Supporting information

Mo-catalyzed cyclization of *N*-vinylindoles and skatoles: synthesis of dihydroindolo[1,2-*c*]-quinazolines and dihydroindolo[3,2-*b*]-indoles, and evaluation of their anticancer activities

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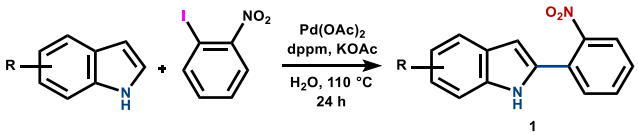
Contents

General considerations

Commercial solvents and reagents were used without further purification unless specified otherwise. The $MoO_2Cl_2(DMF)_2$ was prepared following the Gonçalves procedure.[1] For analytical TLC, Merck silica gel F254 (230-400 mesh) plates were used and analyzed either by UV light or by staining upon heating with vanillin solution (15 g of vanillin, 1g sulfuric acid, 100 mL of EtOH). Purifications were accomplished using flash chromatography with Merck silica gel 60 (230-400 mesh). Solvent peaks were used as reference values, with $CDCl_3$ at 7.26 ppm for ^{1}H NMR and 77.16 ppm for ^{13}C NMR. Chemical shifts δ are given in ppm, and the following abbreviations are used: singlet (s), doublet (d), doublet of doublet (dd), triplet (t), multiplet (m), and broad singlet (br s). In the $^{13}C\{^1H\}$ NMR spectra, signals corresponding to C, CH, CH_2, or CH_3 were assigned from the JMOD sequence. High-resolution mass spectra (HR-MS) were recorded on a MicrOTOF-Q II Spectrometer.

General procedure (A) for the preparation of 2-(2-nitrophenyl)-1*H*-indoles derivatives[2]: synthesis of compounds 1a-f



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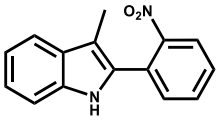
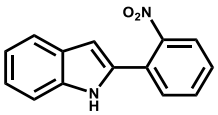
In a round bottom flask, indole (15.0 mmol, 1.0 equiv), 1-iodo-2-nitrobenzene (18.0 mmol, 1.2 equiv). $Pd(OAc)_2$ (5 mol%), bis(diphenylphosphino)methane (dppm) (5 mol%) and KOAc (45.0 mmol, 3.0 equiv) were dissolved in 40 mL of water. The mixture was then heated in an oil bath at 110 °C for 24 hours with a condenser. After the reaction was complete, the reaction mixture was then quenched with an aqueous solution of HCl 1N (70 mL) and diluted with 40 mL of ethyl acetate. Next, the organic layer was separated, and the aqueous layer was extracted with ethyl acetate (4 x 25 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Finally, the crude product was purified by silica gel chromatography using

cyclohexane/ethyl acetate (0 to 15% of ethyl acetate) as eluent to obtain the corresponding 2-(2-nitrophenyl)-1*H*-indole derivative.

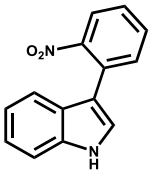


*3-Methyl-2-(2-nitrophenyl)-1H-indole (**1a**).*[3] was prepared according to method A from 3-methyl-1*H*-indole and 1-iodo-2-nitrobenzene. Column chromatography on silica gel provided 2.6 g of the product as a viscous red oil (70% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.81; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 10.23 (br s, 1H), 8.12 – 8.01 (m, 1H), 7.92 – 7.77 (m, 1H), 7.77 – 7.64 (m, 2H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.23 – 7.13 (m, 1H), 7.07 (m, 1H), 2.19 (s, 3H); ^{13}C{1H} NMR (75 MHz, $(CD_3)_2CO$) δ 137.7, 134.0, 133.5, 130.6, 130.1, 129.8, 128.6, 125.2, 123.0, 119.9 (2 C), 119.6, 111.9, 110.6, 9.1 ; HRMS [ESI-TOF] $[M + H]^+$ *m*/*z* calcd for $C_{15}H_{13}N_2O_2$ 253.0977, found 253.0978.

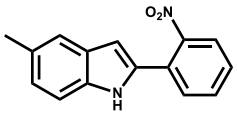


Was prepared according to general method A starting from indole and 1-iodo-2-nitrobenzene. A mixture of 2-(2-Nitrophenyl)-1*H*-indole **1b** and 3-(2-nitrophenyl)-1*H*-indole **1c** was obtained in a ratio of 90/10 **1b**/**1c**.

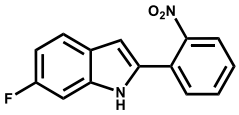
*2-(2-Nitrophenyl)-1H-indole (**1b**).*[4] Column chromatography on silica gel afforded 2.2 g of the product as a red solid (62% yield), mp = 102-104 °C. TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.63; ^{1}H NMR (200 MHz, $(CD_3)_2CO$) δ 10.58 (br s, 1H), 7.91 (d, *J* = 7.9 Hz, 1H), 7.81 (dd, *J* = 4.4, 1.4 Hz, 1H), 7.78 – 7.70 (m, 1H), 7.68 – 7.55 (m, 2H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.27 – 6.95 (m, 2H), 6.63 (s, 1H). *Analytic data is in accordance with literature data.*



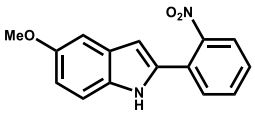
3-(2-nitrophenyl)-1H-indole (***1c***). Column chromatography on silica gel afforded 0.28 g of the product as a red solid (8% yield), mp = 121-123 °C. TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.42; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.90 – 7.81 (m, 1H), 7.69 – 7.39 (m, 5H), 7.32 – 7.13 (m, 3H). $^{13}C\{^1H\}$NMR (75 MHz, $CDCl_3$) δ 136.1, 132.7, 132.1, 129.3, 127.3, 126.4, 124.1, 123.5, 123.0, 120.9, 119.0, 112.8 (2 C), 111.7. HRMS (ESI) *m*/*z*: $(M + H)^+$ $C_{14}H_{11}N_2O_2$ calcd, 239.0821; found, 239.0820



*5-Methyl-2-(2-nitrophenyl)-1H-indole (**1d**).* was prepared according to method A from 5-methyl-1*H*-indole and 1-iodo-2-nitrobenzene. Column chromatography on silica gel afforded 2.6 g of the product as a dark red solid (70% yield), mp = 107-110 °C. TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.63; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 10.43 (br s, 1H), 7.87 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.80 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.74 – 7.66 (m, 1H), 7.63 – 7.51 (m, 1H), 7.46 – 7.37 (m, 1H), 7.40 – 7.22 (m, 1H), 7.12 – 6.88 (m, 1H), 6.78 – 6.30 (m, 1H), 2.41 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $(CD_3)_2CO$) δ 136.8, 134.5, 133.0, 132.0, 129.9, 129.5, 127.9, 125.1, 124.7, 121.1, 118.8, 112.5, 112.0, 102.9, 21.6; HRMS [ESI-TOF] $[M + H]^+$ *m*/*z* calcd for $C_{15}H_{13}N_2O_2$ 253.0977, found 253.0976.

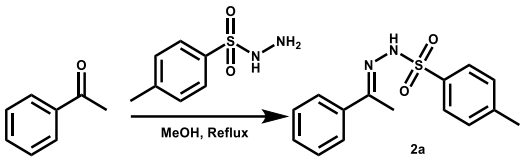


*6-Fluoro-2-(2-nitrophenyl)-1H-indole (**1e**).* was prepared according to method A from 6-fluoro-1*H*-indole and 1-iodo-2-nitrobenzene. Column chromatography on silica gel afforded 3.0 g of the product as a red solid (79% yield), mp = 100-102 °C. TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.41; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 10.68 (br s, 1H), 7.91 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.84 – 7.69 (m, 2H), 7.65 – 7.53 (m, 2H), 7.28 – 7.09 (m, 1H), 6.90 (ddd, *J* = 9.9, 8.7, 2.4 Hz, 1H), 6.66 (dd, *J* = 2.2, 0.9 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $(CD_3)_2CO$) δ 161.0 (d, *J* = 236.6 Hz), 138.3 (d, *J* = 12.8 Hz), 134.5, 133.2, 132.1, 129.8, 127.4, 126.3, 125.3, 124.8, 122.6 (d, *J* = 10.1 Hz), 109.3 (d, *J* = 24.8 Hz), 103.4, 98.2 (d, *J* = 26.2 Hz); $^{19}F\{^1H\}$ NMR (188 MHz, $(CD_3)_2CO$) δ 121.44 (td, *J* = 9.8, 5.4 Hz); HRMS [ESI-TOF] $[M + H]^+$ *m*/*z* calcd for $C_{14}H_{10}FN_2O_2$ 257.0726, found 257.0729.



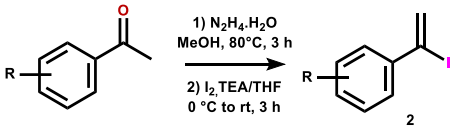
5-Methoxy-2-(2-nitrophenyl)-1H-indole (***1f***).[5] was prepared according to method A from 5-methoxy-1*H*-indole and 1-iodo-2-nitrobenzene. Column chromatography on silica gel provided 3.5 g of the product as a red solid (88% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.66; ^{1}H NMR (200 MHz, $(CD_3)_2CO$) δ 10.44 (br s, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.85 – 7.69 (m, 2H), 7.66 – 7.52 (m, 1H), 7.35 (d, J = 8.8 Hz, 1H), 7.11 (d, J = 2.1 Hz, 1H), 6.83 (dd, J = 8.9, 2.3 Hz, 1H), 6.63 – 6.50 (m, 1H), 3.81 (s, 3H). *Analytic data is in accordance with literature data.*

Synthesis of *N*-tosylhydrazone 2a[6]



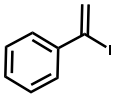
A solution of *p*-toluenesulfonylhydrazide (10 mmol, 1.0 equiv) in methanol (10 mL) was stirred and heated to 60 °C until the sulfonylhydrazide was completely dissolved. Then acetophenone (10 mmol, 1.0 equiv) was slowly added to the mixture. After the completion of the reaction, which was detected by TLC, the crude product was obtained as a white precipitate. The precipitates were then filtered, washed with a small quantity of MeOH and diethyl ether, and then were dried under vacuum to afford the corresponding pure *N*-tosylhydrazone **2a**. The full characterization of *(E)-4-methyl-N'-(1-phenylethylidene)benzenesulfonohydrazide* (***2a***)[7] was reported previously in literature.

General procedure (B) for preparation of iodostyrene derivatives 2c-f[8]

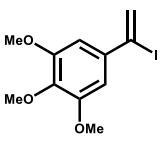


Ketone (20.0 mmol, 1.0 equiv) was solubilized in 20 mL of dry MeOH in a round bottom flask. Then, hydrazine monohydrate (3.0 equiv) was added, and the mixture was heated at 80 °C. After 3 hours, the solvent was removed under *vacuo*. The resulting solid was dissolved in 25 mL of DCM and 25 mL of water. The organic layer was separated, and the aqueous layer was extracted with DCM (3 x 25 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude resulting hydrazone was used for the second step without purification.

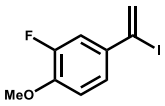
The hydrazone was solubilized in 15 mL of dry THF and 60 mL of triethylamine. The crude reaction was stirred at 0 °C in an ice bath. A solution of iodine (3.0 equiv) in dry THF (15 mL) was added dropwise for 30 min in the reaction mixture, in the dark at 0 °C. The reaction was then warmed up at room temperature, and the stirring was pursued for 3 hours. The reaction mixture was diluted with 100 mL of diethyl ether and quenched with a saturated aqueous solution of $Na_2S_2O_3$ (100 mL). The organic layer was separated, and the aqueous layer was extracted with diethyl ether (3 x 100 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with 0.1% triethylamine and petroleum ether/ethyl acetate (0 to 5% of ethyl acetate) as eluent to give the corresponding iodostyrene.



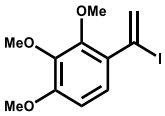
*1-(1-Iodoethenyl)benzene (**2c**).*[9] was prepared according to method B starting from acetophenone. Column chromatography on silica gel afforded 2.4 g of the product as a dark yellow oil (52% yield). N. B. The compound is highly sensitive to light and air. TLC (SiO_2, Cyclohexane/EtOAc: 95/5): R_f = 0.05; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.65 – 7.46 (m, 2H), 7.42 – 7.18 (m, 3H), 6.48 (s, 1H), 6.10 (s, 1H). *Analytic data is in accordance with literature data.*



*5-(1-Iodovinyl)-1,2,3-trimethoxybenzene (**2d**).*[10] was prepared according to method B starting from 1-(3,4,5-trimethoxyphenyl)ethan-1-one. Column chromatography on silica gel provided 4.5 g of the product as a bright yellow oil (70% yield). N. B.: The compound is highly sensitive to light and air. TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.59; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 6.85 (s, 2H), 6.56 (d, J = 1.9 Hz, 1H), 6.07 (d, J = 1.9 Hz, 1H), 3.86 (s, 6H), 3.75 (s, 3H); ^{13}C{1H}NMR (75 MHz, $(CD_3)_2CO$) δ 153.7 (2 C), 140.1, 137.9, 127.8 (2 C), 107.9, 106.9, 60.6, 56.6 (2 C). *Analytic data is in accordance with literature data.*

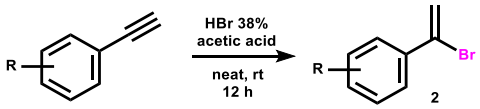


*2-Fluoro-4-(1-iodovinyl)-1-methoxybenzene (**2e**).*[11] was prepared according to method B starting from 1-(3-fluoro-4-methoxyphenyl)ethan-1-one. Column chromatography on silica gel provided 1.8 g of the product as a dark yellow oil (33% yield). N. B.: The compound is highly sensitive to light and air. TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.42; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.36-7.17 (m, 2H), 6.88 (m, 1H), 5.98 (d, J = 2.0 Hz, 1H), 5.66 (d, J = 2.0 Hz, 1H), 3.86 (s, 3H). *Analytic data is in accordance with literature data.*

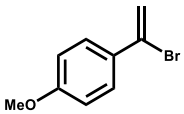


*1-(1-Iodovinyl)-2,3,4-trimethoxybenzene (**2f**).* was prepared according to method B starting from 1-(2,3,4-trimethoxyphenyl)ethan-1-one. Column chromatography on silica gel provided 4.0 g of the product as a bright yellow oil (65% yield). N. B.: The compound is highly sensitive to light and air. TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.62; ^{1}H NMR (200 MHz, $(CD_3)_2CO$) δ 6.96 (d, J = 8.8 Hz, 1H), 6.74 (d, J = 8.8 Hz, 1H), 6.23 (s, 1H), 6.09 (s, 1H), 3.91 (s, 3H), 3.86 (s, 3H), 3.80 (s, 3H). ^{13}C{^{1}H}NMR (75 MHz, $(CD_3)_2CO$) δ 155.5, 151.5, 143.1, 131.1, 130.4, 125.3, 107.9, 101.1, 61.0, 60.9, 56.4.

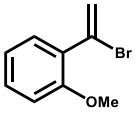
General procedure (C) for preparation of bromostyrene derivatives 2g-k[12]



In a 5 mL sealed tube, alkyne (3.0 mmol, 1.0 equiv) was dissolved in 600 µL of HBr (38% in acetic acid solution). The mixture was stirred at room temperature overnight. Then, 5 mL of a saturated aqueous solution of $NaHCO_3$ and 3 mL of DCM were added. The organic layer was separated, and the aqueous layer was extracted with DCM (3 x 5 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with 0.1% triethylamine and petroleum ether/ethyl acetate (0 to 5% of ethyl acetate) as eluent to give the corresponding bromostyrene.

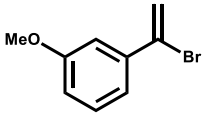


*1-(1-Bromovinyl)-4-methoxybenzene (**2g**).*[13] was prepared according to method C starting from 1-ethynyl-4-methoxybenzene. Column chromatography on silica gel provided 490 mg of the product as a yellow oil (76% yield). N. B.: The compound is highly sensitive to light and air. TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.25; ^{1}H NMR (200 MHz, $(CD_3)_2CO$) δ 7.59 (d, J = 8.9 Hz, 2H), 6.94 (d, J = 8.9 Hz, 2H), 6.15 (d, J = 2.2 Hz, 1H), 5.69 (d, J = 2.2 Hz, 1H), 3.83 (s, 3H). *Analytic data is in accordance with literature data.*

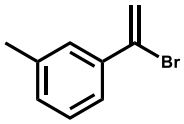


*1-(1-Bromovinyl)-2-methoxybenzene (**2h**).*[14] was prepared according to method C starting from 1-ethynyl-2-methoxybenzene. Column chromatography on silica gel afforded 480 mg of the product as a bright yellow oil (75% yield). N. B.: The compound is highly sensitive to light and air. TLC (SiO_2, 8/2 Cyclohexane/EtOAc: 8/2): R_f = 0.25; ^{1}H NMR (200 MHz, $(CD_3)_2CO$) δ 7.35 (t, J = 7.1 Hz, 2H), 7.10-

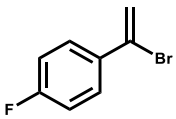
6.88 (m, 2H), 6.05–5.95 (m, 1H), 5.94–5.83 (m, 1H), 3.87 (s, 3H). *Analytic data is in accordance with literature data.*



*1-(1-Bromovinyl)-3-methoxybenzene (**2i**).*[15] was prepared according to method C starting from 1-ethynyl-3-methoxybenzene. Column chromatography on silica gel afforded 288 mg of the product as a yellow oil (45% yield). N. B.: The compound is highly sensitive to light and air. TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.32; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.35 – 7.10 (m, 3H), 6.89 (ddd, *J* = 7.9, 2.7, 1.5 Hz, 1H), 6.13 (d, *J* = 1.9 Hz, 1H), 5.79 (d, *J* = 1.9 Hz, 1H), 3.84 (s, 3H). ^{13}C{^{1}H}NMR (75 MHz, $(CD_3)_2CO$) *δ* 159.5, 140.1, 130.8, 129.4, 119.9, 118.0, 114.8, 113.3, 55.4. *Analytic data is in accordance with literature data.*

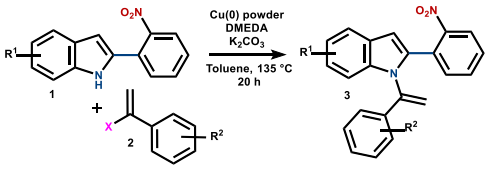


*1-(1-Bromovinyl)-3-methylbenzene (**2j**).*[14] was prepared according to method C starting from 1-ethynyl-3-methylbenzene. Column chromatography on silica gel provided 473 mg of the product as a brown oil (80% yield). N. B.: The compound is highly sensitive to light and air. TLC (SiO_2, Cyclohexane/EtOAc: 9/1): R_f = 0.65; ^{1}H NMR (200 MHz, $(CD_3)_2CO$) *δ* 7.61 – 7.38 (m, 2H), 7.33 – 7.06 (m, 2H), 6.25 (d, *J* = 2.2 Hz, 1H), 5.79 (d, *J* = 2.2 Hz, 1H), 2.36 (s, 3H). *Analytic data is in accordance with literature data.*



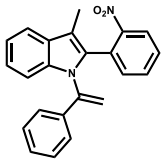
*1-(1-Bromovinyl)-4-fluorobenzene (**2k**).*[14] was prepared according to method C starting from 1-ethynyl-4-fluorobenzene. Column chromatography on silica gel afforded 229 mg of the product as a brown oil (38% yield). N. B.: The compound is highly sensitive to light and air. TLC (SiO_2, Cyclohexane/EtOAc: 9/1): R_f = 0.43; ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 7.73 – 7.39 (m, 2H), 7.04 (t, *J* = 8.6 Hz, 2H), 6.06 (d, *J* = 2.0 Hz, 1H), 5.77 (d, *J* = 2.0 Hz, 1H). *Analytic data is in accordance with literature data.*

General procedure (D) for preparation of *N*-Vinylazole compounds 3a-q

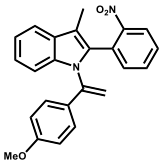


In a sealed tube under argon atmosphere, 2-(2-nitrophenyl)-1*H*-indole derivative (**1**) (0.2 mmol, 1.0 equiv), copper powder (10 mol%), and K_2CO_3 (1.5 equiv) were solubilized in dry toluene (0.8 mL). Then, *N*,*N'*-dimethylethylenediamine (DMEDA) (20 mol%), and the corresponding styrene (**2**) (2.0 equiv) were added. The sealed tube was stirred at 135 °C for 20 hours.

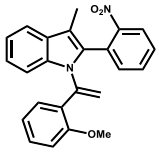
After the reaction was completed, the mixture was filtered through a Celite© pad and concentrated under reduced pressure. The crude product was finally purified by silica gel chromatography using cyclohexane/ethyl acetate (0 to 15% of ethyl acetate) as eluent, resulting in the corresponding *N*-vinylazole.



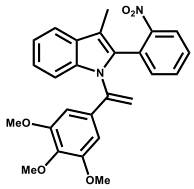
*3-Methyl-2-(2-nitrophenyl)-1-(1-phenylvinyl)-1H-indole (**3a**).* was prepared according to method D starting from 3-methyl-2-(2-nitrophenyl)-1*H*-indole (**1a**) and 1-(1-iodoethenyl)benzene (**2c**). Column chromatography on silica gel provided 60 mg of the product as an orange powder (85% yield), mp = 157-159 °C. TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.34; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 8.03 – 7.93 (m, 1H), 7.69 – 7.63 (m, 1H), 7.61 – 7.54 (m, 2H), 7.45 – 7.36 (m, 1H), 7.29 – 7.20 (m, 3H), 7.19 – 7.06 (m, 5H), 5.79 (s, 1H), 5.29 (s, 1H), 2.20 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 143.9, 138.7, 138.2 (2 C), 134.6, 133.4, 130.4, 129.7, 129.6, 129.2 (3 C), 127.7, 126.9 (2 C), 125.1, 123.6, 120.9, 119.9, 114.0, 112.7, 111.9, 9.2; HRMS [ESI-TOF] $[M + H]^+$ *m/z* calcd for $C_{23}H_{19}N_2O_2$ 355.1446, found 355.1443.



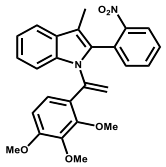
*1-(1-(4-Methoxyphenyl)vinyl)-3-methyl-2-(2-nitrophenyl)-1H-indole (**3b**).* was prepared according to method D starting from 3-methyl-2-(2-nitrophenyl)-1*H*-indole (**1a**) and 1-(1-bromovinyl)-4-methoxybenzene (**2g**). Column chromatography on silica gel provided 60 mg of the product as a yellow oil (78% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.50; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 8.00 (dd, J = 7.0, 2.4 Hz, 1H), 7.69 – 7.53 (m, 3H), 7.42 (dd, J = 6.5, 2.6 Hz, 1H), 7.18 – 7.07 (m, 3H), 7.03 (dt, J = 9.7, 2.9 Hz, 2H), 6.77 (dt, J = 9.7, 2.9 Hz, 2H), 5.65 (s, 1H), 5.14 (s, 1H), 3.76 (s, 3H), 2.20 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 161.3 (2 C), 143.5, 138.7, 134.6, 133.4 (2 C), 130.6, 130.4, 129.6, 128.3 (2 C), 127.9, 125.1, 123.5, 120.9, 119.9, 114.7, 112.6, 112.0 (2 C), 112.0, 55.6, 9.3; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{24}H_{21}N_2O_3$ 385.1552, found 385.1552.



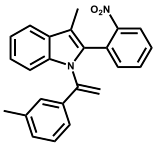
*1-(1-(2-Methoxyphenyl)vinyl)-3-methyl-2-(2-nitrophenyl)-1H-indole (**3c**).* was prepared according to method D starting from 3-methyl-2-(2-nitrophenyl)-1*H*-indole (**1a**) and 1-(1-bromovinyl)-2-methoxybenzene (**2h**). Column chromatography on silica gel provided 61 mg of the product as a bright yellow oil (79% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.49; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 8.88 – 8.72 (m, 1H), 8.46 – 8.37 (m, 1H), 8.37 – 8.27 (m, 2H), 8.08 (dt, J = 7.0, 2.1 Hz, 2H), 7.99 – 7.87 (m, 3H), 7.59 (d, J = 8.3 Hz, 1H), 7.46 (d, J = 4.4 Hz, 2H), 6.49 (s, 1H), 6.26 (s, 1H), 4.28 (s, 3H), 2.93 (s, 3H); ^{13}C{1H} NMR (75 MHz, $(CD_3)_2CO$) δ 158.1 (2 C), 140.5, 134.6, 133.2, 130.6, 130.1, 130.0, 129.5, 128.1, 127.4, 125.0, 123.3, 120.9, 120.5 (2 C), 119.6, 116.6 (2 C), 112.2, 111.9, 111.8, 55.8, 9.1; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{24}H_{21}N_2O_3$ 385.1552, found 385.1550.



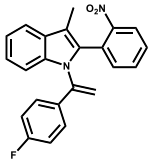
3-Methyl-2-(2-nitrophenyl)-1-(1-(3,4,5-trimethoxyphenyl)vinyl)-1H-indole ***(3d)***. was prepared according to method D starting from 3-methyl-2-(2-nitrophenyl)-1*H*-indole (**1a**) and 5-(1-iodovinyl)-1,2,3-trimethoxybenzene (**2d**). Column chromatography on silica gel afforded 83 mg of the product as a yellow solid (93% yield), mp = 174-176 °C. TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.86; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 8.00 (dd, J = 7.9, 1.5 Hz, 1H), 7.74 – 7.54 (m, 3H), 7.50 (dd, J = 7.5, 1.5 Hz, 1H), 7.23 – 7.08 (m, 3H), 6.37 (s, 2H), 5.70 (s, 1H), 5.18 (s, 1H), 3.69 (s, 3H), 3.64 (s, 6H), 2.21 (s, 3H). ^{13}C{1H} NMR (75 MHz, $(CD_3)_2CO$) δ 154.2 (2 C), 144.0, 140.2, 135.0, 133.8, 133.5, 132.0, 130.4, 129.7, 128.0, 125.2, 123.6, 121.0, 119.9, 112.9 (2 C), 112.1 (2 C), 107.0, 105.1 (2 C), 60.6, 56.4 (2 C), 9.3; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{26}H_{25}N_2O_5$ 445.1763, found 445.1765.



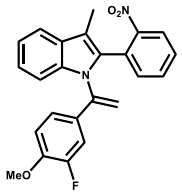
3-Methyl-2-(2-nitrophenyl)-1-(1-(2,3,4-trimethoxyphenyl)vinyl)-1H-indole ***(3e)***. was prepared according to method D starting from 3-methyl-2-(2-nitrophenyl)-1*H*-indole (**1a**) and 1-(1-iodovinyl)-2,3,4-trimethoxybenzene (**2f**). Column chromatography on silica gel afforded 46 mg of the product as a yellow powder (52% yield), mp = 170-172 °C. TLC (SiO_2, Cyclohexane/EtOAc: 7/3): R_f = 0.57; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 8.05 – 7.95 (m, 1H), 7.67 – 7.53 (m, 3H), 7.42 – 7.32 (m, 1H), 7.34 – 7.28 (m, 1H), 7.21 – 7.16 (m, 1H), 7.16 – 7.10 (m, 1H), 6.50 (d, J = 8.8 Hz, 1H), 6.37 (d, J = 8.7 Hz, 1H), 5.66 (s, 1H), 5.37 (s, 1H), 3.77 (s, 3H), 3.70 (s, 3H), 3.24 (s, 3H), 2.16 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 155.4, 152.6, 150.8, 143.2, 140.9, 138.7, 134.7, 133.3, 132.9, 130.2, 129.5, 128.2, 125.1 (2 C), 124.8, 123.4, 120.6, 119.7, 115.6, 112.2, 111.9, 108.0, 60.7, 60.4, 56.3, 9.2; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{26}H_{25}N_2O_5$ 445.1763, found 445.1761.



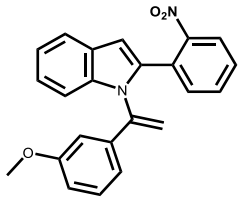
*3-Methyl-2-(2-nitrophenyl)-1-(1-(m-tolyl)vinyl)-1H-indole (**3f**).* was prepared according to method D starting from 3-methyl-2-(2-nitrophenyl)-1*H*-indole (**1a**) and 1-(1-bromovinyl)-3-methylbenzene (**2j**). Column chromatography on silica gel provided 60 mg of the product as a brown oil (82% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.37; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 7.98 (dd, J = 6.9, 2.6 Hz, 1H), 7.68 – 7.61 (m, 1H), 7.61 – 7.51 (m, 2H), 7.41 (dd, J = 6.2, 2.9 Hz, 1H), 7.19 – 7.10 (m, 3H), 7.09 – 7.03 (m, 2H), 6.94 (s, 1H), 6.89 – 6.83 (m, 1H), 5.76 (s, 1H), 5.27 (s, 1H), 2.20 (s, 3H), 2.19 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 144.0 (2 C), 138.8, 138.2, 134.6, 133.3, 130.4, 130.3 (2 C), 129.6, 129.1, 127.8, 127.4, 125.1, 124.1, 123.5, 120.9, 119.9, 113.7, 112.7, 111.9 (2 C), 21.2, 9.3; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{24}H_{21}N_2O_2$ 369.1603, found 369.1600.



*1-(1-(4-Fluorophenyl)vinyl)-3-methyl-2-(2-nitrophenyl)-1H-indole (**3g**).* was prepared according to method D starting from 3-methyl-2-(2-nitrophenyl)-1*H*-indole (**1a**) and 1-(1-bromovinyl)-4-fluorobenzene (**2k**). Column chromatography on silica gel provided 45 mg of the product as a brown oil (60% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.42; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 8.04 – 7.92 (m, 1H), 7.73 – 7.53 (m, 3H), 7.47 – 7.36 (m, 1H), 7.22 – 7.04 (m, 5H), 6.96 (ddd, J = 8.9, 6.8, 2.3 Hz, 2H), 5.77 (s, 1H), 5.29 (s, 1H), 2.20 (s, 3H); ^{13}C{1H} NMR (75 MHz, $(CD_3)_2CO$) δ 163.9 (d, J = 247.2 Hz), 142.5, 133.8, 133.5, 133.2, 130.4, 129.8, 129.7, 129.0, 128.9, 128.4, 124.9, 123.7, 121.8, 121.6, 119.8, 116.2, 115.9, 114.8, 112.9, 112.0, 105.7, 9.1; ^{19}F{^{1}H} NMR (188 MHz, $(CD_3)_2CO$) δ -114.22 (ddd, J = 14.2, 8.7, 5.5 Hz); HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{23}H_{18}FN_2O_2$ 373.1352, found 373.1353.

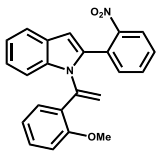


*1-(1-(3-Fluoro-4-methoxyphenyl)vinyl)-3-methyl-2-(2-nitrophenyl)-1H-indole (**3h**).* was prepared according to method D starting from 3-methyl-2-(2-nitrophenyl)-1*H*-indole (**1a**) and 2-fluoro-4-(1-iodovinyl)-1-methoxybenzene (**2e**). Column chromatography on silica gel provided 33 mg of the product as a bright yellow oil (41% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.55; ^{1}H NMR (200 MHz, $(CD_3)_2CO$) δ 7.98 (d, J = 7.2 Hz, 1H), 7.69 – 7.54 (m, 3H), 7.44 (d, J = 6.8 Hz, 1H), 7.20 – 7.05 (m, 3H), 6.99 – 6.67 (m, 3H), 5.71 (s, 1H), 5.18 (s, 1H), 3.81 (s, 3H), 2.17 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 152.8 (d, J = 244.9 Hz), 149.2 (d, J = 10.6 Hz), 150.8, 142.5, 138.6, 134.6, 133.4 (2 C), 133.2, 131.1 (d, J = 6.1 Hz), 130.5, 129.6, 127.7, 125.2, 123.3 (d, J = 3.0 Hz), 121.0, 119.9, 114.5, 114.3, 113.3, 112.9, 111.9, 56.6, 9.3; ^{19}F{^{1}H} NMR (188 MHz, $(CD_3)_2CO$) δ -136.26 (dd, J = 11.8, 8.5 Hz); HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{24}H_{20}FN_2O_3$ 403.1458, found 403.1460.

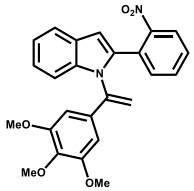


*1-(1-(3-Methoxyphenyl)vinyl)-2-(2-nitrophenyl)-1H-indole (**3i**).* The reaction was conducted with 2-(2-nitrophenyl)-1*H*-indole **1b** (1.9 mmol, 1.0 equiv), 1-(1-bromovinyl)-3-methoxybenzene **2i** (2.4 mmol, 1.3 equiv), Cu(0) (20 mol%), DMEDA (40 mol%), K_2CO_3 (1.5 equiv), 7.2 mL of dry toluene in a sealed tube under argon for 20 hours at 135 °C. Column chromatography on silica gel with petroleum ether/ethyl acetate eluent (0 to 50% of ethyl acetate) afforded 242 mg of the product as an orange oil (42%). TLC (SiO_2, Petroleum ether/EtOAc: 8/2): R_f = 0.27; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 – 7.65 (m, 1H), 7.64 – 7.53 (m, 1H), 7.32 – 7.17 (m, 3H), 7.17 – 7.01 (m, 3H), 6.97 (t, J = 7.9 Hz, 1H), 6.69 – 6.59 (m, 2H), 6.58 – 6.45 (m, 2H), 5.66 (s, 1H), 5.25 (s, 1H), 3.58 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 159.7, 149.4, 142.7, 138.7, 138.7, 135.7, 133.0, 132.0, 129.5, 128.9, 128.3, 127.8, 124.1,

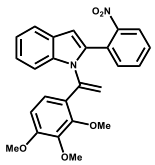
123.0, 121.1, 120.9, 118.8, 114.7, 114.3, 111.7, 111.6, 105.2, 55.4; HRMS [ESI-TOF] $[M + H]^+$ *m/z* calcd for $C_{23}H_{19}N_2O_3$ 371.1396, found 371.1393.



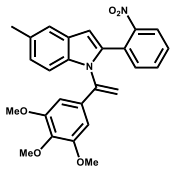
*1-(1-(2-Methoxyphenyl)vinyl)-2-(2-nitrophenyl)-1H-indole (**3j**).* was prepared according to method D starting from 2-(2-nitrophenyl)-1*H*-indole **1b** and 1-(1-bromovinyl)-2-methoxybenzene (**2h**). Column chromatography on silica gel provided 48 mg of the product as yellow oil (65% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.39; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 7.94 – 7.85 (m, 1H), 7.70 – 7.58 (m, 1H), 7.55 – 7.46 (m, 2H), 7.42 – 7.29 (m, 2H), 7.23 – 7.08 (m, 3H), 6.81 (d, *J* = 8.4 Hz, 1H), δ 6.70 (d, *J* = 0.6 Hz, 1H), 6.69 – 6.66 (m, 1H), 6.62 (d, *J* = 0.6 Hz, 1H), 5.81 (s, 1H), 5.53 (s, 1H), 3.49 (s, 3H); ^{13}C{1H} NMR (75 MHz, $(CD_3)_2CO$) δ 158.1 (2 C), 140.4, 136.3, 133.8, 132.9, 131.6, 130.8, 130.1, 129.9, 129.2, 128.5, 127.1, 124.7, 123.3, 121.5, 121.2, 121.0, 117.4, 112.2, 112.0, 105.0, 55.8; HRMS [ESI-TOF] $[M + H]^+$ *m/z* calcd for $C_{23}H_{19}N_2O_3$ 371.1396, found 371.1396.



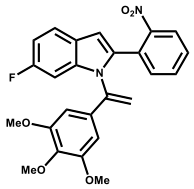
*2-(2-Nitrophenyl)-1-(1-(3,4,5-trimethoxyphenyl)vinyl)-1H-indole (**3k**).* was prepared according to method D starting from 2-(2-nitrophenyl)-1*H*-indole **1b** and 5-(1-iodovinyl)-1,2,3-trimethoxybenzene (**2d**). Column chromatography on silica gel afforded 67 mg of the product as a yellow solid (78% yield), mp = 134-136 °C. TLC (SiO_2, 8/2 Cyclohexane/EtOAc: 8/2): R_f = 0.54; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 7.92 (d, *J* = 8.1 Hz, 1H), 7.69 (dd, *J* = 5.8, 2.7 Hz, 1H), 7.65 – 7.49 (m, 3H), 7.26 (d, *J* = 6.9 Hz, 1H), 7.22 – 7.10 (m, 2H), 6.78 (s, 1H), 6.40 (s, 2H), 5.86 (s, 1H), 5.29 (s, 1H), 3.70 (s, 3H), 3.66 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 154.2 (2 C), 150.3, 143.6 (2 C), 140.2, 139.5, 136.7, 134.0, 133.4, 133.2, 130.2, 129.2, 128.2, 124.9, 123.6, 121.7, 121.6, 113.8, 112.2, 105.8, 105.0 (2 C), 60.6, 56.4; HRMS [ESI-TOF] $[M + H]^+$ *m/z* calcd for $C_{25}H_{23}N_2O_5$ 431.1607, found 430.1610.



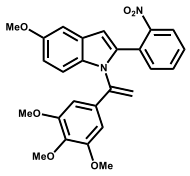
*2-(2-Nitrophenyl)-1-(1-(2,3,4-trimethoxyphenyl)vinyl)-1H-indole (**3l**).* was prepared according to method D starting from 2-(2-nitrophenyl)-1*H*-indole **1b** and 1-(1-iodovinyl)-2,3,4-trimethoxybenzene (**2f**). Column chromatography on silica gel provided 40 mg of the product as a yellow solid (46% yield), mp = 130-132 °C. TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.39; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 7.94 (d, J = 8.1 Hz, 1H), 7.73 (d, J = 4.2 Hz, 2H), 7.57 (dt, J = 8.4, 4.2 Hz, 1H), 7.45 (d, J = 3.2 Hz, 1H), 7.40 (d, J = 3.2 Hz, 1H), 7.27 – 7.01 (m, 4H), 6.85 (d, J = 8.4 Hz, 1H), 5.51 (s, 1H), 5.45 (s, 1H), 3.89 (s, 3H), 3.76 (s, 3H), 3.39 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, CD_2Cl_2) δ 155.7, 152.7, 143.2, 142.8, 136.9, 133.3, 132.7, 132.1, 129.5, 128.0, 127.7, 125.4, 124.7, 123.3, 121.4, 119.4, 113.6, 112.8, 111.8, 109.7, 107.8, 104.4, 61.1, 61.0, 56.5; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{25}H_{23}N_2O_5$ 431.1607, found 431.1606.



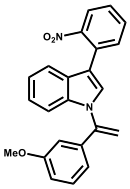
*5-Methyl-2-(2-nitrophenyl)-1-(1-(3,4,5-trimethoxyphenyl)vinyl)-1H-indole (**3m**).* was prepared according to method D starting from 5-methyl-2-(2-nitrophenyl)-1*H*-indole (**1d**) and 5-(1-iodovinyl)-1,2,3-trimethoxybenzene (**2d**). Column chromatography on silica gel afforded 73 mg of the product as a yellow solid (82% yield), mp = 157-159 °C. TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.64; ^{1}H NMR (200 MHz, $(CD_3)_2CO$) δ 7.97 – 7.77 (m, 1H), 7.72 – 7.50 (m, 3H), 7.45 (s, 1H), 7.11 (d, J = 8.4 Hz, 1H), 7.00 (d, J = 8.3 Hz, 1H), 6.66 (s, 1H), 6.39 (s, 2H), 5.80 (s, 1H), 5.22 (s, 1H), 3.68 (s, 3H), 3.65 (s, 6H), 2.42 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 154.3 (2 C), 143.9, 140.3, 138.1, 136.7, 134.0, 133.6, 133.2, 130.7, 130.2, 129.5, 128.3, 125.2, 124.8, 121.4, 113.4 (2 C), 112.0, 105.5, 105.1 (2 C), 60.6, 56.5 (2 C), 21.4; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{26}H_{25}N_2O_5$ 445.1763, found 445.1773.



*6-Fluoro-2-(2-nitrophenyl)-1-(1-(3,4,5-trimethoxyphenyl)vinyl)-1H-indole (**3n**).* was prepared according to method D starting from 6-fluoro-2-(2-nitrophenyl)-1*H*-indole (**1e**) and 5-(1-iodovinyl)-1,2,3-trimethoxybenzene (**2d**). Column chromatography on silica gel afforded 80 mg of the product as a yellow solid (89% yield), mp = 126-128 °C. TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.76; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 7.92 (dd, J = 7.1, 2.3 Hz, 1H), 7.75 – 7.46 (m, 4H), 7.11 – 6.88 (m, 2H), 6.77 (s, 1H), 6.37 (s, 2H), 5.86 (s, 1H), 5.30 (s, 1H), 3.68 (s, 3H), 3.66 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 161.0 (d, J = 237.4 Hz), 154.3 (2 C), 141.9 (d, J = 235.3 Hz), 139.7, 139.5, 137.5, 134.0, 133.3, 133.1, 130.4, 127.9, 125.7, 124.9, 122.9 (d, J = 10.0 Hz), 114.1 (2 C), 110.1 (d, J = 24.6 Hz), 105.8, 105.0 (2 C), 98.5 (d, J = 27.2 Hz), 60.6, 56.4 (2 C); ^{19}F{1H} NMR (188 MHz, $(CD_3)_2CO$) δ 120.40 (td, J = 9.9, 5.4 Hz); HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{25}H_{22}FN_2O_5$ 449.1513, found 449.1518.

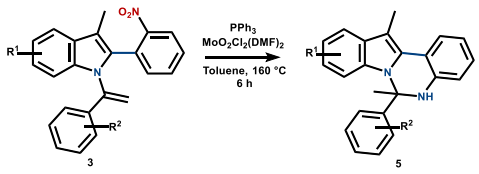


*5-Methoxy-2-(2-nitrophenyl)-1-(1-(3,4,5-trimethoxyphenyl)vinyl)-1H-indole (**3o**).* was prepared according to method D starting from 5-methoxy-2-(2-nitrophenyl)-1*H*-indole (**1f**) and 5-(1-iodovinyl)-1,2,3-trimethoxybenzene (**2d**). Column chromatography on silica gel provided 90 mg of the product as a dark viscous yellow oil (98% yield). TLC (SiO_2, Cyclohexane/EtOAc: 7/3): R_f = 0.64; ^{1}H NMR (200 MHz, $(CD_3)_2CO$) δ 7.89 (dd, J = 7.5, 2.4 Hz, 1H), 7.66 – 7.43 (m, 3H), 7.17 (d, J = 2.5 Hz, 1H), 7.11 (d, J = 9.0 Hz, 1H), 6.82 (dd, J = 9.0, 2.5 Hz, 1H), 6.68 (s, 1H), 6.41 (s, 2H), 5.78 (s, 1H), 5.21 (s, 1H), 3.83 (s, 3H), 3.69 (s, 3H), 3.66 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 155.9, 154.2 (2 C), 143.9, 137.0, 134.8, 133.9, 133.5 (2 C), 133.1, 130.1, 129.7 (2 C), 128.3, 124.8, 113.8, 113.3, 113.0, 105.7, 105.0 (2 C), 103.2, 60.6, 56.4 (2 C), 55.9; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{26}H_{25}N_2O_6$ 461.1713 found, 461.1713.



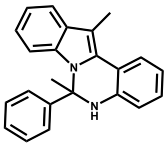
*1-(1-(3-Methoxyphenyl)vinyl)-3-(2-nitrophenyl)-1H-indole (**3q**)*. The reaction was conducted with 3-(2-nitrophenyl)-1*H*-indole (**1c**) (1.9 mmol, 1.0 equiv), 1-(1-bromovinyl)-3-methoxybenzene **2i** (2.4 mmol, 1.3 equiv), Cu(0) (20 mol%), DMEDA (40 mol%), K_2CO_3 (1.5 equiv), 7.2 mL of dry toluene in a sealed tube under argon for 20 hours at 135 °C. Column chromatography on silica gel with petroleum ether/ethyl acetate eluent (0 to 50% of ethyl acetate) afforded 585 mg of the product as an orange oil (83%). TLC (SiO_2, Petroleum ether/EtOAc: 8/2): R_f = 0.42; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 – 7.71 (m, 1H), 7.60 – 7.45 (m, 2H), 7.44 – 7.38 (m, 1H), 7.35 – 7.29 (m, 1H), 7.20 (d, J = 4.1 Hz, 1H), 7.17 – 7.12 (m, 2H), 7.10 – 7.02 (m, 2H), 6.88 – 6.79 (m, 2H), 6.76 (dd, J = 2.5, 1.7 Hz, 1H), 5.56 (d, J = 0.6 Hz, 1H), 5.34 (d, J = 0.6 Hz, 1H), 3.65 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 160.0, 150.1, 144.5 (2 C), 138.2, 136.8, 132.7, 132.1, 129.9, 128.9, 127.7, 127.5, 124.2, 123.0, 121.2, 119.6, 119.1, 115.3, 113.2, 112.4, 112.3, 109.2, 55.4; HRMS [ESI-TOF] $[M + H]^+$ *m/z* calcd for $C_{23}H_{19}N_2O_3$ 371.1396, found 371.1394.

General procedure (E) for Cadogan-like cyclization: synthesis of compounds 5a-h

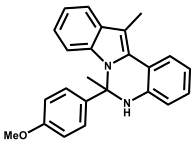


In a sealed tube, 2-(2-nitrophenyl)-1-(1-aryllvinyl)-1*H*-indole (**3**) (0.1 mmol, 1.0 equiv), $MoO_2Cl_2(DMF)_2$ (5 mol%) and PPh_3 (2.4 equiv) were dissolved in toluene (3.0 mL). Next, the solution was degassed with an argon balloon from -196 °C in liquid nitrogen to room temperature before being warmed at 160 °C for 6 hours. After completion, the mixture reaction was filtered through a Celite© pad, and concentrated under reduced pressure. Finally, the crude product was purified by silica gel

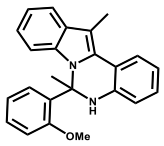
chromatography with cyclohexane/ethyl acetate as eluent (0 to 20% of ethyl acetate) to give the corresponding compounds 5,6-dihydroindolo[1,2-*c*]quinazoline derivatives (**5**).



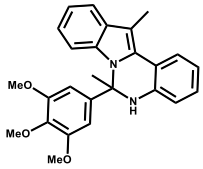
*6,12-Dimethyl-6-phenyl-5,6-dihydroindolo[1,2-c]quinazoline (**5a**).* was prepared according to method E starting from **3a.** Column chromatography on silica gel provided 31 mg of the product as a white oil (95% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.32; ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 7.82 (d, J = 7.3 Hz, 1H), 7.58 (ddd, J = 8.0, 1.2, 0.8 Hz, 1H), 7.46 – 7.43 (m, 1H), 7.42 (d, J = 2.3 Hz, 1H), 7.34 – 7.29 (m, 3H), 7.08 (ddd, J = 8.0, 7.3, 1.4 Hz, 1H), 7.00 (ddd, J = 8.0, 7.0, 0.9 Hz, 1H), 6.90 (dd, J = 8.0, 0.8 Hz, 1H), 6.90 – 6.81 (m, 2H), 6.69 (dt, J = 8.5, 0.8 Hz, 1H), 6.15 (br s, 1H), 2.63 (s, 3H), 2.17 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $(CD_3)_2CO$) δ 145.6, 142.2, 135.4, 131.4, 131.0, 129.4, 129.2, 129.1, 129.0, 128.5, 127.7, 125.7, 122.2, 119.8, 119.7, 119.1, 118.4, 116.0, 112.6, 107.0, 74.7, 26.8, 11.1; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{23}H_{21}N_2$ 325.1705, found 325.1701.



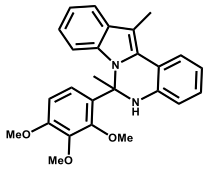
*6-(4-Methoxyphenyl)-6,12-dimethyl-5,6-dihydroindolo[1,2-c]quinazoline (**5b**).* was prepared according to method E starting from **3b.** Column chromatography on silica gel provided 21 mg of the product as a bright yellow oil (60% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.57; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 7.83 (d, J = 7.9 Hz, 1H), 7.56 (d, J = 7.9 Hz, 1H), 7.46 – 7.35 (m, 2H), 7.08 (td, J = 8.0, 7.3, 1.4 Hz, 1H), 6.98 (ddd, J = 7.9, 7.0, 0.9 Hz, 1H), 6.93 – 6.77 (m, 5H), 6.58 (d, J = 8.4 Hz, 1H), 5.98 (br s, 1H), 3.79 (s, 3H), 2.63 (s, 3H), 2.09 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 160.7, 142.3, 137.3, 135.3, 131.4, 131.0, 129.2 (2 C), 128.5, 125.7, 122.1, 119.7, 119.6, 119.0, 118.3, 116.0, 114.4 (2 C), 112.6, 106.9, 74.3, 55.6, 26.2, 11.1; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{24}H_{23}N_2O$ 355.1810, found 355.1816.



