Supporting Information

Transition Metal-free [3+2] Cycloaddition Approach towards Efficient Synthesis of Trisubstituted Pyrrole Derivatives from β-Chlorovinyl Aldehydes

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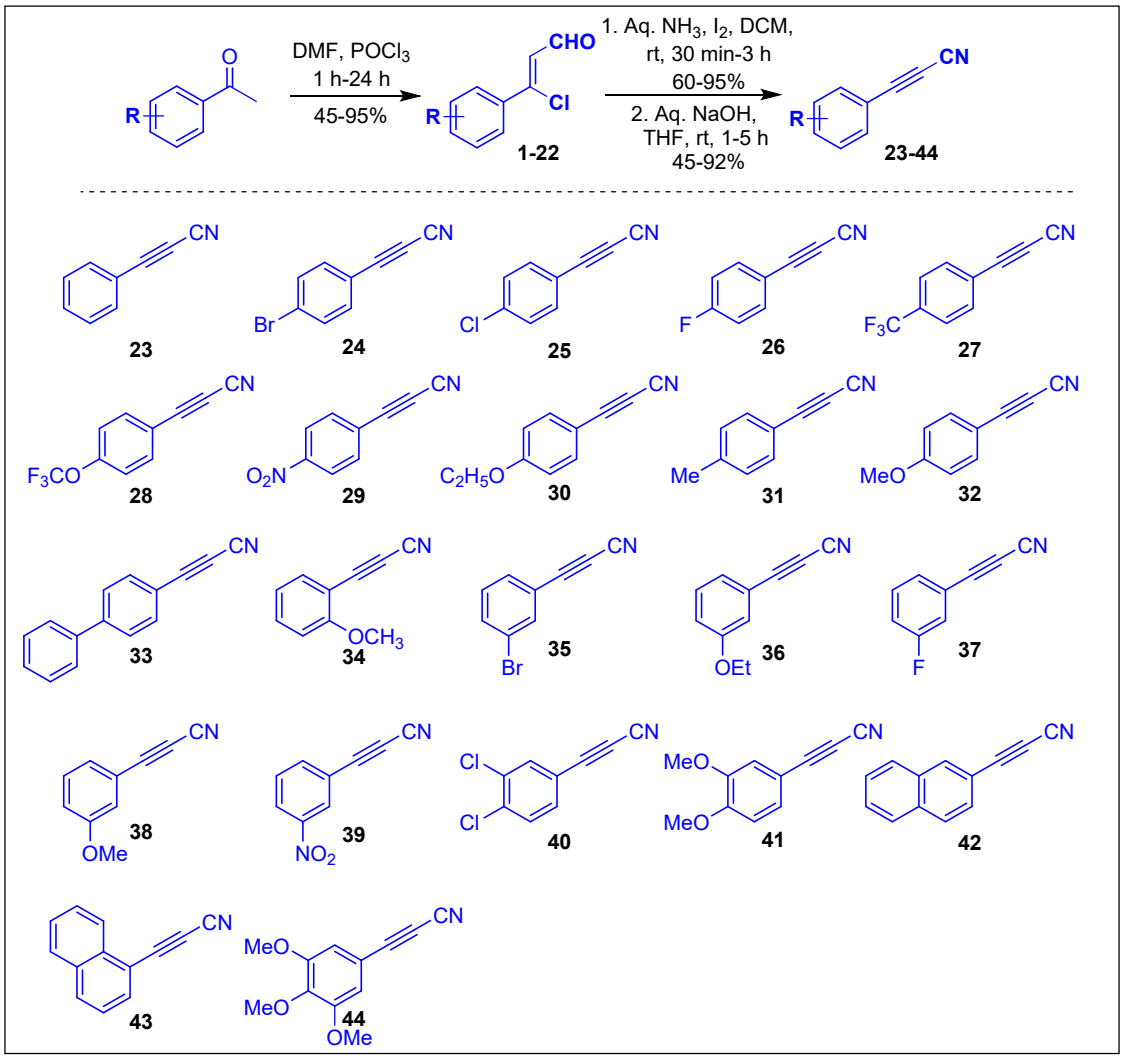
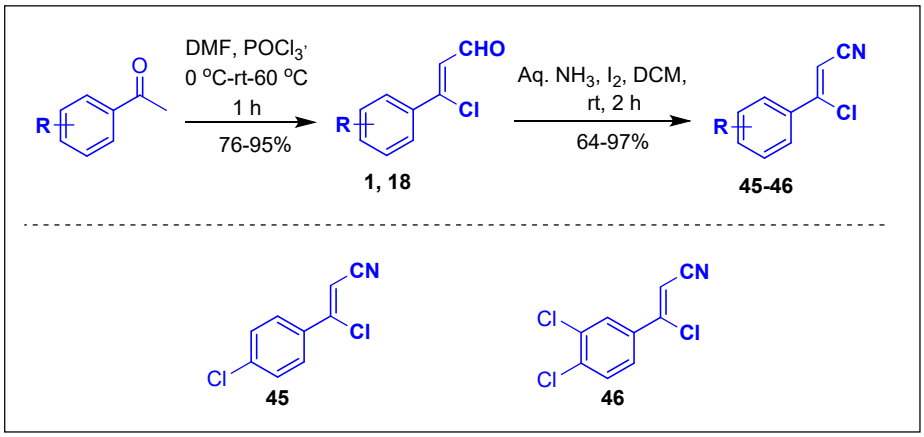
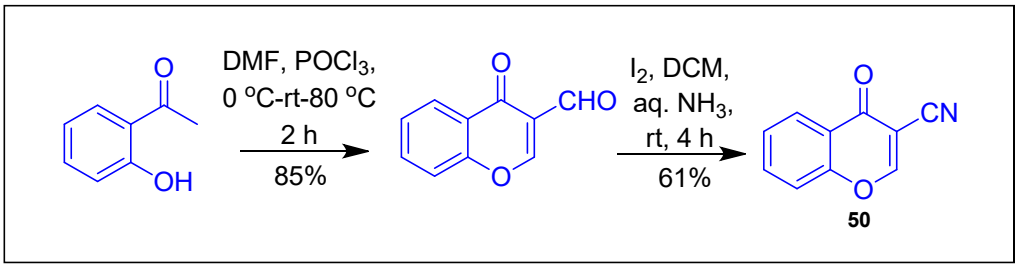
Library of 3-Phenylpropiolonitriles prepared from β-Chlorovinyl Aldehydes



Scheme S1.



Scheme S2.



Scheme S3.

Experimental Data

4-Phenyl-5-tosyl-1*H*-pyrrole-3-carbonitrile (23A). Yield 85% (0.280 g from 0.130 g) as a light brown solid; m.p. 172-174 °C; Rf = 0.33 (hexane/EtOAc, 70:30, v/v); IR (KBr): vmax (cm)-1 = 2168 (CN), 3281 (NH); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.44 (s, 3H, CH_3), 7.12 (d, *J* = 3.0 Hz, 1H, ArH), 7.33 (t, *J* = 7.4 Hz, 1H, ArH), 7.38 (d, *J* = 7.9 Hz, 2H, ArH), 7.40 (d, *J* = 7.4 Hz, 2H, ArH), 7.54 (d, *J* = 7.1 Hz, 2H, ArH), 8.00 (d, *J* = 8.4 Hz, 2H, ArH), 10.23 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.8, 63.9, 95.3, 113.7, 120.1, 127.0, 127.9, 128.3, 129.2, 130.5, 131.2, 135.5, 137.2, 145.8 ppm; HRMS (ESI) m/z: calcd. for $C_{18}H_{14}N_2O_2S$ [M + H+]: 323.0849, found: 323.0853.

4-(4-Bromophenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (24A). Yield 82% (0.160 g from 0.10 g) as a light brown solid; m.p. 122-124 °C; R_f = 0.43 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2167 (CN), 3235 (NH); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.44 (s, 3H, CH_3), 7.11 (s, 1H, ArH), 7.38 (d, *J* = 8.1 Hz, 2H, ArH), 7.41 (d, *J* = 8.5 Hz, 2H, ArH), 7.53 (s, 2H, ArH), 7.99 (d, *J* = 8.4 Hz, 2H, ArH), 10.20 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.9, 60.6, 95.2, 113.3, 119.6, 122.6, 128.0, 128.5, 130.1, 130.5, 132.4, 136.1, 137.1, 146.0 ppm; HRMS (ESI) m/z: calcd. for $C_{18}H_{13}BrN_2O_2S$[M + H^+]: 400.9954, found: 400.9958.

4-(4-Chlorophenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (25A). Yield 91% (0.201 g from 0.10 g) as an off white solid; m.p. 168-170 °C; Rf = 0.31 (hexane/EtOAc, 70:30, v/v); IR (KBr): vmax (cm)-1 = 2167 (CN), 3281 (NH); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.45 (s, 3H, $ArCH_3$) 7.11 (d, *J* = 3.0 Hz, 1H, ArH) 7.37 (d, *J* = 2.0 Hz, 1H, ArH) 7.38 (d, *J* = 2.1 Hz, 2H, ArH) 7.40 (s, 1H, ArH) 7.48 (d, *J* = 8.6 Hz, 2H, ArH) 7.99 (d, *J* = 8.4 Hz, 2H, ArH) 9.90 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, CDCl3) δ = 21.9, 51.0, 95.2, 113.4, 119.7, 128.0, 128.3, 129.4, 129.6, 130.0, 130.5, 134.4, 135.9, 137.1, 146.0 ppm; HRMS (ESI) m/z: calcd. for $C_{18}H_{13}ClN_2O_2S$ [M + H^+]: 357.0459, found: 357.0464.

4-(4-Fluorophenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (26A). Yield = 82% (0.192 g from 0.100 g) as a brown solid; m.p. 178-180 °C; Rf = 0.33 (hexane/EtOAc, 70:30, v/v); IR (KBr): vmax (cm)-1 = 2168 (CN), 3202 (NH); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.44 (s, 3H, $ArCH_3$) 7.07 (d, *J* = 6.7 Hz, 1H, ArH) 7.10 (d, *J* = 8.7 Hz, 2H, ArH) 7.38 (d, *J* = 8.1 Hz, 2H, ArH) 7.50 (d, *J* = 5.2 Hz, 1H, ArH) 7.51 (d, *J* = 5.2 Hz, 1H, ArH) 7.98 (d, *J* = 8.4 Hz, 2H, ArH) 10.39 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.8, 51.0, 95.3, 113.4, 116.2, 116.3 (d, $J_{C,F}$ = 21.5 Hz) 119.46, 128.0, 128.8, 128.9 (d, $J_{C,F}$ = 8.1 Hz), 130.4, 130.5, 135.8, 137.2 (d, $J_{C,F}$ = 205.6 Hz), 145.9 ppm; HRMS (ESI) m/z: calcd. for $C_{18}H_{13}FN_2O_2S$ [M + H+]: 341.0755, found: 341.0759.

5-Tosyl-4-(4-(trifluoromethyl)phenyl)-1H-pyrrole-3-carbonitrile (27A). Yield = 66% (0.132 g from 0.10 g) as a light brown solid; m.p. 178-180 °C; R_f = 0.26 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2168 (CN), 3287 (NH); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.45 (s, 3H, $ArCH_3$), 7.19 (s, 1H, ArH), 7.40 (d, *J* = 7.9 Hz, 2H, ArH), 7.66 (s, 4H, ArH), 8.01 (d, *J* = 8.4 Hz, 2H, ArH), 10.06 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.8, 95.2, 113.4, 120.9, 123.1, 124.9, 126.1(d, $J_{C,F}$ = 3.9 Hz), 126.2, 127.2(q, $J_{C,F}$ = 270 Hz), 127.9, 129.4, 129.9, 130.1, 130.4, 130.6, 134.7, 136.1, 136.8, 146.2 ppm; HRMS (ESI) m/z: calcd. for $C_{19}H_{13}F_3N_2O_2S$ [M + H^+]: 391.0723, found: 391.0730.

5-Tosyl-4-(4-(trifluoromethoxy)phenyl)-1*H*-pyrrole-3-carbonitrile (28A). Yield = 73% (0.226 g from 0.200 g) as a light brown solid ; m.p. 118-120 °C; Rf = 0.36 (hexane/EtOAc, 70:30, v/v); IR (KBr): vmax (cm)-1 = 2211 (CN), 3235 (NH); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.45 (s, 3H, CH_3), 7.12 (s, 1H, ArH), 7.25 (d, *J* = 8.8 Hz, 2H, ArH), 7.39 (d, *J* = 8.0 Hz, 2H, ArH), 7.57 (d, *J* = 8.8 Hz, 2H, ArH), 8.00 (d, *J* = 8.0 Hz, 2H, ArH), 10.06 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 21.8, 95.3, 113.4, 118.0, 119.7, 120.1, 121.4, 121.6, 123.1(q, $J_{C,F}$ = 257 Hz), 127.9, 128.5, 129.8(d, $J_{C,F}$ = 8.1 Hz), 130.6, 135.8, 136.9, 146.1, 149.2 ppm; HRMS (ESI) m/z: calcd. for $C_{19}H_{13}F_3N_2O_3S$ [M + H+]: 407.0672, found: 407.0676.

4-(4-Nitrophenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (29A). Yield = 65% (0.276 g from 0.200 g) as a light brown solid; m.p. 142-144 °C; Rf = 0.34 (hexane/EtOAc, 70:30, v/v); IR (KBr): vmax

(cm)-1 = 2168 (CN), 3180 (NH); 1H NMR (600 MHz, $CDCl_3$) δ = 2.45 (s, 3H, ArCH3), 7.25 (s, 1H, ArH), 7.40 (d, *J* = 8.0 Hz, 2H, ArH), 7.73 (d, *J* = 9.0 Hz, 2H, ArH), 7.99 (d, *J* = 8.0 Hz, 2H, ArH), 8.26 (d, *J* = 8.9 Hz, 2H, ArH), 10.68 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.9, 51.0, 95.4, 113.1, 120.8, 124.6, 127.5, 128.1, 128.5, 130.6, 136.8, 137.1, 137.7, 146.3, 147.5ppm; HRMS (ESI) m/z: calcd. for $C_{18}H_{13}N_3O_4S$[M + H+]: 368.0700, found: 368.0704.

4-(4-Ethoxyphenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (30A). Yield = 90% (0.194 g from 0.100 g) as a light brown solid; m.p. 130-132 °C; R_f = 0.34 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2167 (CN), 3281 (NH); ^1H NMR (600 MHz, $CDCl_3$) δ = 1.41 (t, *J* = 7.0 Hz, 3H, OCH_2CH_3), 2.43 (s, 3H, CH_3), 4.04 (q, *J* = 7.0 Hz, 2H, OCH_2CH_3), 6.91 (d, *J* = 8.8 Hz, 2H, ArH), 7.03 (d, *J* = 2.9 Hz, 1H, ArH), 7.37 (d, *J* = 7.8 Hz, 2H, ArH), 7.46 (d, *J* = 8.8 Hz, 2H, ArH), 7.98 (d, *J* = 8.4 Hz, 2H, ArH), 10.27 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 14.9, 21.8, 51.0, 63.7, 95.1, 113.8, 115.1, 119.2, 123.5, 127.9, 128.2, 130.4, 131.2, 135.2, 137.4, 145.7, 159.1 ppm; HRMS (ESI) m/z: calcd. for $C_{20}H_{18}N_2O_3S$ [M + H^+]: 366.1033, found: 366.1037.

4-(*p*-Tolyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (31A). Yield = 57% (0.136 g from 0.100 g) as a light brown solid; m.p. 136-138 °C; R_f = 0.36 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2135 (CN), 3035(NH); ^1H NMR (600 MHz, $CDCl_3$) δ = 2.36 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 7.09 (d, *J* = 3.0 Hz, 1H, ArH), 7.20 (d, *J* = 7.9 Hz, 2H, ArH), 7.37 (d, *J* = 8.1 Hz, 2H, ArH), 7.43 (d, *J* = 8.1 Hz, 2H, ArH), 7.99 (d, *J* = 8.4 Hz, 2H, ArH), 9.99 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.8, 39.4, 95.3, 113.7, 119.5, 126.9, 127.9, 128.3, 129.9, 129.9, 130.4, 131.4, 135.4, 137.3, 138.3, 145.8 ppm; HRMS (ESI) m/z: calcd. for $C_{19}H_{16}N_2O_2S$[M + H^+]: 337.1005, found: 337.1010.

4-(4-Methoxyphenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (32A). Yield = 87% (0.194 g from 0.10 g) as a light brown solid; m.p. 138-140 °C; Rf = 0.36 (hexane/EtOAc, 70:30, v/v); IR (KBr): vmax (cm)-1 = 2138 (CN), 3013 (NH); ^1H NMR (600 MHz, $CDCl_3$) δ = 2.43 (s, 3H, ArCH3), 3.82 (s, 3H, OCH_3), 6.92 (d, *J* = 8.7 Hz, 2H, ArH), 7.04 (d, *J* = 2.9 Hz, 1H, ArH), 7.37 (d, *J* = 8.1 Hz, 2H, ArH), 7.47 (d, *J* = 8.8 Hz, 2H, ArH), 7.99 (d, *J* = 8.4 Hz, 2H, ArH), 10.08 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.8, 51.0, 55.5, 95.1, 113.8, 114.6, 119.2, 123.7, 127.9, 128.3, 130.5, 131.2, 135.2, 137.3, 145.75, 159.8 ppm; HRMS (ESI) m/z: calcd. for $C_{19}H_{16}N_2O_3S$[M + H+]: 353.0954, found: 353.0959.

4-([1,1'-Biphenyl]-4-yl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (33A). Yield = 87% (0.170g from 0.1g) as a yellow solid ; m.p. 158-160 ^{o}C; Rf = 0.27 (hexane/EtOAc, 70:30, v/v); IR (KBr): vmax (cm)-1 = 2130 (CN), 3074 (NH); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.45 (s, 3H, $ArCH_3$), 7.17 (d, *J* = 3.0 Hz, 1H, ArH), 7.36 (t, *J* = 7.4 Hz, 1H, ArH), 7.39 (d, *J* = 8.0 Hz, 2H, ArH), 7.45 (t, *J* = 7.0 Hz, 2H, ArH), 7.59 (d, *J* = 8.5 Hz, 2H, ArH), 7.63 (d, *J* = 1.7 Hz, 4H, ArH), 8.02 (d, *J* = 8.5 Hz, 2H, ArH), 10.01 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 21.9, 95.3, 113.6, 119.7, 127.1, 127.4, 127.7, 127.8, 128.0, 129.0, 130.1, 130.5, 131.0, 135.7, 137.2, 140.4, 141.2, 145.9 HRMS (ESI) m/z: calcd. for $C_{24}H_{18}N_2O_2S$ [M + H+]: 399.1162, found: 399.1168.

4-(2-Methoxyphenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (34A). Yield = 60% (0.135 g from 0.100 g) as a brown solid; m.p. 150-152 ^{o}C; R_f = 0.24 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2169 (CN), 3235 (NH); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.43 (s, 3H, $ArCH_3$), 3.84 (s, 3H, OCH_3), 6.95 (d, *J* = 8.3 Hz, 1H, ArH), 6.99 (t, *J* = 7.0 Hz, 1H, ArH), 7.24 (d, *J* = 3.0 Hz, 1H, ArH), 7.31 (t, *J* = 7.0 Hz, 1H, ArH), 7.37 (d, *J* = 8.1 Hz, 2H, ArH), 7.48 (dd, *J* = 7.6, 1.7 Hz, 1H, ArH), 8.00 (d, *J* = 8.3 Hz, 2H, ArH), 10.03 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.8, 55.5, 97.1, 111.3, 113.7, 120.0, 121.1, 122.4, 126.9, 127.5, 127.9, 129.5, 129.8, 129.9, 130.4, 134.5, 137.5, 145.6, 156.4 ppm; HRMS (ESI) m/z: calcd. for $C_{19}H_{16}N_2O_3S$[M + H^+]: 353.0954, found: 353.0960.

4-(3-Bromophenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile(35A). Yield = 72% (0.118 g from 0.10 g) as a light brown solid; m.p. 136-138 ^{o}C; R_f = 0.45 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2236 (CN), 3205 (NH); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.45 (s, 3H, $ArCH_3$), 7.13 (s, 1H, ArH), 7.28 (t, *J* = 7.9 Hz, 1H, ArH), 7.39 (d, *J* = 8.0 Hz, 2H, ArH), 7.47 (d, *J* = 9.9 Hz, 1H, ArH), 7.52 (d, *J* = 7.8 Hz, 1H, ArH), 7.63 (s, 1H, ArH), 7.99 (d, *J* = 8.0 Hz, 2H, ArH), 10.08 (brs, 1H, $NH_{pyrrole}$) ppm ; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.9, 95.3, 113.2, 120.1, 123.1, 125.6, 128.0, 129.6, 129.9, 130.6, 130.7, 131.4, 133.1, 136.0, 136.9, 146.1 ppm; HRMS (ESI) m/z: calcd. for $C_{18}H_{13}BrN_2O_2S$ [M + H^+]: 400.9954, found: 400.9959.

4-(3-Ethoxyphenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (36A). Yield = 71% (0.152 g from 0.100 g) as a light brown solid; m.p. 98-100 ^{o}C; R_f = 0.38 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2235(CN), 3244 (NH); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 1.41 (t, *J* = 7.0 Hz, 3H, OCH_2CH_3), 2.44 (s, 3H, $ArCH_3$), 4.05 (q, *J* = 7.0 Hz, 2H, OCH_2CH_3), 6.87 (dd, *J* = 7.4, 2.5 Hz, 1H, ArH), 7.08 (s, 1H, ArH), 7.10 (d, *J* = 7.7 Hz, 1H, ArH), 7.12 (d, *J* = 2.9 Hz, 1H, ArH), 7.29 (t, *J* = 8.0 Hz, 1H,

ArH), 7.38 (d, *J* = 8.2 Hz, 2H, ArH), 8.00 (d, *J* = 8.4 Hz, 2H, ArH), 10.08 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 14.9, 21.8, 63.7, 95.3, 112.9, 113.6, 114.8, 119.2, 120.0, 127.9, 130.2, 130.5, 131.2, 132.3, 135.4, 137.1, 145.9, 159.5 ppm; HRMS (ESI) m/z: calcd. for $C_{20}H_{18}N_2O_3S$ [M + H^+]: 367.1111, found: 367.1118.

4-(3-Fluorophenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (37A) Yield = 66% (0.154g from 0.1g) as a brown solid; m.p. 138-140 °C; R_f = 0.43 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2167(CN), 3282 (NH); ^1H NMR (600 MHz, $CDCl_3$) δ = 2.44 (s, 3H, $ArCH_3$), 7.03 (t, *J* = 8.1 Hz, 1H, ArH), 7.13 (s, 1H, ArH), 7.23 (d, *J* = 9.5 Hz, 1H, ArH), 7.34 – 7.37 (m, 2H, ArH), 7.39 (d, *J* = 8.1 Hz, 2H, ArH), 7.99 (d, *J* = 8.4 Hz, 2H, ArH), 10.08 (brs, 1H, $NH_{pyrrole}$), ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.9, 95.3, 113.3, 113.9, 114.0, 115.2, 115.4 (d, $J_{C,F}$ = 21.6 Hz), 120.0, 122.7, 122.7, 128.0, 130.5, 130.8 (d, $J_{C,F}$ = 8.0 Hz), 136.0, 137.0, 146.0, 162.3, 164.0 (d, $J_{C,F}$ = 245.5 Hz) ppm; HRMS (ESI) m/z: calcd. for $C_{18}H_{133}FN_2O_2S$ [M + H^+]: 341.0755, found: 341.0759.

4-(3-Methoxyphenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (38A). Yield = 69% (0.154g from 0.1g) as a light brown solid; m.p. 128-130 °C; R_f = 0.32 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2205 (CN), 3235 (NH); ^1H NMR (600 MHz, $CDCl_3$) δ = 2.44 (s, 3H, $ArCH_3$), 3.82 (s, 3H, OCH_3), 6.88 (d, *J* = 8.2 Hz, 1H, ArH), 7.09 (s, 1H, ArH), 7.12 (d, *J* = 9.5 Hz, 2H, ArH), 7.31 (t, *J* = 8.0 Hz, 1H, ArH), 7.38 (d, *J* = 7.9 Hz, 2H, ArH), 8.00 (d, *J* = 6.3 Hz, 2H, ArH), 10.02 (brs, 1H, $NH_{pyrrole}$) ppm ; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.8, 55.5, 95.3, 112.4, 113.6, 114.2, 119.4, 120.1, 127.9, 130.2, 130.5, 131.1, 132.4, 135.4, 137.1, 145.9, 160.1 ppm; HRMS (ESI) m/z: calcd. for $C_{19}H_{16}N_2O_3S$ [M + H^+]: 353.0954, found: 353.0959.

4-(3-Nitrophenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (39A). Yield = 82% (0.174g from 0.1g) as a light yellow solid; m.p. 208-210 °C; R_f = 0.28 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2167 (CN), 3244 (NH); ^1H NMR (600 MHz, $CDCl_3$) δ = 2.32 (s, 3H, CH_3), 7.11 (d, J = 3.2 Hz, 1H, ArH), 7.25 (s, 1H, ArH), 7.27 (s, 1H, ArH), 7.48 (t, *J* = 8.0 Hz, 1H, ArH), 7.84 (d, *J* = 13.3 Hz, 2H, ArH), 7.86 (s, 1H, ArH), 8.03 (d, *J* = 8.2 Hz, 1H, ArH), 8.23 (s, 1H, ArH), 13.18 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.5, 29.5, 94.5, 113.4, 121.4, 122.2, 127.3, 127.4, 129.9, 130.1, 132.4, 133.3, 136.2, 137.5, 145.1, 148.4 ppm; HRMS (ESI) m/z: calcd. for $C_{18}H_{13}N_3O_4S$ [M + H^+]: 368.0700, found: 368.0705.

4-(3,4-Dichlorophenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (40A). Yield = 70% (0.139g from 0.1g) as a light brown solid; m.p. 156-158 °C; R_f = 0.36 (hexane/EtOAc, 70:30, v/v); IR (KBr):

ν_{max} $(cm)^{-1}$ = 2167 (CN), 3347 (NH); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.45 (s, 3H, $ArCH_3$), 7.13 (s, 1H, ArH), 7.39 (d, *J* = 8.1 Hz, 2H, ArH), 7.41 – 7.43 (m, 1H, ArH), 7.47 (d, *J* = 8.3 Hz, 1H, ArH), 7.59 (d, *J* = 2.1 Hz, 1H, ArH), 7.99 (d, *J* = 8.0 Hz, 2H, ArH), 10.20 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.9, 113.0, 119.7, 126.2, 128.1, 128.8, 130.6, 131.2, 132.7, 133.4, 136.4, 136.9, 146.1 ppm; HRMS (ESI) m/z: calcd. for $C_{18}H_{12}Cl_2N_2O_2S$ [M + H^+]: 392.2735, found: 392.2739.

4-(3,4-Dimethoxyphenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (41A). Yield = 72% (0.137 g from 0.10 g) as a light brown solid; m.p. 74-76 °C; R_f = 0.18 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2236 (CN), 3205 (NH); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.44 (s, 3H, ArH), 3.89 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 6.89 (d, *J* = 8.0 Hz, 1H, ArH), 7.08 (d, *J* = 3.1 Hz, 2H, ArH), 7.09 (s, 1H, ArH), 7.38 (d, *J* = 8.1 Hz, 2H, ArH), 7.99 (d, *J* = 8.4 Hz, 2H, ArH), 9.90 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.9, 56.1, 56.1, 95.2, 110.3, 111.7, 113.7, 119.0, 119.6, 123.9, 128.0, 130.5, 131.4, 135.4, 137.2, 145.8, 149.3 ppm; HRMS (ESI) m/z: calcd. for $C_{20}H_{18}N_2O_4S$ [M + H^+]: 383.1060, found: 383.1065.

