Thionation reactions of 2-pyrrole carboxylates

*Brandon R. Groves, Deborah A. Smithen, T. Stanley Cameron and Alison Thompson**

Department of Chemistry, Dalhousie University, P.O. Box 15000, Halifax, NS, B3H 4R2, Canada
Alison.Thompson@dal.ca

Supporting Information

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Experimental

General Experimental

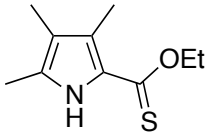
All chemicals were purchased and used as received unless otherwise indicated. Hexanes and dichloromethane used for chromatography were obtained crude and purified via distillation under atmospheric conditions before use. Anhydrous solvents were used as received. Flash chromatography was performed using Silicycle ultra pure silica (230-400 mesh) or Brockmann III (150 mesh) activated basic or neutral alumina oxide as indicated. TLC was performed using glass-backed silica gel plates or plastic-backed neutral alumina plates. Visualization of TLC plates was performed using UV light (254 nm) and/or vanillin stain. Moisture sensitive reactions were performed in oven- or flame-dried glassware under a positive pressure of nitrogen. Air- and moisture-sensitive compounds were introduced via syringe. NMR spectra were recorded using 500 MHz or 300 MHz spectrometers. ^{1}H and ^{13}C chemical shifts are expressed in parts per million (ppm) using the solvent signal ($CDCl_3$ ^{1}H 7.26; ^{13}C 77.16 ppm) as reference. ^{11}B, ^{19}F and ^{31}P chemical shifts were referenced using the absolute referencing procedure standard for digital spectrometers, with BF_3•Et_2O (15% in $CDCl_3$), CCl_3F and 85% H_3PO_4 to define the 0 ppm position, respectively. All coupling constants (*J*) are reported in Hertz (Hz). Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; at, apparent triplet; q, quartet; m, multiplet; a, apparent. All mass spectra were recorded using ESI TOF ionisation. All microwave-promoted reactions were performed using a Biotage Initiator 8 laboratory microwave apparatus, 0–400 W power, 2.45 GHz. Pyrroles were prepared according to literature procedures, as indicated. All X-Ray measurements were made using a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo-Kα radiation. CCDC reference numbers for compounds used as literature comparisons are as follows: **L1** 667280; **2g** 201149; **L2** 1267621; **L3** 263350.

Experimental Procedures

General Procedure for the Synthesis of Pyrrolic Thionoesters (GP1)

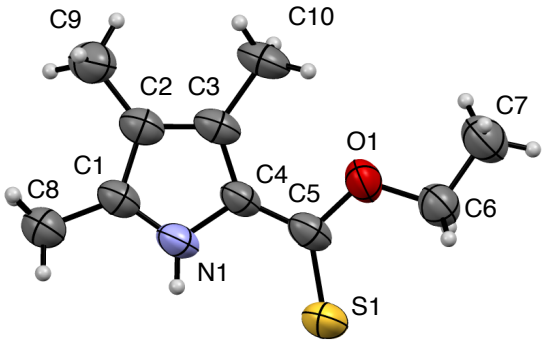
A suspension of pyrrolic ester (0.5 mmol) and Lawesson's reagent (0.3 mmol, 1.2 equiv.) in anhydrous *p*-xylene or anhydrous toluene (0.7 mL, 0.75 M), in a sealed flask under nitrogen, was placed in a sand bath preheated to 140 °C, and then heated with stirring for 1 hour. After this time, the reaction mixture was allowed to cool to room temperature before being diluted with ethyl acetate (1 mL) and the mixture then poured into 20% ethyl acetate/hexanes (20 mL), rinsing the flask with ethyl acetate (2 x 1 mL). The combined solution was then filtered through a short pad of silica, washing with 20% ethyl acetate/hexanes, and the filtrate concentrated to give the crude product, which was purified using column chromatography over silica, eluting with 5-10% ethyl acetate/hexanes, unless otherwise stated.

O-Ethyl-3,4,5-trimethyl-1*H*-pyrrole-2-carbothioate (2a)



Thionoester **2a** was synthesized from **1a**[1] using GP1 to give the title compound as a yellow solid (78 mg, 72% yield). Alternatively, a suspension of pyrrolic ester (0.5 mmol) and Lawesson's reagent (0.3 mmol, 1.2 equiv.) in anhydrous toluene (0.7 mL, 0.75 M), in a sealed microwave

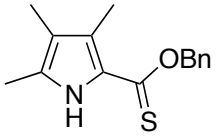
vial under nitrogen, was placed under microwave heating at 160 °C for 20 min. After this time, the reaction mixture was allowed to cool to room temperature before dilution with ethyl acetate (1 mL). The mixture was then poured into 20% ethyl acetate/hexanes (20 mL), rinsing the flask with ethyl acetate (2 x 1 mL). The combined solution was filtered through a short pad of silica, washing with 20% ethyl acetate/hexanes, and the filtrate concentrated to give the crude product, which was purified using column chromatography over silica, eluting with 5% ethyl acetate/hexanes, to give the title compound as a yellow solid (64 mg, 59%) M.p. 83-85 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) 9.06 (br s, 1H, NH), 4.66 (q, 2H, J = 7.2 Hz, CH_2CH_3), 2.25 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 1.91 (s, 3H, CH_3), 1.46 (t, 3H, J = 7.2 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz, UDEFT) 199.5, 134.5, 128.6, 126.1, 119.2, 66.5, 14.3, 12.2, 12.0, 8.8; LRMS: 220.1 $(M+Na)^+$; HRMS: 220.0775 Found, 220.0767 Calculated for $C_{10}H_{15}NSONa$.



Crystal data for compound 2a

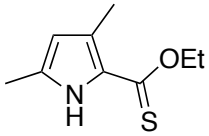
$C_{10}H_{15}NOS$, MM = 197.30 g/mol. Light-yellow plate crystal, dimensions 0.29 x 0.28 x 0.08 mm; triclinic space group, P_{-1} (#2); a = 7.215(2) Å, b = 8.581(3), c = 9.903(2) Å, α = 103.094(9)°, β = 93.3290(16)°, γ = 112.892(9)°, V = 542.8(3) Å^3; d = 1.207 g/cm^3, μ(Mo-Kα) = 2.609 cm^{-1}, 12478 reflections (4181 unique, R_{int} = 0.073), R = 0.0446, R_w = 0.0404, GOF = 1.062. CCDC deposition number: 1455753.

***O*-Benzyl-3,4,5-trimethyl-1*H*-pyrrole-2-carbothioate (2b)**



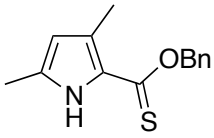
Thionoester **2b** was synthesized from **1b**[1] using GP1 to give the title compound as a yellow solid (105 mg, 49% yield). M.p. 40-43 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) 9.08 (br s, 1H, NH), 7.45 (d, 2H, *J* = 7.5 Hz, ArH), 7.39 (t, 2H, *J* = 7.5 Hz, ArH), 7.34 (t, 1H, *J* = 7.5 Hz, ArH), 5.69 (s, 2H, CH_2Ph), 2.21 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 1.90 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz, UDEFT) 203.2, 136.3, 129.5, 128.72, 128.66, 128.4, 128.3, 127.6, 119.4, 72.1, 12.4, 12.0, 8.8; LRMS: 282.1 $(M+Na)^+$; HRMS: 282.0924 Found, 282.0923 Calculated for $C_{15}H_{17}NSONa$.

***O*-Ethyl-3,5-dimethyl-1*H*-pyrrole-2-carbothioate (2c)**



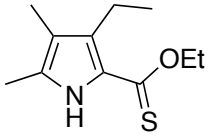
Thionoester **2c** was synthesized from **1c**[2] using GP1 to give the title compound as a yellow solid (392 mg, 72% yield). M.p. 86-88 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) 9.10 (br s, 1H, NH), 5.84 (d, 1H, J = 2.5 Hz, PyH), 4.65 (q, 2H, J = 7.2 Hz, CH_2CH_3), 2.30 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 1.46 (t, 3H, J = 7.2 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz, UDEFT) 199.8, 136.6, 129.5, 129.0, 113.4, 66.7, 14.6, 14.3, 13.5; LRMS: 184.1.1 $(M+H)^+$; HRMS: 184.0789 Found, 184.0791 Calculated for $C_9H_{14}NSO$.

***O*-Benzyl-3,5-dimethyl-1H-pyrrole-2-carbothioate (2d)**



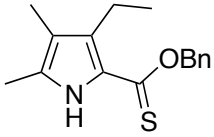
Thionoester **2d** was synthesized from **1d**[3] using GP1 to give the title compound as a yellow solid (108 mg, 50% yield). M.p. 51-53 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) 9.11 (br s, 1H, NH), 7.45 (d, 2H, J = 7.5 Hz, ArH), 7.39 (t, 2H, J = 7.5 Hz, ArH), 7.35 (t, 1H, J = 7.5 Hz, ArH), 5.85 (d, 1H, J = 2.5 Hz, PyH), 5.67 (s, 2H, CH_2Ph), 2.26 (s, 3H, CH_3), 2.25 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz, UDEFT) 199.2, 136.1, 129.5, 128.74, 128.67, 128.5, 128.3, 127.6, 113.6, 72.2, 14.9, 13.5; LRMS: 268.1 $(M+Na)^+$; HRMS: 268.0762 Found, 268.0767 Calculated for $C_{14}H_{15}NSONa$.

***O*-Ethyl-4,5-dimethyl-3-ethyl-1*H*-pyrrole-2-carbothioate (2e)**



Thionoester **2e** was synthesized from **1e**[4] using GP1 to give the title compound as a yellow solid (257 mg, 59% yield). M.p. 52-55 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) 9.08 (br s, 1H, NH), 4.67 (q, 2H, J = 7.2 Hz, CH_2CH_3), 2.72 (q, 2H, J = 7.5 Hz, CH_2CH_3), 2.19 (s, 3H, CH_3), 1.92 (s, 3H, CH_3), 1.46 (t, 3H, J = 7.2 Hz, CH_2CH_3), 1.10 (t, 3H, J = 7.5 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz, UDEFT) 199.4, 134.8, 132.5, 128.0, 118.4, 66.5, 19.6, 14.6, 14.1, 12.0, 8.6; LRMS: 212.1 $(M+H)^+$; HRMS: 212.1108 Found, 212.1104 Calculated for $C_{11}H_{18}NSO$.

