Activation and Deprotection of *F*-BODIPYs using Boron Trihalides

Travis Lundrigan, T. Stanley Cameron and Alison Thompson*

Department of Chemistry, Dalhousie University, PO BOX 15000, 6274 Coburg Road, Halifax, Nova Scotia, B3H 4R2, Canada

Supporting Information

1.1 General Experimental Procedures and Information

All ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz) and ^{11}B NMR (160 MHz) spectra were recorded using a 500 MHz spectrometer. Chemical shifts are expressed in parts per million (ppm) using the solvent signal [$CDCl_3$ (^{1}H 7.26 ppm; ^{13}C 71.16 ppm)] as an internal reference for ^{1}H and ^{13}C and BF_3•OEt_2 as an external reference for ^{11}B. Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. All coupling constants (*J*) are reported in Hertz (Hz). Mass spectra were obtained using ion trap (ESI) instruments operating in positive mode.

General Procedure for the Synthesis of HX Salts, X = Cl, Br (GP1)

The *F*-BODIPY (50 mg) was dissolved in anhydrous dichloromethane (10 mL) and 1 eq of BCl_3 (or BBr_3) was added drop-wise from a 1.0 M solution in anhydrous hexanes. The reaction mixture was stirred for an hour to allow *in situ* formation of the *Cl*-BODIPY. The reaction mixture was then concentrated *in vacuo*. The residue was dissolved in a mixture of acetone:water (10:1) and the solution was stirred for 10 min. The reaction mixture was extracted into dichloromethane and the organic layer was dried over Na_2SO_4. The solution was then concentrated *in vacuo* to obtain the HX salt of the dipyrrin.

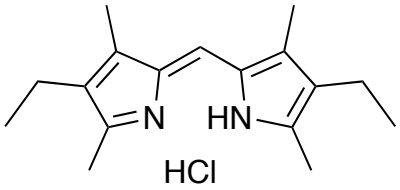
General Procedure for the Synthesis of HBF_4 Salts (GP2)

The *F*-BODIPY (50 mg) was dissolved in anhydrous dichloromethane (10 mL) and 1 eq of $BF_3 \cdot OEt_2$ was added drop-wise. The reaction mixture was stirred for 10 minutes and then 3 eq of water was added and the mixture was further stirred for 3 hours. The reaction

mixture was washed with water and the organic layer dried over Na_2SO_4. The solution was concentrated *in vacuo*. The resulting solid was washed with diethyl ether to remove any unreacted *F*-BODIPY, leaving an orange powder corresponding to the HBF_4 salt of the dipyrrin.

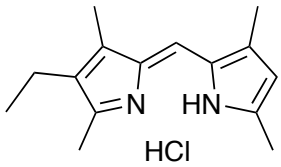
1.2 Procedures and characterization Data

(*Z*)-3-Ethyl-5-((4-ethyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrole hydrochloride (2a)



Using **GP1**, compound **2a** was synthesized from the corresponding *F*-BODIPY.[1] Bright orange solid (48 mg, 99%). δ_H (500 MHz, $CDCl_3$) 13.36 (2H, br s), 7.00 (1H, s), 2.59 (6H, s), 2.40 (4H, q, J = 7.5), 2.24 (6H, s), 1.05 (6H, t, J = 7.5). Data matches that previously reported for this compound.[4]

(*Z*)-2-((4-Ethyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-3,5-dimethyl-1*H*-pyrrole hydrochloride (2b)

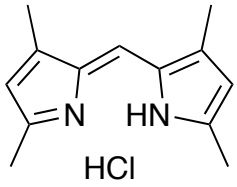


Using **GP1**, compound **2b** was synthesized from the corresponding *F*-BODIPY.[1] Bright orange solid (48 mg, 99%). δ_H (500 MHz, $CDCl_3$) 13.71 (2H, br s), 7.02 (1H, s), 6.11 (1H, s), 2.63 (3H, s), 2.62 (3H, s), 2.42 (2H, q, J = 7.5), 2.33 (3H, s), 2.26 (3H, s), 1.07 (3H, t, J = 7.5); δ_C (125 MHz, $CDCl_3$) 155.4, 148.8, 141.9, 139.1, 131.0, 126.84, 126.82, 119.4, 116.8, 17.4, 14.53, 14.51, 13.0, 12.2, 10.1. LRMS-ESI (m/z): 229.2 $[M + H]^+$

;

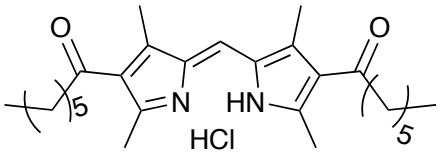
HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{15}H_{21}N_2$ 229.1699; found, 229.1691.

(*Z*)-2-((3,5-Dimethyl-2*H*-pyrrol-2-ylidene)methyl)-3,5-dimethyl-1*H*-pyrrole hydrochloride (2c)



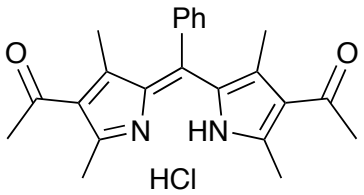
Using **GP1**, compound **2c** was synthesized from the corresponding *F*-BODIPY.[2] Bright orange solid (48 mg, 99%). δ_H (500 MHz, $CDCl_3$) 13.72 (2H, br s), 7.03 (1H, s), 6.13 (2H, s), 2.62 (6H, s), 2.32 (6H, s). Data matches that previously reported for this compound.[5]

(*Z*)-1-(2-((4-Heptanoyl-3,5-dimethyl-1*H*-pyrrol-2-yl)methylene)-3,5-dimethyl-2*H*-pyrrol-4-yl)heptan-1-one hydrochloride (2d)



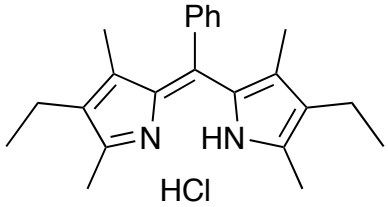
Using **GP1**, compound **2d** was synthesized from the corresponding *F*-BODIPY.[3] Bright orange solid (49 mg, 99%). δ_H (500 MHz, $CDCl_3$) 7.44 (1H, s), 3.00 (6H, s), 2.76 (4H, t, J = 7.2), 2.51 (6H, s), 1.74-1.66 (4H, m), 1.39-1.28 (12H, m), 0.90 (6H, t, J = 6.6); δ_C (125 MHz, $CDCl_3$) 198.4, 165.7, 142.1, 136.8, 132.0, 123.1, 43.8, 31.9, 29.9, 24.2, 22.7, 17.5, 14.2, 12.4. LRMS-ESI (m/z): 425.3 $[M + H]^+$; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{27}H_{41}N_2O_2$ 425.3163; found, 425.3147.

(*Z*)-1-(2-((4-Acetyl-3,5-dimethyl-1*H*-pyrrol-2-yl)(phenyl)methylene)-3,5-dimethyl-2*H*-pyrrol-4-yl)ethanone hydrochloride (2e)



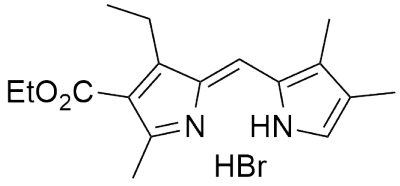
Using **GP1**, compound **2e** was synthesized from the corresponding *F*-BODIPY.[3] Bright orange solid (49 mg, 99%). δ_H (500 MHz, $CDCl_3$) 13.93 (2H, brs), 7.50-7.46 (3H, m), 7.30-7.28 (2H, m), 2.58 (6H, s), 2.39 (6H, s), 1.53 (6H, s); δ_C (125 MHz, $CDCl_3$) 196.7, 154.5, 143.7, 143.6, 137.2, 137.1, 131.0, 129.4, 129.3, 129.2, 31.8, 18.1, 14.5. LRMS-ESI (m/z): 361.2 $[M + H]^+$; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{23}H_{25}N_2O_2$ 361.1916; found, 361.1913.

(*Z*)-3-Ethyl-5-((4-ethyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)(phenyl)methyl)-2,4-dimethyl-1*H*-pyrrole hydrochloride (2f)



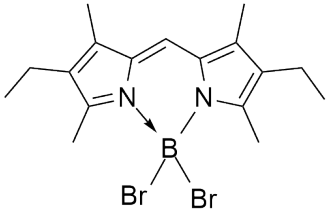
Using **GP1**, compound **2f** was synthesized from the corresponding *F*-BODIPY.[1] Bright orange solid (48 mg, 99%). δ_H (500 MHz, $CDCl_3$) 11.46 (2H, brs), 7.55-7.41 (3H, m), 7.26-7.25 (2H, m), 2.58 (6H, s), 2.33 (4H, q, J = 7.5), 1.31 (6H, s), 0.99 (6H, t, J = 7.5). Data matches that previously reported for this compound.[2]

(*Z*)-Ethyl 2-((3,4-dimethyl-1*H*-pyrrol-2-yl)methylene)-3-ethyl-5-methyl-2*H*-pyrrole-4-carboxylate hydrobromide (2g)



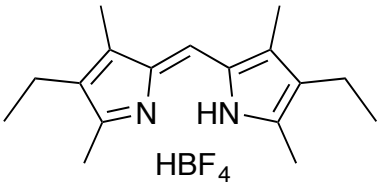
Using **GP1**, compound **2g** was synthesized from the corresponding *F*-BODIPY. Bright orange solid (55 mg, 99%). δ_H (500 MHz, $CDCl_3$) 13.73 (1H, br s), 13.35 (1H, br s), 7.76 (1H, d, J = 3.5), 7.34 (1H, s), 4.36 (2H, q, J = 7.0), 3.07 (2H, q, J = 7.5), 2.96 (3H, s), 2.33 (3H, s), 2.10 (3H, s), 1.40 (3H, t, J = 7.0), 1.27 (3H, t, J = 7.5); δ_C (125 MHz, $CDCl_3$) 163.2, 158.6, 155.6, 144.7, 144.5, 128.9, 126.6, 125.3, 122.9, 118.2, 60.7, 19.6, 16.9, 15.6, 14.4, 10.5, 10.2. LRMS-ESI (m/z): 287.2 $[M + H]^+$; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{17}H_{23}N_2O_2$ 287.1754; found, 287.1752.