4-(Naphthalen-1-yl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (42A). Yield = 70% (0.296 g from 0.200 g) as a light brown solid; m.p. 80-82 °C; Rf = 0.48 (hexane/EtOAc, 70:30, v/v); IR (KBr): vmax (cm)-1 = 2219 (CN), 3235 (NH); 1H NMR (600 MHz, CDCl3) δ = 2.46 (s, 3H, ArCH3), 7.12 (s, 1H, ArH), 7.41 (d, J = 7.9 Hz, 2H, ArH), 7.45 (t, J = 6.6 Hz, 2H, ArH), 7.50 - 7.48 (m, 2H, ArH), 7.84 (d, J = 8.2 Hz, 1H, ArH), 7.88 (t, J = 7.5 Hz, 2H, ArH), 8.04 (d, J = 8.0 Hz, 2H, ArH), 10.08 (brs, 1H, NHpyrrole) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.9, 98.3, 112.9, 122.0, 125.0, 125.5, 126.3, 126.8, 128.1, 128.3, 128.5, 128.7, 128.7, 129.2, 129.7, 130.5, 131.6, 133.9, 135.1, 137.2, 145.9 ppm; HRMS (ESI) m/z: calcd. for C22H16N2O2S [M + H+]: 373.4495, found: 373.4501.

4-(Naphthalen-2-yl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (43A). Yield = 68% (0.288 g from 0.200 g) as a light brown solid; m.p. 118-120 °C; R_f = 0.34 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2219 (CN), 3235 (NH); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.44 (s, 3H, CH_3), 7.24 (d, *J* = 3.0 Hz, 1H, ArH), 7.39 (d, *J* = 8.2 Hz, 2H, ArH), 7.50 – 7.48 (m, 2H, ArH), 7.62 (d, *J* = 8.5 Hz, 1H, ArH), 7.82 (d, *J* = 9.1 Hz, 1H, ArH), 7.86 (d, *J* = 8.5 Hz, 2H, ArH), 8.02 (d, *J* = 8.4 Hz, 2H, ArH), 8.06 (s, 1H, ArH), 10.04 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.8, 95.4, 113.7, 120.1, 124.8, 125.9, 126.6, 126.7, 127.8, 127.9, 128.3, 128.5, 128.9, 130.5, 131.2,

133.5, 133.5, 135.8, 137.2, 145.9ppm; HRMS (ESI) m/z: calcd. for $C_{22}H_{16}N_2O_2S$[M + H^+]: 373.4495, found: 373.4499.

5-Tosyl-4-(3,4,5-trimethoxyphenyl)-1*H*-pyrrole-3-carbonitrile (44A). Yield = 72% (0.137 g from 0.10 g) as a light brown solid; m.p. 78-80 °C; R_f = 0.21 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2236 (CN), 3205 (NH); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.45 (s, 3H, $ArCH_3$), 3.86 (s, 3H, OCH_3), 3.88 (s, 6H, 2(OCH_3)), 6.75 (s, 2H, ArH), 7.11 (d, *J* = 2.7 Hz, 1H, ArH), 7.39 (d, *J* = 8.1 Hz, 2H, ArH), 7.99 (d, *J* = 8.4 Hz, 2H, ArH), 10.12 (brs, 1H, $NH_{pyrrole}$) ppm ; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.9, 56.4, 61.1, 95.3, 104.3, 113.7, 119.6, 126.7, 127.9, 130.5, 131.4, 135.5, 137.2, 138.2, 145.9, 153.7 ppm; HRMS (ESI) m/z: calcd. for $C_{21}H_{20}N_2O_5S$ [M + H^+]: 413.1166, found: 413.1170.

Ethyl 4-cyano-2-tosyl-1*H*-pyrrole-3-carboxylate(49A). Yield = 46% (0.092 g from 0.10 g) as a brown solid; m.p. 182-184 °C; R_f = 0.46 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2240 (CN), 3235 (NH), 1735 (COOEt); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 1.17 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 2.26 (s, 3H, $ArCH_3$), 4.13 (q, *J* = 7.2 Hz, 2H, $CO_2CH_2CH_3$), 7.19 (d, *J* = 6.3 Hz, 2H, ArH), 7.32 (s, 1H, ArH), 7.77 (d, *J* = 8.4 Hz, 2H, ArH), 13.28 (brs, 1H, $NH_{pyrrole}$)ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 13.9, 21.4, 60.7, 97.0, 111.9, 119.9, 127.4, 130.0, 130.0, 136.7, 137.1, 145.3, 161.2 ppm; HRMS (ESI) m/z: calcd. for $C_{15}H_{14}N_2O_4S$ [M + H^+]: 319.0747, found: 319.0754.

3-Tosylchromeno[2,3-*c*]pyrrol-9(2*H*)-one (50A). Yield = 40% (0.080 g from 0.10 g) as a brown solid; m.p. 90-92 °C; R_f = 0.23 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 3245 (NH), 1715 (C=O); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.40 (s, 3H, $ArCH_3$), 7.32 (d, *J* = 8.0 Hz, 2H, ArH), 7.36 (t, *J* = 7.5 Hz, 1H, ArH), 7.54 (d, *J* = 8.4 Hz, 1H, ArH), 7.66 (s, 1H), 7.68 – 7.71 (m, 1H, ArH), 7.96 (d, *J* = 8.7 Hz, 1H, ArH), 8.28 (d, *J* = 7.9 Hz, 2H, ArH), 10.36 (brs, 1H, $NH_{pyrrole}$) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.7, 112.0, 113.5, 118.3, 120.0, 122.2, 124.2, 126.9, 127.0, 130.1, 134.6, 139.0, 144.7, 145.7, 156.9, 174.8 ppm; HRMS (ESI) m/z: calcd. for $C_{19}H_{15}NO_3S$ [M + H^+]: 338.4005, found: 338.4010.

1-Benzyl-4-(4-chlorophenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile(51) Yield = 96% (0.120 g from 0.10 g) as a light brown solid; m.p. 190-192 °C; R_f = 0.55 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2238 (CN),; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.36 (s, 3H, $ArCH_3$), 5.52 (s, 2H, CH_2Ph),

6.87 (s, 1H, ArH), 6.98 (d, *J* = 7.0 Hz, 2H, ArH), 7.17 (d, *J* = 8.2 Hz, 2H, ArH), 7.24 (d, *J* = 7.1 Hz, 1H, ArH), 7.27 (s, 1H, ArH), 7.29 (d, *J* = 7.2 Hz, 1H, ArH), 7.33 (d, *J* = 8.5 Hz, 2H, ArH), 7.46 (d, *J* = 8.5 Hz, 2H, ArH), 7.66 (d, *J* = 8.2 Hz, 2H, ArH) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.8, 52.8, 98.3, 114.0, 125.4, 127.4, 127.7, 128.3, 128.4, 128.6, 129.2, 129.3, 129.5, 130.2, 134.3, 135.0, 135.4, 137.7, 145.4 ppm; HRMS (ESI) m/z: calcd. for $C_{25}H_{19}ClN_2O_2S$ [M + H^+]: 447.0929, found: 447.0934.

4-(4-Chlorophenyl)-1-ethynyl-5-tosyl-1*H*-pyrrole-3-carbonitrile (52). Yield = 93% (0.123 g from 0.10 g) as a brown solid; m.p. 144-146 ^oC; R_f = 0.49 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2240 (CN); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.45 (s, 3H, $ArCH_3$), 2.56 (s, 1H, $CH_{propargyl}$), 5.19 (d, *J* = 2.6 Hz, 2H, $CH_{2propargylic}$), 7.27 (s, 1H, ArH), 7.38 (d, *J* = 8.5 Hz, 4H, ArH), 7.50 (d, *J* = 8.5 Hz, 2H, ArH), 8.00 (d, *J* = 8.3 Hz, 2H, ArH) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.9, 39.0, 84.0, 98.9, 113.6, 124.3, 127.9, 128.5, 129.4, 130.5, 134.5, 137.7, 145.9 ppm; HRMS (ESI) m/z: calcd. for $C_{20}H_{13}ClN_2O_2S$ [M + H^+]: 381.0459, found: 381.0463.

1-Allyl-4-(4-chlorophenyl)-5-tosyl-1*H*-pyrrole-3-carbonitrile (53). Yield = 95% (0.102 g from 0.10 g) as an off white solid; m.p. 138-140 ^oC; R_f = 0.52 (hexane/EtOAc, 70:30, v/v); IR (KBr): ν_{max} $(cm)^{-1}$ = 2333 (CN); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.44 (s, 3H, $ArCH_3$), 4.94 (d, *J* = 5.9 Hz, 2H, $CH_{2allylic}$), 5.12 (d, *J* = 17.0 Hz, 1H, =CH*H*), 5.27 (d, *J* = 10.2 Hz, 1H, =C*H*H), 5.86-5.95 (m, 1H, =CH), 6.95 (s, 1H,), 7.37 (dd, *J* = 8.4, 4.2 Hz, 4H, ArH), 7.50 (d, *J* = 8.5 Hz, 2H, ArH), 7.95 (d, *J* = 8.2 Hz, 2H, ArH) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 21.8, 51.7, 98.1, 113.9, 120.1, 124.7, 127.8, 128.4, 128.4, 129.3, 129.5, 130.4, 131.9, 134.3, 135.0, 137.9, 145.7 ppm; HRMS (ESI) m/z: calcd. for $C_{21}H_{17}ClN_2O_2S$ [M + H^+]: 397.0772, found: 397.0776.

^{1}H and ^{13}C NMR spectra of synthesized novel compounds

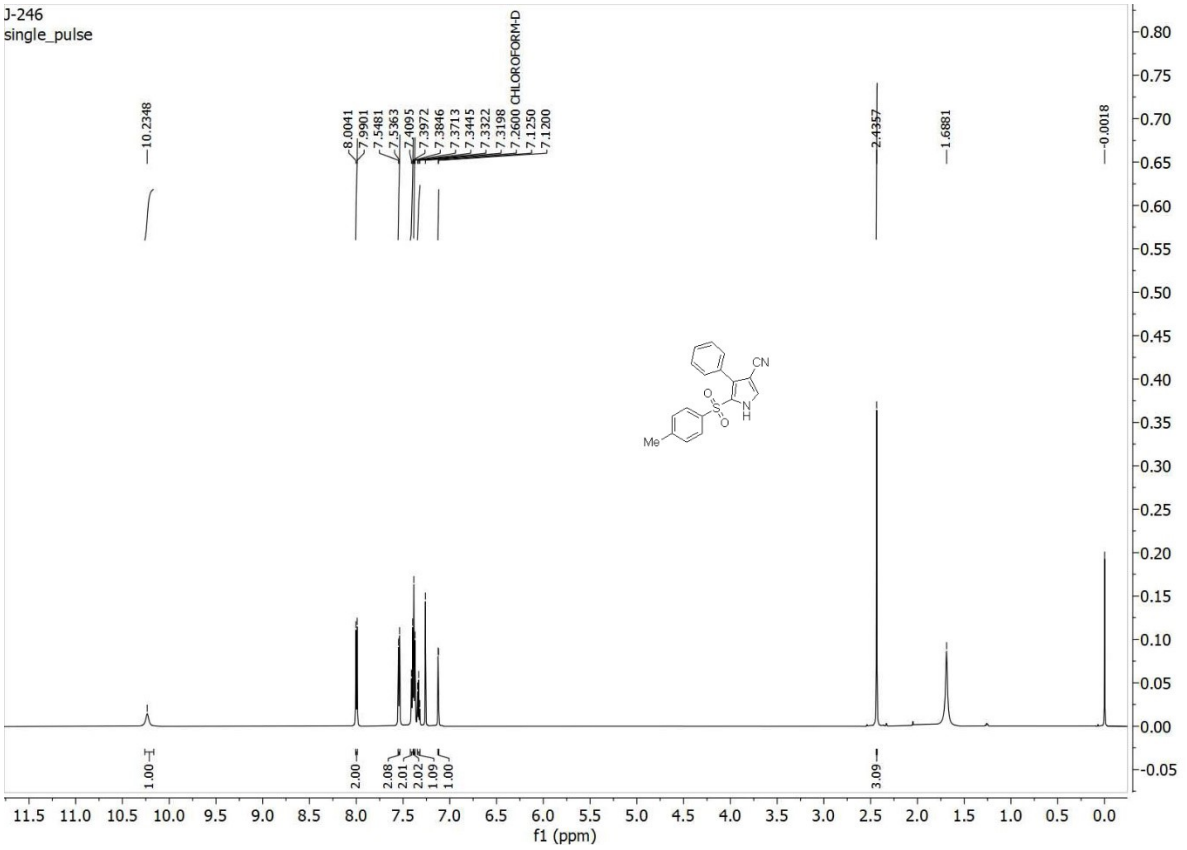


Figure S1. ^{1}H NMR spectrum of **23A** in $CDCl_3$.

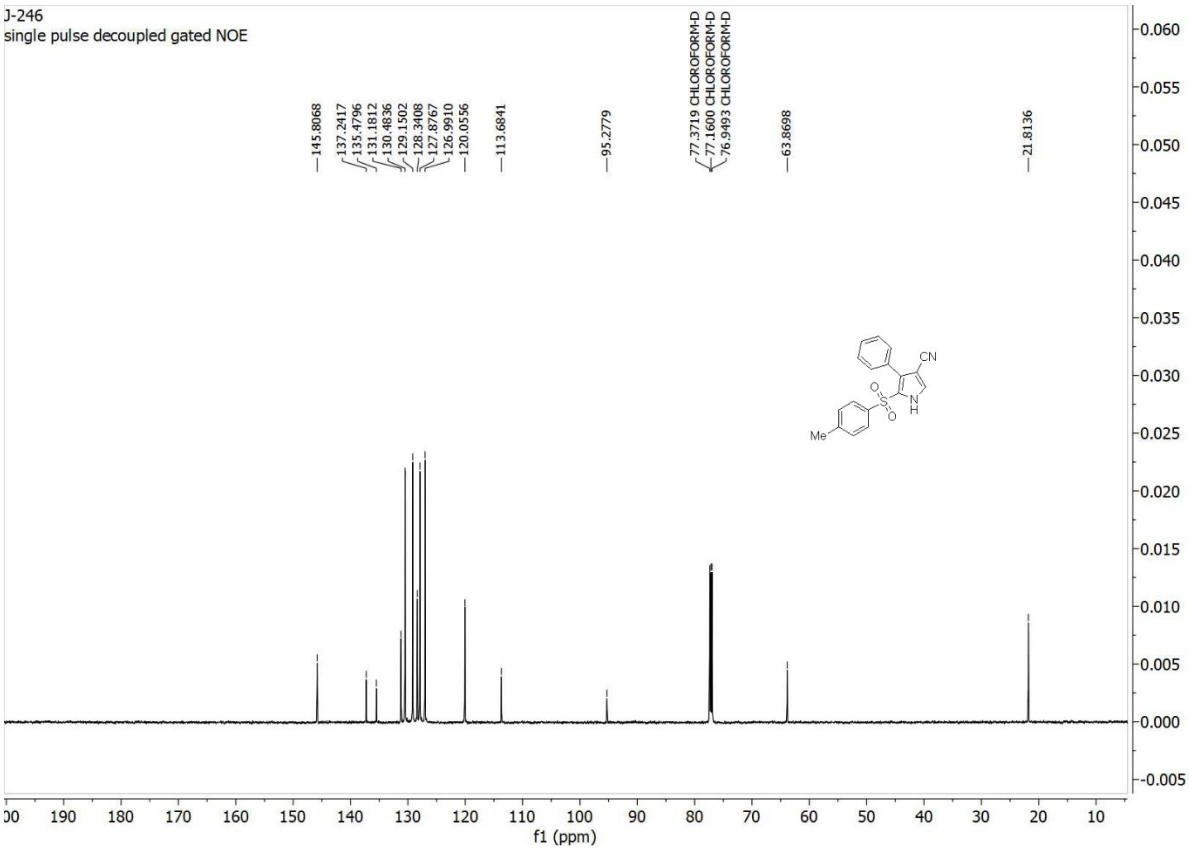


Figure S2. ^{13}C NMR spectrum of **23A** in $CDCl_3$.

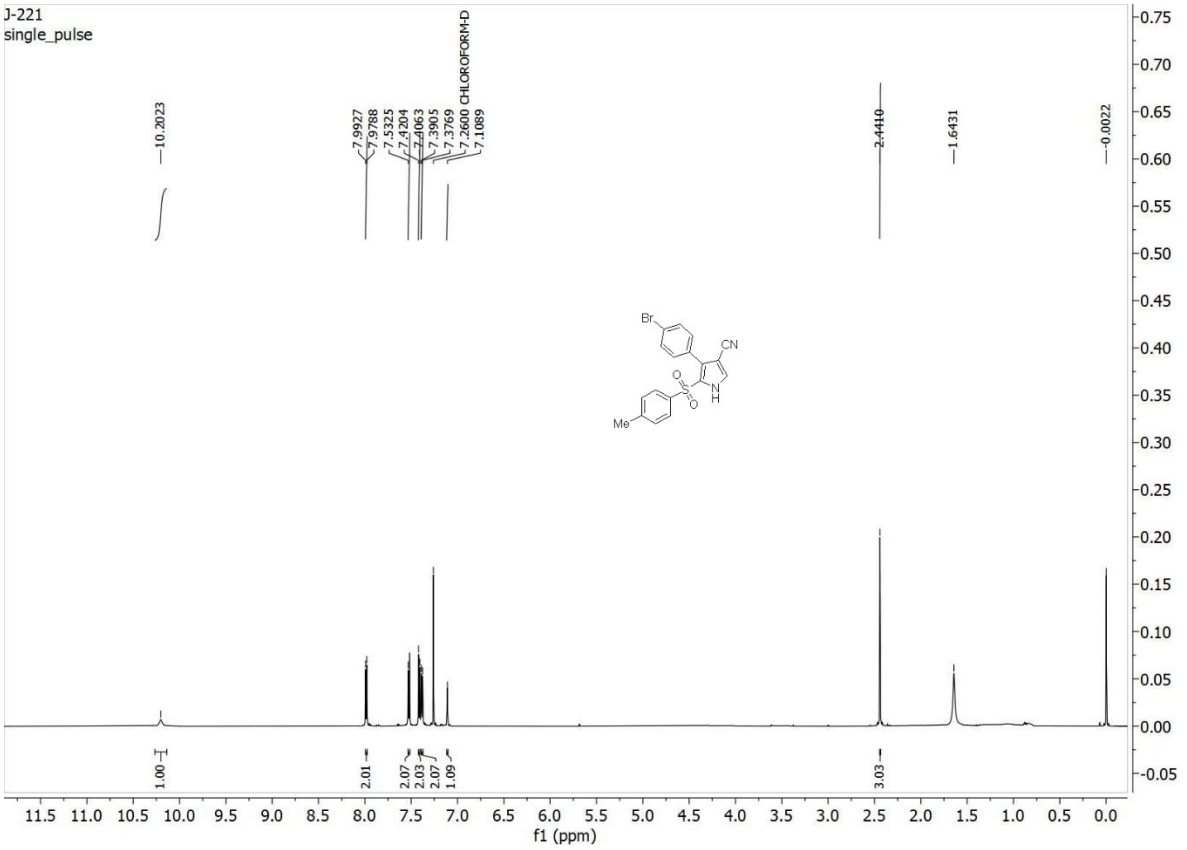


Figure S3. ^{1}H NMR spectrum of **24A** in $CDCl_3$.

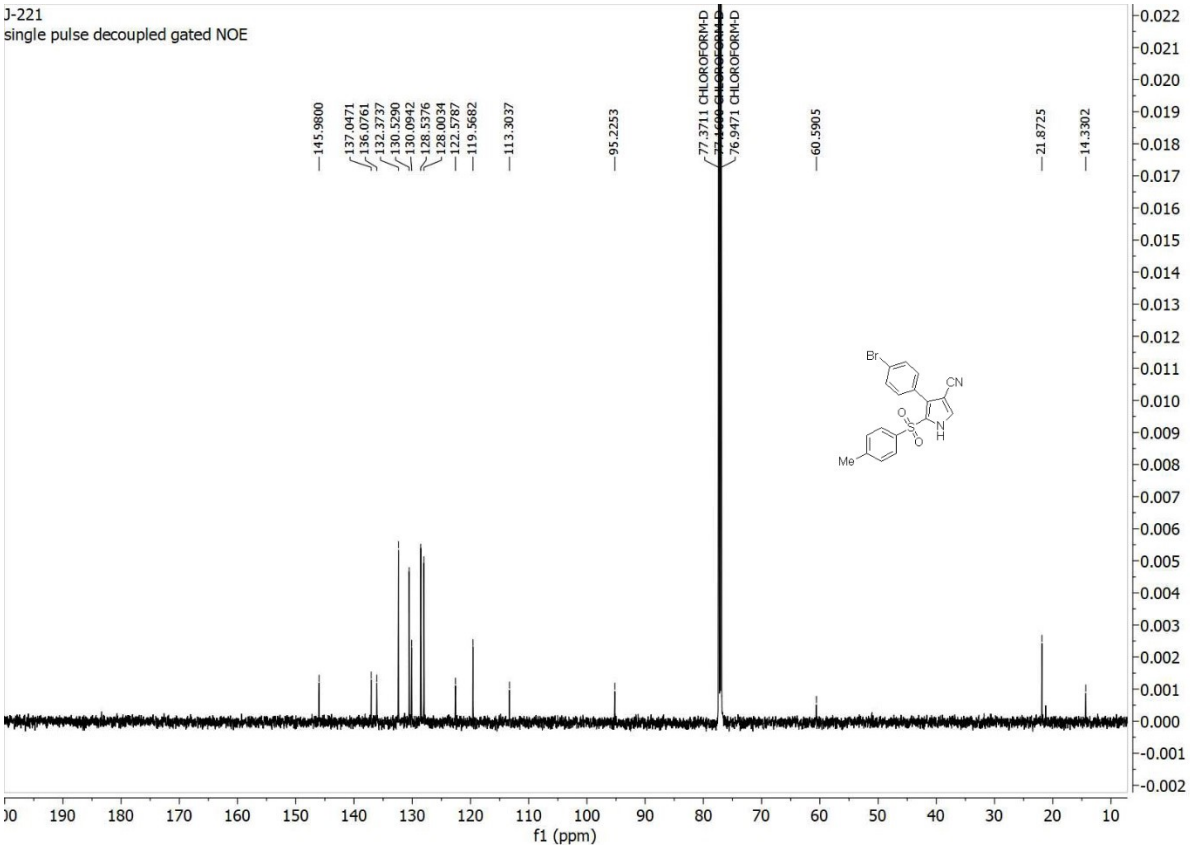


Figure S4. ^{13}C NMR spectrum of **24A** in $CDCl_3$.

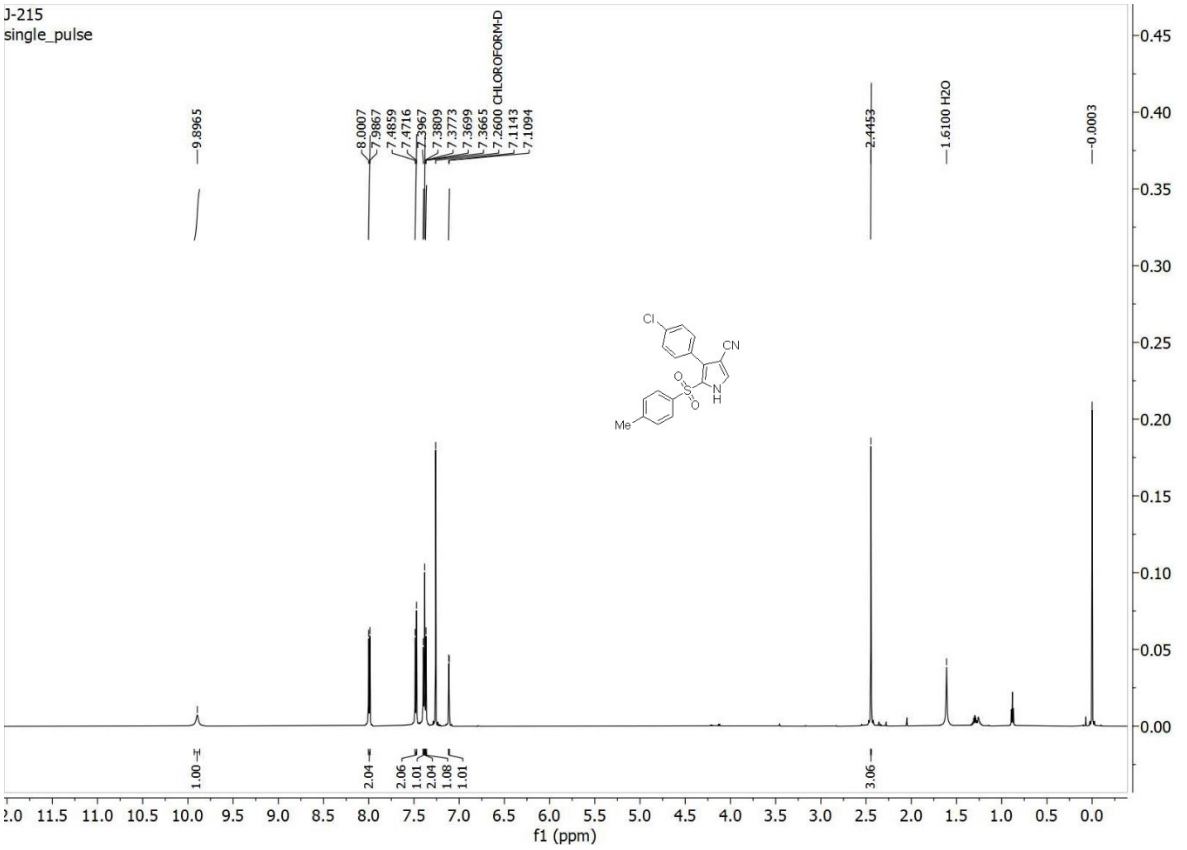


Figure S5. ^{1}H NMR spectrum of **25A** in $CDCl_3$.

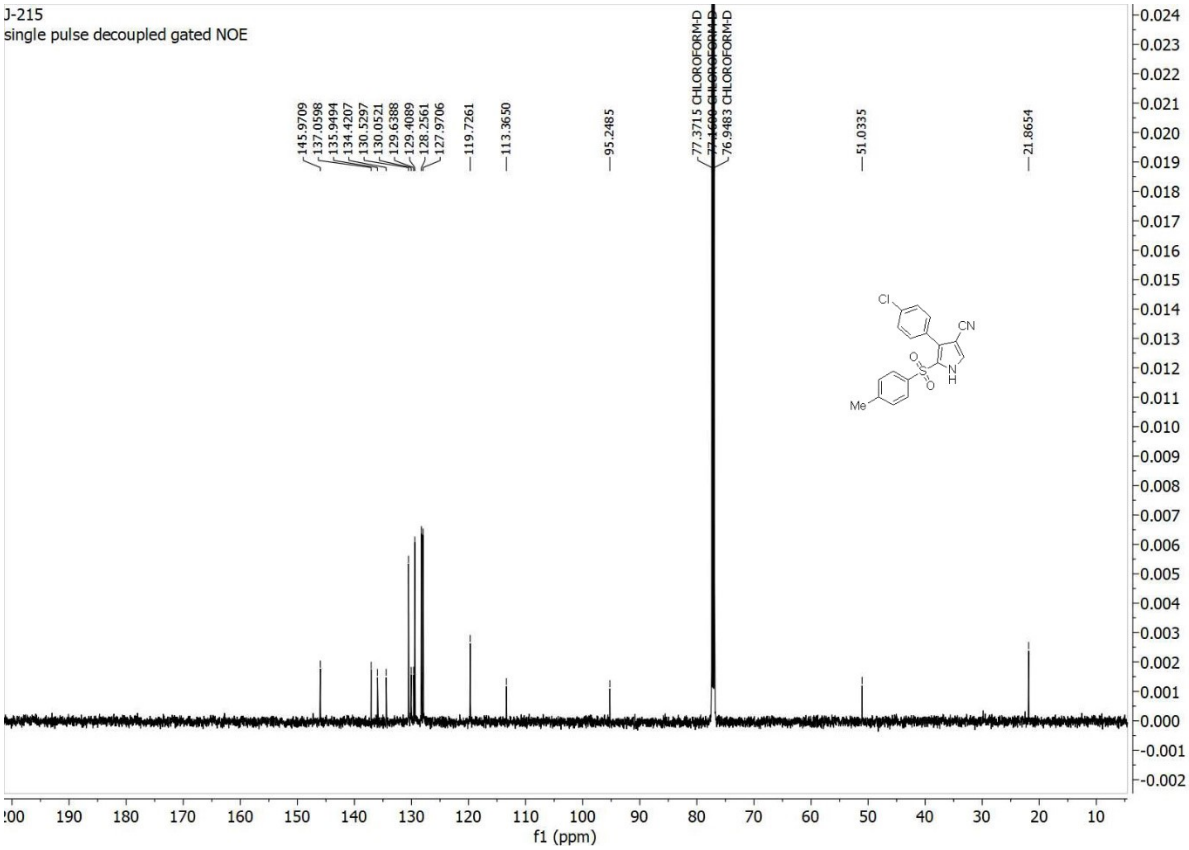


Figure S6. ^{13}C NMR spectrum of **25A** in $CDCl_3$.

