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Supporting Information

Easy Access to Indole-based Bi-Sulfurylate-Heterocyclic Scaffolds

Giacomo Mari,* Lucia De Crescentini, Gianfranco Favi, Michele Mancinelli, Stefania Santeusanio, and Fabio Mantellini*

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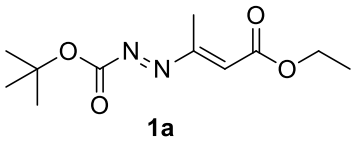
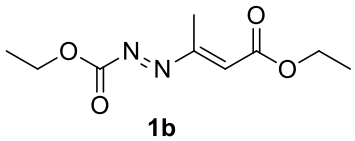
1 General experimental details.

All the commercially available reagents and solvents were used without further purification. 1,2-diaza-1,3-dienes (DDs) **1a-h** were synthesized as a mixture of *E/Z* isomers as previously reported.[1] The indoline-2-thiones **2a-h** were prepared according to the procedures reported in the literature.[2] Chromatographic purification of compounds was carried out on silica gel (60–200 μm). TLC analysis was performed on pre-loaded (0.25 mm) glass supported silica gel plates (Kieselgel 60); compounds were visualized by exposure to UV light and by dipping the plates in 1% $Ce(SO_4)\cdot 4H_2O$, 2.5% $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ in 10% sulphuric acid followed by heating on a hot plate. All ^1H NMR and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, using $[D_6]$DMSO or $CDCl_3$ as solvent. Chemical shift (δ scale) are reported in parts per million (ppm) relative to the central peak of the solvent and are sorted in ascending order within each group. The following abbreviations are used to describe peak patterns where appropriate: s = singlet, d = doublet, dd = doublet of doublet, dt = doublet of triplet, t = triplet, q = quartet, sept = septet, m = multiplet and br = broad signal. All coupling constants (J value) are given in Hertz [Hz]. High-and low-resolution mass spectroscopy was performed on a Micromass Q-ToF Micro mass spectrometer (Micromass, Manchester, UK) using an ESI source. Melting points were determined in open capillary tubes and are uncorrected. Elemental analyses were within ± 0.4 of the theoretical values (C, H, N).

2 Starting materials; Table S1: Substituted 1,2-diaza-1,3-dienes (DDs) 1a-h employed.[1]



1a



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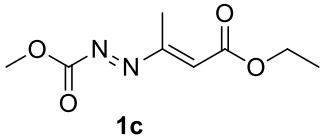

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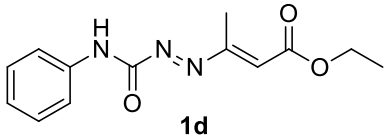

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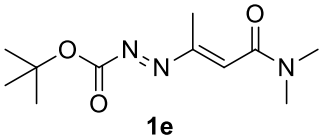
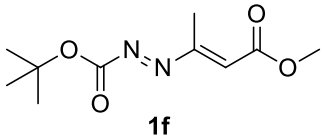


1e



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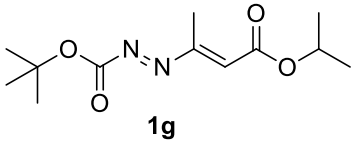
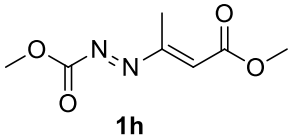
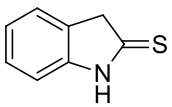


1g

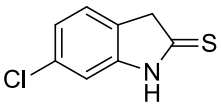


1h

3 Starting materials; Table S2: Substituted-indoline-2-thiones 2a-h employed.[2]



2a



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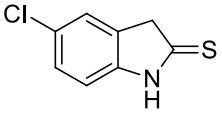

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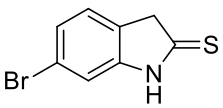
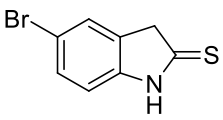


2d



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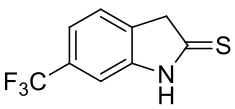

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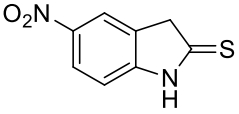
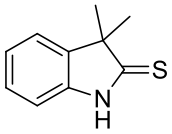


2g



2h

4 General procedure for the synthesis of *tert*-butyl 2-(3-((1*H*-indol-2-yl)thio)-4-ethoxy-4-oxobutan-2-ylidene)hydrazinecarboxylate 3a and methyl 2-(3-((1*H*-indol-2-yl)thio)-4-(dimethylamino)-4-oxobutan-2-ylidene)hydrazinecarboxylate 3b.

To a solution of 1,2-diaza-1,3-dienes **1a,e**[1] (1.0 mmol) in acetonitrile (6.0 mL) at room temperature, indoline-2-thione **2a**[2] (1.0 mmol) dissolved in acetonitrile (6.0 mL) was added and the reaction mixture was stirred at room temperature until the disappearance of the reagents (TLC monitoring, 0.10-0.50 h) as also evidenced by the colour change from red, typical of DDs, to pale yellow. Then, the solvent was evaporated under reduced pressure and the α-thio-functionalized hydrazones **3a,b** were purified by column chromatography on silica gel (elution mixture: cyclohexane : ethyl acetate, 80 : 20 for compounds **3a** and cyclohexane : ethyl acetate, 65 : 35 for compounds **3b**. The pure products **3a,b** were precipitated in ethyl acetate/petrol ether.

5 General procedure for the synthesis of 4-((1*H*-indol-2-yl)thio)-5-oxo-4,5-dihydro-1*H*-pyrazole-1-carboxylates 4a-o.

To a solution of 1,2-diaza-1,3-dienes **1a-d**[1] (1.0 mmol) in acetonitrile (6.0 mL) at room temperature indoline-2-thiones **2a-g**[2] (1.0 mmol) dissolved in acetonitrile (6.0 mL) were added and the reaction mixture was stirred at room temperature until the disappearance of the reagents (TLC monitoring, 0.10-0.50 h) as also evidenced by the color change from red, typical of DDs, to pale yellow. Then, directly to the reaction mixture, sodium acetate (2.0 mmol) was added and the reaction was stand under magnetic stirring for 13.0-17.0 h until the disappearance of the hydrazone intermediates **3** (TLC monitoring). The sodium acetate was removed by filtration, the solvent evaporated under reduced pressure and compounds **4a-o** were purified by chromatography on silica gel (elution mixture: cyclohexane: ethyl acetate, 80 : 20).

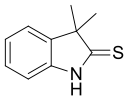
6 General procedure for the synthesis of 4-((6-chloro-1*H*-indol-2-yl)thio)-3-methyl-1*H*-pyrazol-5(4*H*)-one 4p.

To a solution of methyl 4-((6-chloro-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-4,5-dihydro-1*H*-pyrazole-1-carboxylate **4i** (0.50 mmol) in acetonitrile (5.0 mL) , sodium acetate (2.0 mmol) was added and the reaction was refluxed until the disappearance of the starting material (TLC monitoring 8.0 h). Then, the sodium acetate was removed by filtration, the solvent evaporated under reduced pressure and compounds **4p** was purified by chromatography on silica gel (elution mixture: cyclohexane : ethyl acetate, 70 : 30).

7 General procedure for the synthesis of 3,3-dimethyl-3'*H*-spiro-indoline-2,2'-thiazoles 5a-e.

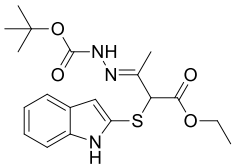
A solution of 1,2-diaza-1,3-dienes **1**[1] (0.5 mmol) and 3,3-dimethylindoline-2-thione **2h**[2] in chloroform (3.0 mL) was stirred at room temperature for DDs **1a,f** (3.5 and 4.5 h respectively), or refluxed in the case of DDs **1c,g,h** (3-4.5 h), until the disappearance of the reagents (TLC monitoring) and as also evidenced by the colour change from red, typical of DDs, to pale yellow. Then, the solvent was evaporated under reduced pressure and compounds **5a-e** were purified by chromatography on silica gel (elution mixture: cyclohexane : ethyl acetate, 85 : 15) and the pure products were precipitated in ethyl acetate/petrol ether.

8 Spectral data of compounds 2h, 3a,b, 4a-q and 5a-e.



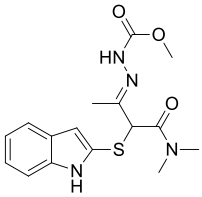
3,3-dimethylindoline-2-thione 2h.

2h was isolated by column chromatography on silica gel (acetate/cyclohexane) in 81% yield. Pale yellow solid; mp: 100–102 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.30 (s, 6H, 2CH$_3$), 7.03 (d, 1H, *J* = 8.0 Hz), 7.11 (dt, 1H, *J* = 7.6 Hz, *J* = 0.8 Hz, Ar), 7.25 (dt, 1H, *J* = 7.6 Hz, *J* = 1.2 Hz, Ar), 7.41 (d, 1H, *J* = 7.2 Hz), 12.57 (brs, 1H, NH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 27.3, 54.6, 110.4, 123.2, 123.4, 127.8, 140.6, 142.2, 213.0; anal. calcd. for $C_{10}H_{11}NS$ (177.27): C 67.76, H 6.25, N 7.90; found: C 67.93, H 6.12, N 7.76.



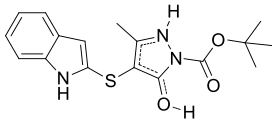
***Tert*-butyl 2-(3-((1*H*-indol-2-yl)thio)-4-ethoxy-4-oxobutan-2-ylidene)hydrazinecarboxylate 3a.**[3]

3a was isolated by column chromatography on silica gel (acetate/cyclohexane) in 98% yield. White powder; mp: 138–140 °C with decomposition; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.11 (t, 3H, *J* = 7.2 Hz, OCH$_2$*CH$_3$*), 1.45 (s, 9H, OC(*CH$_3$*)$_3$), 1.91 (s, 3H, *CH$_3$*), 4.09 (q, 2H, *J* = 7.2 Hz, O*CH$_2$*CH$_3$), 4.79 (s, 1H, *CH*), 6.58 (dd, 1H, *J* = 1.6 Hz, *J* = 0.8 Hz, Ar), 6.98 (dt, 1H, *J* = 8.0 Hz, *J* = 0.8 Hz, Ar), 7.12 (dt, 1H, *J* = 7.2 Hz, *J* = 1.2 Hz, Ar), 7.33 (dd, 1H, *J* = 8.0 Hz, *J* = 0.8 Hz, Ar), 7.47 (d, 1H, *J* = 8.0 Hz, Ar), 9.92 (brs, 1H, NH), 11.58 (brs, 1H, NH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.8, 14.6, 28.0, 58.3, 61,5, 79.8, 109.6, 111.0, 119.2, 119.9, 122.2, 124.6, 127.5, 137.7, 146.8, 153.4, 167.9; MS *m/z* (ESI): 392 (M + H$^+$); anal. calcd. for $C_{19}H_{25}N_3O_4S$ (391.48): C 58.29, H 6.44, N 10.73; found: C 58.07, H 6.58, N 10.58.



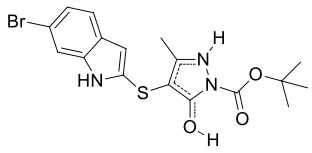
Methyl 2-(3-((1*H*-indol-2-yl)thio)-4-(dimethylamino)-4-oxobutan-2-ylidene)hydrazinecarboxylate 3b.

3b was isolated by column chromatography on silica gel (acetate/cyclohexane) in 96% yield. White powder; mp: 146–148 °C with decomposition; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.93 (s, 3H, CH$_3$), 2.85 (s, 3H, N(*CH$_3$*)$_2$), 3.08 (s, 3H, N(*CH$_3$*)$_2$), 3.59 (s, 3H, O*CH$_3$*), 5.10 (s, 1H, *CH*), 6.52 (dd, 1H, *J* = 2.0 Hz, *J* = 0.8 Hz, Ar), 6.97 (dt, 1H, *J* = 7.6 Hz, *J* = 1.2 Hz, Ar), 7.10 (dt, 1H, *J* = 7.6 Hz, *J* = 1.2 Hz, Ar), 7.32 (dd, 1H, *J* = 8.4 Hz, *J* = 0.8 Hz, Ar), 7.44 (d, 1H, *J* = 7.6 Hz, Ar), 9.96 (brs, 1H, NH), 11.35 (brs, 1H, NH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.4 (q), 35.5 (q), 37.2 (q), 51.8 (q), 58.4 (d), 108.8 (d), 110.9 (d), 119.0 (d), 119.7 (s), 121.9 (d), 125.8 (s), 127.6 (s), 137.5 (s), 149.2 (s), 154.5 (s), 166.2 (s); MS *m/z* (ESI): 349 (M + H$^+$); anal. calcd. for $C_{16}H_{20}N_4O_3S$ (348.42): C 55.16, H 5.79, N 16.08; found: C 54.97, H 5.94, N 16.32.



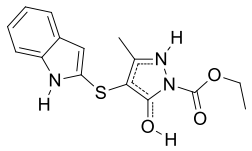
***Tert*-butyl 4-((1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4a**

4a was isolated by column chromatography on silica gel (acetate/cyclohexane) in 90% yield. Brown powder; mp: 190–192 °C with decomposition; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.23, 1.36 and 1.48 (brs, s, brs, 9H, OC(*CH$_3$*)$_3$), 1.99, and 2.04 (s, s, 3H, *CH$_3$*), 6.02 and 6.14 (s, s, 1H, Ar), 6.85–7.00 (m, 2H, Ar), 7.21 (d, 1H, *J* = 7.6 Hz, Ar), 7.29 (d, 1H, *J* = 7.6 Hz, Ar), 10.88 (s, 1H, NH), 11.06 and 11.79 (brs, brs 1H, OH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.4, 27.5, 29.0, 80.9, 84.5, 99.6, 110.4, 110.7, 118.3, 118.9, 120.0, 128.4, 135.1, 136.8, 152.0, 156.1, 165.9; MS *m/z* (ESI): 346 (M + H$^+$); anal. calcd. for $C_{17}H_{19}N_3O_3S$ (345.42): C 59.11, H 5.54, N 12.17; found: C 59.20, H 5.63, N 11.95.



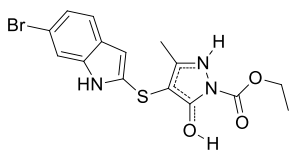
***Tert*-butyl 4-((6-bromo-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4b**

4b was isolated by column chromatography on silica gel (acetate/cyclohexane) in 81% yield. Brown powder; mp: 202–204 °C with decomposition; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.34 (s, 9H, OC(*CH$_3$*)$_3$), 2.04 (s,3H, *CH$_3$*), 6.02 (s, 1H, Ar), 7.03 (dd, 1H, *J* = 8.4 Hz, *J* = 1.6 Hz, Ar), 7.26 (d, 1H, *J* = 8.4 Hz, Ar), 7.38 (brs, 1H, Ar), 11.08 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 14.1, 27.5, 80.2, 84.5, 99.4, 112.4, 112.9, 119.9, 121.6, 127.5, 136.7, 137.6, 152.0, 156.0, 165.9; MS *m/z* (ESI): 425 (M + H$^+$); anal. calcd. for $C_{17}H_{18}BrN_3O_3S$ (424.31): C 48.12, H 4.28, N 9.90; found: C 48.28, H 4.17, N 9.75.



Ethyl 4-((1H-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1H-pyrazole-1-carboxylate 4c

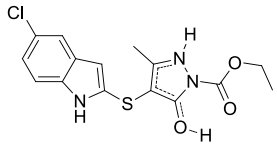
4c was isolated by column chromatography on silica gel (acetate/cyclohexane) in 51% yield. Light brown powder; mp: 194–196 °C with decomposition; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.07–1.31 (m, 3H, OCH$_2$*CH$_3$*), 1.99, 2.06 (2brs, 3H, *CH$_3$*), 4.12–4.28 (m, 2H, O*CH$_2$*CH$_3$), 6.04 (d, 1H, *J* = 1.2 Hz, Ar), 6.82–6.96 (m, 2H, Ar), 7.22 (d, 1H, *J* = 7.6 Hz, Ar), 7.29 (d, 1H, *J* = 7.6 Hz, Ar), 10.89 and 10.92 (2brs, 1H, NH), 11.85 (brs, 1H, OH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ =13.6, 14.0, 14.3, 61.0, 63.3, 78.5, 81.2, 99.2, 99.8, 110.5, 118.4, 118.8, 120.0, 128.4, 134.8, 136.8, 151.1, 153.0, 155.0, 157.0, 165.9, 166.6; MS *m/z* (ESI): 318 (M + H$^+$); anal. calcd. for $C_{15}H_{15}N_3O_3S$ (317.36): C 56.77, H 4.76, N 13.24; found: C 56.61, H 4.86, N 13.45.



Ethyl 4-((6-bromo-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4d

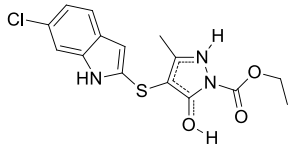
4d was isolated by column chromatography on silica gel (acetate/cyclohexane) in 87% yield. Light brown powder; mp: 202–204 °C with decomposition; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.16–1.28 (m, 3H, OCH$_2$*CH$_3$*), 1.99, 2.00 and 2.06 (s,s,brs,

3H, *CH*$_3$), 4.21 (q, 2H, *J* = 7.2 Hz, O*CH*$_2$CH$_3$), 6.06 (s, 1H, Ar), 7.01 (d, 1H, *J* = 8.4 Hz, Ar), 7.26 (d, 1H, *J* = 8.4 Hz, Ar), 7.42 (s, 1H, Ar), 11.10 (s, 1H, NH), 11.95 (brs, 1H OH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 14.1, 14.6, 14.9, 21.2, 21.5, 60.2, 61.5, 78.3, 99.4, 112.8, 113.5, 120.3, 122.0, 128.0, 138.0, 151.4, 155.4, 166.8, 170.9; MS *m/z* (ESI): 397 (M + H$^+$); anal. calcd. for $C_{15}H_{14}BrN_3O_3S$ (396.26): C 45.47, H 3.56, N 10.60; found: C 45.53, H 3.79, N 10.38.



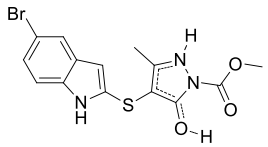
Ethyl 4-((5-chloro-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4e

4e was isolated by column chromatography on silica gel (acetate/cyclohexane) in 95% yield. Brown powder; mp: 192–195 °C with decomposition; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.15–1.36 (m, 3H, OCH$_2$*CH*$_3$), 1.99, 2.00 and 2.06 (s,s,brs, 3H, *CH*$_3$), 4.21 (q, 2H, *J* = 7.2 Hz, OCH$_2$*CH*$_3$), 6.00 (s, 1H, Ar), 6.92 (d, 1H, *J* = 8.4 Hz, Ar), 7.22 (d, 1H, *J* = 7.6 Hz, Ar), 7.33 (s, 1H, Ar), 11.13 (s, 1H, NH), 11.99 (brs, 1H, OH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.7, 14.4, 20.8, 21.1, 59.8, 61.0, 77.4, 98.4, 111.8, 117.3, 119.5, 123.4, 129.7, 135.2, 139.4, 151.0, 153.0, 155.1, 156.9, 165.9, 166.5, 170.4, 172.0; MS *m/z* (ESI): 352 (M + H$^+$); anal. calcd. for $C_{15}H_{14}ClN_3O_3S$ (351.81): C 51.21, H 4.01, N 10.08; found: C 51.07, H 4.16, N 9.95.



Ethyl 4-((6-chloro-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4f

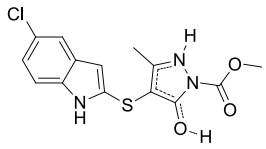
4f was isolated by column chromatography on silica gel (acetate/cyclohexane) in 82% yield. Brown powder; mp: 198–200 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.08–1.31 (m, 3H, OCH$_2$*CH*$_3$), 1.99 and 2.05 (s, brs, 3H, *CH*$_3$), 4.02–4.30 (m, 2H, OCH$_2$*CH*$_3$), 6.05 (s, 1H, Ar), 6.90 (d, 1H, *J* = 8.0 Hz, Ar), 7.23 (brs, 1H, Ar), 7.28 (d, 1H, *J* = 8.4 Hz, Ar), 11.08 (s, 1H, NH), 11.95(brs, 1H, OH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.5, 14.1, 20.7, 59.7, 63.4, 80.6, 99.3, 110.0, 119.1, 119.5, 124.5, 127.2, 136.5, 137.1, 153.0, 157.0, 165.8, 166.5, 170.4; MS *m/z* (ESI): 352 (M + H$^+$); anal. calcd. for $C_{15}H_{14}ClN_3O_3S$ (351.81): C 51.21, H 4.01, N 10.08; found: C 51.39, H 3.86, N 10.19.



Methyl 4-((5-bromo-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4g

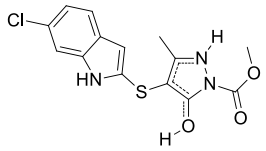
4g was isolated by column chromatography on silica gel (acetate/cyclohexane) in 93% yield. Brown powder; mp: 220–224 °C with decomposition; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.92, 1.96 (s, brs, 3H, *CH*$_3$), 3.74 (s, 3H, O*CH*$_3$), 5.99 (d, 1H, *J* = 1.2 Hz, Ar), 7.03 (d, 1H, *J* = 8.4 Hz, Ar), 7.19 (d, 1H, *J* = 8.8 Hz, Ar), 7.47 (d, 1H, *J* = 2.0 Hz, Ar), 11.16 and 11.24 (2s, 1H, NH), 11.91 (brs, 1H, OH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ =

13.8, 21.1, 52.2, 76.9, 98.2, 111.4, 112.2, 120.3, 122.0, 130.4, 135.4, 139.6, 151.4, 155.0, 166.4, 170.4, 172.0; MS *m/z* (ESI): 383 (M + H^+); anal. calcd. for $C_{14}H_{12}BrN_3O_3S$ (382.23): C 43.99, H 3.16, N 10.99; found: C 43.80, H 3.25, N 11.15.



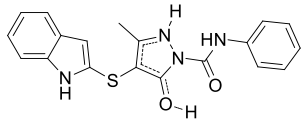
Methyl 4-((5-chloro-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4h

4h was isolated by column chromatography on silica gel (acetate/cyclohexane) in 63% yield. Brown powder; mp: 210–213 °C with decomposition; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.96 (s, 3H, *CH$_3$*), 3.74 (s, 3H, O*CH$_3$*), 5.98 (d, 1H, *J* = 1.6 Hz, Ar), 6.91 (dd, 1H, *J* = 8.4 Hz, *J* = 2.0 Hz, Ar), 7.22 (d, 1H, *J* = 8.4 Hz, Ar), 7.32 (d, 1H, *J* = 2.0 Hz, Ar), 11.12 (s, 1H, NH), 12.04 (brs, 1H, NH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.8, 52.2, 77.0, 98.2, 111.7, 117.2, 119.4, 123.3, 129.7, 135.2, 139.6, 151.6, 155.2, 166.6; MS *m/z* (ESI): 338 (M + H^+); anal. calcd. for $C_{14}H_{12}ClN_3O_3S$ (337.78): C 49.78, H 3.58, N 12.44; found: C 49.94, H 3.67, N 12.28.



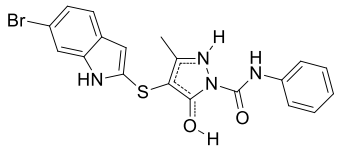
Methyl 4-((6-chloro-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4i

4i was isolated by column chromatography on silica gel (acetate/cyclohexane) in 58% yield. Light brown powder; mp: 196–198 °C with decomposition; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.99 (s, 3H, *CH$_3$*), 3.76 (s, 3H, O*CH$_3$*), 6.06 (s, 1H, Ar), 6.91 (dd, 1H, *J* = 8.4 Hz, *J* = 1.6 Hz, Ar), 7.24–7.32 (m, 2H, Ar), 11.11 (s, 1H, NH), 11.23 (brs, 1H, OH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 10.3, 87.6, 101.6, 110.3, 119.4, 120.1, 125.2, 127.0, 133.9, 137.2, 144.0, 144.3, 161.7; MS *m/z* (ESI): 338 (M + H^+); anal. calcd. for $C_{14}H_{12}ClN_3O_3S$ (337.78): C 49.78, H 3.58, N 12.44; found: C 49.63, H 3.69, N 12.31.



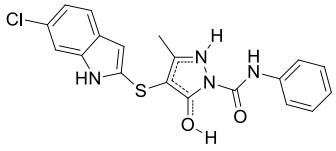
4-((1*H*-Indol-2-yl)thio)-3-methyl-5-oxo-*N*-phenyl-2,5-dihydro-1*H*-pyrazole-1-carboxamide 4j

4j was isolated by column chromatography on silica gel (acetate/cyclohexane) in 56% yield. Light brown powder; mp: 176–178 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 2.33 (s, 3H, *CH$_3$*), 6.35 (s, 1H, Ar), 6.94 (t, 1H, *J* = 7.6 Hz, Ar), 7.02 (t, 1H, *J* = 8.0 Hz, Ar), 7.14 (t, 1H, *J* = 7.6 Hz, Ar), 7.27 (d, 1H, *J* = 8.0 Hz, Ar), 7.37–7.41 (m, 3H, Ar), 7.54 (d, 2H, *J* = 8.4 Hz, Ar), 11.04 (s, 1H, NH), 11.27 (s, 1H, NH), 13.09 (brs, 1H, NH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 11.4, 89.3, 102.4, 110.8, 119.0, 119.2, 119.6, 120.9, 124.0, 128.2, 129.2, 130.6, 136.9, 137.0, 146.4, 153.9, 162.5; MS *m/z* (ESI): 365 (M + H^+); anal. calcd. for $C_{19}H_{16}N_4O_2S$ (364.42): C 62.62, H 4.43, N 15.37; found: C 62.81, H 4.32, N 15.52.



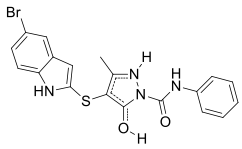
4-((6-bromo-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-*N*-phenyl-2,5-dihydro-1*H*-pyrazole-1-carboxamide 4k

4k was isolated by column chromatography on silica gel (acetate/cyclohexane) in 93% yield. Light brown powder; mp: 206–208 °C; ^{1}H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 2.31 (s, 3H, CH_3), 6.36 (s, 1H, Ar), 7.07 (dd, 1H, *J* = 8.4 Hz, *J* = 1.2 Hz, Ar), 7.14 (t, 1H, *J* = 7.2 Hz, Ar), 7.33–7.43 (m, 4H, Ar), 7.54 (d, 2H, *J* = 8.0 Hz, Ar), 11.21 (s, 2H, 2NH), 13.3 (brs, 1H, OH); ^{13}C NMR (100 MHz, $DMSO_{d6}$, 25 °C): δ = 11.8, 89.3, 102.7, 113.7, 113.9, 121.1, 122.5, 124.6, 127.8, 129.7, 132.6, 137.4, 138.2, 146.8, 154.4, 162.8; MS *m/z* (ESI): 444 (M + H^+); anal. calcd. for $C_{19}H_{15}BrN_4O_2S$ (443.32): C 51.48, H 3.41, N 12.64; found: C 51.69, H 3.54, N 12.48.



