Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Ambident Reactivity of 5-Aminopyrazoles towards Donor-Acceptor Cyclopropanes

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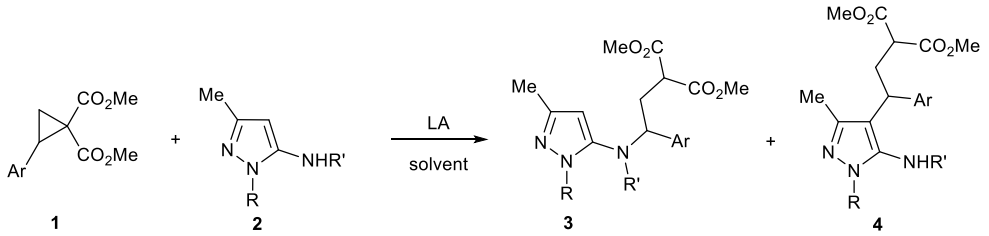
General Information

NMR spectra were acquired on Bruker Avance 500 spectrometer at room temperature; the chemical shifts δ were measured in ppm with respect to solvent (^{1}H: $CDCl_3$, δ = 7.26 ppm; DMSO-d_6, δ = 2.50 ppm; ^{13}C: $CDCl_3$, δ = 77.16; DMSO-d_6, δ = 39.52 ppm). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quadruplet; m, multiplet; dd, double doublet. Coupling constants (*J*) are in Hertz. Structural assignments were made with additional information from gHSQC and gHMBC experiments. Infrared spectra were recorded on Bruker FTIR spectrometer ALPHA II. High resolution and accurate mass measurements were carried out using a BrukermicrOTOF-Q^{TM} ESI-TOF (Electro Spray Ionization/Time of Flight). Elemental analyses were performed with Fisons EA-1108 CHNS elemental analyser instrument. Melting points (mp) were determined using the Stuart® SMP3 melting point apparatus. X-Ray analysis was performed on Bruker D8 Quest diffractometer. Analytical thin layer chromatography (TLC) was carried out with silica gel plates (silica gel 60, F_{254}, supported on aluminium); the revelation was done by UV lamp (260 and 365 nm). Column chromatography was performed on Macherey-Nagel silica gel (230-400 mesh). Cyclopropanes **1** were synthesized similarly to the reported procedures.[S1,S2]

Lewis acid-induced *N*- and *C*-alkylation of 5-aminopyrazoles 2 with donor-acceptor cyclopropanes 1



General procedure A

$GaCl_3$ (1.2 equiv) was added to 0.12 M solution of cyclopropane **1** (1 equiv) and 1,3-dimethyl-1*H*-pyrazol-5-amine (1 equiv) in dichloromethane. The resulting mixture was stirred under argon atmosphere at room temperature for 0.5–1 h. Then the mixture was quenched with aq. solution of $NaHCO_3$ and extracted with dichloromethane (3×15 mL). The combined organic fractions were dried with Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on a silica gel to afford the desired product.

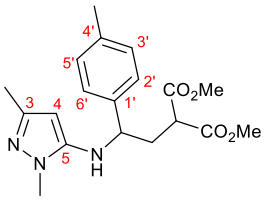
General procedure B

$Sc(OTf)_3$ (10 mol.%) was added to 0.24 M solution of cyclopropane **1** (1 equiv) and 1,3-dimethyl-1*H*-pyrazol-5-amine (1 equiv) in acetonitrile. The resulting mixture was stirred under reflux or at 60 °C for 2–6 h. Then the reaction mixture was quenched with aq. solution of $NaHCO_3$ and extracted with ethyl acetate (3×15 mL). The combined organic fractions were dried with Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on a silica gel to afford the desired product.

General procedure C

$Sc(OTf)_3$ (10 mol.%) was added to 0.24 M solution of cyclopropane **1** (1 equiv) and 1,3-dimethyl-1*H*-pyrazol-5-amine (1 equiv) in dichloromethane. The resulting mixture was stirred under reflux for 4–8 h. Then the reaction mixture was quenched with aq. solution of $NaHCO_3$ and treated as described above.

Dimethyl 2-{2-[(1,3-dimethyl-1H-pyrazol-5-yl)amino]-2-(p-tolyl)ethyl}malonate **(3a)** was synthesized



from 1,3-dimethyl-1*H*-pyrazol-5-amine **2a** (90 mg, 0.81 mmol) and dimethyl 2-(*p*-tolyl)cyclopropane-1,1-dicarboxylate **1a** (200 mg, 0.81 mmol) using **General procedure A**. Reaction time: 1 h. Yield: 168 mg (58%). Yellow oil; R_f=0.33 (ethyl acetate).

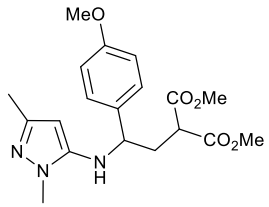
^{1}H NMR (500 MHz; $CDCl_3$): δ = 7.17 (d, ^3J = 8.1 Hz, 2 H, C(2')H, C(6')H), 7.13 (d, ^3J = 8.1 Hz, 2 H, C(3')H, C(5')H), 5.06 (s, 1 H, C(4)H), 4.18–4.16 (m, 2 H, CH, NH), 3.73 (s, 3 H, CH_3O), 3.69 (s, 3 H, CH_3O), 3.59 (s, 3 H, CH_3N), 3.46 (dd, ^3J = 7.6 Hz, ^3J = 5.5 Hz, 1 H, CH), 2.47 (ddd, ^2J =14.5 Hz, ^3J = 8.3 Hz, ^3J = 7.6 Hz, 1 H, CH_2), 2.36–2.29 (m, 1 H, CH_2), 2.32 (s, 3 H, CH_3C(3)), 2.07 (s, 3 H, CH_3C(4')).[1]

^{13}C NMR (126 MHz; $CDCl_3$): δ = 170.1 (CO_2Me), 169.8 (CO_2Me), 147.8 (C(5)), 146.9 (C(3)), 138.5 (C(4')), 137.7 (C(1')), 129.7 (C(3')H, C(5')H), 126.3 (C(2')H, C(6')H), 89.7 (C(4)H), 58.7 (CHNH), 52.9 (2×CH_3O), 49.2 (CH), 36.4 (CH_2), 34.0 (CH_3N), 21.2 (CH_3C(4')), 13.7 (CH_3C(3)).

IR (film): 3357, 3242, 3097, 3006, 2951, 2734, 2589, 2351, 2307, 2122, 2013, 1909, 1761, 1730, 1612, 1585, 1553, 1537, 1516, 1452, 1434, 1417, 1390, 1355, 1335, 1264, 1181, 1147, 1116, 1098, 1081, 1055, 1018, 970, 946, 916, 874, 820, 769, 731 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{19}H_{26}N_3O_4$: 360.1918; found: 360.1919.

Dimethyl 2-{2-[(1,3-dimethyl-1H-pyrazol-5-yl)amino]-2-(4-methoxyphenyl)ethyl}malonate **(3b)** was



synthesized from 1,3-dimethyl-1*H*-pyrazol-5-amine **2a** (126 mg, 1.14 mmol) and dimethyl 2-(4-methoxyphenyl)cyclopropane-1,1-dicarboxylate **1b** (300 mg, 1.14 mmol) using **General procedure A**. Reaction time: 50 min. Yield: 166 mg (52%). Yellow oil, R_f=0.31 (ethyl acetate).

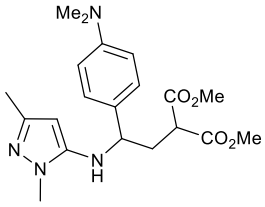
^{1}H NMR (500 MHz; $CDCl_3$): δ = 7.19 (br. d, ^3J = 8.6 Hz, 2 H, C(2')H, C(6')H), 6.84 (br. d, ^3J = 8.6 Hz, 2 H, C(3')H, C(5')H), 5.04 (s, 1 H, C(4)H), 4.14 (dd, ^3J = 8.6 Hz, ^3J = 5.5 Hz, 1 H, CH), 3.91 (br. s, 1 H, NH), 3.77 (s, 3 H, CH_3O), 3.71 (s, 3 H, CH_3O), 3.68 (s, 3 H, CH_3O), 3.55 (s, 3 H, CH_3N), 3.44 (dd, ^3J = 7.5 Hz, ^3J = 6.3 Hz, 1 H, CH), 2.46 (ddd, ^3J = 14.0 Hz, ^3J = 8.6 Hz, ^3J = 6.3 Hz, 1 H, CH_2), 2.31 (ddd, ^3J = 14.0 Hz, ^3J = 7.5 Hz, ^3J = 5.5 Hz, 1 H, CH_2), 2.06 (s, 3 H, CH_3).

^{13}C NMR (126 MHz; $CDCl_3$): δ = 170.1 (CO_2Me), 169.8 (CO_2Me), 159.2 (C(4')), 147.2 (C), 147.0 (C), 134.0 (C(1')), 127.6 (C(2')H, C(6')H), 114.3 (C(3')H, C(5')H), 89.6 (C(4)H), 58.4 (CHNH), 55.3 (CH_3O), 52.8 (2×CH_3O), 49.2 (CH), 36.5 (CH_2), 33.9 (CH_3N), 13.8 (CH_3).

IR (film): 3350, 3246, 3001, 2954, 2839, 1754, 1733, 1612, 1569, 1514, 1438, 1389, 1355, 1247, 1178, 1154, 1115, 1096, 1033, 970, 916, 872, 835, 791, 737 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{19}H_{26}N_3O_5$: 376.1867; found: 376.1873.

Dimethyl 2-{2-[(1,3-dimethyl-1H-pyrazol-5-yl)amino]-2-(4-(dimethylamino)phenyl)ethyl}malonate **(3c)** was synthesized from 1,3-dimethyl-1*H*-pyrazol-5-amine **2a** (80 mg, 0.72 mmol) and dimethyl 2-[4-(dimethylamino)phenyl]cyclopropane-1,1-dicarboxylate **1c** (200 mg, 0.72 mmol) using **General procedure A**. Reaction time: 30 min. Yield: 142 mg (51%). Yellow oil; R_f=0.27 (ethyl acetate).



^{1}H NMR (500 MHz; DMSO-d_6): δ = 7.14 (d, ^3J = 8.7 Hz, 2 H, C(2')H, C(6')H), 6.66 (d, ^3J = 8.7 Hz, 2 H, C(3')H, C(5')H), 5.69 (d, ^3J = 8.5 Hz, 1 H, NH), 4.87 (s, 1 H, C(4)H), 3.89 (ddd, ^3J = 8.5

[1] Here and below, the numbering of atoms in the compound corresponds to that shown in the structures, *i.e.*, differ from IUPAC nomenclature.

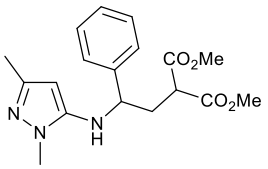
Hz, ^3J = 8.2 Hz, ^3J = 6.6 Hz, 1 H, CH), 3.67 (s, 3 H, CH_3O), 3.60 (s, 3 H, CH_3O), 3.48 (dd, ^3J = 7.5 Hz, ^3J = 7.0 Hz, 1 H, CH), 3.45 (s, 3 H, CH_3N), 2.85 (s, 6 H, $N(CH_3)_2$), 2.34 (ddd, ^2J = 14.0 Hz, ^3J = 8.2 Hz, ^3J = 7.5 Hz, 1 H, CH_2), 2.09 (ddd, ^2J = 14.0 Hz, ^3J = 7.0 Hz, ^3J = 6.6 Hz, 1 H, CH_2), 1.87 (s, 3 H, CH_3).

^{13}C NMR (126 MHz; DMSO-d_6): δ = 169.3 (CO_2Me), 169.2 (CO_2Me), 149.6 (C(4')), 147.8 (C(5)), 144.7 (C(3)), 130.4 (C(1')), 127.1 (C(2')H, C(6')H), 112.3 (C(3')H, C(5')H), 87.6 (C(4)H), 56.8 (CHNH), 52.4 (2×CH_3O), 48.8 (CH), 40.2 ($N(CH_3)_2$), 36.5 (CH_2), 34.0 (CH_3N), 13.7 (CH_3).

IR (film): 3455, 3264, 3074, 3011, 2957, 2923, 2894, 2854, 2810, 2389, 2352, 1889, 1753, 1737, 1617, 1561, 1527, 1436, 1390, 1354, 1317, 1293. 1267, 1244, 1222, 1198, 1148, 1097, 1070, 1008, 969, 937, 872, 839, 815, 748, 796 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{20}H_{29}N_4O_4$: 389.2183; found: 389.2173.

Dimethyl 2-{2-[(1,3-dimethyl-1H-pyrazol-5-yl)amino]-2-phenylethyl}malonate **(3d)** was synthesized from 1,3-dimethyl-1*H*-pyrazol-5-amine **2a** (109 mg, 0.98 mmol) and dimethyl 2-phenylcyclopropane-1,1-dicarboxylate **1d** (230 mg, 0.98 mmol) using **General procedure A**. Reaction time: 1 h. Yield: 100 mg (56%). Yellow oil; R_f=0.55 (ethyl acetate).



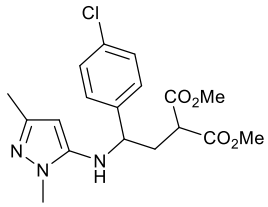
^{1}H NMR (500 MHz; $CDCl_3$): δ = 7.30–7.21 (m, 5 H, 5×CH, Ar), 5.00 (s, 1 H, C(4)H), 4.18 (br. dd, ^3J = 7.9 Hz, ^3J = 5.8 Hz, 1 H, CH), 4.12–4.10 (br. s, 1 H, NH), 3.69 (s, 3 H, CH_3O), 3.65 (s, 3 H, CH_3O), 3.52 (s, 3 H, CH_3N), 3.46 (dd, ^3J = 7.5 Hz, ^3J = 6.5 Hz, 1 H, CH), 2.44 (ddd, ^2J = 14.4 Hz, ^3J = 7.9 Hz, ^3J = 7.5 Hz, 1 H, CH_2), 2.33 (ddd, ^2J = 14.4 Hz, ^3J = 6.5 Hz, ^3J=5.8 Hz, 1 H, CH_2), 2.02 (s, 3 H, CH_3).

^{13}C NMR (126 MHz; $CDCl_3$): δ = 169.9 (CO_2Me), 169.7 (CO_2Me), 147.1 (C), 146.9 (C), 141.7 (C(1')), 128.8 (C(3')H, C(5')H), 127.8 (C(4')H), 126.3 (C(2')H, C(6')H), 89.5 (C(4)H), 58.8 (CH), 52.7 (2×CH_3O), 49.1 (CH), 36.4 (CH_2), 33.9 (CH_3N), 13.7 (CH_3).

IR (film): 3603, 3354, 3246, 3086, 3063, 3029, 3004, 2954, 2848, 1749, 1743, 1729, 1646, 1569, 1563, 1494, 1451, 1437, 1391, 1356, 1267, 1239, 1212, 1155, 1101, 1053, 1015, 969, 915, 874, 845 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{18}H_{24}N_3O_4$: 346.1761; found: 346.1761.

Dimethyl 2-{2-(4-chlorophenyl)-2-[(1,3-dimethyl-1H-pyrazol-5-yl)amino]ethyl}malonate **(3e)** was synthesized from 1,3-dimethyl-1*H*-pyrazol-5-amine **2a** (83 mg, 0.74 mmol) and dimethyl 2-(4-chlorophenyl)cyclopropane-1,1-dicarboxylate **1e** (200 mg, 0.74 mmol) using **General procedure A**. Reaction time: 1 h. Yield: 156 mg (55%). Yellow oil; R_f=0.40 (ethyl acetate).



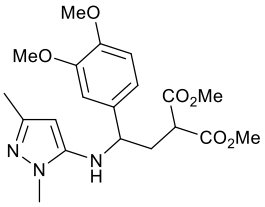
^{1}H NMR (500 MHz; $CDCl_3$): δ = 7.30 (d, ^3J = 8.4 Hz, 2 H, Ar), 7.24 (d, ^3J = 8.4 Hz, 2 H, Ar), 4.97 (s, 1 H, CH), 4.26–4.23 (br. d, ^3J = 5.4 Hz, 1 H, NH), 4.20 (ddd, ^3J = 8.0 Hz, ^3J = 6.2 Hz, ^3J = 5.4 Hz, 1 H, CH), 3.73 (s, 3 H, CH_3O), 3.71 (s, 3 H, CH_3O), 3.60 (s, 3 H, CH_3N), 3.48 (dd, ^3J = 7.0 Hz, ^3J = 5.8 Hz, 1 H, CH), 2.44 (ddd, ^2J = 14.4 Hz, ^3J = 8.0 Hz, ^3J = 7.0 Hz, 1 H, CH_2), 2.34 (ddd, ^2J = 14.4 Hz, ^3J = 6.2 Hz, ^3J = 5.8 Hz, 1 H, CH_2), 2.06 (s, 3 H, CH_3).

