Supplementary Material (ESI) for Chemical Communications

Electronic Supplementary Information

One-Pot nitro-Mannich/hydroamination cascades for the direct synthesis of 2,5-disubstituted pyrroles using base and gold catalysis

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Contents

General Experimental

All non-aqueous reactions were conducted using oven-dried glassware under a positive pressure of dry nitrogen and were magnetically stirred unless otherwise stated. Yields refer to chromatographically purified and spectroscopically pure compounds, unless otherwise stated.

Solvents and Reagents

Concentration under reduced pressure was performed by rotary evaporation at 40 °C at the appropriate pressure. Reagents used were obtained from commercial suppliers or purified according to standard procedures. Triethylamine was distilled from calcium hydride under a positive pressure of dry nitrogen and stored over potassium hydroxide. Petroleum ether (PE) refers to distilled light petroleum of fraction 30-40 °C. Anhydrous methanol was freshly distilled from magnesium iodide under an atmosphere of dry nitrogen. Anhydrous toluene was freshly distilled from sodium/benzophenone ketyl under an atmosphere of dry nitrogen. Anhydrous tetrahydrofuran, dichloromethane, diethyl ether and acetonitrile were dried by filtration through activated alumina (powder ~150 mesh, pore size 58Å, basic, Sigma-Aldrich) columns. Dimethyl sulfoxide was used as supplied. Deuterated solvents were used as supplied.

Chromatography

Reactions were monitored by thin layer chromatography (TLC) using Merck silica gel 60 F_{254} plates and visualised by fluorescence quenching under UV light. In addition, TLC plates were stained with vanillin or potassium permanganate solution. Chromatographic purification was performed on VWR 60 silica gel 40-63 μm using technical grade solvents that were used as supplied.

Melting Points

Melting points were obtained on a Leica Galen III Hot-stage melting point apparatus and microscope and are uncorrected.

NMR Spectra

NMR spectra were recorded on a Bruker Spectrospin spectrometer operating at 400 MHz or 500 MHz (^{1}H acquisitions) and 100 MHz or 125 MHz (^{13}C acquisitions). Chemical shifts (δ) are reported in ppm with the solvent resonance as the internal standard (e.g. Chloroform δ 7.27 ppm for ^{1}H and 77.0 ppm for ^{13}C). Coupling constants (*J*) are reported in hertz (Hz).

Data are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, ddd = doublet of doublets of doublets, dt = doublet of triplets, td = triplet of doublets, tt = triplet of triplets, tq = triplet of quartets, qt = quartet of triplets, m = multiplet, br = broad, coupling constants in Hz, integration, assignment. Two-dimensional spectroscopy (COSY, HMQC and HMBC) was used to assist in the assignment. The data is not reported.

Mass Spectra

Low-resolution mass spectra (ESI) were recorded on a Waters LCT Premier XE Micromass mass spectrometer. High-resolution mass spectra (ESI) were recorded on Bruker Daltonics MicroTOF mass spectrometer. High-resolution mass spectra (EI) were recorded on a Bruker FT-ICR Apex III mass spectrometer.

Infrared Spectra

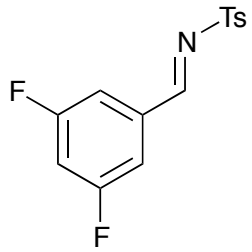
Infrared spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer as a thin film on a sodium chloride plate. Only selected maximum absorbances are reported.

Starting Materials

The starting *p*-toluenesulfonyl imines **1a**, **1b**, **1c**, **1d** and **1k** were synthesised by condensation of the corresponding aromatic aldehyde with *p*-toluenesulfonamide using titanium tetrachloride and anhydrous triethylamine in dry CH_2Cl_2.[S1] The starting *p*-toluenesulfonyl imines **1e** and **1j** were synthesised by condensation of the corresponding aromatic aldehyde with *p*-toluenesulfonamide mediated by *p*-toluenesulfinic acid in an aqueous media, followed by elimination using saturated sodium bicarbonate solution.[S2] The starting *p*-toluenesulfonyl imines **1f**, **1g**, **1h**, **1i**, **1l**, **1m**, **1n** and *p*-nitrobezenesulfonyl imine **1o** were synthesised by condensation of the corresponding aldehyde and *p*-toluenesulfonamide or *p*-nitrobenzenesulfonamide using tetraethylorthosilicate with azeotropic removal of ethanol.[S3] The starting *tert*-butyl (phenylmethylene)carbamate imine **1p** was synthesized by condensation of the corresponding aldehyde with *tert*-butyl carbamate mediated by *p*-toluenesulfinic acid in an aqueous media, followed by elimination using sodium carbonate in anhydrous THF.[S4] Experimental procedures and characterisation data are supplied for the novel *p*-toluenesulfonyl imines **1i** and **1l**.

Synthesis of compounds 1i and 1l

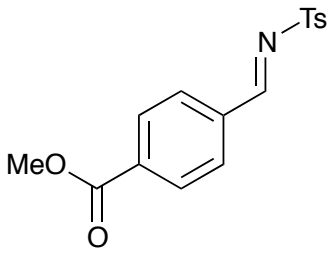
N-[(3,5-Difluorophenyl)methylene]-4-methylbenzenesulfonamide (1i)



Prepared according to a literature procedure described by Metzner.[S3] To a mixture of the 3,5-difluorobenzaldehyde (0.72 g, 5.50 mmol, 1.1 eq.) and *p*-toluenesulfonamide (0.86 g, 5.00 mmol, 1.0 eq.) at r.t. was added tetraethylorthosilicate (1.15 g, 5.50 mmol, 1.23 mL, 1.1 eq.). The resulting mixture was heated to 170 °C for 3 h in a flask equipped with a Dean-Stark trap. The reaction mixture was cooled to r.t. and the resulting solid was triturated with Et_2O to yield imine **1i** (1.13 g, 77%) as a white solid.

Melting Point: 131-134 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 8.95 (s, 1H, C*H*=N), 7.90 (AA′, part of AA′BB′ system, J = 8.5 Hz, 2H, $H_{aromatic}$), 7.49 - 7.43 (m, 2H, $H_{aromatic}$), 7.38 (BB′, part of AA′BB′ system, J = 8.5 Hz, 2H, $H_{aromatic}$), 7.07 (tt, J = 8.5 Hz, 2.5 Hz, 1H, $H_{aromatic}$), 2.46 (s, 3H, tosyl CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_c 167.4 (t, J = 3.0 Hz, 1C, *C*H=N), 163.1 (dd, J = 251.5 Hz, 12.0 Hz, 2C, $C_{aromatic}$), 145.1 (1C, $C_{aromatic}$), 135.3 (t, J = 9.0 Hz, 1C, $C_{aromatic}$), 134.3 (1C, $C_{aromatic}$), 129.9 (2C, $CH_{aromatic}$), 128.2 (2C, $CH_{aromatic}$), 113.6 (dd, J = 19.0 Hz, 7.0 Hz, 2C, $CH_{aromatic}$), 110.0 (t, J = 25.5 Hz, 1C, $CH_{aromatic}$), 21.6 (1C, tosyl CH_3); **IR** (thin film): ν_{max} 1584 cm^{-1} (-CH=N-), 1316 cm^{-1} (-SO_2N-), 1162 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 296.10 [(M + H)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{15}H_{15}F_2NNaO_3S$ [(M + Na + MeOH)$^+$], 350.0633; found 350.0637.

Methyl 4-[{[(4-methylphenyl)sulfonyl]imino}methyl]benzoate (1l)



Prepared according to a literature procedure described by Metzner.[S3] To a mixture of the methyl 4-formylbenzoate (0.41 g, 2.50 mmol, 1.1 eq.) and *p*-toluenesulfonamide (0.39 g, 2.27 mmol, 1.0 eq.) at r.t. in toluene (3.0 mL) was added tetraethylorthosilicate (0.52 g,

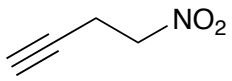
2.50 mmol, 0.56 mL, 1.1 eq.). The resulting mixture was heated to 170 °C for 3 h in a flask equipped with a Dean-Stark trap. The reaction mixture was cooled to r.t. and the resulting solid was triturated with Et_2O to yield imine **1l** (0.34 g, 47%) as a white solid.

Melting Point: 183-185 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 9.07 (s, 1H, C*H*=N), 8.13 (AA', part of AA'BB' system, J = 6.5 Hz, 1.5 Hz, 2H, $H_{aromatic}$), 8.00 (BB', part of AA'BB' system, J = 6.5 Hz, 1.5 Hz, 2H, $H_{aromatic}$), 7.93 - 7.87 (m, 2H, $H_{aromatic}$), 7.39 - 7.33 (m, 2H, $H_{aromatic}$), 3.95 (s, 3H, COOCH_3), 2.45 (s, 3H, tosyl CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 168.8 (1C, *C*H=N), 165.8 1C, *C*=O), 144.9 (1C, $C_{aromatic}$), 135.8 (1C, $C_{aromatic}$), 135.3 (1C, $C_{aromatic}$), 134.5 (1C, $C_{aromatic}$), 131.0 (2C, $CH_{aromatic}$), 130.1 (2C, $CH_{aromatic}$), 129.9 (2C, $CH_{aromatic}$), 128.2 (2C, $CH_{aromatic}$), 52.6 (1C, COO*C*H$_3$), 21.6 (1C, tosyl *C*H$_3$); **IR** (thin film): ν_{max} 1717 cm^{-1} (C=O), 1603 cm^{-1} (-CH=N-) 1323 cm^{-1} (-SO_2N-), 1160 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 318.11 [(M + H)$^+$]; **HRMS** (EI/FI): exact mass calculated for $C_{16}H_{15}NO_4S$ $[M]^+$, 317.0722; found 317.0722.

Synthesis of compounds 2a, 2b and 3

4-Bromobut-1-yne is commercially available.

4-Nitrobut-1-yne (2a)

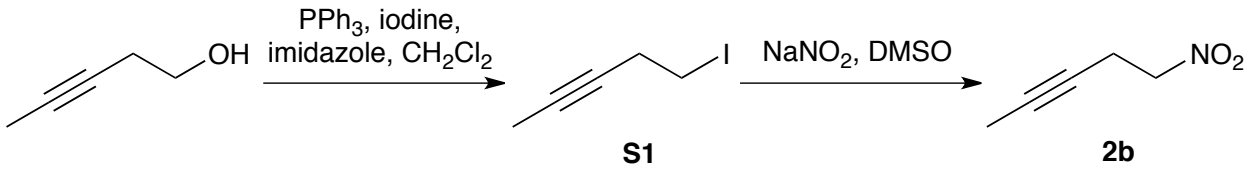


Prepared according to a modified literature procedure described by McMurry.[S5] To a stirred solution of 4-bromobut-1-yne (3.85 g, 29.0 mmol, 1.0 eq.) in DMSO (29 mL) at r.t. was added $NaNO_2$ (4.00 g, 58.0 mmol, 2.0 eq.) behind a blast shield. The resulting mixture was stirred at r.t. for 2 h. The reaction mixture was diluted with ice water (100 mL) and extracted with Et_2O (3 × 100 mL). The combined organic extracts were washed with ice water (100 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography eluting with PE : Et_2O (19:1) yielded **2a** (1.1 g, 38%) as a colourless oil.

TLC: R_f = 0.21 (PE : Et_2O 19:1, $KMnO_4$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 4.48 (t, J = 7.0 Hz, 2H, $CH_2CH_2NO_2$), 2.88 (td, J = 7.0 Hz, 2.5 Hz, 2H, $CH_2CH_2NO_2$), 2.09 (t, J = 2.5 Hz, 1H, H_{alkyne}); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 77.6 (1C, C_{alkyne}), 73.0 (1C, $CH_2CH_2NO_2$), 71.6 (1C, CH_{alkyne}), 17.3 (1C, $CH_2CH_2NO_2$); **IR** (thin film): ν_{max} 3309 cm^{-1} (-C≡CH),

1560 cm^{-1} (-NO_2), 1378 cm^{-1} (-NO_2); **HRMS** (EI/FI): exact mass calculated for $C_4H_5NO_2$ $[M]^+$, 99.0320; found 99.0321.

5-Nitropent-2-yne (2b)



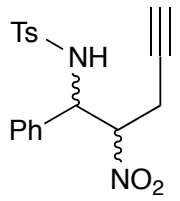
S1 **2b**

Compound **S1** was prepared according to a literature procedure described by Lange.[S6] To a stirred solution of PPh_3 (3.42 g, 13.0 mmol, 1.30 eq.) in dry CH_2Cl_2 (40 mL) at r.t. was firstly added imidazole (0.90 g, 13.0 mmol, 1.30 eq.) and then iodine (3.29 g, 13.0 mmol, 1.30 eq.). The resulting mixture was stirred at r.t. for 10 minutes and 3-pentyn-1-ol (0.841 g, 10.0 mmol, 0.922 mL, 1.0 eq.) was added in one portion. The resulting mixture was protected from light and stirred at r.t. for 3 h. The reaction mixture was concentrated under a stream of nitrogen and the resulting residue was purified by flash column chromatography eluting with PE to yield **S1** (1.07 g, 55%) as a colourless oil.

TLC: R_f = 0.40 (PE, $KMnO_4$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 3.21 (t, *J* = 7.5 Hz, 2H, CH_2CH_2I), 2.73 (tq, *J* = 7.5 Hz, 2.5 Hz, 2H, CH_2CH_2I), 1.79 (t, *J* = 2.5 Hz, 3H, alkyne CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ_C 77.9 (1C, C_{alkyne}), 77.8 (1C, C_{alkyne}), 24.1 (1C, CH_2), 3.5 (1C, CH_3), 2.6 (1C, CH_2). Data was in accordance with that reported in the literature.[S7] To a stirred solution of the **S1** (1.07 g, 5.50 mmol, 1.0 eq.) in DMSO (5.5 mL) at r.t. was added $NaNO_2$ (0.76 g, 11.0 mmol, 2.0 eq.). The resulting mixture was stirred at r.t. for 2 h. The reaction mixture was diluted with ice water (10 mL) and extracted with Et_2O (3 × 25 mL). The combined organic extracts were washed with ice water (20 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography eluting with PE : Et_2O (19:1) yielded **2b** (0.25 g, 39%) as a pale yellow oil.

TLC: R_f = 0.26 (PE : Et_2O 19:1, $KMnO_4$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 4.46 (t, *J* = 7.0 Hz, 2H, $CH_2CH_2NO_2$), 2.85 (qt, *J* = 7.0 Hz, 2.5 Hz, 2H, $CH_2CH_2NO_2$), 1.78 (t, J = 2.5 Hz, 3H, alkyne CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 79.1 (1C, C_{alkyne}), 73.8 (1C, $CH_2CH_2NO_2$), 72.4 (1C, C_{alkyne}), 17.7 (1C, $CH_2CH_2NO_2$), 3.3 (1C, alkyne CH_3); **IR** (thin film): ν_{max} 1558 cm^{-1} (-NO_2), 1380 cm^{-1} (-NO_2); **HRMS** (EI/FI): exact mass calculated for $C_5H_7NO_2$ $[M]^+$, 113.0477; found 113.0475.

4-Methyl-*N*-(2-nitro-1-phenylpent-4-yn-1-yl)benzenesulfonamide (3)



To a stirred solution of **2a** (20.8 mg, 0.21 mmol, 1.5 eq.) and imine **1a** (36.3 mg, 0.14 mmol, 1.0 eq.) in dry MeOH (1.5 mL) at r.t. was added KO^{t}Bu (1.60 mg, 0.01 mmol, 10 mol %). The resulting mixture was stirred at r.t. for 24 h. The white precipitate was filtered and dried to yield nitro amine **3** (18.0 mg, 36%) as a white solid (d.r. = 98:2). The mother liquor was concentrated under reduced pressure and the residue (d.r. = 75:25) was purified by flash column chromatography eluting with PE : EtOAc (4:1) to yield nitro amine **3** (27.0 mg, 54%, d.r. = 75:25) as an off-white solid. 90% combined yield.

Major *syn* diastereoisomer 3: TLC: R_f = 0.33 (PE : EtOAc 4:1, UV, vanillin); **Melting Point**: 166-169 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ_H 7.53 (AA′, part of AA′BB′ system, J = 8.5 Hz, 2H, $H_{aromatic}$), 7.25 - 7.18 (m, 3H, $H_{aromatic}$), 7.11 (BB′, part of AA′BB′ system, J = 8.5 Hz, 2H, $H_{aromatic}$), 7.03 - 6.98 (m, 2H, $H_{aromatic}$), 5.65 (d, J = 10.0 Hz, 1H, N*H*), 4.93 (dd, J = 10.0 Hz, 6.0 Hz, 1H, C*H*NH), 4.85 (dt, J = 9.0 Hz, 5.5 Hz, 1H, C*H*NO_2), 2.93 (ddd, J = 17.5 Hz, 9.0 Hz, 2.5 Hz, 1H, CH_2CHNO_2), 2.67 (ddd, J = 17.5 Hz, 5.5 Hz, 2.5 Hz, 1H, CH_2CHNO_2), 2.34 (s, 3H, tosyl CH_3), 2.15 (t, J = 2.5 Hz, 1H, H_{alkyne}); **^{13}C NMR** (125 MHz, $CDCl_3$): δ_C 143.7 (1C, $C_{aromatic}$), 136.9 (1C, $C_{aromatic}$), 134.8 (1C, $C_{aromatic}$), 129.4 (2C, $CH_{aromatic}$), 129.1 (2C, $CH_{aromatic}$), 128.8 (1C, $CH_{aromatic}$), 127.0 (2C, $CH_{aromatic}$), 126.3 (2C, $CH_{aromatic}$), 89.9 (1C, $CHNO_2$), 76.4 (1C, C_{alkyne}), 73.1 (1C, CH_{alkyne}), 58.5 (1C, *C*HNH), 21.5 (1C, CH_2CHNO_2), 21.5 (1C, tosyl CH_3); **IR** (thin film): ν_{max} 3281 cm^{-1} (-C≡CH), 1561 cm^{-1} (-NO_2), 1371 cm^{-1} (-SO_2N-), 1325 cm^{-1} (-NO_2), 1162 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 381.11 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{18}H_{18}N_2NaO_4S$ [(M + Na)$^+$], 381.0879; found 381.0883.

Minor *anti* diastereoisomer 3: TLC: R_f = 0.33 (PE : EtOAc 4:1, UV, vanillin); **Melting Point**: 121-124 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.54 (d, J = 8.0 Hz, 2H, $H_{aromatic}$), 7.25 - 7.09 (m, 5H, $H_{aromatic}$), 6.93 (d, J = 7.5 Hz, 2H, $H_{aromatic}$), 5.84 (d, J = 9.0 Hz, 1H, N*H*), 4.89 - 4.79 (m, 2H, NHC*H*C*H*NO_2), 2.95 - 2.90 (m, 2H, CH_2CHNO_2), 2.36 (s, 3H, tosyl CH_3), 2.18 (t, J = 2.5 Hz, 1H, H_{alkyne}); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 143.9 (1C, $C_{aromatic}$), 136.5 (1C, $C_{aromatic}$), 133.9 (1C, $C_{aromatic}$), 129.6 (2C, $CH_{aromatic}$), 129.0 (1C, $CH_{aromatic}$), 128.9 (2C,

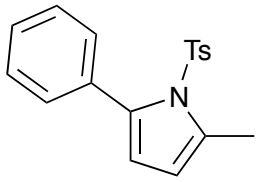
*C*H$_{aromatic}$), 127.1 (2C, *C*H$_{aromatic}$), 126.7 (2C, *C*H$_{aromatic}$), 88.9 (1C, C*H*NO$_2$), 77.2 (1C, *C*$_{alkyne}$), 72.9 (1C, *C*H$_{alkyne}$), 58.7 (1C, *C*HNH), 21.5 (1C, tosyl *C*H$_3$), 20.7 (1C, *C*H$_2$CHNO$_2$); **IR** (thin film): ν_{max} 3287 cm^{-1} (-C≡CH), 1559 cm^{-1} (-NO$_2$), 1370 cm^{-1} (-SO$_2$N-), 1324 cm^{-1} (-NO$_2$), 1161 cm^{-1} (-SO$_2$N-); **MS** (ESI): *m/z* 381.13 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{18}H_{18}N_2NaO_4S$ [(M + Na)$^+$], 381.0879; found 381.0873

General procedure for the nitro-Mannich/hydroamination cascade

To a stirred solution of 4-nitrobut-1-yne **2a** (60 mg, 0.60 mmol, 1.5 eq.) and the corresponding *p*-toluenesulfonyl imine **1a-p** (0.40 mmol, 1.0 eq.) in freshly distilled MeOH (3.2 mL) at r.t. in a vial equipped with a rubber septum, was added KO^{t}Bu (4.5 mg, 0.04 mmol, 10 mol %). The resulting mixture was stirred at r.t. and monitored by TLC. Once the imine had been consumed (typically 4-8 h), $AuCl_3$ (6.1 mg, 0.02 mmol, 5 mol %) was added. The reaction mixture was sealed in a microwave vial, purged with nitrogen (×2), protected from light and heated to 70 ºC (typically 24-48 h). The reaction mixture was cooled to r.t. and concentrated under a stream of nitrogen. The resulting residue was purified by chromatography on silica gel to yield the desired pyrrole **4a-q**.

Synthesis and characterisation of compounds 4a-q

2-Methyl-1-[(4-methylphenyl)sulfonyl]-5-phenyl-1*H*-pyrrole (4a)

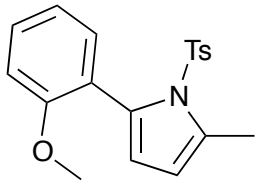


Prepared according to the general procedure, compound **4a** (95 mg) was isolated as a white solid in 76% yield after flash column chromatography.