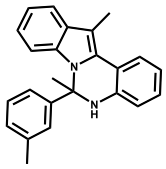
*6-(2-Methoxyphenyl)-6,12-dimethyl-5,6-dihydroindolo[1,2-c]quinazoline (**5c**).* was prepared according to method E starting from **3c.** Column chromatography on silica gel provided 21 mg of the product as a white oil (59% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.53; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 7.70 (d, J = 7.8 Hz, 1H), 7.71 – 7.62 (m, 1H), 7.60 – 7.54 (m, 1H), 7.17 – 7.04 (m, 3H), 7.00 (d, J = 7.2 Hz, 1H), 6.98 – 6.95 (m, 1H), 6.82 (d, J = 7.8 Hz, 1H), 6.77 (td, J = 7.5, 1.3 Hz, 1H), 6.48 (td, J = 7.5, 1.3 Hz, 1H), 6.27 (br s, 1H), 5.71 (dd, J = 7.8, 1.6 Hz, 1H), 4.01 (s, 3H), 2.63 (s, 3H), 2.54 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 157.1, 142.9, 136.0, 133.1, 131.3, 131.0, 130.0, 128.4, 127.8, 125.7, 122.7, 120.9, 120.0 (2 C), 119.4, 119.0, 115.9, 113.1, 112.8, 107.0, 75.5, 56.2, 27.6, 11.0; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{24}H_{23}N_2O$ 355.1810, found 355,1816.



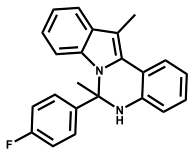
*6,12-Dimethyl-6-(3,4,5-trimethoxyphenyl)-5,6-dihydroindolo[1,2-c]quinazoline (**5d**).* was prepared according to method E starting from **3d**. Column chromatography on silica gel provided 37 mg of the product as a colorless oil (89% yield). TLC (SiO_2, Cyclohexane/EtOAc: 6/4): R_f = 0.64; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 7.83 (d, J = 7.9 Hz, 1H), 7.57 (ddd, J = 7.9, 1.2, 0.7 Hz, 1H), 7.09 (ddd, J = 8.0, 7.3, 1.4 Hz, 1H), 7.01 (ddd, J = 8.0, 6.9, 1.2 Hz, 1H), 6.95 – 6.92 (m, 1H), 6.89 (ddd, J = 6.9, 2.3, 1.1 Hz, 1H), 6.87 – 6.83 (m, 1H), 6.81 (dt, J = 8.4, 0.9 Hz, 1H), 6.77 (s, 2H), 6.13 (br s, 1H), 3.71 (s, 3H), 3.65 (s, 6H), 2.63 (s, 3H), 2.15 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 154.2 (2 C), 142.3, 140.9, 139.4, 135.6, 131.4, 131.2, 128.5, 125.8, 122.3, 119.9, 119.8, 119.0, 118.5, 116.1, 112.7, 107.2, 105.9 (2 C), 74.9, 60.6, 56.5 (2 C), 27.0, 11.2; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{26}H_{27}N_2O_3$ 415.2022, found 415.2021.



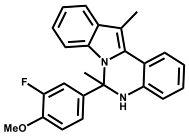
*6,12-Dimethyl-6-(2,3,4-trimethoxyphenyl)-5,6-dihydroindolo[1,2-c]quinazoline (**5e**).* was prepared according to method E starting from **3e**. Column chromatography on silica gel provided 30 mg of the product as a bright yellow oil (72% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.56; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 7.75 (d, J = 7.8 Hz, 1H), 7.69 – 7.58 (m, 1H), 7.54 – 7.37 (m, 1H), 7.15 – 6.96 (m, 3H), 6.84 (d, J = 8.1 Hz, 1H), 6.79 (t, J = 8.1 Hz, 1H), 6.30 (d, J = 8.8 Hz, 1H), 6.05 (br s, 1H), 5.59 (d, J = 8.8 Hz, 1H), 3.98 (s, 3H), 3.73 (s, 3H), 3.67 (s, 3H), 2.63 (s, 3H), 2.47 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 154.8, 152.0, 143.5, 142.5, 135.7, 131.1, 131.0, 130.0, 128.4, 125.7, 122.5, 122.0, 119.9, 119.7, 119.2, 118.6, 115.9, 113.0, 110.9, 106.7, 74.8, 61.5, 60.5, 56.0, 27.5, 11.1; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{26}H_{27}N_2O_3$ 415.2022, found 415.2024.



*6,12-Dimethyl-6-(m-tolyl)-5,6-dihydroindolo[1,2-c]quinazoline (**5f**).* was prepared according to method E starting from **3f**. Column chromatography on silica gel provided 18 mg of the product as a brown oil (53% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.42; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 7.83 (d, J = 7.9 Hz, 1H), 7.56 (dt, J = 7.9, 0.9 Hz, 1H), 7.41 – 7.33 (m, 1H), 7.24 – 7.18 (m, 1H), 7.18 – 7.12 (m, 1H), 7.11 – 7.03 (m, 2H), 6.98 (ddd, J = 8.0, 6.0, 0.9 Hz, 1H), 6.93 – 6.79 (m, 3H), 6.64 (dt, J = 8.4, 0.8 Hz, 1H), 6.04 (br s, 1H), 2.63 (s, 3H), 2.27 (s, 3H), 2.13 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 145.4, 142.2, 138.7, 131.4, 129.8, 129.0, 128.5, 128.4, 127.2, 125.7, 124.9, 123.9, 122.1, 119.8, 119.6, 119.0, 118.3, 115.9, 112.6, 107.0, 74.5, 26.5, 21.5, 11.1; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{24}H_{23}N_2$ 339.1861, found 339.1857.

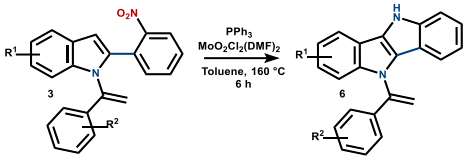


*6-(4-Fluorophenyl)-6,12-dimethyl-5,6-dihydroindolo[1,2-c]quinazoline (**5g**).* was prepared according to method E starting from **3g**. Column chromatography on silica gel provided 23 mg of the product as a colorless oil (67% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.53; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 7.83 (d, J = 7.8 Hz, 1H), 7.58 (d, J = 7.8 Hz, 1H), 7.47 (dd, J = 8.9, 5.4 Hz, 2H), 7.16 – 7.04 (m, 3H), 7.04 – 6.97 (m, 1H), 6.92 – 6.82 (m, 3H), 6.69 (d, J = 8.4 Hz, 1H), 6.15 (br s, 1H), 2.63 (s, 3H), 2.17 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 163.4 (d, J = 246.0 Hz), 142.0, 141.8, 141.8, 135.2, 132.2, 131.4, 130.9, 129.9 (d, J = 8.2 Hz), 128.6, 125.7, 122.3, 119.9, 119.8, 119.1, 118.3, 116.0 (d, J = 8.5 Hz), 115.6, 112.5, 107.2, 74.3, 26.7, 11.0; ^{19}F{^{1}H} NMR (188 MHz, $(CD_3)_2CO$) δ -115.71 (tt, J = 8.8, 5.4 Hz); HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{23}H_{20}FN_2$ $[M + H]^+$ 343.1611, found 343.1616.

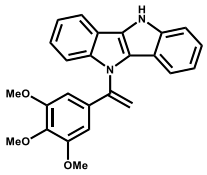


*6-(3-Fluoro-4-methoxyphenyl)-6,12-dimethyl-5,6-dihydroindolo[1,2-c]quinazoline (**5h**).* was prepared according to method E starting from **3h**. Column chromatography on silica gel provided 19 mg of the product as a colorless oil (51% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.67; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 7.82 (d, J = 7.9 Hz, 1H), 7.59 (ddd, J = 7.9, 1.2, 0.7 Hz, 1H), 7.19 (dd, J = 12.8, 2.3 Hz, 1H), 7.15 – 7.10 (m, 1H), 7.10 – 7.05 (m, 1H), 7.05 – 7.02 (m, 1H), 7.00 (dd, J = 5.6, 1.4 Hz, 1H), 6.96 – 6.83 (m, 3H), 6.78 (dd, J = 8.4, 0.8 Hz, 1H), 6.12 (br s, 1H), 3.86 (s, 3H), 2.63 (s, 3H), 2.16 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 152.9 (d, J = 244.6 Hz), 148.5 (d, J = 10.7 Hz), 142.0, 138.6 (d, J = 4.6 Hz), 135.3, 131.4, 130.9, 128.56, 125.7, 123.6 (d, J = 3.2 Hz), 122.4, 119.9, 119.9, 119.1, 118.4, 116.0, 115.5 (d, J = 19.5 Hz), 113.9, 112.5, 107.2, 74.2, 56.5, 26.8, 11.0; ^{19}F{^{1}H} NMR (188 MHz, $(CD_3)_2CO$) δ -136.26 (dd, J = 12.2, 8.1 Hz); HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{24}H_{22}FN_2O$ 373.1716, found 373.1718.

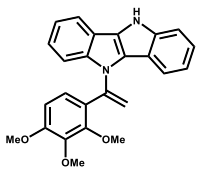
General procedure (F) for Cadogan-like cyclization: synthesis of compounds 6a-f



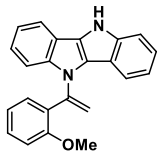
In a sealed tube, 2-(2-nitrophenyl)-1-(1-aryllvinyl)-1*H*-indole (**3**) (0.1 mmol, 1.0 equiv), $MoO_2Cl_2(DMF)_2$ (5 mol%) and PPh_3 (2.4 equiv) were dissolved in toluene (3.0 mL). The solution was then degassed with an argon balloon from -196 °C in liquid nitrogen to room temperature before being warmed at 160 °C for 6 hours. After the reaction was complete, the mixture reaction was filtered through a Celite© pad and concentrated under reduced pressure. Finally, the crude product was purified by silica gel chromatography with cyclohexane/ethyl acetate as eluent (0 to 20% of ethyl acetate) to give the corresponding compounds 5,10-dihydroindolo[3,2-*b*]indole derivatives (**6** or **8**).



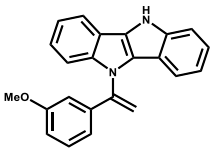
*5-(1-(3,4,5-Trimethoxyphenyl)vinyl)-5,10-dihydroindolo[3,2-b]indole (**6a**).* was prepared according to method F starting from **3k**. Column chromatography on silica gel provided 29 mg of the product as a white solid (72% yield), mp = 104-106 °C. TLC (SiO_2, Cyclohexane/EtOAc: 7/3): R_f = 0.48; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 10.44 (br s, 1H), 7.84 (ddd, J = 6.3, 3.1, 2.0 Hz, 1H), 7.52 (dt, J = 7.9, 1.0 Hz, 1H), 7.33 (ddd, J = 8.0, 3.1, 1.7 Hz, 1H), 7.19 – 7.08 (m, 4H), 6.93 (ddd, J = 8.0, 7.4, 1.0 Hz, 1H), 6.81 (s, 2H), 5.95 (s, 1H), 5.52 (s, 1H), 3.77 (s, 3H), 3.67 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 154.7 (2 C), 145.1, 142.4, 141.8, 141.3, 133.6, 123.1, 122.8, 120.5, 119.4, 119.0, 118.8, 117.4, 116.3, 114.4, 113.3, 113.0, 108.4, 105.8 (2 C), 104.3, 60.8, 56.6 (2 C); HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{25}H_{23}N_2O_3$ 399.1709, found 399.1705.



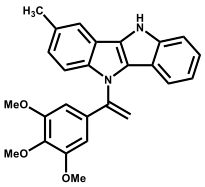
*5-(1-(2,3,4-Trimethoxyphenyl)vinyl)-5,10-dihydroindolo[3,2-b]indole (**6b**).* was prepared according to method F starting from **3l**. Column chromatography on silica gel provided 26 mg of the product as a white oil (64% yield). TLC (SiO_2, Cyclohexane/EtOAc: 7/3): R_f = 0.60; ^{1}H NMR (200 MHz, $(CD_3)_2CO$) δ 10.28 (br s, 1H), 7.87 (d, J = 7.0 Hz, 2H), 7.42 (d, J = 8.4 Hz, 1H), 7.25 – 6.90 (m, 6H), 6.83 (d, J = 8.6 Hz, 1H), 5.69 (s, 1H), 5.68 (s, 1H), 3.88 (s, 3H), 3.72 (s, 3H), 3.28 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 156.1, 153.0, 145.5, 143.5, 141.2, 139.9, 139.7, 125.9, 125.5, 123.8, 123.7, 123.2, 121.3, 120.8, 120.6, 120.3, 118.9, 112.7, 112.5, 110.9, 108.4, 101.5, 60.7, 60.6, 56.3; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{25}H_{23}N_2O_3$ 399.1708, found 399.1702.



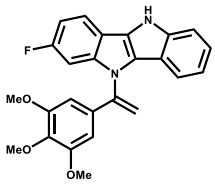
*5-(1-(2-Methoxyphenyl)vinyl)-5,10-dihydroindolo[3,2-b]indole (**6c**).* was prepared according to method F starting from **3j**. Column chromatography on silica gel afforded 20 mg of the product as a white oil (58% yield). TLC (SiO_2, Cyclohexane/EtOAc: 7/3): R_f = 0.68; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 10.39 (br s, 1H), 7.80 (dd, J = 5.9, 3.1 Hz, 1H), 7.50 (d, J = 8.2 Hz, 1H), 7.39 – 7.30 (m, 2H), 7.30 – 7.24 (m, 1H), 7.16 (dd, J = 7.6, 1.8 Hz, 1H), 7.11 (dd, J = 6.1, 3.1 Hz, 3H), 7.06 (d, J = 8.2 Hz, 1H), 6.97 – 6.83 (m, 2H), 5.98 (s, 1H), 5.77 (s, 1H), 3.63 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 158.9, 142.1, 141.9, 141.8, 131.1, 130.8, 130.0, 129.5, 127.1, 126.6, 122.8, 122.5, 121.4, 120.0, 119.1, 118.8, 118.6, 116.9, 116.3, 112.9, 112.8, 112.7, 56.1; HRMS [ESI-TOF] calcd for HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{23}H_{19}N_2O$ 339.1497, found 339.1497.



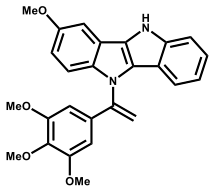
*5-(1-(3-Methoxyphenyl)vinyl)-5,10-dihydroindolo[3,2-b]indole (**6d**).* was prepared according to method F starting from **3i**. Column chromatography on silica gel provided 22 mg of the product as a white oil (65% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.70; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 10.45 (s, 1H), 7.90 – 7.80 (m, 1H), 7.52 (dt, J = 8.2, 0.9 Hz, 1H), 7.36 – 7.26 (m, 2H), 7.23 – 7.10 (m, 4H), 7.05 – 6.88 (m, 4H), 6.02 (s, 1H), 5.60 (s, 1H), 3.72 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 161.1, 145.0, 142.3, 141.8, 139.7, 130.7, 123.1, 122.8, 122.7, 120.4, 120.0, 119.4 (2 C), 118.8, 117.2, 116.2, 115.5, 113.3, 113.1, 113.0, 112.2, 110.0, 55.6; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{23}H_{19}N_2O$ 339.1497, found 339.1492.



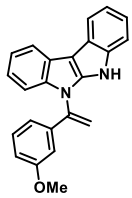
*3-Methyl-10-(1-(3,4,5-trimethoxyphenyl)vinyl)-5,10-dihydroindolo[3,2-b]indole (**6e**).* was prepared according to method F starting from **3m**. Column chromatography on silica gel provided 18 mg of the product as a white oil (43% yield). TLC (SiO_2, Cyclohexane/EtOAc: 8/2): R_f = 0.59; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 10.39 (br s, 1H), 7.66 – 7.58 (m, 1H), 7.50 (d, J = 8.8 Hz, 1H), 7.20 (d, J = 8.5 Hz, 1H), 7.16 – 7.07 (m, 2H), 6.99 (dd, J = 8.5, 1.7 Hz, 1H), 6.95 – 6.85 (m, 1H), 6.81 (s, 2H), 5.89 (s, 1H), 5.47 (s, 1H), 3.77 (s, 3H), 3.67 (s, 6H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 154.6 (2 C), 145.2, 141.7, 140.9, 140.6, 133.7, 132.7, 129.5, 124.5, 122.6, 119.3, 118.9, 118.6, 117.5, 116.4, 113.1, 112.9, 112.9, 107.7, 105.9 (2 C), 60.7, 56.6 (2 C), 21.4; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{26}H_{25}N_2O_3$ 413.1865, found 413.1868.



*2-Fluoro-10-(1-(3,4,5-trimethoxyphenyl)vinyl)-5,10-dihydroindolo[3,2-b]indole (**6f**).* was prepared according to method F starting from **3n**. Column chromatography on silica gel provided 29 mg of the product as a bright yellow solid (70% yield), mp = 251-253 °C. TLC (SiO_2, Cyclohexane/EtOAc: 7/3): R_f = 0.63; ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 10.49 (br s, 1H), 7.83 (dd, J = 8.6, 5.5 Hz, 1H), 7.58 – 7.41 (m, 1H), 7.19 – 7.10 (m, 2H), 7.04 (dd, J = 10.8, 2.1 Hz, 1H), 7.00 – 6.95 (m, 1H), 6.95 – 6.90 (m, 1H), 6.81 (s, 2H), 5.98 (s, 1H), 5.55 (s, 1H), 3.77 (s, 3H), 3.68 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $(CD_3)_2CO$) δ 160.6 (d, J = 236.8 Hz), 154.7 (2 C), 144.8, 142.4 (d, J = 11.8 Hz), 141.5, 140.8, 133.1, 127.5, 126.4, 122.7, 119.7 (d, J = 10.2 Hz), 119.5, 118.8, 116.3, 114.3, 113.1, 108.9, 108.5 (d, J = 24.7 Hz), 105.8 (2 C), 99.9 (d, J = 27.7 Hz), 60.8, 56.6 (2 C); ^{19}F{^{1}H} NMR (376 MHz, $(CD_3)_2CO$) δ -120.63 (ddd, J = 10.6, 9.7, 5.5 Hz); HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{25}H_{22}FN_2O_3$ 417.1614, found 417.1614.



*3-Methoxy-10-(1-(3,4,5-trimethoxyphenyl)vinyl)-5,10-dihydroindolo[3,2-b]indole (**6g**).* was prepared according to method F starting from **3o**. Column chromatography on silica gel provided 28 mg of the product as a bright yellow oil (65% yield). TLC (SiO_2, Cyclohexane/EtOAc: 7/3): R_f = 0.71; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 10.32 (br s, 1H), 7.57 – 7.41 (m, 1H), 7.32 (d, J = 12.2 Hz, 1H), 7.20 (d, J = 9.0 Hz, 1H), 7.15 – 7.07 (m, 2H), 6.95 – 6.87 (m, 1H), 6.85 – 6.74 (m, 3H), 5.86 (s, 1H), 5.46 (s, 1H), 3.86 (s, 3H), 3.77 (s, 3H), 3.68 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 155.1, 154.7 (2 C), 145.3, 141.8, 140.6, 137.6, 133.7, 122.8, 119.3, 119.0, 117.7, 116.4, 114.1, 113.0, 112.2, 107.4, 106.9, 105.9 (2 C), 105.3, 101.5, 60.7, 56.6 (2 C), 56.0; HRMS [ESI-TOF] $[M + H]^+$ m/z calcd for $C_{26}H_{25}N_2O_4$ 429.1814, found 429.1814.



*5-(1-(3-Methoxyphenyl)vinyl)-5,6-dihydroindolo[2,3-b]indole (**8a**).* was prepared according to method F starting from **3q**. Column chromatography on silica gel provided 59 mg of the product as orange oil (79% yield). TLC (SiO_2, Petroleum ether/EtOAc: 8/2): R_f = 0.50; ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 10.36 (s, 1H), 8.05 – 7.81 (m, 2H), 7.41 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.31 – 7.15 (m, 4H), 7.17 – 7.08 (m, 3H), 7.08 – 7.00 (m, 1H), 7.03 – 6.93 (m, 3H), 6.89 (dt, *J* = 7.6, 1.2 Hz, 1H), 5.99 (d, *J* = 0.8 Hz, 1H), 5.69 (d, *J* = 0.8 Hz, 1H); ^{13}C{^{1}H} NMR (75 MHz, $(CD_3)_2CO$) δ 161.0, 143.2, 140.3, 139.8, 138.2, 130.7, 123.9, 123.3, 121.6, 120.9, 120.8, 120.6, 120.6, 119.8, 119.0 (2 C), 115.6, 113.2, 112.7, 112.7, 112.5, 111.0, 55.6; HRMS [ESI-TOF] $[M + H]^+$ *m*/*z* calcd for $C_{23}H_{19}N_2O$ 339.1497, found 339.1495.

Biological assays

Cell culture and proliferation assay: The cancer cell lines used in this study were obtained from the American type of Culture Collection (Rockville, MD) and were cultured according to the supplier's instructions. In brief, HCT-116 cells were grown in RPMI 1640 containing 10% FCS and 1% glutamine. All cell lines were maintained at 37 °C in a humidified atmosphere containing 5% CO_2. The maximum number of passages for each cell line was eight. Cell viability was assessed using Promega CellTiter-Blue TM reagent according to the manufacturer's instructions. Cells were seeded in 96-well plates (5 ×103 cells/well) containing 50 µL growth medium. After 24 h of culture, the cells were supplemented with 50 µL of the tested compound dissolved in DMSO (less than 0.1% in each preparation). After 72 h of incubation, 20 µL of resazurin was added for 2 h (the supplier's protocol recommends 1-4 h) before recording fluorescence (λex =560 nm, λem = 590 nm) using a Victor microtiter plate fluorimeter (Perkin-Elmer, USA). The IC_{50} corresponds to the concentration of the tested compound that caused a decrease of 50% in fluorescence of drug treated cells compared with untreated cells. For IC_{50} determination, products **3o**, and **6g** were tested at 10 different concentrations, each concentration being tested in triplicate.

Molecular modeling

Atomic coordinates for tubulin α,β-dimer were retrieved from the Protein Data Bank (accession code 6H9B).[16] Missing hydrogen atoms were added using the Dock Prep module from the UCSF Chimera v1.13 software package,[17] and atoms from the ligand co-crystallized in the colchicine binding at the interface between chains C and D were deleted. Coordinates for a low energy starting conformer of compound **6g** were obtained using the conformers function from MarvinSketch v19.12 software package with default parameters. Molecular docking was performed using AutoDock Vina v1.1.2 software package,[18] with default parameters and the binding site defined as the box circumscribed to all the protein residues in contact with the co-crystallized ligand. Analysis and depiction of poses were performed using UCSF Chimera v1.13 software package.

X-ray Crystallography

X-ray Diffraction. Crystals suitable for Single Crystal X-ray Diffraction analyses were obtained for the following five compounds **5a**, **5f**, **6a**, **6c**, **6f** and **8a** in saturated solution after slow evaporation of diethyl ether. Samples were selected under a binocular with polarized light, cleansed and isolated in Paratone® oil. Subsequently, they were mounted on a suitable support for analysis at room temperature utilizing RIGAKU diffractometers. Data for compounds **5a**, **5f**, **6f** and **8a** were recorded using the XtaLABpro apparatus, which is equipped with a Mo(*Kα*) microfocus sealed tube generator coupled to a double-bounce confocal Max-Flux® multilayer optics, and an HPAD PILATUS3R 200K detector. *CrysAlisPro*[19] software was employed for data acquisition and data reduction, applying absorption correction that combines an empirical approach using spherical harmonics, implemented in the SCALE3 ABSPACK scaling algorithm, with a numerical correction based on a Gaussian integration over a multifaceted crystal model. Data for compounds **6a** and **6c** were recorded using a MM007 HF rotating anode, which delivered Cu(*Kα*) radiation through Osmic CMF confocal optics and equipped with a Rapid II curved Image Plate. They were integrated and reduced using *Fs_process*[20] software, as implemented in the GUI *CrystalClear 2.0* [20] and corrected for the radiation absorption using the multi-scan *Abscor* option.[21]

The very thin needle obtained for **6c** poorly diffracted no further than atomic resolution, even though a fairly lengthy exposure time was employed with the copper rotating anode. Consequently, a resolution cut-off of 1.01 Å was applied to the recorded data set. The **6c** structure was nevertheless solved by intrinsic phasing methods (*SHELXT* program),[22] as were the other five structures, which were then refined by full-matrix least-squares methods on F^2 using *SHELX-L*.[23] All non-hydrogen thermal parameters were refined anisotropically. The hydrogen atoms, which were mainly located in the difference Fourier maps, were then refined using a riding model with U_{iso} set to $1.2U_{eq}$(C) for the aromatic carbons or $1.5U_{eq}$(C) for those carried by methyl carbons. The methyl hydrogens were allowed to rotate but not to tilt. Except for the **6c** structure (the limited resolution enforced us to use a riding model), the coordinates of the amine hydrogen atom were freely refined and its U_{iso} set to $1.2U_{eq}$(N). If,

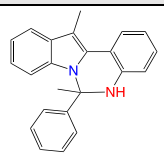
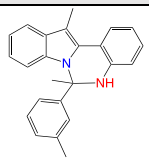
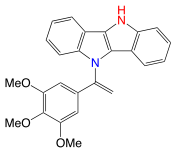
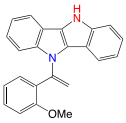
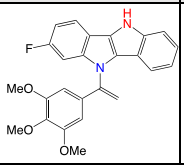
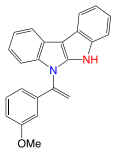
in the monoclinic unit cells of **5a** and **5f**, the amine hydrogen develops edge-to face interaction with the adjacent indole ring at 1-x, y-½, ½-z (resp. in **5f** x, ½-y, z-1/2), it is involved in conventional H-bonds with the oxygen atoms from the methoxy groups in the other crystals. This is exemplified in the case of **8a** where two independent molecules are paired in the asymmetric unit of the $P2_1/c$ unit cell (see figure S1). Regarding the geometry of the structures, the orientation of the tolyl group in **5f** is found to be flipped around its attachment to the N-hetero-6-membered ring with a refined occupancy ratio of 0.590(5):0.410(5). Compounds **6a** and **6f** differ by substitution of a fluorine atom at C14 but they have crystallized in the same P-1 unit cell with a slight volume expansion for **6f** (*ca* 1130 *vs* 1150Å^3). In both crystals, the tri-methoxy phenyl group exhibited some disorder due to their promiscuity in the crystal packing which propagates along the crystallographic ***a***-axis (see figure S2a,b). If that disorder is delineated to two methoxy groups over two sites for **6a**, the presence of the fluorine atoms in that crystal area extends the disorder to all the atoms of this tri-MeO-phenyl. This implies refinement of the phenyl position over two close sites, with fixed occupancy factors 0.84/0.16, bearing different methoxy orientations (see Figure S). The two crystal forms also present cavities of about 116 ± 6Å^{21} volume at position ½ 0 ½ (see figure S2c) as estimated by the *Squeeze* procedure in *PLATON*.[24] That procedure further estimated the structure factor contribution from the void content (between 21 and 33 electrons per unit cell of **6a** and **6f,** respectively, which are likely to be partially occupied by diffuse diethyl ether molecules -about 1/3 per unit cell-) in order to correct the original *hkl* file from this unprofitable contribution. Therefore, the molecular solvent information was not included in table S1, which summarized all the crystal data, data collection, and structure refinement details.

Additionally, the disordered structures were treated on a case-by-case basis, applying combinations of restraints with upon geometrical (*DFIX, SADI*) and atomic displacement parameters (ADPs) (*DELU, SIMU, RIGU*) to accommodate them. Furthermore, the BUMP instruction was also used in **6a** to prevent bad contact between vicinal methyl hydrogens of the disordered tolyl group. Finally, limited data over parameter ratio in **6c** was compensated by using *DELU (sd 0.01), SIMU (sd 0.02),* and *RIGU (sd 0.01)* instructions to make ADPs regular throughout the entire structure.

A search of the Cambridge Structural Database (CSD version 5.44 June. 2023 update)[25] revealed a former crystal structure (CSD RefCode WOMBAE),[26] with a trifluoromethyl group instead of the methyl group, similar to **5a** (and somewhat to **5c**), (see the overlays in figure S3). Only non-substituted DINI (5,10-dihydroindolo[3,2-*b*]indole) structures have been deposited in the CSD under the following refcodes UNEFEA, UNEFIE, and UNEFOK.[27] To the best of our knowledge, structure **8a** represents the first characterization of 5,6-dihydroindolo[2,3-b]indole using SCXRD to date (Figure 4d). All the figures were drawn using Mercury.[28]

CCDC 2310238-2310243 (compounds **5a**, **5f**, **6a**, **6c**, **6f** and **8a** respectively) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Table S1 Crystal data of **5a**, **5f**, **6a**, **6c**, **6f**, and **8a**.

Identification code	**5a**	**5f**	**6a**	**6c**	**6f**	**8a**
						
Empirical formula	$C_{23}H_{20}N_2$	$C_{24}H_{22}N_2$	$C_{25}H_{22}N_2O_3$ [+solvent]	$C_{23}H_{18}N_2O$	$C_{25}H_{21}FN_2O_3$ [+solvent]	$C_{23}H_{18}N_2O$
Formula weight	324.41	338.43	398.44	338.39	416.44	338.39
Diffractometer	Rigaku® XTALabPro μ-*S* mm003, Dectris® PILATUS 200 K		Rigaku® SPIDER mm007, Rapid 2		Rigaku® XTALabPro μ-*S* mm003, Dectris® PILATUS 200 K	
Temp. (K), Wavelength (Å)	293.0 (2), 0.71073	293.0 (2), 0.71073	293.0 (2), 1.54187	293.0 (2), 1.54187	293.0 (2), 0.71073	293.0 (2), 0.71073
Crystal system, Space group	Monoclinic, I 2/a	Monoclinic, P 2_1/c	Triclinic, P -1	Monoclinic, P 2_1/c	Triclinic, P -1	Monoclinic, P 2_1/c
Unit cell dimensions	17.1017(11) 10.1324(6) 21.8754(15) 90 111.523(8) 90	8.1403(4) 17.9909(9) 13.1138(7) 90 97.700(5) 90	8.4557(5) 11.5977(7) 12.3663(9) 79.089(6) 84.728(6) 72.178(5)	12.7466(12) 17.1840(13) 7.9788(7) 90 93.746(7) 90	8.6051(3) 11.7265(6) 12.2507(6) 79.867(4) 86.096(4) 70.779(4)	11.2201(4) 19.8758(7) 16.7325(6) 90 107.865(4) 90
Volume	3526.3(4)	1903.22(17)	1132.91(13)	1743.9(3)	1149.0(1)	3551.6(2)
Z, Calculated density (Mg/mm^{-3})	8, 1.222	4, 1.181	2, 1.168	4, 1.289	2, 1.204	8, 1.266
Absorption coefficient (mm^{-1})	0.072	0.069	0.621	0.626	0.085	0.078
F(000)	1376	720	420	712	436	1424
Crystal size	0.60 x 0.30 x 0.12	0.20 x 0.14 x 0.13	0.58 x 0.55 x 0.28	0.19 x 0.09 x 0.04	0.25 x 0.18 x 0.15	0.23 x 0.19 x 0.12
θ range for data collection	4.239 to 25.344	2.264 to 25.345	3.643 to 66.699	3.475 to 52.624	2.507 to 25.358	2.558 to 25.350
Limiting indices	$-20 \le h \le 20$, $-11 \le k \le 12$, $-26 \le l \le 26$	$-9 \le h \le 9$, $-21 \le k \le 21$, $-15 \le l \le 15$	$-9 \le h \le 10$, $-13 \le k \le 12$, $-14 \le l \le 14$	$-13 \le h \le 13$, $-17 \le k \le 14$, $-8 \le l \le 7$	$-10 \le h \le 10$, $-13 \le k \le 14$, $-14 \le l \le 14$	$-12 \le h \le 13$, $-23 \le k \le 23$, $-20 \le l \le 20$
Reflections collected / unique Rint	21551 / 3225 0.0934	23102 / 3487 0.0391	14682 / 3919 0.0494	10893 / 1986 0.054	22443 / 4211 0.0399	43740 / 6510 0.0338
Completeness to θ_{full} (23.5°†/ 25.4°)	99.3	99.9	97.3	99.4	99.9	99.9
Absorption correction	Empirical absorption & Gaussian		Empirical absorption		Empirical absorption & Gaussian	
Max. and min. transmission	1.000 and 0.351	1.000 and 0.495	1.000 and 0.856	1.000 and 0.607	1.000 and 0.374	1.000 and 0.417
Refinement method	Full-matrix least-squares on F^2					
Data / restraints / parameters	32086 / 0 / 231	3485 / 261 / 282	3903 / 120 / 317	1760 / 392 / 236	4208 / 569 / 416	6508 / 0 / 489
Goodness-of-fit on F^2	1.011	1.085	0.931	1.028	1.044	1.076
Final R indices [$I>2\sigma(I)$]	0.0413, 0.1091	0.0464, 0.1198	0.0499, 0.1303	0.0656, 0.1721	0.0572, 0.1746	0.0462, 0.1038
R indices (all data)	0.0467, 0.1136	0.0558, 0.1268	0.0732, 0.1498	0.0888, 0.1880	0.0655 0.1850	0.0602, 0.1113

Largest diff. peak and hole	0.194 and -0.165	0.116 and -0.110	0.162 and -0.195	0.412 and -0.144	0.290 and -0.208	0.149 and -0.144
CCDC deposit n°	2310238	2310239	2310240	2310241	2310242	2310243

Figure S1 View of the content of the asymmetric unit of **8a**, highlighting the dimer association in an $R^2_2(18)$ graph set motif involving N-H… O hydrogen bonding and π-π stacking interactions. Distance values between H and O atoms are given in Å, as is the centroid-to-centroid distance (red dots linked by cyan dotted lines).

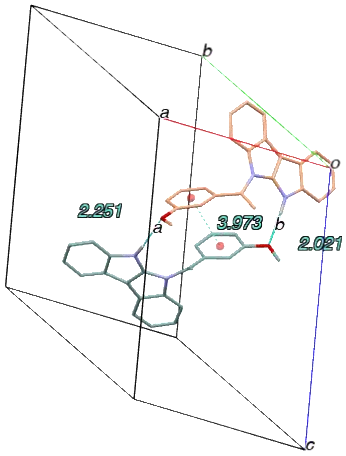
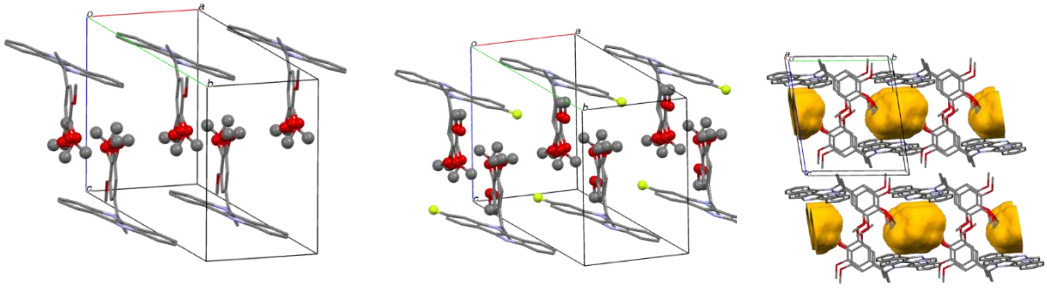


Figure S2 Partial view of the crystal packing for **6a** (a) and **6f** (b), highlighting the disordered parts (ball-and-stick representation) of the respective structures propagating along the ***a*** direction. A view down the ***a*** axis to display the cavities (in gold) inside the **6a** crystal packing (c).



(a) (b) (c)

Figure S3 View of the overlay diagrams (above the 3-methylindole group) between **5a** (carbons in grey), and **5f** (in pale yellow) (left), and in addition with refcode CSD WOMBAE (in dark green) (right).

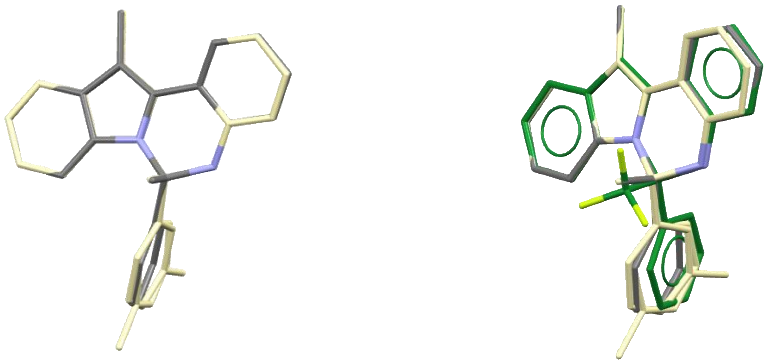
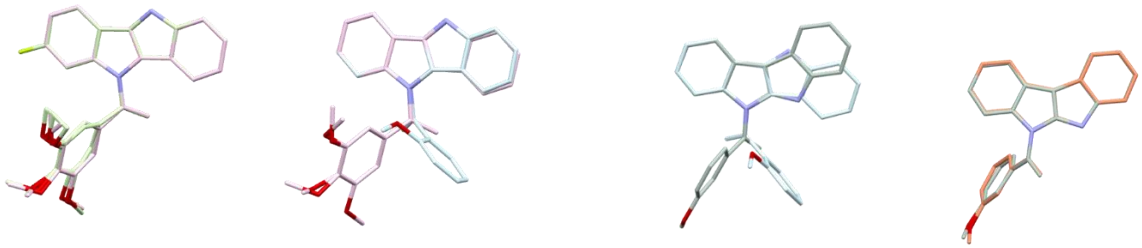


Figure S4 Overlay diagrams (above the left indole moiety) (a) between **6a** (carbons in pink), and **6f** (in light green); (b) **6a** and **6c**; (c) **6c** and **8a**; (d) the two conformers of **8a** in the asu with a rmsd of 0.1631Å and a max of deviation of 0.3715Å.



a) b) c) d)

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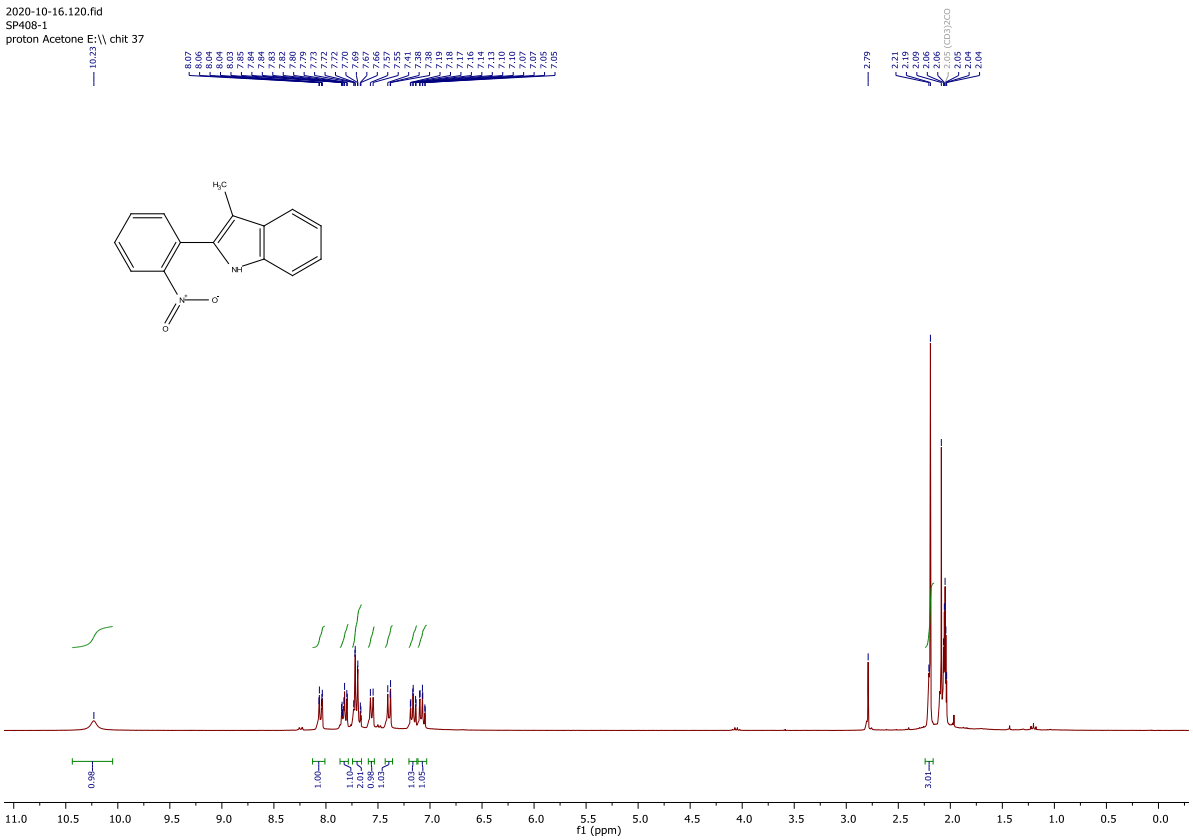
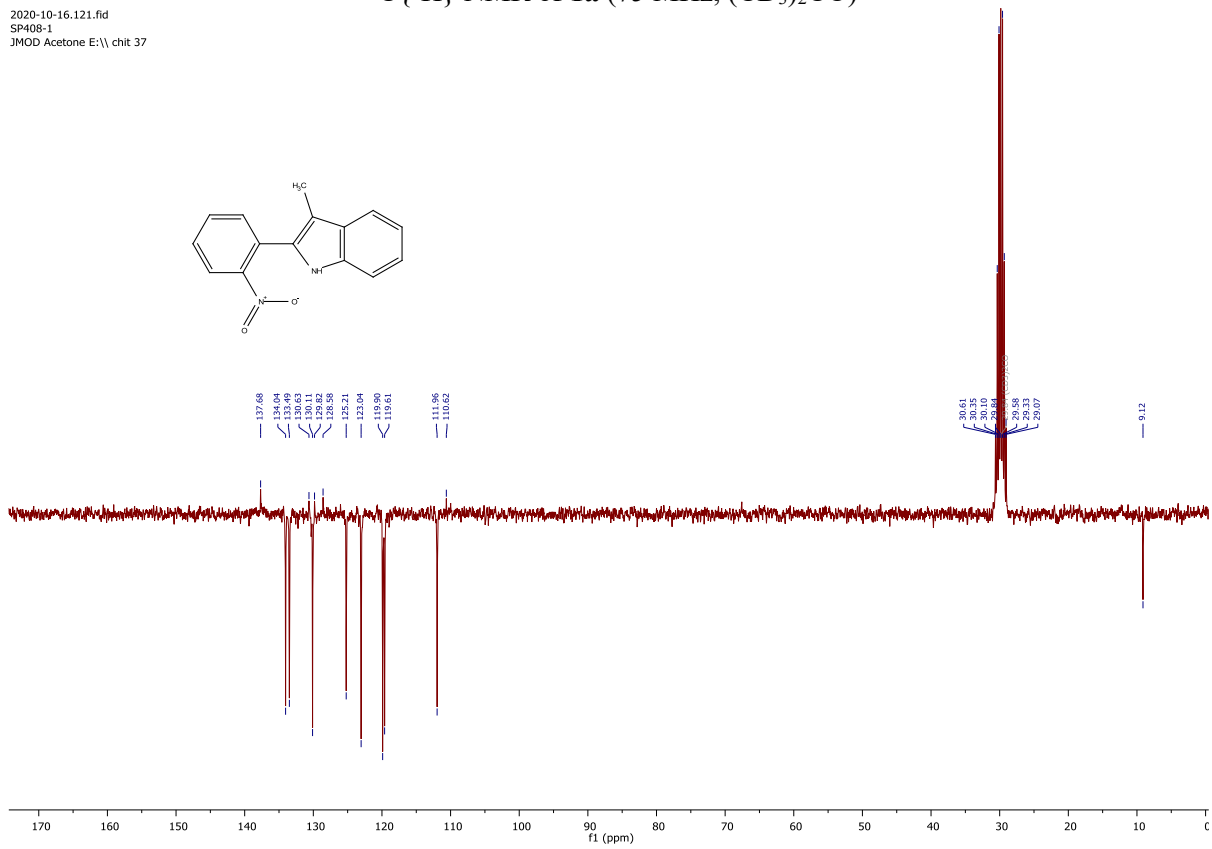
^{1}H, ^{13}C, ^{19}F NMR Spectra

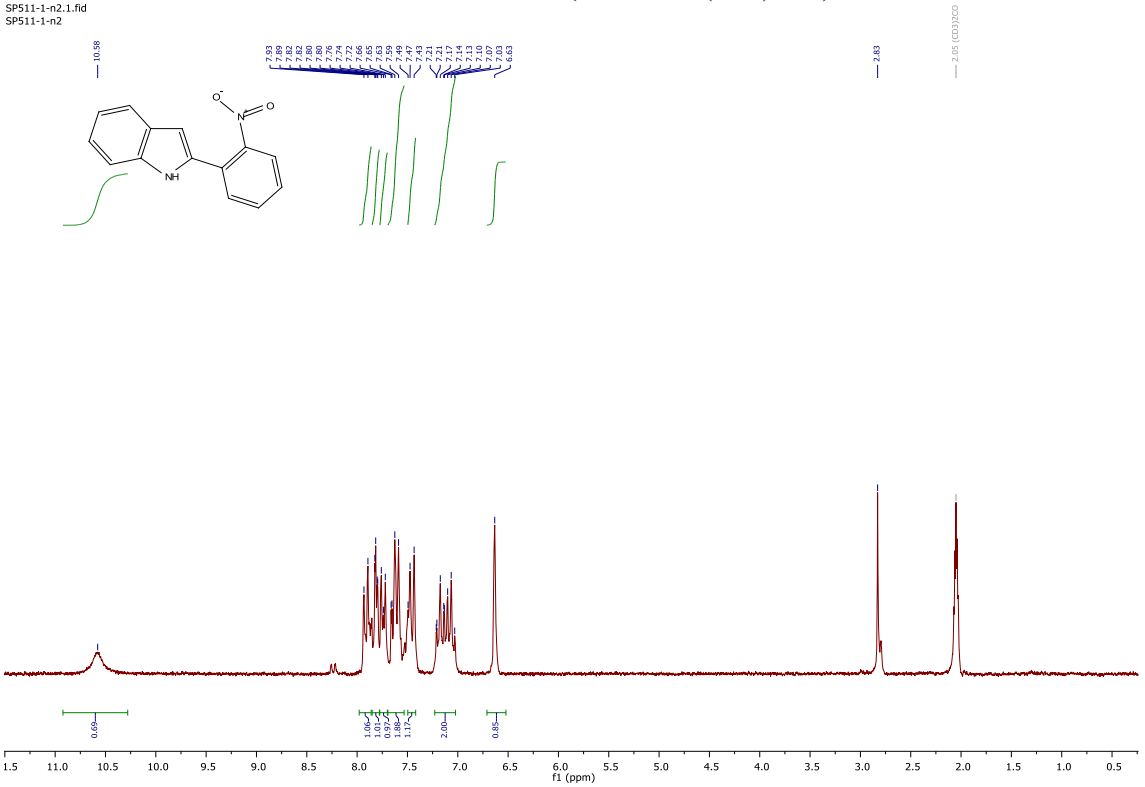
^{1}H NMR of **1a** (300 MHz, $(CD_3)_2CO$)



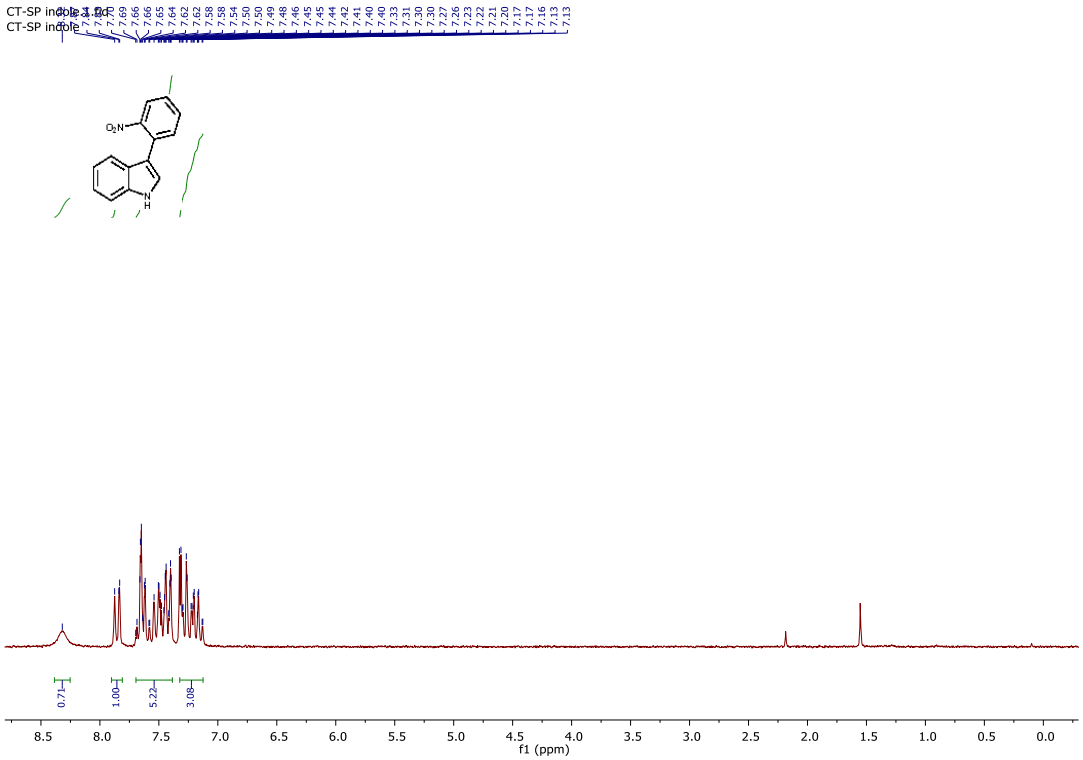
$^{13}C\{^{1}H\}$ NMR of **1a** (75 MHz, $(CD_3)_2CO$)



