A Practical and Effective Method for the N–N-bond cleavage of *N*-Amino-heterocycles

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

Department of Biomolecular Sciences, Section of Organic Chemistry and Organic Natural Compounds, University of Urbino "Carlo Bo", Via I Maggetti 24, 61029 Urbino (PU), Italy

e-mail: fabio.mantellini@uniurb.it

SUPPORTING INFORMATION

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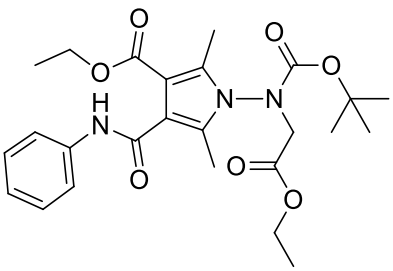
1. General information. All the commercially available reagents and solvents were used without further purification. 1,2-Diaza-1,3-dienes **2a,b** were synthesized as a mixture of *E/Z* isomers as previously reported.[1,2] Chromatographic purification of compounds was carried out on silica gel (60–200 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 ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 and 100.56 MHz, respectively. Proton and carbon spectra were referenced internally to solvent signals, using values of δ = 2.50 ppm for proton (middle peak) and δ = 39.50 ppm for carbon (middle peak) in DMSO-d_6 and δ = 7.27 ppm for proton and δ = 77.00 ppm for carbon (middle peak) in $CDCl_3$. The following abbreviations are used to describe peak patterns where appropriate: s = singlet, d = doublet, t = triplet q = quartet, sex = sextet, m = multiplet and br = broad signal. All coupling constants (*J*) are given in Hz. FT-IR spectra were obtained as Nujol mulls. Mass spectra were obtained by ESI-MS analyses. Elemental analyses were within ± 0.4 of the theoretical values (C, H, N). Melting points were determined in open capillary tubes and are uncorrected.

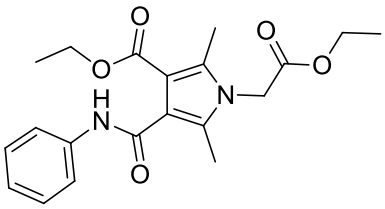
2. Synthesis of 1-amino-1*H*-pyrrole 3a and 1*H*-pyrrole 5a by treatment of 1-amino-1*H*-pyrrole 1a with Magnus' conditions. To a magnetically stirred solution of 1-amino-1*H*-pyrrole **1a** (0.5 mmol) in MeCN (10 mL), ethyl bromoacetate 7 (1.0 mmol) and Cs_2CO_3 (1.25 mmol) were added and then the reaction mixture was refluxed for 18 hours, according to the Magnus' procedure. After this time, a TLC analysis revealed the disappearance of the starting reagent **1** and the formation 1-amino-1*H*-pyrrole **3a** and of 1*H*-pyrrole **5a**, in 52% and 39% yields, respectively. After the filtration of Cs_2CO_3, the solvent was removed in vacuo and the residue was purified by silica gel column chromatography using cyclohexane/ethyl acetate mixtures as eluent: product **3a** is oil, while product **5a** was crystallized from ethyl acetate/petroleum ether.

3. Spectral data of 1-amino-1*H*-pyrrole 3a and 1*H*-pyrrole 5a.

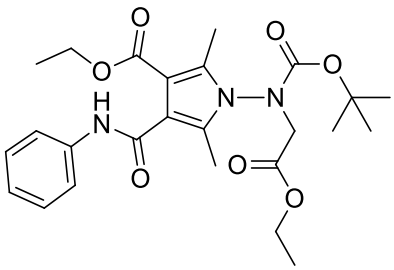


Ethyl 1-((*tert*-butoxycarbonyl)(2-ethoxy-2-oxoethyl)amino)-2,5-dimethyl-4-(phenylcarbamoyl)-1*H*-pyrrole-3-carboxylate (3a). The compound was obtained as yellow oil (126.9 mg, 52%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.25–1.45 (m, 6H, $2OCH_2CH_3$), 1.38 and 1.49 (2s, 9H, $OC(CH_3)_3$), 2.48 and 2.48 (2s, 3H, CH_3), 2.53 and 2.55 (2brs, 3H, CH_3), 4.06–4.11 (m, 1H, OCH_2CO), 4.23 (q, *J*=7.2 Hz, 2H, OCH_2CH_3), 4.31–4.43 (m, 3H, OCH_2CO and OCH_2CH_3), 7.05 (t, *J*=7.6 Hz, $1H_{ar}$), 7.29–7.33 (m, $2H_{ar}$), 7.69–7.74 (m, $2H_{ar}$), 11.40 and 11.64 (2brs, *1H*, *NH*); ^{13}C

NMR (100 MHz, $CDCl_3$, 25 °C): δ = 11.2 (q), 11.4 (q), 11.9 (q), 12.1 (q), 14.0 (q), 14.1 (q), 14.1 (q), 52.6 (t), 53.8 (t), 60.9 (t), 61.0 (t), 61.6 (t), 83.4 (s), 84.0 (s), 107.4 (s), 107.7 (s), 114.2 (s), 114.6 (s), 119.9 (d), 119.9 (d), 123.2 (d), 128.6 (d), 136.8 (s), 137.2 (s), 137.4 (s), 137.5 (s), 139.2 (s), 152.4 (s), 153.1 (s), 162.6 (s), 162.7 (s), 167.2 (s), 167.3 (s), 167.4 (s), 167.6 (s); IR (nujol): ν_{max} = 3300, 1759, 1653, 1648, 1630 cm^{-1}; MS *m/z* (ESI): 488.26 ($M + H^+$); anal. calcd. for $C_{25}H_{33}N_3O_7$ (487.55): C 61.59, H 6.82, N 8.62; found: C 61.47, H 6.88, N 8.69.

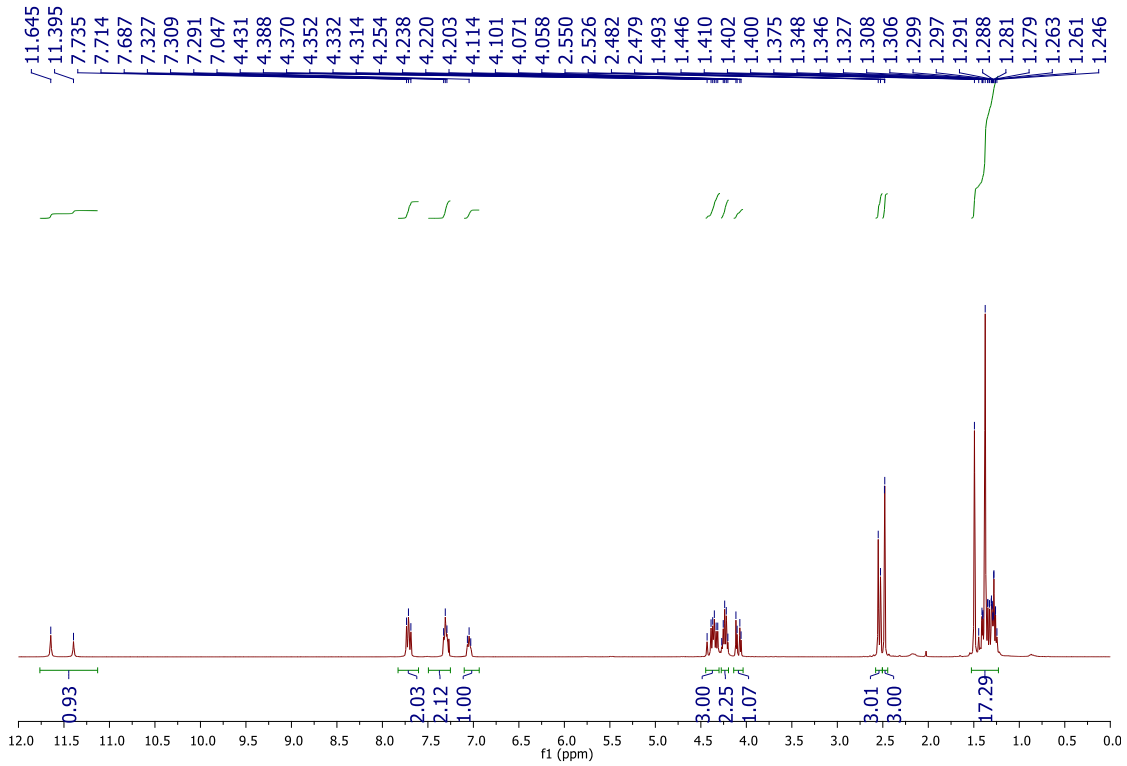


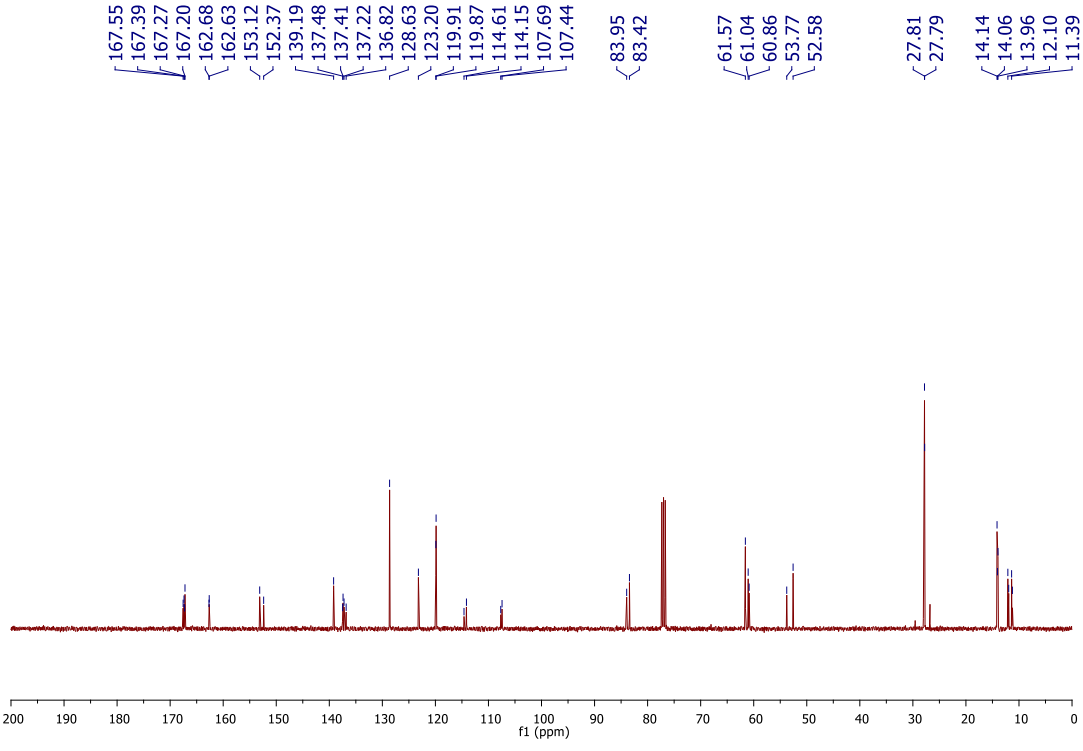
Ethyl 1-(2-ethoxy-2-oxoethyl)-2,5-dimethyl-4-(phenylcarbamoyl)-1*H*-pyrrole-3-carboxylate (5a). The compound was obtained as white solid (73.2 mg, 39%); mp: 90–92 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.30 (q, *J*=7.2 Hz, 3H, $OCH_2\mathit{CH_3}$), 1.36 (q, *J*=7.2 Hz, 3H, $OCH_2\mathit{CH_3}$), 2.46 (s, 3H, $\mathit{CH_3}$), 2.57 (s, 3H, $\mathit{CH_3}$), 4.26 (q, *J*=7.2 Hz, 2H, $O\mathit{CH_2}CH_3$), 4.36 (q, *J*=7.2 Hz, 2H, $O\mathit{CH_2}CH_3$), 4.62 (s, 2H, $O\mathit{CH_2}CO$), 7.07 (t, *J*=7.2 Hz, $1H_{ar}$), 7.33 (t, *J*=8.4 Hz, $2H_{ar}$), 7.72 (d, *J*=7.6 Hz, $2H_{ar}$), 11.11 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 11.9 (q), 12.6 (q), 14.1 (q), 14.3 (q), 45.2 (t), 60.9 (t), 62.2 (t), 109.6 (s), 116.2 (s), 120.0 (d), 123.3 (d), 128.7 (d), 136.0 (s), 136.4 (s), 139.3 (s), 163.4 (s), 167.3 (s), 167.6 (s); IR (nujol): ν_{max} = 3322, 1692, 1649, 1637 cm^{-1}; MS *m/z* (ESI): 373.10 ($M + H^+$); anal. calcd. for $C_{20}H_{24}N_2O_5$ (372.42): C 64.50, H 6.50, N 7.52; found: C 64.62, H 6.54, N 7.47.

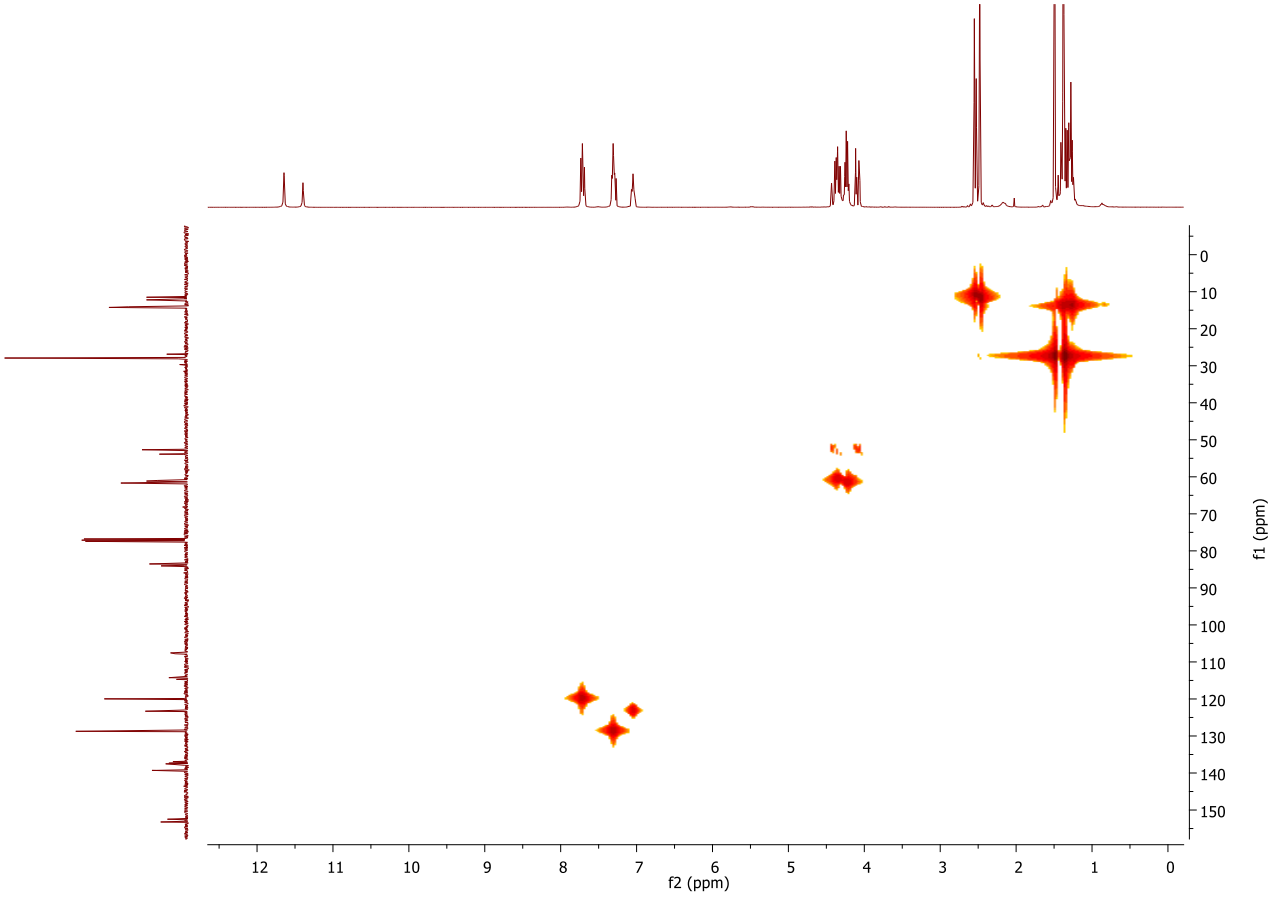


4. ^{1}H and ^{13}C spectra of 1-amino-1*H*-pyrrole 3a and 1*H*-pyrrole 5a.

Ethyl 1-((*tert*-butoxycarbonyl)(2-ethoxy-2-oxoethyl)amino)-2,5-dimethyl-4-(phenylcarbamoyl)-1*H*-pyrrole-3-carboxylate (3a).



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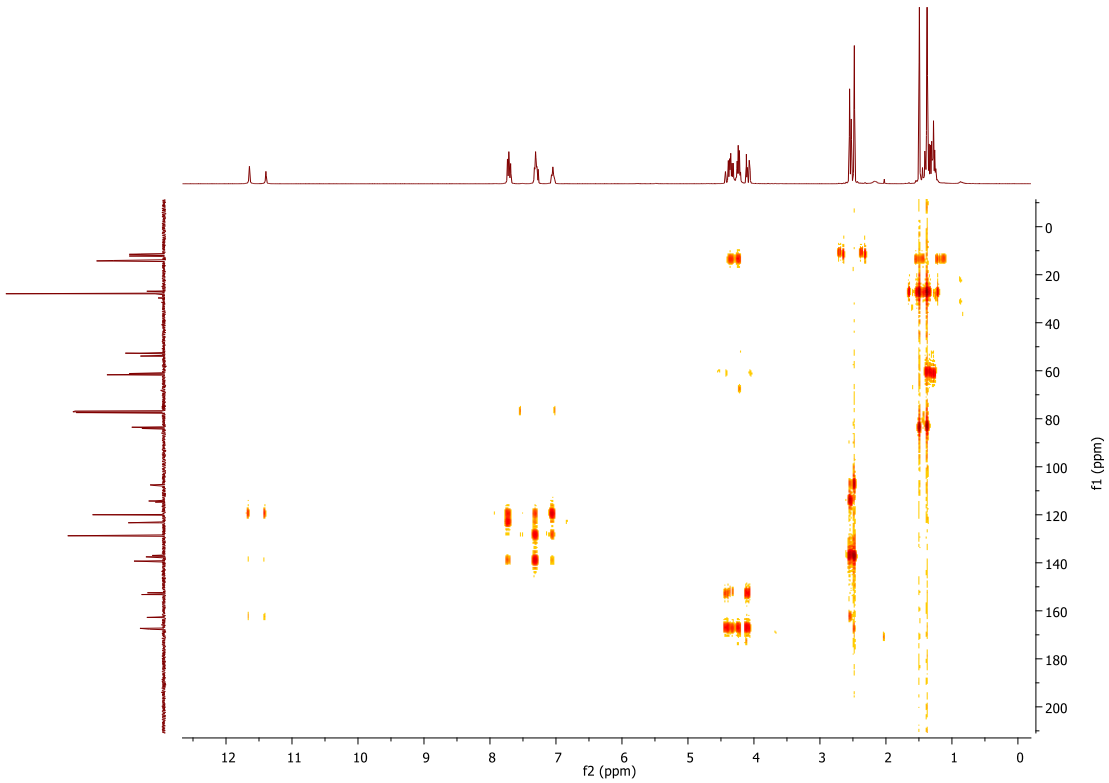
f1 (ppm)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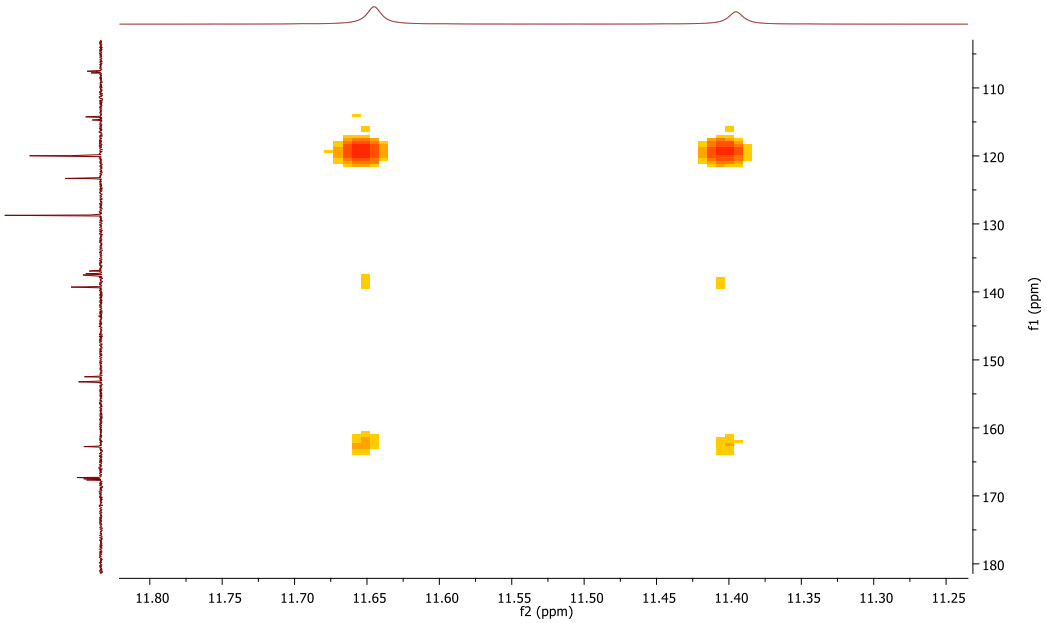
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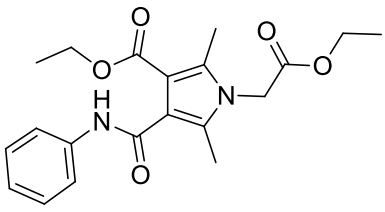
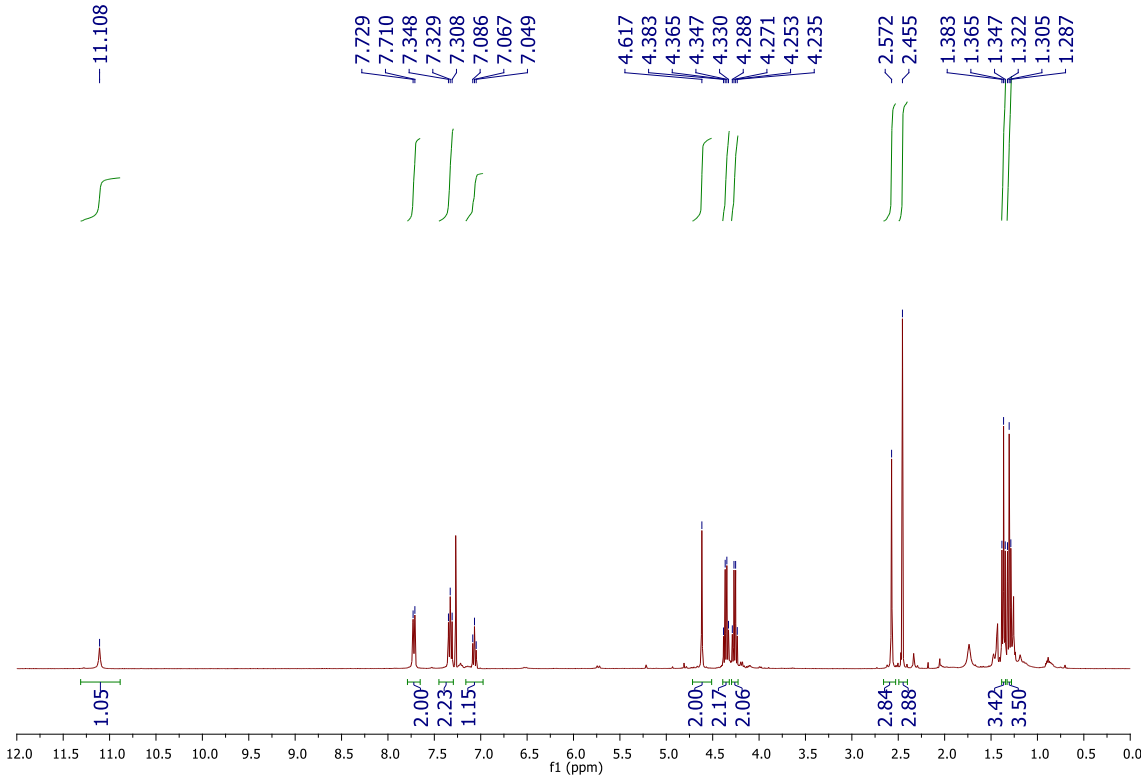
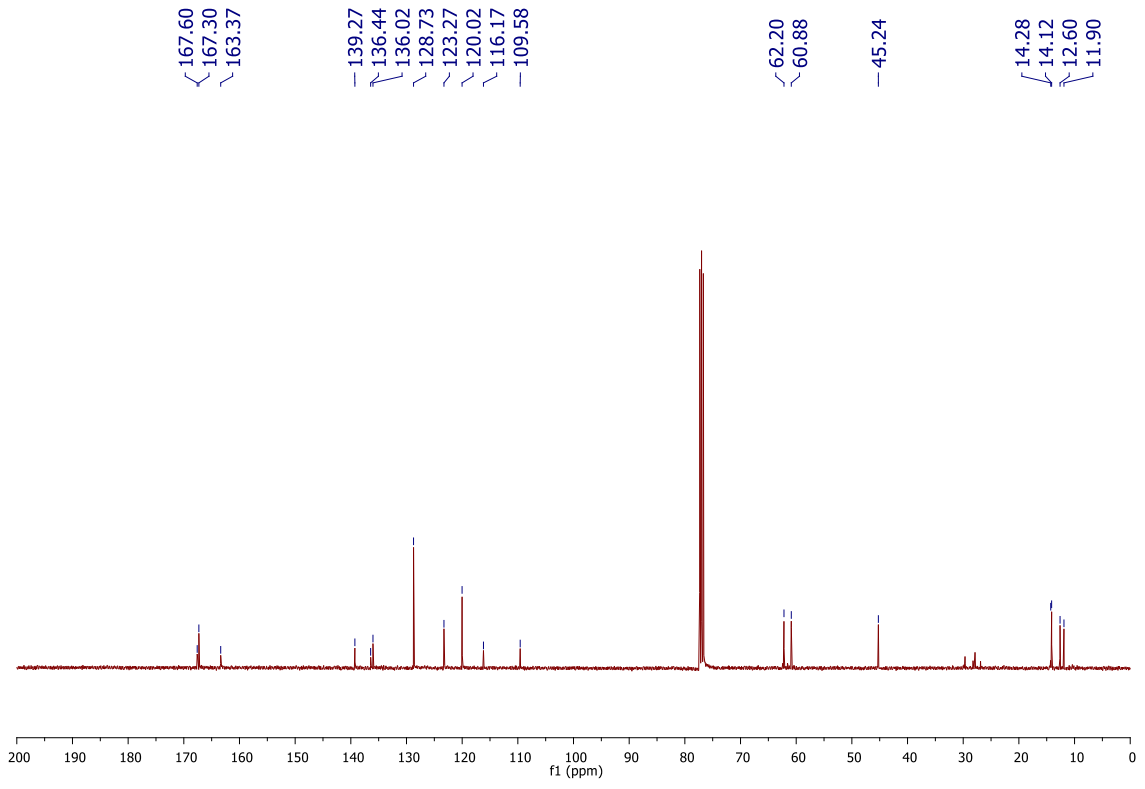
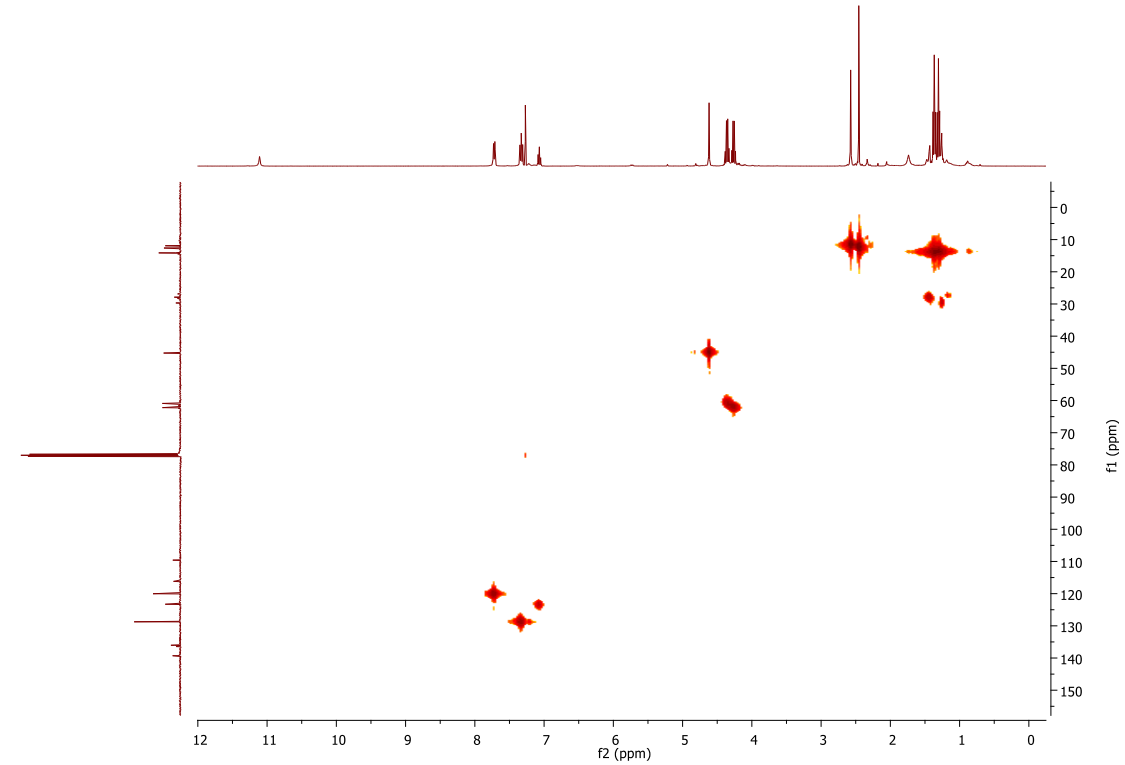
11.25
f2 (ppm)



Ethyl 1-(2-ethoxy-2-oxoethyl)-2,5-dimethyl-4-(phenylcarbamoyl)-1*H*-pyrrole-3-carboxylate (5a).