TLC: R_f = 0.28 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 115-118 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.38 - 7.29 (m, 7H, *H*$_{aromatic}$), 7.17 (d, *J* = 8.0 Hz, 2H, *H*$_{aromatic}$), 6.09 - 6.05 (m, 1H, *H*$_{pyrrole}$), 6.03 - 5.98 (m, 1H, *H*$_{pyrrole}$), 2.54 (s, 3H, pyrrole C*H*$_3$), 2.38 (s, 3H, tosyl C*H*$_3$); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_c 144.3 (1C, *C*$_{aromatic}$), 137.6 (1C, *C*$_{aromatic}$), 136.4 (1C, *C*$_{aromatic}$), 134.3 (1C, *C*$_{aromatic}$), 133.2 (1C, *C*$_{aromatic}$), 130.6 (2C, *C*H$_{aromatic}$), 129.4 (2C, *C*H$_{aromatic}$), 127.7 (1C, *C*H$_{aromatic}$), 127.2 (2C, *C*H$_{aromatic}$), 126.4 (2C, *C*H$_{aromatic}$), 115.3 (1C, *C*H$_{pyrrole}$), 113.5 (1C, *C*H$_{pyrrole}$), 21.5 (1C, tosyl *C*H$_3$), 16.1 (1C, pyrrole *C*H$_3$); **IR** (thin film):

ν_{max} 1369 cm^{-1} (-SO_2N-), 1173 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 334.11 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{18}H_{17}NNaO_2S$ [(M + Na)$^+$], 334.0872; found 334.0874.

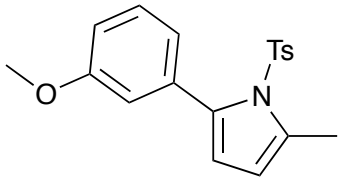
2-(2-Methoxyphenyl)-5-methyl-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrole (4b)



Prepared according to the general procedure, compound **4b** (93 mg) was isolated as a white solid in 68% yield after flash column chromatography.

TLC: R_f = 0.18 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 125-127 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.42 (d, *J* = 8.5 Hz, 2H, $H_{aromatic}$), 7.40 - 7.34 (m, 1H, $H_{aromatic}$), 7.21 (d, *J* = 8.5 Hz, 2H, $H_{aromatic}$), 7.14 (dd, *J* = 7.5 Hz, 2.0 Hz, 1H, $H_{aromatic}$), 6.97 - 6.92 (m, 1H, $H_{aromatic}$), 6.89 (d, *J* = 8.5 Hz, 1H, $H_{aromatic}$), 6.09 - 6.06 (m, 1H, $H_{pyrrole}$), 6.06 - 6.03 (m, 1H, $H_{pyrrole}$), 3.75 (s, 3H, OCH_3), 2.45 (s, 3H, pyrrole CH_3), 2.40 (s, 3H, tosyl CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 158.6 (1C, $C_{aromatic}$), 144.0 (1C, $C_{aromatic}$), 137.2 (1C, $C_{aromatic}$), 133.2 (1C, $C_{aromatic}$), 133.1 (1C, $C_{aromatic}$), 131.9 (1C, $CH_{aromatic}$), 129.8 (1C, $CH_{aromatic}$), 129.4 (2C, $CH_{aromatic}$), 126.5 (2C, $CH_{aromatic}$), 122.9 (1C, $C_{aromatic}$), 119.5 (1C, $CH_{aromatic}$), 114.1 (1C, $CH_{pyrrole}$), 112.8 (1C, $CH_{pyrrole}$), 110.2 (1C, $CH_{aromatic}$), 55.3 (1C, OCH_3), 21.5 (1C, tosyl CH_3), 15.7 (1C, pyrrole CH_3); **IR** (thin film): ν_{max} 1368 cm^{-1} (-SO_2N-), 1175 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 364.09 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{20}NO_3S$ [(M + H)$^+$], 342.1158; found 342.1158.

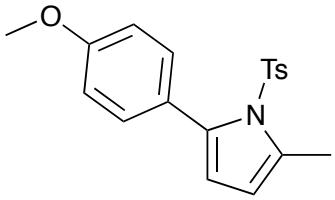
2-(3-Methoxyphenyl)-5-methyl-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrole (4c)



Prepared according to the general procedure, compound **4c** (118 mg) was isolated as a white solid in 86% yield after flash column chromatography.

TLC: R_f = 0.23 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 112-114 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.34 (d, *J* = 8.5 Hz, 2H, $H_{aromatic}$), 7.24 (t, *J* = 8.0 Hz, 1H, $H_{aromatic}$), 7.17 (d, *J* = 8.5 Hz, 2H, $H_{aromatic}$), 6.95 - 6.84 (m, 3H, $H_{aromatic}$), 6.09 - 6.04 (m, 1H, $H_{pyrrole}$), 6.02 - 5.96 (m, 1H, $H_{pyrrole}$), 3.81 (s, 3H, OCH_3), 2.53 (s, 3H, pyrrole CH_3), 2.38 (s, 3H, tosyl CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 158.4 (1C, $C_{aromatic}$), 144.3 (1C, $C_{aromatic}$), 137.4 (1C, $C_{aromatic}$), 136.3 (1C, $C_{aromatic}$), 134.4 (1C, $C_{aromatic}$), 134.4 (1C, $C_{aromatic}$), 129.4 (2C, CH$_{aromatic}$), 128.1 (1C, CH$_{aromatic}$), 126.5 (2C, CH$_{aromatic}$), 123.1 (1C, CH$_{aromatic}$), 116.0 (1C, CH$_{aromatic}$), 115.2 (1C, CH$_{aromatic}$), 113.6 (1C, CH$_{aromatic}$), 113.4 (1C, CH$_{aromatic}$), 55.2 (1C, OCH$_3$), 21.5 (1C, toysl CH$_3$), 16.1 (1C, pyrrole CH$_3$); **IR** (thin film): ν_{max} 1369 cm^{-1} (-SO_2N-), 1174 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 364.12 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{19}NNaO_3S$ [(M + Na)$^+$], 364.0978; found 364.0985.

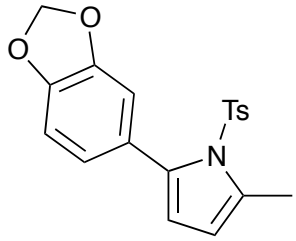
2-(4-Methoxyphenyl)-5-methyl-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrole (4d)



Prepared according to the general procedure, compound **4d** (75 mg) was isolated as a white solid in 55% yield after flash column chromatography.

TLC: R_f = 0.23 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 114-117 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ_H 7.30 (d, *J* = 8.5 Hz, 2H, $H_{aromatic}$), 7.22 (AA′, part of AA′BB′ system, *J* = 6.5 Hz, 2.0 Hz, 2H, $H_{aromatic}$), 7.17 (d, *J* = 8.5 Hz, 2H, $H_{aromatic}$), 6.86 (BB′, part of AA′BB′ system, *J* = 6.5 Hz, 2.0 Hz, 2H, $H_{aromatic}$), 6.01 - 5.97 (m, 2H, $H_{pyrrole}$), 3.85 (s, 3H, OCH_3), 2.52 (s, 3H, pyrrole CH_3), 2.38 (s, 3H, tosyl CH_3); **^{13}C NMR** (125 MHz, $CDCl_3$): δ_C 159.3 (1C, $C_{aromatic}$), 144.2 (1C, $C_{aromatic}$), 137.3 (1C, $C_{aromatic}$), 136.6 (1C, $C_{aromatic}$), 133.9 (1C, $C_{aromatic}$), 131.9 (2C, CH$_{aromatic}$), 129.4 (2C, CH$_{aromatic}$), 126.5 (2C, CH$_{aromatic}$), 125.6 (1C, $C_{aromatic}$), 114.7 (1C, CH$_{pyrrole}$), 113.3 (1C, CH$_{pyrrole}$), 112.6 (2C, CH$_{aromatic}$), 55.2 (1C, OCH$_3$), 21.6 (1C, tosyl CH$_3$), 16.2 (1C, pyrrole CH$_3$); **IR** (thin film): ν_{max} 1368 cm^{-1} (-SO_2N-), 1175 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 364.11 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{20}NO_3S$ [(M + H)$^+$], 342.1158; found 342.1158.

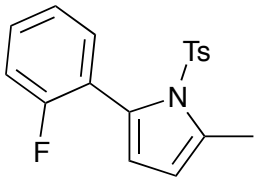
2-(1,3-Benzodioxol-5-yl)-5-methyl-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrole (4e)



Prepared according to the general procedure, compound **4e** (91 mg) was isolated as a white solid in 64% yield after flash column chromatography.

TLC: R_f = 0.18 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 134-136 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ_H 7.35 (AA′, part of AA′BB′ system, J = 8.0 Hz, 2H, $H_{aromatic}$), 7.19 (BB′, part of AA′BB′ system, J = 8.0 Hz, 2H, $H_{aromatic}$), 6.82 (d, J = 1.5 Hz, 1H, $H_{aromatic}$), 6.76 (d, J = 8.0 Hz, 1H, $H_{aromatic}$), 6.74 (dd, J = 8.0 Hz, 1.5 Hz, 1H, $H_{aromatic}$), 6.02 - 5.99 (m, 3H, [1H, $H_{pyrrole}$], [2H, OCH_2O]), 5.97 (dd, J = 3.0 Hz, 1.0 Hz, 1H, $H_{pyrrole}$), 2.52 - 2.49 (m, 3H, pyrrole CH_3), 2.38 (s, 3H, tosyl CH_3); **^{13}C NMR** (125 MHz, $CDCl_3$): δ_C 147.4 (1C, $C_{aromatic}$), 146.6 (1C, $C_{aromatic}$), 144.3 (1C, $C_{aromatic}$), 137.1 (1C, $C_{aromatic}$), 136.5 (1C, $C_{aromatic}$), 134.1 (1C, $C_{aromatic}$), 129.4 (2C, CH$_{aromatic}$), 127.0 (1C, $C_{aromatic}$), 126.5 (2C, CH$_{aromatic}$), 124.2 (1C, CH$_{aromatic}$), 115.0 (1C, CH$_{pyrrole}$), 113.3 (1C, CH$_{pyrrole}$), 111.5 (1C, CH$_{aromatic}$), 107.2 (1C, CH$_{aromatic}$), 101.2 (1C, OCH$_2$O), 21.6 (1C, tosyl CH$_3$), 16.1 (1C, pyrrole CH$_3$); **IR** (thin film): ν_{max} 1368 cm^{-1} (-SO_2N-), 1175 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 378.10 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{17}NNaO_4S$ [(M + Na)$^+$], 378.0770; found 378.0771.

2-(2-Fluorophenyl)-5-methyl-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrole (4f)

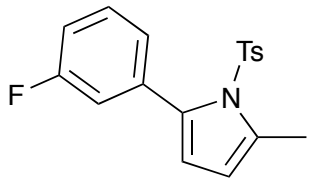


Prepared according to the general procedure, compound **4f** (100 mg) was isolated as a white solid in 76% yield after flash column chromatography.

TLC: R_f = 0.24 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 105-108 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.38 (AA', part of AA'BB' system, J = 8.0 Hz, 2H, $H_{aromatic}$), 7.36 - 7.30 (m, 1H, $H_{aromatic}$), 7.24 (td, J = 7.5 Hz, 2.0 Hz, 1H, $H_{aromatic}$), 7.19 (BB', part of AA'BB' system, J = 8.0 Hz, 2H, $H_{aromatic}$), 7.11 (td, J = 7.5 Hz, 1.0 Hz, 1H, $H_{aromatic}$), 7.08 - 7.02 (m, 1H,

$H_{aromatic}$), 6.12 (d, J = 3.0 Hz, 1H, $H_{pyrrole}$), 6.03 (m, 1H, $H_{pyrrole}$), 2.45 - 2.42 (m, 3H, pyrrole CH_3), 2.36 (s, 3H, tosyl CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 160.8 (d, J = 247.5 Hz, 1C, $C_{aromatic}$), 144.5 (1C, $C_{aromatic}$), 136.5 (1C, $C_{aromatic}$), 134.1 (1C, $C_{aromatic}$), 132.5 (d, J = 2.5 Hz, 1C, CH$_{aromatic}$), 130.1 (1C, $C_{aromatic}$), 130.0 (d, J = 8.0 Hz, 1C, CH$_{aromatic}$), 129.6 (2C, CH$_{aromatic}$), 126.4 (2C, CH$_{aromatic}$), 123.0 (d, J = 3.0 Hz, 1C, CH$_{aromatic}$), 121.6 (d, J = 16.0 Hz, 1C, $C_{aromatic}$), 115.8 (1C, CH$_{pyrrole}$), 115.0 (d, J = 21.5 Hz, 1C, CH$_{aromatic}$), 113.2 (1C, CH$_{pyrrole}$), 21.5 (1C, tosyl CH$_3$), 15.6 (1C, pyrrole CH$_3$); **IR** (thin film): ν_{max} 1370 cm^{-1} (-SO_2N-), 1175 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 352.09 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{18}H_{16}FNNaO_2S$ [(M + Na)$^+$], 352.0778; found 352.0787.

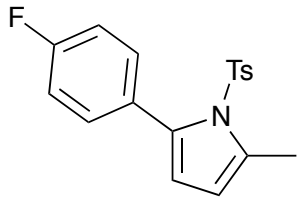
2-(3-Fluorophenyl)-5-methyl-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrole (4g)



Prepared according to the general procedure, compound **4g** (80 mg) was isolated as a pale pink solid in 61% yield after flash column chromatography.

TLC: R_f = 0.38 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 135-138 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.34 (AA', part of AA'BB' system, J = 8.0 Hz, 2H, $H_{aromatic}$), 7.31 - 7.28 (m, 1H, $H_{aromatic}$), 7.20 (BB', part of AA'BB' system, J = 8.0 Hz, 2H, $H_{aromatic}$), 7.15 (dt, J = 7.5 Hz, 1.0 Hz, 1H, $H_{aromatic}$), 7.08 - 7.00 (m, 2H, $H_{aromatic}$), 6.09 (d, J = 3.0 Hz, 1H, $H_{pyrrole}$), 6.03 - 5.99 (m, 1H, $H_{pyrrole}$), 2.54 - 2.50 (m, 3H, pyrrole CH_3), 2.39 (s, 3H, tosyl CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 161.8 (d, J = 245.5 Hz, 1C, $C_{aromatic}$), 144.6 (1C, $C_{aromatic}$), 136.2 (1C, $C_{aromatic}$), 135.2 (d, J = 9.0 Hz, 1C, $C_{aromatic}$), 134.9 (1C, $C_{aromatic}$), 129.5 (2C, CH$_{aromatic}$), 128.6 (d, J = 9.0 Hz, 1C, CH$_{aromatic}$), 126.4 (2C, CH$_{aromatic}$), 126.4 (d, J = 3.0 Hz, 1C, CH$_{aromatic}$), 117.3 (d, J = 22.5 Hz, 1C, CH$_{aromatic}$), 115.8 (1C, CH$_{pyrrole}$), 114.6 (d, J = 21.0 Hz, 1C, CH$_{aromatic}$), 113.6 (1C, CH$_{pyrrole}$), 21.6 (1C, tosyl CH$_3$), 16.0 (1C, pyrrole CH$_3$); **IR** (thin film): ν_{max} 1370 cm^{-1} (-SO_2N-), 1173 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 352.09 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{18}H_{16}FNNaO_2S$ [(M + Na)$^+$], 352.0778; found 352.0787.

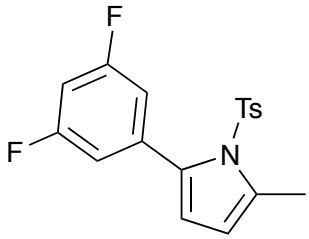
2-(4-Fluorophenyl)-5-methyl-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrole (4h)



Prepared according to the general procedure, compound **4h** (97 mg) was isolated as a white solid in 74% yield after flash column chromatography.

TLC: R_f = 0.23 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 126-129 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.32 - 7.24 (m, 4H, $H_{aromatic}$), 7.20 - 7.16 (m, 2H, $H_{aromatic}$), 7.04 - 6.97 (m, 2H, $H_{aromatic}$), 6.03 (d, J = 3.0 Hz, 1H, $H_{pyrrole}$), 6.01 - 5.98 (m, 1H, $H_{pyrrole}$), 2.52 (d, J = 1.0 Hz, 3H, pyrrole CH_3), 2.38 (s, 3H, tosyl CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 162.5 (d, J = 247.5 Hz, 1C, $C_{aromatic}$), 144.4 (1C, $C_{aromatic}$), 136.4 (1C, $C_{aromatic}$), 136.3 (1C, $C_{aromatic}$), 134.4 (1C, $C_{aromatic}$), 132.3 (d, J = 8.0 Hz, 2C, CH$_{aromatic}$), 129.5 (2C, CH$_{aromatic}$), 129.2 (d, J = 3.0 Hz, 1C, $C_{aromatic}$), 126.4 (2C, CH$_{aromatic}$), 115.3 (1C, CH$_{pyrrole}$), 114.2 (d, J = 21.5 Hz, 2C, CH$_{aromatic}$), 113.4 (1C, CH$_{pyrrole}$), 21.5 (1C, tosyl CH$_3$), 16.0 (1C, pyrrole CH$_3$); **IR** (thin film): ν_{max} 1369 cm^{-1} (-SO_2N-), 1174 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 330.12 [(M + H)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{18}H_{17}FNO_2S$ [(M + H)$^+$], 330.0959; found 330.0954.

2-(3,5-Difluorophenyl)-5-methyl-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrole (4i)

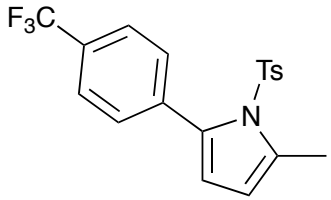


Prepared according to the general procedure, compound **4i** (91 mg) was isolated as a white solid in 66% yield after flash column chromatography.

TLC: R_f = 0.38 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 167-169 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.35 (AA′, part of AA′BB′ system, J = 8.5 Hz, 2H, $H_{aromatic}$), 7.22 (BB′, part of AA′BB′ system, J = 8.5 Hz, 2H, $H_{aromatic}$), 6.90 - 6.83 (m, 2H, $H_{aromatic}$), 6.79 (tt, J = 9.0 Hz, 2.5 Hz, 1H, $H_{aromatic}$), 6.11 (d, J = 3.5 Hz, 1H, $H_{pyrrole}$), 6.03 - 5.97 (m, 1H, $H_{pyrrole}$), 2.51 (s, 3H, pyrrole CH_3), 2.40 (s, 3H, tosyl CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 161.9 (dd, J = 247.5 Hz, 13.5 Hz, 2C, $C_{aromatic}$), 144.8 (1C, $C_{aromatic}$), 136.2 (1C, $C_{aromatic}$), 136.1 (1C,

$C_{aromatic}$), 135.5 (1C, $C_{aromatic}$), 135.2 (t, J = 2.5 Hz, 1C, $C_{aromatic}$), 129.6 (2C, $CH_{aromatic}$), 126.4 (2C, $CH_{aromatic}$), 116.4 (1C, $CH_{pyrrole}$), 113.7 (1C, $CH_{pyrrole}$), 113.4 (dd, J = 18.5 Hz, 7.0 Hz, 2C, $CH_{aromatic}$), 103.1 (t, J = 25.0 Hz, 1C, $CH_{aromatic}$), 21.6 (1C, tosyl CH_3), 15.9 (1C, pyrrole CH_3); **IR** (thin film): ν_{max} 1369 cm^{-1} (-SO_2N-), 1169 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 348.10 [(M + H)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{18}H_{16}F_2NO_2S$ [(M + H)$^+$], 348.0864; found 348.0858.

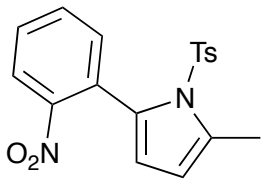
2-Methyl-1-[(4-methylphenyl)sulfonyl]-5-[4-(trifluoromethyl)phenyl]-1*H*-pyrrole (4j)



Prepared according to the general procedure, compound **4j** (108 mg) was isolated as a white solid in 71% yield after flash column chromatography.

TLC: R_f = 0.30 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 111-113 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ_H 7.59 (d, J = 8.0 Hz, 2H, $H_{aromatic}$), 7.46 (d, J = 8.0 Hz, 2H, $H_{aromatic}$), 7.31 (d, J = 8.0 Hz, 2H, $H_{aromatic}$), 7.19 (d, J = 8.0 Hz, 2H, $H_{aromatic}$), 6.12 (d, J = 3.5 Hz, 1H, $H_{pyrrole}$), 6.03 (dd, J = 3.5 Hz, 1.0 Hz, 1H, $H_{pyrrole}$), 2.52 (d, J = 1.0 Hz, 3H, pyrrole CH_3), 2.39 (s, 3H, tosyl CH_3); **^{13}C NMR** (125 MHz, $CDCl_3$): δ_C 144.7 (1C, $C_{aromatic}$), 136.9 (1C, $C_{aromatic}$), 136.2 (1C, $C_{aromatic}$), 136.1 (1C, $C_{aromatic}$), 135.4 (1C, $C_{aromatic}$), 130.5 (2C, $CH_{aromatic}$), 129.6 (2C, $CH_{aromatic}$), 129.6 (q, J = 32.5 Hz, 1C, $C_{aromatic}$), 126.3 (2C, $CH_{aromatic}$), 124.2 (q, J = 272.0 Hz, 1C, CF_3), 124.2 (q, J = 4.0 Hz, 2C, $CH_{aromatic}$), 116.6 (1C, $CH_{pyrrole}$), 113.9 (1C, $CH_{pyrrole}$), 21.6 (1C, tosyl CH_3), 16.0 (1C, pyrrole CH_3); **IR** (thin film): ν_{max} 1371 cm^{-1} (-SO_2N-), 1174 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 402.09 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{16}F_3NNaO_2S$ [(M + Na)$^+$], 402.0746; found 402.0747.

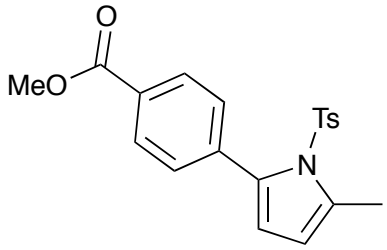
2-Methyl-1-[(4-methylphenyl)sulfonyl]-5-(2-nitrophenyl)-1*H*-pyrrole (4k)



Prepared according to the general procedure, compound **4k** (90 mg) was isolated as a yellow solid in 63% yield after flash column chromatography.