^{13}C NMR (126 MHz; $CDCl_3$): δ = 169.9 (CO_2Me), 169.8 (CO_2Me), 147.1 (C), 147.0 (C), 140.2 (C), 133.7 (C), 129.2 (2×CH), 127.9 (2×CH), 89.9 (CH), 58.4 (CH), 53.0 (2×CH_3O), 49.2 (CH), 36.4 (CH_3N), 34.1 (CH_2), 13.7 (CH_3).

IR (film): 3600, 3585, 3546, 3498, 3466, 3434, 3399, 3370, 3372, 3248, 3233, 3117, 3084, 3015, 2996, 2952, 2916, 2840, 2378, 2346, 1847, 1751, 1735, 1617, 1565, 1492, 1437, 1410, 1393, 1365, 1279, 1237, 1213, 1153, 1092, 1052, 1013, 968, 830 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{18}H_{23}ClN_3O_4$: 380.1372; found: 380.1354.

***Dimethyl 2-{2-[(1,3-dimethyl-1H-pyrazol-5-yl)amino]-2-(3,4-dimethoxyphenyl)ethyl}malonate* (3f)**



was synthesized from 1,3-dimethyl-1*H*-pyrazol-5-amine **2a** (76 mg, 0.68 mmol) and dimethyl 2-(3,4-dimethoxyphenyl)cyclopropane-1,1-dicarboxylate **1f** (200 mg, 0.68 mmol) using **General procedure A**. Reaction time: 50 min. Yield: 157 mg (57%). Colorless oil; R_f=0.28 (ethyl acetate).

^{1}H NMR (500 MHz; DMSO-d$_6$): δ = 7.00 (d, ^4J = 1.4 Hz, 1 H, Ar), 6.86 (d, ^3J = 8.5 Hz, 1 H, Ar), 6.84 (dd, ^3J = 8.5 Hz, ^4J = 1.4 Hz, 1 H, Ar), 5.79 (d, ^3J = 8.8 Hz, 1 H, NH), 4.92 (s, 1 H, CH), 3.96 (ddd, ^3J = 8.8 Hz, ^3J = 7.9 Hz, ^3J = 7.1 Hz, 1 H, CH), 3.73 (s, 3 H, CH$_3$O), 3.70 (s, 3 H, CH$_3$O), 3.66 (s, 3 H, CH$_3$O), 3.64 (dd, ^3J = 8.0 Hz, ^3J = 5.8 Hz, 1 H, CH), 3.60 (s, 3 H, CH$_3$O), 3.45 (s, 3 H, CH$_3$N), 2.35 (ddd, ^2J = 14.0 Hz, ^3J = 8.0 Hz, ^3J = 7.1 Hz, 1 H, CH$_2$), 2.13 (ddd, ^2J = 14.0 Hz, ^3J = 7.9 Hz, ^3J = 5.8 Hz, 1 H, CH$_2$), 1.87 (s, 3 H, CH$_3$).

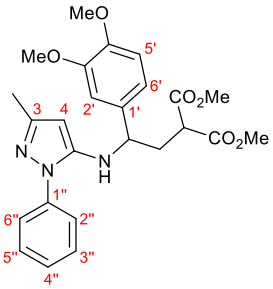
^{13}C NMR (126 MHz; DMSO-d$_6$): δ = 169.6 (*C*O$_2$Me), 169.3 (*C*O$_2$Me), 148.9 (C), 148.0 (C), 147.9 (C), 145.1 (C), 135.8 (C), 118.9 (CH), 111.6 (CH), 110.2 (CH), 87.9 (CH), 57.4 (CH), 55.61 (CH$_3$O), 55.59 (CH$_3$O), 52.6 (2×CH$_3$O), 49.1 (CH), 36.5 (CH$_3$N), 34.2 (CH$_2$), 13.8 (CH$_3$).

IR (film): 3465, 3434, 3396, 3272, 3252, 3236, 3000, 2954, 2838, 1751, 1734, 1606, 1593, 1564, 1516, 1463, 1439, 1391, 1343, 1261, 1238, 1203, 1143, 1101, 1055, 1026, 969, 858, 812, 764, 737 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{20}H_{28}N_3O_6$: 406.1973; found: 406.1973.

When reaction was performed using 1.00 g (3.4 mmol) of **1f** and 378 mg (3.4 mmol) of **2a**, using **General Procedure A** for 1 h, product **3f** was isolated in 55% yield (757 mg).

***Dimethyl 2-{2-[(3-methyl-1-phenyl-1H-pyrazol-5-yl)amino]-2-(3,4-dimethoxyphenyl)ethyl}malonate* (3g)**



was synthesized from 3-methyl-1-phenyl-1*H*-pyrazol-5-amine **2b** (118 mg, 0.68 mmol) and dimethyl 2-(3,4-dimethoxyphenyl)cyclopropane-1,1-dicarboxylate **1f** (200 mg, 0.68 mmol) using **General procedure A**. Reaction time: 44 min. Yield: 139 mg (44%). Colorless oil; R_f=0.30 (ethyl acetate).

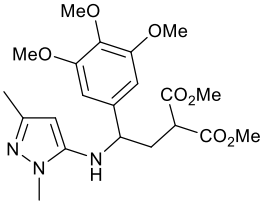
^{1}H NMR (500 MHz; DMSO-d$_6$): δ = 7.57–7.55 (m, 2 H, Ar), 7.51–7.48 (m, 2 H, Ar), 7.34–7.30 (m, 1 H, Ar), 7.05 (br. s, 1 H, Ar), 6.87 (br. s, 2 H, Ar), 5.89 (d, ^3J = 8.6 Hz, 1 H, NH), 5.20 (s, 1 H, C(4)H), 4.03 (ddd, ^3J = 8.6 Hz, ^3J = 7.8 Hz, ^3J = 7.0 Hz, 1 H, CH), 3.72 (s, 6 H, 2×CH$_3$O), 3.65 (s, 3 H, CH$_3$O), 3.61 (s, 3 H, CH$_3$O), 3.49 (dd, ^3J = 8.2 Hz, ^3J = 6.6 Hz, 1 H, CH), 2.41 (ddd, ^3J = 14.3 Hz, ^3J = 8.2 Hz, ^3J = 7.8 Hz, 1 H, CH$_2$), 2.14 (ddd, ^3J = 14.3 Hz, ^3J = 7.0 Hz, ^3J = 6.6 Hz, 1 H, CH$_2$), 2.00 (s, 3 H, CH$_3$).

^{13}C NMR (126 MHz; DMSO-d$_6$): δ = 169.3 (*C*O$_2$Me), 169.1 (*C*O$_2$Me), 148.8 (C), 147.9 (C), 147.7 (2×C), 139.5 (C(1'')), 135.3 (C(1')), 129.1 (C(3'')H, C(5'')H), 126.0 (C(4'')H), 123.2 (C(2'')H, C(6'')H), 118.9 (C(6')H), 111.5 (C(5')H), 110.3 (C(2')H), 89.9 (C(4)H), 57.6 (CH), 55.5 (2×CH$_3$O), 52.4 (2×CH$_3$O), 48.8 (CH), 36.0 (CH$_2$), 13.8 (CH$_3$).

IR (film): 3403, 3118, 300, 2953, 2837, 2602, 2356, 2054, 1750, 1732, 1595, 1564, 1516, 1455, 1438, 1387, 1363, 1313, 1260, 1235, 1141, 1096, 1073, 1057, 1025, 970, 914, 857, 812 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{25}H_{30}N_3O_6$: 468.2129; found: 468.2129.

***Dimethyl 2-{2-[(1,3-dimethyl-1H-pyrazol-5-yl)amino]-2-(3,4,5-trimethoxyphenyl)ethyl}malonate* (3h)**



was synthesized from 1,3-dimethyl-1*H*-pyrazol-5-amine **2a** (69 mg, 0.62 mmol) and dimethyl 2-(3,4,5-trimethoxyphenyl)cyclopropane-1,1-dicarboxylate **1g** (200 mg, 0.62 mmol) using **General procedure C**. Reaction time: 6 h. Yield: 178 mg (66%). Yellow oil; R_f=0.23 (ethyl acetate).

^{1}H NMR (500 MHz; $CDCl_3$): δ = 6.48 (s, 2 H, Ar), 5.06 (s, 1 H, Ar), 4.09 (br. dd, ^3J = 8.2 Hz, ^3J = 5.5 Hz, 1 H, CH), 3.99–3.97 (m, 1 H, NH), 3.82 (s, 6 H, 2×CH_3O), 3.80 (s, 3 H, CH_3O), 3.73 (s, 3 H, CH_3O), 3.69 (s, 3 H, CH_3O), 3.56 (s, 3 H, CH_3N), 3.46 (dd, ^3J =7.6 Hz, ^3J = 6.2 Hz, 1 H, CH), 2.45 (ddd, ^2J = 14.3 Hz, ^3J = 8.2 Hz, ^3J = 7.6 Hz, 1 H, CH_2), 2.31 (ddd, ^2J = 14.3 Hz, ^3J = 6.2 Hz, ^3J = 5.5 Hz, 1 H, CH_2), 2.06 (s, 3 H, CH_3).

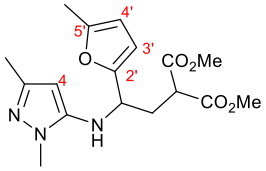
^{13}C NMR (126 MHz; $CDCl_3$): δ = 170.1 (CO_2Me), 169.8 (CO_2Me), 153.6 (2×C), 147.2 (C), 147.1 (C), 137.5 (C), 137.4 (C), 103.3 (2×CH), 89.8 (CH), 60.9 (CH_3O), 59.4 (CH), 56.2 (CH_3O), 52.9 (3×CH_3O), 49.2 (CH), 36.4 (CH_2), 34.0 (CH_3N), 13.8 (CH_3).

IR (film): 3346, 2999, 2951, 2841, 1748, 1737, 1595, 1561, 1509, 1464, 1427, 1388, 1351, 1328, 1239, 1152, 1126, 1039, 1006, 918, 869, 835 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{21}H_{30}N_3O_7$: 436.2078; found: 436.2076.

When **1g** (200 mg, 0.62 mmol) and **2a** (69 mg, 0.62 mmol) were heated under reflux for 5 h according to the **General procedure B**, product **3h** was obtained in 52% yield (140 mg).

Dimethyl 2-{2-[(1,3-dimethyl-1H-pyrazol-5-yl)amino]-2-(5-methylfuran-2-yl)ethyl}malonate **(3i)** was synthesized from 1,3-dimethyl-1*H*-pyrazol-5-amine **2a** (47 mg, 0.42 mmol) and dimethyl 2-(5-methylfuran-2-yl)cyclopropane-1,1-dicarboxylate **1h** (100 mg, 0.42 mmol) using **General procedure A**. Reaction time: 30 min. Yield: 63 mg (43%). Yellow oil; R_f=0.45 (ethyl acetate).



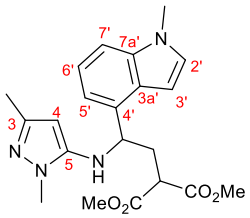
^{1}H NMR (500 MHz; $CDCl_3$): δ = 6.04 (d, ^3J = 2.4 Hz, 1 H, C(3')H), 5.84 (br. d, ^3J = 2.4 Hz, C(4')H), 5.27 (s, 1 H, C(4)H), 4.24–4.19 (m, 1 H, CHN), 3.94 (br. s, 1 H, NH), 3.71 (s, 3 H, CH_3O), 3.69 (s, 3 H, CH_3O), 3.55 (s, 3 H, CH_3N), 3.51 (t, ^3J = 7.1 Hz, 1 H, CH), 2.54–2.47 (m, 1 H, CH_2), 2.44–2.37 (m, 1 H, CH_2), 2.23 (s, 3 H, CH_3), 2.12 (s, 3 H, CH_3).

^{13}C NMR (126 MHz; $CDCl_3$): δ = 169.8 (CO_2Me), 169.6 (CO_2Me), 151.6 (C), 152.0 (C), 147.1 (C), 147.0 (C), 107.9 (C(3')H), 106.2 (C(4')H), 89.9 (C(4)H), 52.8 (2×CH_3O), 52.7 (CH), 48.9 (CH), 34.0 (CH_3), 33.4 (CH_2), 13.7 (CH_3), 13.6 (CH_3).

IR (film): 3219, 2954, 2927, 1750, 1735, 1612, 1564, 1437, 1391, 1346, 1314, 1271, 1242, 1220, 1156, 1098, 1049, 1021, 962, 939, 914, 840 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{17}H_{24}N_3O_5$: 350.1710; found: 350.1721.

Dimethyl 2-{2-[(1,3-dimethyl-1H-pyrazol-5-yl)amino]-2-(1-methyl-1H-indol-3-yl)ethyl}malonate **(3j)** was synthesized from 1,3-dimethyl-1*H*-pyrazol-5-amine **2a** (65 mg, 0.58 mmol) and dimethyl 2-(1-methyl-1*H*-indol-3-yl)cyclopropane-1,1-dicarboxylate **1i** (200 mg, 0.58 mmol) using **General procedure C**. Reaction time: 6 h. Yield: 164 mg (62%). Colorless oil; R_f=0.48 (ethyl acetate).

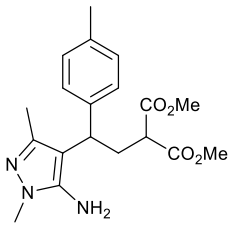


^{1}H NMR (500 MHz; DMSO-d_6): δ = 7.32 (d, ^3J = 3.1 Hz, 1 H, C(2')H), 7.29 (br. d, ^3J = 7.8 Hz, 1 H, C(7')H), 7.11 (dd, ^3J = 7.8 Hz, ^3J = 7.3 Hz, 1 H, C(6')H), 6.65 (dd, ^3J = 3.1 Hz, ^5J = 0.5 Hz, 1 H, C(3')H), 6.01 (d, ^3J = 8.4 Hz, 1 H, NH), 4.77 (s, 1 H, C(4)H), 4.52 (ddd, ^3J = 9.2 Hz, ^3J = 8.4 Hz, ^3J = 5.6 Hz, 1 H, CH), 3.77 (s, 3 H, CH_3), 3.71 (dd, ^3J = 8.4 Hz, ^3J=6.4 Hz, CH), 3.67 (s, 3 H, CH_3), 3.66 (s, 3 H, CH_3), 3.55 (s, 3 H, CH_3), 2.42 (ddd, ^2J = 14.2 Hz, ^3J = 9.2 Hz, ^3J = 6.4 Hz, 1 H, CH_2), 2.36 (ddd, ^2J = 14.2 Hz, ^3J = 8.4 Hz, ^3J = 5.6 Hz, 1 H, CH_2), 1.83 (s, 3 H, CH_3).

^{13}C NMR (126 MHz; DMSO-d_6): δ = 169.4 (CO_2Me), 169.3 (CO_2Me), 148.1 (C), 144.8 (C), 136.5 (C), 134.6 (C), 129.5 (CH), 126.2 (C), 121.1 (CH), 115.6 (CH), 108.6 (CH), 98.1 (CH), 87.3 (CH), 55.2 (CH), 52.5 (CH_3O), 52.4 (CH_3O), 48.8 (CH), 35.8 (CH_2), 34.1 (CH_3), 32.5 (CH_3), 13.5 (CH_3).

IR (film): 3353, 3255, 2952, 2846, 1754, 1610, 1563, 1570, 1515, 1497, 1440, 1391, 1370, 1347, 1267, 1238, 1207, 1180, 1153, 1092, 1047, 1013, 968, 951, 874, 837 cm^{-1}.
HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{21}H_{27}N_4O_4$: 399.2027; found: 399.2023.

Dimethyl 2-[2-(5-amino-1,3-dimethyl-1H-pyrazol-4-yl)-2-(p-tolyl)ethyl]malonate **(4a)** was synthesized

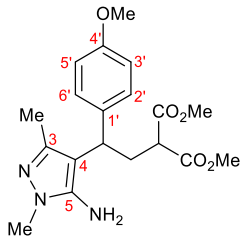


from 1,3-dimethyl-1*H*-pyrazol-5-amine **2a** (90 mg, 0.81 mmol) and dimethyl 2-(*p*-tolyl)cyclopropane-1,1-dicarboxylate **1a** (200 mg, 0.81 mmol) using **General procedure B** under reflux for 6 h. Yield: 153 mg (53%). Yellow oil, R_f=0.20 (ethyl acetate : methanol; 12:1).