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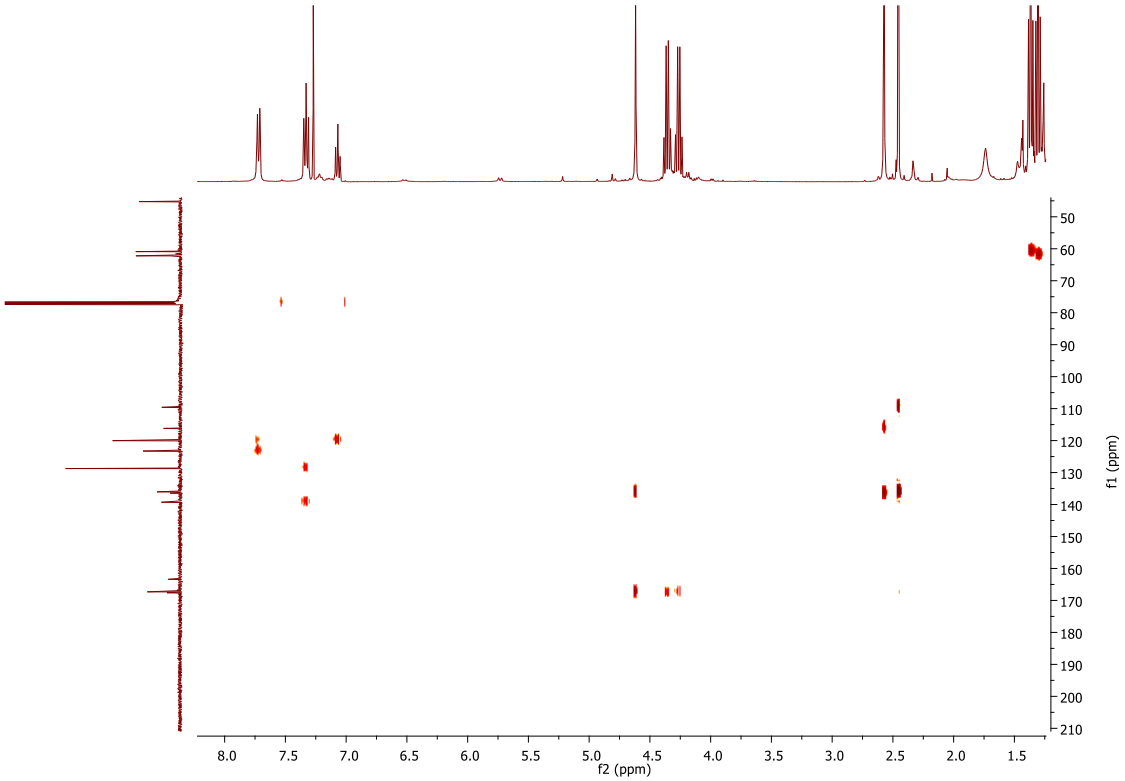
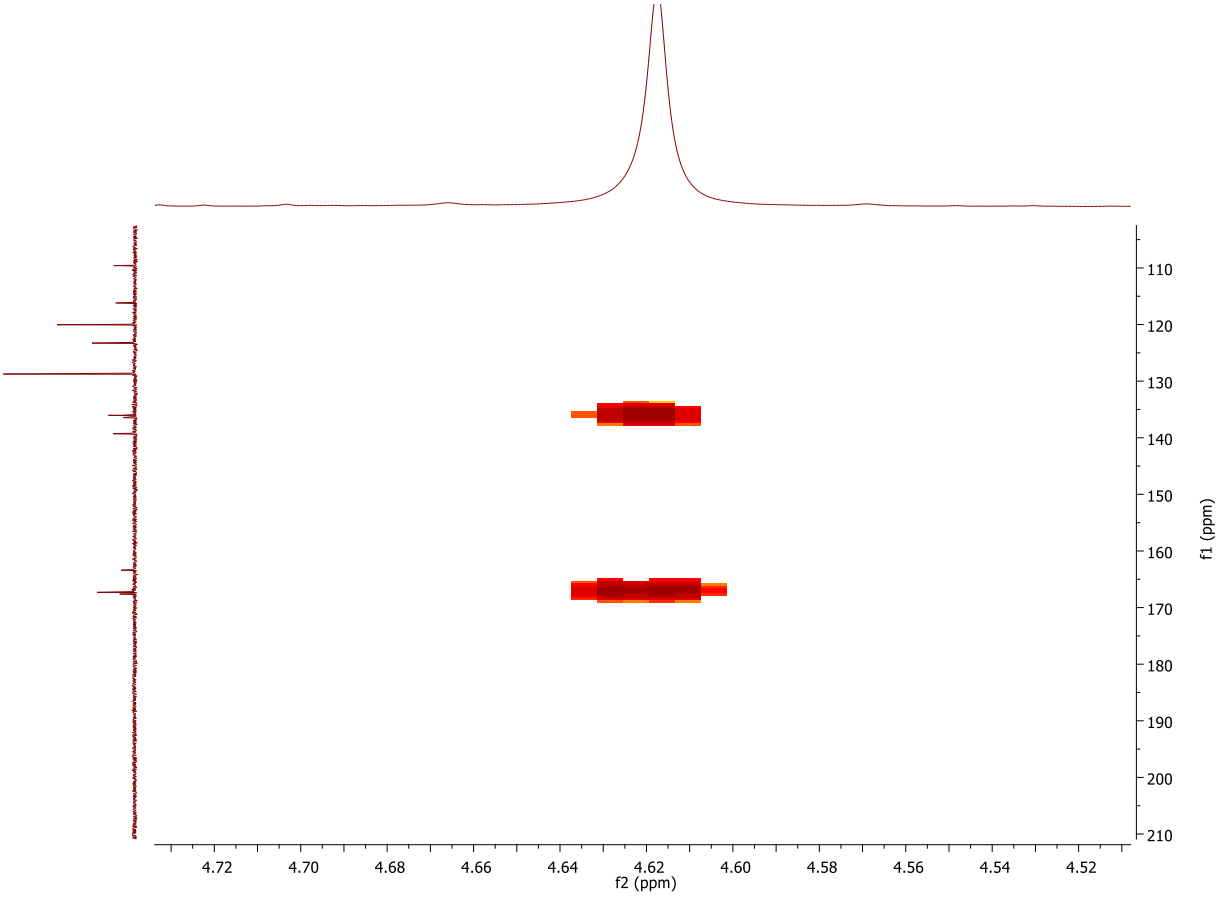

f2 (ppm)
f1 (ppm)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f1 (ppm)
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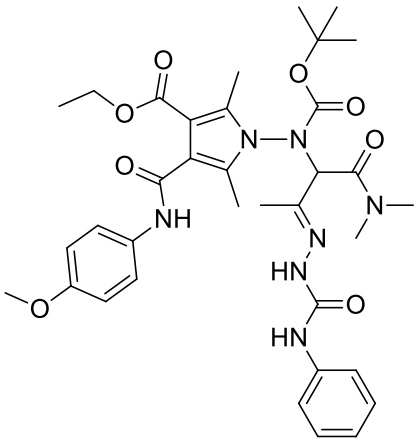
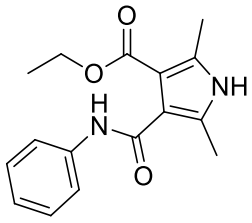
4.66
4.64
4.62
4.60
4.58
4.56
4.54
4.52
f2 (ppm)

5. General procedure for the synthesis of 1amino-1*H*-pyrrole 6a and 1*H*-pyrroles 4a–l by basic treatment of 1-amino-1*H*-pyrroles 1a–m and DDs 2a,b. To a magnetically stirred solution of 1-amino-1*H*-pyrroles **1a–m** (0.5 mmol) in MeCN (10 mL), the appropriate DD **2a,b** (1.0 mmol) and K_2CO_3 (1.5 mmol) were added and then the reaction mixture was refluxed for 1 hour, until the TLC analysis revealed the disappearance of the starting reagent **1** and the formation of 1*H*-pyrroles **4a–l**. After the filtration of K_2CO_3, the solvent was removed in vacuo; the so-formed products **4** were purified by silica gel column chromatography using cyclohexane/ethyl acetate mixtures as eluent and then were crystallized from ethyl acetate/petroleum ether. Only in the case of the reaction between 1-amino-1*H*-pyrrole **1e** with the DD **2b**, after 0.5 hours, the TLC check detected the presence of a transient further spot, together with the one of the expected 1*H*-pyrrole **4d**, that was occasionally isolated and characterized as ethyl 1-((*tert*-butoxycarbonyl)(1-(dimethylamino)-1-oxo-3-(2-(phenylcarbamoyl)hydrazono)butan-2yl)amino)-4-((4-methoxyphenyl)carbamoyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate **6a**.

6. Spectral data of 1amino-1*H*-pyrrole 6a and 1*H*-pyrroles 4a–l.

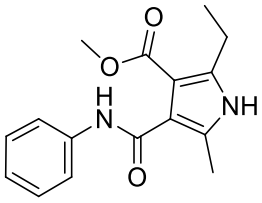


Ethyl 1-((*tert*-butoxycarbonyl)(1-(dimethylamino)-1-oxo-3-(2-(phenylcarbamoyl)hydrazono)butan-2yl)amino)-4-((4-methoxyphenyl)carbamoyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (6a). The compound was obtained as white solid; mp: 107–109 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.22 (t, *J*=6.8 Hz, 3H, OCH_2CH_3), 1.40 (brs, 9H, $OC(CH_3)_3$), 1.60 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.91 (s, 3H, CH_3), 3.05 (s, 3H, $N(CH_3)_2$), 3.17 (s, 3H, $N(CH_3)_2$), 3.80 (s, 3H, OCH_3), 4.24–4.29 (m, 2H, OCH_2CH_3), 5.67 (brs, 1H, *CH*), 6.86 (d, *J*=8.8 Hz, $2H_{ar}$), 7.11 (t, *J*=7.2 Hz, $1H_{ar}$), 7.34 (t, *J*=7.6 Hz, $2H_{ar}$), 7.45 (d, *J*=8.0 Hz, $2H_{ar}$),7.62 (d, *J*=8.0 Hz, $2H_{ar}$), 7.97 (s, 1H, *NH*), 8.40 (brs, 1H, *NH*), 11.23 and 11.42 (2brs, 1H, *NH*).

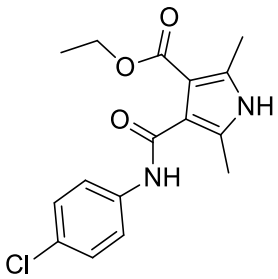


Ethyl 2,5-dimethyl-4-(phenylcarbamoyl)-1*H*-pyrrole-3-carboxylate (4a). The compound was obtained as white solid (141.3 mg, 99%); mp: 203–204 °C; ^{1}H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 1.17 (t, *J*=7.2 Hz, 3H, OCH_2CH_3), 2.31 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 4.17 (q, *J*=7.2 Hz, 2H, OCH_2CH_3), 7.00 (t, *J*=7.2 Hz, $1H_{ar}$), 7.29 (t, *J*=7.2 Hz, $2H_{ar}$), 7.67 (d, *J*=7.2 Hz, $2H_{ar}$), 10.80 (s, 1H, *NH*), 11.47 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, $DMSO_{d6}$, 25 °C): δ = 12.4 (q), 13.6 (q), 14.0 (q), 59.5 (t), 108.2 (s), 116.3 (s), 119.0 (d), 122.5 (d), 128.5 (d), 131.4 (s), 134.7 (s), 139.8 (s), 163.4 (s),

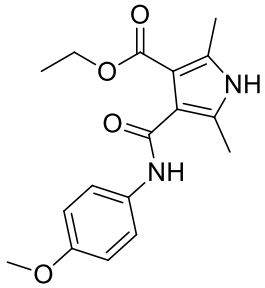
165.9 (s); IR (nujol): ν_{max} = 3226, 3124, 1673, 1653 cm^{-1}; MS *m/z* (ESI): 287.21 (M + H^+); anal. calcd. for $C_{16}H_{18}N_2O_3$ (286.33): C 67.12, H 6.34, N 9.78; found: C 67.25, H 6.42, N 9.65.



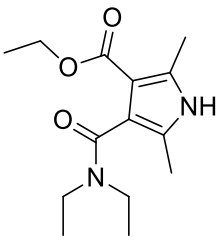
Methyl 2-ethyl-5-methyl-4-(phenylcarbamoyl)-1*H*-pyrrole-3-carboxylate (4b). The compound was obtained as white solid (83.2 mg, 58%); mp: 200–202 °C; ^{1}H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 1.16 (t, *J*=7.2 Hz, 3H, CH_2CH_3), 2.30 (s, 3H, CH_3), 2.81 (q, *J*=7.2 Hz, 2H, CH_2CH_3), 3.68 (s, 3H, OCH_3), 7.01 (t, *J*=7.2 Hz, $1H_{ar}$), **7**.29 (t, *J*=7.6 Hz, $2H_{ar}$), 7.66 (d, *J*=8.0 Hz, $2H_{ar}$), 10.52 (s, 1H, *NH*), 11.39 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.2 (q), 14.2 (q), 20.3 (t), 51.0 (q), 107.4 (s), 116.6 (s), 119.1 (d), 122.6 (d), 128.5 (d), 130.8 (s), 139.8 (s), 140.2 (s), 163.6 (s), 165.9 (s); IR (nujol): ν_{max} = 3264, 3198, 1654, 1627 cm^{-1}; MS *m/z* (ESI): 287.01 (M + H^+); anal. calcd. for $C_{16}H_{18}N_2O_3$ (286.33): C 67.12, H 6.34, N 9.78; found: C 66.98, H 6.28, N 9.83.



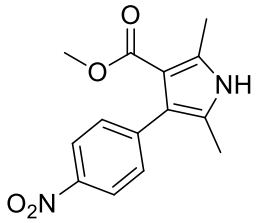
Ethyl 4-((4-chlorophenyl)carbamoyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (4c). The compound was obtained as white solid (158.7 mg, 99% from **2c** and **1a**, 101.2 mg, 63% from **2d** and **1a**); mp: 212–214 °C; ^{1}H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 1.14 (t, *J*=7.2 Hz, 3H, OCH_2CH_3), 2.30 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 4.14 (q, *J*=7.2 Hz, 2H, OCH_2CH_3), 7.34 (d, *J*=8.8 Hz, $2H_{ar}$), 7.71 (d, *J*=8.8 Hz, $2H_{ar}$), 10.88 (s, 1H, *NH*), 11.51 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.4 (q), 13.5 (q), 14.1 (q), 59.5 (t), 108.2 (s), 116.2 (s), 120.4 (d), 126.0 (s), 128.5 (d), 131.4 (s), 134.8 (s), 138.8 (s), 163.7(s), 165.8 (s); IR (nujol): ν_{max} = 3216, 3124, 1652, 1592 cm^{-1}; MS *m/z* (ESI): 321.26 (M + H^+); anal. calcd. for $C_{16}H_{17}ClN_2O_3$ (320.77): C 59.91, H 5.34, N 8.73; found: C 60.06, H 5.28, N 8.80.



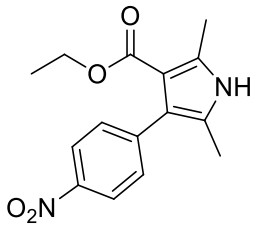
Ethyl 4-((4-methoxyphenyl)carbamoyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (4d). The compound was obtained as white solid (129.4 mg, 82%); mp: 198–200 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.38 (t, *J*=7.2 Hz, 3H, OCH_2CH_3), 2.40 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 4.35 (q, *J*=7.2 Hz, 2H, OCH_2CH_3), 6.86 (d, *J*=8.8 Hz, $2H_{ar}$), 7.62 (d, *J*=8.8 Hz, $2H_{ar}$), 9.36 (brs, 1H, *NH*), 11.84 (s, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.3 (q), 14.3 (q), 15.1 (q), 55.5 (q), 60.7 (t), 108.5 (s), 114.0 (d), 115.2 (s), 121.9 (d), 132.5 (s), 135.8 (s), 135.9 (s), 155.8 (s), 163.6 (s), 168.1 (s); IR (nujol): ν_{max} = 3232, 3142, 1653, 1634 cm^{-1}; MS *m/z* (ESI): 317.81 (M + H^+); anal. calcd. for $C_{17}H_{20}N_2O_4$ (316.35): C 64.54, H 6.37, N 8.86; found: C 64.67, H 6.31, N 8.76.



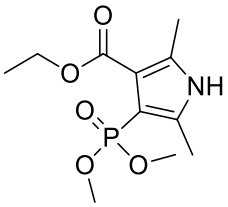
Ethyl 4-(diethylcarbamoyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (4e). The compound was obtained as white solid (98.6 mg, 74%); mp: 202–204 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 0.91 (t, *J*=7.2 Hz, 3H, N(CH$_2$*CH$_3$*)$_2$), 1.10 (t, *J*=7.2 Hz, 3H, N(CH$_2$*CH$_3$*)$_2$), 1.16 (t, *J*=7.2 Hz, 3H, OCH$_2$*CH$_3$*), 1.98 (s, 3H, *CH$_3$*), 2.35 (s, 3H, *CH$_3$*), 3.03–3.22 (m, 2H, N(*CH$_2$*CH$_3$)$_2$), 3.29–3.42 (m, 2H, N(*CH$_2$*CH$_3$)$_2$), 4.02–4.08 (m, 2H, O*CH$_2$*CH$_3$), 11.15 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, CDCl$_3$, 25 °C): δ = 10.6 (q), 12.6 (q), 12.8 (q), 13.9 (q), 14.3 (q), 38.2 (t), 42.3 (t), 58.4 (t), 108.0 (s), 117.4 (s), 122.7 (s), 133.7 (s), 164.0 (s), 166.7 (s); IR (nujol): ν_{max} = 3232, 1653, 1634 cm^{-1}; MS *m/z* (ESI): 267.33 (M + H$^+$); anal. calcd. for $C_{14}H_{22}N_2O_3$ (266.16): C 63.13, H 8.33, N 10.52; found: C 63.01, H 8.38, N 10.64.



Methyl 2,5-dimethyl-4-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (4f). The compound was obtained as yellow solid (89.3 mg, 65%); mp: 170–172 °C; ^{1}H NMR (400 MHz, CDCl$_3$, 25 °C): δ = 2.13 (s, 3H, *CH$_3$*), 2.51 (s, 3H, *CH$_3$*), 3.65 (s, 3H, O*CH$_3$*), 7.40 (d, *J*=8.8 Hz, 2H$_{ar}$), 8.19 (d, *J*=8.8 Hz, 2H$_{ar}$), 8.41 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, CDCl$_3$, 25 °C): δ = 11.2 (q), 13.6 (q), 50.5 (t), 110.4 (s), 120.7 (s), 122.7 (d), 124.6 (s), 130.9 (d), 134.9 (s), 143.6 (s), 145.9 (s), 165.3 (s); IR (nujol): ν_{max} = 3232, 1725, 1634 cm^{-1}; MS *m/z* (ESI): 275.81 (M + H$^+$); anal. calcd. for $C_{14}H_{14}N_2O_4$ (274.10): C 61.31, H 5.14, N 10.21; found: C 61.22, H 5.11, N 10.28.

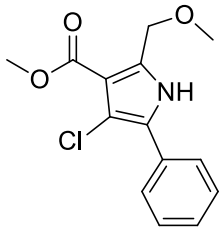


Ethyl 2,5-dimethyl-4-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (4g).[3] The compound was obtained as yellow solid (82.3 mg, 57%); mp: 164–165 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.04 (t, *J*=7.2 Hz, 3H, OCH$_2$*CH$_3$*), 2.09 (s, 3H, *CH$_3$*), 2.41 (s, 3H, *CH$_3$*), 4.00 (q, *J*=7.2 Hz, 2H, O*CH$_2$*CH$_3$), 7.43 (d, *J*=8.8 Hz, 2H$_{ar}$), 7.43 (d, *J*=8.8 Hz, 2H$_{ar}$), 11.36 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, CDCl$_3$, 25 °C): δ = 11.0 (q), 13.1 (q), 14.0 (q), 58.5 (t), 109.0 (s), 119.3 (s), 122.3 (d), 125.0 (s), 131.0 (d), 134.6 (s), 143.9 (s), 145.0 (s), 164.4 (s); IR (nujol): ν_{max} = 3276, 1722, 1668 cm^{-1}; MS *m/z* (ESI): 289.81 (M + H$^+$); anal. calcd. for $C_{15}H_{16}N_2O_4$ (288.30): C 62.49, H 5.59, N 9.72; found: C 62.62, H 5.61, N 9.62.

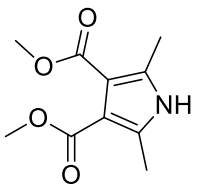


Ethyl 4-(dimethoxyphosphoryl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (4h). The compound was obtained as yellow solid (90.9 mg, 66%); mp: 178–180 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.23 (t, *J*=7.2 Hz, 3H, OCH$_2$*CH$_3$*), 2.32 (s, 3H, *CH$_3$*), 2.33 (d, *J$_{3HP}$*=1.6 Hz, 3H, *CH$_3$*), 3.52 (s, 3H, O*CH$_3$*), 3.55 (s, 3H, O*CH$_3$*), 4.11 (q, *J*=7.2 Hz, 2H, OCH$_2$*CH$_3$*), 11.55 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 12.5 (q), 12.7 (q), 14.1 (q), 51.4 (q), 51.5 (q), 58.9 (t), 102.0 (s, *J$_{1CP}$*=213.7 Hz,), 112.8 (s, *J$_{2CP}$*=11.4 Hz,), 135.0 (s, *J$_{3CP}$*=13.1 Hz,), 137.3 (s, *J$_{2CP}$*=22.4 Hz,), 163.9 (s); IR (nujol): ν_{max} = 3232,

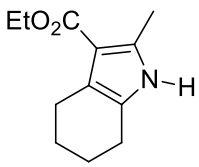
1652, 1634 cm^{-1}; MS *m/z* (ESI): 276.38 ($M + H^+$); anal. calcd. for $C_{11}H_{18}NO_5P$ (275.09): C 48.00, H 6.59, N 5.09; found: C 48.09, H 6.56, N 5.06.



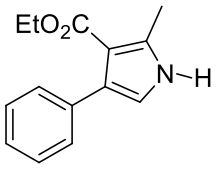
Methyl 4-chloro-2-(methoxymethyl)-5-phenyl-1*H*-pyrrole-3-carboxylate (4i). The compound was obtained as white solid (99.1 mg, 71%); mp: 209–211 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 3.51 (s, 3H, O*CH*$_3$), 3.87 (s, 3H, O*CH*$_3$), 4.80 (s, 2H, *CH*$_2$OCH$_3$), 7.33 (t, *J*=7.2 Hz, 1H$_{ar}$), 7.44 (t, *J*=8.0 Hz, 2H$_{ar}$), 7.64 (d, *J*=8.0 Hz, 2H$_{ar}$), 9.00 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 51.1 (q), 59.1 (q), 67.8 (t), 109.5 (s), 110.0 (s), 126.7 (d), 127.1 (s), 127.7 (d), 128.8 (d), 130.4 (s), 136.0 (s), 164.2 (s); IR (nujol): ν_{max} = 3226, 1729, 1713, 1683 cm^{-1}; MS *m/z* (ESI): 280.81 ($M + H^+$); anal. calcd. for $C_{14}H_{14}ClNO_3$ (279.72): C 60.11, H 5.04, N 5.01; found: C 60.19, H 4.99, N 5.04.



Dimethyl 2,5-dimethyl-1*H*-pyrrole-3,4-dicarboxylate (4j).[4] The compound was obtained as pale yellow solid (54.9 mg, 52%); mp: 112–113 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.31 (s, 6H, 2*CH*$_3$), 3.78 (s, 6H, 2O*CH*$_3$), 8.97 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.3 (q), 51.3 (q), 112.0 (s), 132.8 (s), 166.0 (s); IR (nujol): ν_{max} = 3262, 1736, 1715, 1675 cm^{-1}; MS *m/z* (ESI): 212.22 ($M + H^+$); anal. calcd. for $C_{10}H_{13}NO_4$ (211.08): C 56.86, H 6.20, N 6.63; found: C 56.98, H 6.16, N 6.66.

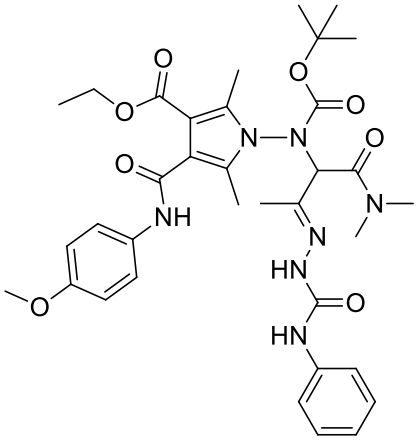


Ethyl 2-methyl-4,5,6,7-tetrahydro-1*H*-indole-3-carboxylate (4k). The compound was obtained as pale yellow solid (68.4 mg, 66%); mp: 121–122 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.34 (t, *J*=7.2 Hz, 3H, OCH$_2$*CH*$_3$), 1.71–1.81 (m, 4H, CH$_2$*CH*$_2$*CH*$_2$CH$_2$), 2.48–2.51 (m, 5H, *CH*$_2$CH$_2$CH$_2$CH$_2$ and *CH*$_3$), 2.70 (t, *J*=5.6 Hz, 2H, CH$_2$CH$_2$CH$_2$*CH*$_2$), 4.25 (q, *J*=7.2 2H, Hz, O*CH*$_2$CH$_3$), 7.83 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.6 (q), 14.5 (q), 22.4 (t), 22.9 (t), 23.3 (t), 23.5 (t), 58.9 (t), 109.6 (s), 118.7 (s), 125.3 (s), 134.0 (s), 166.3 (s); IR (nujol): ν_{max} = 3258, 1736, 1675 cm^{-1}; MS *m/z* (ESI): 208.38 ($M + H^+$); anal. calcd. for $C_{12}H_{17}NO_2$ (207.27): C 69.54, H 8.27, N 6.76; found: C 69.36, H 8.34, N 6.82.

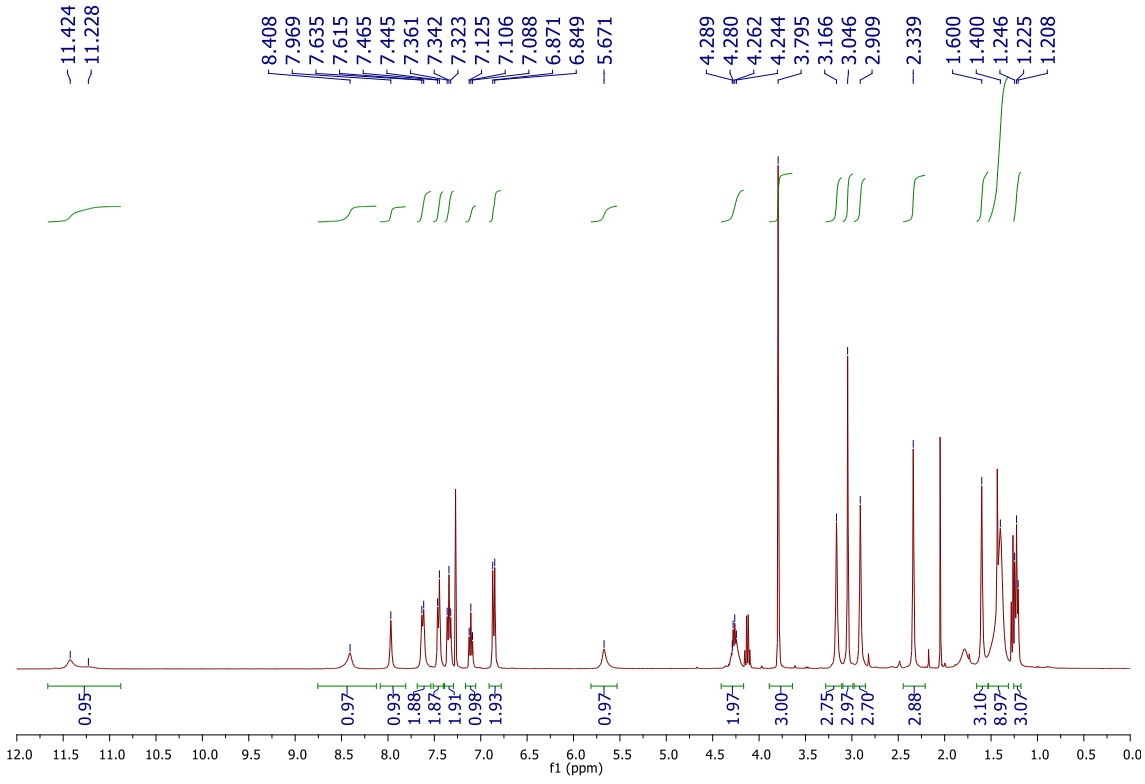


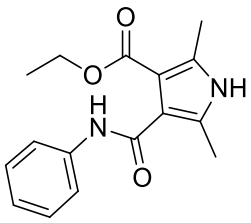
Ethyl 2-methyl-4-phenyl-1*H*-indole-3-carboxylate (4l). The compound was obtained as pale yellow solid (61.1 mg, 53%); mp: 118–120 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.37 (t, *J*=7.2 Hz, 3H, OCH$_2$*CH*$_3$), 2.59 (s, 3H, *CH*$_3$), 4.31 (q, *J*=7.2, 2H, Hz, O*CH*$_2$CH$_3$), 6.85 (d, *J*=2.8 Hz, 1H, *CH*), 7.22 (t, *J*=7.2 Hz, 1H, Ar), 7.36 (t, *J*=8.0 Hz, 2H, Ar), 7.47 (d, *J*=7.2 Hz, 2H, Ar), 8.81 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.4 (q), 14.5 (q), 59.6 (t), 107.3 (d), 113.3 (d), 123.6 (d), 126.5 (d), 128.9 (d), 130.0 (s), 131.8 (s), 136.2 (s), 165.7 (s); IR (nujol): ν_{max} = 3266, 1738, 1677 cm^{-1}; MS *m/z* (ESI): 230.31 ($M + H^+$); anal. calcd. for $C_{14}H_{15}NO_2$ (229.27): C 73.34, H 6.59, N 6.11; found: C 73.46, H 6.56, N 6.14.

7. ^{1}H and ^{13}C spectra of 1amino-1*H*-pyrrole 6a and 1*H*-pyrroles 4a–l.

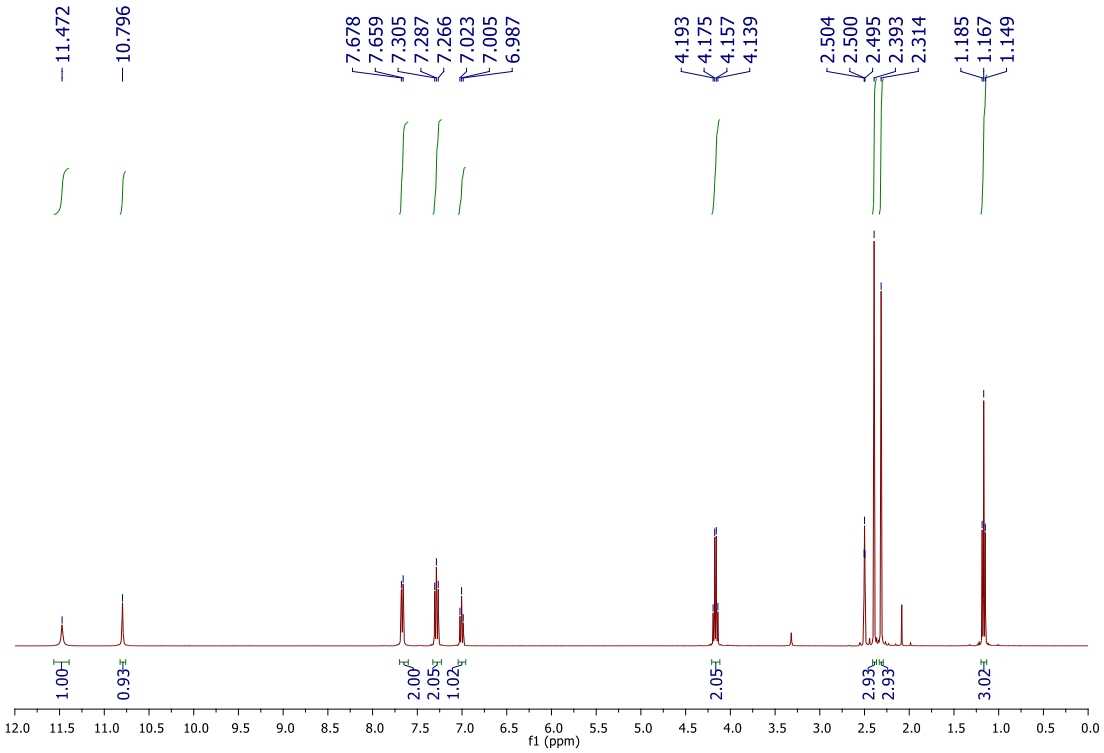


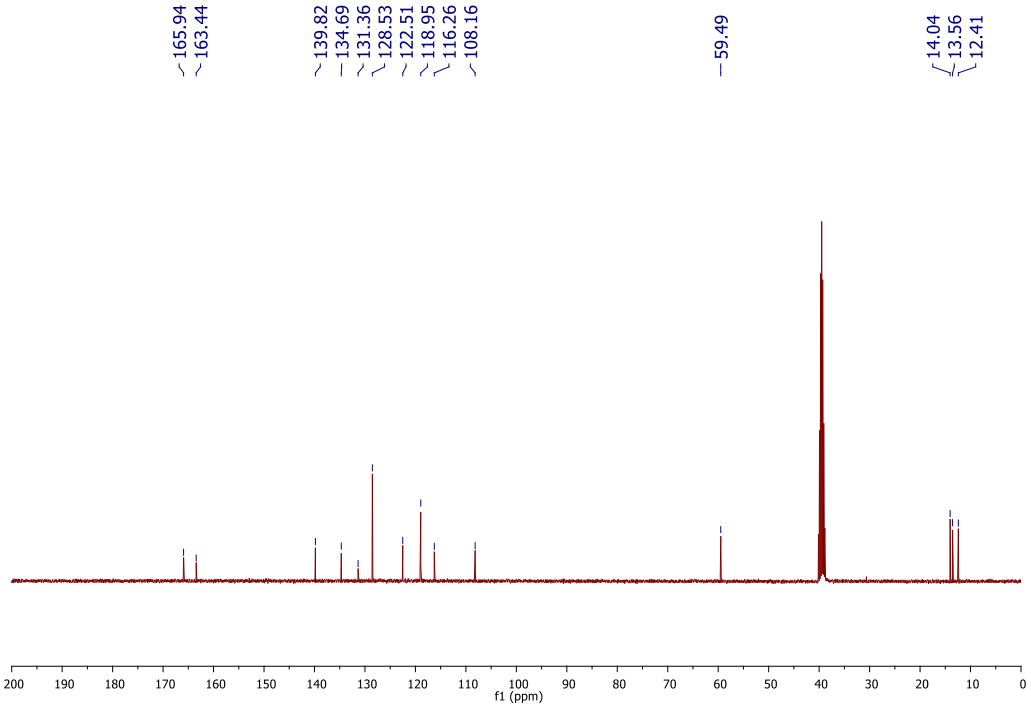
Ethyl 1-((*tert*-butoxycarbonyl)(1-(dimethylamino)-1-oxo-3-(2-(phenylcarbamoyl)hydrazono)butan-2yl)amino)-4-((4-methoxyphenyl)carbamoyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (6a).