TLC: R_f = 0.12 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 129-132 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 8.08 (dd, *J* = 8.0 Hz, 2.0 Hz, 1H, $H_{aromatic}$), 7.61 - 7.48 (m, 2H, $H_{aromatic}$), 7.39 (d, *J* = 8.5 Hz, 2H, $H_{aromatic}$), 7.32 (dd, *J* = 7.5 Hz, 2.0 Hz, 1H, $H_{aromatic}$), 7.22 (d, *J* = 8.5 Hz, 2H, $H_{aromatic}$), 6.11 (d, *J* = 3.0 Hz, 1H, $H_{pyrrole}$), 6.08 - 6.04 (m, 1H, $H_{pyrrole}$), 2.45 (s, 3H, pyrrole CH_3), 2.39 (s, 3H, tosyl CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 149.2 (1C, $C_{aromatic}$), 144.7 (1C, $C_{aromatic}$), 136.4 (1C, $C_{aromatic}$), 134.1 (1C, $C_{aromatic}$), 133.5 (1C, $CH_{aromatic}$), 132.0 (1C, $CH_{aromatic}$), 131.3 (1C, $C_{aromatic}$), 129.7 (2C, $CH_{aromatic}$), 129.1 (1C, $CH_{aromatic}$), 128.4 (1C, $C_{aromatic}$), 126.6 (2C, $CH_{aromatic}$), 124.1 (1C, $CH_{aromatic}$), 114.8 (1C, $CH_{pyrrole}$), 113.1 (1C, $CH_{pyrrole}$), 21.5 (1C, tosyl CH_3), 15.4 (1C, pyrrole CH_3); **IR** (thin film): ν_{max} 1527 cm^{-1} (-NO_2), 1366 cm^{-1} (-SO_2N-), 1348 cm^{-1} (-NO_2), 1174 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 379.10 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{18}H_{16}N_2NaO_4S$ [(M + Na)$^+$], 379.0723; found 379.0726.

Methyl 4-{5-methyl-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrol-2-yl}benzoate (4l)

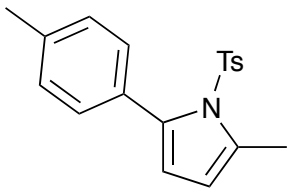


Prepared according to the general procedure using THF as a co-solvent (3.0 ml, added at the same time as $AuCl_3$), compound **4l** (89 mg) was isolated as an off-white solid in 60% yield after flash column chromatography.

TLC: R_f = 0.16 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 115-117 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 8.01 (AA', part of AA'BB' system, *J* = 6.5 Hz, 2.0 Hz, 2H, $H_{aromatic}$), 7.43

(AA', part of AA'BB' system, J = 6.5 Hz, 2.0 Hz, 2H, $H_{aromatic}$), 7.33 - 7.28 (m, 2H, $H_{aromatic}$), 7.21 - 7.15 (m, 2H, $H_{aromatic}$), 6.12 (d, J = 3.5 Hz, 1H, $H_{pyrrole}$), 6.02 (dd, J = 3.5 Hz, 1.0 Hz, 1H, $H_{pyrrole}$), 3.94 (s, 3H, COOCH_3), 2.51 (d, J = 1.0 Hz, 3H, pyrrole CH_3), 2.38 (s, 3H, tosyl CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 166.9 (1C, *C*=O), 144.6 (1C, $C_{aromatic}$), 137.8 (1C, $C_{aromatic}$), 136.7 (1C, $C_{aromatic}$), 136.0 (1C, $C_{aromatic}$), 135.5 (1C, $C_{aromatic}$), 130.2 (2C, $CH_{aromatic}$), 129.5 (2C, $CH_{aromatic}$), 129.1 (1C, $C_{aromatic}$), 128.5 (2C, $CH_{aromatic}$), 126.3 (2C, $CH_{aromatic}$), 116.5 (1C, $CH_{pyrrole}$), 114.0 (1C, $CH_{pyrrole}$), 52.1 (1C, COOCH_3), 21.5 (1C, tosyl CH_3), 16.0 (1C, pyrrole CH_3); **IR** (thin film): ν_{max} 1721 cm^{-1} (C=O), 1370 cm^{-1} (-SO_2N-), 1175 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 392.11 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{20}H_{19}NNaO_4S$ [(M + Na)$^+$], 392.0927; found 392.0938.

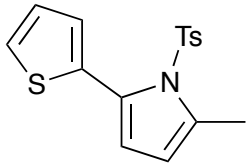
2-Methyl-5-(4-methylphenyl)-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrole (4m)



Prepared according to the general procedure, compound **4m** (79 mg) was isolated as a white solid in 61% yield after flash column chromatography.

TLC: R_f = 0.42 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 100-103 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.33 (AA′, part of AA′BB′ system, J = 6.5 Hz, 2H, $H_{aromatic}$), 7.23 (AA′, part of AA′BB′ system, J = 6.5 Hz, 1.0 Hz, 2H, $H_{aromatic}$), 7.19 - 7.12 (m, 4H, $H_{aromatic}$), 6.03 (d, J = 3.0 Hz, 1H, $H_{pyrrole}$), 5.99 (dd, J = 3.0 Hz, 1.0 Hz, 1H, $H_{pyrrole}$), 2.53 - 2.50 (m, 3H, pyrrole CH_3), 2.40 (s, 3H, phenyl CH_3), 2.38 (s, 3H, tosyl CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 144.2 (1C, $C_{aromatic}$), 137.8 (1C, $C_{aromatic}$), 137.6 (1C, $C_{aromatic}$), 136.5 (1C, $C_{aromatic}$), 134.1 (1C, $C_{aromatic}$), 130.4 (2C, $CH_{aromatic}$), 130.4 (1C, $C_{aromatic}$), 129.4 (2C, $CH_{aromatic}$), 128.0 (2C, $CH_{aromatic}$), 126.4 (2C, $CH_{aromatic}$), 115.0 (1C, $CH_{pyrrole}$), 113.5 (1C, $CH_{pyrrole}$), 21.6 (1C, tosyl CH_3), 21.3 (1C, phenyl CH_3), 16.1 (1C, pyrrole CH_3); **IR** (thin film): ν_{max} 1369 cm^{-1} (-SO_2N-), 1174 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 326.15 [(M + H)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{20}NO_2S$ [(M + H)$^+$], 326.1209; found 326.1201.

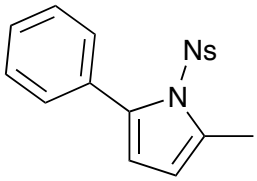
2-Methyl-1-[(4-methylphenyl)sulfonyl]-5-(2-thienyl)-1*H*-pyrrole (4n)



Prepared according to the general procedure, compound **4n** (90 mg) was isolated as a white solid in 71% yield after flash column chromatography.

TLC: R_f = 0.28 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 71-74 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.37 (d, J = 8.5 Hz, 2H, $H_{aromatic}$), 7.29 (dd, J = 5.0 Hz, 1.0 Hz, 1H, $H_{thiophene}$), 7.18 (d, J = 8.5 Hz, 2H, $H_{aromatic}$), 7.09 (dd, J = 4.0 Hz, 1.0 Hz, 1H, $H_{thiophene}$), 7.02 (dd, J = 5.0 Hz, 4.0 Hz, 1H, $H_{thiophene}$), 6.18 (d, J = 3.5 Hz, 1H, $H_{pyrrole}$), 6.01 (dd, J = 3.5 Hz, 1.0 Hz, 1H, $H_{pyrrole}$), 2.56 (s, 3H, pyrrole CH_3), 2.38 (s, 3H, tosyl CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_c 144.4 (1C, $C_{aromatic}$), 136.5 (1C, $C_{aromatic}$), 135.1 (1C, $C_{aromatic}$), 133.1 (1C, $C_{aromatic}$), 130.0 (1C, $CH_{thiophene}$), 129.5 (2C, $CH_{aromatic}$), 128.3 (1C, $C_{aromatic}$), 126.6 (2C, $CH_{aromatic}$), 126.4 (1C, $CH_{thiophene}$), 126.4 (1C, $CH_{thiophene}$), 116.7 (1C, $CH_{pyrrole}$), 112.8 (1C, $CH_{pyrrole}$), 21.5 (1C, tosyl CH_3), 16.2 (1C, pyrrole CH_3); **IR** (thin film): ν_{max} 1370 cm^{-1} (-SO_2N-), 1174 cm^{-1} (-SO_2N-); **MS** (ESI): *m/z* 340.07 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{16}H_{16}NO_2S_2$ [(M + H)$^+$], 318.0617; found 318.0620.

2-Methyl-1-[(4-nitrophenyl)sulfonyl]-5-phenyl-1*H*-pyrrole (4o)

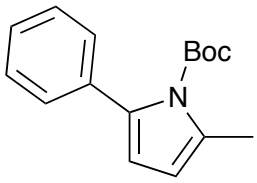


Prepared according to the general procedure, compound **4o** (76 mg) was isolated as a pale yellow solid in 56% yield after flash column chromatography.

TLC: R_f = 0.27 (PE : EtOAc 19:1, UV, vanillin); **Melting Point**: 130-133 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 8.21 (AA′, part of AA′BB′ system, J = 7.0 Hz, 2.0 Hz, 2H, $H_{aromatic}$), 7.55 (BB′, part of AA′BB′ system, J = 7.0 Hz, 2.0 Hz, 2H, $H_{aromatic}$), 7.39 - 7.32 (m, 3H, $H_{aromatic}$), 7.30 - 7.25 (m, 2H, $H_{aromatic}$), 6.11 (d, J = 3.5 Hz, 1H, $H_{pyrrole}$), 6.09 - 6.05 (m, 1H, $H_{pyrrole}$), 2.56 (s, 3H, pyrrole CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 150.3 (1C, $C_{aromatic}$), 144.2 (1C, $C_{aromatic}$), 137.8 (1C, $C_{aromatic}$), 134.7 (1C, $C_{aromatic}$), 132.3 (1C, $C_{aromatic}$), 130.5 (2C, $CH_{aromatic}$),

128.2 (1C, *C*H$_{aromatic}$), 127.8 (2C, *C*H$_{aromatic}$), 127.5 (2C, *C*H$_{aromatic}$), 124.0 (2C, *C*H$_{aromatic}$), 116.2 (1C, *C*H$_{pyrrole}$), 114.8 (1C, *C*H$_{pyrrole}$), 16.2 (1C, pyrrole *C*H$_3$); **IR** (thin film): ν_{max} 1532 cm^{-1} (-NO$_2$), 1376 cm^{-1} (-SO$_2$N-), 1349 cm^{-1} (-NO$_2$), 1183 cm^{-1} (-SO$_2$N-); **MS** (ESI): *m/z* 365.12 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{17}H_{14}N_2NaO_4S$ [(M + Na)$^+$], 365.0566; found 365.0568.

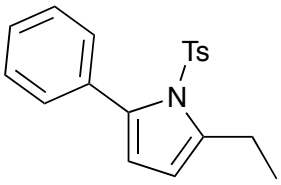
***tert*-Butyl 2-methyl-5-phenyl-1*H*-pyrrole-1-carboxylate (4p)**



Prepared according to the general procedure using MeCN as solvent, compound **4p** (23 mg) was isolated as a colourless oil in 35% yield after flash column chromatography.

TLC: R$_f$ = 0.30 (2% Et$_2$O in PE, UV, vanillin); **^{1}H NMR** (500 MHz, CDCl$_3$): δ_H 7.37 - 7.32 (m, 2H, *H*$_{aromatic}$), 7.31 - 7.25 (m, 3H, *H*$_{aromatic}$), 6.08 (d, *J* = 3.0 Hz, 1H, *H*$_{pyrrole}$), 5.98 - 5.94 (m, 1H, *H*$_{pyrrole}$), 2.47 - 2.45 (m, 3H, pyrrole C*H*$_3$), 1.27 (s, 9H, C(C*H*$_3$)$_3$); **^{13}C NMR** (125 MHz, CDCl$_3$): δ_C 150.2 (1C, *C*=O), 135.4 (1C, *C*$_{aromatic}$), 134.8 (1C, *C*$_{aromatic}$), 133.1 (1C, *C*$_{aromatic}$), 128.1 (2C, *C*H$_{aromatic}$), 127.7 (2C, *C*H$_{aromatic}$), 126.6 (1C, *C*H$_{aromatic}$), 112.1 (1C, *C*H$_{pyrrole}$), 110.3 (1C, *C*H$_{pyrrole}$), 83.3 (1C, *C*(CH$_3$)$_3$), 27.3 (3C, C(*C*H$_3$)$_3$), 15.3 (1C, pyrrole *C*H$_3$); **IR** (thin film): ν_{max} 1742 cm^{-1} (C=O); **MS** (ESI): *m/z* 280.13 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{16}H_{19}NNaO_2$ [(M + Na)$^+$], 280.1308; found 280.1307.

2-Ethyl-1-[(4-methylphenyl)sulfonyl]-5-phenyl-1*H*-pyrrole (4q)



Prepared according to the general procedure using nitro alkyne **2b**, PPh$_3$AuCl (9.9 mg, 0.02 mmol, 5 mol %) and AgOTf (5.2 mg, 0.02 mmol, 5 mol %) heated at reflux for 3 days. Compound **4q** (27 mg) was isolated as a colourless oil in 21% yield after flash column chromatography.

TLC: R$_f$ = 0.33 (PE : EtOAc 19:1, UV, vanillin); **^{1}H NMR** (500 MHz, CDCl$_3$): δ_H 7.36 - 7.31 (m, 5H, *H*$_{aromatic}$), 7.30 (AA′, part of AA′BB′ system, *J* = 8.0 Hz, 2H, *H*$_{aromatic}$), 7.16 (BB′, part

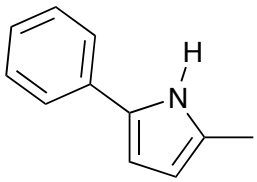
of AA′BB′ system, J = 8.0 Hz, 2H, $H_{aromatic}$), 6.10 (d, J = 3.0 Hz, 1H, $H_{pyrrole}$), 6.07 - 6.04 (m, 1H, $H_{pyrrole}$), 2.97 (dq, J = 7.5 Hz, 1.0 Hz, 2H, CH_2CH$_3$), 2.37 (s, 3H, tosyl CH_3), 1.31 (t, J = 7.5 Hz, 3H, CH$_2$CH_3); **^{13}C NMR** (125 MHz, $CDCl_3$): 144.2 (1C, $C_{aromatic}$), 141.1 (1C, $C_{aromatic}$), 138.0 (1C, $C_{aromatic}$), 136.4 (1C, $C_{aromatic}$), 133.3 (1C, $C_{aromatic}$), 130.5 (2C, CH$_{aromatic}$), 129.4 (2C, CH$_{aromatic}$), 127.7 (1C, CH$_{aromatic}$), 127.2 (2C, CH$_{aromatic}$), 126.4 (2C, CH$_{aromatic}$), 115.5 (1C, CH$_{pyrrole}$) 111.7 (1C, CH$_{pyrrole}$), 22.8 (1C, CH$_2$CH$_3$), 21.5 (1C, tosyl CH$_3$), 13.5 (1C, CH$_2$$CH_3$); **IR** (thin film): ν_{max} 1360 cm^{-1} (-SO$_2$N-), 1176 cm^{-1} (-SO$_2$N-); **MS** (ESI): *m/z* 348.11 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{19}NNaO_2S$ [(M + Na)$^+$], 348.1029; found 348.1029.

General procedure for deprotection of pyrroles

Using a modified literature procedure described by Samet.[S8] To a stirred mixture of the corresponding pyrrole (0.20 mmol) in MeOH (2.0 mL) at r.t. was added powdered KOH (1.40 mmol, 7.0 eq.). The resulting mixture was heated to reflux and stirred for 72 h. The reaction mixture was cooled to r.t. and concentrated under a stream of nitrogen. The residue was purified by flash column chromatography to yield the desired deprotected pyrrole.

Synthesis of compounds 5a, 5j and 5k

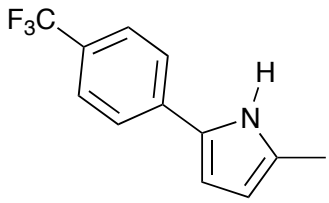
2-Methyl-5-phenyl-1*H*-pyrrole (5a)



Prepared according to the general procedure on a 0.20 mmol scale, compound **5a** (25.5 mg) was isolated as a white solid in 81% yield after flash column chromatography.

TLC: R_f = 0.26 (PE : Et$_2$O 19:1, UV, vanillin); **Melting Point:** 91-94 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 8.11 (br s, 1H, NH), 7.46 - 7.42 (m, 2H, $H_{aromatic}$), 7.38 - 7.32 (m, 2H, $H_{aromatic}$), 7.20 - 7.14 (m, 1H, $H_{aromatic}$), 6.41 (t, J = 3.0 Hz, 1H, $H_{pyrrole}$), 5.98 - 5.95 (m, 1H, $H_{pyrrole}$), 2.35 (s, 3H, pyrrole CH_3); **MS** (ESI): *m/z* 156.10 [(M - H)$^-$]. Data was in accordance with that reported in the literature.[S9]

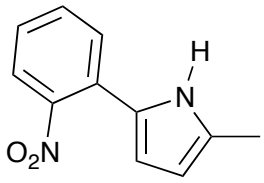
2-Methyl-5-[4-(trifluoromethyl)phenyl]-1*H*-pyrrole (5j)



Prepared according to the general procedure on a 0.135 mmol scale, compound **5j** (18.8 mg) was isolated as a white solid in 62% yield after flash column chromatography**.**

TLC: R_f = 0.30 (PE : EtOAc 19:1, UV, vanillin); **Melting Point:** 127-130 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 8.19 (br s, 1H, N*H*), 7.58 (d, *J* = 8.0 Hz, 2H, $H_{aromatic}$), 7.50 (d, *J* = 8.0 Hz, 2H, $H_{aromatic}$), 6.52 (t, *J* = 3.0 Hz, 1H, $H_{pyrrole}$), 6.02 - 5.99 (m, 1H, $H_{pyrrole}$), 2.37 (s, 3H, pyrrole CH_3); **MS** (ESI): *m/z* 224.07 [(M - H)$^-$]. Data was in accordance with that reported in the literature.[S9]

2-Methyl-5-(2-nitrophenyl)-1*H*-pyrrole (5k)



Prepared according to the general procedure on 0.10 mmol scale, compound **5k** (17.0 mg) was isolated as a yellow solid in 84% yield after flash column chromatography.

TLC: R_f = 0.17 (PE : EtOAc 19:1, UV, vanillin); **Melting Point:** 51-54 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 8.64 (br s, 1H, N*H*), 7.72 - 7.68 (m, 1H, $H_{aromatic}$), 7.62 - 7.58 (m, 1H, $H_{aromatic}$), 7.56 - 7.50 (m, 1H, $H_{aromatic}$), 7.33 - 7.28 (m, 1H, $H_{aromatic}$), 6.40 (t, *J* = 3.0 Hz, 1H, $H_{pyrrole}$), 6.02 - 5.98 (m, 1H, $H_{pyrrole}$), 2.34 (s, 3H, pyrrole CH_3); **MS** (ESI): *m/z* 201.05 [(M - H)$^-$]. Data was in accordance with that reported in the literature.[S10]

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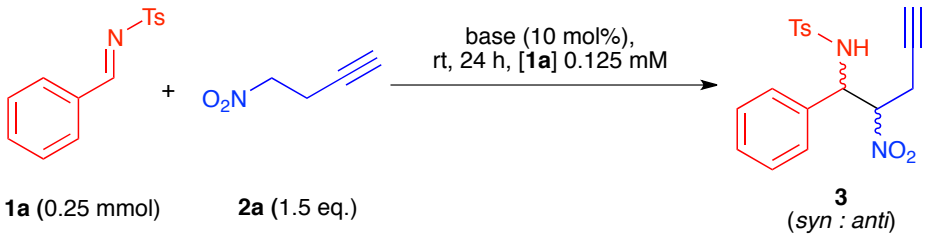
Appendix 1

Table 1 Nitro-Mannich optimisation studies



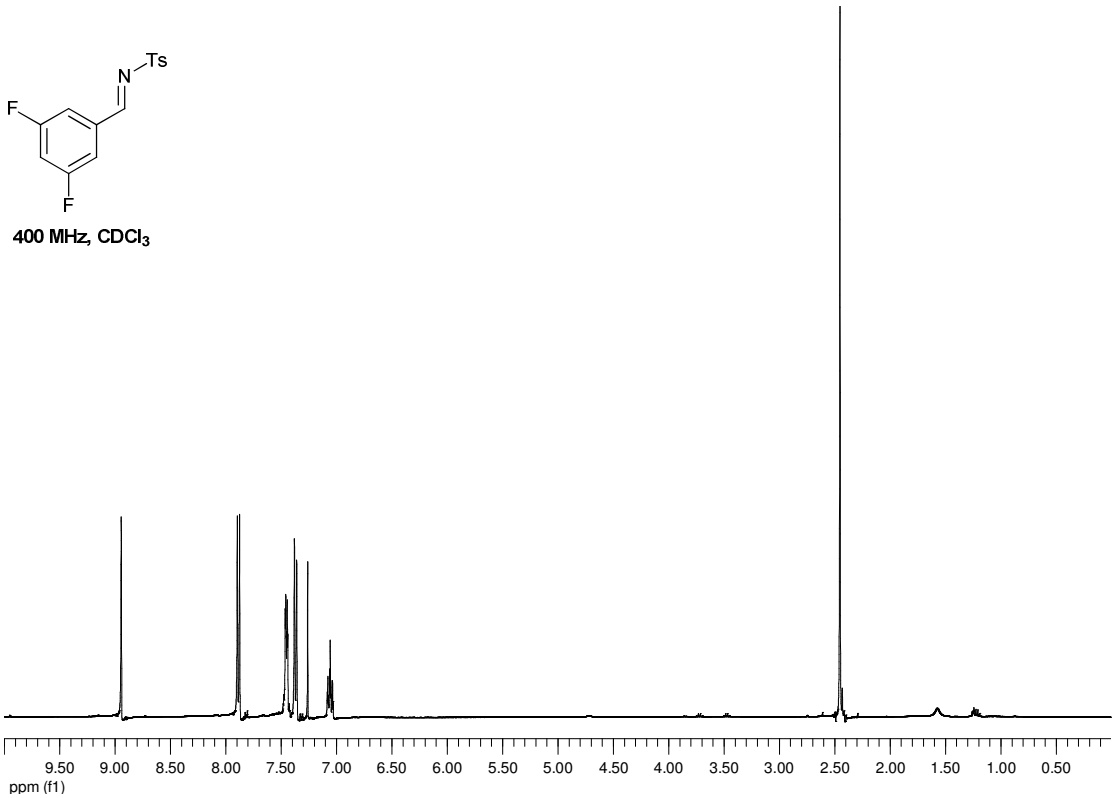
1a (0.25 mmol) **2a** (1.5 eq.) **3** (*syn : anti*)