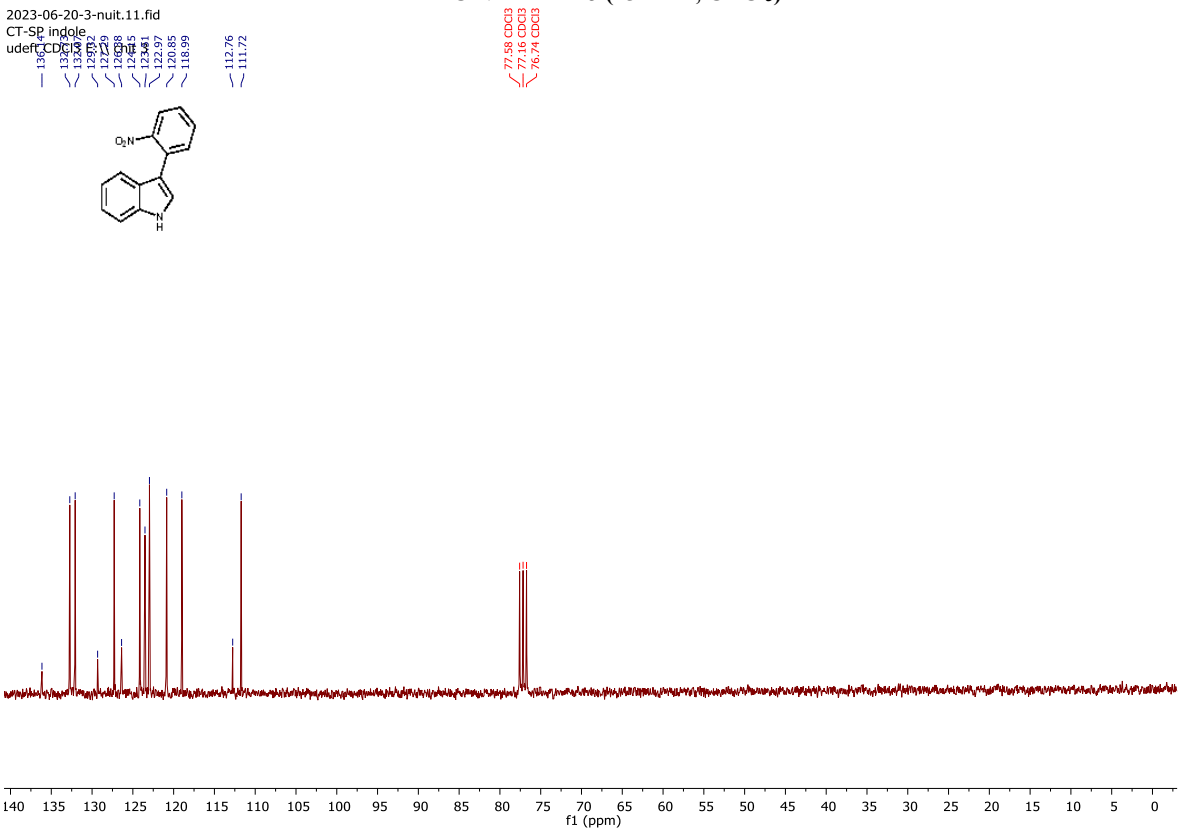
^{1}H NMR of **1b** (200 MHz, $(CD_3)_2CO$)



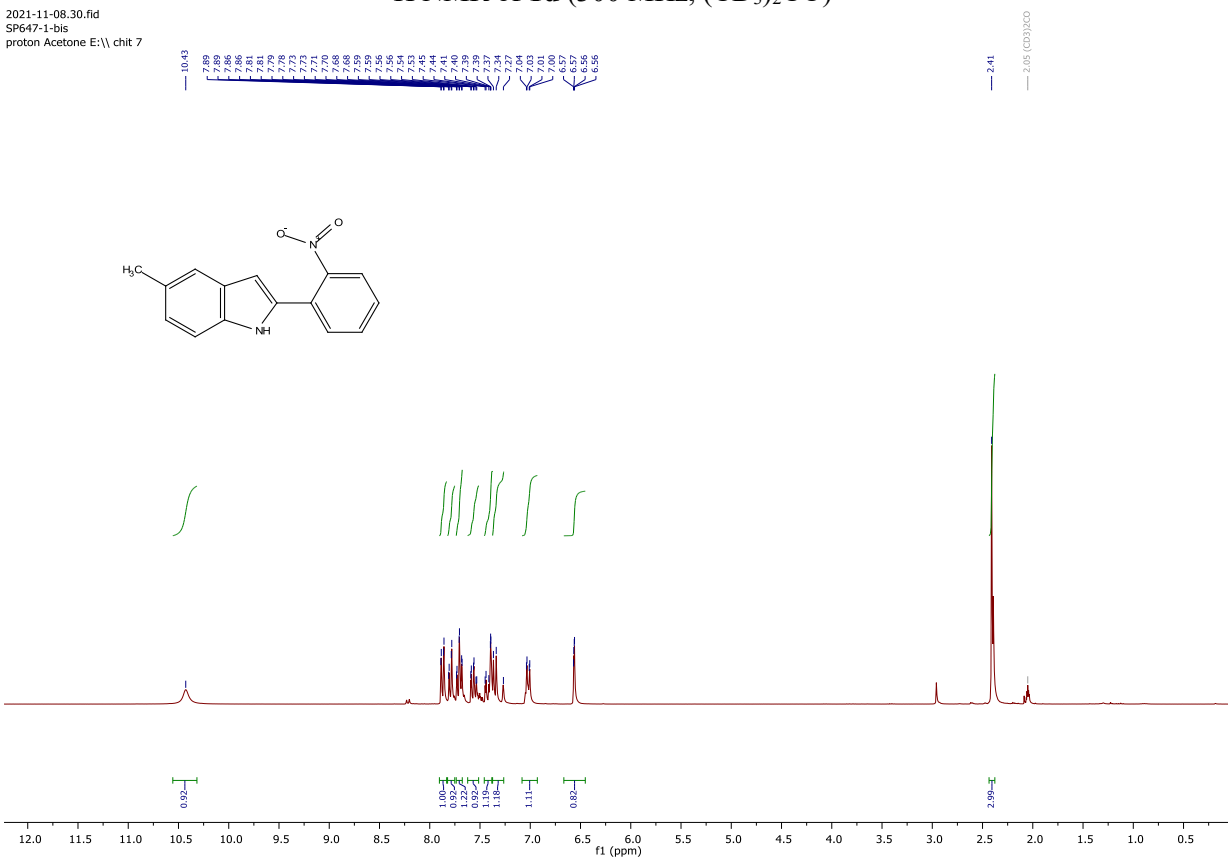
^{1}H NMR of 1c (300 MHz, $CDCl_3$)



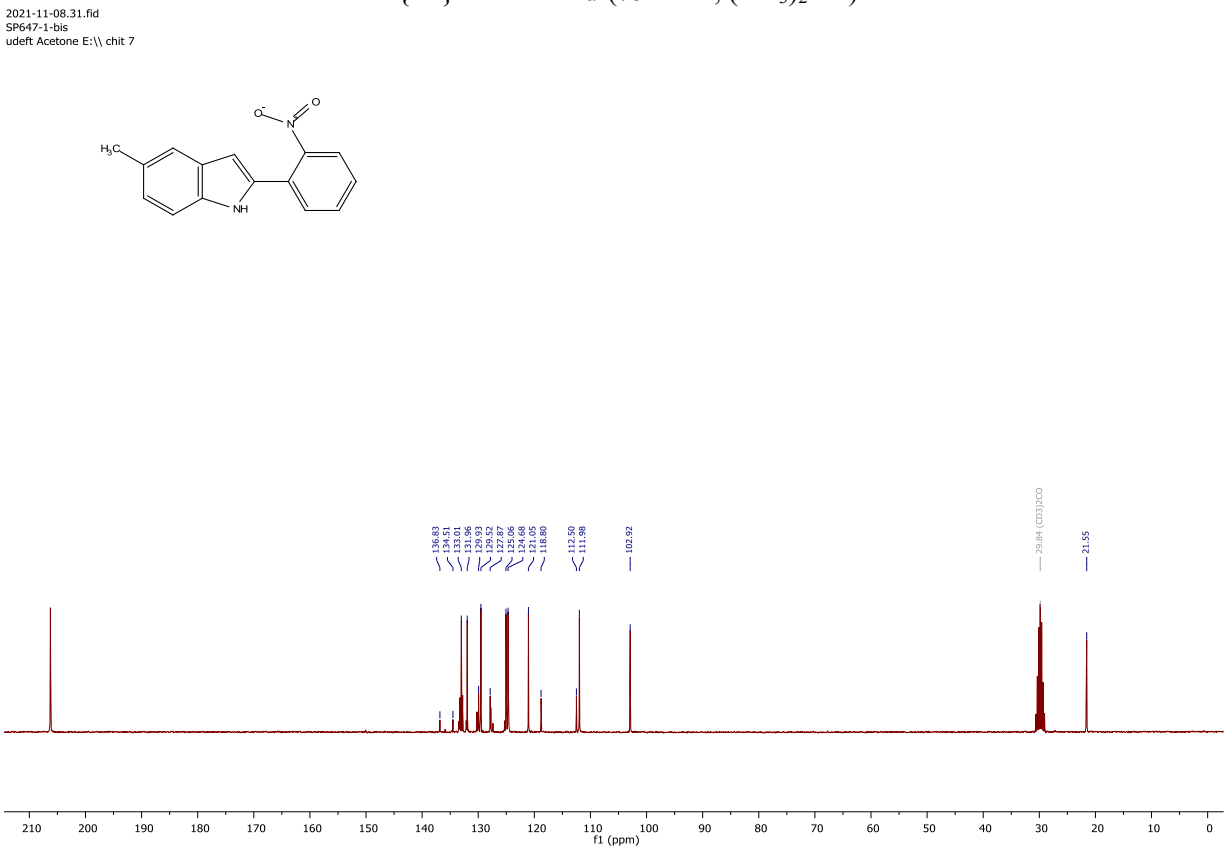
^{13}C NMR of **1c** (75 MHz, $CDCl_3$)



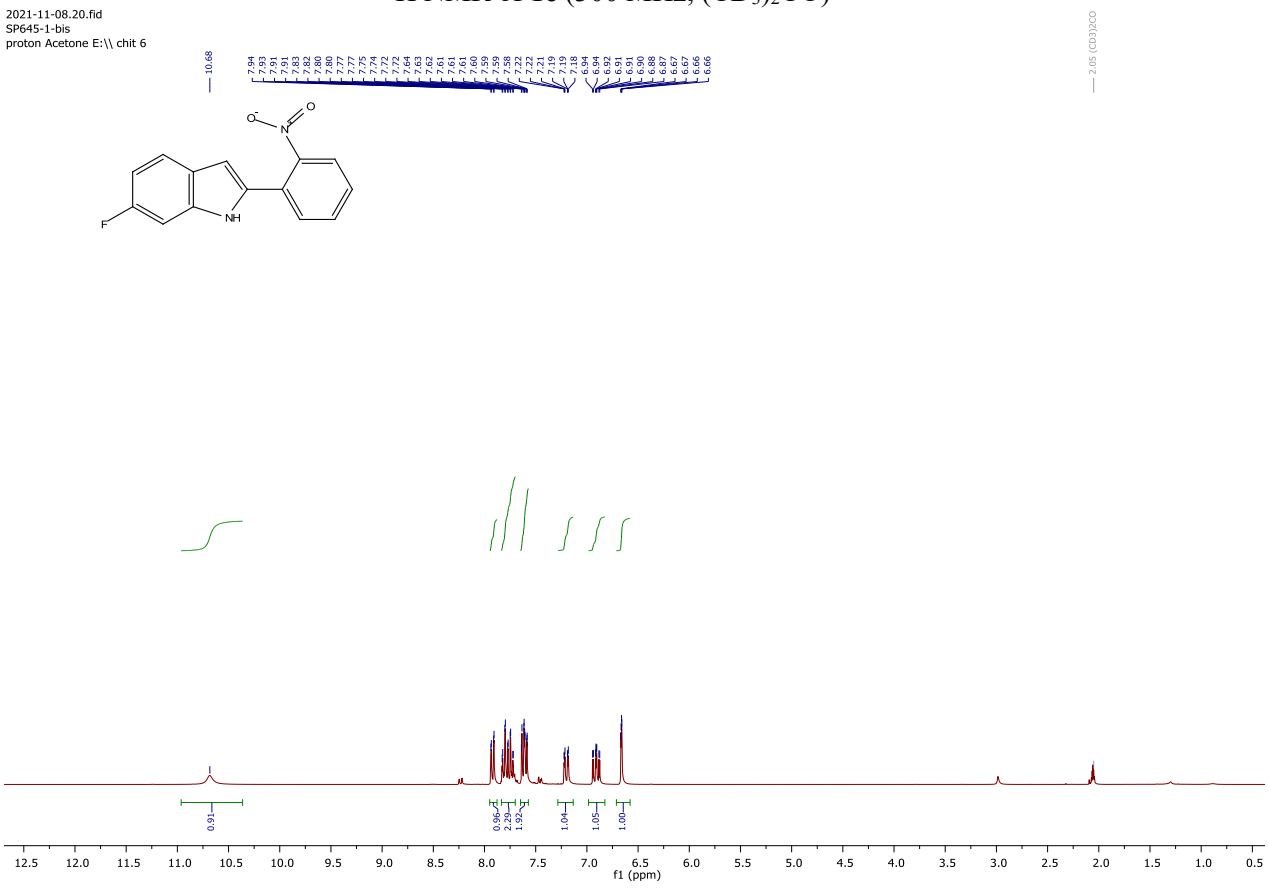
^{1}H NMR of **1d** (300 MHz, $(CD_3)_2CO$)



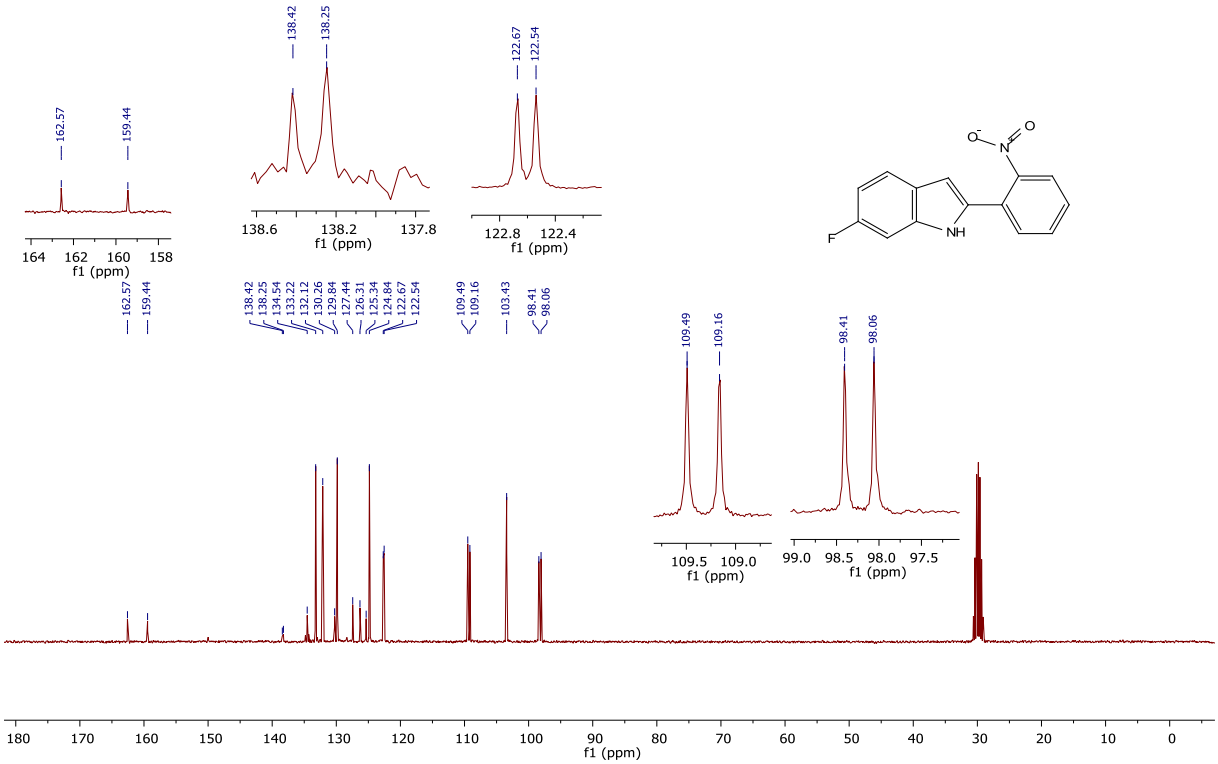
$^{13}C\{^{1}H\}$ NMR of **1d** (75 MHz, $(CD_3)_2CO$)



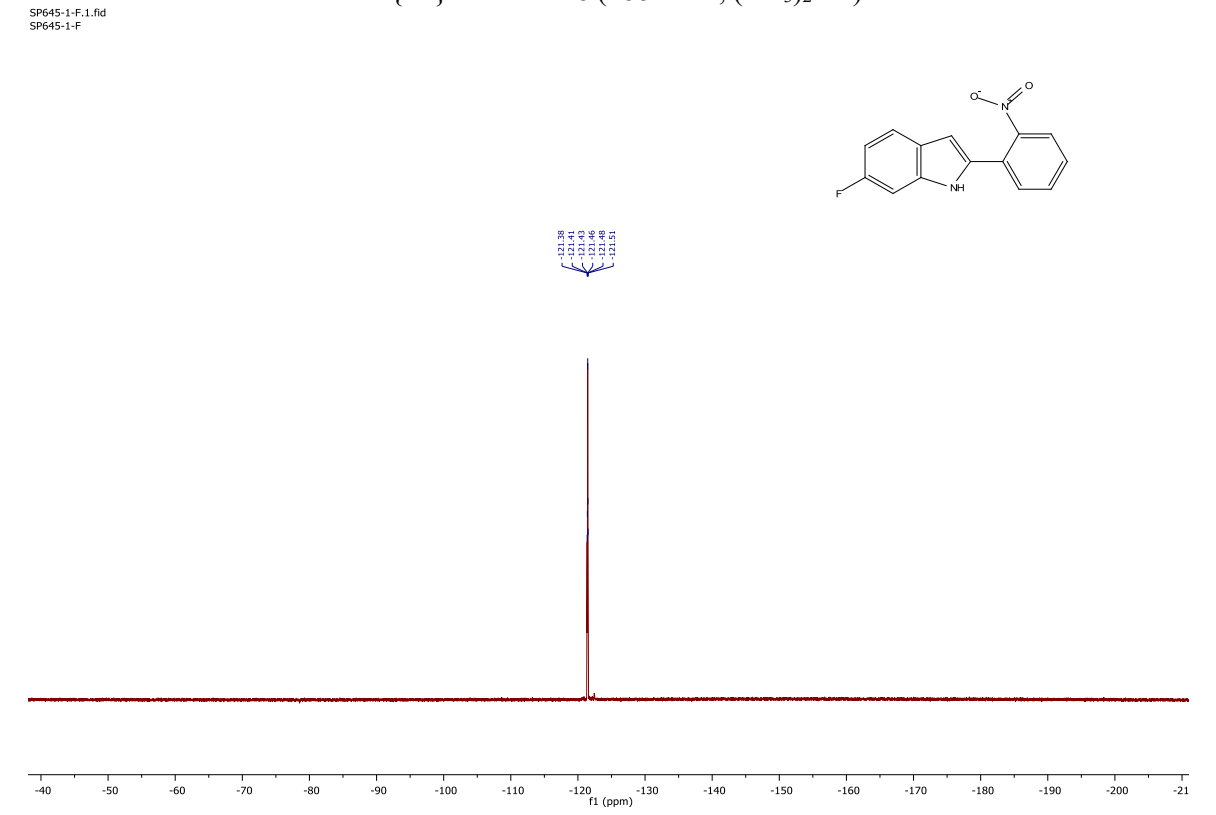
^{1}H NMR of **1e** (300 MHz, $(CD_3)_2CO$)



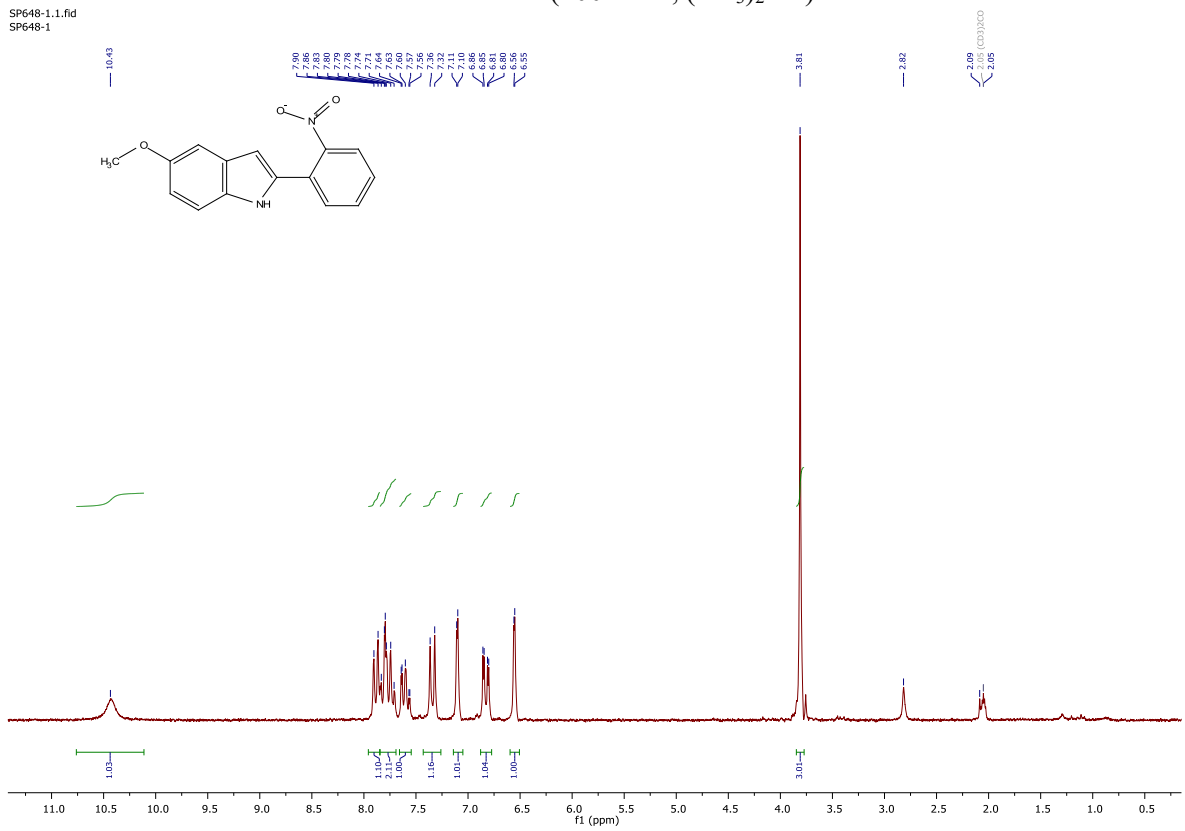
$^{13}C\{^{1}H\}$ NMR of **1e** (75 MHz, $(CD_3)_2CO$)



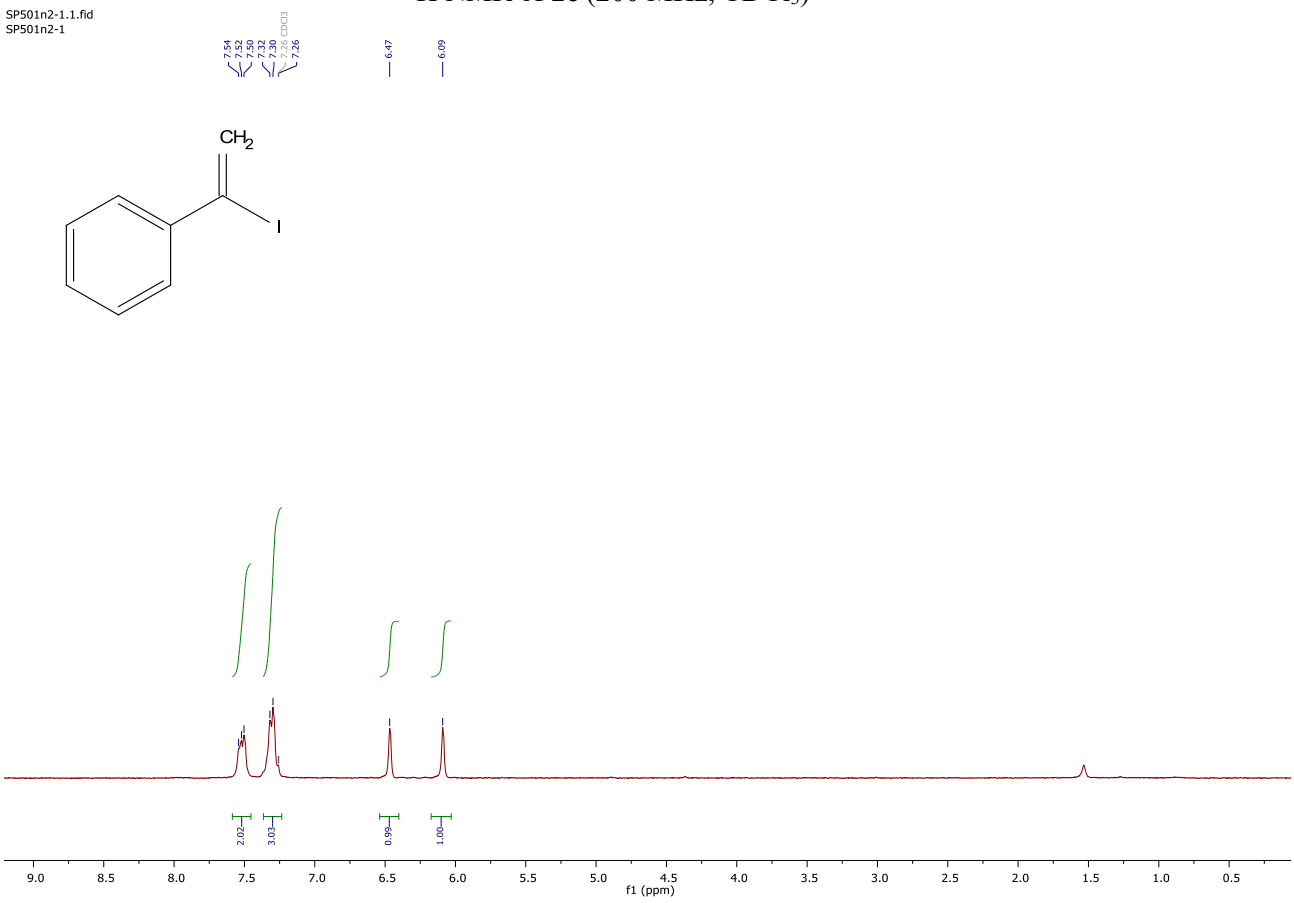
$^{19}F\{^{1}H\}$ NMR of **1e** (188 MHz, $(CD_3)_2CO$)



^{1}H NMR of **1f** (200 MHz, $(CD_3)_2CO$)



^{1}H NMR of **2c** (200 MHz, $CDCl_3$)



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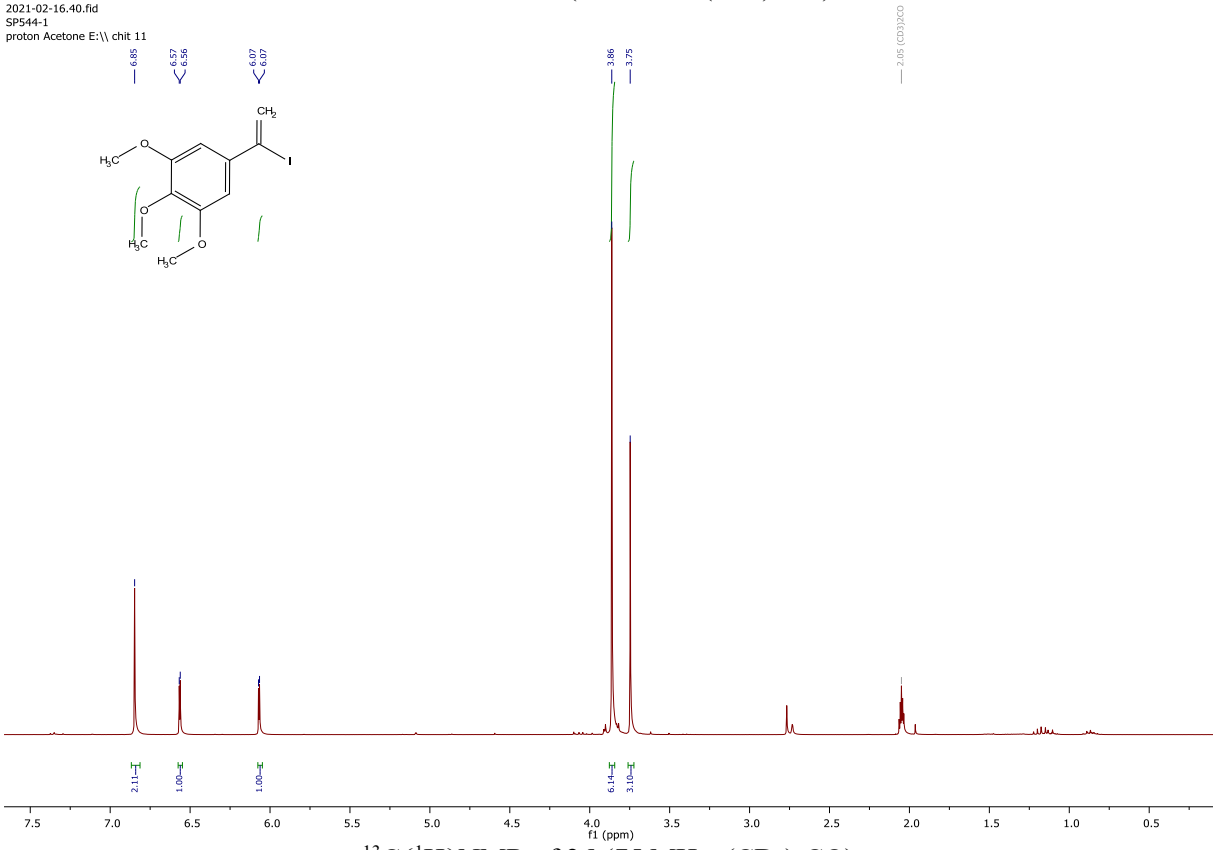

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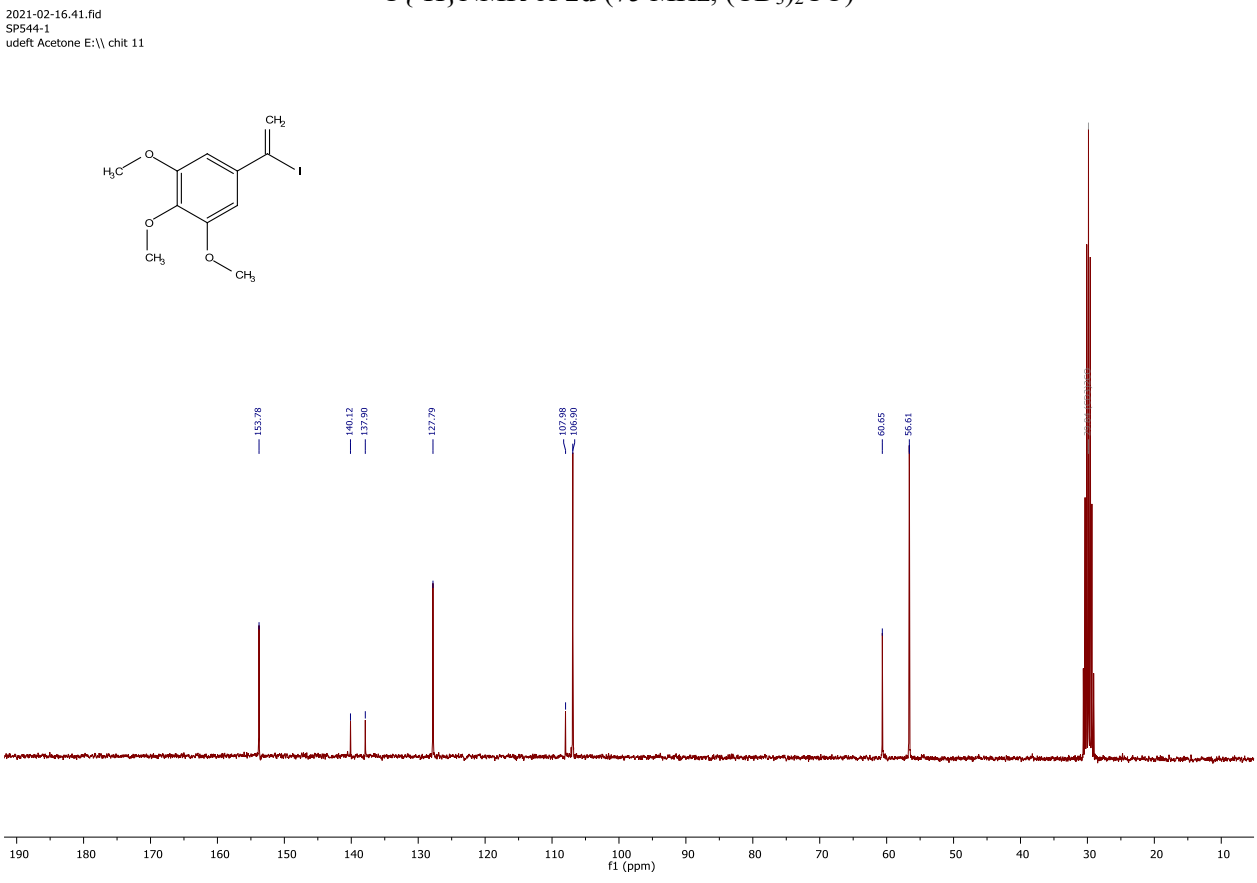

^{1}H NMR of **2e** (200 MHz, $CDCl_3$)

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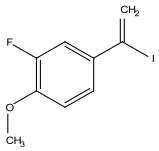
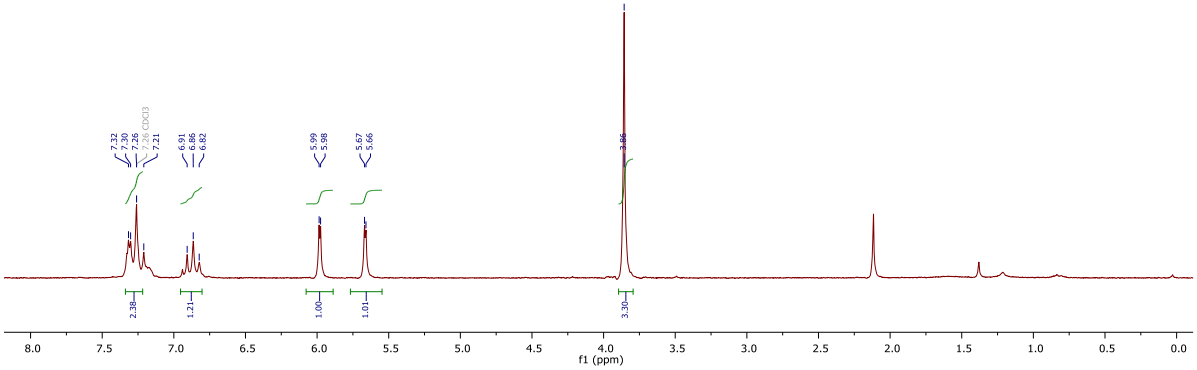
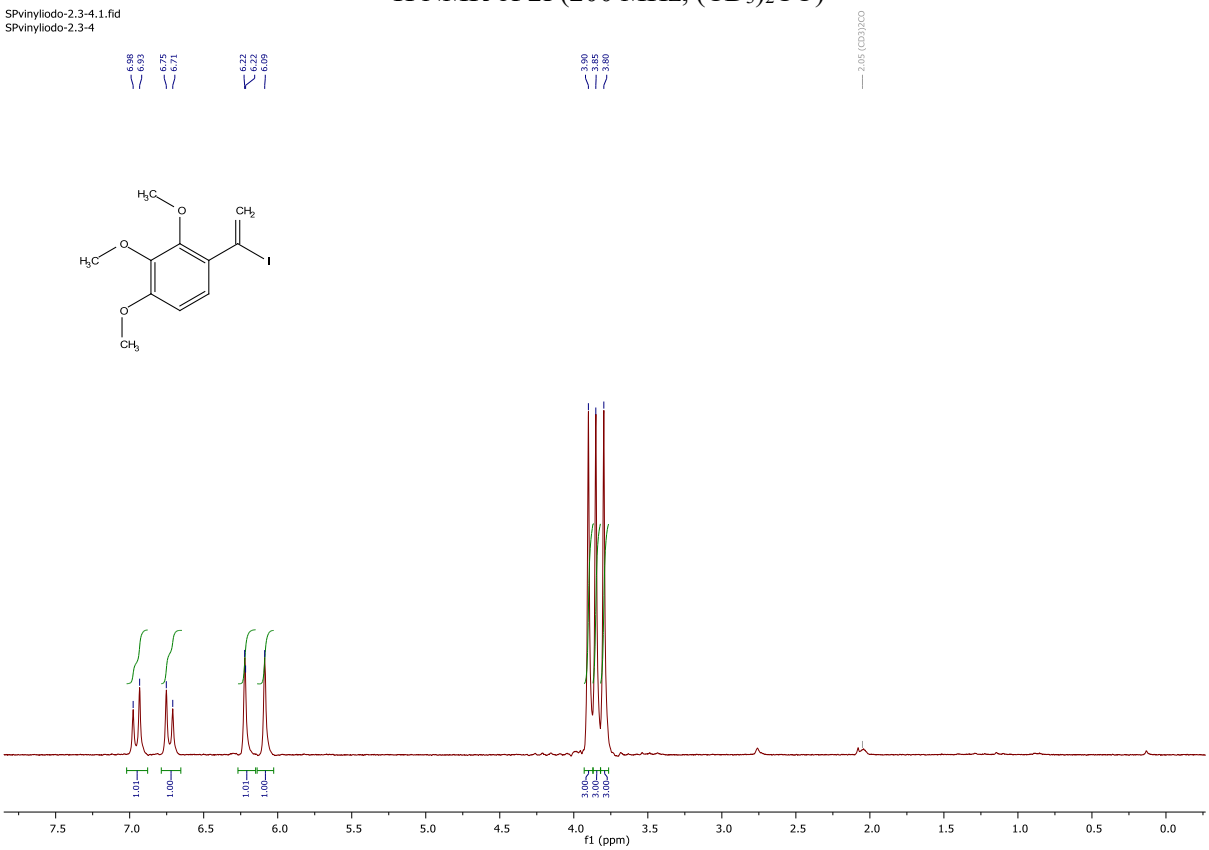
SP607-1



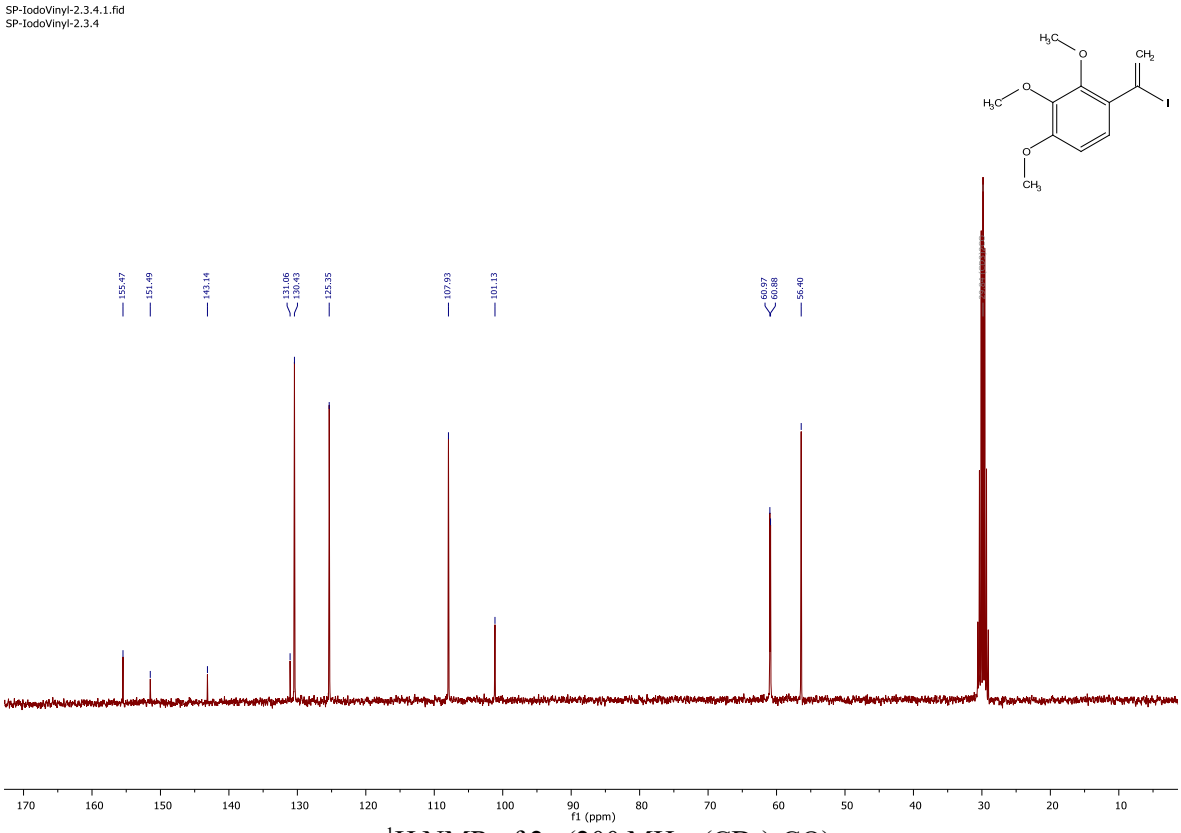


^{1}H NMR of **2f** (200 MHz, $(CD_3)_2CO$)

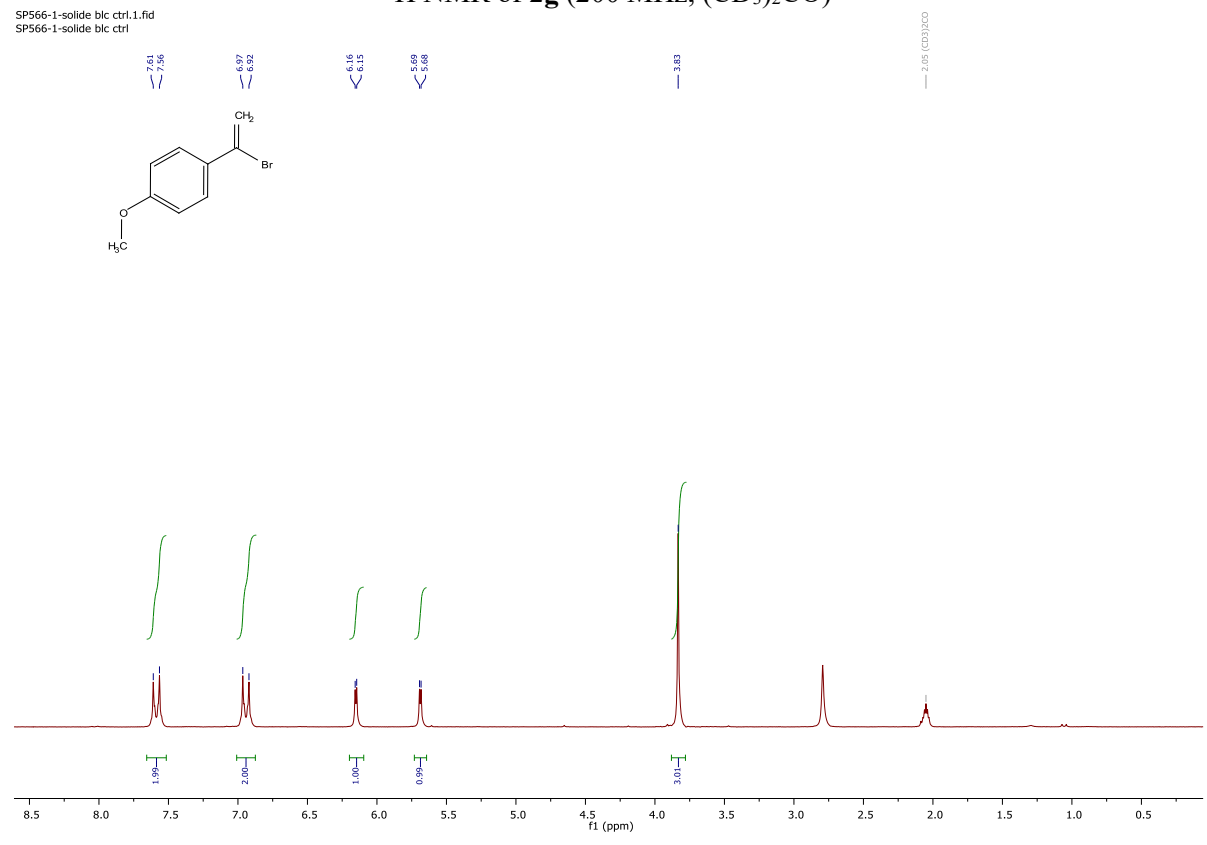
SPvinyliodo-2.3-4.1.fid
SPvinyliodo-2.3-4



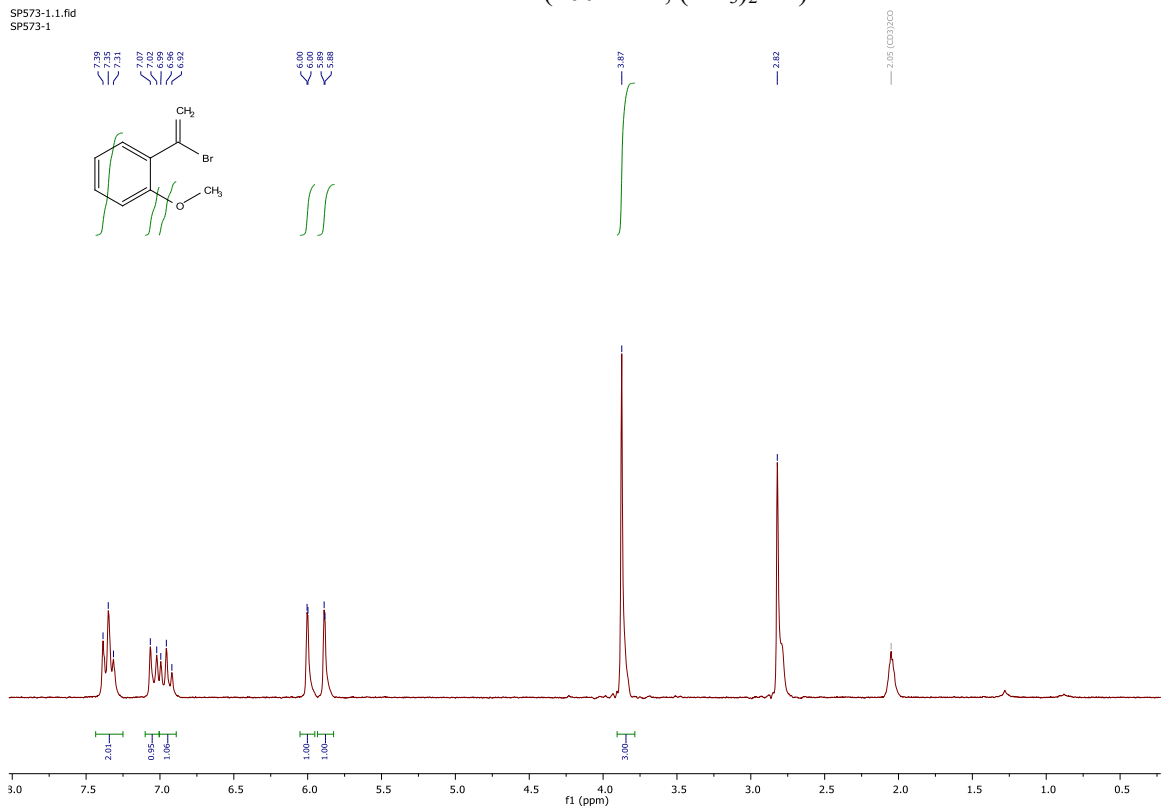
$^{13}C\{^{1}H\}$NMR of **2f** (75 MHz, $(CD_3)_2CO$)