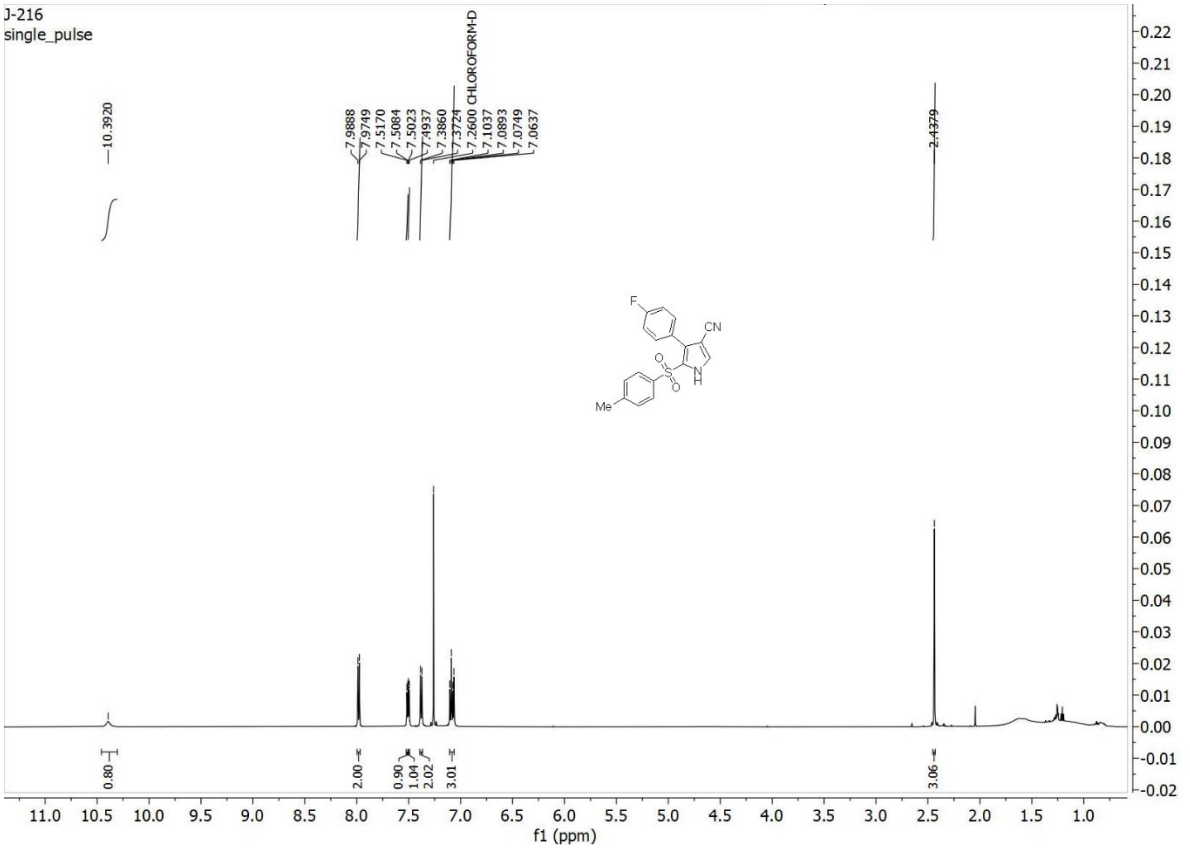


Figure S7. ^{1}H NMR spectrum of **26A** in $CDCl_3$.

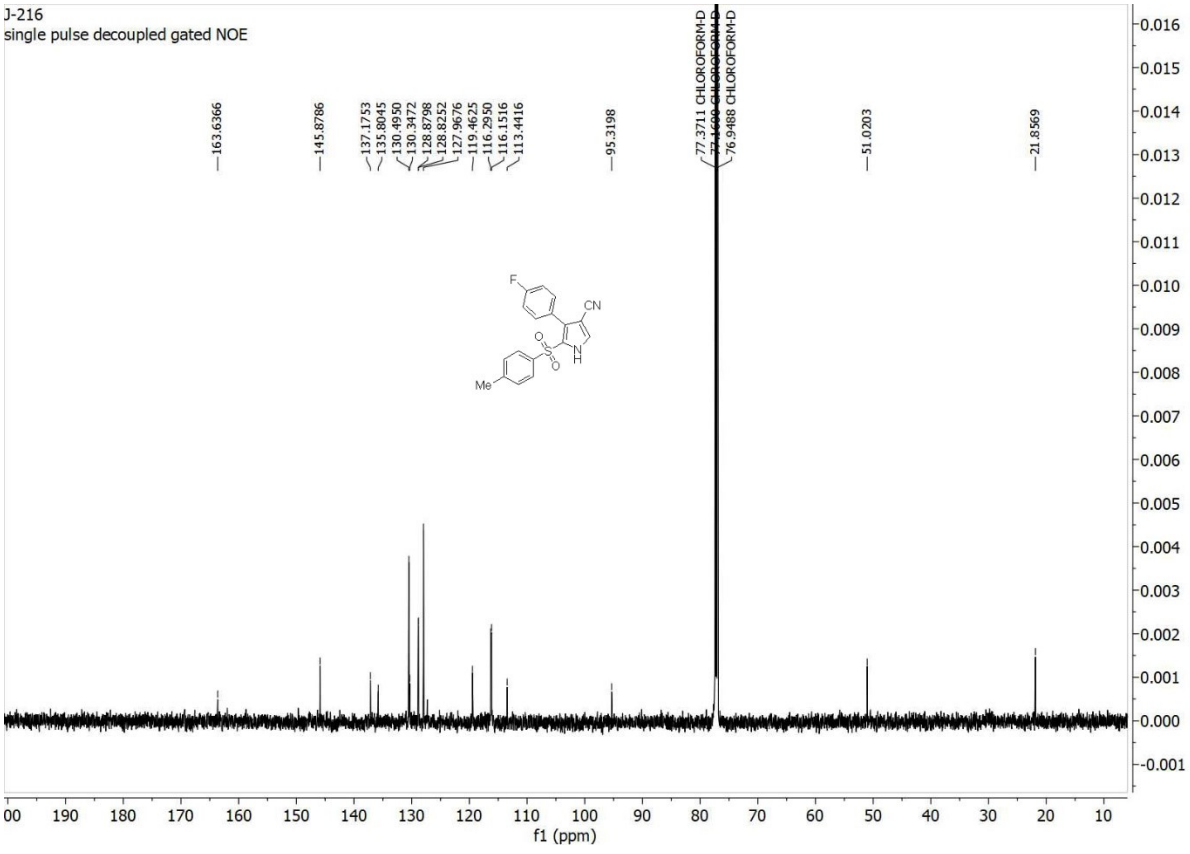


Figure S8. ^{13}C NMR spectrum of **26A** in $CDCl_3$.

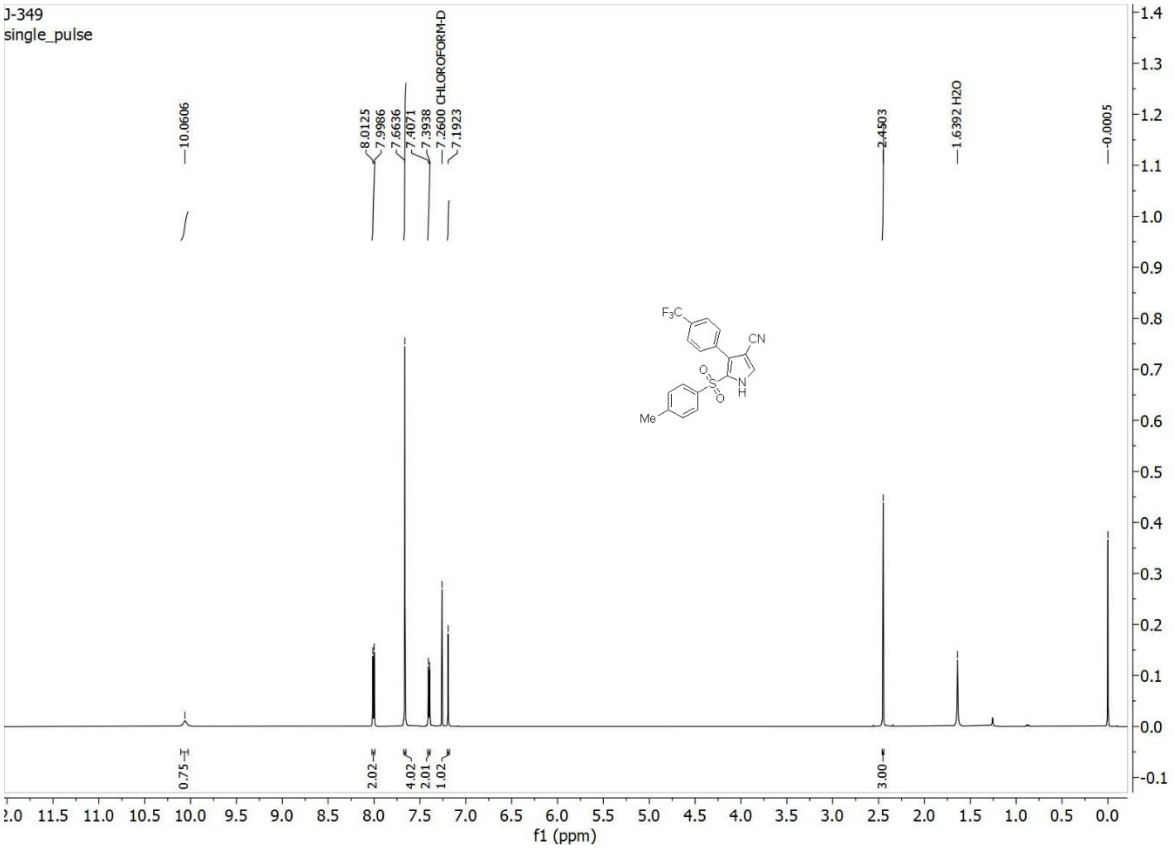


Figure S9. ^{1}H NMR spectrum of **27A** in $CDCl_3$.

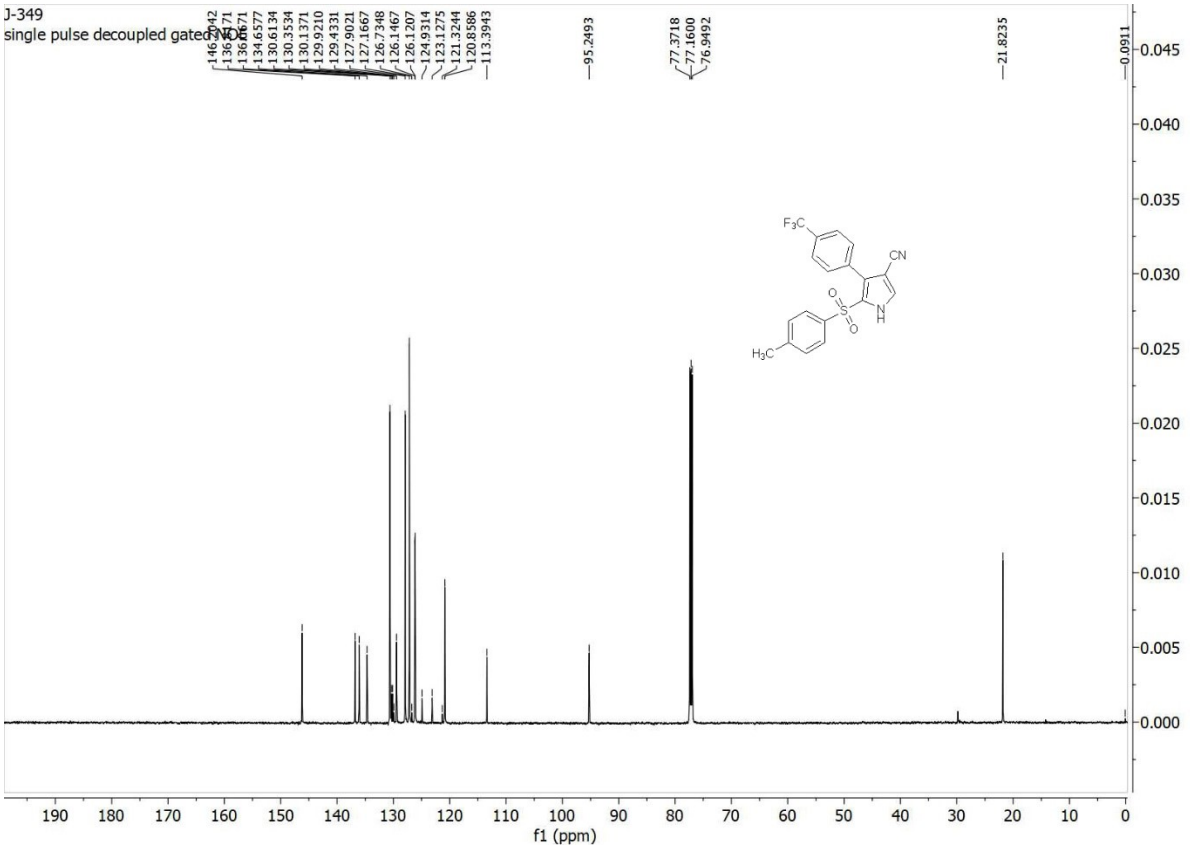


Figure S10. ^{13}C NMR spectrum of **27A** in $CDCl_3$.

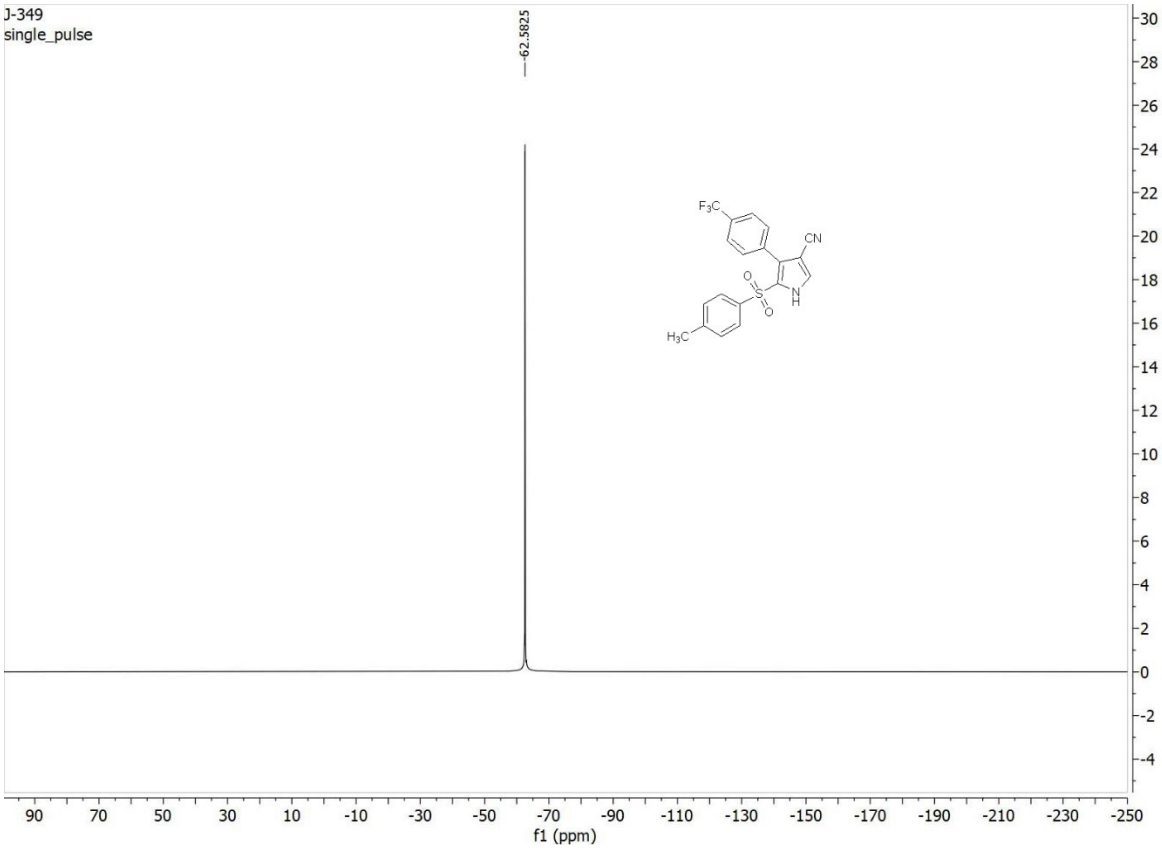


Figure S11. ^{19}F NMR spectrum of **27A** in $CDCl_3$.

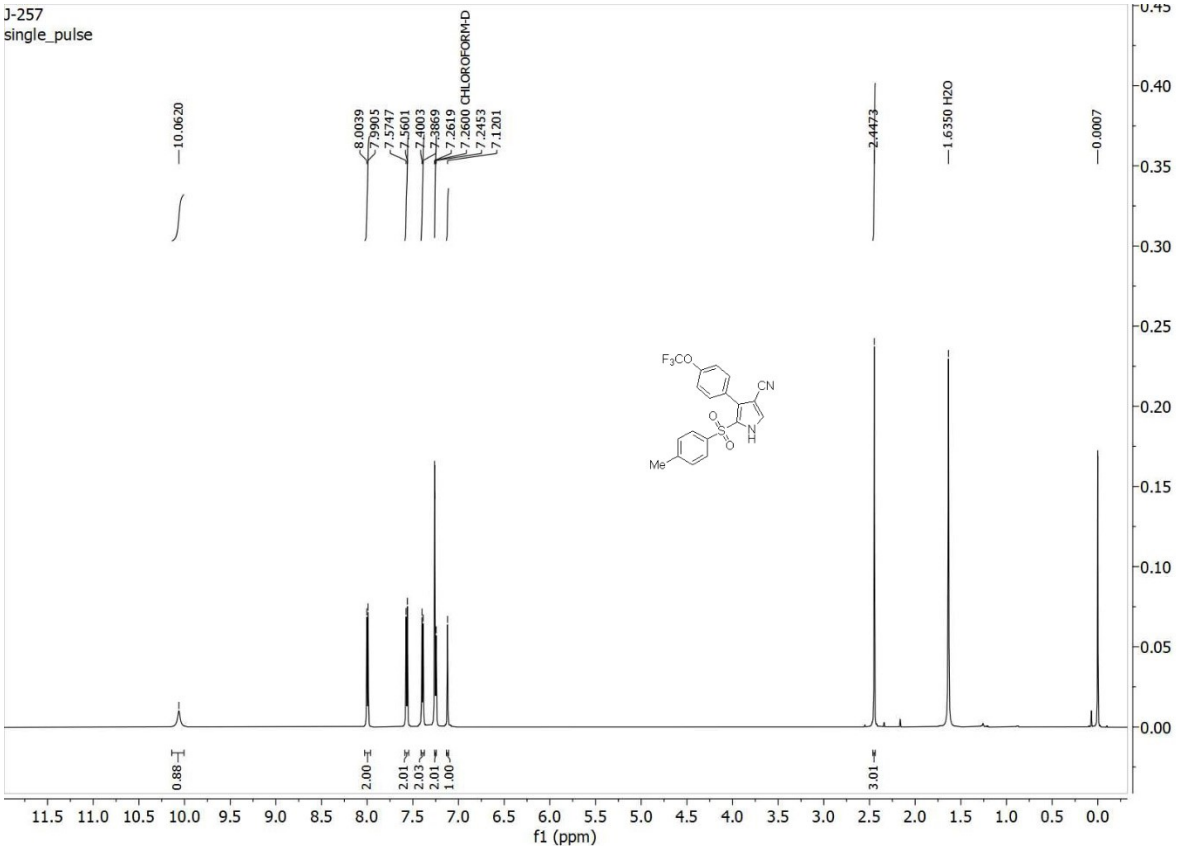


Figure S12. ^{1}H NMR spectrum of **28A** in $CDCl_3$.

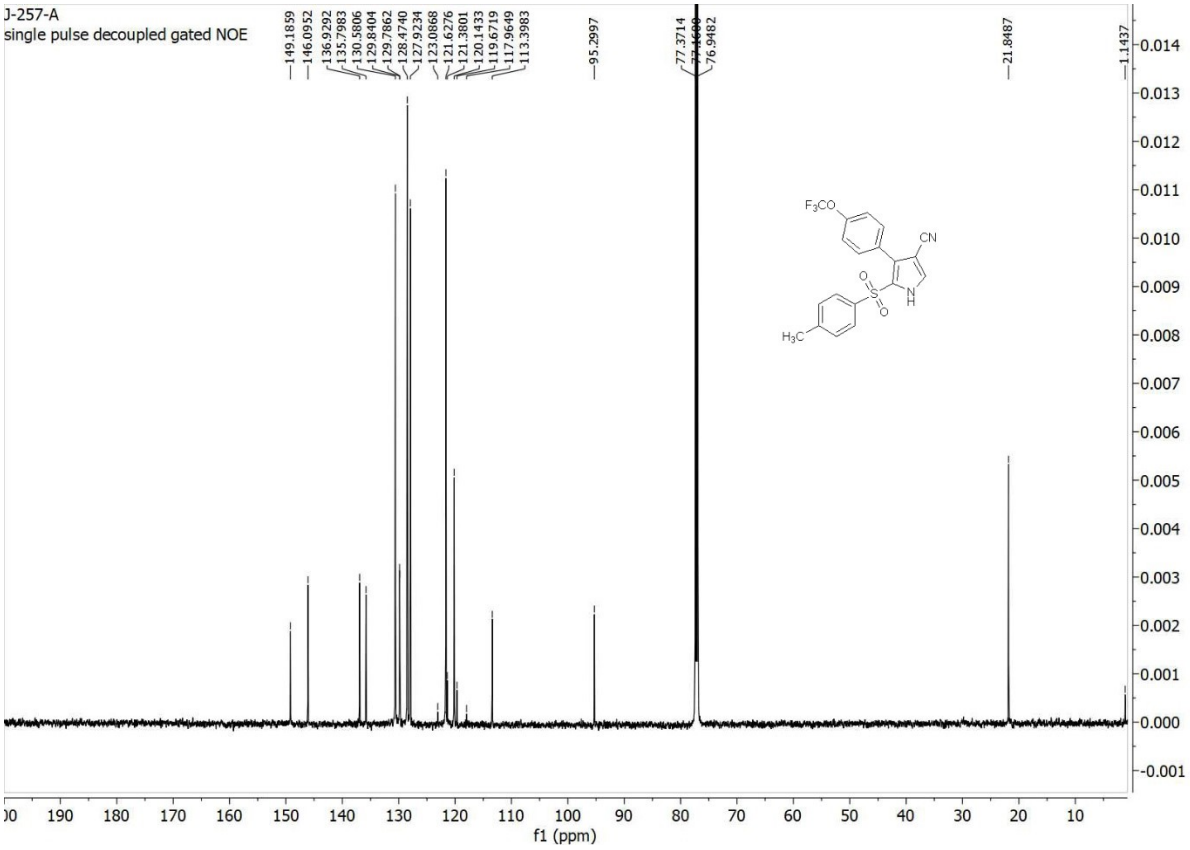


Figure S13. ^{13}C NMR spectrum of **28A** in $CDCl_3$.

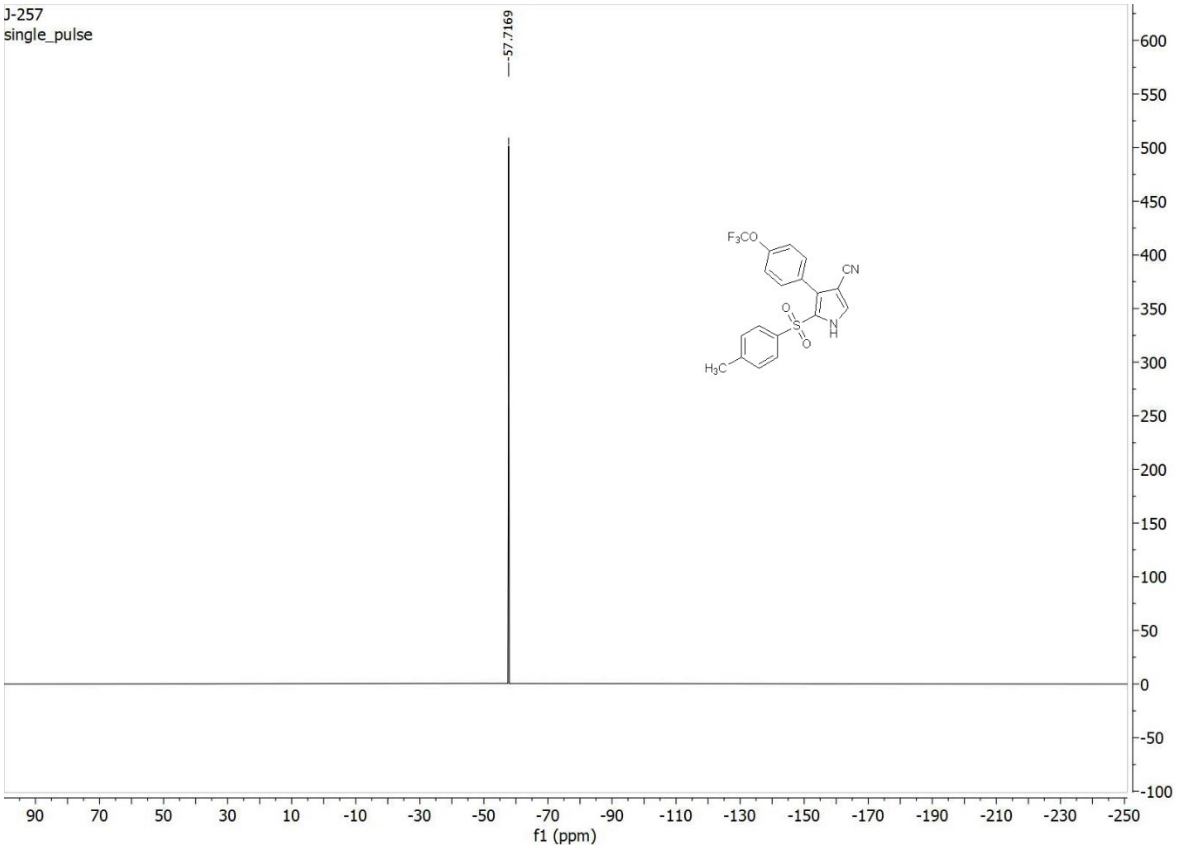


Figure S14. ^{19}F NMR spectrum of **28A** in $CDCl_3$.