^{1}H NMR (500 MHz; DMSO-d_6): δ = 7.12 (br. d, ^3J = 8.1 Hz, 2 H, Ar), 7.07 (br. d, ^3J = 8.1 Hz, 2 H, Ar), 5.01 (br. s, 2 H, NH_2), 3.73 (dd, ^3J = 9.9 Hz, ^3J = 6.6 Hz, 1 H, CH), 3.65 (s, 3 H, CH_3O), 3.57 (s, 3 H, CH_3O), 3.44 (s, 3 H, CH_3N), 3.28 (dd, ^3J = 7.8 Hz, ^3J = 6.5 Hz, 1 H, CH), 2.50–2.45 (m, 2 H, CH_2), 2.24 (s, 3 H, CH_3), 1.85 (s, 3 H, CH_3).
^{13}C NMR (126 MHz; DMSO-d_6): δ = 169.3 (*C*O_2Me), 169.2 (*C*O_2Me), 144.8 (C), 143.2 (C), 140.8 (C), 134.8 (C), 128.7 (2×CH), 127.1 (2×CH), 100.5 (C), 52.5 (CH_3O), 52.2 (CH_3O), 49.9 (CH), 36.7 (CH), 33.8 (CH_3N), 31.9 (CH_2), 20.5 (CH_3), 12.7 (CH_3).
IR (film): 3434, 3235, 3118, 3088, 2954, 2926, 2854, 2735, 2594, 2389, 2352, 2315, 1911, 1733, 1632, 1570, 1538, 1514, 1438, 1393, 1376, 1334, 1262, 1234, 1152, 1097, 1029, 924, 812, 750, 728, 699 cm^{-1}.
HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{19}H_{26}N_3O_4$: 360.1918; found: 360.1923.

When reaction was performed using 1.00 g (4.03 mmol) of **1a** and 448 mg (4.03 mmol) of **2a**, using **General Procedure B** under reflux for 6 h, product **4a** was isolated in 56% yield (811 mg).

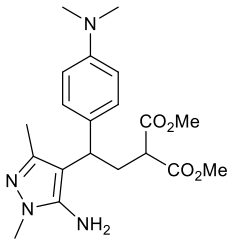
Dimethyl 2-[2-(5-amino-1,3-dimethyl-1H-pyrazol-4-yl)-2-(4-methoxyphenyl)ethyl]malonate **(4b)** was



synthesized from 1,3-dimethyl-1*H*-pyrazol-5-amine **2a** (84 mg, 0.76 mmol) and dimethyl 2-(4-methoxyphenyl)cyclopropane-1,1-dicarboxylate **1b** (200 mg, 0.76 mmol) using **General procedure B** under reflux for 4 h. Ratio **3b** : **4b** = 59 : 41 (on the basis of analysis ^{1}H NMR spectrum of reaction mixture). The column chromatography yielded 71 mg (25%) of **3b** and 102 mg (36%) of **4b** as yellow oil, R_f=0.55 (ethyl acetate).

^{1}H NMR (500 MHz; $CDCl_3$): δ = 7.10 (br. d, ^3J = 8.6 Hz, 2 H, C(2')H, C(6')H), 6.76 (br. d, ^3J = 8.6 Hz, 2 H, C(3')H, C(5')H), 3.73 (dd, ^3J = 10.3 Hz, ^3J = 6.0 Hz, 1 H, CH), 3.70 (s, 3 H, CH_3O), 3.66 (s, 3 H, CH_3O), 3.60 (s, 3 H, CH_3O), 3.48 (s, 3 H, CH_3N), 3.40 (br. s, 2 H, NH_2), 3.32 (dd, ^3J = 8.3 Hz, ^3J = 6.2 Hz, 1 H, CH), 2.59 (ddd, ^2J = 13.8 Hz, ^3J = 8.3 Hz, ^3J = 6.0 Hz, 1 H, CH_2), 2.45 (ddd, ^2J = 13.8 Hz, ^3J=10.3 Hz, ^3J = 6.2 Hz, 1 H, CH_2), 1.95 (s, 3 H, CH_3).
^{13}C NMR (126 MHz; $CDCl_3$): δ = 169.9 (*C*O_2Me), 169.8 (*C*O_2Me), 158.0 (C(4')), 145.3 (C(3)), 142.4 (C(5)), 134.5 (C(1')), 128.3 (C(2')H, C(6')H), 113.8 (C(3')H, C(5')H), 103.4 (C(4)), 55.2 (CH_3O), 52.6 (CH_3O), 52.5 (CH_3O), 50.1 (CH), 36.7 (CH), 33.8 (CH_3N), 32.4 (CH_2), 12.7 (CH_3).
IR (film): 3422, 3351, 3197, 3000, 2954, 2838, 1755, 1740, 1722, 1691, 1636, 1612, 1571, 1566, 1540, 1530, 1438, 1393, 1243, 1180, 1152, 1033, 963, 833, 781, 754, 733, 706 cm^{-1}.
HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{19}H_{26}N_3O_5$: 376.1867; found: 376.1854.

Dimethyl 2-{2-(5-amino-1,3-dimethyl-1H-pyrazol-4-yl)-2-[4-(dimethylamino)phenyl]ethyl}-malonate **(4c)** was synthesized from 1,3-dimethyl-1*H*-pyrazol-5-amine **2a** (80 mg, 0.72 mmol) and dimethyl 2-[(4-dimethylamino)phenyl]cyclopropane-1,1-dicarboxylate **1c** (200 mg, 0.72 mmol) under heating at 55 °C for 3 h according to the **General procedure B**. Yield: 137 mg (49%). Colorless oil, R_f=0.35 (ethyl acetate).



^{1}H NMR (500 MHz; DMSO-d$_6$): δ = 7.05 (d, ^3J = 8.7 Hz, 2 H, C(2')H, C(6')H), 6.64 (d, ^3J = 8.7 Hz, 2 H, C(3')H, C(5')H), 4.65 (br. s, 2 H, NH_2), 3.65 (s, 3 H, CH_3O), 3.63 (t, ^3J = 7.8 Hz, 1 H, CH), 3.58 (s, 3 H, CH_3O), 3.42 (s, 3 H, CH_3N), 3.27 (t, ^3J = 7.3 Hz, 1 H, CH), 2.83 (s, 6 H, $N(CH_3)_2$), 2.49–2.42 (m, 2 H, CH_2), 1.83 (s, 3 H, CH_3).

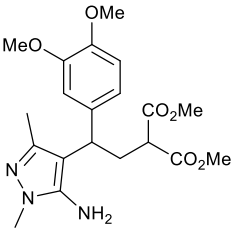
^{13}C NMR (500 MHz; DMSO-d$_6$): δ = 169.4 (CO_2Me), 169.3 (CO_2Me), 148.7 (C(4')), 143.9 (C), 143.3 (C), 131.7 (C(1')), 127.7 (C(2')H, C(6')H), 112.4 (C(3')H, C(5')H), 100.8 (C(4)), 52.4 (CH_3O), 52.3 (CH_3O), 50.0 (CH), 40.3 ($N(CH_3)_2$), 36.4 (CH), 33.8 (CH_3N), 32.4 (CH_2), 13.1 (CH_3).

IR (film): 3430, 3230, 2954, 2850, 2800, 2096, 1885, 1760, 1632, 1569, 1535, 1516, 1482, 1467, 1451, 1392, 1356, 1060, 1017, 947, 817 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{20}H_{29}N_4O_4$: 389.2183 ; found: 389.2178.

When **1c** (200 mg, 0.72 mmol) and **2a** (80 mg, 0.72 mmol) were heated under reflux for 6 h according to the **General procedure C**, both **3c** (78 mg, 28%) and **4c** (117 mg, 42%) were isolated.

Dimethyl 2-[2-(5-amino-1,3-dimethyl-1H-pyrazol-4-yl)-2-(3,4-dimethoxyphenyl)ethyl]malonate **(4f)** was synthesized from 1,3-dimethyl-1*H*-pyrazol-5-amine **2a** (94 mg, 0.85 mmol) and dimethyl 2-(3,4-dimethoxyphenyl)cyclopropane-1,1-dicarboxylate **1f** (250 mg, 0.85 mmol) using **General procedure B** under reflux for 6 h. Ratio **3f** : **4f** = 63 : 37 (on the basis of ^{1}H NMR spectrum of reaction mixture). The column chromatography yielded 86 mg (25%) of **3f** and 145 mg (42%) of **4f** as yellow oil, R_f=0.19 (ethyl acetate).



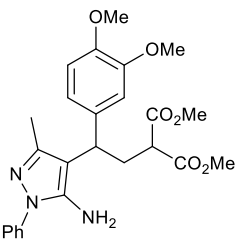
^{1}H NMR (500 MHz; DMSO-d$_6$): δ = 6.84 (dd, ^3J = 8.4 Hz, ^4J = 2.1 Hz, 1 H, CH), 6.83–6.81 (m, 1 H, CH), 6.75 (br. d, ^3J = 8.4 Hz, 1 H, CH), 4.75 (s, 2 H, NH_2), 3.70 (s, 3 H, CH_3O), 3.69 (s, 3 H, CH_3O), 3.67 (dd, ^3J = 9.7 Hz, ^3J = 7.1 Hz, 1 H, CH), 3.64 (s, 3 H, CH_3O), 3.57 (s, 3 H, CH_3O), 3.41 (s, 3 H, CH_3N), 3.27 (t, ^3J = 7.1 Hz, 1 H, CH), 2.49–2.41 (m, 2 H, CH_2), 1.88 (s, 3 H, CH_3).

^{13}C NMR (126 MHz; DMSO-d$_6$): δ = 169.5 (CO_2Me), 169.4 (CO_2Me), 148.6 (C), 147.1 (C), 144.1 (C), 143.4 (C), 136.9 (C), 119.0 (CH), 111.8 (CH), 111.7 (CH), 100.5 (C), 55.61 (CH_3O), 55.58 (CH_3O), 52.5 (CH_3O), 52.4 (CH_3O), 50.0 (CH), 37.2 (CH), 33.9 (CH_3N), 32.4 (CH_2), 13.2 (CH_3).

IR (film): 3432, 3234, 3119, 3080, 2997, 2953, 2838, 2590, 2387, 287, 2350, 2290, 2063, 1750, 1732, 1634, 1591, 1570, 1515, 1441, 1418, 1393, 1267, 1250, 1143, 1026, 964, 910, 853, 811, 763 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{20}H_{28}N_3O_6$: 406.1973; found: 406.1966.

Dimethyl 2-[2-(5-amino-3-methyl-1-phenyl-1H-pyrazol-4-yl)-2-(3,4-dimethoxyphenyl)ethyl]malonate **(4g)** was synthesized from 3-methyl-1-phenyl-1*H*-pyrazol-5-amine **2b** (118 mg, 0.68 mmol) and dimethyl 2-(3,4-dimethoxyphenyl)cyclopropane-1,1-dicarboxylate **1f** (200 mg, 0.68 mmol) using **General procedure B** under reflux for 6 h. Ratio **3g** : **4g** = 89 : 11 (on the basis of ^{1}H NMR spectrum of reaction mixture). The column chromatography yielded 25 mg (7%) of **3g** and 197 mg (55%) of **4g** as colorless oil, R_f=0.30 (ethyl acetate : petroleum ether; 1:1).



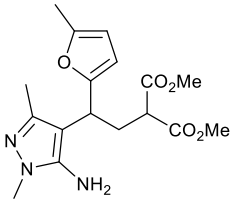
^{1}H NMR (500 MHz; DMSO-d_6): δ = 7.55 (d, ^3J = 7.5 Hz, 2 H, Ph), 7.46–7.42 (m, 2 H, Ph), 7.28–7.25 (m, 1 H, Ph), 6.88 (br. d, ^4J = 1.8 Hz, 1 H, Ar), 6.87 (br. d, ^3J = 8.4 Hz, 1 H, Ar), 6.82 (dd, ^3J = 8.4 Hz, ^4J = 1.8 Hz, 1 H, Ar), 4.92 (s, 2 H, NH_2), 3.85 (dd, ^3J = 9.7 Hz, ^3J = 6.6 Hz, 1 H, CH), 3.73 (s, 3 H, CH_3O), 3.71 (s, 3 H, CH_3O), 3.66 (s, 3 H, CH_3O), 3.55 (s, 3 H, CH_3O), 3.38 (t, ^3J = 7.1 Hz, 1 H, CH), 2.57–2.50 (m, 2 H, CH_2), 1.97 (s, 3 H, CH_3).

^{13}C NMR (126 MHz; DMSO-d_6): δ = 169.4 (CO$_2$Me), 169.3 (CO$_2$Me), 148.5 (C), 147.1 (C), 146.4 (C), 144.0 (C), 137.0 (C), 136.6 (C), 129.0 (2×CH), 125.7 (CH), 122.7 (2×CH), 119.0 (CH), 111.7 (2×CH), 102.4 (C), 55.5 (2×CH_3O), 52.5 (CH_3O), 52.3 (CH_3O), 50.1 (CH), 36.8 (CH), 32.1 (CH_2), 13.6 (CH_3).

IR (film): 3434, 3119, 2997, 2954, 2931, 2837, 2388, 2353, 2317, 1731, 1625, 1600, 1569, 1515, 1440, 1415, 1392, 1252, 1143, 1074, 1026, 962, 912, 852, 810 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{25}H_{30}N_3O_6$: 468.2129; found: 468.2122.

Dimethyl 2-[2-(5-amino-1,3-dimethyl-1H-pyrazol-4-yl)-2-(5-methylfuran-2-yl)ethyl]malonate **(4i)** was synthesized from 1,3-dimethyl-1*H*-pyrazol-5-amine **2a** (93 mg, 0.84 mmol) and dimethyl 2-(5-methylfuran-2-yl)cyclopropane-1,1-dicarboxylate **1h** (200 mg, 0.84 mmol) under heating at 55 °C for 3 h according to the **General procedure B**. Yield: 167 mg (57%). Orange oil, R_f=0.39 (ethyl acetate).



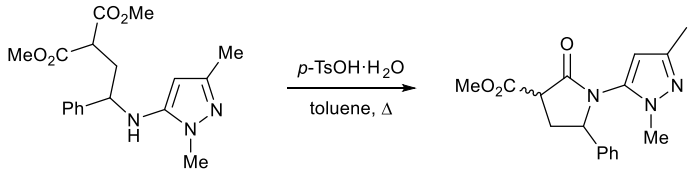
^{1}H NMR (500 MHz; DMSO-d_6): δ = 5.94–5.93 (m, 1 H, CH, Ar), 5.92–5.91 (m, 1 H, CH, Ar), 4.80 (br. s, 2 H, NH_2), 3.79 (dd, ^3J = 10.4 Hz, ^3J = 5.7 Hz, 1 H, CH), 3.56 (s, 3 H, CH_3O), 3.54 (s, 3 H, CH_3O), 3.43 (s, 3 H, CH_3N), 3.31 (dd, ^3J = 7.5 Hz, ^3J = 6.6 Hz, 1 H, CH), 2.46 (ddd, ^2J = 13.6 Hz, ^3J = 7.5 Hz, ^3J = 5.7 Hz, 1 H, CH_2), 2.32 (ddd, ^2J = 13.6 Hz, ^3J = 10.4 Hz, ^3J = 6.6 Hz, 1 H, CH_2), 2.19 (s, 3H, CH_3), 1.84 (s, 3 H, CH_3).

^{13}C NMR (126 MHz; DMSO-d_6): δ = 169.3 (CO$_2$Me), 169.2 (CO$_2$Me), 154.8 (C), 149.8 (C), 144.5 (C), 143.5 (C), 106.0 (CH), 105.6 (CH), 97.5 (C), 52.5 (CH_3O), 52.3 (CH_3O), 49.4 (CH), 33.8 (CH_3N), 31.9 (CH), 31.1 (CH_2), 13.3 (CH_3), 12.6 (CH_3).

IR (film): 3414, 3342, 2952, 1747, 1733, 1630, 1568, 1438, 1395, 1267, 1237, 1155, 1025, 960, 789, 760, 639 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{17}H_{24}N_3O_5$: 350.1710; found: 350.1708.