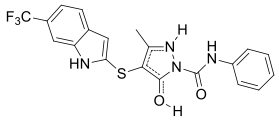
4-((6-Chloro-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-*N*-phenyl-2,5-dihydro-1*H*-pyrazole-1-carboxamide 4l

4l was isolated by column chromatography on silica gel (acetate/cyclohexane) in 86% yield. Light brown powder; mp: 190–192 °C; ^{1}H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 2.25 (s, 3H, CH_3), 6.30 (s, 1H, Ar), 6.94 (dd, 1H, *J* = 8.4 Hz, *J* = 2.0 Hz, Ar), 7.11 (t, 1H, *J* = 7.2 Hz, Ar), 7.27 (d, 1H, *J* = 2.0 Hz, Ar), 7.34–7.41 (m, 3H, Ar), 7.53 (d, 2H, *J* = 7.6 Hz, Ar), 11.16 (s, 1H, NH), 11.53 (brs, 1H, NH), 13.69 (brs, 1H, NH); ^{13}C NMR (100 MHz, $DMSO_{d6}$, 25 °C): δ = 11.9, 86.2, 101.5, 110.3, 119.4, 120.0, 123.7, 125.2, 127.1, 129.2, 137.2, 147.2, 153.7, 163.3; (ESI): 399 (M + H^+); anal. calcd. for $C_{19}H_{15}ClN_4O_2S$ (398.87): C 57.21, H 3.79, N 14.05; found: C 57.03, H 3.95, N 13.82.



4-((5-bromo-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-*N*-phenyl-2,5-dihydro-1*H*-pyrazole-1-carboxamide 4m

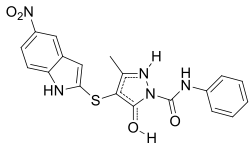
4m was isolated by column chromatography on silica gel (acetate/cyclohexane) in 91% yield. Whitish powder; mp: 198–200 °C; ^{1}H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 2.32 (s, 3H, CH_3), 6.32 (s, 1H, Ar), 7.11-7.23 (m, 2H, Ar), 7.22 (d, 1H, *J* = 8.8 Hz, Ar), 7.38 (d, 2H, *J* = 8.0 Hz, Ar), 7.52-7.58 (m, 3H, Ar), 11.17 (s, 1H, NH), 11.26 (s, 1H, NH), 13.65 (brs, 1H, OH); ^{13}C NMR (100 MHz, $DMSO_{d6}$, 25 °C): δ = 11.2, 88.8, 101.3, 111.7, 112.6, 119.6, 121.0, 123.2, 124.1, 129.2, 130.2, 132.8, 135.6, 136.8, 146.2, 154.0, 162.2; MS *m/z* (ESI): 444 (M + H^+); anal. calcd. for $C_{19}H_{15}BrN_4O_2S$ (443.32): C 51.48, H 3.41, N 12.64; found: C 51.26, H 3.60, N 12.46.



3-methyl-5-oxo-*N*-phenyl-4-((6-(trifluoromethyl)-1*H*-indol-2-yl)thio)-2,5-dihydro-1*H*-pyrazole-1-carboxamide 4n

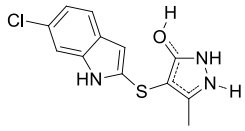
4n was isolated by column chromatography on silica gel

(acetate/cyclohexane) in 72% yield. Whitish powder; mp: 240–243 °C with decomposition; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 2.12 (s, 3H, *CH$_3$*), 6.22 (d, 1H, *J* = 1.2 Hz, Ar), 7.05 (t, 1H, *J* = 7.2 Hz, Ar), 7.18 (dd, 1H, *J* = 8.4 Hz, *J* = 1.2 Hz, Ar), 7.34 (t, 2H, *J* = 8.0 Hz, Ar), 7.49–7.57 (m, 4H, Ar), 11.36 (s, 1H, NH), 12.21 (s, 2H, NH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.0, 80.0, 99.4, 107.6, 115.3, 118.8, 119.2, 120.1 (*J$_{2CF}$*= 31 Hz), 123.0, 125.5 (*J$_{1CF}$*= 270 Hz), 129.0, 131.3, 135.6, 138.4, 139.8, 149.3, 153.8, 165.2; MS *m/z* (ESI): 433 (M + H$^+$); anal. calcd. for $C_{20}H_{15}F_3N_4O_2S$ (432.42): C 55.55, H 3.50, N 12.96; found: C 55.81, H 3.36, N 12.74.



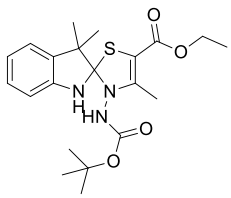
3-methyl-4-((5-nitro-1*H*-indol-2-yl)thio)-5-oxo-*N*-phenyl-2,5-dihydro-1*H*-pyrazole-1-carboxamide 4o

4o was isolated by column chromatography on silica gel (acetate/cyclohexane) in 79% yield. Whitish powder; mp: 206–209 °C with decomposition; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 2.04 (s, 3H, *CH$_3$*), 6.26 (s, 1H, Ar), 7.02 (d, 1H, *J* = 7.2 Hz, Ar), 7.32 (t, 2H, *J* = 8.0 Hz, Ar), 7.39 (d, 1H, *J* = 8.8 Hz, Ar), 7.52 (d, 2H, *J* = 8.0 Hz, Ar), 7.85 (dd, 1H, *J* = 8.8 Hz, *J* = 2.0 Hz, Ar), 8.31 (d, 1H, *J* = 2.0 Hz, Ar), 11.77 (brs, 1H, NH), 12.58 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.6, 77.0, 100.4, 110.6, 114.8, 115.3, 118.9, 122.5, 128.1, 128.9, 138.9, 140.2, 140.5, 141.8, 150.0, 166.0, 174.8; MS *m/z* (ESI): 410 (M + H$^+$); anal. calcd. for $C_{19}H_{15}N_5O_4S$ (409.42): C 55.74, H 3.69, N 17.11; found: C 55.58, H 3.83, N 17.32.



4-((6-Chloro-1*H*-indol-2-yl)thio)-5-methyl-1*H*-pyrazol-3(2*H*)-one 4p

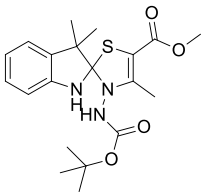
4p was isolated by column chromatography on silica gel (acetate/cyclohexane) in 57% yield. Whitish powder; mp: 185–187 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 2.19 (s, 3H, *CH$_3$*), 6.15 (dd, 1H, *J* = 2.0 Hz, *J* = 0.8 Hz, Ar), 6.94 (dd 1H, *J* = 8.4 Hz, *J* = 2.0 Hz, Ar), 7.27 (brs, 1H, CH), 7.36 (d, 1H, *J* = 8.4 Hz, Ar), 10.46 (brs, 1H, OH), 11.15 (s, 1H, NH), 11.72 (brs, 1H, NH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 10.3, 87.6, 101.6, 110.3, 119.4, 120.1, 125.2, 127.0, 133.9, 137.2, 144.0, 161.7; MS *m/z* (ESI): 280 (M + H$^+$); anal. calcd. for $C_{12}H_{10}ClN_3OS$ (279.75): C 51.52, H 3.60, N 15.02; found: C 51.68, H 3.77, N 15.24.



Ethyl 3'-((tert-butoxycarbonyl)amino)3,3,4'-trimethyl-3'*H*-spiro[indoline-2,2'thiazole]-5'-carboxylate 5a.

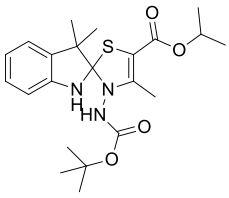
5a was isolated by column chromatography on silica gel (acetate/cyclohexane) in 68% yield. Pale yellow powder; mp: 150–152 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.16 (s, 3H, CH$_3$), 1.21 (t, 3H, *J* = 7.2 Hz, OCH$_2$*CH$_3$*), 1.27 (s, 3H, CH$_3$), 1.31 (s, 9H,C(CH$_3$)$_3$), 2.02 (s, 3H,CH$_3$), 4.08–4.14 (m, 2H, O*CH$_2$*CH$_3$), 5.86 (s, 1H, NH), 6.42 (d, 1H, *J* = 7.6 Hz, Ar), 6.66 (t, 1H, *J* = 7.2 Hz, Ar), 6.91 (dt, 1H, *J* = 7.6 Hz, *J* = 1.2 Hz, Ar), 7.01 (d, 1H, *J* = 7.2 Hz, Ar), 9.08 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): ^{13}C

NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 12.5, 14.4, 18.7, 27.9, 29.2, 48.4, 59.5, 80.5, 88.3, 106.1, 106.5, 118.6, 121.2, 126.6, 135.2, 146.4, 148.8, 156.5, 163.0; HRMS (ESI) calcd for $C_{21}H_{30}N_3O_4S$ $[M + H]^+$: 420.1952; found: 420.1954.



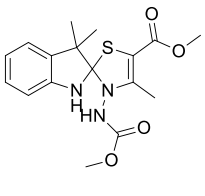
Methyl 3'-((tert-butoxycarbonyl)amino)3,3,4'-trimethyl-3'*H*-spiro[indoline-2,2'thiazole]-5'-carboxylate 5b.

5b was isolated by column chromatography on silica gel (acetate/cyclohexane) in 76% yield. Pale yellow powder; mp: 148–150 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.16 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.32 (s, 9H,C(CH_3)$_3$), 2.03 (s, 3H,CH_3), 3.65 (s, 3H, O*CH$_3$*), 5.87 (s, 1H, NH), 6.43 (d, 1H, *J* = 7.6 Hz, Ar), 6.67 (dt, 1H, *J* = 7.2 Hz, *J* = 0.8 Hz, Ar), 6.92 (dt, 1H, *J* = 7.6 Hz, *J* = 1.2 Hz, Ar), 7.01 (d, 1H, *J* = 7.2 Hz, Ar), 9.10 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 12.5, 18.7, 27.8, 29.1, 48.4, 51.0, 80.5, 87.8, 106.1, 106.5, 118.6, 121.1, 126.6, 135.1, 146.4, 149.1, 156.4, 163.3; HRMS (ESI) calcd for $C_{20}H_{28}N_3O_4S$ $[M + H]^+$: 406.1795; found: 406.1812.



Isopropyl 3'-((tert-butoxycarbonyl)amino)3,3,4'-trimethyl-3'*H*-spiro[indoline-2,2'thiazole]-5'-carboxylate 5c.

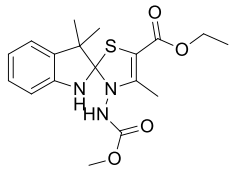
5c was isolated by column chromatography on silica gel (acetate/cyclohexane) in 38% yield. Pale yellow powder; mp: 138–140 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.15 (s, 3H, CH_3), 1.21 (d, 6H, *J* = 6.4 Hz, OCH(*CH$_3$*)$_2$), 1.27 (s, 3H, CH_3), 1.31 (s, 9H,C(CH_3)$_3$), 2.02 (s, 3H,CH_3), 4.94 (sep, 1H, *J* = 6.4 Hz, O*CH*(CH_3)$_2$), 5.87 (s, 1H, NH), 6.41 (d, 1H, *J* = 7.6 Hz, Ar), 6.66 (t, 1H, *J* = 7.2 Hz, Ar), 6.91 (t, 1H, *J* = 7.2 Hz, *J* = 1.2 Hz, Ar), 7.01 (d, 1H, *J* = 7.2 Hz, Ar), 9.08 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 12.5, 18.7, 21.8, 21.9, 27.9, 29.2, 48.3, 66.8, 80.4, 88.8, 106.1, 106.5, 118.6, 121.1, 126.6, 135.2, 146.4, 148.5, 156.5, 162.6; MS *m/z* (ESI): 434 ($M + H^+$); anal. calcd. for $C_{22}H_{31}N_3O_4S$ (433.66): C 60.94, H 7.21, N 9.69; found: C 61.13, H 7.02, N 9.84.



Methyl 3'-((methoxycarbonyl)amino)3,3,4'-trimethyl-3'*H*-spiro[indoline-2,2'thiazole]-5'-carboxylate 5d.

5d was isolated by column chromatography on silica gel (acetate/cyclohexane) in 43% yield. Pale yellow powder; mp: 100–102 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.16 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 2.04 (s, 3H,CH_3), 3.48 (s, 3H, O*CH$_3$*), 3.64 (s, 3H, O*CH$_3$*), 5.88 (s, 1H, NH), 6.44 (d, 1H, *J* = 7.6 Hz, Ar), 6.65 (t, 1H, *J* = 7.6 Hz, Ar), 6.92 (dt, 1H, *J* = 7.6 Hz, *J* = 1.2 Hz, Ar), 7.01 (d, 1H, *J* = 6.8 Hz, Ar), 9.31 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 12.5, 18.8, 28.9, 48.5, 51.0, 52.5, 88.0, 105.9, 106.2, 118.7, 121.2, 126.9, 135.0, 146.5, 149.0, 157.9, 163.3; MS *m/z* (ESI): 364 (M +

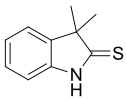
H^+); anal. calcd. for $C_{17}H_{21}N_3O_4S$ (363.43): C 56.18, H 5.82, N 11.56; found: C 56.41, H 5.95, N 11.37.



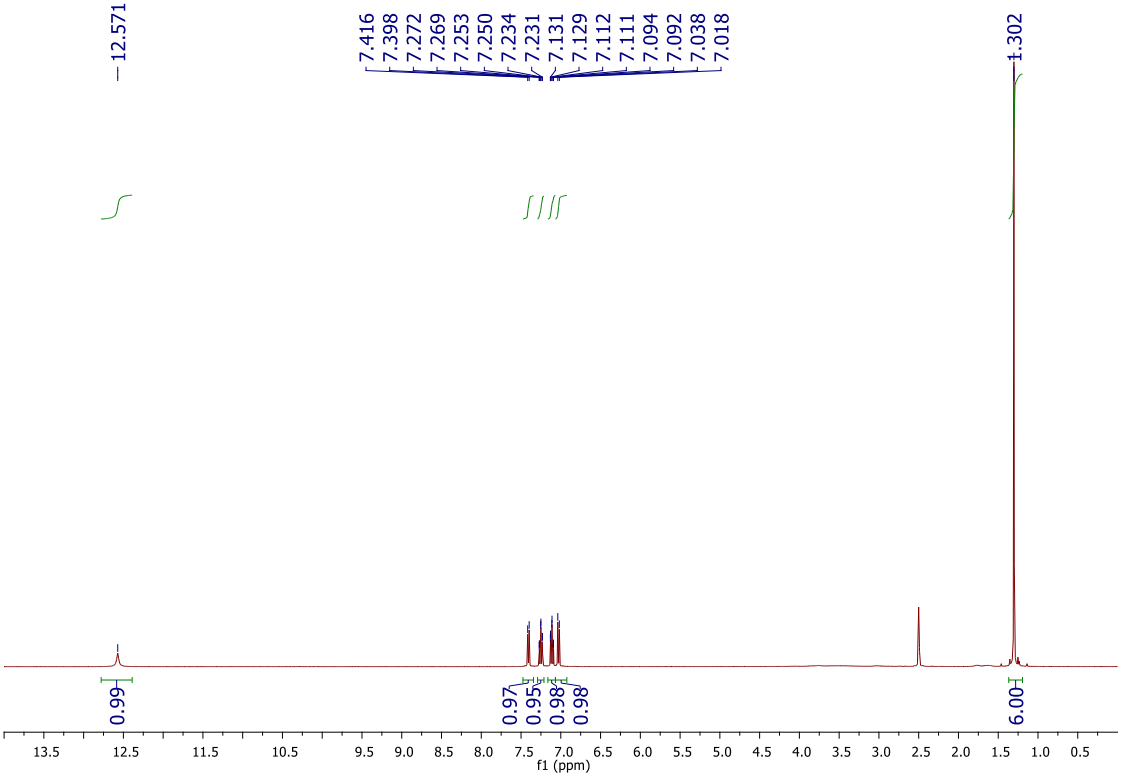
Ethyl 3'-((methoxycarbonyl)amino)-3,3,4'-trimethyl-3'H-spiro[indoline-2,2'-thiazole]-5'-carboxylate 5e

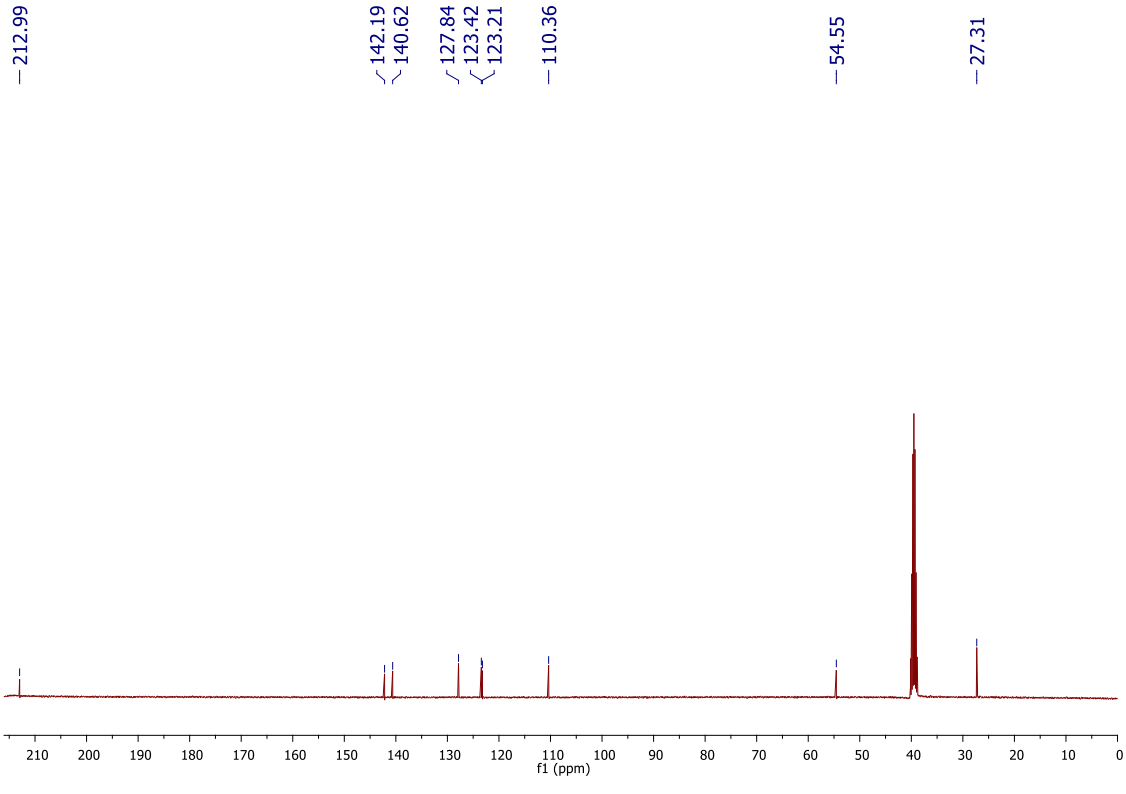
5e was isolated by column chromatography on silica gel (acetate/cyclohexane) in 47% yield. Pale yellow powder; mp: 111–113 °C; ^{1}H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 1.16 and 1.33 (2s, 3H, CH_3), 1.21 (t, 3H, *J* = 7.2 Hz, OCH_2CH_3), 1.27 and 1.38 (2s, 3H, CH_3), 2.04 and 2.16 (2s, 3H, CH_3), 3.48 and 3.65 (2s, 3H, OCH3), 4.00–4.17 (m, 2H, OCH_2CH_3), 5.45 and 5.87 (s, 1H, NH), 6.43 and 6.49 (2d, 1H, *J* = 7.6 Hz, and *J* = 6.8 Hz, Ar), 6.59–6.67 (m, 1H, Ar), 6.87–6.97 (m, 1H, Ar), 7.00–7.12 (m, 1H, Ar), 9.30 and 10.74 (2s, 1H, NH); ^{13}C NMR (100 MHz, $DMSO_{d6}$, 25 °C): ^{13}C NMR (100 MHz, $DMSO_{d6}$, 25 °C): δ = 12.6 ,14.4, 18.8, 28.9, 48.4, 52.5, 59.6,.88.4, 105.9, 106.2, 118.7, 121.2, 126.9, 135.1, 146.5, 148.7, 157.9, 163.0 (s); MS *m/z* (ESI): 378 ($M + H^+$); anal. calcd. for $C_{18}H_{23}N_3O_4S$ (377.46): C 57.28, H 6.14, N 11.13; found: C 57.37, H 6.02, N 11.27.

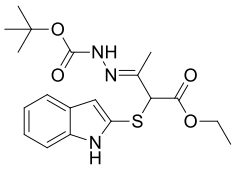
9 NMR spectra of compounds 2h, 3a,b, 4a-p and 5a-e.



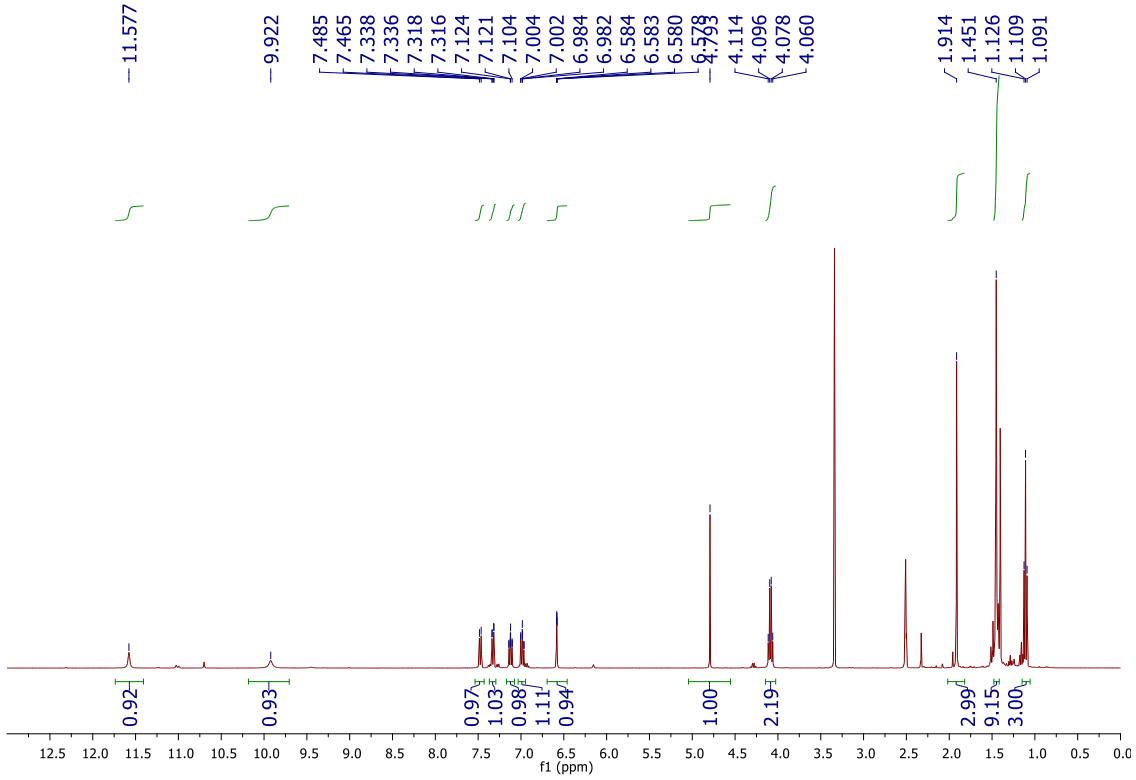
3,3-dimethylindoline-2-thione 2h.