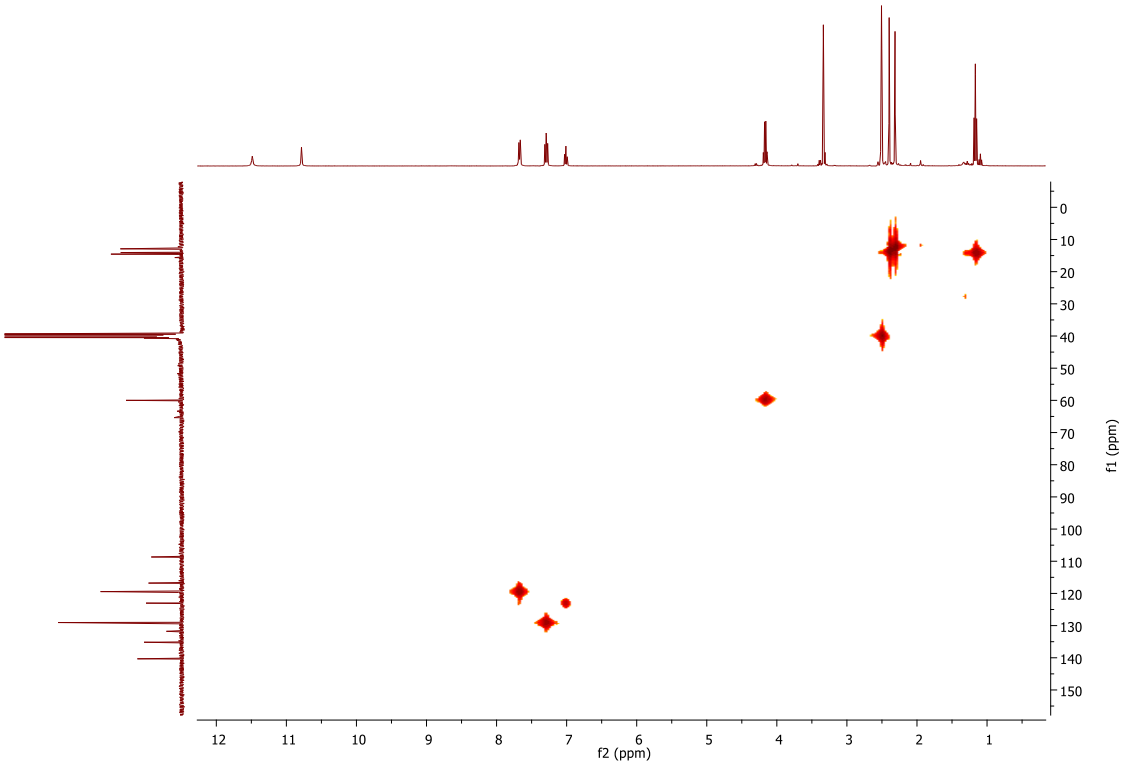




Ethyl 2,5-dimethyl-4-(phenylcarbamoyl)-1*H*-pyrrole-3-carboxylate (4a).



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6
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2
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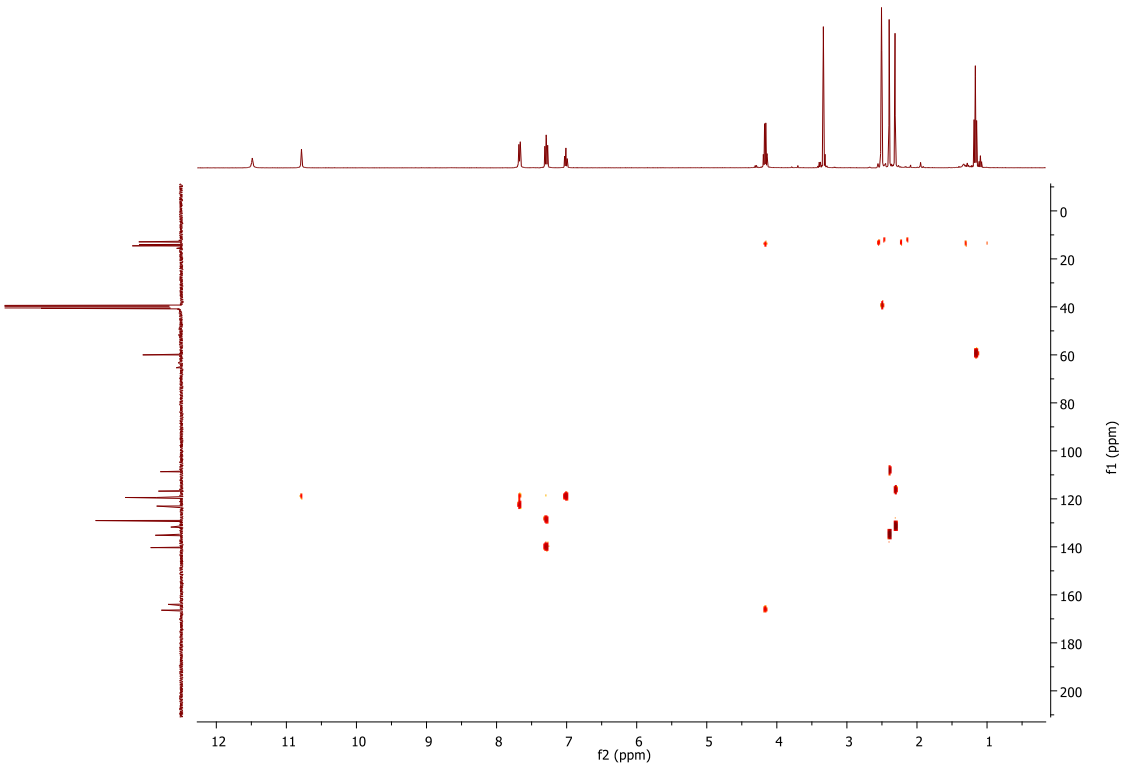
f2 (ppm)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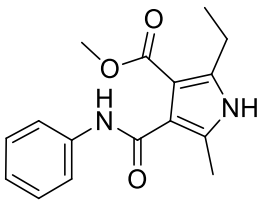
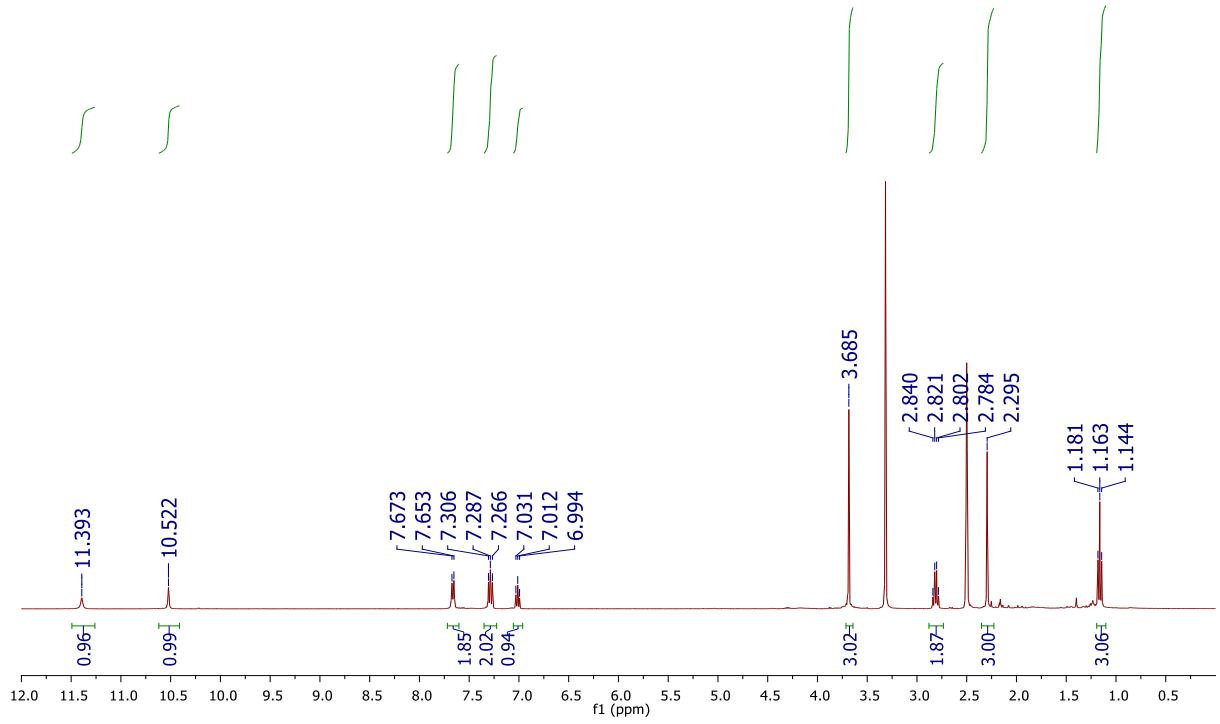
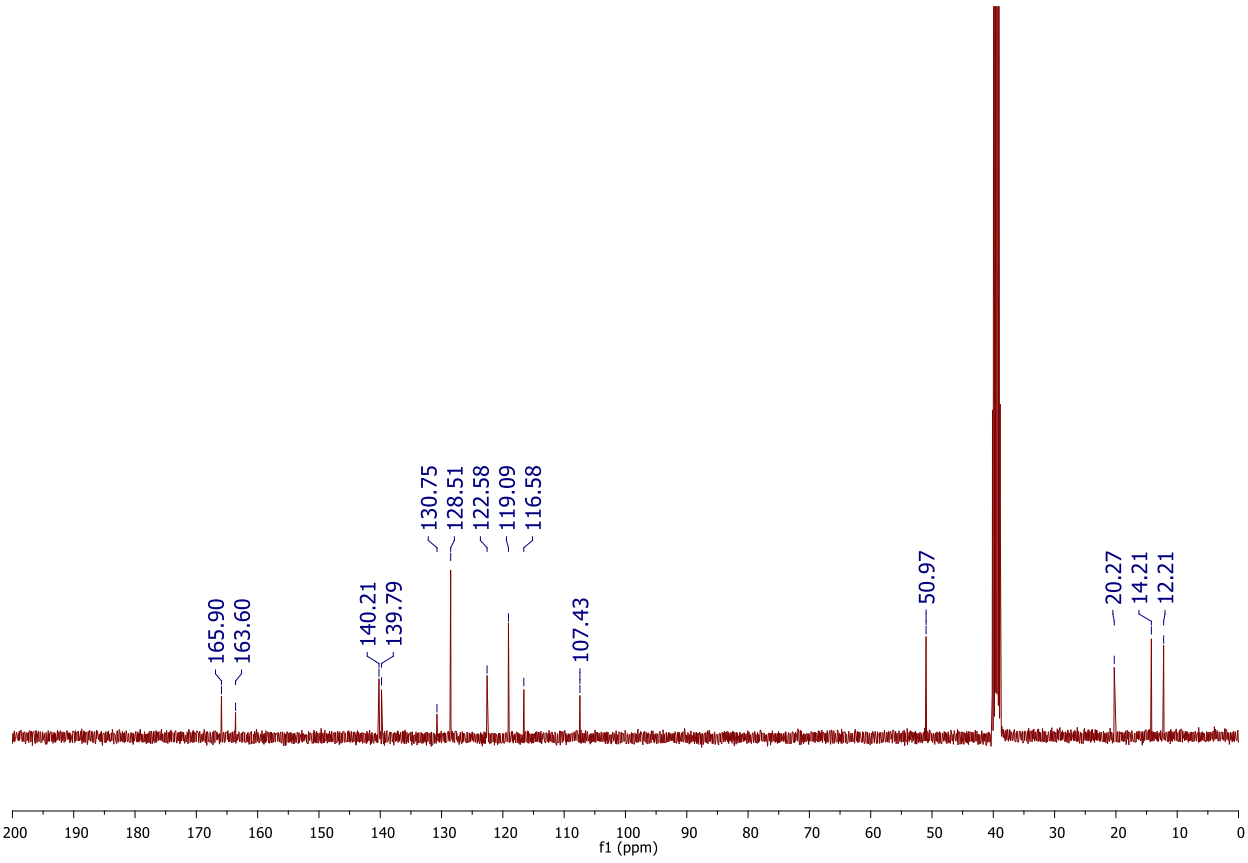
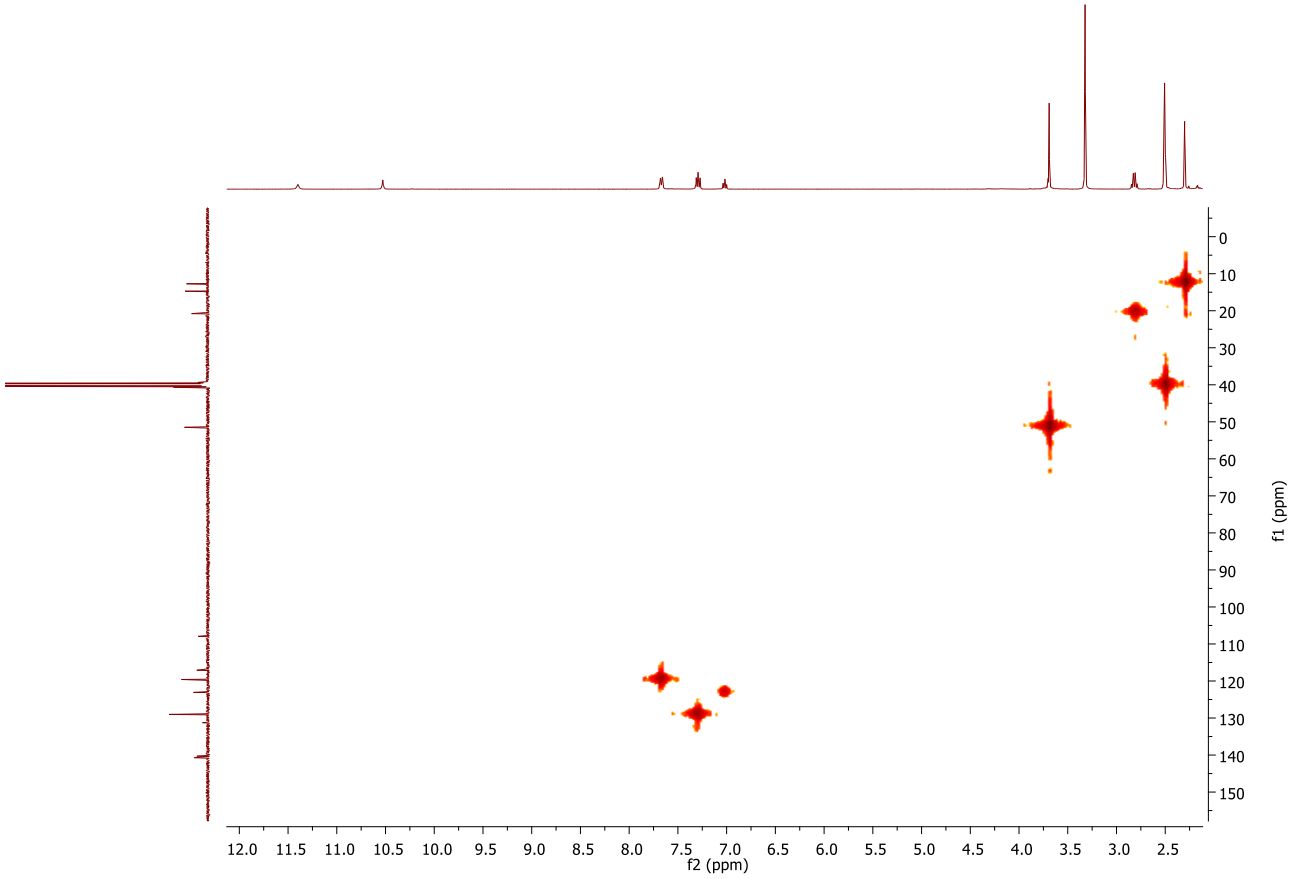
f2 (ppm)



Methyl 2-ethyl-5-methyl-4-(phenylcarbamoyl)-1H-pyrrole-3-carboxylate (4b).



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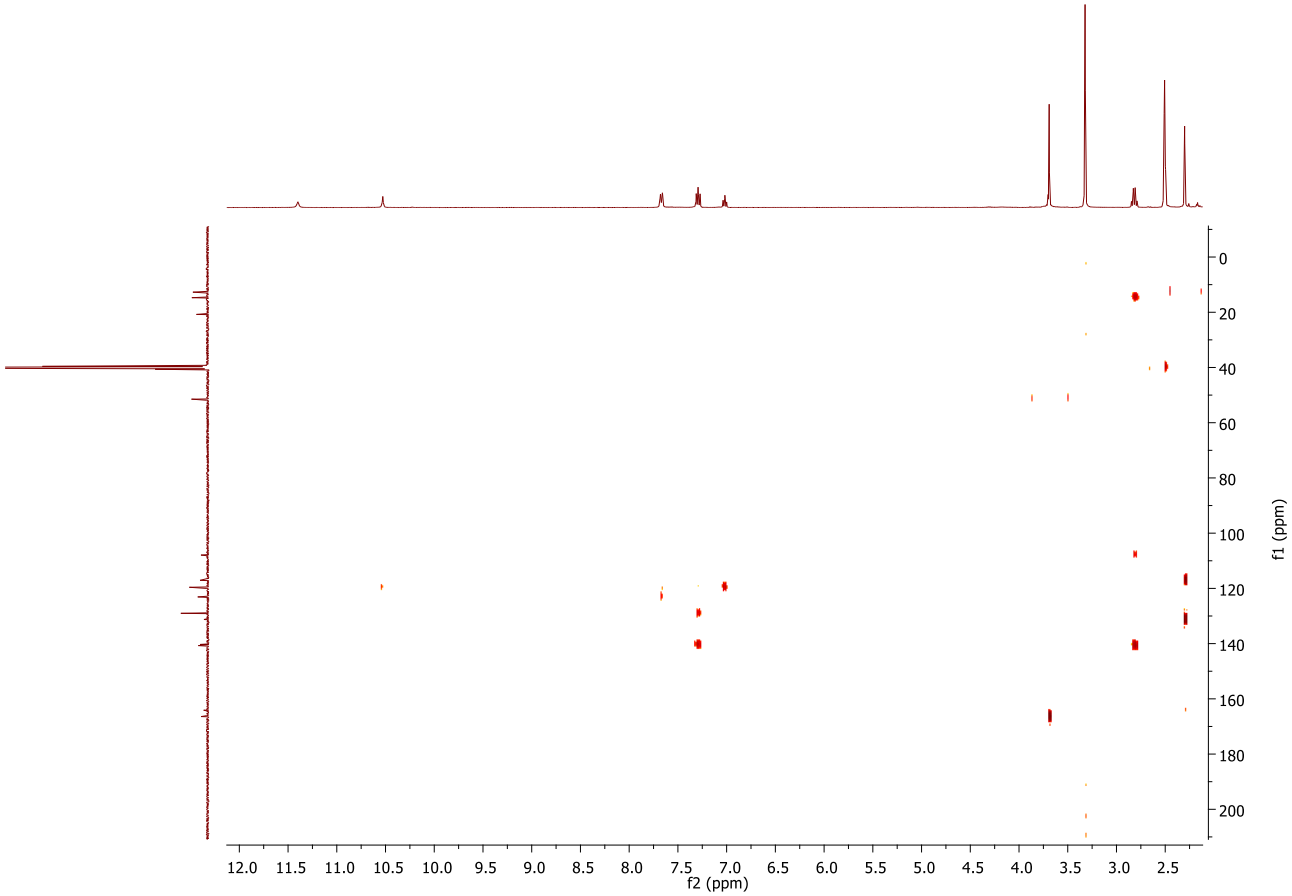
f2 (ppm)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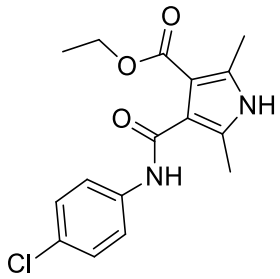
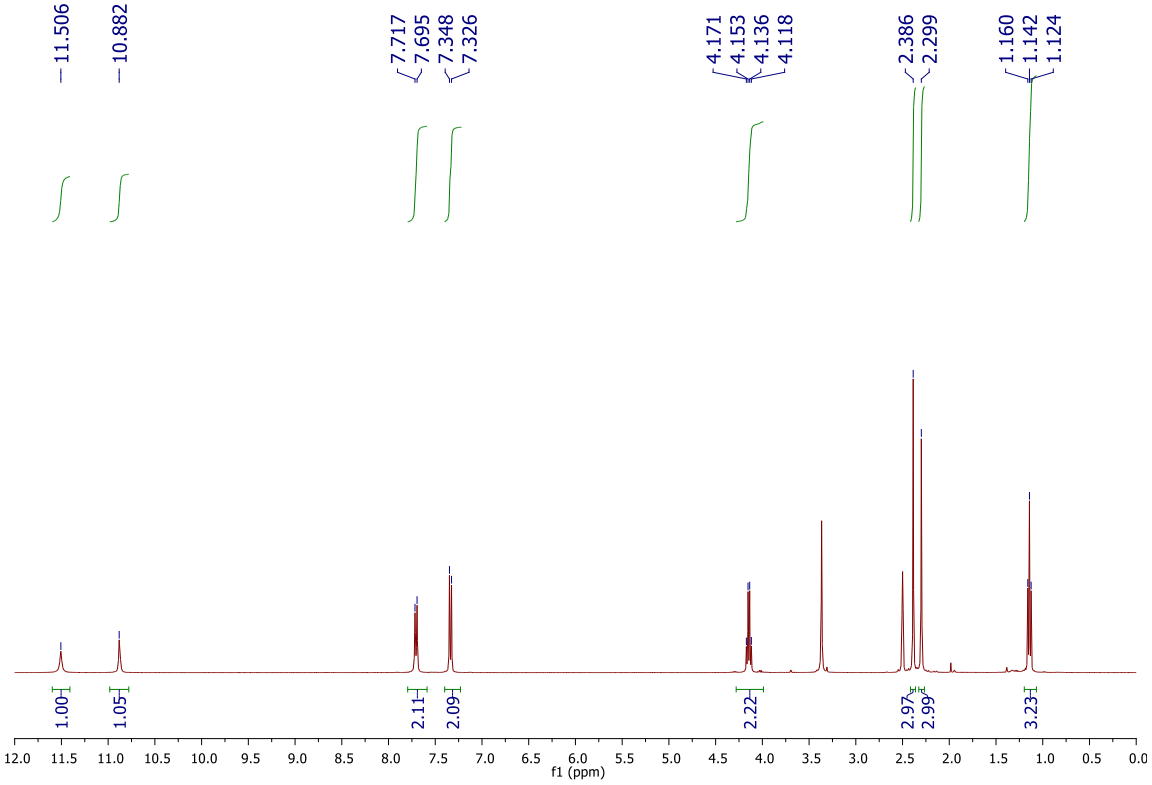
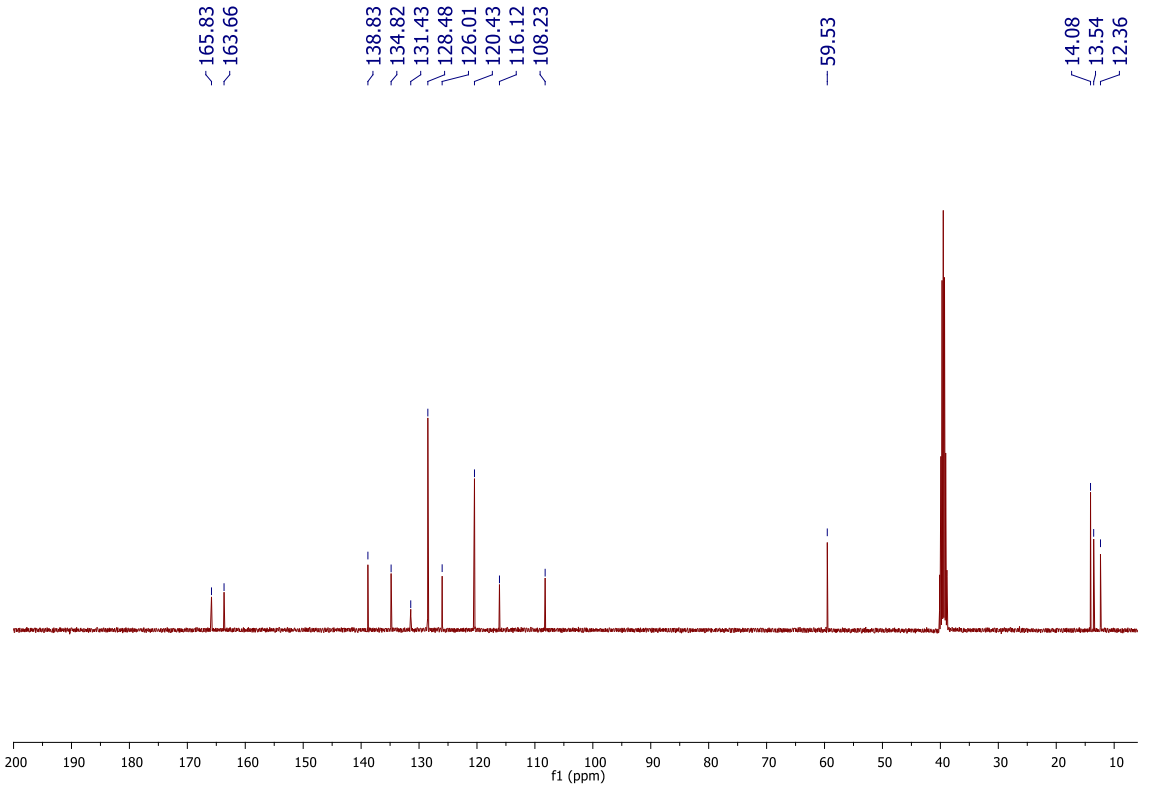
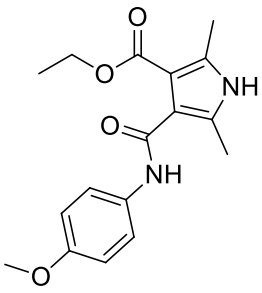
f2 (ppm)



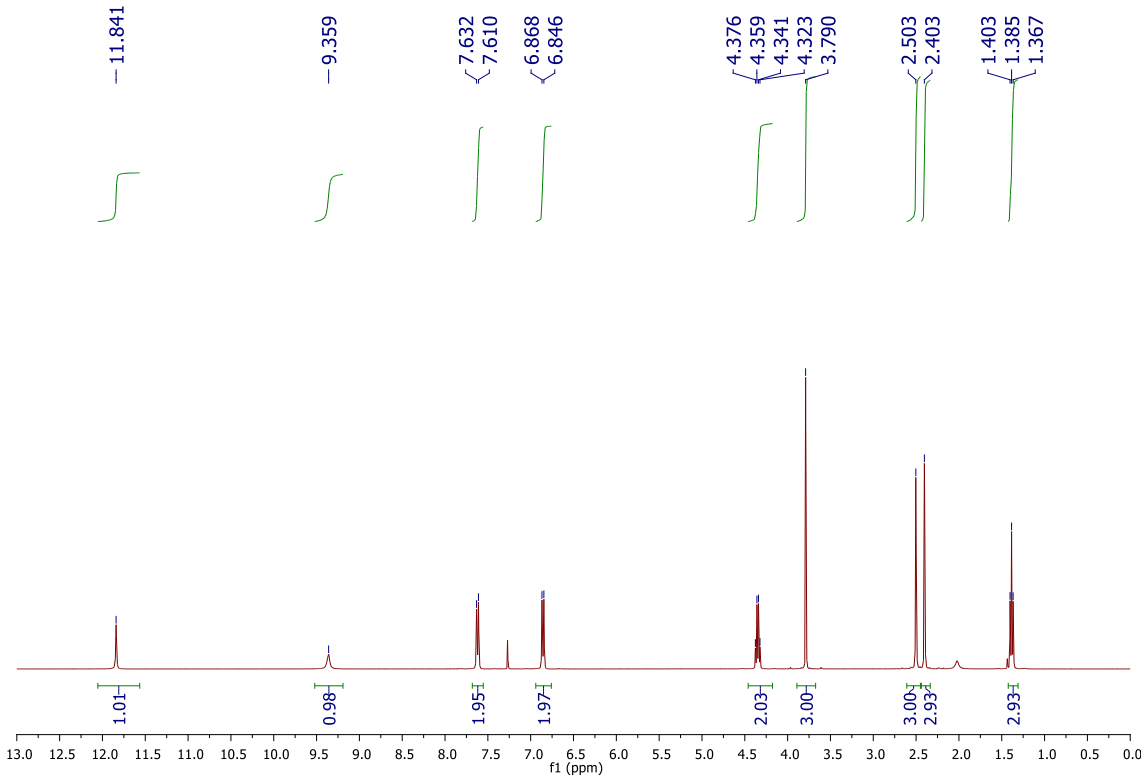
Ethyl 4-((4-chlorophenyl)carbamoyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (4c).

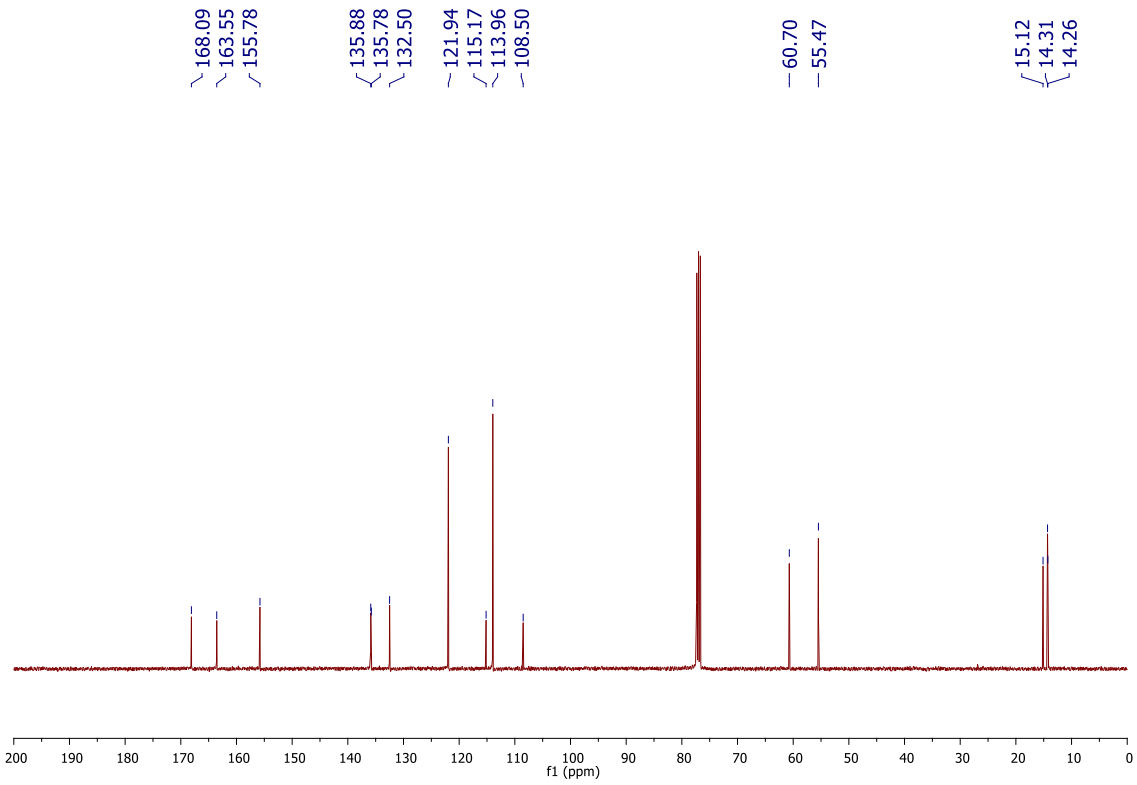






Ethyl 4-((4-methoxyphenyl)carbamoyl)-2,5-dimethyl-1H-pyrrole-3-carboxylate (4d).