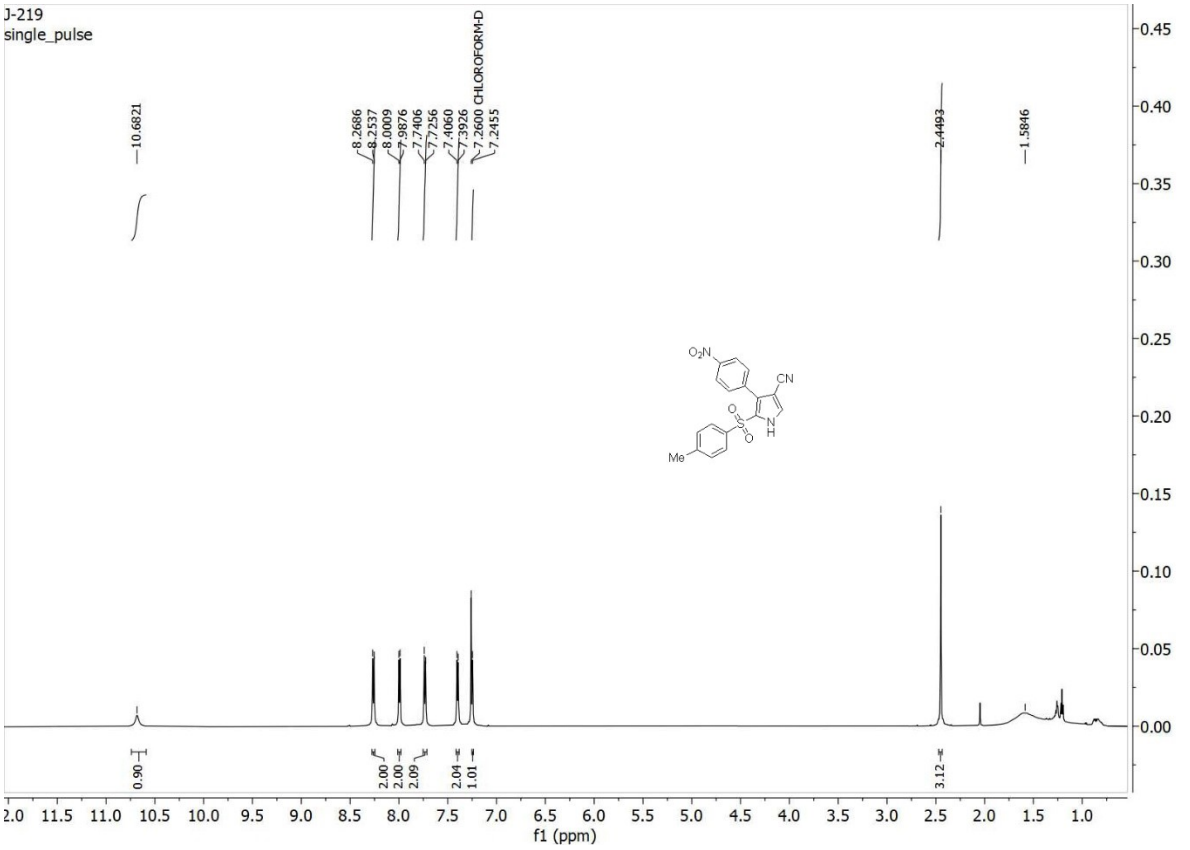


Figure S15. ^{1}H NMR spectrum of **29A** in $CDCl_3$.

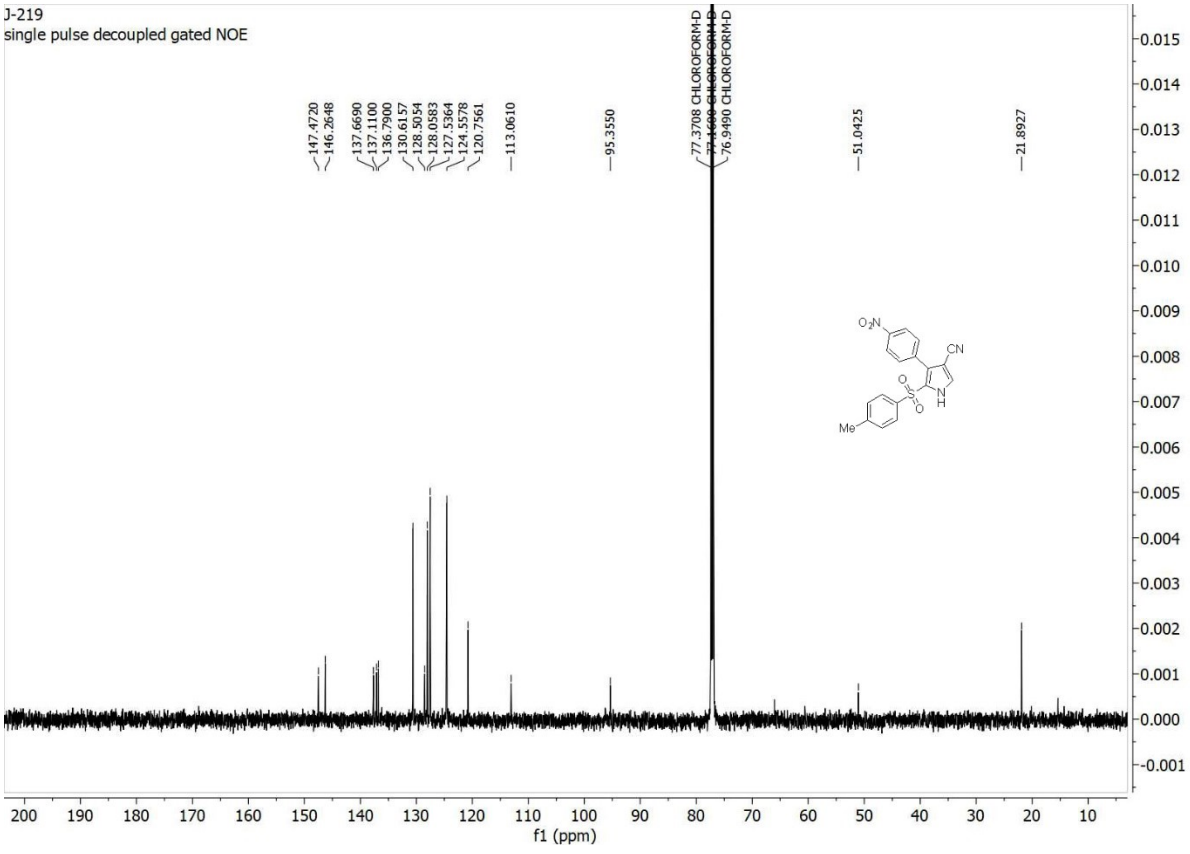


Figure S16. ^{13}C NMR spectrum of **29A** in $CDCl_3$.

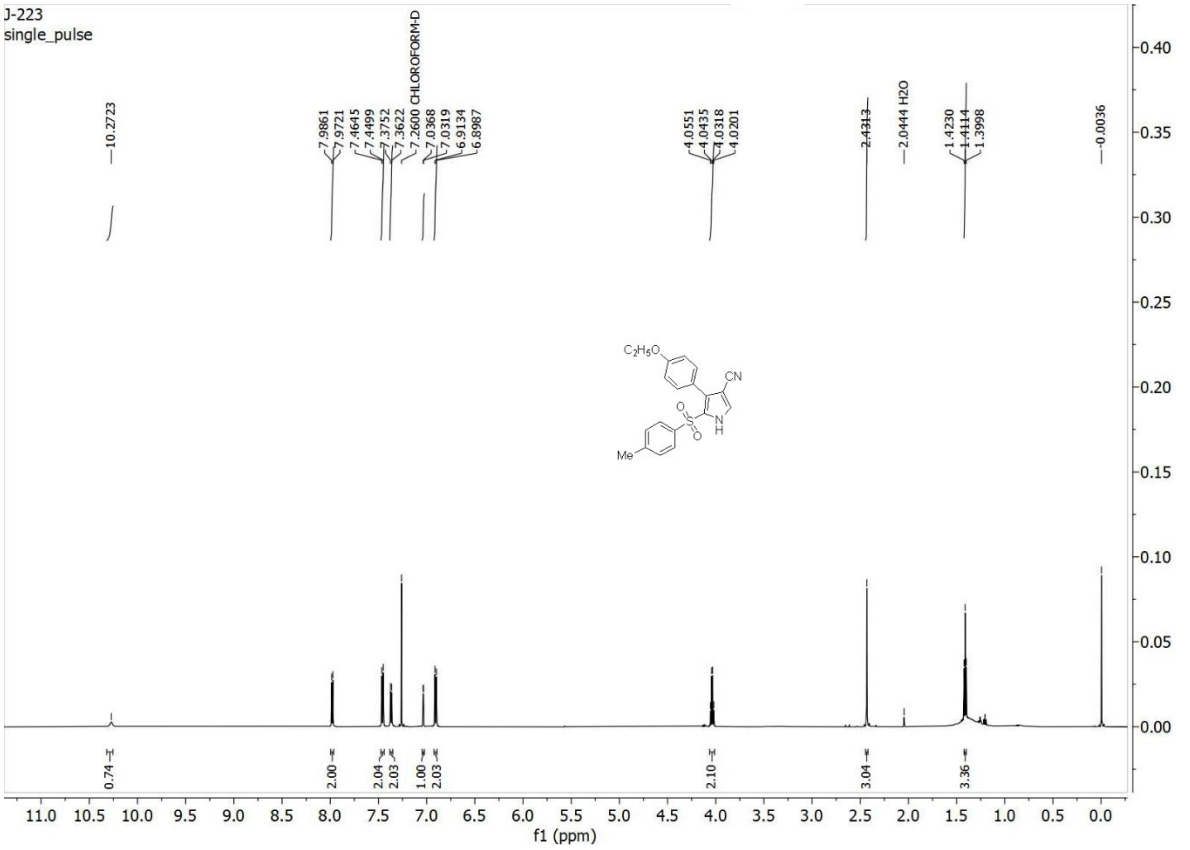


Figure S17. ^{1}H NMR spectrum of **30A** in $CDCl_3$.

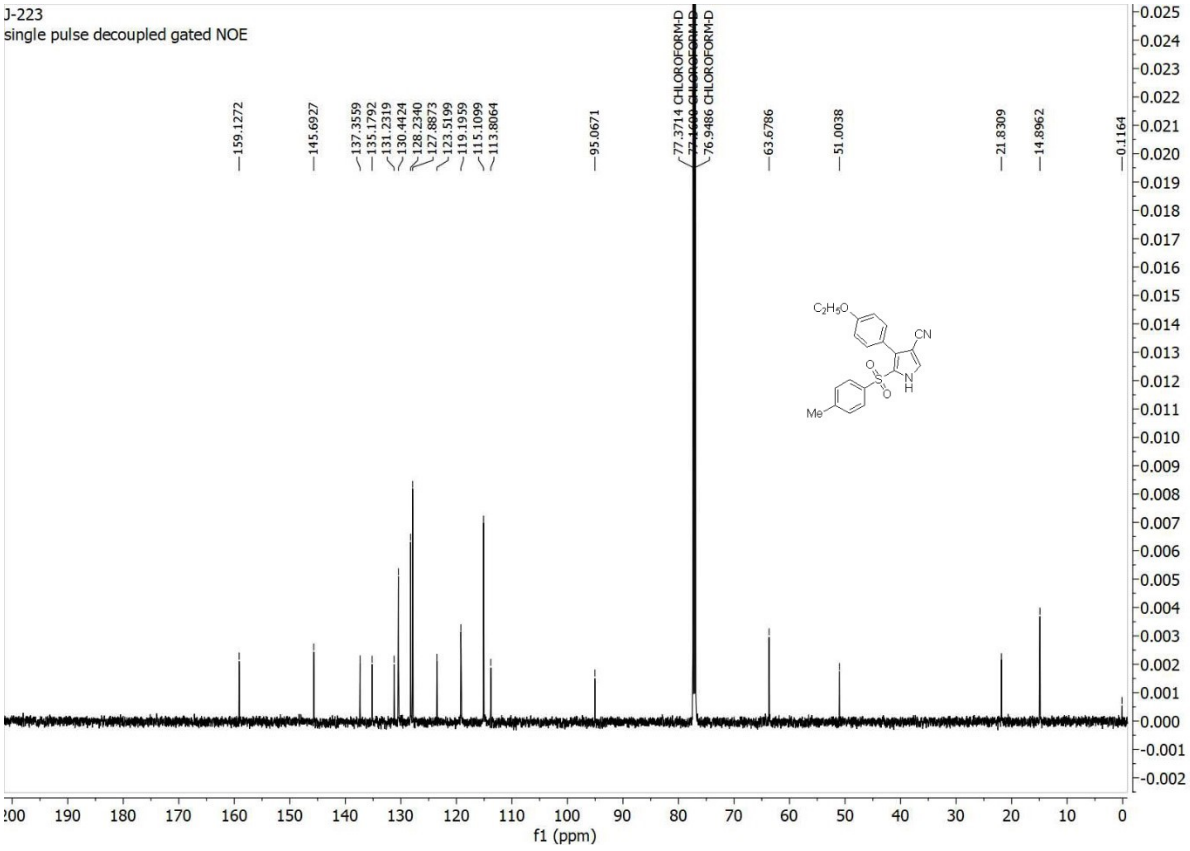


Figure S18. ^{1}H NMR spectrum of **30A** in $CDCl_3$.

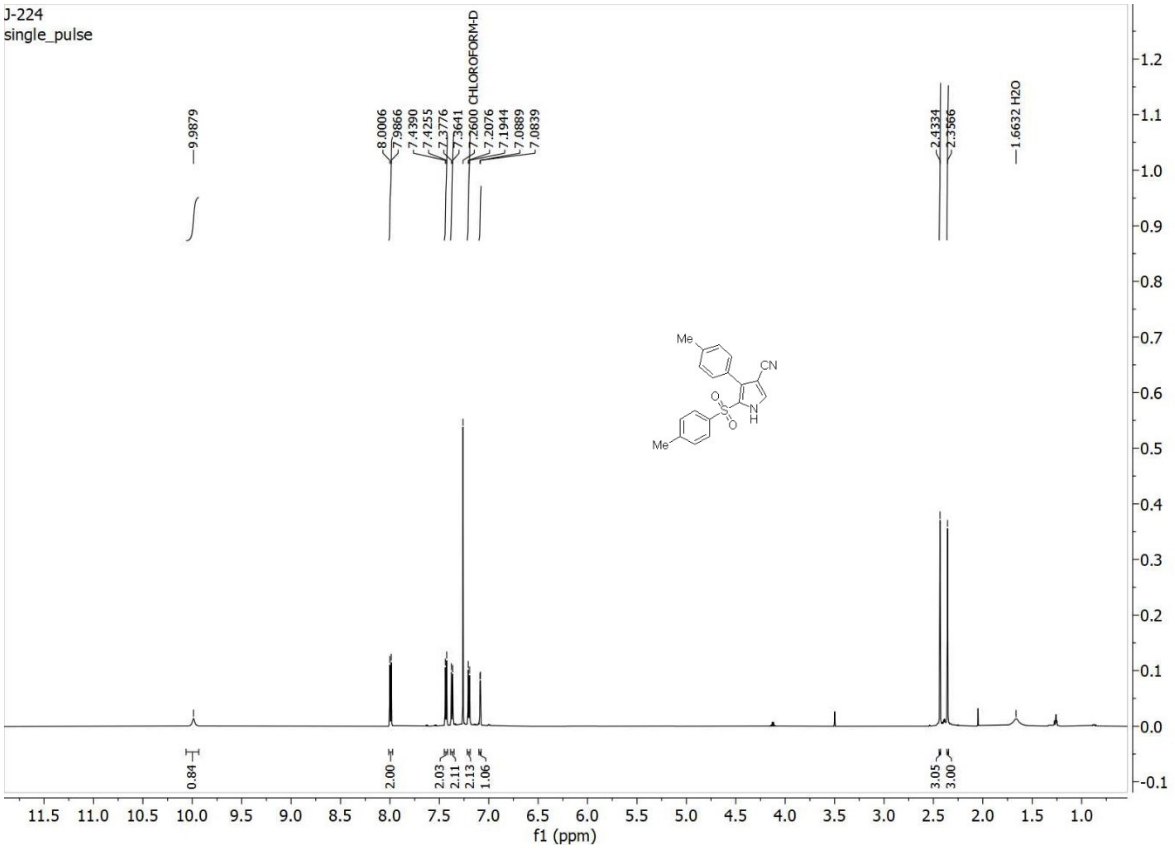


Figure S19. ^{1}H NMR spectrum of **31A** in $CDCl_3$.

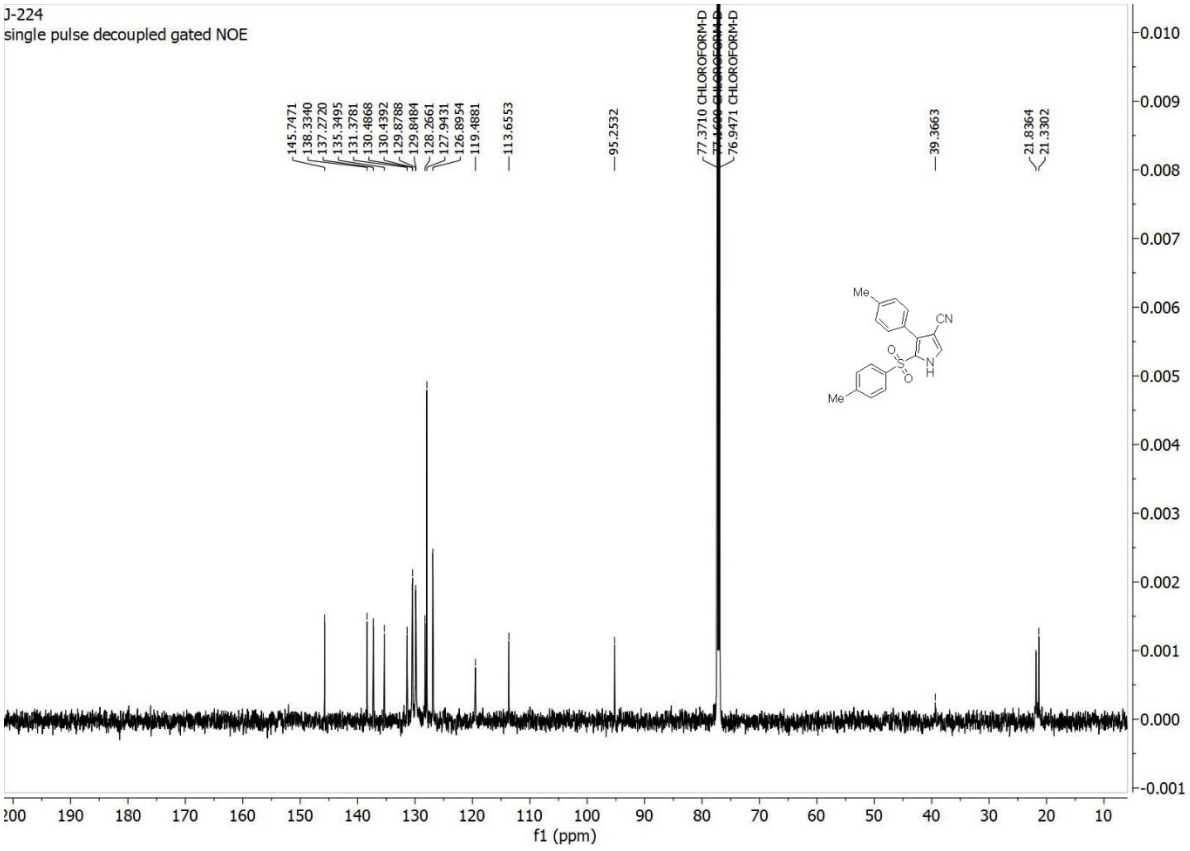


Figure S20. ^{13}C NMR spectrum of **31A** in $CDCl_3$.

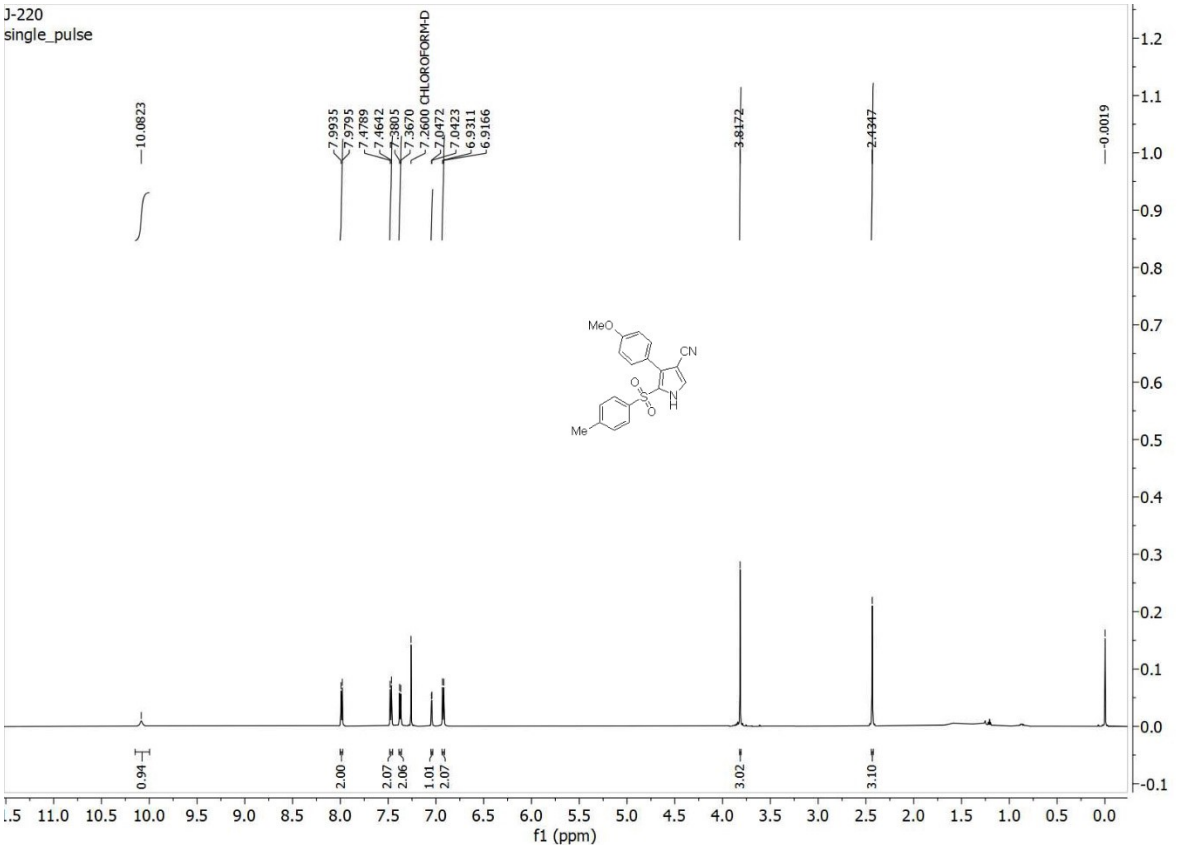


Figure S21. ^{1}H NMR spectrum of **32A** in $CDCl_3$.

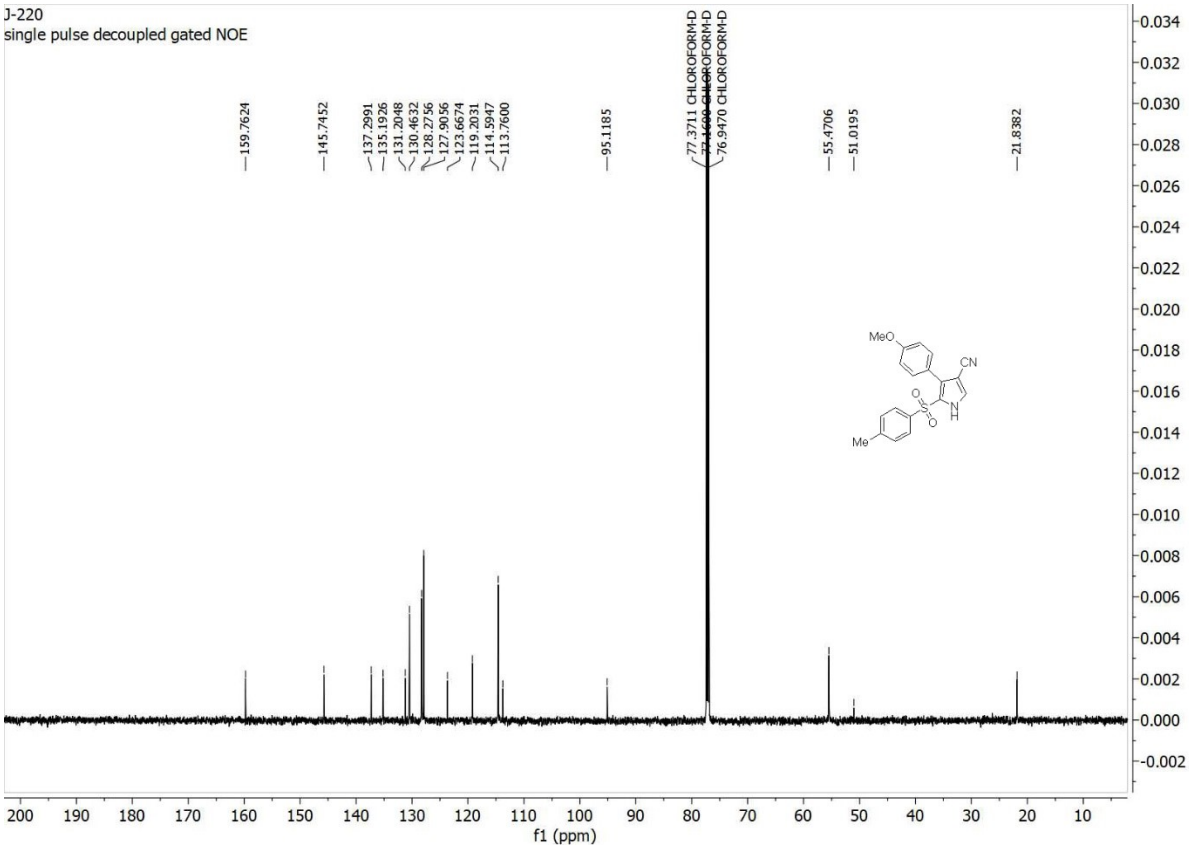


Figure S22. ^{13}C NMR spectrum of **32A** in $CDCl_3$.