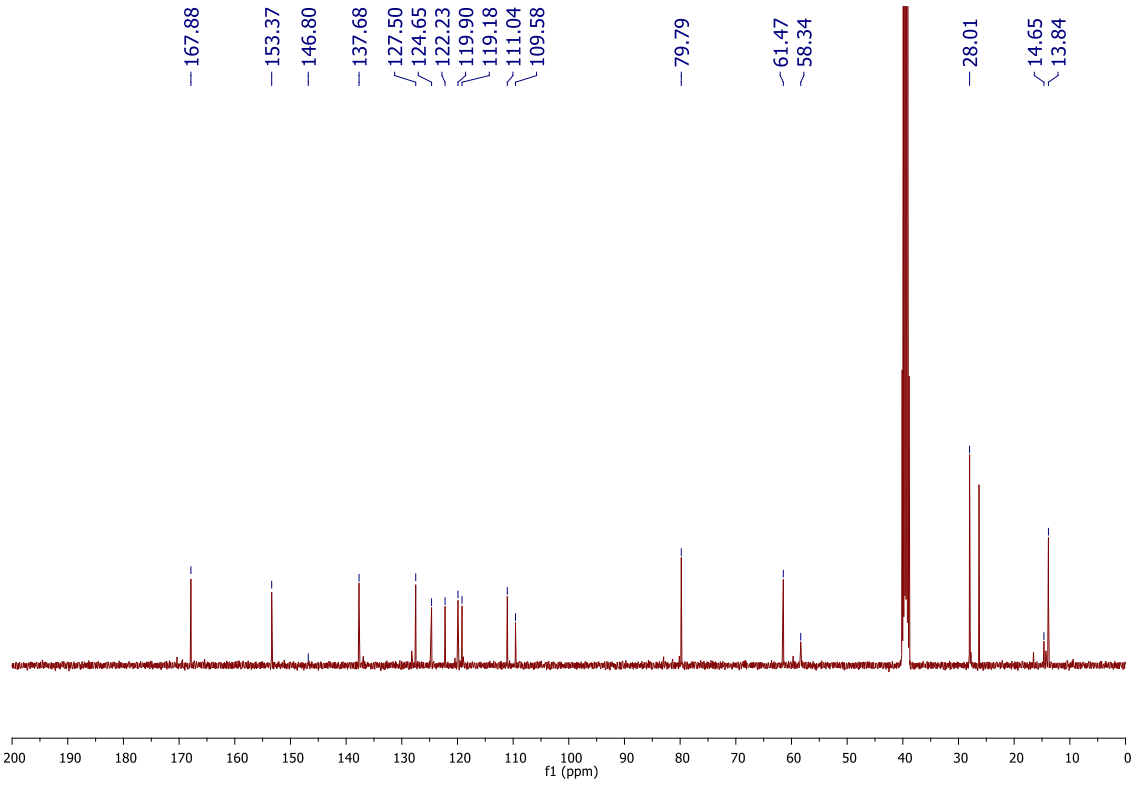


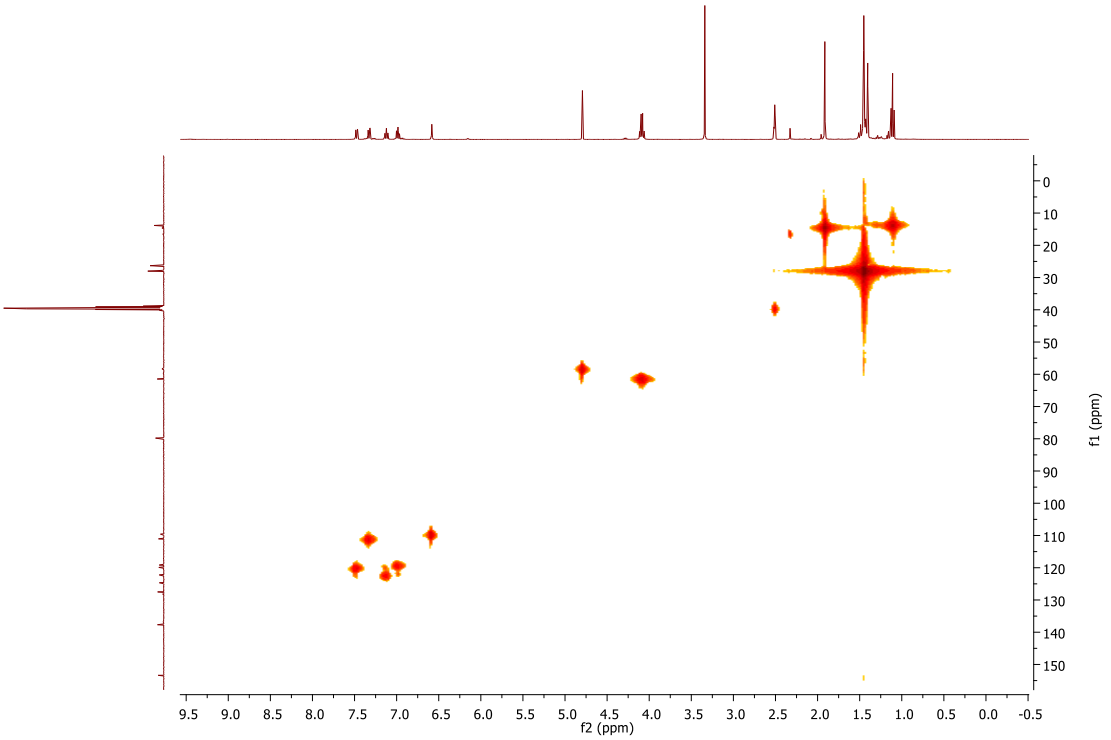




***Tert*-butyl 2-(3-((1*H*-indol-2-yl)thio)-4-ethoxy-4-oxobutan-2-ylidene)hydrazinecarboxylate 3a.**



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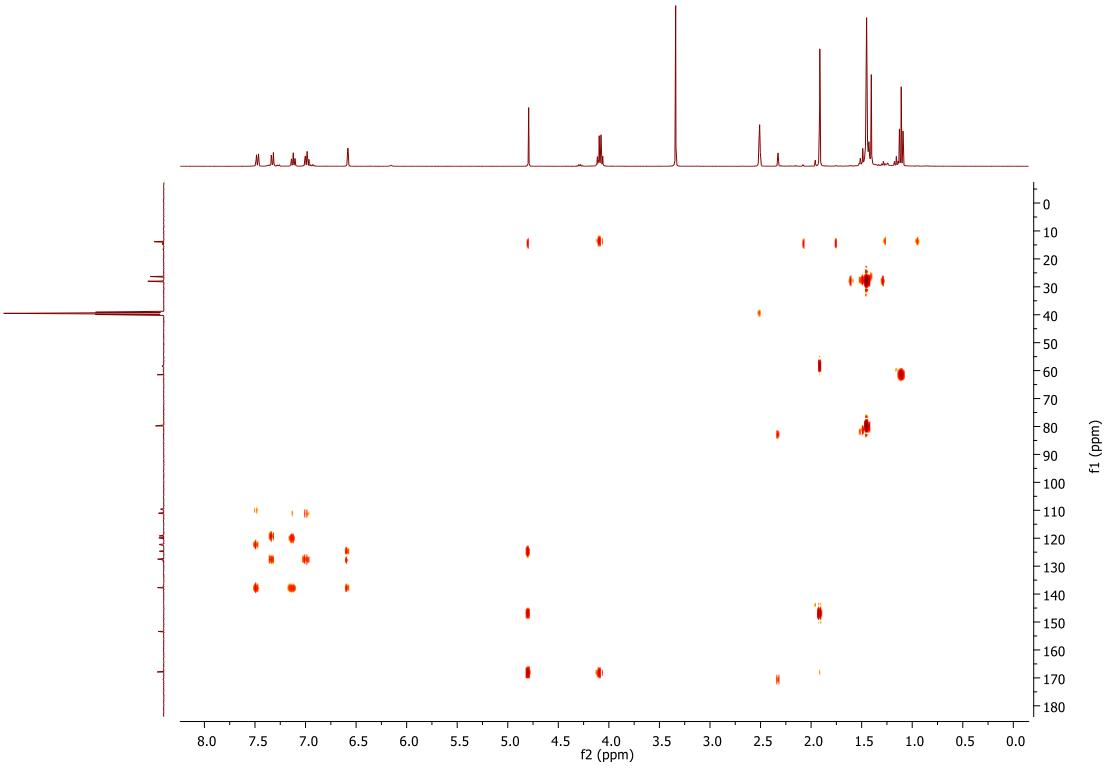
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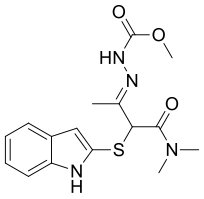
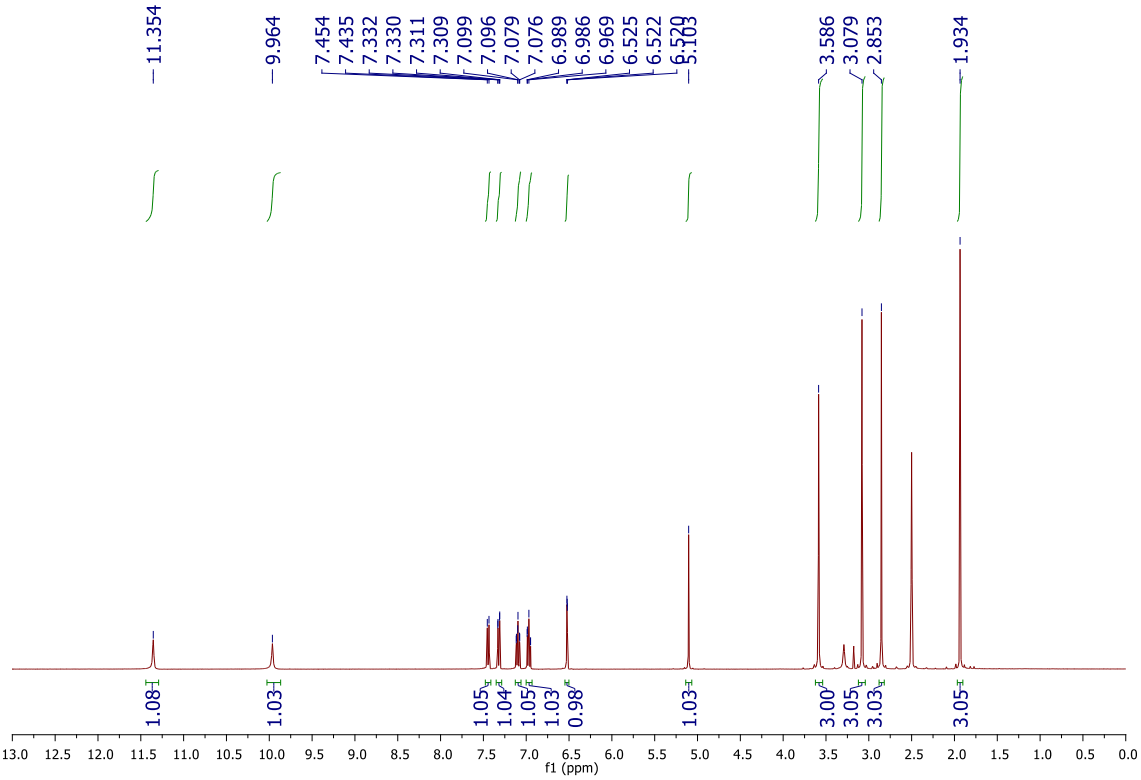
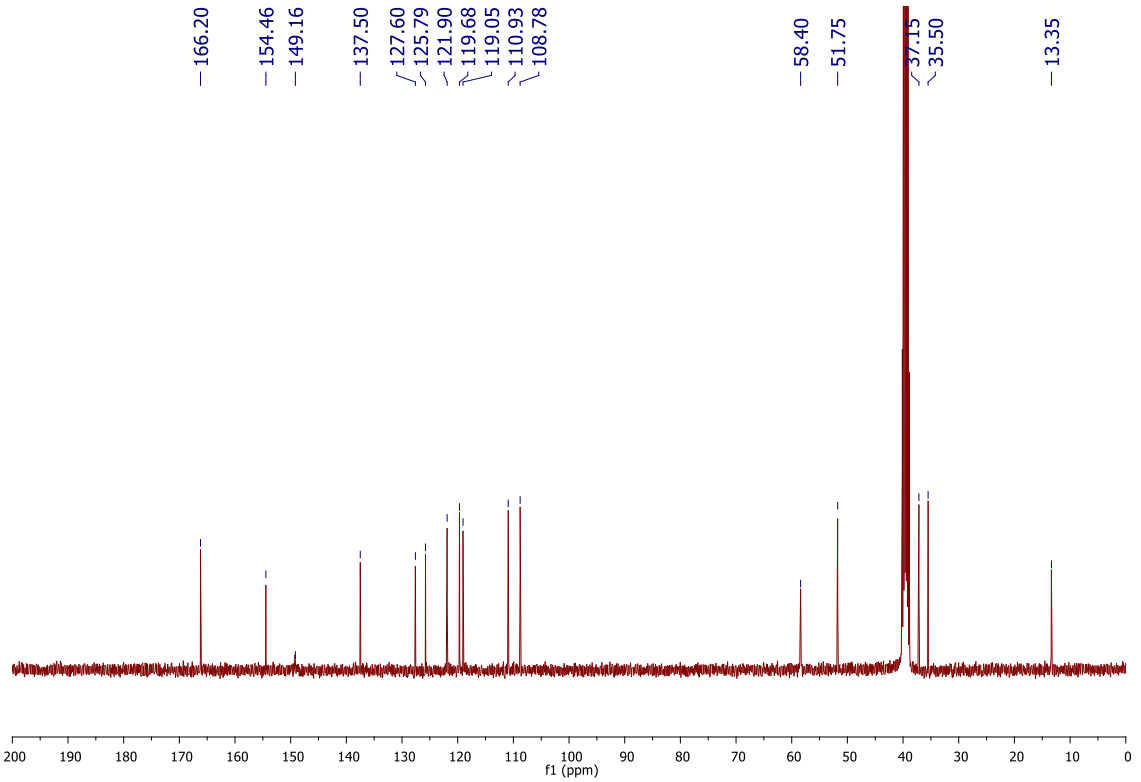
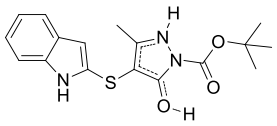


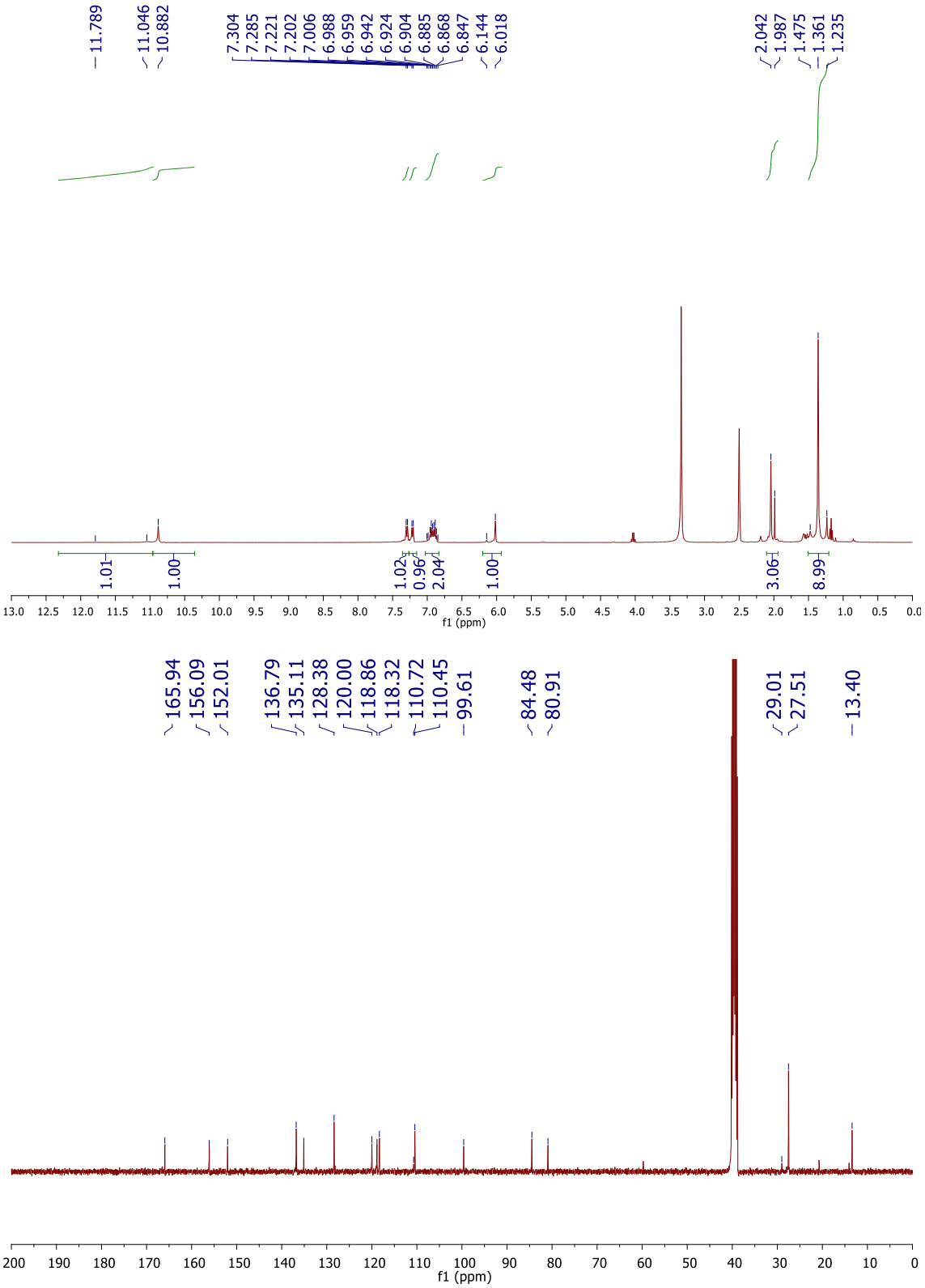
Methyl 2-(3-((1*H*-indol-2-yl)thio)-4-(dimethylamino)-4-oxobutan-2-ylidene)hydrazinecarboxylate 3b.

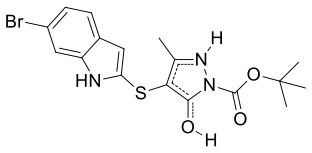




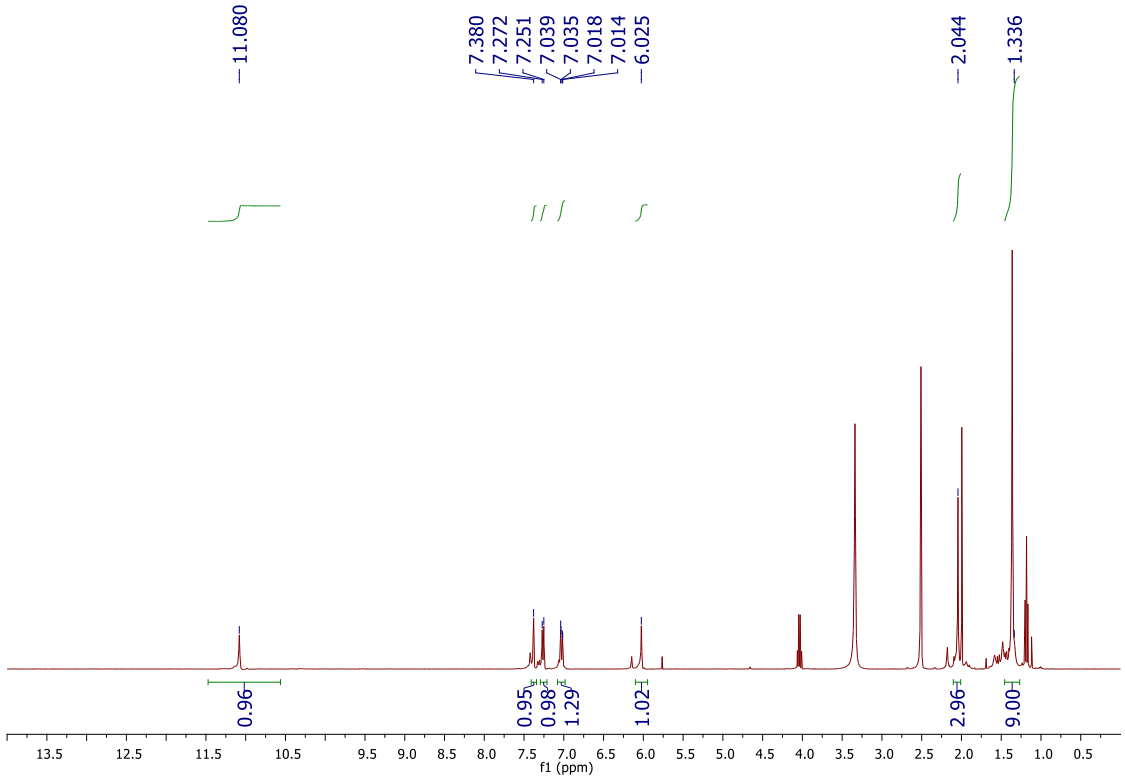


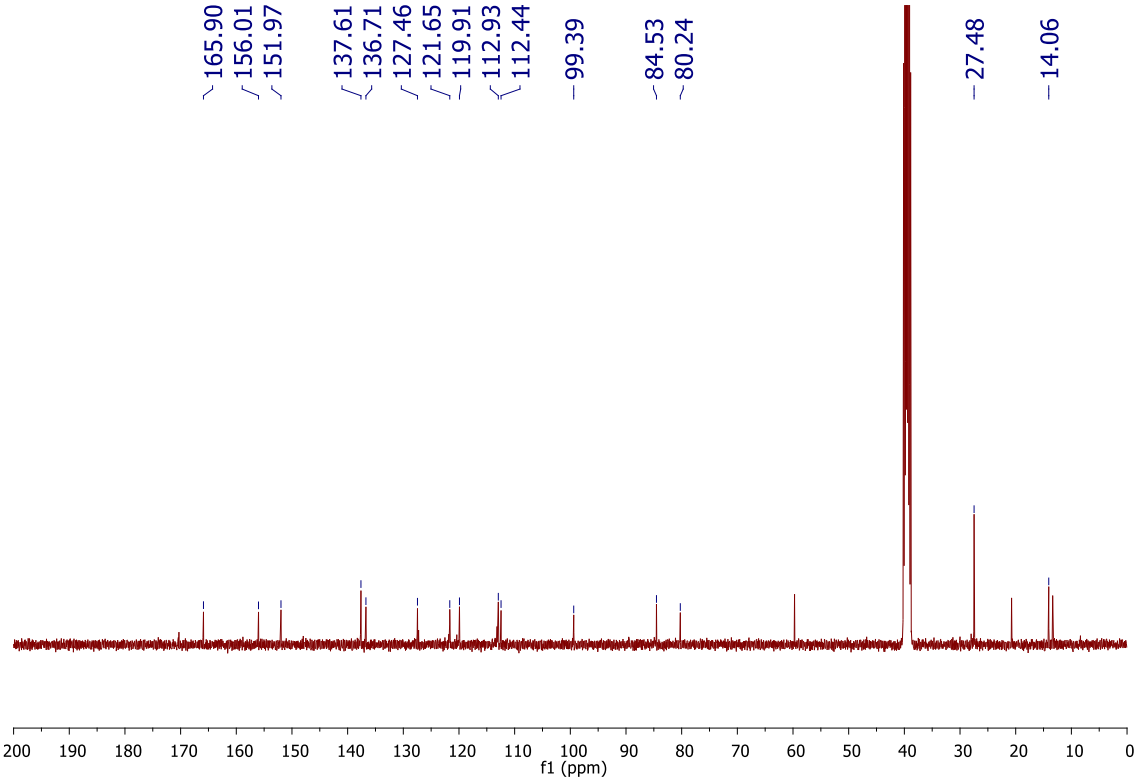
Tert-butyl 4-((1_H_-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1_H_-pyrazole-1-carboxylate 4a

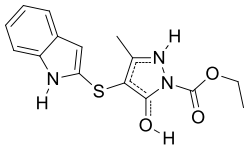




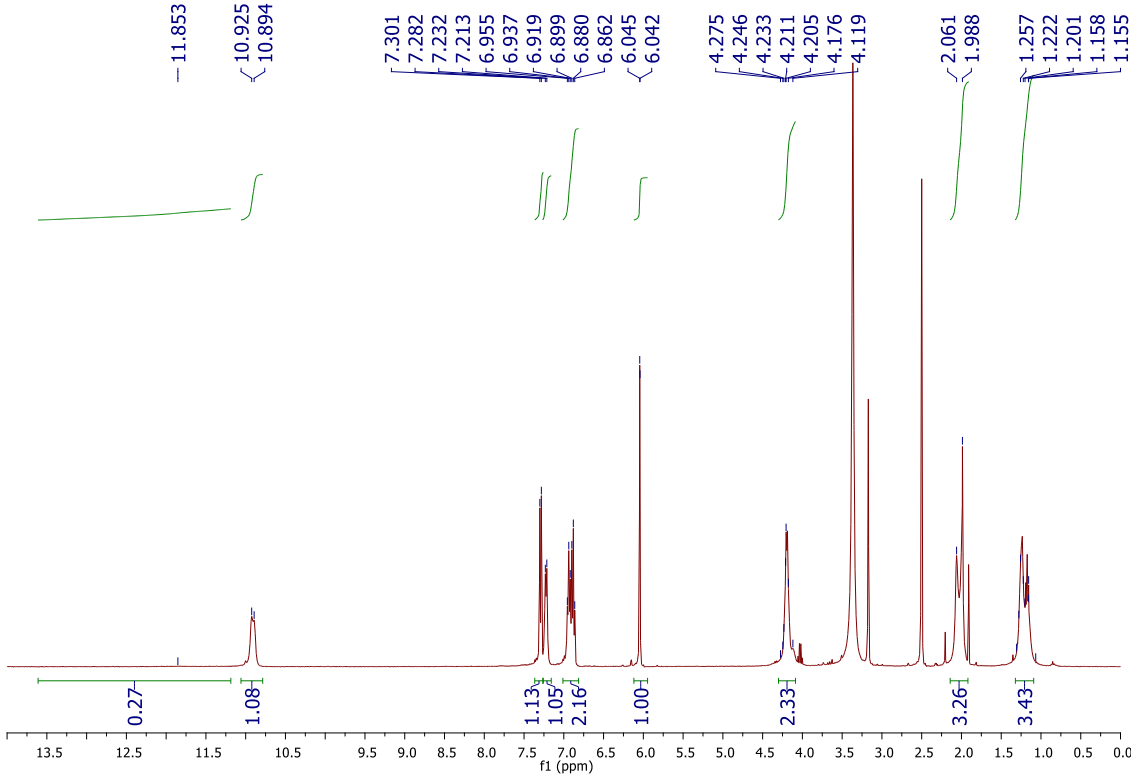
***Tert*-butyl 4-((6-bromo-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4b**

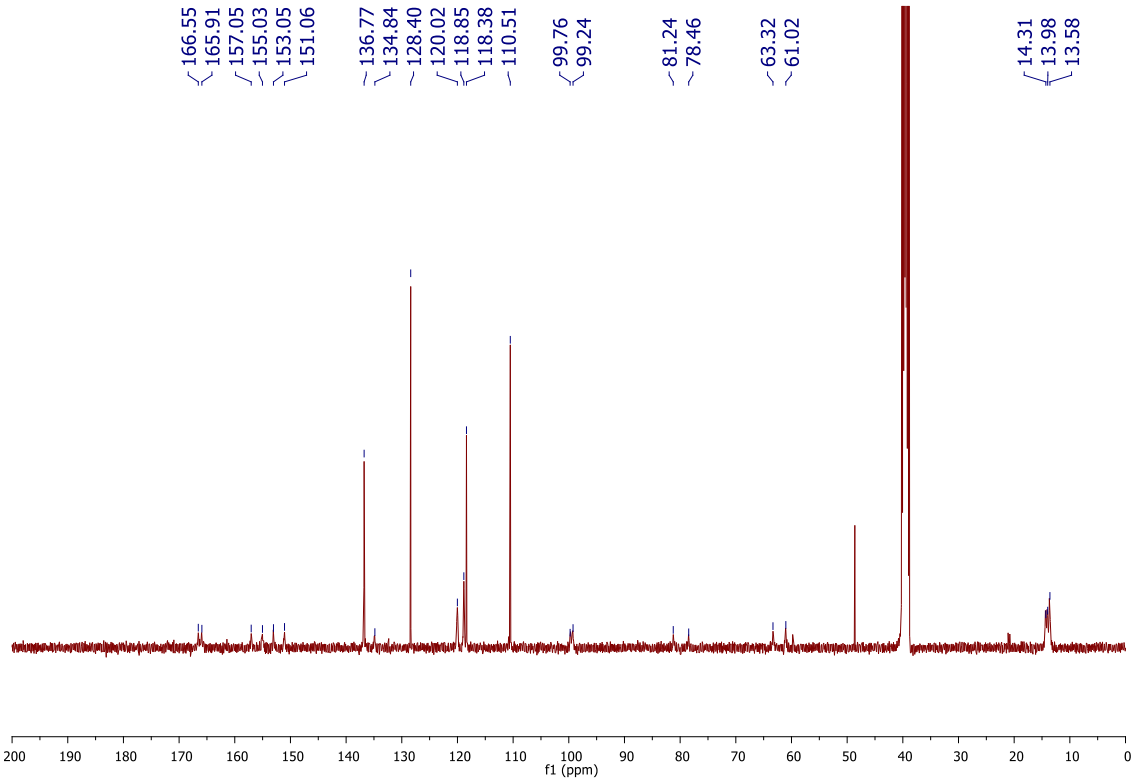


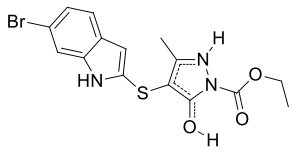




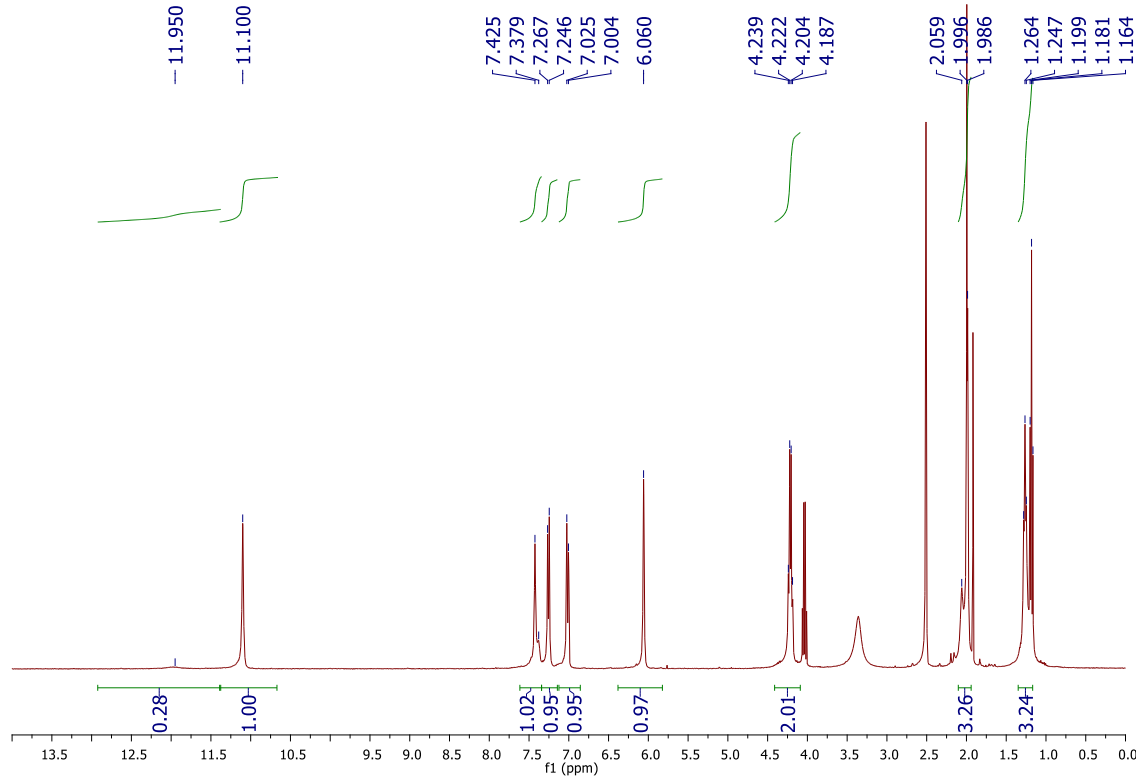
Ethyl 4-((1H-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1H-pyrazole-1-carboxylate 4c