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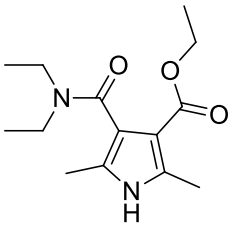
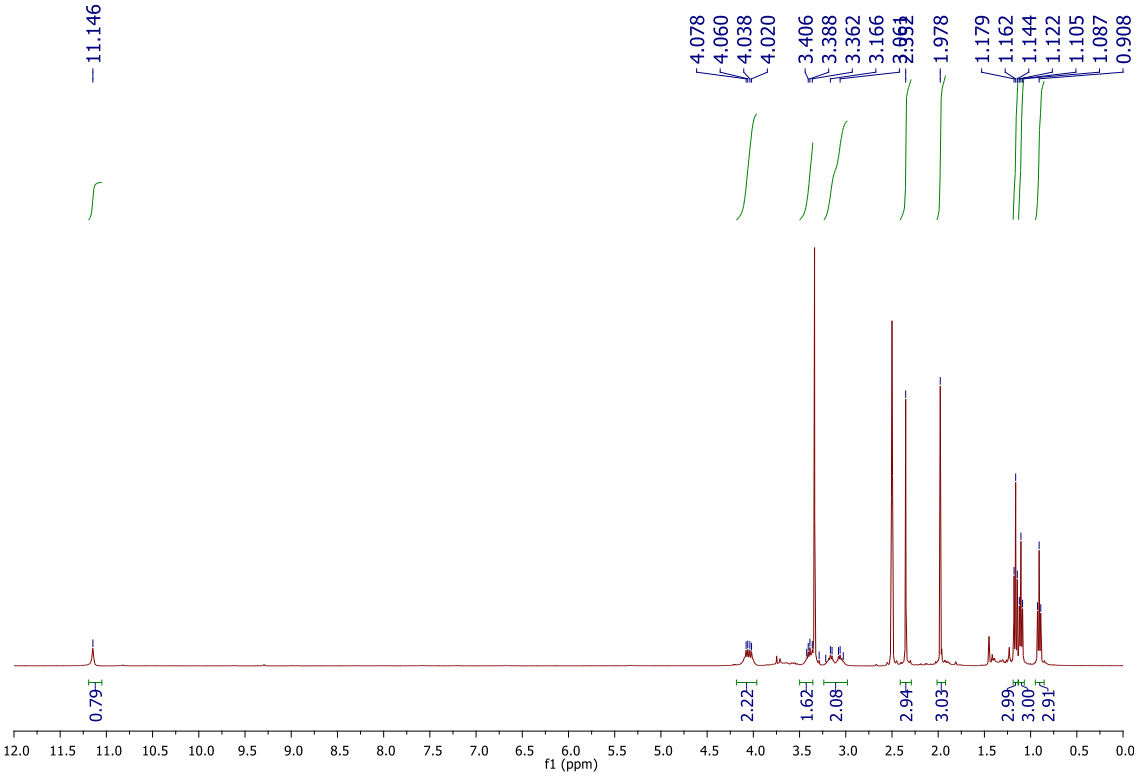
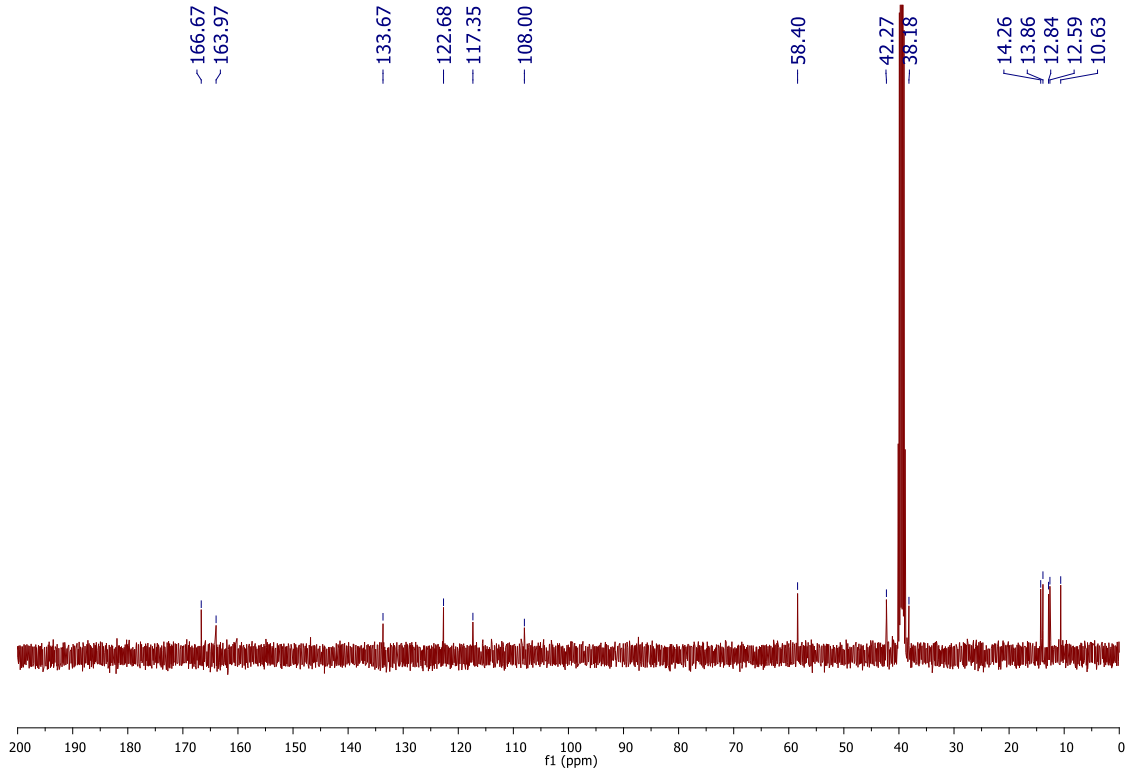
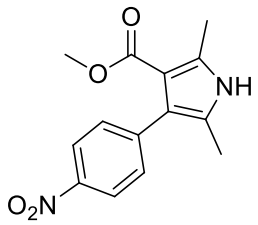
f1 (ppm)



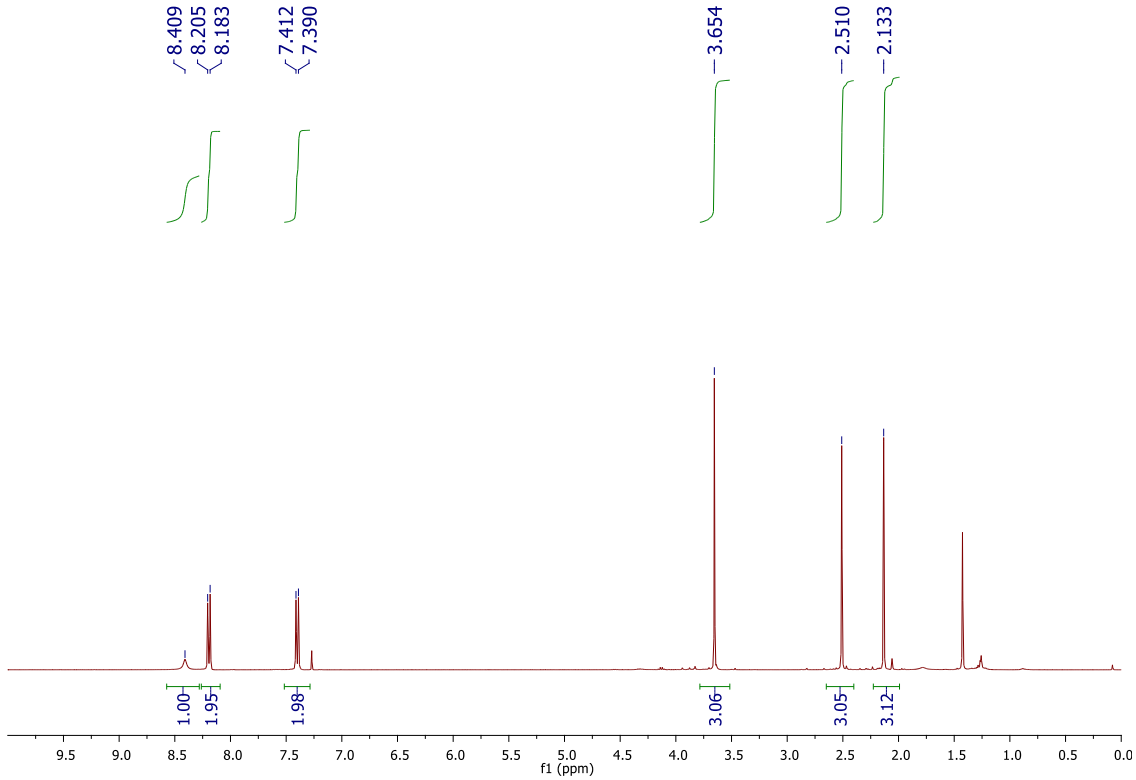
Ethyl 4-(diethylcarbamoyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (4e).

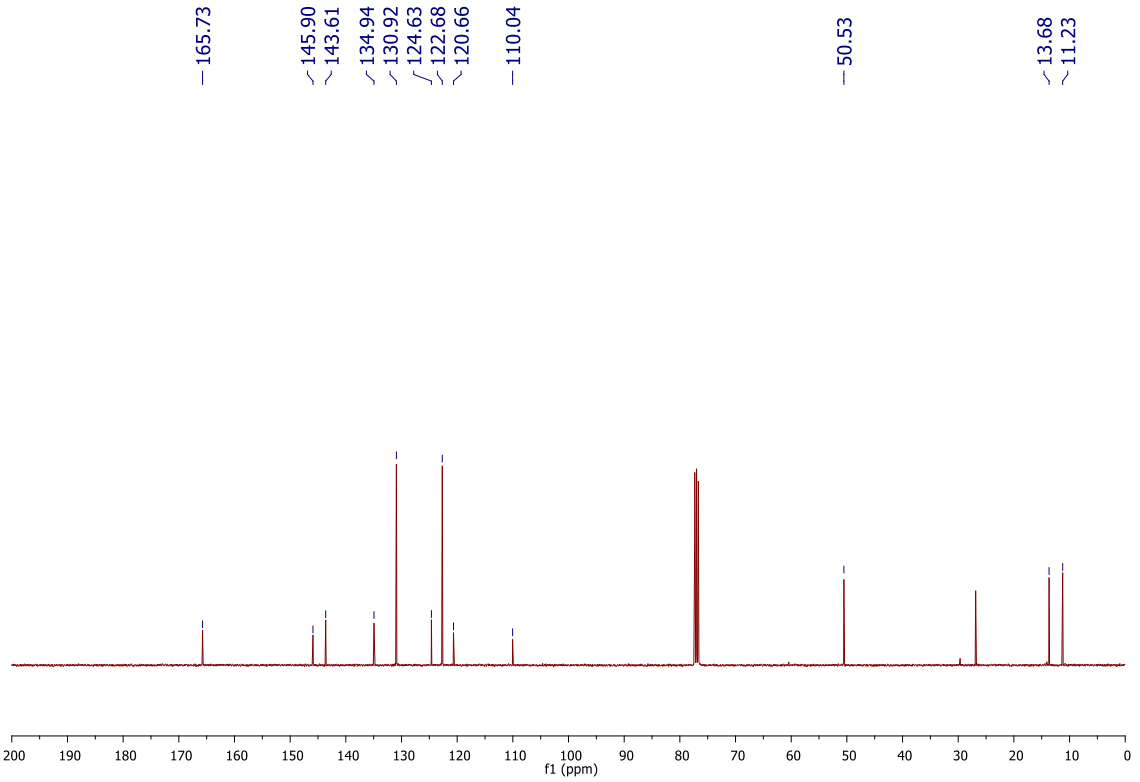


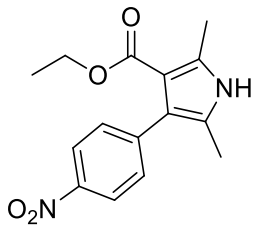




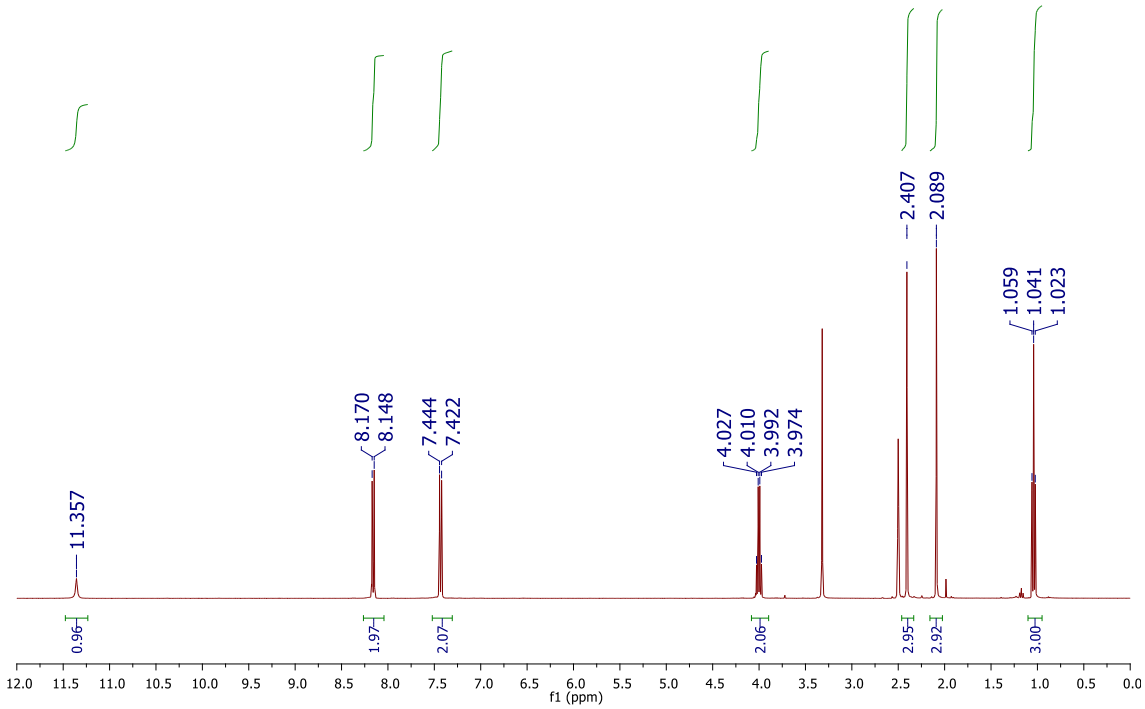
Methyl 2,5-dimethyl-4-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (4f).

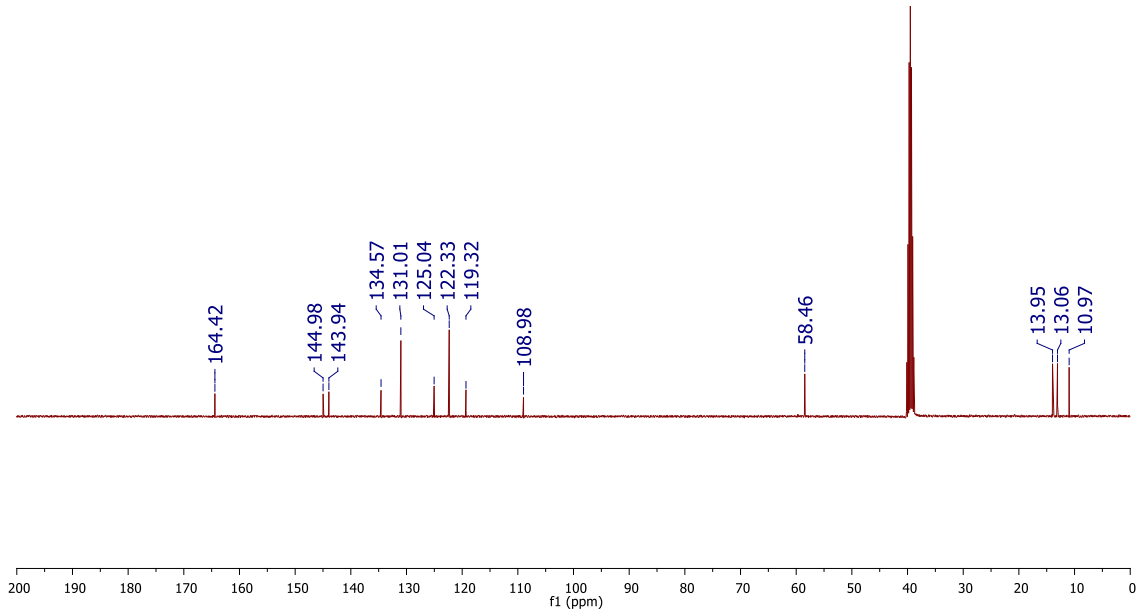


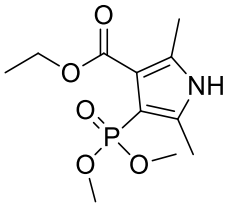




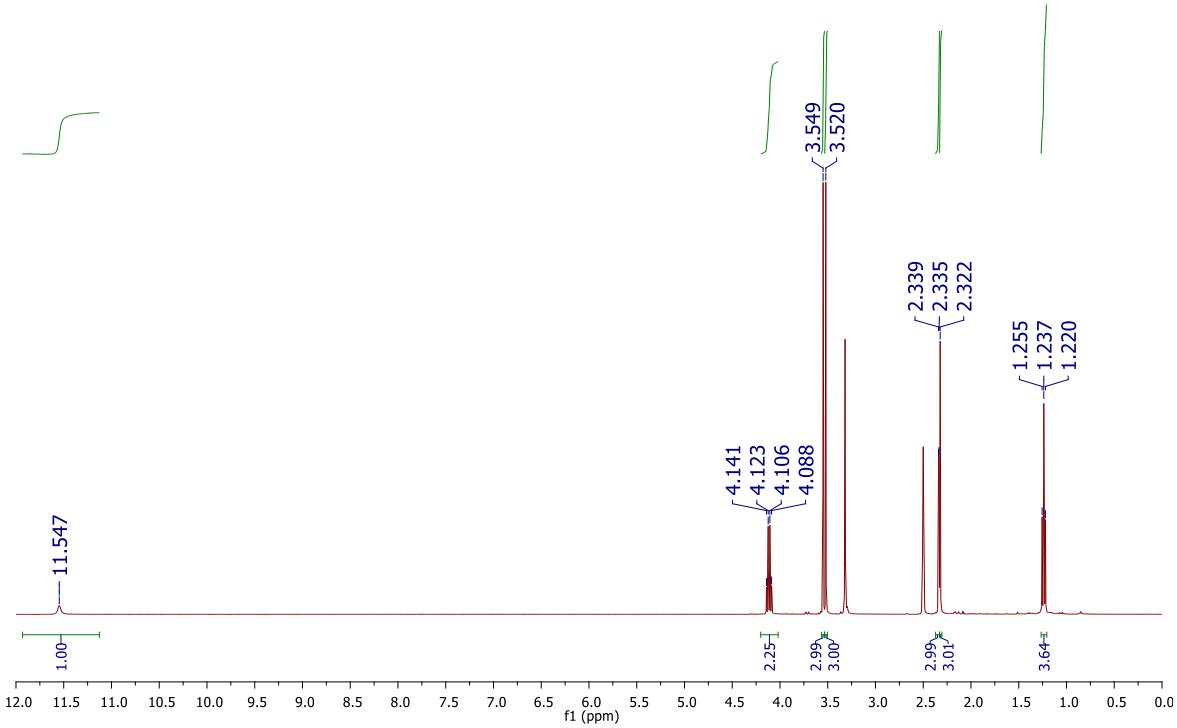
Ethyl 2,5-dimethyl-4-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (4g).[3]

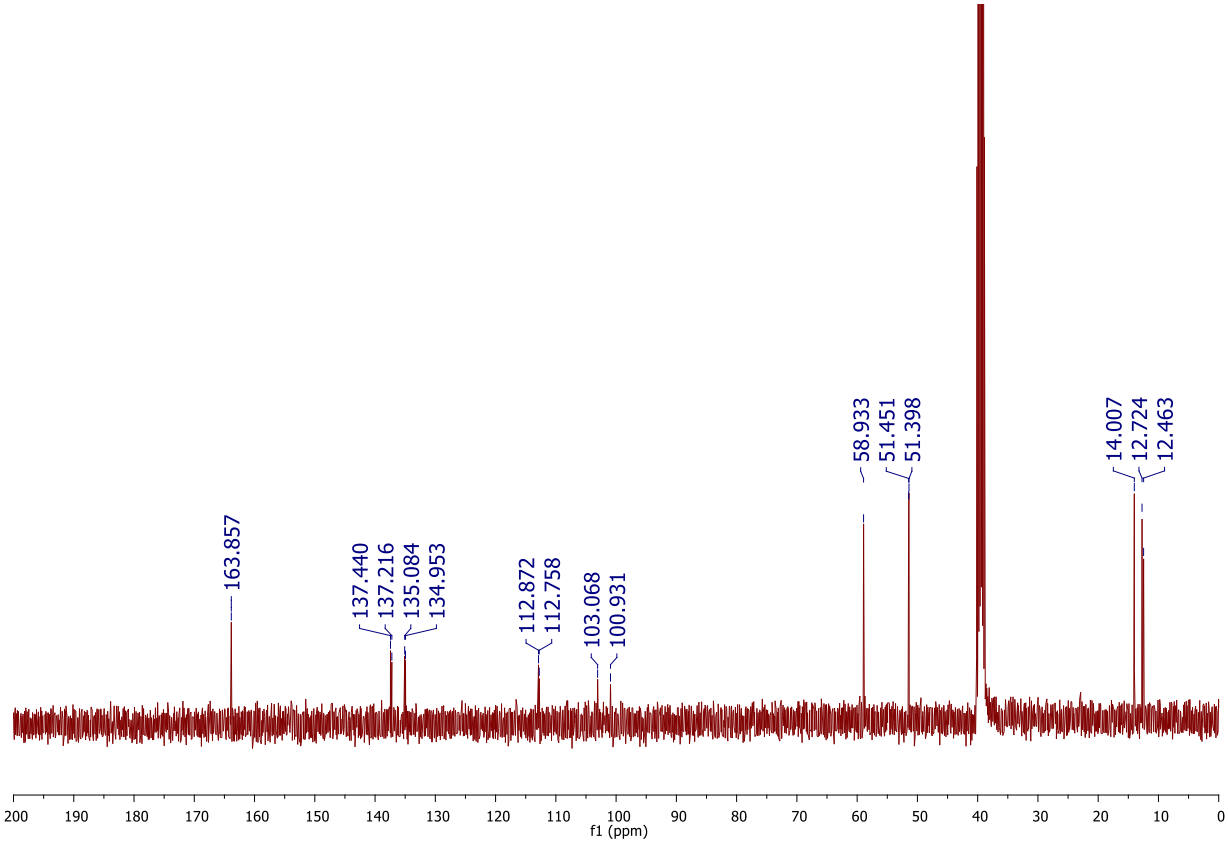


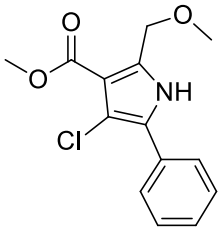




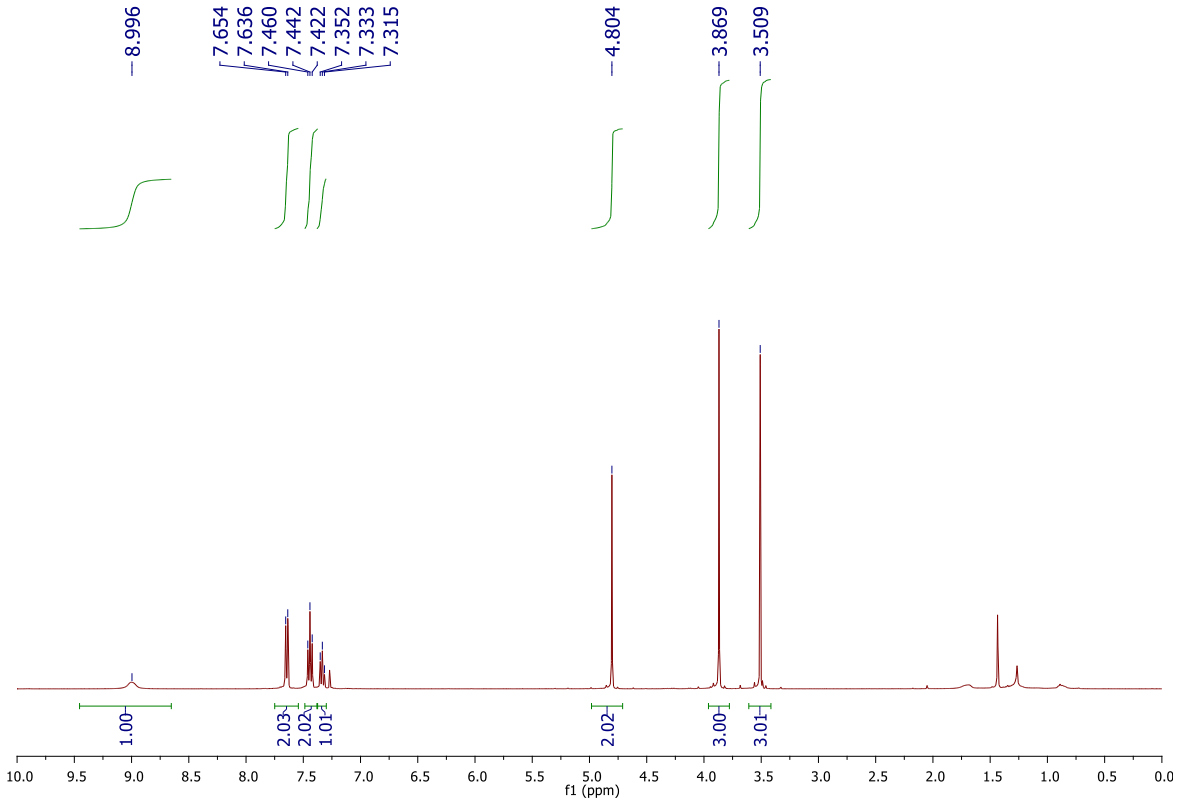
Ethyl 4-(dimethoxyphosphoryl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (4h).

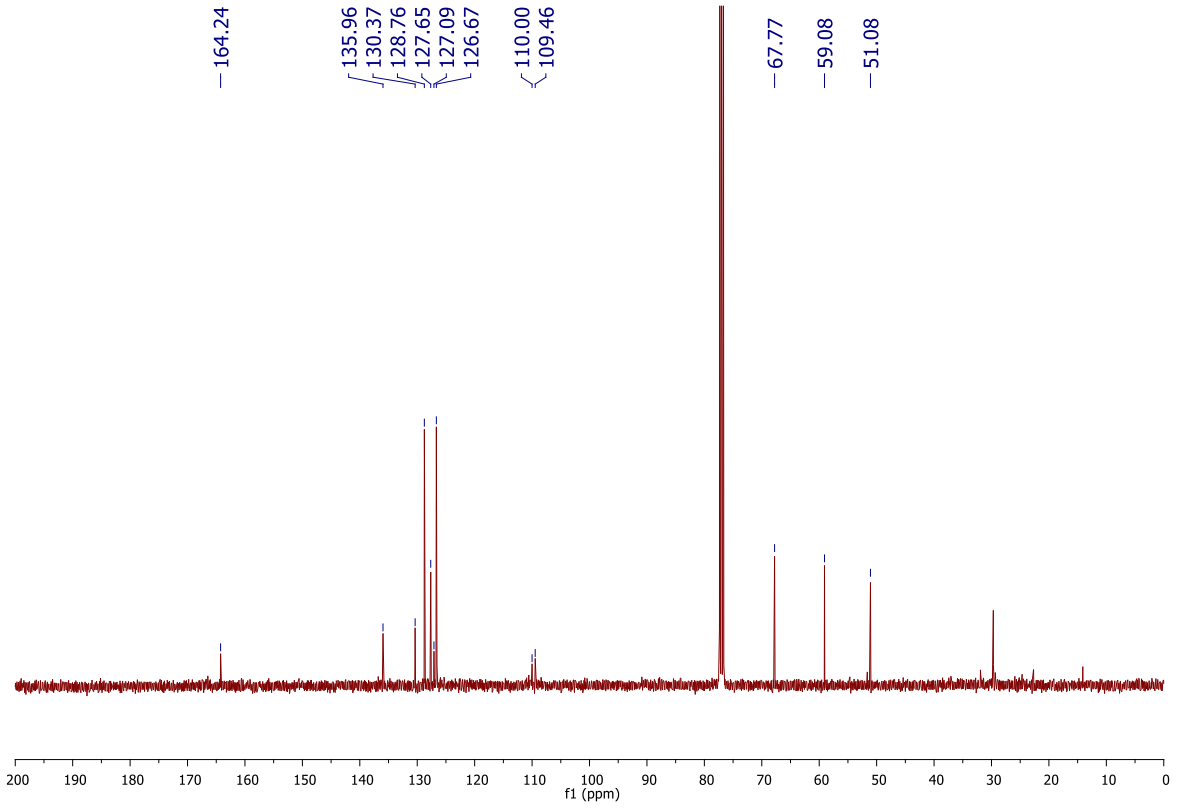


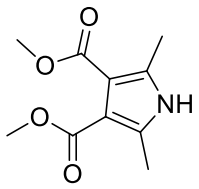




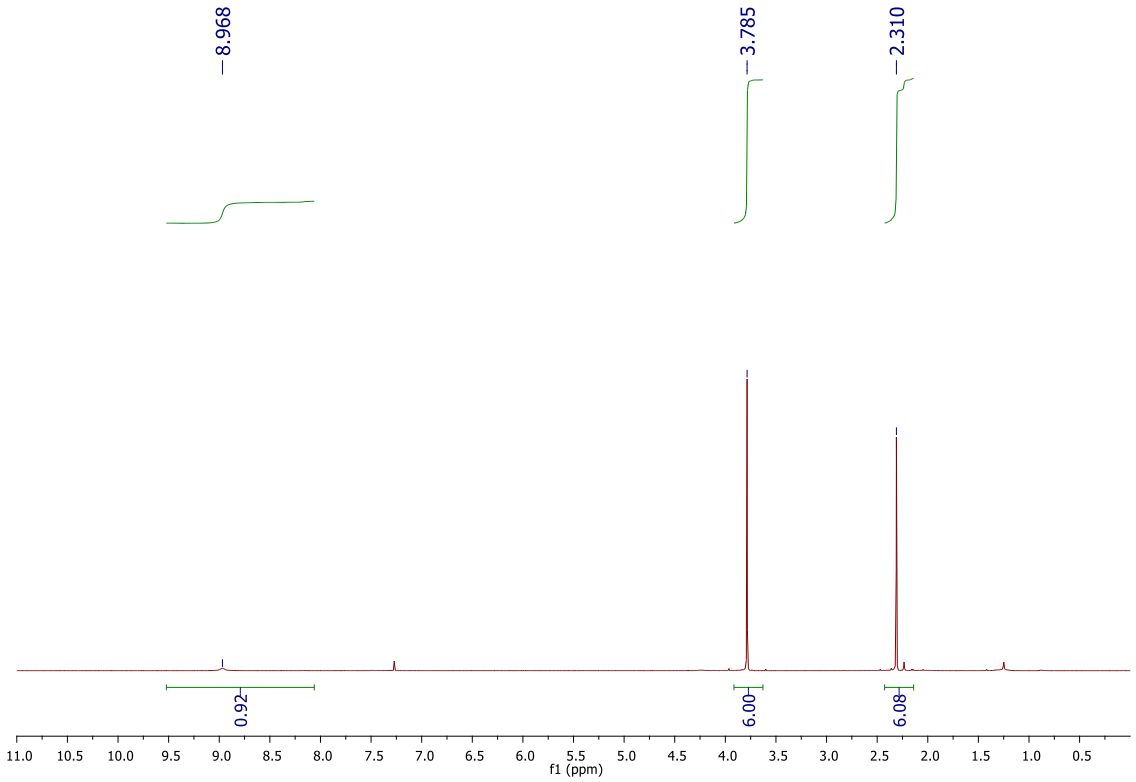
Methyl 4-chloro-2-(methoxymethyl)-5-phenyl-1*H*-pyrrole-3-carboxylate (4i).