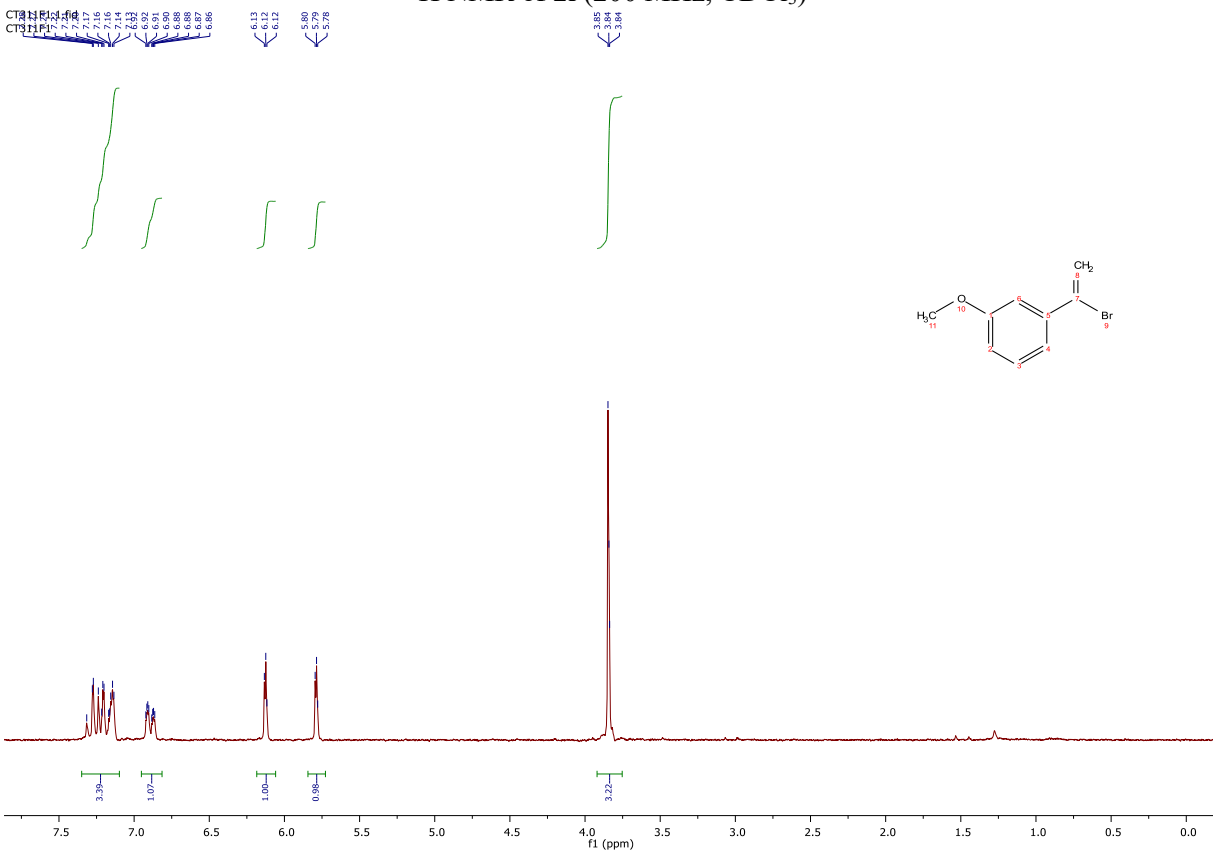
^{1}H NMR of **2g** (200 MHz, $(CD_3)_2CO$)



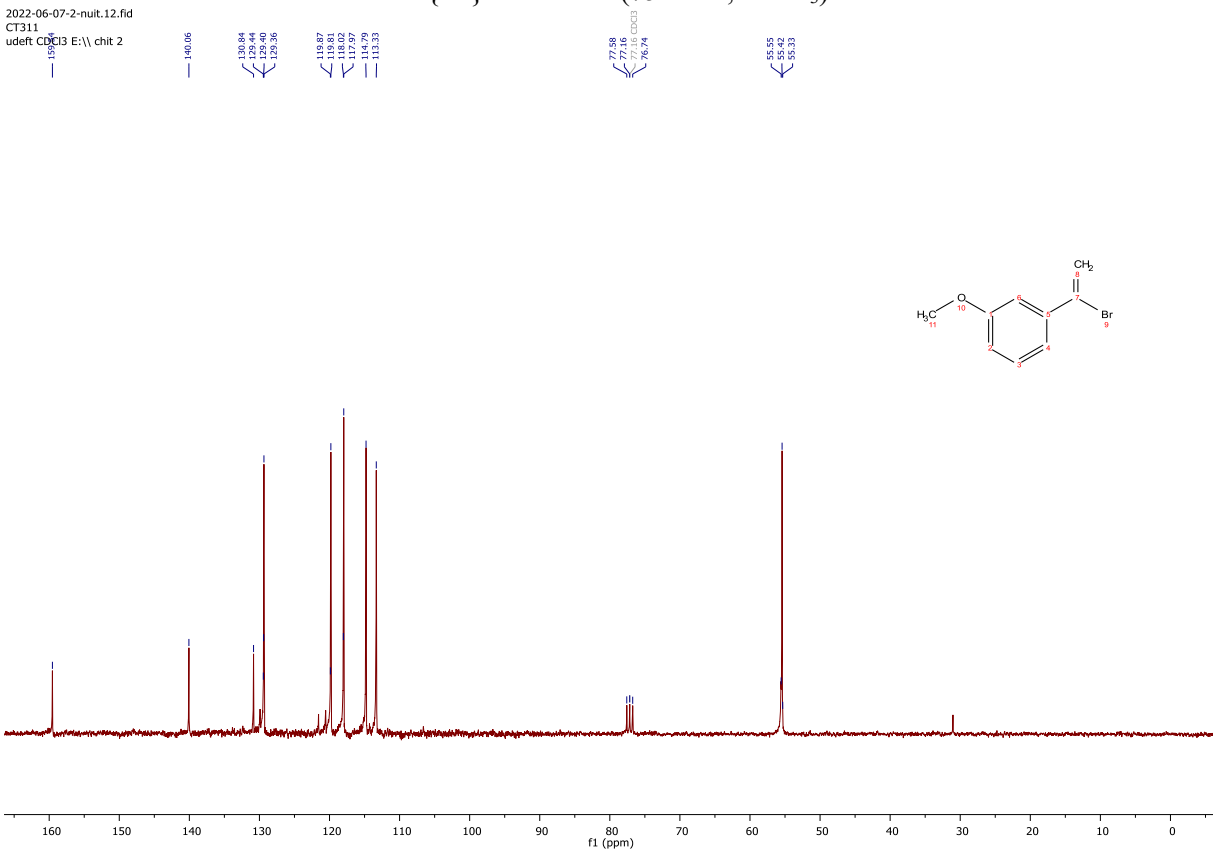
^{1}H NMR of **2h** (200 MHz, $(CD_3)_2CO$)



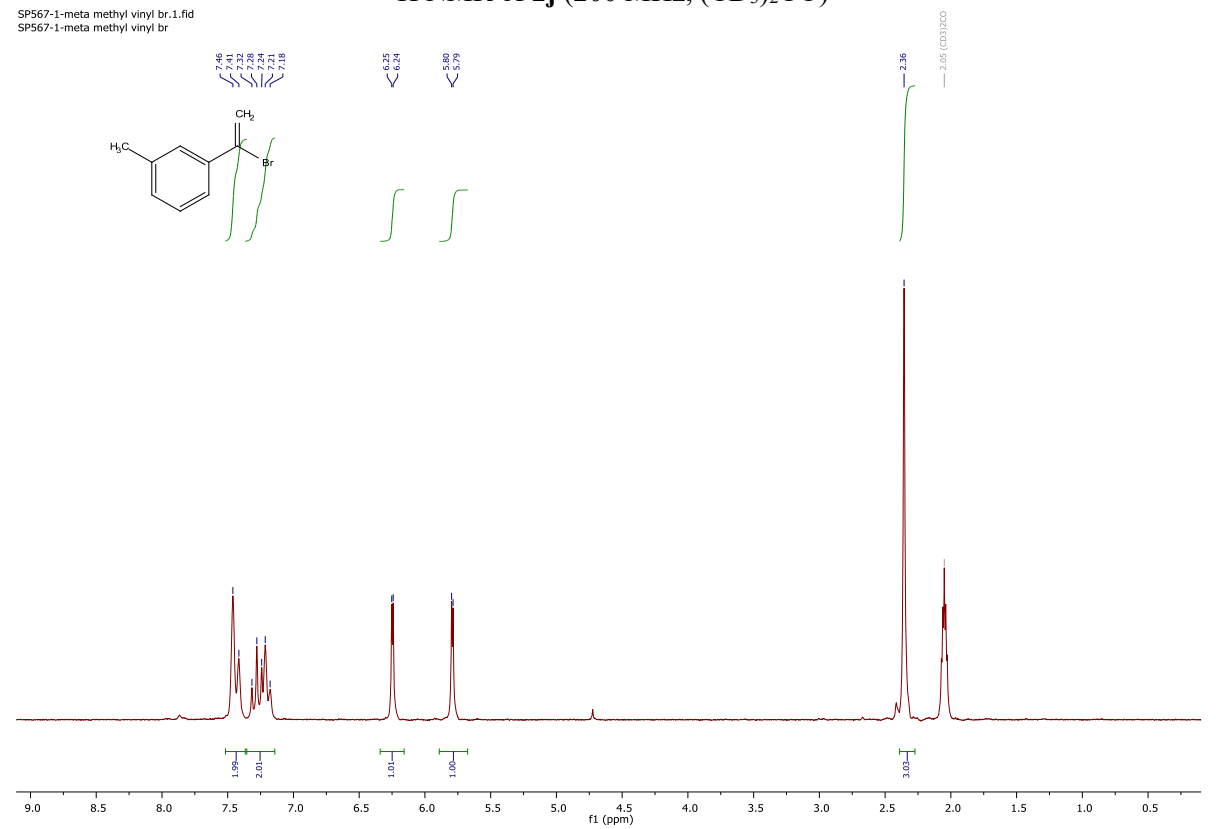
^{1}H NMR of **2i** (200 MHz, $CDCl_3$)



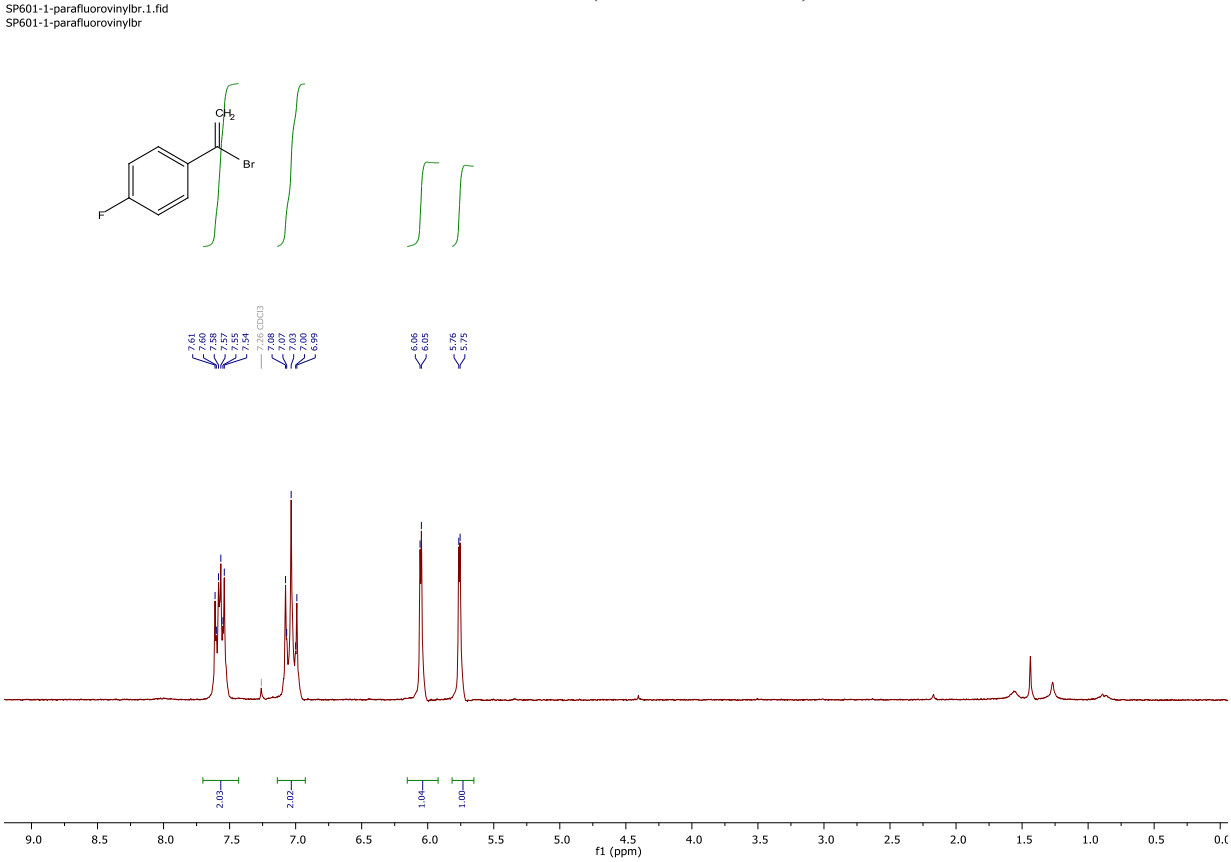
$^{13}C\{^{1}H\}$NMR of **2i** (75 MHz, $CDCl_3$)



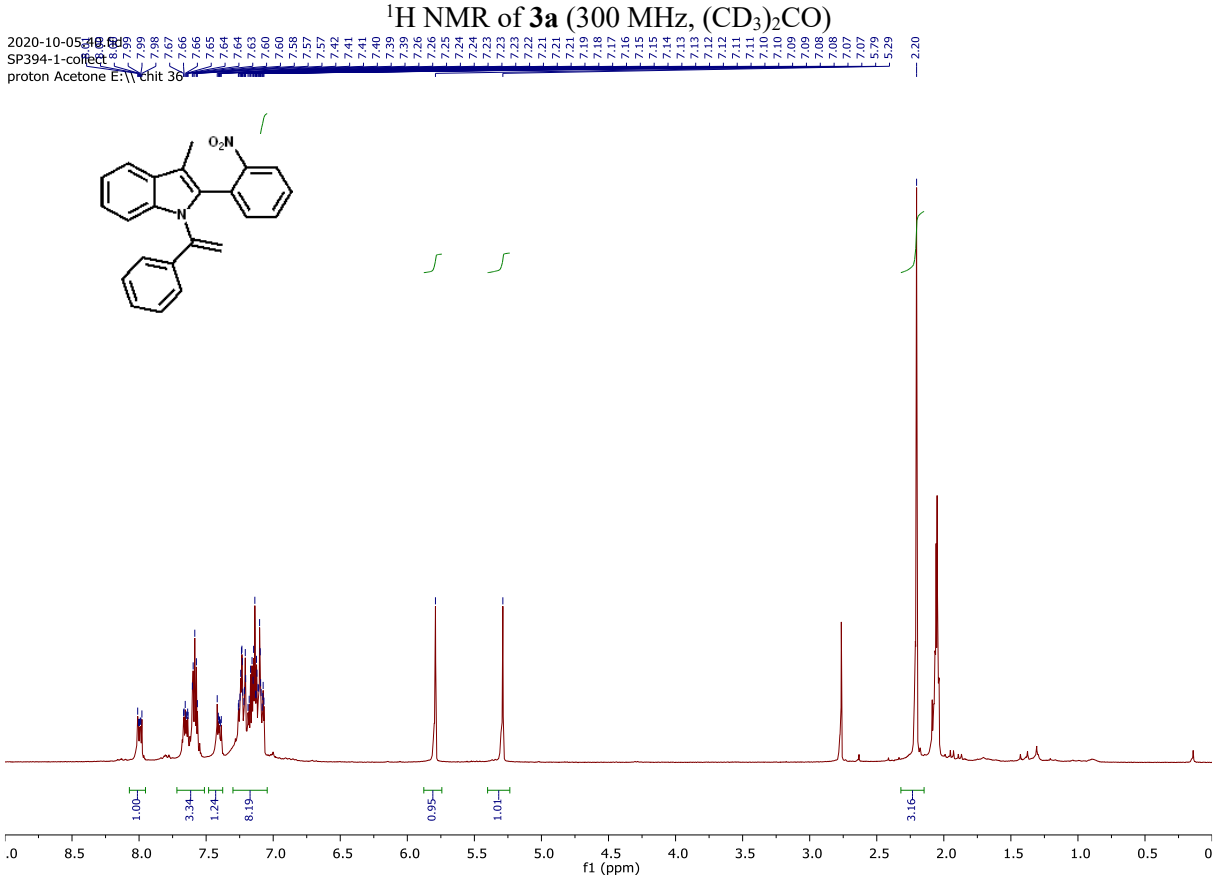
^{1}H NMR of **2j** (200 MHz, $(CD_3)_2CO$)



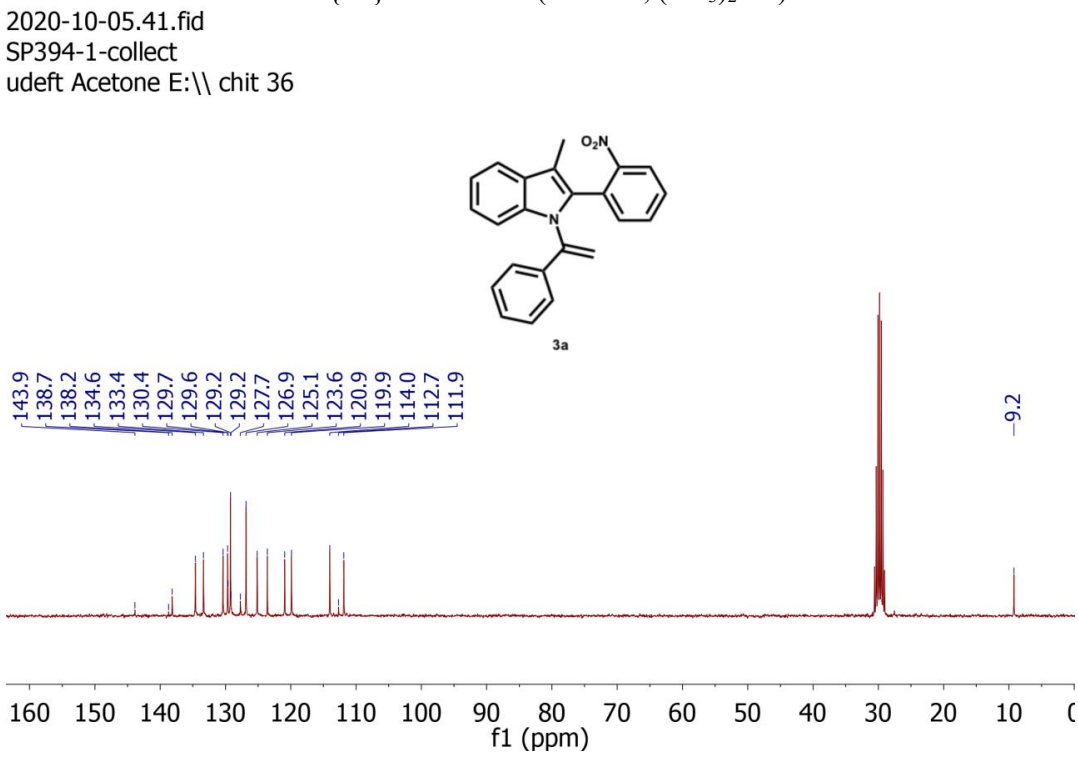
^{1}H NMR of **2k** (200 MHz, $CDCl_3$)



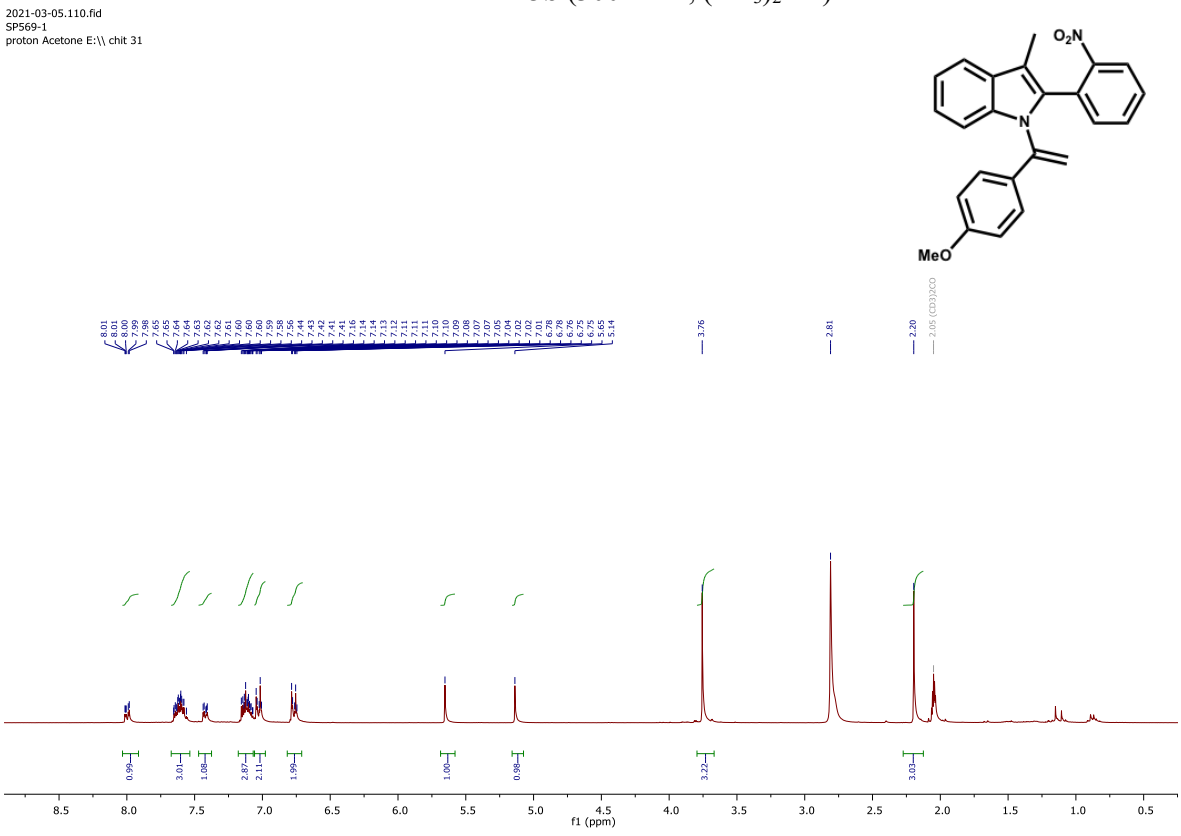
^{1}H NMR of **3a** (300 MHz, $(CD_3)_2CO$)



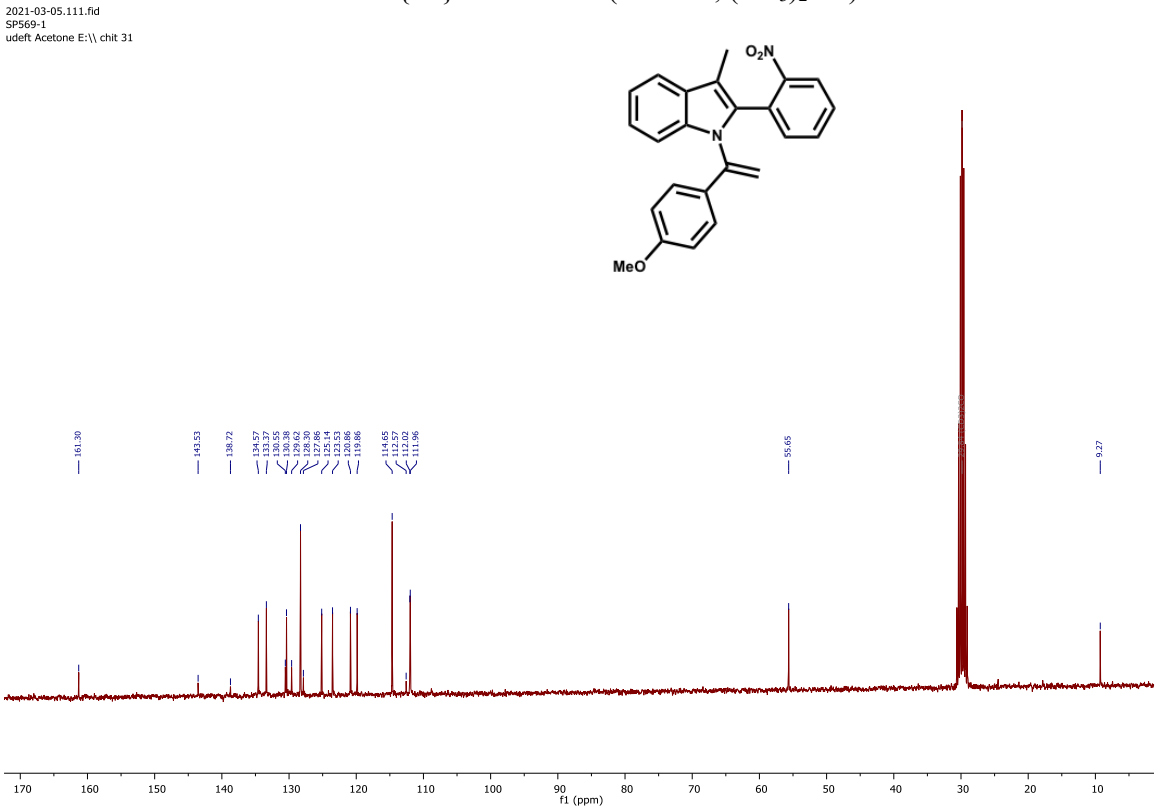
$^{13}C\{^{1}H\}$ NMR of **3a** (75 MHz, $(CD_3)_2CO$)



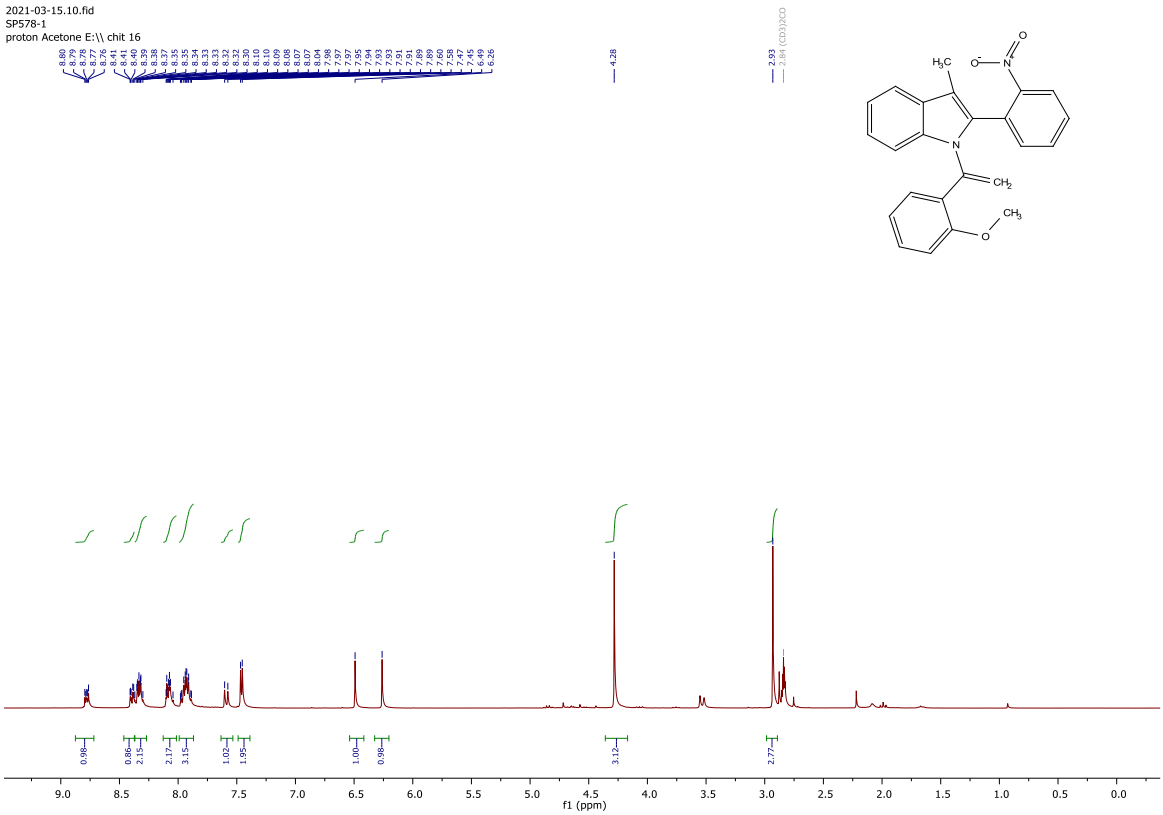
^{1}H NMR of **3b** (300 MHz, $(CD_3)_2CO$)



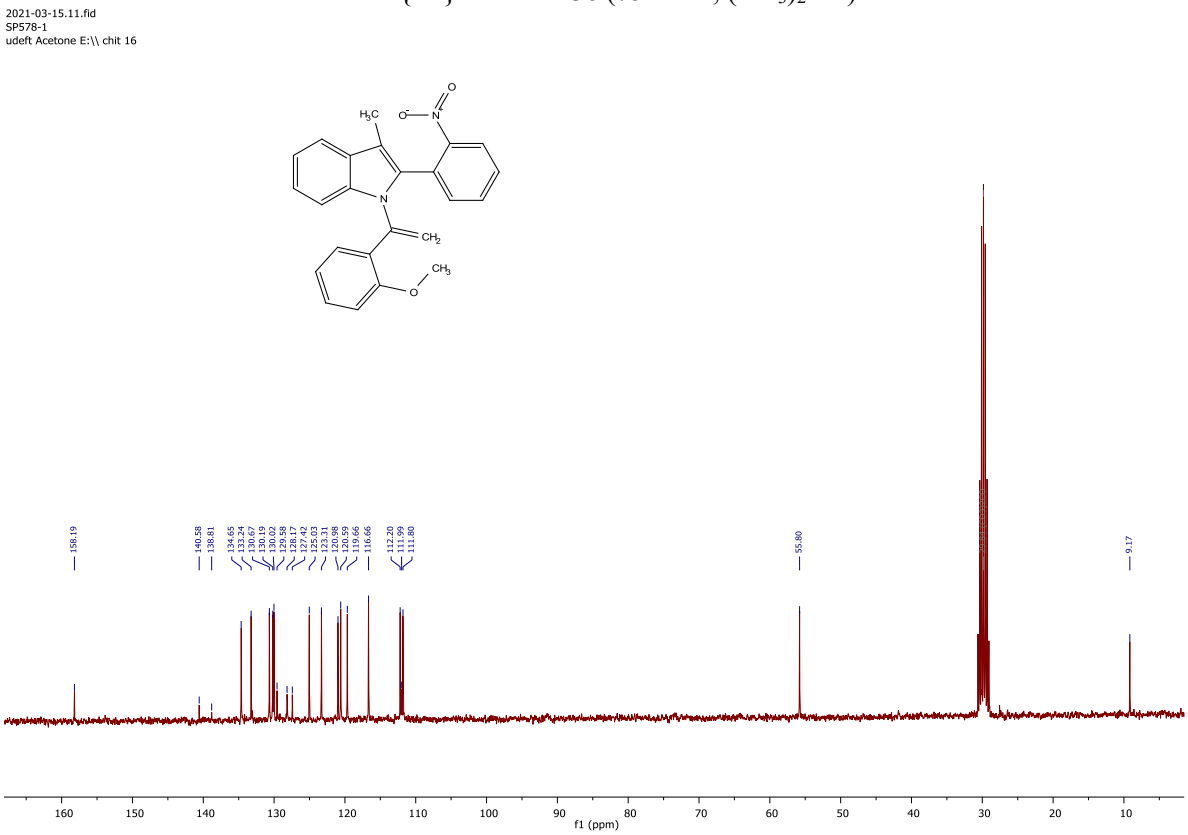
$^{13}C\{^{1}H\}$ NMR of **3b** (75 MHz, $(CD_3)_2CO$)



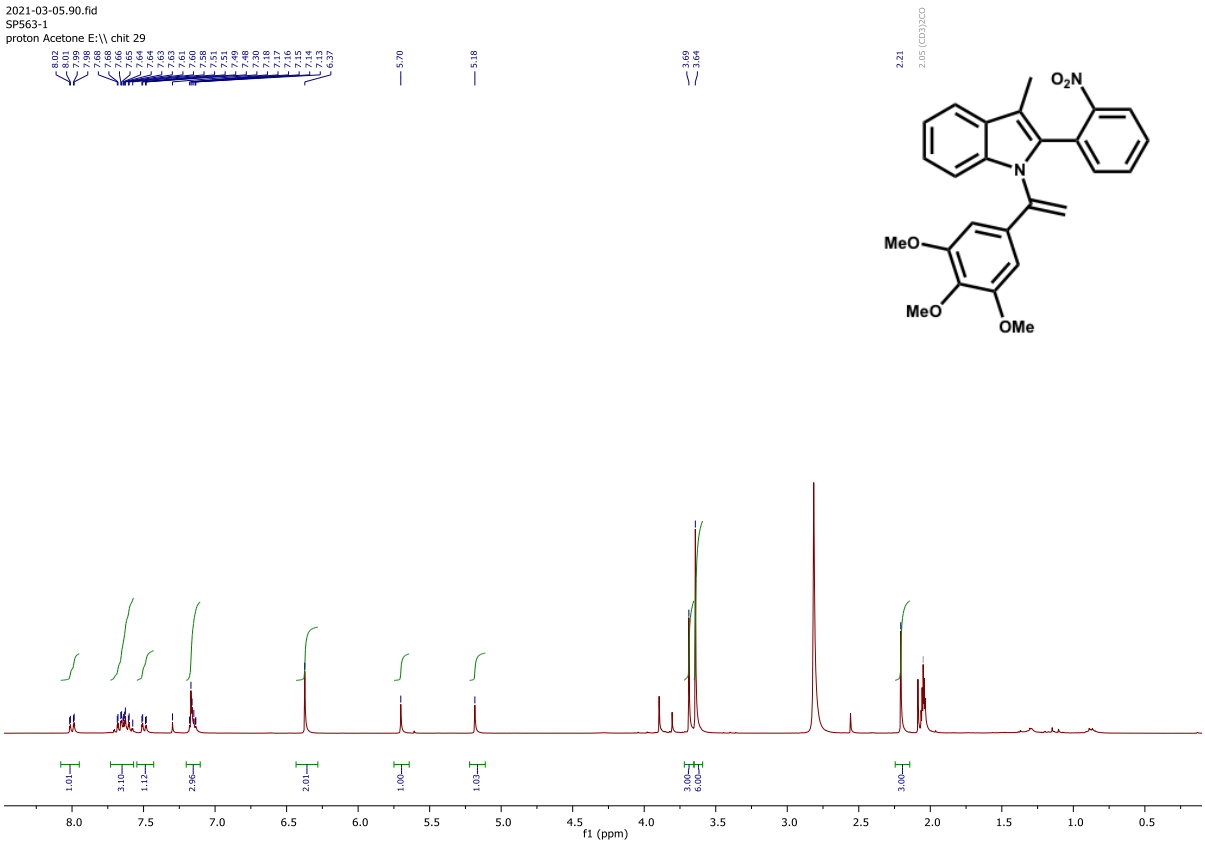
^{1}H NMR of **3c** (300 MHz, $(CD_3)_2CO$)



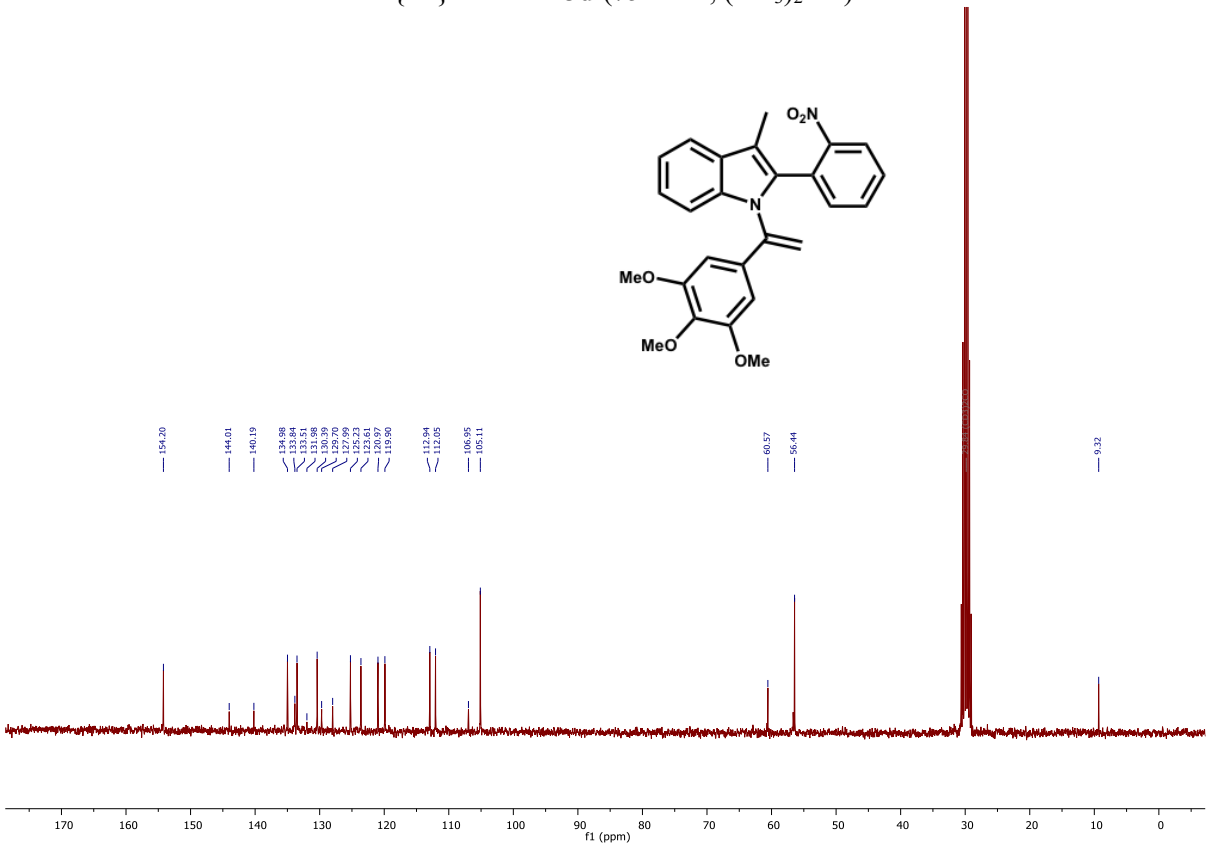
$^{13}C\{^{1}H\}$ NMR of **3c** (75 MHz, $(CD_3)_2CO$)



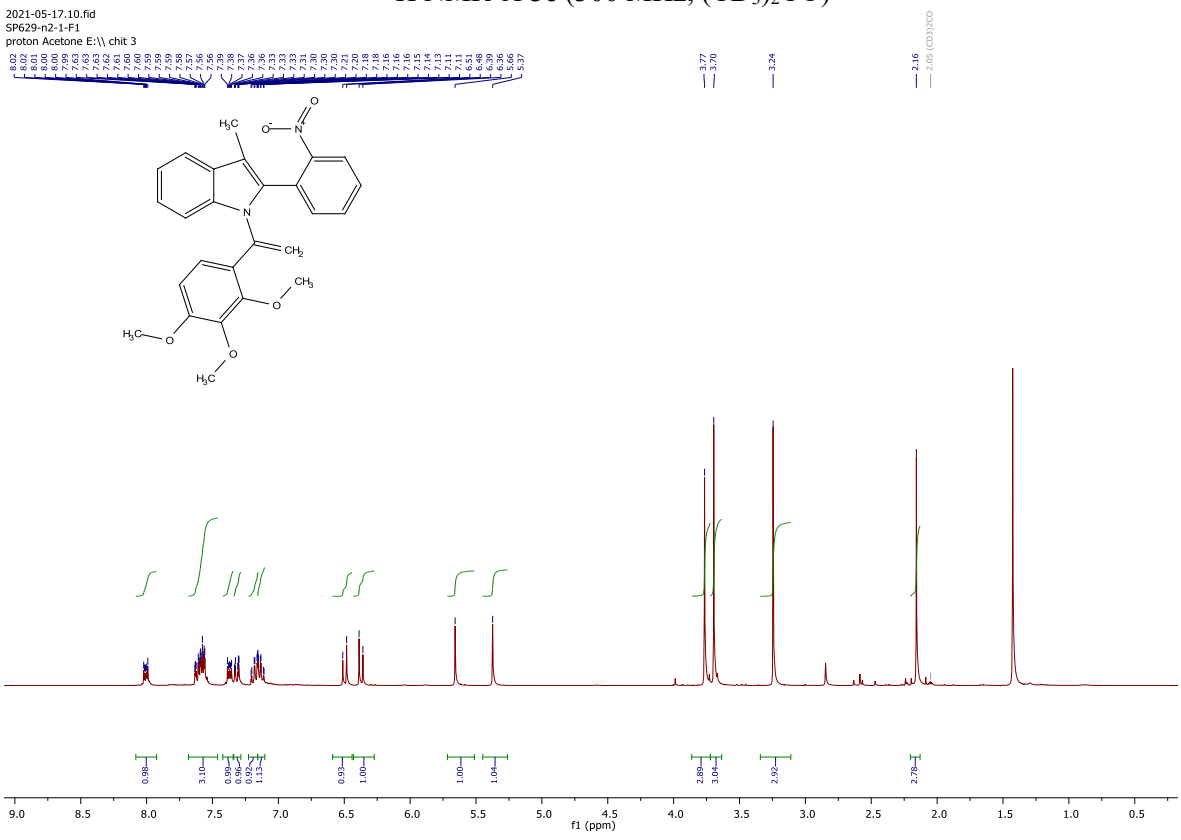
^{1}H NMR of **3d** (300 MHz, $(CD_3)_2CO$)



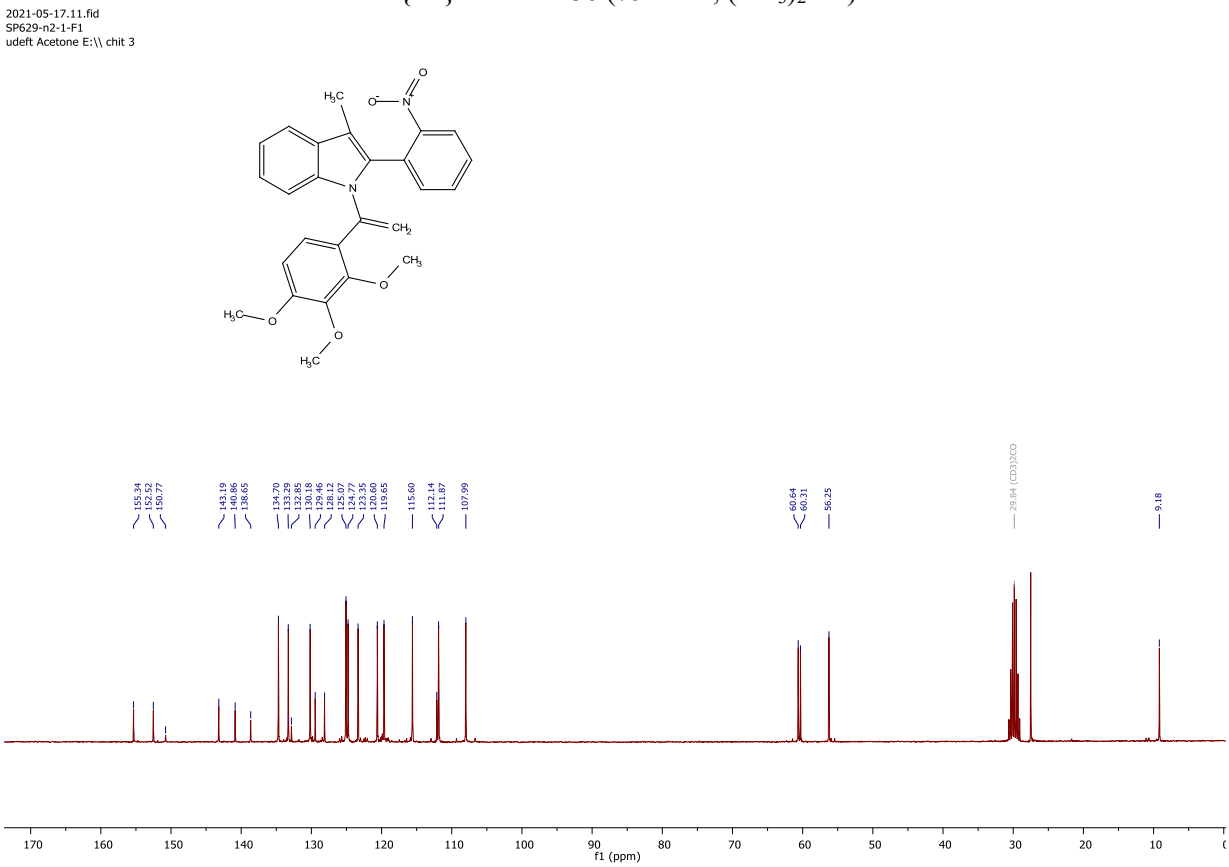
$^{13}C\{^{1}H\}$ NMR of **3d** (75 MHz, $(CD_3)_2CO$)



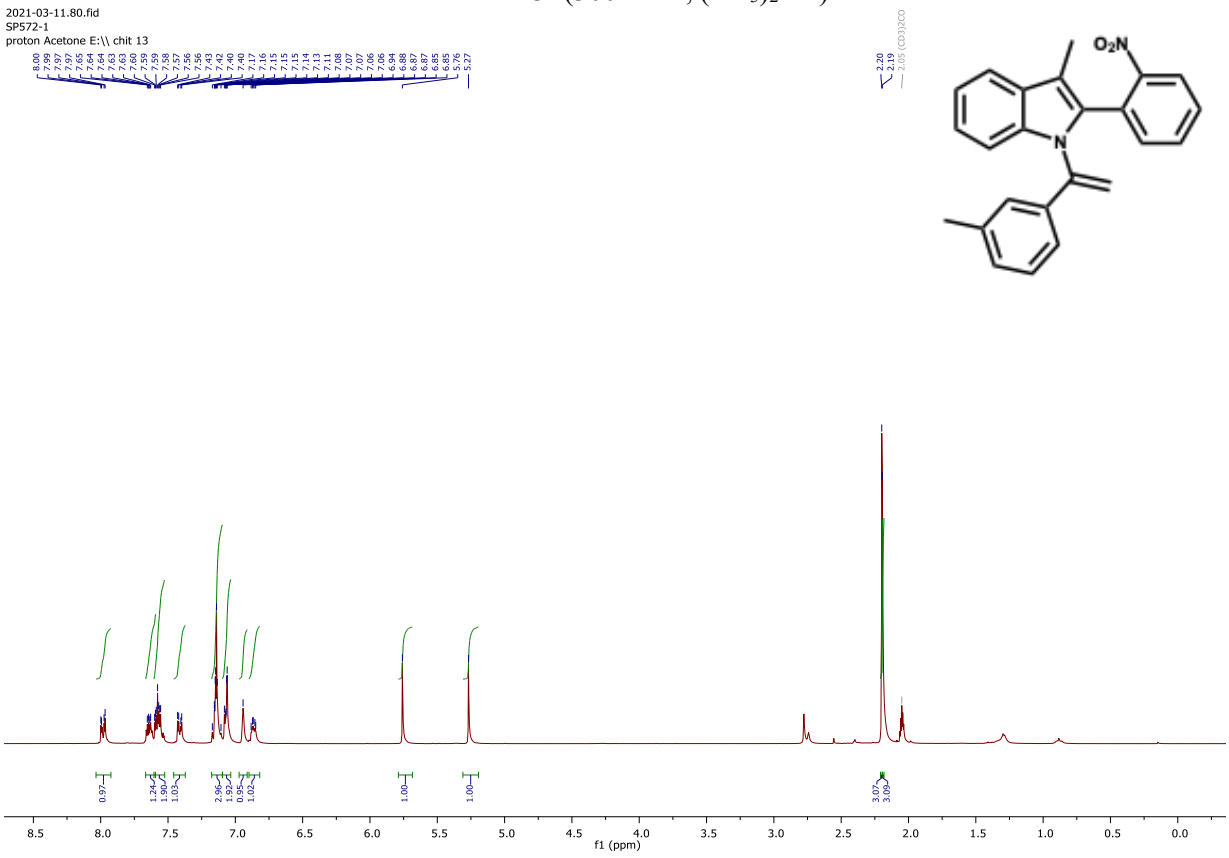
^{1}H NMR of **3e** (300 MHz, $(CD_3)_2CO$)