Entry	Solvent	Base (10 mol%)	dr[a] (*syn : anti*)	Yield[b] (%)
1[c]	THF	KO^{t}Bu	38:62	57
2[c]	MeOH	KO^{t}Bu	58:42	37
3	MeCN	KO^{t}Bu	77:23	75
4	CH_2Cl_2	KO^{t}Bu	63:37	63
5	$PhCH_3$	KO^{t}Bu	54:46	47
6	THF	KO^{t}Bu	52:48	35
7	MeOH	KO^{t}Bu	83:17	90
8	MeOH	Et_3N	73:27	93
9	MeOH	DBU	82:18	73
10	MeOH	TMG	82:18	78
11	MeOH	BEMP[d]	86:14	84
12[e]	MeOH	KO^{t}Bu	55:45	84
13[f]	MeOH	—	64:36	56
14[e]	MeOH	—	59:41	4
15[g]	MeOH	—	—	—

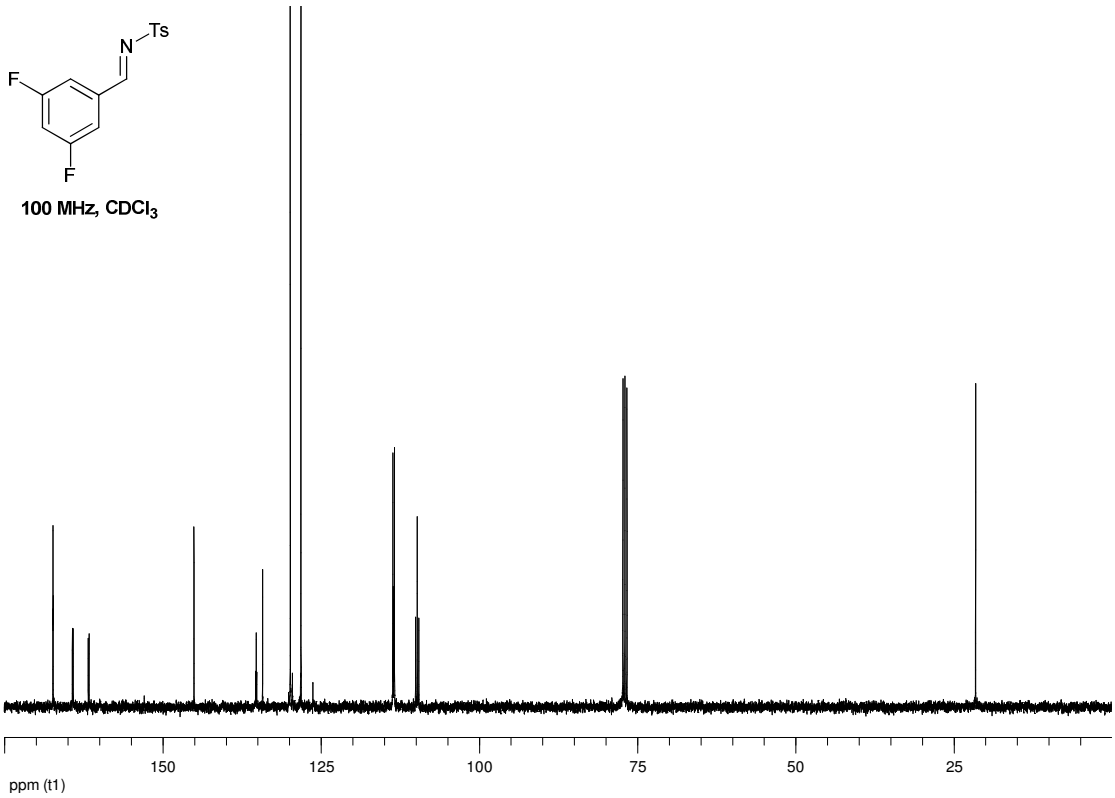
[a] Determined by crude ^{1}H NMR. [b] Isolated yield after flash column chromatography. [c] **1a** (1.5 eq.), **2a** (1.0 eq.). [d] BEMP = 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazophosphorine, commercially available from Sigma-Aldrich. [e] Reaction time of 4 hours. [f] Reaction time of 9 days. [g] Reaction conducted at reflux.