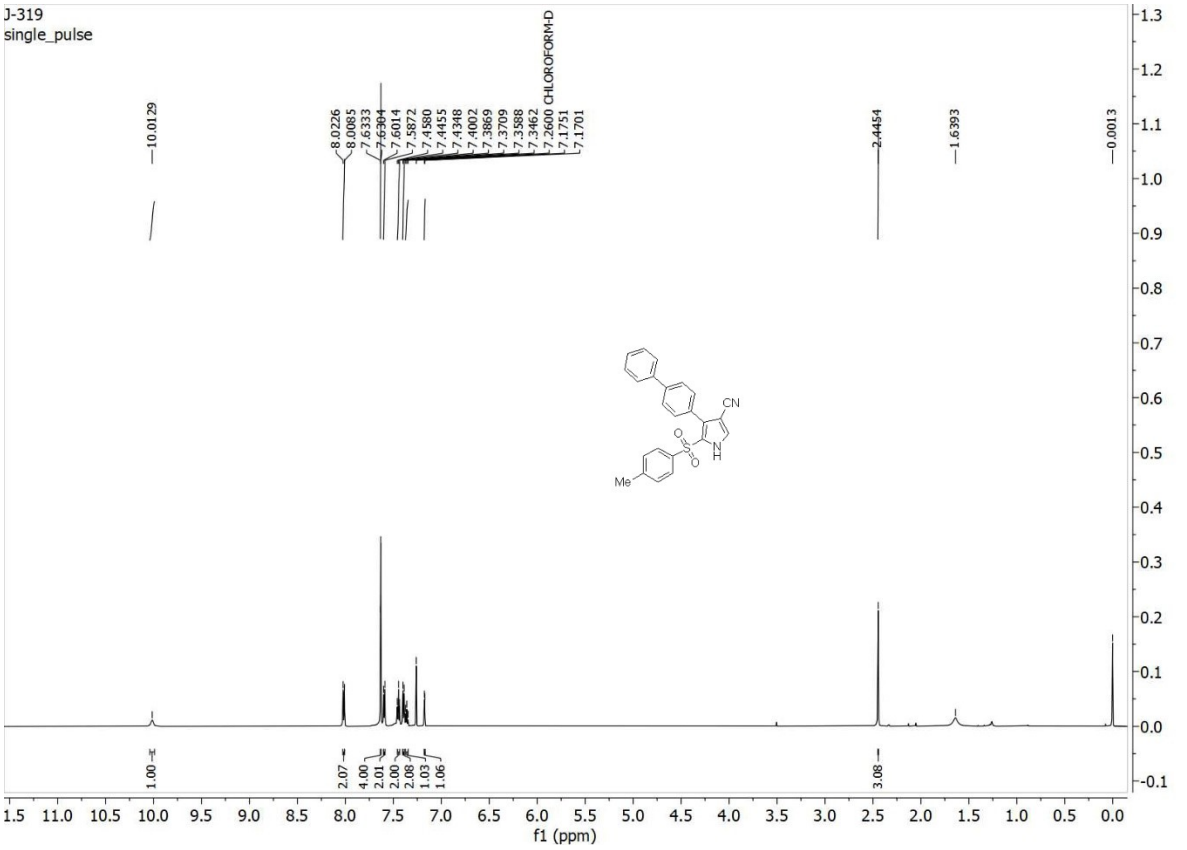


Figure S23. ^{1}H NMR spectrum of **33A** in $CDCl_3$.

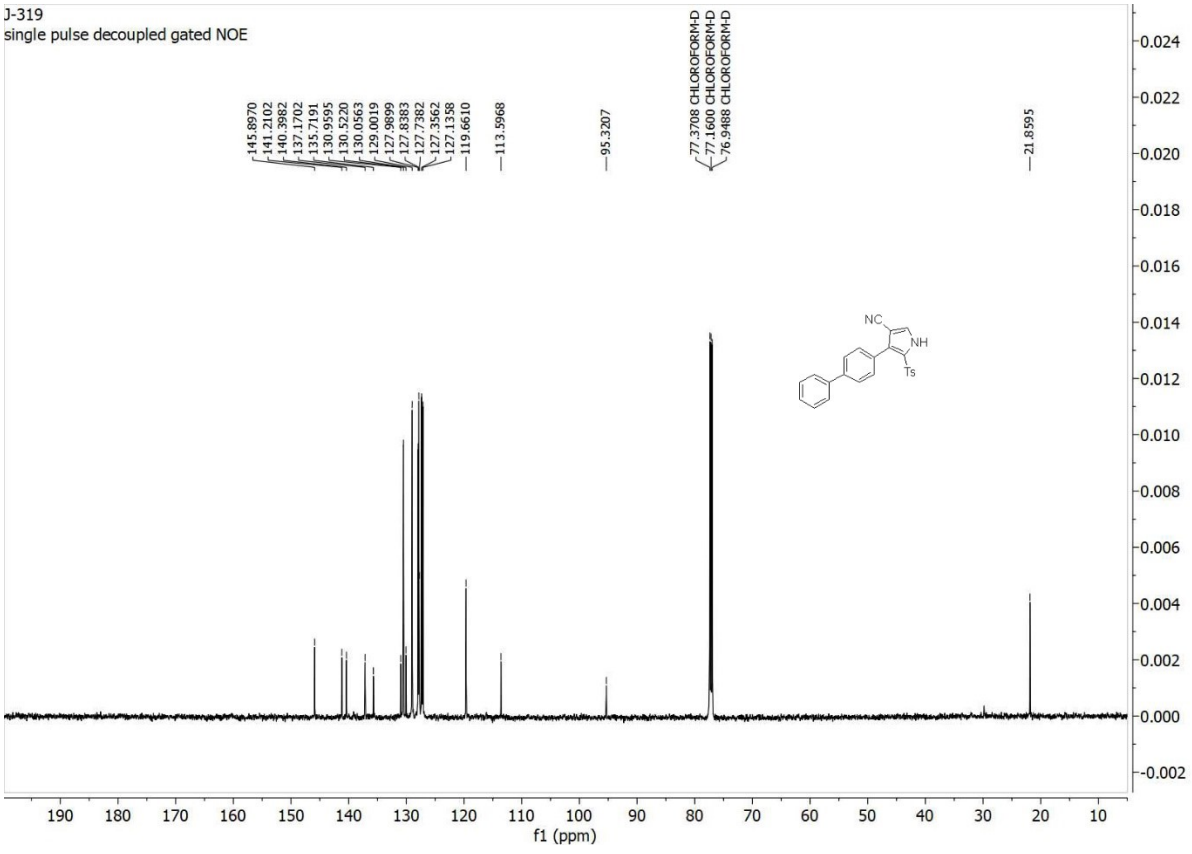


Figure S24. ^{13}C NMR spectrum of **33A** in $CDCl_3$.

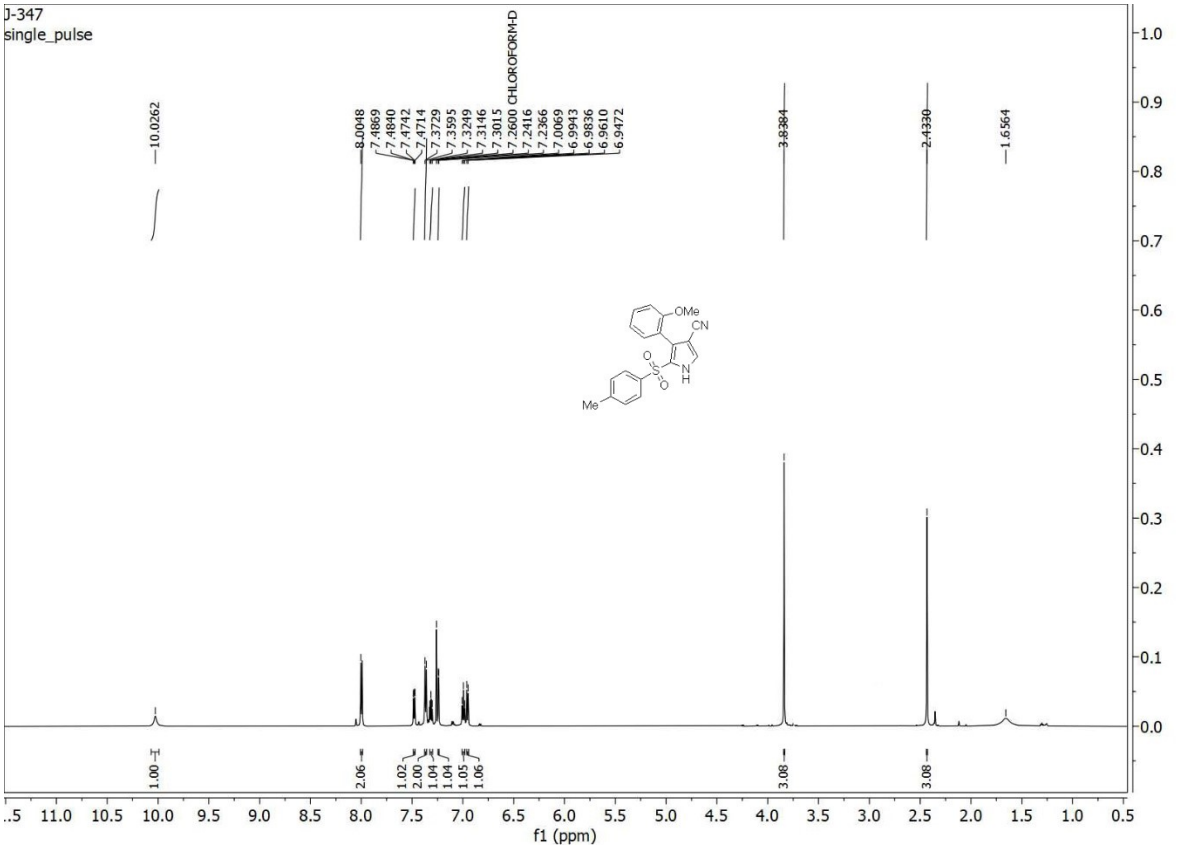


Figure S25 . ^{1}H NMR spectrum of **34A** in $CDCl_3$.

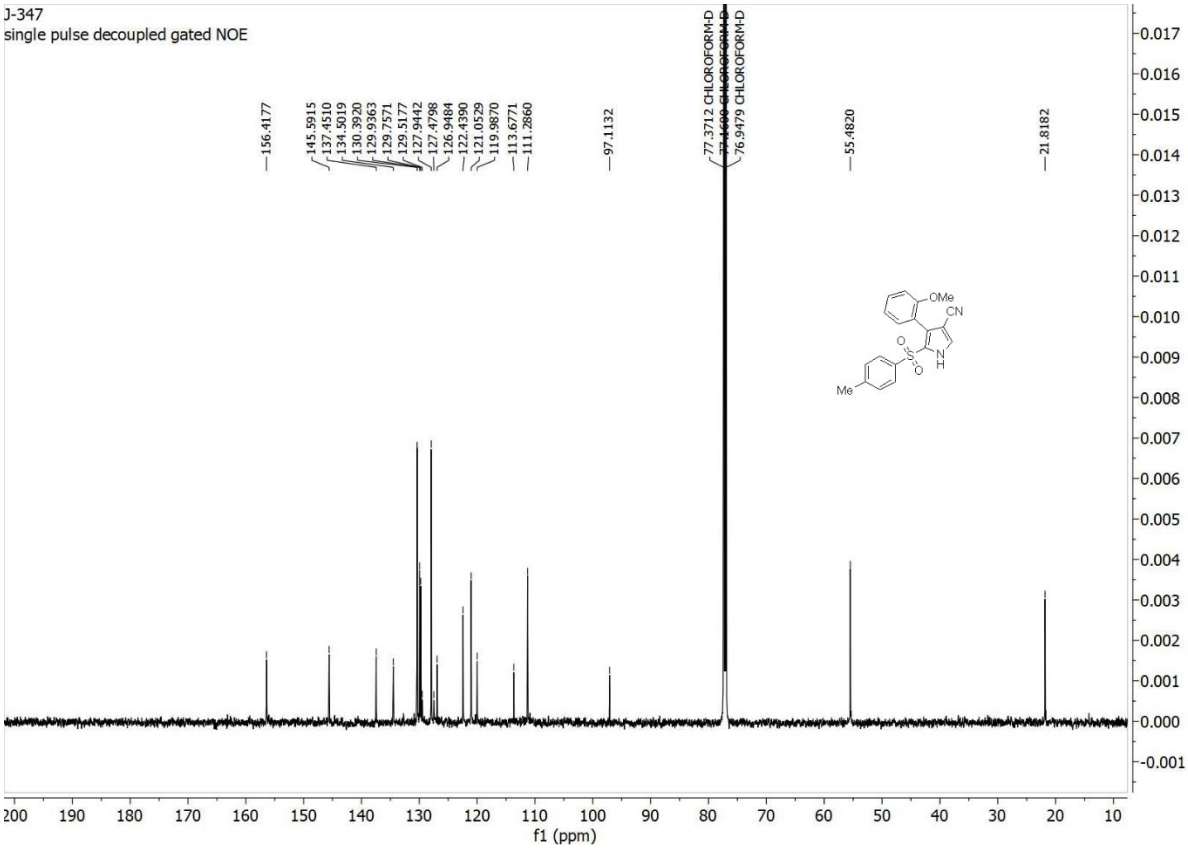


Figure S26. ^{13}C NMR spectrum of **34A** in $CDCl_3$.

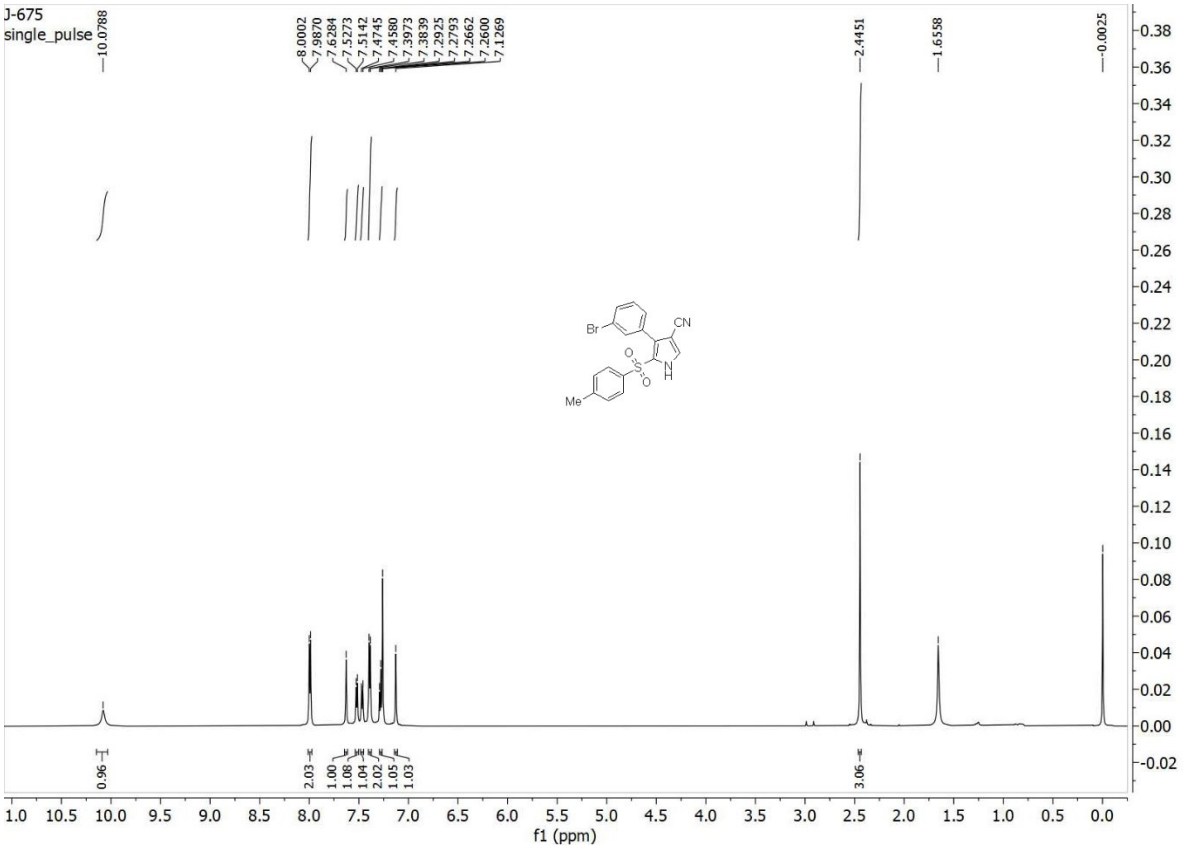


Figure S27. ^{1}H NMR spectrum of **35A** in $CDCl_3$.

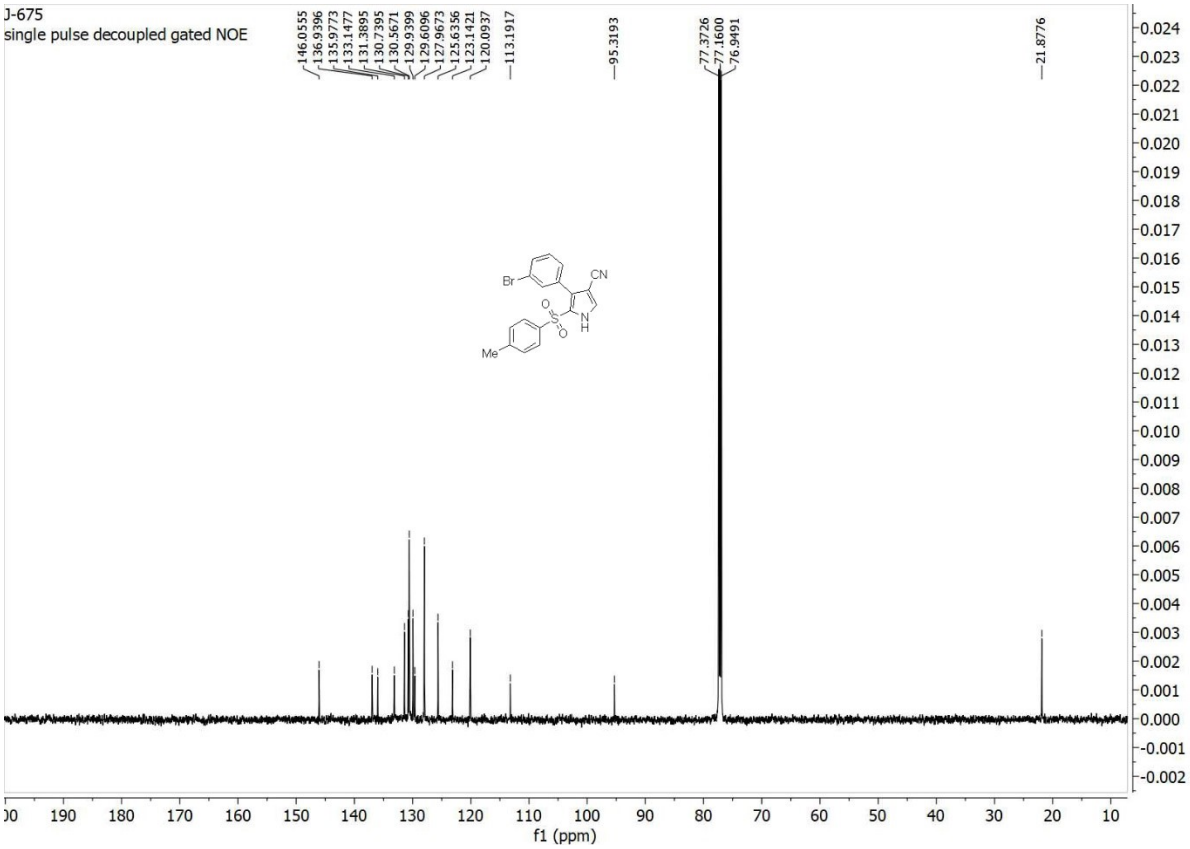


Figure S28. ^{13}C NMR spectrum of **35A** in $CDCl_3$.

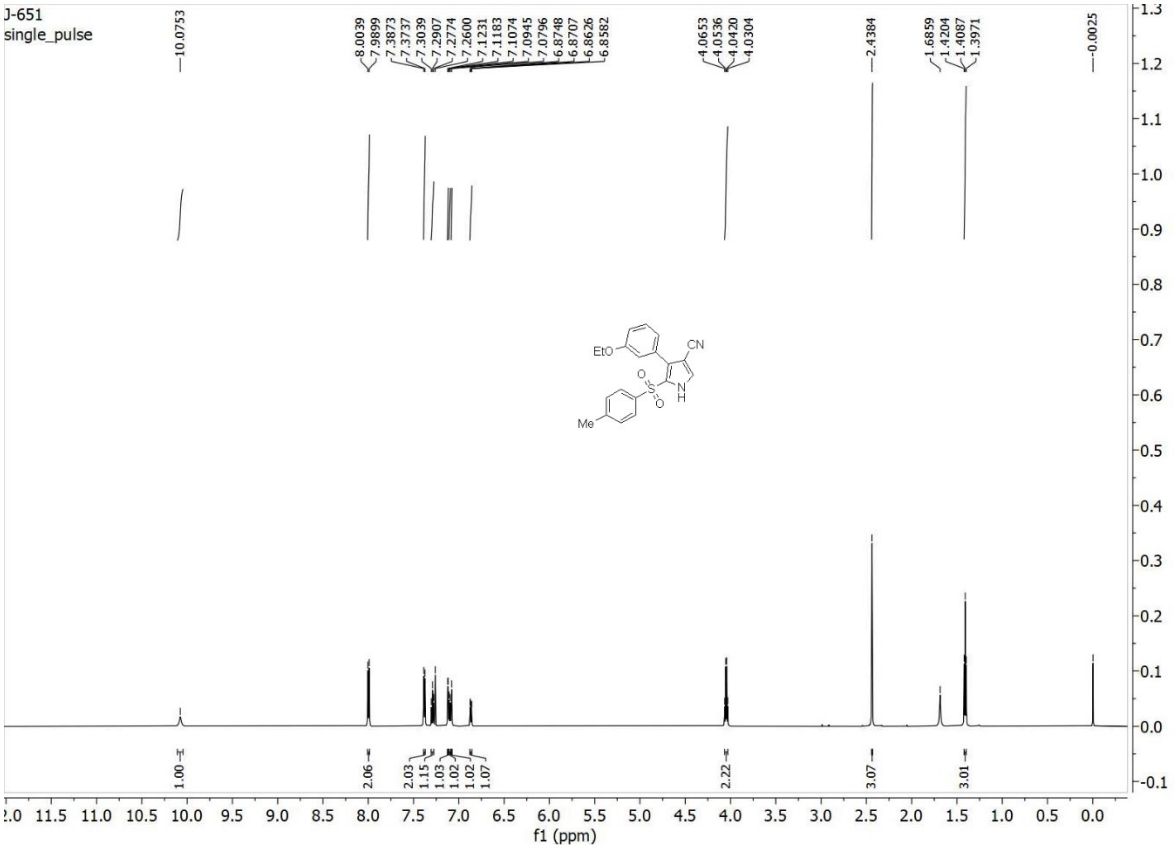


Figure S29. ^{1}H NMR spectrum of **36A** in $CDCl_3$.

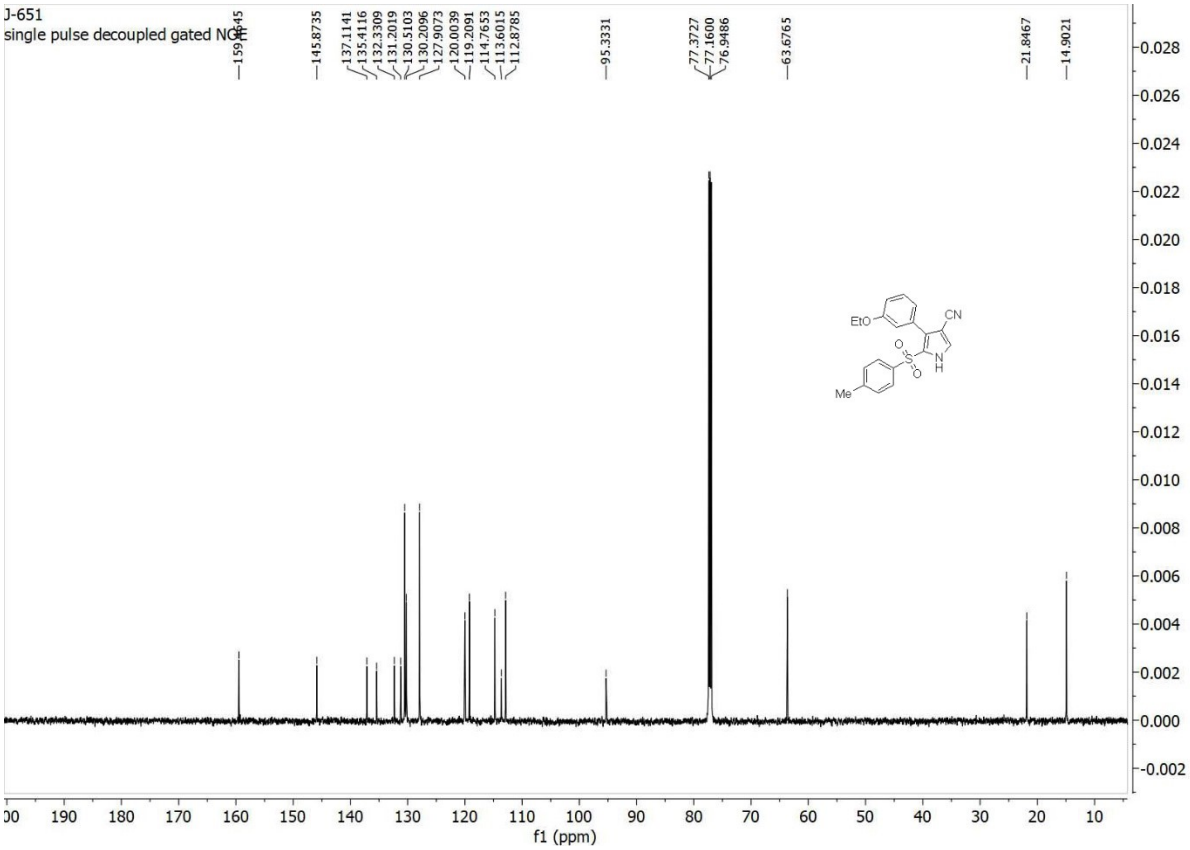


Figure S30. ^{13}C NMR spectrum of **36A** in $CDCl_3$.

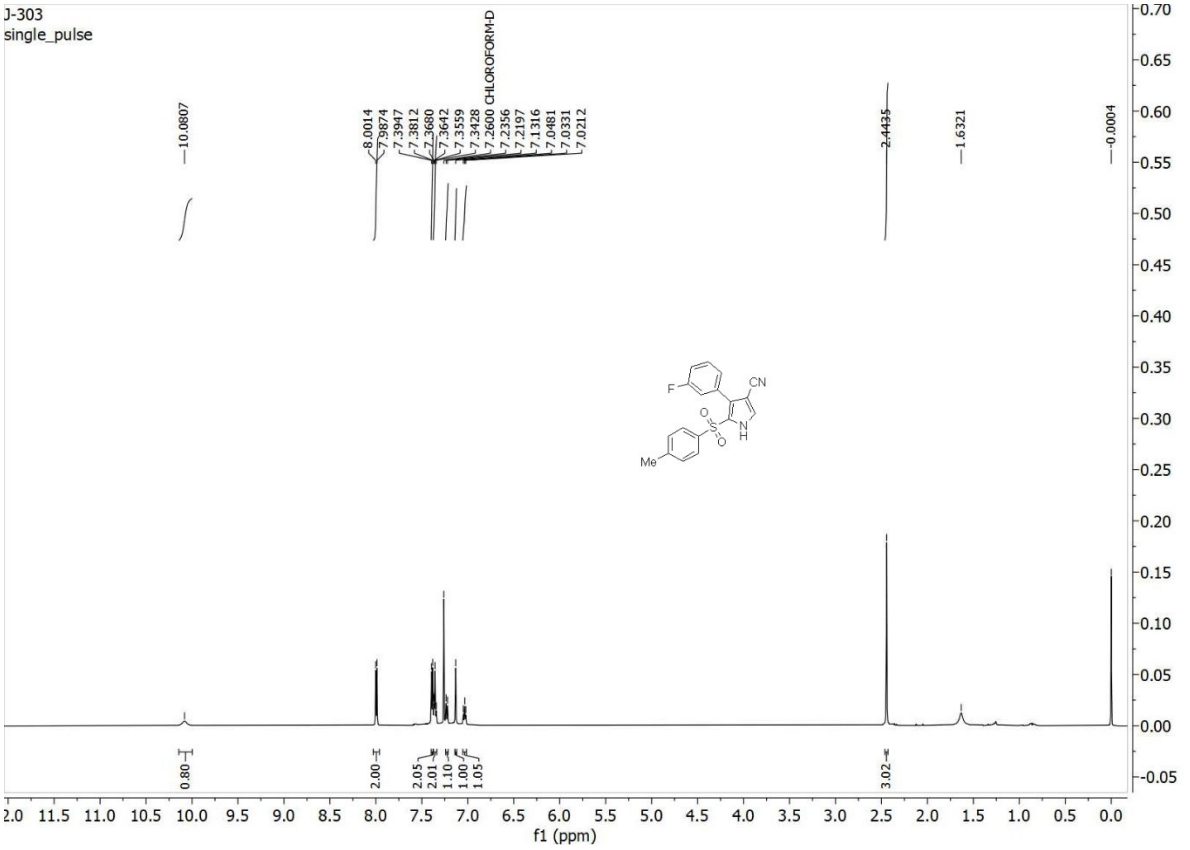


Figure S31. ^{1}H NMR spectrum of **37A** in $CDCl_3$.