1,3,5,7-Tetramethyl-2,6-diethyl-8-*H*-4,4'-dibromo-bora-3a,4a-diaza-*s*-indacene (3a)



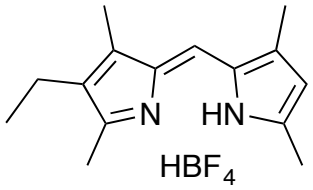
The analogous *F*-BODIPY (50 mg) was dissolved in anhydrous CCl_4 (10 mL) and treated with 1 eq of BBr_3. The bright orange solution became dark red/purple in colour. The solution was concentrated *in vacuo* and compound **3a** was isolated as a dark red solid (70 mg, 99%). δ_H (500 MHz, $CDCl_3$) 7.02 (1H, s), 2.80 (6H, s), 2.40 (4H, q, J = 7.5), 2.21 (6H, s), 1.08 (6H, t, J = 7.5); δ_C (125 MHz, $CDCl_3$) 154.2, 139.6, 134.1, 131.6, 119.4, 17.4, 14.7, 14.4, 10.2; δ_B (160 MHz, $CDCl_3$) -5.89 (s).

(*Z*)-3-Ethyl-5-((4-ethyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrole tetrafluoroborate (4a)



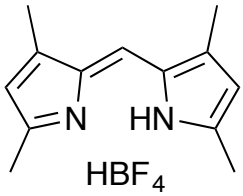
Using **GP2**, compound **4a** was synthesized from the corresponding *F*-BODIPY.[1] Bright orange solid (56 mg, 99%). δ_H (500 MHz, $CDCl_3$) 10.78 (2H, brs), 7.06 (1H, s), 2.55 (6H, s), 2.44 (4H, q, J = 7.5), 2.28 (6H, s), 1.09 (6H, t, J = 7.5); δ_C (125 MHz, $CDCl_3$) 154.3, 142.6, 131.1, 126.9, 118.9, 17.4, 14.5, 12.8, 10.2; δ_B (160 MHz, $CDCl_3$) -0.65 (s); δ_F (282 MHz, $CDCl_3$) -155.1 (s). LRMS-ESI (m/z): 87.0 $[M]^-$.

(*Z*)-2-((4-Ethyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-3,5-dimethyl-1*H*-pyrrole tetrafluoroborate (4b)



Using **GP2**, compound **4b** was synthesized from the corresponding *F*-BODIPY.[1] Bright orange solid (52 mg, 91%). δ_H (500 MHz, $CDCl_3$) 10.83 (1H, br s), 10.73 (1H, brs), 7.09 (1H, s), 6.19 (1H, s), 2.57 (6H, s, 2 x CH_3), 2.45 (2H, q, J = 7.5), 2.35 (3H, s), 2.29 (3H, s). 1.09 (3H, t, J = 7.5); δ_C (125 MHz, $CDCl_3$) 156.1, 154.8, 146.2, 143.5, 131.7, 127.30, 127.28, 119.5, 117.4, 17.5, 14.4, 12.9, 12.3, 10.2 (1C signal missing); δ_B (160 MHz, $CDCl_3$) -0.65 (s); δ_F (282 MHz, $CDCl_3$) -155.0 (s). LRMS-ESI (m/z): 87.0 $[M]^-$.

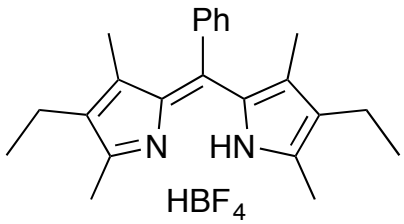
(*Z*)-2-((3,5-Dimethyl-2*H*-pyrrol-2-ylidene)methyl)-3,5-dimethyl-1*H*-pyrrole tetrafluoroborate (4c)



Using **GP2**, compound **4c** was synthesized from the corresponding *F*-BODIPY.[2] Bright orange solid (46 mg, 80%). δ_H (500 MHz, $CDCl_3$) 10.84 (2H, brs), 7.09 (1H, s), 6.21 (2H, s), 2.58 (6H, s), 2.34 (6H, s); δ_C (125 MHz, $CDCl_3$) 156.2, 147.4, 133.5, 127.6, 120.3,

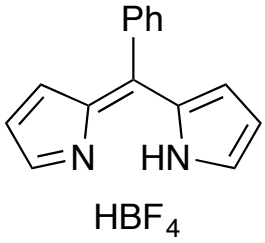
14.5, 12.2; δ_B (160 MHz, $CDCl_3$) -0.65 (s); δ_F (282 MHz, $CDCl_3$) -154.9 (s). LRMS-ESI (m/z): 87.0 $[M]^-$.

(*Z*)-3-Ethyl-5-((4-ethyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)(phenyl)methyl)-2,4-dimethyl-1*H*-pyrrole tetrafluoroborate (4e)



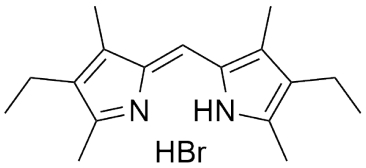
Using **GP2**, compound **4d** was synthesized from the corresponding *F*-BODIPY.[1] Bright orange solid (25 mg, 45%). δ_H (500 MHz, $CDCl_3$) 9.89 (2H, br s), 7.53-7.45 (3H, m), 7.35-7.31 (2H, m), 2.52 (6H, s), 2.41 (4H, q, *J*=7.5), 1.45 (6H, s), 1.06 (6H, t, *J* = 7.5); δ_C (125 MHz, $CDCl_3$) 153.7, 138.5, 136.6, 135.9, 133.8, 132.2, 129.3, 129.1, 128.3, 17.5, 14.3, 12.7, 12.1; δ_B (160 MHz, $CDCl_3$) -1.01 (s); δ_F (282 MHz, $CDCl_3$) -157.4 (s). LRMS-ESI (m/z): 87.0 $[M]^-$.

(*Z*)-2-(Phenyl(2*H*-pyrrol-2-ylidene)methyl)-1*H*-pyrrole tetrafluoroborate (4h)



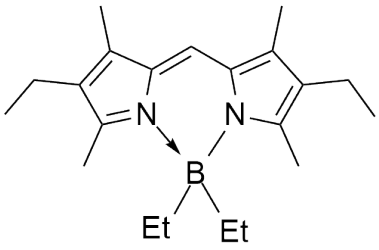
Using **GP2**, compound **4e** was synthesized from the corresponding *F*-BODIPY.[1] Bright orange solid (3 mg, 5%). δ_H (500 MHz, $CDCl_3$) 8.46 (2H, brs), 7.68 (2H, t, *J* = 1.2), 7.52-7.42 (5H, m), 6.62 (2H, dd, *J* = 4.2, 1.2), 6.41 (2H, dd, *J* = 4.2, 1.5); δ_C (125 MHz, $CDCl_3$) 143.8, 142.7, 140.3, 137.4, 131.0, 129.5, 129.2, 127.7, 117.7; δ_B (160 MHz, $CDCl_3$) -1.00 (s); δ_F (282 MHz, $CDCl_3$) -157.0 (s). LRMS-ESI (m/z): 87.0 $[M]^-$.

(*Z*)-3-Ethyl-5-((4-ethyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrole hydrobromide (4a-HBr)



Compound **4a-HBF4** (50 mg) was dissolved in anhydrous dichloromethane (10 mL) and treated with excess (0.1 mL) aqueous HBr (48%). The resulting solution was stirred for 15 min and then washed with water. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to give **4a-HBr** as a bright orange solid (49 mg, 99%). δ_H (500 MHz, $CDCl_3$) 12.87 (2H, br s), 7.02 (1H, s), 2.66 (6H, s), 2.41 (4H, q, J = 7.5), 2.26 (6H, s), 1.06 (6H, t, J = 7.5). Data matches that previously reported for this compound.[7]

1,3,5,7-Tetramethyl-2,6-diethyl-8-*H*-4,4'-diethyl-bora-3a,4a-diaza-*s*-indacene (5a)



F-BODIPY **1a** (50 mg) was dissolved in anhydrous dichloromethane (10 mL) and treated with 1 eq of $BF_3{\cdot}OEt_2$, followed by the addition of 2 eq of EtMgBr (3.0 M in THF) added drop-wise. The solution was then washed with water and the organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to give **5a** as a bright orange solid (53 mg, 99%). δ_H (500 MHz, $CDCl_3$) 6.99 (1H, s), 2.44-2.39 (10H, m, 2x(CH_3+CH_2)), 2.18 (6H, s), 1.06 (6H, t, J=7.6), 0.82 (4H, q, J=7.6), 0.31 (6H, t, J=7.6). Compound has been previously characterized.[6]

1.3 References

[1] Lundrigan, T.L.; Baker, A.E.G.; Longobardi, L.E.; Wood, T.E.; Smithen, D.A.; Crawford, S.M.; Cameron, T.S.; Thompson, A. *Org. Lett.* **2012**, *14*, 2158-2161.

