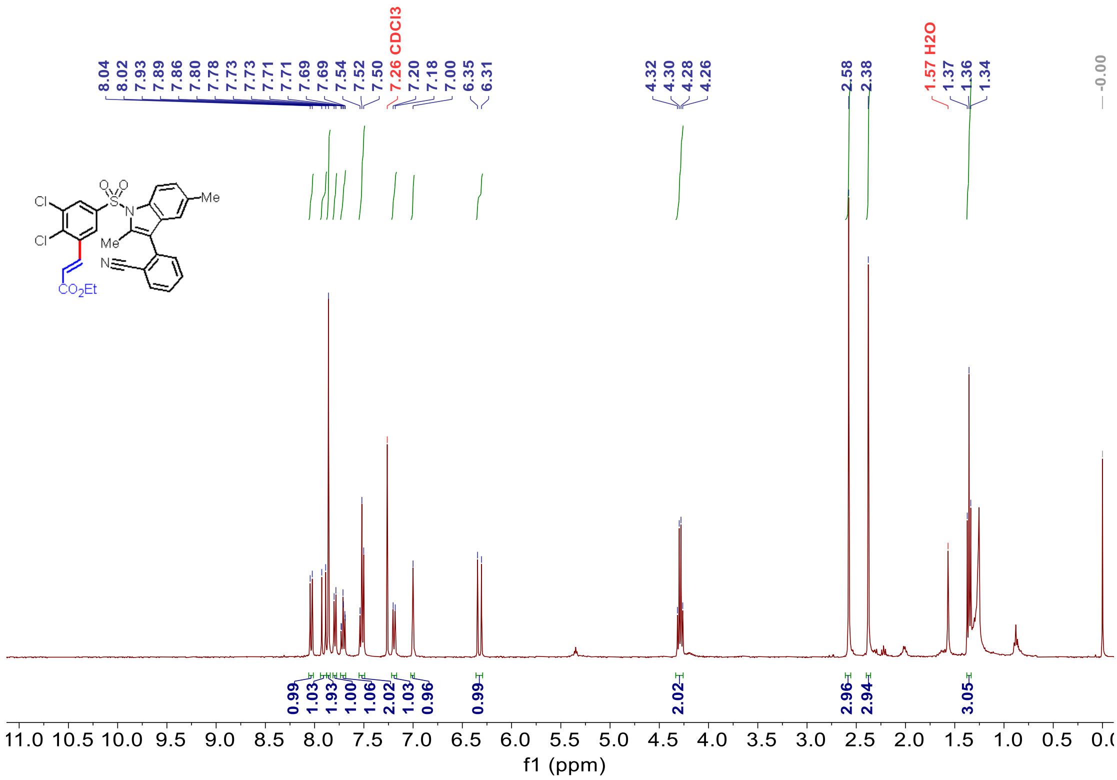


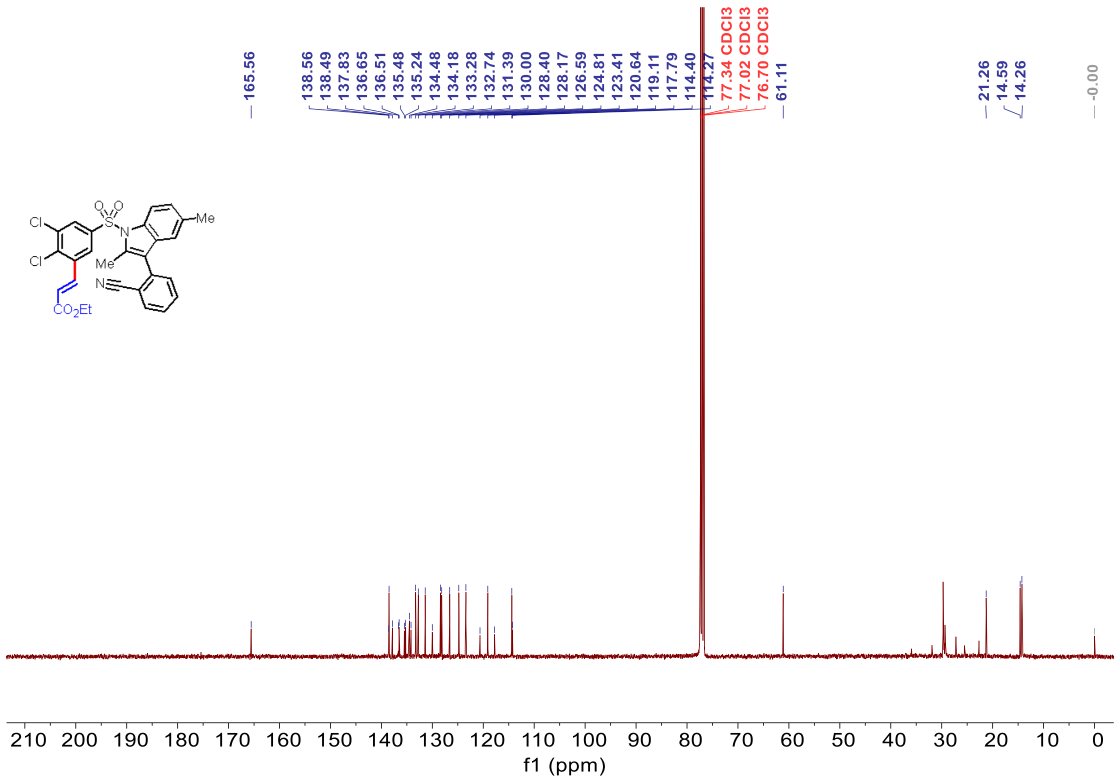
^{1}H NMR spectra of **2p**



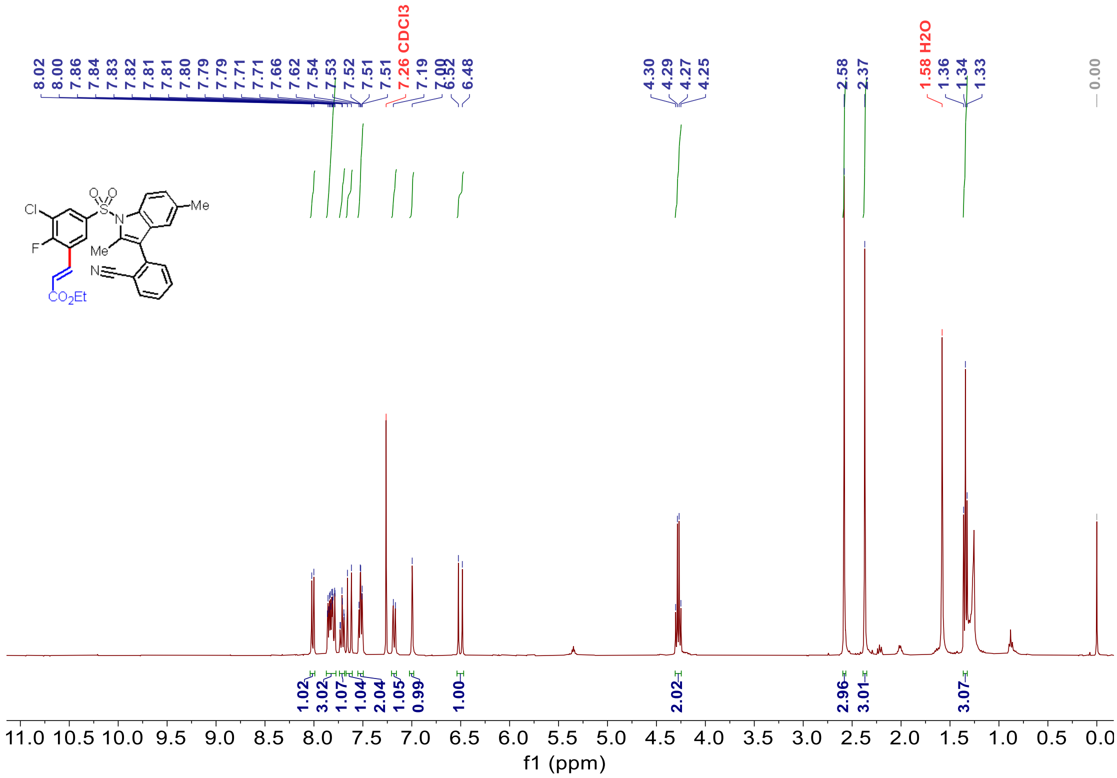
^{13}C NMR spectra of **2p**



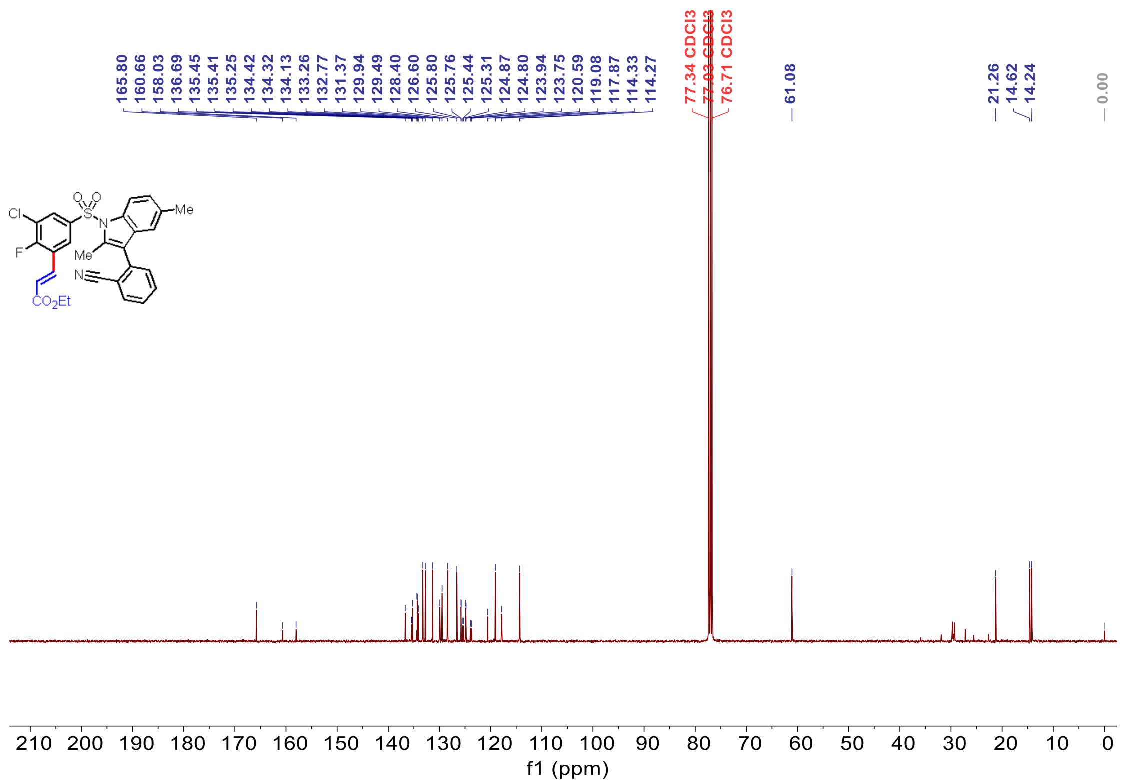
^{1}H NMR spectra of **2q**



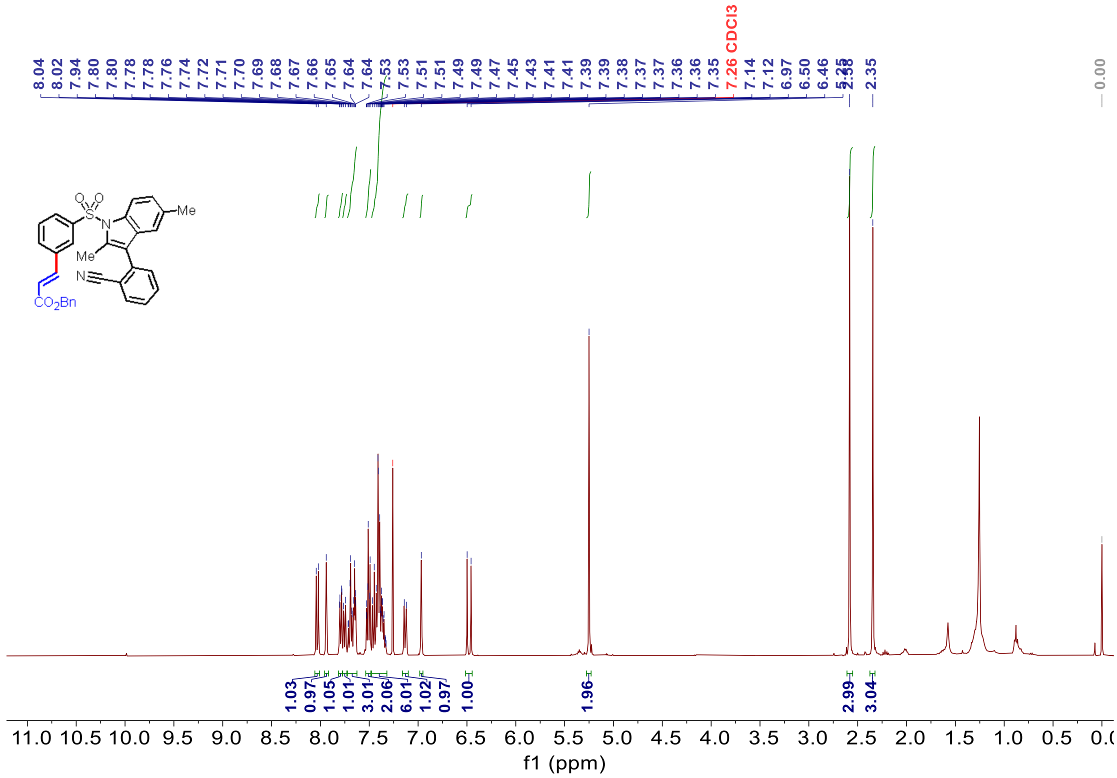
^{13}C NMR spectra of **2q**



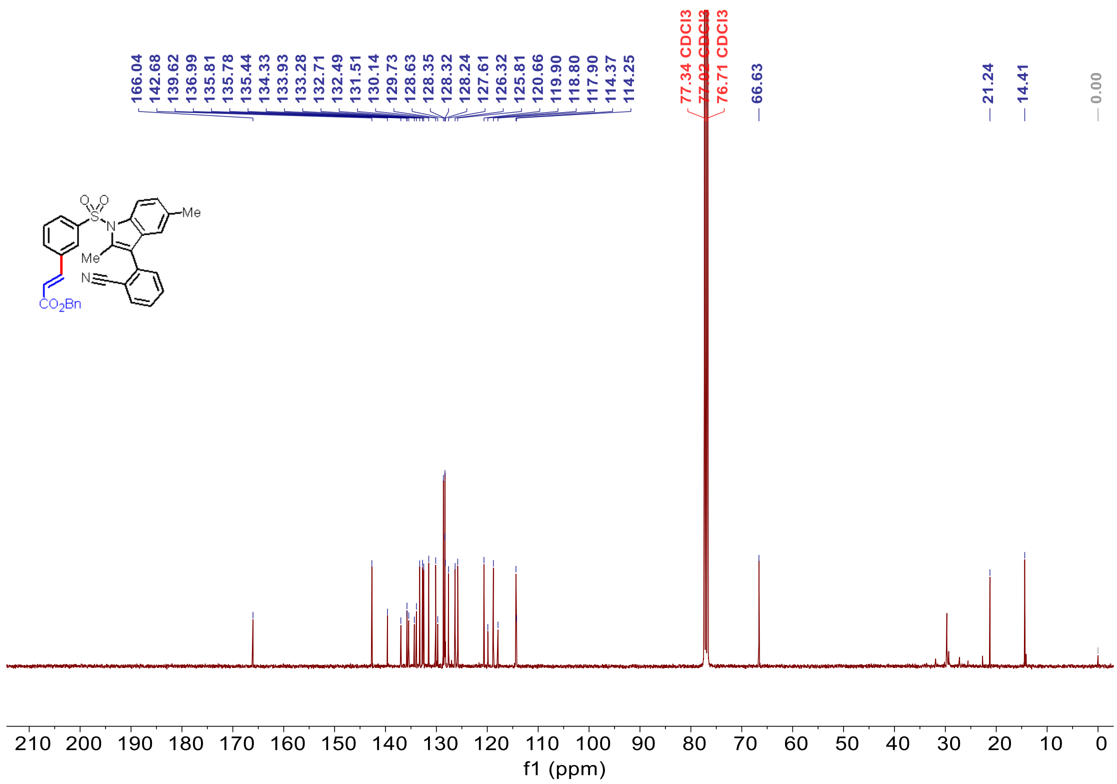
^{1}H NMR spectra of **2r**



^{13}C NMR spectra of **2r**



^{1}H NMR spectra of **3a**



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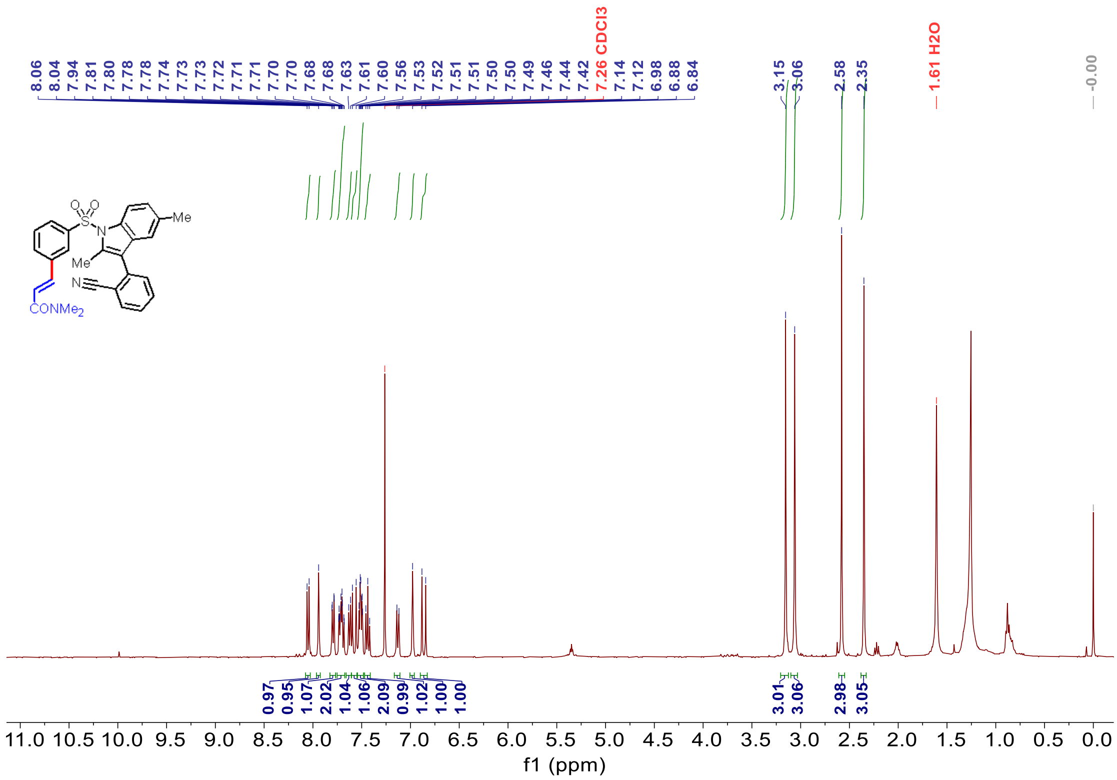
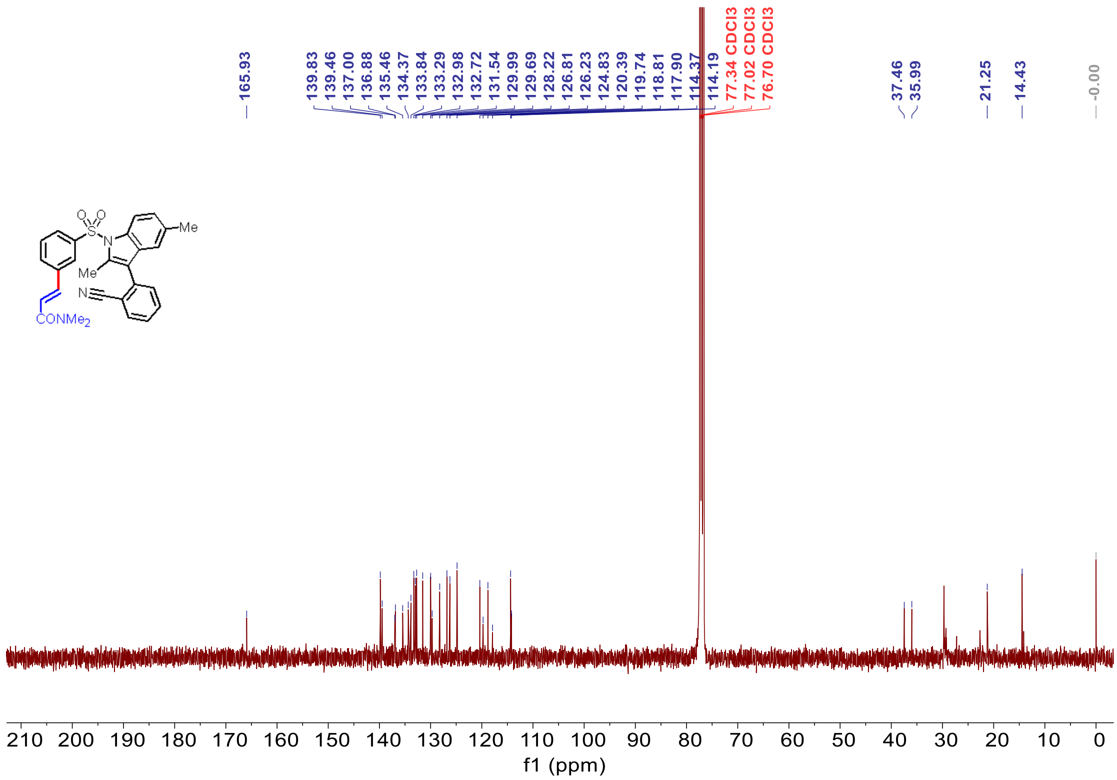
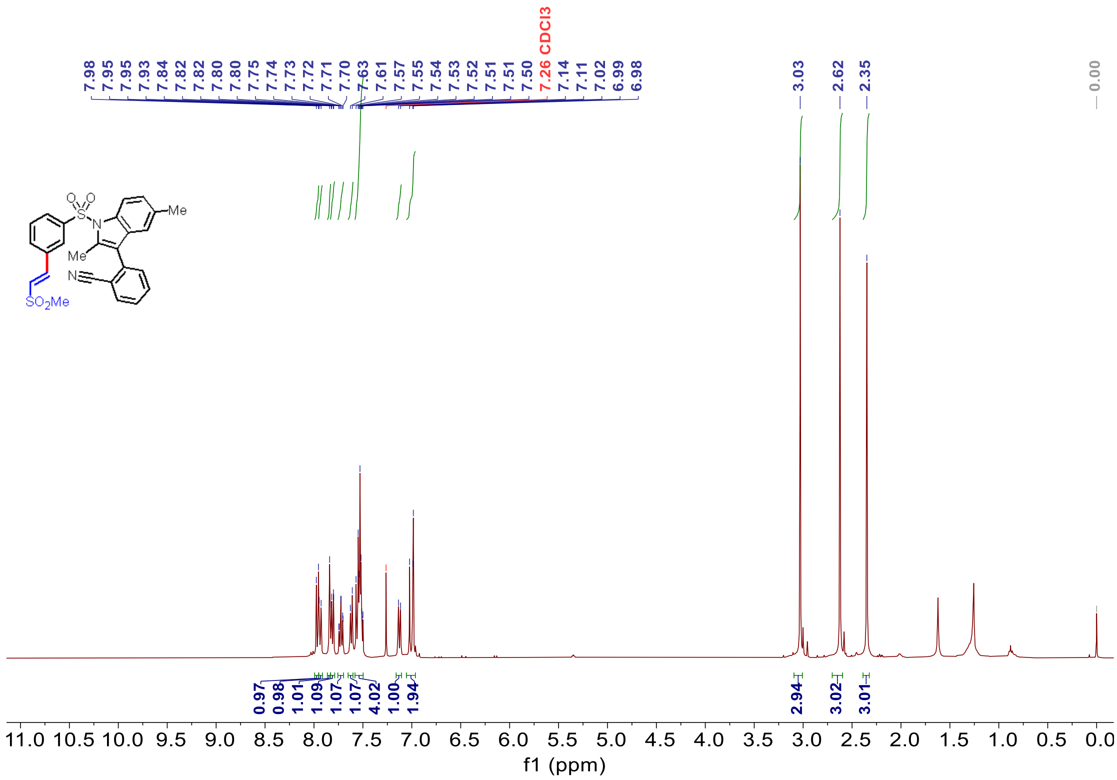