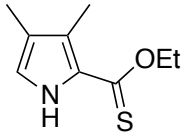
***O*-Benzyl-3-ethyl-4,5-dimethyl-1*H*-pyrrole-2-carbothioate (2f)**



Thionoester **2f** was synthesized from **1f**[5] using GP1 to give the title compound as a yellow oil (99 mg, 47% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) 9.13 (br s, 1H, NH), 7.47 (d, 2H, J = 7.5 Hz, ArH), 7.42-7.34 (m, 3H, ArH), 5.70 (s, 2H, CH_2Ph), 2.69 (q, 2H, J = 7.5 Hz, CH_2CH_3), 2.21 (s, 3H, CH_3), 1.93 (s, 3H, CH_3), 1.02 (t, 3H, J = 7.5 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz,

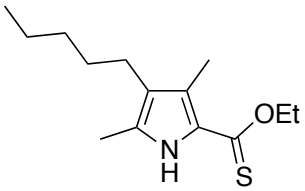
UDEFT) 198.6, 136.0, 129.5, 128.64, 128.56 (2 x C), 128.5, 128.3, 118.6, 72.2, 19.5, 14.7, 11.9, 8.5; LRMS: 296.1 $(M+H)^+$; HRMS: 296.1074 Found, 296.1080 Calculated for $C_{16}H_{19}NNaSO$.

***O*-Ethyl-3,4-dimethyl-1*H*-pyrrole-2-carbothioate (2g)**



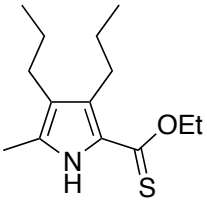
Thionoester **2g** was synthesized from **1g**[5] using GP1 to give the title compound as a yellow solid (192 mg, 58% yield). M.p. 36-38 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) 9.20 (br s, 1H, NH), 6.78 (ad, 1H, J = 2.5 Hz, PyH), 4.68 (q, 2H, J = 7.0 Hz, CH_2CH_3), 2.27 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 1.48 (t, 3H, J = 7.0 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz, UDEFT) 201.0, 130.5, 124.8, 123.9, 122.0, 66.9, 14.2, 11.8, 10.1; LRMS: 184.1 $(M+H)^+$; HRMS: 184.0798 Found, 184.0791 Calculated for $C_9H_{14}NSO$.

***O*-Ethyl-3,5-dimethyl-4-pentyl-1*H*-pyrrole-2-carbothioate (2h)**



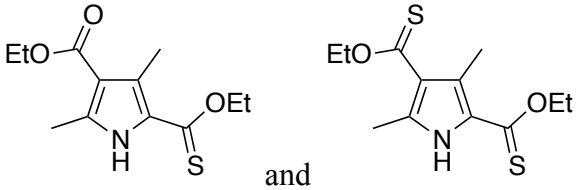
Thionoester **2h** was synthesized from **1h**[6] using GP1 to give the title compound as a yellow solid (343 mg, 64% yield). M.p. 44-47 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) 9.07 (br s, 1H, NH), 4.66 (q, 2H, J = 7.0 Hz, CH_2CH_3), 2.33 (t, 2H, J = 7.8 Hz, PyrrCH$_2$), 2.25 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 1.46 (t, 3H, J = 7.0 Hz, CH_2CH_3), 1.43-1.38 (m, 2H, CH_2), 1.34-1.26 (m, 4H, 2 x CH_2), 0.89 (t, 3H, J = 7.0 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz, UDEFT) 199.5, 134.6, 128.7, 126.1, 124.5, 66.5, 31.7, 30.6, 24.0, 22.7, 14.3, 14.2, 12.2, 12.0; LRMS: 254.2 $(M+H)^+$; HRMS: 254.1573 Found, 254.1573 Calculated for $C_{14}H_{24}NSO$.

***O*-Ethyl-3,4-dipropyl-5-methyl-1*H*-pyrrole-2-carbothioate (2i)**



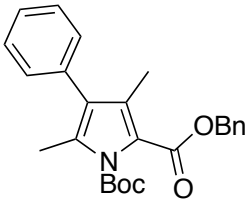
Thioester **2i** was synthesized from **1j**[4] using GP1 to give the title compound as a yellow solid (292 mg, 68% yield). M.p. 31-33 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) 9.06 (br s, 1H, NH), 4.66 (q, 2H, J = 7.1 Hz, CH_2CH_3), 2.52 (t, 2H, J = 7.8 Hz, CH_2Py), 2.32 (t, 2H, J = 7.8 Hz, CH_2Py), 2.26 (s, 3H, CH_3), 1.68-1.60 (m, 2H, CH_2), 1.46 (t, 3H, J = 7.1 Hz, CH_2CH_3), 1.47-1.41 (m, 2H, CH_2), 0.98 (t, 3H, J = 7.5 Hz, CH_2CH_3), 0.92 (t, 3H, J = 7.5 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz, UDEFT) 199.6, 139.2, 128.8, 125.6, 124.1, 66.5, 28.4, 26.0, 24.3, 22.7, 14.3, 14.1 (2 x C), 12.2; LRMS: 254.2 $(M+H)^+$; HRMS: 254.1563 Found, 254.1573 Calculated for $C_{14}H_{24}NSO$.

Ethyl 5-(ethoxycarbonothioyl)-2,4-dimethyl-1*H*-pyrrole-3-carboxylate (2j) and *O*,*O*-diethyl 3,5-dimethyl-1H-pyrrole-2,4-bis(carbothioate) (2jS)



Thionoester **2j** was synthesized from **1j7** using GP1 with a reaction time of 4 hours to give the title compound as a pale yellow solid (111 mg, 52% yield). M.p. 107-109 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) 9.36 (br s, 1H, NH), 4.68 (q, 2H, J = 7.3 Hz, CH_2CH$_3$), 4.30 (q, 2H, J = 7.3 Hz, CH_2CH$_3$), 2.58 (s, 3H, CH$_3$), 2.51 (s, 3H, CH$_3$), 1.49 (t, 3H, J = 7.3 Hz, CH$_2$CH_3), 1.36 (t, 3H, J = 7.3 Hz, CH$_2$CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz, UDEFT) 201.3, 165.6, 141.7, 128.7, 128.5, 115.0, 67.5, 59.8, 14.9, 14.6, 14.1, 13.2; LRMS: 278.1 $(M+Na)^+$; HRMS: 278.0832 Found, 278.0821 Calculated for $C_{12}H_{17}NSO_3Na$. After column chromatography according to GP1, dthionoester **2jS** was also isolated as a yellow solid (17 mg, 7% yield). M.p. 77-79 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) 9.40 (br s, 1H, NH), 4.69 (q, 2H, J = 7.0 Hz, CH_2CH_3), 4.64 (q, 2H, J = 7.0 Hz, CH_2CH_3), 2.58 (s, 3H, CH_3), 2.57 (s, 3H, CH_3), 1.48 (aq, 6H, J = 7.0 Hz, 2 x CH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz, UDEFT) 207.7, 201.4, 141.2, 128.2, 126.2, 126.1, 67.6, 66.8, 16.2, 14.1, 14.0, 13.9; LRMS: 272.1 $(M+H)^+$; HRMS (APCI): 272.0771 Found, 272.0773 Calculated for $C_{12}H_{18}NS_2O_2$.

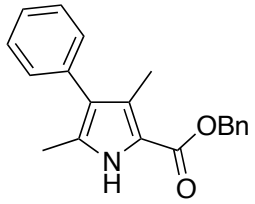
Benzyl 3,5-dimethyl-4-phenyl-1-Boc-pyrrole-2-carboxylate (1kBOC)



NaHMDS (1 M in THF, 1.55 mL, 1.55 mmol) was added drop-wise over several minutes to a solution of benzyl 4-iodo-3,5-dimethyl-1H-pyrrole-2-carboxylate[8] (500 mg, 1.41 mmol) in THF (20 mL), with stirring under nitrogen at 0 °C. After 1 hour, $(BOC)_2O$ (323 mg, 1.48 mmol) was added to the reaction mixture in one portion. After stirring at 40 °C overnight, the reaction mixture was separated between diethyl ether (30 mL) and water (30 mL). The aqueous phase was extracted with diethyl ether (2 x 30 mL) and the combined organic extracts were washed with brine (80 mL), then dried over anhydrous magnesium sulfate and concentrated to give the crude product, which was partially purified over silica, eluting with 10% ethyl acetate/hexanes. The crude BOC-protected pyrrole was then subjected to Suzuki coupling reaction conditions, without further purification. Tetrakis(triphenylphosphine)palladium (38 mg, 0.033 mmol) and potassium carbonate (91 mg, 0.66 mmol) were added to a stirred solution of BOC protected **1kSM**, (200 mg, 0.33 mmol) and phenylboronic acid (48 mg, 0.39 mmol) in toluene (2.0 mL) and the resulting suspension was bubbled with nitrogen for 10 minutes. Degassed (N_2) water (0.7 mL) was then added and the flask was sealed before heating the reaction mixture to 120 °C, with stirring for 24 hours. After cooling to room temperature, the reaction mixture was separated between dichloromethane (20 mL) and water (20 mL). The aqueous phase was extracted with dichloromethane (3 x 20 mL) and the combined organic extracts were washed with brine (80

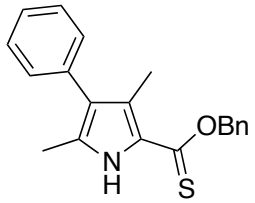
mL), then dried over anhydrous sodium sulfate and concentrated to give the crude product. Purification using column chromatography on silica, eluting with 15% diethyl ether/hexanes gave the title compound (**1kBOC**, 133 mg, 42% over two steps) as a colourless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) 7.46-7.29 (m, 8H, ArH), 7.22-7.19 (m, 2H, ArH), 5.34 (s, 2H, CH_2), 2.29 (s, 2H, CH_3), 2.15 (s, 2H, CH_3), 1.54 (s, 9H, ^{t}Bu); LRMS: 428.1 $(M+Na)^+$; HRMS: 428.1850 Found, 428.1832 Calculated for $C_{25}H_{27}NO_4Na$. This material was used for the synthesis of **1k**, without further characterization.