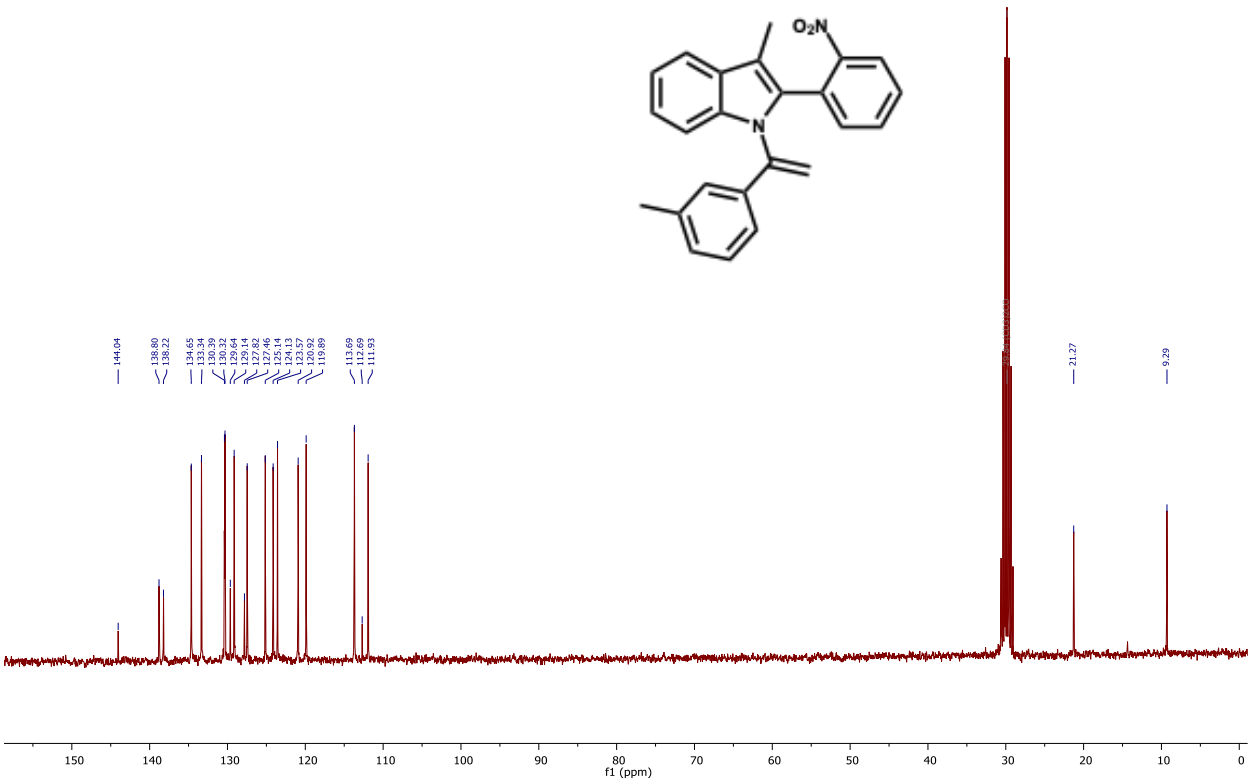
$^{13}C\{^{1}H\}$ NMR of **3e** (75 MHz, $(CD_3)_2CO$)



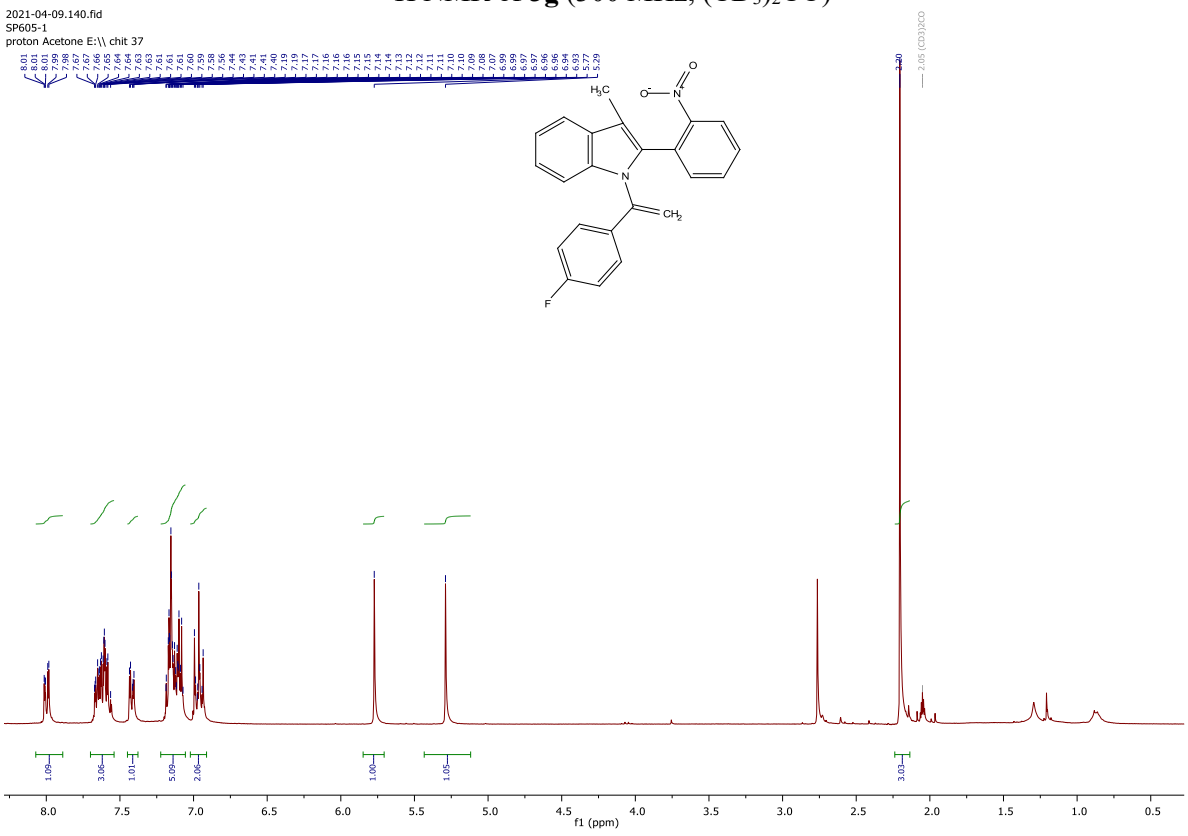
^{1}H NMR of **3f** (300 MHz, $(CD_3)_2CO$)



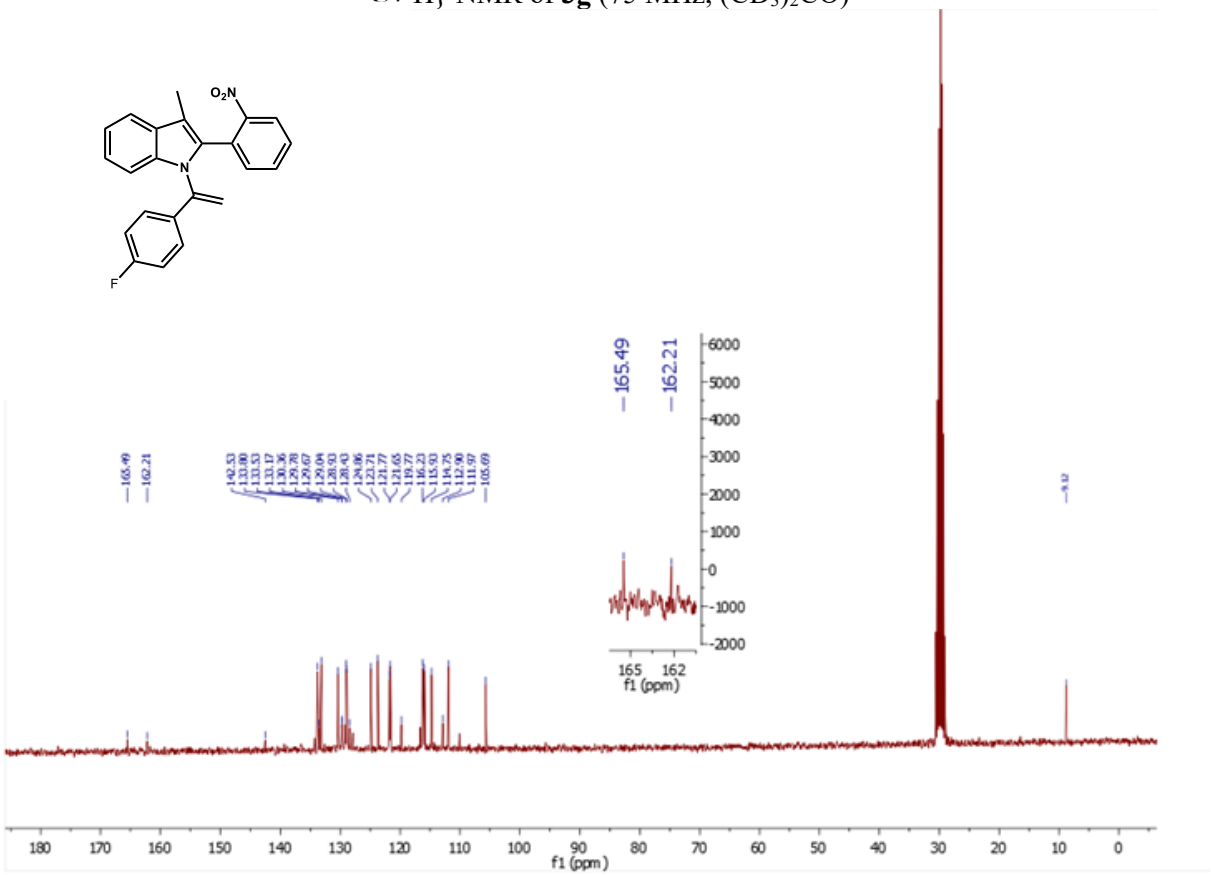
$^{13}C\{^{1}H\}$ NMR of **3f** (75 MHz, $(CD_3)_2CO$)



^{1}H NMR of **3g** (300 MHz, $(CD_3)_2CO$)

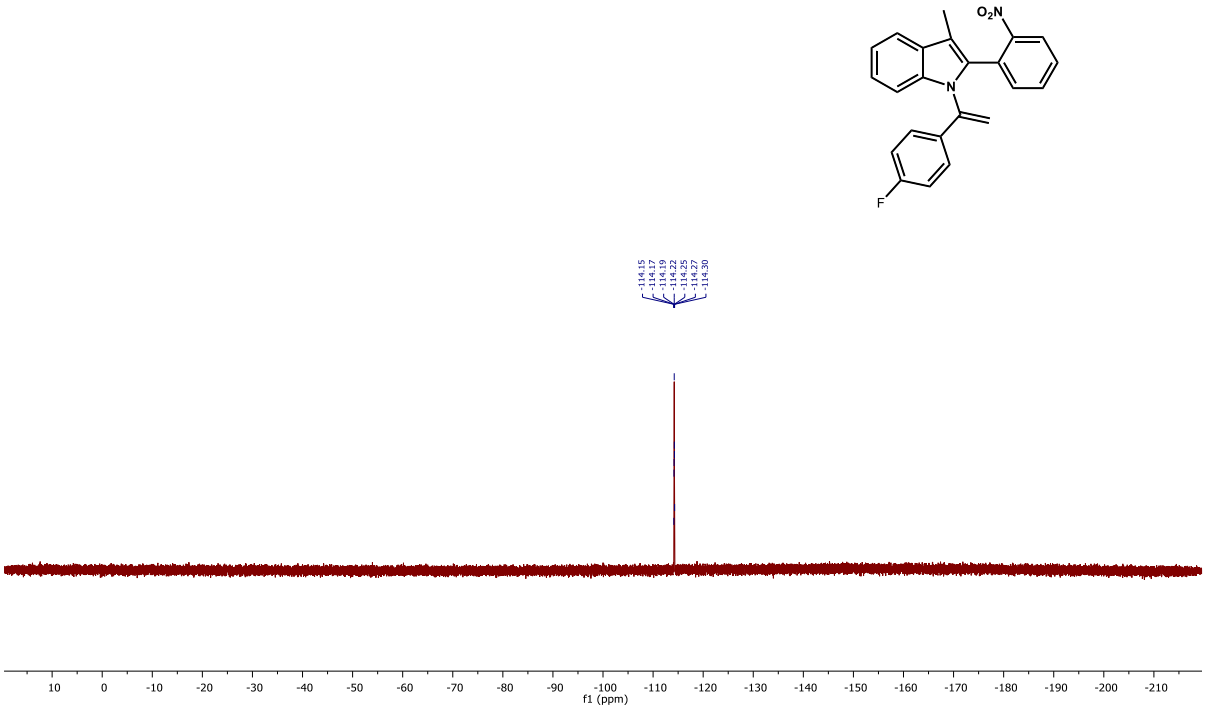


$^{13}C\{^{1}H\}$ NMR of **3g** (75 MHz, $(CD_3)_2CO$)

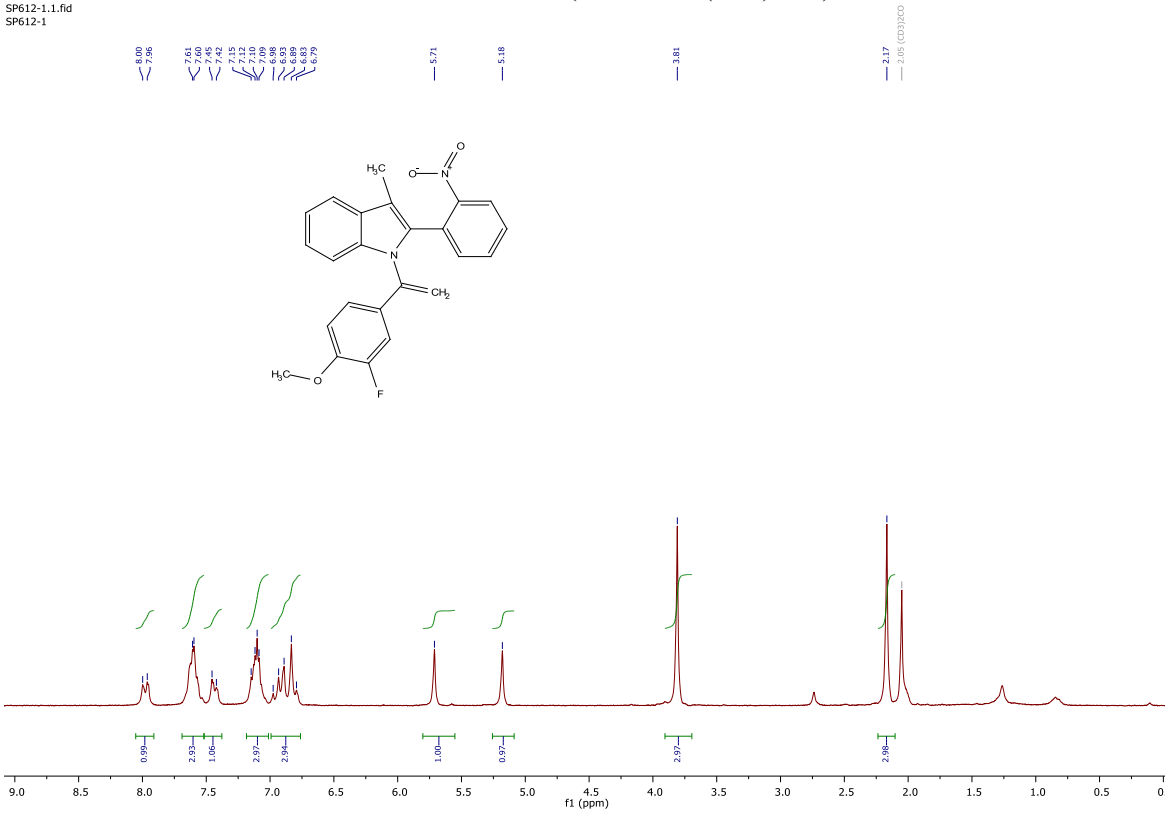


$^{19}F\{^{1}H\}$ NMR of **3g** (188 MHz, $(CD_3)_2CO$)

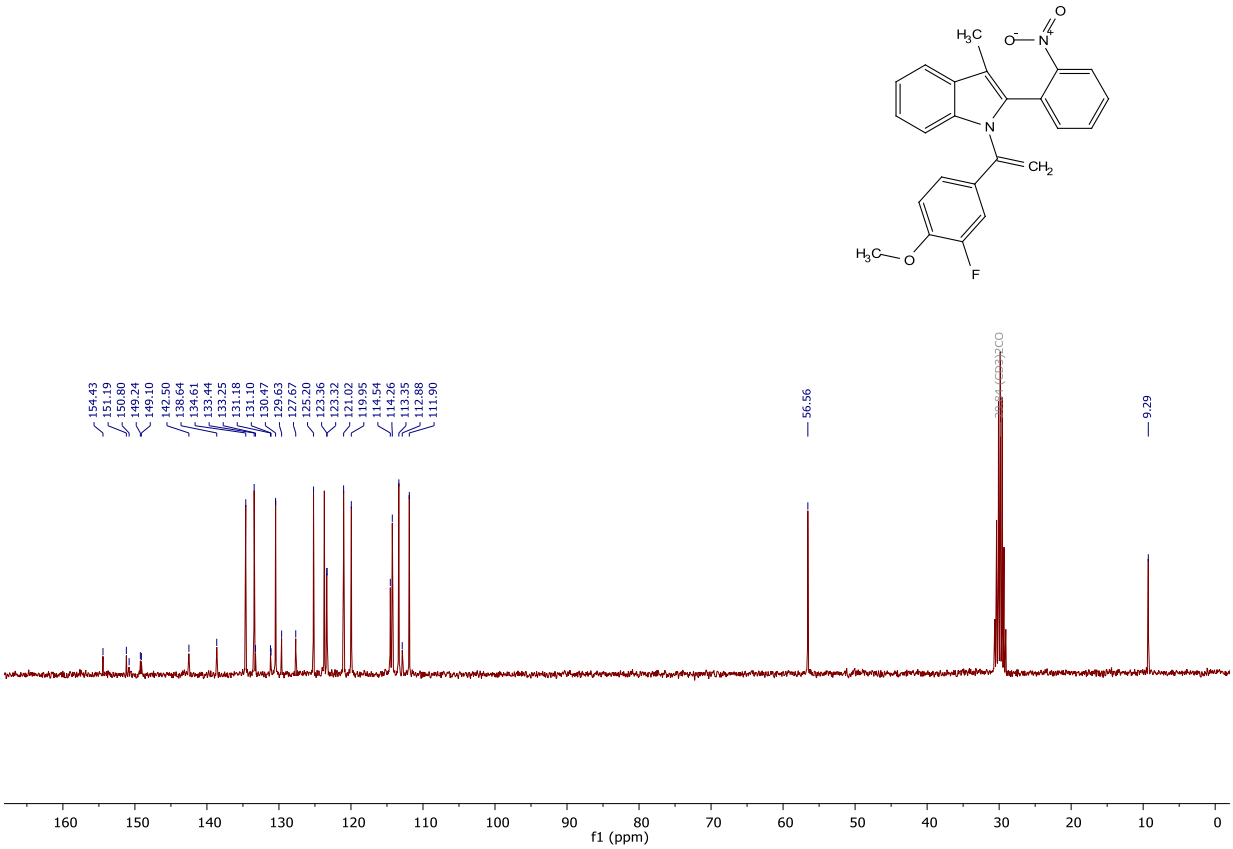
SP605-1-fluor.1.fid
SP605-1-fluor



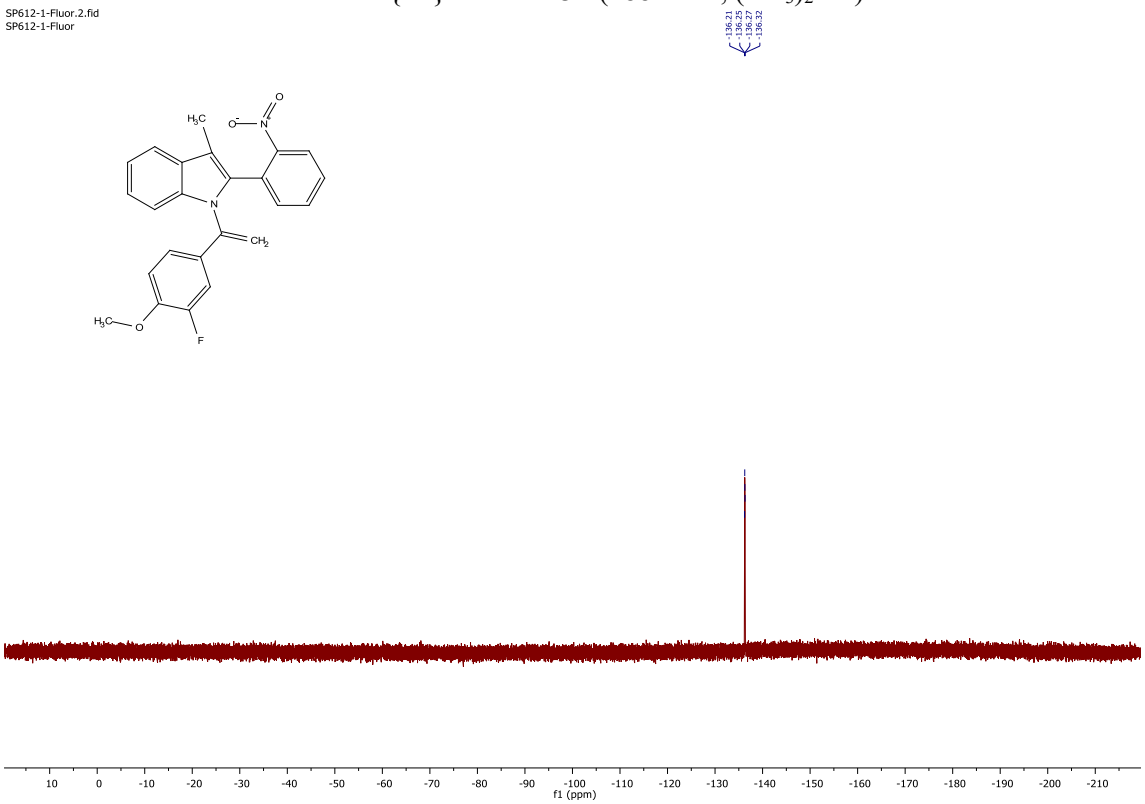
^{1}H NMR of **3h** (200 MHz, $(CD_3)_2CO$)



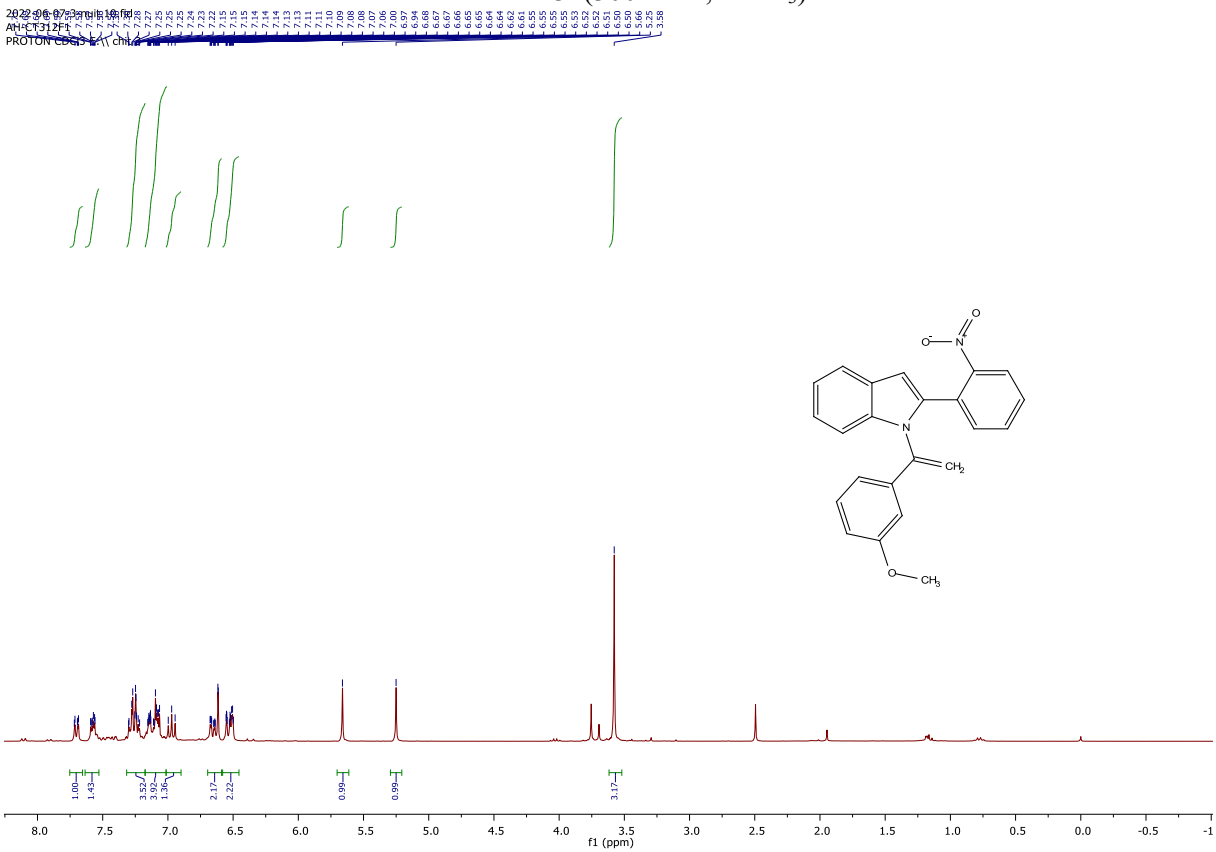
^{13}C{^{1}H} NMR of **3h** (75 MHz, $(CD_3)_2CO$)



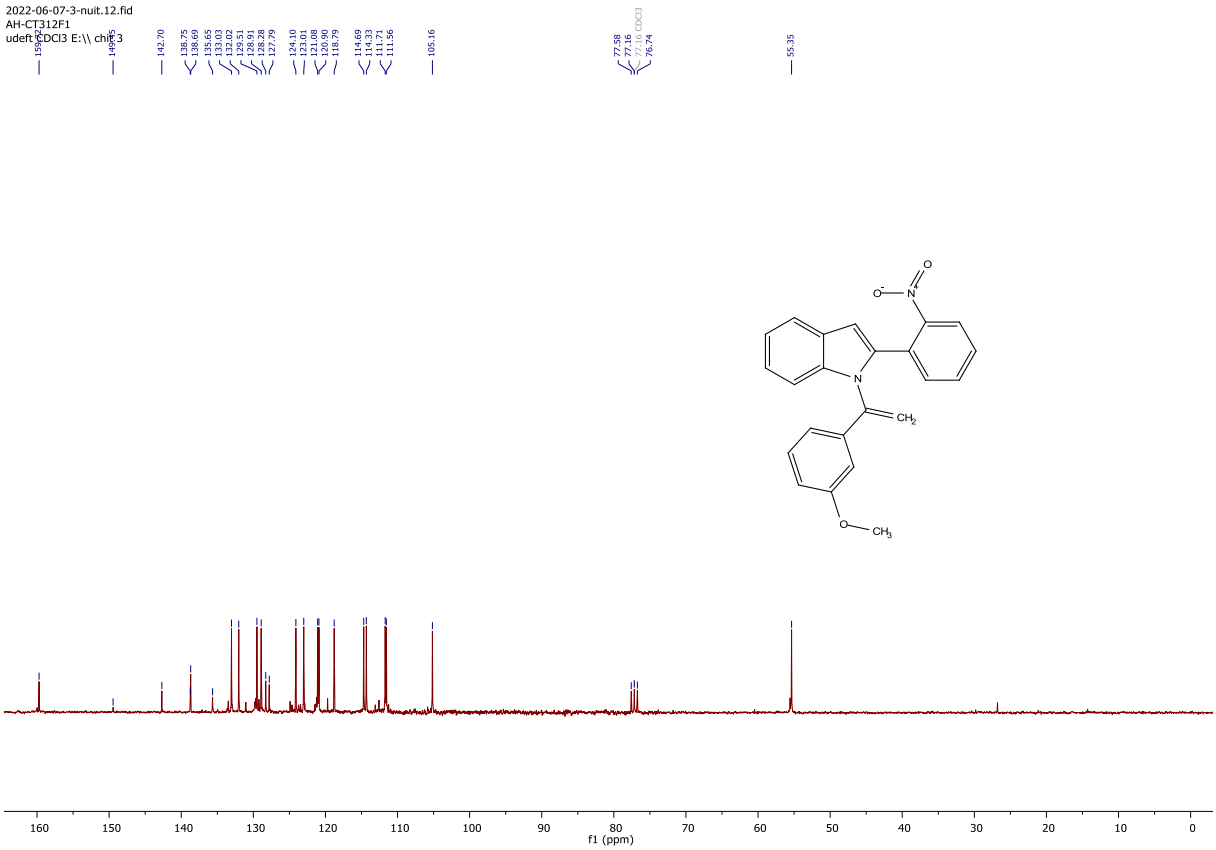
$^{19}F\{^{1}H\}$ NMR of **3h** (188 MHz, $(CD_3)_2CO$)



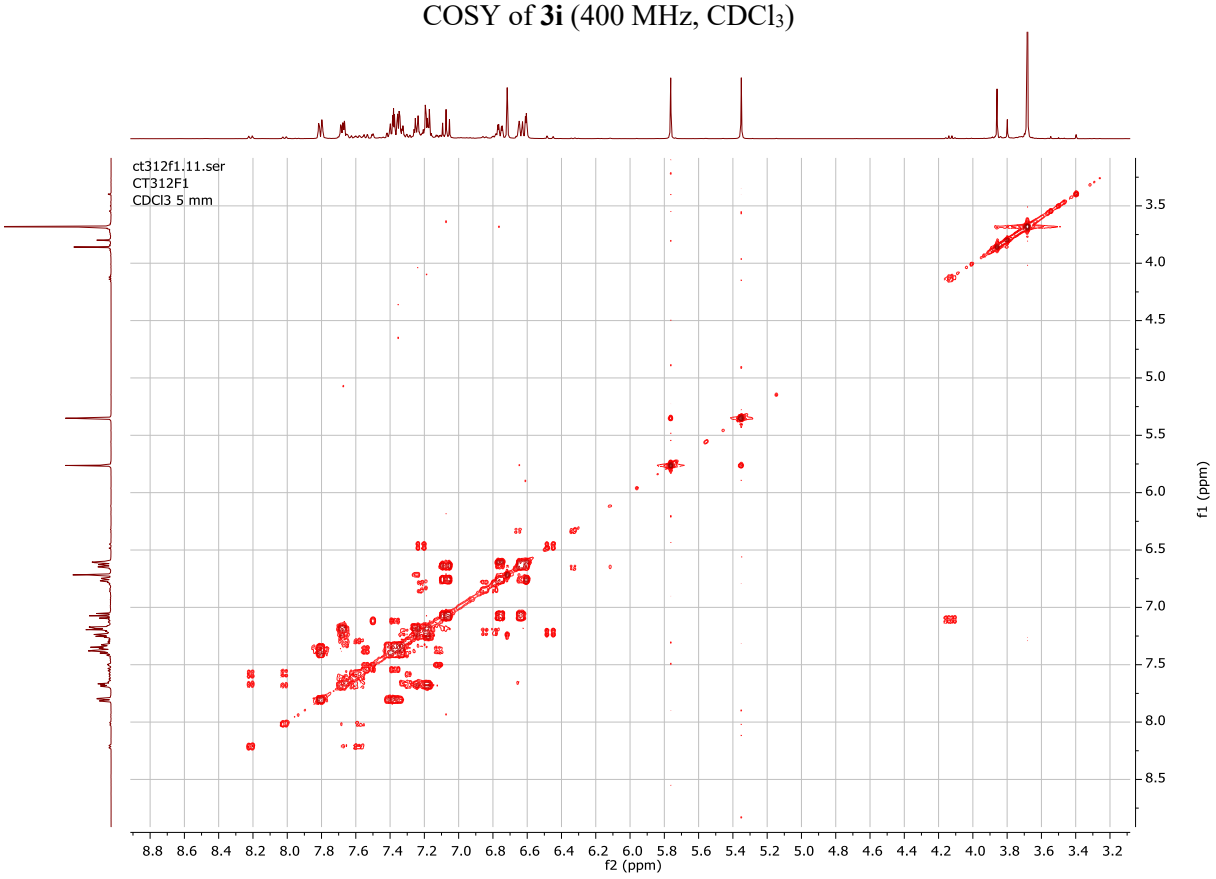
^{1}H NMR of **3i** (300 MHz, $CDCl_3$)



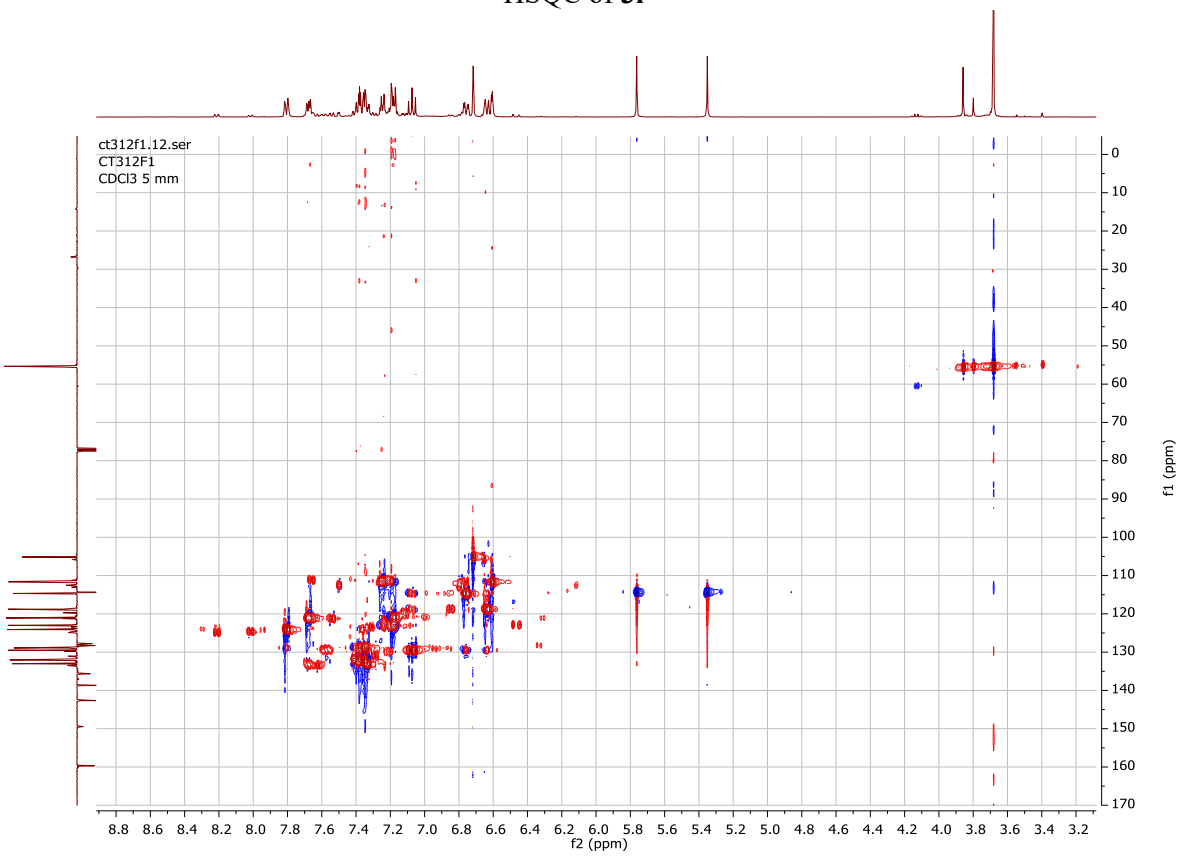
$^{13}C\{^{1}H\}$ NMR of **3i** (75 MHz, $CDCl_3$)



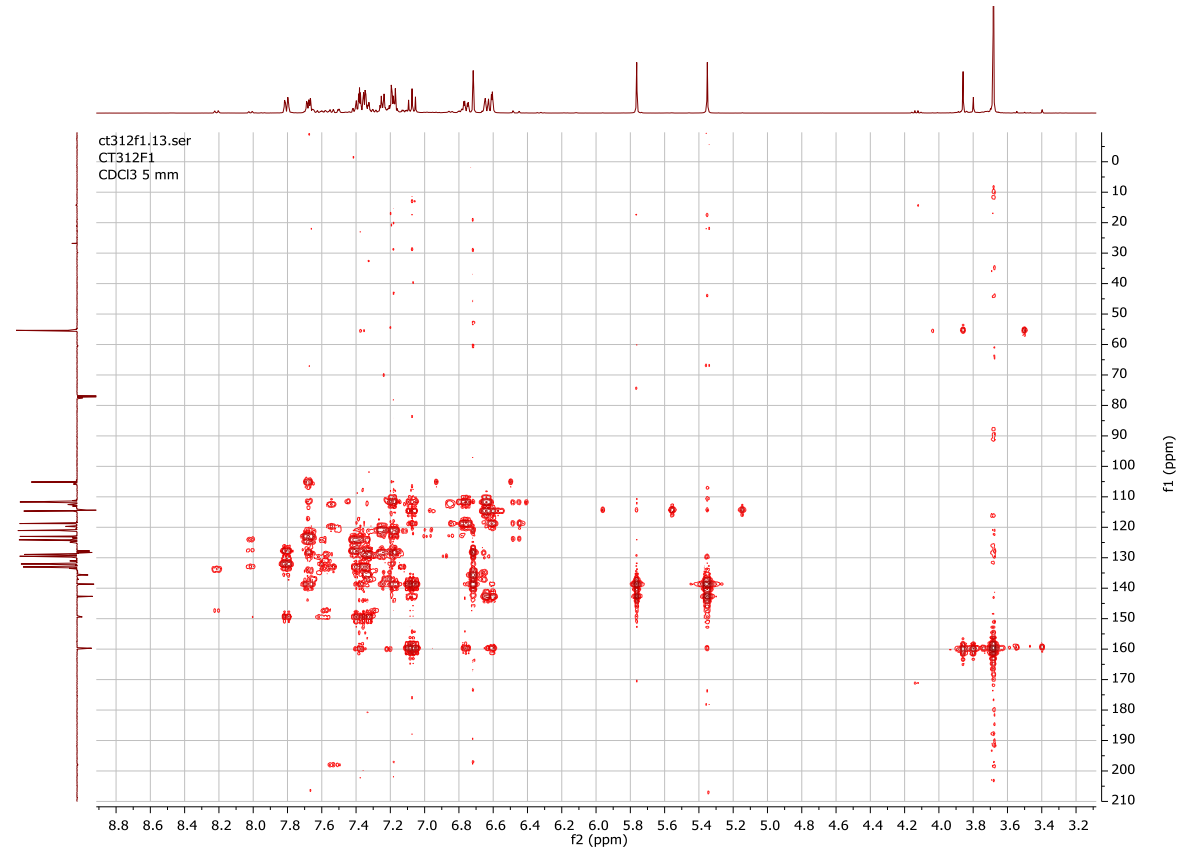
COSY of **3i** (400 MHz, $CDCl_3$)



HSQC of **3i**



HMBC of **3i**



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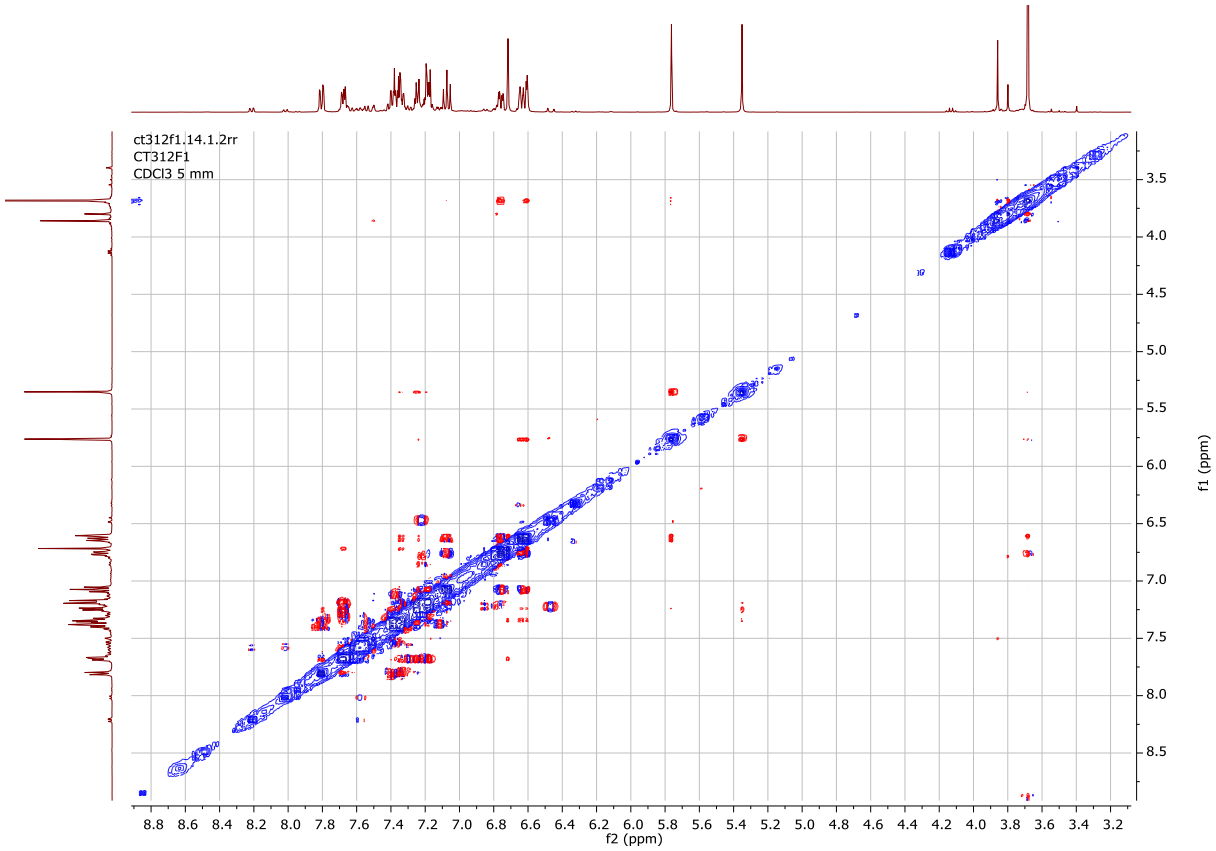
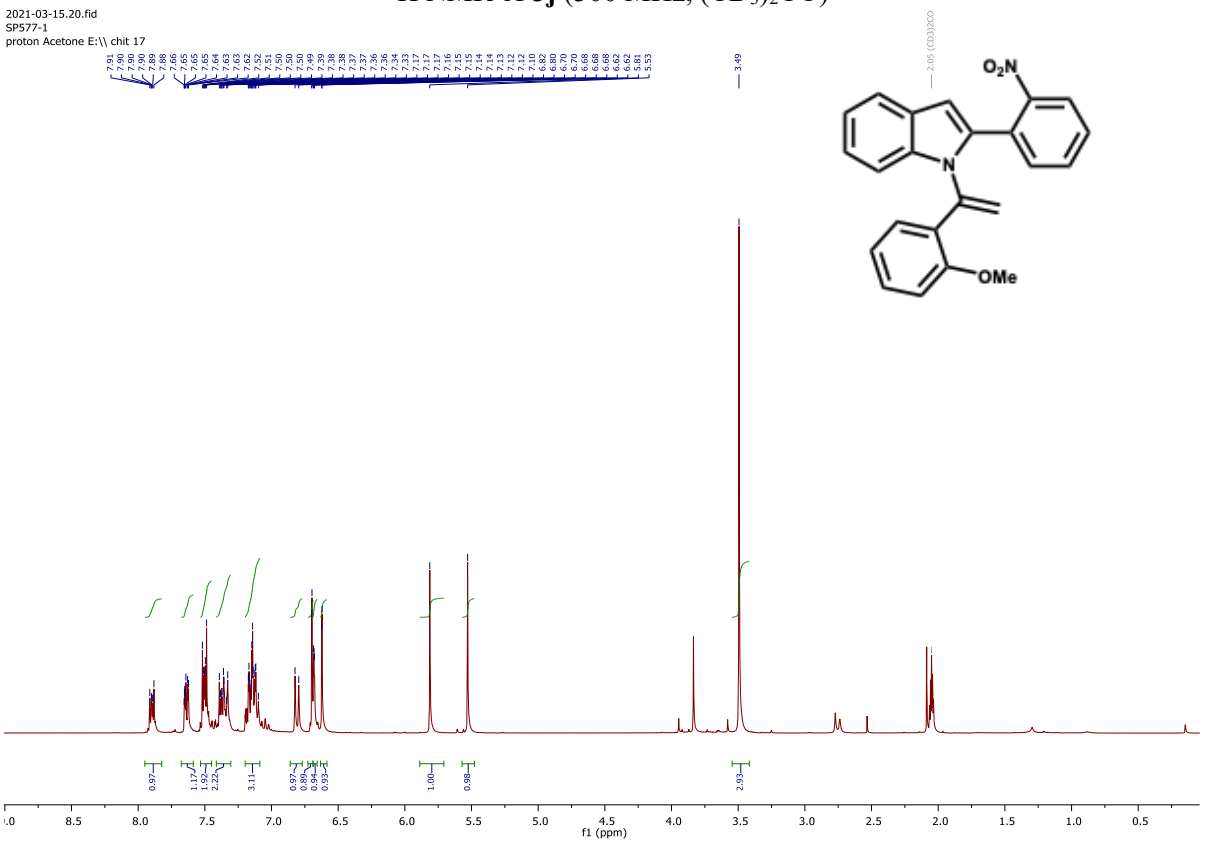
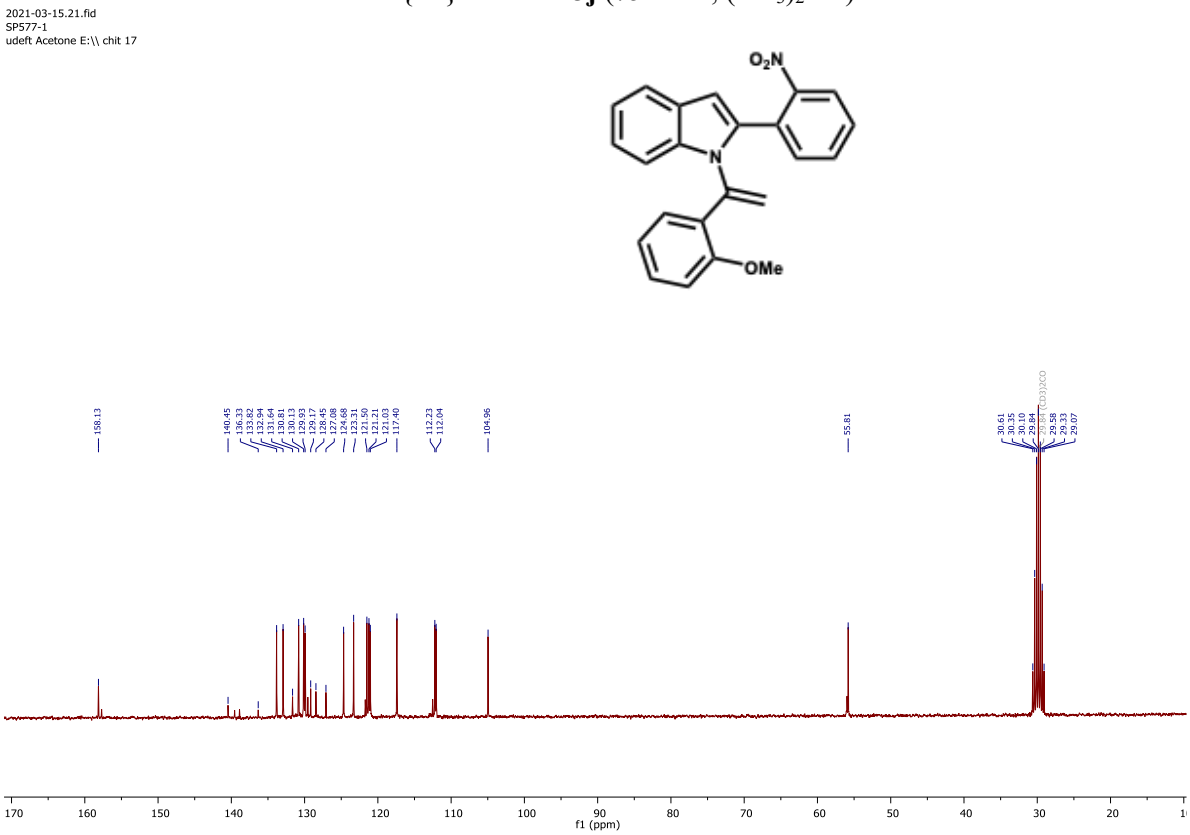