Synthesis of methyl 1-(1,3-dimethyl-1*H*-pyrazol-5-yl)-2-oxo-5-phenylpyrrolidine-3-carboxylate (5)



3d **5**, 42%, *dr* 55:45

A 0.15 M solution of TsOH·H_2O (110 mg, 0.58 mmol) in toluene was added to aminopyrazole **3d** (100 mg, 0.29 mmol). The resulting mixture was heated under reflux for 6 h. Then the reaction mixture was quenched with aq. solution of $NaHCO_3$ and extracted with ethyl acetate (3×15 mL), dried with Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on a silica gel to afford product **5** as a mixture of two diastereomers (**A**:**B**) in 55:45 ratio. Yield: 38 mg (42%). Colorless oil, R_f=0.54 (ethyl acetate).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39–7.27 (m, 10 H, 5×CH+5×CH, **A**, **B**), 5.75 (s, 1 H, CH, **A**), 5.68 (s, 1 H, CH, **B**), 5.14 (dd, ^3J = 8.0 Hz, ^3J = 6.3 Hz, 1 H, CH, **B**), 5.04 (dd, ^3J = 9.0 Hz, ^3J = 7.4 Hz, 1 H, CH, **A**), 3.98

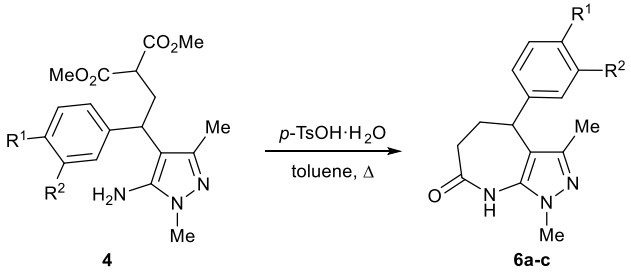
(dd, ^3J = 10.0 Hz, ^3J = 9.4 Hz, 1 H, CH, **A**), 3.96 (dd, ^3J = 9.9 Hz, ^3J = 5.3 Hz, 1 H, CH, **B**), 3.74 (s, 3 H, CH_3, **A**), 3.73 (s, 3 H, CH_3, **B**), 3.50 (s, 3 H, CH_3, **A**), 3.49 (s, 3 H, CH_3, **B**), 2.87 (ddd, ^2J = 12.9 Hz, ^3J = 9.4 Hz, ^3J = 7.4 Hz, 1 H, CH_2, **A**), 2.84 (ddd, ^2J = 13.3 Hz, ^3J =8.0 Hz, ^3J = 5.3 Hz, 1 H, CH_2, **B**), 2.39 (ddd, ^2J = 13.3 Hz, ^3J = 9.9 Hz, ^3J = 6.3 Hz, 1 H, CH_2, **B**), 2.29 (ddd, ^2J = 12.9 Hz, ^3J = 10.0 Hz, ^3J = 9.0 Hz, 1 H, CH_2, **A**), 1.97 (s, 3 H, CH_3, **B**), 1.96 (s, 3 H, CH_3, **A**).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.2 (C), 170.1 (C), 170.0 (C), 169.8 (C), 145.7 (C), 145.6 (C), 140.1 (C), 139.8 (C), 135.8 (C), 135.7 (C), 128.9 (CH), 128.4 (2×CH), 128.3 (2×CH), 127.3 (2×CH), 127.2 (2×CH), 126.9 (CH), 100.5 (CH), 100.2 (CH), 63.2 (CH), 62.3 (CH), 52.6 (CH_3O), 52.5 (CH_3O), 47.9 (CH), 47.6 (CH), 35.7 (CH_3N), 35.6 (CH_3N), 33.0 (CH_2), 32.4 (CH_2), 13.5 (2×CH_3).

IR (film): 3413, 3131, 3064, 3033, 2953, 2928, 2854, 2255, 2126, 1962, 1891, 1744, 1605, 1557, 1494, 1457, 1438, 1413, 1385, 1354, 1283, 1256, 1223, 1196, 1169, 1095, 1030, 1008, 930, 870, 759 cm^{-1}.

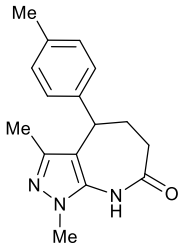
HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{17}H_{20}N_3O_3$: 314.1499; found: 314.1494.

Synthesis of tetrahydropyrazolo[3,4-*b*]azepines 6a-c



A 0.15 M solution of TsOH·H_2O (2 equiv) in toluene was added to 5-aminopyrazole derivative **4** (1 equiv). The resulting mixture was heated under reflux for 3–8 h. Then the mixture was quenched with aq. solution of $NaHCO_3$ and extracted with ethyl acetate (3×15 mL), dried with Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on a silica gel to afford the desired product.

1,3-Dimethyl-4-(*p*-tolyl)-4,5,6,8-tetrahydropyrazolo[3,4-*b*]azepin-7(1*H*)-one (6a) was synthesized from dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(*p*-tolyl)ethyl}malonate **4a** (100 mg, 0.28 mmol) and TsOH·H_2O (106 mg, 0.56 mmol). Yield: 39 mg (52%). Colorless solid, R_f=0.49 (ethyl acetate).



^{1}H NMR (500 MHz; DMSO-d_6): δ = 9.86 (br. s, 1 H, NH), 7.08 (d, ^3J = 8.7 Hz, 2 H, Ar), 6.98 (d, ^3J = 8.7 Hz, 2 H, Ar), 4.01 (dd, ^3J = 8.6 Hz, ^3J = 6.8 Hz, 1 H, CH), 3.62 (s, 3 H, CH_3N), 2.45–2.34 (m, 2 H, CH_2), 2.25 (s, 3 H, CH_3), 2.26–2.19 (m, 1 H, CH_2), 1.76 (ddd, ^2J = 14.4 Hz, ^3J = 9.6 Hz, ^3J = 8.6 Hz, 1 H, CH_2), 1.55 (s, 3 H, CH_3).

^{13}C NMR (126 MHz; DMSO-d_6): δ = 173.5 (CO), 145.2 (C), 142.2 (C), 135.6 (C), 135.0 (C), 128.9 (2×CH), 127.3 (2×CH), 106.0 (C), 40.1 (CH), 35.1 (CH_3N), 33.4 (CH_2), 30.9 (CH_2), 20.5 (CH_3), 12.5 (CH_3).

IR (KBr): 3295, 2997, 2956, 2843, 2826, 2590, 1712, 1668, 1615, 1555, 1509, 1453, 1416, 1364, 1334, 1302, 1227, 1189, 1158, 1126, 1087, 1073, 1043, 1013, 985, 972, 947, 911, 833, 784, 769, 726 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{16}H_{20}N_3O$: 270.1601; found: 270.1600.

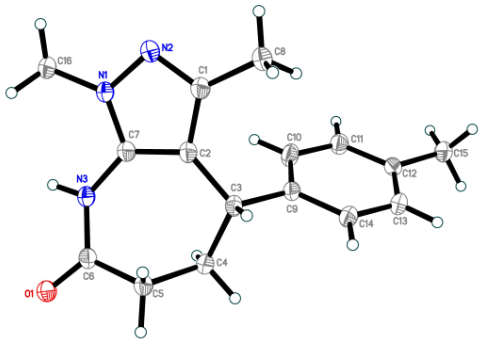
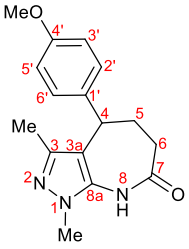


Figure S1. Molecular structure (ORTEP-3[S3]) from single crystal X-ray study of **6a** (CCDC 2144481).

4-(4-Methoxyphenyl)-1,3-dimethyl-4,5,6,8-tetrahydropyrazolo[3,4-*b*]azepin-7(1*H*)-one (6b) was



synthesized from dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(4-methoxyphenyl)ethyl}malonate **4b** (100 mg, 0.27 mmol) and TsOH·H_2O (101 mg, 0.53 mmol). Yield: 41 mg (54%); colorless solid, R_f=0.12 (ethyl acetate : petroleum ether; 2:1).

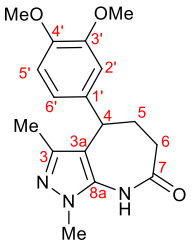
^{1}H NMR (500 MHz; DMSO-d_6): δ = 9.87 (br. s, 1 H, NH), 7.01 (br. d, ^3J = 8.7 Hz, 2 H, C(2')H), C(6')H), 6.84 (br. d, ^3J = 8.7 Hz, 2 H, C(3')H), C(5')H), 4.01 (dd, ^3J = 8.7 Hz, ^3J = 6.6 Hz, 1 H, C(4)H), 3.71 (s, 3 H, CH_3O), 3.62 (s, 3 H, CH_3N), 2.44–2.33 (m, 2 H, C(5)H_2), 2.21 (dd, ^2J = 14.4 Hz, ^3J = 8.5 Hz, ^3J = 6.5 Hz, 1 H, C(6)H_2), 1.75 (ddd, ^2J = 14.4 Hz, ^3J = 9.6 Hz, ^3J = 8.7 Hz, 1 H, C(6)H_2), 1.55 (s, 3 H, CH_3).

^{13}C NMR (126 MHz; DMSO-d_6): δ = 173.6 (CO), 157.6 (C(4')), 145.3 (C(3)), 137.2 (C(1')), 135.6 (C(8a)), 128.5 (C(2')H), C(6')H), 113.8 (C(3')H), C(5')H), 106.3 (C(3a)), 55.0 (CH_3O), 40.1 (C(4)H), 35.2 (CH_3N), 33.4 (C(5)H_2), 31.0 (C(6)H_2), 12.6 (CH_3).

IR (KBr): 3436, 3238, 3183, 3118, 3053, 3026, 2999, 2954, 2919, 2857, 2838, 2356, 1880, 1737, 1672, 1614, 1578, 1512, 1468, 1447, 1430, 1381, 1328, 1309, 1296, 1264, 1253, 1203, 1186, 1170, 1073, 1031, 994, 942, 882, 820, 781, 765, 728 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{16}H_{20}N_3O_2$: 286.1550; found: 286.1539.

4-(3,4-Dimethoxyphenyl)-1,3-dimethyl-4,5,6,8-tetrahydropyrazolo[3,4-*b*]azepin-7(1*H*)-one (6c) was



synthesized from dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(3,4-dimethoxyphenyl)ethyl}malonate **4f** (120 mg, 0.30 mmol) and TsOH·H_2O (113 mg, 0.59 mmol). Yield: 55 mg (58%). Colorless solid, R_f=0.21 (ethyl acetate).

^{1}H NMR (500 MHz; DMSO-d_6): δ = 9.84 (br. s, 1H, NH), 6.84 (br. d, ^3J = 8.2 Hz, 1 H, C(5')H), 6.75 (br. s, 1 H, C(2')H), 6.55 (dd, ^3J = 8.2 Hz, ^3J = 1.7 Hz, 1 H, C(6')H)), 4.00 (t, ^3J=7.5 Hz, 1 H, C(4)H), 3.71 (s, 3 H, CH_3O), 3.69 (s, 3 H, CH_3O), 3.62 (s, 3 H, CH_3N), 2.41–2.35 (m, 2 H, C(5)H_2), 2.26–2.19 (m, 1 H, C(6)H_2), 1.87–1.77 (m, 1 H, C(6)H_2), 1.53 (s, 3 H, CH_3).

^{13}C NMR (126 MHz; DMSO-d_6): δ = 173.6 (CO), 148.6 (C), 147.2 (C), 145.3 (C(3)), 137.8 (C(1')), 135.6 (C(8a)), 119.3 (C(6')), 111.7 (C(5')H), 111.6 (C(2')H)), 106.0 (C(3a)), 55.5 (CH_3O), 55.4 (CH_3O), 40.1 (C(4)H), 35.2 (CH_3N), 33.4 (C(5)H_2), 30.8 (C(6)H_2), 12.6 (CH_3).

IR (KBr): 3434, 3235, 3177, 3054, 3004, 2958, 2920, 2851, 2281, 2012, 1738, 1678, 1606, 1593, 1539, 1449, 1416, 1387, 1342, 1320, 1296, 1271, 1253, 1239, 1207, 1186, 1154, 1133, 1206, 947, 914, 871, 849 cm^{-1}.

HRMS (ESI-TOF): *m/z* [*M*+H]$^+$ calcd for $C_{17}H_{22}N_3O_3$: 316.1656; found: 316.1651.

DFT analysis of transformation of D–A cyclopropane 1a to pyrazoles 3a and 4a

Diverse conformational isomers of products (pyrazoles **3a** and **4a**) were optimized using the density functional theory at the B3LYP[S4,S5] level of theory with the 6-311++G** basis set for all atoms. The most stable conformers of **3a** and **4a** were reoptimized at B3LYP-D3[S6]/6-311++G**/SMD[S7](MeCN) level. The obtained results showed that *C*-alkylated pyrazole **4a** is 3.9 kcal/mol more stable than *N*-alkylated pyrazole **3a**, and it is the thermodynamically favourable product.

Reactants – 2-(*p*-tolyl)cyclopropane-1,1-diester **1a** and 1,3-dimethyl-5-aminopyrazole **2a** – were optimized at the same level of theory. Starting geometries of reactants were based on molecular structures of related compounds in the crystalline state. Additionally, for aminopyrazole **2a**, the Natural Bond Orbital (NBO) analysis[S8] was carried out. The calculated natural atomic charges on C(4) and exocyclic N atom are –0.409 and –0.828, respectively (Fig. S2). The charge distribution indicates that exocyclic N atom is more electronegative than C(4), and it is the preferred nucleophilic center/Lewis base. On the other hand, visualization of the frontier molecular orbitals showed that HOMO is a bonding orbital localized on C(4)=C(5) bond, while a lone pair localized on N atom of exocyclic amino group is HOMO–3 (Fig. S3). Energy difference between HOMO and HOMO–3 is 1.59 eV.

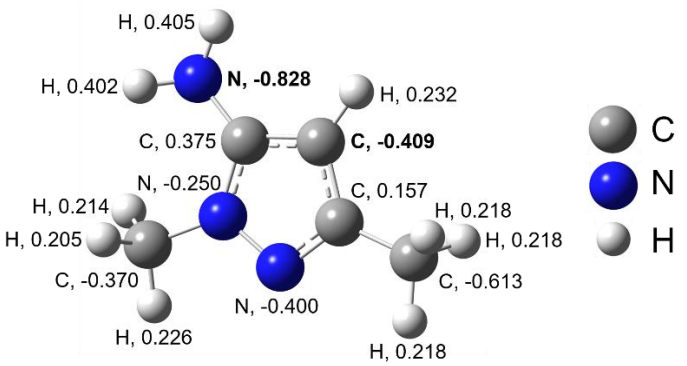


Figure S2. Atomic charges in compound **2a** calculated using natural population analysis at B3LYP-D3/6-311++G**/SMD(MeCN) level.

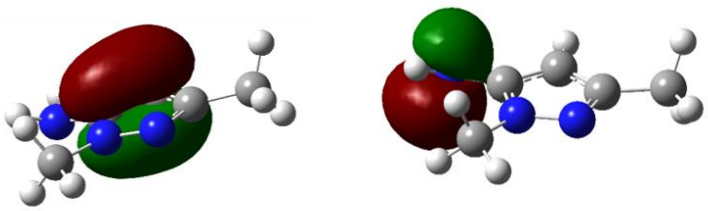


Figure S3. Atomic contributions to HOMO and (HOMO – 3) of compound **2a** (MOs visualized with an isovalue of 0.04).

All optimized geometries were characterized to be a minimum with no imaginary frequencies. Calculations were performed using Gaussian 16 software package.[S9] CYLview v1.0.600 Beta[S10] and GaussView 6.0.16[S11] programs were used to visualize the optimized structures and the frontier molecular orbitals. The optimized geometries are given after copies of NMR spectra.