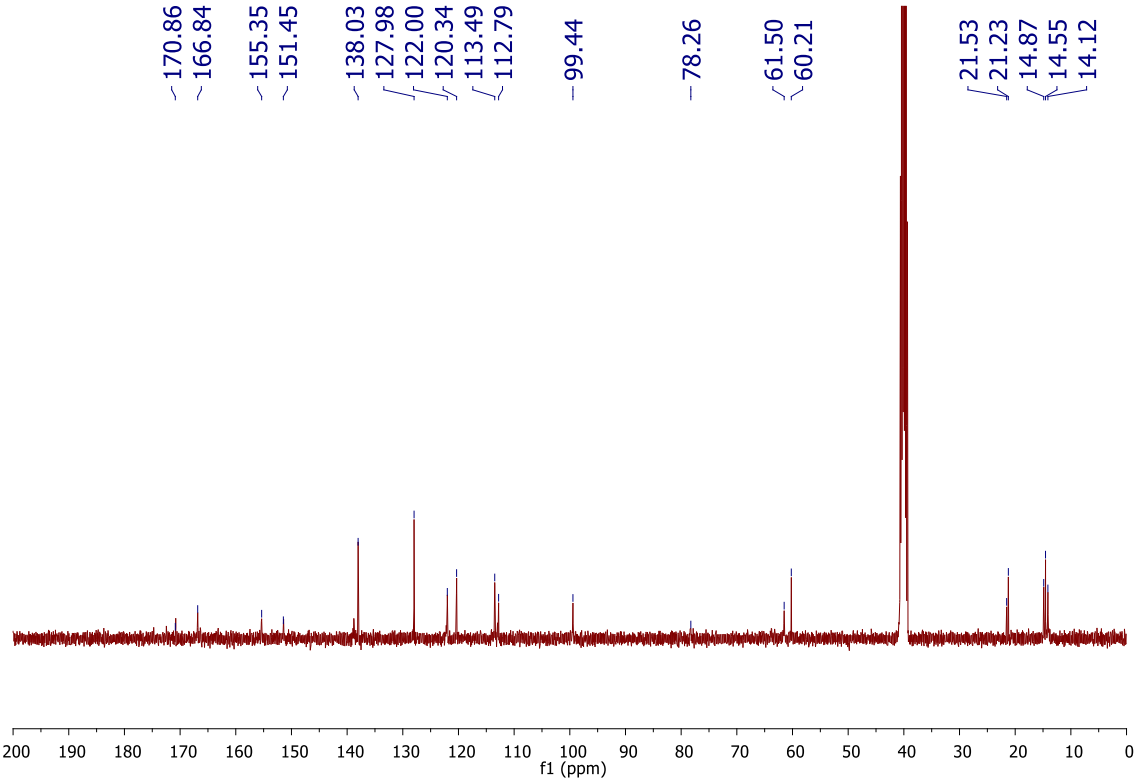


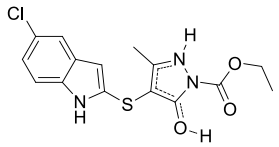




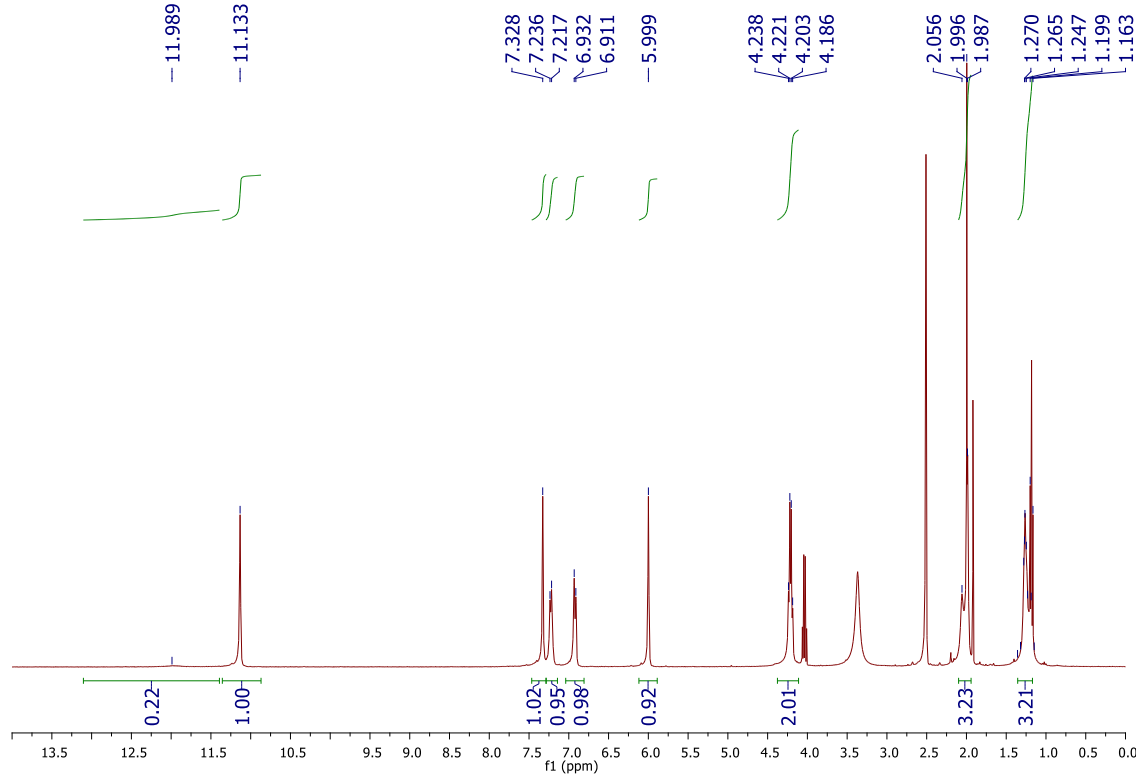
Ethyl 4-((6-bromo-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4d

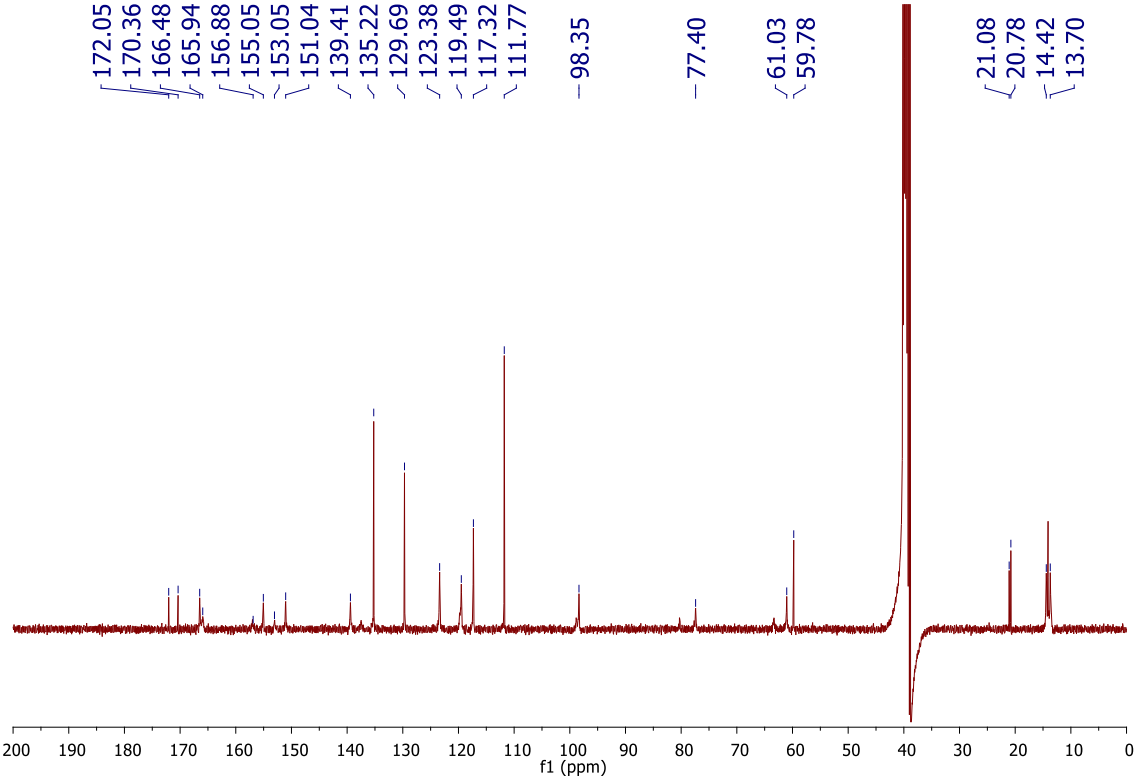


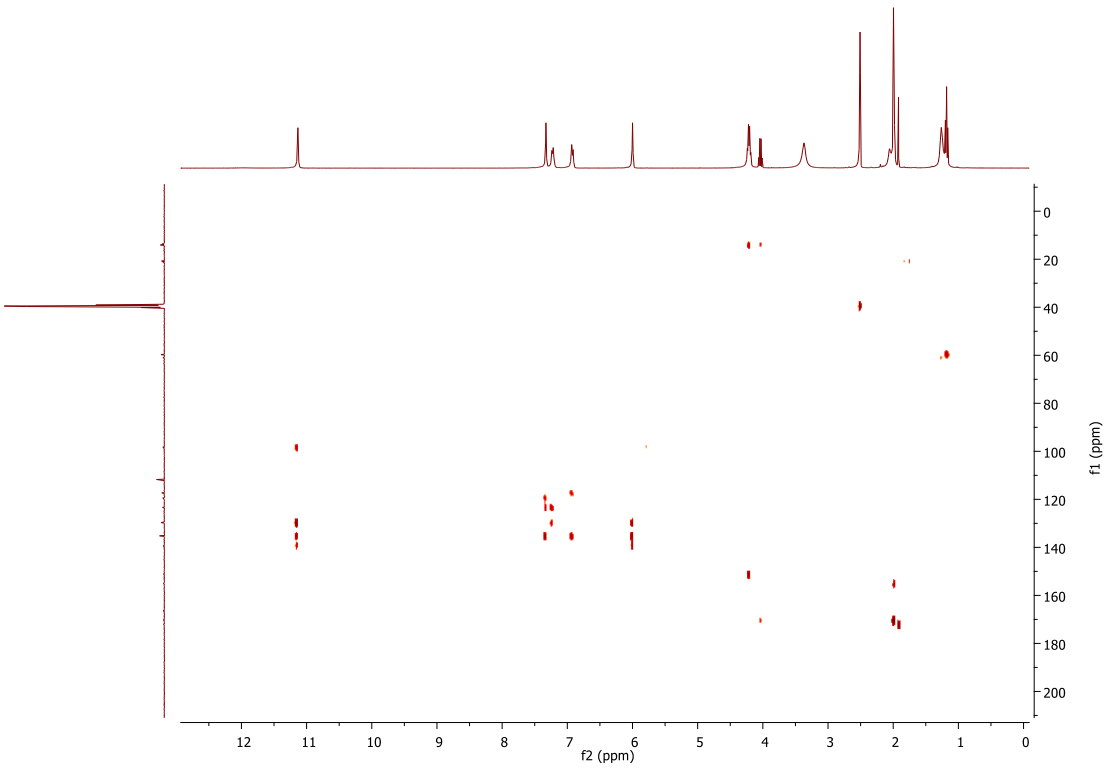




Ethyl 4-((5-chloro-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4e



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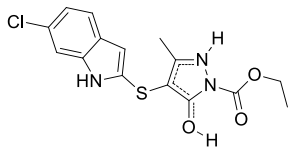
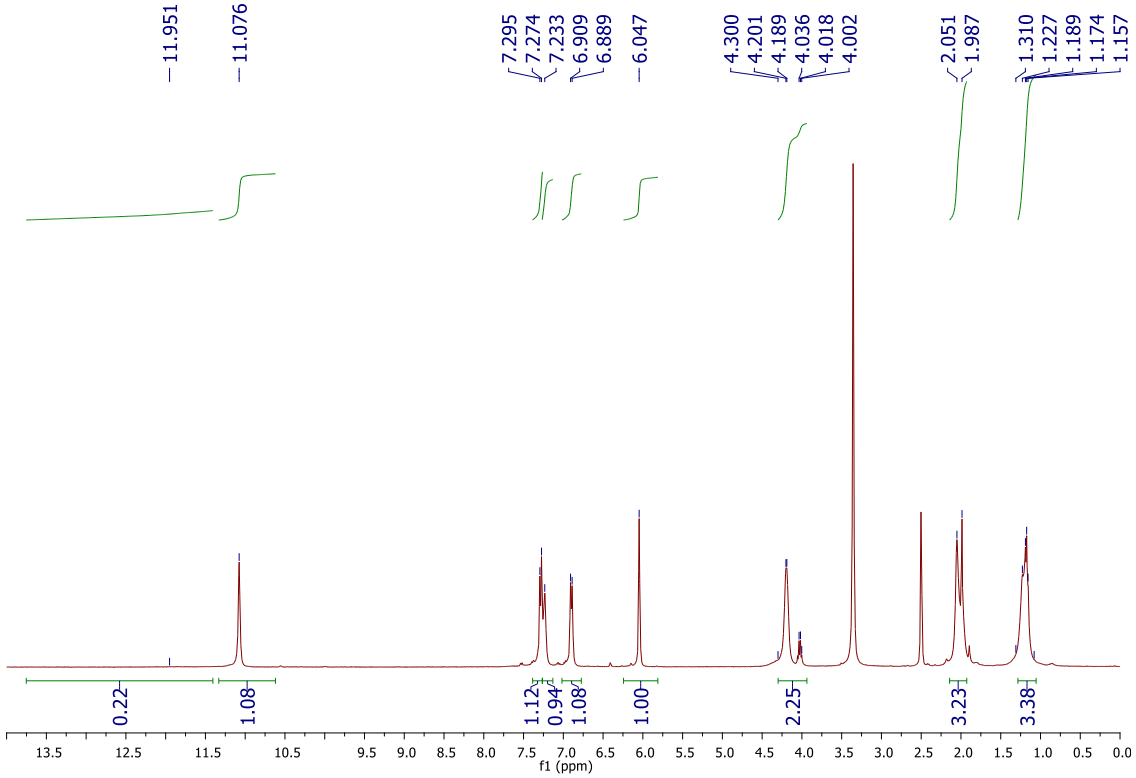
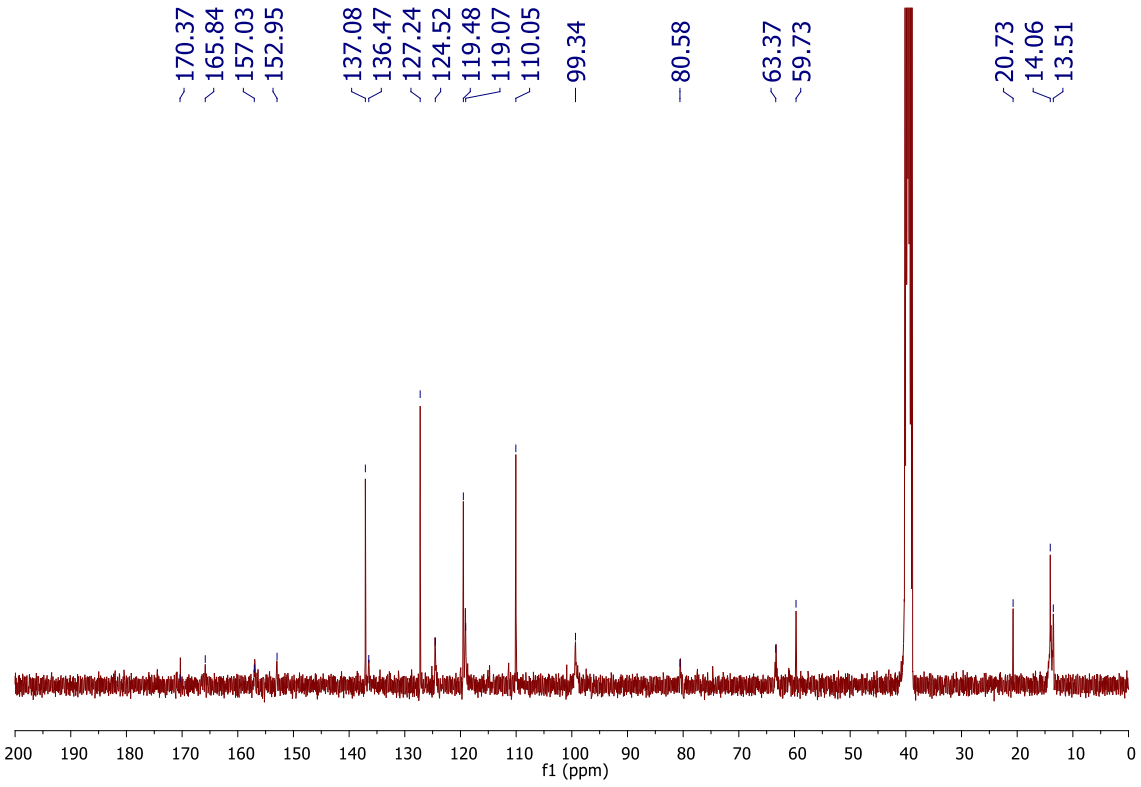
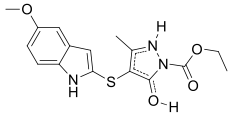
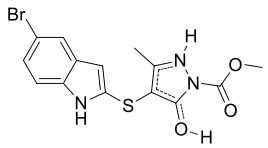


Ethyl 4-((6-chloro-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4f

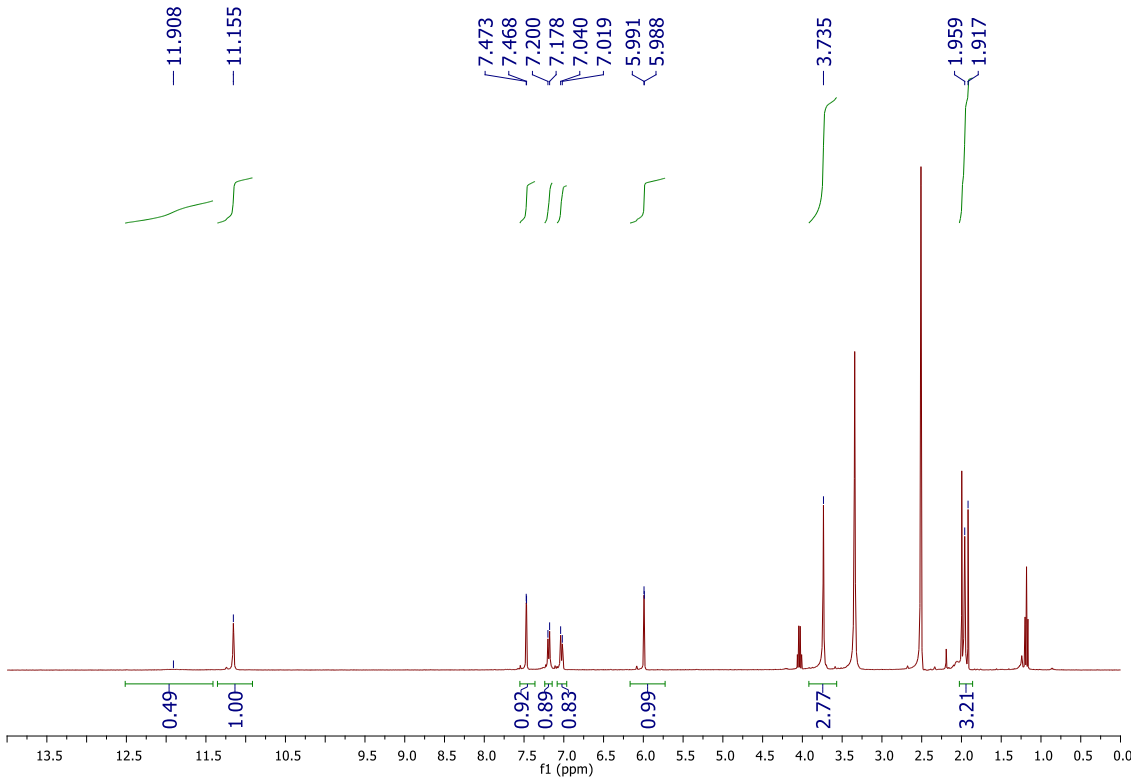


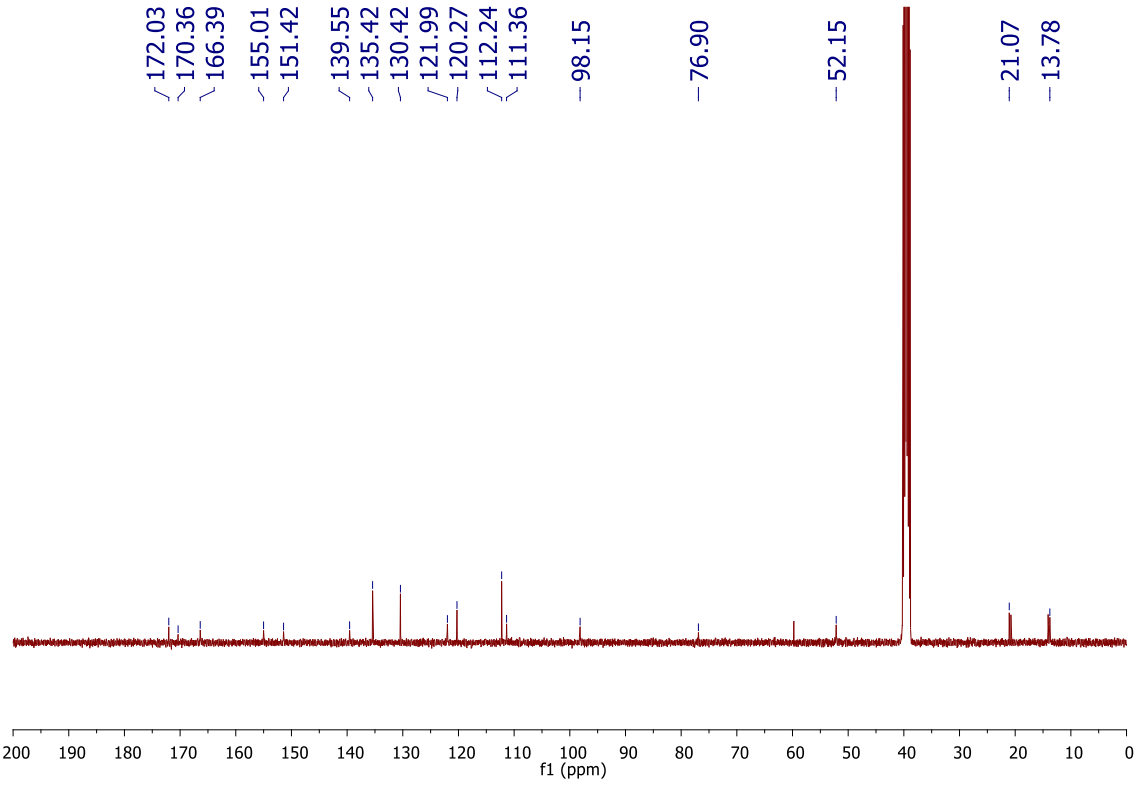


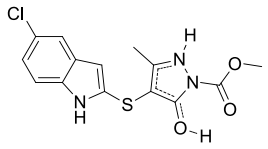




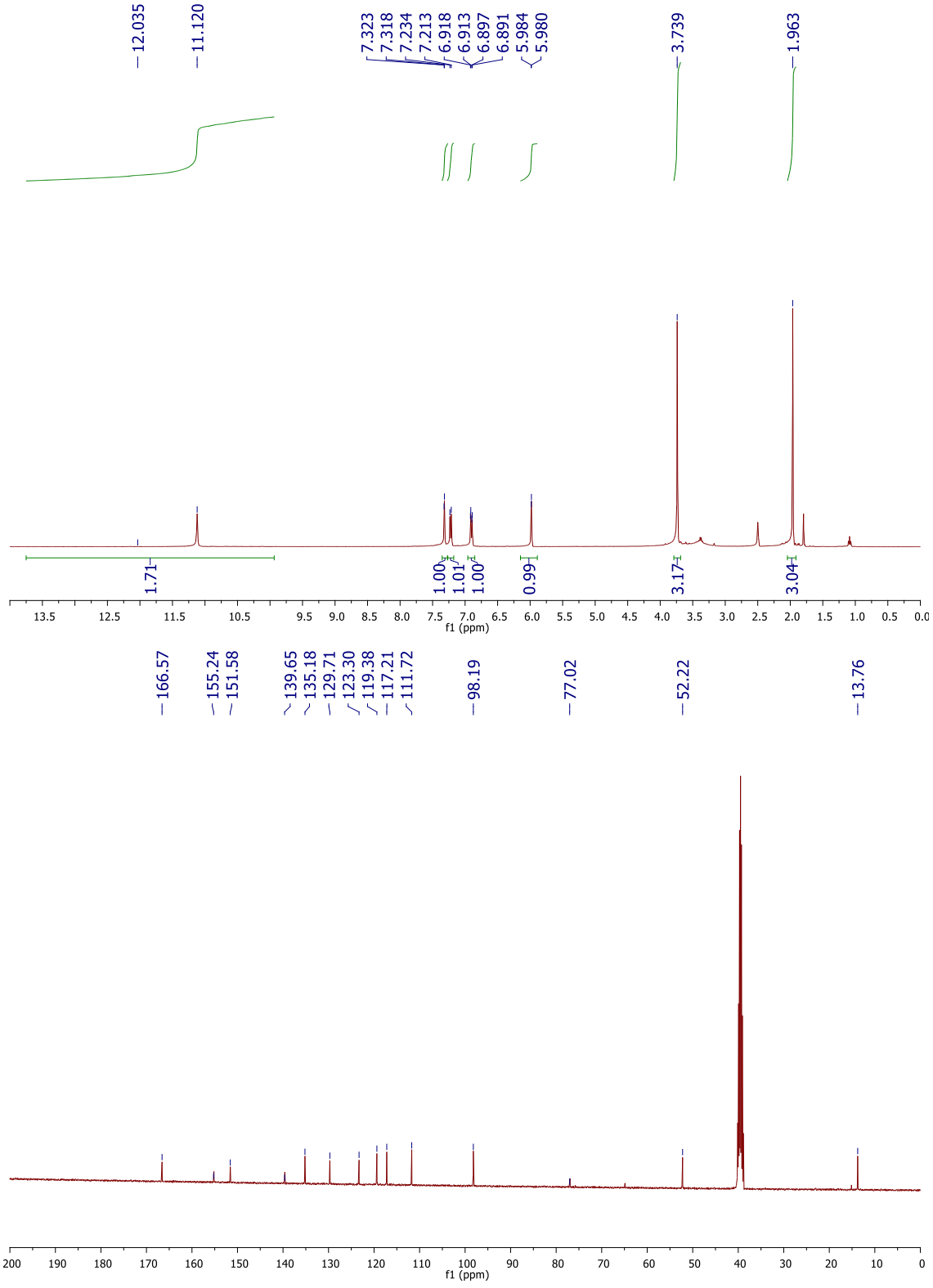
Methyl 4-((5-bromo-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4g