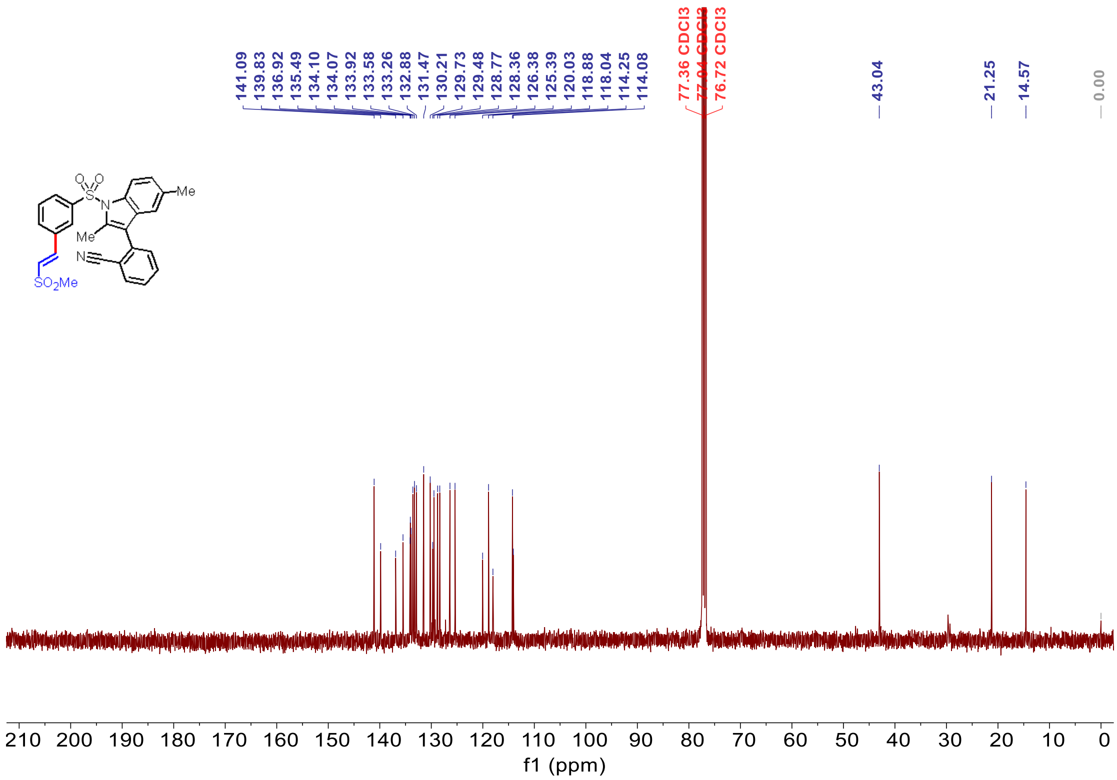
^{1}H NMR spectra of **3b**



^{13}C NMR spectra of **3b**



^{1}H NMR spectra of **3c**



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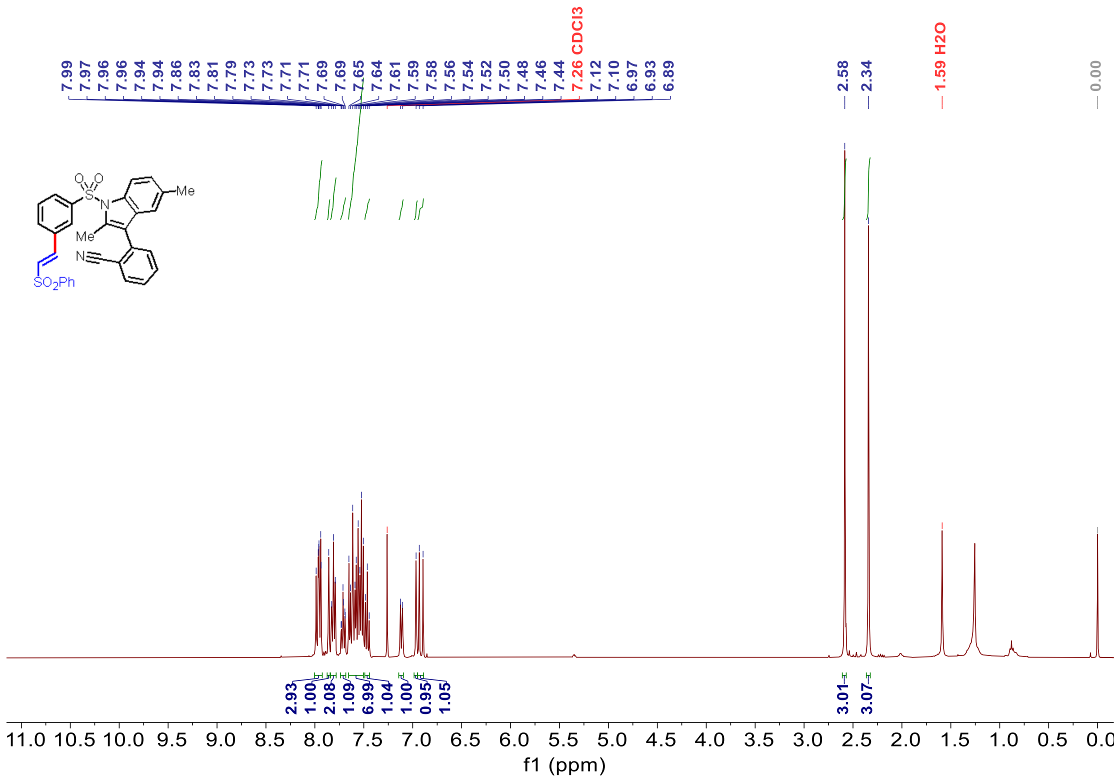
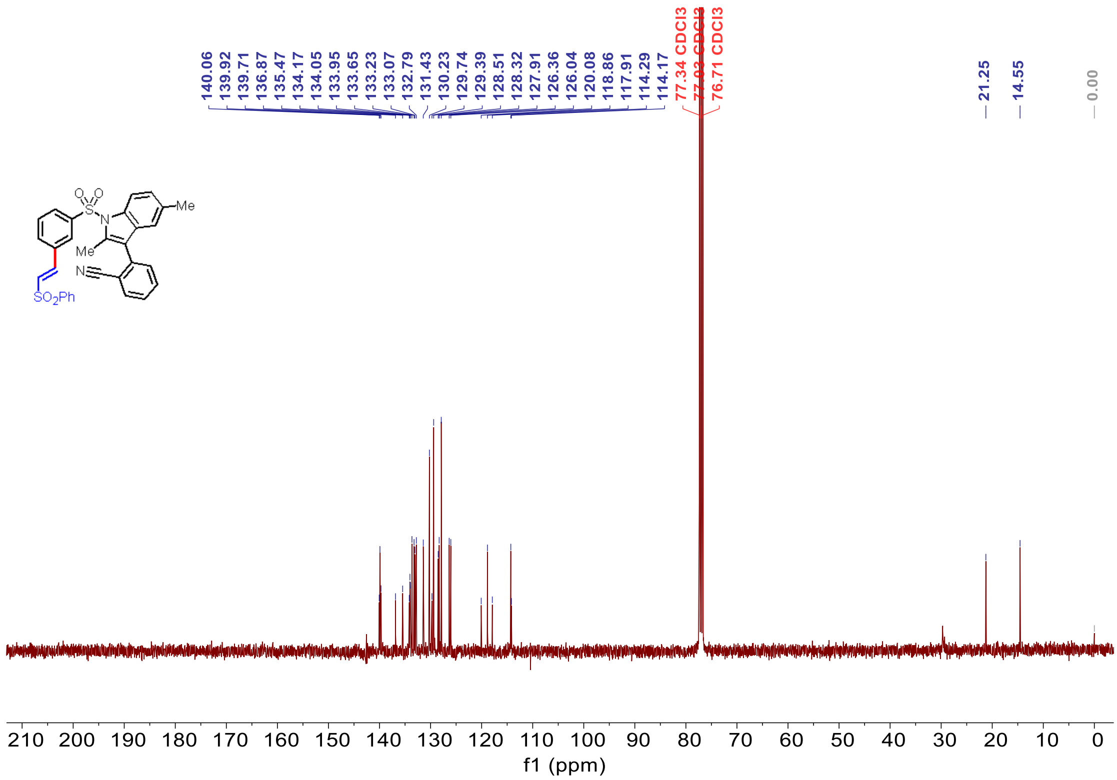


^{1}H NMR spectra of **3d**



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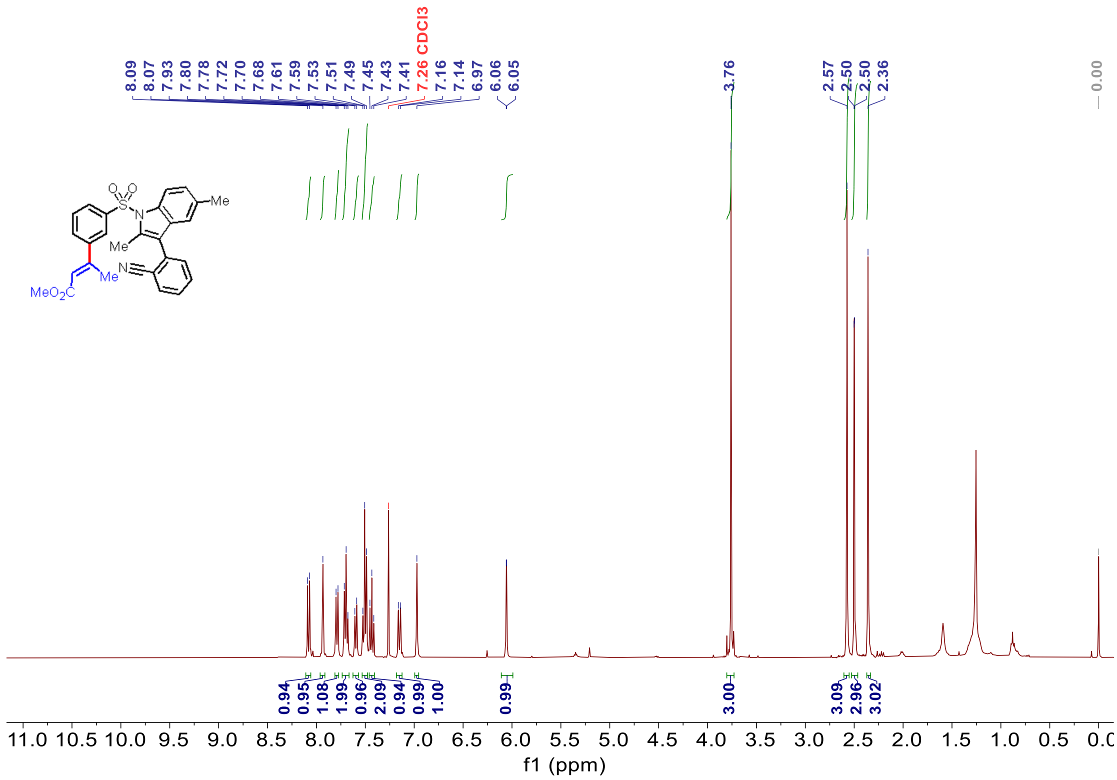

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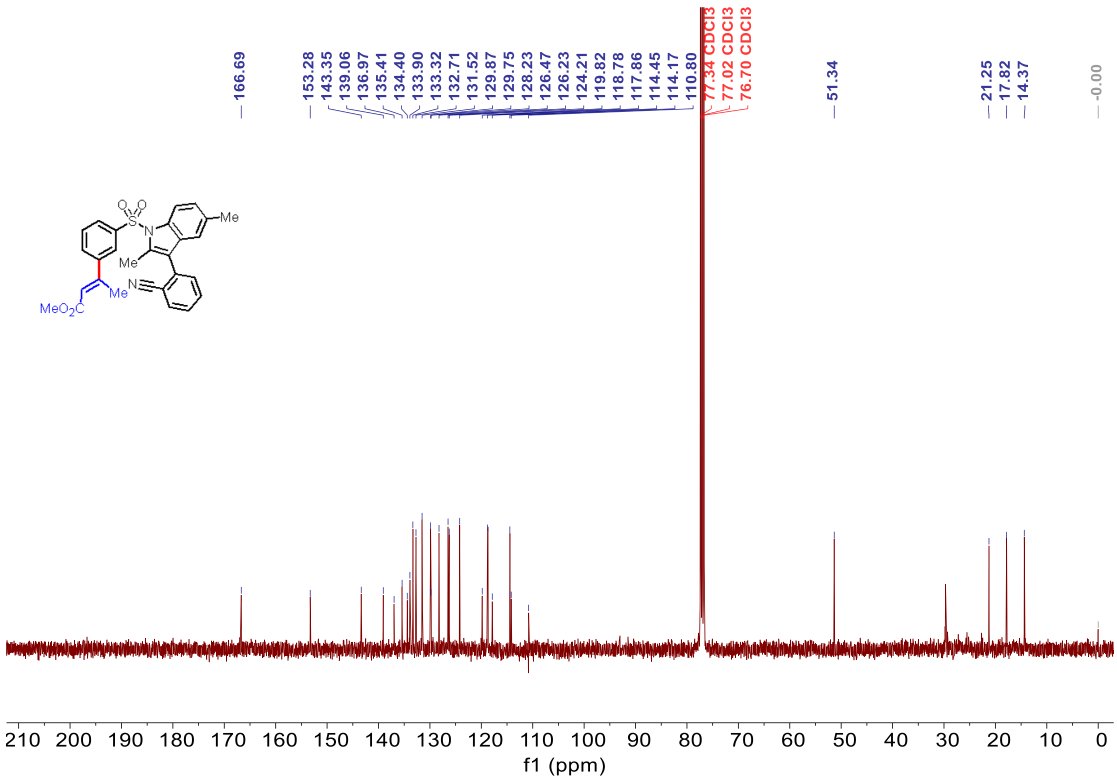

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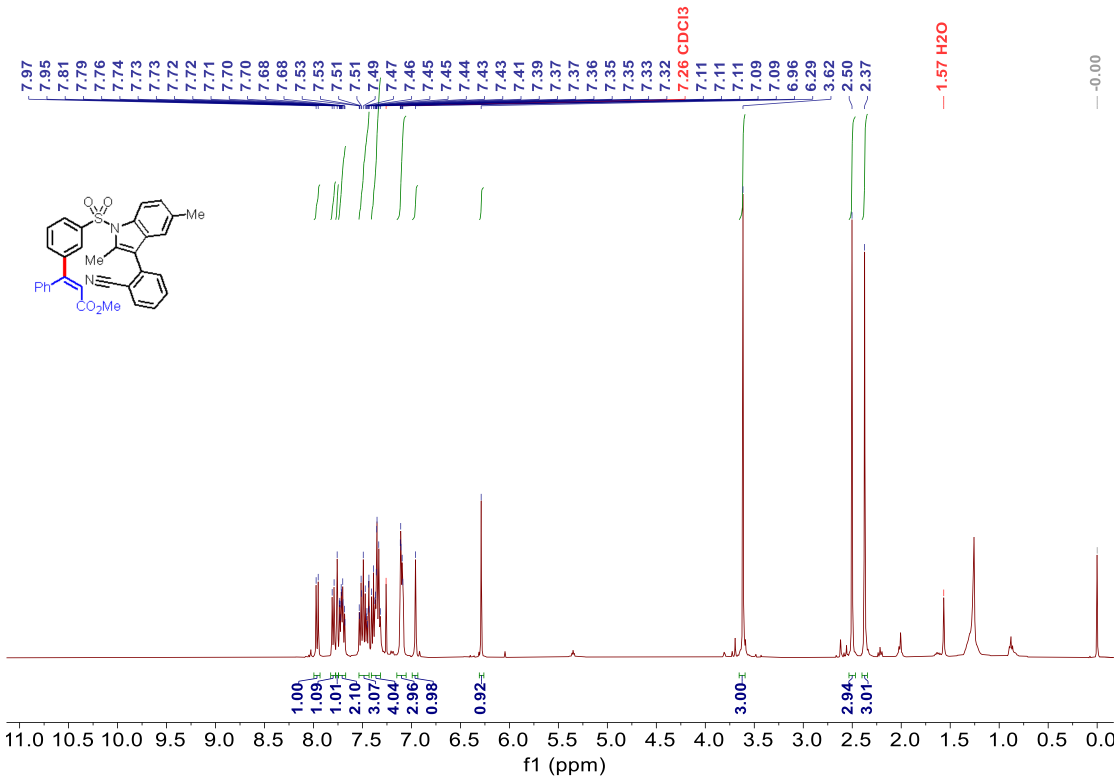
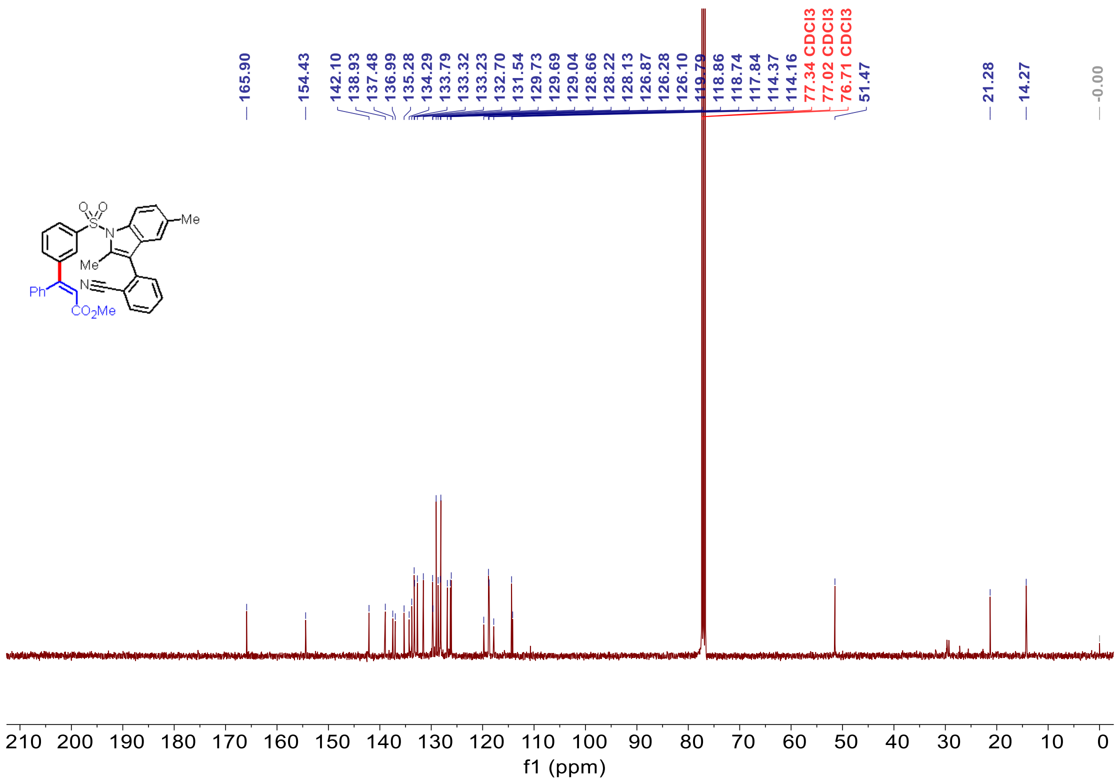