[2] Crawford, S.M.; Thompson, A. *Org. Lett*, **2010**, *12*, 1424-1427.

[3] Smithen, D.A.; Baker, A.E.G.; Offman, M.; Crawford, S.M.; Cameron, T.S.; Thompson, A. *J. Org. Chem*. **2012**, *77*, 3439−3453

[4] Tu, B.; Wang, C.; Ma, J. *Org. Prep. Proced. Int.*, **1999**, *31*, 349-352.

[5] Sessler, J.L.; Eller, L.R.; Cho, W.-S.; Nicolaou, S.; Aguilar, A.; Lee, J.T.; Lynch, V.M.; Magda, D.J. *Angew. Chem*. **2005**, *117*, 6143–6146.

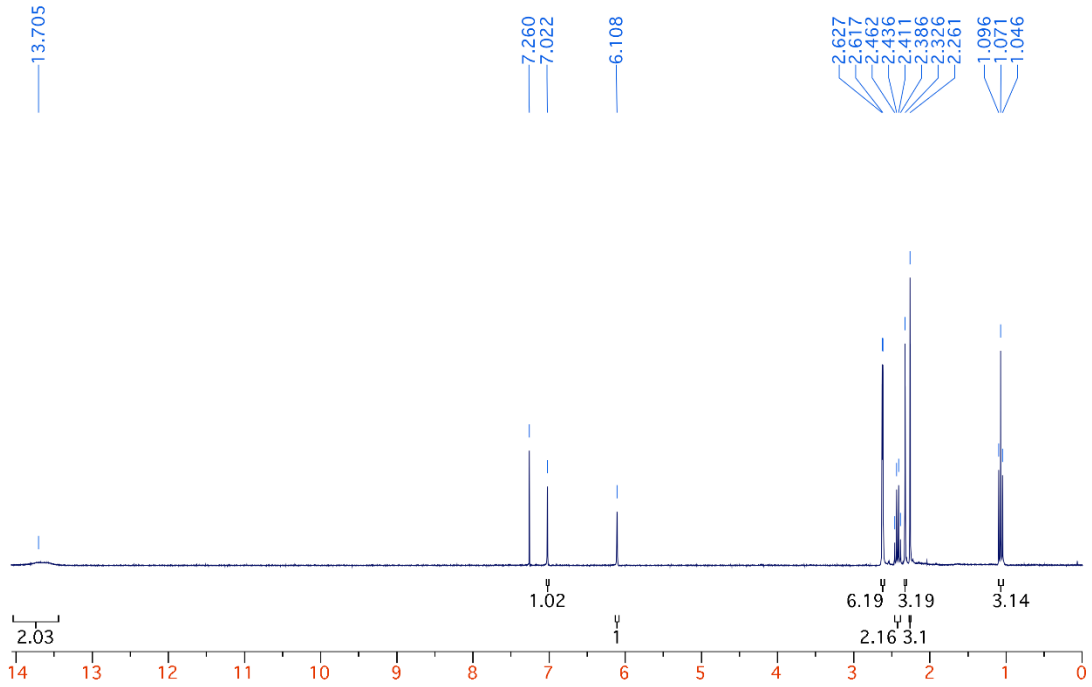
[6] Lundrigan, T.L.; Crawford, S.M.; Cameron, T.S.; Thompson, A. *Chem. Commun.* **2012**, *48*, 1003-1005.

[7] Semeikin, A.S.; Berezin, M.B.; Chernova, O.M.; Antina, E.V.; Syrbu, S.A.; Lyubimova, T.V.; Kutepov, A.M. *Russ.Chem.Bull., Int.Ed*., **2003**, *52*, 1807-1813.

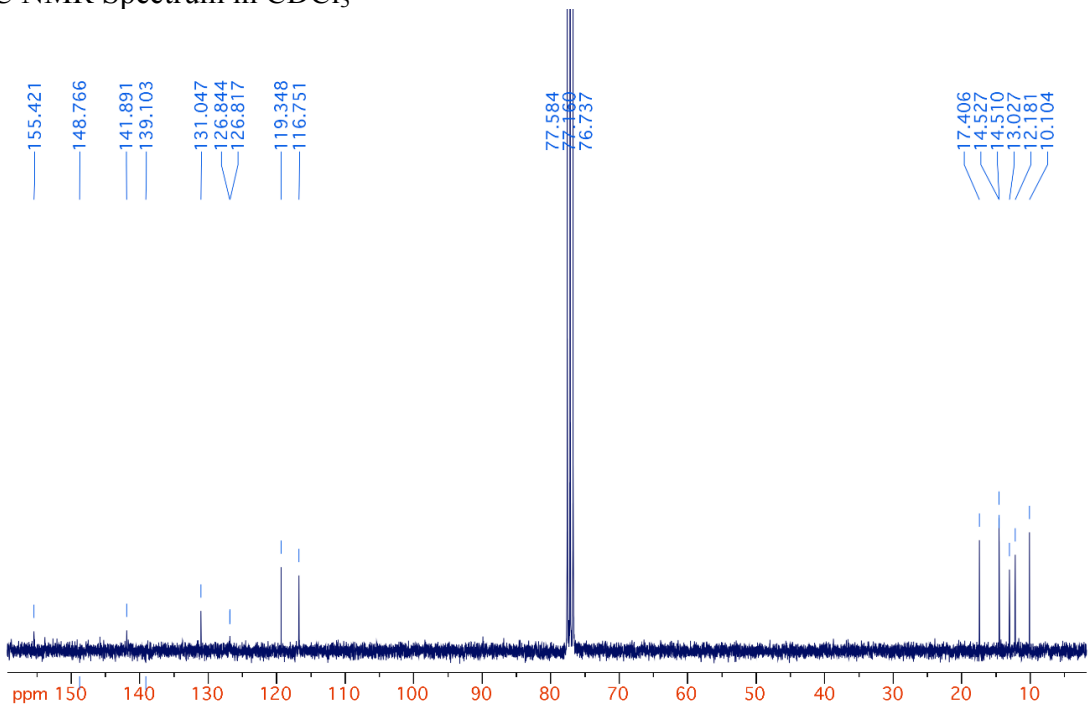
1.4 ^{1}H and ^{13}C NMR Spectra

(*Z*)-2-((4-Ethyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-3,5-dimethyl-1*H*-pyrrole hydrochloride (2b)