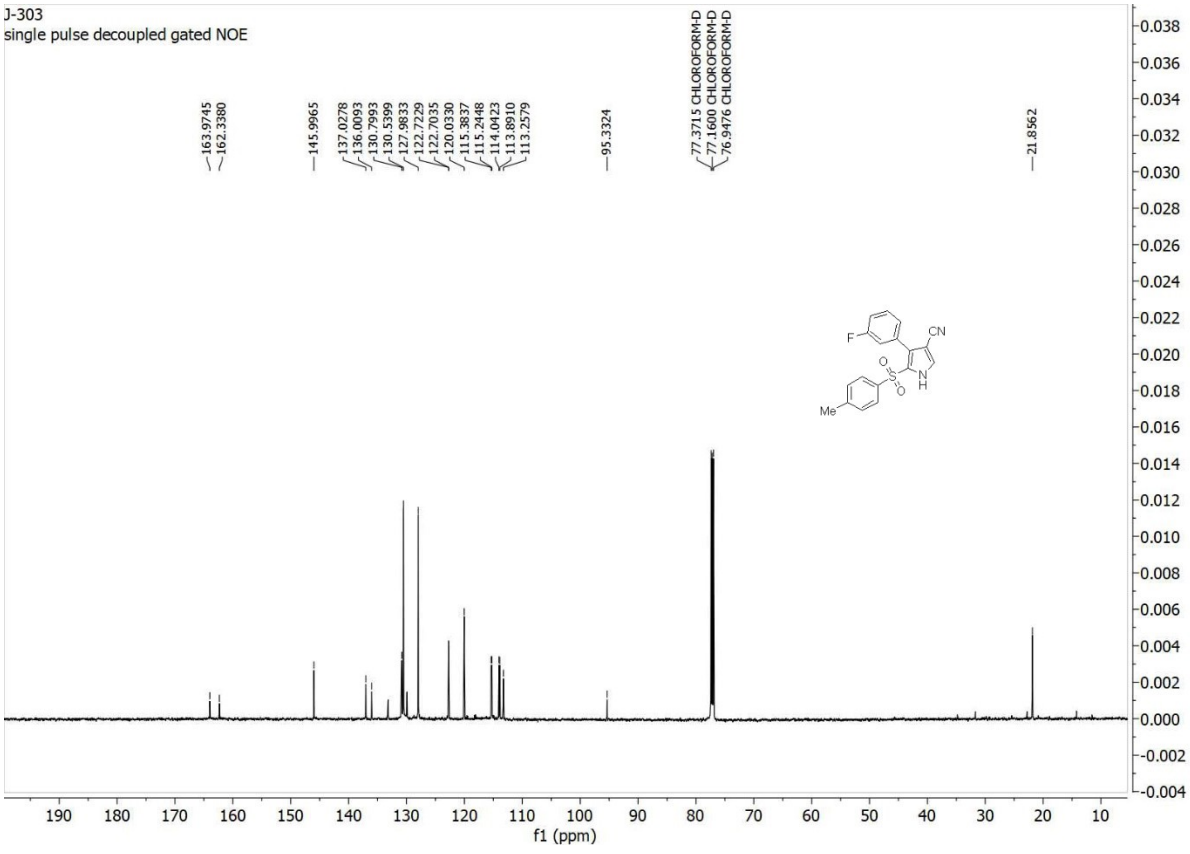


Figure S32. ^{13}C NMR spectrum of **37A** in $CDCl_3$.

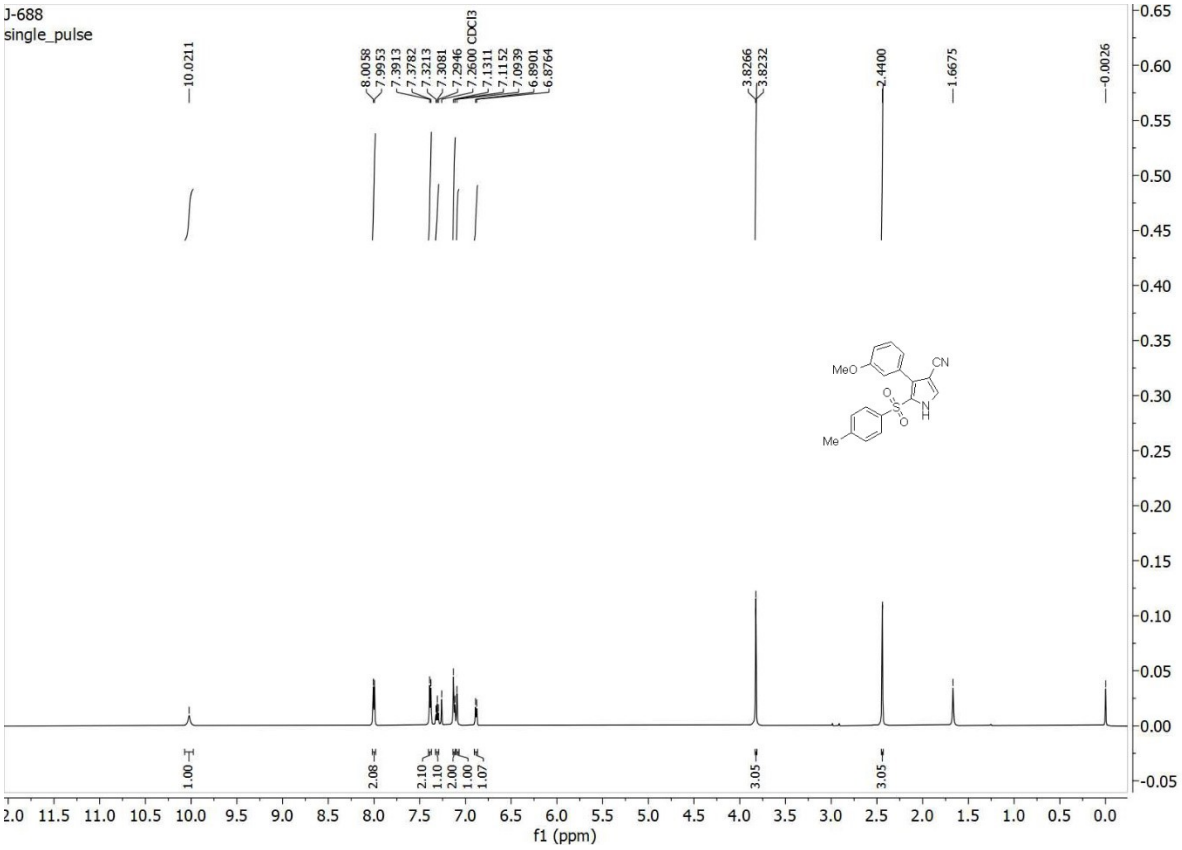


Figure S33. ^{1}H NMR spectrum of **38A** in $CDCl_3$.

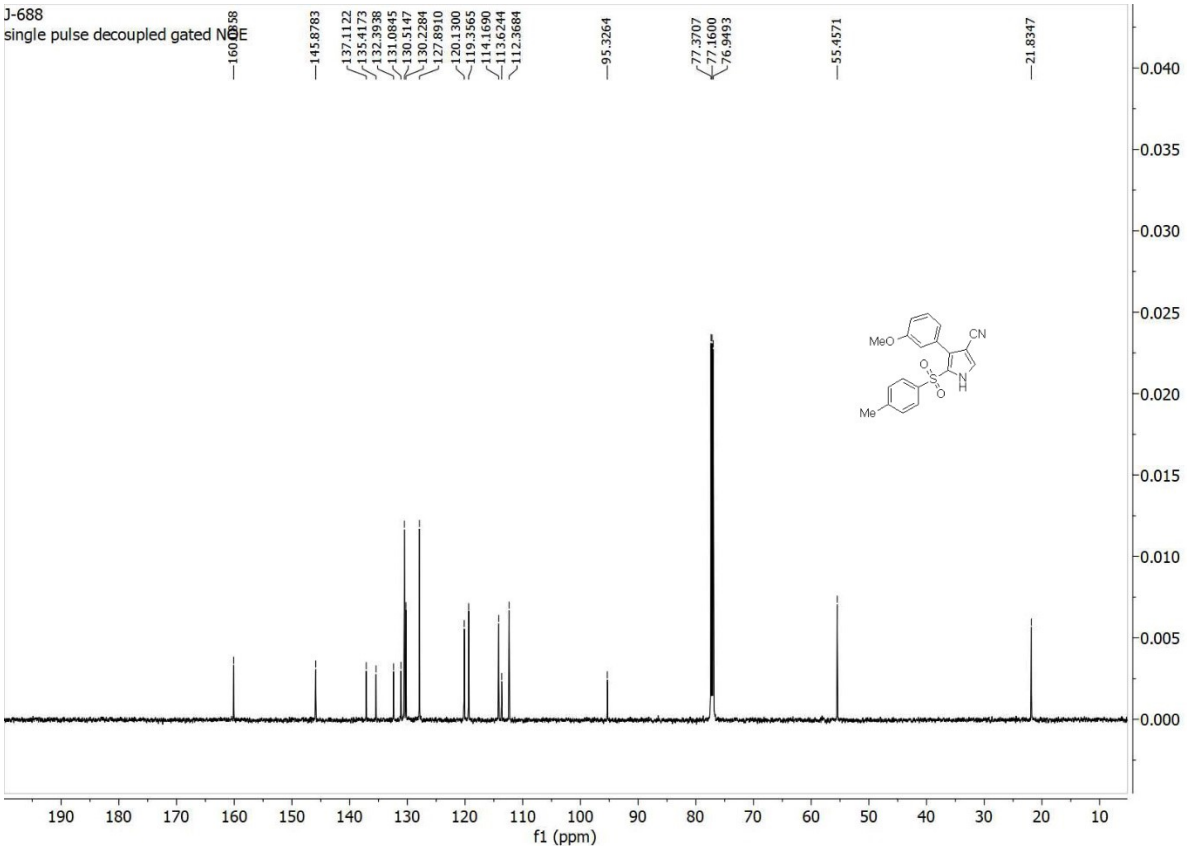


Figure S34. ^{13}C NMR spectrum of **38A** in $CDCl_3$.

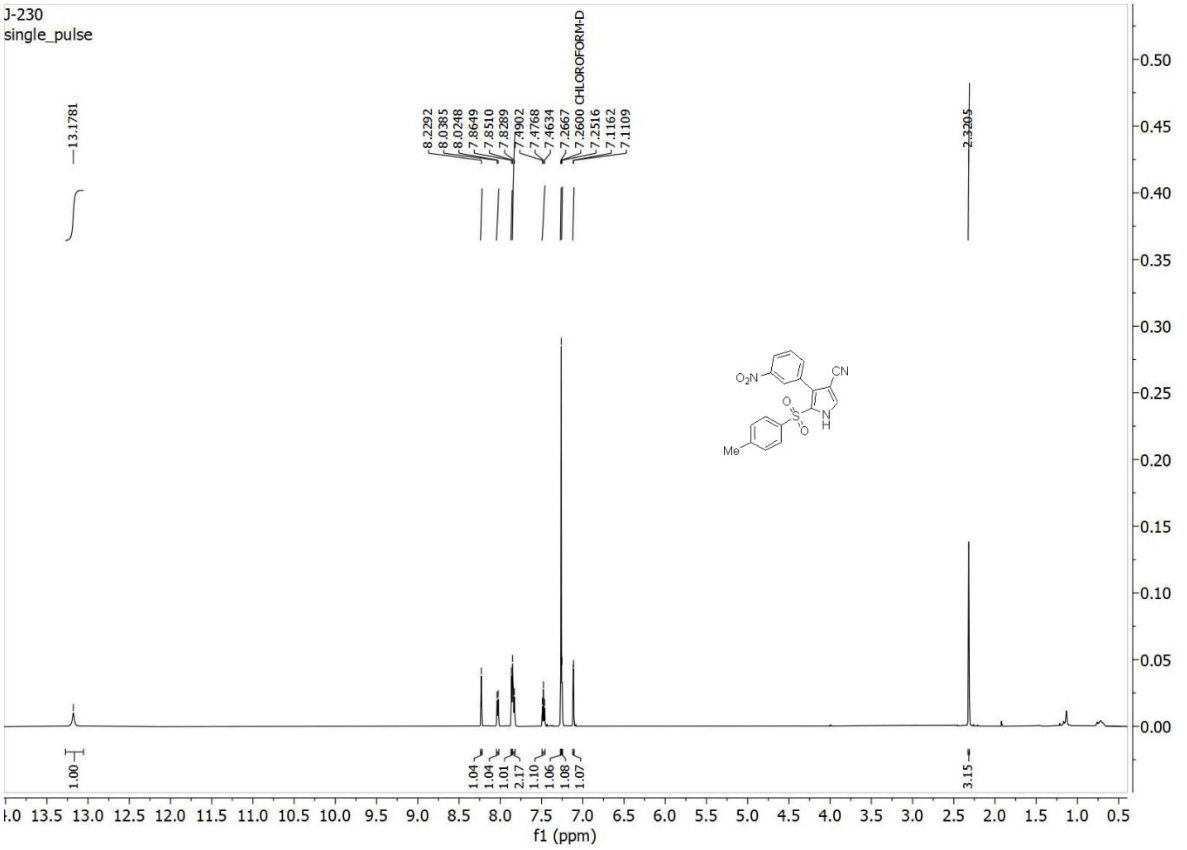


Figure S35. ^{1}H NMR spectrum of **39A** in $CDCl_3$.

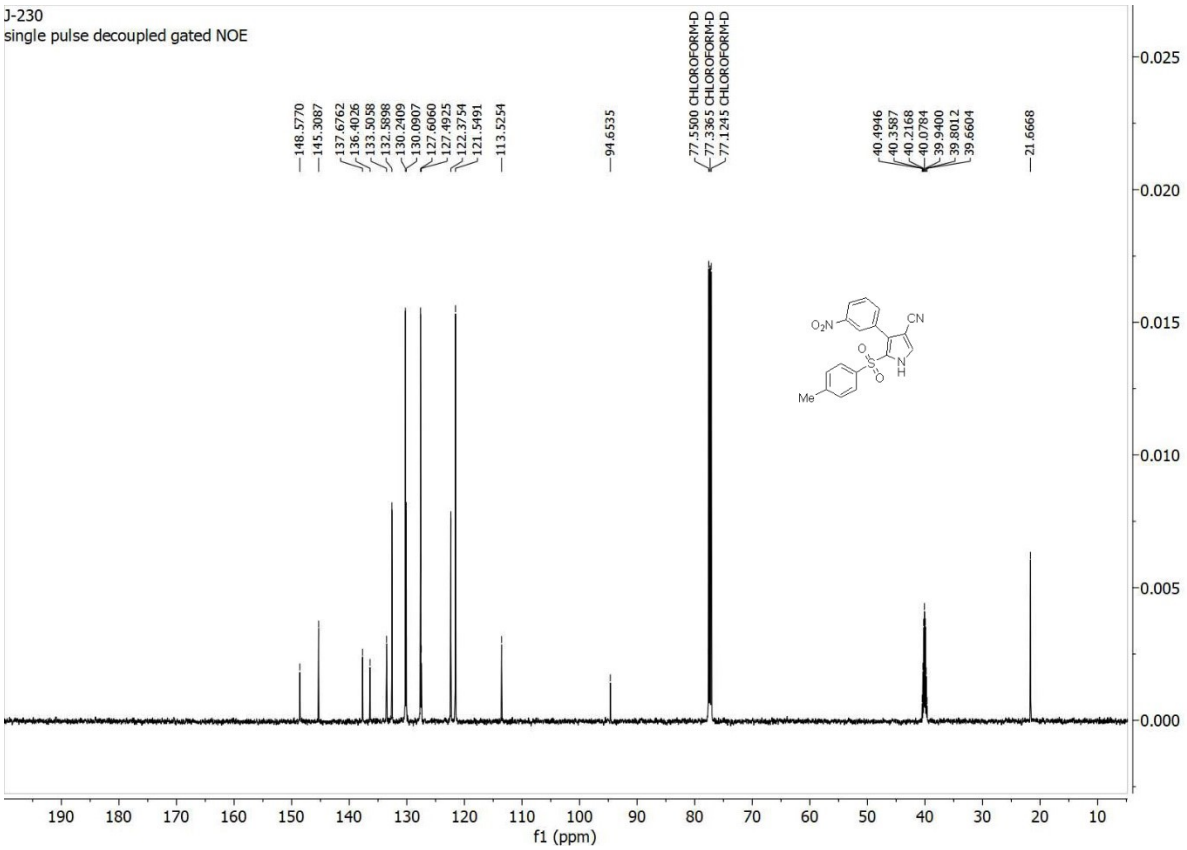


Figure S36. ^{13}C NMR spectrum of **39A** in $CDCl_3$ +DMSO.

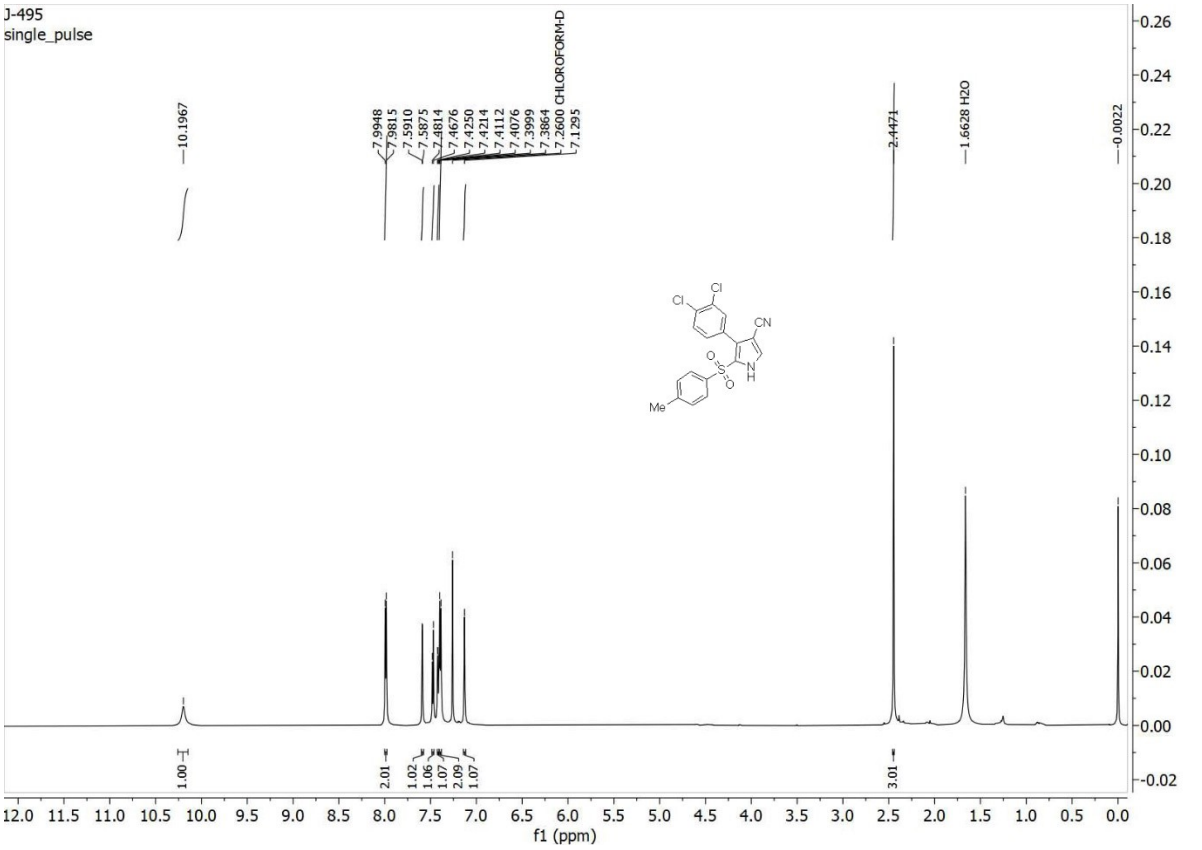


Figure S37. ^{1}H NMR spectrum of **40A** in $CDCl_3$.

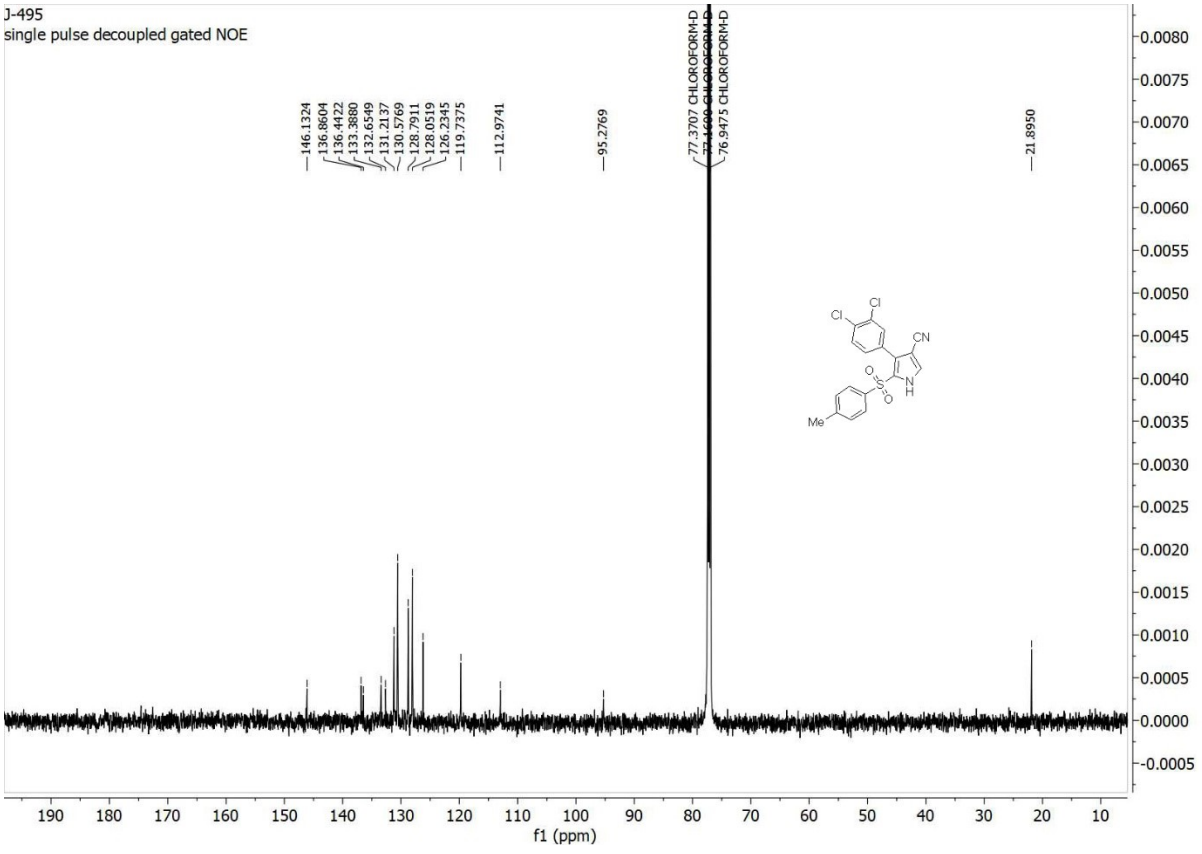


Figure S38. ^{13}C NMR spectrum of **40A** in $CDCl_3$.

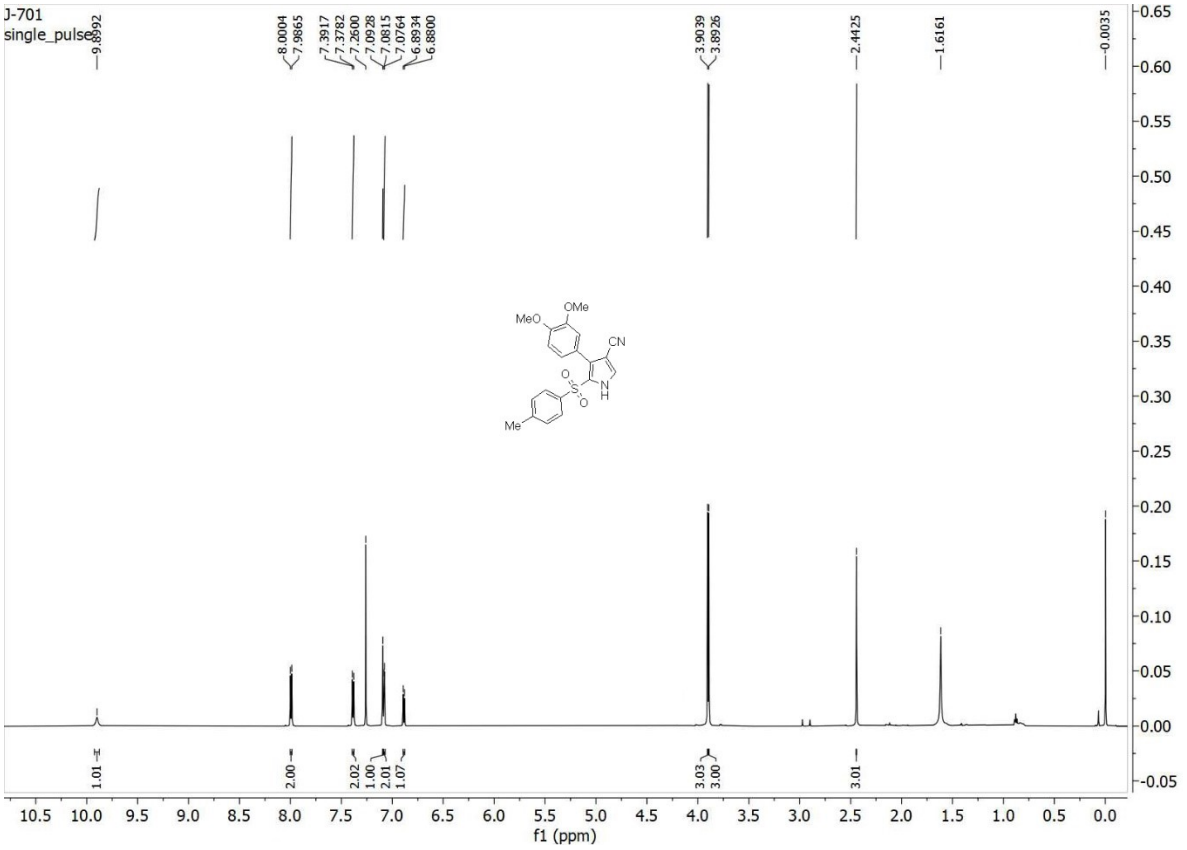


Figure S39. ^{1}H NMR spectrum of **41A** in $CDCl_3$.