^{1}H NMR spectra of **3f**



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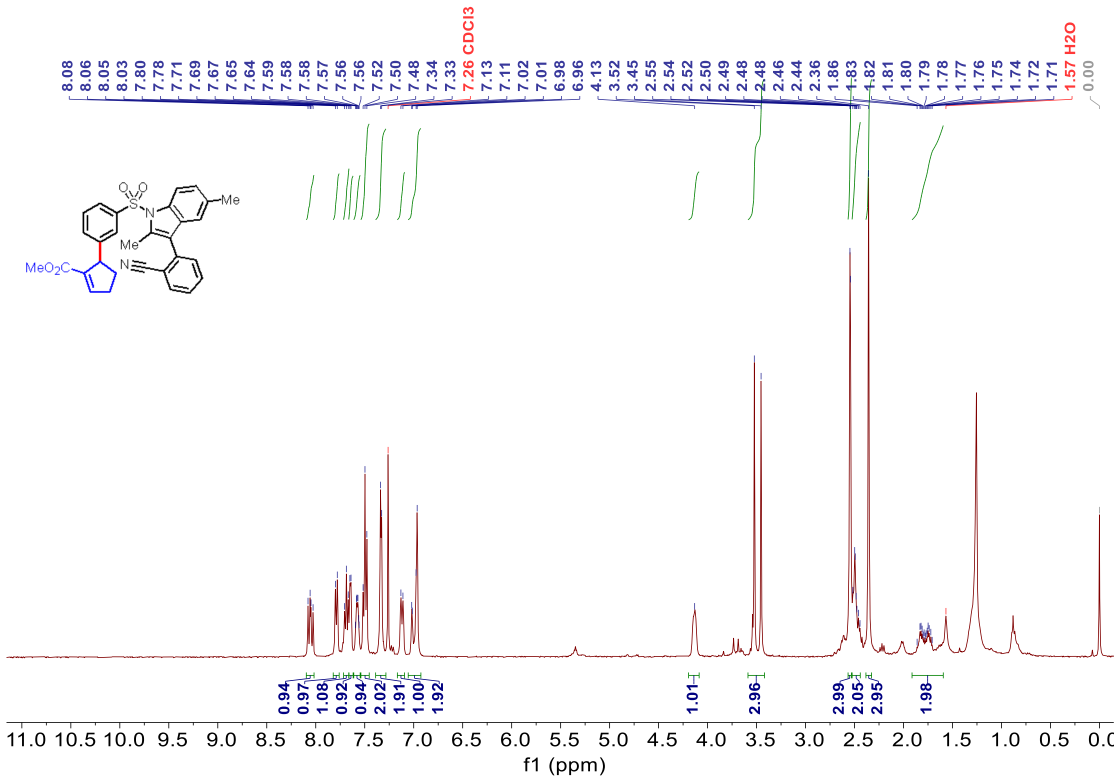
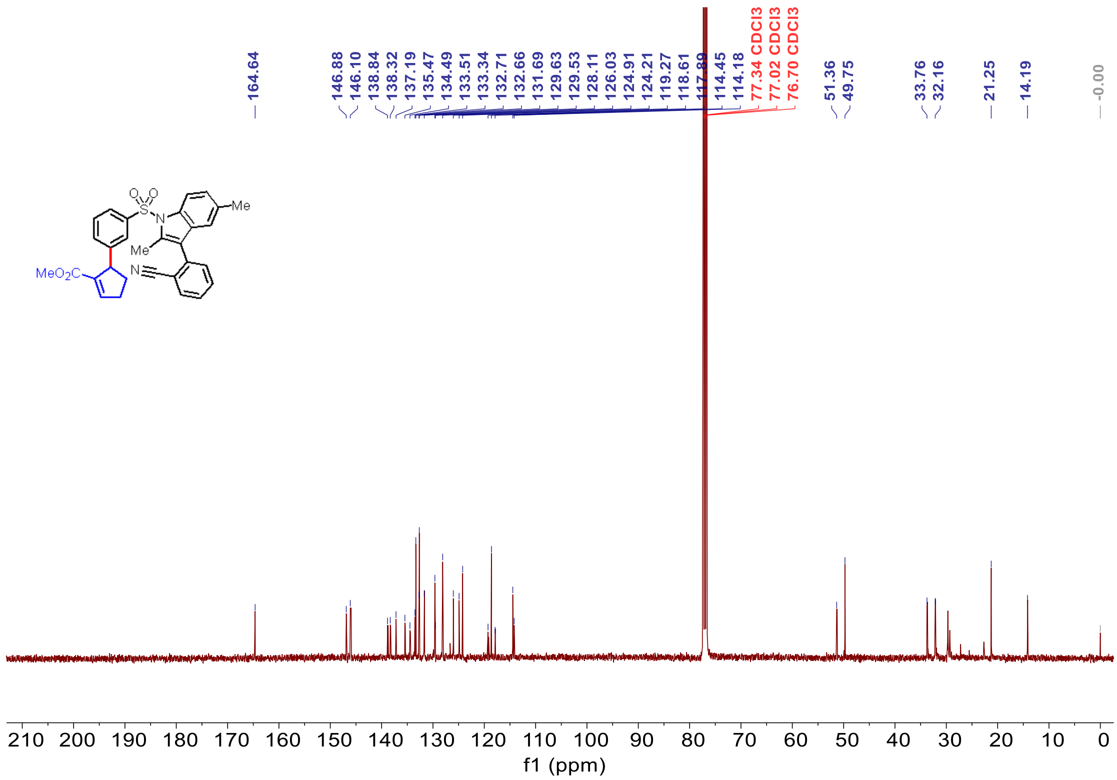
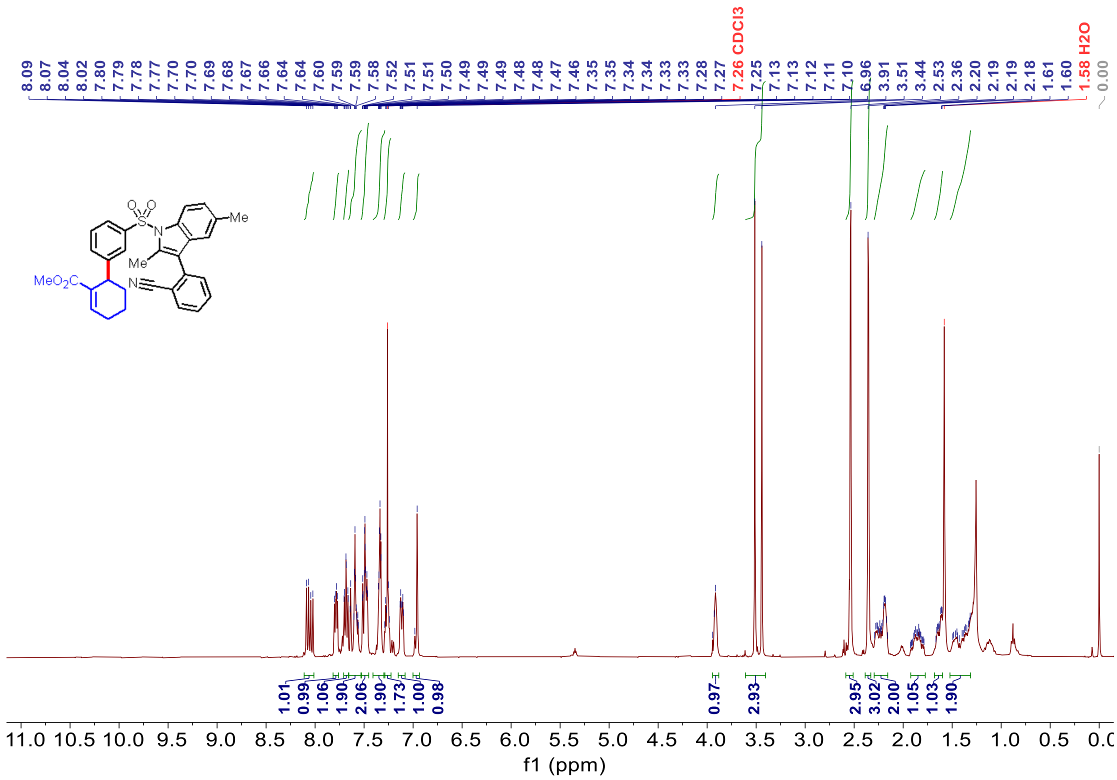


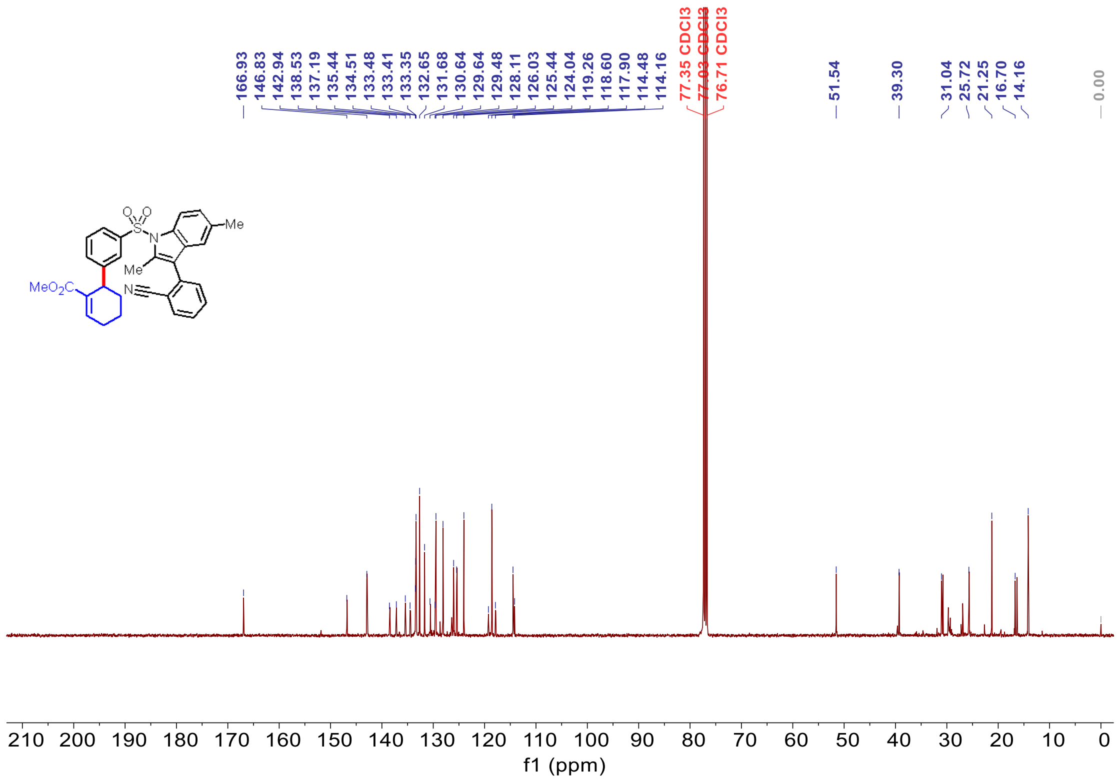
^{1}H NMR spectra of **3g**



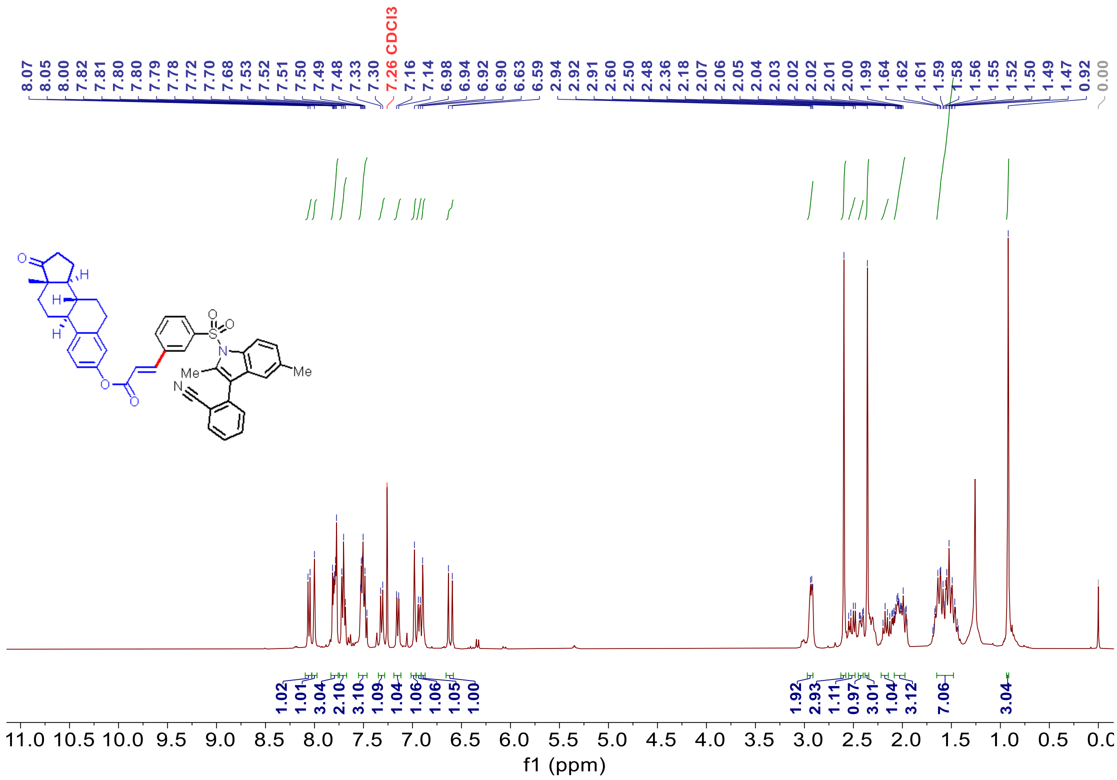
^{13}C NMR spectra of **3g**



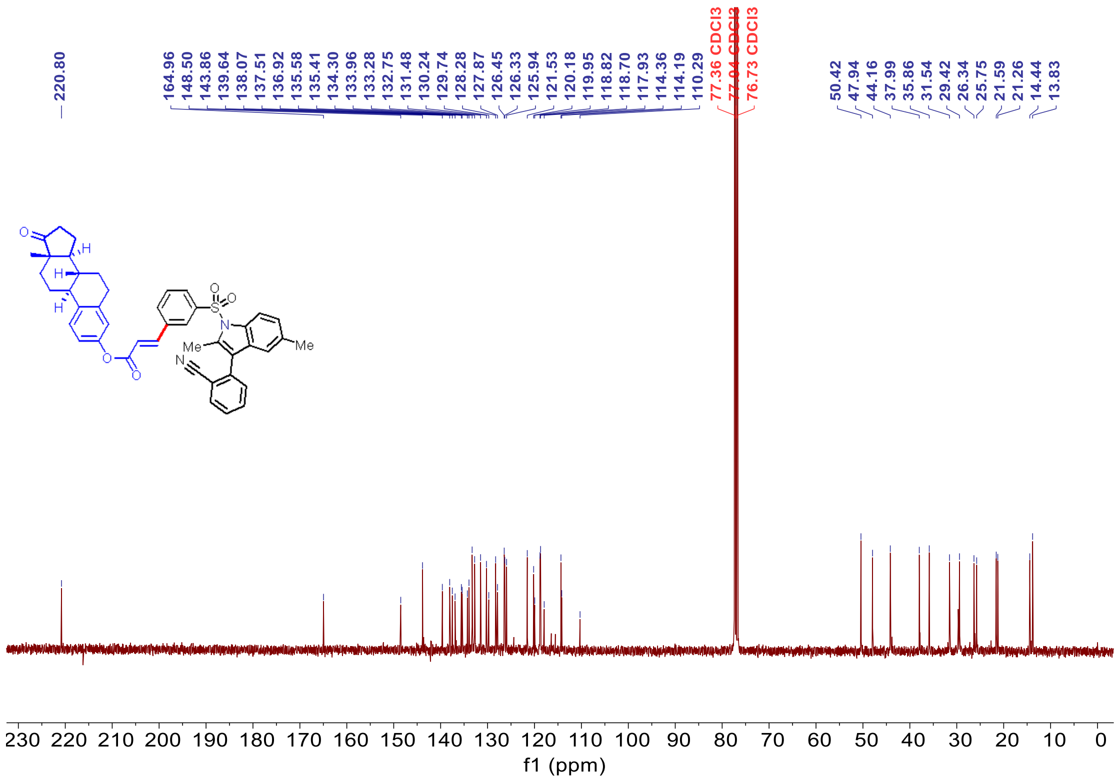
^{1}H NMR spectra of **3h**



^{13}C NMR spectra of **3h**



^{1}H NMR spectra of **3i**



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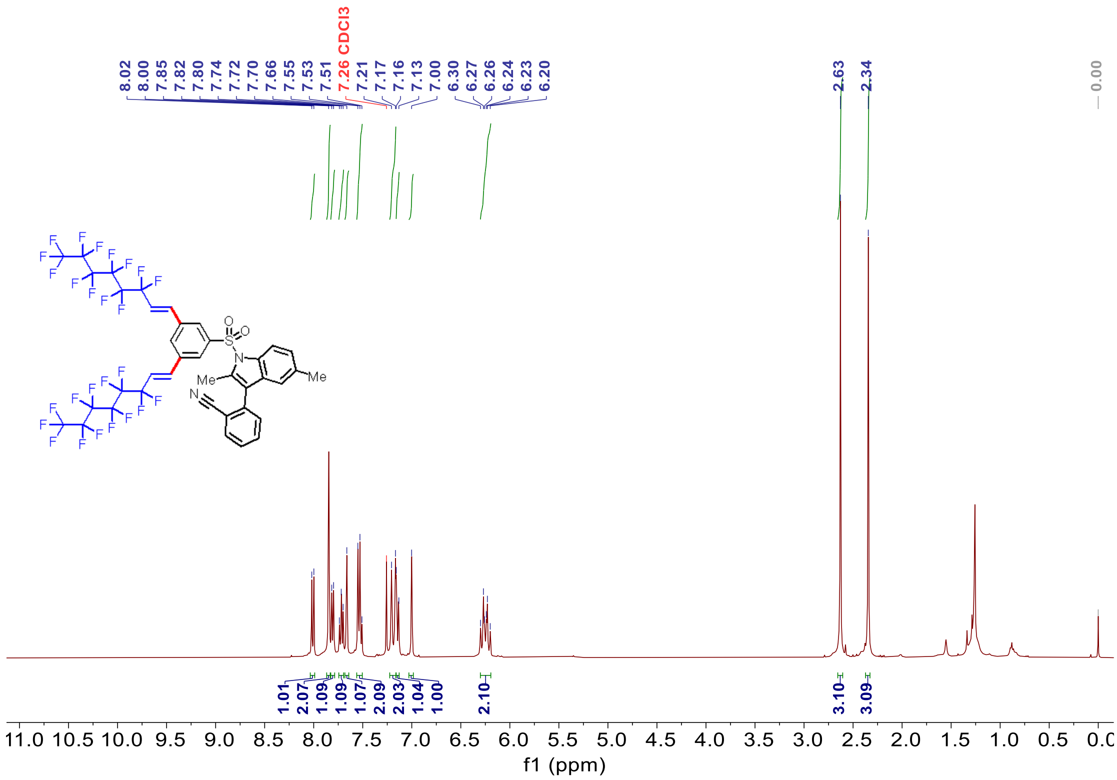

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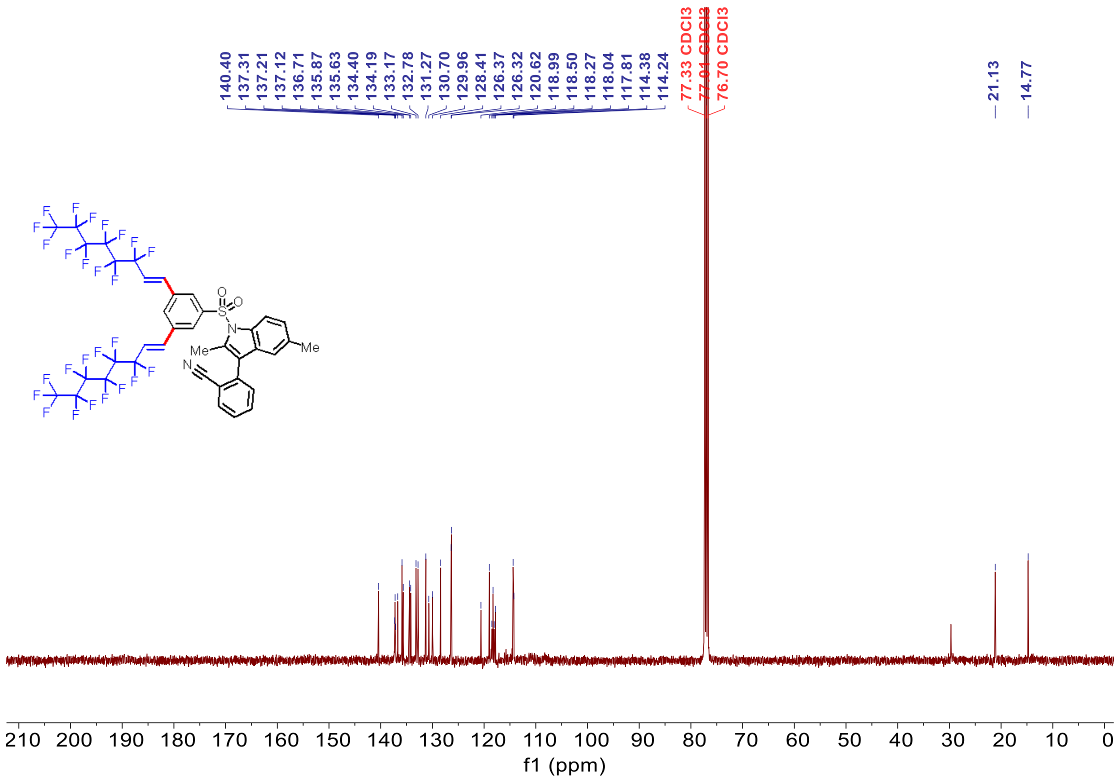

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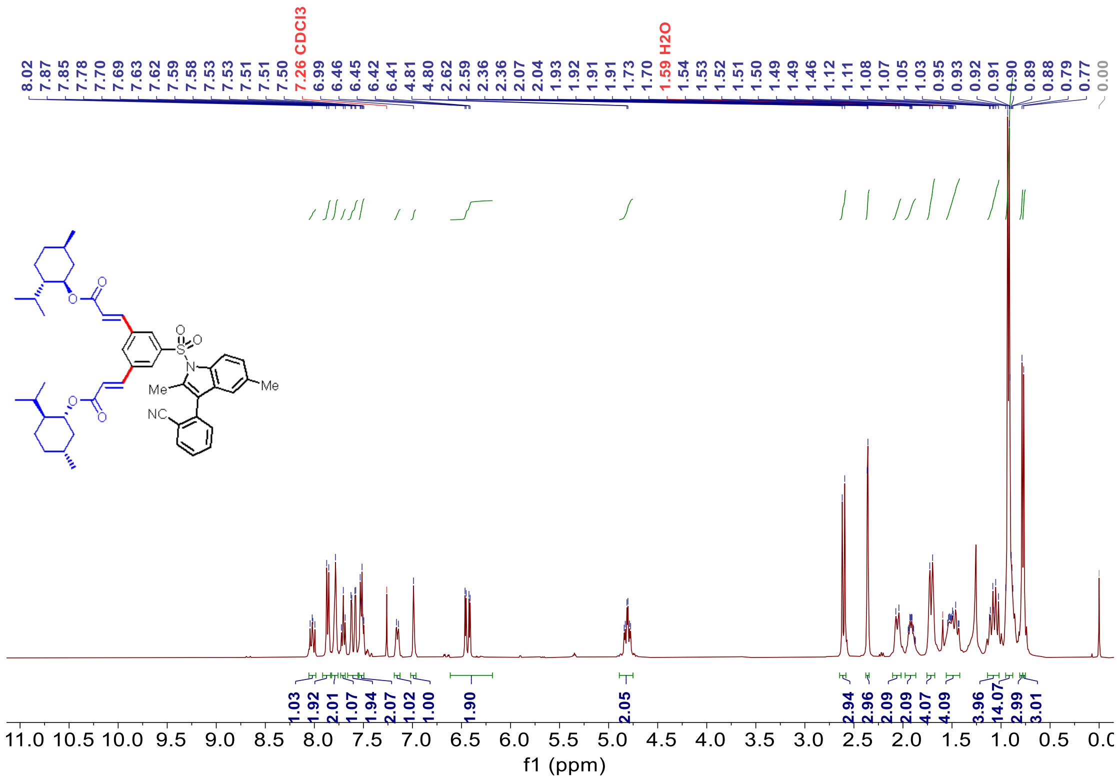

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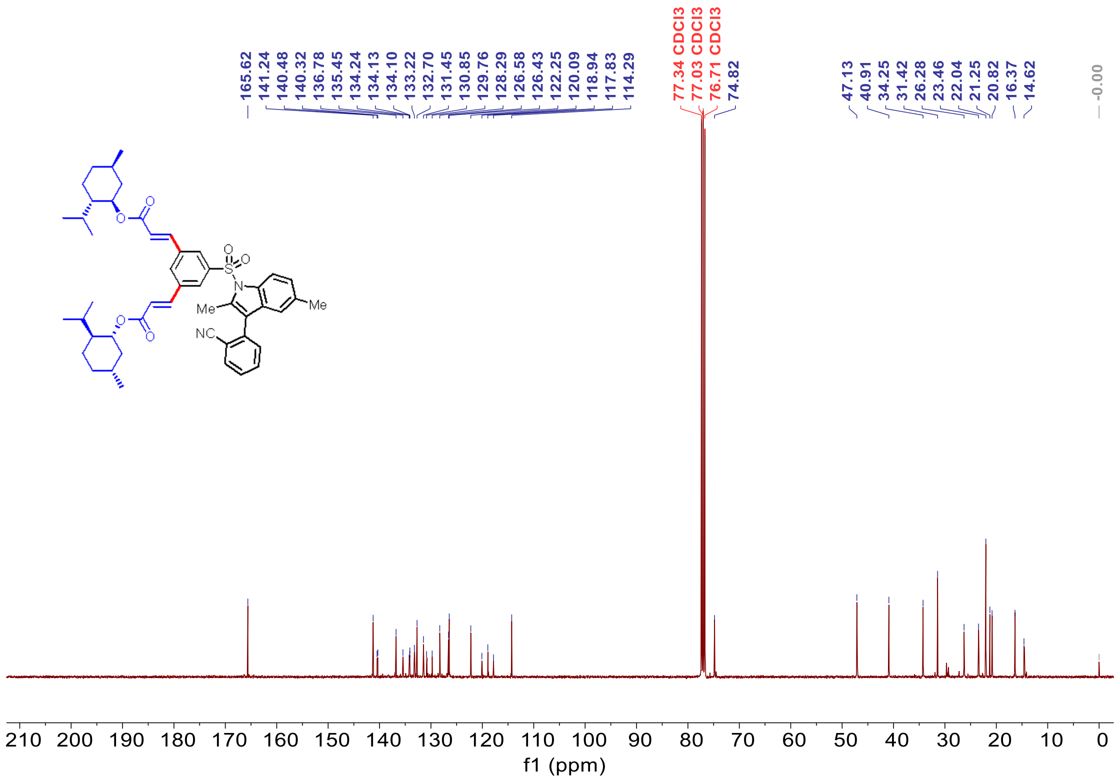