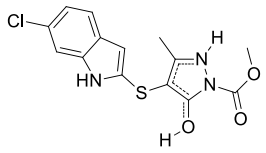




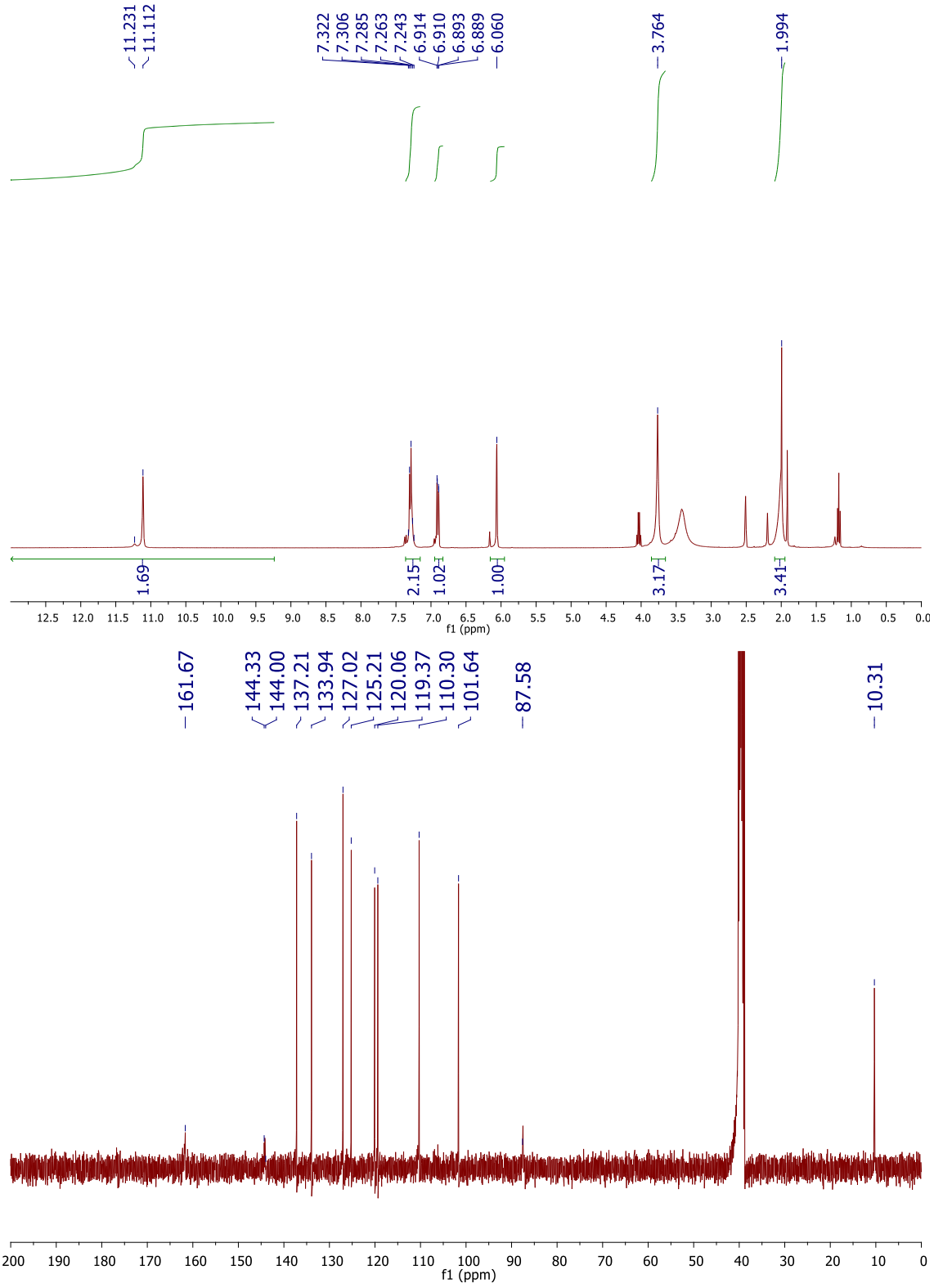


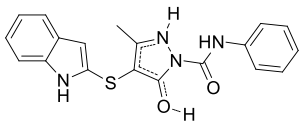
Methyl 4-((5-chloro-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4h



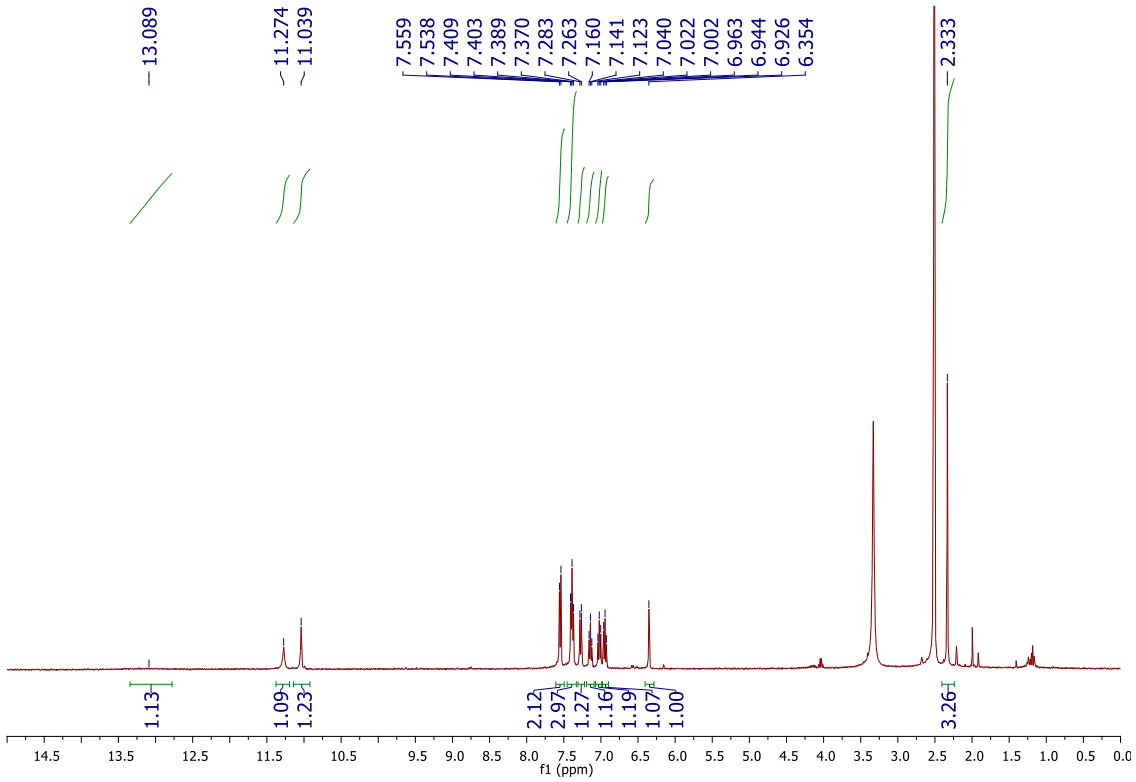


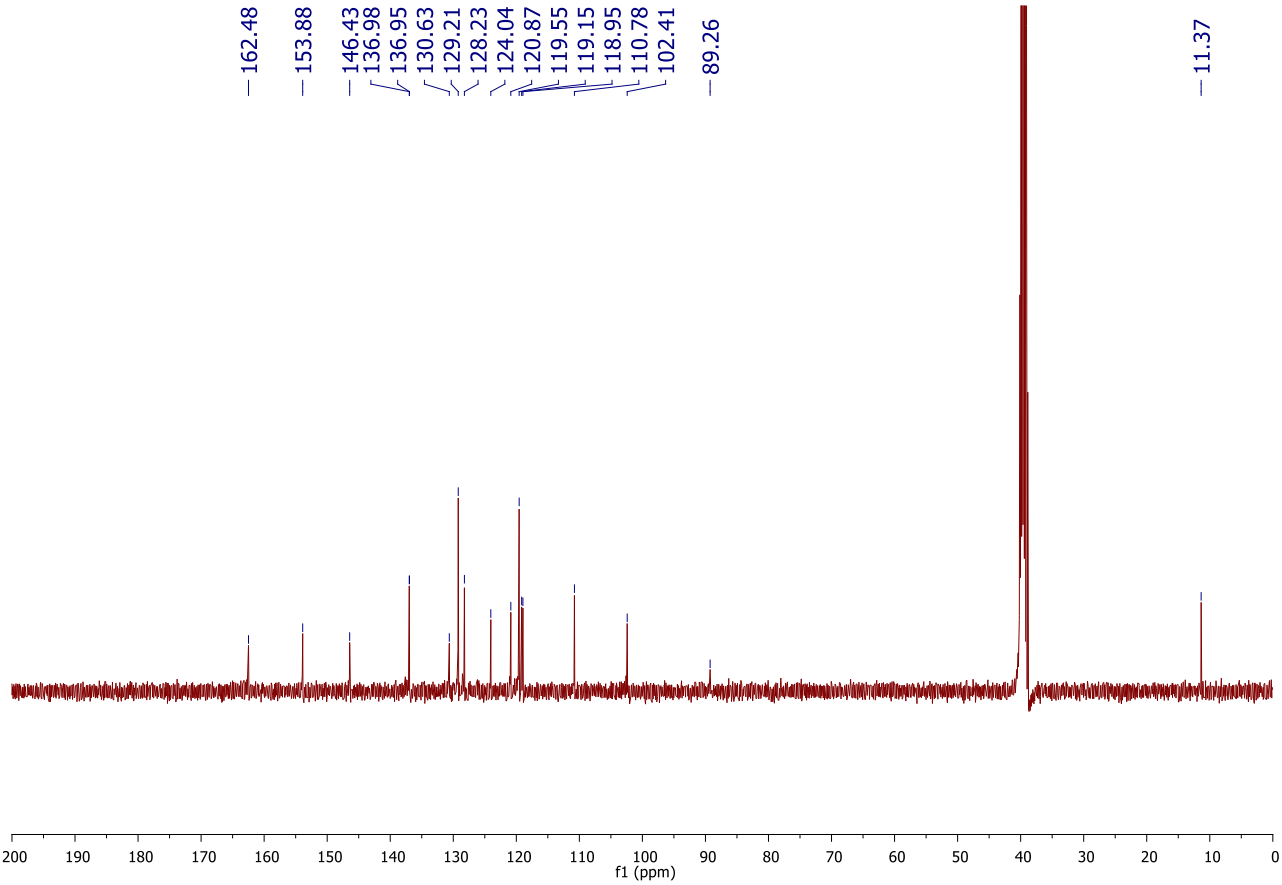
Methyl 4-((6-chloro-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carboxylate 4i

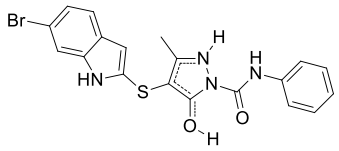




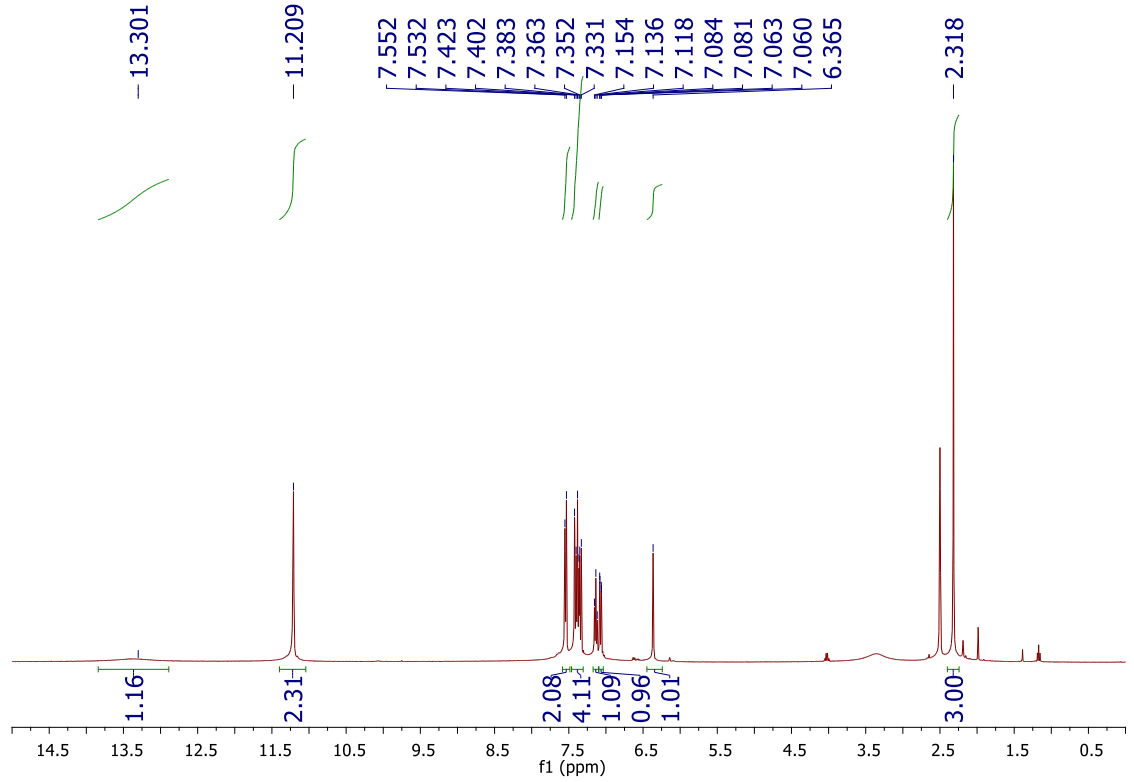
4-((1*H*-Indol-2-yl)thio)-3-methyl-5-oxo-*N*-phenyl-2,5-dihydro-1*H*-pyrazole-1-carboxamide 4j

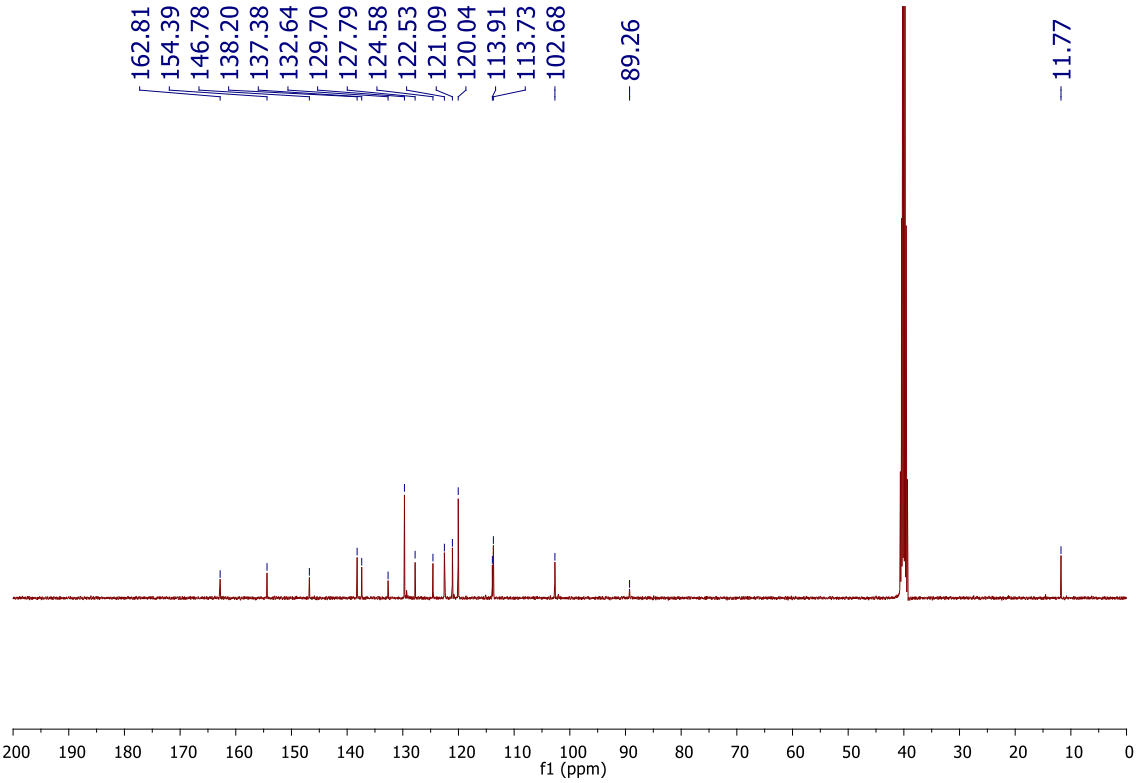




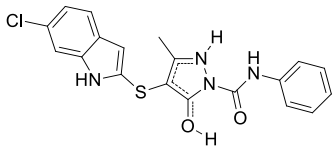


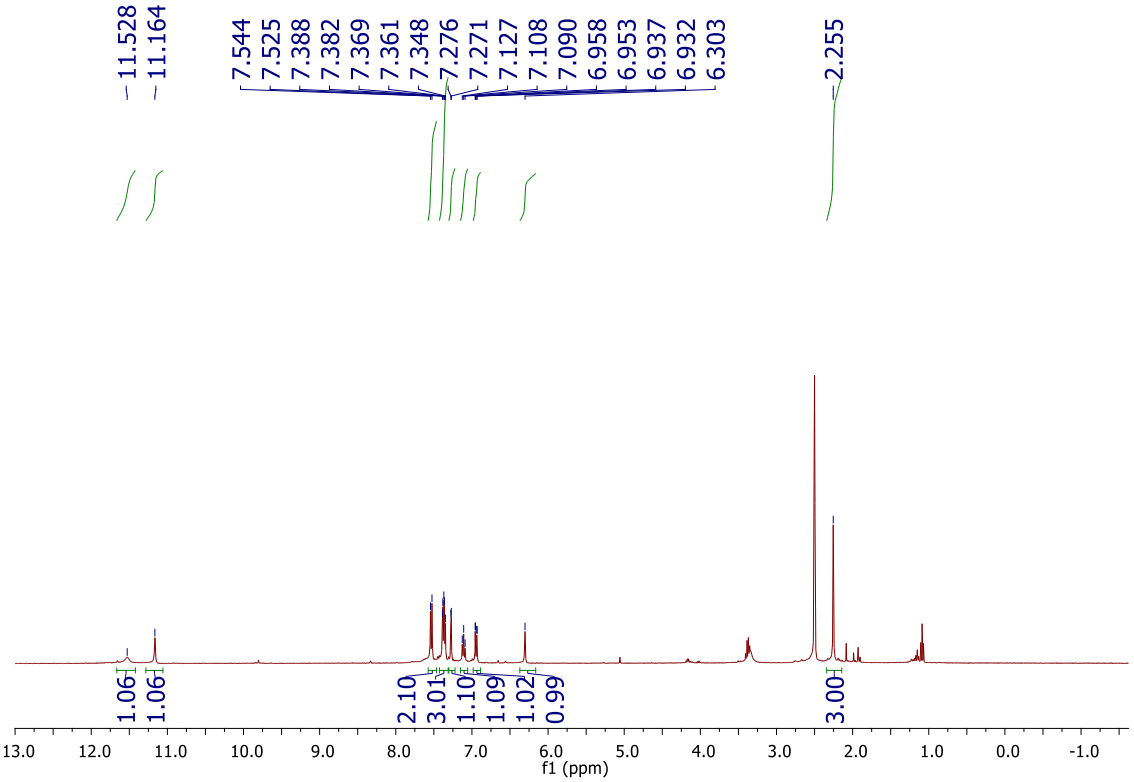
4-((6-bromo-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-*N*-phenyl-2,5-dihydro-1*H*-pyrazole-1-carboxamide 4k

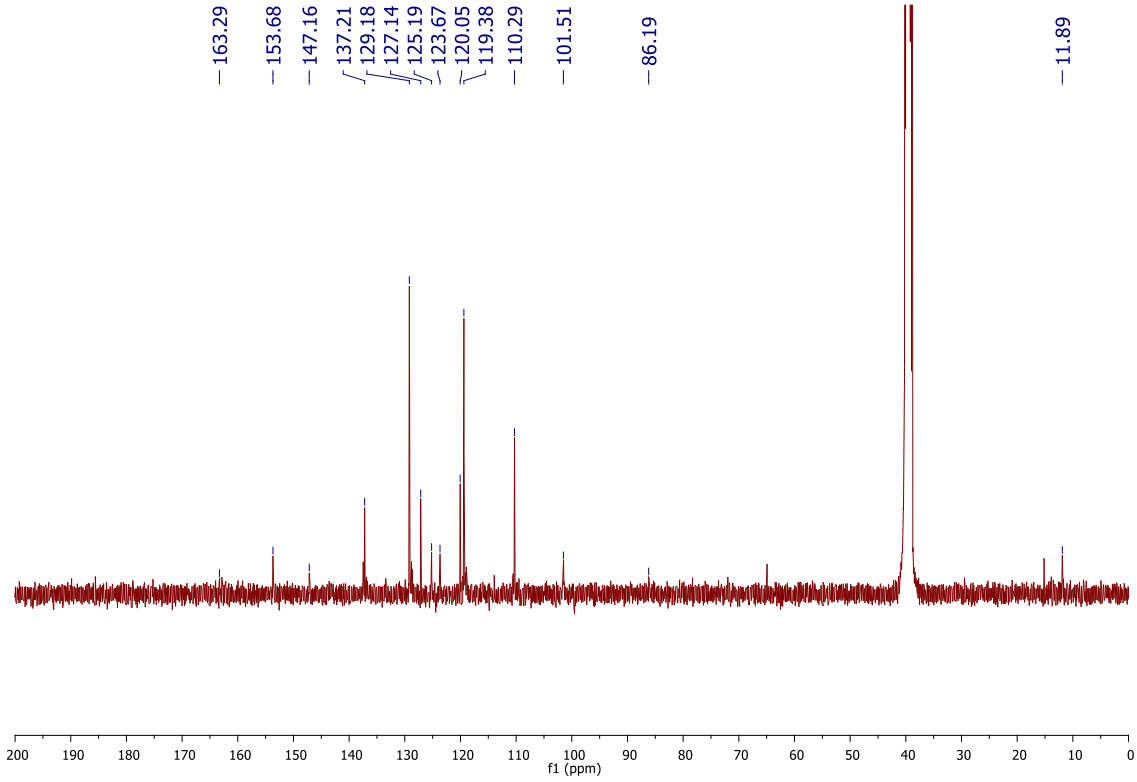


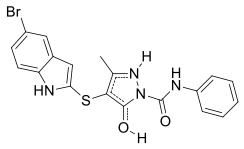


4-((6-Chloro-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-*N*-phenyl-2,5-dihydro-1*H*-pyrazole-1-carboxamide 4l

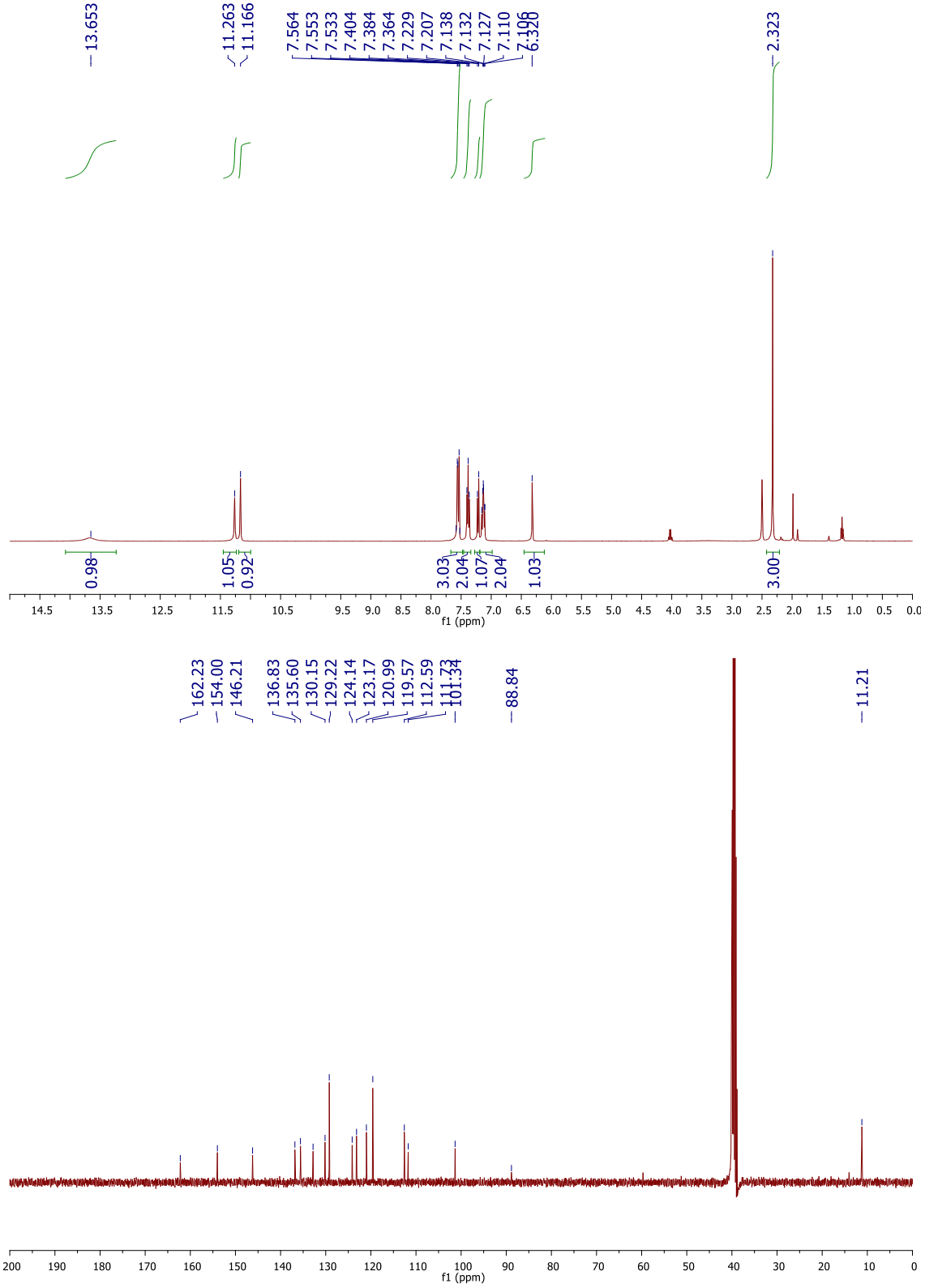


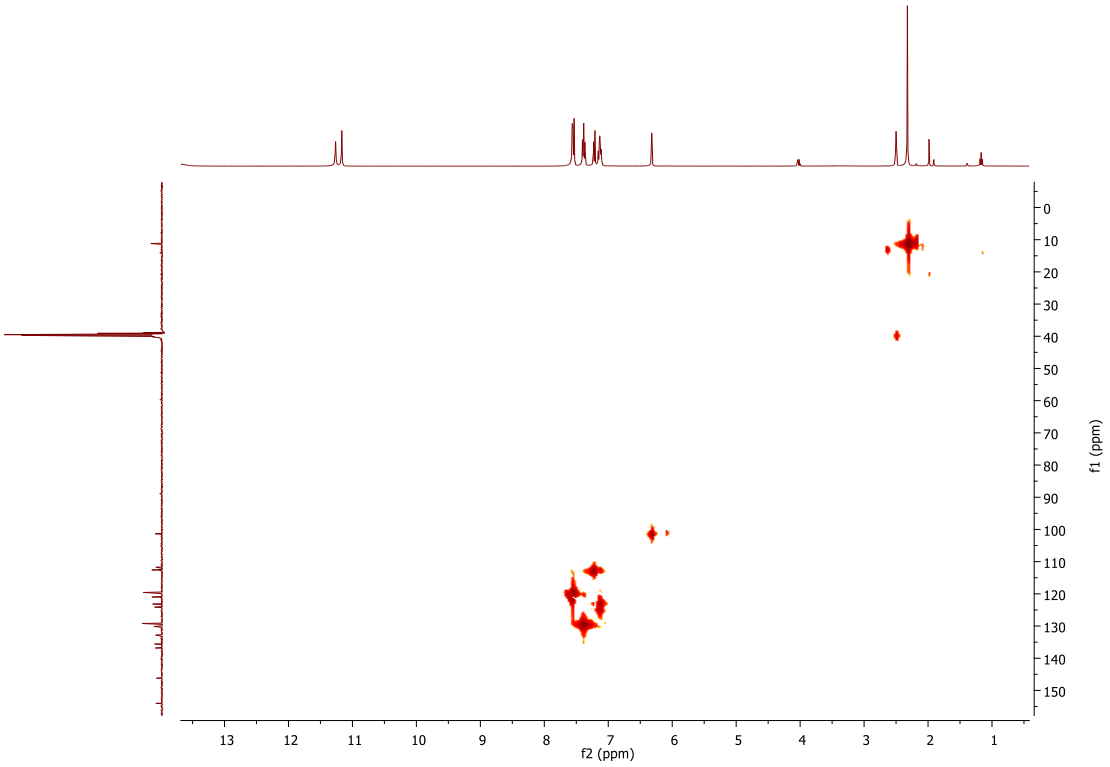






4-((5-bromo-1*H*-indol-2-yl)thio)-3-methyl-5-oxo-*N*-phenyl-2,5-dihydro-1*H*-pyrazole-1-carboxamide 4m