NMR Spectra

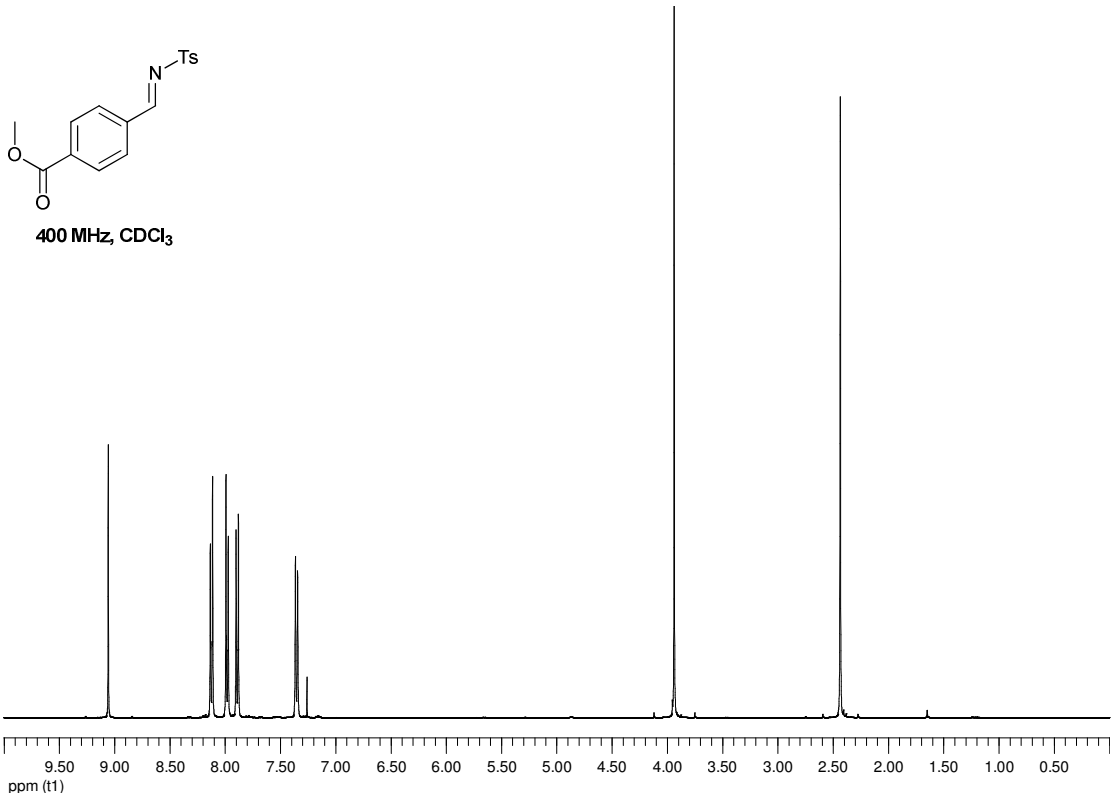
^{1}H NMR of imine 1i



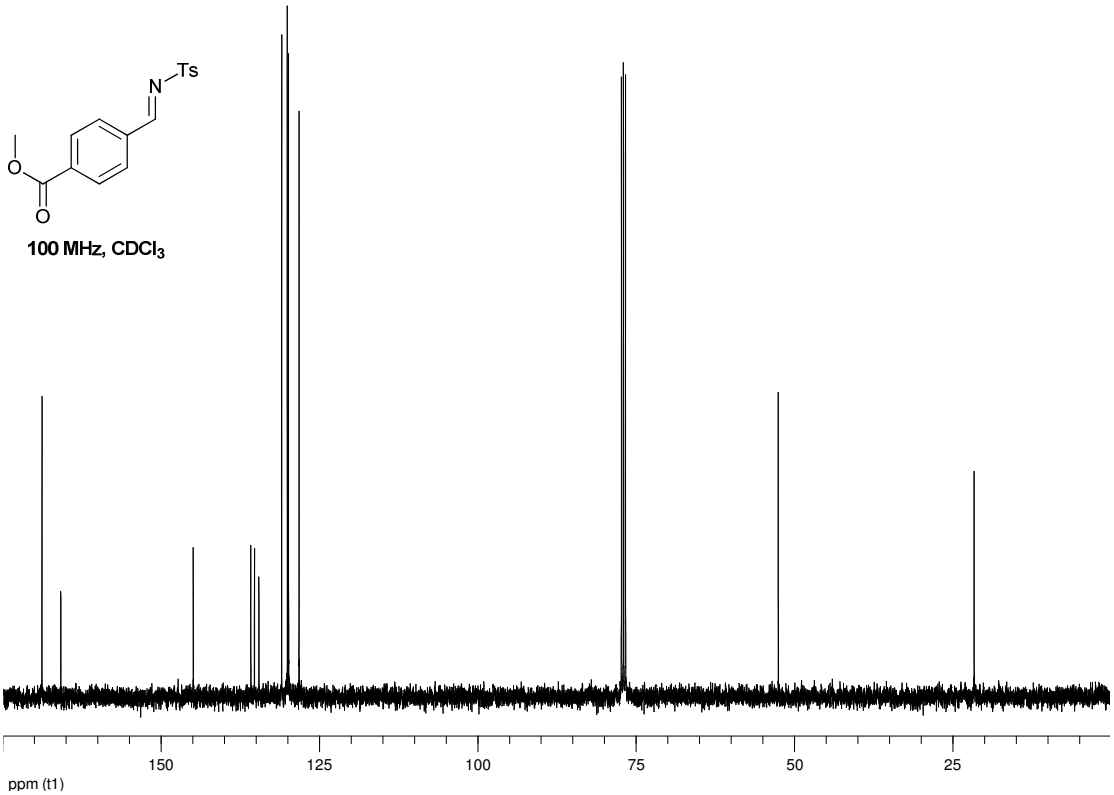
^{13}C NMR of imine 1i



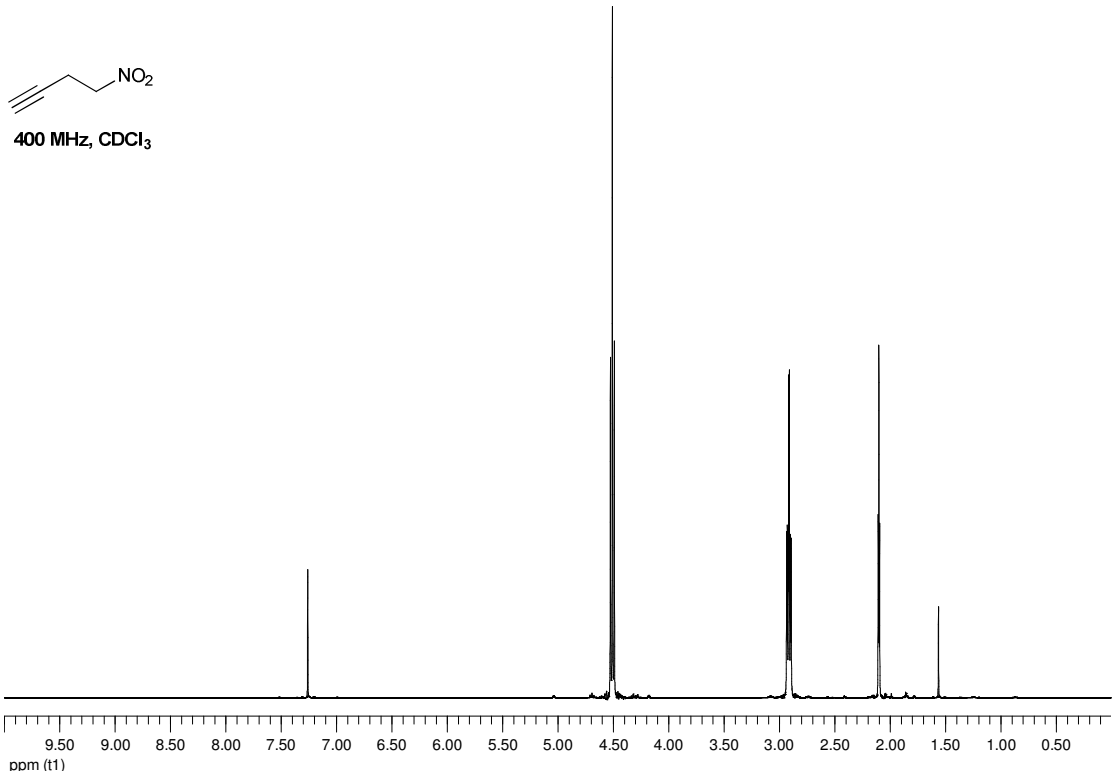
^{1}H NMR of imine 1l



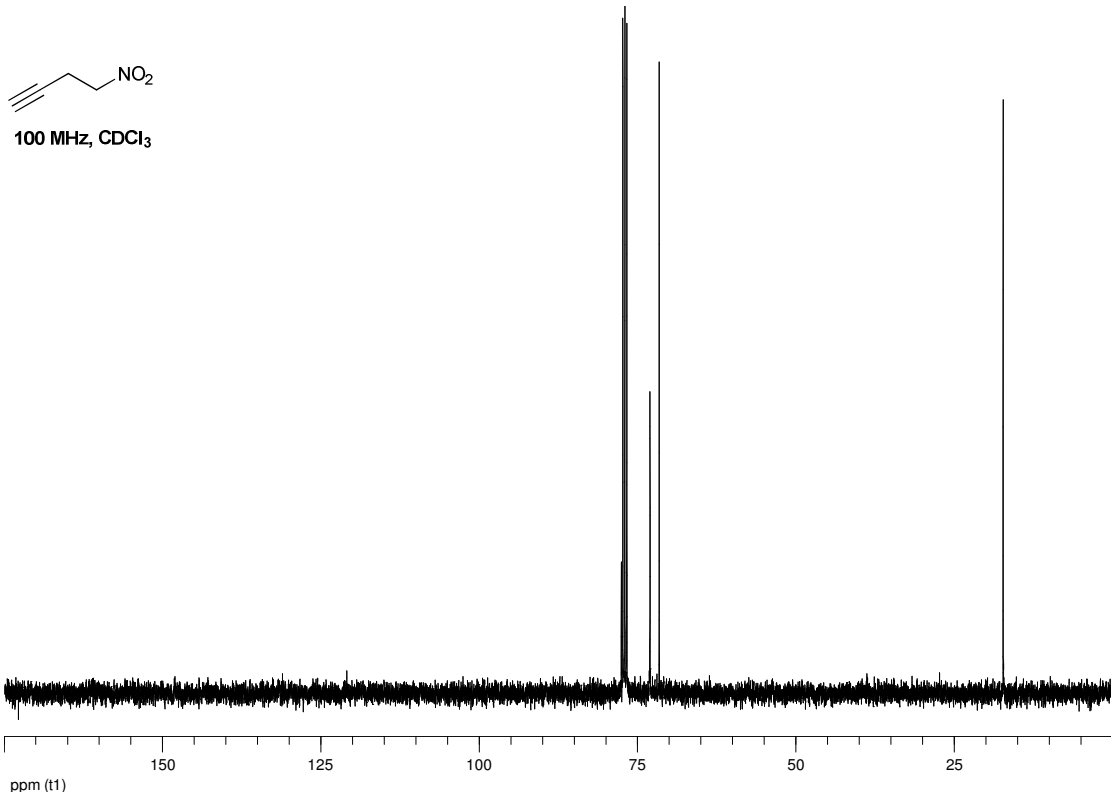
^{13}C NMR of imine 1l



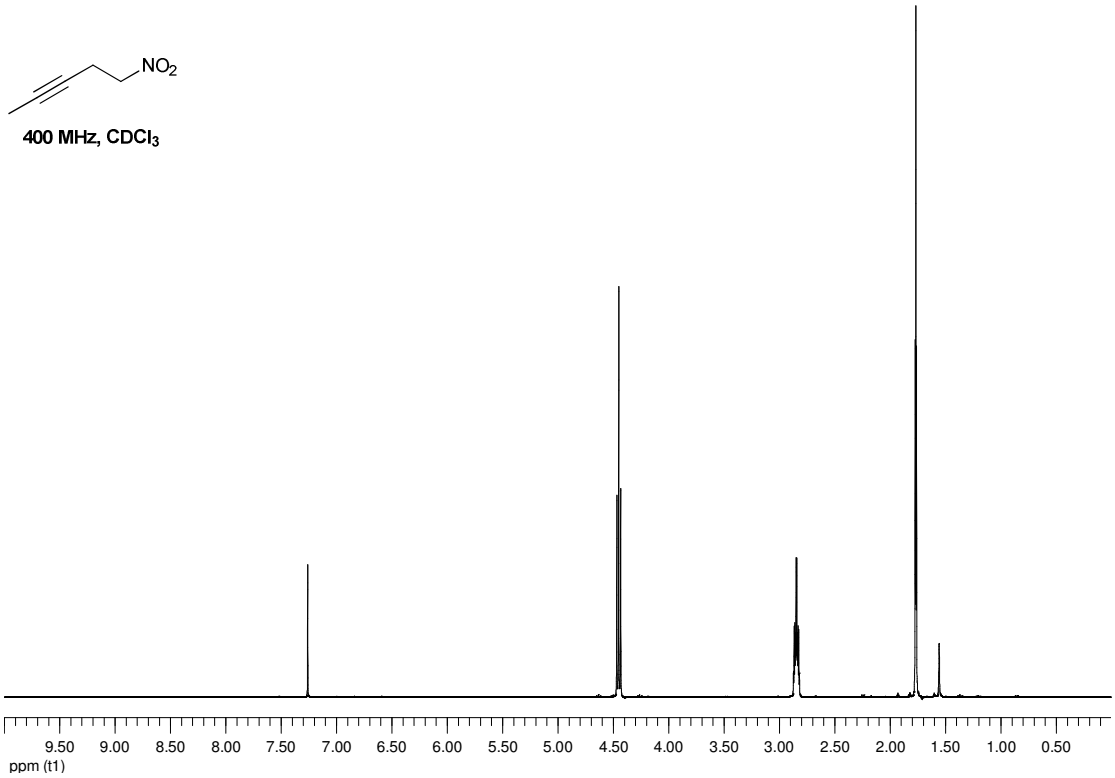
^{1}H NMR of nitro compound 2a



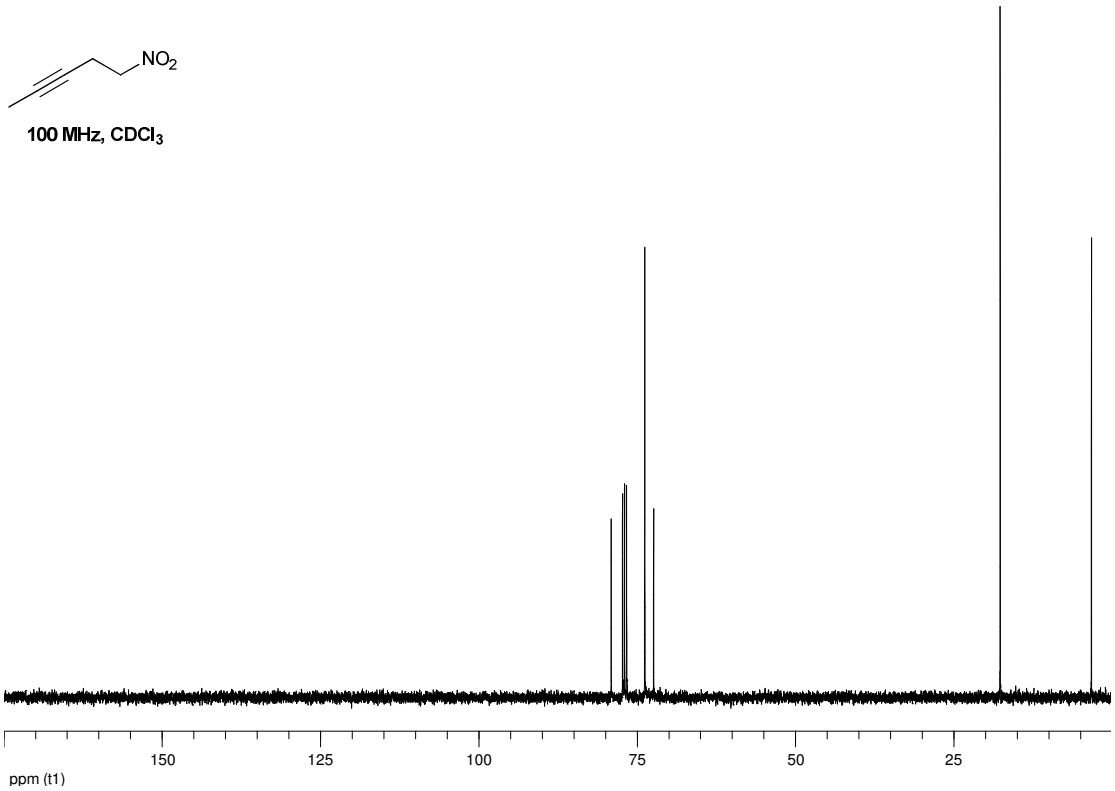
^{13}C NMR of nitro compound 2a



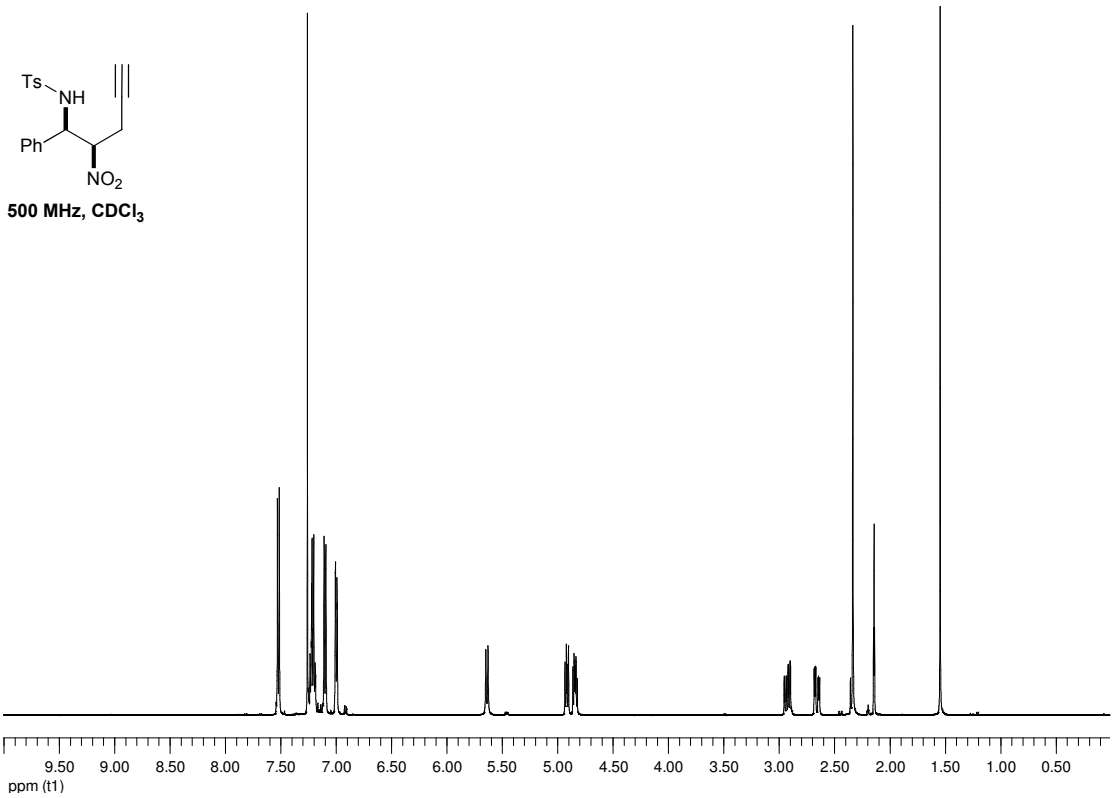
^{1}H NMR of nitro compound 2b



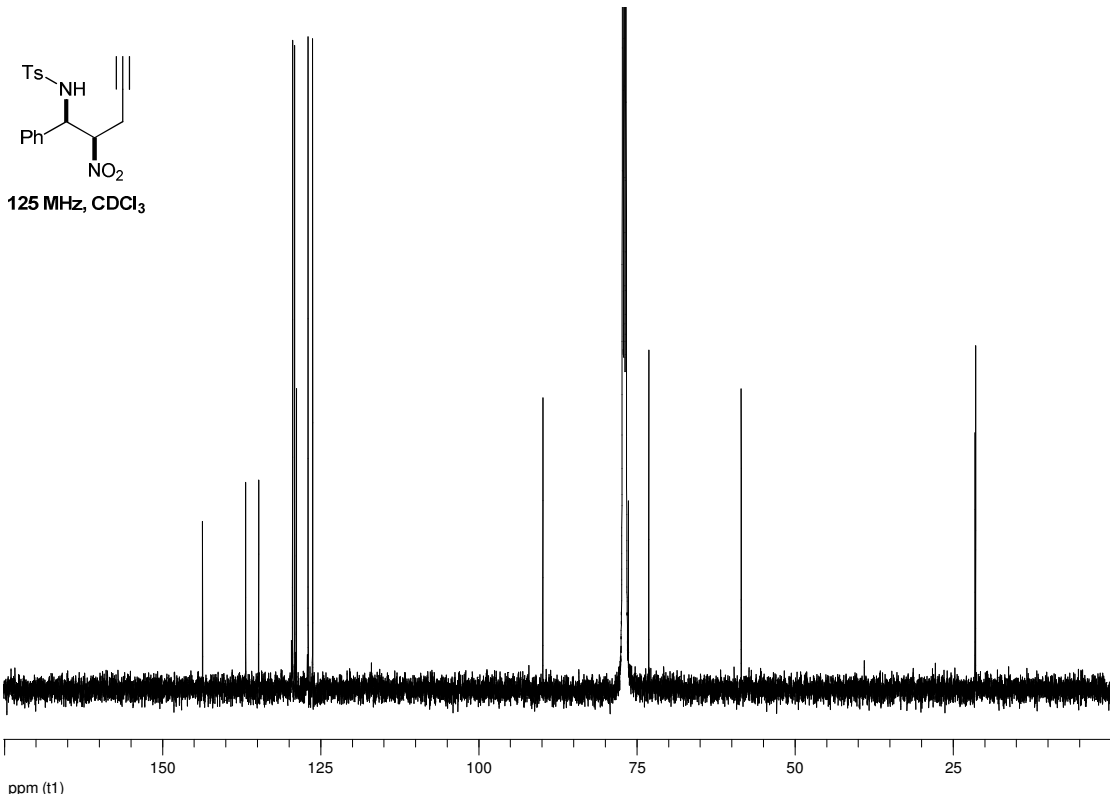
^{13}C NMR of nitro compound 2b



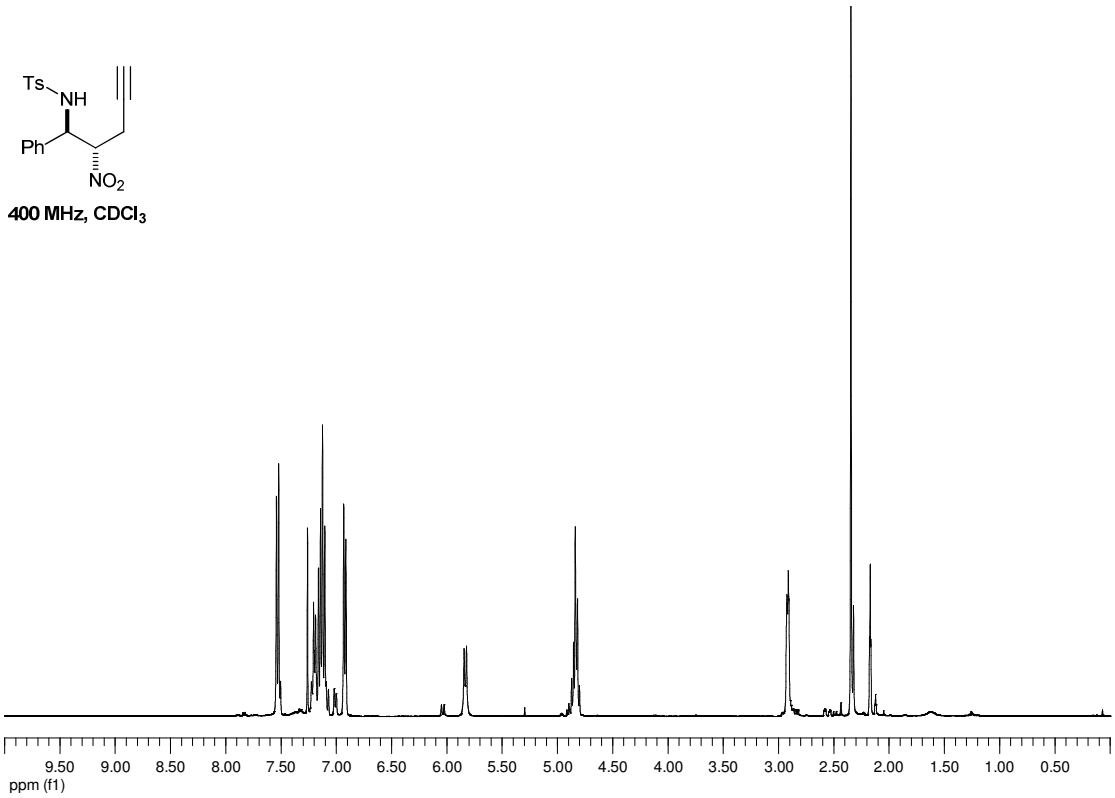
^{1}H NMR of nitro-Mannich *syn* diastereoisomer 3



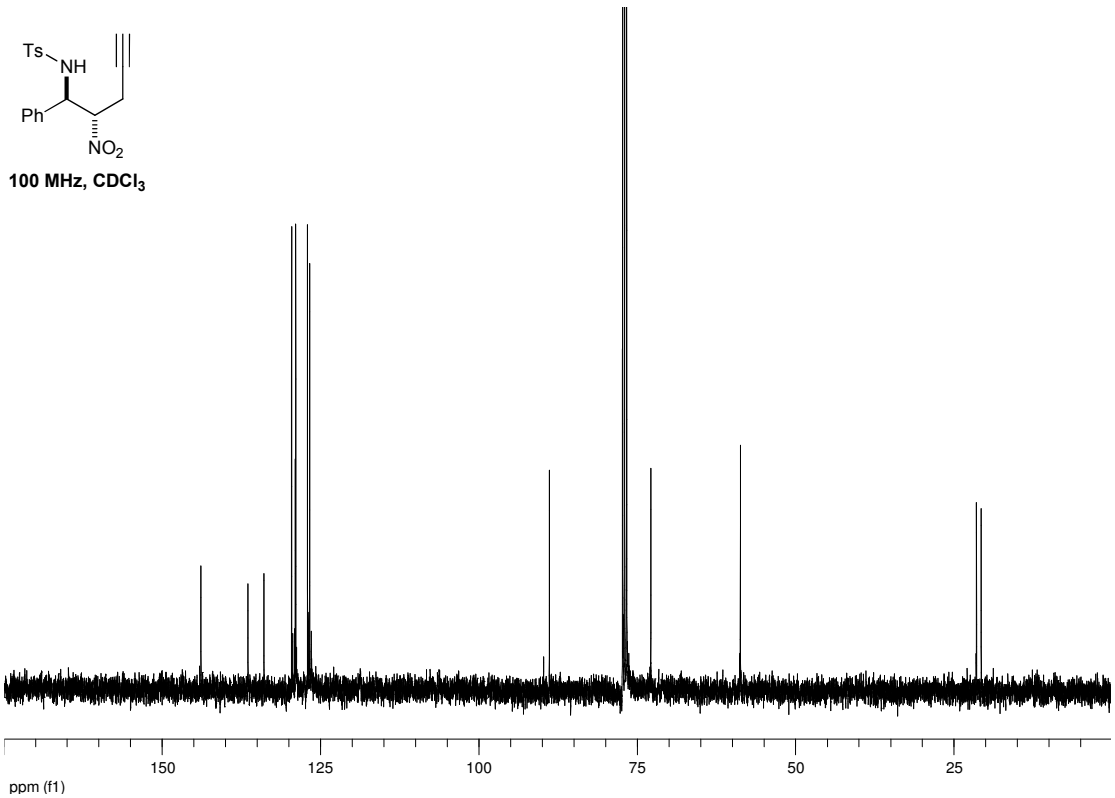
^{13}C NMR of nitro-Mannich *syn* diastereoisomer 3



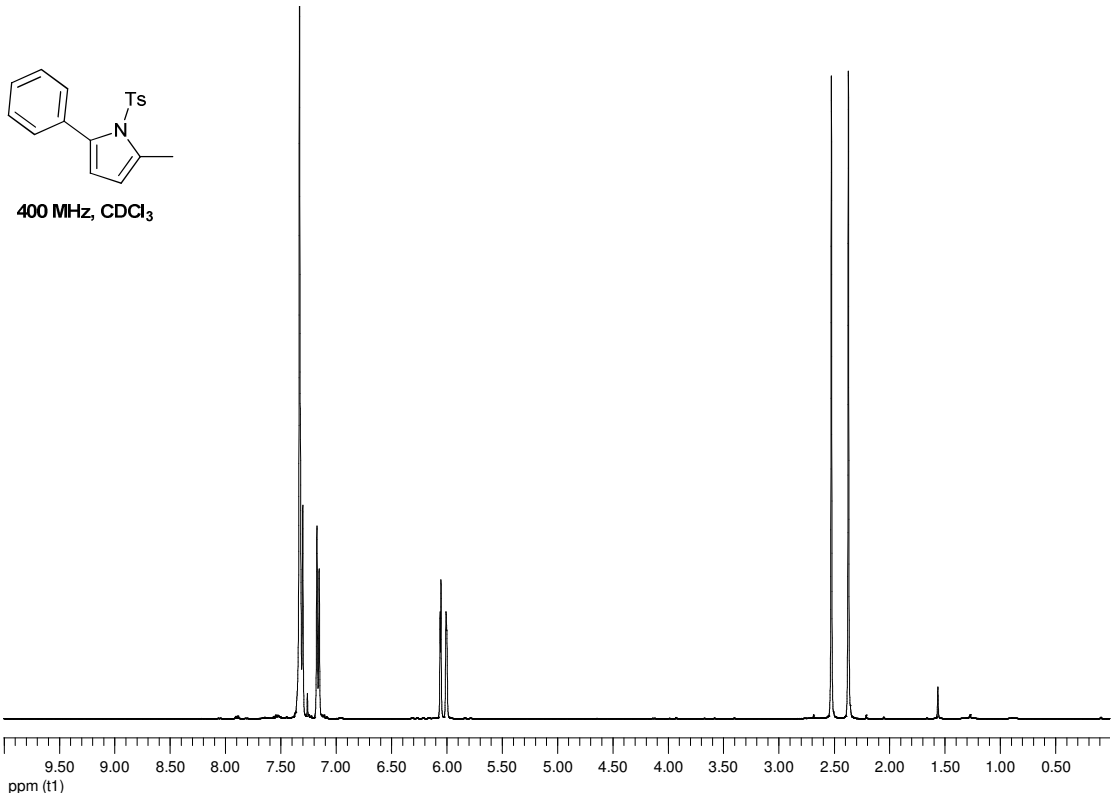
^{1}H NMR of nitro-Mannich *anti* diastereoisomer 3 (minor diastereoisomer characterised by isolating product from reaction shown in Table 1, Entry 1).



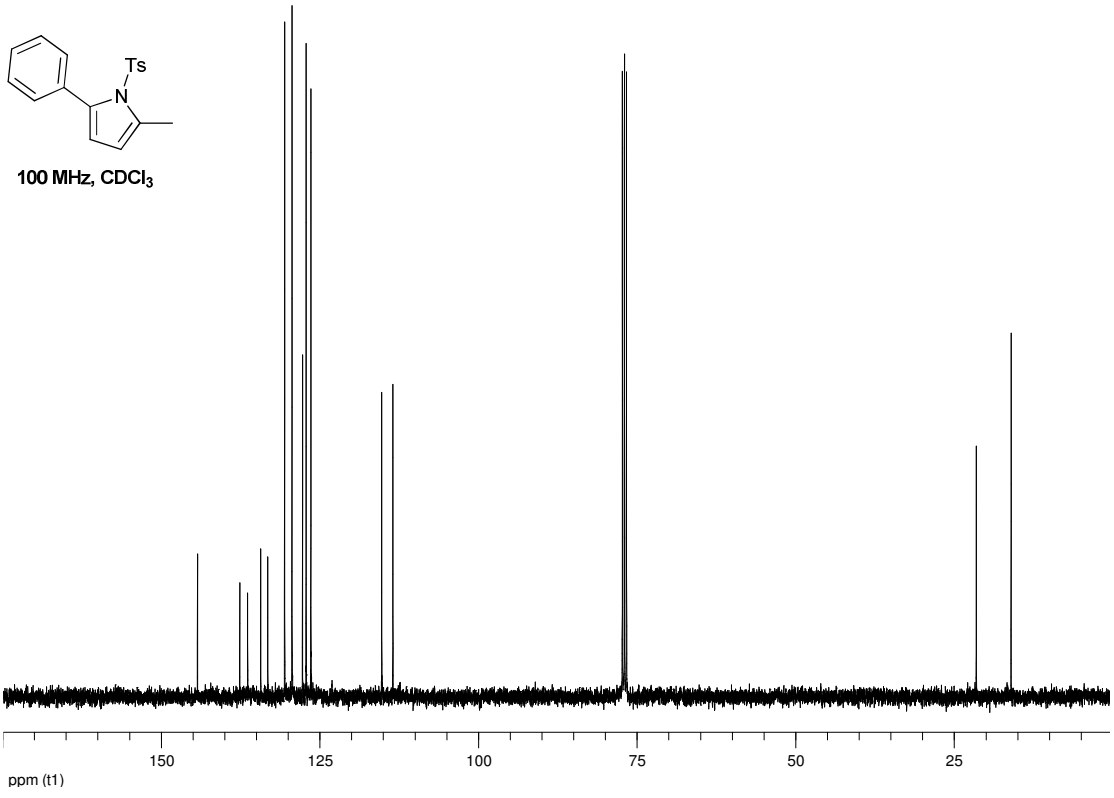
^{13}C NMR of nitro-Mannich *anti* diastereoisomer 3