Benzyl 3,5-dimethyl-4-phenyl-1*H*-pyrrole-2-carboxylate (1k)



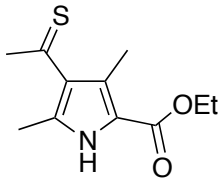
TFA (0.5 mL, 6.63 mmol) was added drop-wise to a solution of **1kBOC** (128 mg, 0.316 mmol) in anhydrous dichloromethane (1 mL), with stirring at room temperature under nitrogen for 45 minutes. The reaction mixture was then cooled to 0 °C and neutralized slowly with 6 M aq. NaOH (1.1 mL), before partitioning between dichloromethane (20 mL) and water (20 mL). The aqueous phase was extracted with dichloromethane (2 x 20 mL) and the combined organic extracts were washed with brine (50 mL), then dried over anhydrous sodium sulfate and concentrated to give the crude product. Purification using column chromatography on silica, eluting with 30% ethyl acetate/hexanes, gave the title compound as a pale pink solid (91 mg, 94% yield). M.p. 116-119 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) 8.78 (br s, 1H, NH), 7.44 (d, 2H, J = 7.5 Hz, ArH), 7.40 (aq, 4H, J = 7.8 Hz, ArH), 7.34 (t, 1H, J = 7.3 Hz, ArH), 7.29 (t, 1H, J = 7.3 Hz, ArH), 7.24 (d, 2H, J = 7.0 Hz, ArH), 5.34 (s, 2H, CH_2Ph), 2.32 (s, 3H, CH_3), 2.25 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz, UDEFT) 161.5, 136.7, 135.0, 130.2 (2 x C), 128.7, 128.4, 128.3, 128.2, 126.4, 125.0, 117.2, 65.7, 12.3, 11.6 (1 x C missing); LRMS: 328.1 $(M+Na)^+$; HRMS: 328.1313 Found, 328.1308 Calculated for $C_{20}H_{19}NO_2Na$.

***O*-Benzyl 3,5-dimethyl-4-phenyl-1*H*-pyrrole-2-carbothioate (2k)**



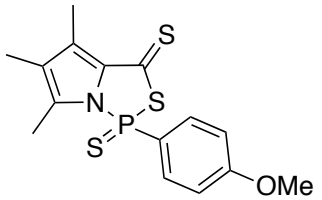
Thionoester **2k** was synthesized from **1k** using GP1 and a reaction time of 4 hours to give the title compound as a yellow solid (73 mg, 55% yield). M.p. 78-80 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) 9.29 (br s, 1H, NH), 7.47 (d, 2H, J = 7.5 Hz, ArH), 7.42-7.38 (m, 4H, ArH), 7.36-7.33 (m, 1H, ArH), 7.30 (t, 1H, J = 7.5 Hz, ArH), 7.21 (d, 2H, J = 7.0 Hz, ArH), 5.72 (s, 2H, CH_2Ph), 2.26 (s, 3H, CH_3), 2.25 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz, UDEFT) 199.4, 136.1, 134.5, 130.4, 130.3, 129.6, 128.7, 128.5, 128.42, 128.38, 126.8, 126.7, 72.4, 13.2, 12.6 (1 x C missing); LRMS: 344.1 $(M+Na)^+$; HRMS: 344.1081 Found, 344.1080 Calculated for $C_{20}H_{19}NSONa$.

Ethyl 4-ethanethioyl-3,5-dimethyl-1*H*-pyrrole-2-carboxylate (2l)

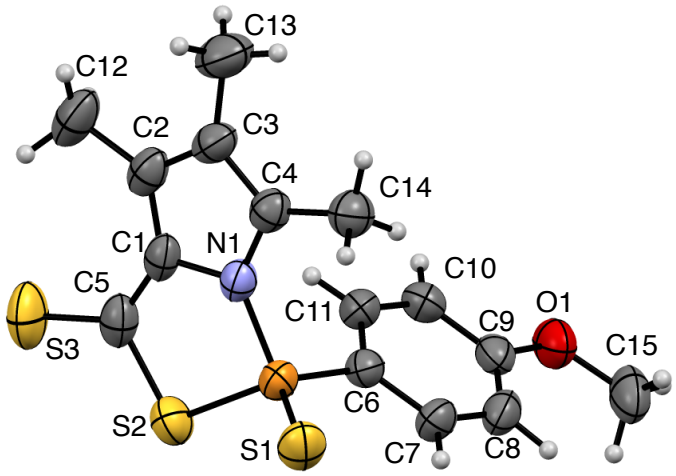


Thionoester **2l** was synthesized from **1l**[9] using GP1 and purified using column chromatography over silica, eluting with 20% ethyl acetate/hexanes, to give the title compound as a pink solid (132 mg, 61% yield). M.p. 155-160 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) 8.99 (br s, 1H NH), 4.35 (q, 2H, J = 7.0 Hz, CH_2CH_3), 3.03 (s, 3H, C(S)CH_3), 2.60 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 1.38 (t, 3H, J = 7.0 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz, UDEFT) 235.0, 161.7, 137.5, 134.8, 127.3, 118.2, 60.7, 42.6, 16.6, 14.6, 13.6; LRMS: 248.1 $(M+Na)^+$; HRMS: 248.0720 Found, 248.0716 Calculated for $C_{11}H_{15}NSO_2Na$. Crystal data for **2l**, included for completeness and verification of position of C=S bond: $C_{12}H_{18}NO_{3.50}S$, MM = 264.34 g/mol. Dark red needle, dimensions 0.31 x 0.03 x 0.02 mm; monoclinic space group, P21/n (#14); a = 4.2608(3) Å, b = 25.2486(15), c = 14.5750(9) Å, β = 98.524(4) º, V = 1550.65(17) Å3; d = 1.132 g/cm^3, μ(Mo-Kα) = 2.100 cm^{-1}, 19739 reflections (5366 unique, R_{int} = 0.235), R = 0.0446, R_w = 0.1497, GOF = 1.206. Not desposited in CCDC as data is obviously inadequate beyond showing location of sulfur atom (beta thiocarbonyl functionality). Attempts to grow larger crystals were met with disappointment.

1-(4-Methoxyphenyl)-4,5,6-trimethylpyrrolo[1,2-c][1,3,2]thiazaphosphole-3(1H)-thione-1-sulfide (3)



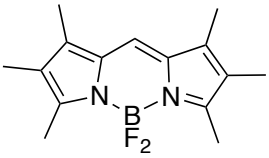
A suspension of thionoester **2a** (50 mg, 0.25 mmol) and Lawesson's reagent (77 mg, 0.19 mmol, 1.5 equiv.) in anhydrous *p*-xylene (0.5 mL), in a sealed flask under nitrogen, was placed in a sand bath preheated to 140 °C and heated with stirring for 1.5 hours. After this time, the reaction mixture was allowed to cool to room temperature before being poured into 30% ethyl acetate/hexanes (20 mL), rinsing the flask with ethyl acetate. The solution was then filtered, washing with 30% ethyl acetate/hexanes, and the filtrate concentrated to give the crude product, which was purified quickly using column chromatography over silica eluting with 15% ethyl acetate/hexanes, then again eluting with 45% dichloromethane in hexanes, if necessary, to give the title compound as an orange solid (30 mg, 33% yield). M.p. 125-127 °C; λ_{max} CH_2Cl_2 404 (ε 29 000), 279 (ε 20 000); ^{1}H NMR ($CDCl_3$, 500 MHz) 7.82 (dd, 2H, J = 15.2, 9.0 Hz, ArH), 6.99 (dd, 2H, J = 9.0, 3.5 Hz, ArH), 3.88 (s, 3H, OMe), 2.43 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 1.94 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) 194.0, 164.0, 139.5, 138.2 (d), 134.0 (d), 130.2 (d), 124.8, 124.0, 114.7 (d), 55.8, 12.0, 11.3, 9.4; ^{31}P NMR ($CDCl_3$, 202 MHz) 63.4 (t, J = 15.2 Hz); LRMS: 376.0 $(M+Na)^+$; HRMS: 376.0014 Found, 376.0024 Calculated for $C_{15}H_{16}NPS_3O$.



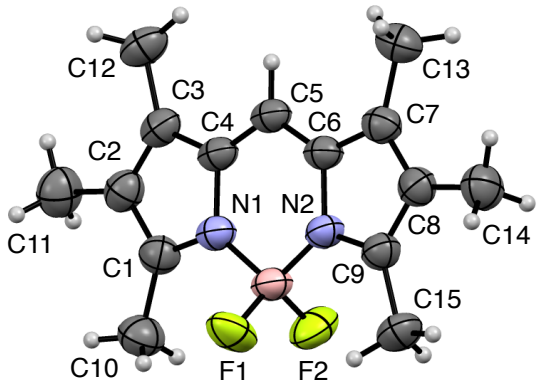
Crystal data for compound 3

$C_{15}H_{16}NPS_3O$, MM = 353.46 g/mol. Orange plate crystal, dimensions 0.27 x 0.26 x 0.09 mm; monoclinic space group, $P2_1/n$; a = 7.4515(15) Å, b = 11.579(2), c = 19.631(3) Å, α = 90 º, β = 97.168(6) º, γ = 90 º, V = 1680.5(5) $Å^3$; d = 1.397 g/cm^3, μ(Mo-Kα) = 5.33 cm^{-1}, 21248 reflections (5767 unique, R_{int} = 0.048), R = 0.0292, R_w = 0.0357, GOF = 1.096. CCDC deposition number: 1455752.