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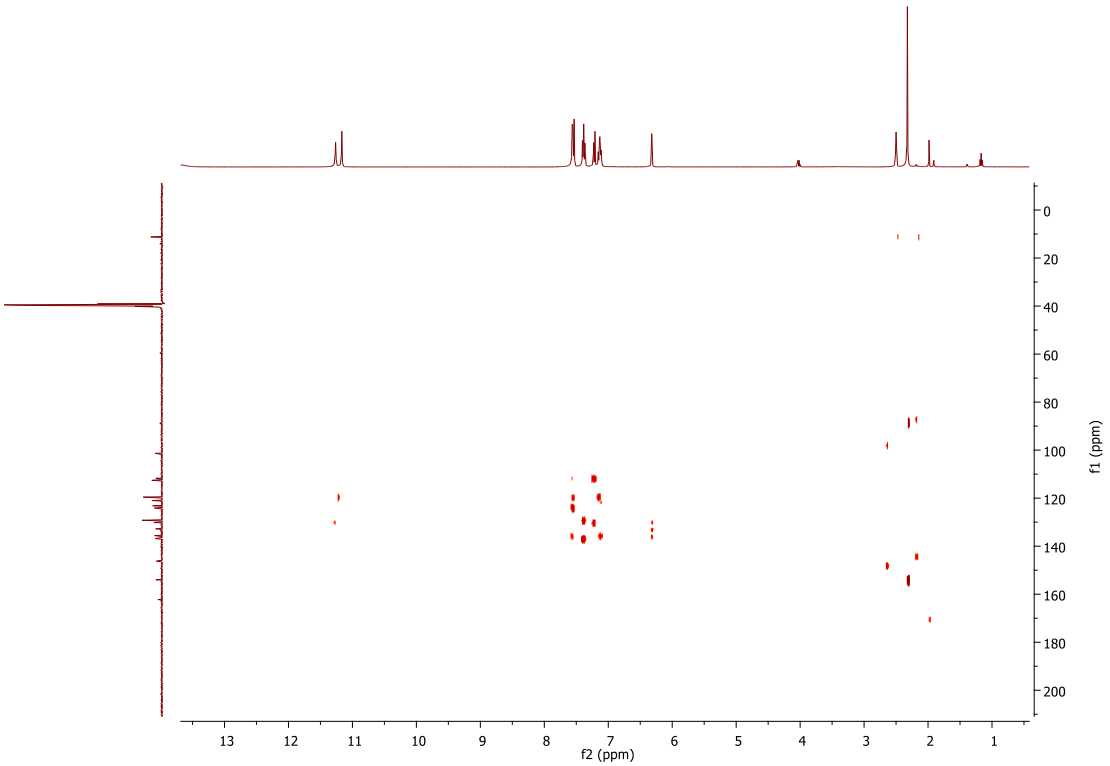
f1 (ppm)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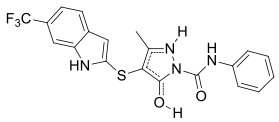
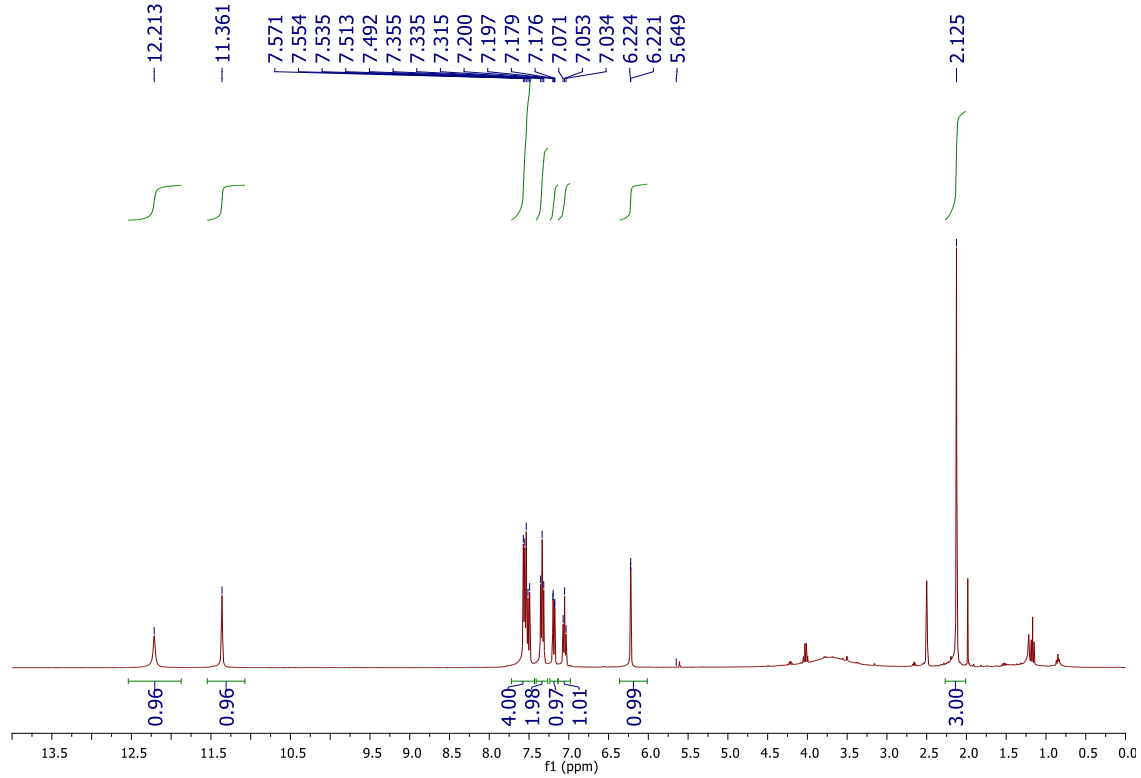
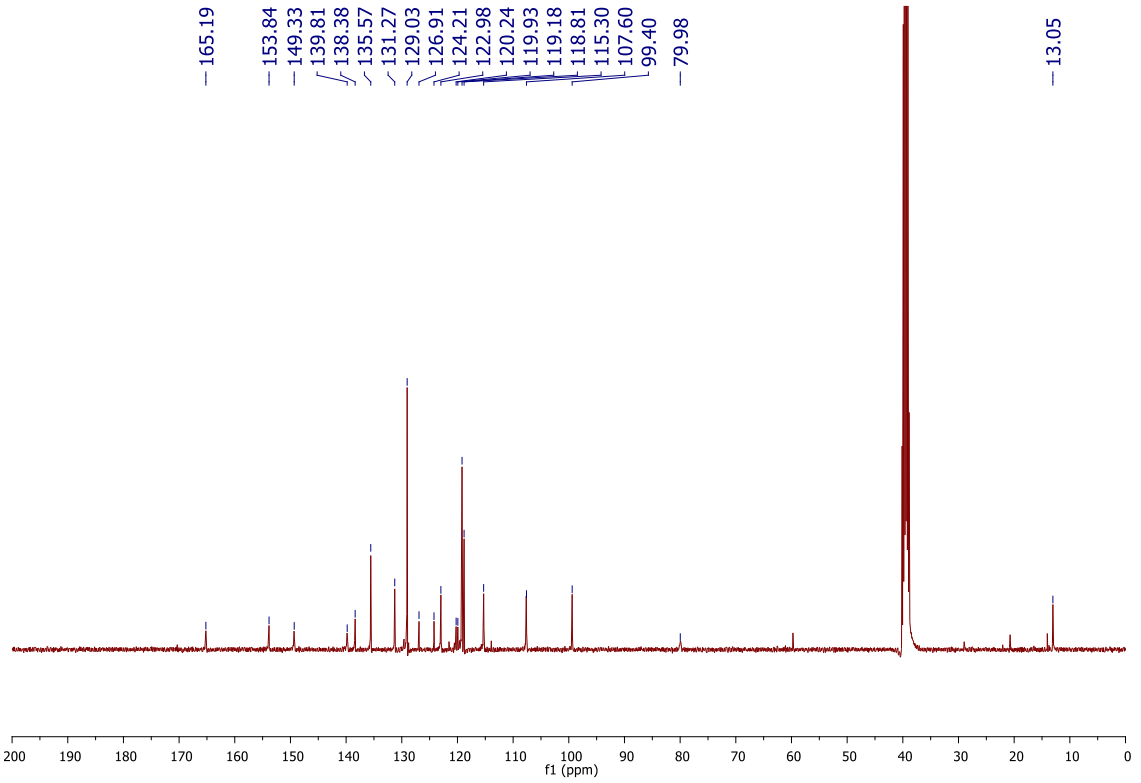
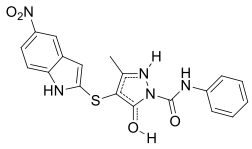
f1 (ppm)



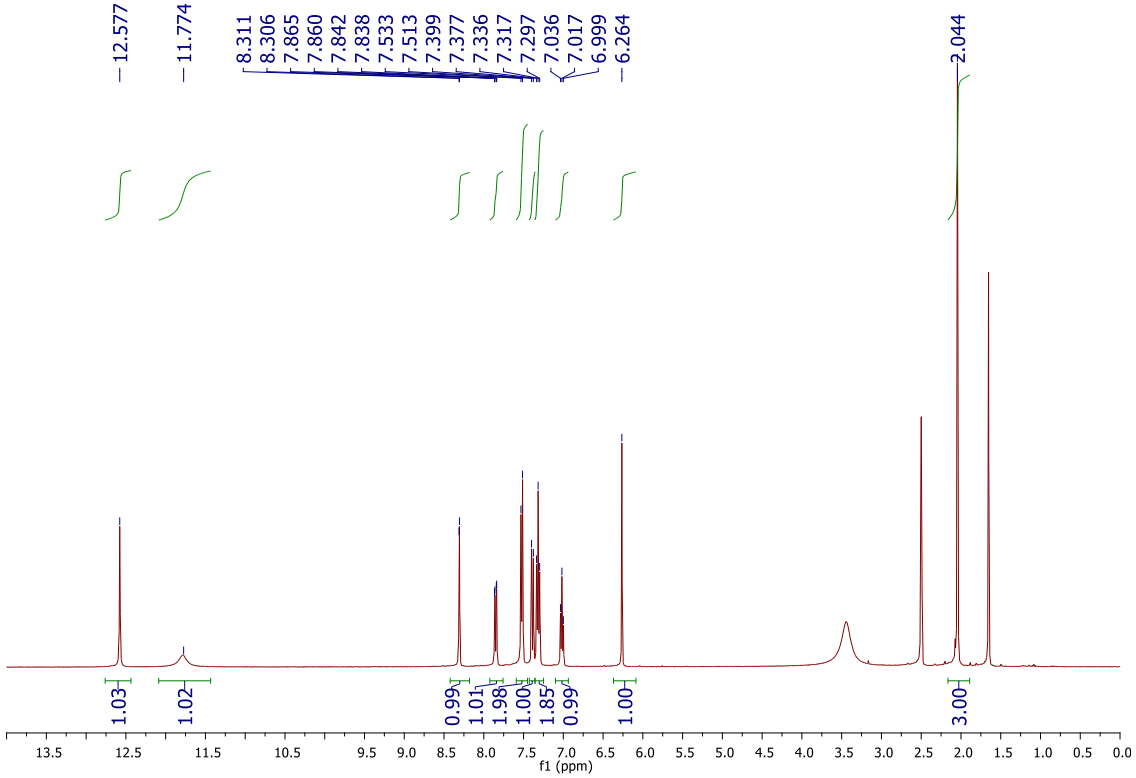
3-methyl-5-oxo-*N*-phenyl-4-((6-(trifluoromethyl)-1*H*-indol-2-yl)thio)-2,5-dihydro-1*H*-pyrazole-1-carboxamide 4n

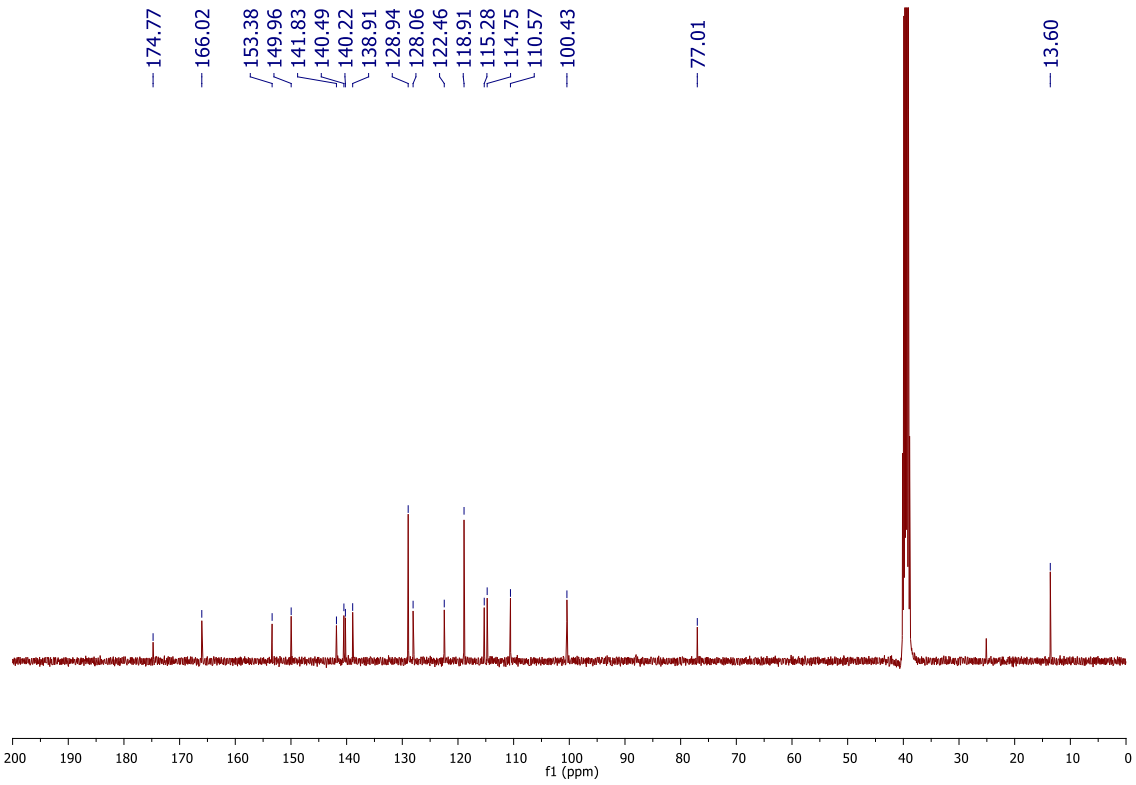


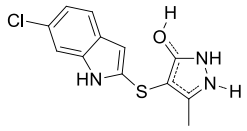




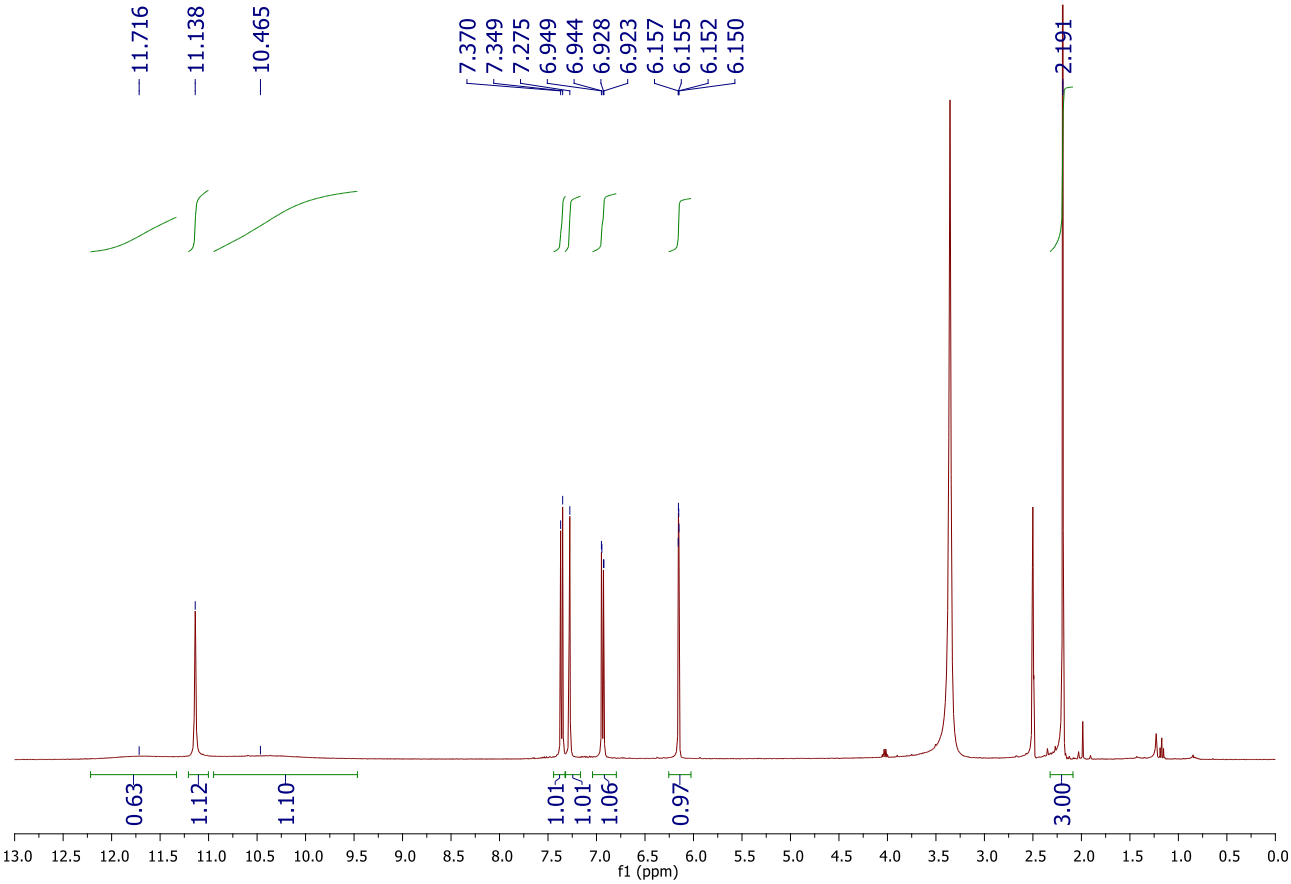
3-methyl-4-((5-nitro-1*H*-indol-2-yl)thio)-5-oxo-*N*-phenyl-2,5-dihydro-1*H*-pyrazole-1-carboxamide 4o

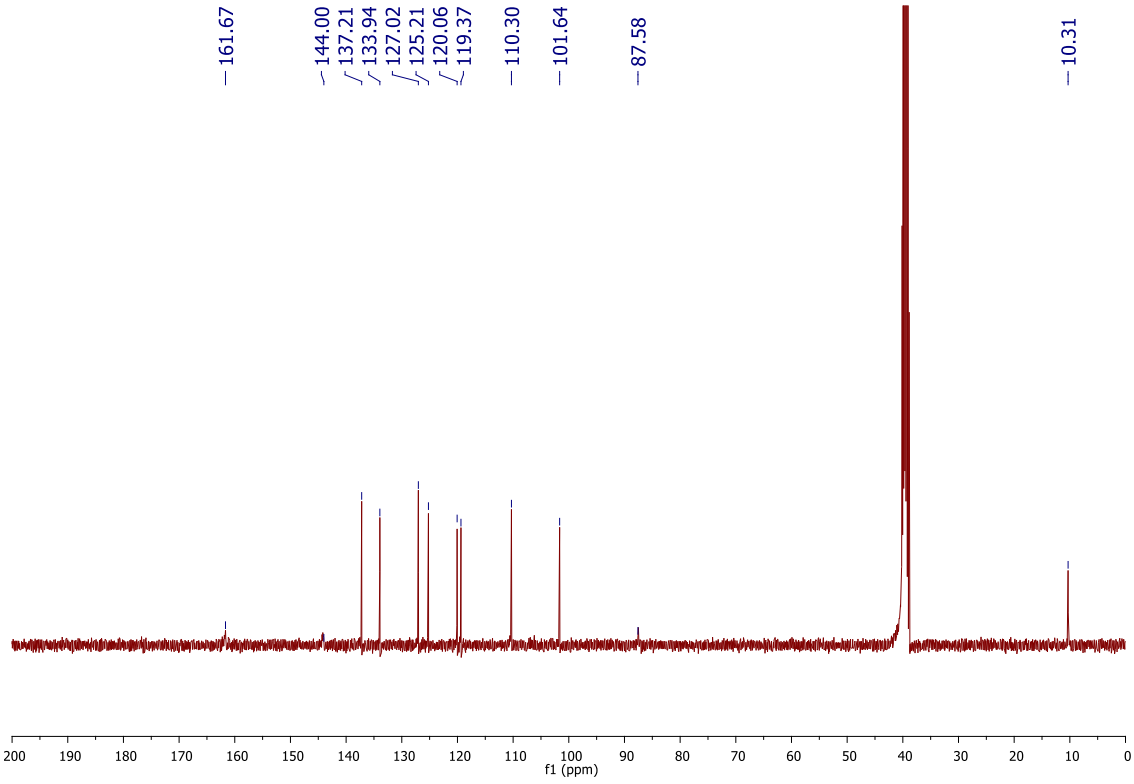


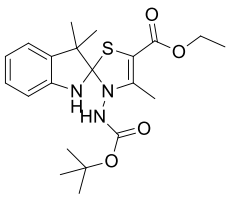




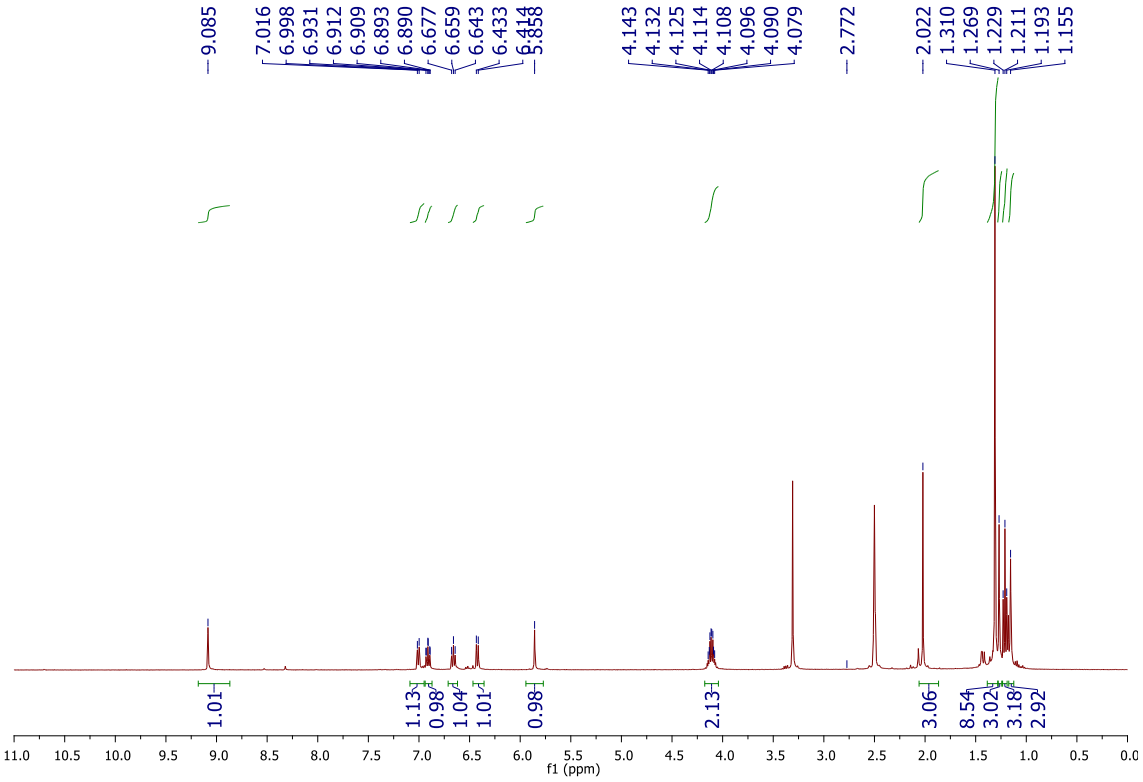
4-((6-Chloro-1*H*-indol-2-yl)thio)-5-methyl-1*H*-pyrazol-3(2*H*)-one 4p