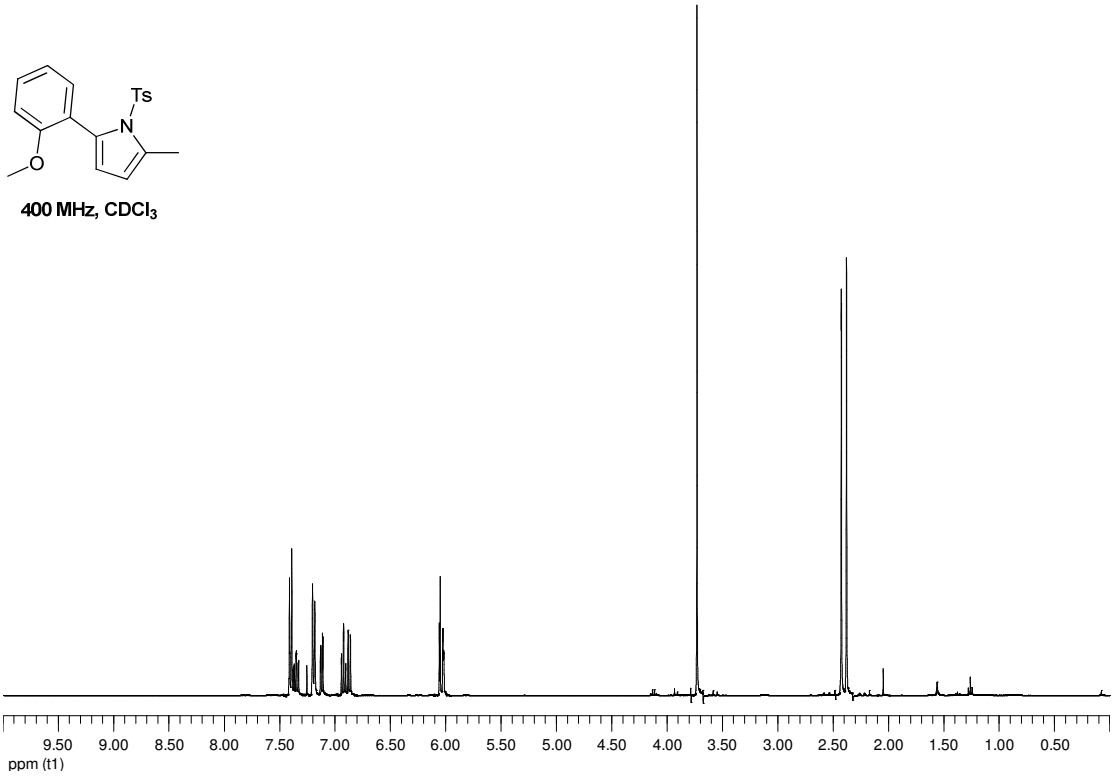
^{1}H NMR of pyrrole 4a



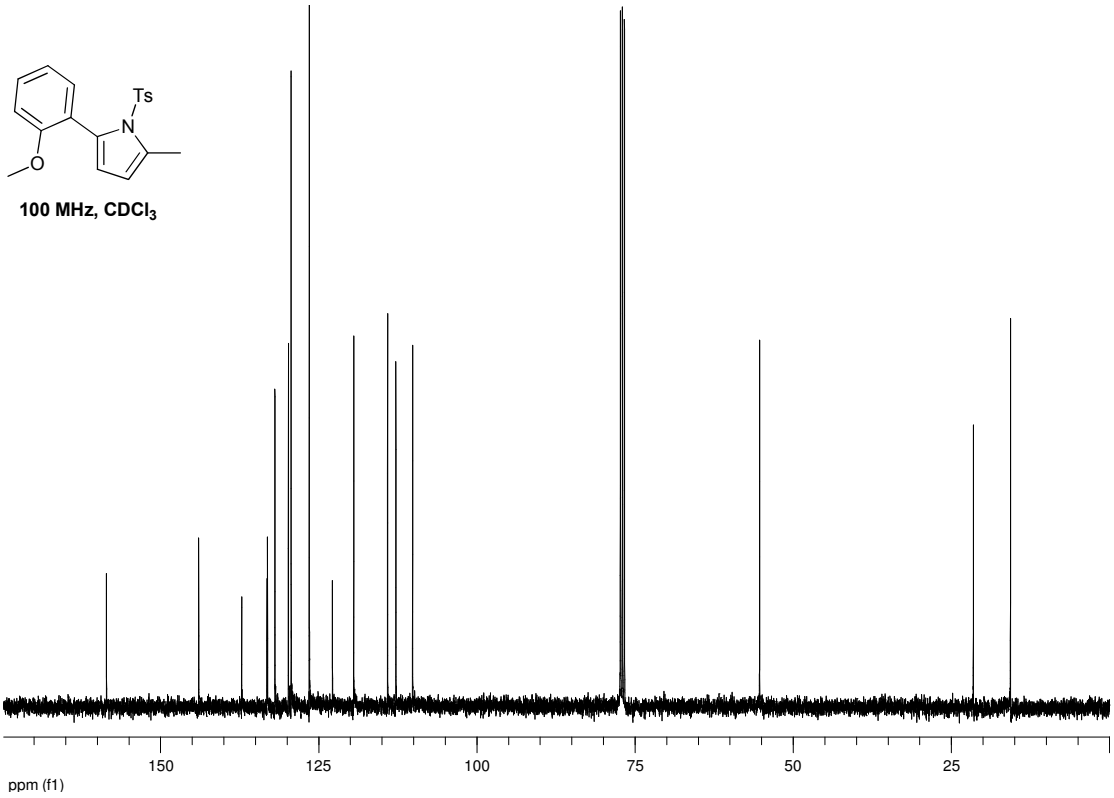
^{13}C NMR of pyrrole 4a



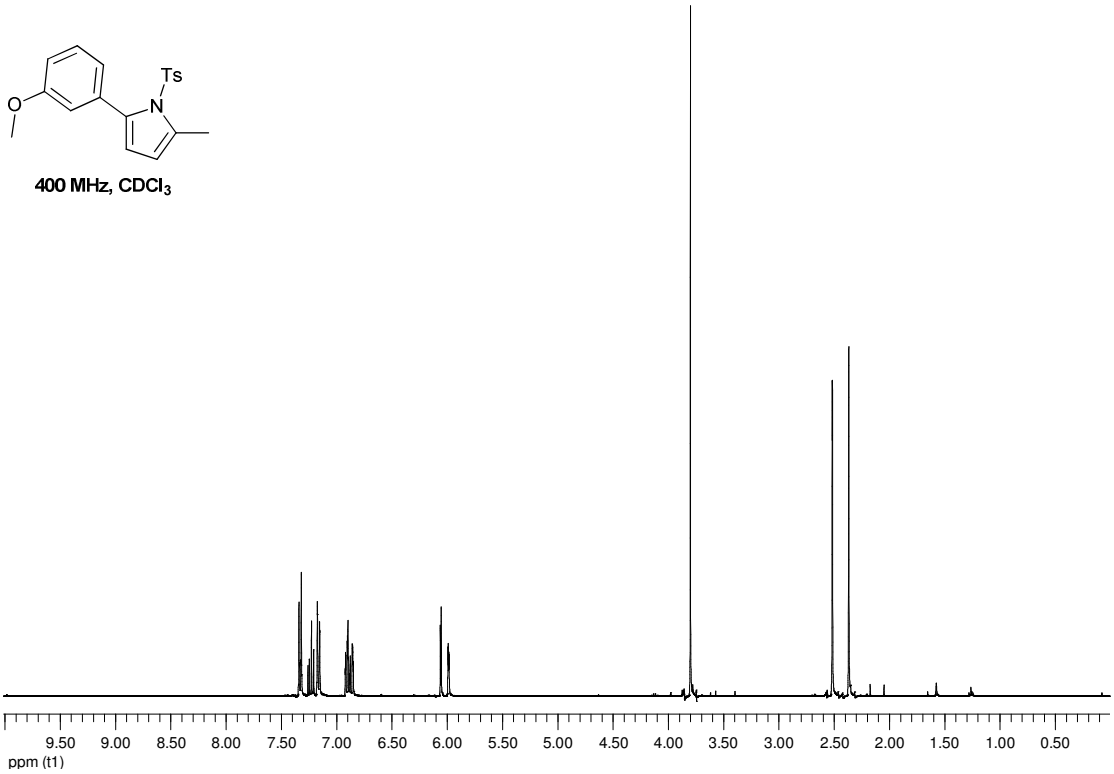
^{1}H NMR of pyrrole 4b



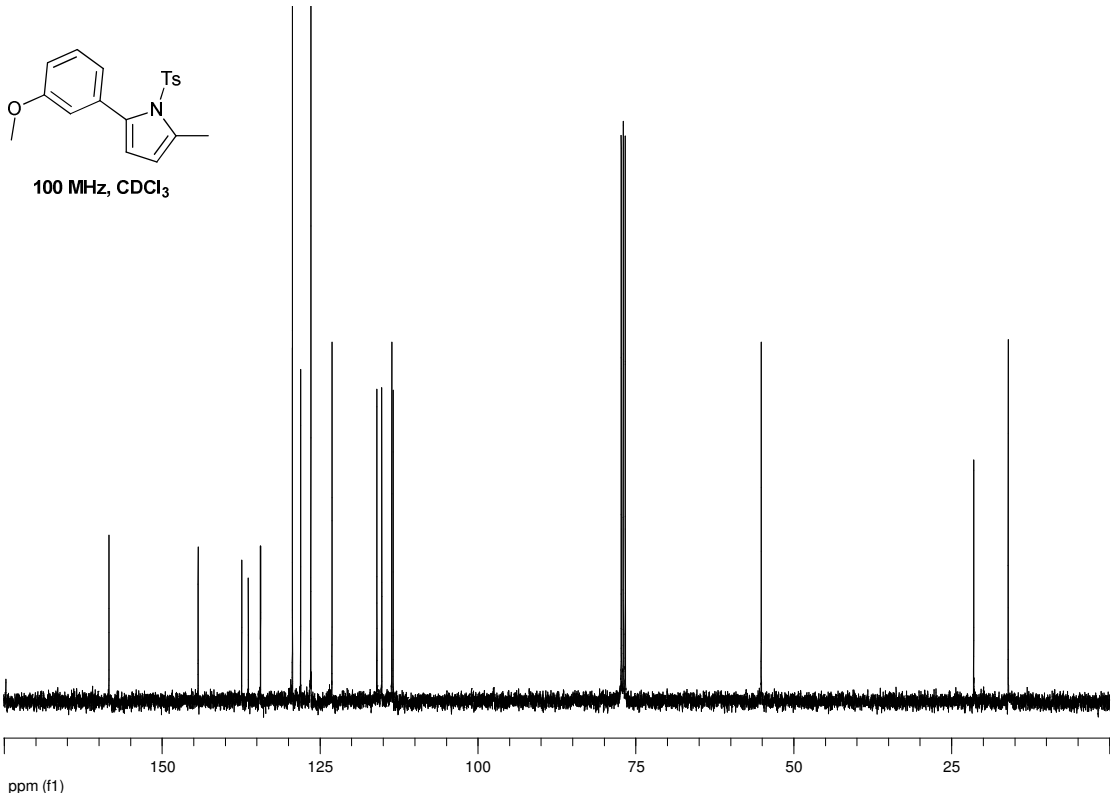
^{13}C NMR of pyrrole 4b



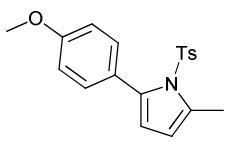
^{1}H NMR of pyrrole 4c



^{13}C NMR of pyrrole 4c

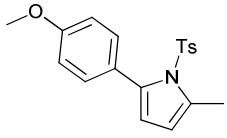


^{1}H NMR for pyrrole 4d



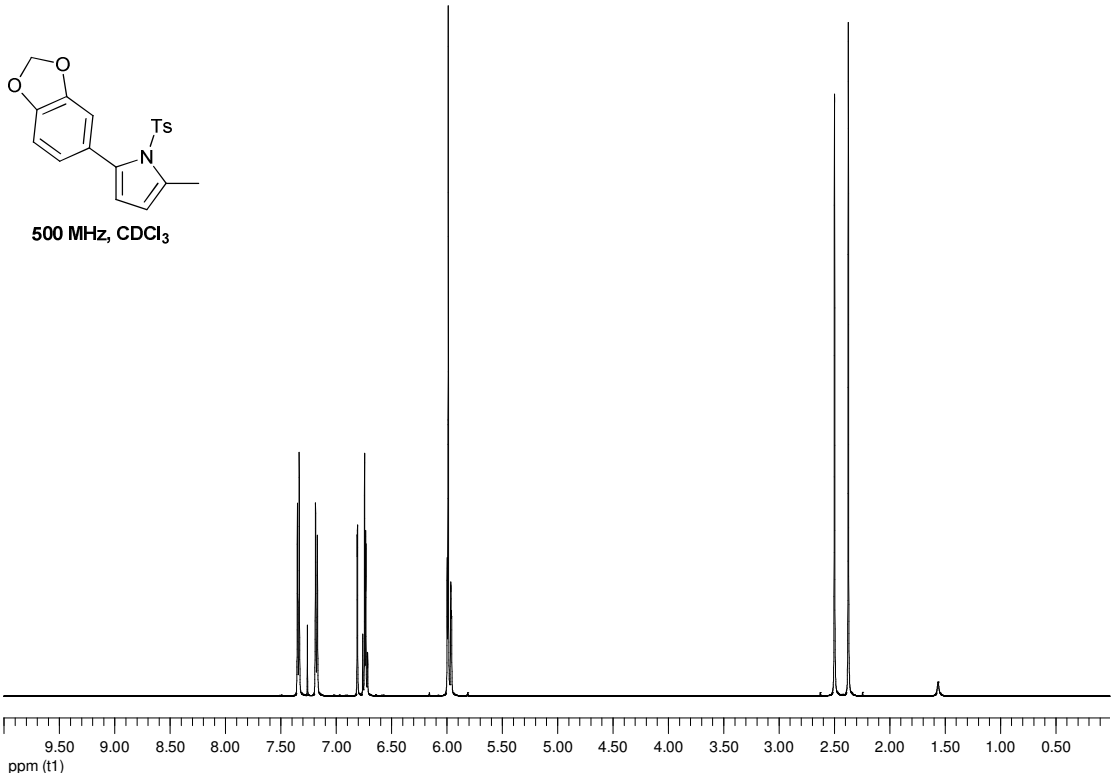
500 MHz, $CDCl_3$

^{13}C NMR of pyrrole 4d

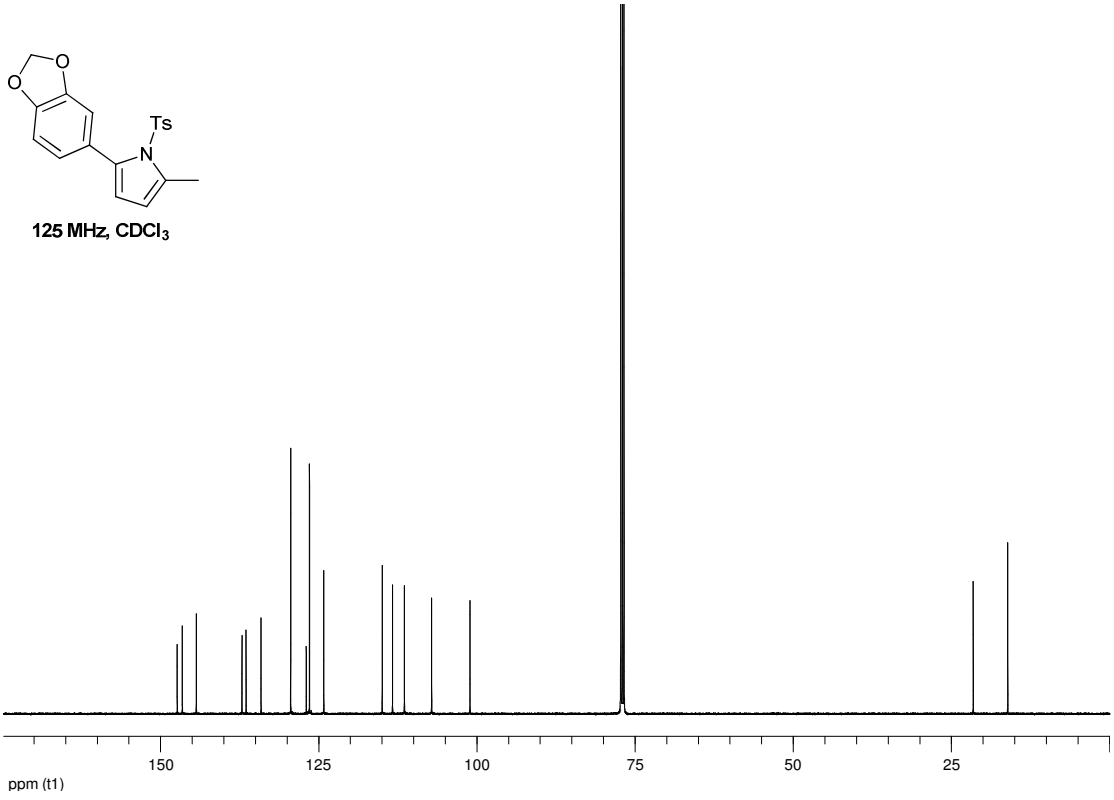


125 MHz, $CDCl_3$

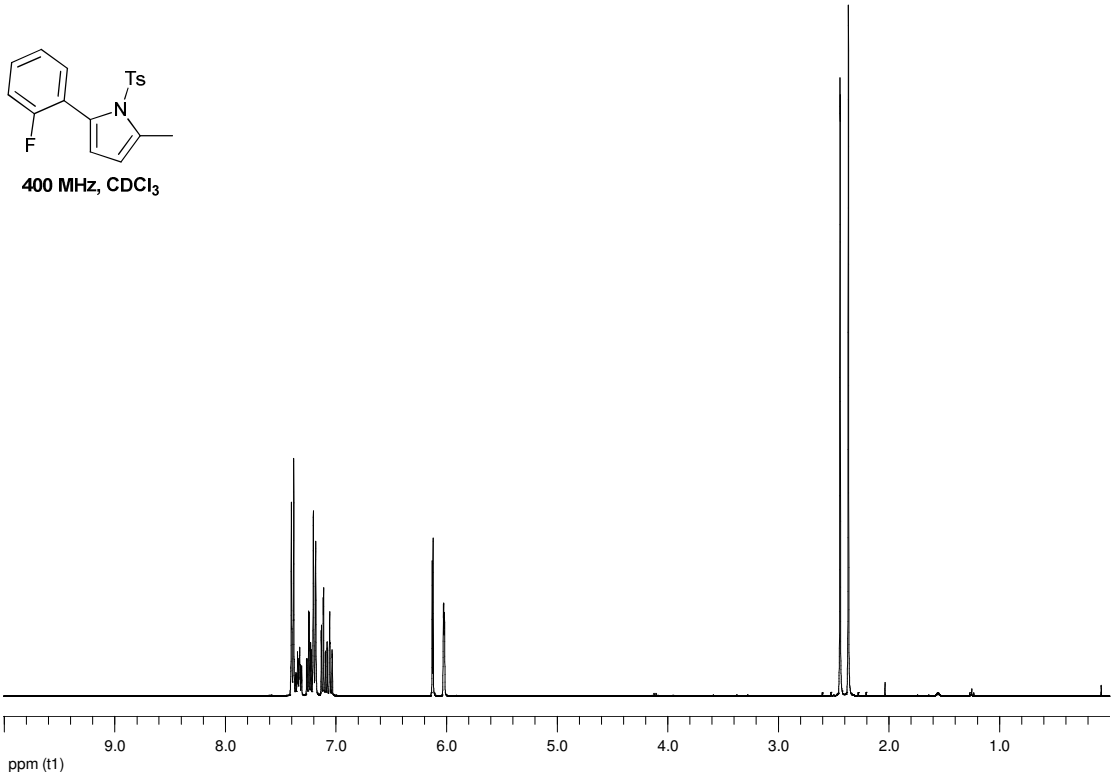
^{1}H NMR of pyrrole 4e



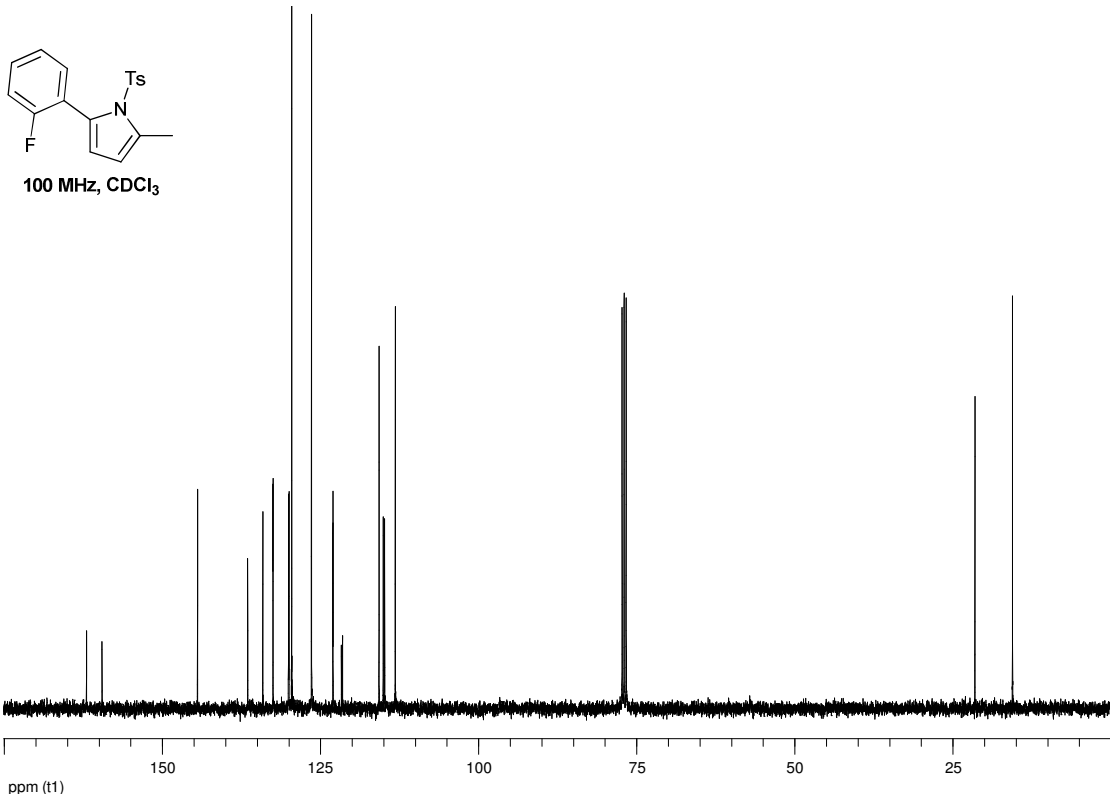
^{13}C NMR of pyrrole 4e



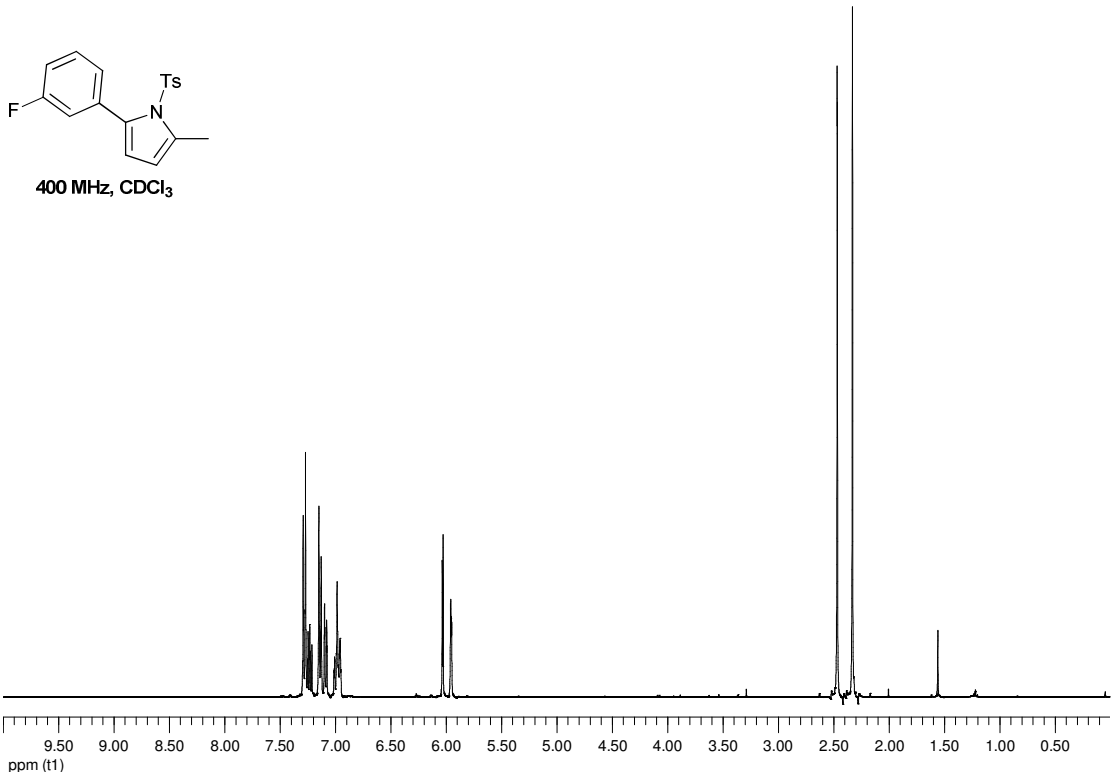