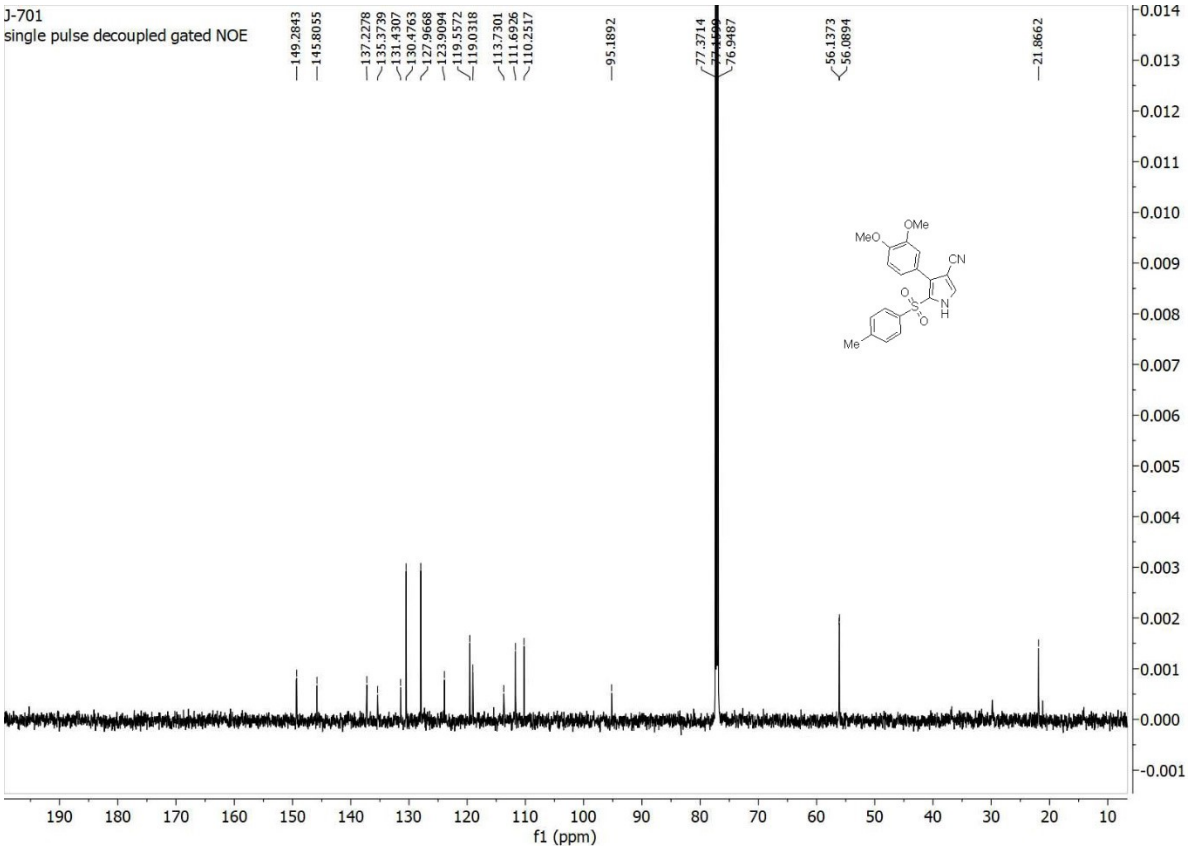


Figure S40. ^{1}H NMR spectrum of **41A** in $CDCl_3$.

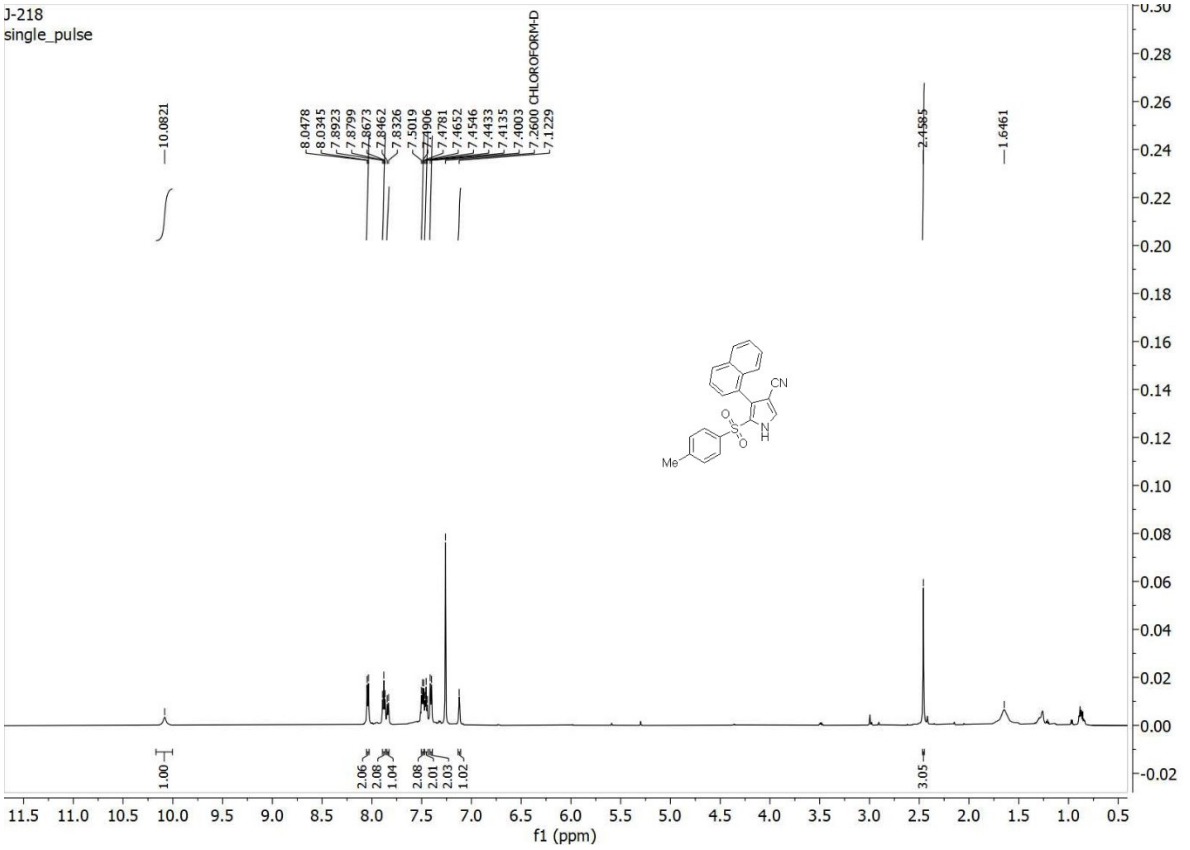


Figure S41. ^{1}H NMR spectrum of **42A** in $CDCl_3$.

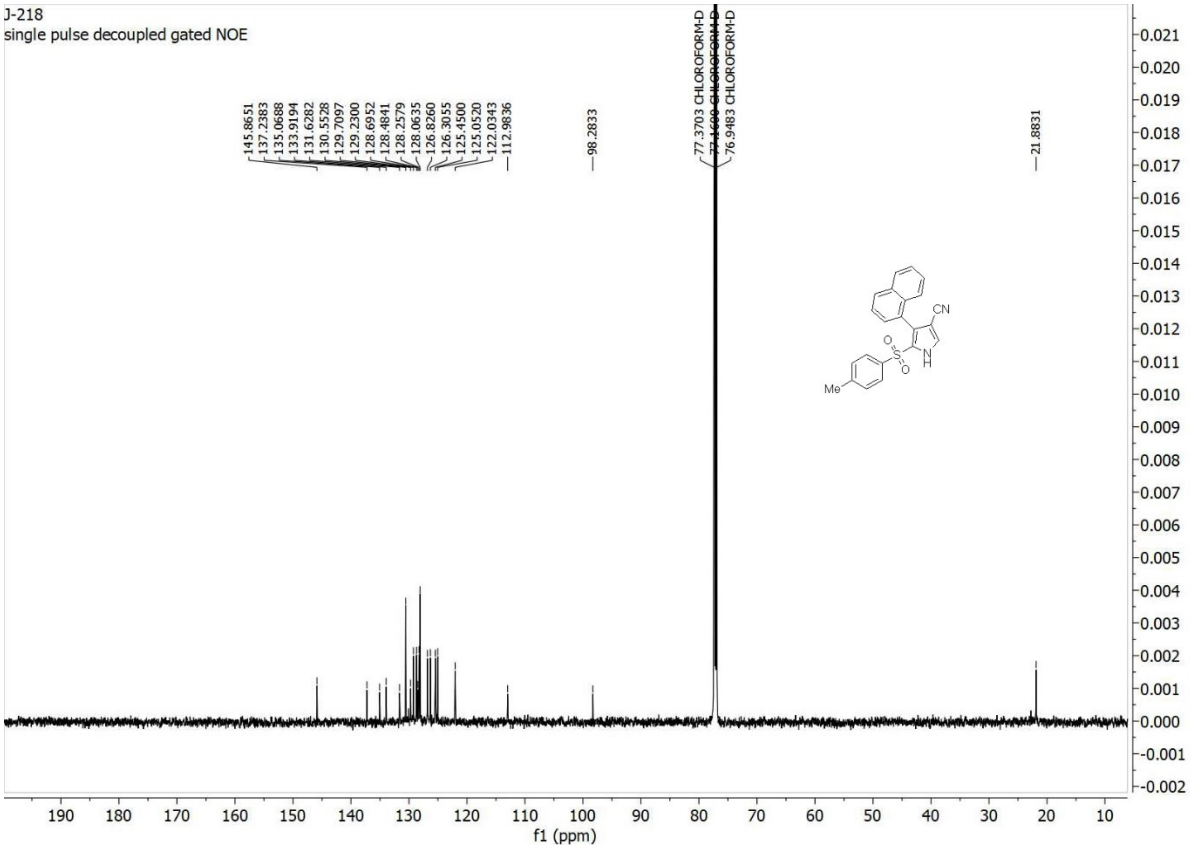


Figure S42. ^{1}H NMR spectrum of **42A** in $CDCl_3$.

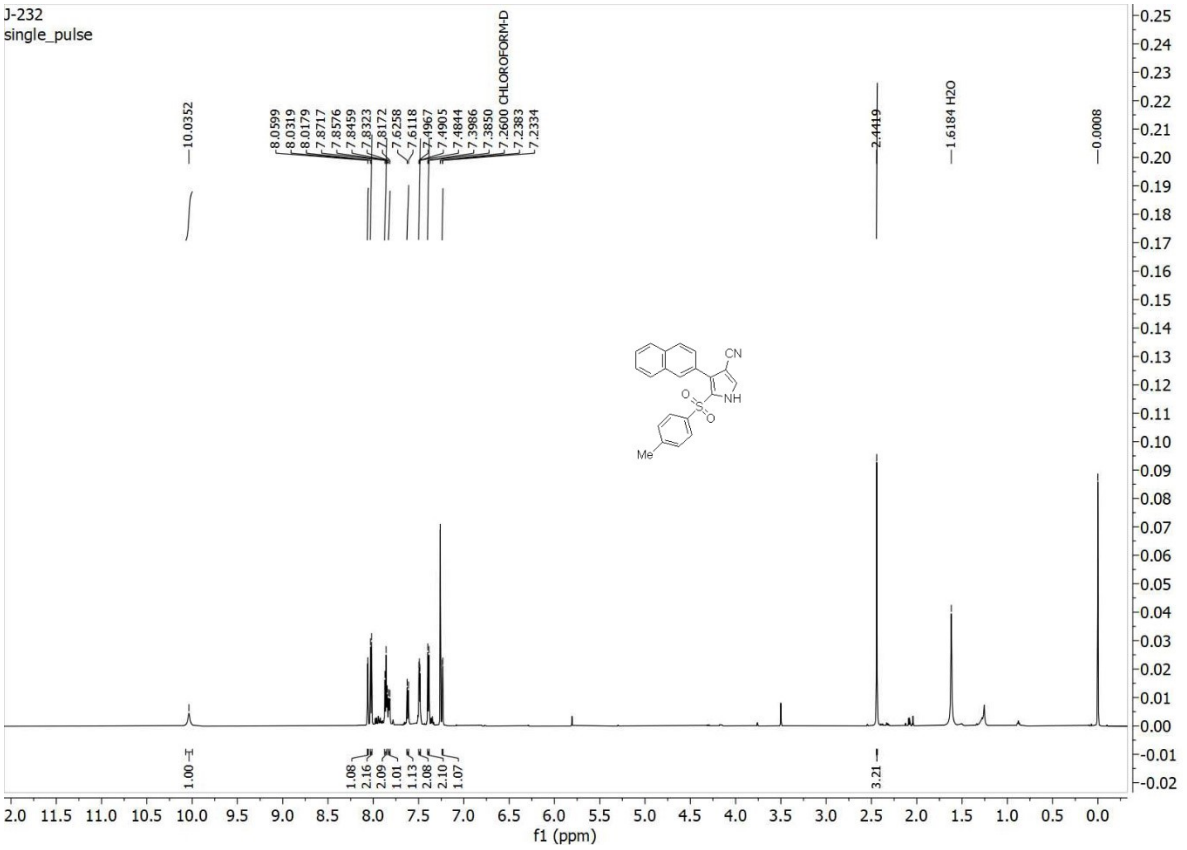


Figure S43. ^{1}H NMR spectrum of **43A** in $CDCl_3$.

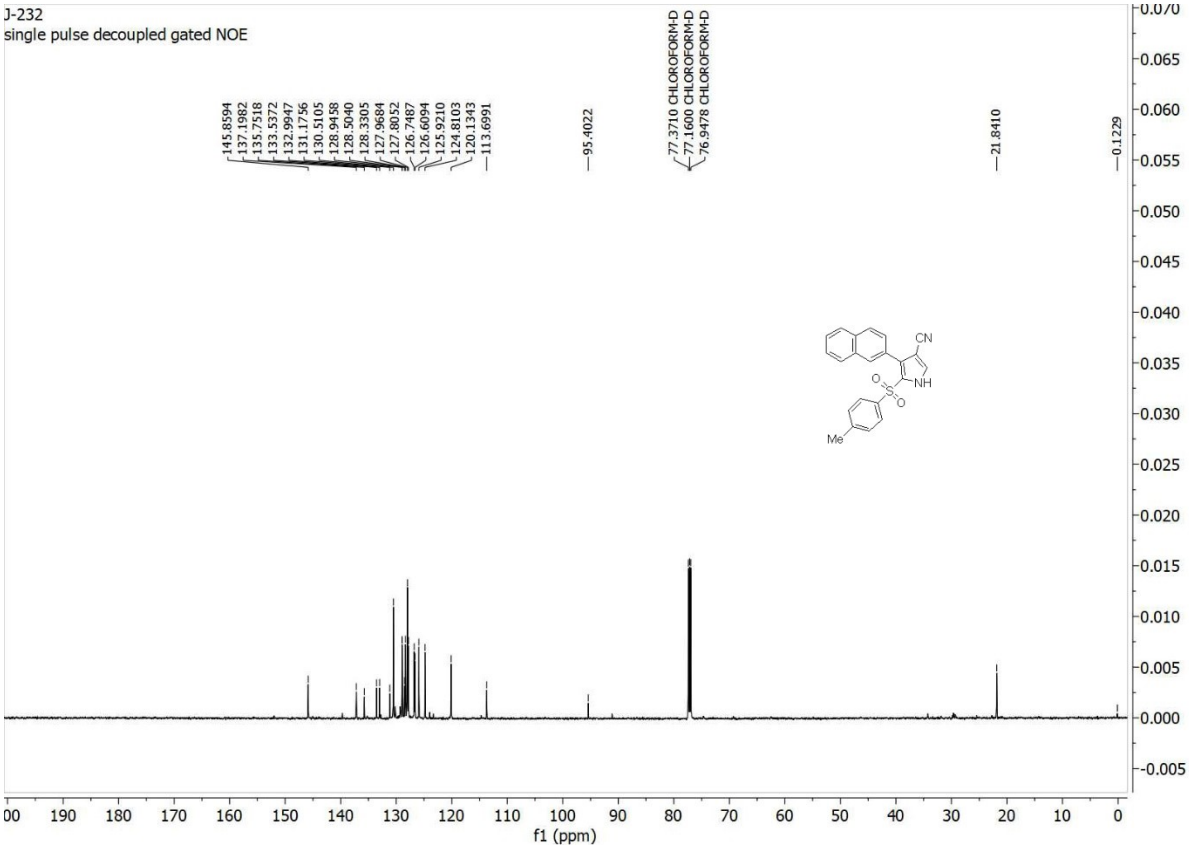


Figure S44. ^{13}C NMR spectrum of **43A** in $CDCl_3$.

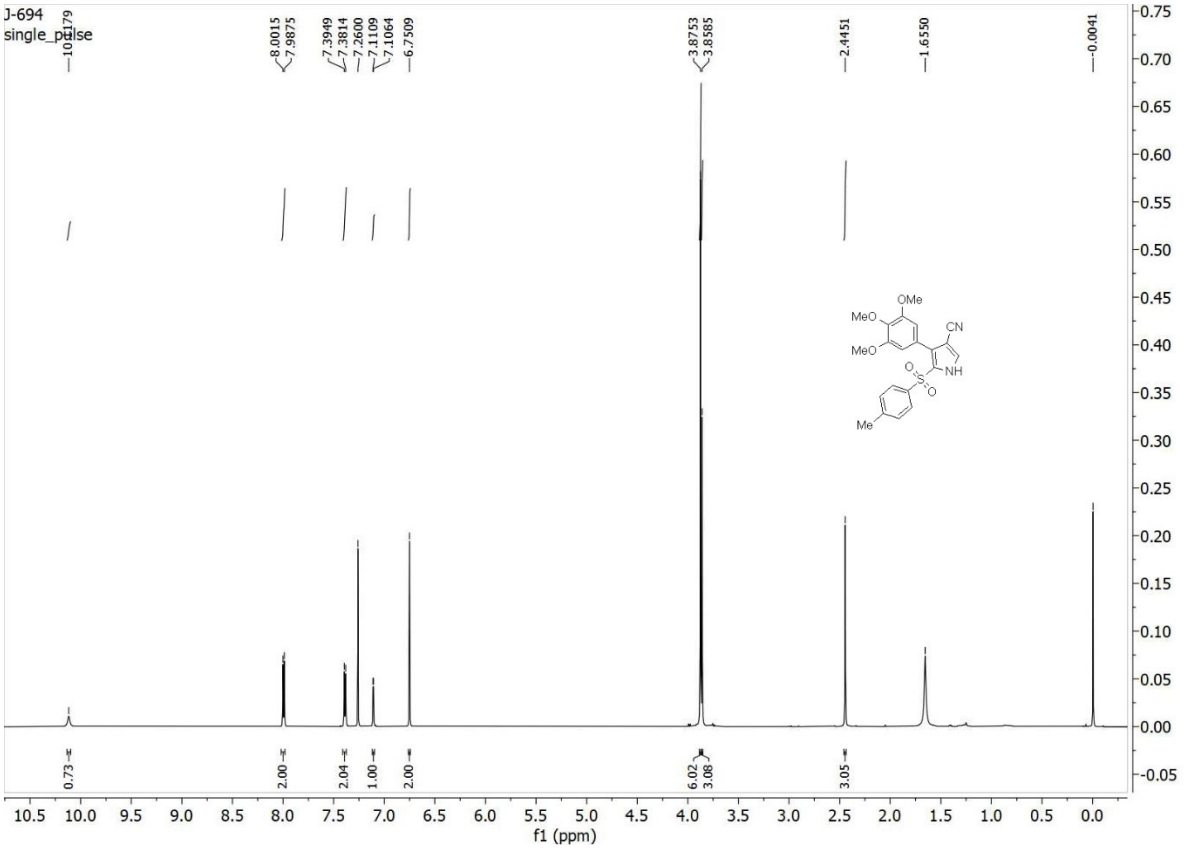


Figure S45. ^{1}H NMR spectrum of **44A** in $CDCl_3$.

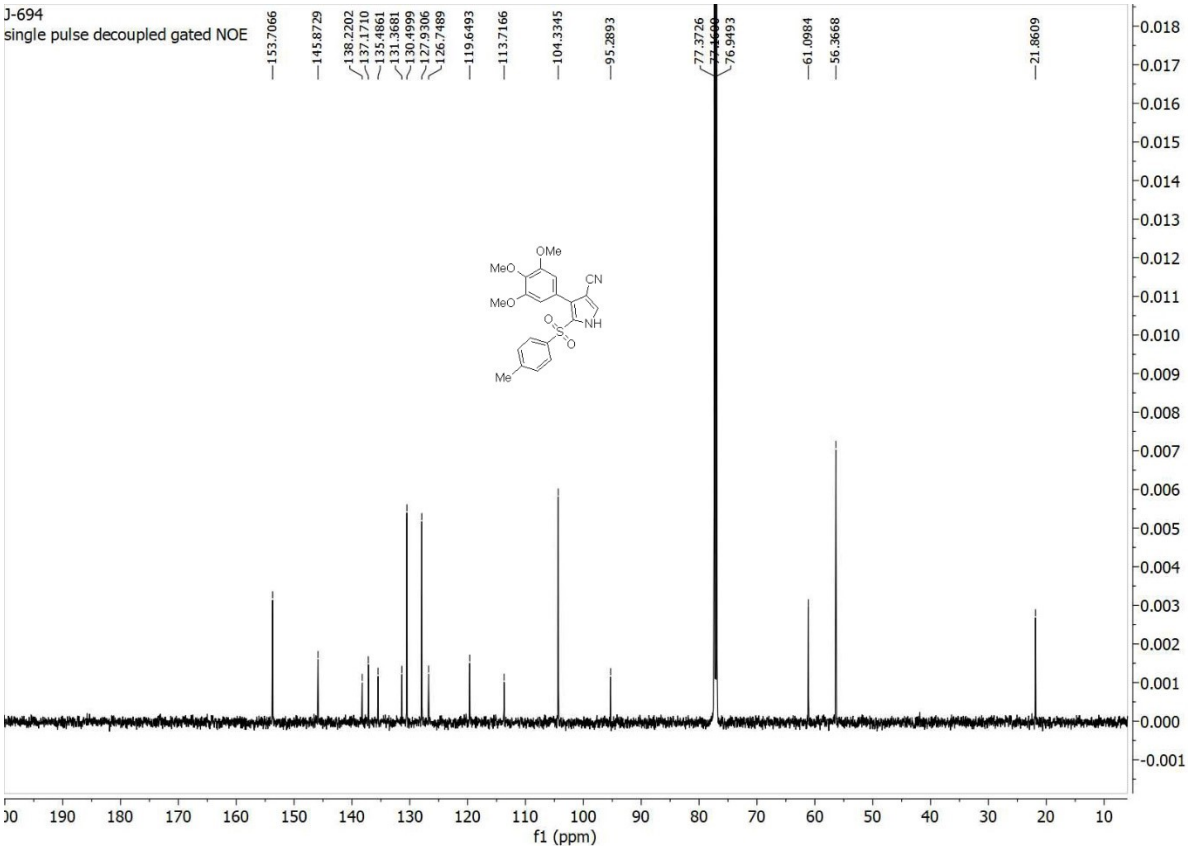


Figure S46. ^{13}C NMR spectrum of **44A** in $CDCl_3$.

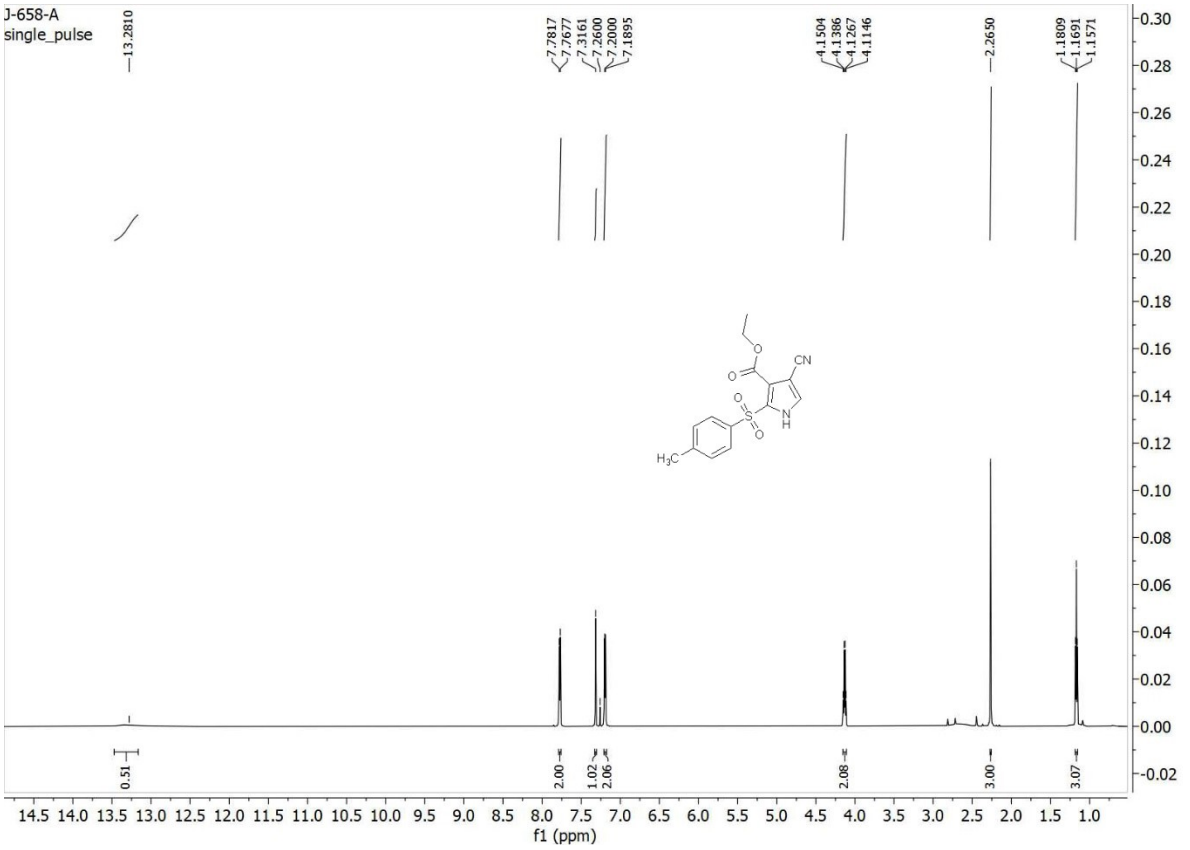


Figure S47. ^{1}H NMR spectrum of **49A** in $CDCl_3$.

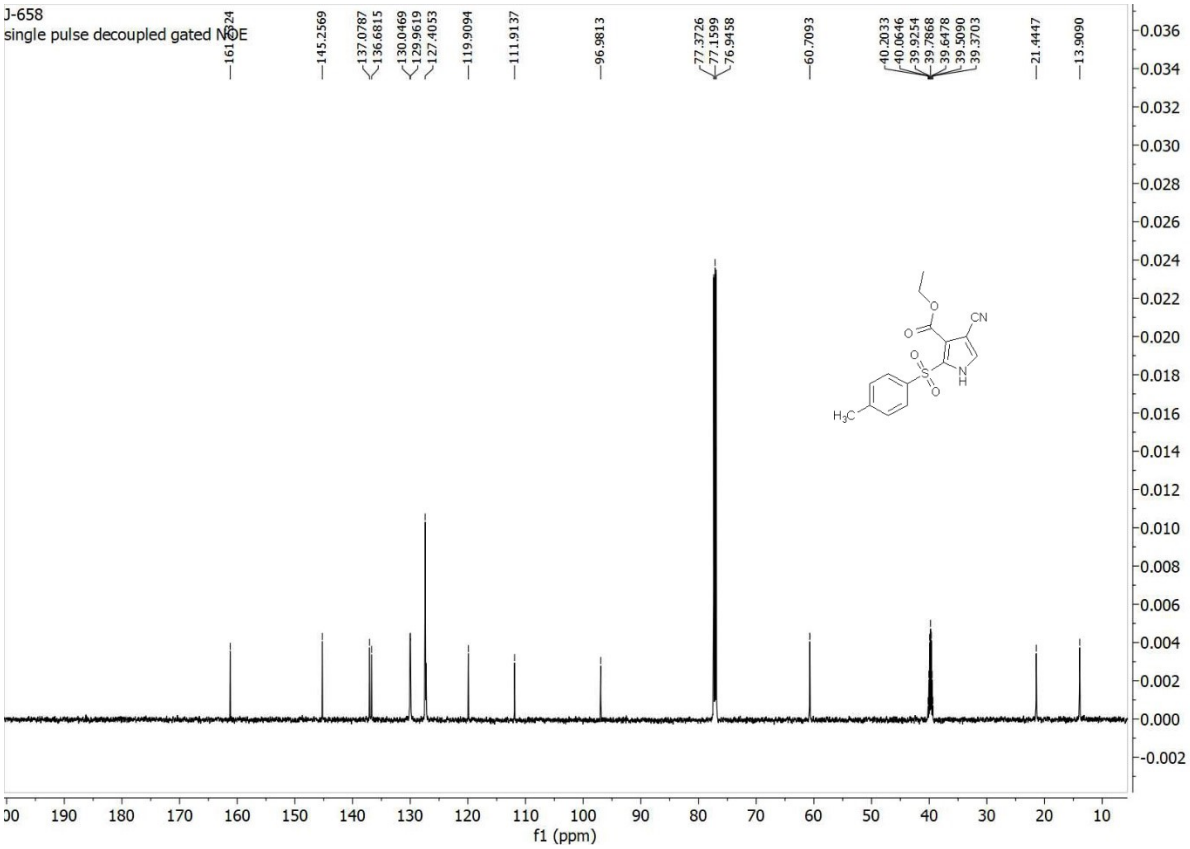


Figure S48. ^{13}C NMR spectrum of **49A** in $CDCl_3$+DMSO d_6.