4,4-Difluoro-1,2,3,5,6,7-hexamethyl-8*H*-4-bora-3a,4a-diaza-s-indacene (4a)



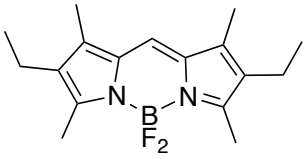
A mixture of **1a** (100 mg, 0.55 mmol) and Lawesson's reagent (223 mg, 0.55 mmol) was prepared in a 0.5-2.0 mL capacity microwave vial under nitrogen using a cap bearing a septum. A suspension was formed upon addition of toluene (1 mL) with vigorous stirring. $BF_3 \square OEt_2$ (0.27 mL, 2.2 mmol, 4 equiv.) was then added drop-wise, via the septum, and the vial was heated in a microwave reactor at 160 °C for 20 minutes before being allowed to cool to room temperature. The reaction mixture was diluted with ethyl acetate (2 mL), then poured into a 20% ethyl acetate/hexanes solution (30 mL). The solution was filtered through a short pad of silica, washing with 30% ethyl acetate/hexanes, and then concentrated. The crude product was purified over neutral alumina (Brockmann type III), eluting slowly with 5-20% dichloromethane/hexanes, to give the title compound as a deep red crystalline solid (8 mg, 11% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) 6.94 (s, 1H, *meso*-H), 2.48 (s, 6H, 2 x CH_3), 2.15 (s, 6H, 2 x CH_3), 1.93 (s, 6H, 2 x CH_3); ^{11}B NMR ($CDCl_3$, 160 MHz) 0.87 (t, J = 33 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz): -146.4 (q, J = 34 Hz); this data matches literature values.[10]



Crystal data for compound 4a

$C_{15}H_{19}N_2BF_2$, MM = 197.30 g/mol. Deep-red needle crystal, dimensions 0.42 x 0.19 x 0.08 mm; monoclinic space group, $P2_1/n$; a = 7.2351(6) Å, b = 16.6785(14), c = 11.8701(10) Å, α = 90 º, β = 98.682(4)°, γ = 90 º, V = 1416.0(2) $Å^3$; d = 1.295 g/cm^3, μ(Mo-Kα) = 0.940 cm^{-1}, 12329 reflections (3788 unique, R_{int} = 0.025), R = 0.0485, R_w = 0.0576 , GOF = 1.089. CCDC deposition number: 1468172.

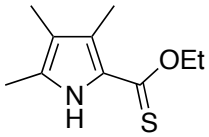
2,6-Diethyl-4,4-difluoro-1,3,5,7-tertamethyl-8-H-4-bora-3a,4a-diaza-s-indacene (4b)



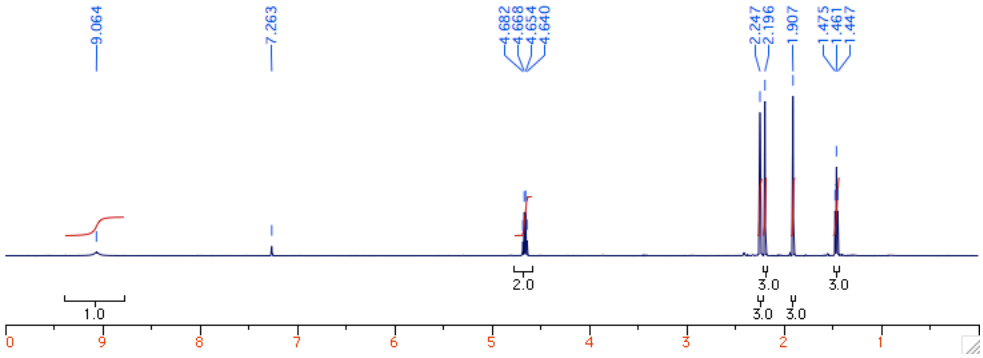
A mixture of **1p** (0.55 mmol, 1 equiv.) and Lawesson's reagent (223 mg, 0.55 mmol, 2 equiv.) was prepared in a 0.5-2.0 mL capacity microwave vial under nitrogen using a cap bearing a septum. A suspension was formed upon addition of toluene (1 mL) with vigorous stirring. BF_3□OEt_2 (0.27 mL, 2.2 mmol, 4 equiv.) was then added drop-wise, via the septum, and the vial was heated in a microwave reactor at 160 °C for 20 minutes before being cooled to room temperature. The mixture was diluted with ethyl acetate (2 mL), then poured into a 20% ethyl acetate/hexanes solution (30 mL). The solution was filtered through a short pad of silica, washing with 30% ethyl acetate/hexanes, and then concentrated. The crude product was purified over neutral alumina (Brockmann type III), eluting slowly with 5-20% DCM/hexanes, to give the title compound as a deep red crystalline solid (8 mg, 11% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) 6.95 (s, 1H, *meso*-H), 2.50 (s, 6H, 2 x CH_3), 2.38 (q, *J* = 7.6 Hz, 4H, 2 x CH_2), 2.16 (s, 6H, 2 x CH_3), 1.06 (t, *J* = 7.6 Hz, 6H, 2 x CH_2*CH_3*); ^{11}B NMR ($CDCl_3$, 160 MHz): 0.89 (t, J = 34 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz): -146.3 (q, *J* = 34 Hz); this data matches literature values.[11]

Copies of NMR spectra

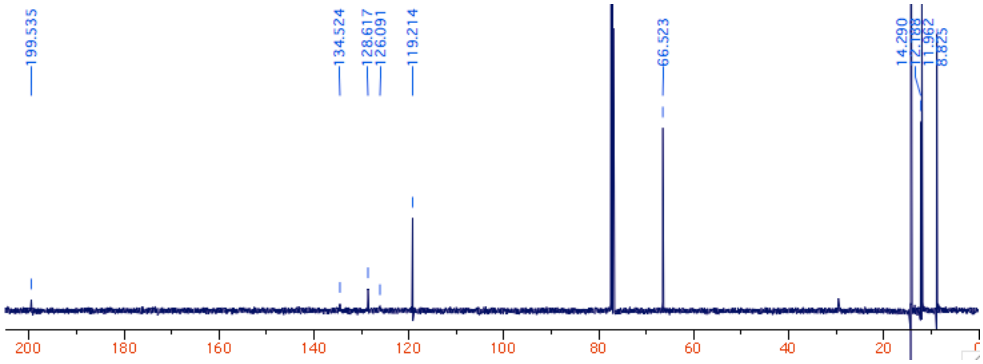
O-Ethyl-3,4,5-trimethyl-1H-pyrrole-2-carbothioate (2a)



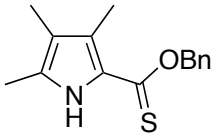
^{1}H NMR ($CDCl_3$, 500 MHz):



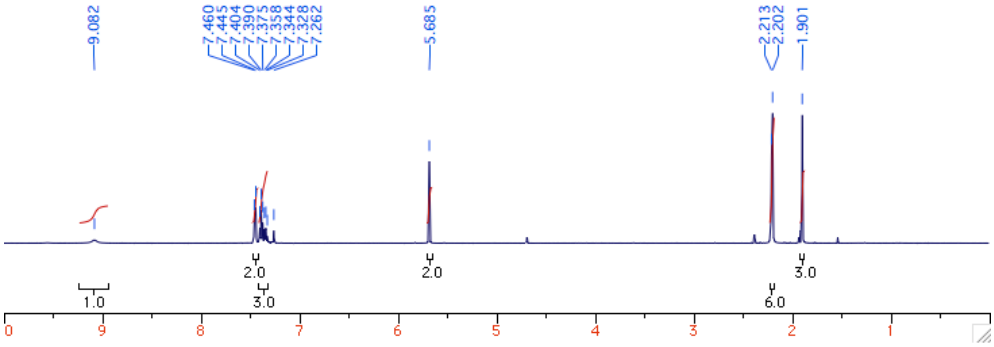
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



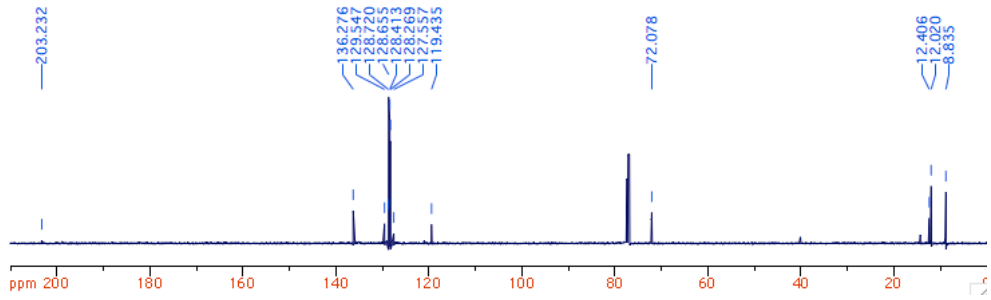
O-Benzyl-3,4,5-trimethyl-1H-pyrrole-2-carbothioate (2b)



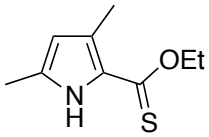
^{1}H NMR ($CDCl_3$, 500 MHz):



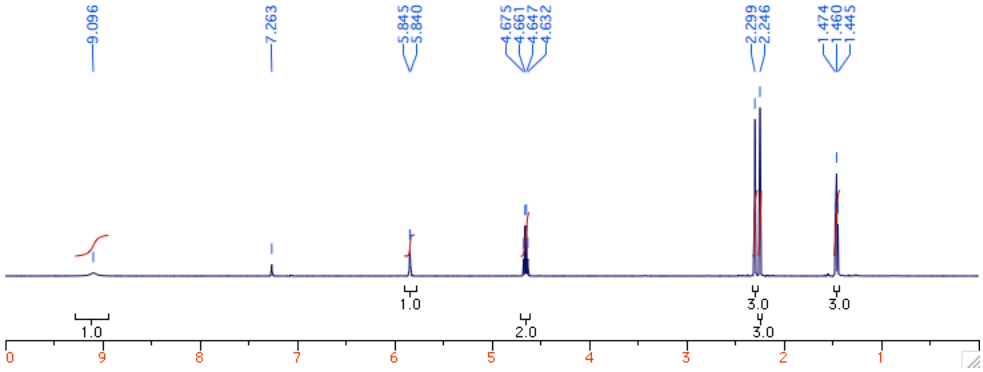
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