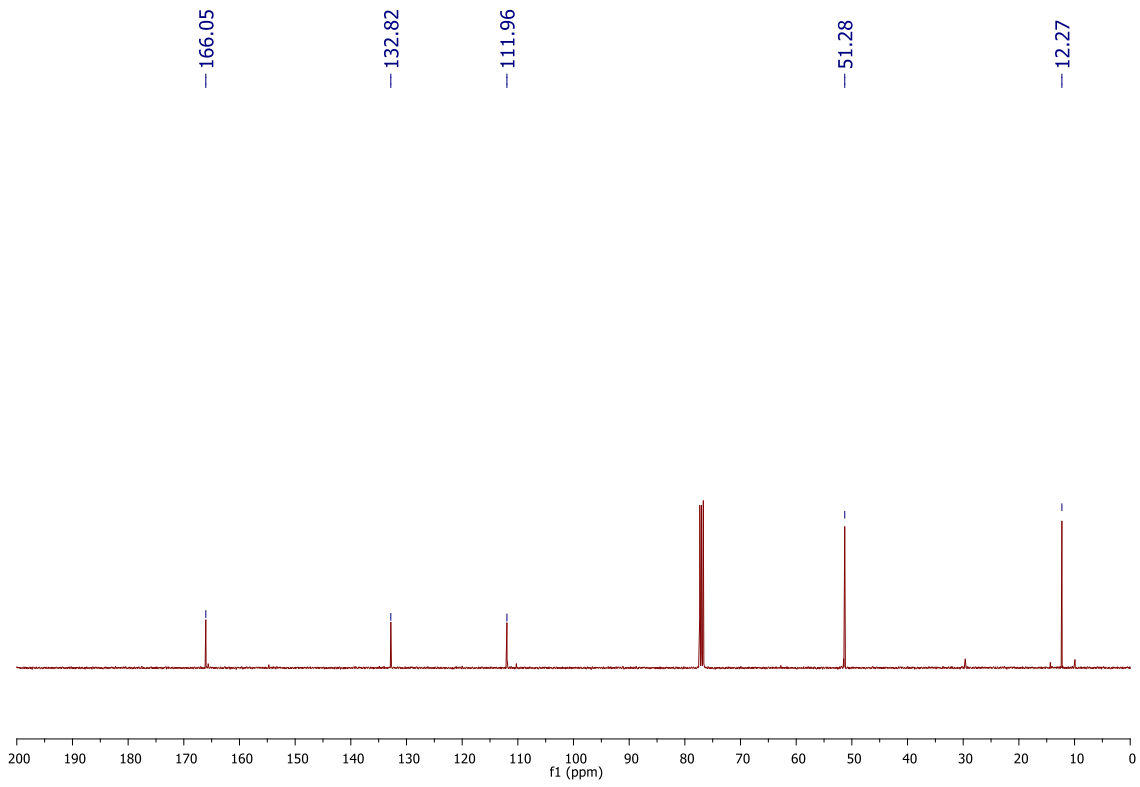


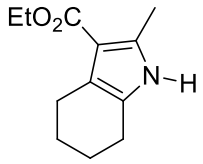




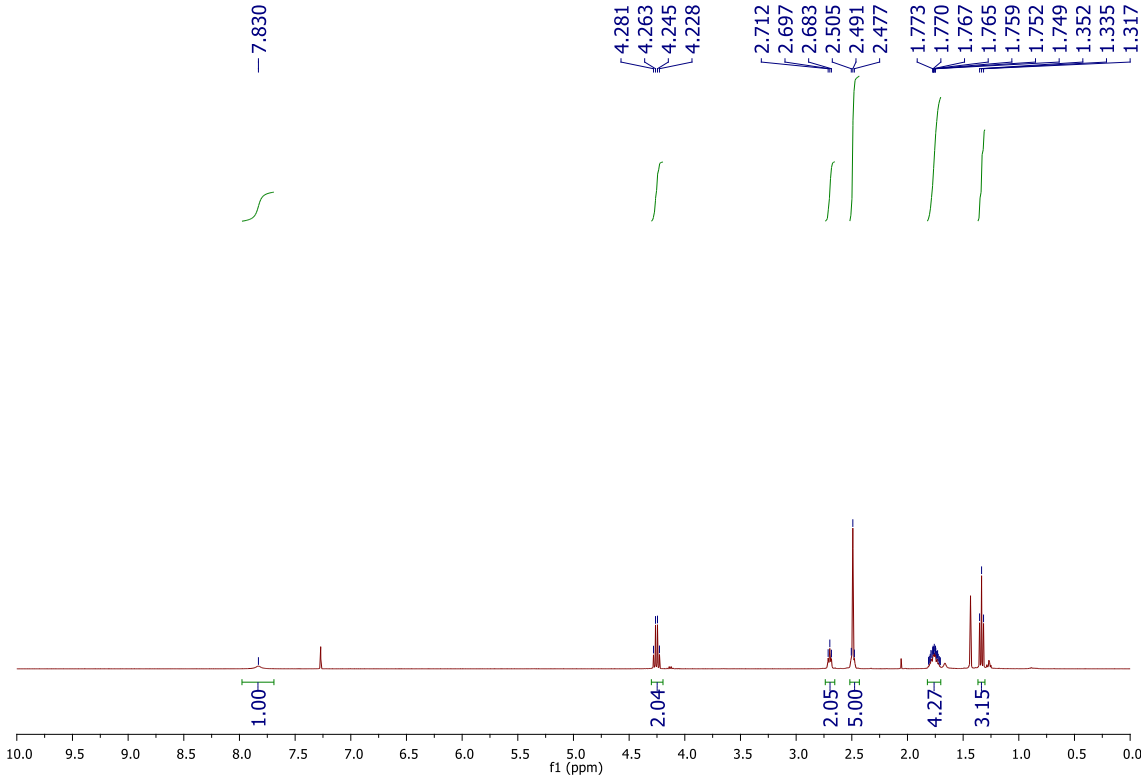
Dimethyl 2,5-dimethyl-1*H*-pyrrole-3,4-dicarboxylate (4j).[4]

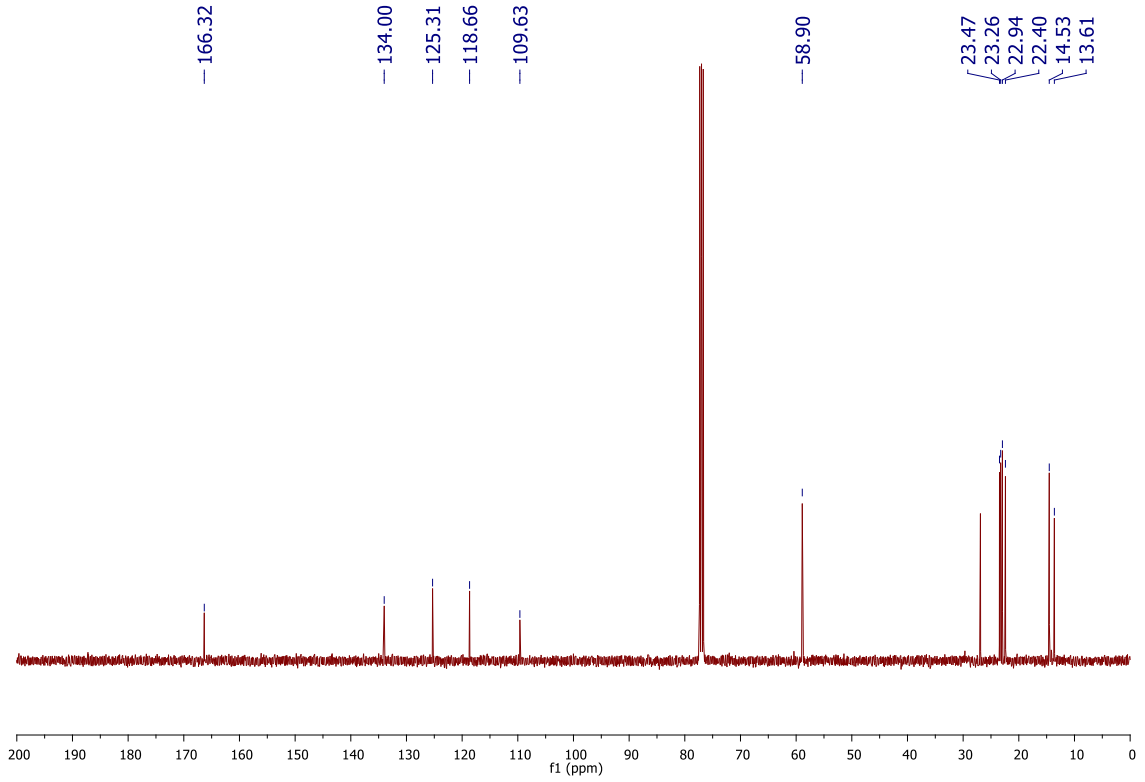


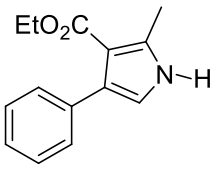




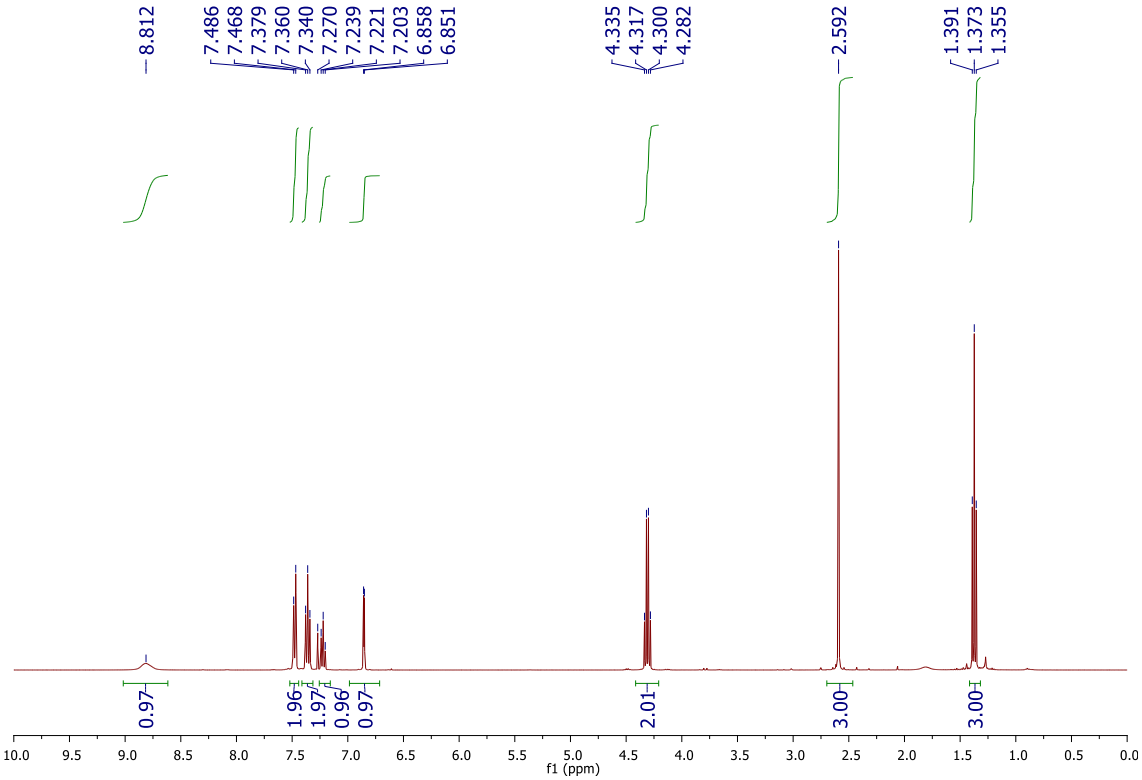
Ethyl 2-methyl-4,5,6,7-tetrahydro-1*H*-indole-3-carboxylate (4k).

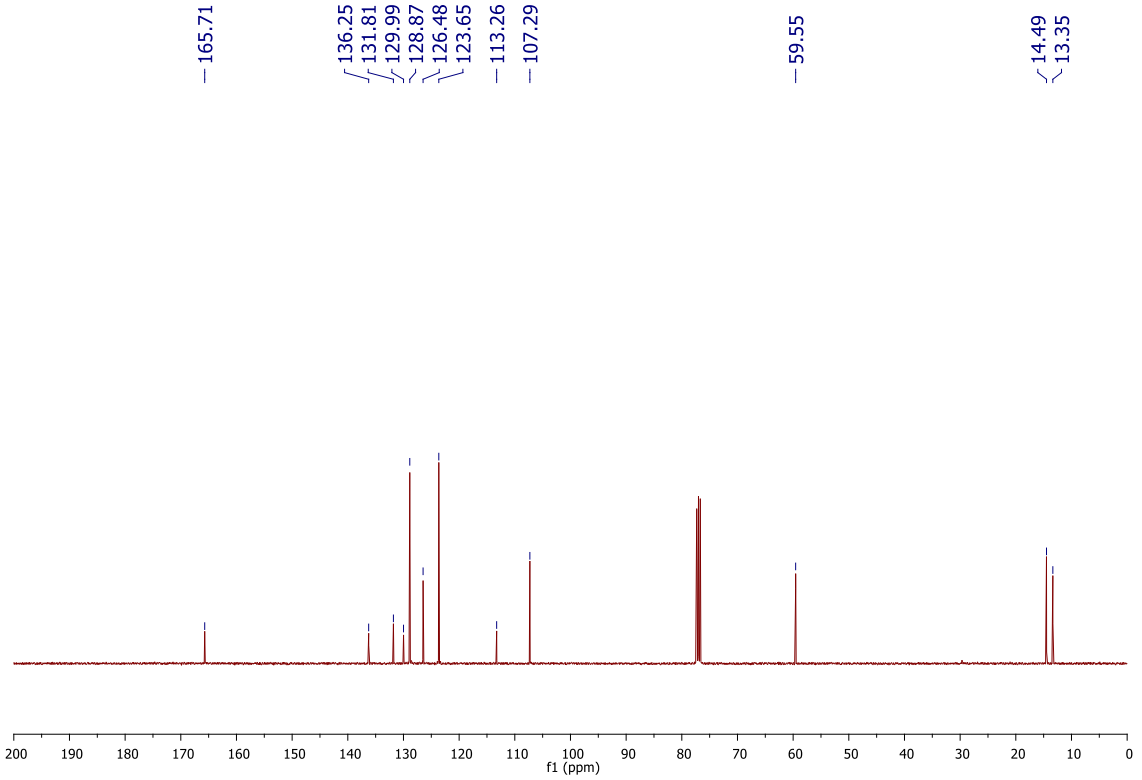






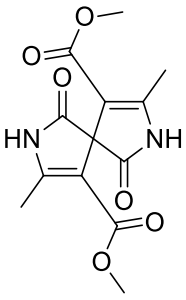
Ethyl 2-methyl-4-phenyl-1H-indole-3-carboxylate (4l).



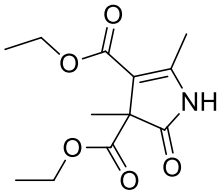


8. General procedure for the synthesis of 1*H*-pyrrol-2-ones 10a–e by basic treatment of 1-amino-1*H*-pyrrol-2-ones 9a–e and DD 2a. To a magnetically stirred solution of 1-amino-1*H*-pyrrol-2-ones **9a–e** (0.5 mmol) in MeCN (10 mL), DD **2a** (1.0 mmol) and K_2CO_3 (1.5 mmol) were added and then the reaction mixture was refluxed for 1 hour, until the TLC analysis revealed the disappearance of the starting reagent **9** and the formation of 1*H*-pyrrol-2-ones **10a–e**. After the filtration of K_2CO_3, the solvent was removed in vacuo; the so-formed products **10** were purified by silica gel column chromatography using cyclohexane/ethyl acetate mixtures as eluent and then were crystallized from ethyl acetate/petroleum ether.

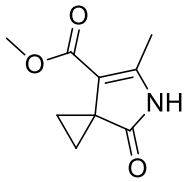
9. Spectral data of 1*H*-pyrrol-2-ones 10a–e.



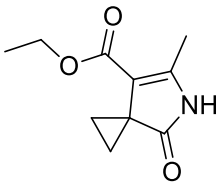
Dimethyl 3,8-dimethyl-1,6-dioxo-2,7-diazaspiro[4.4]nona-3,8-diene-4,9-dicarboxylate (10a). The compound was obtained as yellow solid (92.5 mg, 63%); mp: 140–142 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 2.32 (s, 6H, 2*CH*$_3$), 3.54 (s, 6H, 2O*CH*$_3$), 10.64 (s, 2H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.4 (q), 50.7 (q), 64.8 (s), 105.6 (s), 156.3 (s), 162.8 (s), 173.2 (s); IR (nujol): ν_{max} = 3313, 3252, 1760, 1739, 1713, 1704 cm^{-1}; MS *m/z* (ESI): 295.11 (M + H$^+$); anal. calcd. for $C_{13}H_{14}N_2O_6$ (294.08): C 53.06, H 4.80, N 9.52; found: C 53.18, H 4.75, N 9.44.



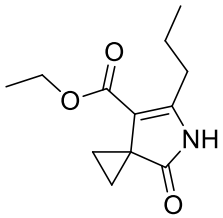
Diethyl 3,5-dimethyl-2-oxo-2,3-dihydro-1*H*-pyrrole-3,4-dicarboxylate (10b).[5] The compound was obtained as white solid (117.3 mg, 92%); mp: 104–105 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.09 (t, *J*=7.2 Hz, 3H, OCH_2CH_3), 1.16 (t, *J*=7.2 Hz, 3H, OCH_2CH_3), 1.41 (s, 3H, *CH*$_3$), 2.30 (s, 3H, *CH*$_3$), 4.00–4.11 (m, 4H, 2O*CH*$_2$CH$_3$), 10.62 (s, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.0 (q), 13.9 (q), 14.1 (q), 19.0 (q), 56.3 (s), 59.0 (t), 60.9 (t), 109.7 (s), 154.3 (s), 162.6 (s), 168.2 (s), 176.3 (s); IR (nujol): ν_{max} = 3142, 1723, 1645, 1634 cm^{-1}; MS *m/z* (ESI): 256.44 (M + H$^+$); anal. calcd. for $C_{12}H_{17}NO_5$ (255.27): C 56.46, H 6.71, N 5.49; found: C 56.62, H 6.77, N 5.41.



Methyl 6-methyl-4-oxo-5-azaspiro[2.4]hept-6-ene-7-carboxylate (10c). The compound was obtained as white solid (48.2 mg, 53%); mp: 142–144 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.42–1.45 (m, 2H, CH_2CH_2), 1.88–1.91 (m, 2H, CH_2CH_2), 2.44 (s, 3H, *CH*$_3$), 3.70 (s, 3H, O*CH*$_3$), 9.20 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.4 (q), 18.2 (t), 29.9 (s), 50.7 (q), 107.6 (s), 149.5 (s), 163.9 (s), 180.9 (s); IR (nujol): ν_{max} = 3180, 1713, 1683 cm^{-1}; MS *m/z* (ESI): 182.31 (M + H$^+$); anal. calcd. for $C_9H_{11}NO_3$ (181.19): C 59.66, H 6.12, N 7.73; found: C 59.77, H 6.07, N 7.65.

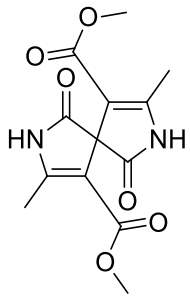


Ethyl 6-methyl-4-oxo-5-azaspiro[2.4]hept-6-ene-7-carboxylate (10d). The compound was obtained as white solid (46.6 mg, 48%); mp: 130–132 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.13–1.16 (m, 2H, CH_2CH_2), 1.19 (t, *J*=7.2 Hz, 3H, OCH_2CH_3), 1.66–1.69 (m, 2H, CH_2CH_2), 2.32 (s, 3H, CH_3), 4.05 (q, *J*=7.2 Hz, 2H, OCH_2CH_3), 10.53 (s, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.8 (q), 14.1 (q), 16.3 (t), 28.8 (s), 58.8 (t), 105.1 (s), 151.3 (s), 162.7 (s), 178.7 (s); IR (nujol): ν_{max} = 3190, 1719, 1693 cm^{-1}; MS *m/z* (ESI): 196.42 (M + H$^+$); anal. calcd. for $C_{10}H_{13}NO_3$ (195.21): C 61.53, H 6.71, N 7.18; found: C 61.38, H 6.75, N 7.13.

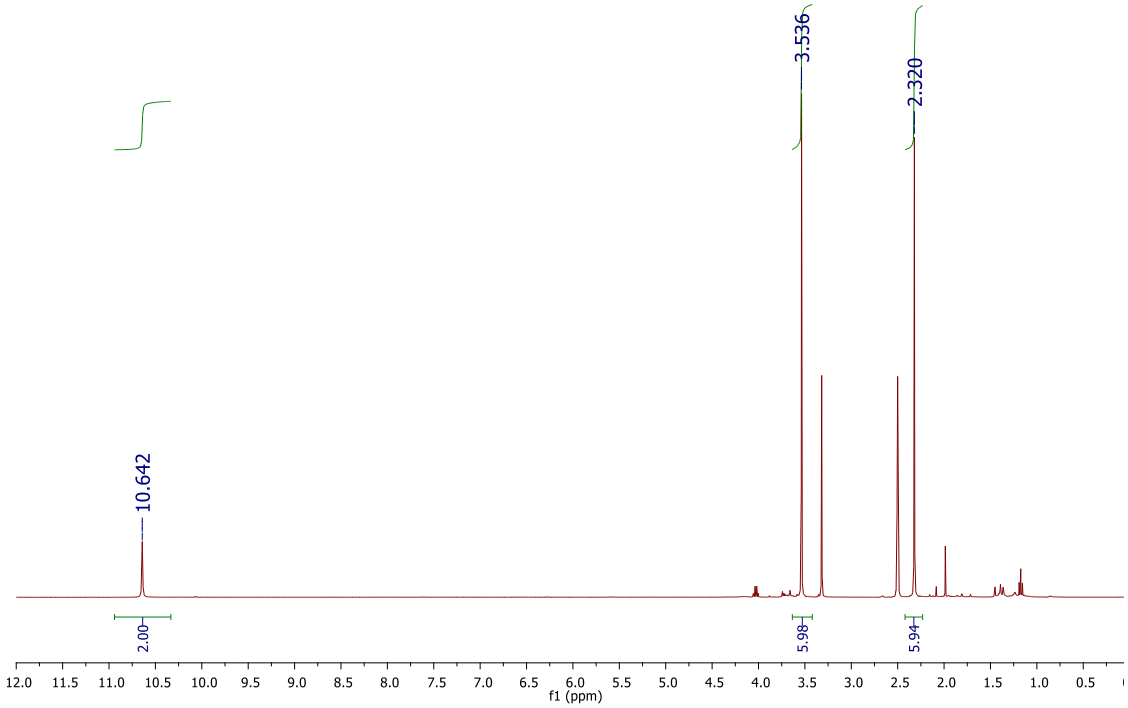


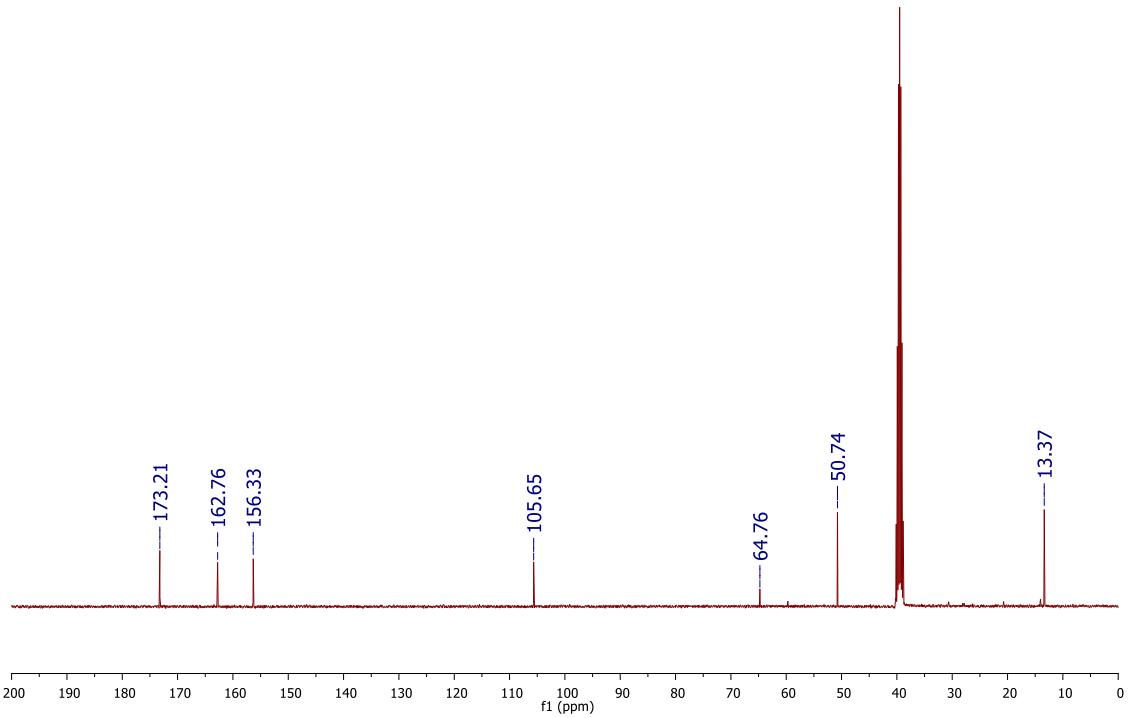
Ethyl 4-oxo-6-propyl-5-azaspiro[2.4]hept-6-ene-7-carboxylate (10e). The compound was obtained as white solid (60.4 mg, 54%); mp: 70–72 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.00 (t, *J*=7.6 Hz, 3H, $CH_2CH_2CH_3$), 1.28 (t, *J*=7.2 Hz, 3H, OCH_2CH_3), 1.42–1.45 (m, 2H, CH_2CH_2), 1.66 (sex, *J*=7.6 Hz, 2H, $CH_2CH_2CH_3$), 1.90–1.93 (m, 2H, CH_2CH_2), 2.85 (t, *J*=7.6 Hz, 2H, $CH_2CH_2CH_3$), 4.16 (q, *J*=7.2 Hz, 2H, OCH_2CH_3), 9.13 (s, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.8 (q), 14.2 (q), 18.3 (t), 21.2 (t), 29.7 (s), 29.7 (t), 29.9 (t), 59.4 (t), 107.4 (s), 153.6 (s), 163.4 (s), 180.9 (s); IR (nujol): ν_{max} = 3160, 1688, 1634 cm^{-1}; MS *m/z* (ESI): 224.77 (M + H$^+$); anal. calcd. for $C_{12}H_{17}NO_3$ (223.27): C 64.55, H 7.67, N 6.27; found: C 64.68, H 7.69, N 6.21.

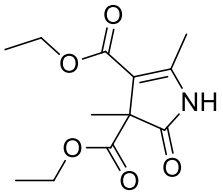
10. ^{1}H and ^{13}C spectra of 1*H*-pyrrol-2-ones 10a–e.



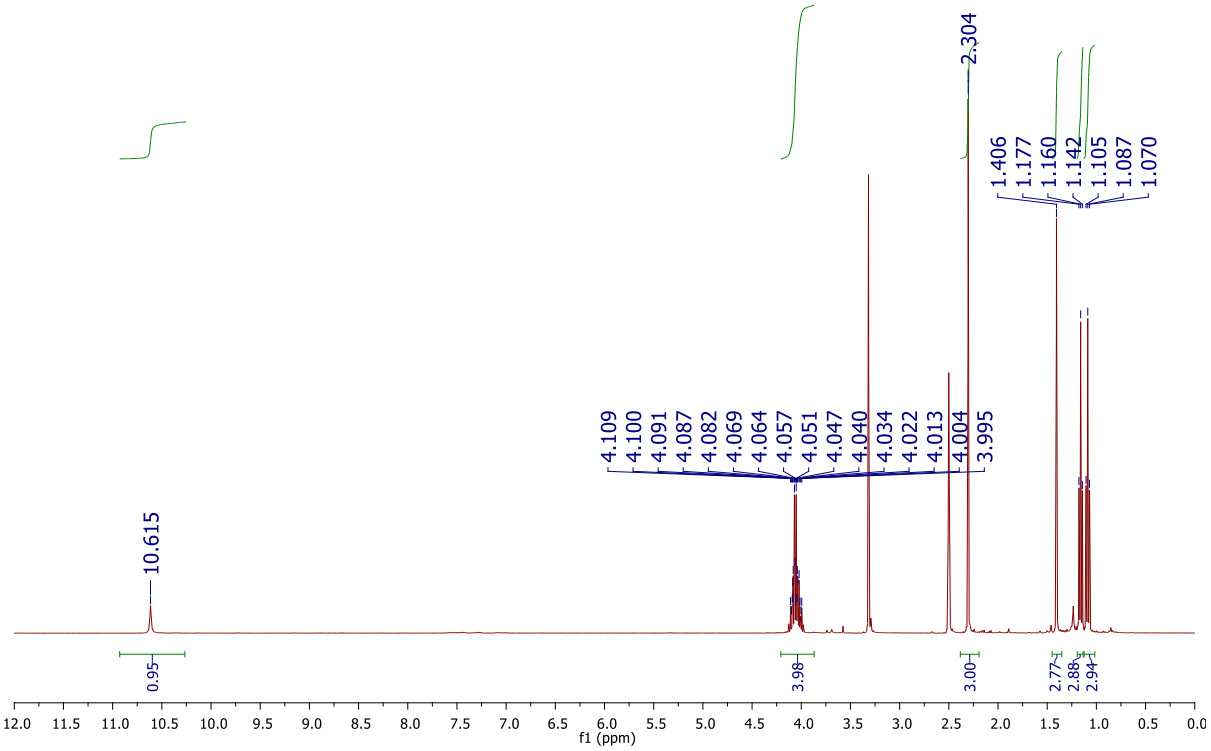
Dimethyl 3,8-dimethyl-1,6-dioxo-2,7-diazaspiro[4.4]nona-3,8-diene-4,9-dicarboxylate (10a).

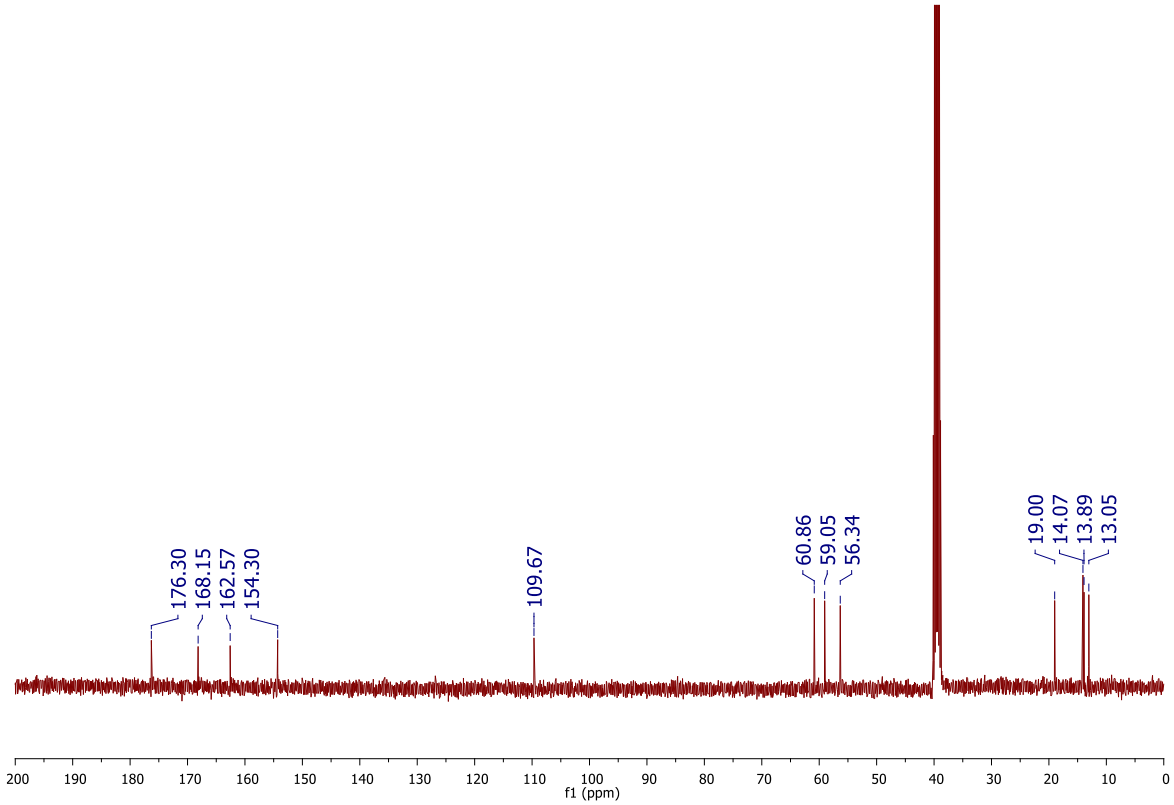


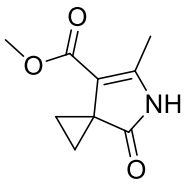




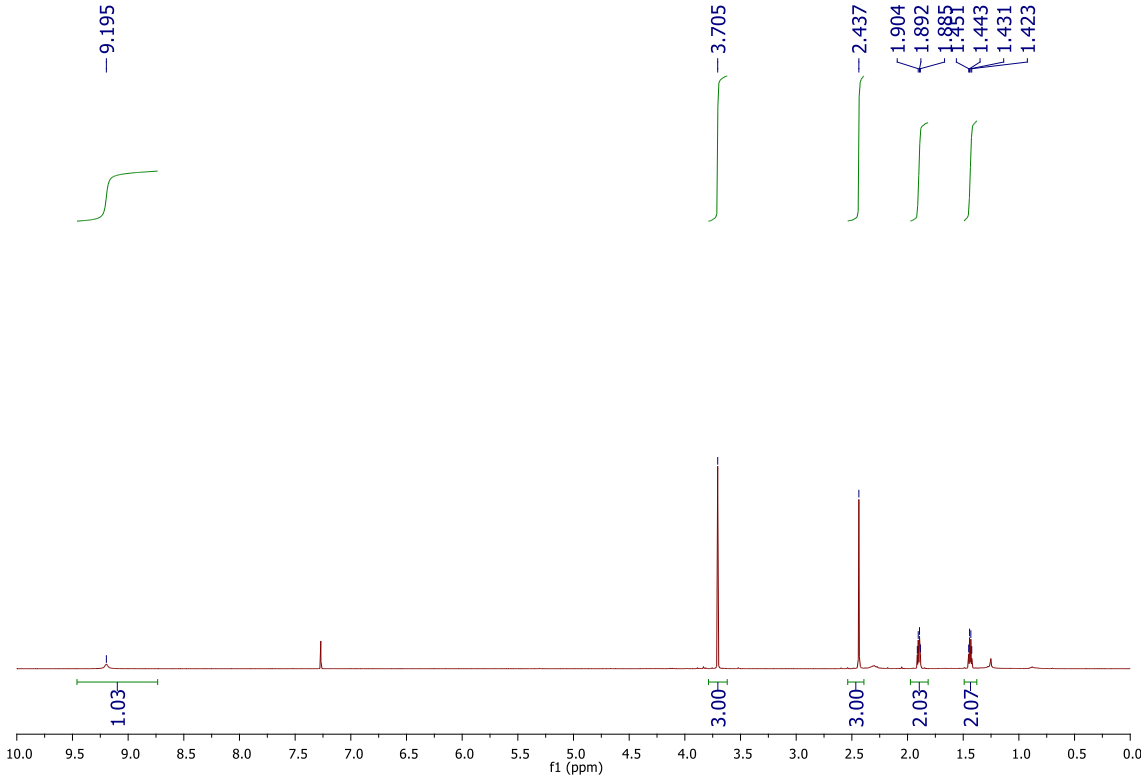
Diethyl 3,5-dimethyl-2-oxo-2,3-dihydro-1*H*-pyrrole-3,4-dicarboxylate (10b).