^{1}H NMR Spectrum in $CDCl_3$

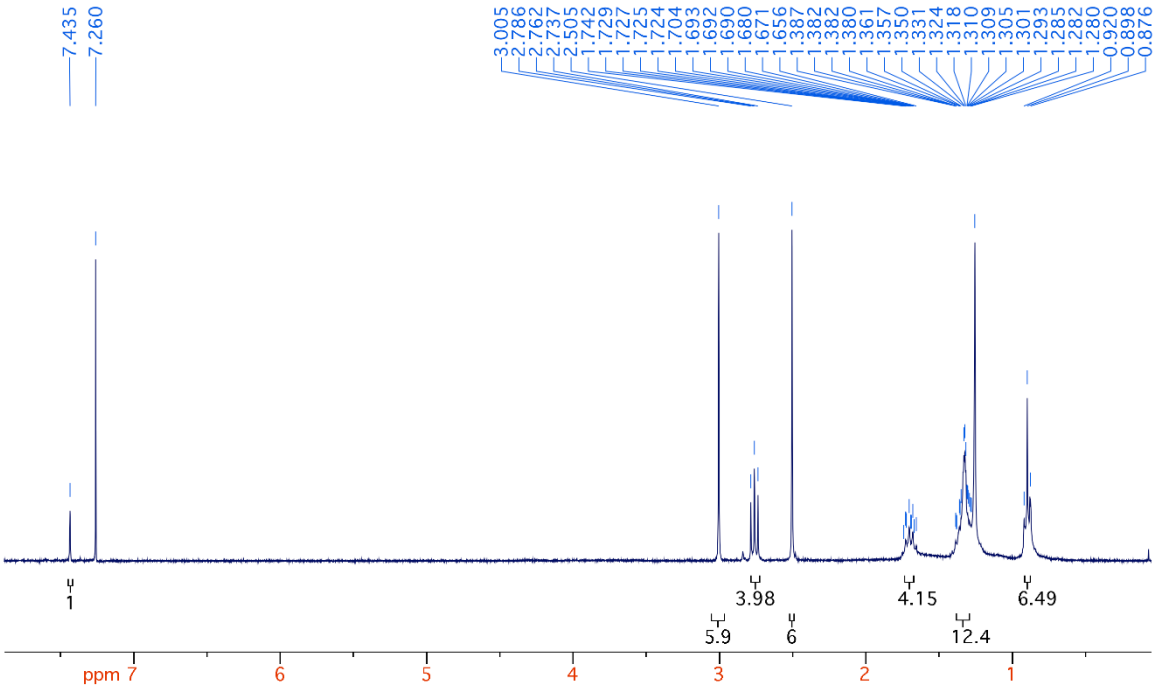


^{13}C NMR Spectrum in $CDCl_3$

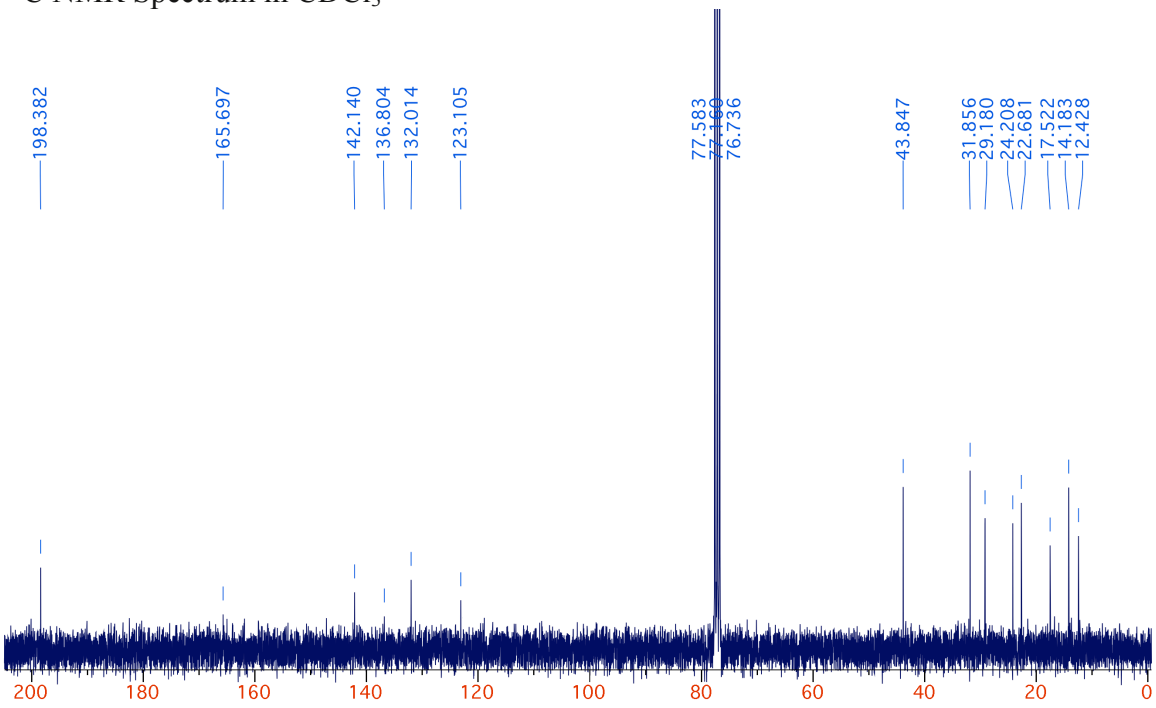


(*Z*)-1-(2-((4-Heptanoyl-3,5-dimethyl-1*H*-pyrrol-2-yl)methylene)-3,5-dimethyl-2*H*-pyrrol-4-yl)heptan-1-one hydrochloride (2d)

^{1}H NMR Spectrum in $CDCl_3$

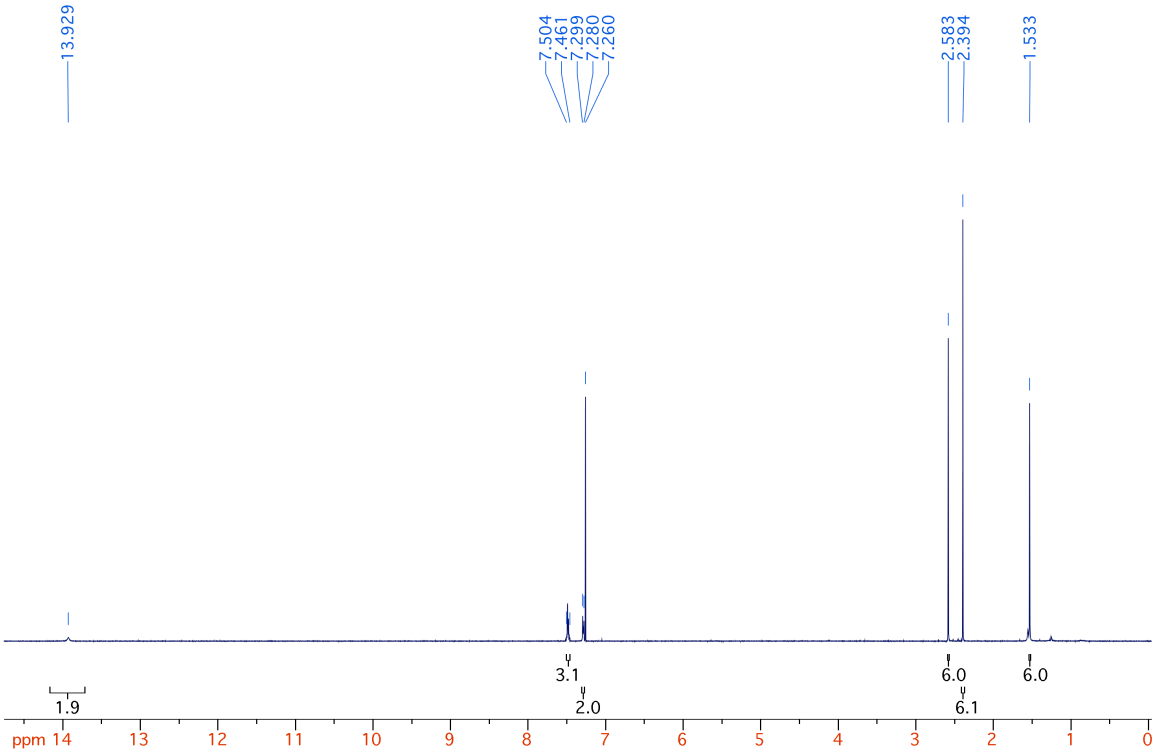


^{13}C NMR Spectrum in $CDCl_3$

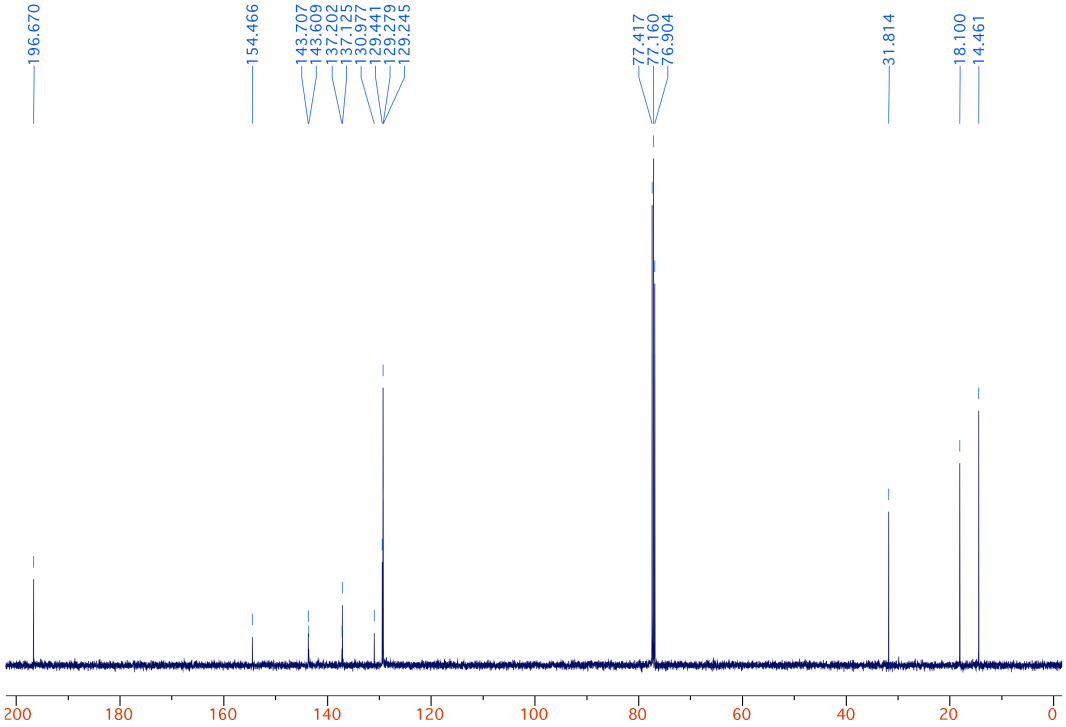


(*Z*)-1-(2-((4-Acetyl-3,5-dimethyl-1*H*-pyrrol-2-yl)(phenyl)methylene)-3,5-dimethyl-2*H*-pyrrol-4-yl)ethanone hydrochloride (2e)