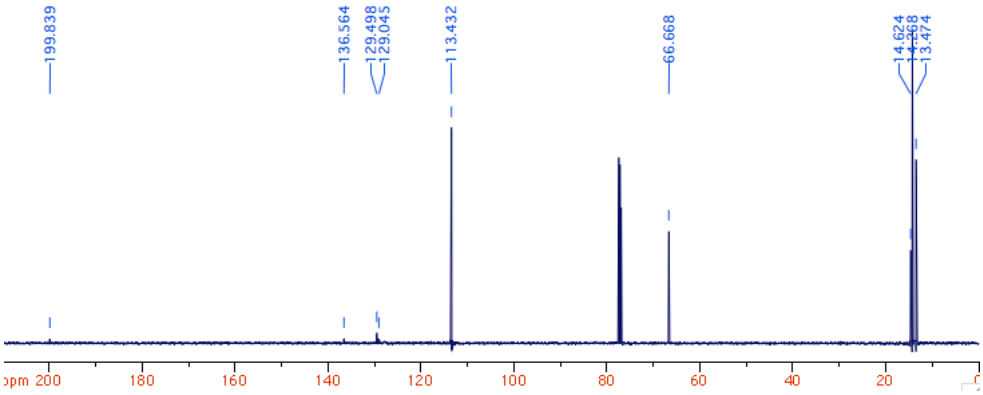
O-Ethyl-3,5-dimethyl-1H-pyrrole-2-carbothioate (2c)



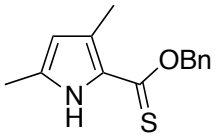
^{1}H NMR ($CDCl_3$, 500 MHz):



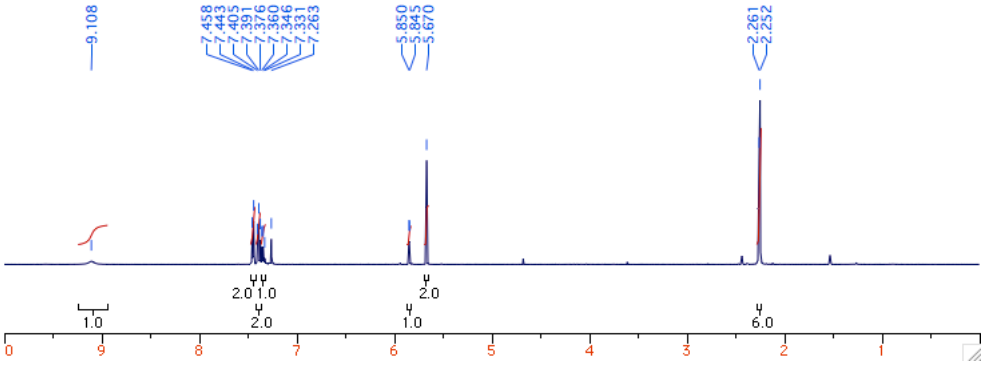
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



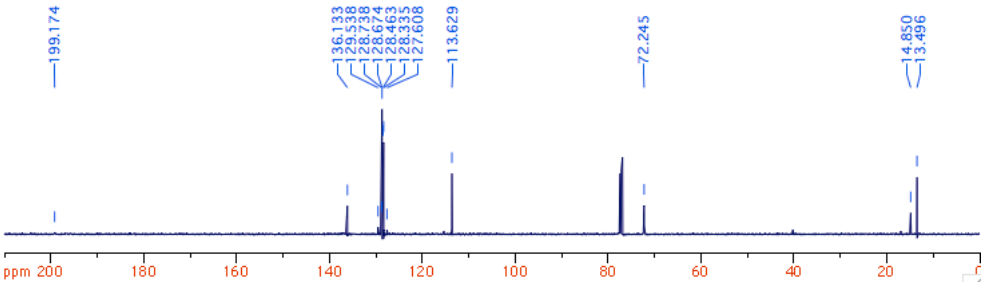
O-Benzyl-3,5-dimethyl-1H-pyrrole-2-carbothioate (2d)



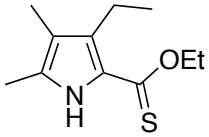
^{1}H NMR ($CDCl_3$, 500 MHz):



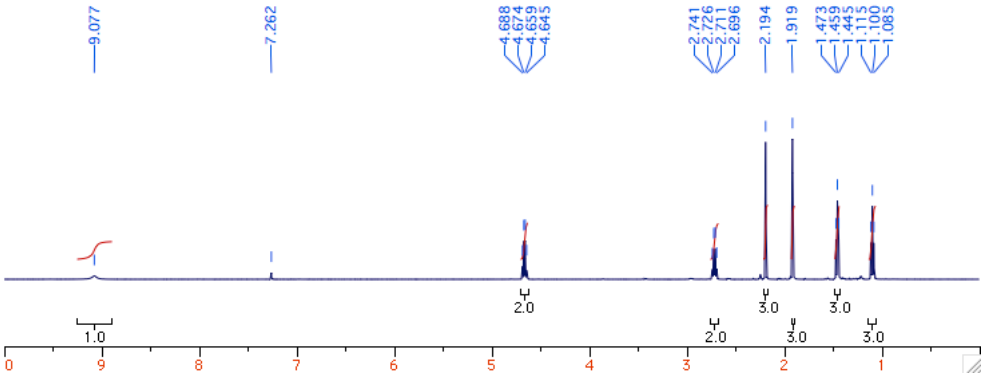
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



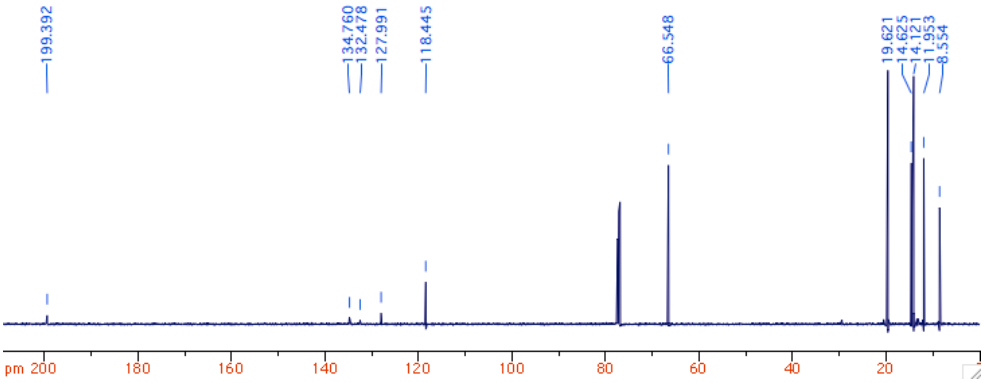
O-Ethyl-4,5-dimethyl-3-ethyl-1H-pyrrole-2-carbothioate (2e)



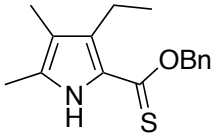
^{1}H NMR ($CDCl_3$, 500 MHz):



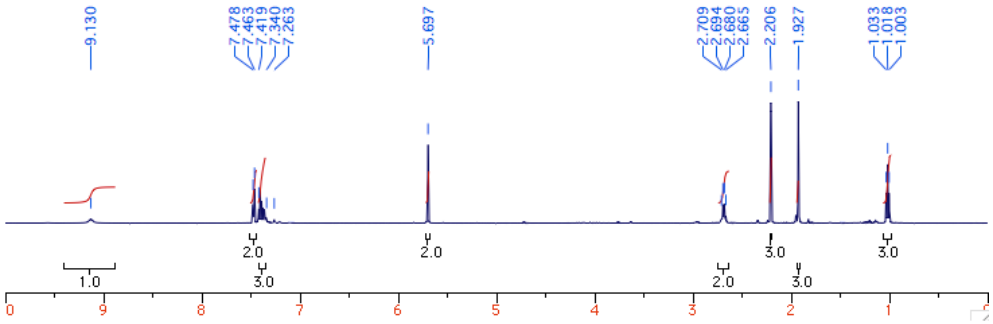
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



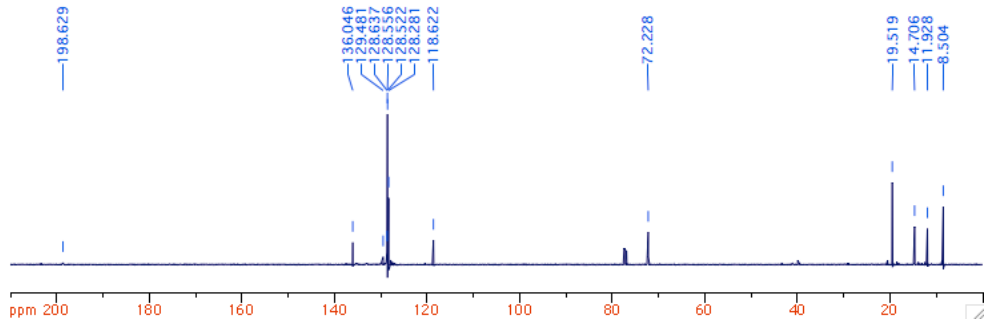
O-Benzyl-3-ethyl-4,5-dimethyl-1H-pyrrole-2-carbothioate (2f)



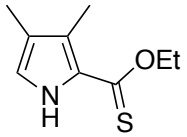
^{1}H NMR ($CDCl_3$, 500 MHz):