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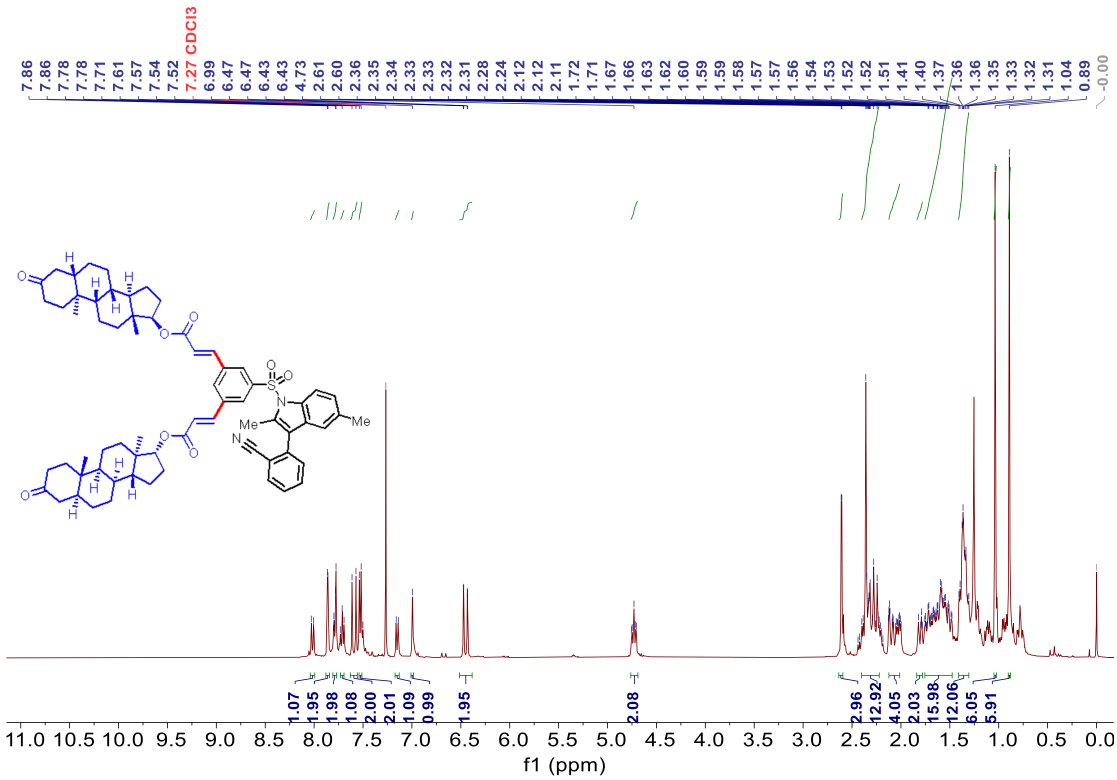

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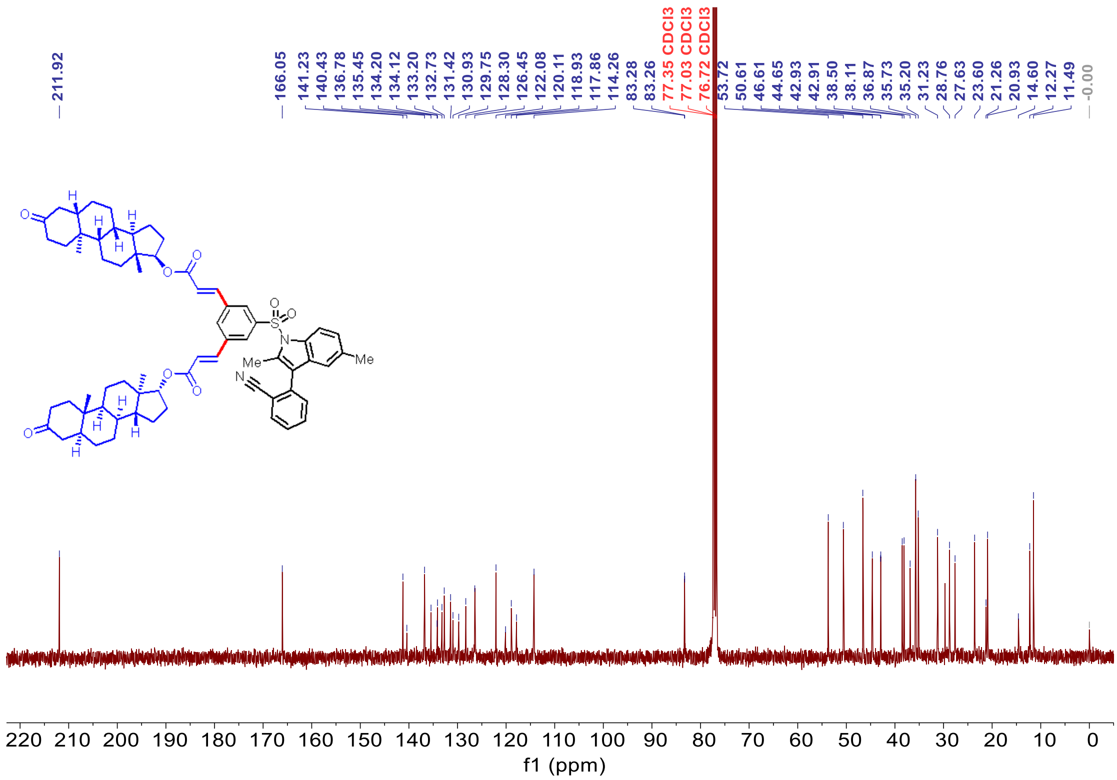

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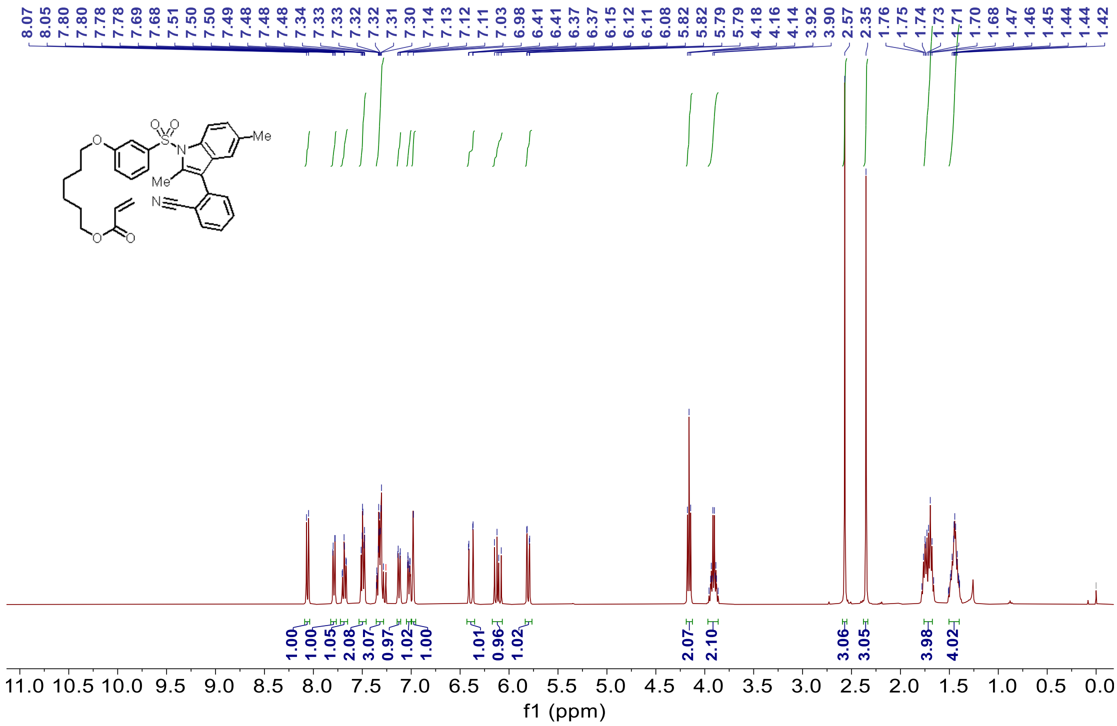
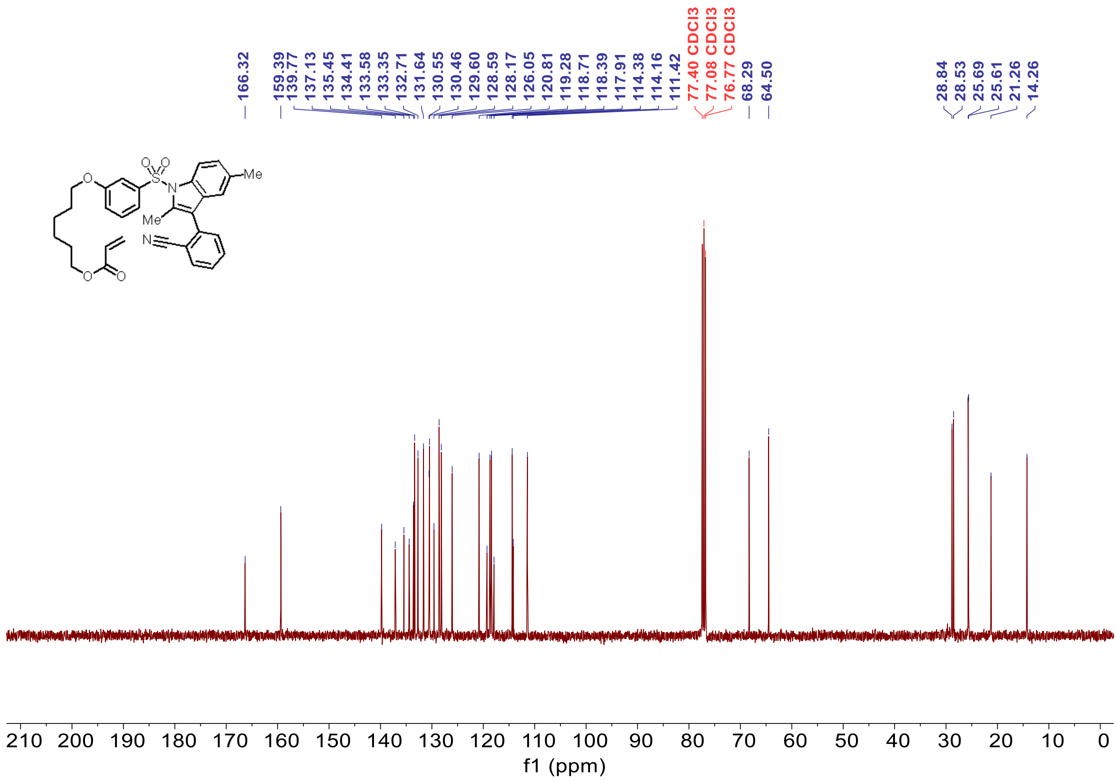
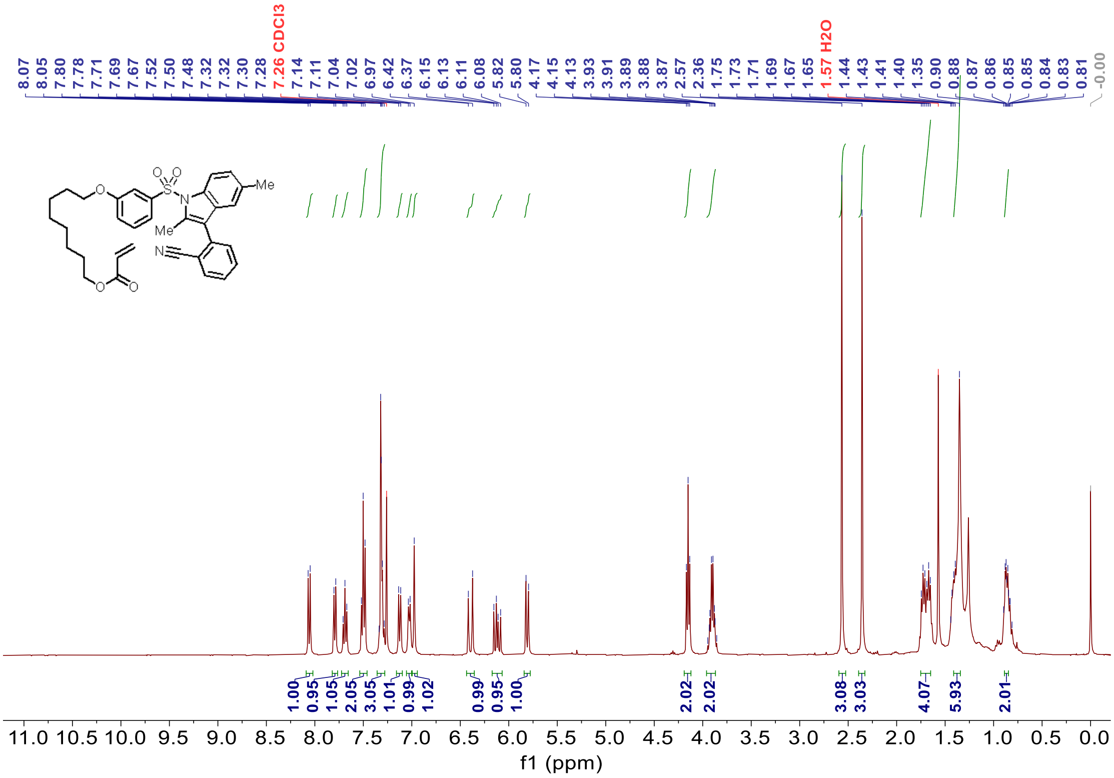


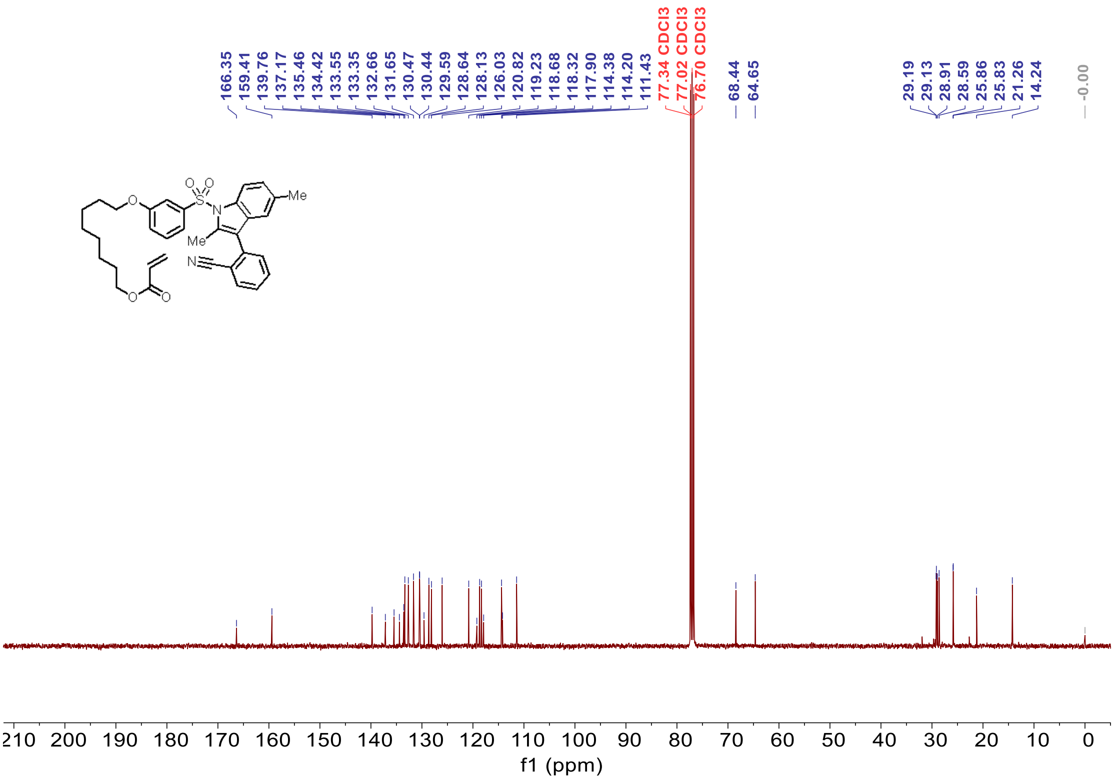
^{1}H NMR spectra of **4a**



^{13}C NMR spectra of **4a**



^{1}H NMR spectra of **4b**



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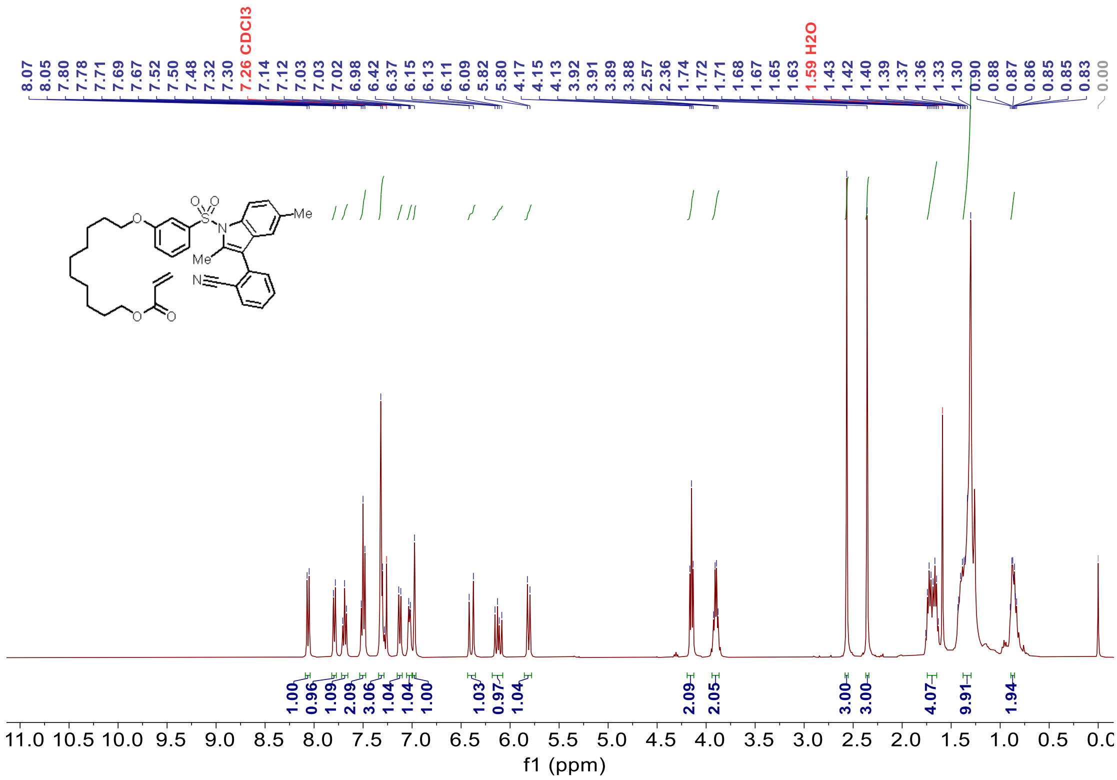
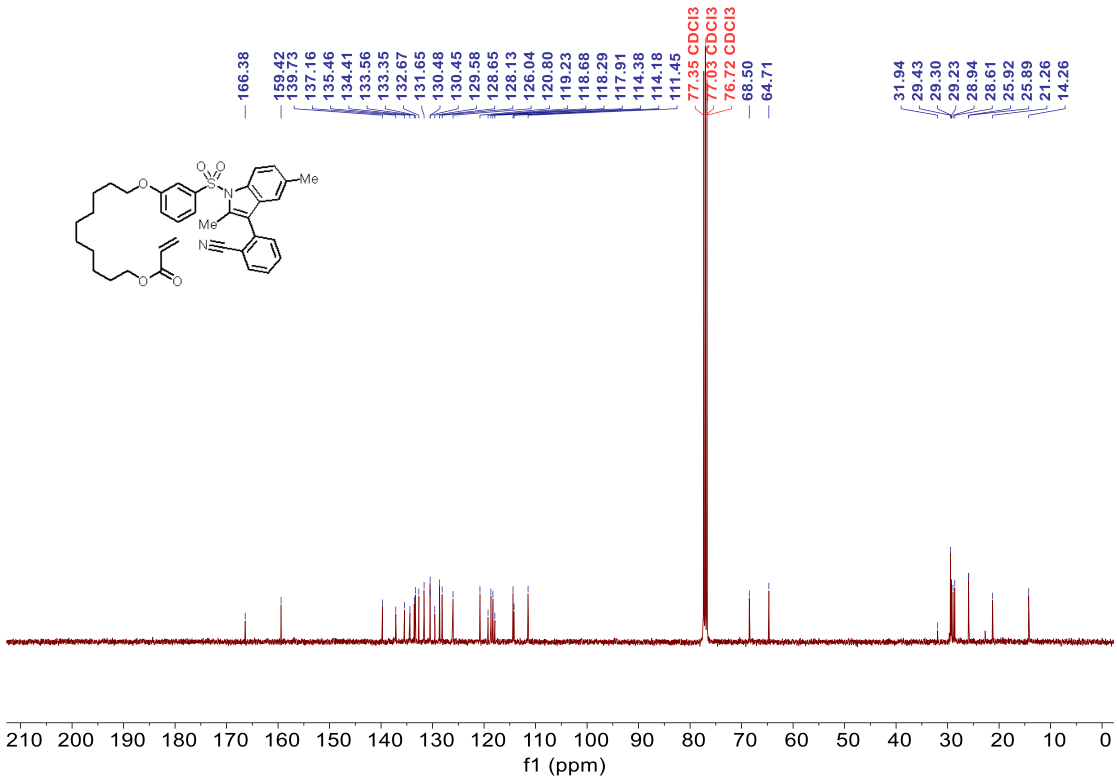


^{1}H NMR spectra of **4c**



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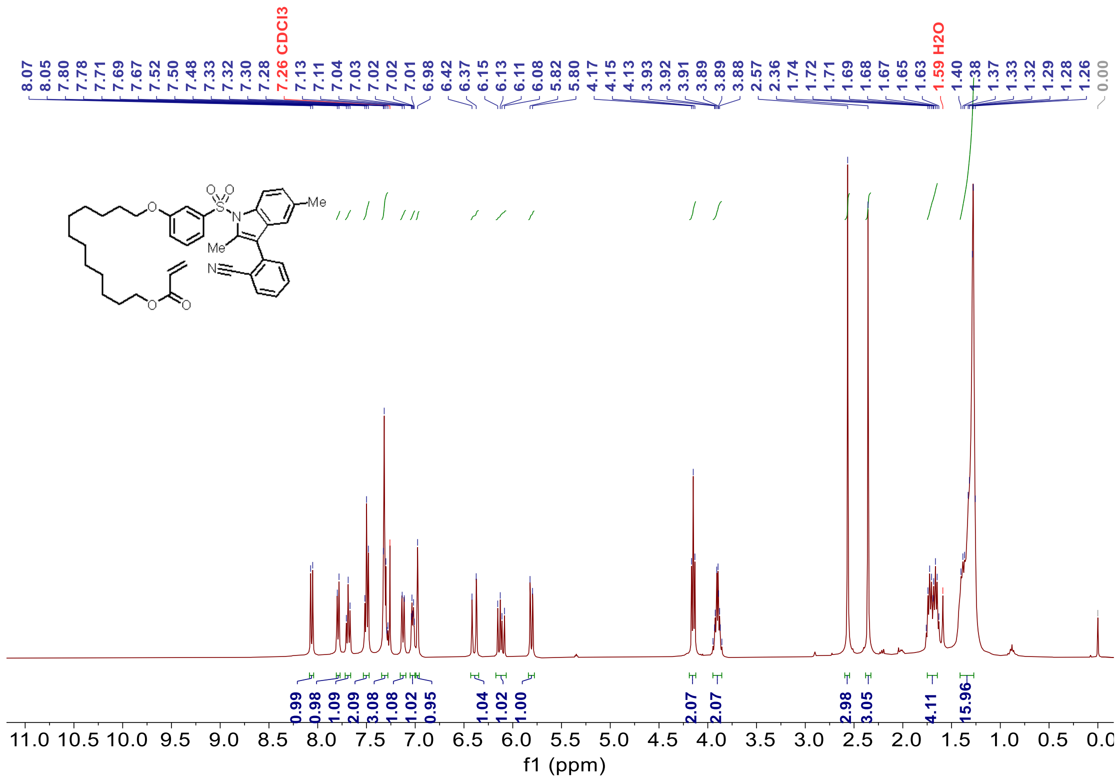