^{1}H NMR of pyrrole 4f



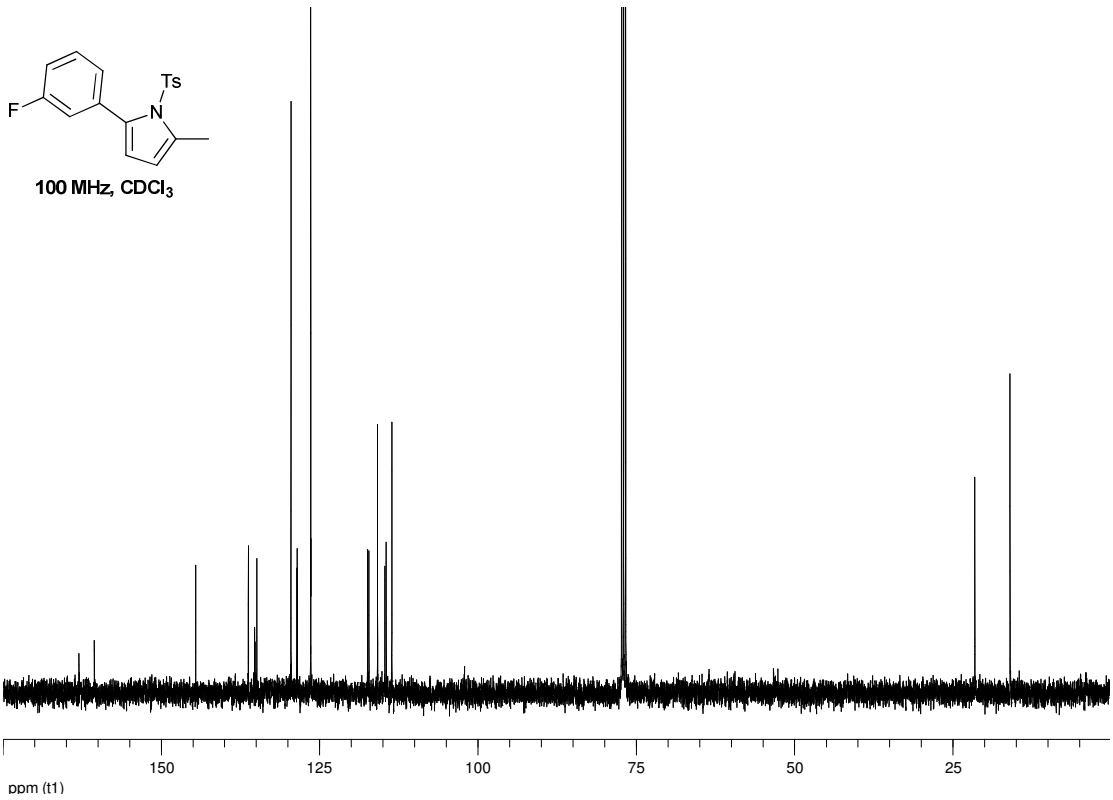
^{13}C NMR of pyrrole 4f



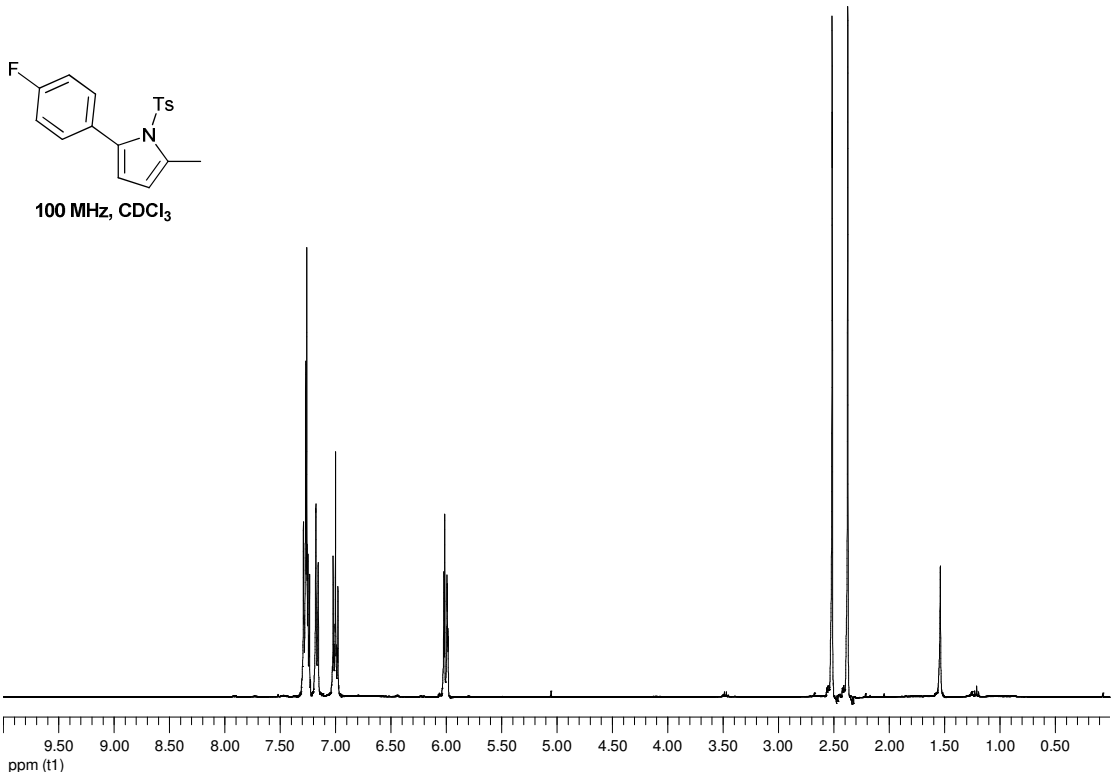
^{1}H NMR of pyrrole 4g



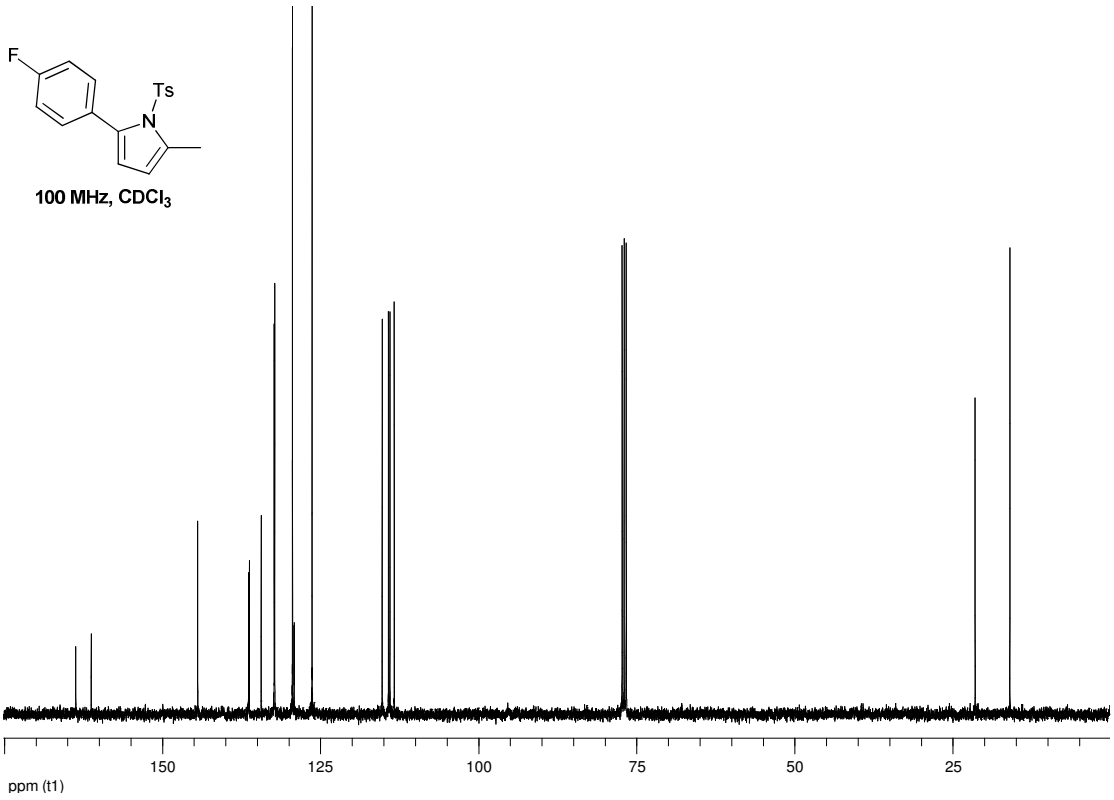
^{13}C NMR of pyrrole 4g



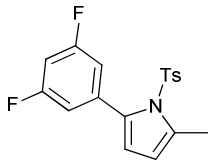
^{1}H NMR of pyrrole 4h



^{13}C NMR of pyrrole 4h

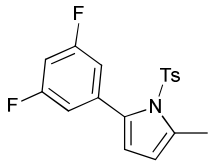


^{1}H NMR of pyrrole 4i



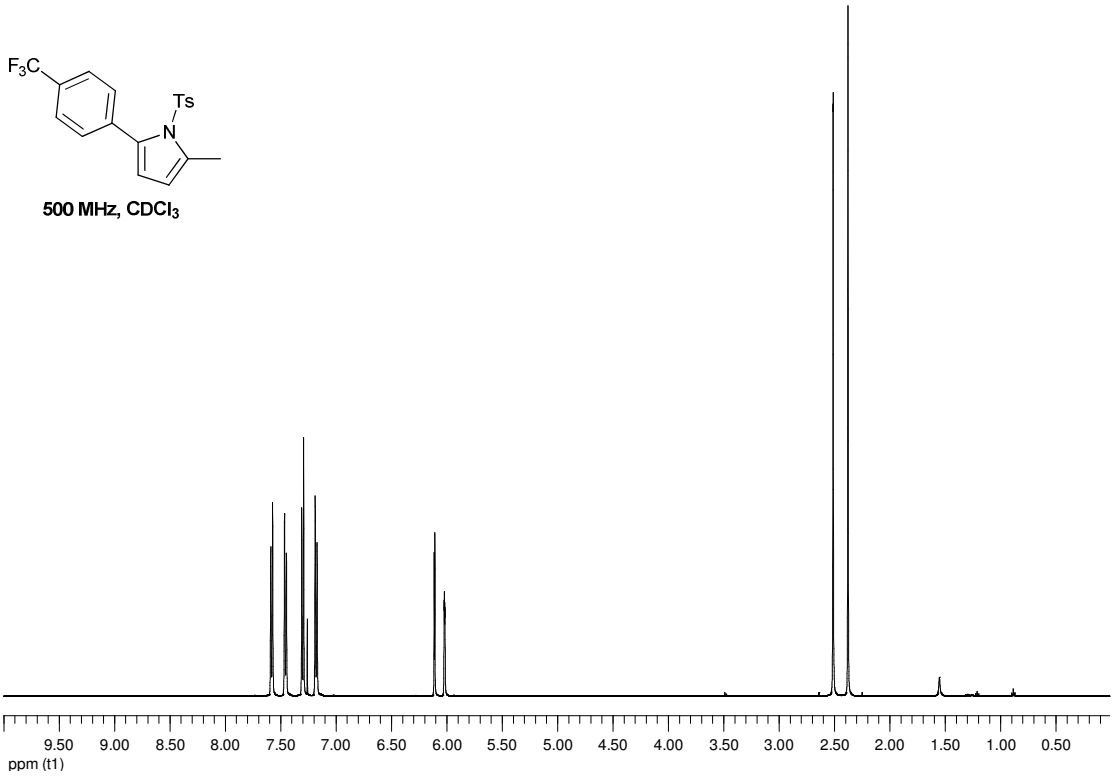
400 MHz, $CDCl_3$

^{13}C NMR of pyrrole 4i

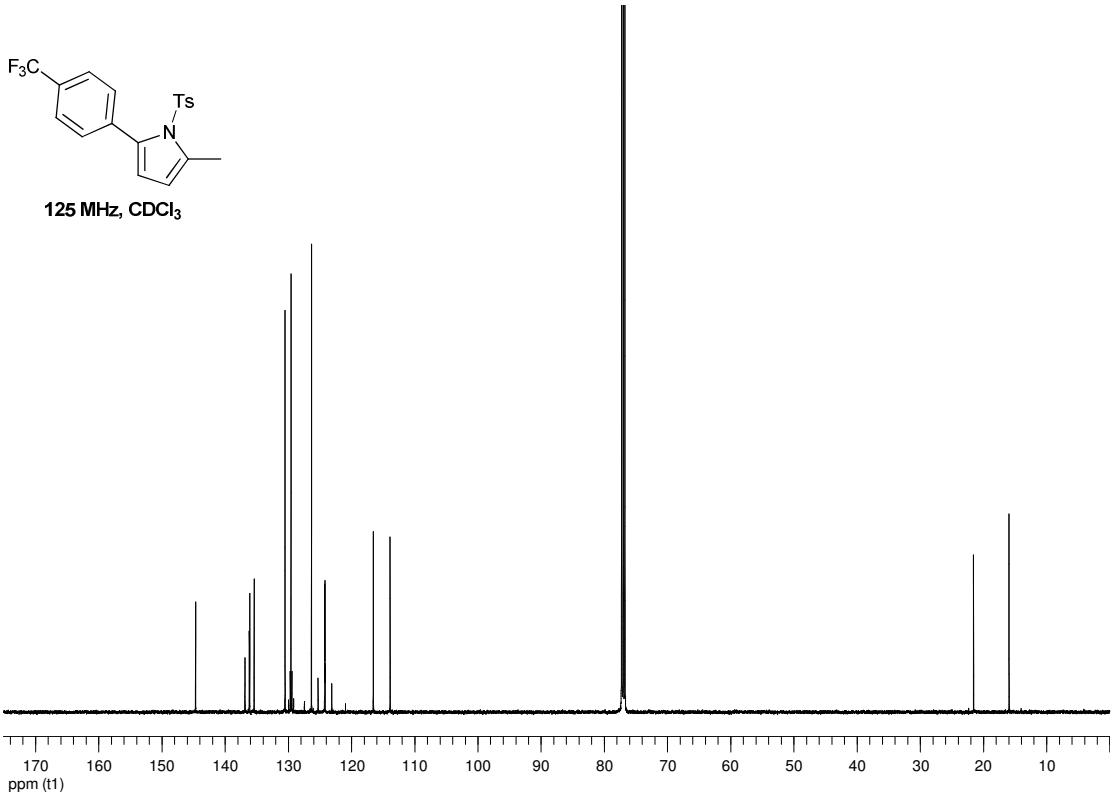


100 MHz, $CDCl_3$

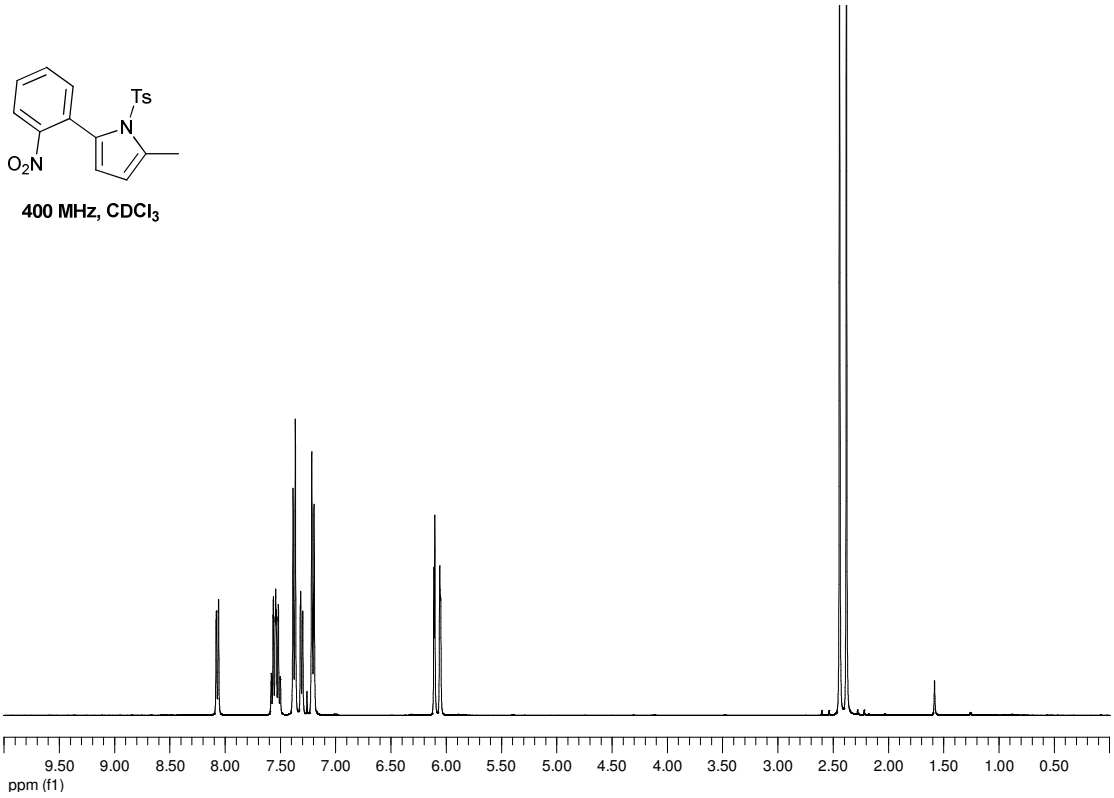
^{1}H NMR of pyrrole 4j



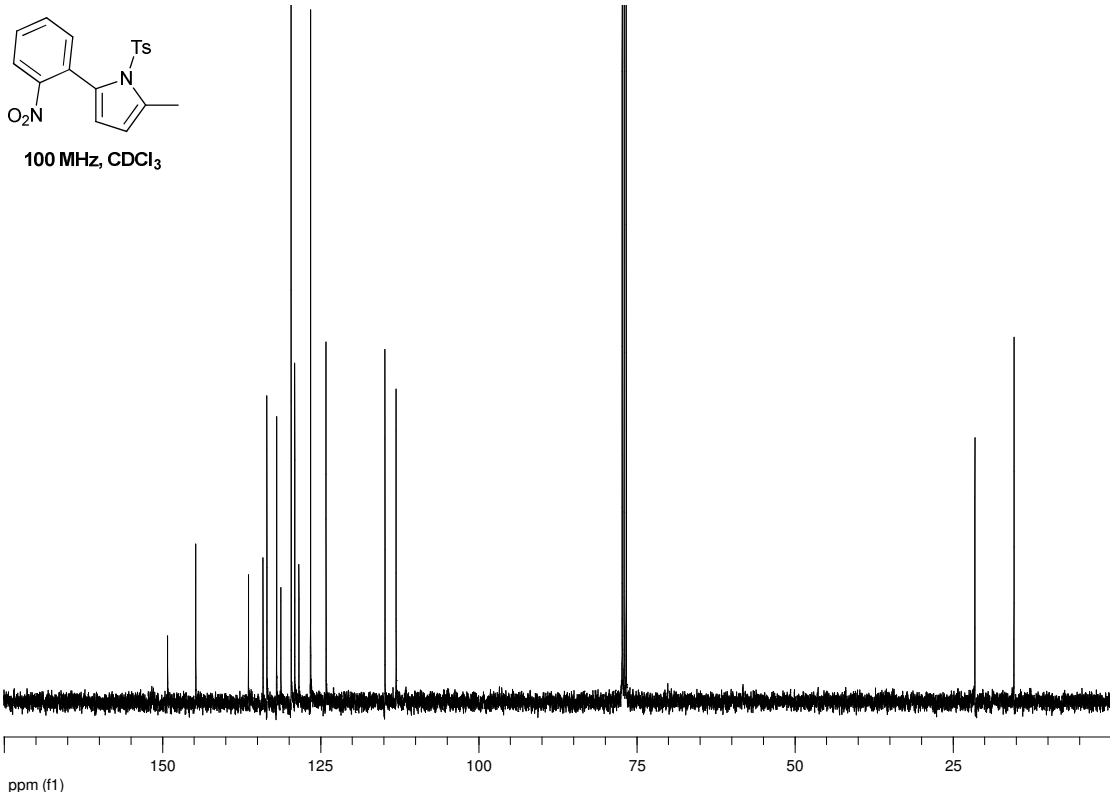
^{13}C NMR of pyrrole 4j



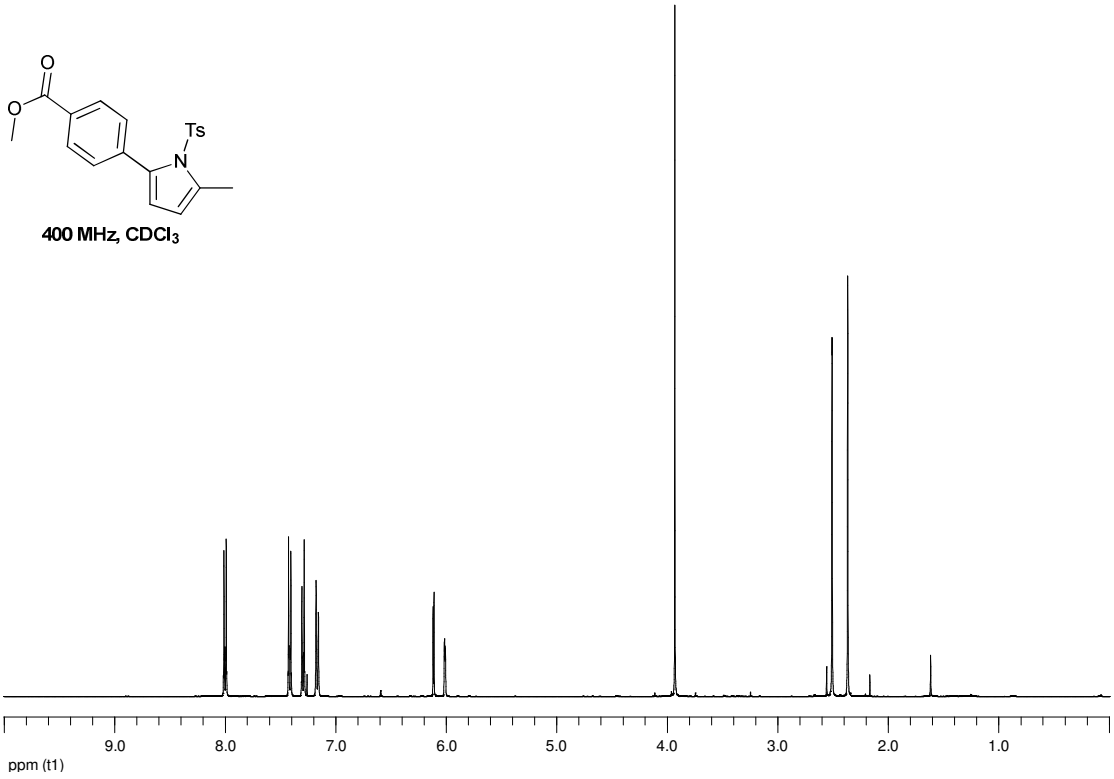
^{1}H NMR of pyrrole 4k



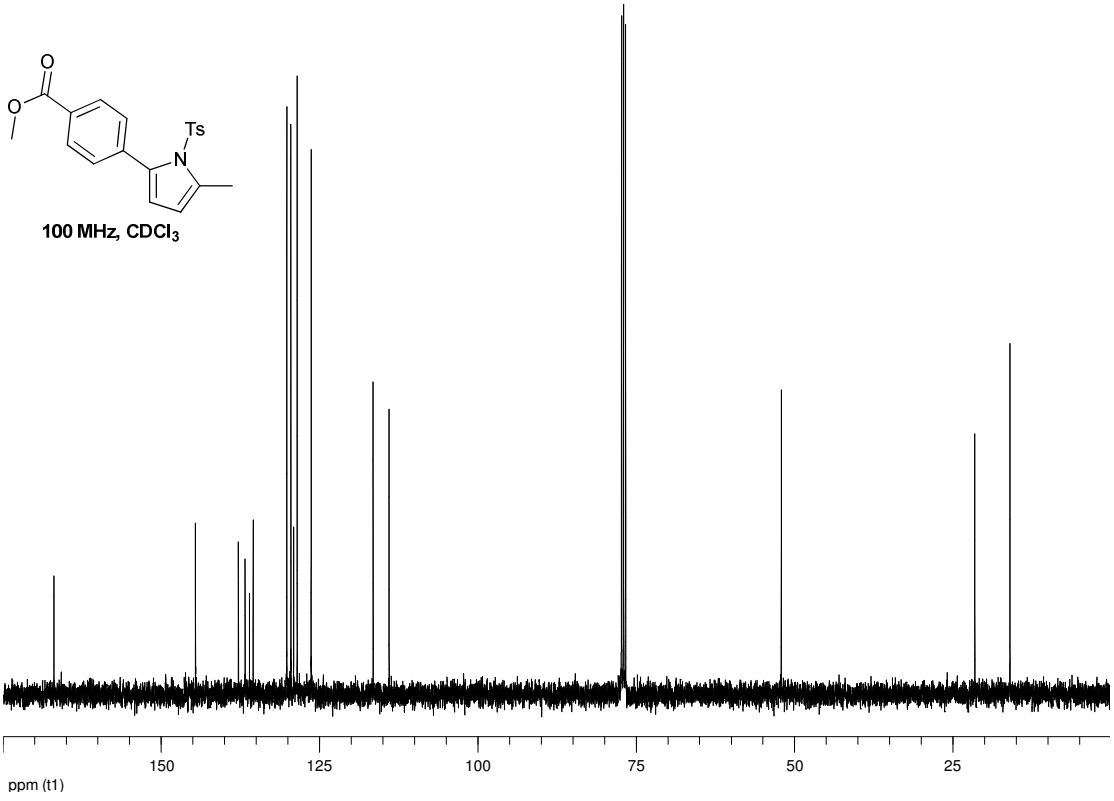