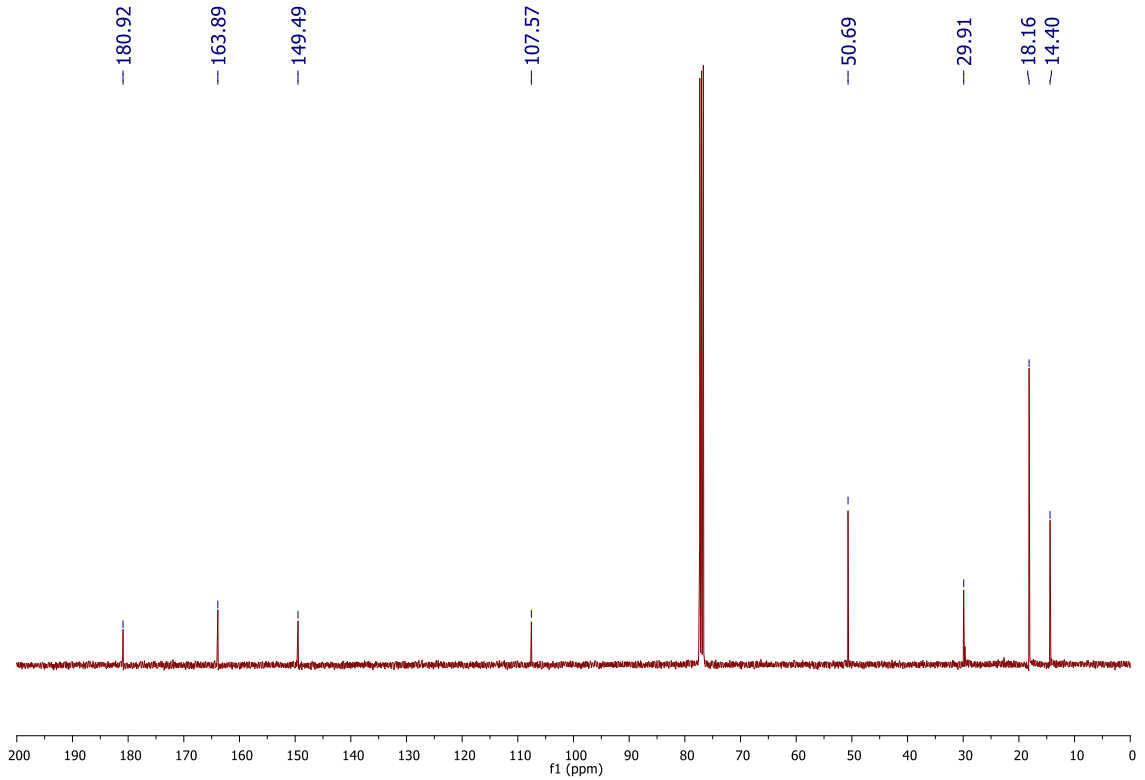


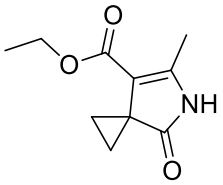




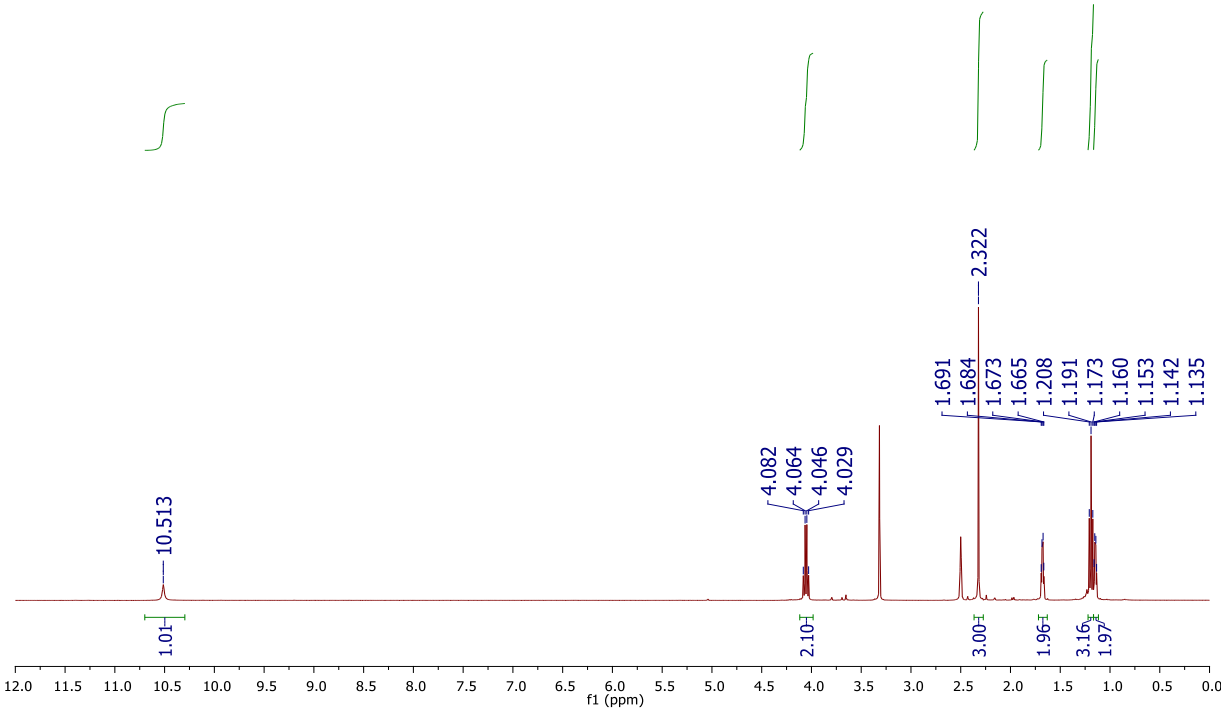
Methyl 6-methyl-4-oxo-5-azaspiro[2.4]hept-6-ene-7-carboxylate (10c).

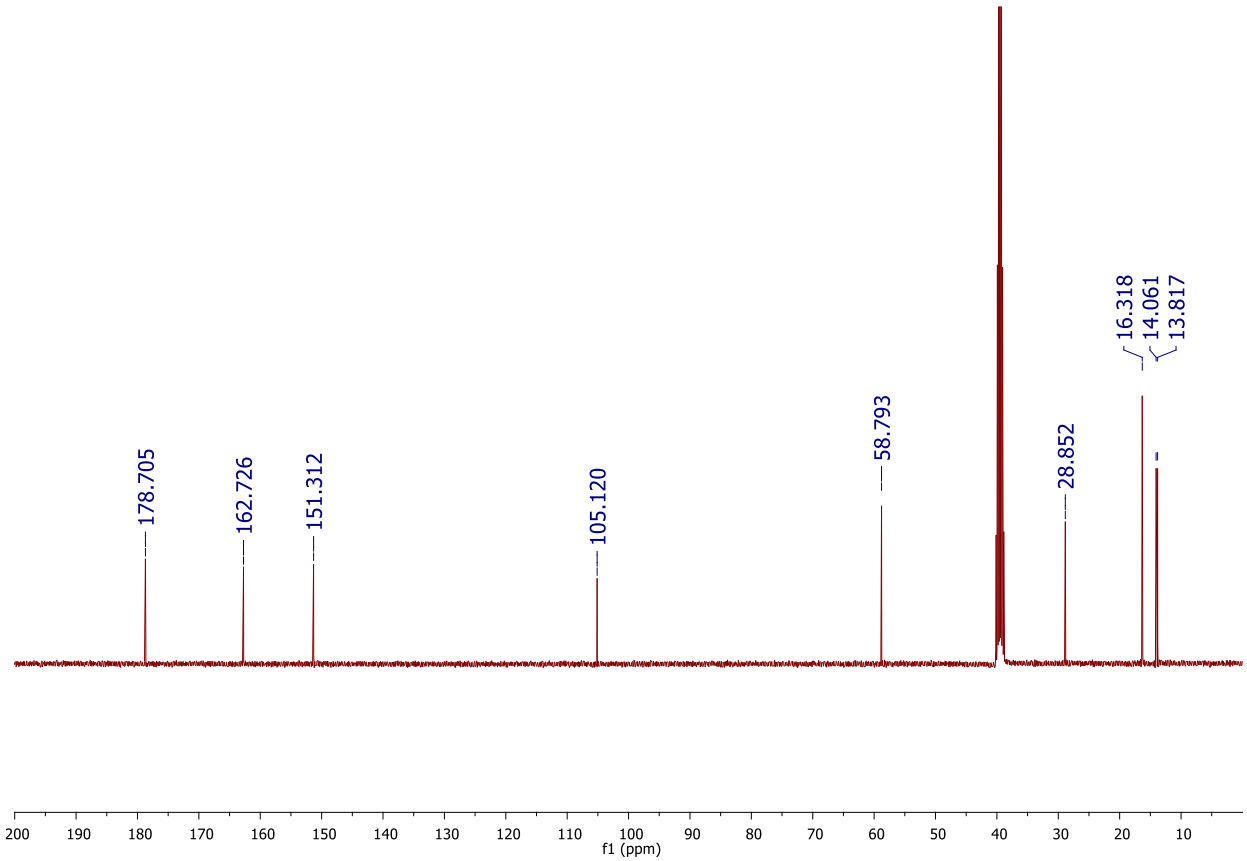


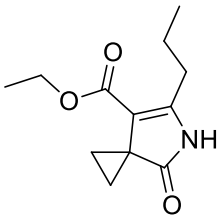




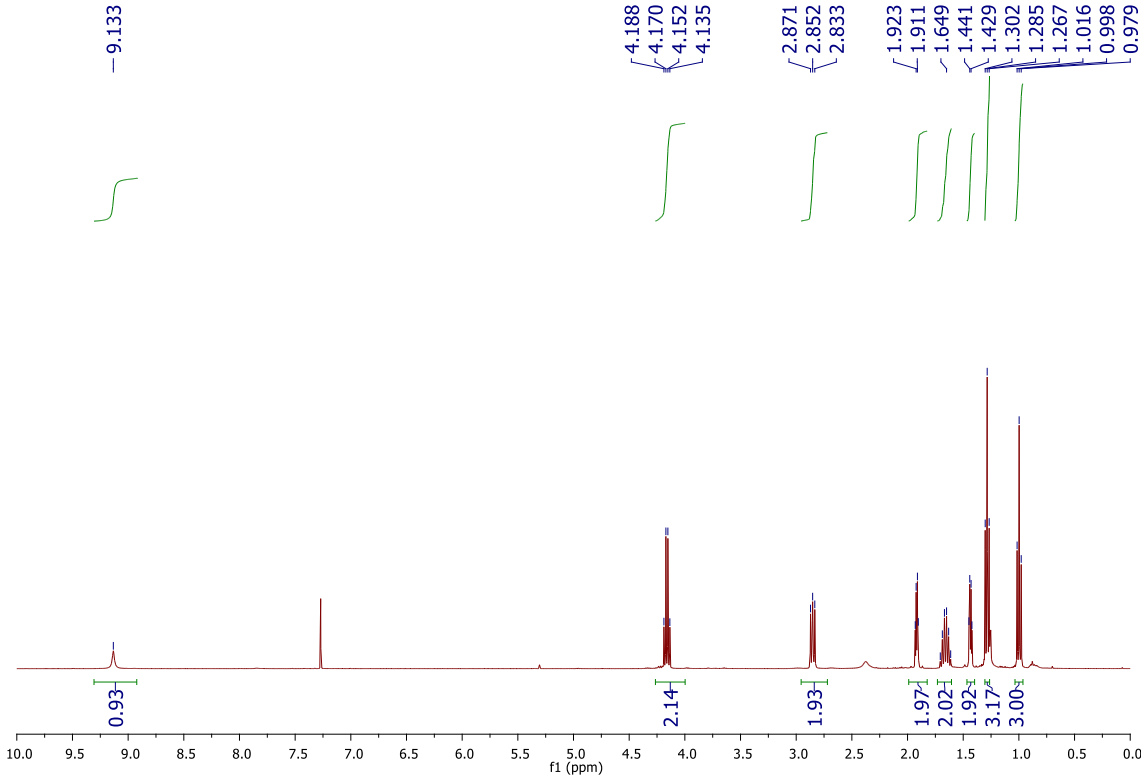
Ethyl 6-methyl-4-oxo-5-azaspiro[2.4]hept-6-ene-7-carboxylate (10d).

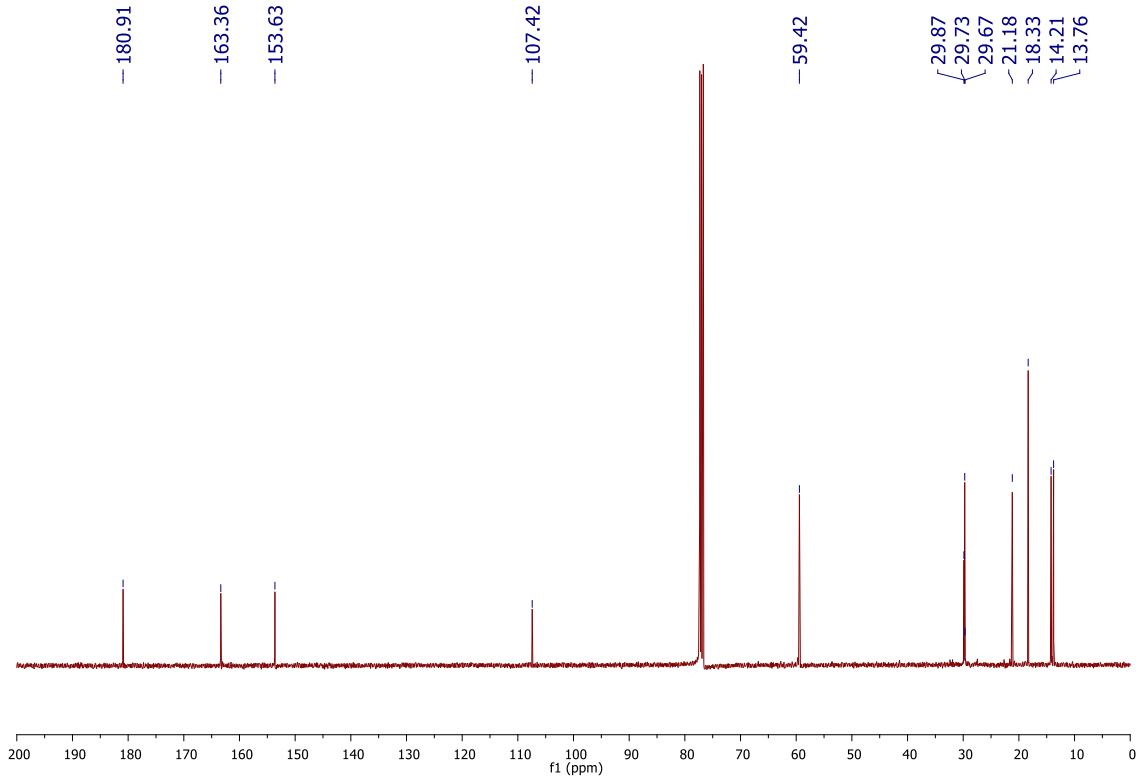






Ethyl 4-oxo-6-propyl-5-azaspiro[2.4]hept-6-ene-7-carboxylate (10e).





11. General procedure for the synthesis of 1*H*-imidazoles 12a–c by basic treatment of 1-amino-1*H*-imidazoles 11a–c and DD 2a. To a magnetically stirred solution of 1-amino-1*H*-imidazoles **11a–c** (0.5 mmol) in MeCN (10 mL), the DD **2a** (1.0 mmol) and K_2CO_3 (1.5 mmol) were added and then the reaction mixture was refluxed for 1 hour, until the TLC analysis revealed the disappearance of the starting reagent **11** and the formation of 1*H*-imidazoles **12a–c**. After the filtration of K_2CO_3, the solvent was removed in vacuo; the so-formed products **12** were purified by silica gel column chromatography using cyclohexane/ethyl acetate mixtures as eluent and then were crystallized from ethyl acetate/petroleum ether.

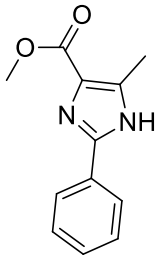
12. Spectral data of 1*H*-imidazoles 12a–c.

Methyl 5-methyl-2-phenyl-1*H*-imidazole-4-carboxylate (12a). The compound was obtained as white solid (103.6 mg, 96%); mp: 154–156 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.55 (s, 3H, *CH*$_3$), 3.84 (s, 3H, O*CH*$_3$), 7.34–7.36 (m, 3H$_{ar}$), 7.41 (brs, 1H, *NH*), 7.90-7.92 (m, 2H$_{ar}$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.9 (q), 51.6 (q), 123.2 (s), 125.9 (d), 128.6 (s), 128.9 (d), 129.7 (d), 142.1 (s), 146.7 (s), 162.6 (s); IR (nujol): ν_{max} = 3313, 1693, 1653 cm^{-1}; MS *m/z* (ESI): 217.38 (M + H$^+$); anal. calcd. for $C_{12}H_{12}N_2O_2$ (216.24): C 66.65, H 5.59, N 12.96; found: C 66.73, H 5.64, N 12.89.

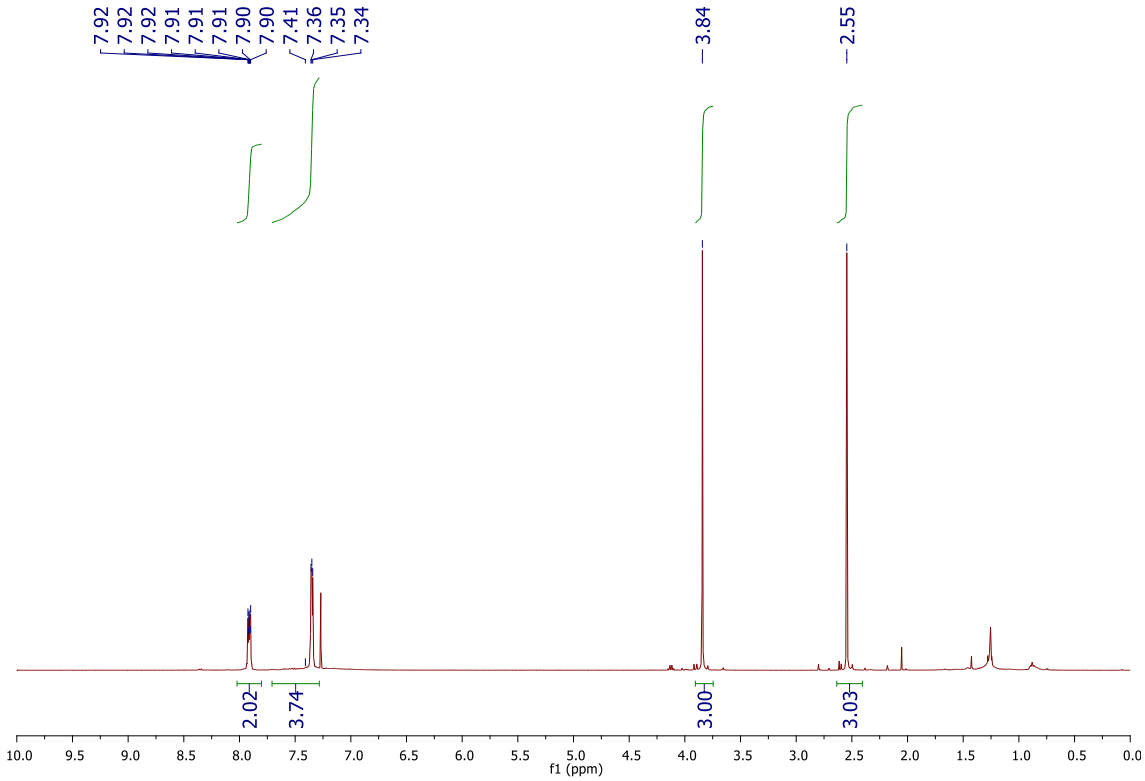
Ethyl 5-methyl-2-phenyl-1*H*-imidazole-4-carboxylate (12b). The compound was obtained as white solid (96.6 mg, 84%); mp: 183–185 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.31 (t, *J*=7.2 Hz, 3H, OCH$_2$*CH*$_3$), 2.55 (s, 3H, *CH*$_3$), 4.33 (q, *J*=7.2 Hz, 2H, O*CH*$_2$CH$_3$), 7.34–7.36 (m, 3H$_{ar}$), 7.90–7.93 (m, 2H$_{ar}$), 9.48 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.7 (q), 14.3 (q), 60.8 (t), 122.8 (s), 126.2 (d), 127.8 (s), 128.9 (d), 130.0 (d), 141.7 (s), 146.4 (s), 161.6 (s); IR (nujol): ν_{max} = 3328, 1729, 1644 cm^{-1}; MS *m/z* (ESI): 231.44 (M + H$^+$); anal. calcd. for $C_{13}H_{14}N_2O_2$ (230.26): C 67.81, H 6.13, N 12.17; found: C 67.67, H 6.16, N 12.08.

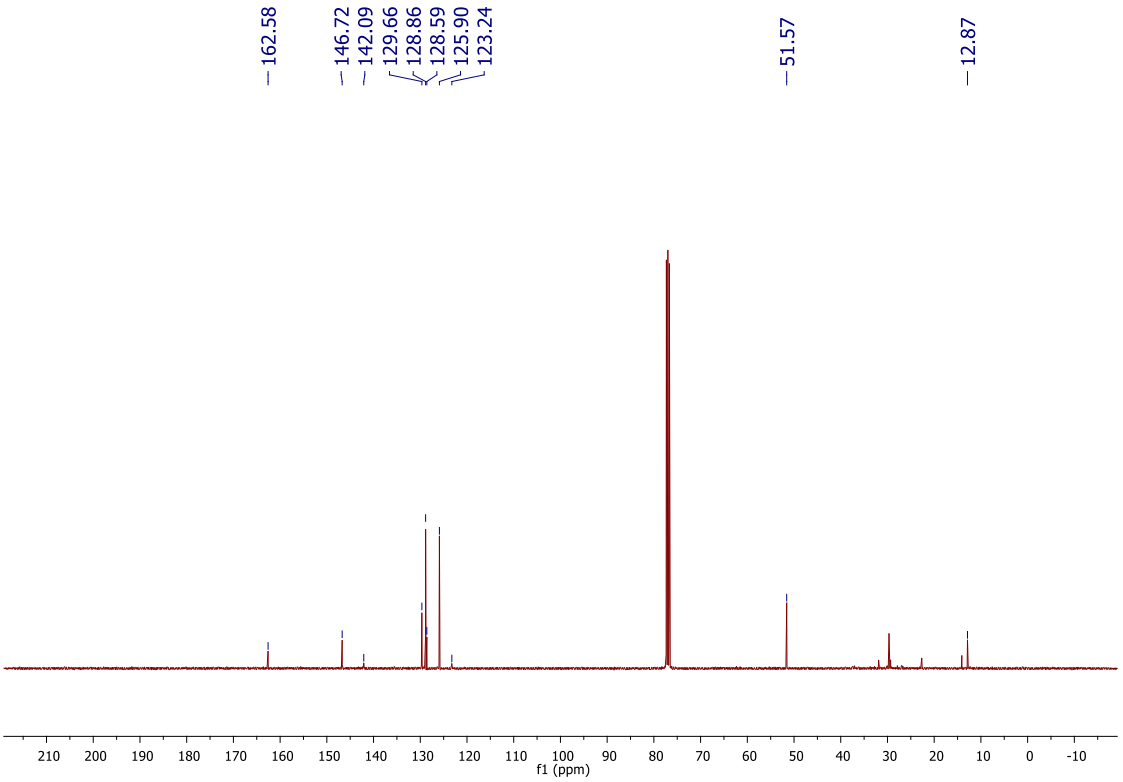
Methyl 5-ethyl-2-phenyl-1*H*-imidazole-4-carboxylate (12c). The compound was obtained as white solid (112.6 mg, 98%); mp: 172–174 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.31 (t, *J*=7.6 Hz, 3H, CH$_2$*CH*$_3$), 3.03 (q, *J*=7.6 Hz, 2H, *CH*$_2$CH$_3$), 3.88 (s, 3H, O*CH*$_3$), 4.64 (brs, 1H, *NH*), 7.37–7.39 (m, 2H$_{ar}$), 7.97–7.99 (m, 3H$_{ar}$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.9 (q), 20.1 (t), 51.8 (q), 126.4 (d), 128.7 (s), 129.0 (d), 130.4 (d), 146.2 (s), 147.2 (s), 160.2 (s), 161.5 (s); IR (nujol): ν_{max} = 3314, 1739, 1634 cm^{-1}; MS *m/z* (ESI): 231.08 (M + H$^+$); anal. calcd. for $C_{13}H_{14}N_2O_4$ (230.26): C 67.81, H 6.13, N 12.17; found: C 67.73, H 6.09, N 12.24.

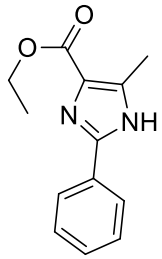
13. ^{1}H and ^{13}C spectra of 1*H*-imidazoles 12a–c.



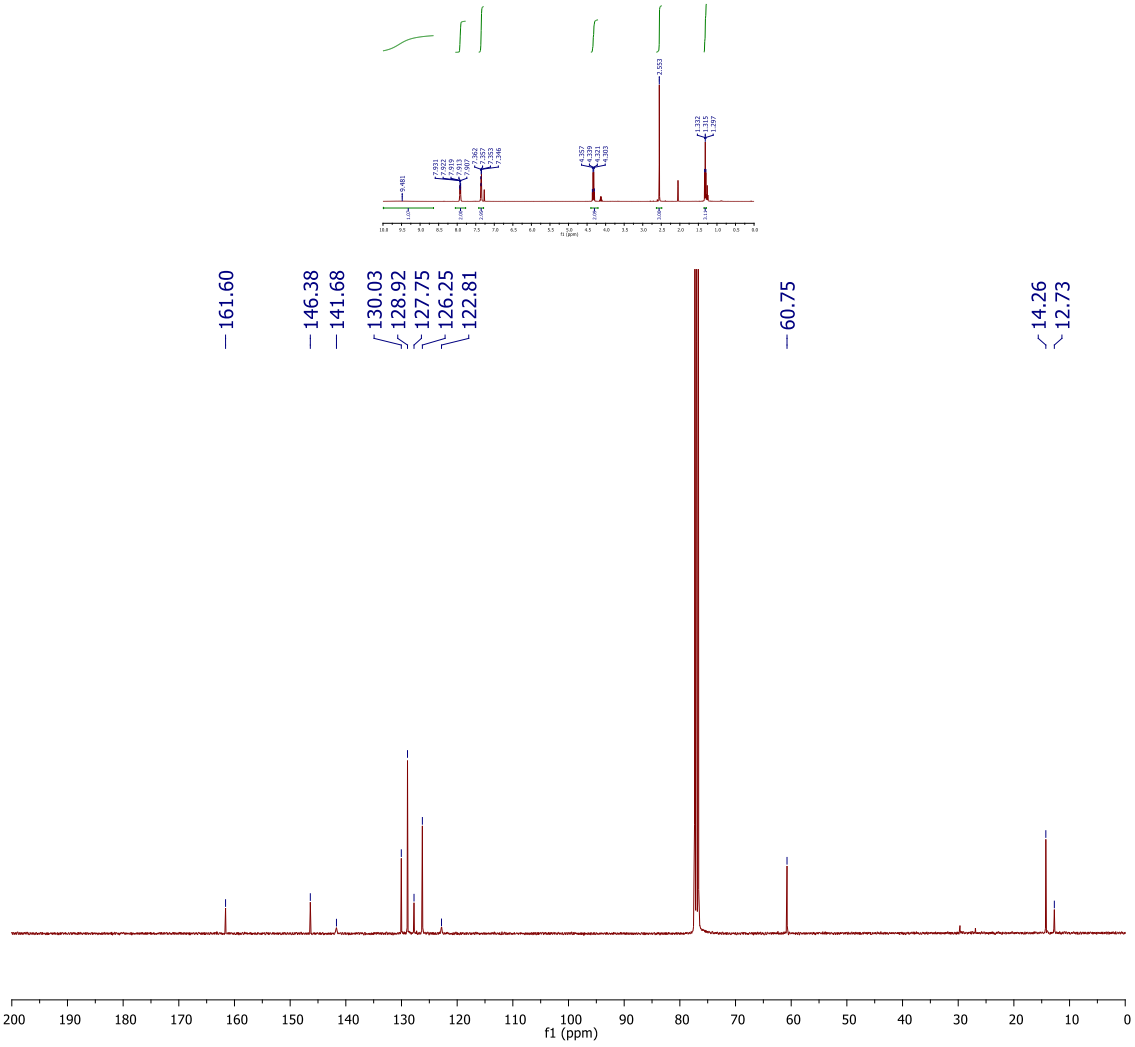
Methyl 5-methyl-2-phenyl-1*H*-imidazole-4-carboxylate (12a).