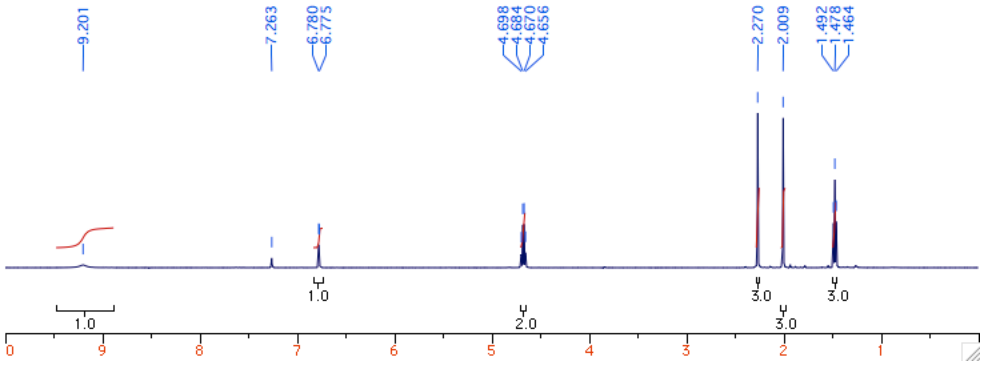
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



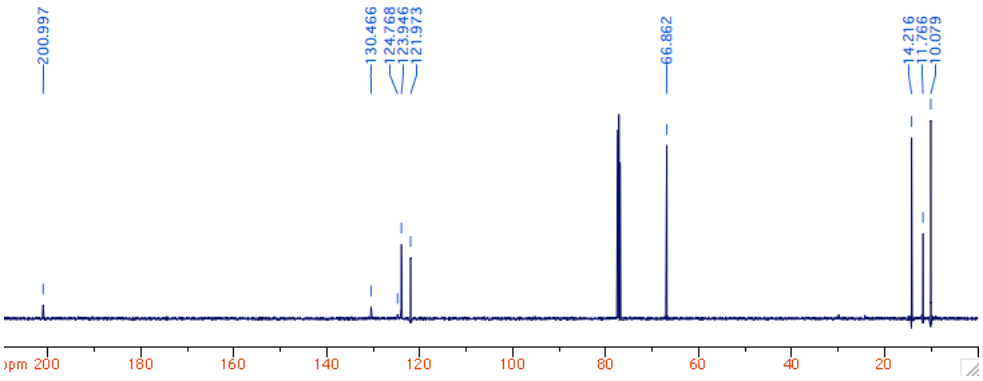
O-Ethyl-3,4-dimethyl-1H-pyrrole-2-carbothioate (2g)



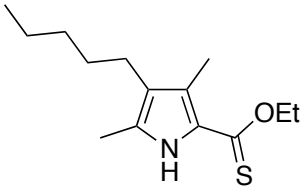
^{1}H NMR ($CDCl_3$, 500 MHz):



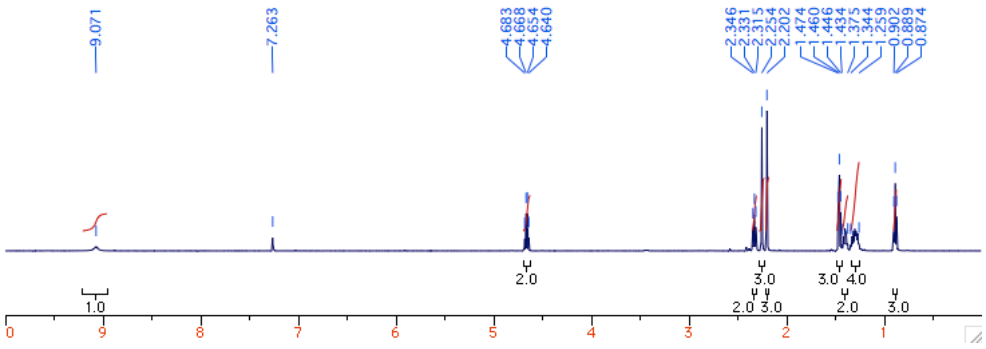
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



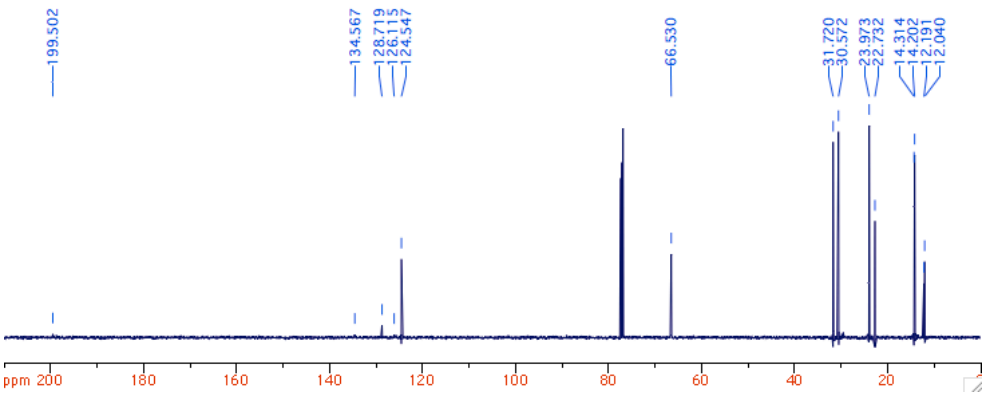
O-Ethyl-3,5-dimethyl-4-pentyl-1H-pyrrole-2-carbothioate (2h)



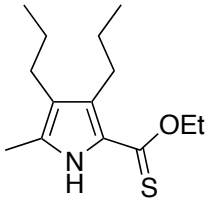
^{1}H NMR ($CDCl_3$, 500 MHz):



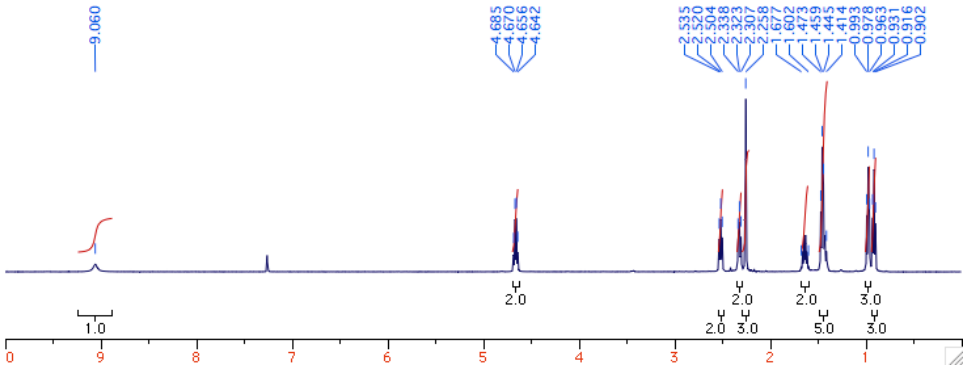
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



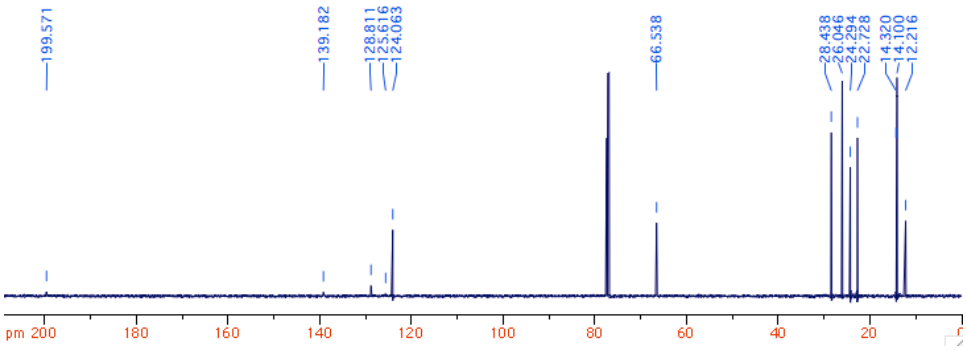
O-Ethyl-3,4-dipropyl-5-methyl-1H-pyrrole-2-carbothioate (2i)



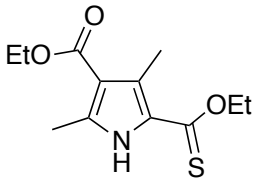
^{1}H NMR ($CDCl_3$, 500 MHz):



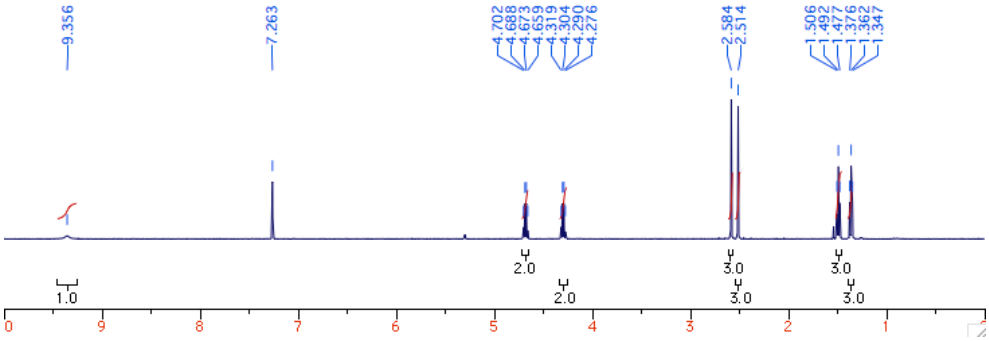
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



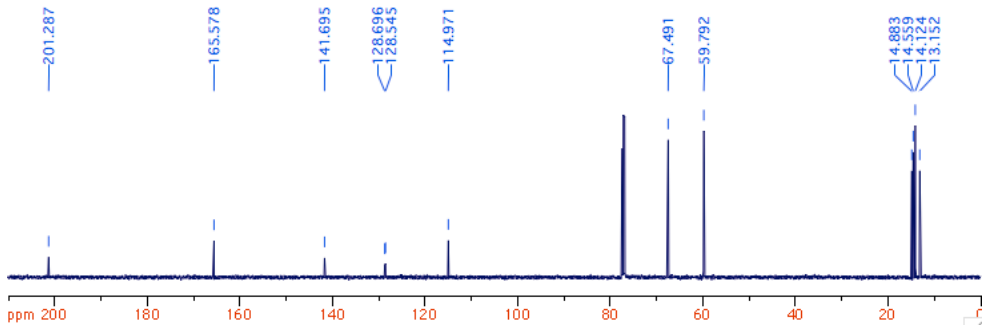
Ethyl 4-(ethoxycarbonothioyl)-3,5-dimethyl-1H-pyrrole-2-carboxylate (2j)
major product, as determined via X-ray structure after chromatographic separation of product mixture)