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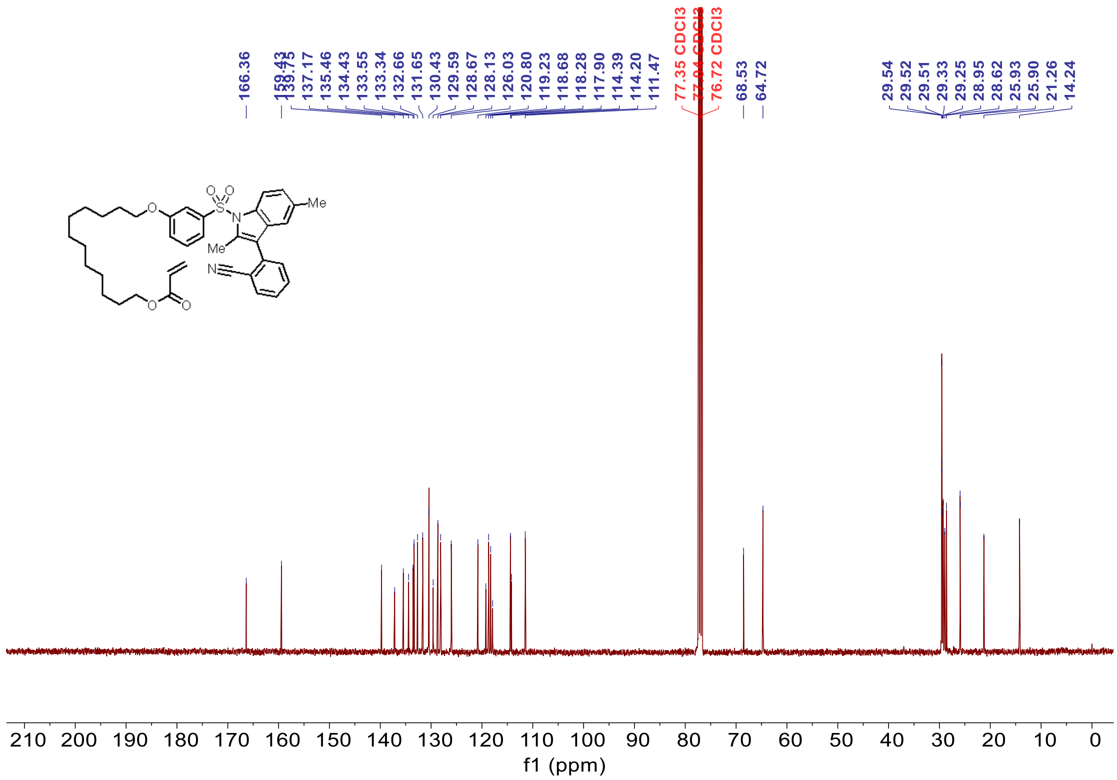

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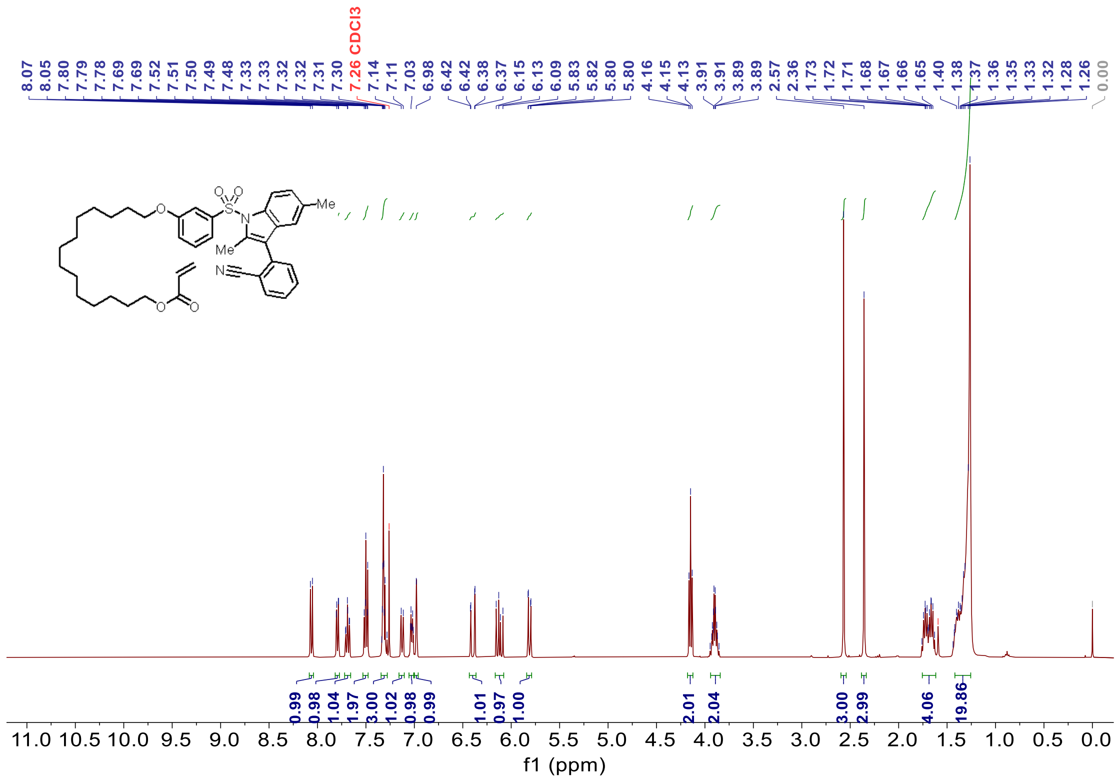

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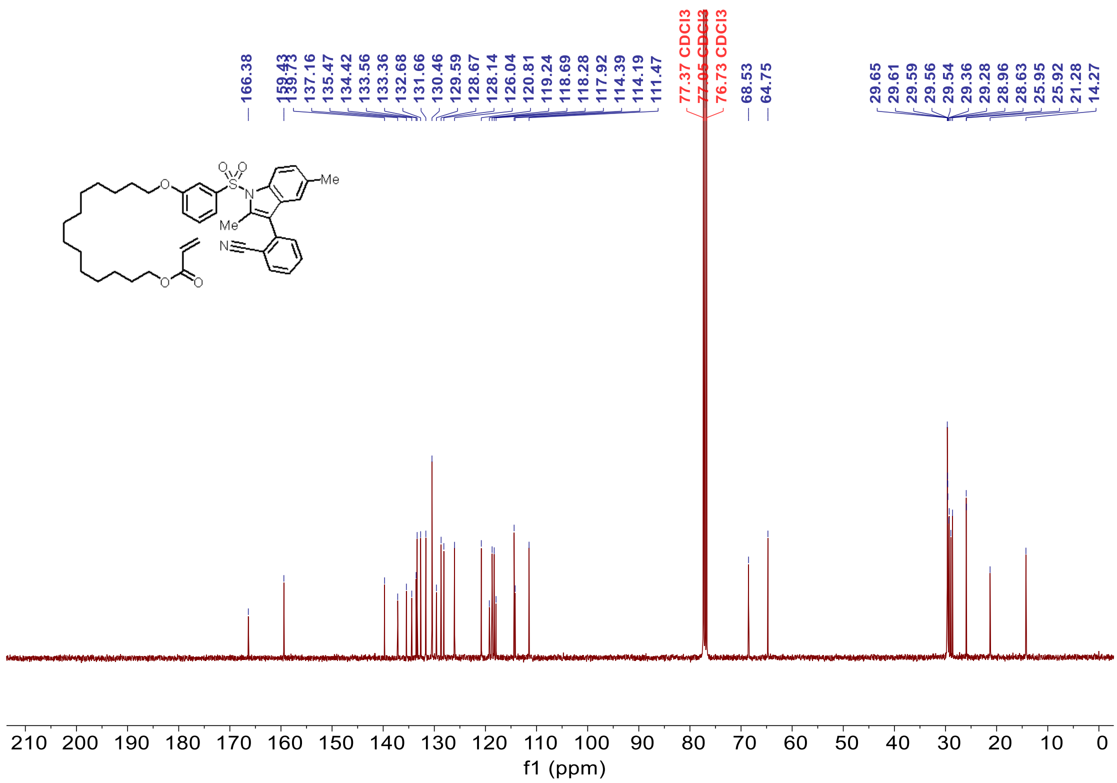

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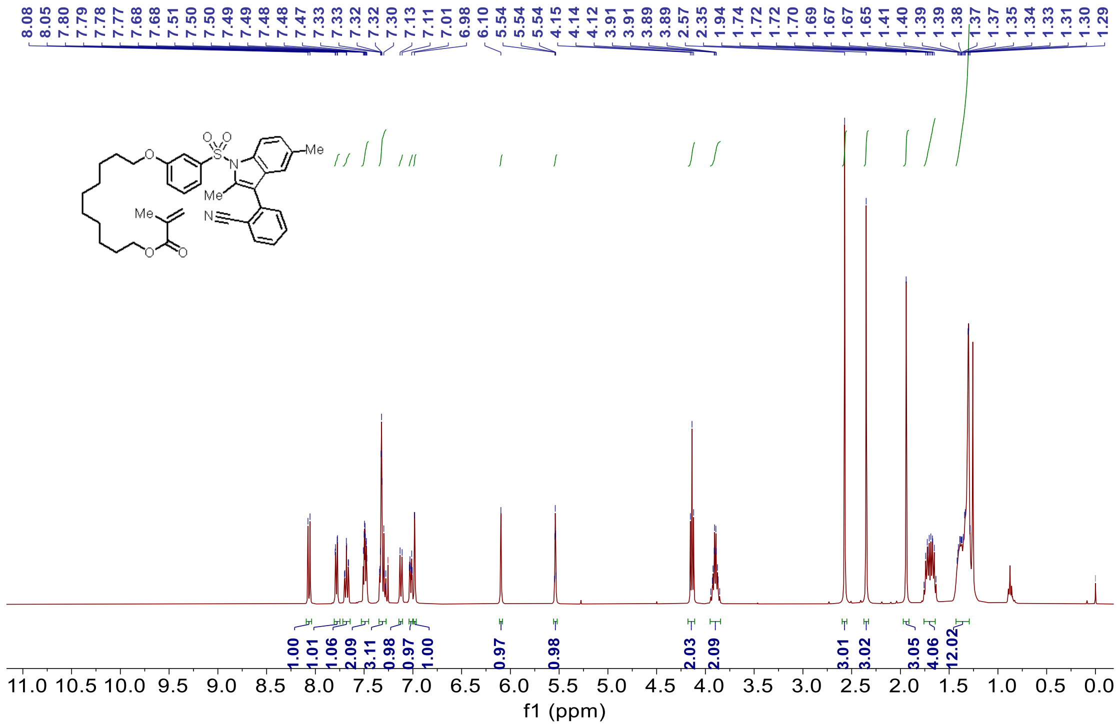

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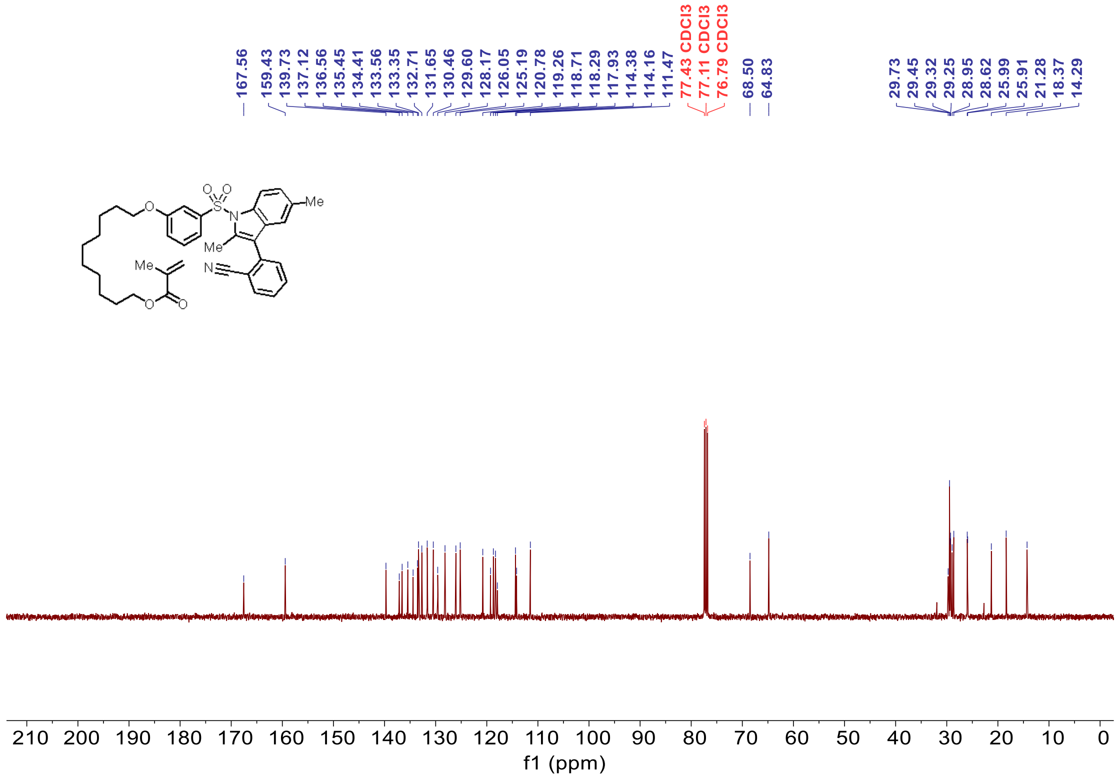

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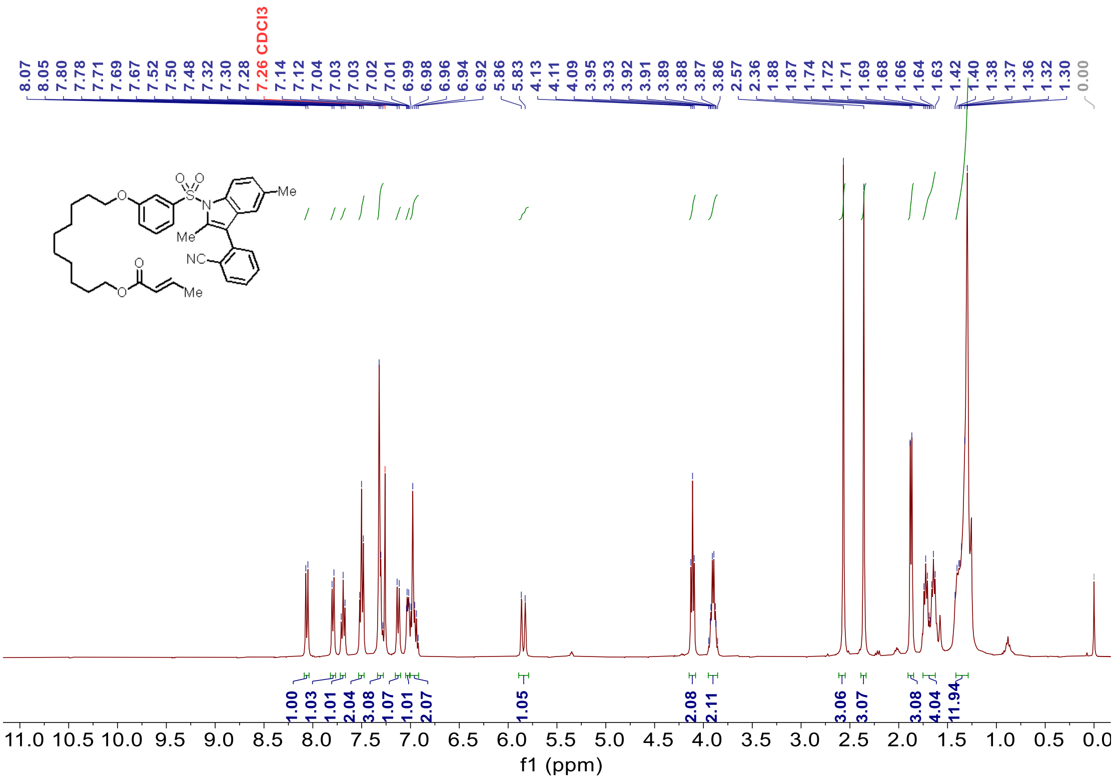

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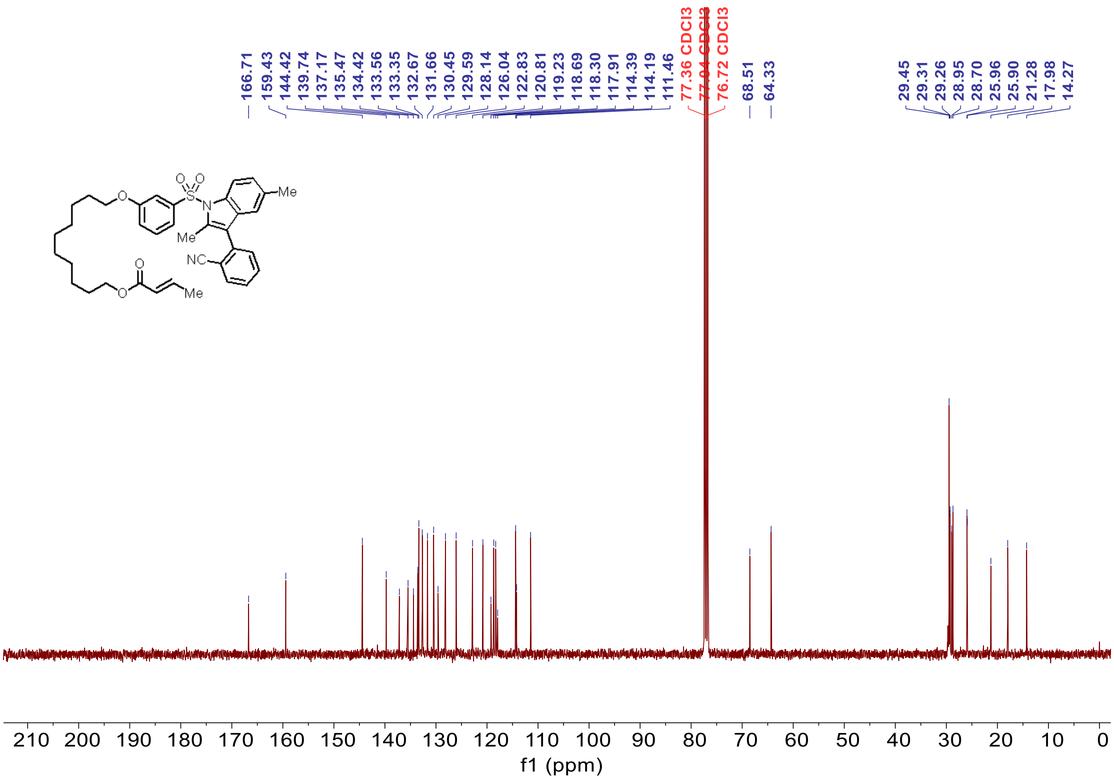

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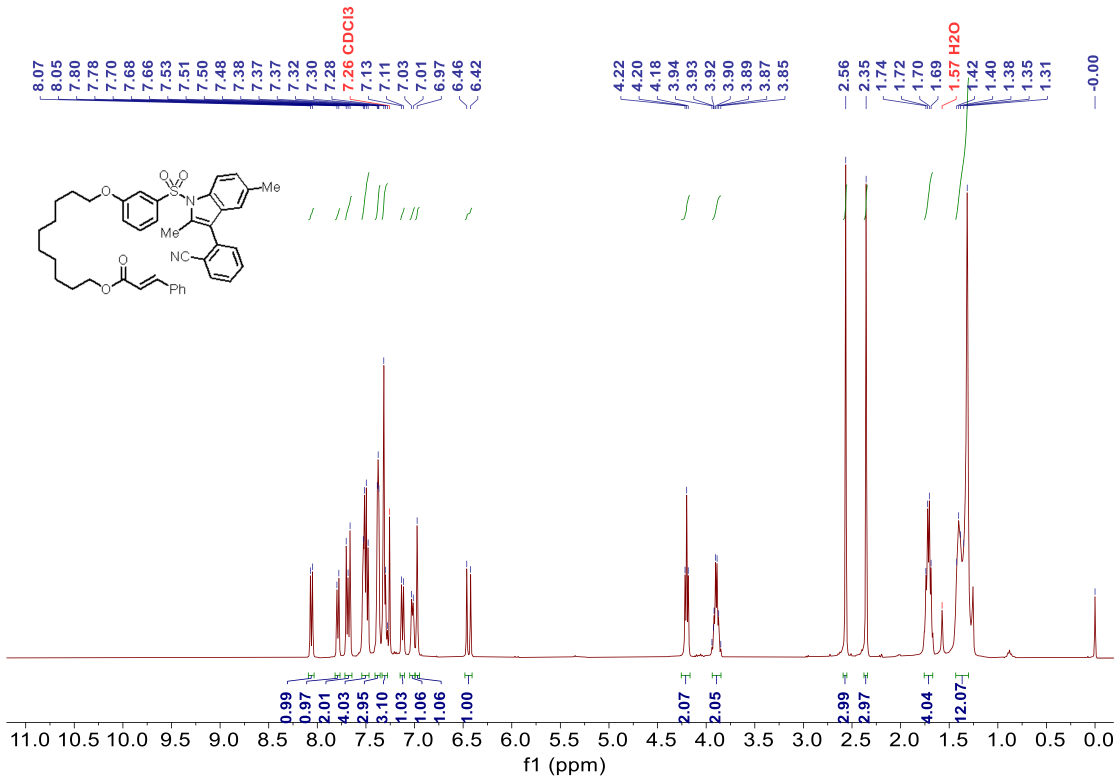
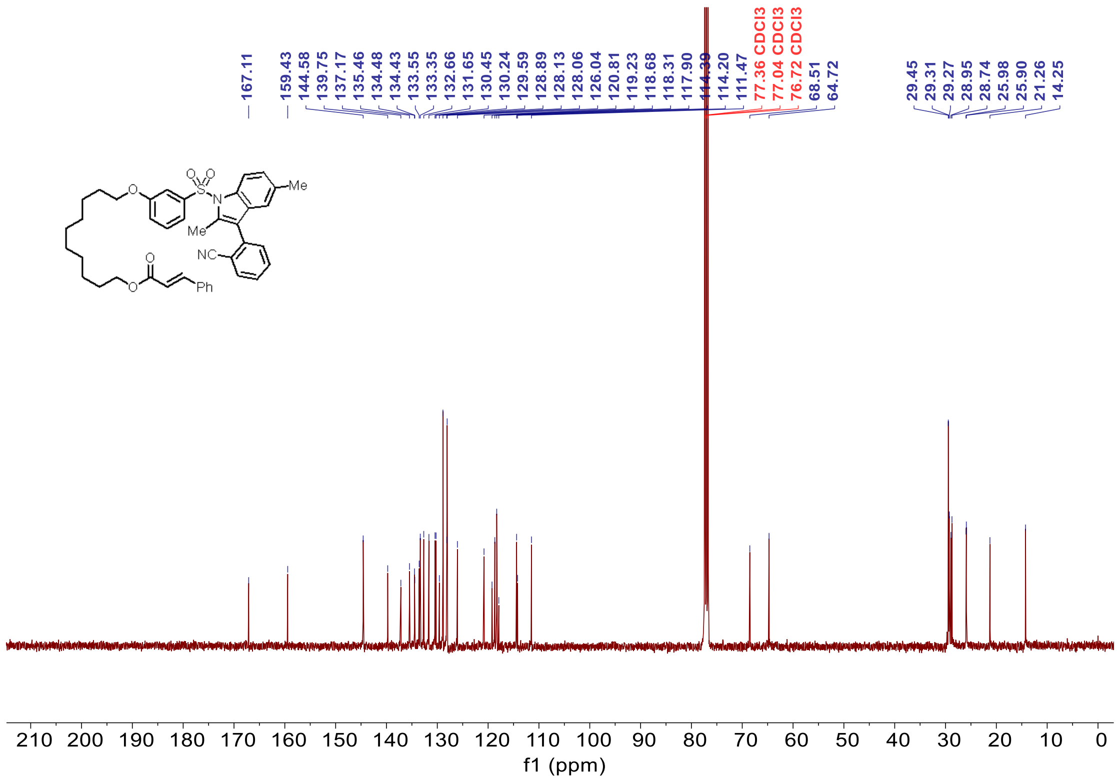