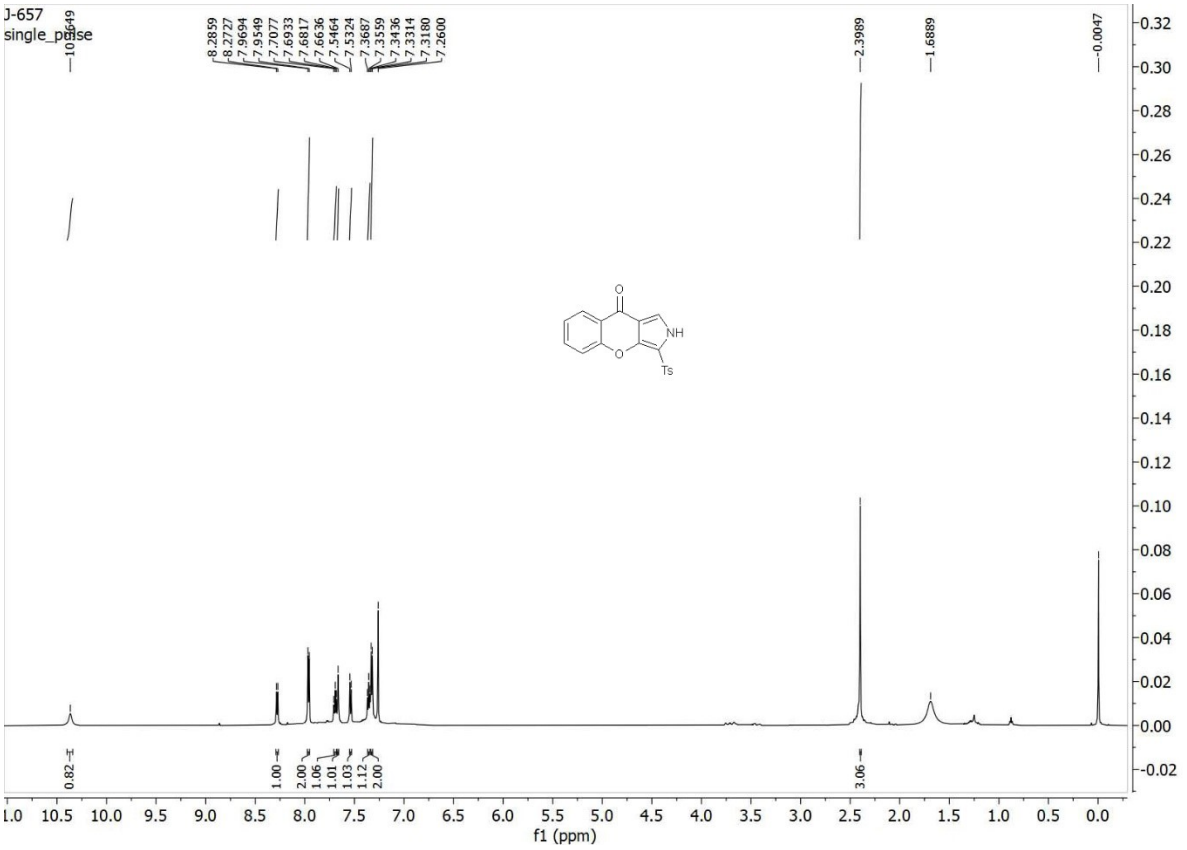


Figure S49. ^{1}H NMR spectrum of **50A** in $CDCl_3$.

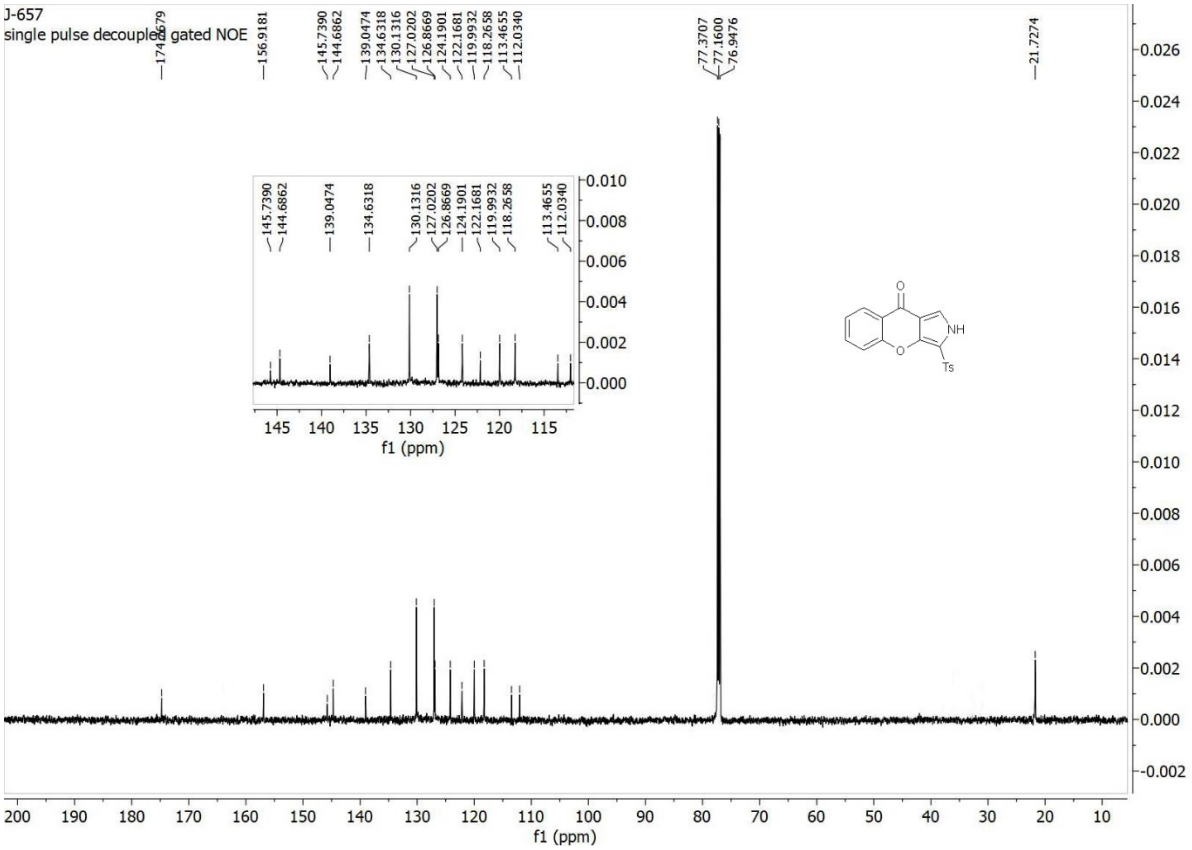


Figure S50. ^{13}C NMR spectrum of **50A** in $CDCl_3$.

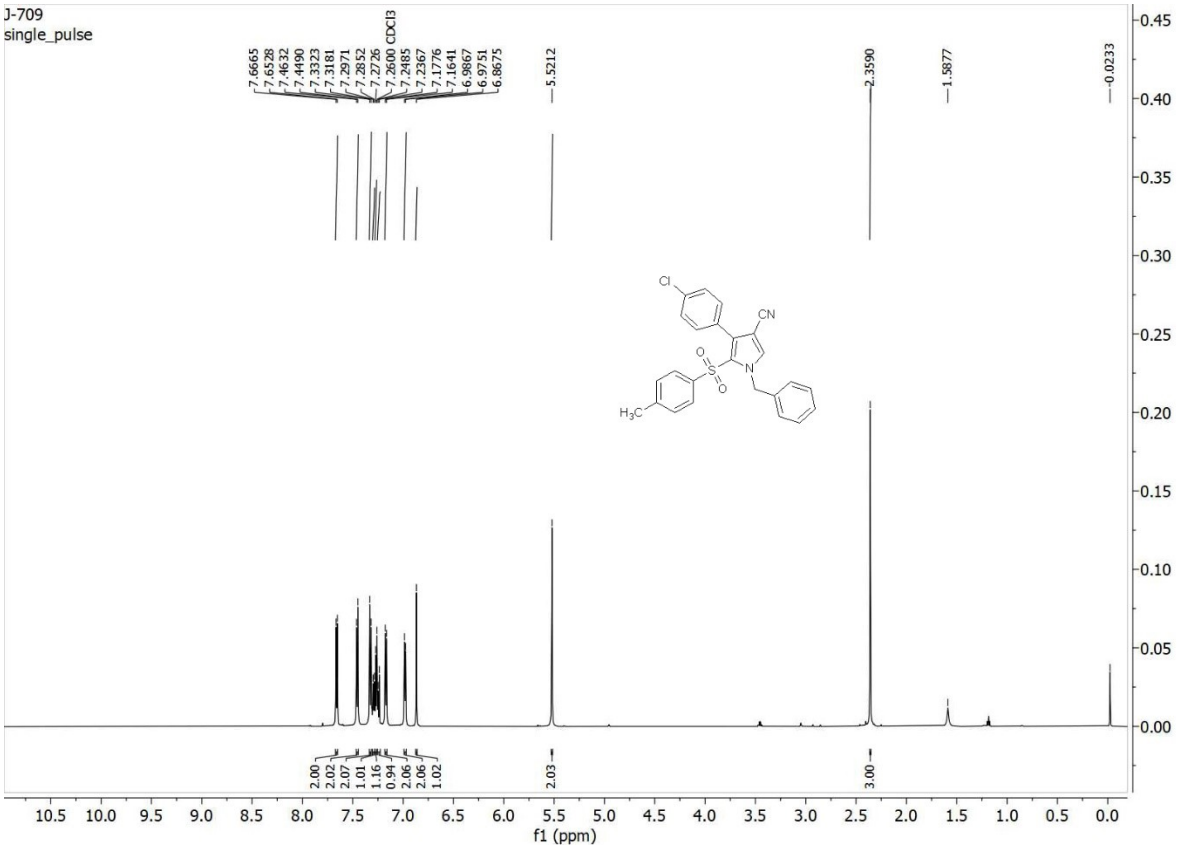


Figure S51. ^{1}H NMR spectrum of **51** in $CDCl_3$.

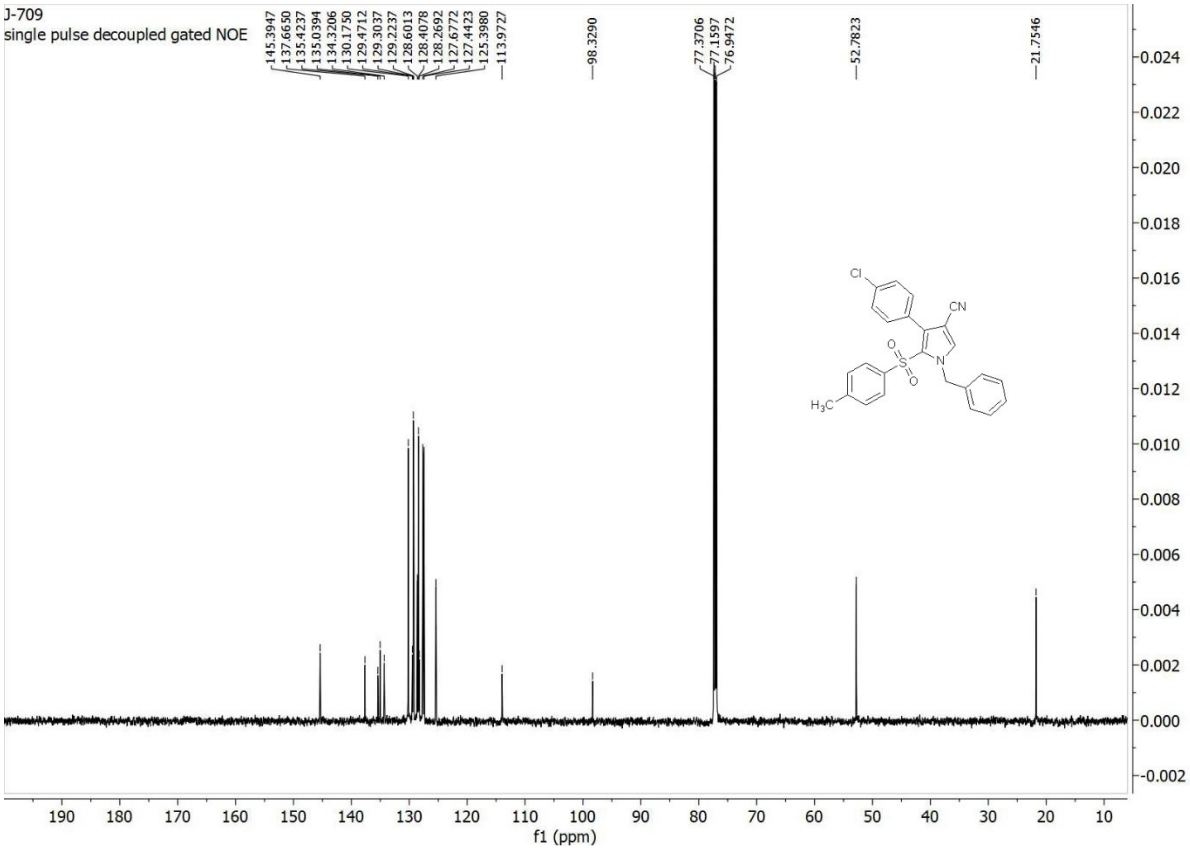


Figure S52. ^{13}C NMR spectrum of **51**in $CDCl_3$.

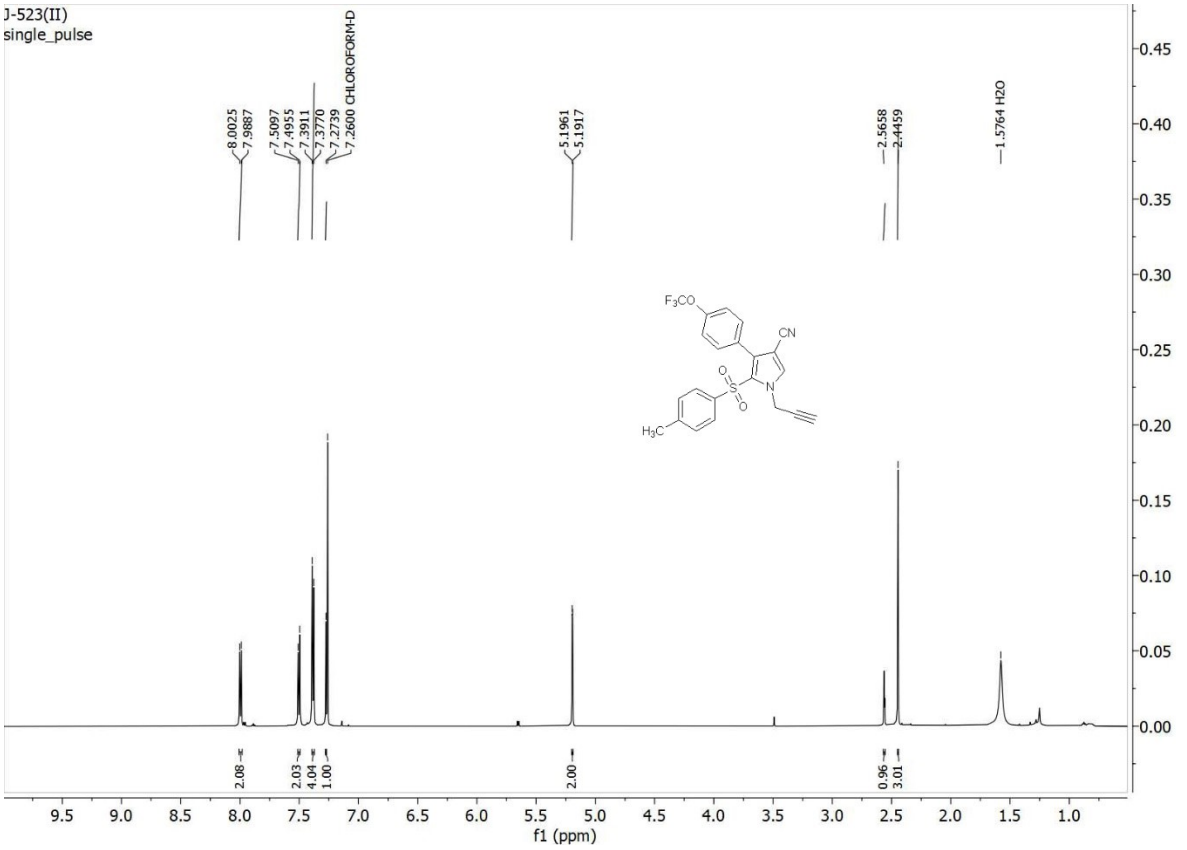


Figure S53. ^{1}H NMR spectrum of **52** in $CDCl_3$.

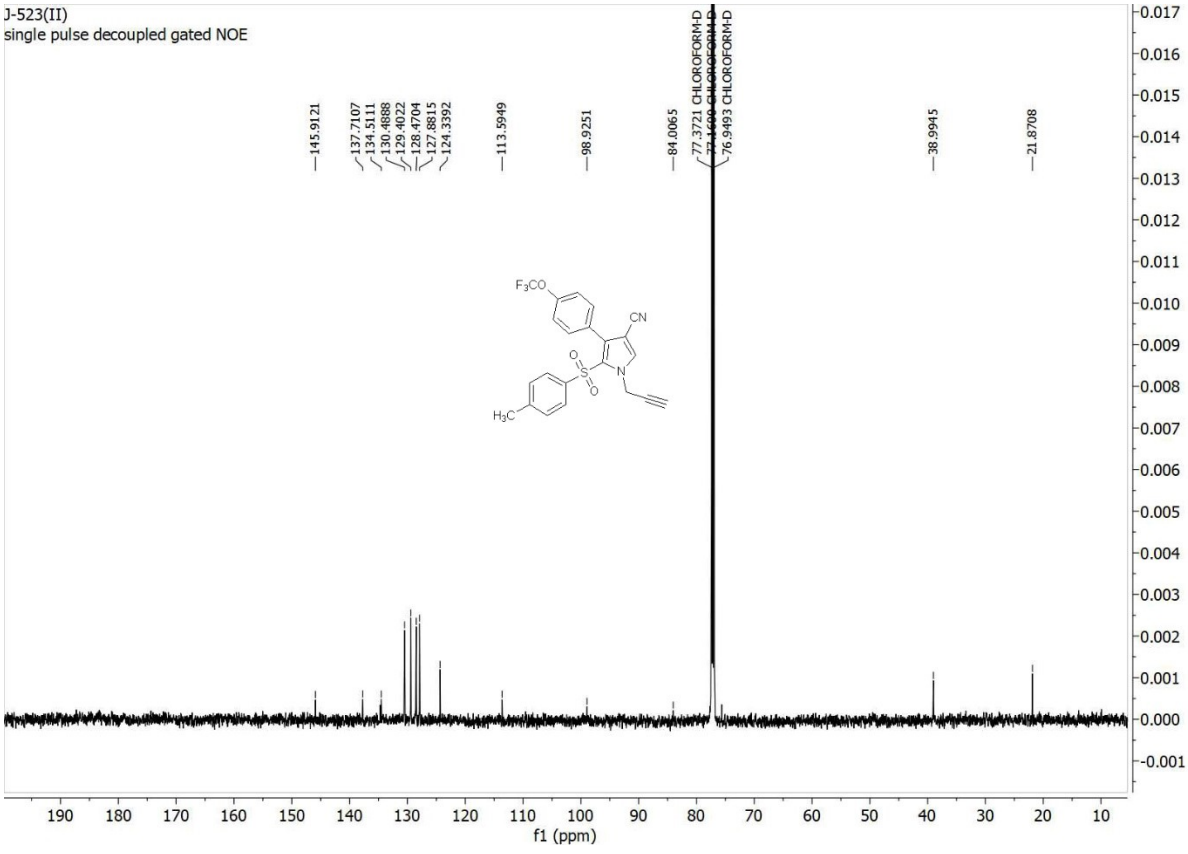


Figure S54. ^{13}C NMR spectrum of **52** in $CDCl_3$.

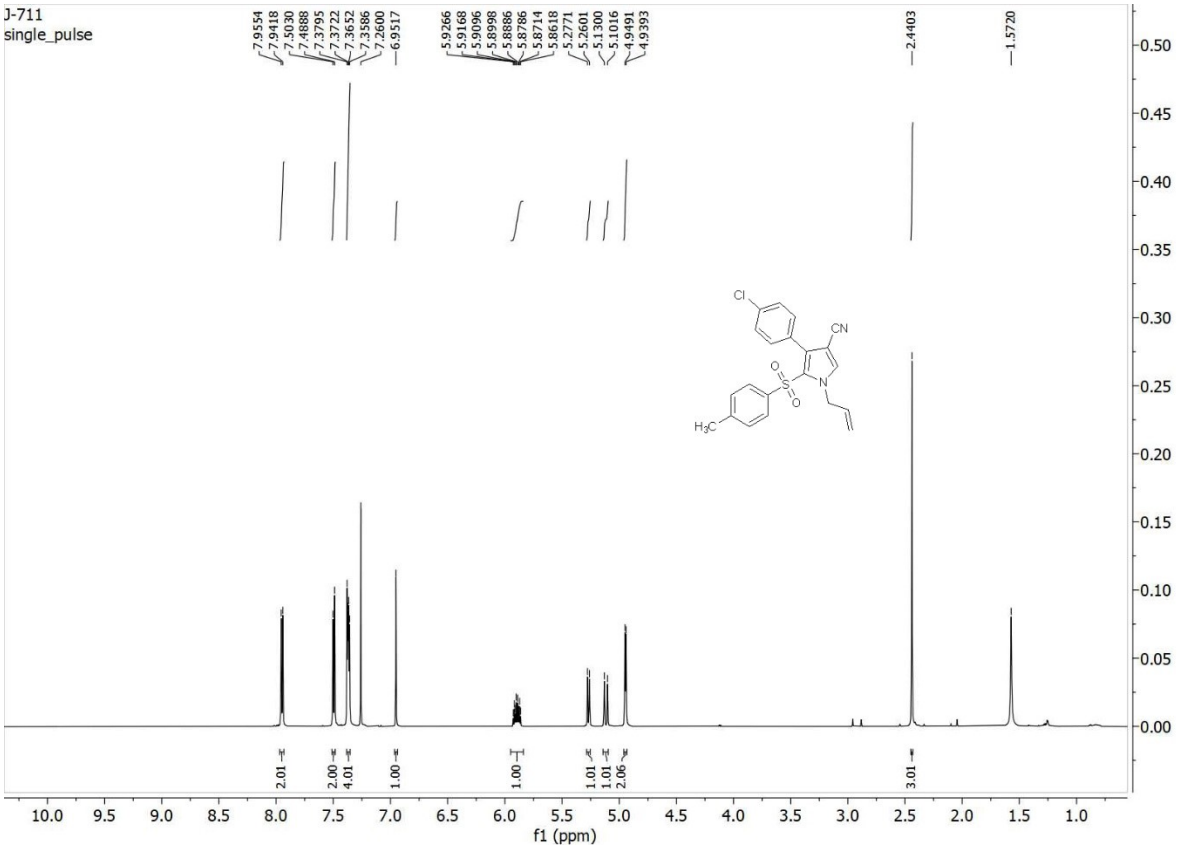


Figure S55. ^{1}H NMR spectrum of **53** in $CDCl_3$.

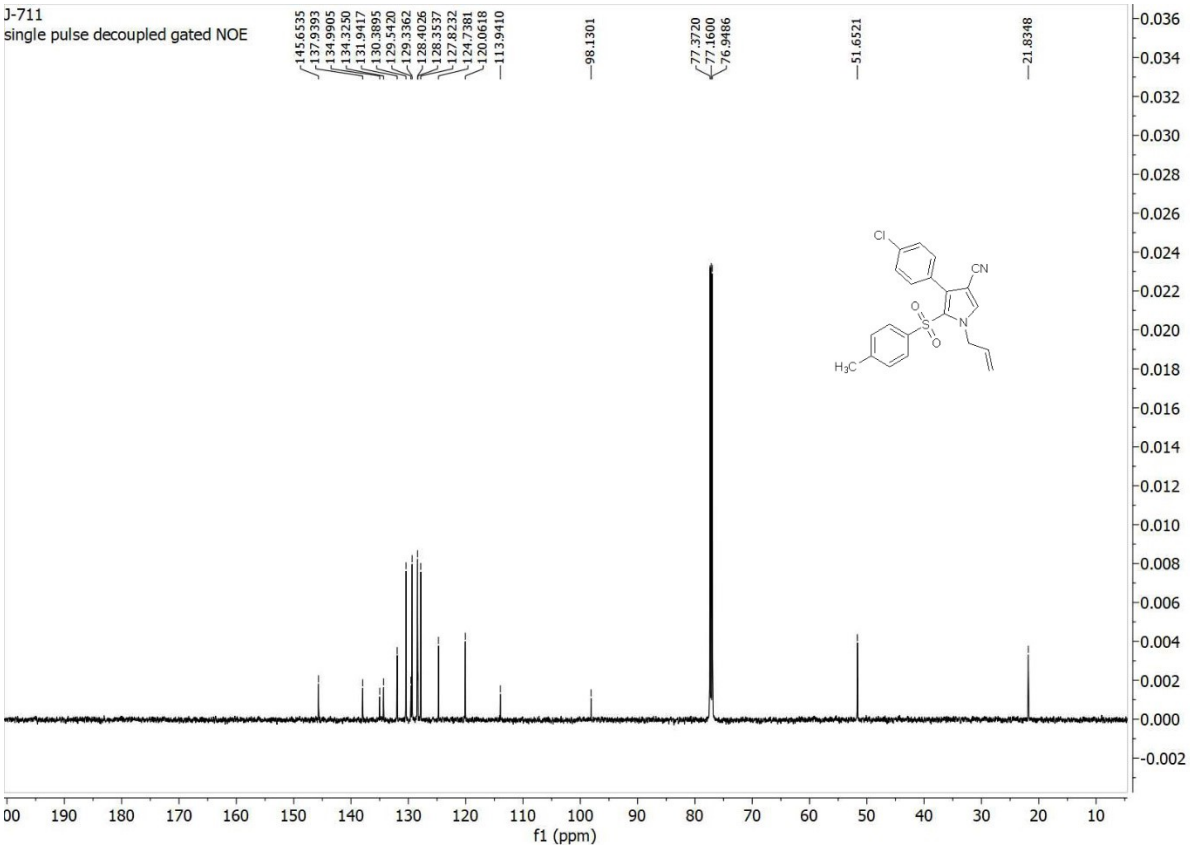


Figure S56. ^{13}C NMR spectrum of **53** in $CDCl_3$.