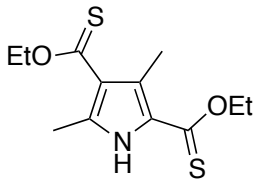
^{1}H NMR ($CDCl_3$, 500 MHz):



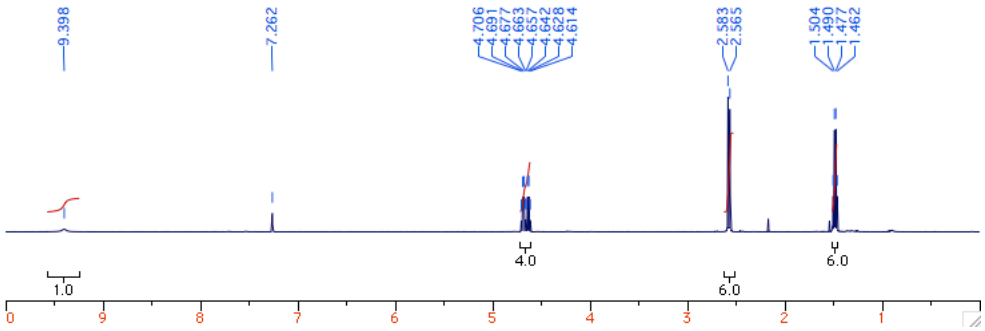
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



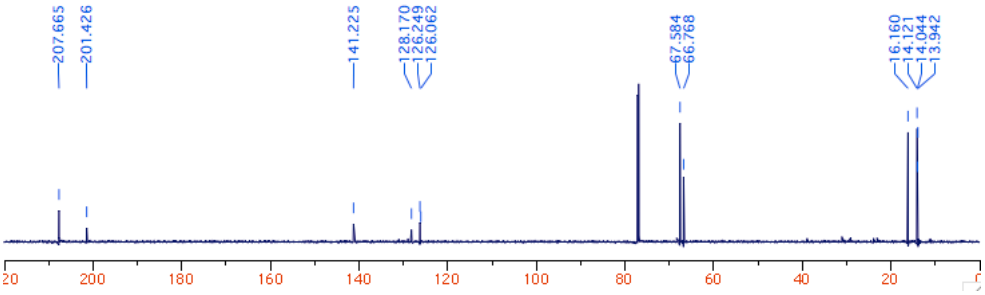
O,*O*-Diethyl 3,5-dimethyl-1H-pyrrole-2,4-bis(carbothioate) (2jS)



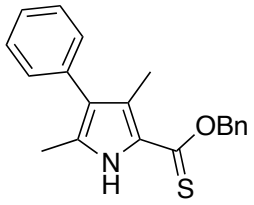
^{1}H NMR ($CDCl_3$, 500 MHz):



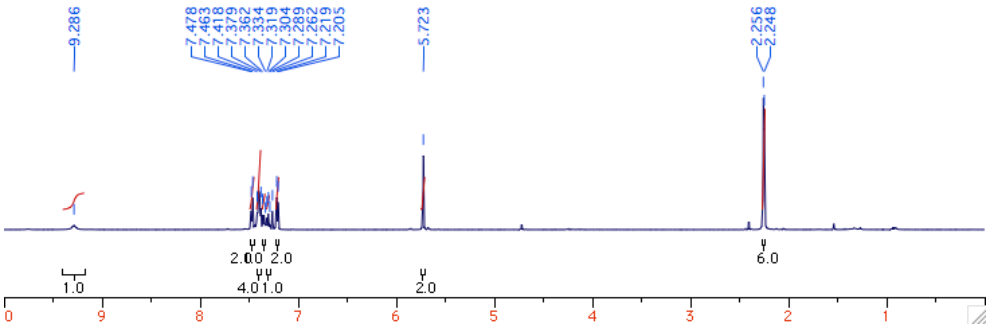
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



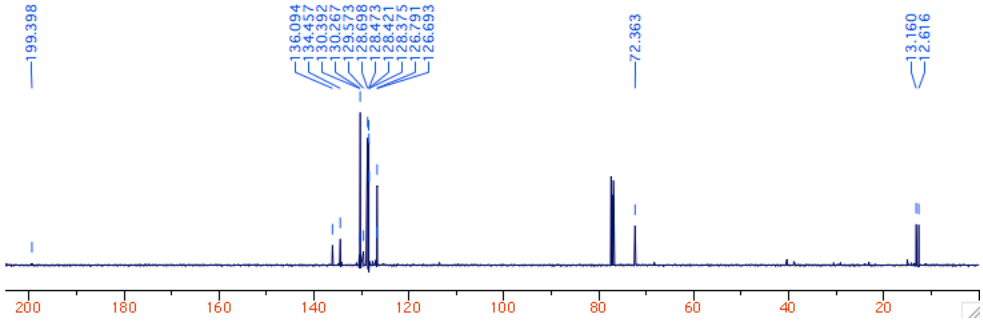
O-Benzyl 3,5-dimethyl-4-phenyl-1H-pyrrole-2-carbothioate (2k)



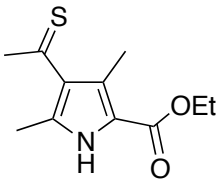
^{1}H NMR ($CDCl_3$, 500 MHz):



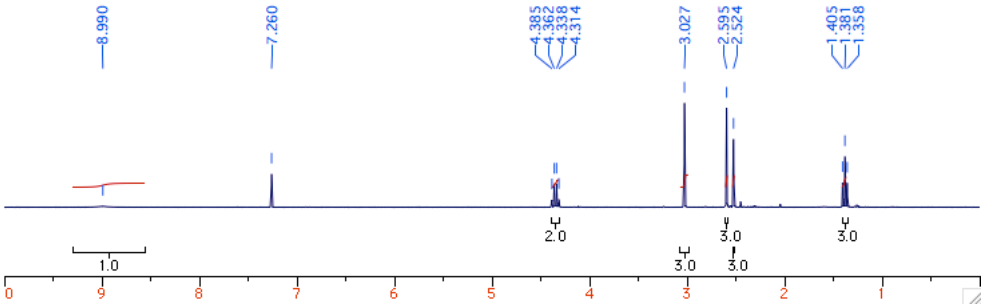
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



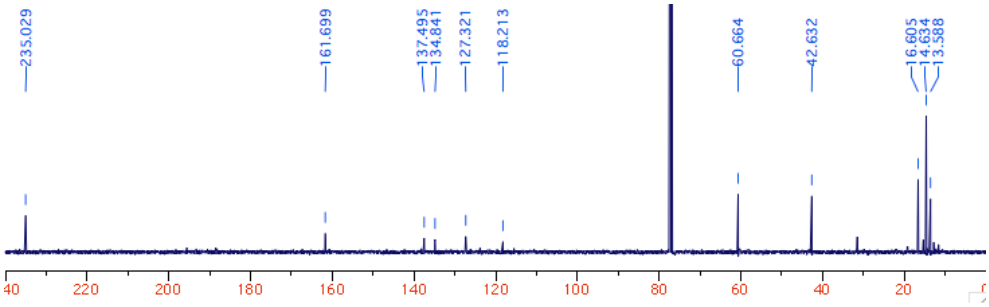
Ethyl 4-ethanethioyl-3,5-dimethyl-1H-pyrrole-2-carboxylate (2l)



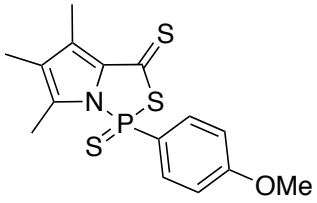
^{1}H NMR ($CDCl_3$, 500 MHz):



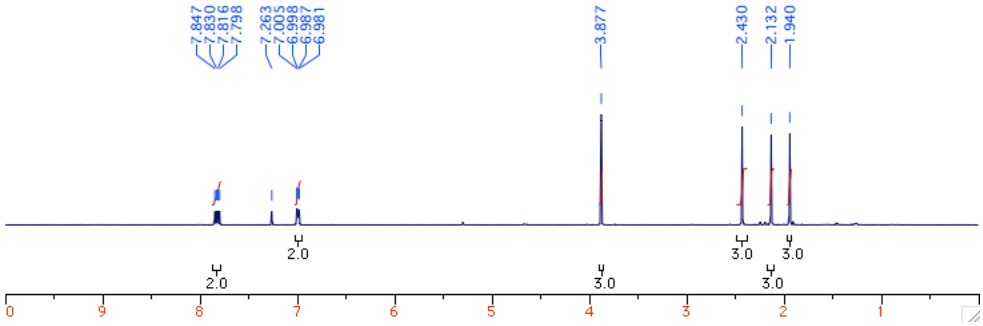
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



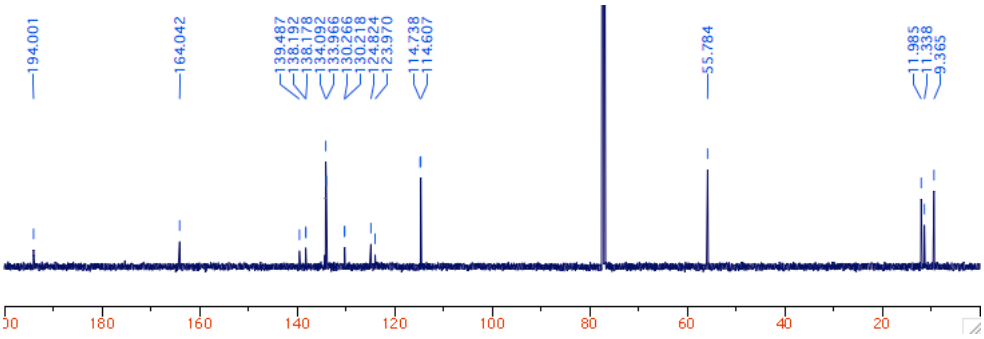
1-(4-Methoxyphenyl)-4,5,6-trimethylpyrrolo[1,2-c][1,3,2]thiazaphosphole-3(1H)-thione-1-sulfide (3)