^{1}H NMR spectra of **4h**



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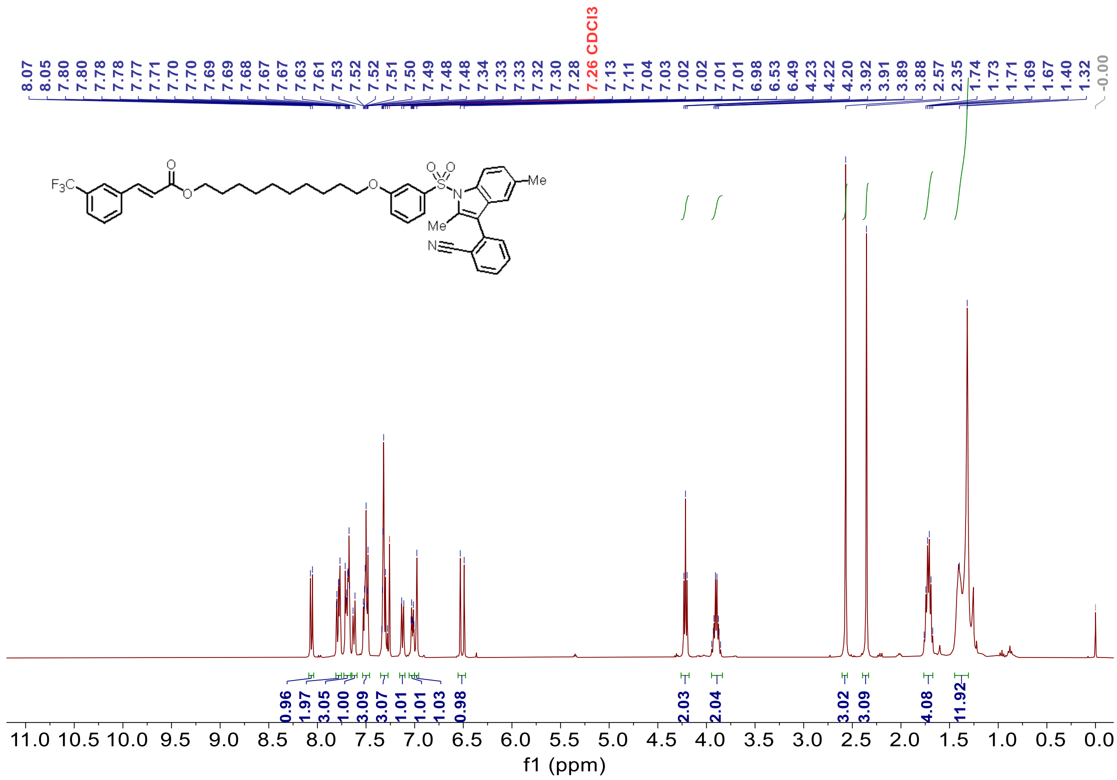
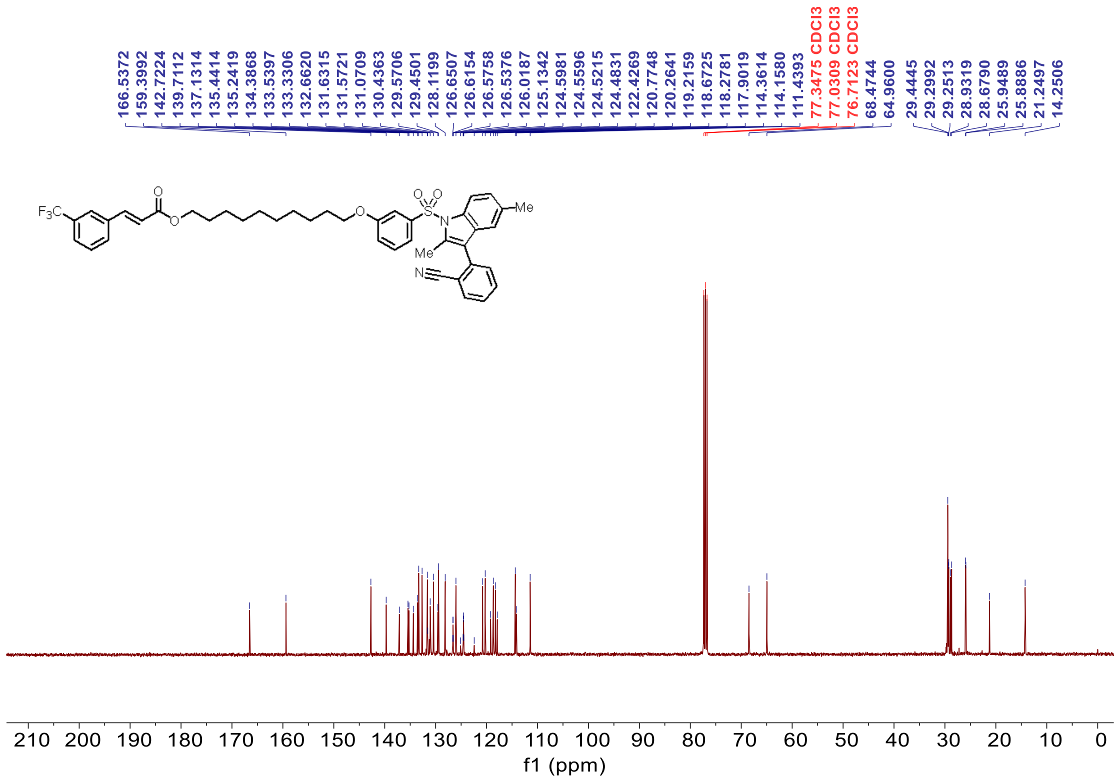


[1]H NMR spectra of **4i**



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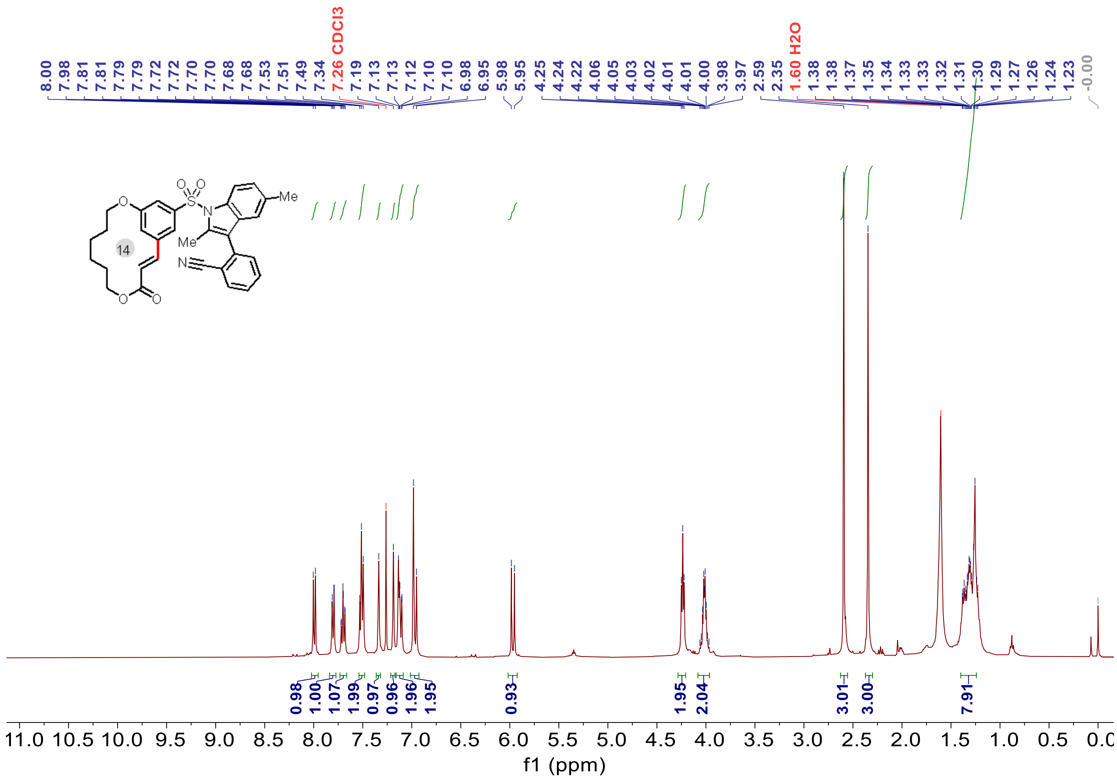

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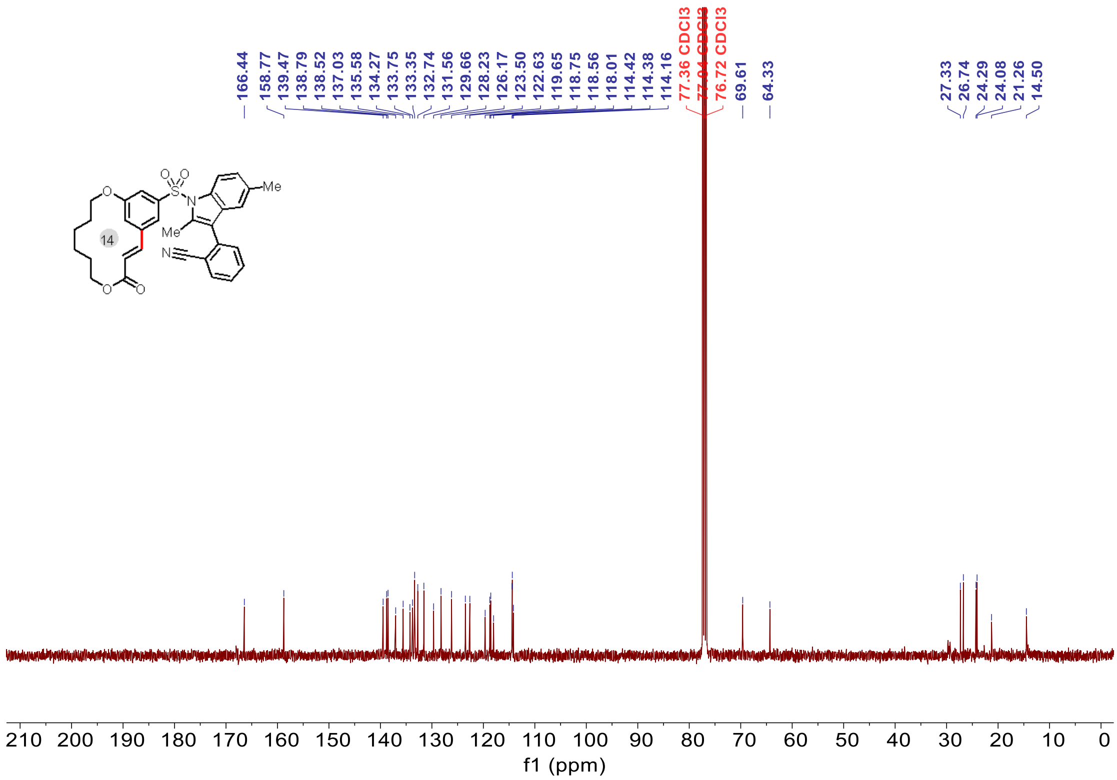
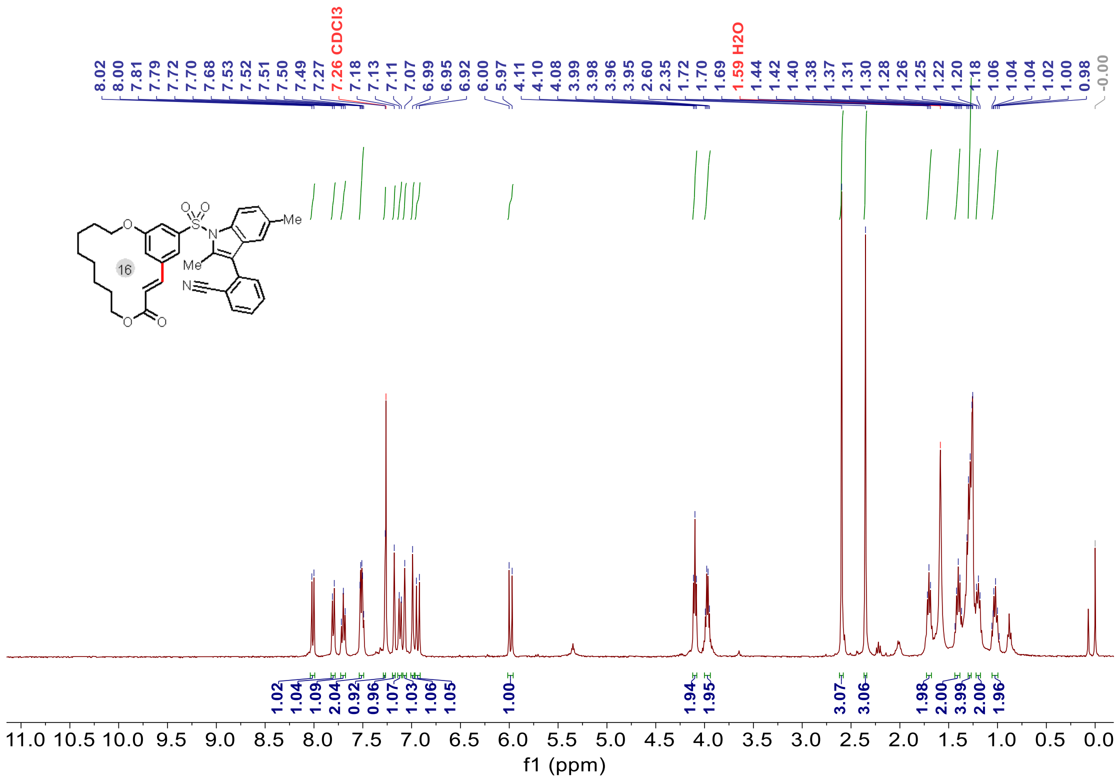


^{13}C NMR spectra of **5a**



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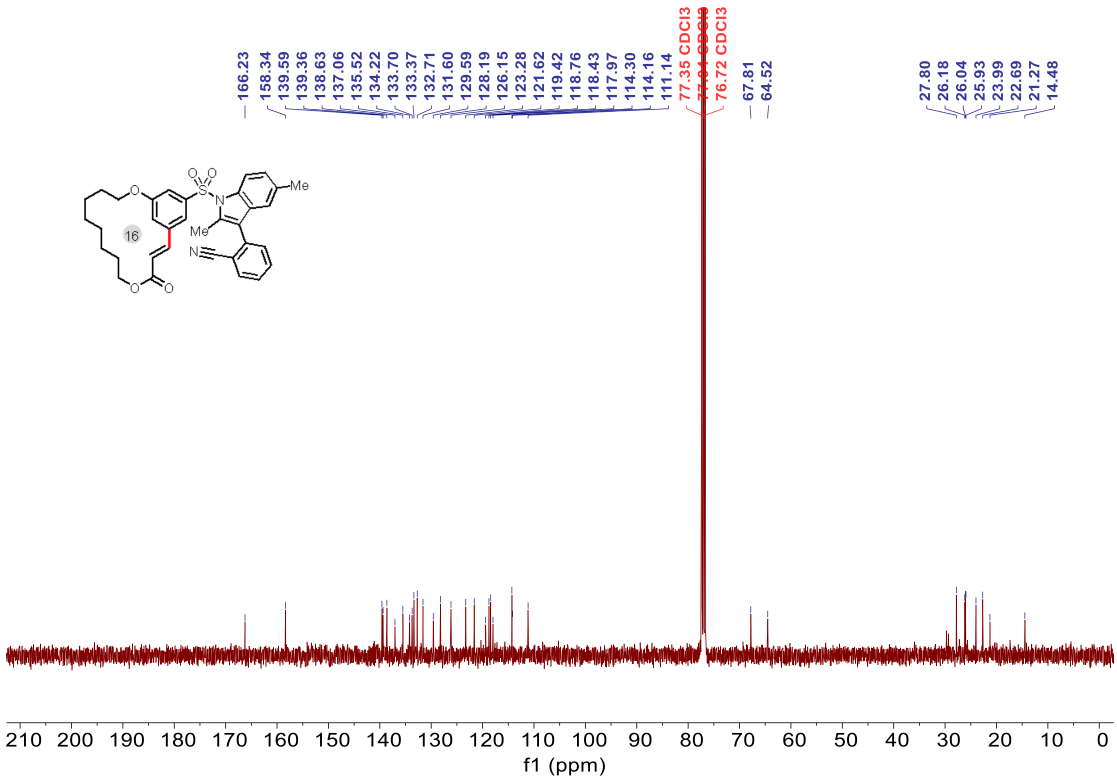

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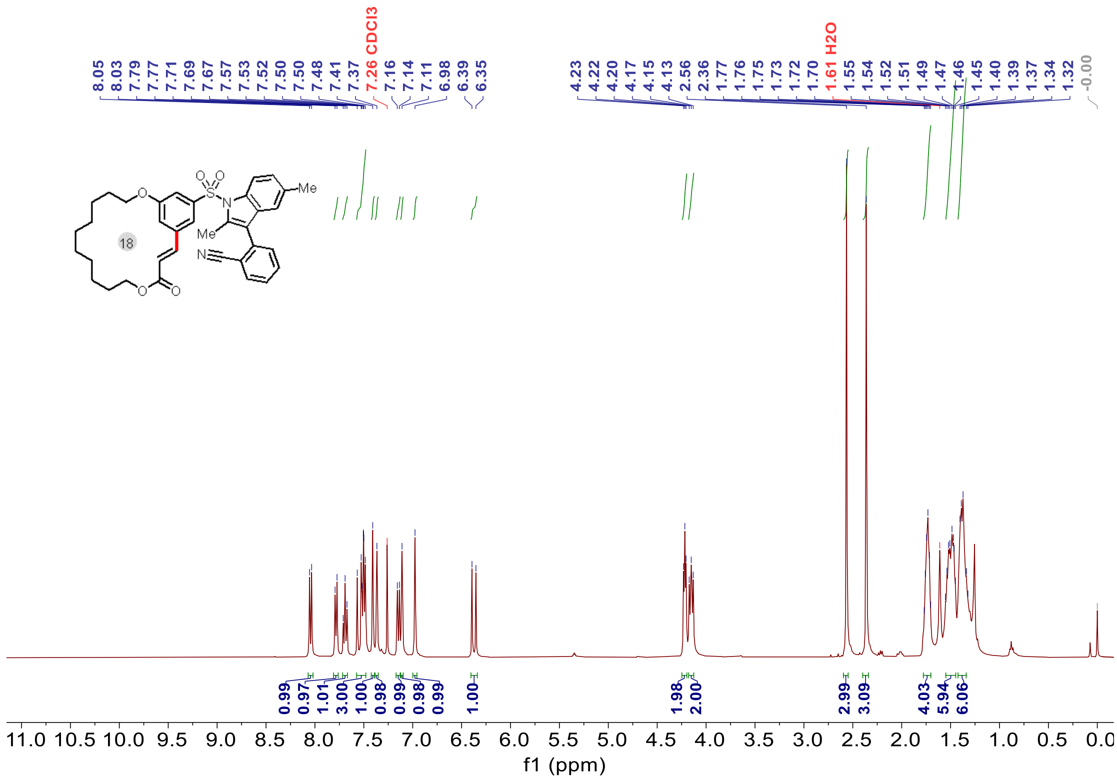

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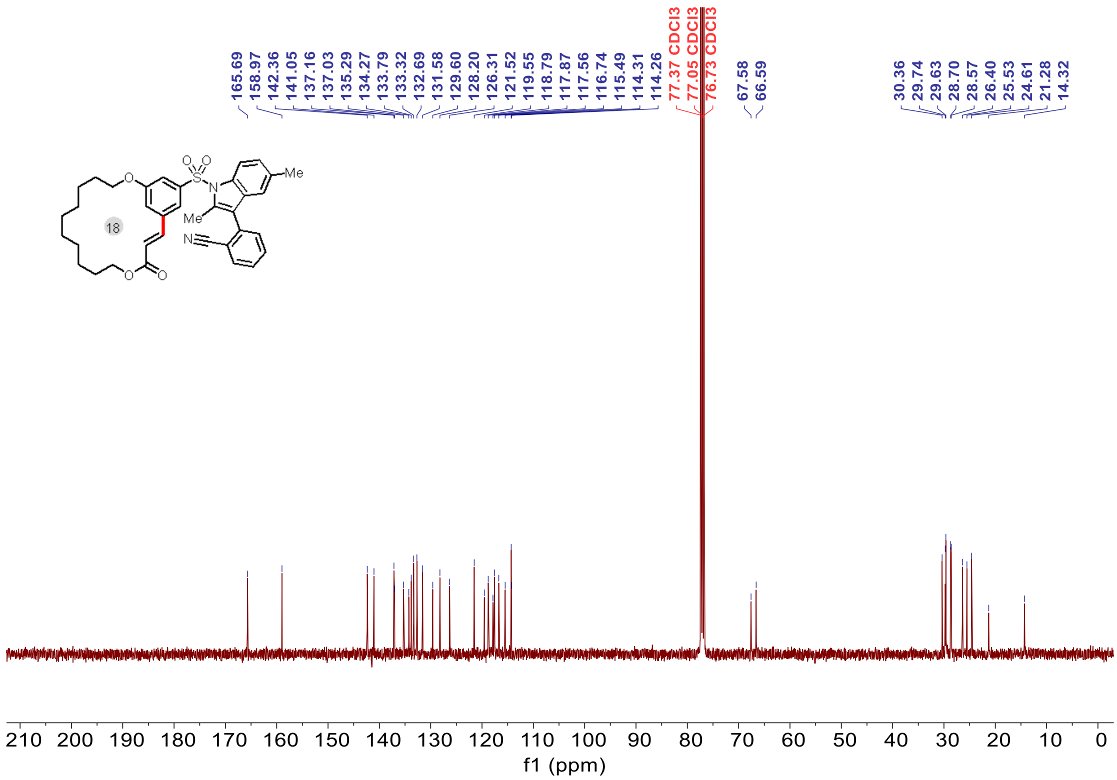
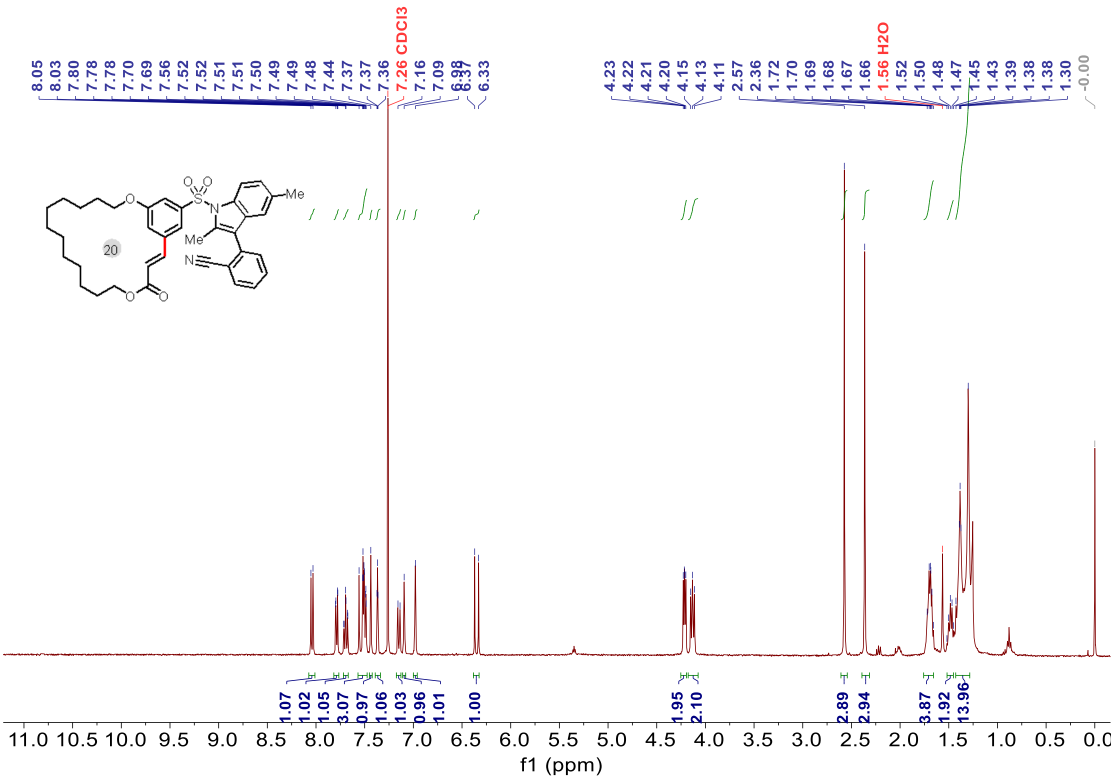