^{1}H NMR Spectrum in $CDCl_3$

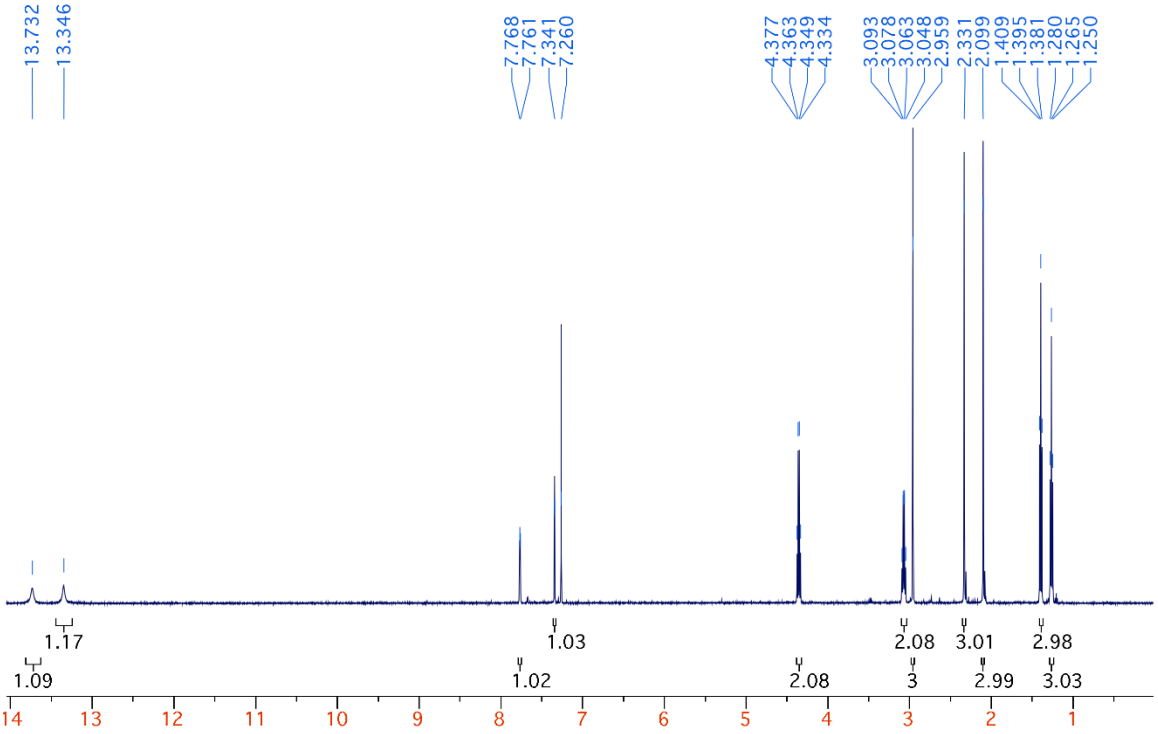


^{13}CNMR Spectrum in $CDCl_3$

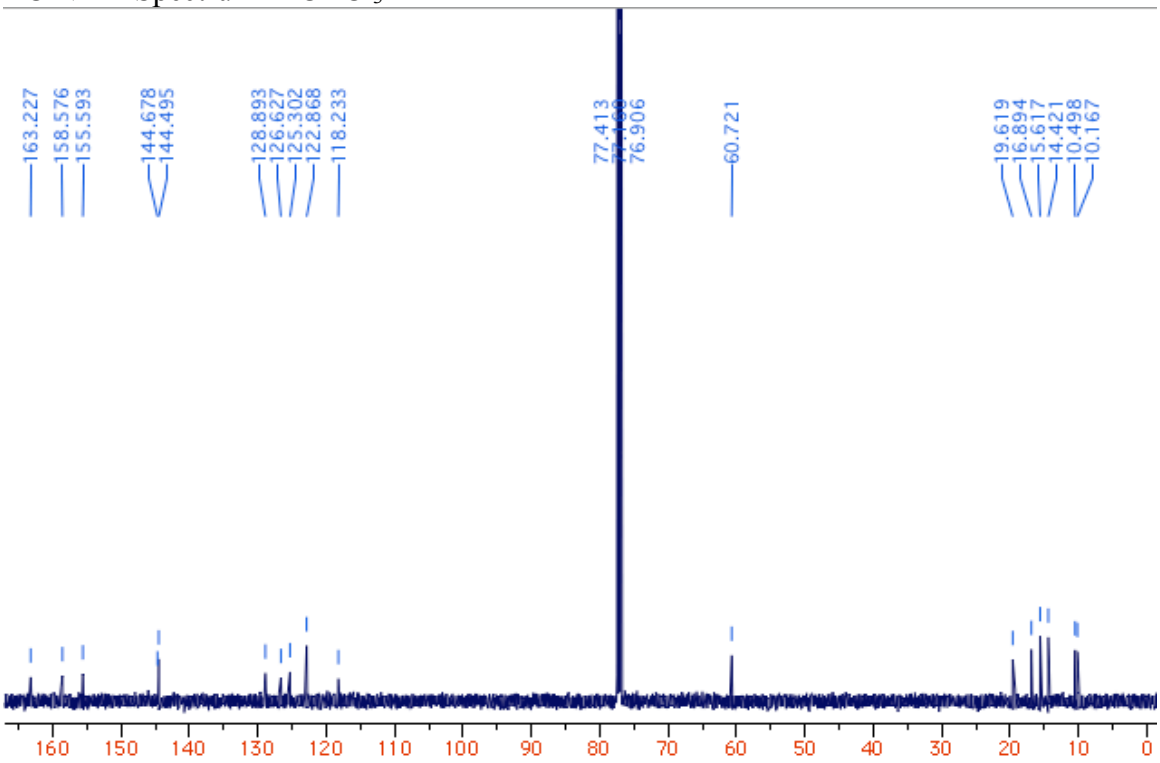


(*Z*)-Ethyl 2-((3,4-dimethyl-1*H*-pyrrol-2-yl)methylene)-3-ethyl-5-methyl-2*H*-pyrrole-4-carboxylate hydrobromide (2g)