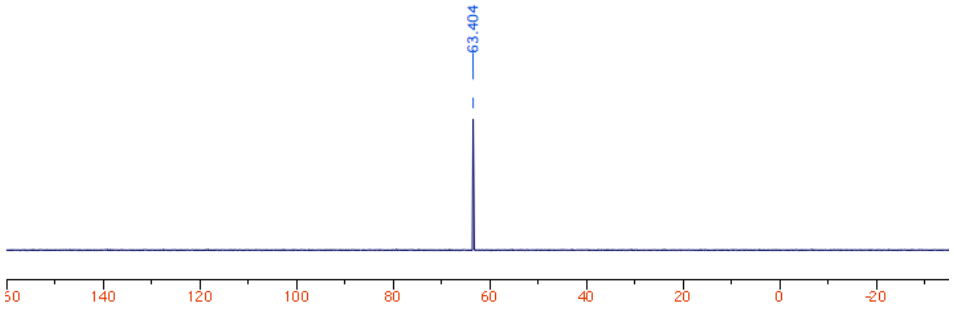
^{1}H NMR ($CDCl_3$, 500 MHz):



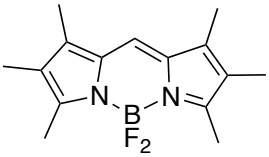
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



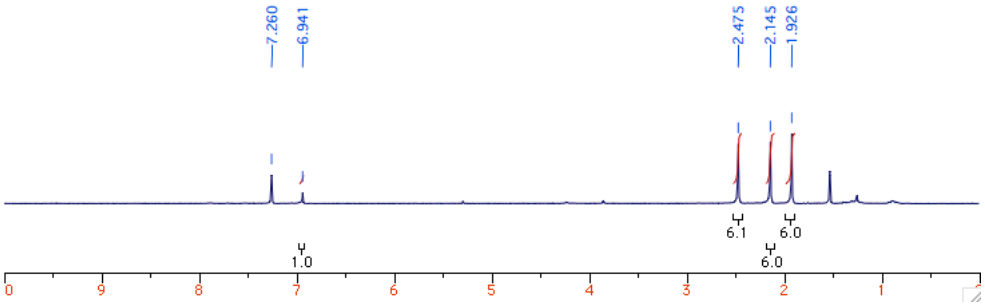
^{31}P NMR ($CDCl_3$, 202 MHz):



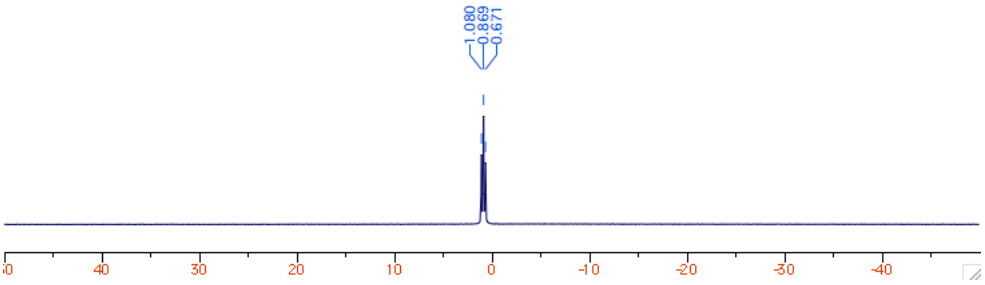
4,4-Difluoro-1,2,3,5,6,7-hexamethyl-8-H-4-bora-3a,4a-diaza-*s*-indacene (4a)



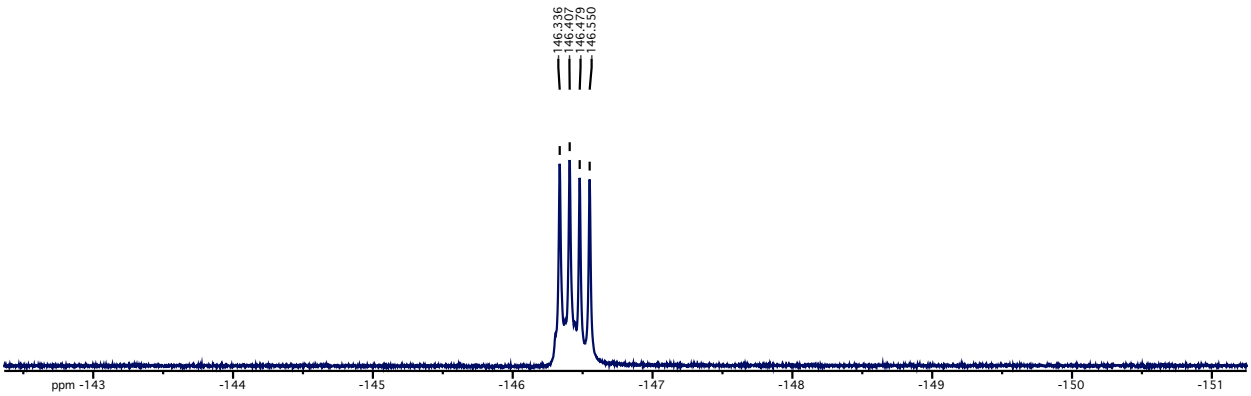
^{1}H NMR ($CDCl_3$, 500 MHz):



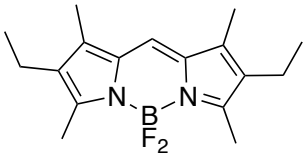
^{11}B NMR ($CDCl_3$, 160 MHz):



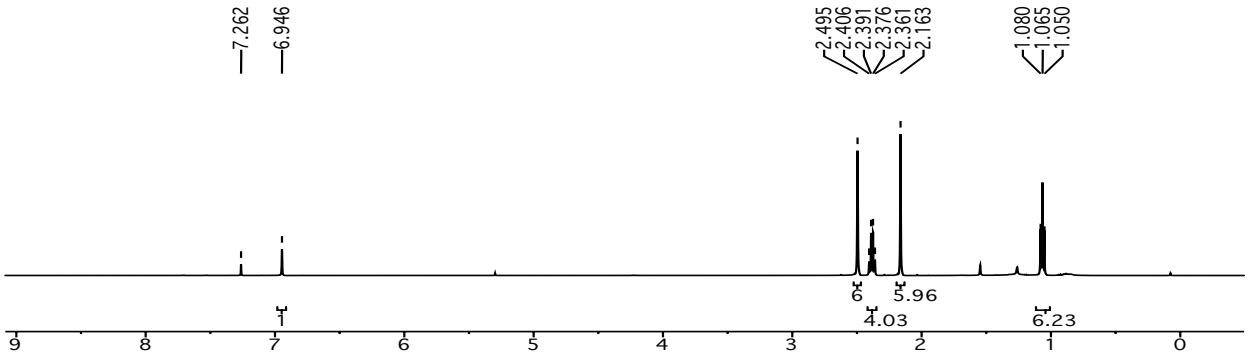
^{19}F NMR ($CDCl_3$, 470 MHz):



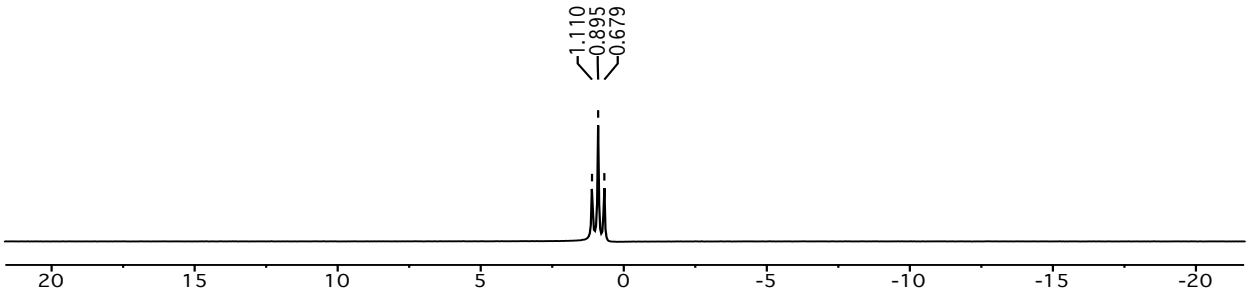
2,6-Diethyl-4,4-difluoro-1,3,5,7-tertamethyl-8-H-4-bora-3a,4a-diaza-*s*-indacene (4b)



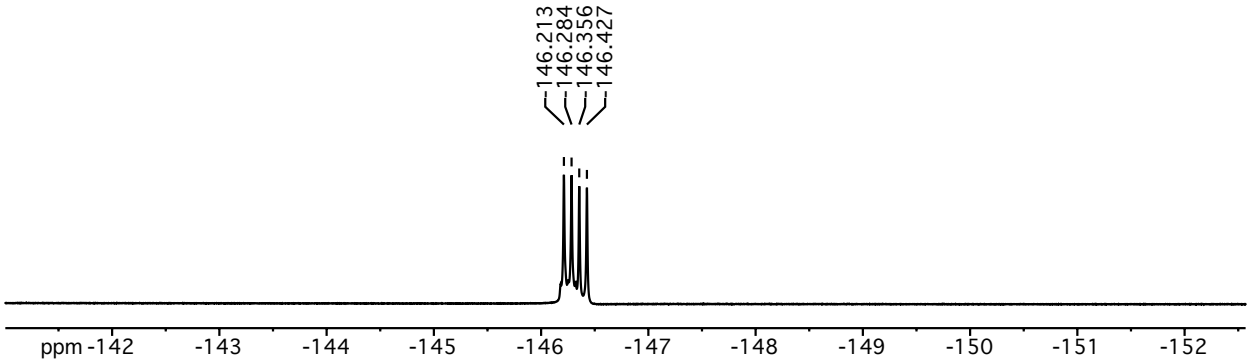
^{1}H NMR ($CDCl_3$, 500 MHz):



^{11}B NMR ($CDCl_3$, 160 MHz):



^{19}F NMR ($CDCl_3$, 470 MHz):



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