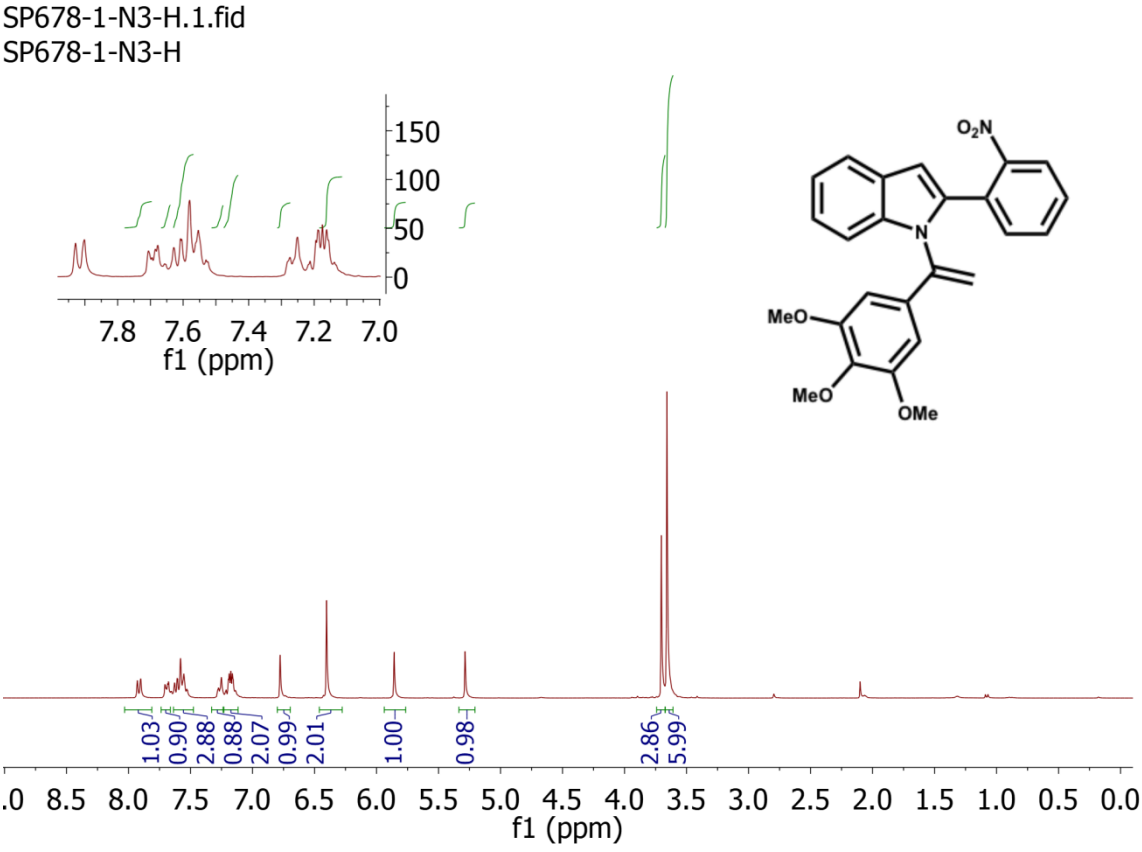
^{1}H NMR of **3j** (300 MHz, $(CD_3)_2CO$)



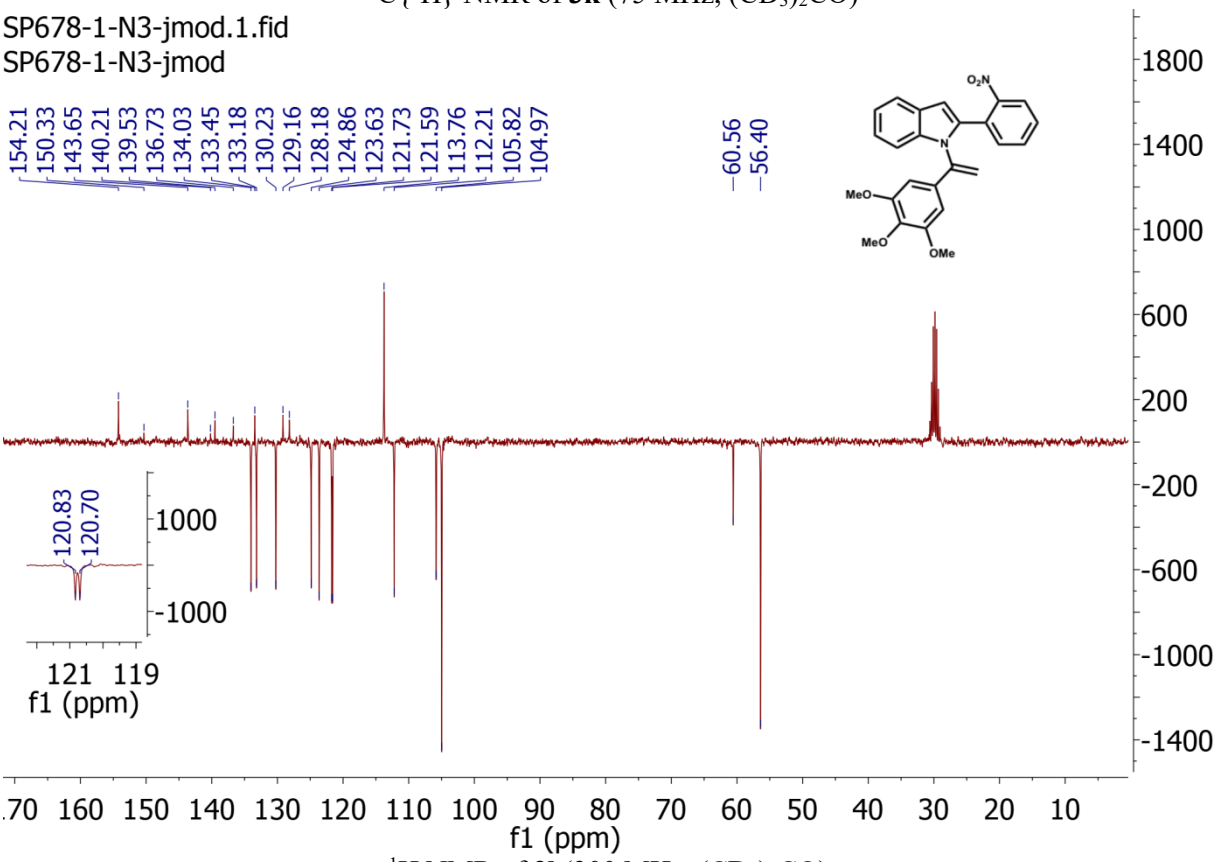
$^{13}C\{^{1}H\}$ NMR of **3j** (75 MHz, $(CD_3)_2CO$)



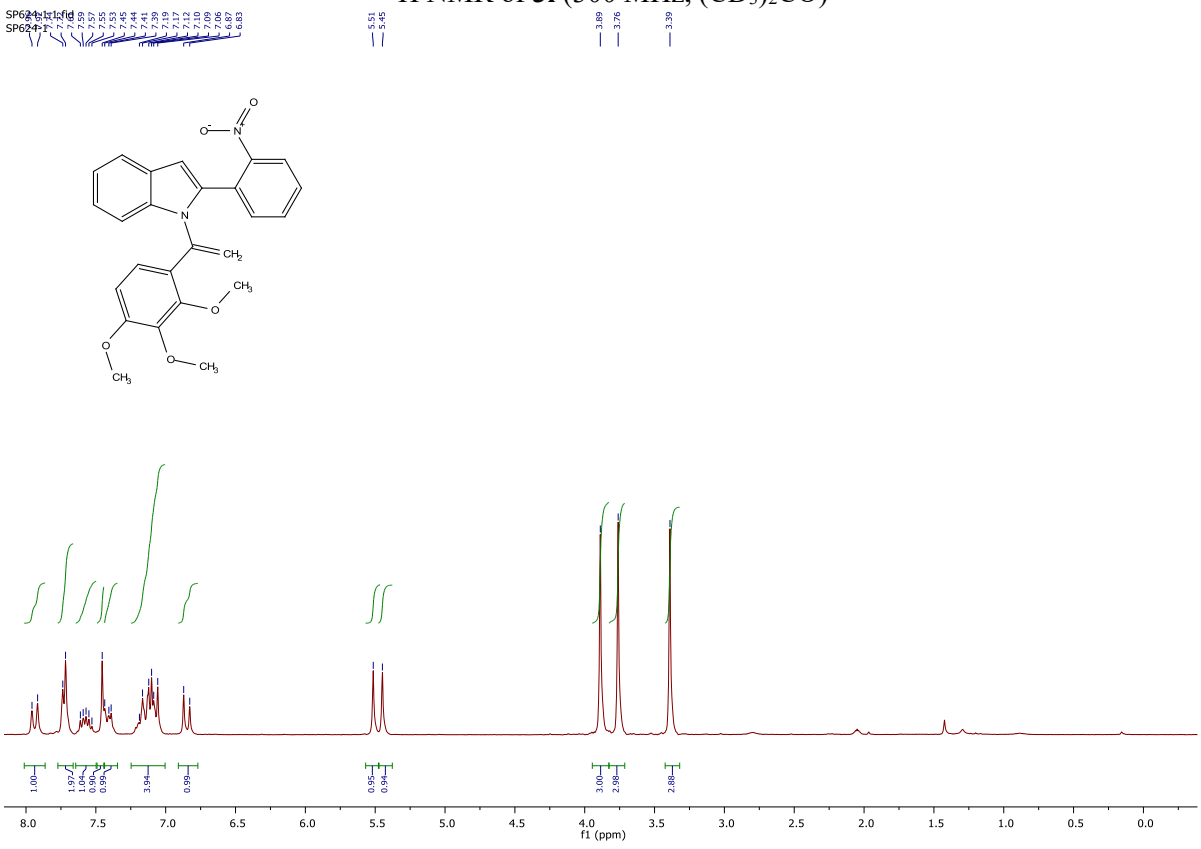
^{1}H NMR of **3k** (300 MHz, $(CD_3)_2CO$)



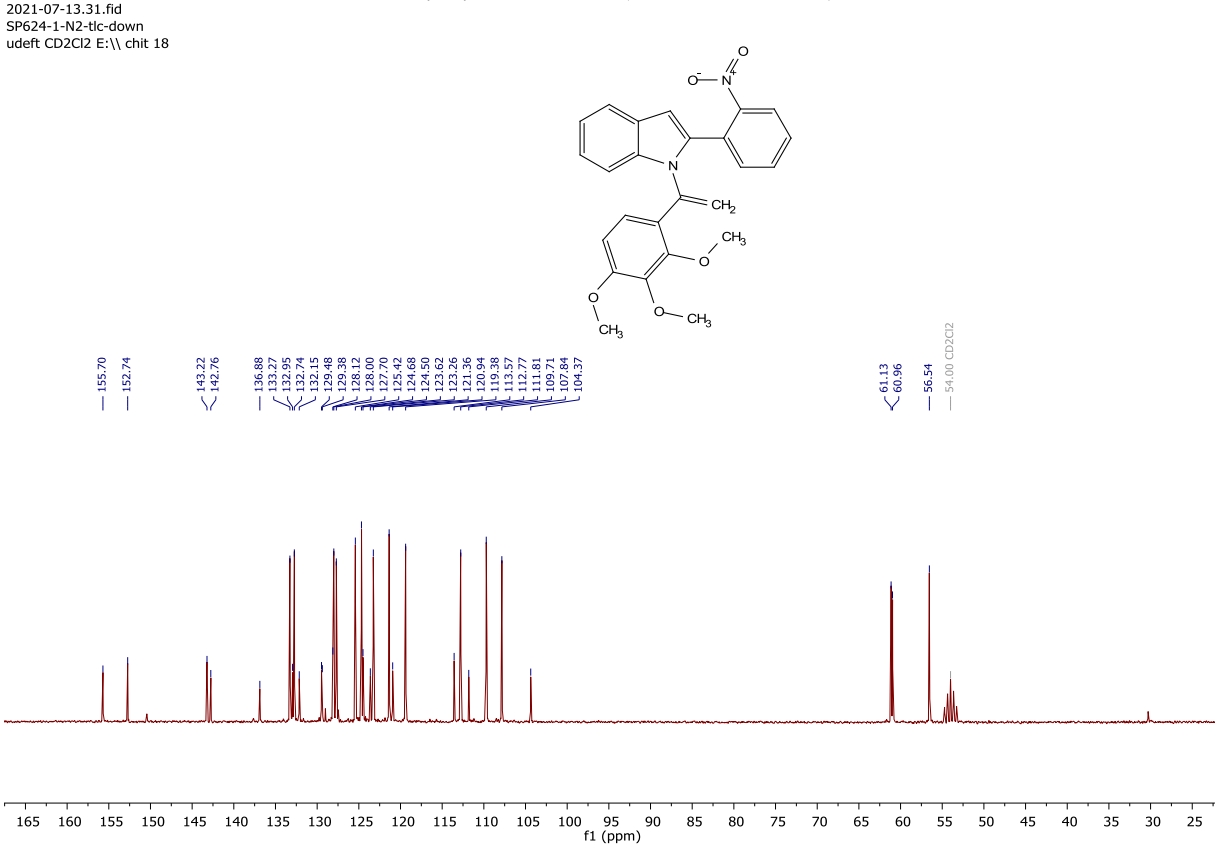
$^{13}C\{^{1}H\}$ NMR of **3k** (75 MHz, $(CD_3)_2CO$)



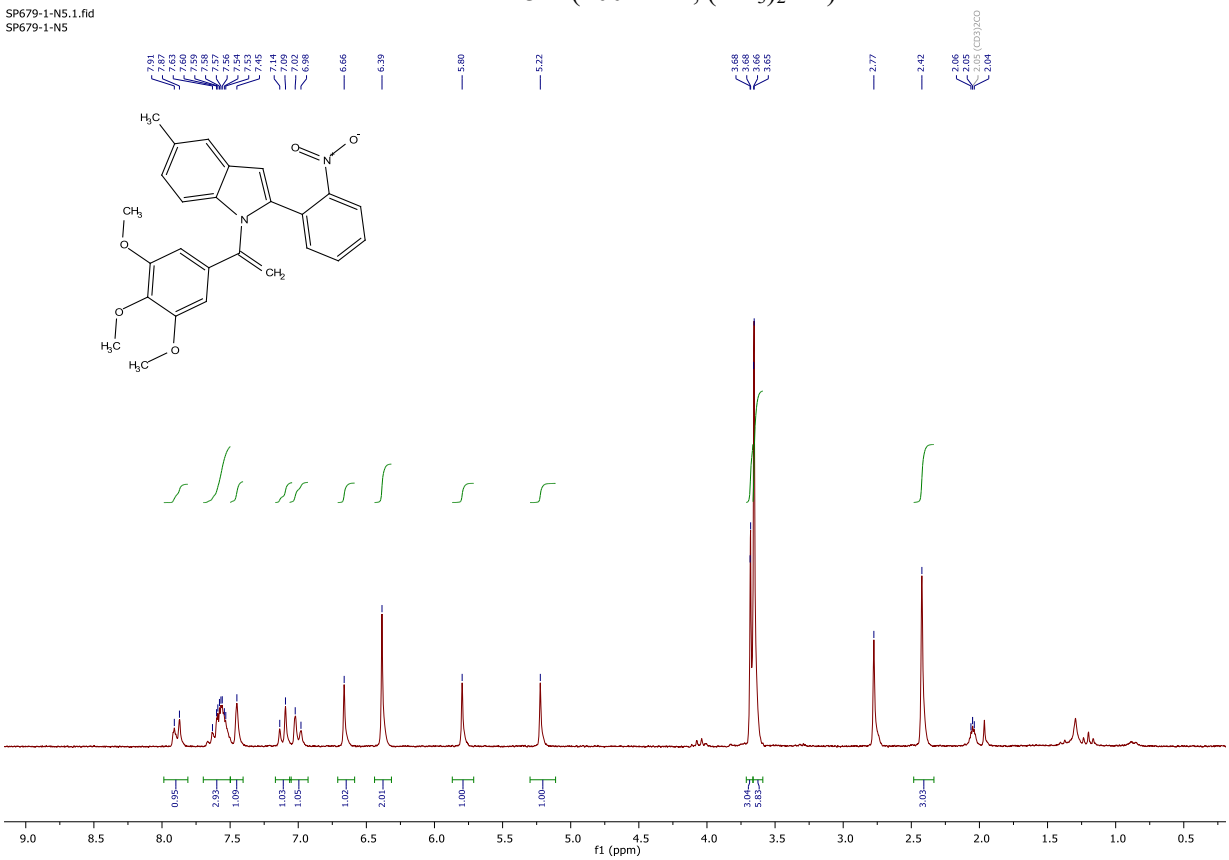
^{1}H NMR of **3l** (300 MHz, $(CD_3)_2CO$)



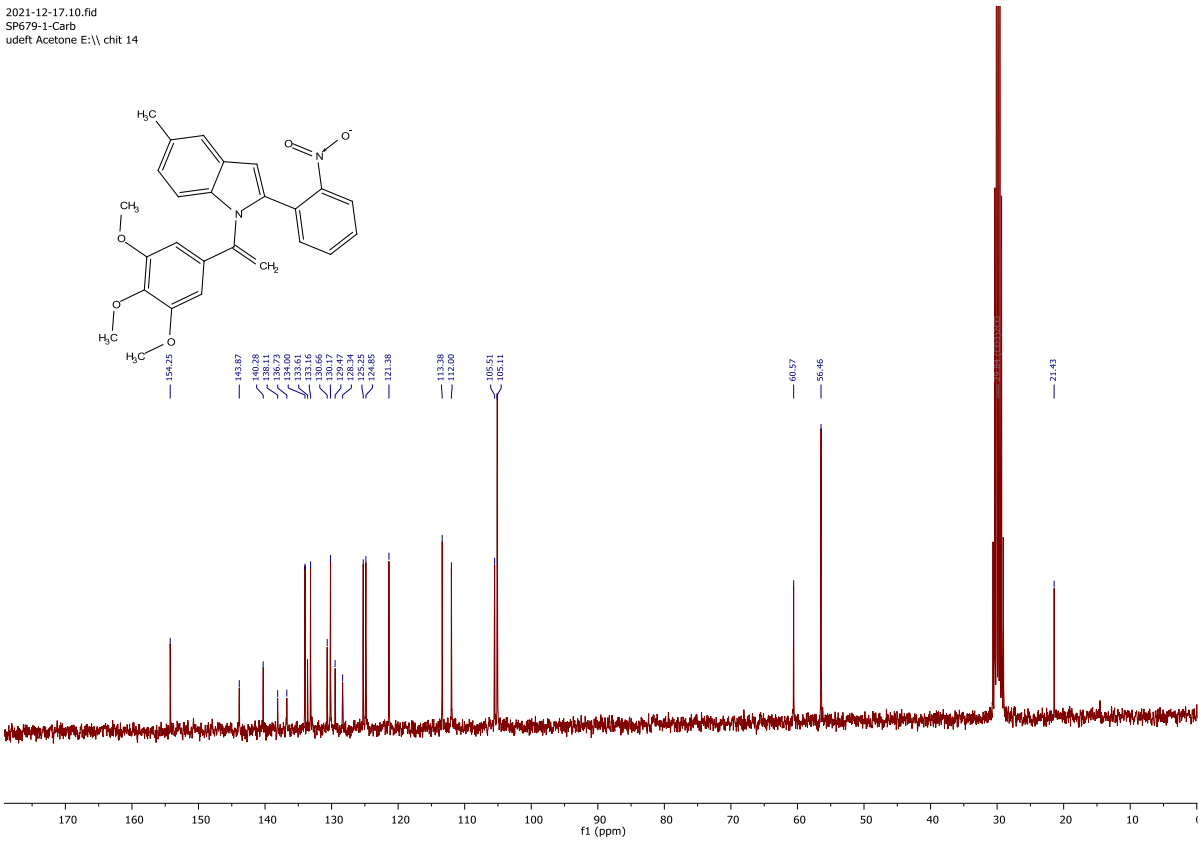
$^{13}C\{^{1}H\}$ NMR of **3l** (75 MHz, CD_2Cl_2)



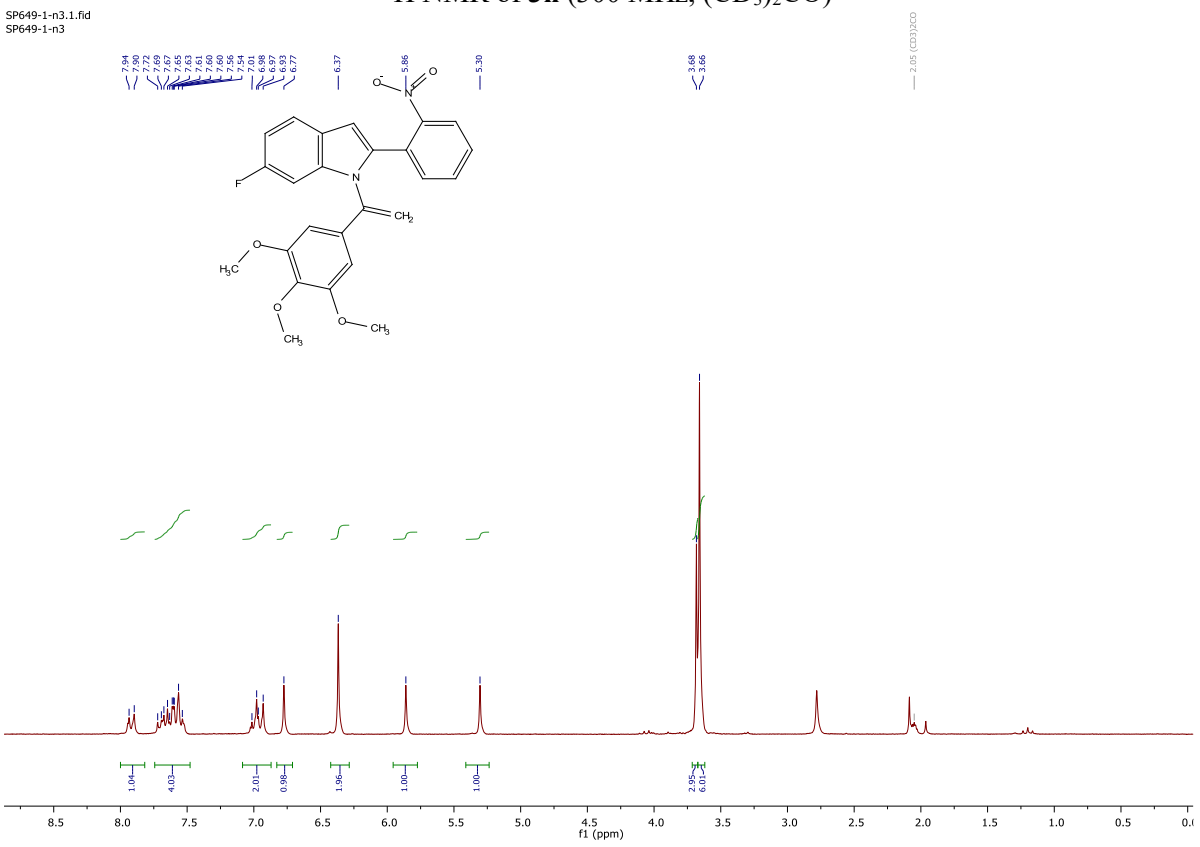
^{1}H NMR of **3m** (200 MHz, $(CD_3)_2CO$)



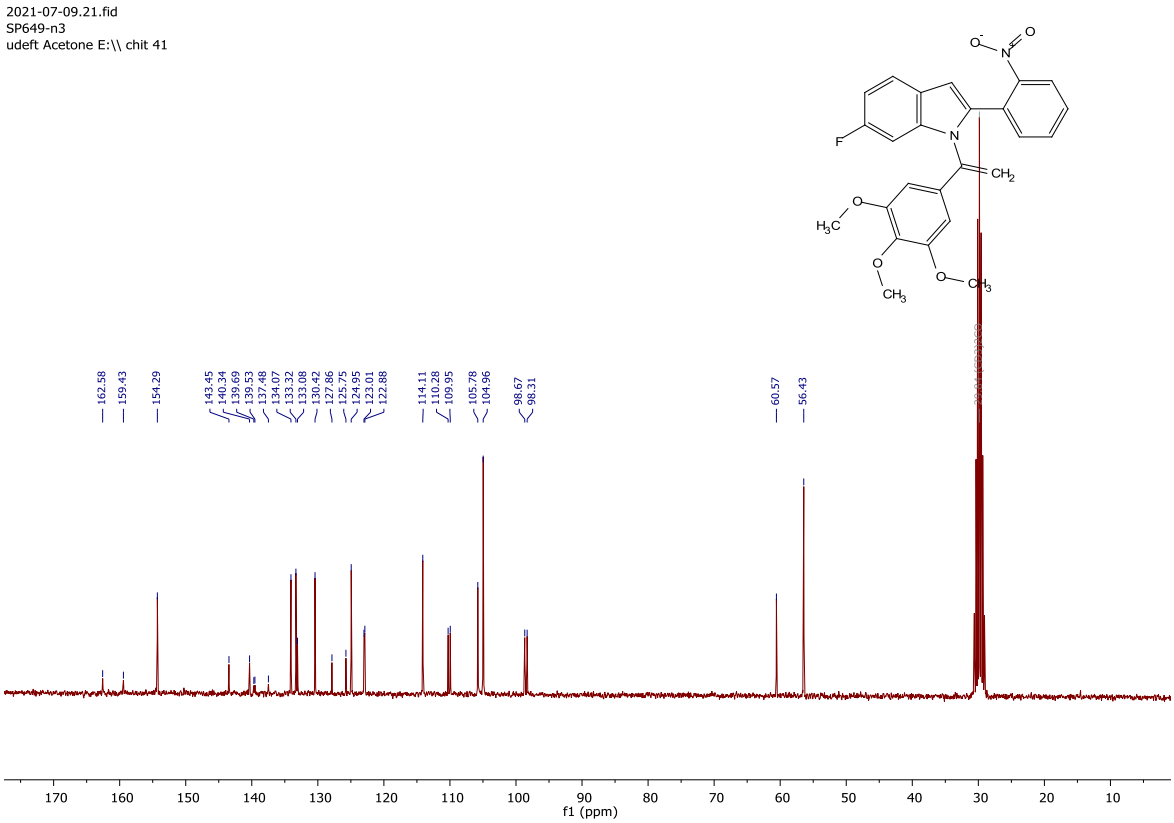
$^{13}C\{^{1}H\}$ NMR of **3m** (75 MHz, $(CD_3)_2CO$)



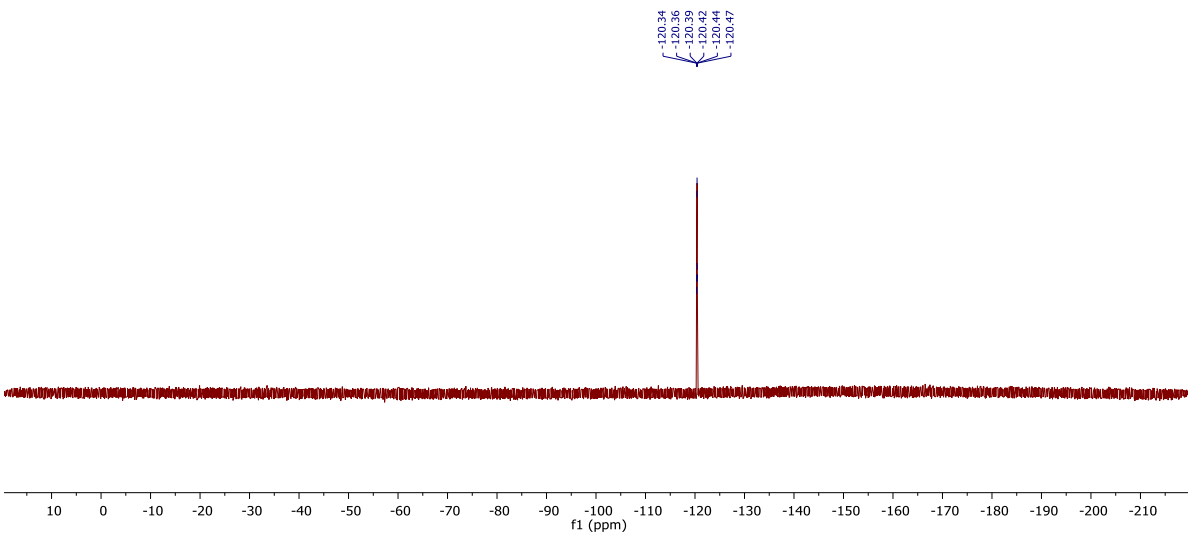
^{1}H NMR of **3n** (300 MHz, $(CD_3)_2CO$)



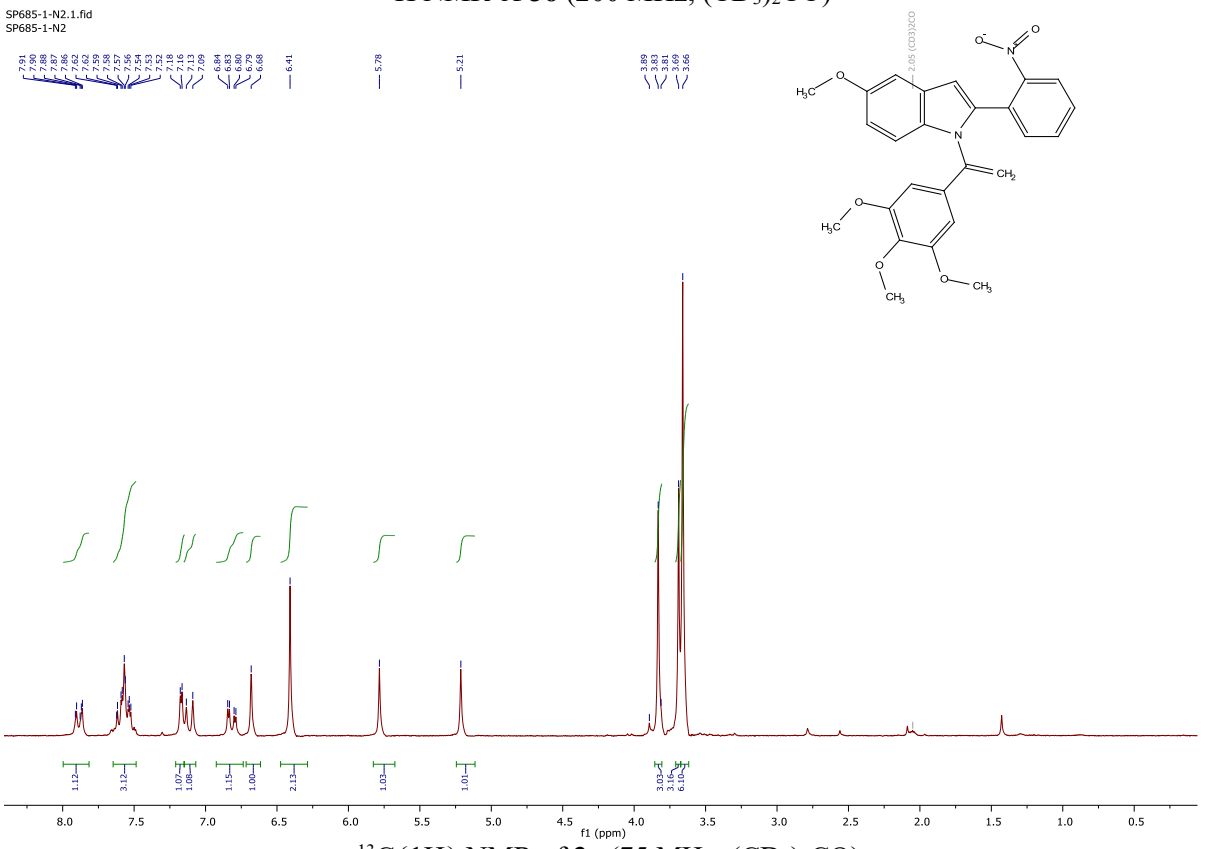
$^{13}C\{^{1}H\}$ NMR of **3n** (75 MHz, $(CD_3)_2CO$)



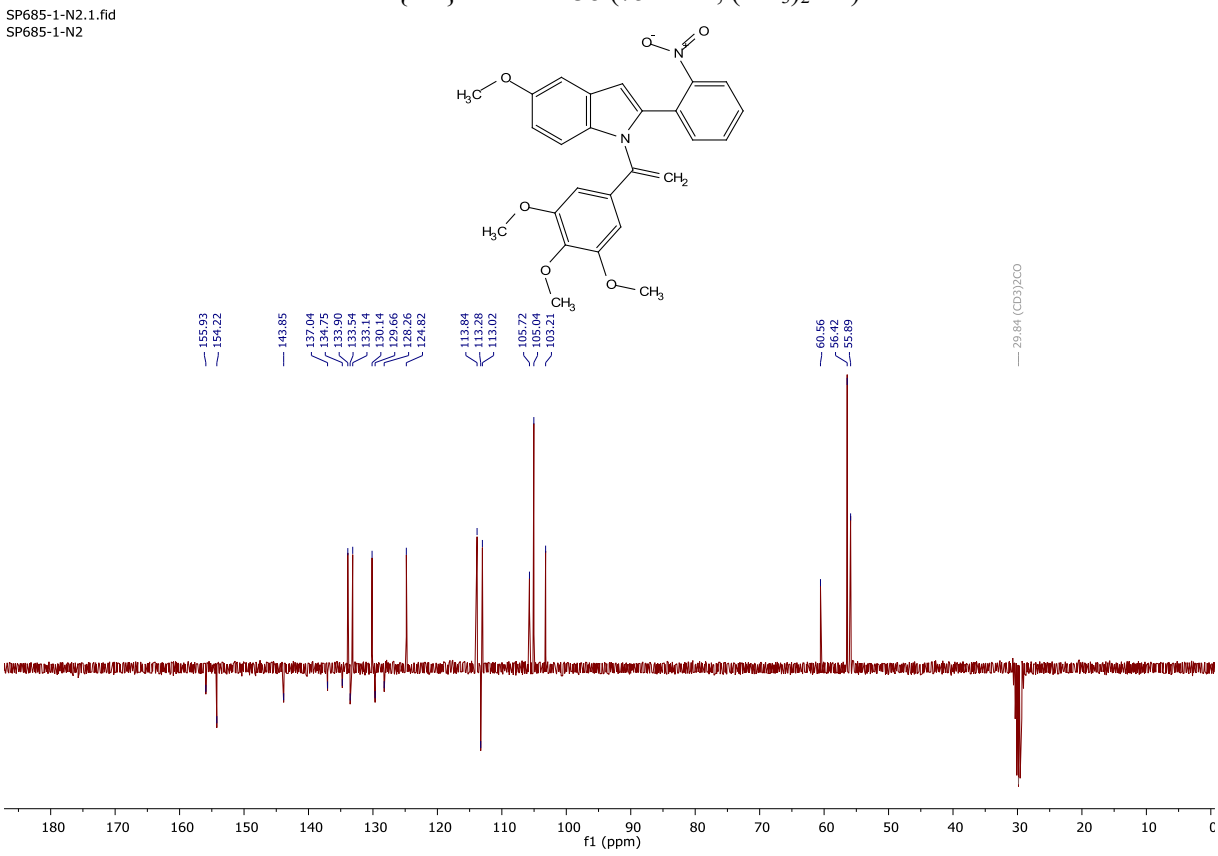
$^{19}F\{^{1}H\}$ NMR of **3n** (188 MHz, $(CD_3)_2CO$)



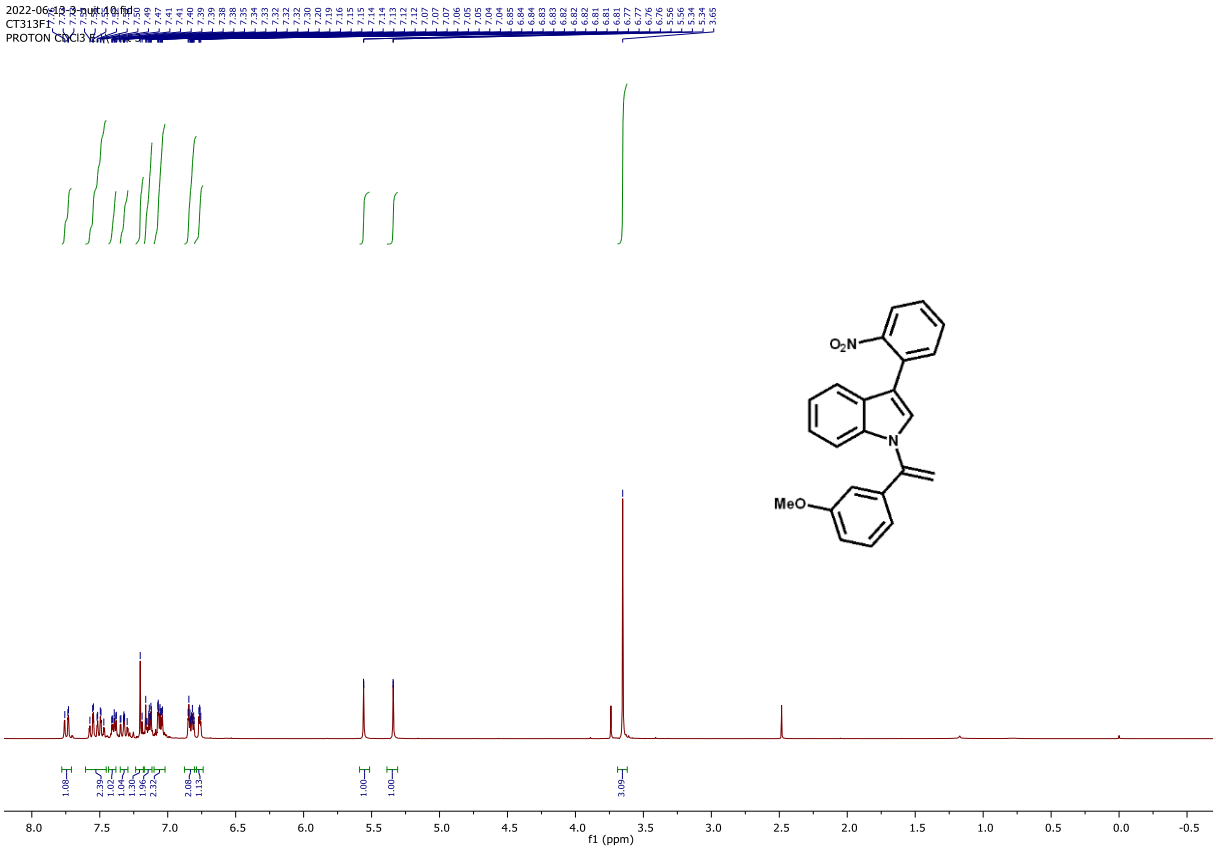
^{1}H NMR of **3o** (200 MHz, $(CD_3)_2CO$)



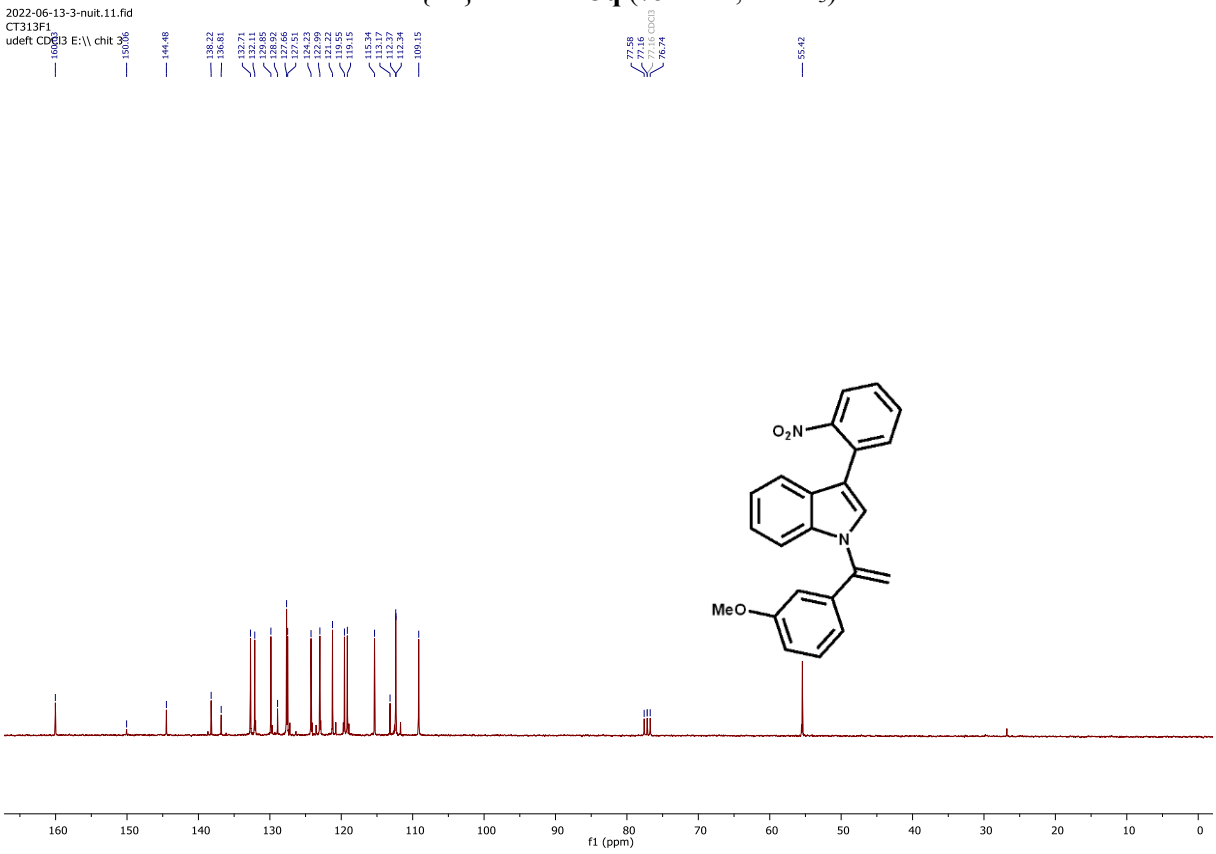
^{13}C{1H} NMR of **3o** (75 MHz, $(CD_3)_2CO$)



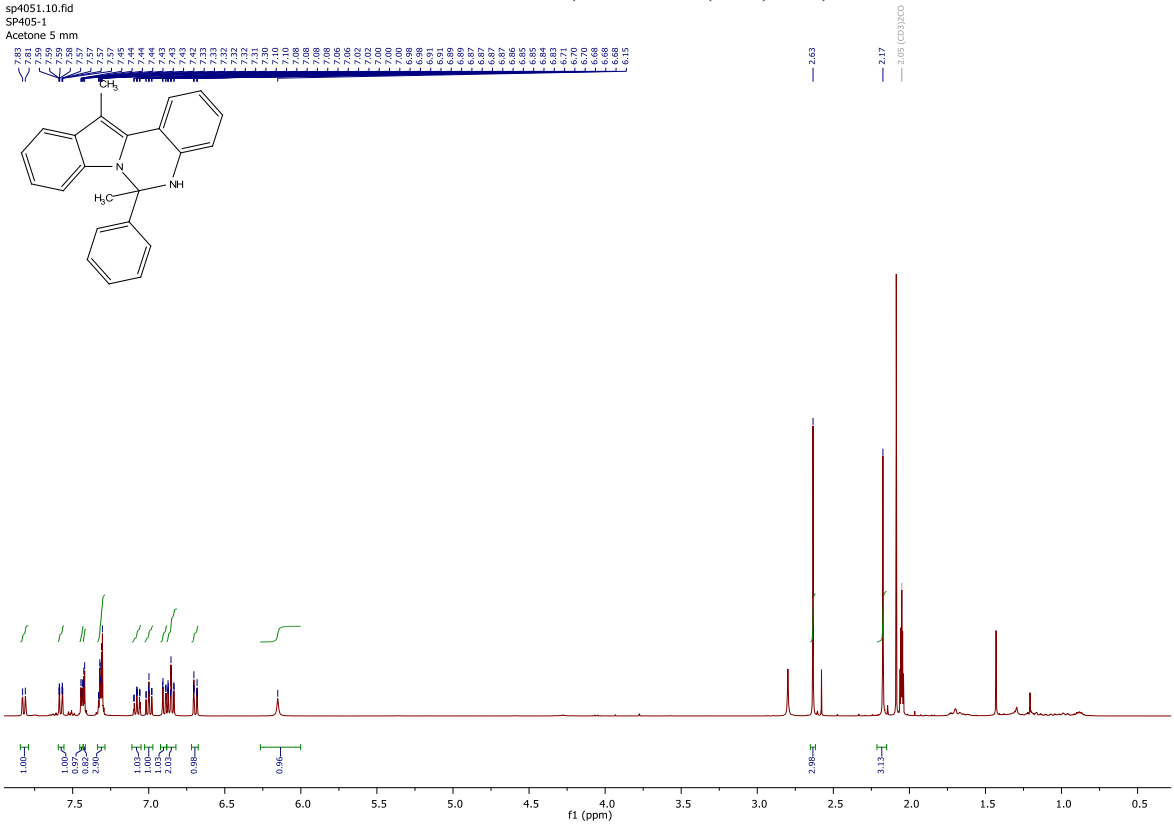
^{1}H NMR of **3q** (300 MHz, $CDCl_3$)



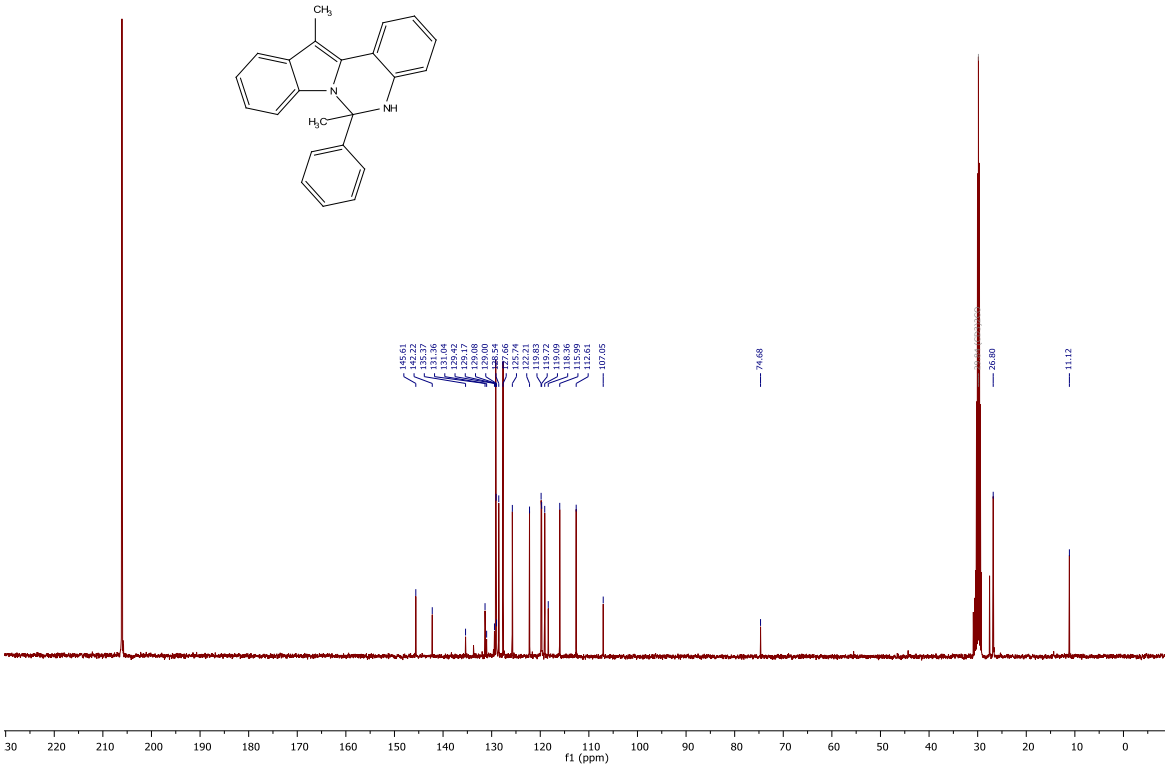
^{13}C{^{1}H} NMR of **3q** (75 MHz, $CDCl_3$)



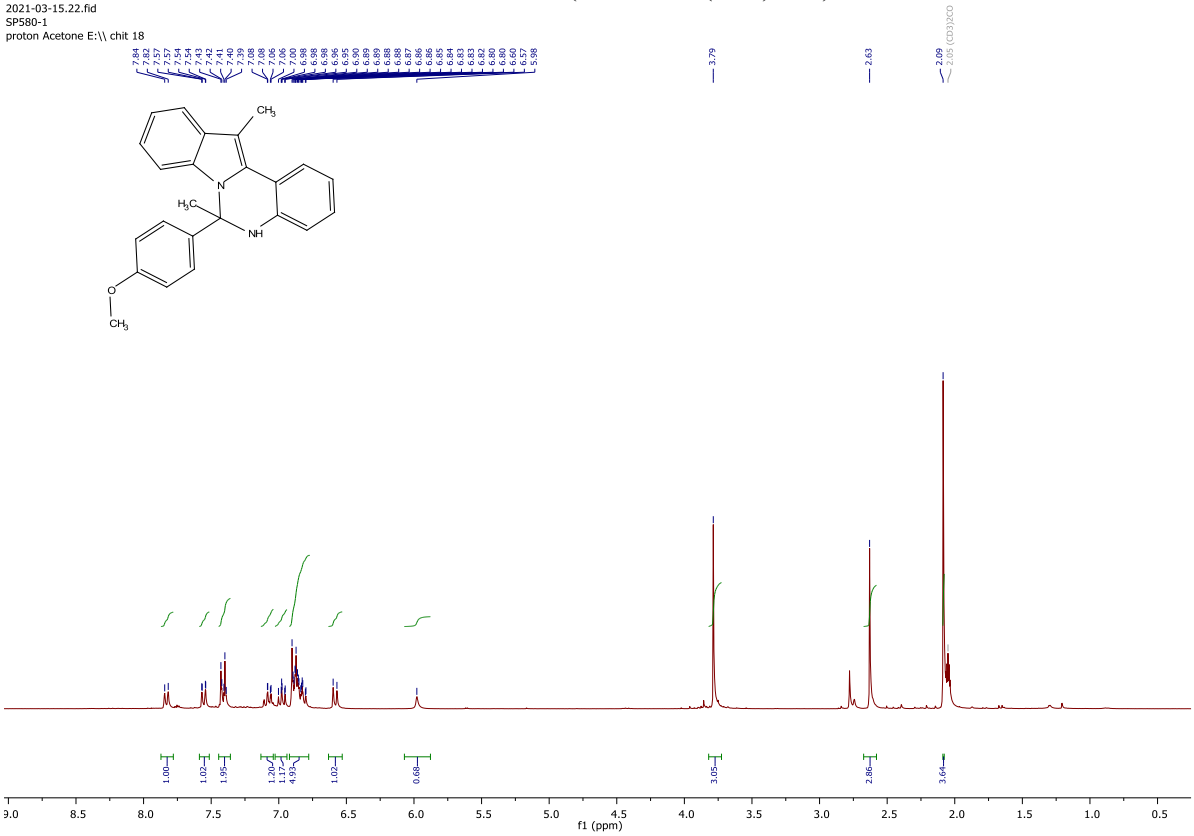
^{1}H NMR of **5a** (400 MHz, $(CD_3)_2CO$)