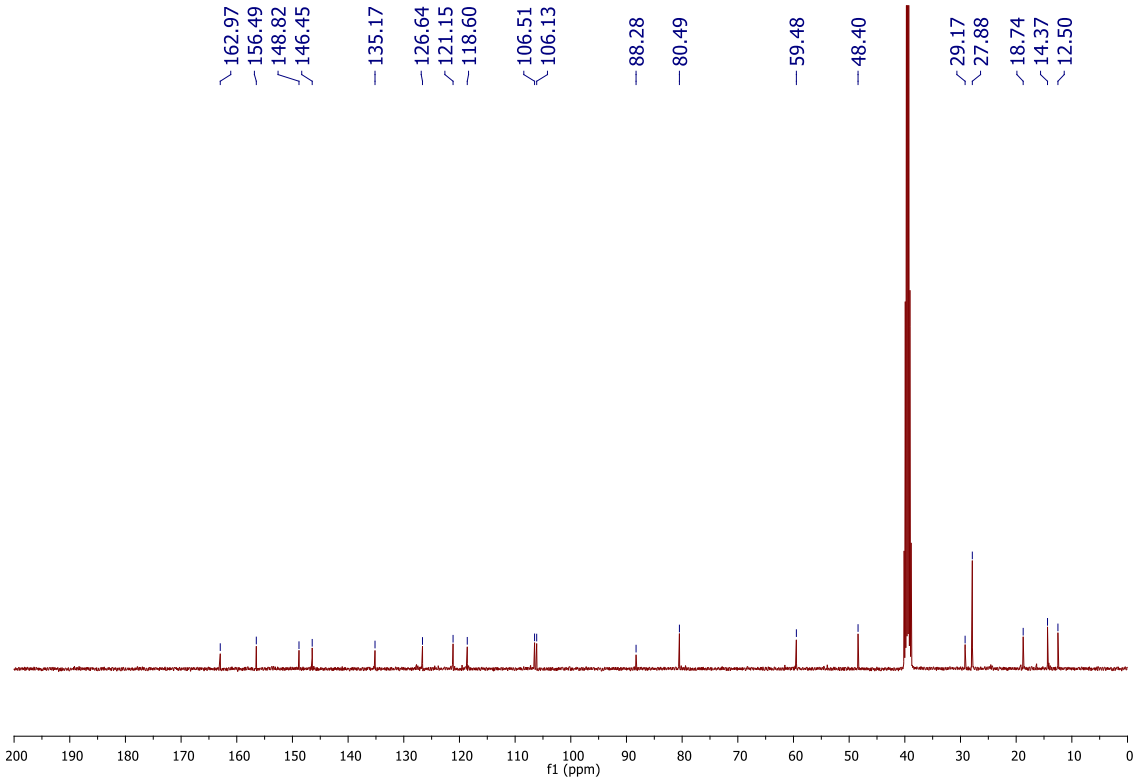


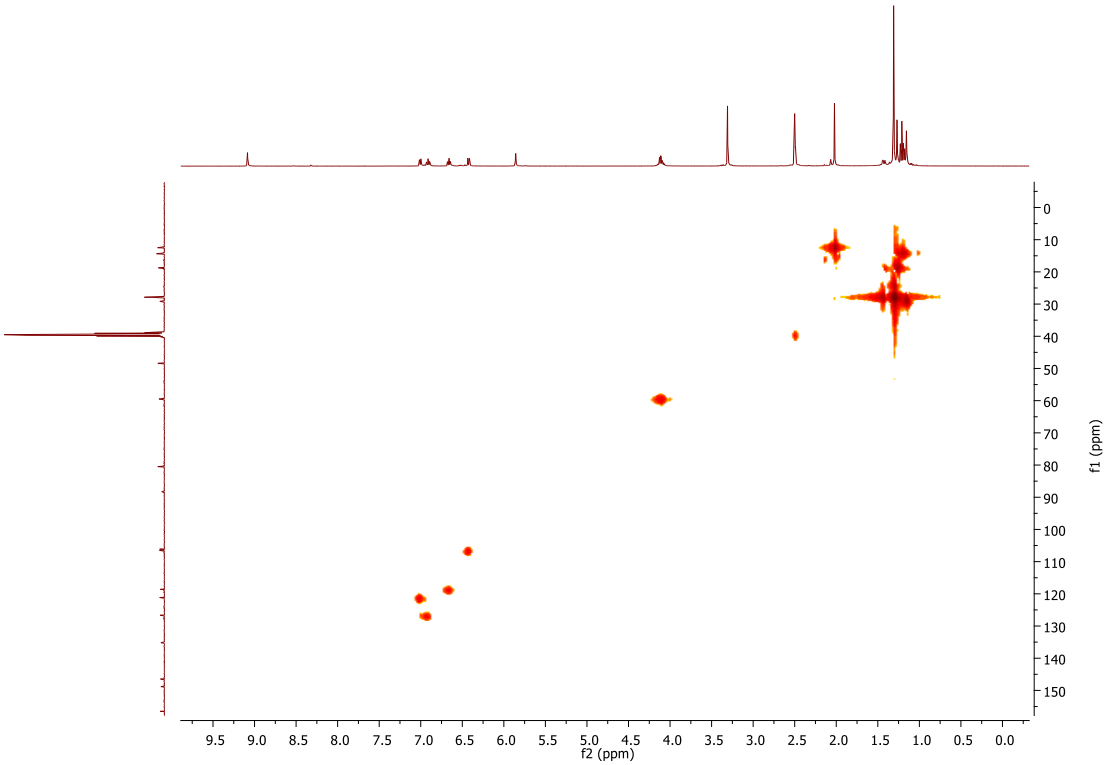


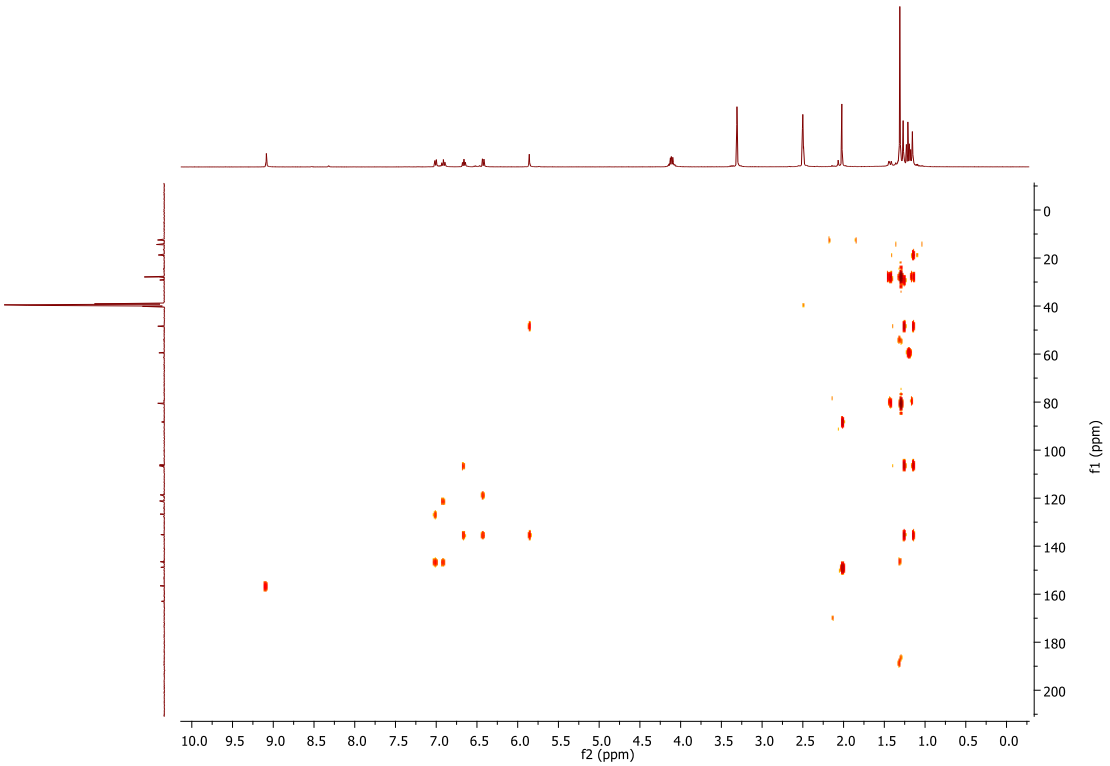


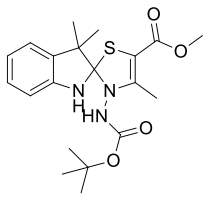
Ethyl 3'-((tert-butoxycarbonyl)amino)3,3,4'-trimethyl-3'*H*-spiro[indoline-2,2'thiazole]-5'-carboxylate 5a.



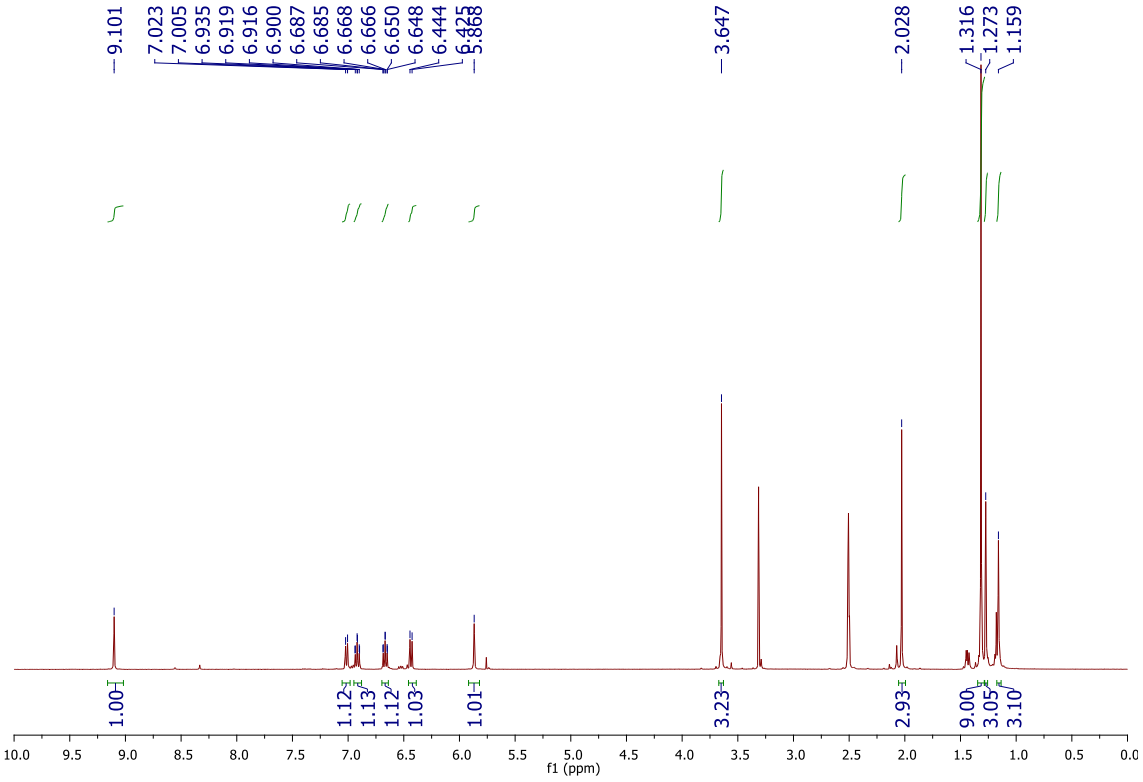


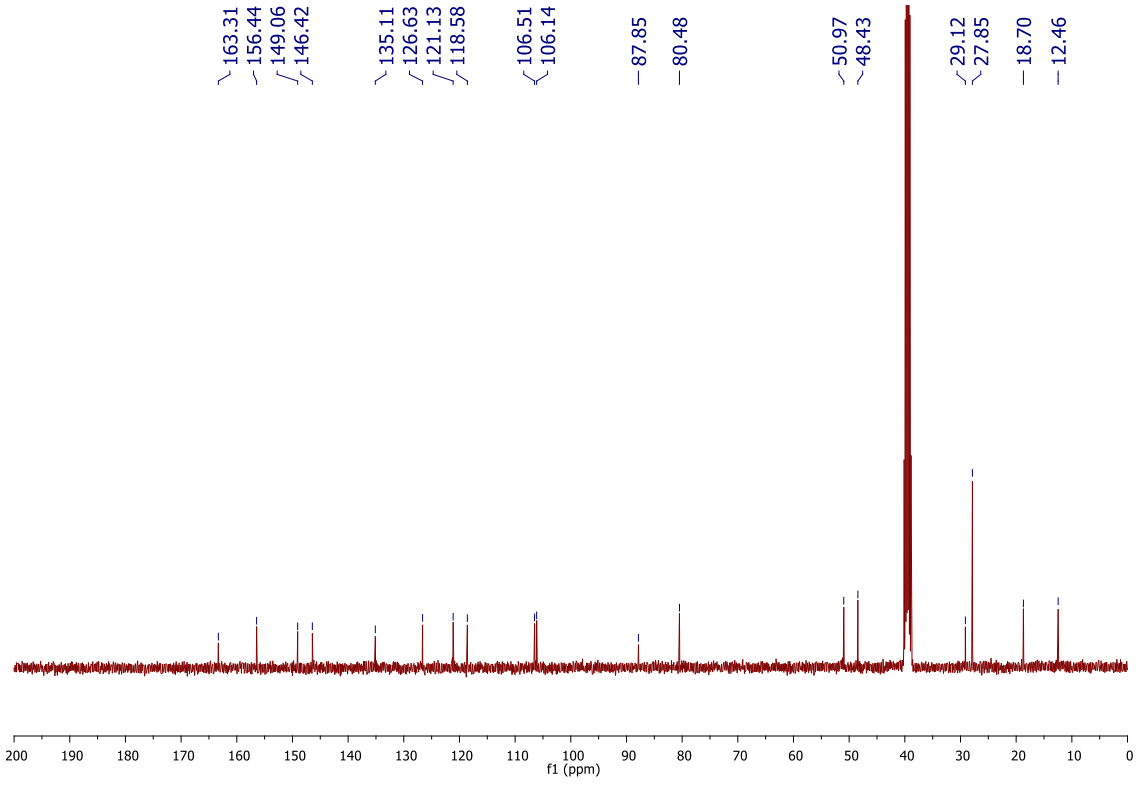

0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
f1 (ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f2 (ppm)

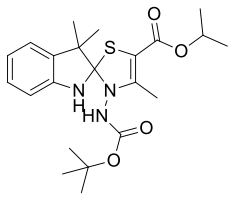

0
20
40
60
80
100
120
140
160
180
200
f1 (ppm)
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f2 (ppm)



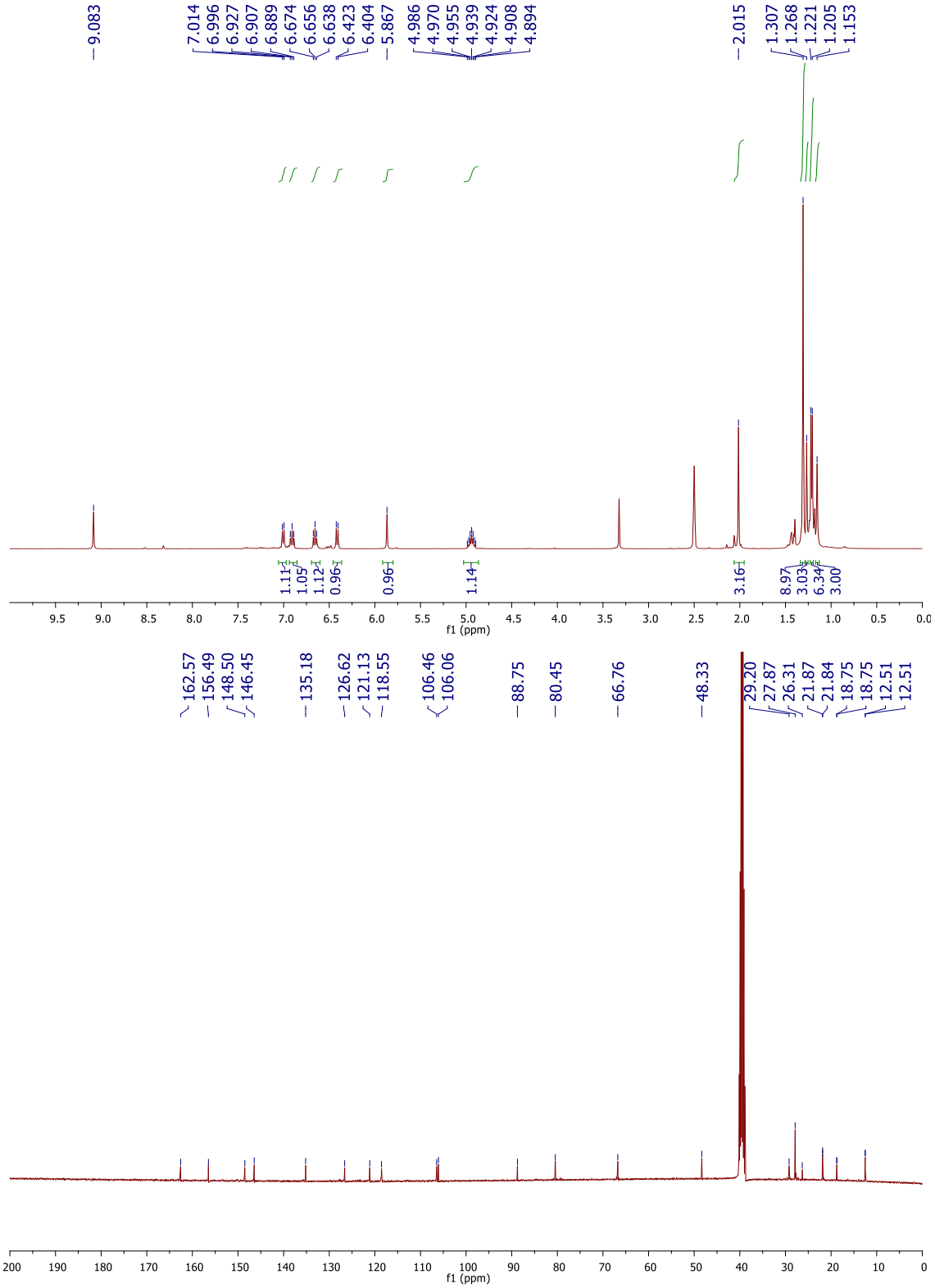
Methyl 3'-((tert-butoxycarbonyl)amino)3,3,4'-trimethyl-3'*H*-spiro[indoline-2,2'thiazole]-5'-carboxylate 5b.

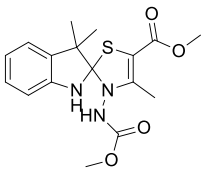




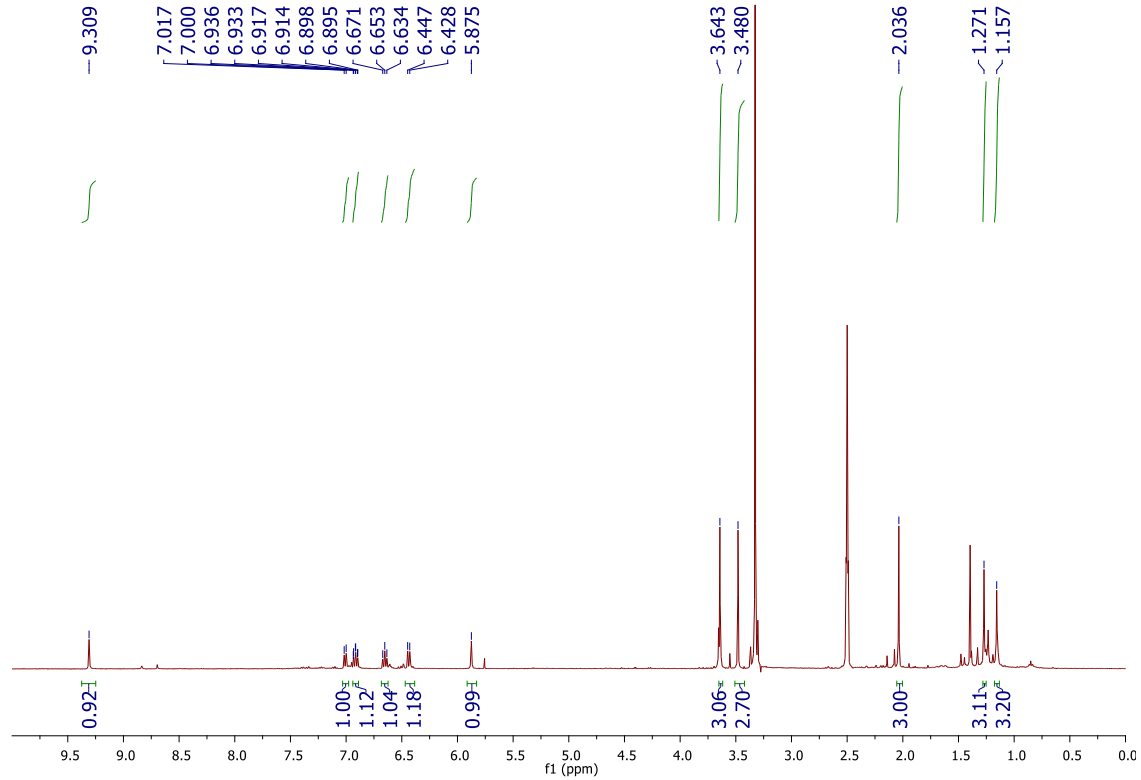


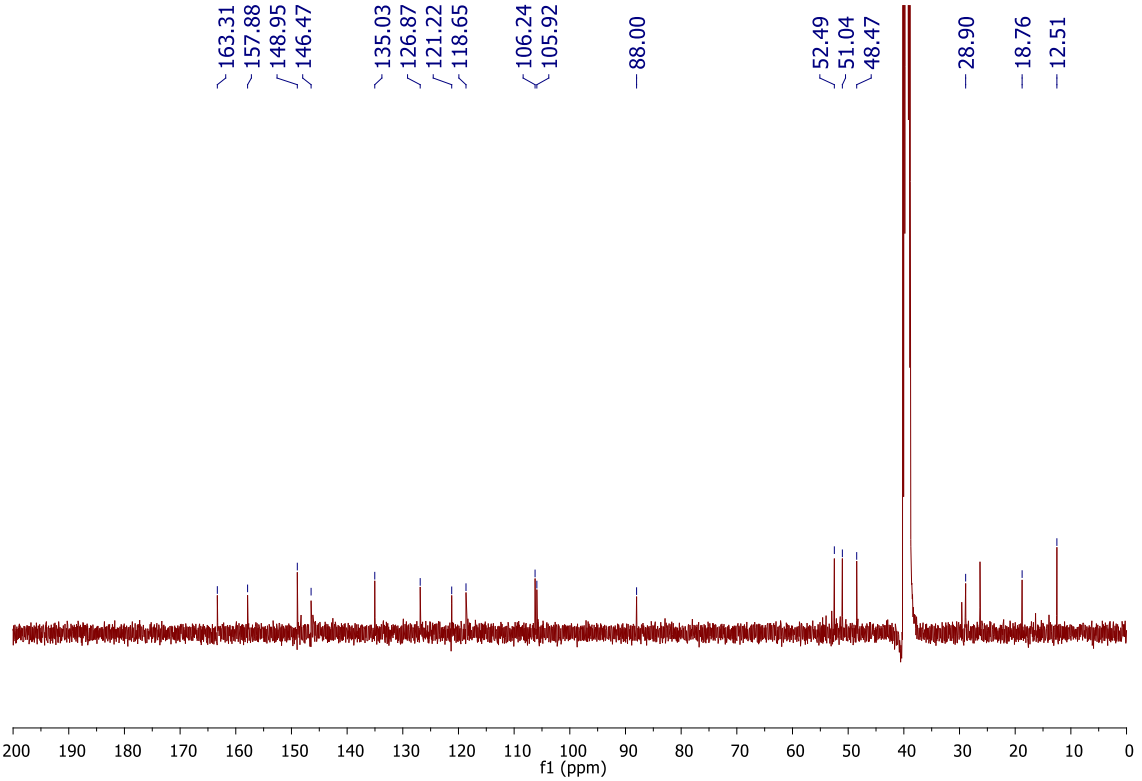
Isopropyl 3'-((tert-butoxycarbonyl)amino)3,3,4'-trimethyl-3'*H*-spiro[indoline-2,2'thiazole]-5'-carboxylate 5c.

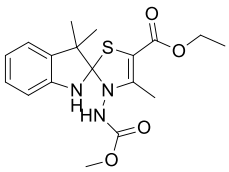




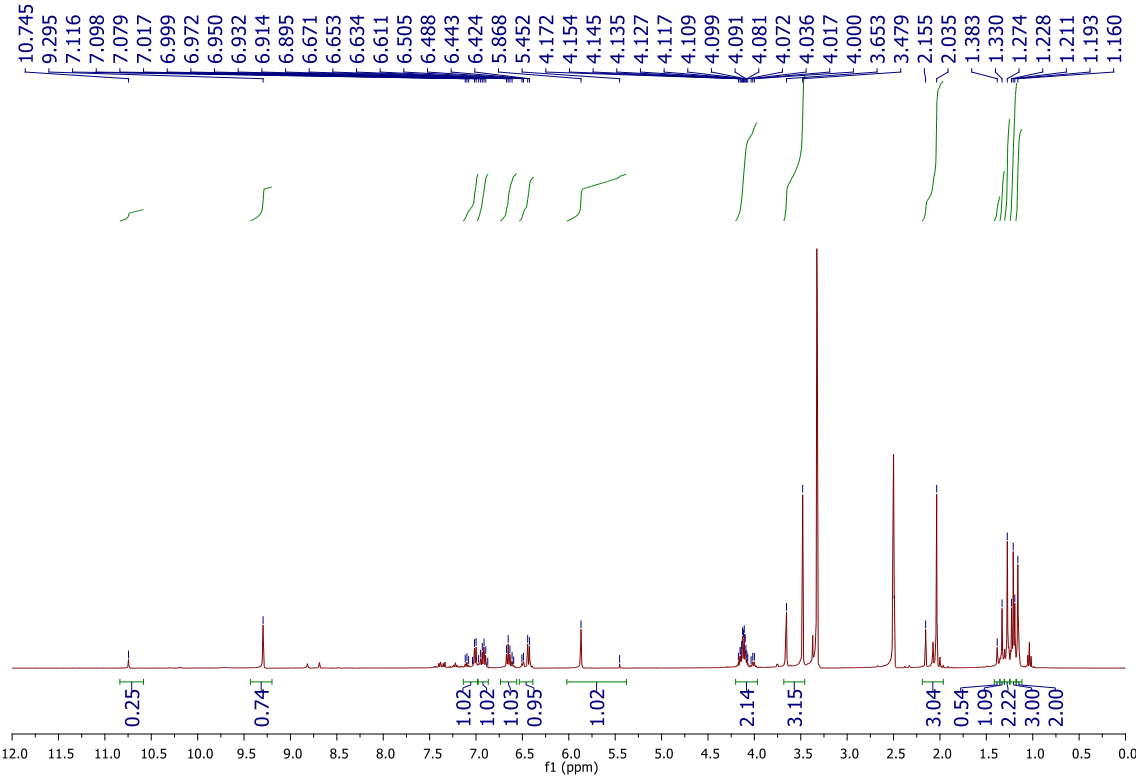
Methyl 3'-((methoxycarbonyl)amino)3,3,4'-trimethyl-3'*H*-spiro[indoline-2,2'thiazole]-5'-carboxylate 5d.