^{1}H NMR Spectrum in $CDCl_3$

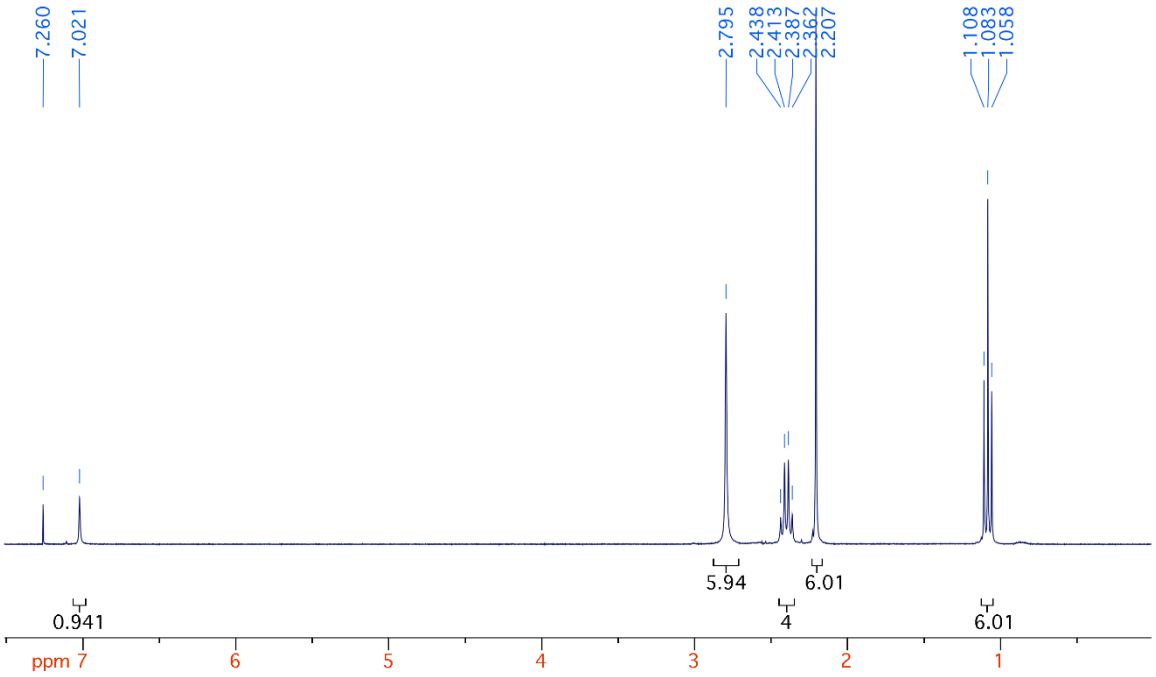


^{13}C NMR Spectrum in $CDCl_3$

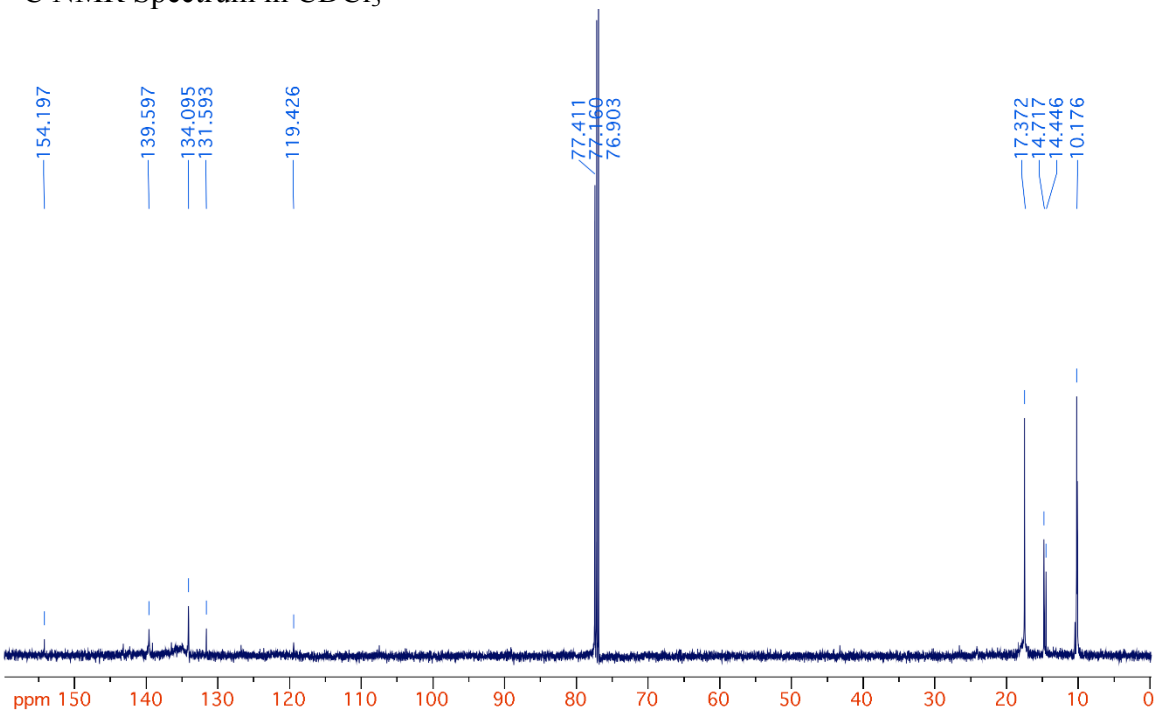


1,3,5,7-Tetramethyl-2,6-diethyl-8-*H*-4,4'-dibromo-bora-3a,4a-diaza-*s*-indacene (3a)

^{1}H NMR Spectrum in $CDCl_3$

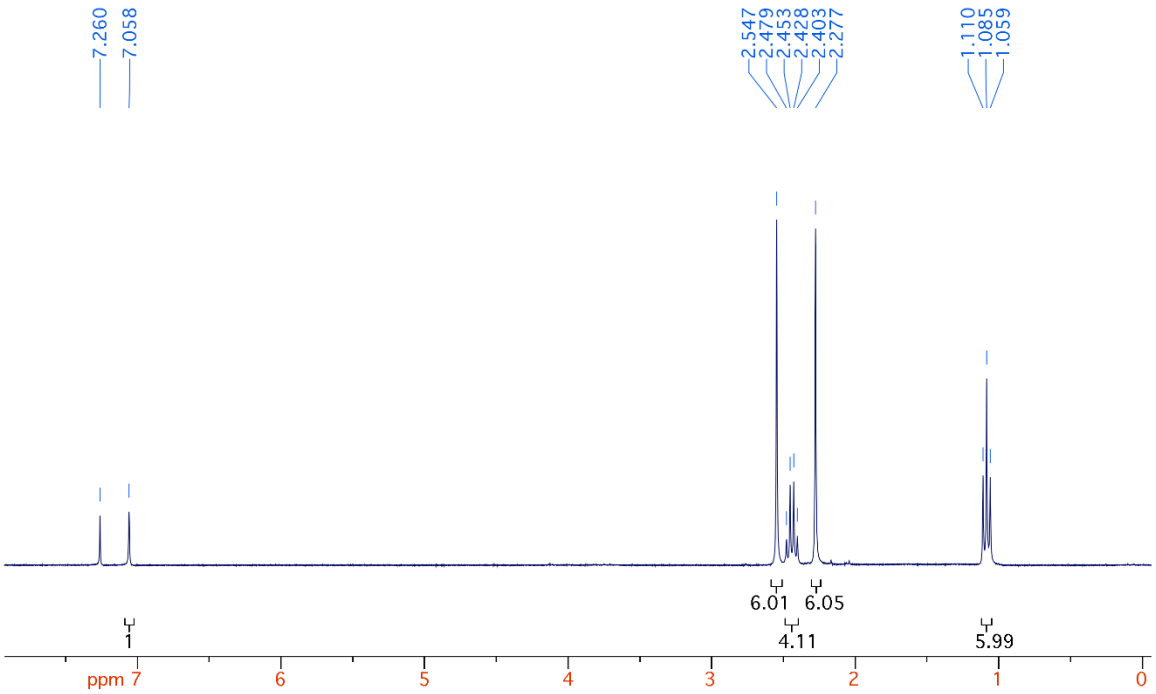


^{13}C NMR Spectrum in $CDCl_3$

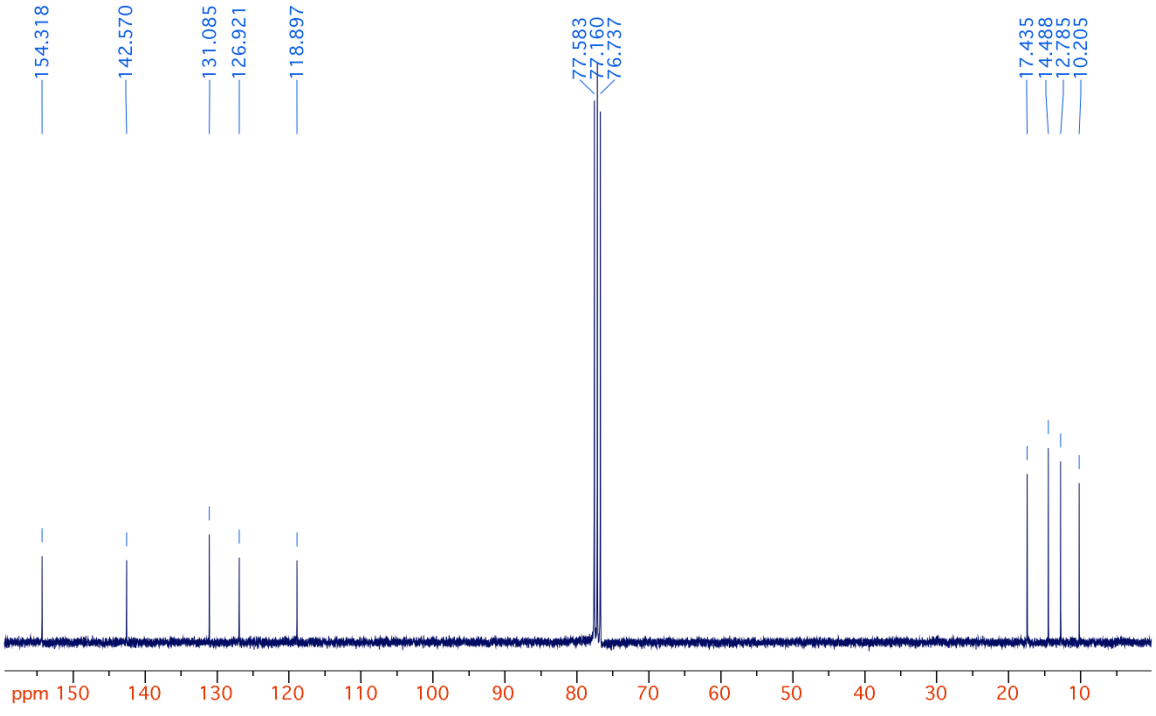


(*Z*)-3-Ethyl-5-((4-ethyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrole tetrafluoroborate (4a)