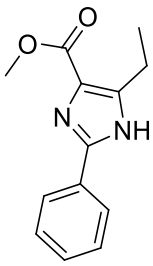




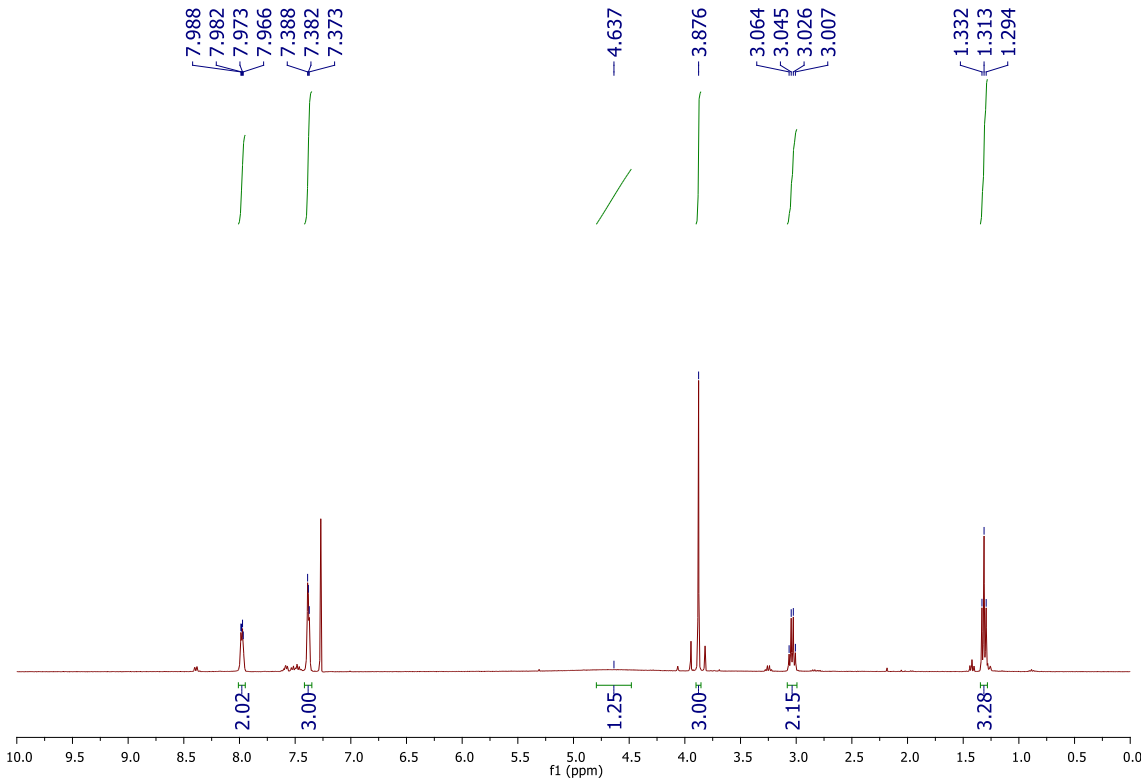


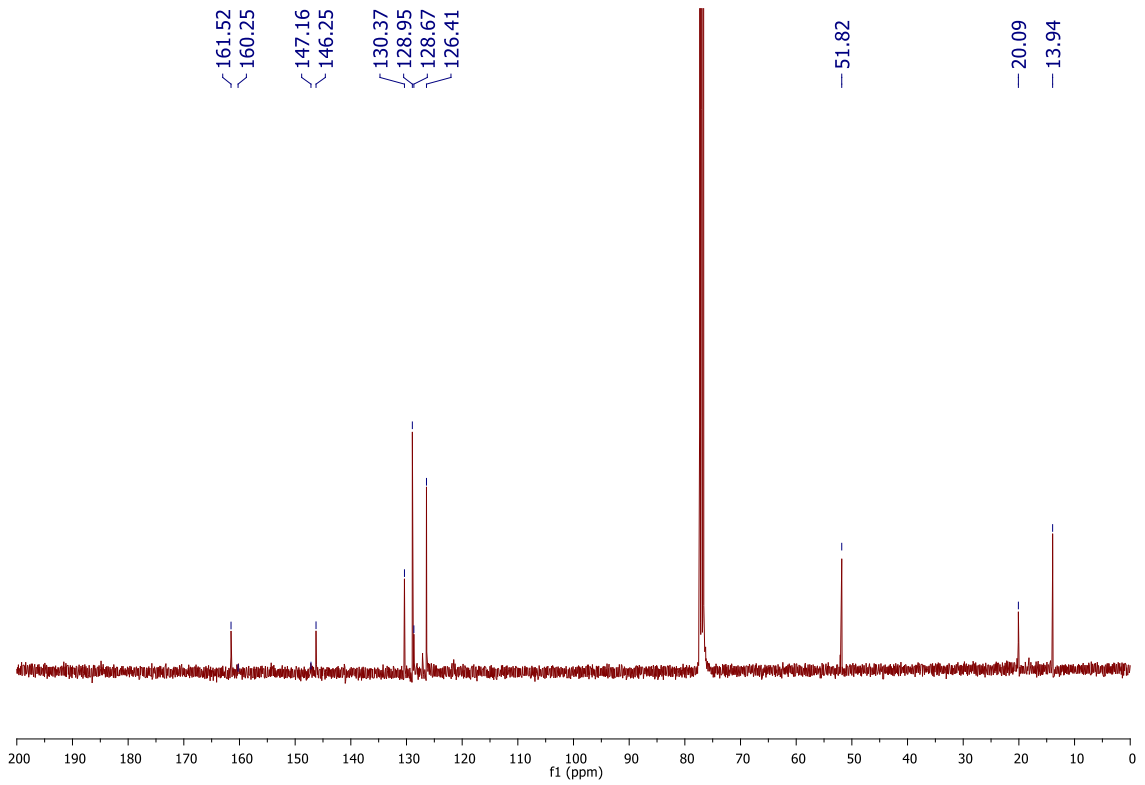
Ethyl 5-methyl-2-phenyl-1*H*-imidazole-4-carboxylate (12b).





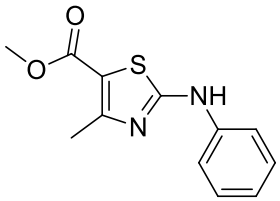
Methyl 5-ethyl-2-phenyl-1*H*-imidazole-4-carboxylate (12c).



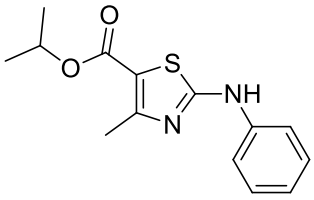


14. General procedure for the synthesis of thiazoles 14a–d by basic treatment of 3-amino-2,3-dihydrothiazoles 13a–d and DD 2a. To a magnetically stirred solution of 3-amino-2,3-dihydrothiazoles **13a–d** (0.5 mmol) in MeCN (10 mL), DD **2a** (1.0 mmol) and K_2CO_3 (1.5 mmol) were added and then the reaction mixture was refluxed for 1 hour, until the TLC analysis revealed the disappearance of the starting reagent **13** and the formation of thiazoles **14a–d**. After the filtration of K_2CO_3, the solvent was removed in vacuo; the so-formed products **14** were purified by silica gel column chromatography using cyclohexane/ethyl acetate mixtures as eluent and then were crystallized from ethyl acetate/petroleum ether.

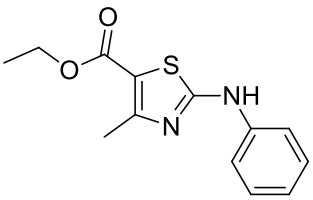
15. Spectral data of thiazoles 14a–d.



Methyl 4-methyl-2-(phenylamino)thiazole-5-carboxylate (14a).[6] The compound was obtained as white solid (101.6 mg, 82%); mp: 96–98 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.52 (s, 3H, *CH*$_3$), 3.73 (s, 3H, O*CH*$_3$), 7.03 (t, *J*=7.2 Hz, 1H$_{ar}$), 7.34 (t, *J*=8.0 Hz, 2H$_{ar}$), 7.60 (d, *J*=8.0 Hz, 2H$_{ar}$), 10.68 (s, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 17.2 (q), 51.1 (q), 108.4 (s), 118.0 (d), 122.5 (d), 129.0 (d), 140.0 (s), 158.8 (s), 162.2 (s), 165.0 (s); IR (nujol): ν_{max} = 3232, 1653, 1634 cm^{-1}; MS *m/z* (ESI): 249.03 (M + H$^+$); anal. calcd. for $C_{12}H_{12}N_2O_2S$ (248.30): C 58.05, H 4.87, N 11.28; found: C 57.91, H 4.91, N 11.35.

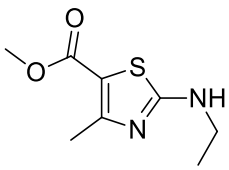


Methyl 4-methyl-2-(phenylamino)thiazole-5-carboxylate (14b). The compound was obtained as white solid (109.2 mg, 79%); mp: 101–103 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ =1.31 (d, *J*=6.4 Hz, 6H, OCH(*CH*$_3$)$_2$), 2.53 (s, 3H, *CH*$_3$), 5.15 (ep, *J*=6.4 Hz, 1H, OC*H*(*C*H$_3$)$_2$), 7.18 (t, *J*=7.2 Hz, 1H$_{ar}$), 7.34–7.43 (m, 4H$_{ar}$), 8.29 (brs, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 17.2 (q), 22.0 (q), 68.2 (d), 110.1 (s), 120.3 (d), 124.8 (d), 129.7 (d), 139.2 (s), 157.6 (s), 162.0 (s), 167.8 (s); IR (nujol): ν_{max} = 3175, 1657, 1634 cm^{-1}; MS *m/z* (ESI): 277.41 (M + H$^+$); anal. calcd. for $C_{14}H_{16}N_2O_2S$ (276.35): C 60.85, H 5.84, N 11.58; found: C 60.94, H 5.80, N 11.63.



Ethyl 4-methyl-2-(phenylamino)thiazole-5-carboxylate (14c).[7] The compound was obtained as white solid (85.3 mg, 65%); mp: 134–136 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.34 (t, *J*=7.2 Hz, 3H, OCH$_2$*CH*$_3$), 2.56 (s, 3H, *CH*$_3$), 4.28 (q, *J*=7.2 Hz, 2H, O*CH*$_2$CH$_3$), 6.96 (brs, 1H, *NH*), 7.17–7.21 (m, 1H$_{ar}$), 7.33–7.36 (m, 2H$_{ar}$), 7.39–7.43 (m, 2H$_{ar}$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.4 (q), 17.2 (q), 60.7 (t), 109.6 (s), 120.2 (d), 124.8 (d), 129.7 (d), 139.1 (s), 158.0 (s), 162.4 (s), 167.8 (s); IR (nujol): ν_{max} = 3200, 3166, 1698 cm^{-1}; MS *m/z* (ESI):

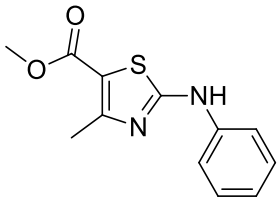
263.21 (M + H^+); anal. calcd. for $C_{13}H_{14}N_2O_2S$ (262.33): C 59.52, H 5.38, N 10.68; found: C 59.38, H 5.41, N 10.59.

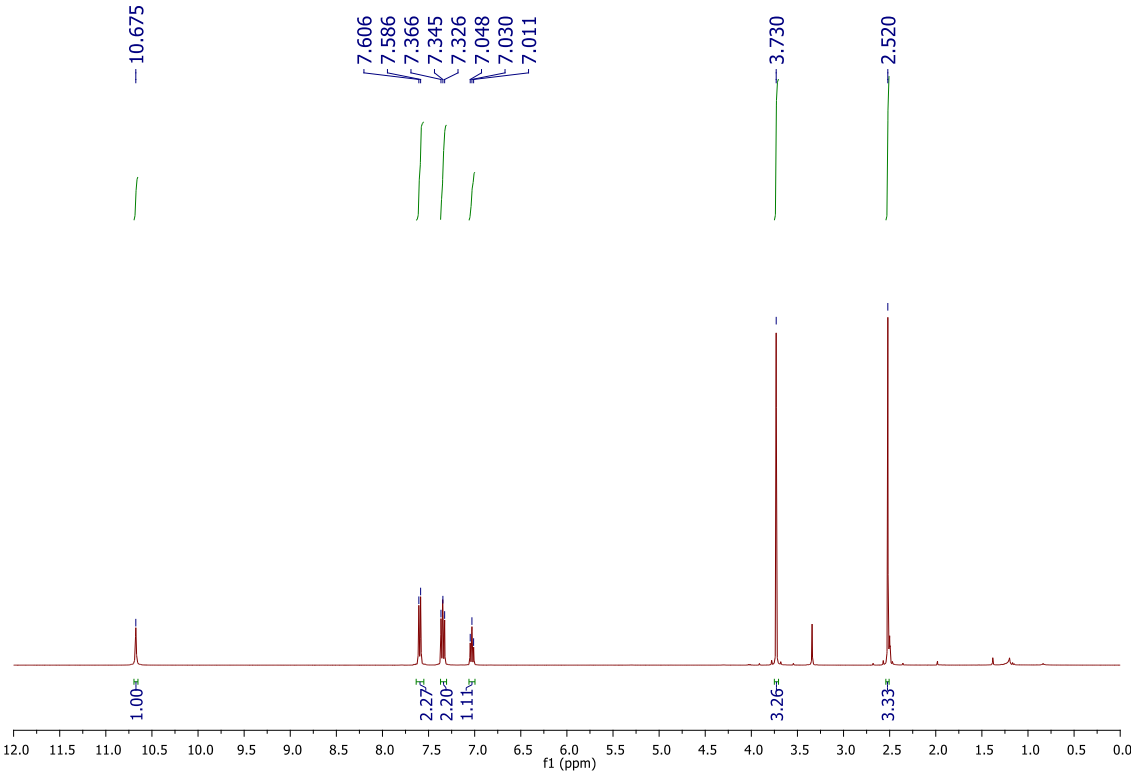


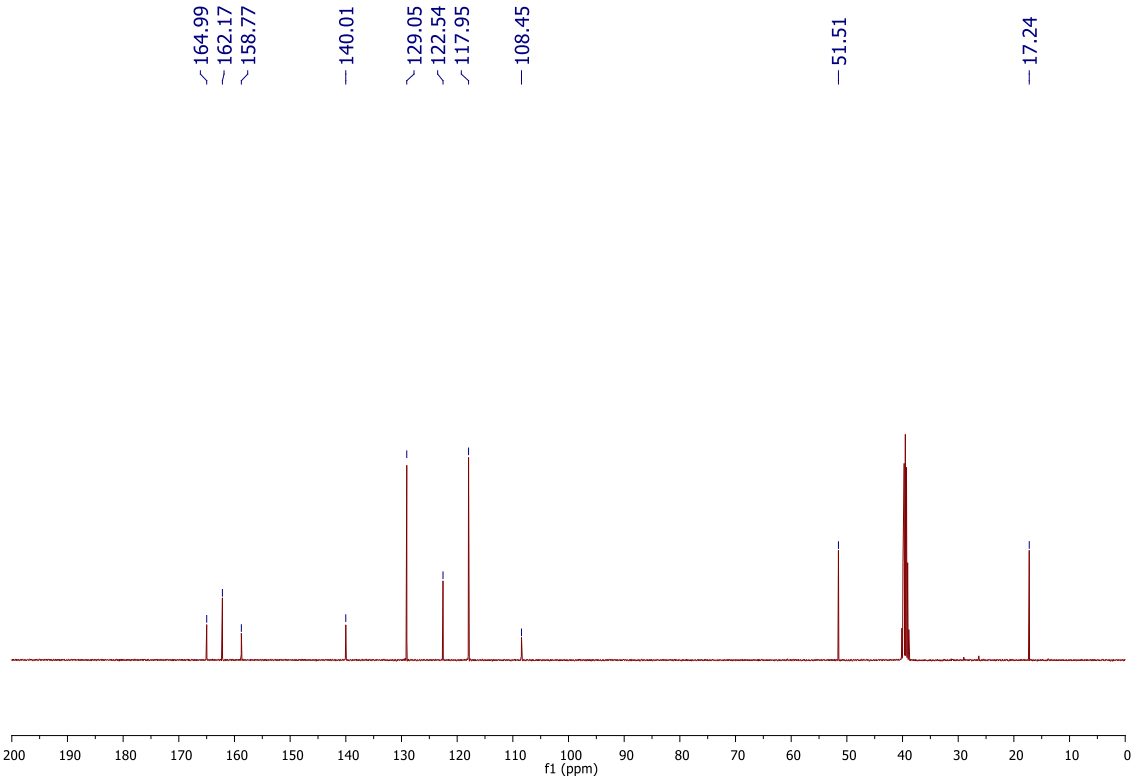
Methyl 2-(ethylamino)-4-methylthiazole-5-carboxylate (14d). The compound was obtained as white solid (51.2 mg, 51%); mp: 105–107 °C; ^{1}H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 1.14 (t, *J*=7.2 Hz, 3H, OCH_2CH_3), 2.40 (s, 3H, CH_3), 3.23 (dq, *J*=7.2 Hz, *J*=5.2 Hz, 2H, CH_2), 3.68 (s, 3H, OCH_3), 8.32 (t, *J*=5.2 Hz, 1H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.0 (q), 17.2 (q), 40.0 (t), 51.2 (q), 106.3 (s), 159.8 (s), 162.3 (s), 169.7 (s); IR (nujol): ν_{max} = 3221, 1709, 1639 cm^{-1}; MS *m/z* (ESI): 201.27 (M + H^+); anal. calcd. for $C_8H_{12}N_2O_2S$ (200.06): C 47.98, H 6.04, N 13.99; found: C 48.06, H 5.98, N 13.92.

16. ^{1}H and ^{13}C spectra of thiazoles 14a–d.

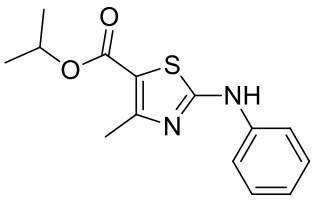
Methyl 4-methyl-2-(phenylamino)thiazole-5-carboxylate (14a).[6]

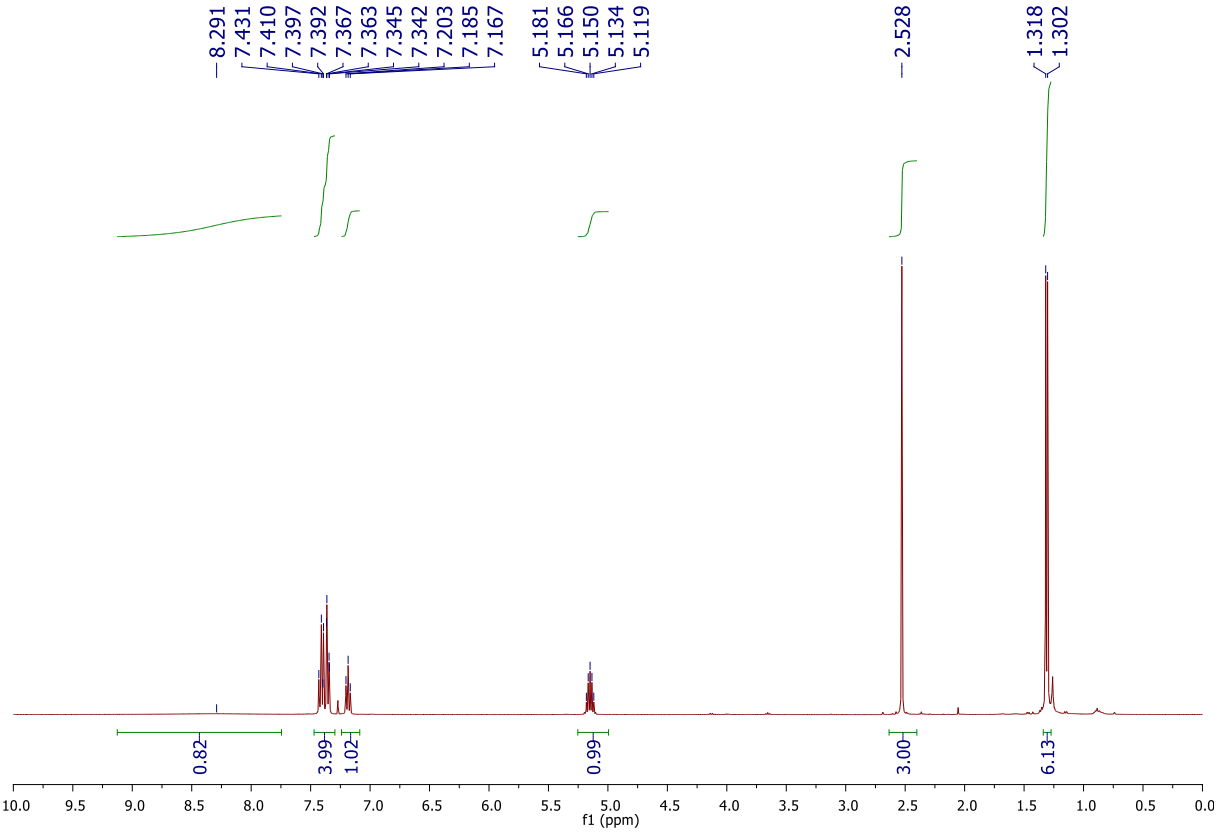


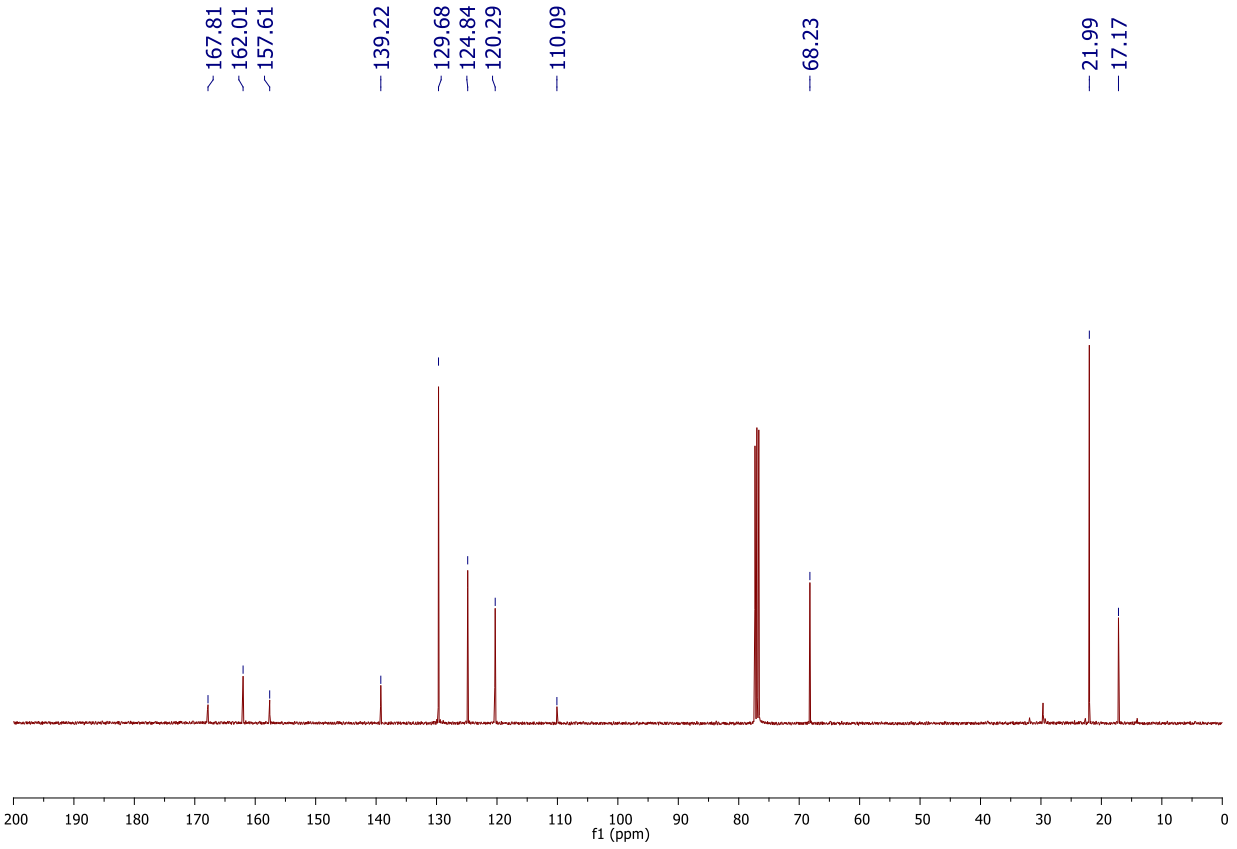




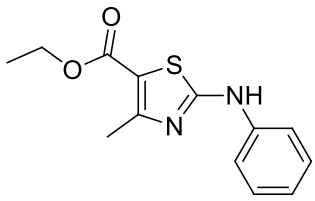
Methyl 4-methyl-2-(phenylamino)thiazole-5-carboxylate (14b).

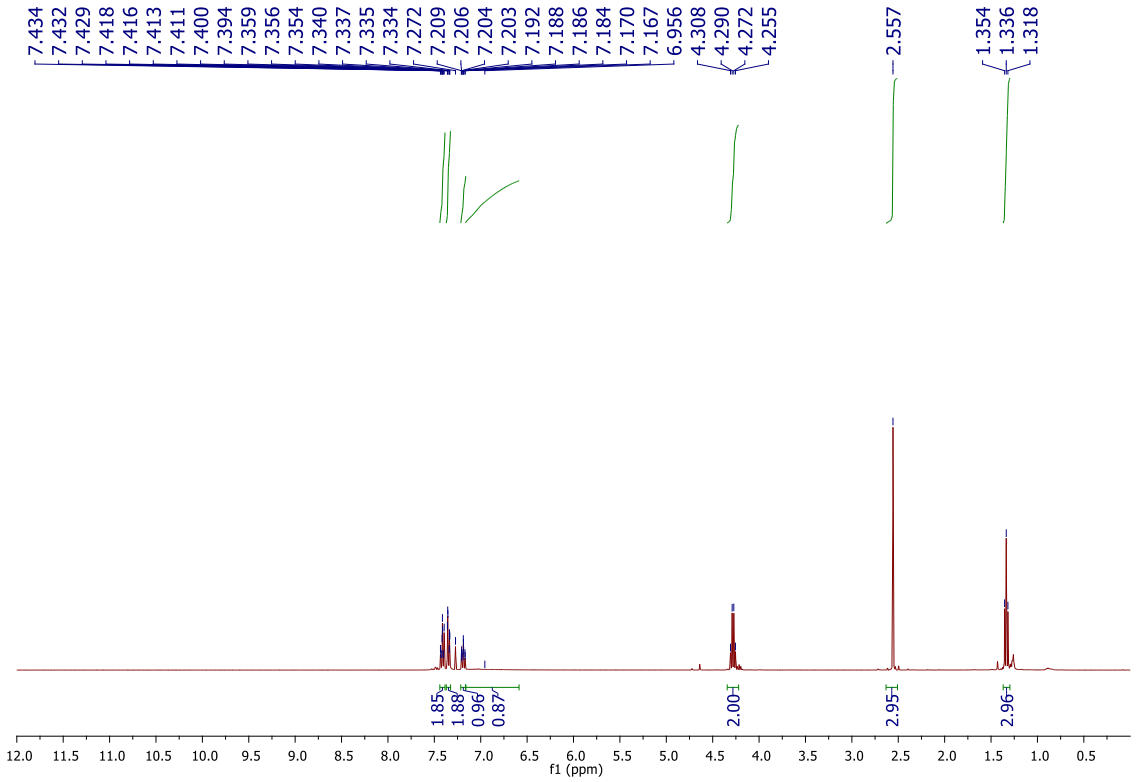


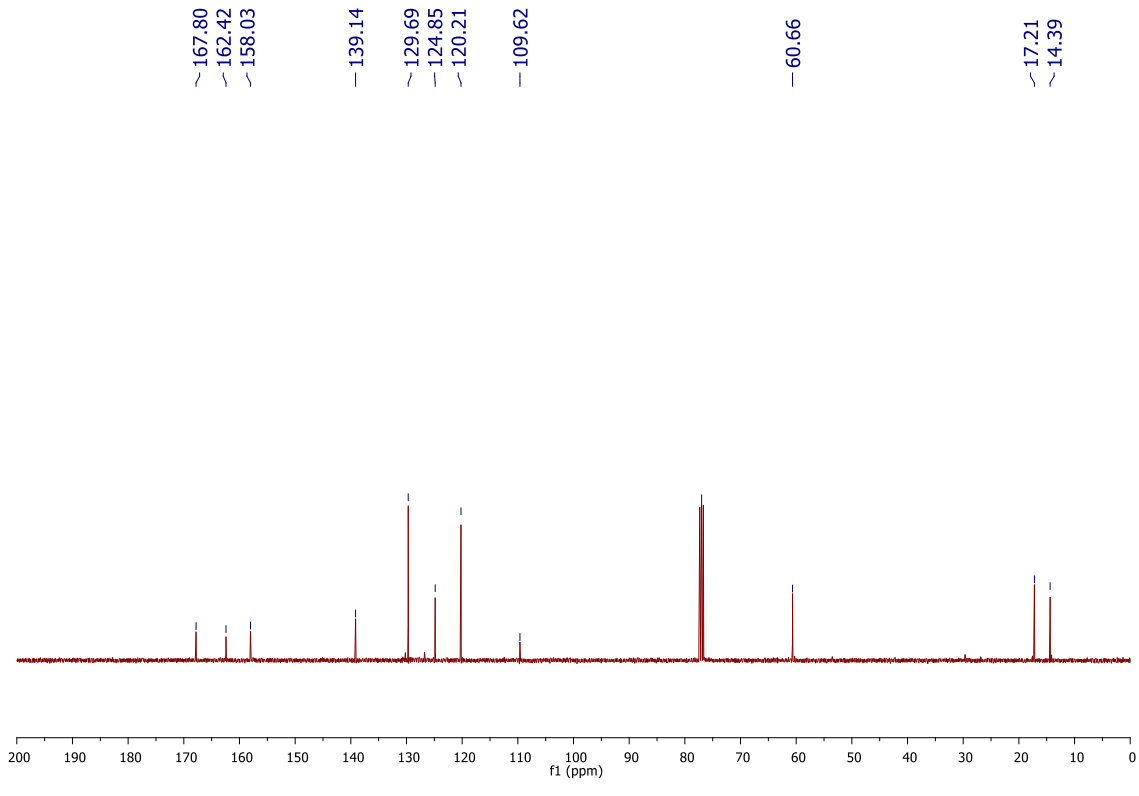




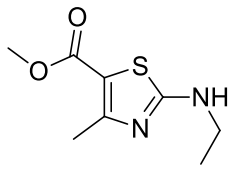
Ethyl 4-methyl-2-(phenylamino)thiazole-5-carboxylate (14c).[7]

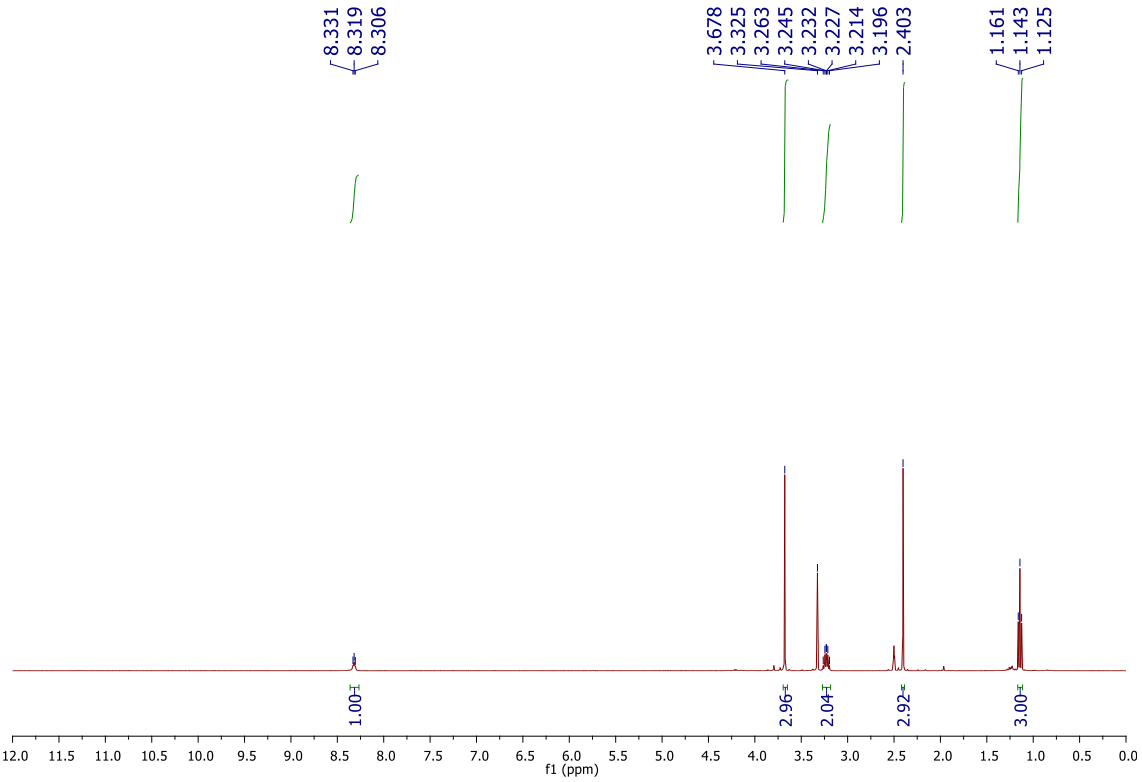


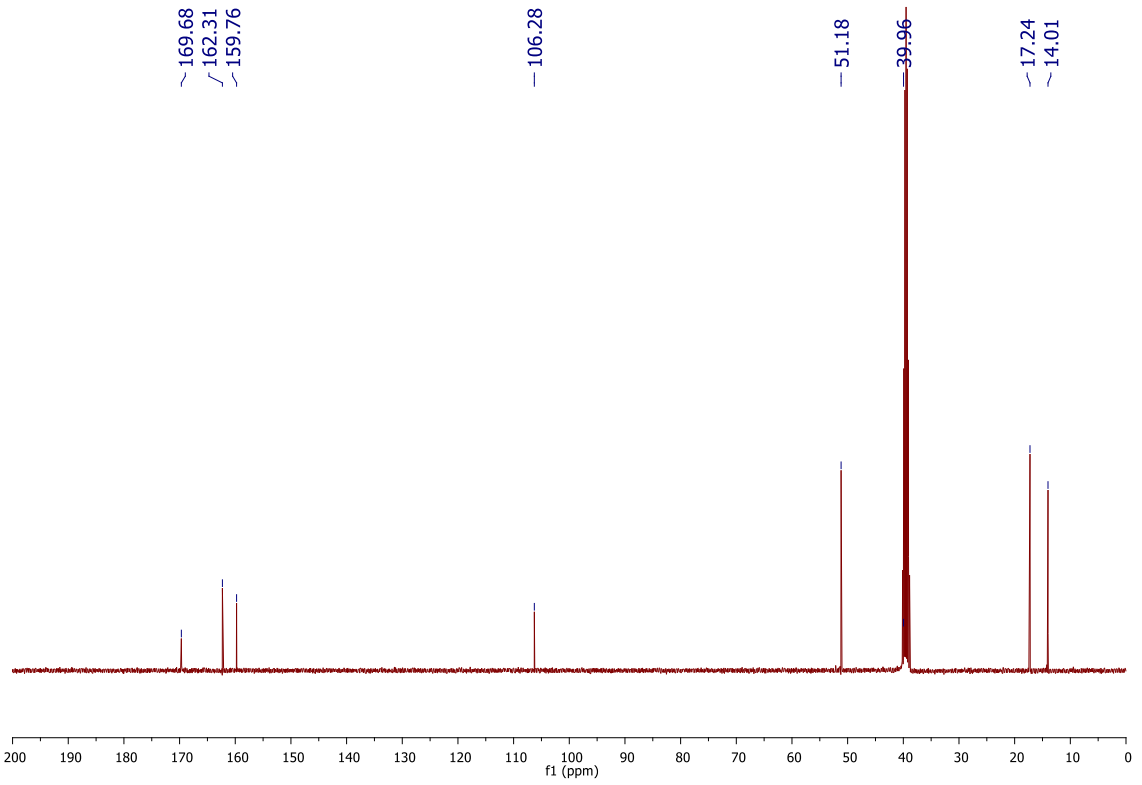




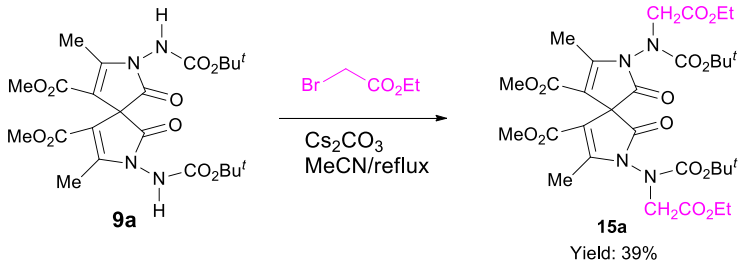
Methyl 2-(ethylamino)-4-methylthiazole-5-carboxylate (14d).