References

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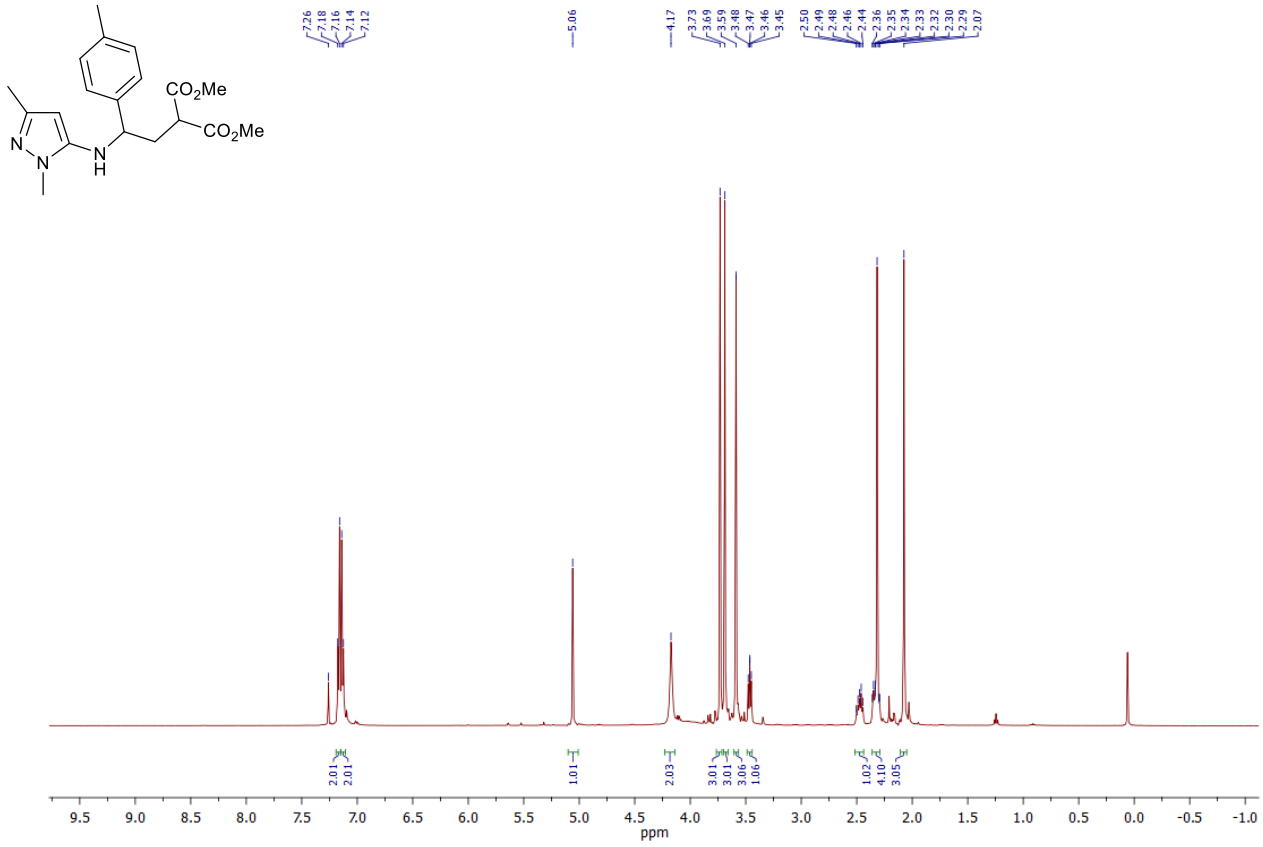
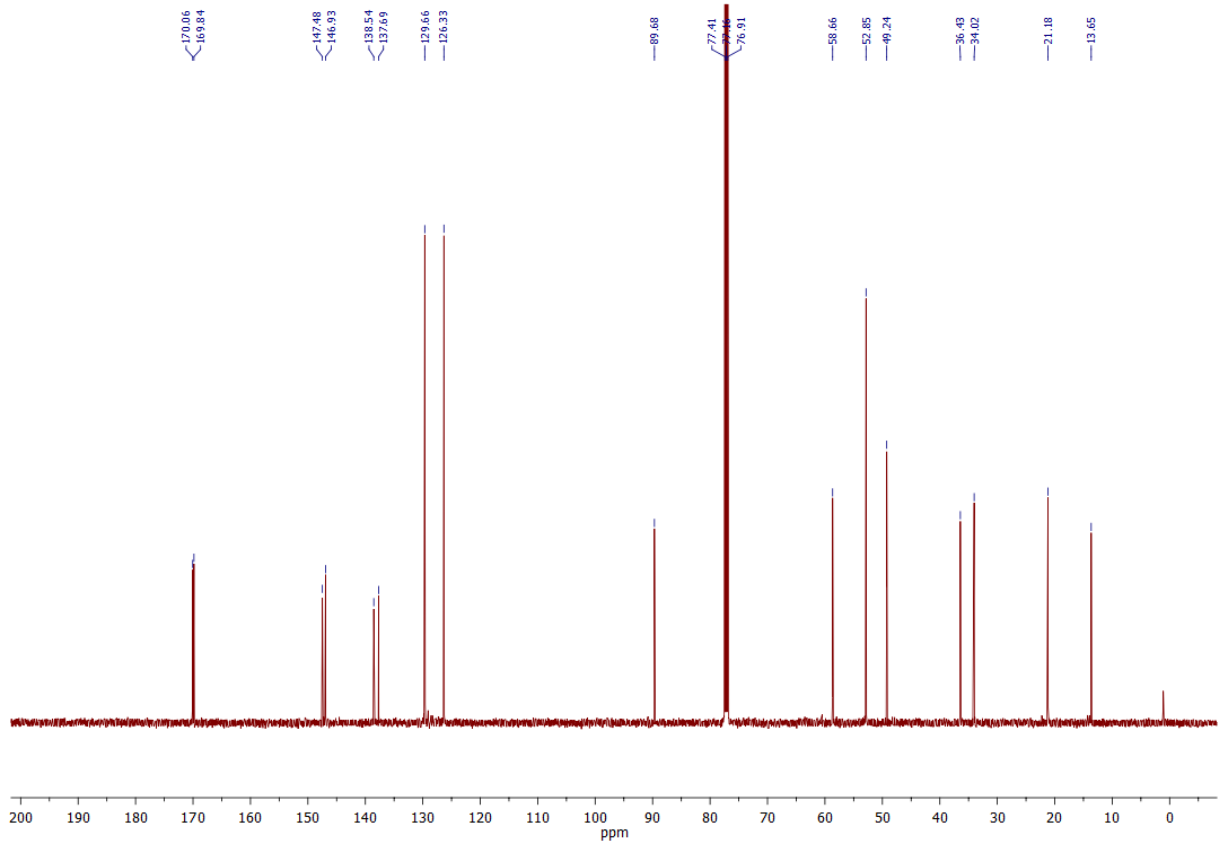
Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(*p*-tolyl)ethyl}malonate (3a)

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

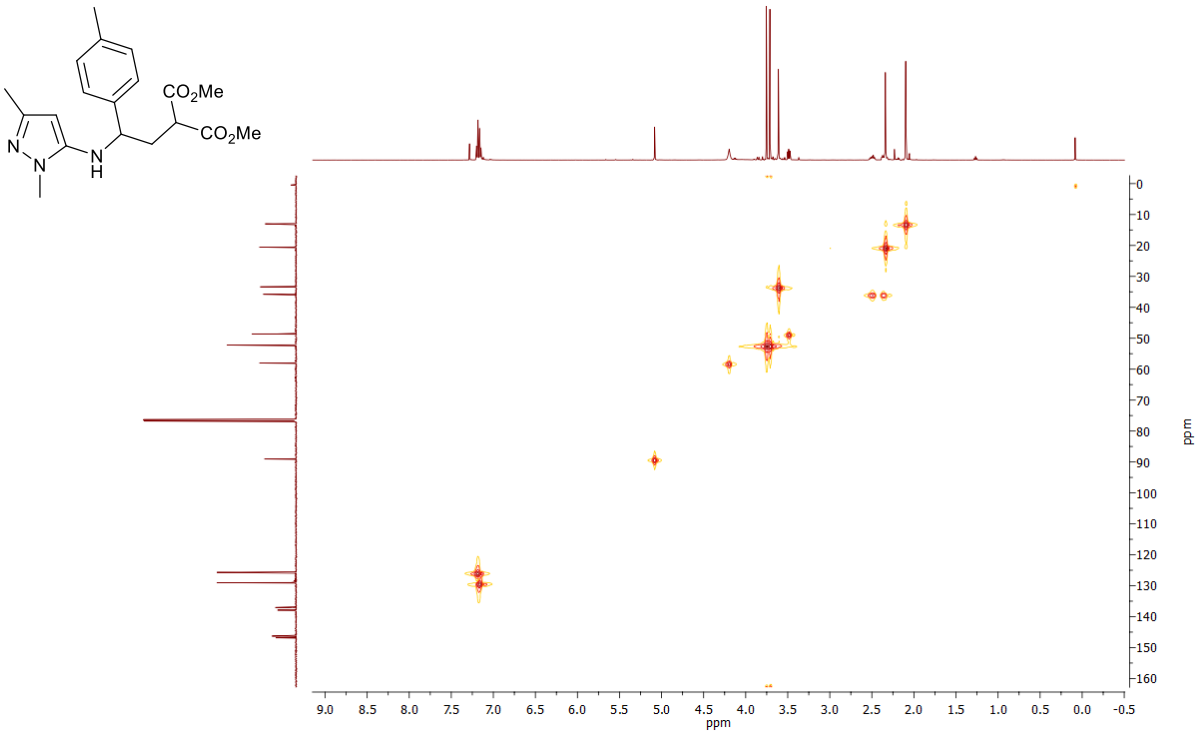


^{13}C NMR (126 MHz, $CDCl_3$)

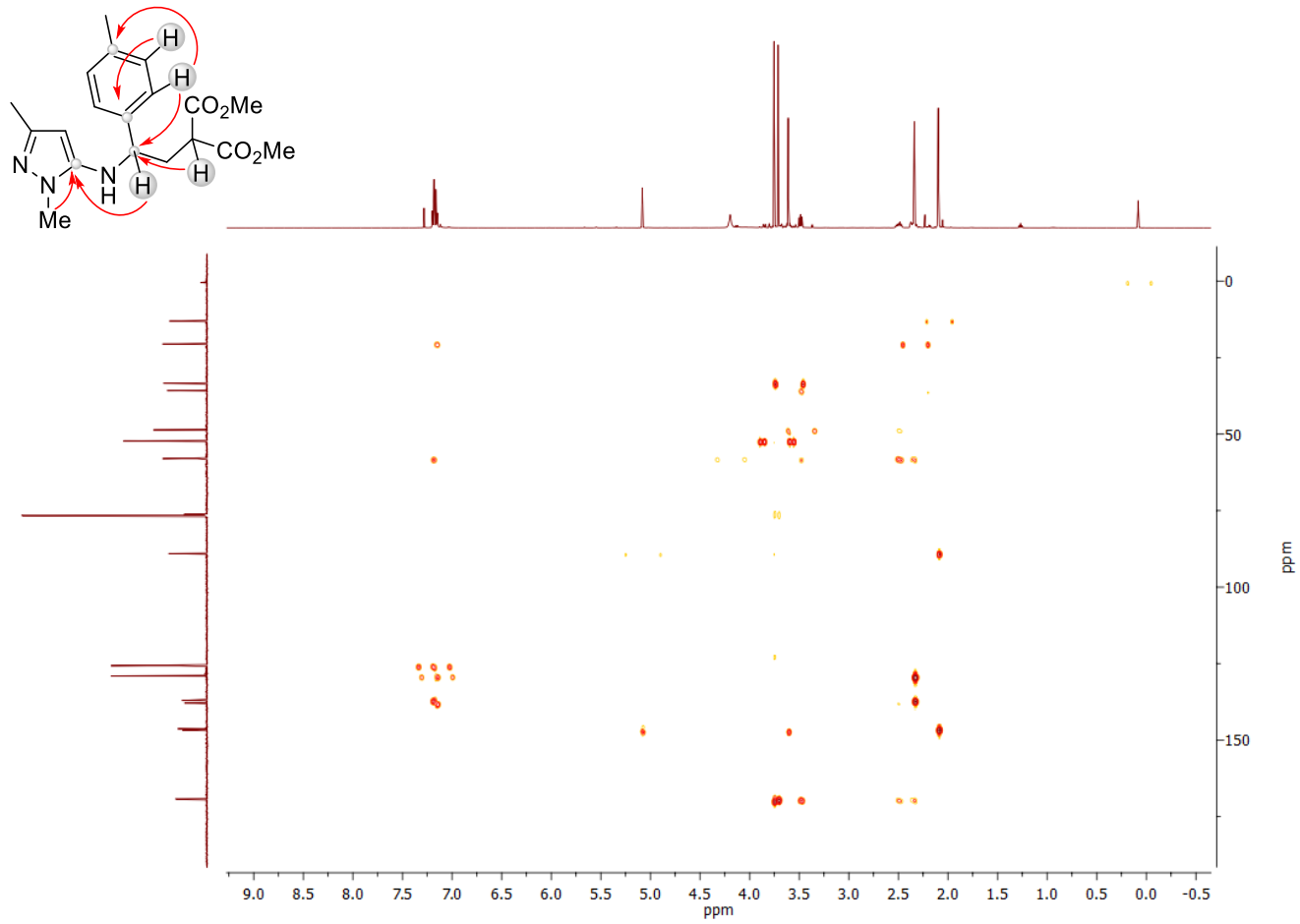


Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(*p*-tolyl)ethyl}malonate (3a)

HSQC ^{1}H-^{13}C ($CDCl_3$)

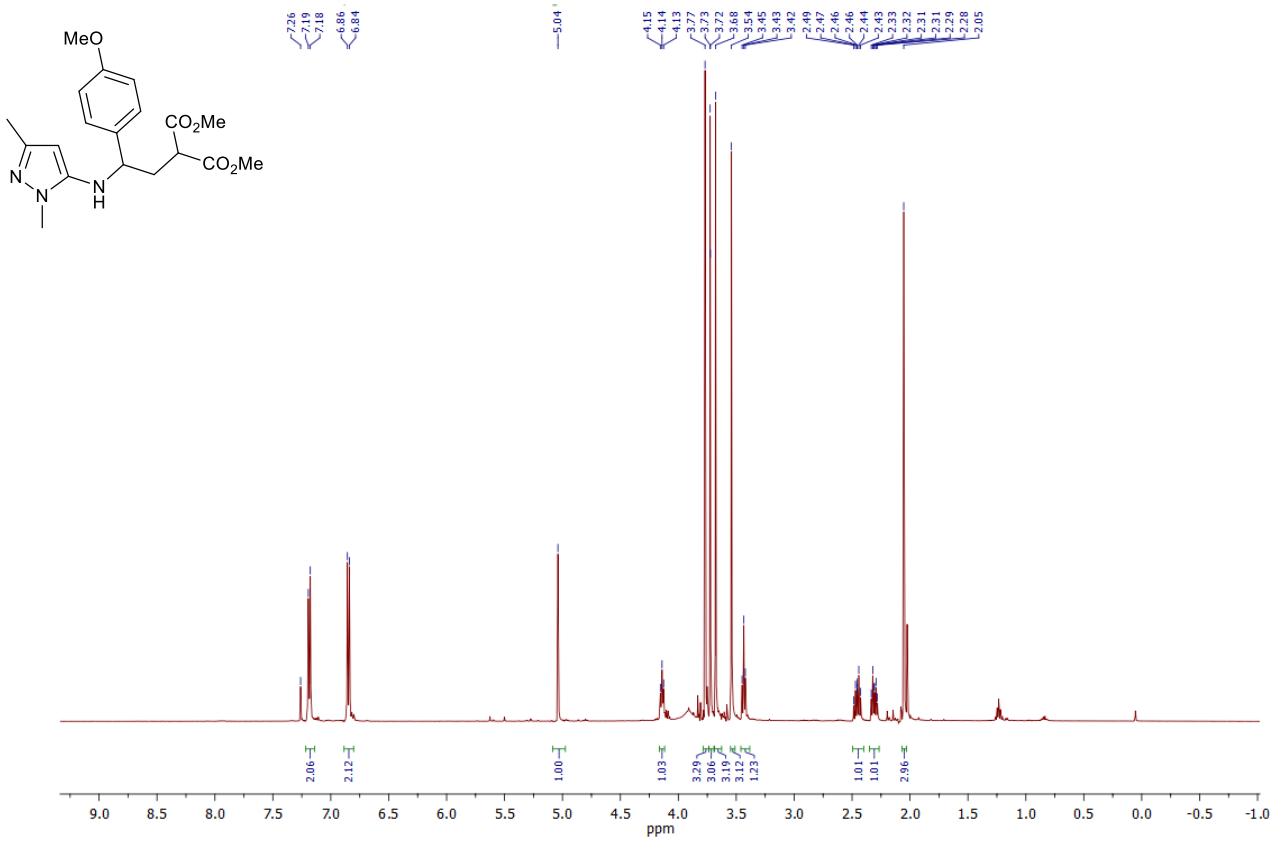


HMBC ^{1}H-^{13}C ($CDCl_3$)

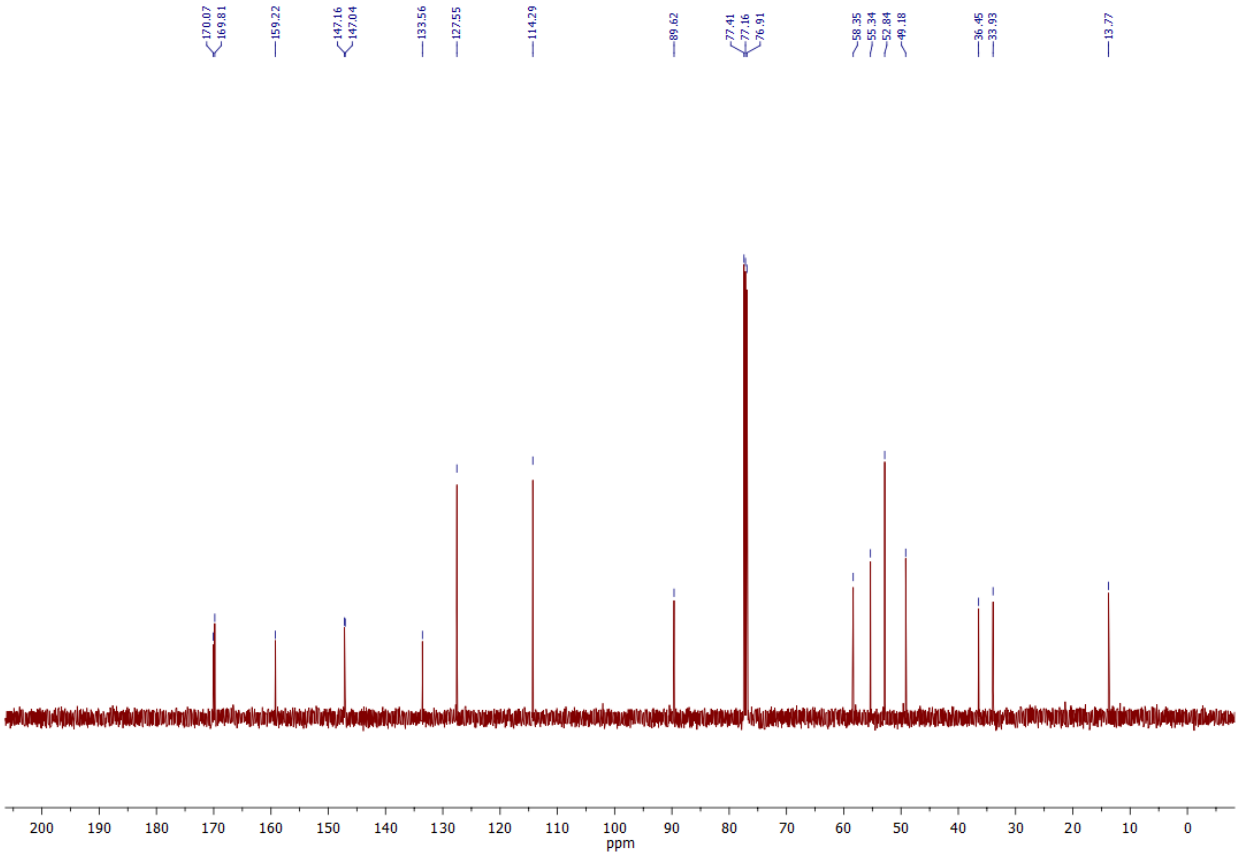


Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(4-methoxyphenyl)ethyl}malonate (3b)