^{1}H NMR Spectrum in $CDCl_3$

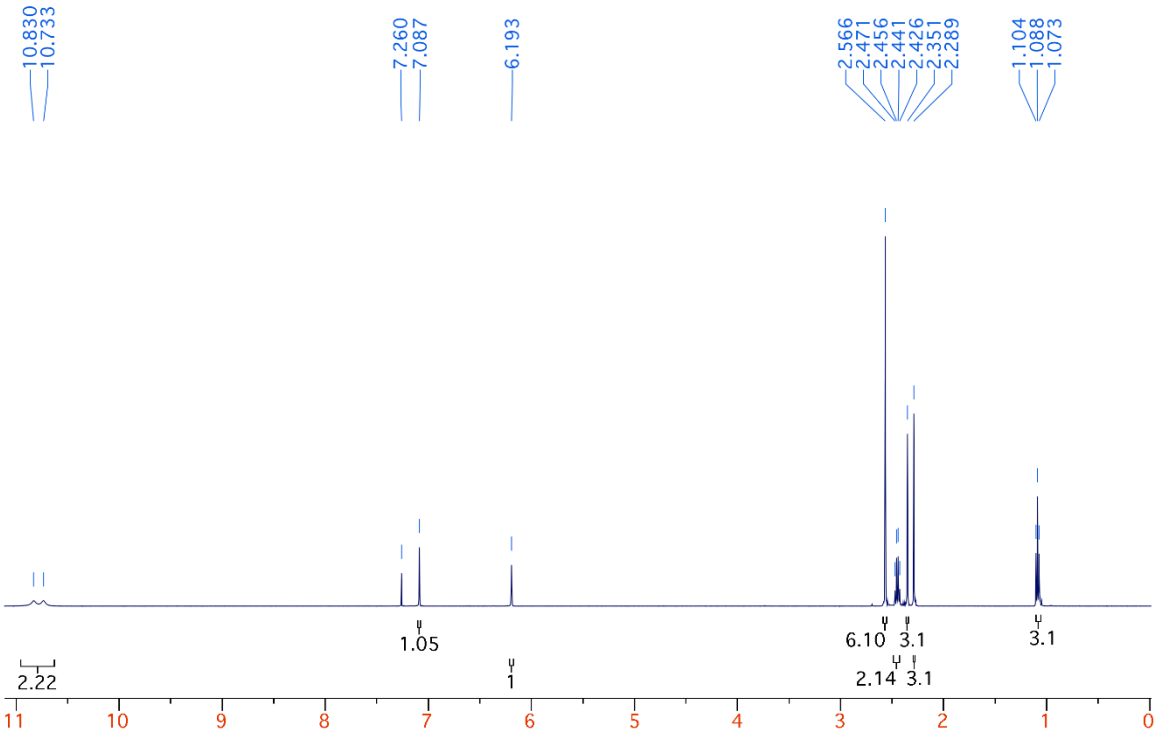


^{13}C NMR Spectrum in $CDCl_3$

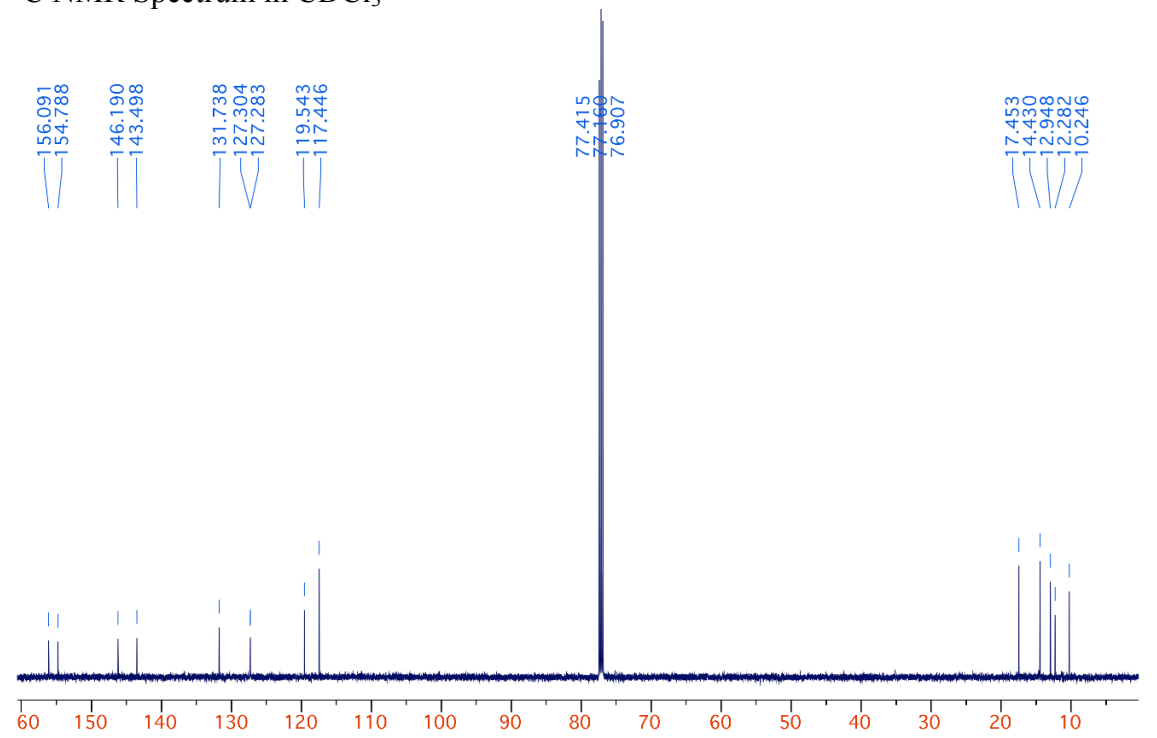


(*Z*)-2-((4-Ethyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-3,5-dimethyl-1*H*-pyrrole tetrafluoroborate (4b)

^{1}H NMR Spectrum in $CDCl_3$

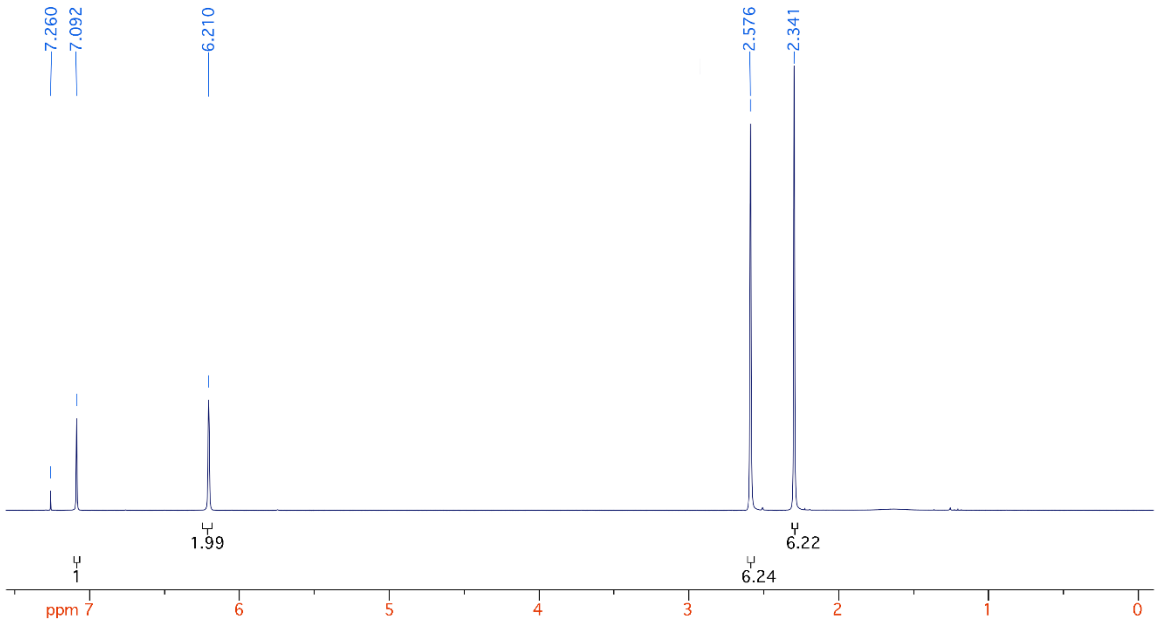


^{13}C NMR Spectrum in $CDCl_3$

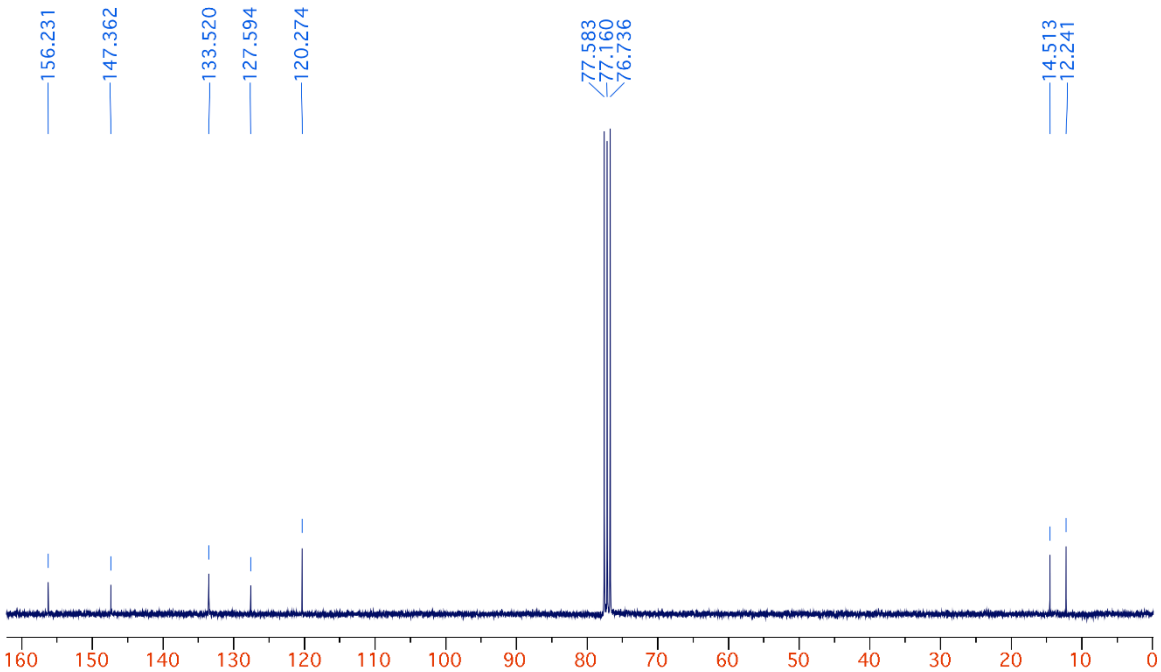


(*Z*)-2-((3,5-Dimethyl-2*H*-pyrrol-2-ylidene)methyl)-3,5-dimethyl-1*H*-pyrrole tetrafluoroborate (4c)