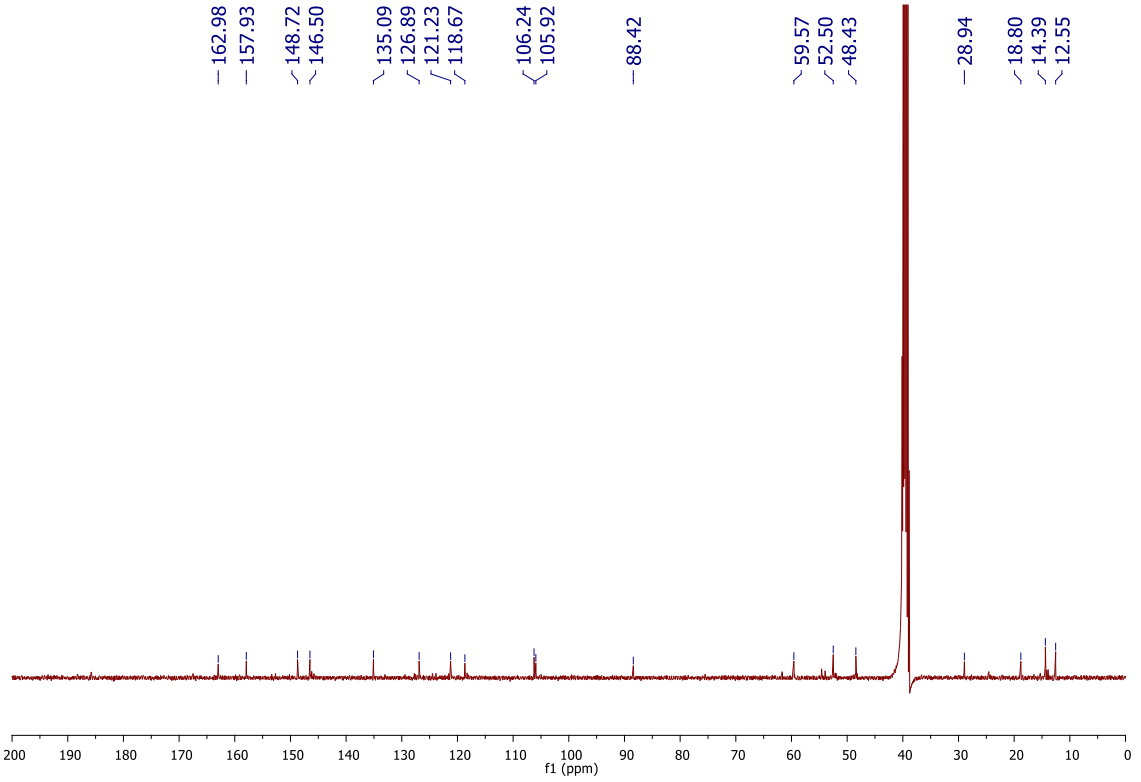




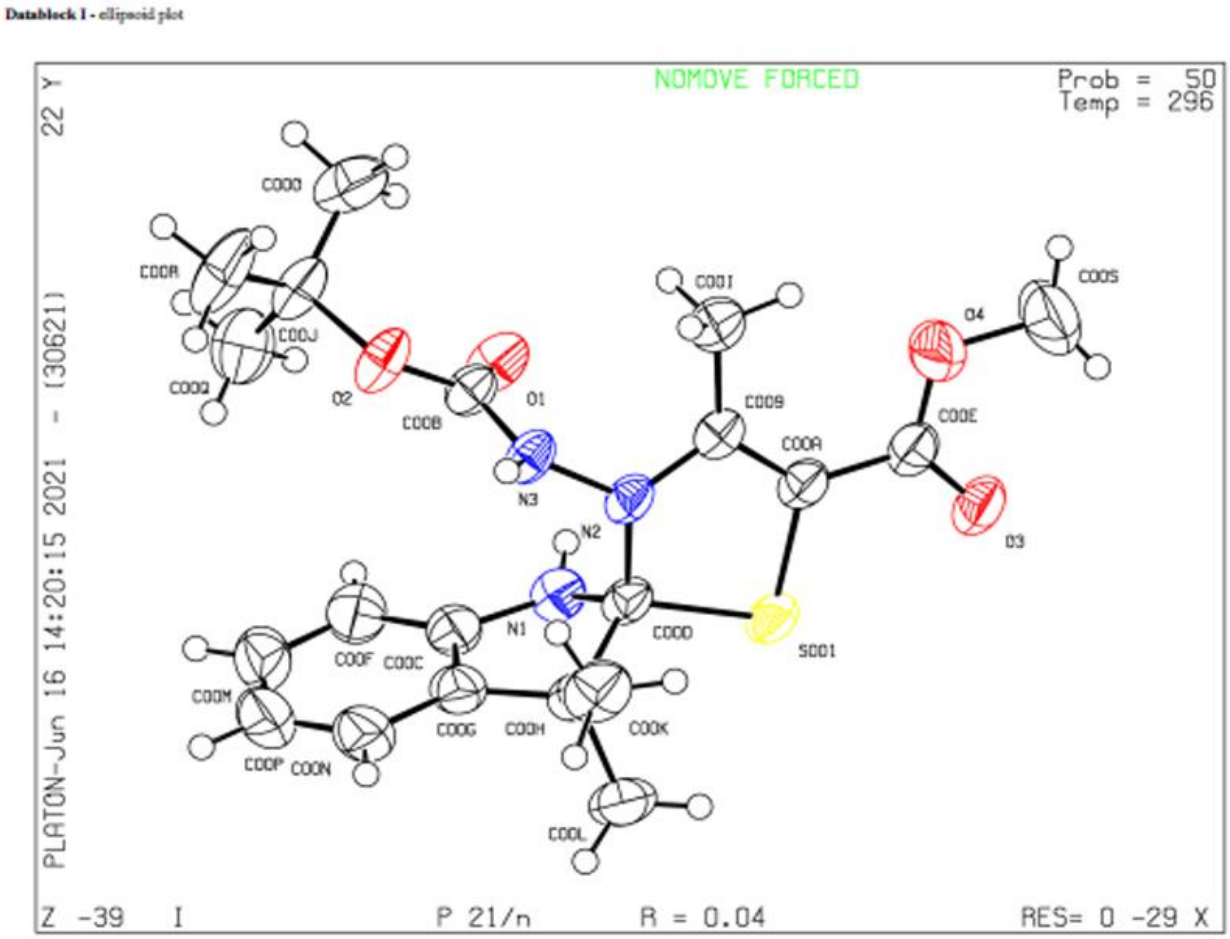


Ethyl 3'-((methoxycarbonyl)amino)-3,3,4'-trimethyl-3'H-spiro[indoline-2,2'-thiazole]-5'-carboxylate 5e





10 Crystal data of compounds 5b (CCDC-2172327)



A specimen of $C_{20}H_{27}N_3O_4S$, approximate dimensions 0.160 mm x 0.180 mm x 0.350 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured.

The total exposure time was 6.78 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 35360 reflections to a maximum θ angle of 27.50° (0.77 Å resolution), of which 4970 were independent (average redundancy 7.115, completeness = 99.5%, R_{int} = 2.51%, R_{sig} = 1.41%) and 4486 (90.26%) were greater than $2\sigma(F^2)$. The final cell constants of a = 10.9192(6) Å, b = 13.5240(7) Å, c = 14.7809(7) Å, β = 95.131(2)°, volume = 2173.97(19) $Å^3$, are based upon the refinement of the XYZ-centroids of 4970 reflections above 20 σ(I) with 4.851° < 2θ < 58.77°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.942. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9620 and 0.9720.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 21/n, with Z = 4 for the formula unit, $C_{20}H_{27}N_3O_4S$. The final anisotropic full-matrix least-squares refinement on F^2 with 268 variables converged at R1 = 4.23%, for the observed data and wR2 = 11.61% for all data. The goodness-of-fit was 1.065. The largest peak in the final difference electron density synthesis was 0.218 $e^-/Å^3$ and the largest hole was -0.233 $e^-/Å^3$ with an RMS deviation of 0.044 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.239 g/cm^3 and F(000), 864 e^-.

Table 1. Sample and crystal data for 5b.

Identification code	**5b**
Chemical formula	$C_{20}H_{27}N_3O_4S$
Formula weight	405.50 g/mol
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal size	0.160 x 0.180 x 0.350 mm
Crystal system	monoclinic
Space group	P 21/n
Unit cell dimensions	a = 10.9192(6) Å α = 90°
	b = 13.5240(7) Å β = 95.131(2)°
	c = 14.7809(7) Å γ = 90°
Volume	2173.97(19) $Å^3$
Z	4
Density (calculated)	1.239 g/cm^3
Absorption coefficient	0.178 mm^{-1}
F(000)	864

Table 2. Data collection and structure refinement for mancio2101.

Theta range for data collection	2.43 to 27.50°
Index ranges	-14<=h<=14, -17<=k<=17, -19<=l<=19
Reflections collected	35360
Independent reflections	4970 [R(int) = 0.0251]
Coverage of independent reflections	99.5%
Absorption correction	Multi-Scan
Max. and min. transmission	0.9720 and 0.9620
Structure solution technique	direct methods
Structure solution program	XT, VERSION 2014/5
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2014/7 (Sheldrick, 2014)
Function minimized	$\Sigma\ w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	4970 / 0 / 268
Goodness-of-fit on F^2	1.065
Δ/σ_{max}	0.001

Final R indices	4486 data; I>2σ(I)	R1 = 0.0423, wR2 = 0.1131
	all data	R1 = 0.0459, wR2 = 0.1161
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0576P)^2+0.5452P]$	
	where $P=(F_o^2+2F_c^2)/3$	
Largest diff. peak and hole	0.218 and -0.233 eÅ^{-3}	
R.M.S. deviation from mean	0.044 eÅ^{-3}	

Table 3. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2) for mancio2101.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
S001	0.65338(4)	0.30245(2)	0.70929(3)	0.04720(12)
O1	0.57262(11)	0.59708(7)	0.55396(7)	0.0529(3)
O2	0.55452(11)	0.72976(7)	0.64690(7)	0.0514(3)
O3	0.86981(11)	0.21618(8)	0.63547(7)	0.0529(3)
N3	0.61995(11)	0.59077(8)	0.70668(7)	0.0396(3)
N2	0.65843(10)	0.49330(8)	0.70928(7)	0.0385(2)
N1	0.46328(11)	0.42298(9)	0.64723(8)	0.0434(3)
O4	0.97060(12)	0.35610(9)	0.61129(11)	0.0727(4)
C009	0.76424(12)	0.46589(9)	0.67222(9)	0.0391(3)
C00A	0.77625(13)	0.36623(10)	0.66590(9)	0.0416(3)

C00B	0.58007(13)	0.63626(9)	0.62752(9)	0.0395(3)
C00C	0.37114(13)	0.48089(10)	0.67887(10)	0.0453(3)
C00D	0.56332(13)	0.41550(9)	0.71684(9)	0.0383(3)
C00E	0.87394(14)	0.30569(10)	0.63653(9)	0.0453(3)
C00F	0.27477(14)	0.52779(12)	0.62976(13)	0.0571(4)
C00G	0.38695(14)	0.48659(11)	0.77342(11)	0.0492(3)
C00H	0.49629(14)	0.42368(11)	0.80625(9)	0.0469(3)
C00I	0.85231(15)	0.54380(11)	0.64903(13)	0.0563(4)
C00J	0.50723(17)	0.79995(11)	0.57577(10)	0.0534(4)
C00K	0.57839(18)	0.46318(14)	0.88682(10)	0.0617(4)
C00L	0.44698(19)	0.32093(13)	0.82987(13)	0.0649(5)
C00M	0.19336(16)	0.58087(15)	0.67819(17)	0.0714(5)
C00N	0.30433(18)	0.53928(14)	0.81988(14)	0.0661(5)
C00O	0.5946(2)	0.80798(14)	0.50260(14)	0.0740(5)
C00P	0.20731(18	0.58675(15	0.77131(17	0.0765(6)

	)	)	)	
C00Q	0.37956(19)	0.76700(17)	0.53962(15)	0.0773(6)
C00R	0.5039(3)	0.89581(13)	0.62915(15)	0.0869(7)
C00S	0.0748(2)	0.29760(18)	0.5899(2)	0.0974(8)

Table 4. Bond lengths (Å) for mancio2101.

S001-C00A	1.7634(14)	S001-C00D	1.8265(13)
O1-C00B	1.2057(16)	O2-C00B	1.3316(16)
O2-C00J	1.4751(16)	O3-C00E	1.2115(17)
N3-C00B	1.3587(17)	N3-N2	1.3830(15)
N3-H3N	0.854(17)	N2-C009	1.3731(17)
N2-C00D	1.4896(17)	N1-C00C	1.3887(19)
N1-C00D	1.4356(18)	N1-H1N	0.817(18)
O4-C00E	1.3373(19)	O4-C00S	1.444(2)
C009-C00A	1.3581(18)	C009-C00I	1.487(2)
C00A-C00E	1.4421(19)	C00C-C00F	1.378(2)
C00C-C00G	1.395(2)	C00D-C00H	1.5709(18)
C00F-C00M	1.390(3)	C00F-H00F	0.93
C00G-	1.380(2)	C00G-	1.510(2)

C00N		C00H	
C00H-C00K	1.522(2)	C00H-C00L	1.542(2)
C00I-H00A	0.96	C00I-H00B	0.96
C00I-H00C	0.96	C00J-C00O	1.509(3)
C00J-C00Q	1.515(3)	C00J-C00R	1.520(2)
C00K-H00D	0.96	C00K-H00E	0.96
C00K-H00G	0.96	C00L-H00H	0.96
C00L-H00I	0.96	C00L-H00J	0.96
C00M-C00P	1.373(3)	C00M-H00M	0.93
C00N-C00P	1.383(3)	C00N-H00N	0.93
C00O-H00K	0.96	C00O-H00L	0.96
C00O-H00O	0.96	C00P-H00P	0.93
C00Q-H00Q	0.96	C00Q-H00R	0.96
C00Q-H00S	0.96	C00R-H00T	0.96
C00R-	0.96	C00R-	0.96

H00U		H00V	
C00S-H00W	0.96	C00S-H00$	0.96
C00S-H00	0.96		

Table 5. Bond angles (°) for mancio2101.

C00A-S001-C00D	92.52(6)	C00B-O2-C00J	121.63(11)
C00B-N3-N2	121.92(11)	C00B-N3-H3N	119.3(11)
N2-N3-H3N	118.7(11)	C009-N2-N3	120.70(11)
C009-N2-C00D	117.15(10)	N3-N2-C00D	117.59(10)
C00C-N1-C00D	109.04(11)	C00C-N1-H1N	120.5(12)
C00D-N1-H1N	116.0(12)	C00E-O4-C00S	116.03(14)
C00A-C009-N2	112.65(12)	C00A-C009-C00I	128.24(13)
N2-C009-C00I	119.02(12)	C009-C00A-C00E	131.51(13)
C009-C00A-S001	112.28(11)	C00E-C00A-S001	116.05(10)
O1-C00B-O2	127.79(12)	O1-C00B-N3	124.62(12)
O2-C00B-N3	107.57(11)	C00F-C00C-N1	128.62(15)
C00F-C00C-C00G	121.49(15)	N1-C00C-C00G	109.88(13)

N1-C00D-N2	112.79(10)	N1-C00D-C00H	102.48(11)
N2-C00D-C00H	113.19(10)	N1-C00D-S001	113.23(9)
N2-C00D-S001	101.77(9)	C00H-C00D-S001	113.84(9)
O3-C00E-O4	122.36(14)	O3-C00E-C00A	122.93(14)
O4-C00E-C00A	114.71(12)	C00C-C00F-C00M	117.38(17)
C00C-C00F-H00F	121.3	C00M-C00F-H00F	121.3
C00N-C00G-C00C	119.96(16)	C00N-C00G-C00H	131.62(15)
C00C-C00G-C00H	108.32(12)	C00G-C00H-C00K	116.56(13)
C00G-C00H-C00L	107.37(14)	C00K-C00H-C00L	109.42(14)
C00G-C00H-C00D	100.58(11)	C00K-C00H-C00D	113.38(13)
C00L-C00H-C00D	108.99(12)	C009-C00I-H00A	109.5
C009-C00I-H00B	109.5	H00A-C00I-H00B	109.5

C009-C00I-H00C	109.5	H00A-C00I-H00C	109.5
H00B-C00I-H00C	109.5	O2-C00J-C00O	110.72(15)
O2-C00J-C00Q	108.34(14)	C00O-C00J-C00Q	112.92(16)
O2-C00J-C00R	101.66(12)	C00O-C00J-C00R	110.91(17)
C00Q-C00J-C00R	111.70(18)	C00H-C00K-H00D	109.5
C00H-C00K-H00E	109.5	H00D-C00K-H00E	109.5
C00H-C00K-H00G	109.5	H00D-C00K-H00G	109.5
H00E-C00K-H00G	109.5	C00H-C00L-H00H	109.5
C00H-C00L-H00I	109.5	H00H-C00L-H00I	109.5
C00H-C00L-H00J	109.5	H00H-C00L-H00J	109.5
H00I-C00L-H00J	109.5	C00P-C00M-C00F	121.82(18)
C00P-C00M-H00M	119.1	C00F-C00M-H00M	119.1

C00G-C00N-C00P	119.06(18)	C00G-C00N-H00N	120.5
C00P-C00N-H00N	120.5	C00J-C00O-H00K	109.5
C00J-C00O-H00L	109.5	H00K-C00O-H00L	109.5
C00J-C00O-H00O	109.5	H00K-C00O-H00O	109.5
H00L-C00O-H00O	109.5	C00M-C00P-C00N	120.29(17)
C00M-C00P-H00P	119.9	C00N-C00P-H00P	119.9
C00J-C00Q-H00Q	109.5	C00J-C00Q-H00R	109.5
H00Q-C00Q-H00R	109.5	C00J-C00Q-H00S	109.5
H00Q-C00Q-H00S	109.5	H00R-C00Q-H00S	109.5
C00J-C00R-H00T	109.5	C00J-C00R-H00U	109.5
H00T-C00R-H00U	109.5	C00J-C00R-H00V	109.5

H00T-C00R-H00V	109.5	H00U-C00R-H00V	109.5
O4-C00S-H00W	109.5	O4-C00S-H00$	109.5
H00W-C00S-H00$	109.5	O4-C00S-H00	109.5
H00W-C00S-H00	109.5	H00$-C00S-H00	109.5

Table 6. Torsion angles (°) for mancio2101.

C00B-N3-N2-C009	67.87(17)	C00B-N3-N2-C00D	-87.53(15)
N3-N2-C009-C00A	-168.74(11)	C00D-N2-C009-C00A	-13.23(16)
N3-N2-C009-C00I	14.36(18)	C00D-N2-C009-C00I	169.86(12)
N2-C009-C00A-C00E	-176.15(13)	C00I-C009-C00A-C00E	0.4(3)
N2-C009-C00A-S001	-1.12(15)	C00I-C009-C00A-S001	175.44(12)
C00D-S001-C00A-C009	11.05(11)	C00D-S001-C00A-C00E	-173.09(11)
C00J-O2-C00B-O1	2.1(2)	C00J-O2-C00B-N3	-179.26(13)
N2-N3-C00B-O1	1.2(2)	N2-N3-C00B-O2	-177.56(12)
C00D-N1-C00C-C00F	161.99(14)	C00D-N1-C00C-C00G	-18.48(16)
C00C-N1-C00D-N2	-92.07(13)	C00C-N1-C00D-	29.96(14)

		C00H	
C00C-N1-C00D-S001	153.02(10)	C009-N2-C00D-N1	-101.94(13)
N3-N2-C00D-N1	54.34(15)	C009-N2-C00D-C00H	142.27(12)
N3-N2-C00D-C00H	-61.45(14)	C009-N2-C00D-S001	19.70(12)
N3-N2-C00D-S001	175.98(9)	C00A-S001-C00D-N1	105.31(10)
C00A-S001-C00D-N2	-16.03(9)	C00A-S001-C00D-C00H	-138.15(10)
C00S-O4-C00E-O3	-5.1(3)	C00S-O4-C00E-C00A	174.26(18)
C009-C00A-C00E-O3	179.69(15)	S001-C00A-C00E-O3	4.81(19)
C009-C00A-C00E-O4	0.4(2)	S001-C00A-C00E-O4	-174.53(11)
N1-C00C-C00F-C00M	179.24(15)	C00G-C00C-C00F-C00M	-0.2(2)

C00F-C00C-C00G-C00N	0.7(2)	N1-C00C-C00G-C00N	-178.91(14)
C00F-C00C-C00G-C00H	177.28(13)	N1-C00C-C00G-C00H	-2.29(16)
C00N-C00G-C00H-C00K	-41.3(2)	C00C-C00G-C00H-C00K	142.57(14)
C00N-C00G-C00H-C00L	81.7(2)	C00C-C00G-C00H-C00L	-94.35(14)
C00N-C00G-C00H-C00D	-164.35(17)	C00C-C00G-C00H-C00D	19.56(15)
N1-C00D-C00H-C00G	-29.10(13)	N2-C00D-C00H-C00G	92.67(13)
S001-C00D-C00H-C00G	-151.75(10)	N1-C00D-C00H-C00K	-154.29(12)
N2-C00D-C00H-C00K	-32.52(16)	S001-C00D-C00H-C00K	83.06(14)
N1-C00D-C00H-	83.57(14)	N2-C00D-C00H-	-154.66(13)

C00L		C00L	
S001-C00D-C00H-C00L	-39.08(16)	C00B-O2-C00J-C00O	-57.37(19)
C00B-O2-C00J-C00Q	66.96(19)	C00B-O2-C00J-C00R	-175.26(17)
C00C-C00F-C00M-C00P	-0.1(3)	C00C-C00G-C00N-C00P	-0.7(3)
C00H-C00G-C00N-C00P	-176.42(17)	C00F-C00M-C00P-C00N	0.1(3)
C00G-C00N-C00P-C00M	0.4(3)		

Table 7. Anisotropic atomic displacement parameters ($Å^2$) for mancio2101.

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S001	0.0621(2)	0.02645(17)	0.0545(2)	0.00369(13)	0.01373(16)	0.00212(13)
O1	0.0838(8)	0.0380(5)	0.0359(5)	-0.0035(4)	-0.0009(5)	0.0004(5)
O2	0.0809(7)	0.0308(5)	0.0402(5)	-0.0011(4)	-0.0081(5)	0.0113(5)
O3	0.0752(7)	0.0353(5)	0.0490(6)	0.0039(4)	0.0097(5)	0.0129(5)
N3	0.0578(7)	0.0256(5)	0.0345(5)	-0.0042(4)	-0.0006(5)	0.0035(4)
N2	0.0497(6)	0.0245(5)	0.0414(6)	0.0001(4)	0.0041(5)	0.0007(4)
N1	0.0536(7)	0.0388(6)	0.0378(6)	-0.0042(5)	0.0037(5)	-0.0008(5)
O4	0.0665(7)	0.0469(6)	0.1096(10)	0.0001(7)	0.0345(7)	0.0064(6)
C009	0.0470(7)	0.0319(6)	0.0375(6)	0.0010(5)	-0.0002(5)	0.0004(5)
C00A	0.0521(7)	0.0324(6)	0.0405(7)	0.0027(5)	0.0050(5)	0.0020(5)
C00B	0.0501(7)	0.0295(6)	0.0383(6)	-0.0016(5)	0.0001(5)	-0.0011(5)
C00C	0.0459(7)	0.0355(7)	0.0549(8)	-0.0030(6)	0.0070(6)	-0.0063(5)
C00D	0.0518(7)	0.0271(6)	0.0364(6)	-0.0002(5)	0.0059(5)	0.0000(5)
C00E	0.0581(8)	0.0384(7)	0.0393(7)	0.0038(5)	0.0047(6)	0.0085(6)
C00F	0.0485(8)	0.0497(9)	0.0720(10)	-0.0011(7)	-0.0016(7)	-0.0065(7)

C00G	0.0550(8)	0.0401(7)	0.0545(8)	-0.0006(6)	0.0168(6)	-0.0032(6)
C00H	0.0638(9)	0.0390(7)	0.0395(7)	0.0017(5)	0.0144(6)	-0.0003(6)
C00I	0.0552(8)	0.0375(7)	0.0773(11)	0.0024(7)	0.0110(8)	-0.0037(6)
C00J	0.0759(10)	0.0354(7)	0.0464(8)	0.0060(6)	-0.0076(7)	0.0098(7)
C00K	0.0885(12)	0.0606(10)	0.0364(7)	-0.0018(7)	0.0074(7)	0.0037(9)
C00L	0.0867(12)	0.0469(9)	0.0652(10)	0.0119(8)	0.0295(9)	-0.0045(8)
C00M	0.0463(9)	0.0583(10)	0.1099(17)	0.0071(10)	0.0092(9)	0.0022(7)
C00N	0.0741(11)	0.0584(10)	0.0705(11)	0.0001(8)	0.0324(9)	0.0049(8)
C00O	0.1004(15)	0.0508(10)	0.0719(12)	0.0132(8)	0.0136(11)	-0.0108(9)
C00P	0.0642(11)	0.0642(12)	0.1066(17)	0.0017(11)	0.0376(11)	0.0095(9)
C00Q	0.0711(12)	0.0816(14)	0.0758(12)	0.0063(11)	-0.0121(10)	0.0131(10)
C00R	0.148(2)	0.0382(9)	0.0700(12)	-0.0010(8)	-0.0144(13)	0.0295(11)
C00S	0.0737(13)	0.0746(14)	0.151(2)	-0.0109(14)	0.0480(15)	0.0140(11)

Table 8. Hydrogen atomic coordinates and isotropic atomic displacement parameters (Å^2) for mancio2101.

	x/a	y/b	z/c	U(eq)
H00F	0.2646	0.5241	0.5667	0.069
H00A	0.9289	0.5137	0.6371	0.085
H00B	0.8659	0.5890	0.6990	0.085
H00C	0.8190	0.5790	0.5960	0.085
H00D	0.5968	0.5315	0.8767	0.093
H00E	0.6534	0.4258	0.8935	0.093
H00G	0.5367	0.4572	0.9410	0.093
H00H	0.3974	0.3268	0.8801	0.097
H00I	0.5148	0.2773	0.8461	0.097
H00J	0.3981	0.2947	0.7782	0.097
H00M	0.1276	0.6133	0.6467	0.086
H00N	0.3137	0.5428	0.8830	0.079
H00K	0.6766	0.8185	0.5301	0.111
H00L	0.5708	0.8626	0.4634	0.111
H00O	0.5921	0.7480	0.4678	0.111
H00P	0.1513	0.6228	0.8018	0.092
H00Q	0.3845	0.7041	0.5101	0.116

H00R	0.3446	0.8148	0.4968	0.116
H00S	0.3286	0.7612	0.5890	0.116
H00T	0.4522	0.8875	0.6779	0.13
H00U	0.4716	0.9478	0.5897	0.13
H00V	0.5856	0.9127	0.6536	0.13
H00W	1.1016	0.2567	0.6410	0.146
H00$	1.1406	0.3406	0.5762	0.146
H00	1.0515	0.2565	0.5382	0.146
H3N	0.6250(14)	0.6239(12)	0.7560(11)	0.043(4)
H1N	0.4823(15)	0.4295(13)	0.5953(12)	0.050(5)

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