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

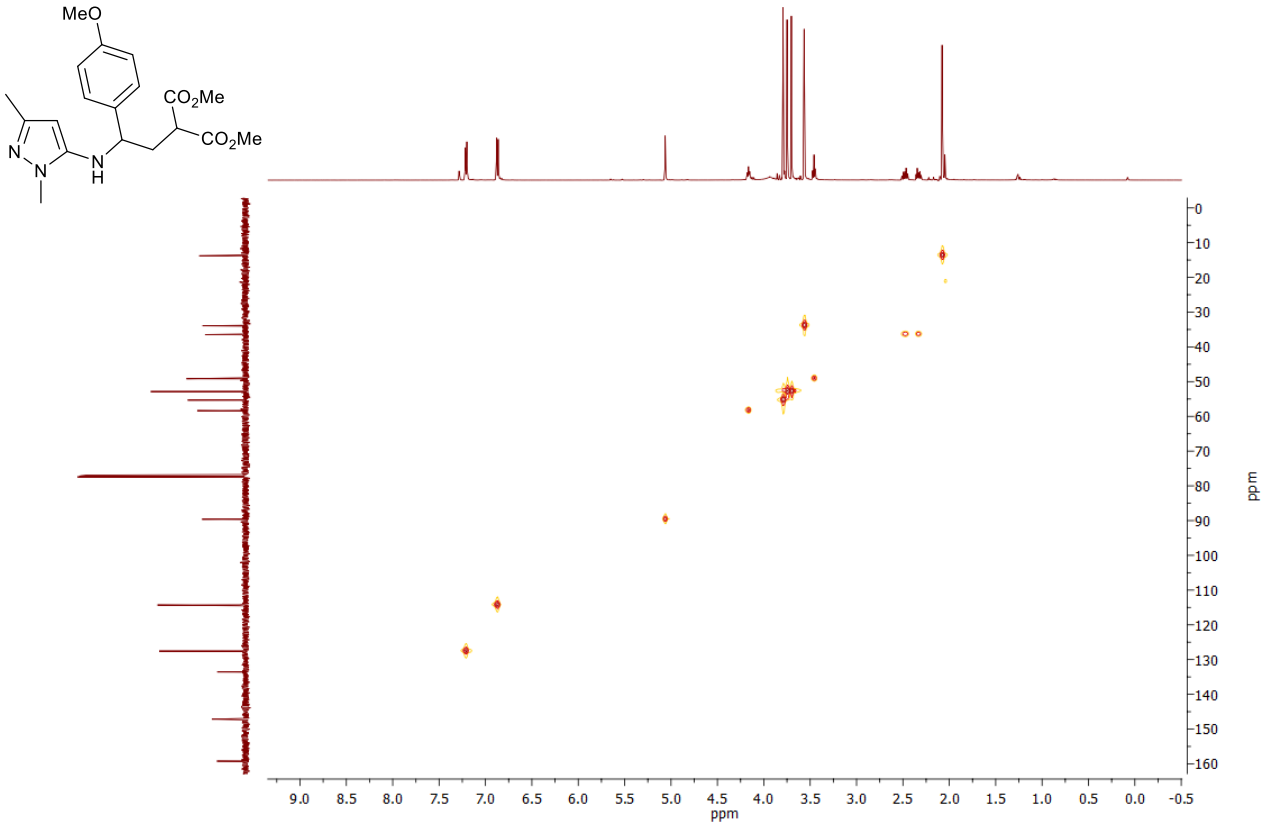


^{13}C NMR (126 MHz, $CDCl_3$)

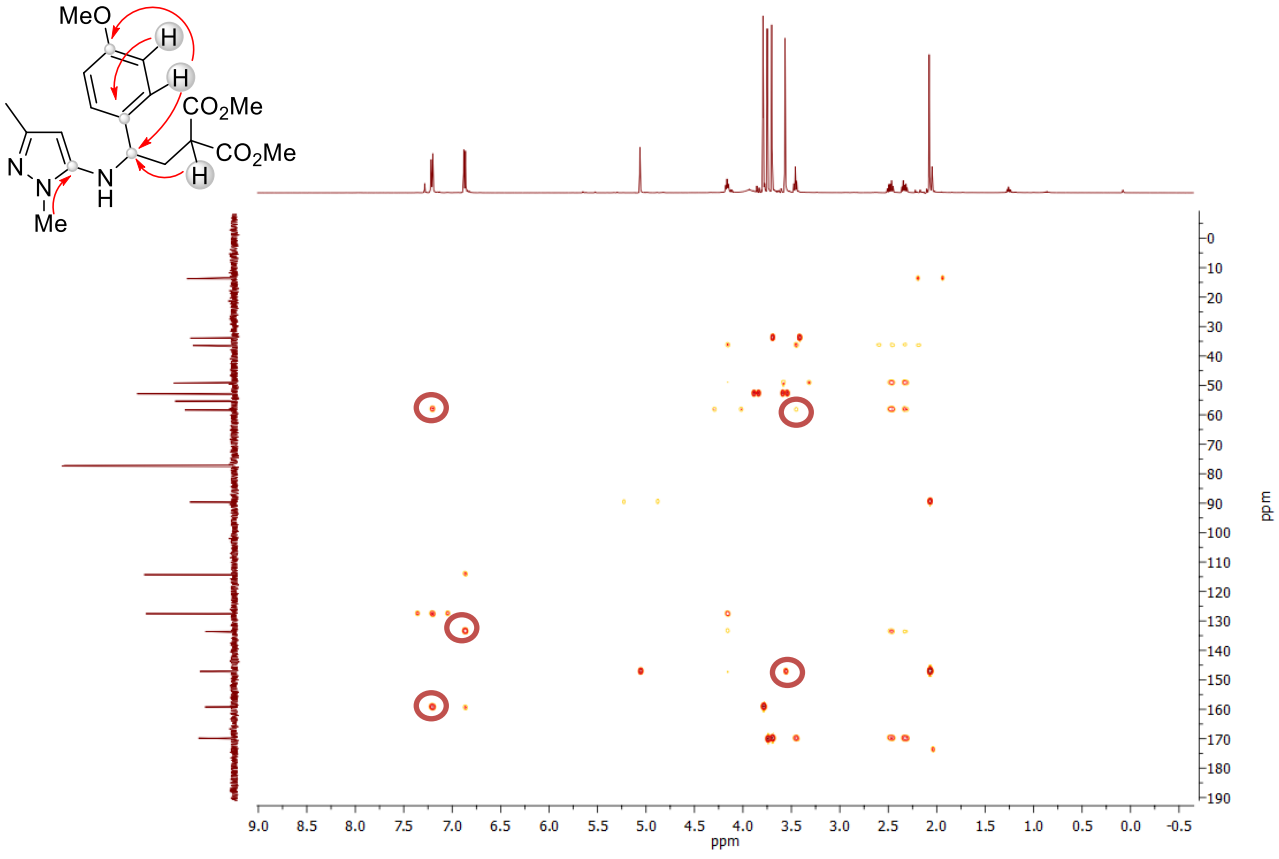


Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(4-methoxyphenyl)ethyl}malonate (3b)

HSQC ^{1}H-^{13}C ($CDCl_3$)

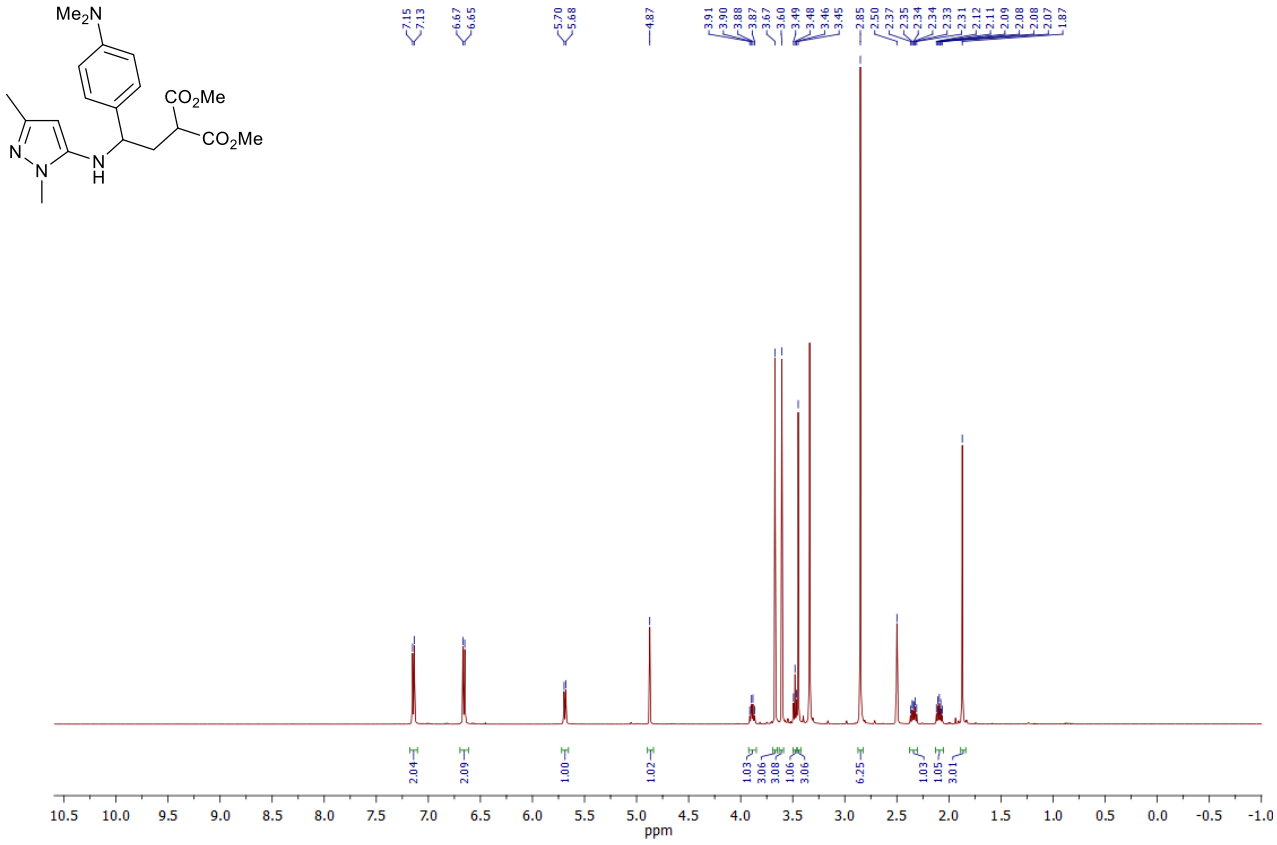


HMBC ^{1}H-^{13}C ($CDCl_3$)

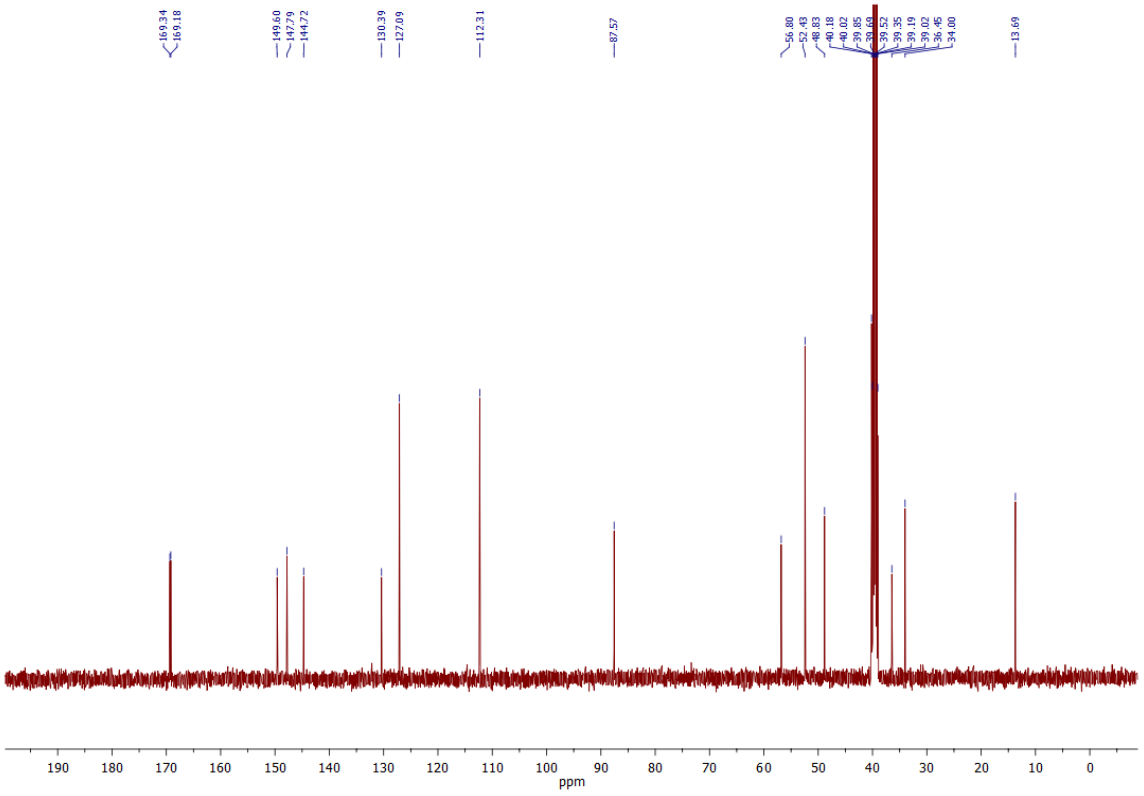


Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-[4-(dimethylamino)phenyl]ethyl}malonate (3c)

^{1}H NMR (500 MHz, DMSO-d_6)

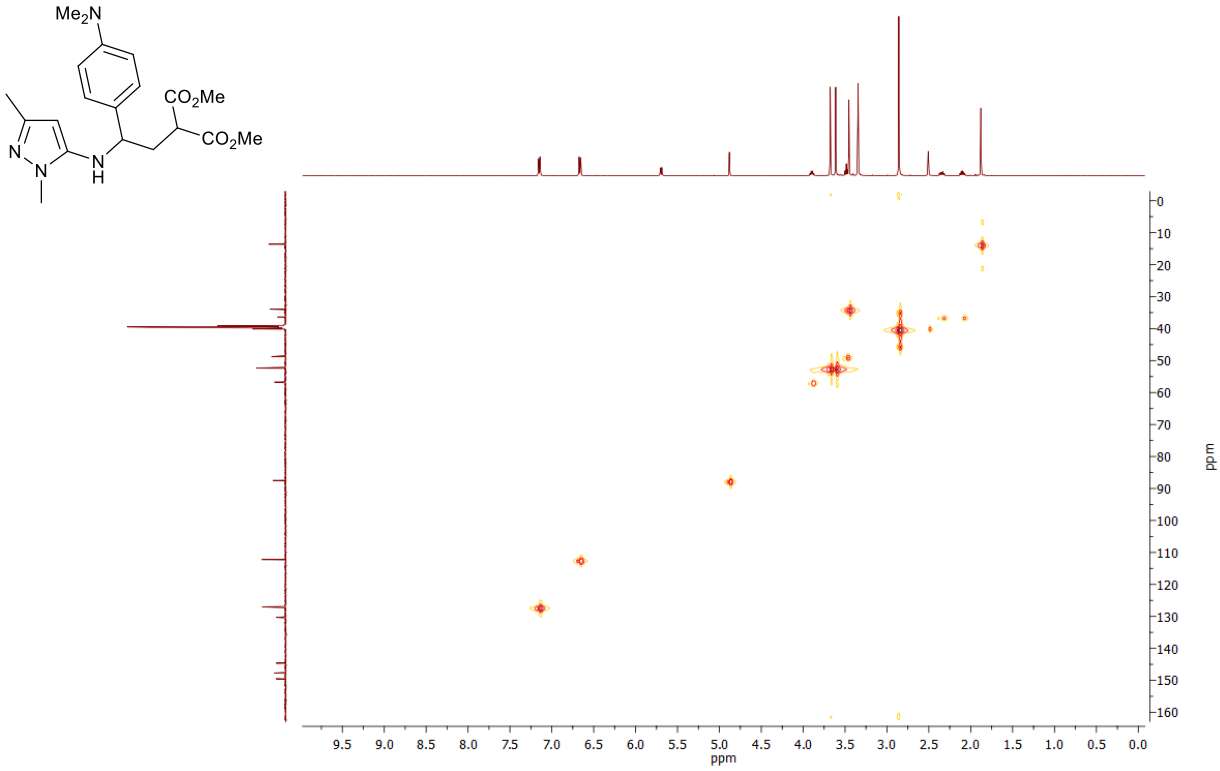


^{13}C NMR (126 MHz, DMSO-d_6)