^{1}H NMR Spectrum in $CDCl_3$

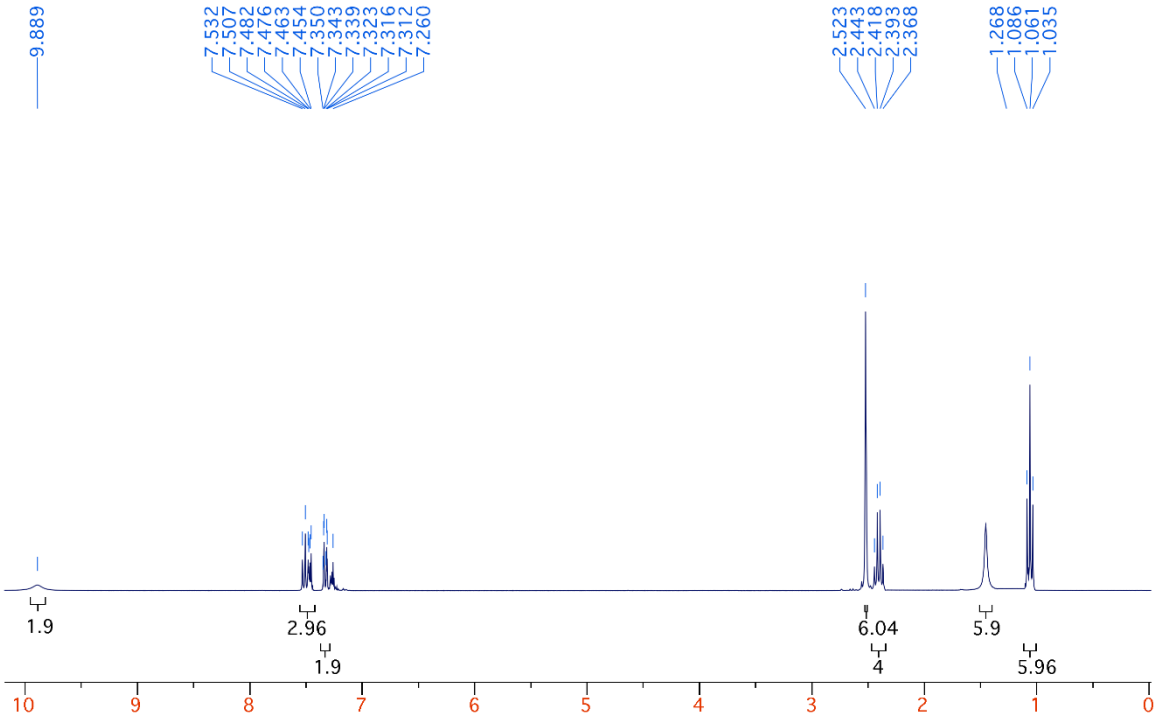


^{13}C NMR Spectrum in $CDCl_3$

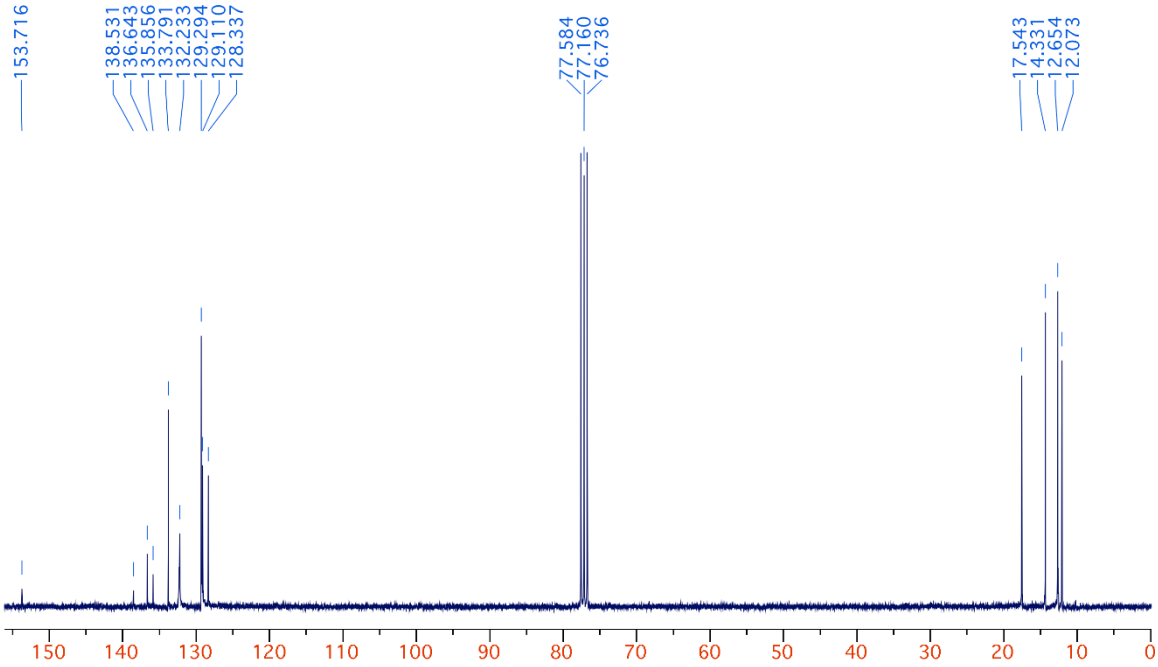


(*Z*)-3-Ethyl-5-((4-ethyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)(phenyl)methyl)-2,4-dimethyl-1*H*-pyrrole tetrafluoroborate (4e)

^{1}H NMR Spectrum in $CDCl_3$

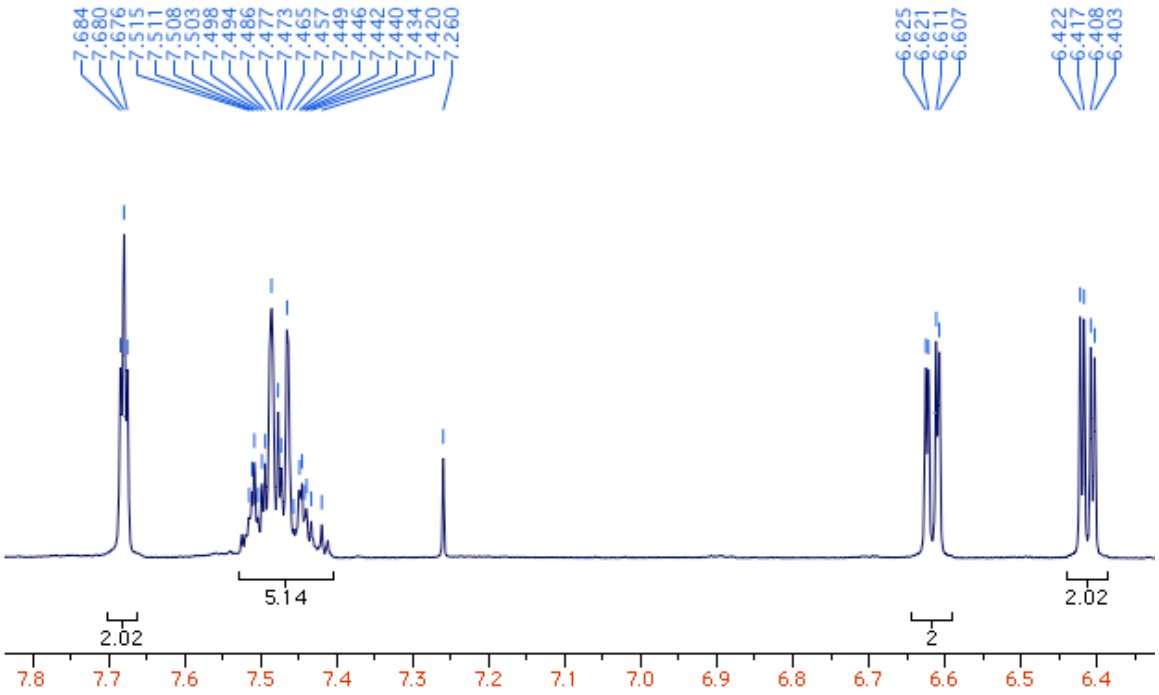


^{13}C NMR Spectrum in $CDCl_3$



(*Z*)-2-(Phenyl(2*H*-pyrrol-2-ylidene)methyl)-1*H*-pyrrole tetrafluoroborate (4h)

^{1}H NMR Spectrum in $CDCl_3$



^{13}C NMR Spectrum in $CDCl_3$