^{13}C NMR of pyrrole 4k



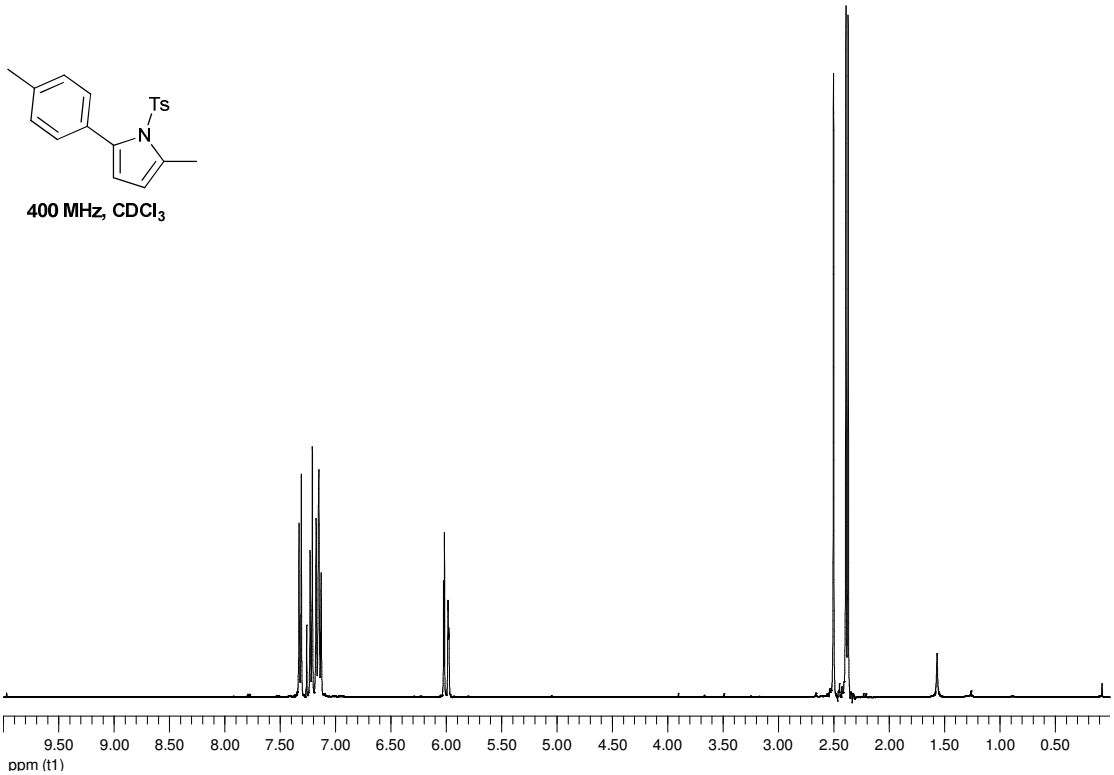
^{1}H NMR of pyrrole 4l



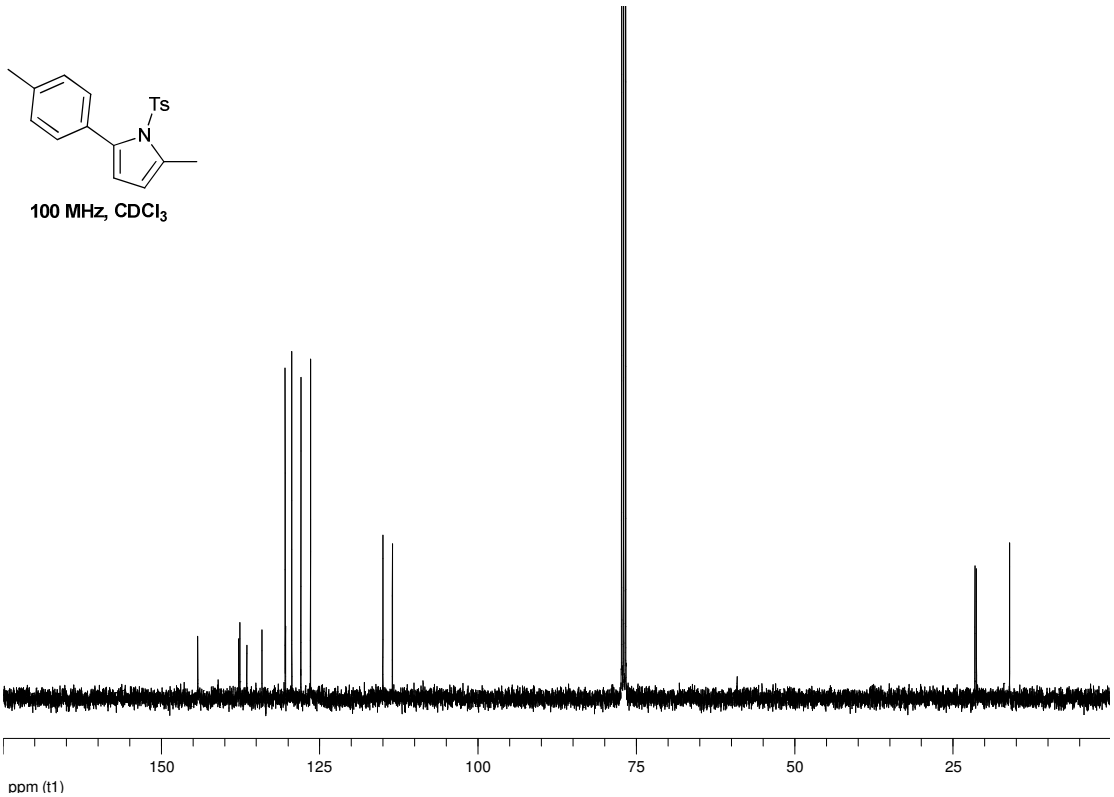
^{13}C NMR of pyrrole 4l



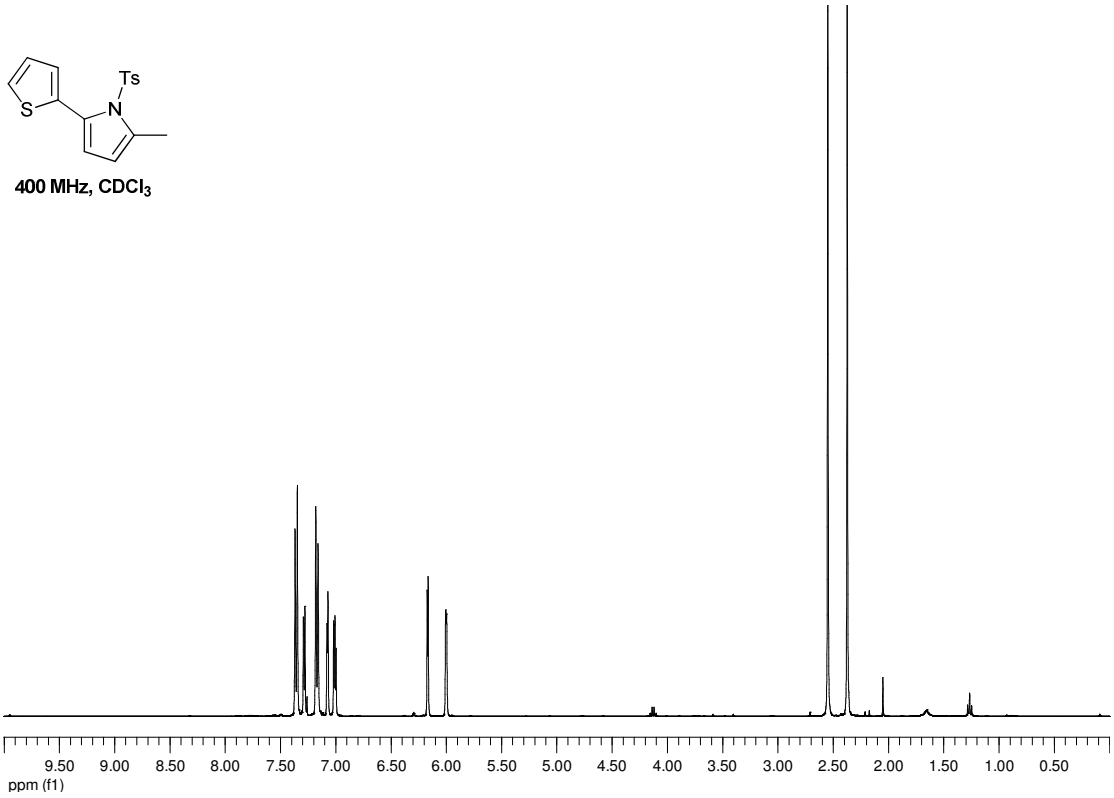
^{1}H NMR of pyrrole 4m



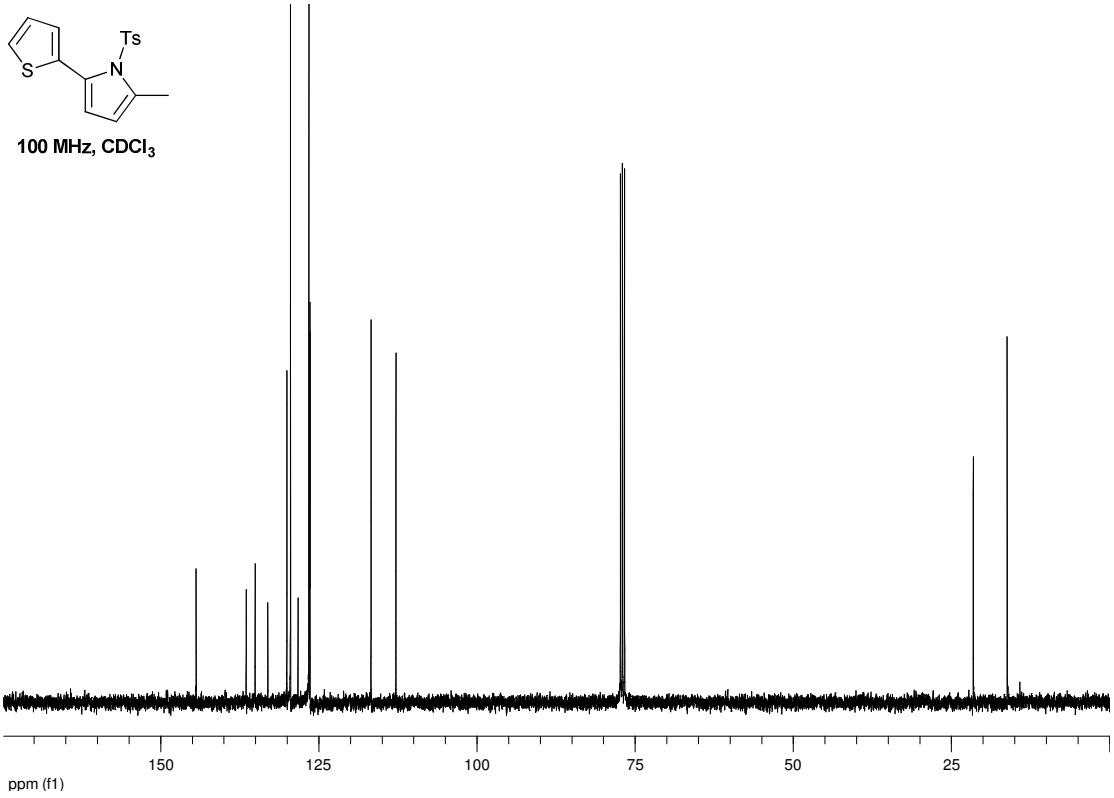
^{13}C NMR of pyrrole 4m



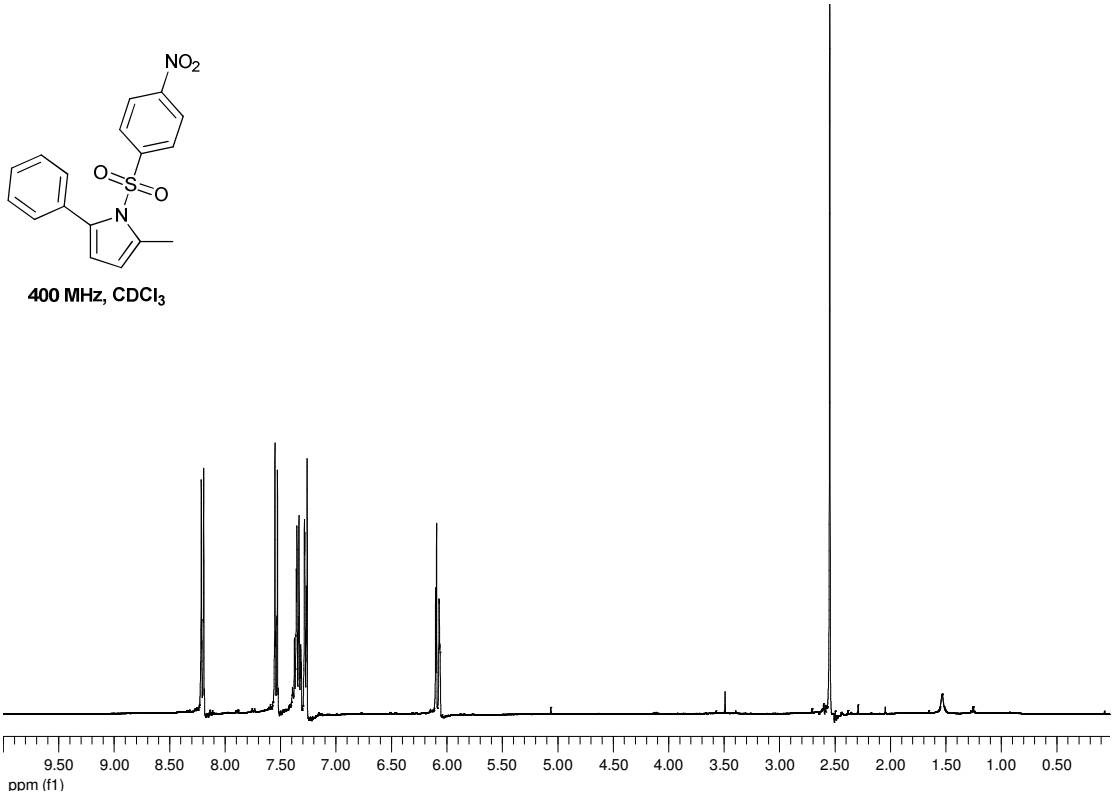
^{1}H NMR of pyrrole 4n



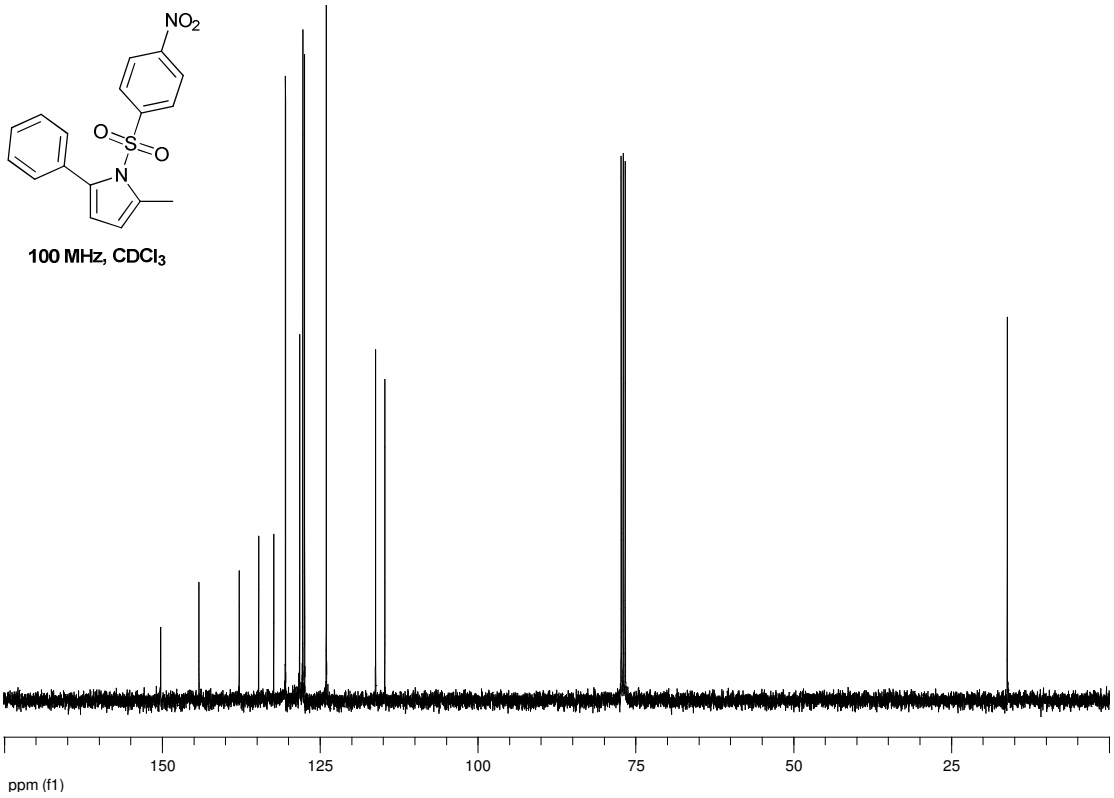
^{13}C NMR of pyrrole 4n



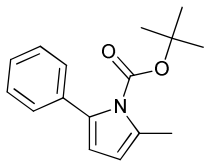
^{1}H NMR of pyrrole 4o



^{13}C NMR of pyrrole 4o

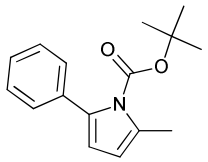


^{1}H NMR of pyrrole 4p



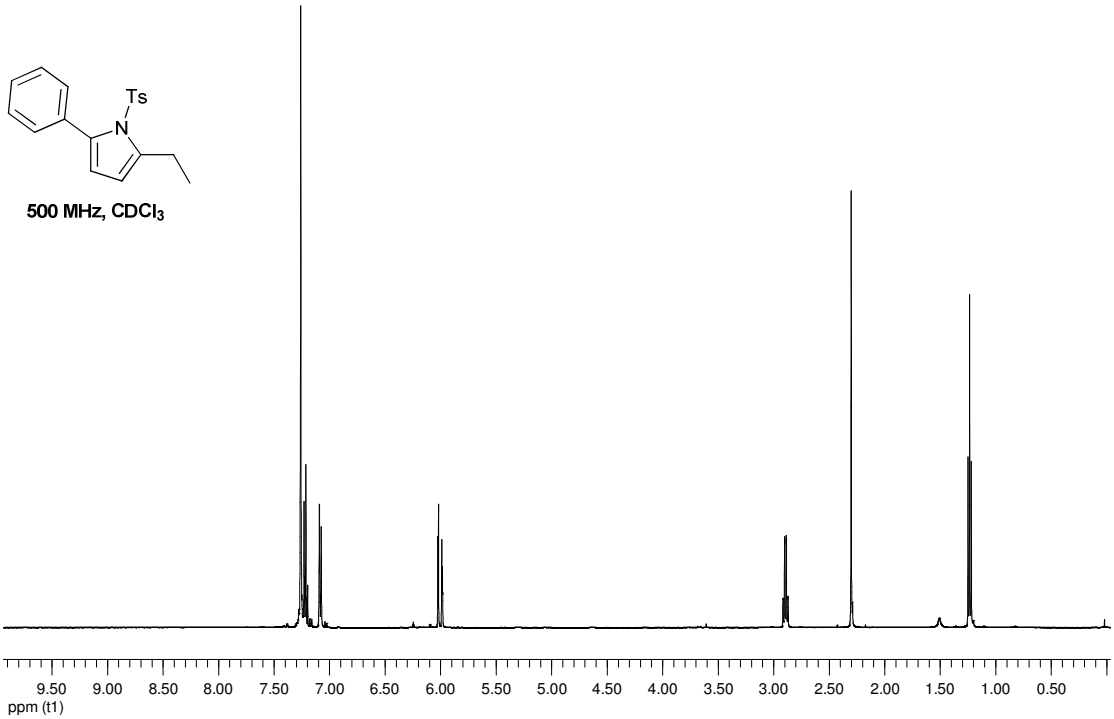
500 MHz, $CDCl_3$

^{13}C NMR of pyrrole 4p



125 MHz, $CDCl_3$

^{1}H NMR of pyrrole 4q



^{13}C NMR of pyrrole 4q