^{13}C NMR spectra of **5c**



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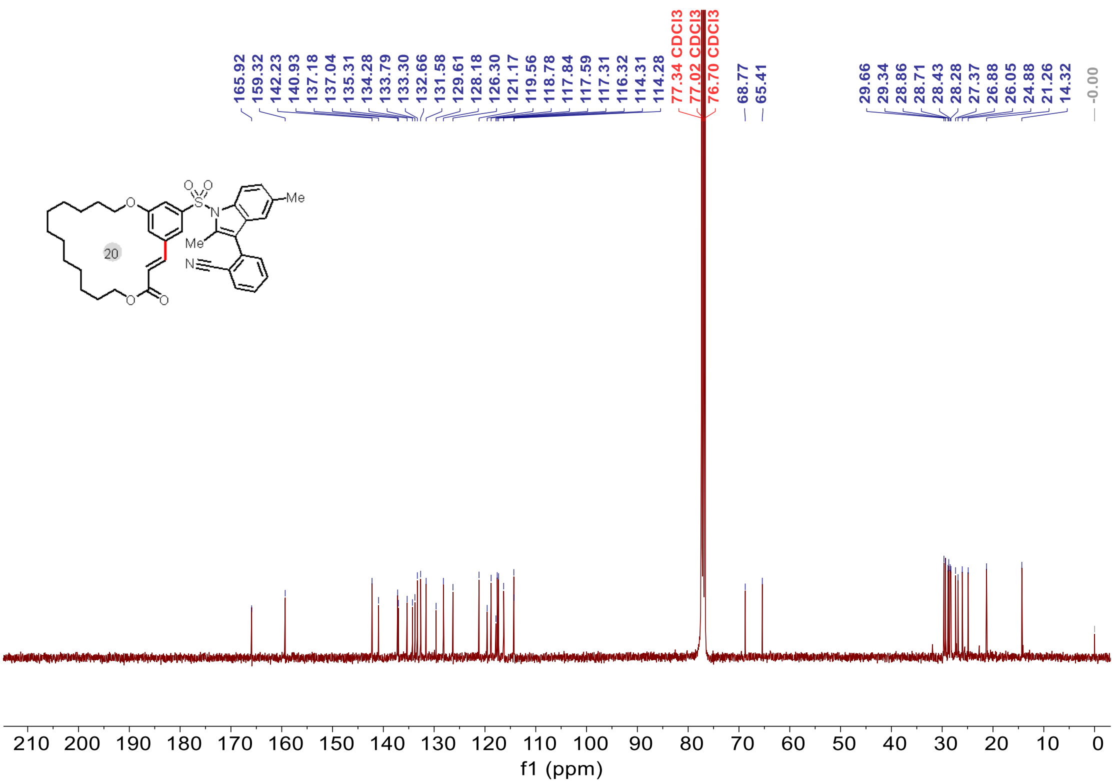

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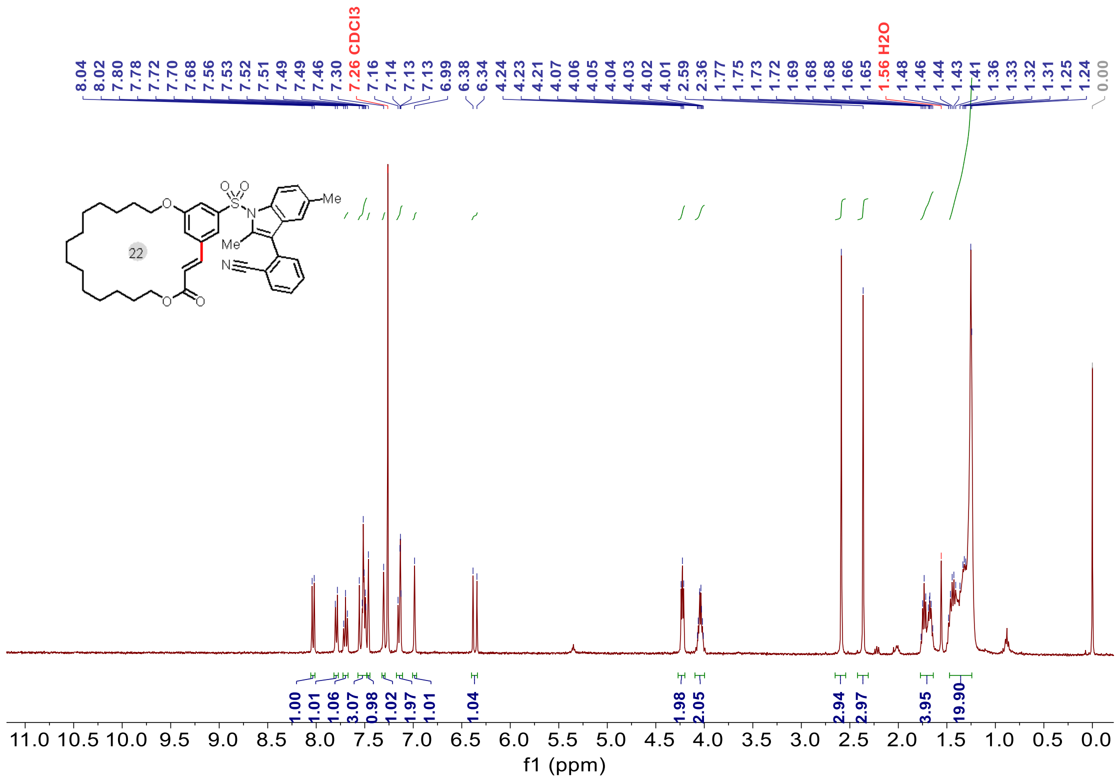

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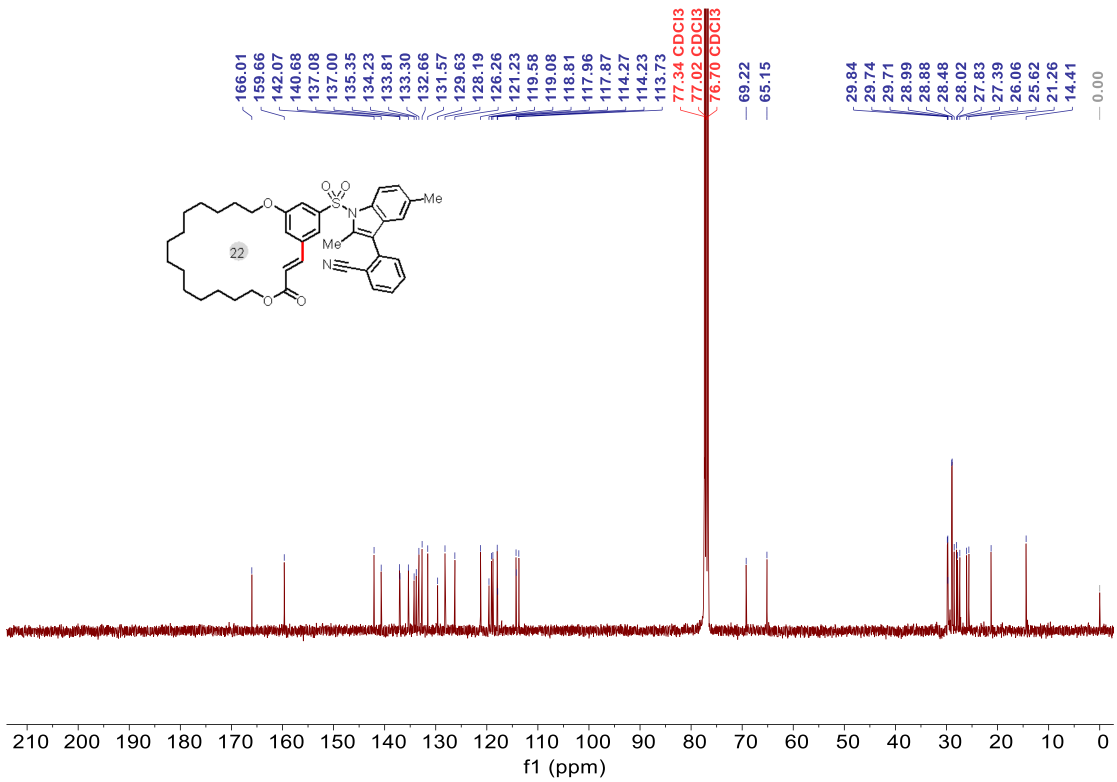
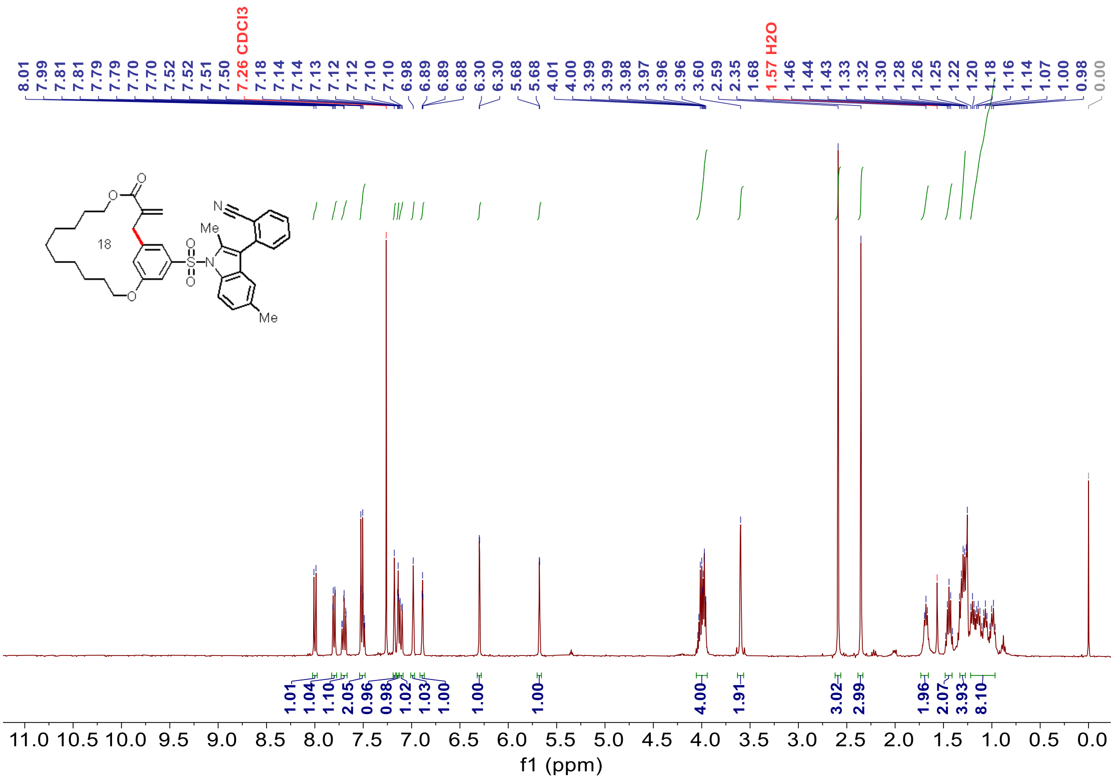
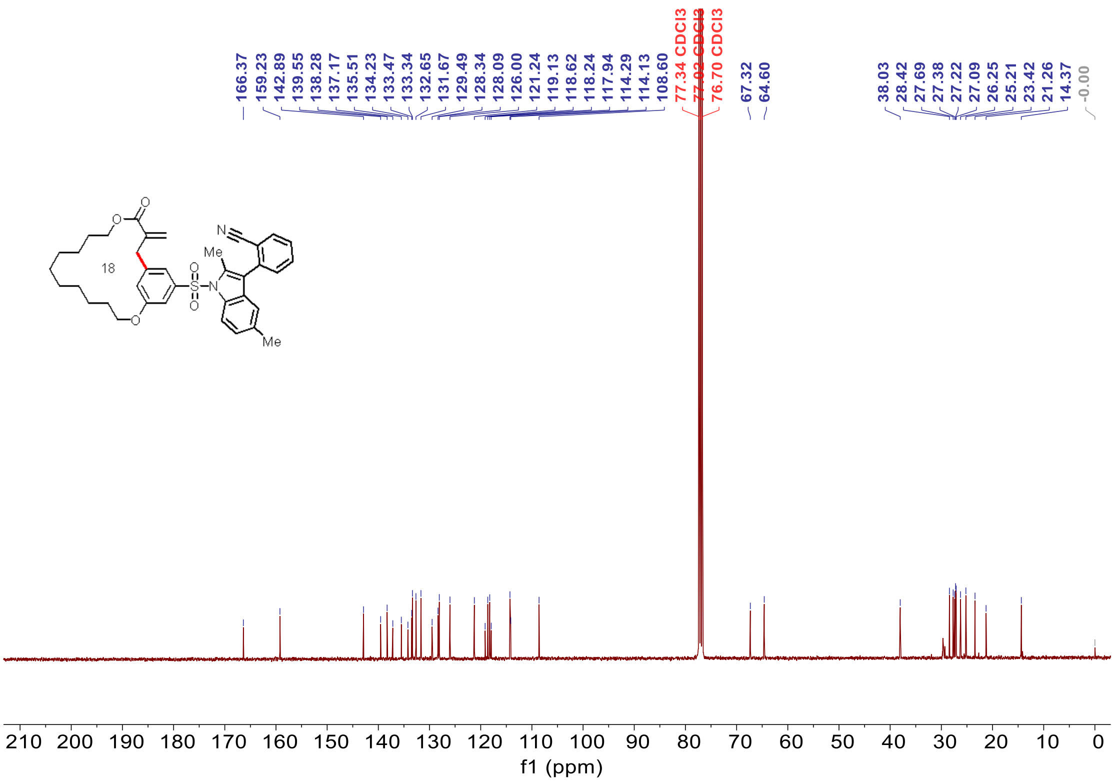