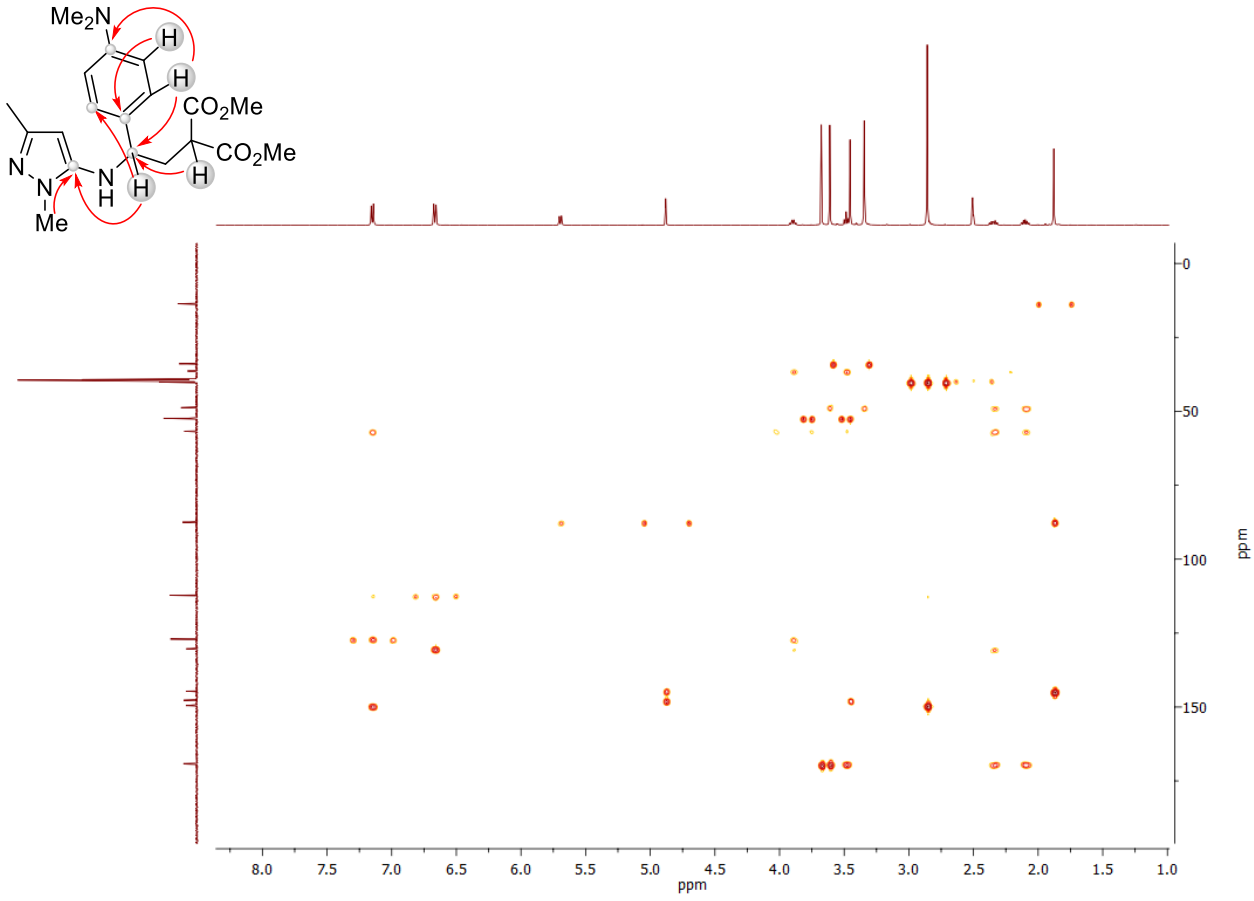


Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-[4-(dimethylamino)phenyl]ethyl}malonate (3c)

HSQC ^{1}H-^{13}C (DMSO-d_6)

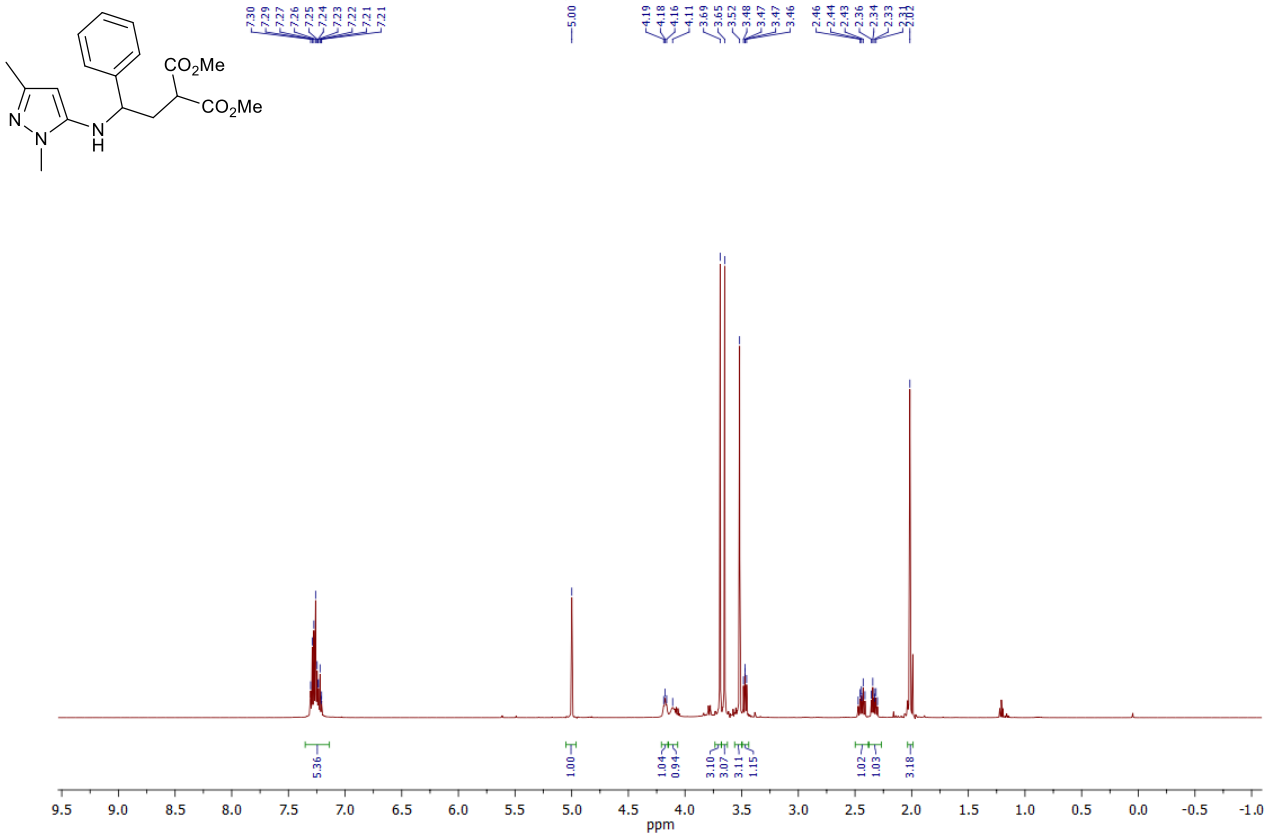


HMBC ^{1}H-^{13}C (DMSO-d_6)

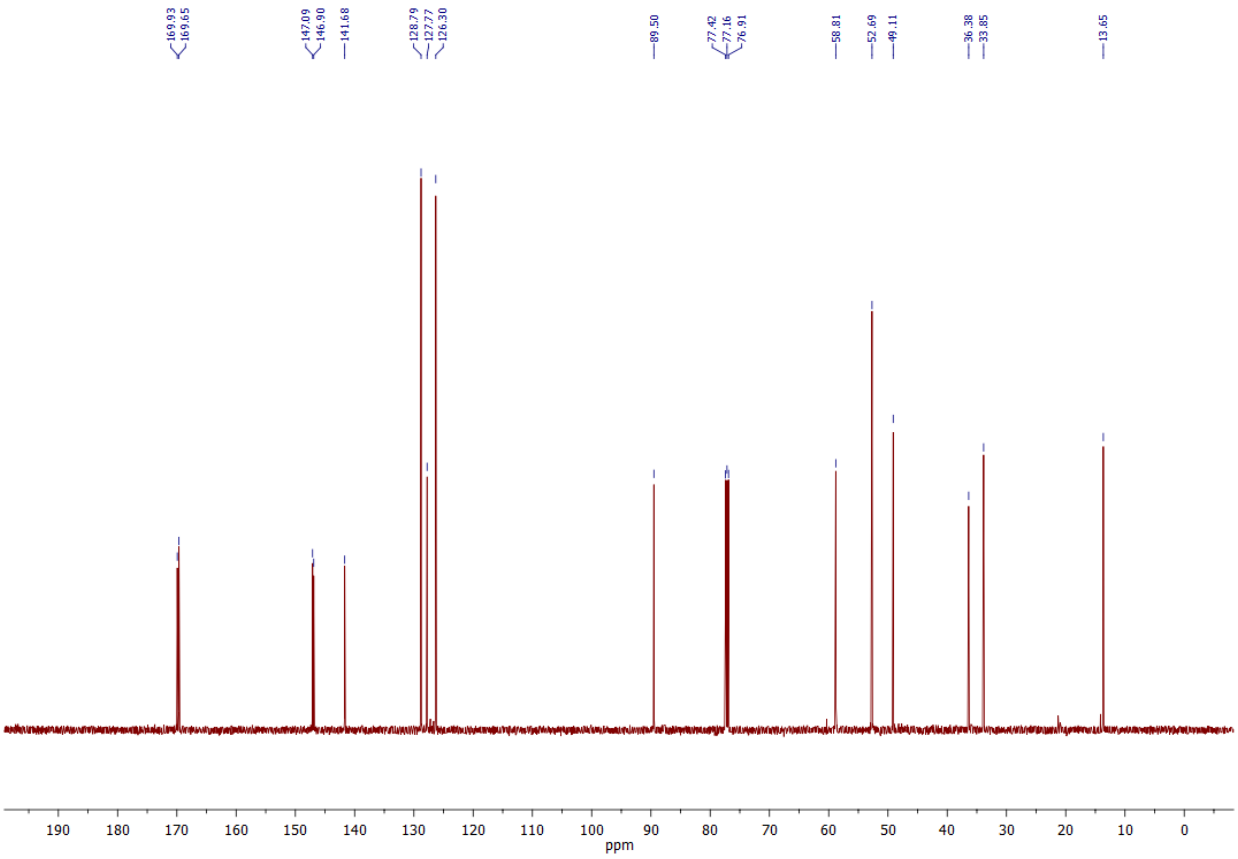


Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-phenylethyl}malonate (3d)

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

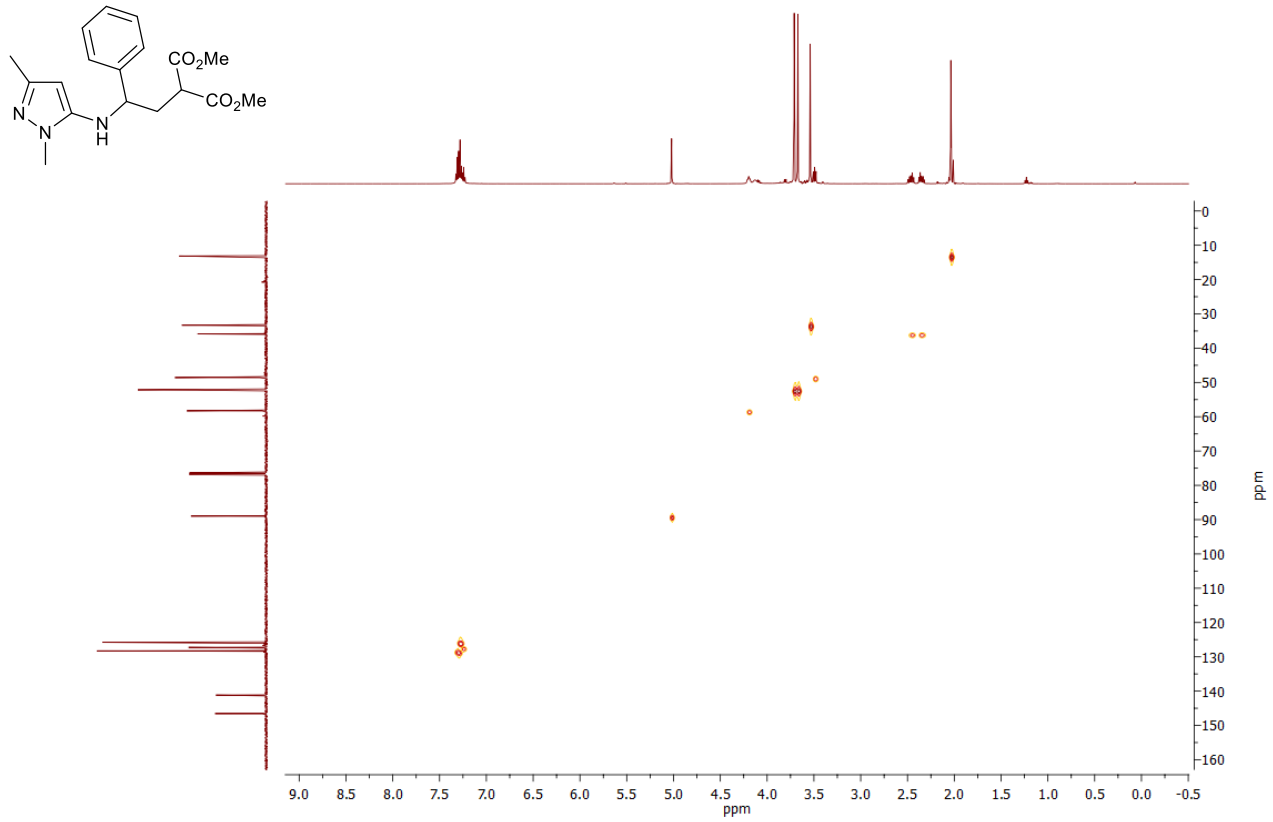


^{13}C NMR (126 MHz, $CDCl_3$)

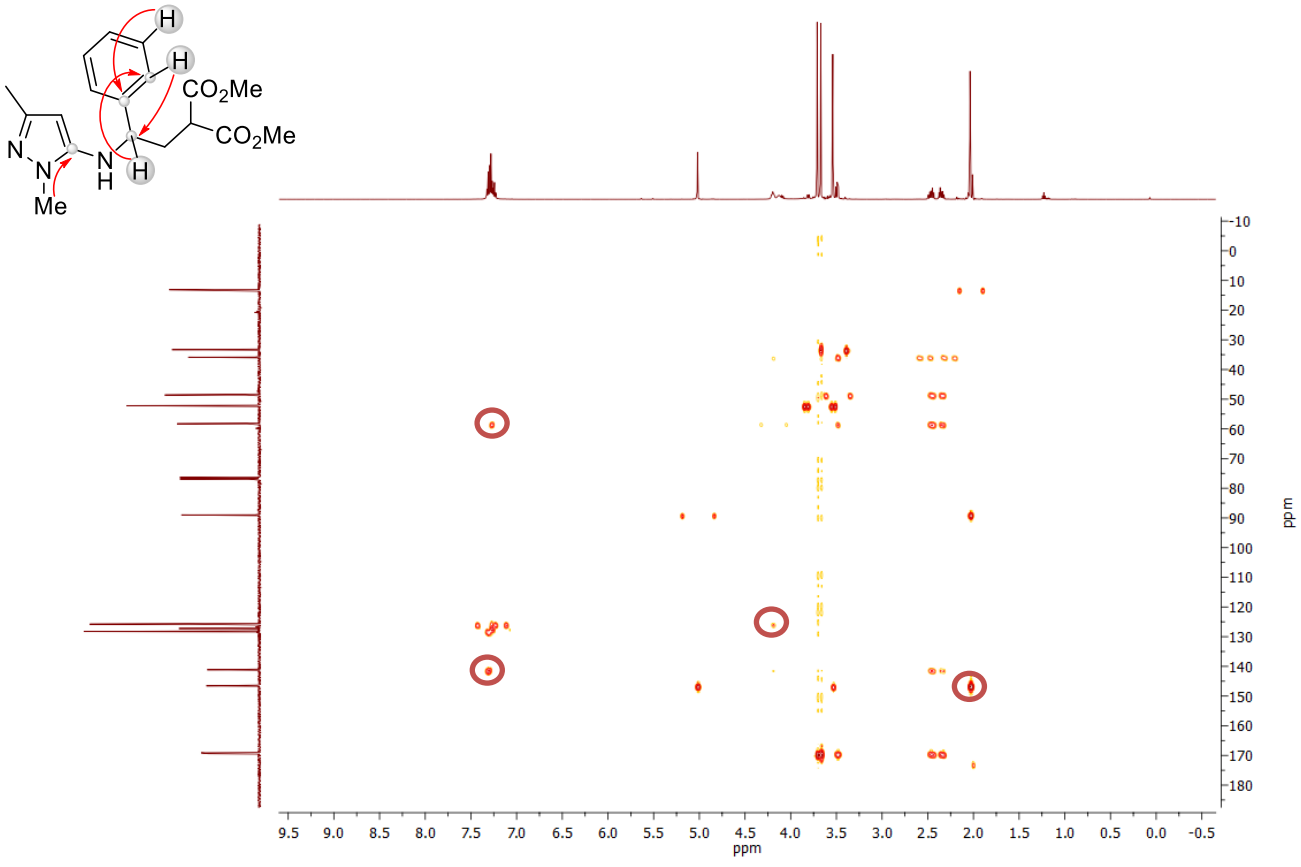


Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-phenylethyl}malonate (3d)