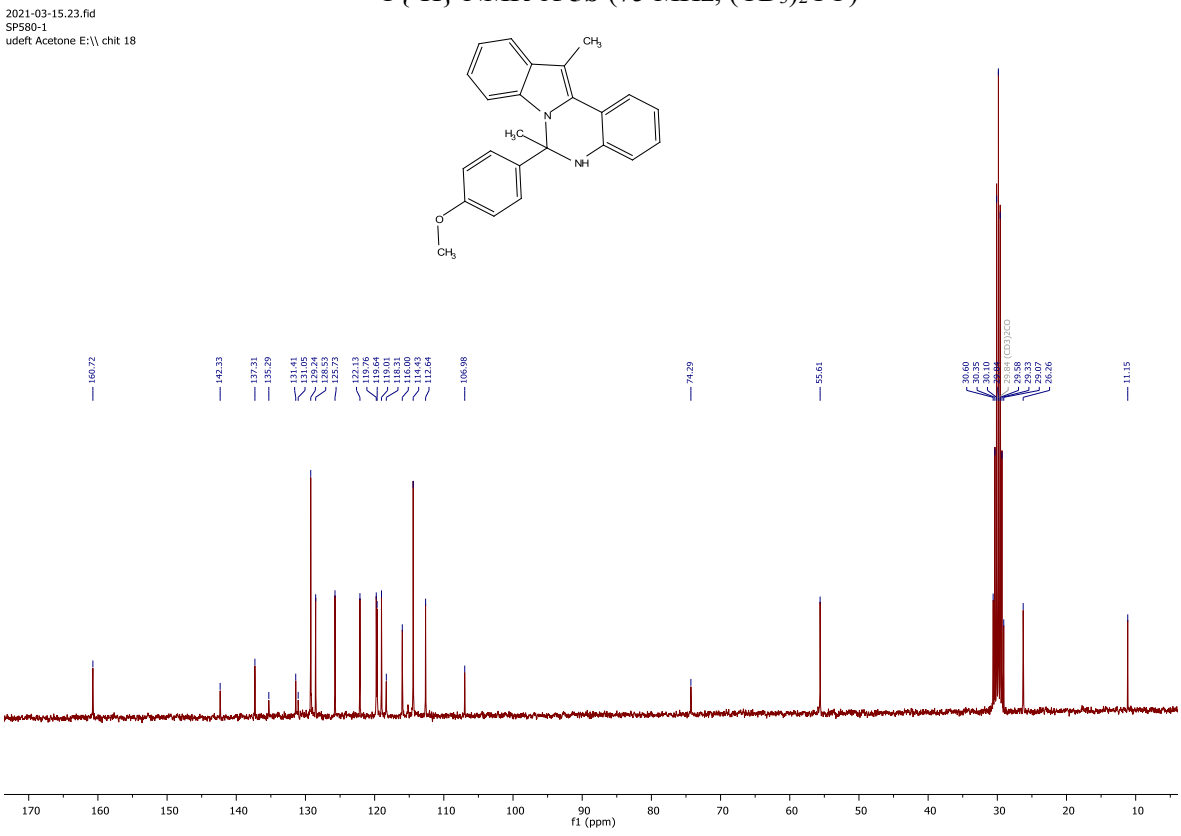
^{13}C{^{1}H} NMR of **5a** (101 MHz, $(CD_3)_2CO$)



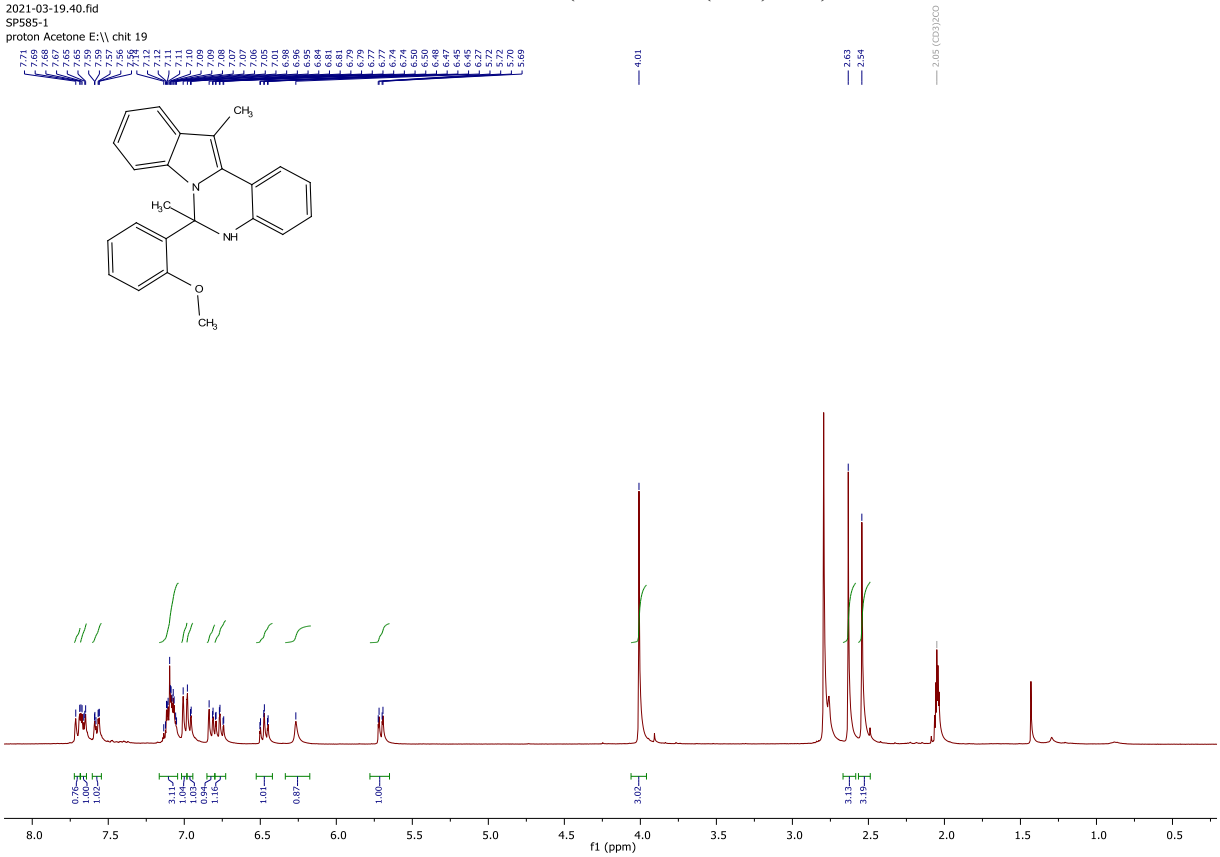
^{1}H NMR of **5b** (300 MHz, $(CD_3)_2CO$)



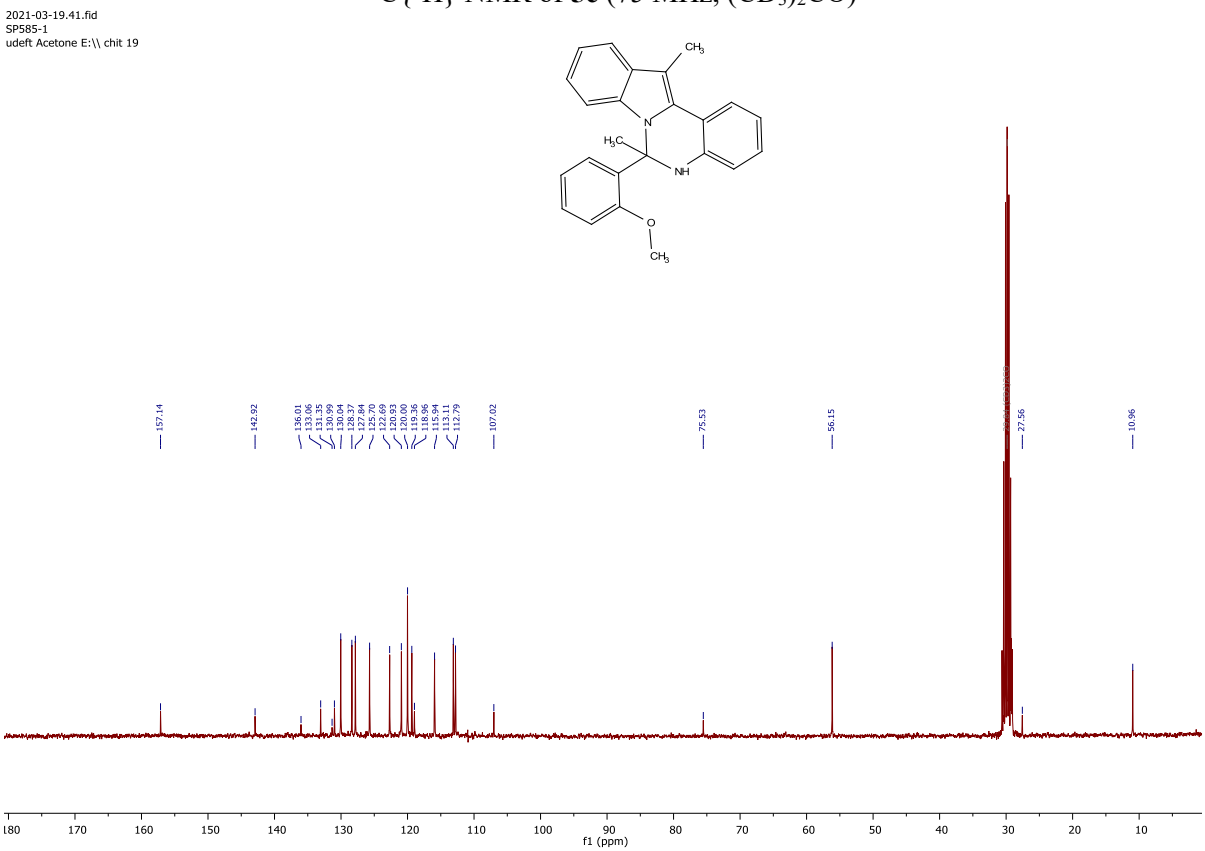
^{13}C{^{1}H} NMR of **5b** (75 MHz, $(CD_3)_2CO$)



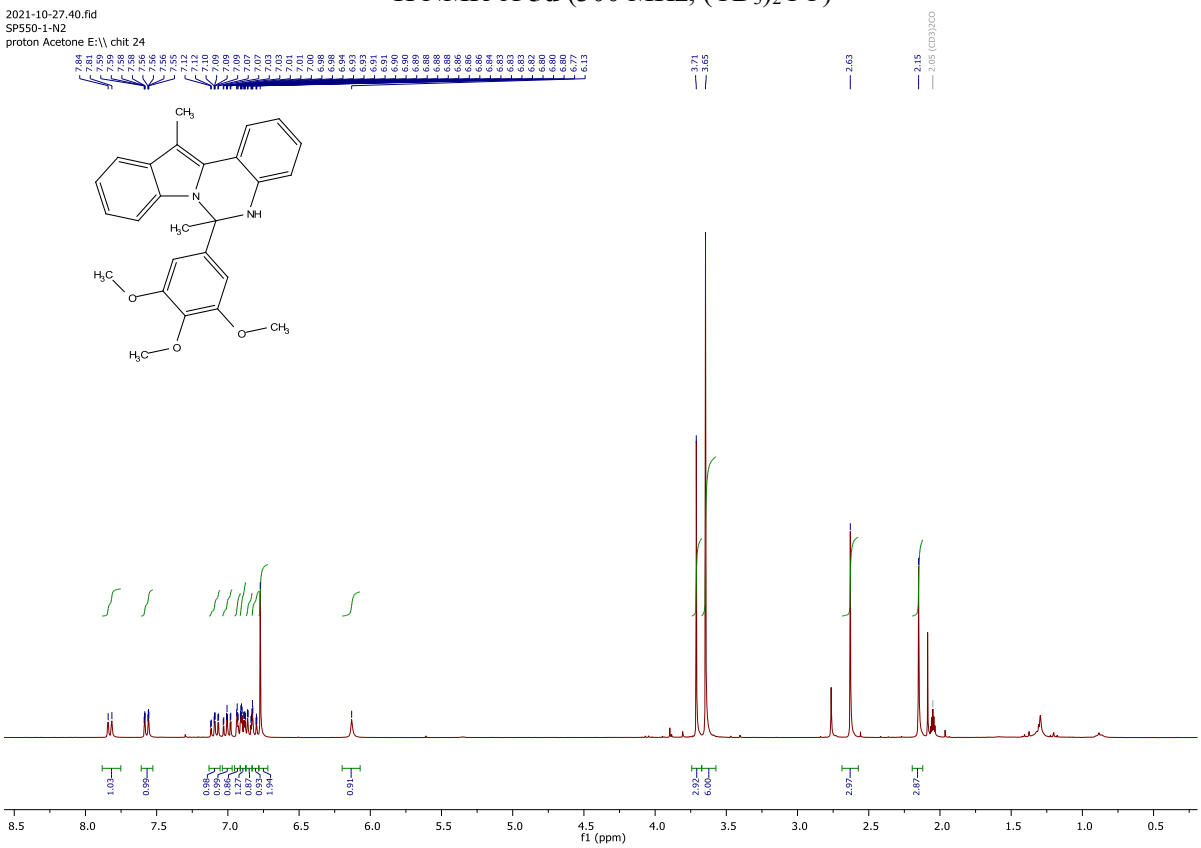
^{1}H NMR of **5c** (300 MHz, $(CD_3)_2CO$)



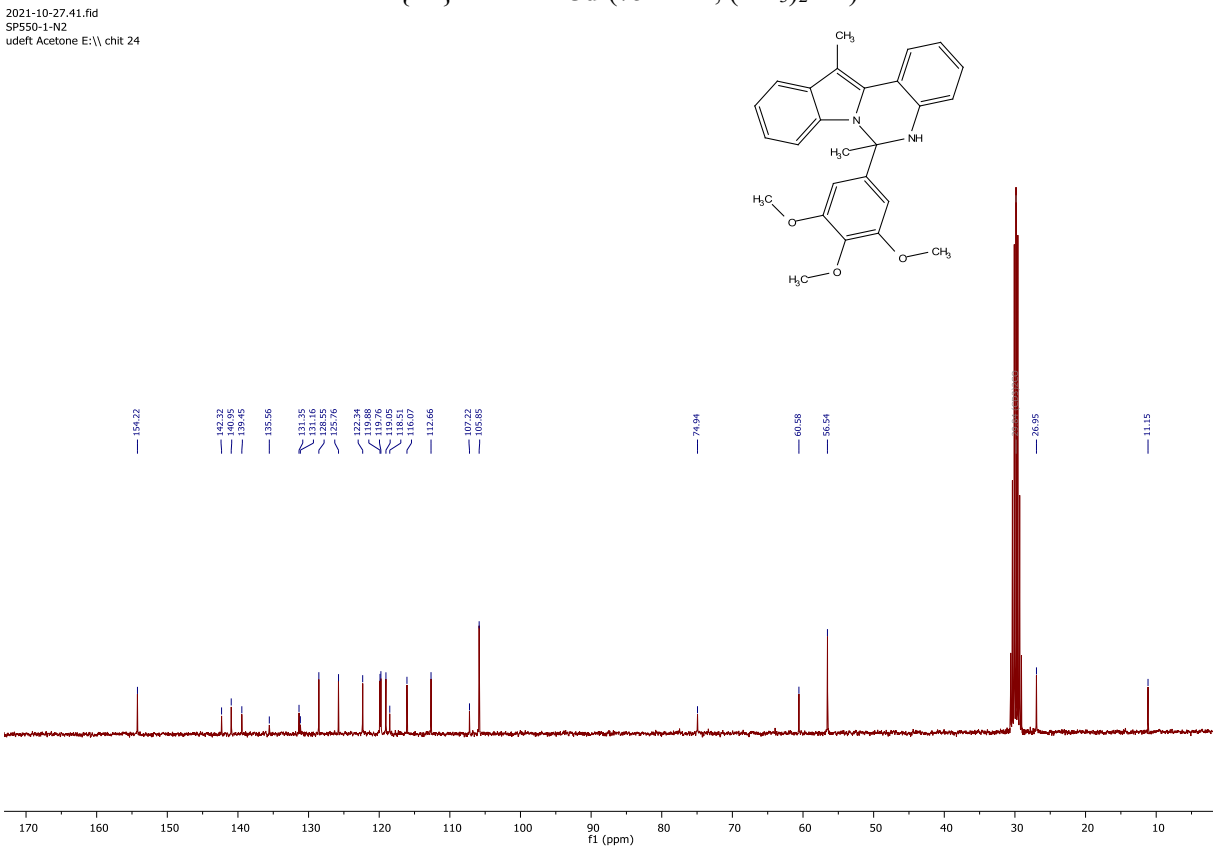
^{13}C{^{1}H} NMR of **5c** (75 MHz, $(CD_3)_2CO$)



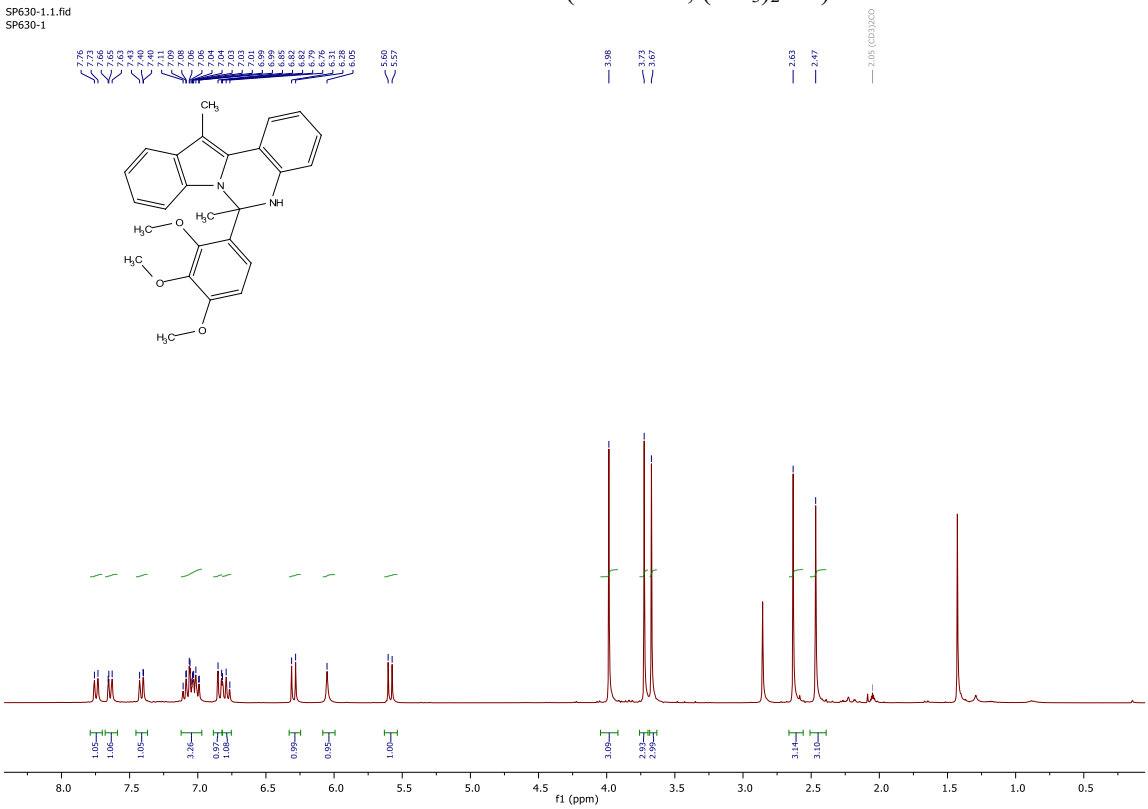
^{1}H NMR of **5d** (300 MHz, $(CD_3)_2CO$)



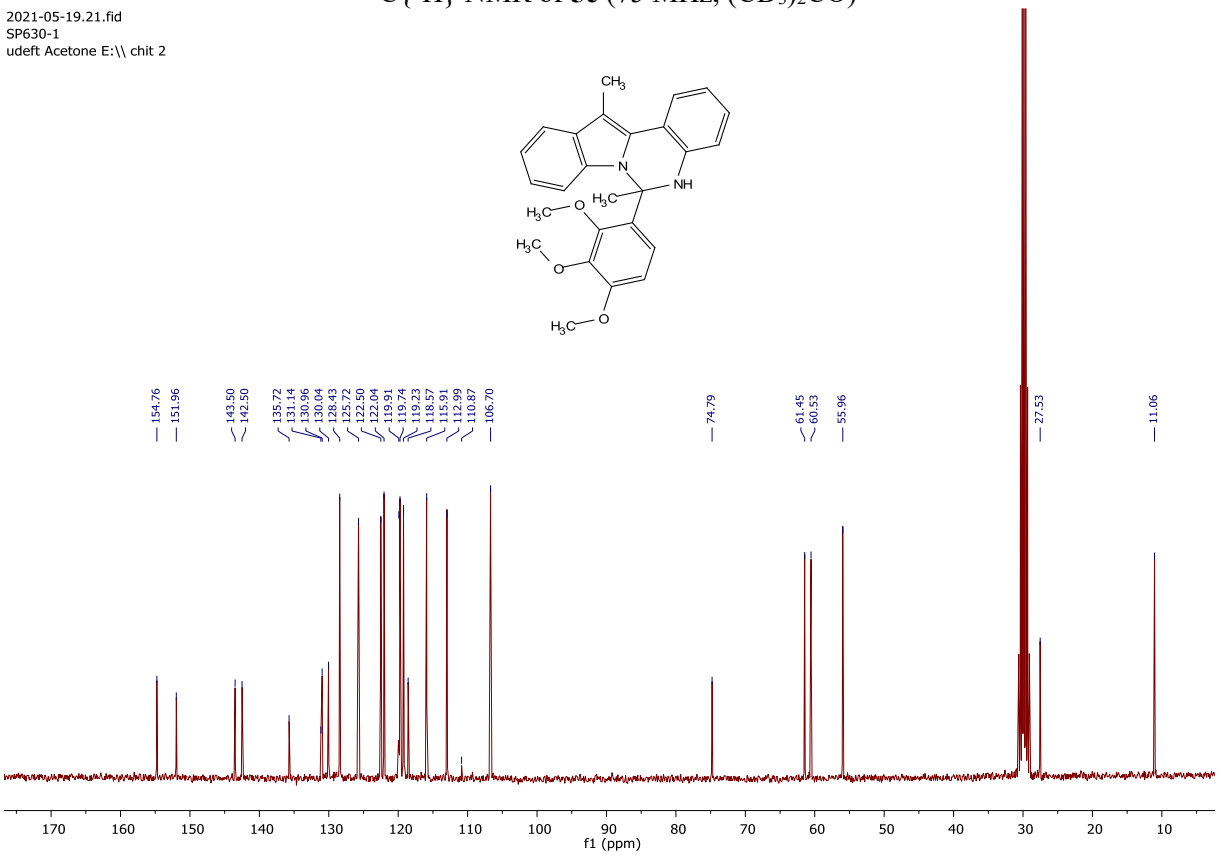
^{13}C{^{1}H} NMR of **5d** (75 MHz, $(CD_3)_2CO$)



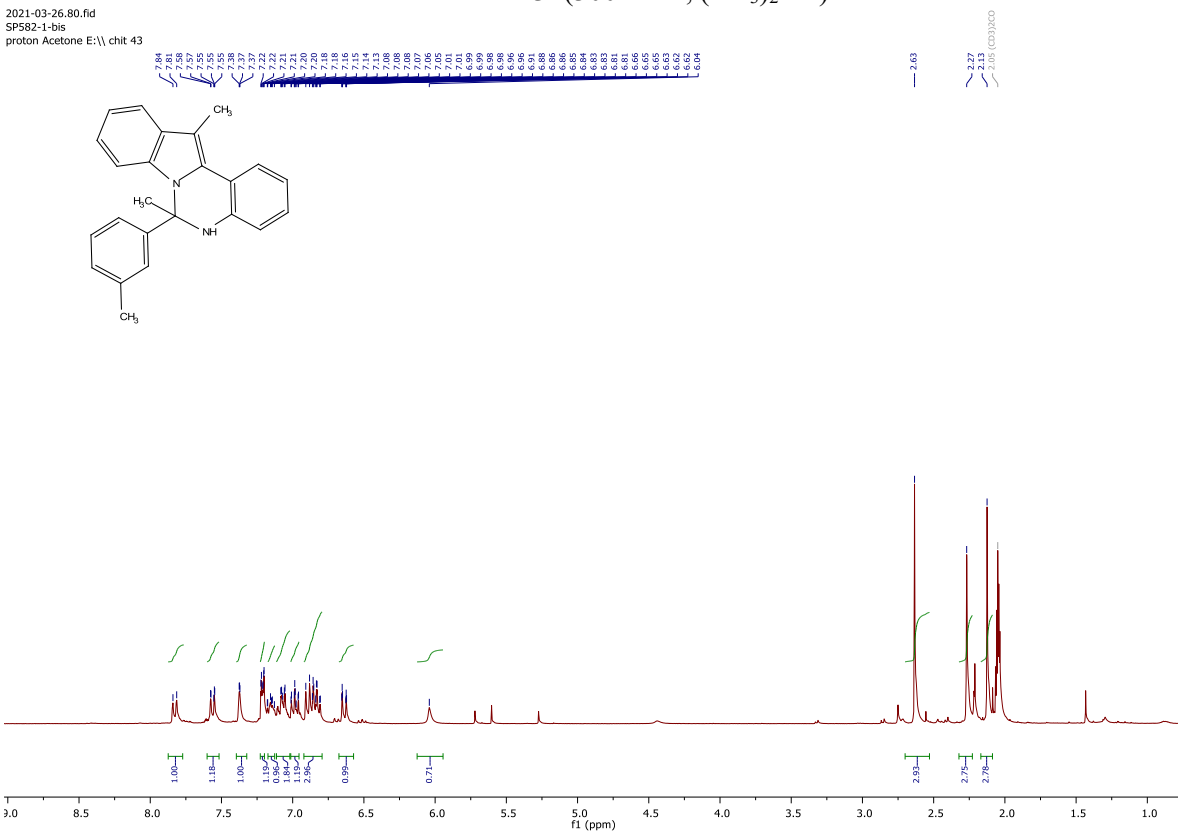
^{1}H NMR of **5e** (300 MHz, $(CD_3)_2CO$)



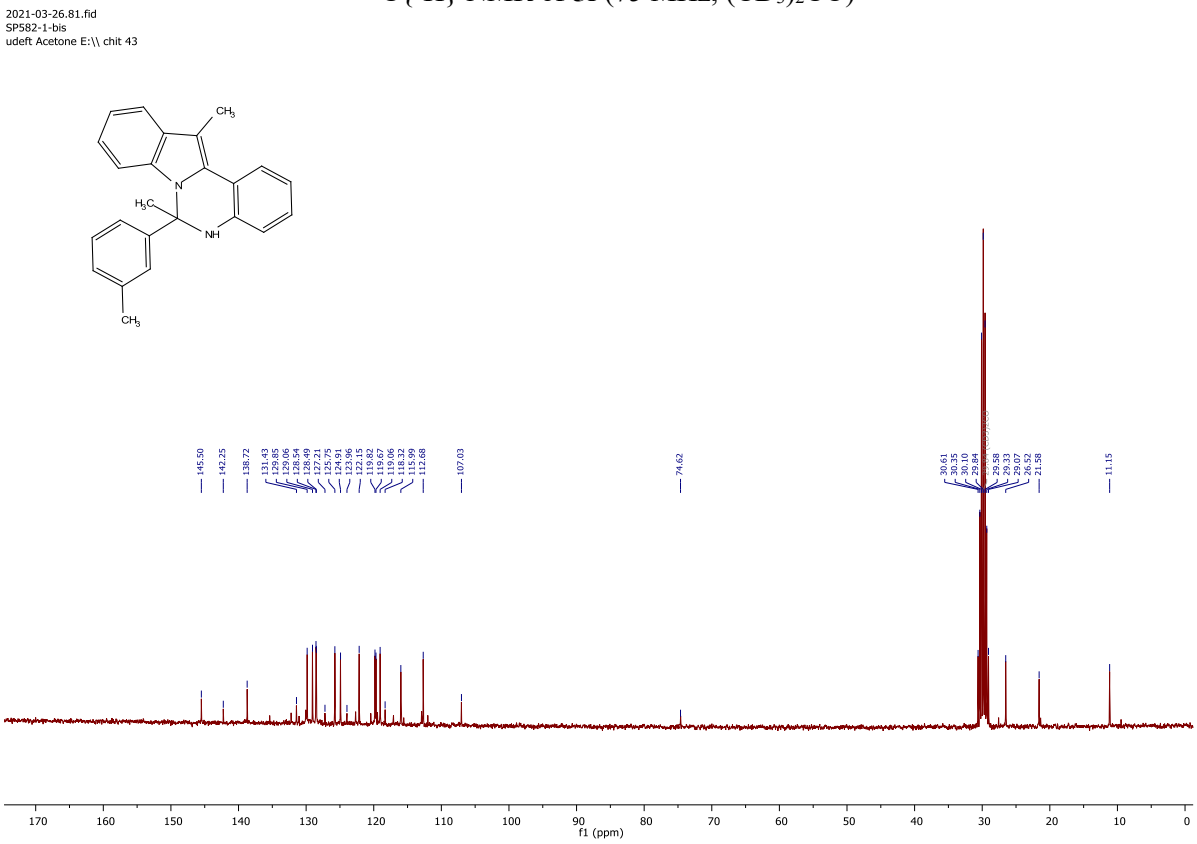
^{13}C{^{1}H} NMR of **5e** (75 MHz, $(CD_3)_2CO$)



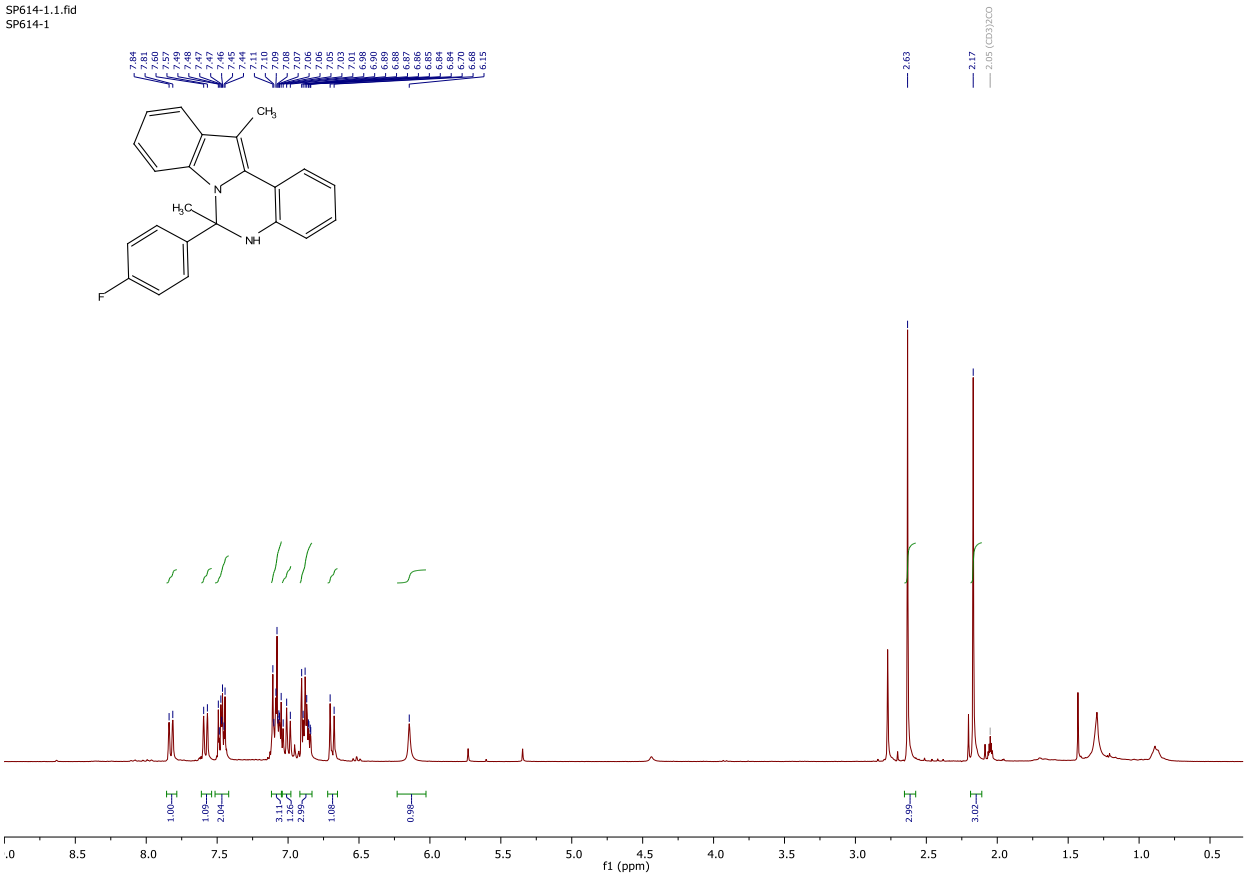
^{1}H NMR of **5f** (300 MHz, $(CD_3)_2CO$)



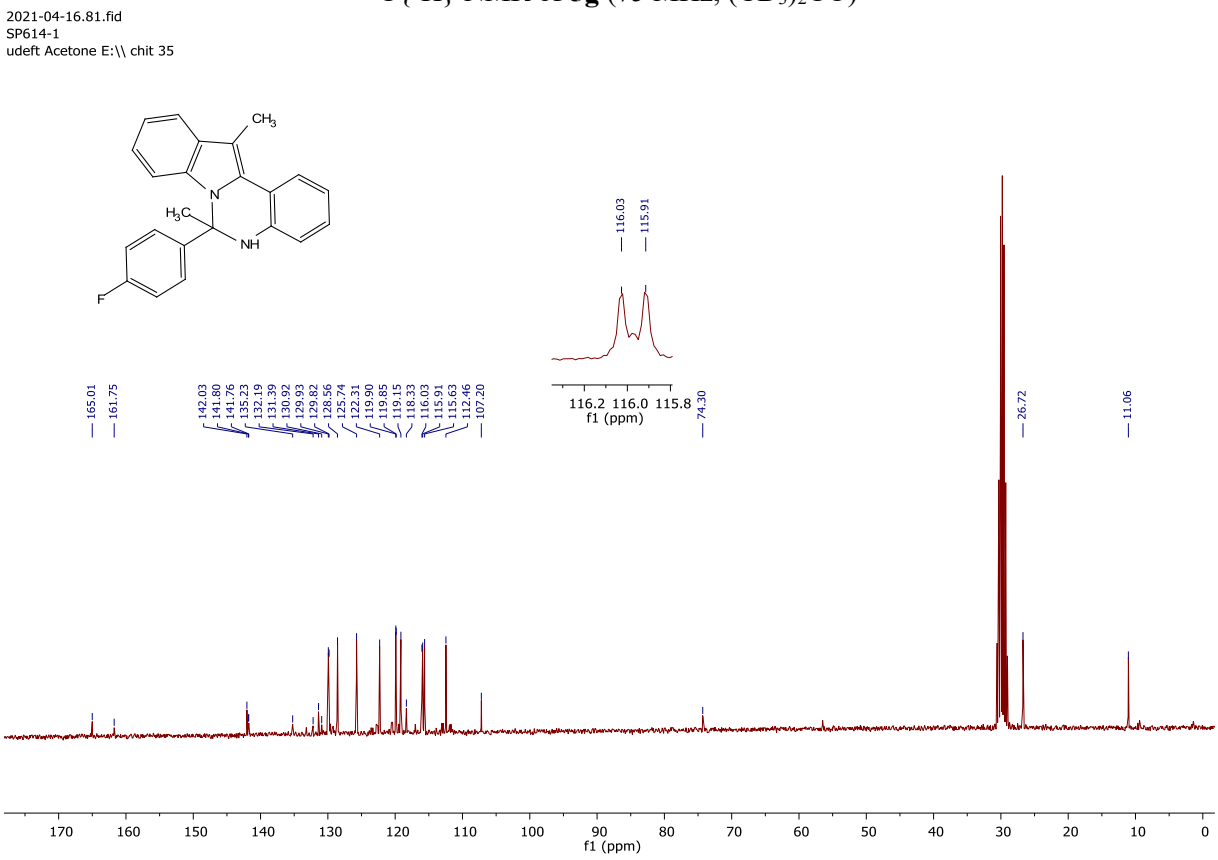
^{13}C{^{1}H} NMR of **5f** (75 MHz, $(CD_3)_2CO$)



^{1}H NMR of **5g** (300 MHz, $(CD_3)_2CO$)



$^{13}C\{^{1}H\}$ NMR of **5g** (75 MHz, $(CD_3)_2CO$)



$^{19}F\{^{1}H\}$ NMR of **5g** (188 MHz, $(CD_3)_2CO$)

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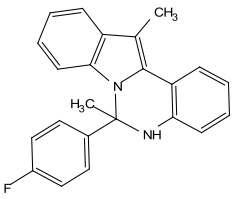

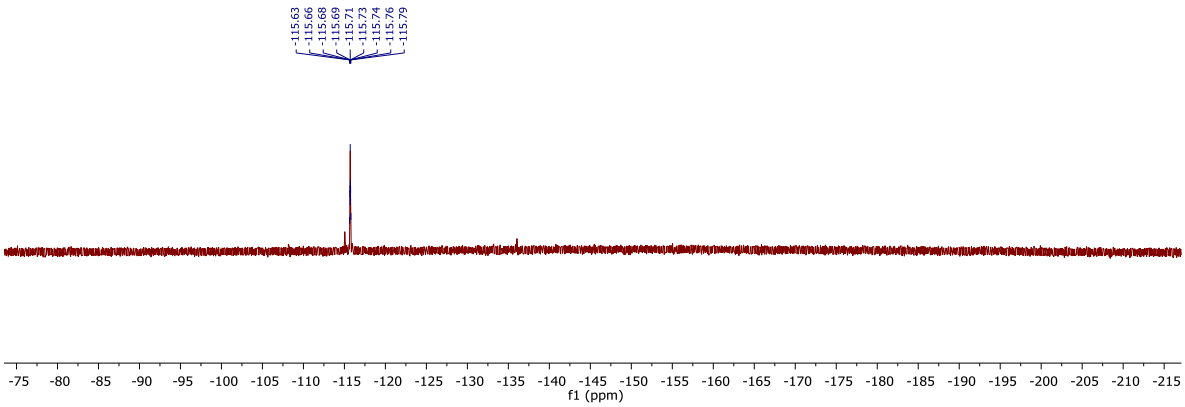

^{1}H NMR of **5h** (300 MHz, $(CD_3)_2CO$)

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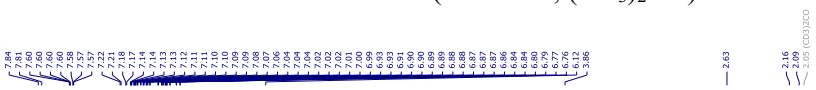
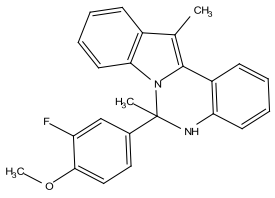
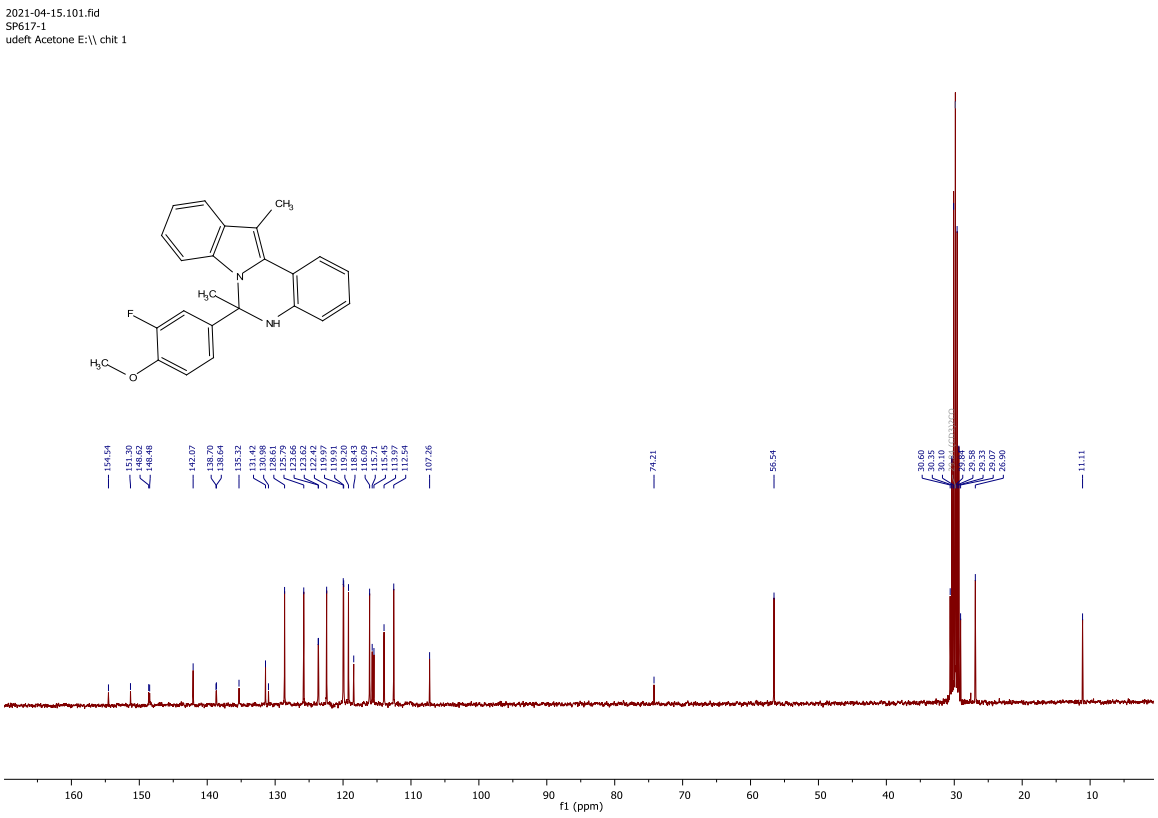
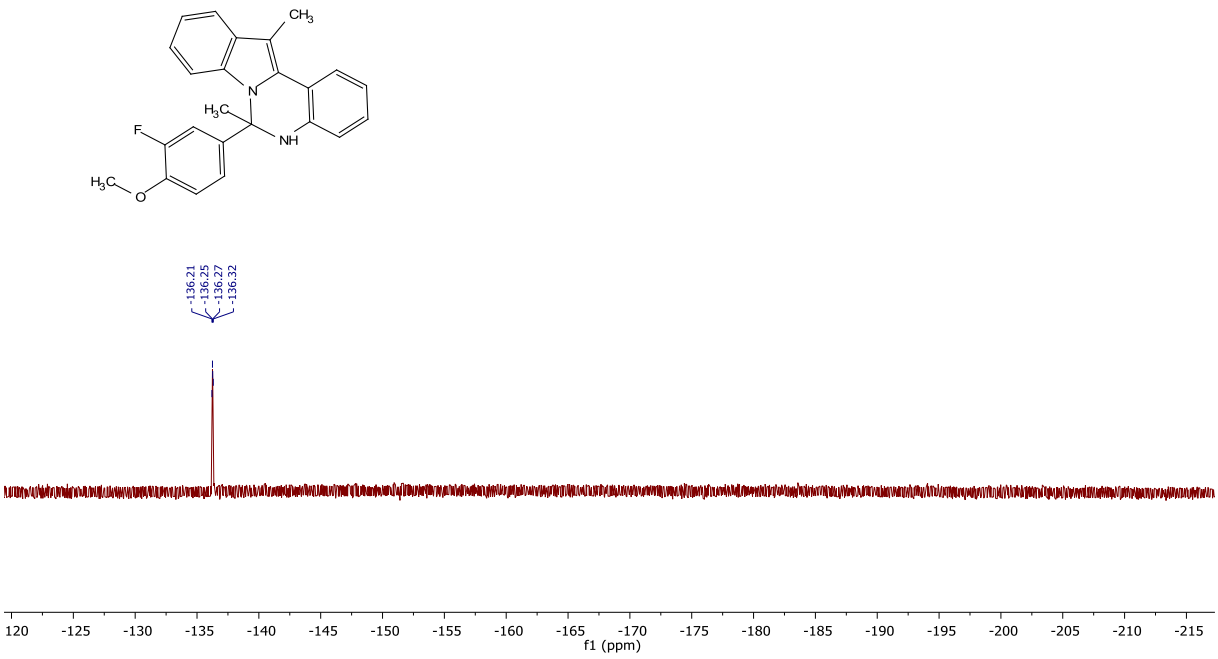




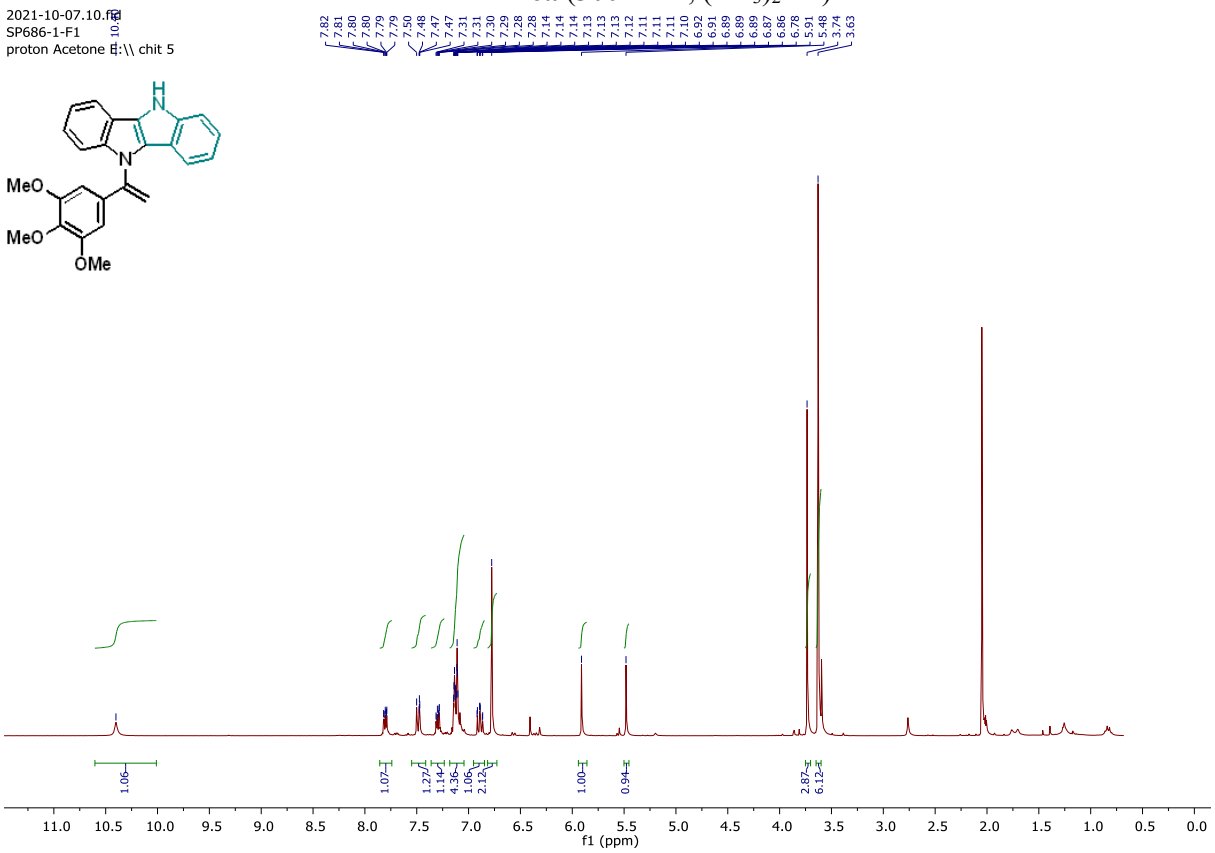
$^{13}C\{^{1}H\}$ NMR of **5h** (75 MHz, $(CD_3)_2CO$)