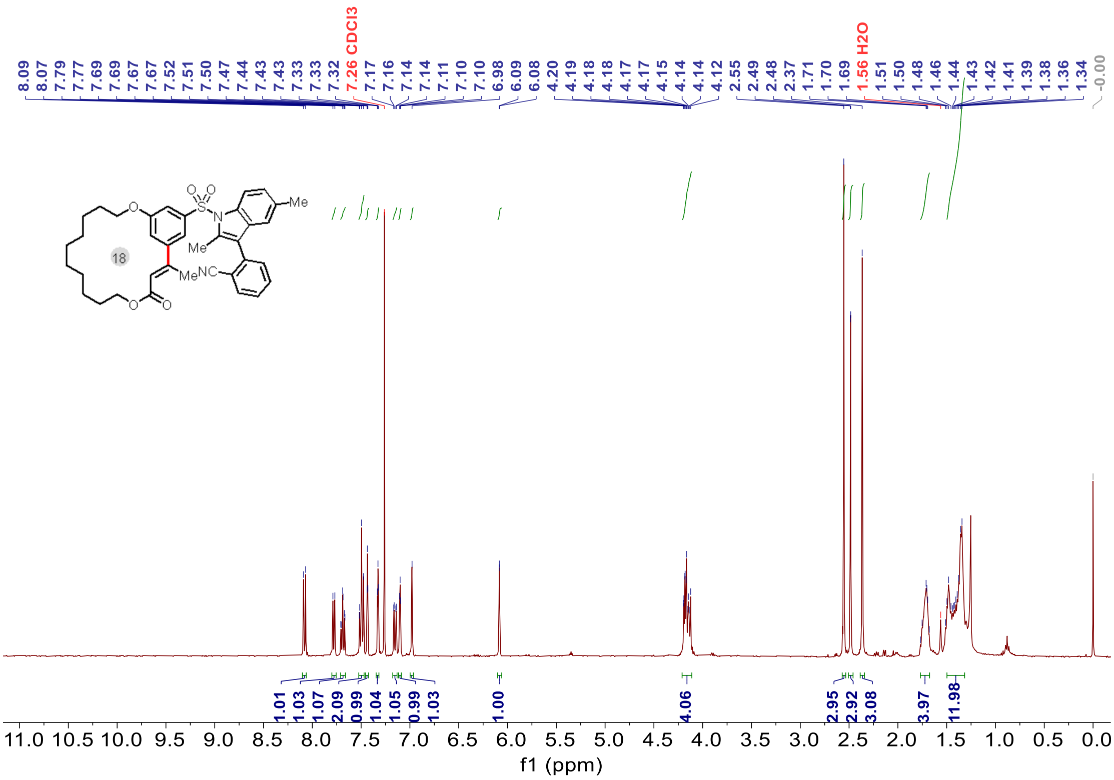
^{13}C NMR spectra of **5e**



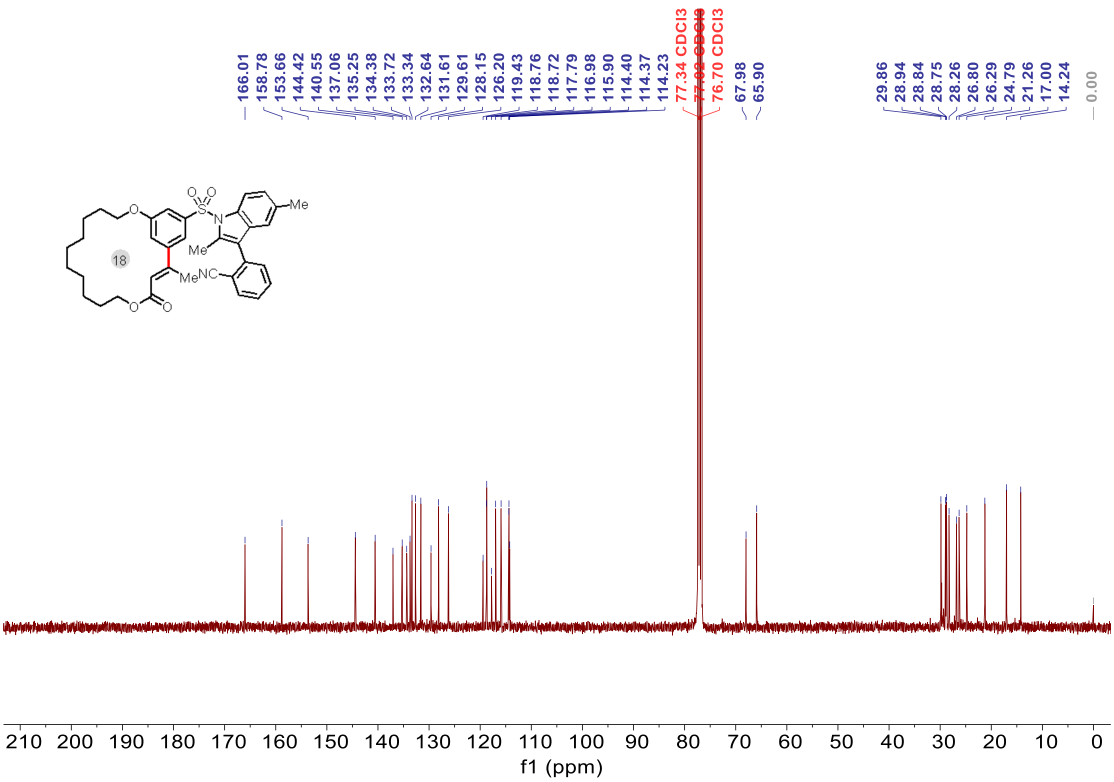
[1]H NMR spectra of **5f**



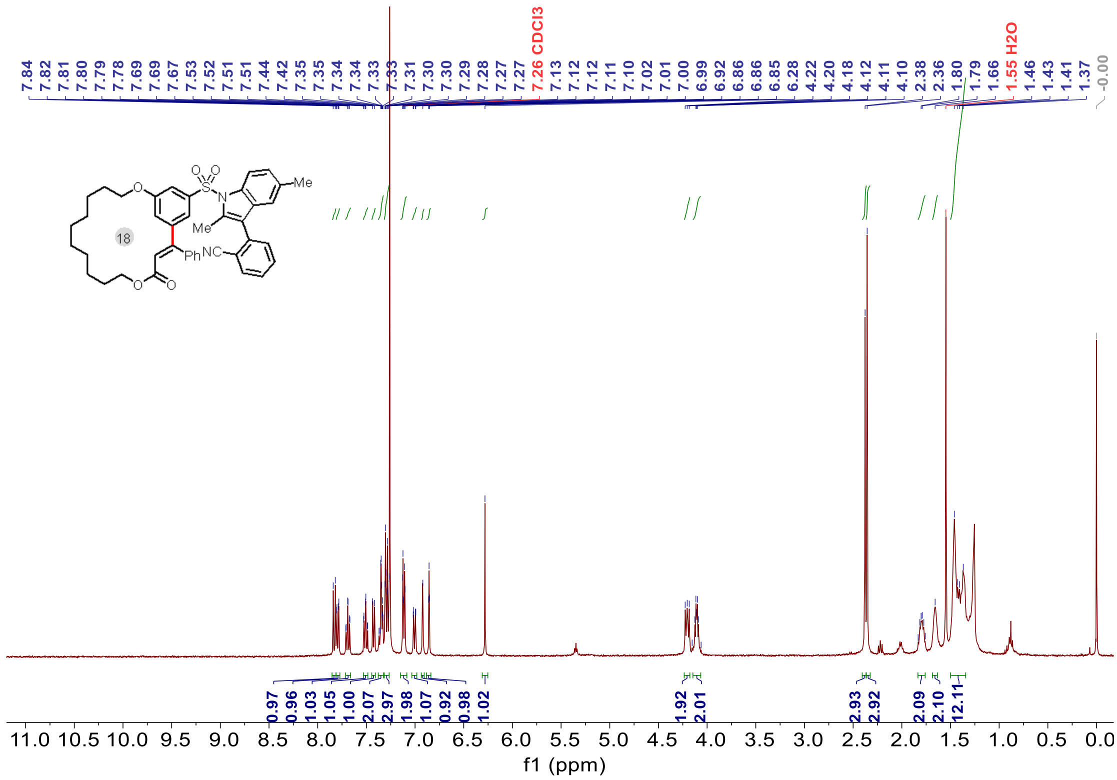
[13]C NMR spectra of **5f**



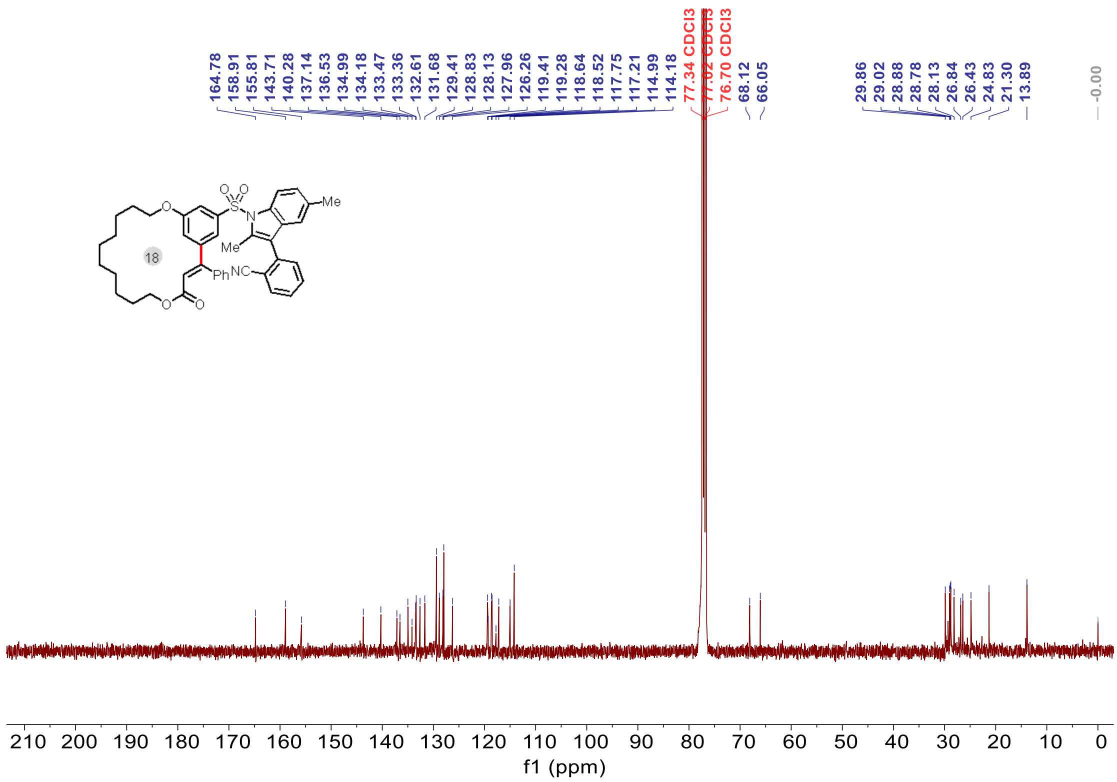
^{1}H NMR spectra of **5g**



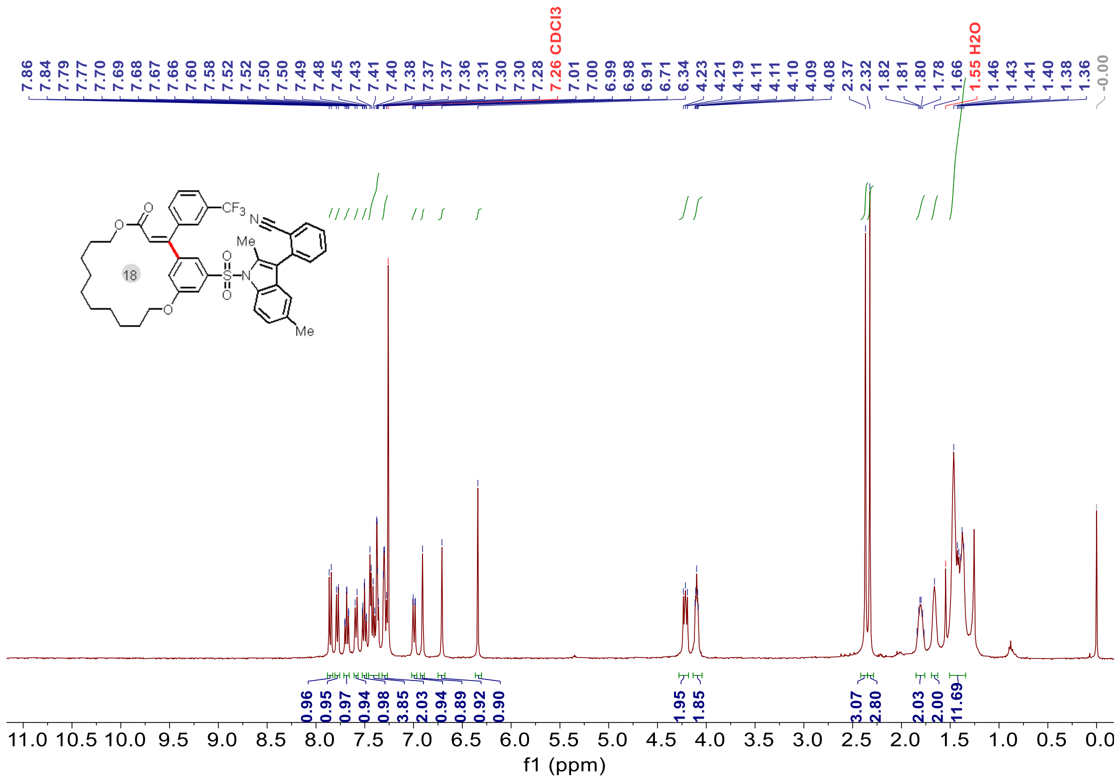
^{13}C NMR spectra of **5g**



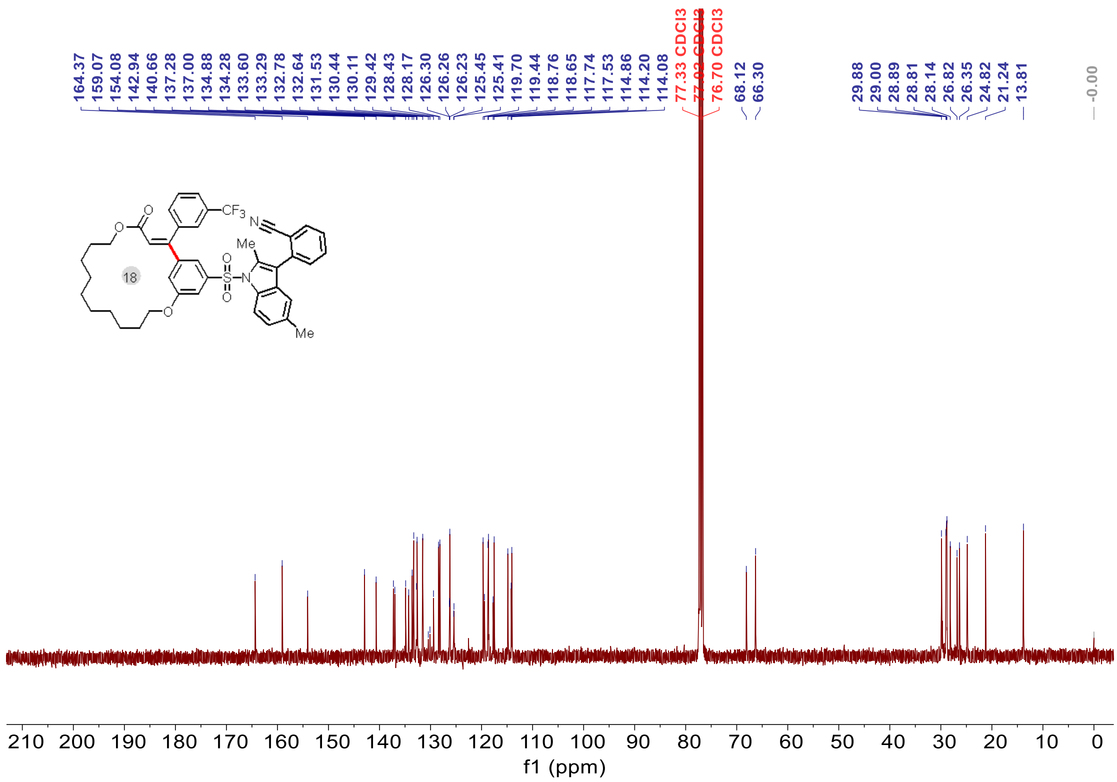
^{1}H NMR spectra of **5h**



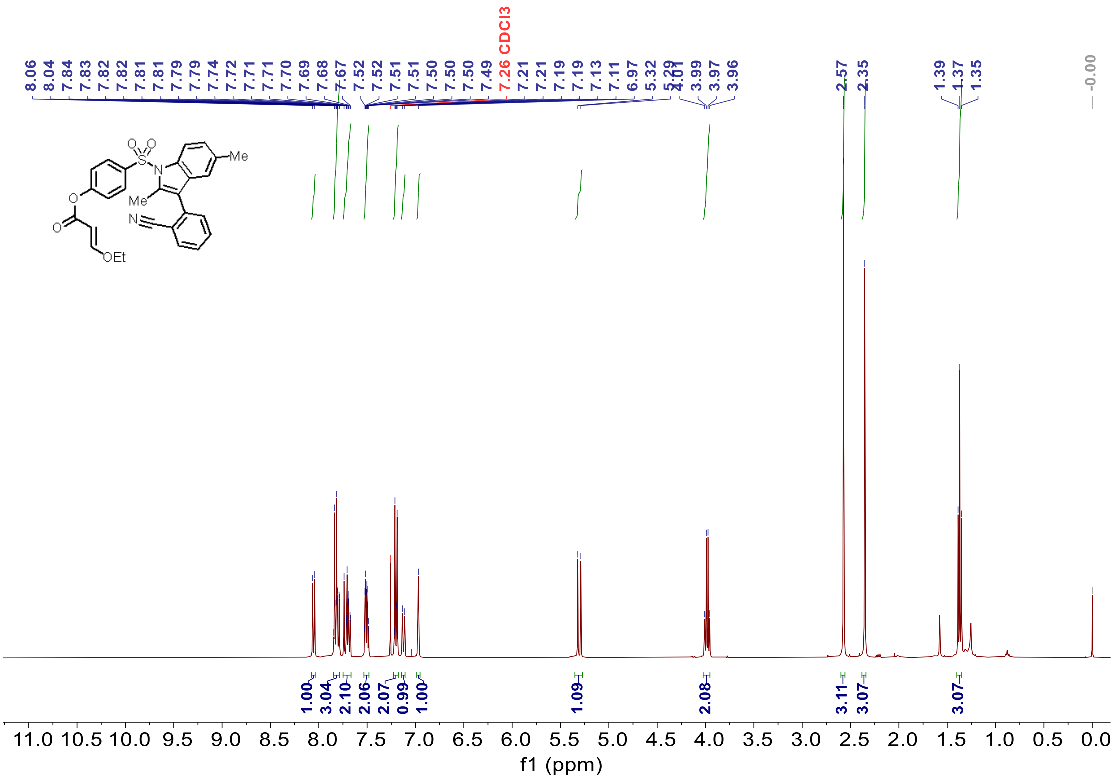
^{13}C NMR spectra of **5h**



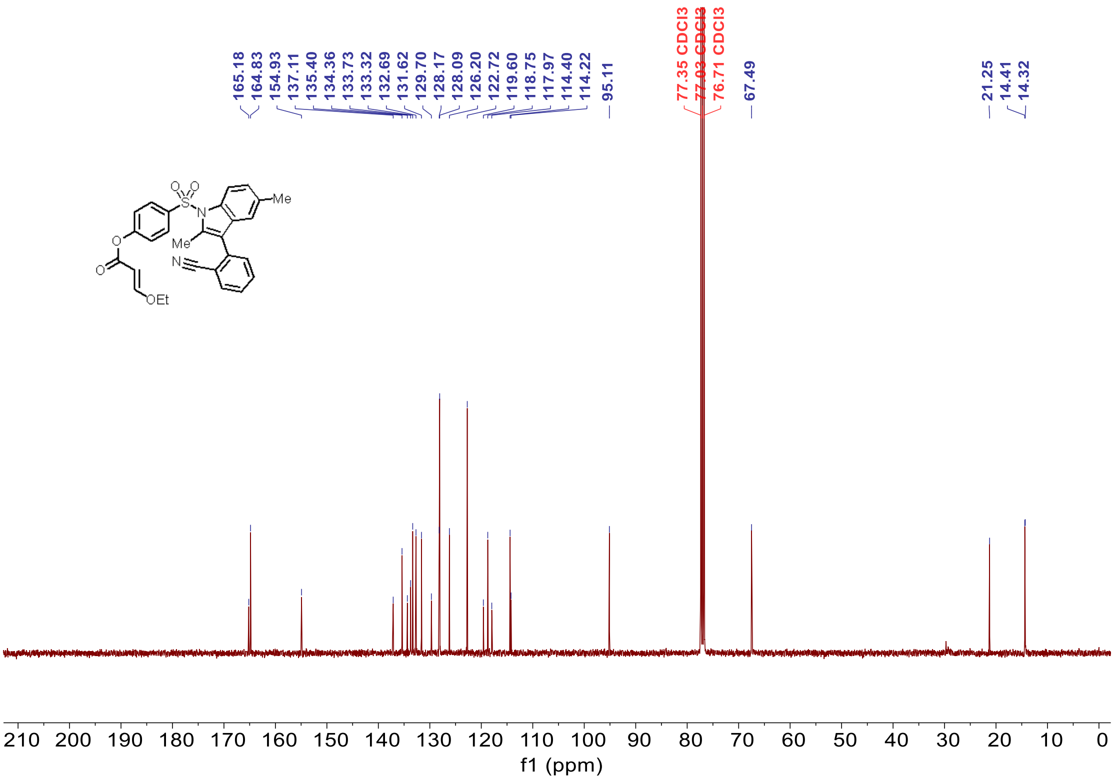
^{1}H NMR spectra of **5i**



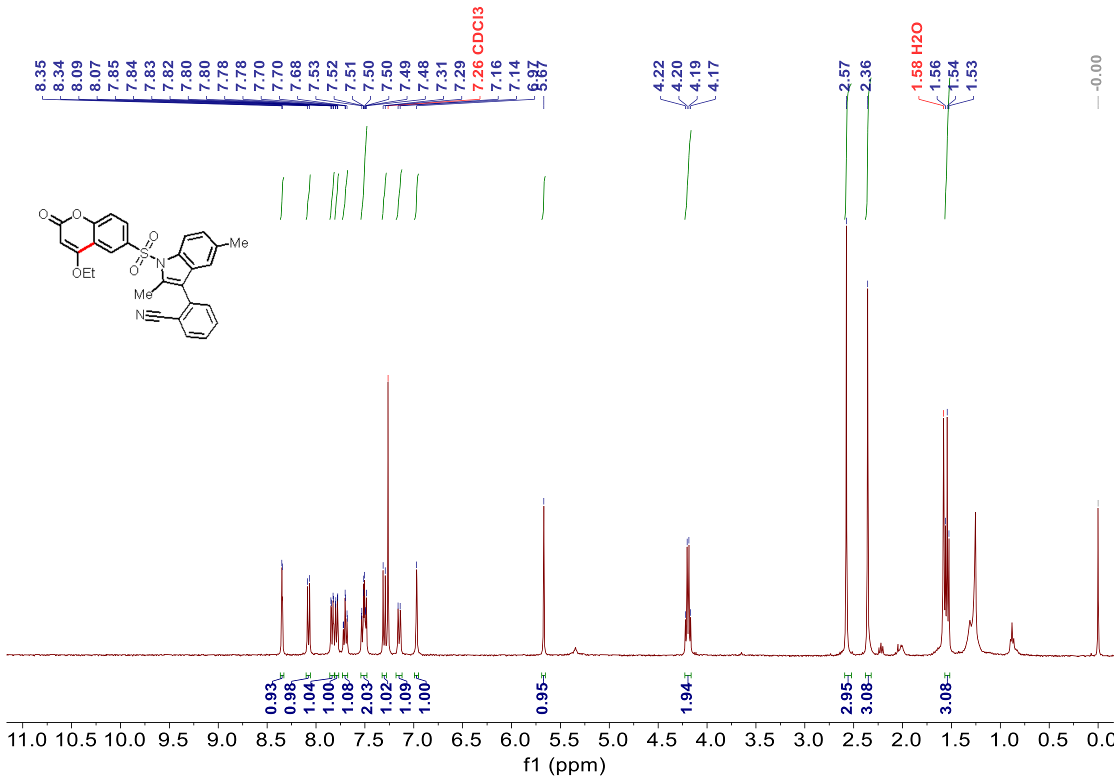
^{13}C NMR spectra of **5i**



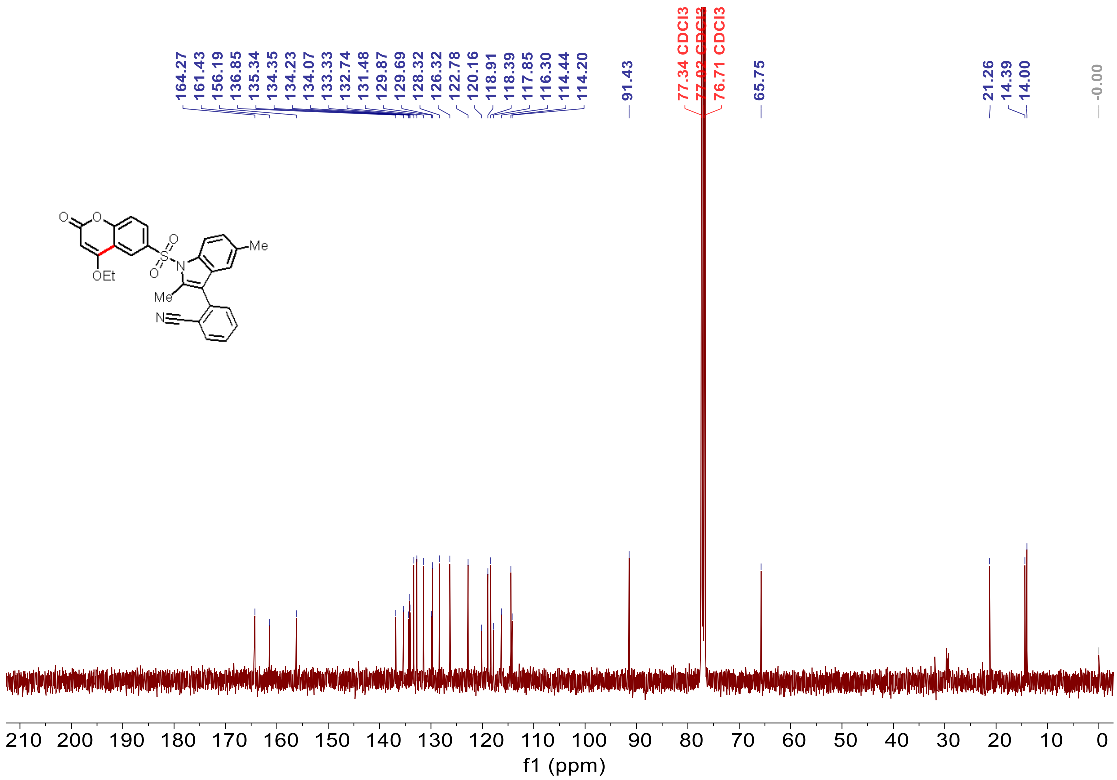
[1]H NMR spectra of **6**



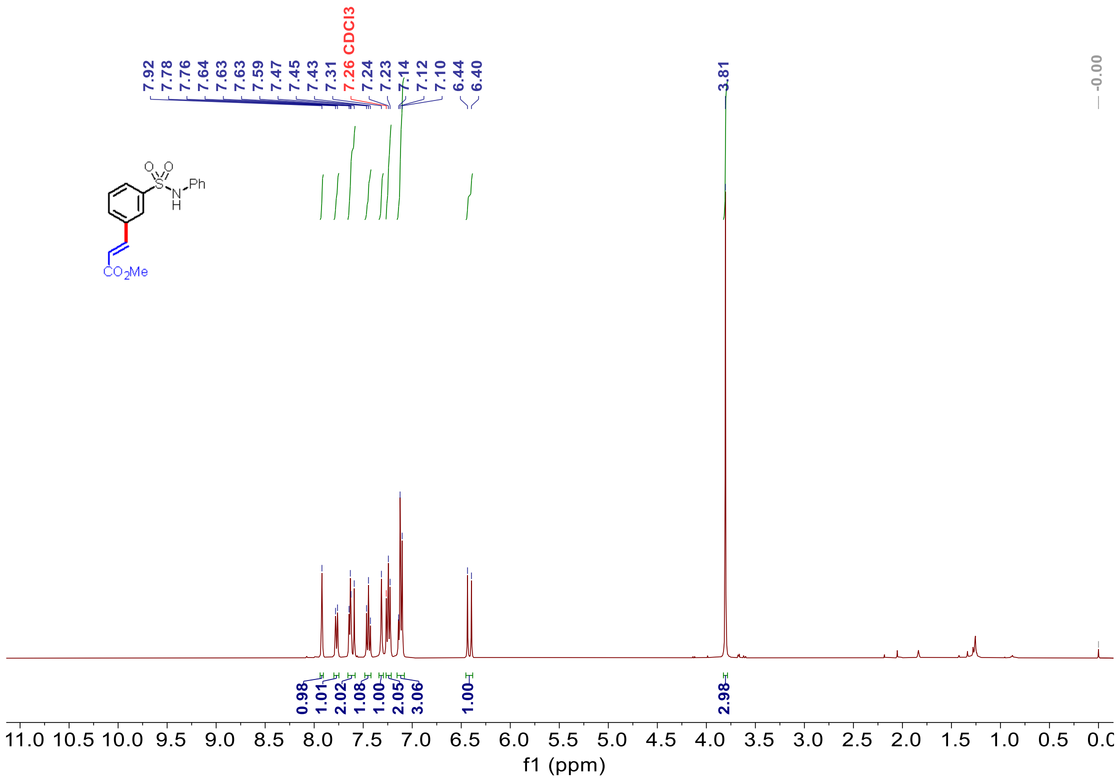
[13]C NMR spectra of **6**



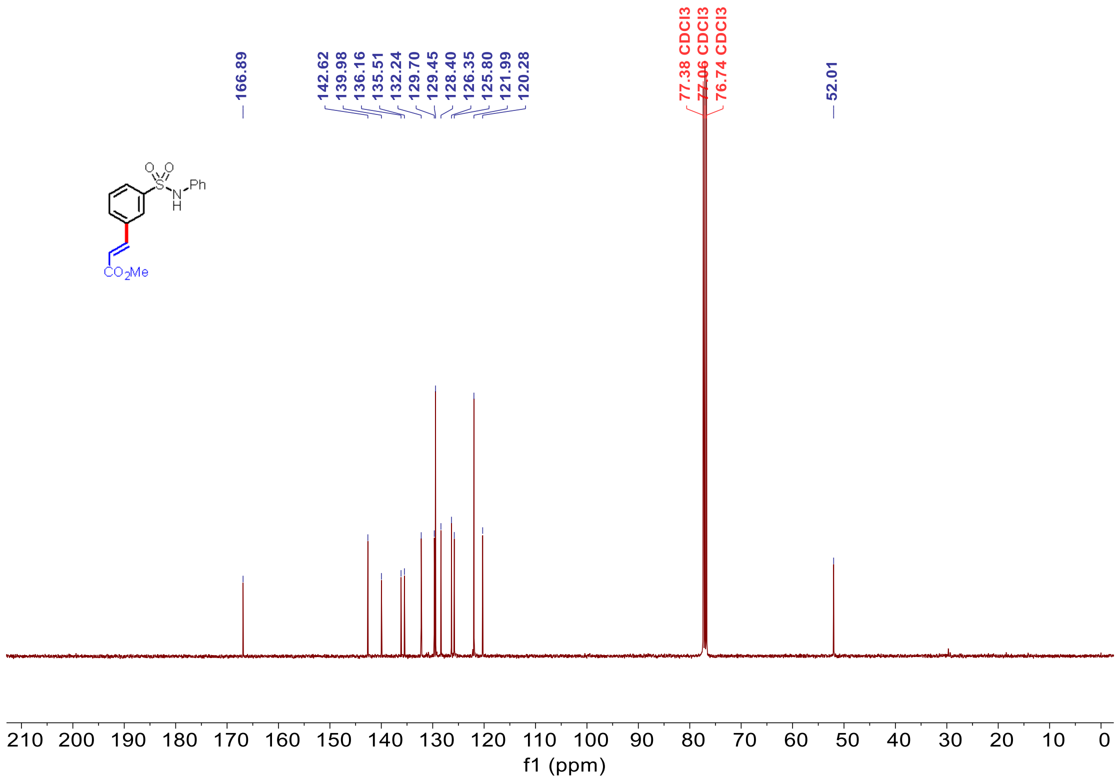
[1]H NMR spectra of **7**



[13]C NMR spectra of **7**



[1]H NMR spectra of **8**



[13]C NMR spectra of **8**