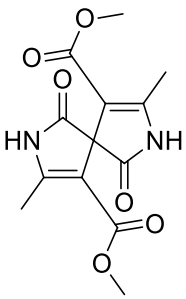


17. Synthesis of *N*-dialkylated 1-amino-1*H*-bis-pyrrol-2-one 15a by treatment of 1-amino-1*H*-bis-pyrrole 9a under Magnus' conditions (see Section 2)



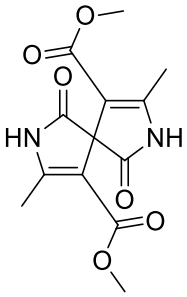
Scheme 1: Synthesis of *N*-dialkylated 1-amino-1*H*-bis-pyrrol-2-one **15a** by treatment of 1-amino-1*H*-bis-pyrrole **9a** under Magnus' conditions.

18. Spectral data of *N*-dialkylated 1-amino-1*H*-bis-pyrrol-2-one 15a.

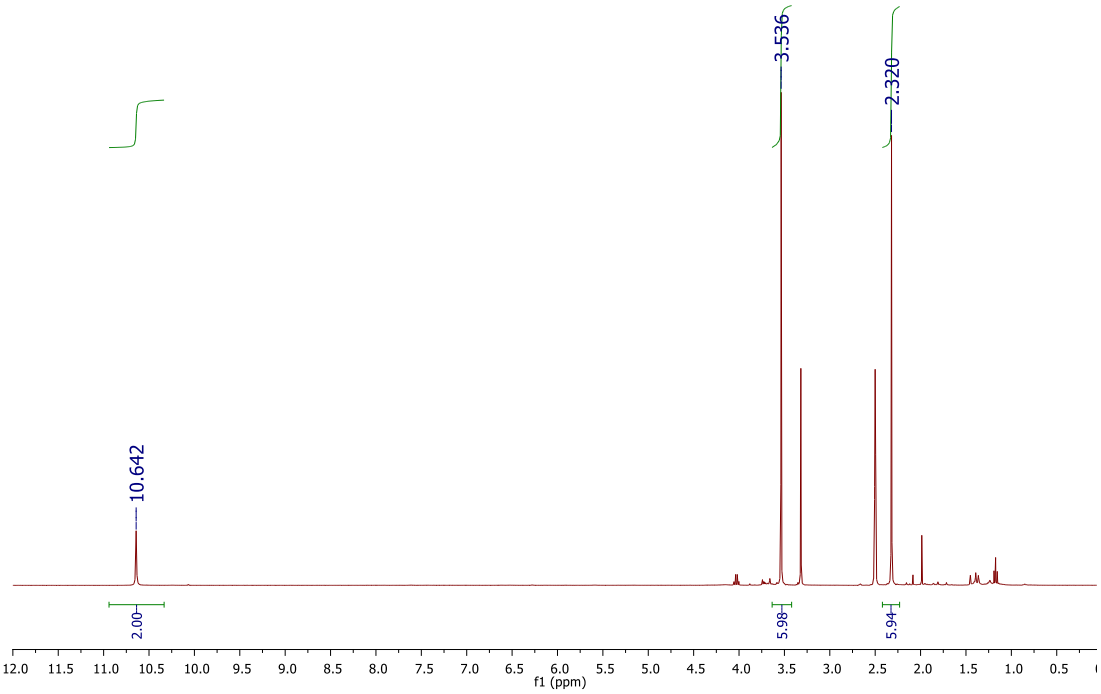


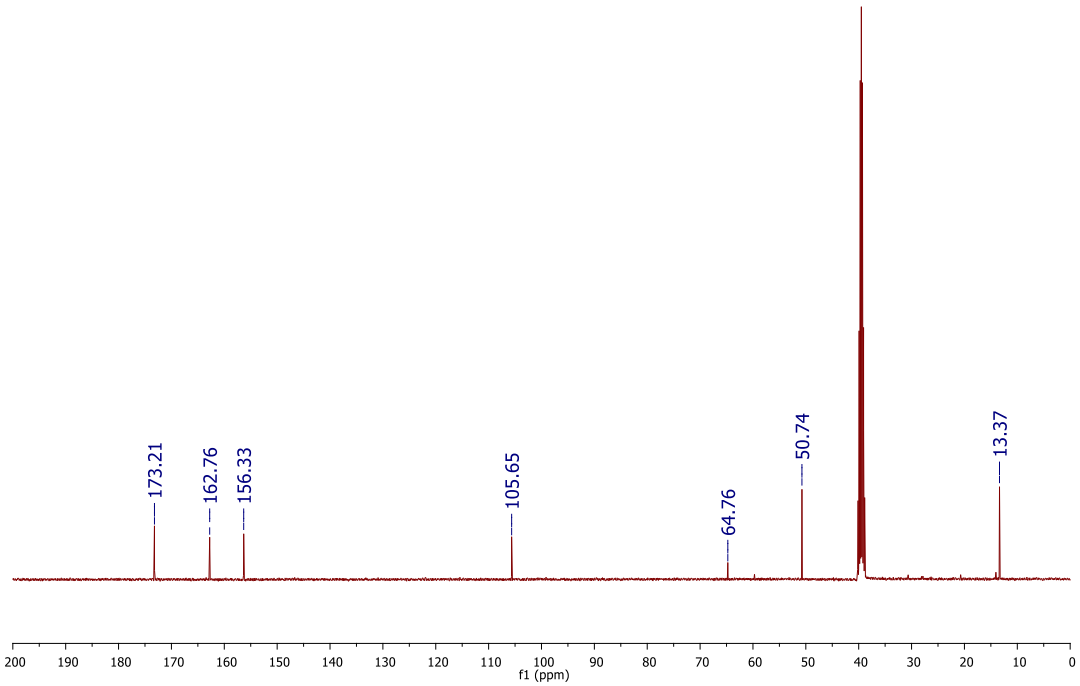
Dimethyl 3,8-dimethyl-1,6-dioxo-2,7-diazaspiro[4.4]nona-3,8-diene-4,9-dicarboxylate (15a). The compound was obtained as yellow solid (92.5 mg, 63%); mp: 140–142 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 2.32 (s, 6H, 2*CH*$_3$), 3.54 (s, 6H, 2O*CH*$_3$), 10.64 (s, 2H, *NH*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.4 (q), 50.7 (q), 64.8 (s), 105.6 (s), 156.3 (s), 162.8 (s), 173.2 (s); IR (nujol): ν_{max} = 3313, 3252, 1760, 1739, 1713, 1704 cm^{-1}; MS *m/z* (ESI): 295.11 (M + H$^+$); anal. calcd. for $C_{13}H_{14}N_2O_6$ (294.08): C 53.06, H 4.80, N 9.52; found: C 53.18, H 4.75, N 9.44.

19. ^{1}H and ^{13}C spectra of of *N*-dialkylated 1-amino-1*H*-bis-pyrrol-2-one 15a.

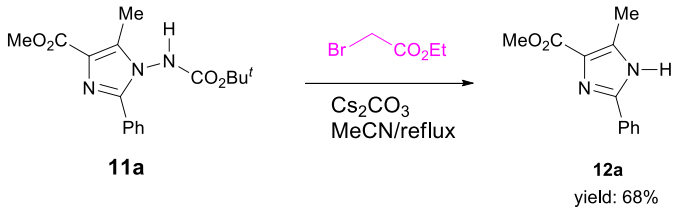


Dimethyl 3,8-dimethyl-1,6-dioxo-2,7-diazaspiro[4.4]nona-3,8-diene-4,9-dicarboxylate (15a).



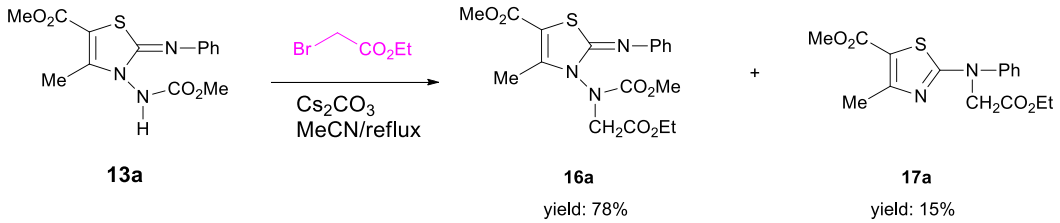


20. Synthesis of 1*H*-imidazole 12a, by treatment of 1-amino-1*H*-imidazole 11a under Magnus' conditions (see Section 2)



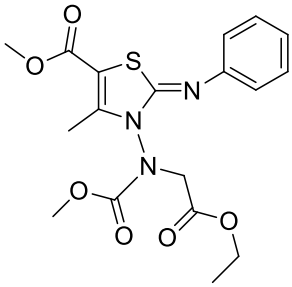
Scheme 2. Synthesis of 1*H*-imidazole **12a**, by treatment of 1-amino-1*H*-imidazole **11a** under Magnus' conditions.

21. Synthesis of *N*-alkylated 2,3-dihydrothiazole 16a and of *N*-alkylated 2-aminothiazole 17a, by treatment of 3-amino-2,3-dihydrothiazole 13a under Magnus' conditions.

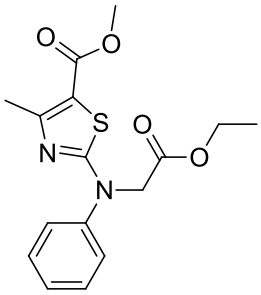


Scheme 3. Synthesis of *N*-alkylated 2,3-dihydrothiazole **16a** and of *N*-alkylated 2-aminothiazole **17a**, by treatment of 3-amino-2,3-dihydrothiazole **13a** under Magnus' conditions.

22. Spectral data of *N*-alkylated 2,3-dihydrothiazole 16a and of *N*-alkylated 2-aminothiazole 17a.

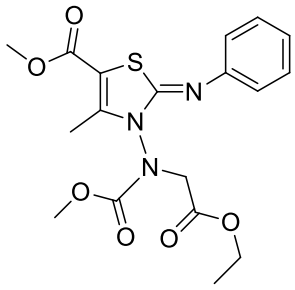


Methyl 3-((2-ethoxy-2-oxoethyl)(methoxycarbonyl)amino)-4-methyl-2-(phenylimino)-2,3-dihydrothiazole-5-carboxylate (16a). The compound was obtained as colorless oil (158.8 mg, 78%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.28–1.33 (m, 3H, $OCH_2\mathit{CH_3}$), 2.67 (s, 3H, $\mathit{CH_3}$), 3.77, 3.79, 3.80 and 3.88 (4brs, 6H, $2O\mathit{CH_3}$), 4.17–4.31 (m, 3H, $O\mathit{CH_2}CO$ and $O\mathit{CH_2}CH_3$), 4.89–5.05 (m, 1H, $O\mathit{CH_2}CO$), 7.02–7.11 (m, 3H_{ar}), 7.34 (t, *J*=8.0 Hz, 2H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.6 (q), 14.1 (q), 51.4 (q), 51.9 (q), 54.5 (t), 54.6 (t), 61.5 (t), 61.6 (t), 97.5 (s), 121.2 (d), 121.3 (d), 124.1 (d), 124.3 (d), 129.3 (d), 129.5 (d), 147.7 (s), 148.0 (s), 148.5 (s), 152.4 (s), 155.3 (s), 156.4 (s), 162.0 (s), 168.4 (s); IR (nujol): ν_{max} = 1749, 1734, 1653, 1637 cm^{-1}; MS *m/z* (ESI): 408.09 (M + H^+); anal. calcd. for $C_{18}H_{21}N_3O_6S$ (407.12): C 53.06, H 5.20, N 10.31; found: C 52.94, H 5.24, N 10.27.

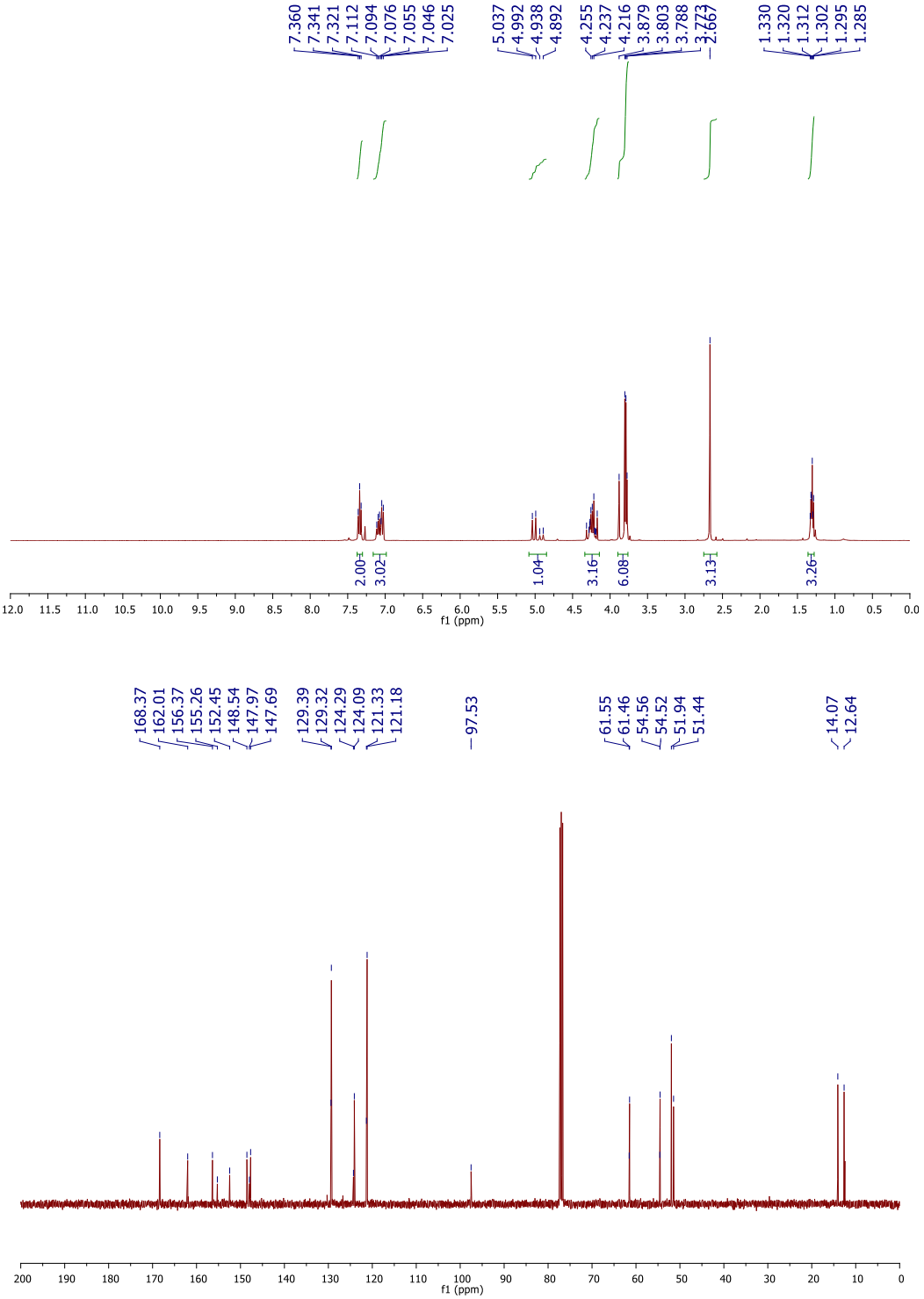


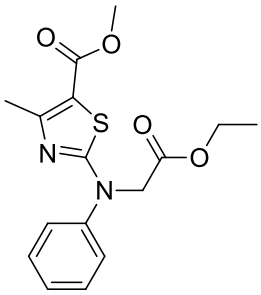
Methyl 2-((2-ethoxy-2-oxoethyl)(phenyl)amino)-4-methylthiazole-5-carboxylate (17a). The compound was obtained as white solid (25.2 mg, 15%); mp: 112–114 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.28 (t, *J*=7.6 Hz, 3H, $OCH_2\mathit{CH_3}$), 2.56 (s, 3H, $\mathit{CH_3}$), 3.74 (s, 3H, $O\mathit{CH_3}$), 4.23 (q, *J*=7.6 Hz, 2H, $O\mathit{CH_2}CH_3$), 4.64 (s, 2H, $\mathit{CH_2}CO$), 7.36–7.40 (m, $1H_{ar}$), 7.44–7.53 (m, $4H_{ar}$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.2 (q), 17.5 (q), 51.4 (q), 53.6 (t), 61.4 (t), 110.6 (s), 126.8 (d), 128.4 (d), 130.2 (d), 144.3 (s), 160.0 (s), 163.0 (s), 169.1 (s), 170.6 (s); IR (nujol): ν_{max} = 1723, 1653, 1644 cm^{-1}; MS *m/z* (ESI): 335.27 ($M + H^+$); anal. calcd. for $C_{16}H_{18}N_2O_4S$ (334.39): C 57.47, H 5.43, N 8.38; found: C 57.34, H 5.48, N 8.47.

23. ^{1}H and ^{13}C spectra of *N*-alkylated 2,3-dihydrothiazole 16a and of *N*-alkylated 2-aminothiazole 17a.

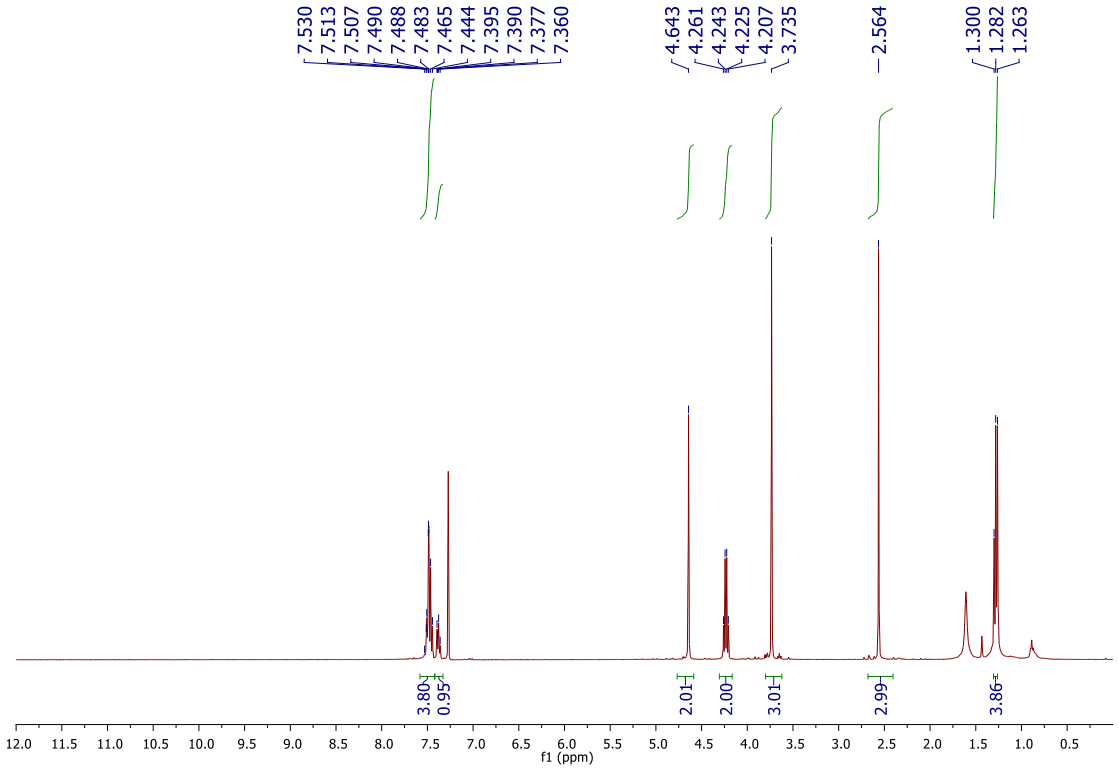


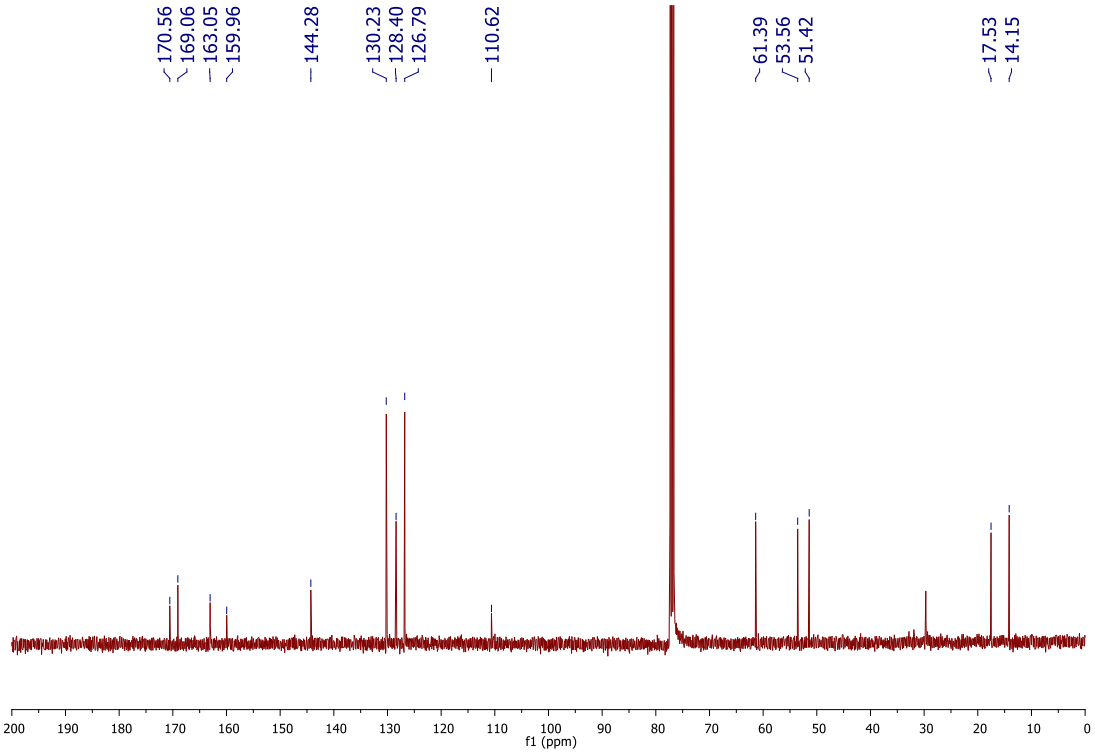
Methyl 3-((2-ethoxy-2-oxoethyl)(methoxycarbonyl)amino)-4-methyl-2-(phenylimino)-2,3-dihydrothiazole-5-carboxylate (16a).

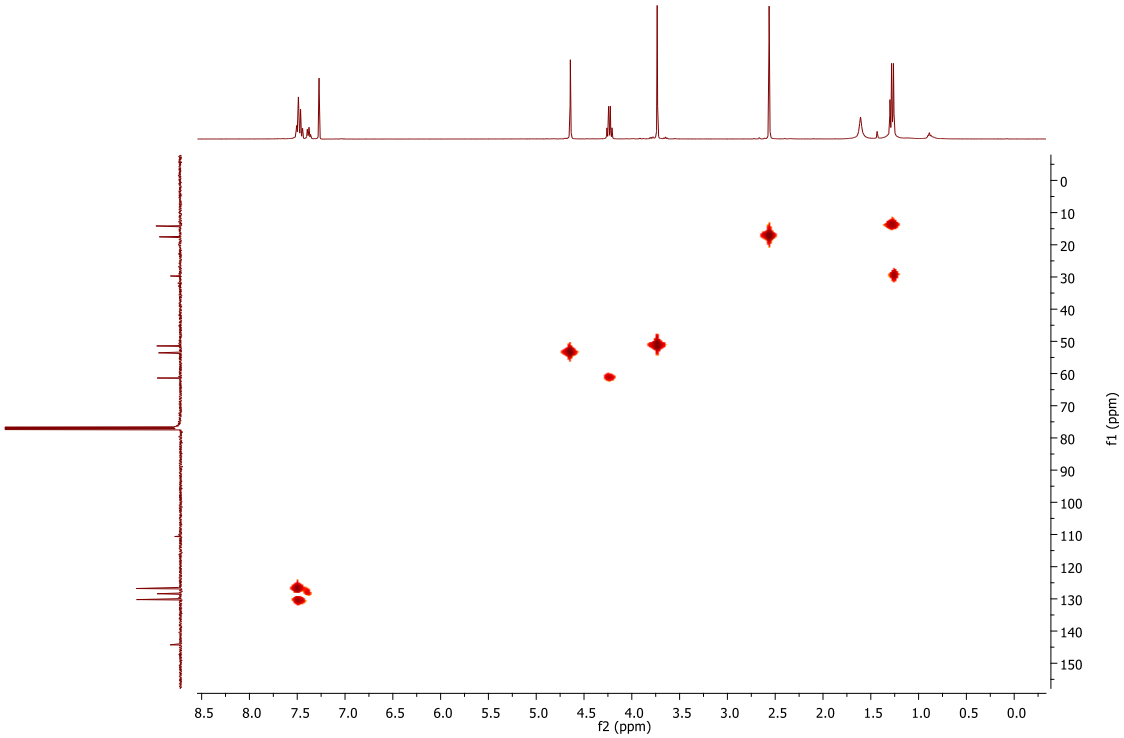


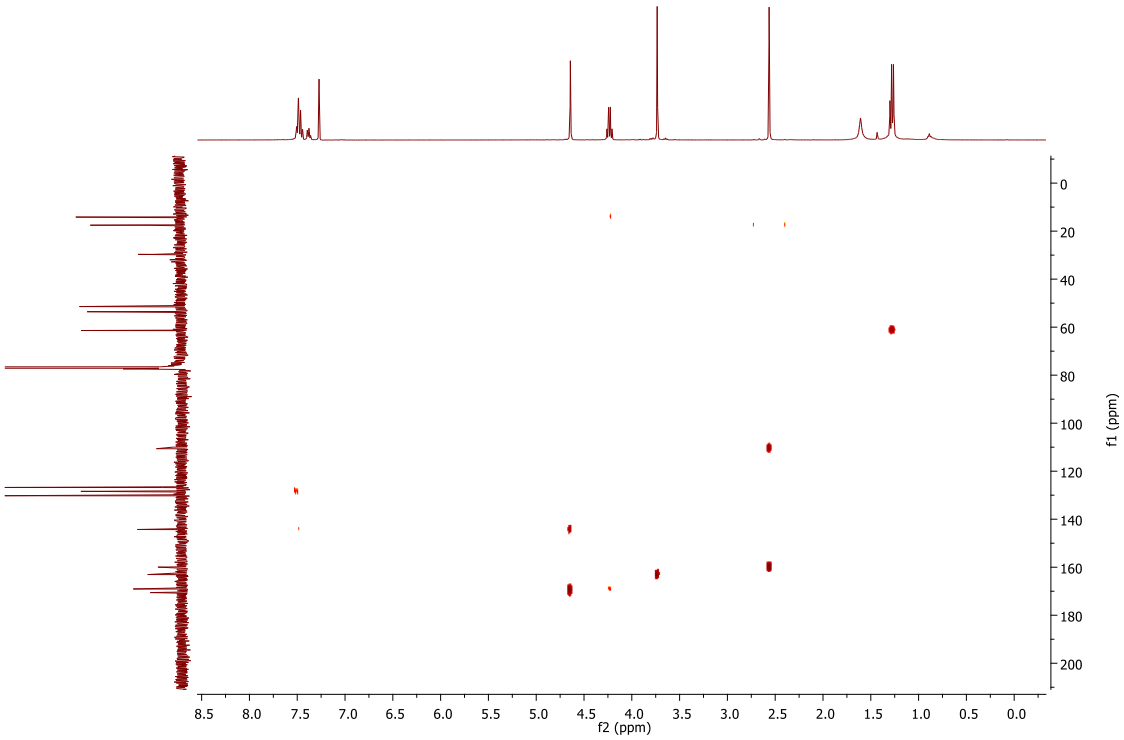


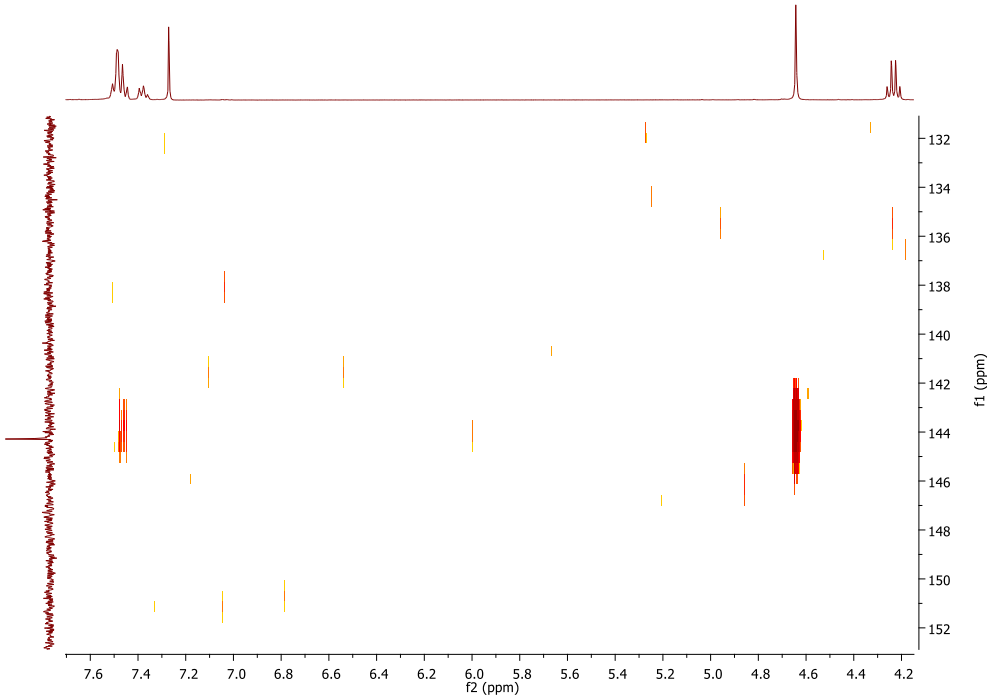
Methyl 2-((2-ethoxy-2-oxoethyl)(phenyl)amino)-4-methylthiazole-5-carboxylate (17a).






f1 (ppm)
f2 (ppm)


f1 (ppm)
f2 (ppm)


132
134
136
138
140
142
144
146
148
150
152
f1 (ppm)
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
f2 (ppm)

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