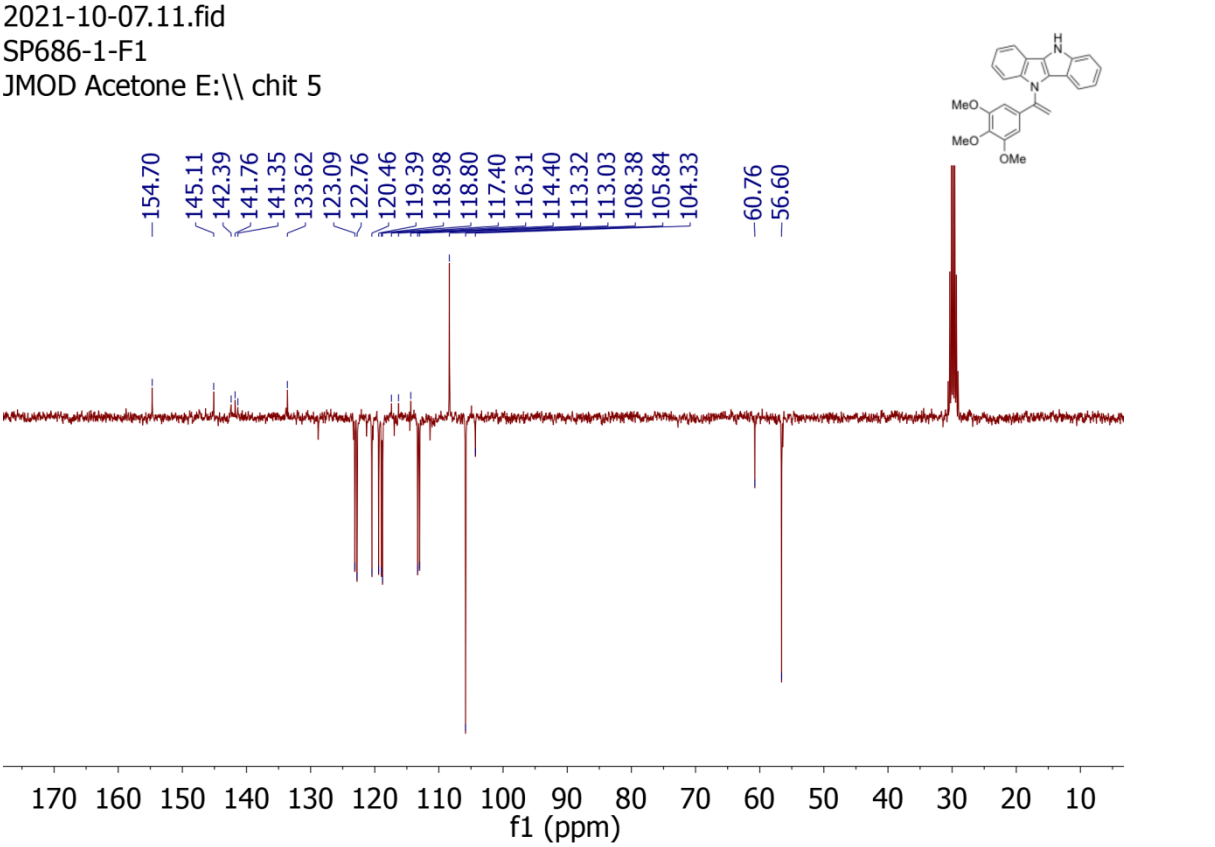
$^{19}F\{^{1}H\}$ NMR of **5h** (188 MHz, $(CD_3)_2CO$)



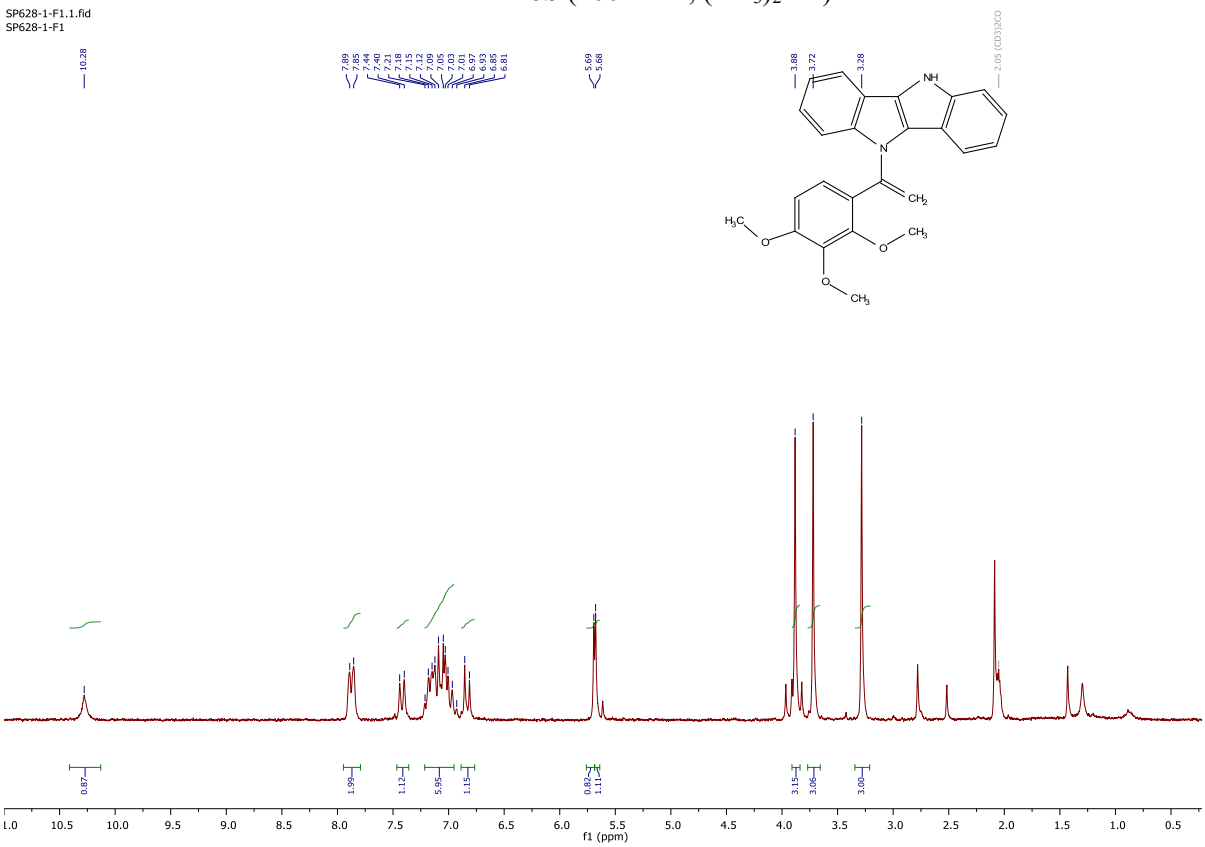
^{1}H NMR of **6a** (300 MHz, $(CD_3)_2CO$)



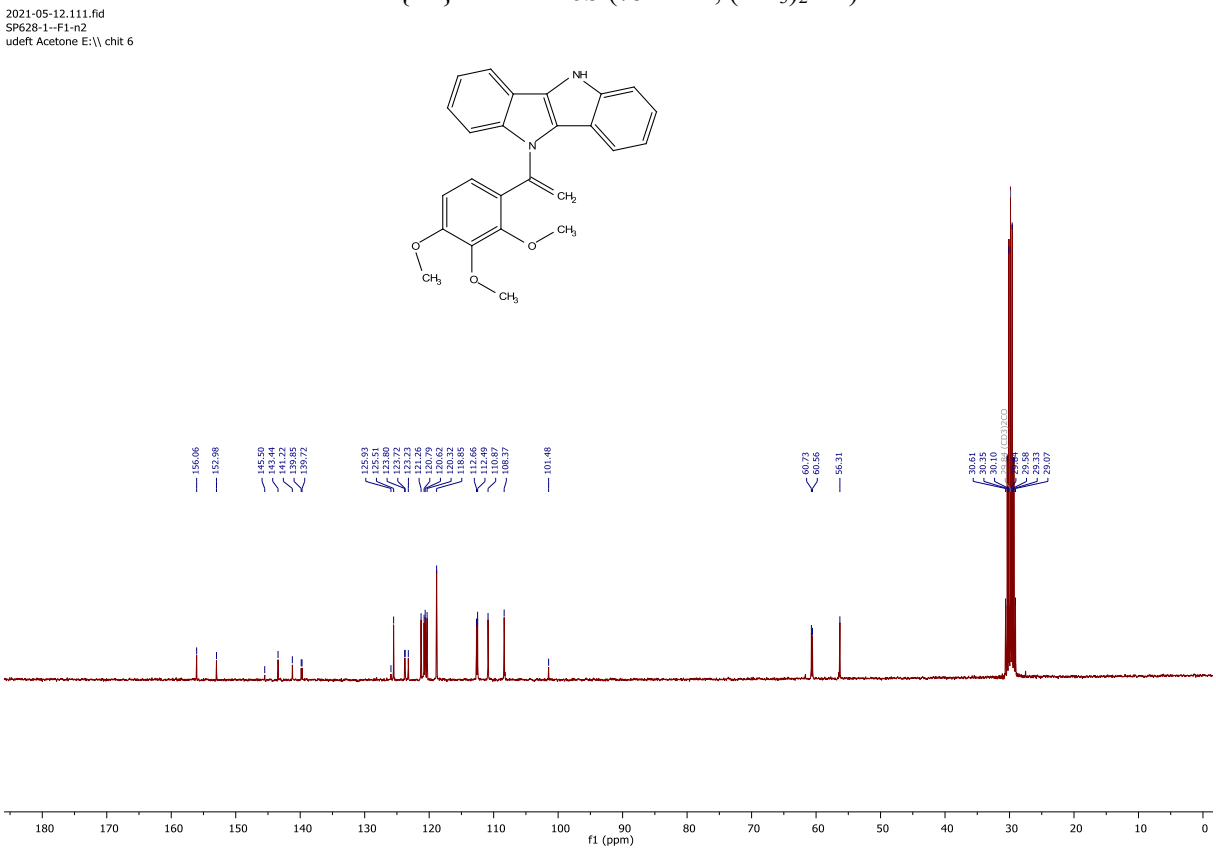
^{13}C{^{1}H} NMR of **6a** (75 MHz, $(CD_3)_2CO$)



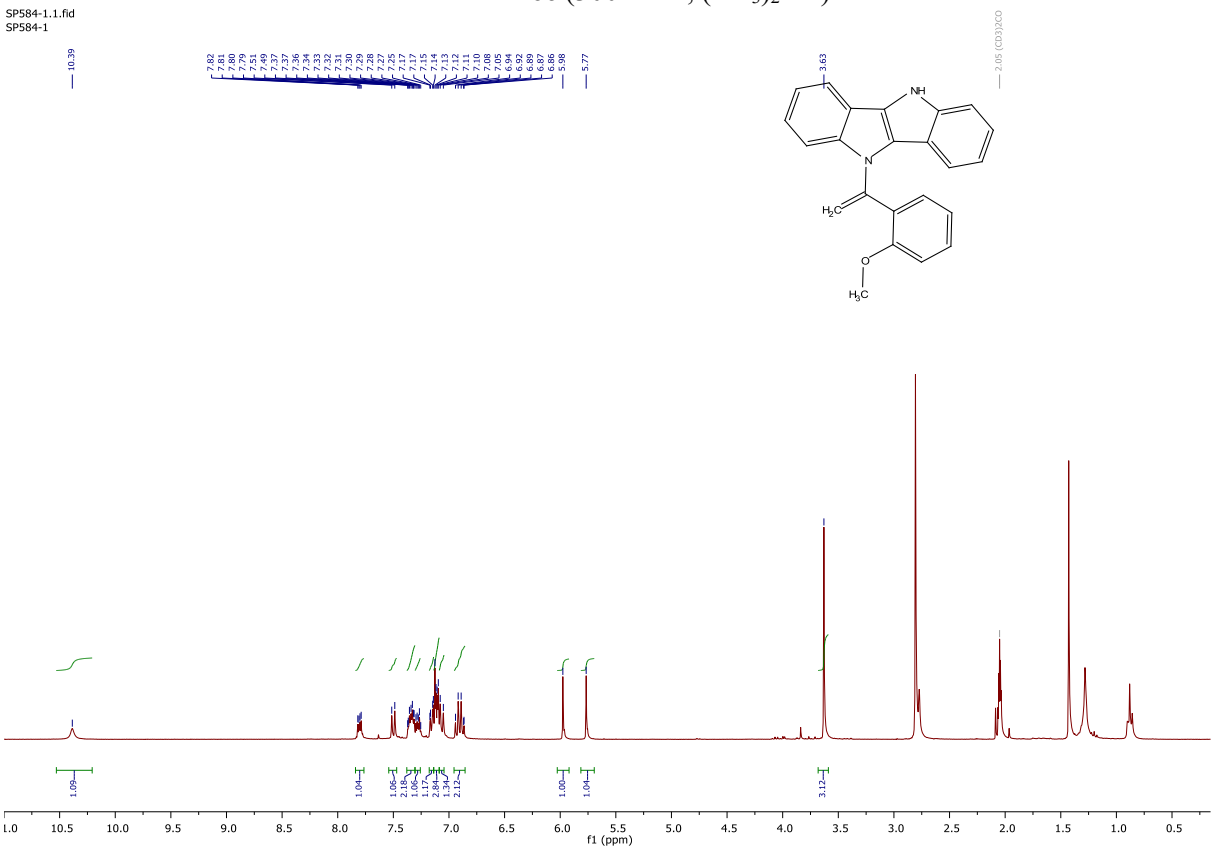
^{1}H NMR of **6b** (200 MHz, $(CD_3)_2CO$)



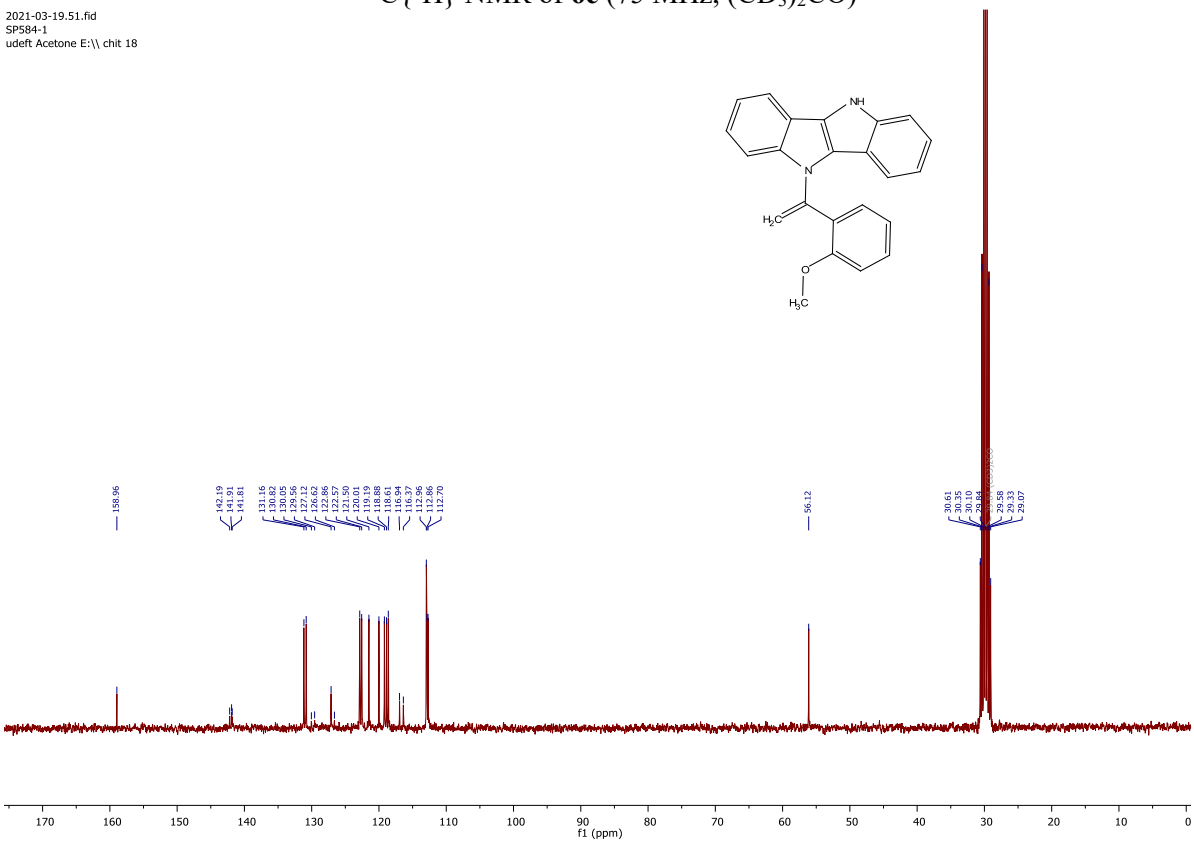
^{13}C{^{1}H} NMR of **6b** (75 MHz, $(CD_3)_2CO$)



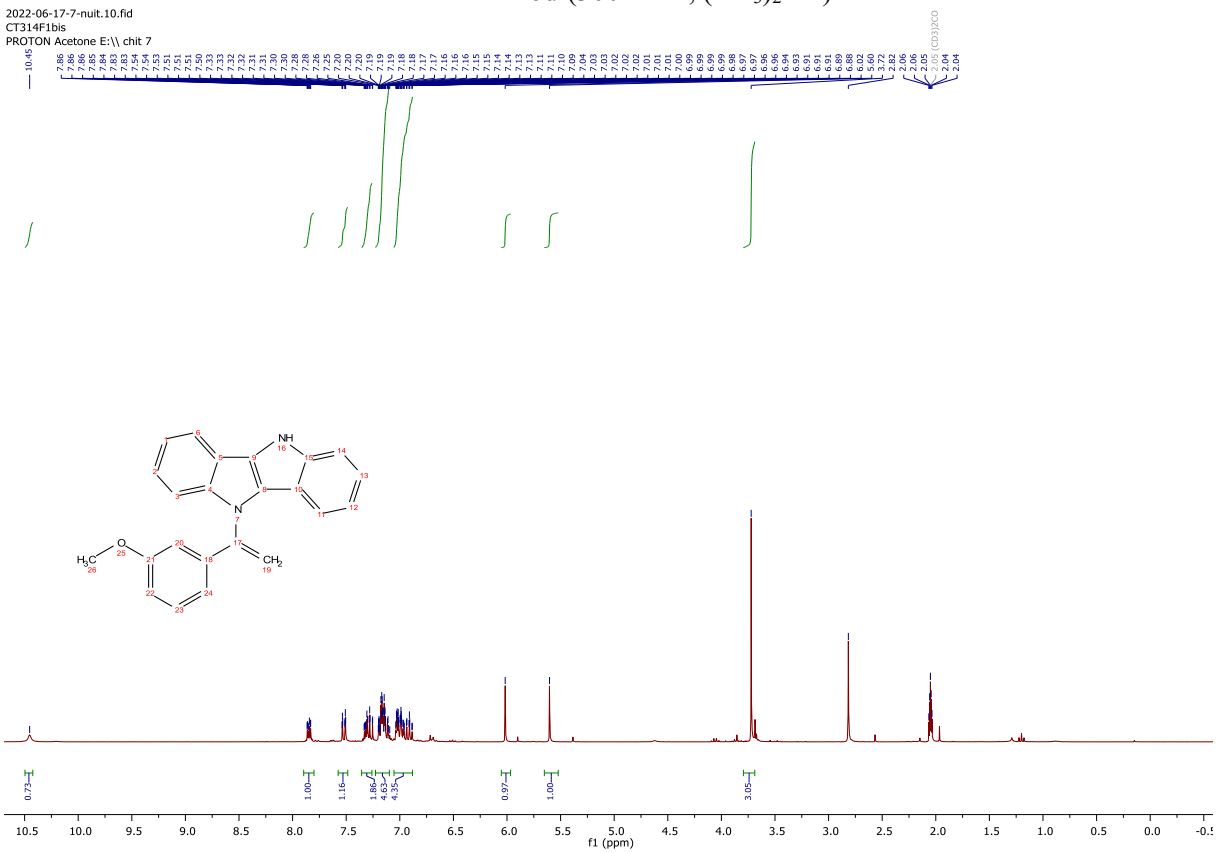
^{1}H NMR of **6c** (300 MHz, $(CD_3)_2CO$)



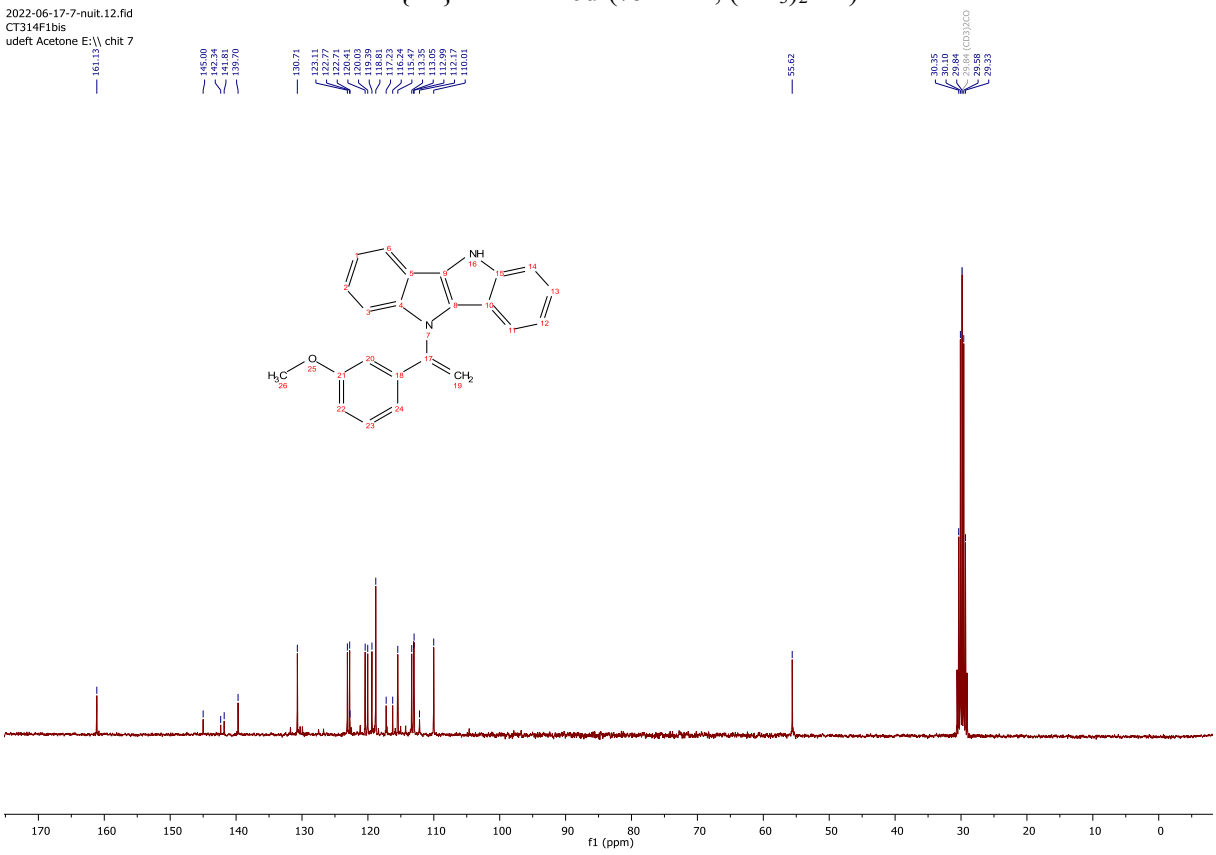
^{13}C{^{1}H} NMR of **6c** (75 MHz, $(CD_3)_2CO$)



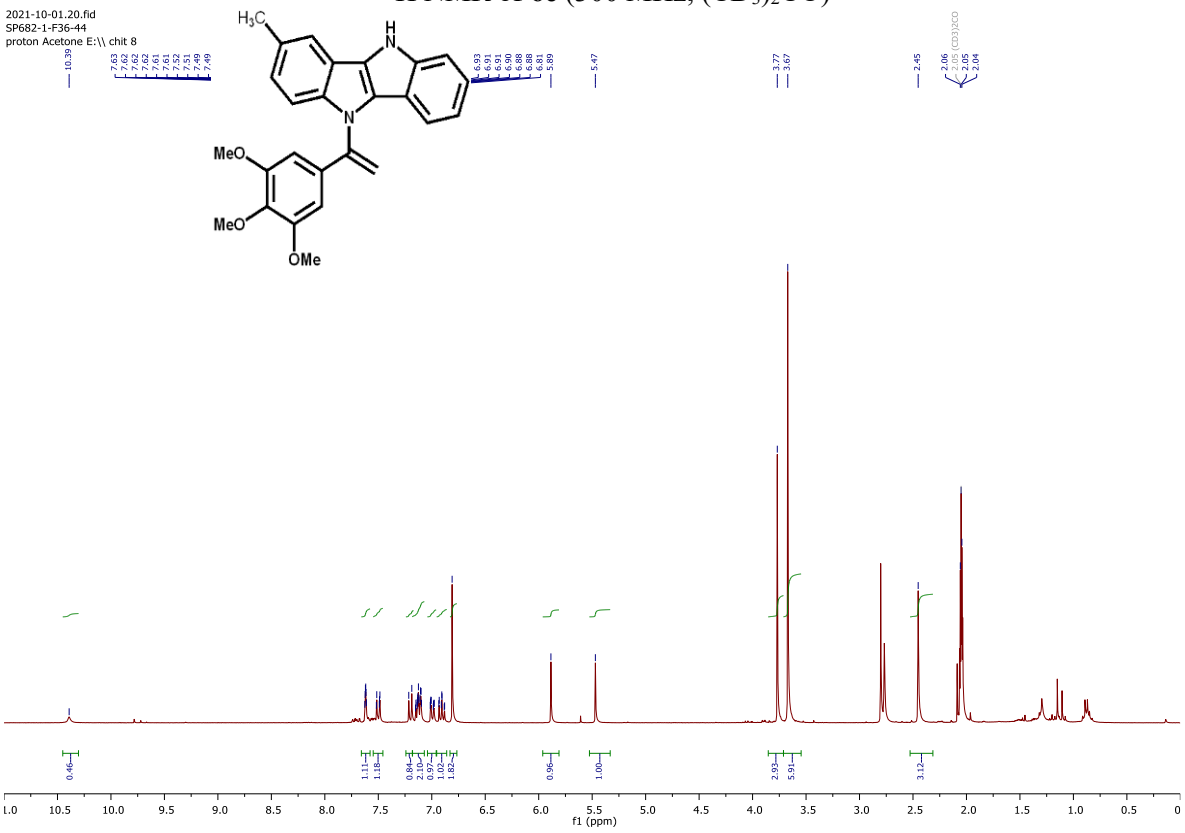
^{1}H NMR of **6d** (300 MHz, $(CD_3)_2CO$)



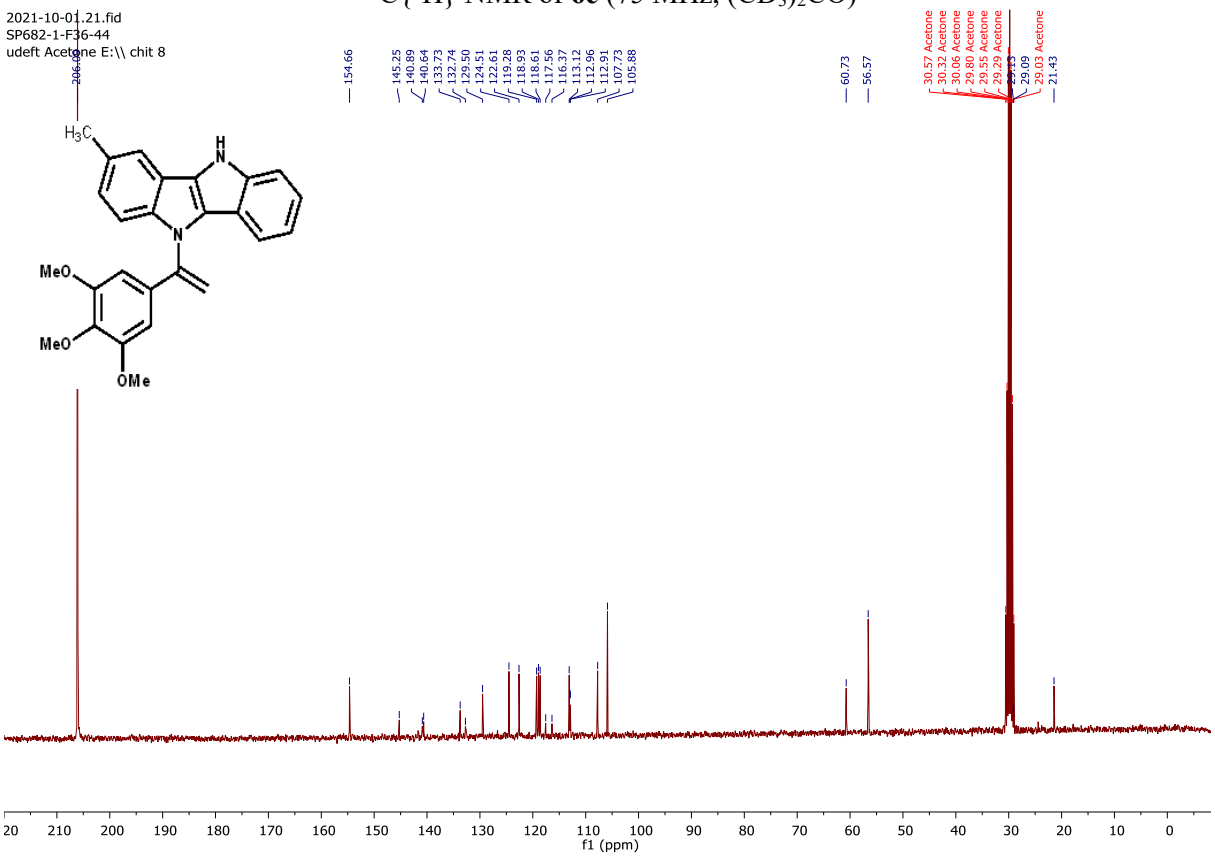
^{13}C{^{1}H} NMR of **6d** (75 MHz, $(CD_3)_2CO$)



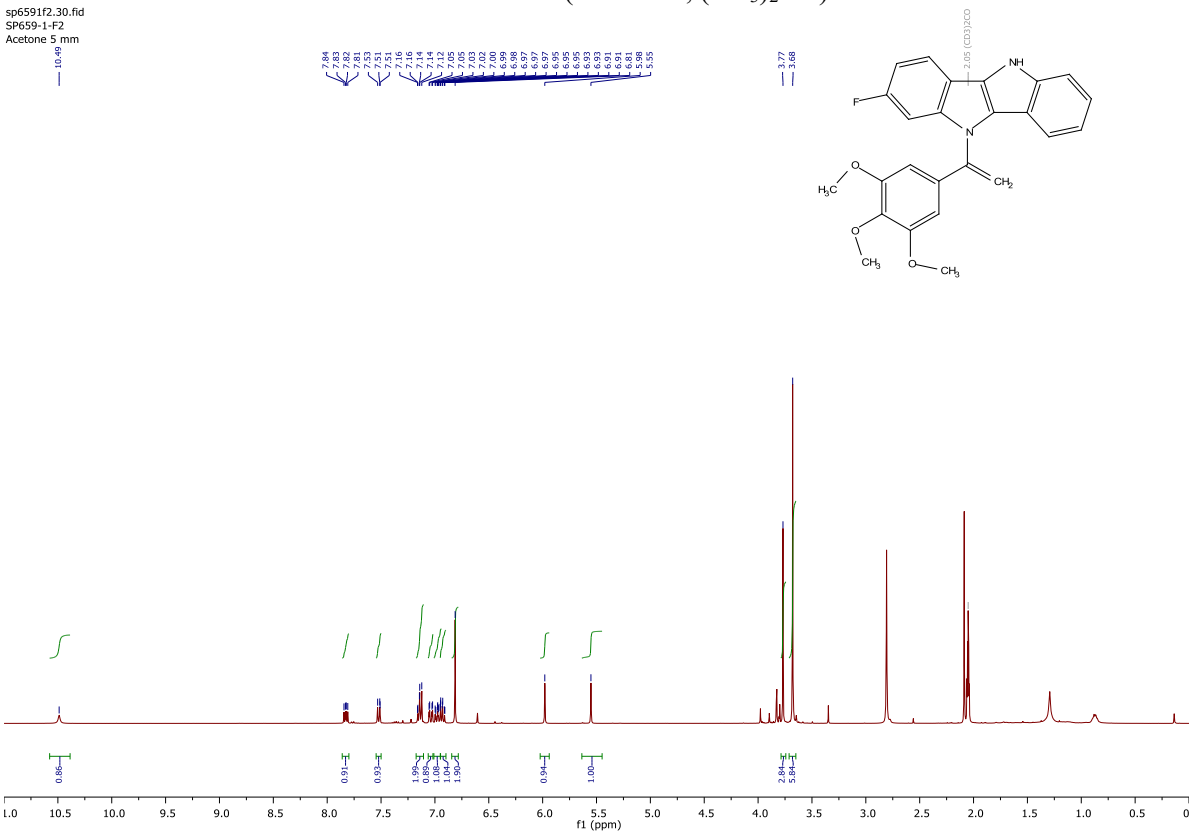
^{1}H NMR of **6e** (300 MHz, $(CD_3)_2CO$)



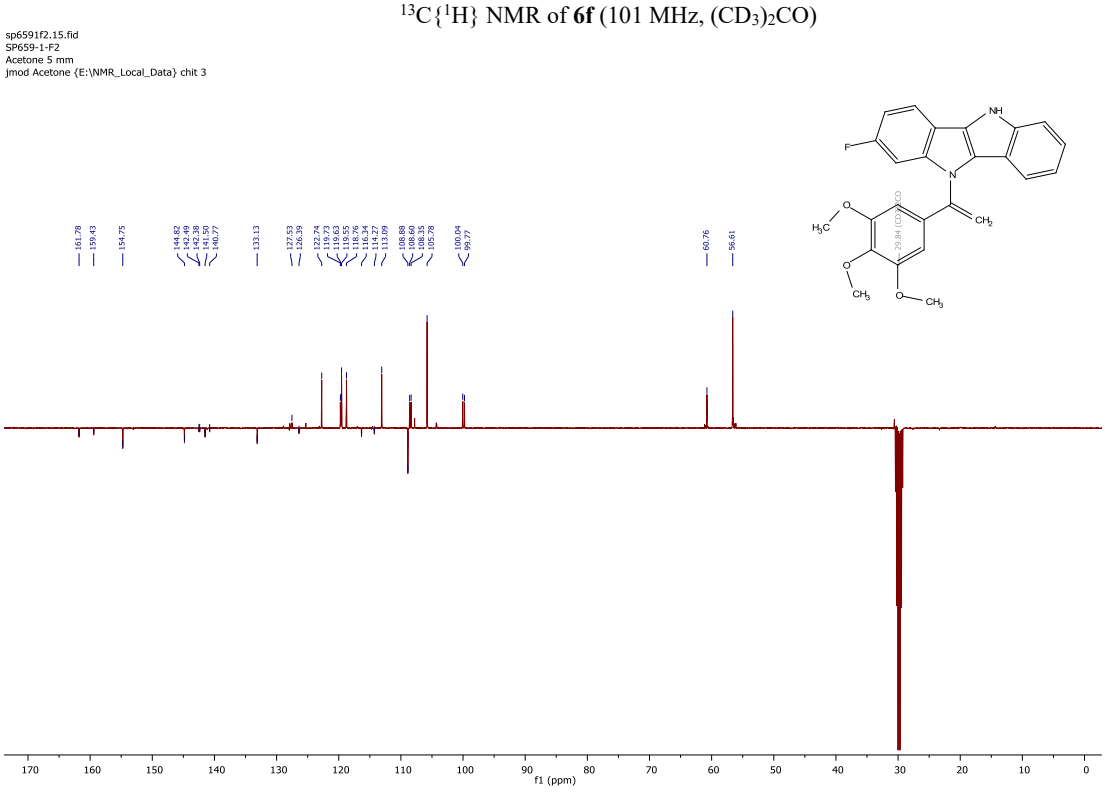
^{13}C{^{1}H} NMR of **6e** (75 MHz, $(CD_3)_2CO$)



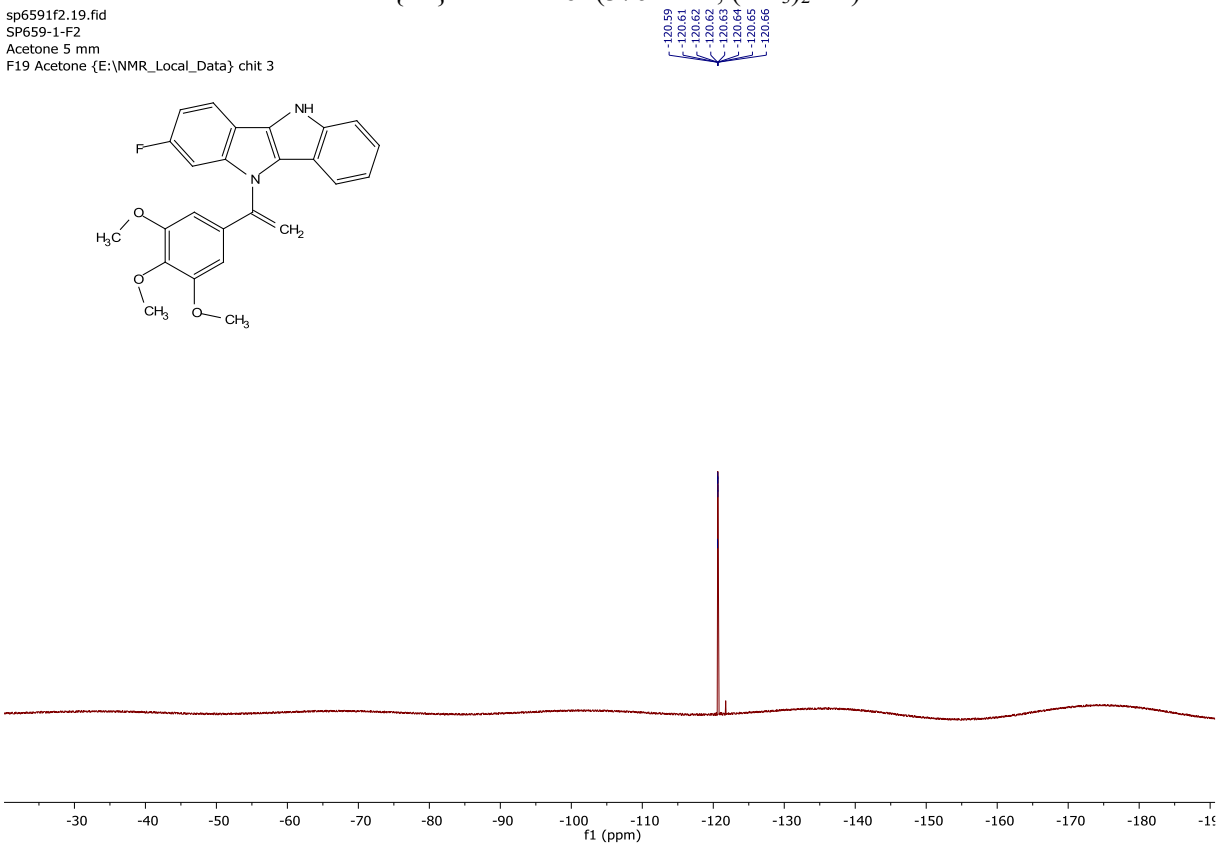
^{1}H NMR of **6f** (400 MHz, $(CD_3)_2CO$)



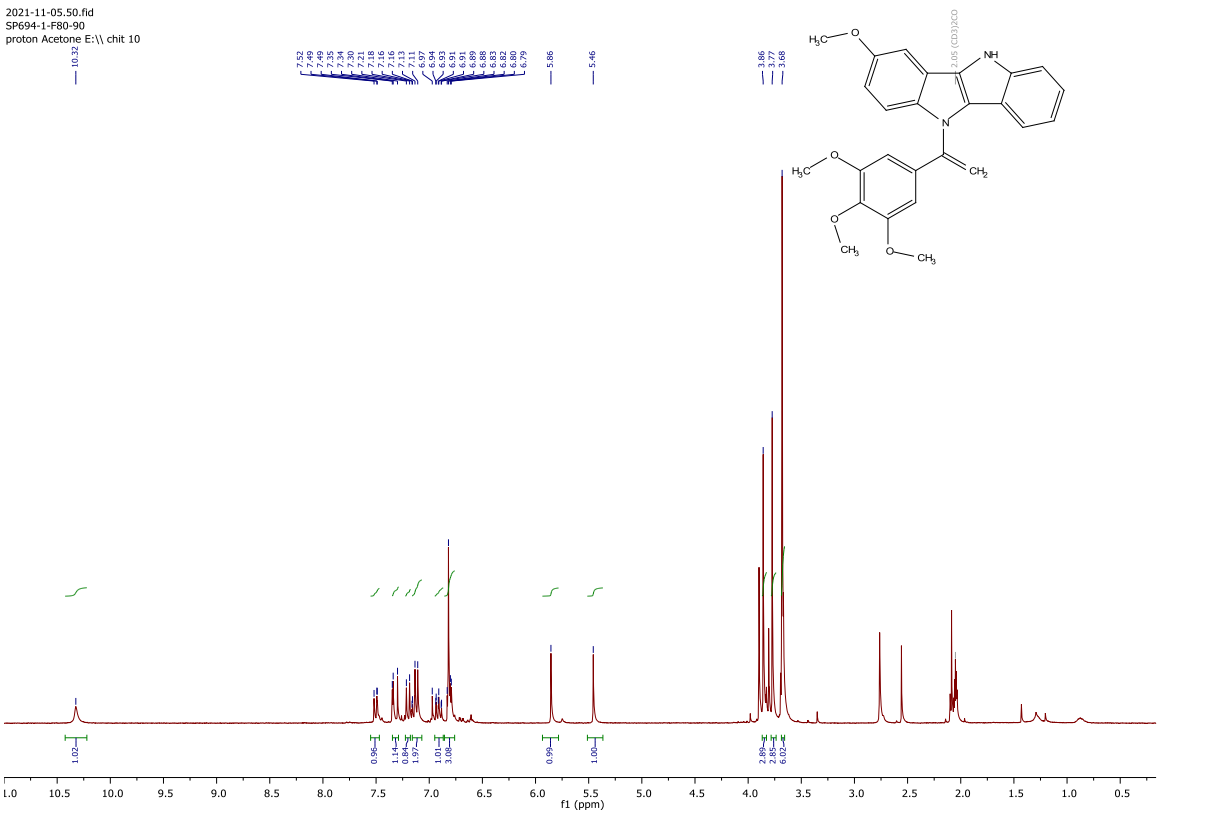
^{13}C{^{1}H} NMR of **6f** (101 MHz, $(CD_3)_2CO$)



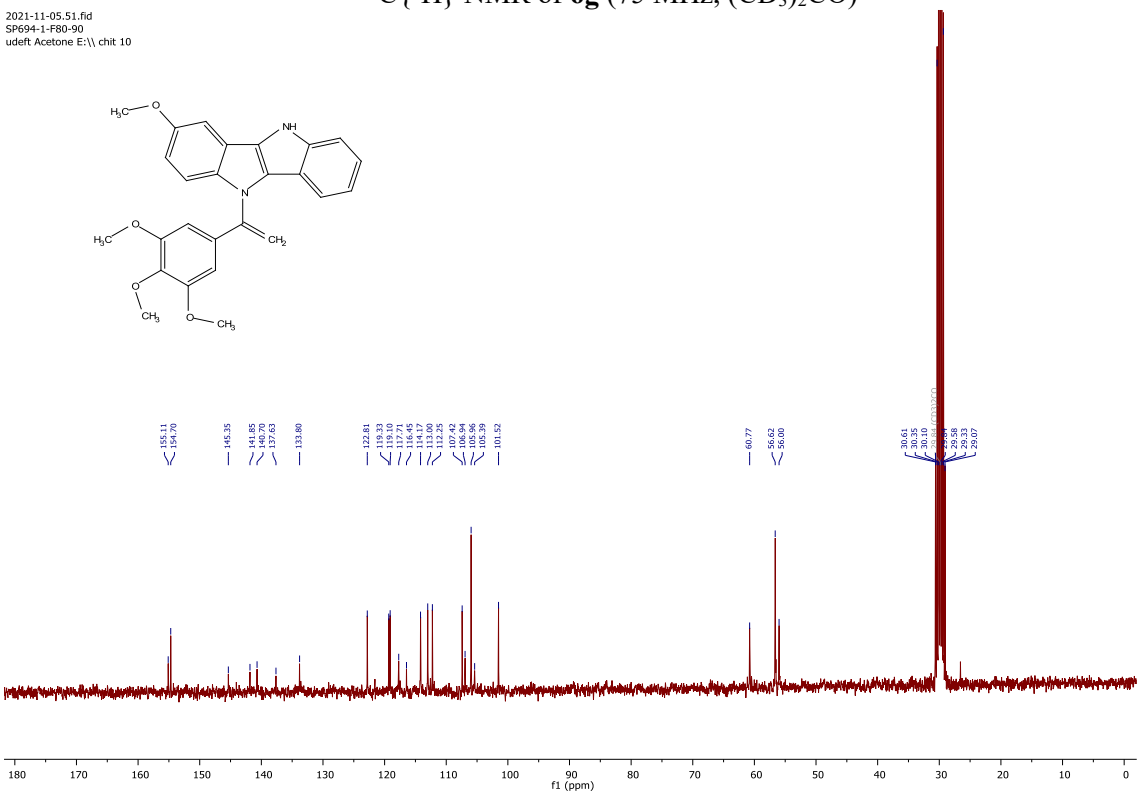
$^{19}F\{^{1}H\}$ NMR of **6f** (376 MHz, $(CD_3)_2CO$)



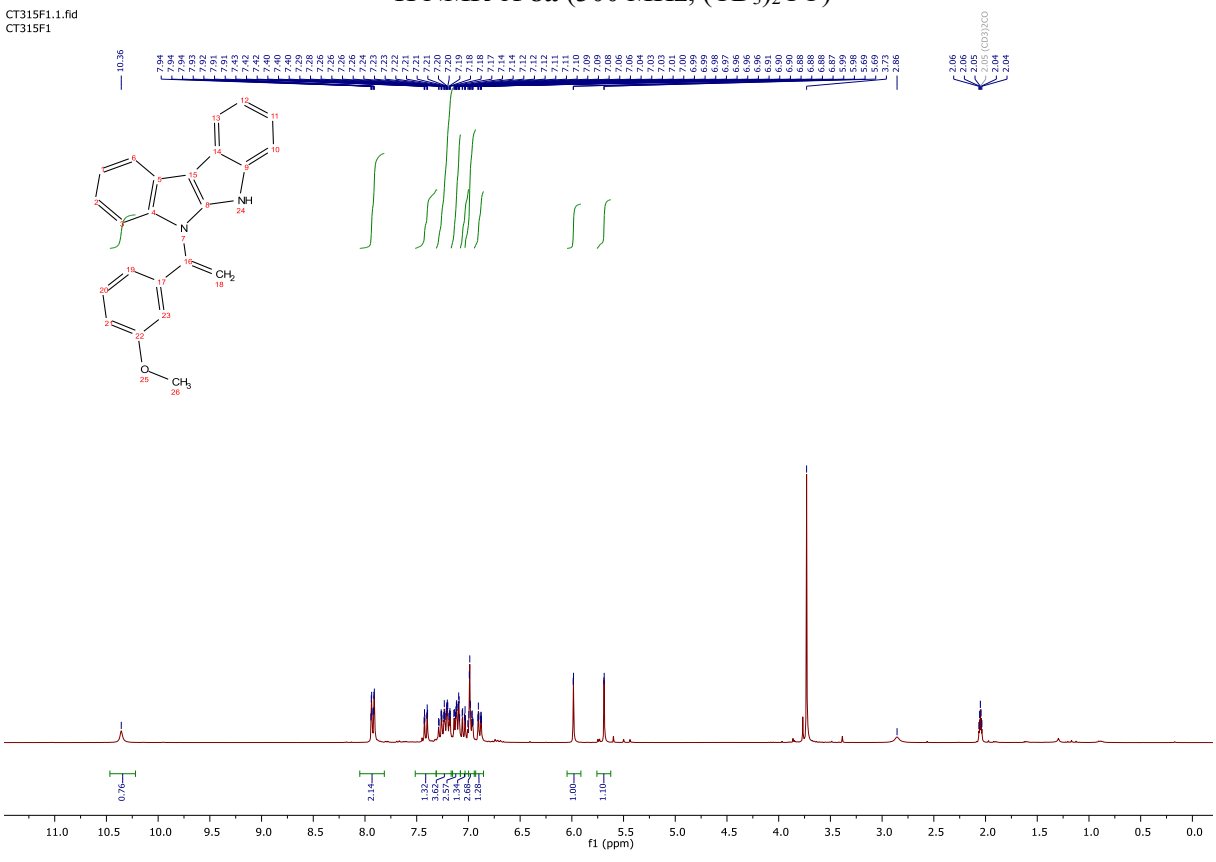
^{1}H NMR of **6g** (300 MHz, $(CD_3)_2CO$)



$^{13}C\{^{1}H\}$ NMR of **6g** (75 MHz, $(CD_3)_2CO$)



^{1}H NMR of **8a** (300 MHz, $(CD_3)_2CO$)



$^{13}C\{^{1}H\}$ NMR of **8a** (75 MHz, $(CD_3)_2CO$)