HSQC ^{1}H-^{13}C ($CDCl_3$)

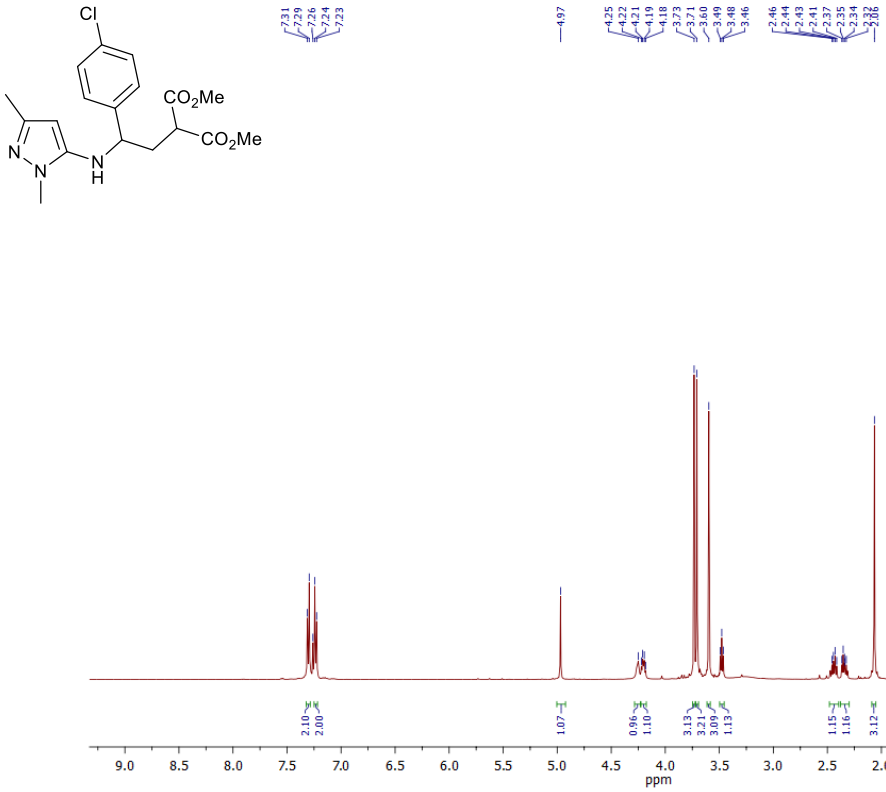


HMBC ^{1}H-^{13}C ($CDCl_3$)

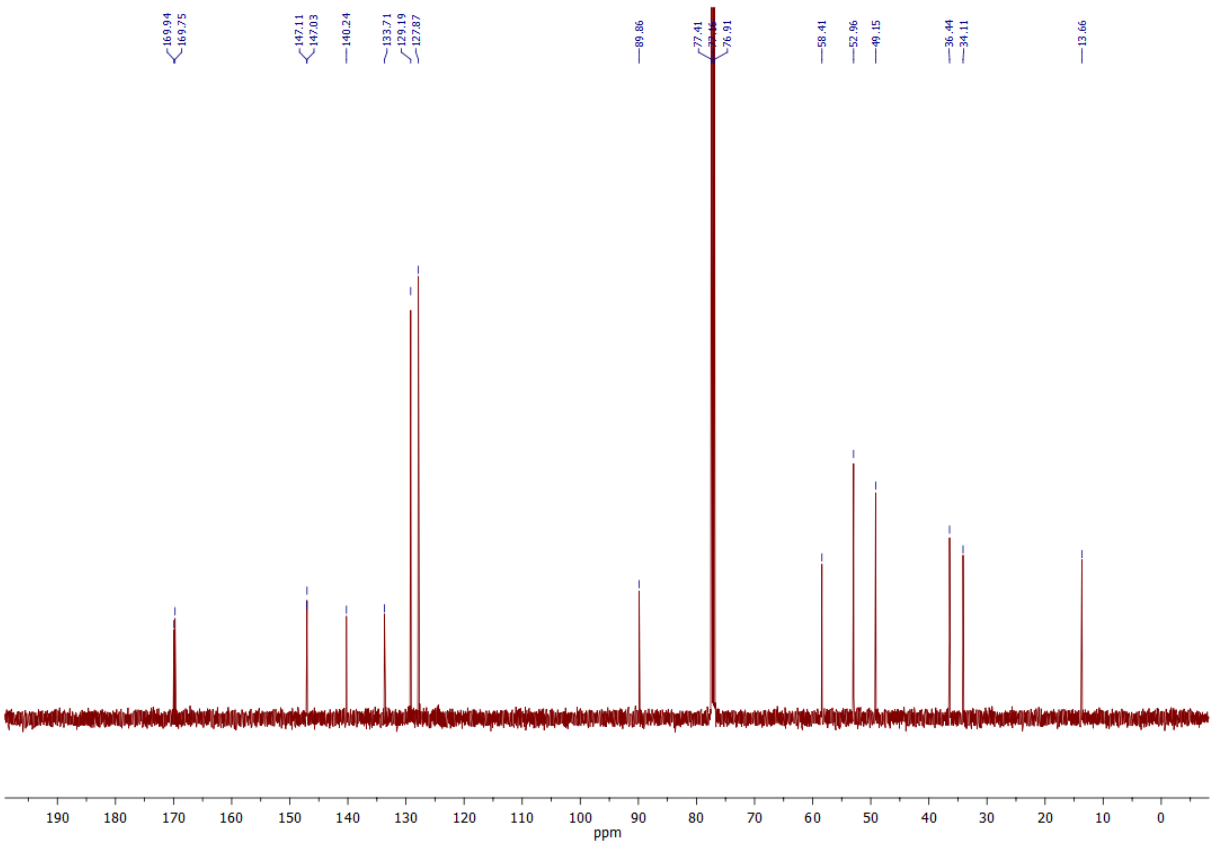


Dimethyl 2-{2-(4-chlorophenyl)-2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]ethyl}malonate (3e)

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

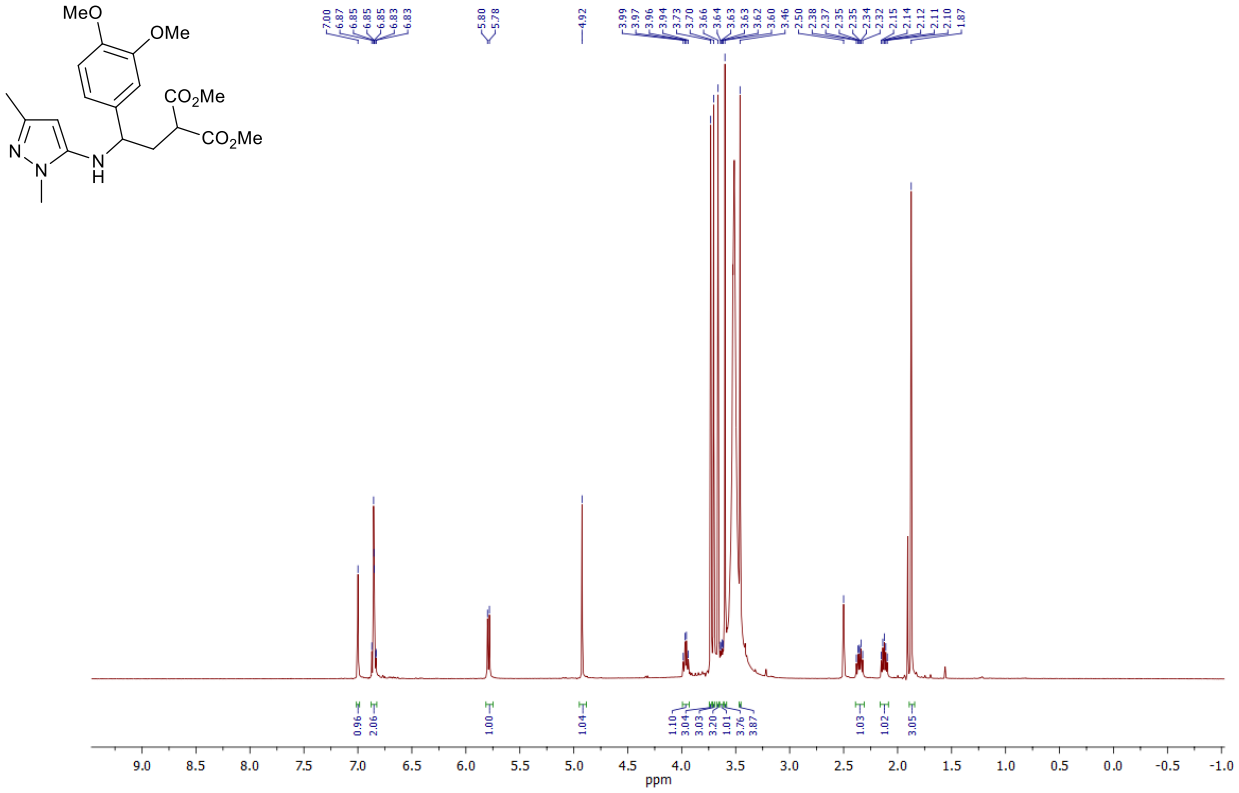


^{13}C NMR (126 MHz, $CDCl_3$)

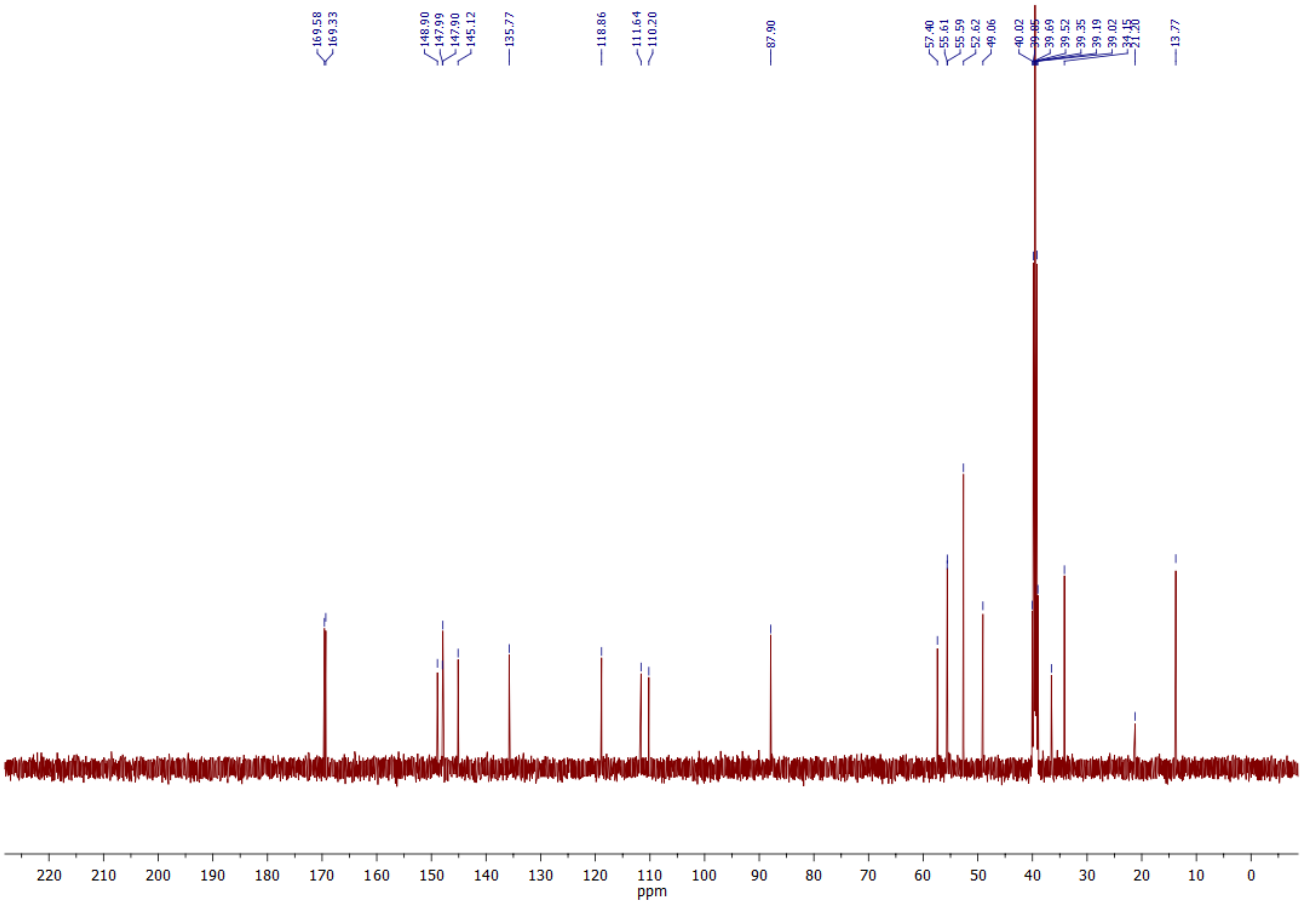


Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(5-methylfuran-2-yl)ethyl}malonate (3f)

^{1}H NMR (500 MHz, DMSO-d_6)

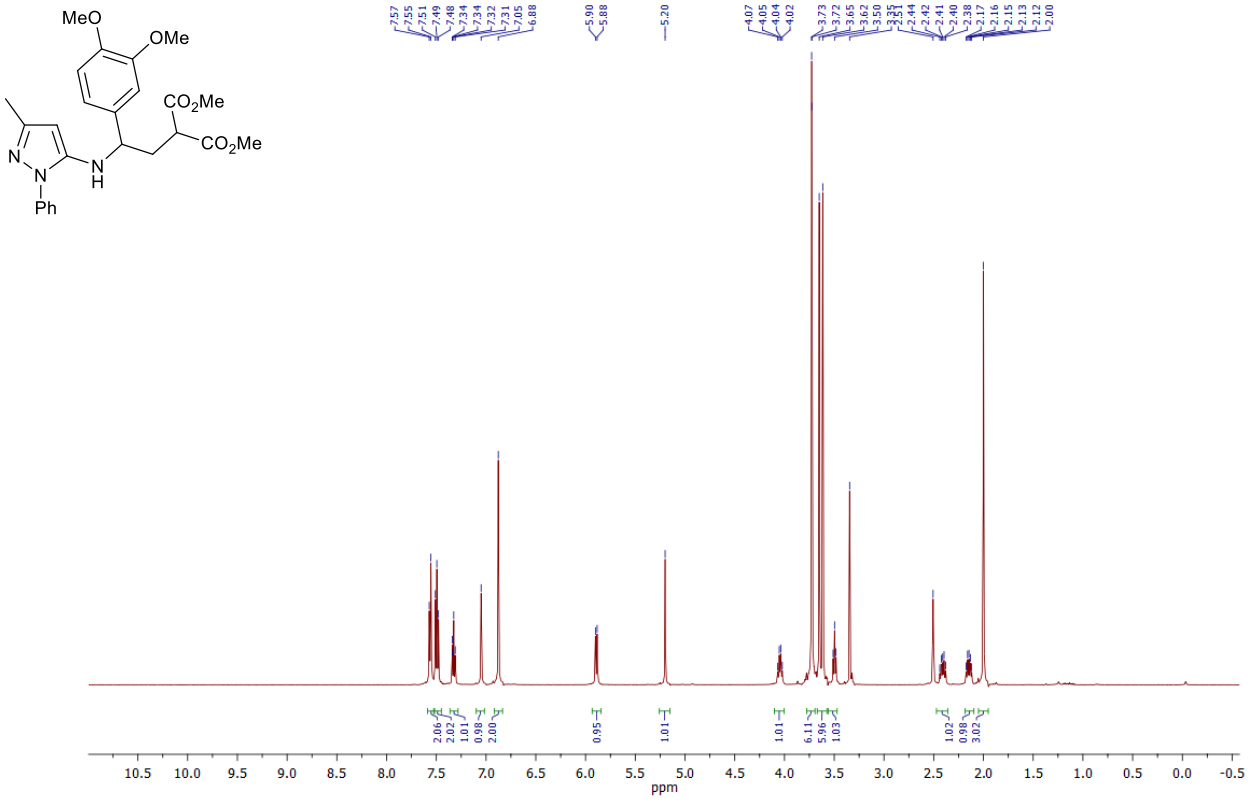


^{13}C NMR (126 MHz, DMSO-d_6)

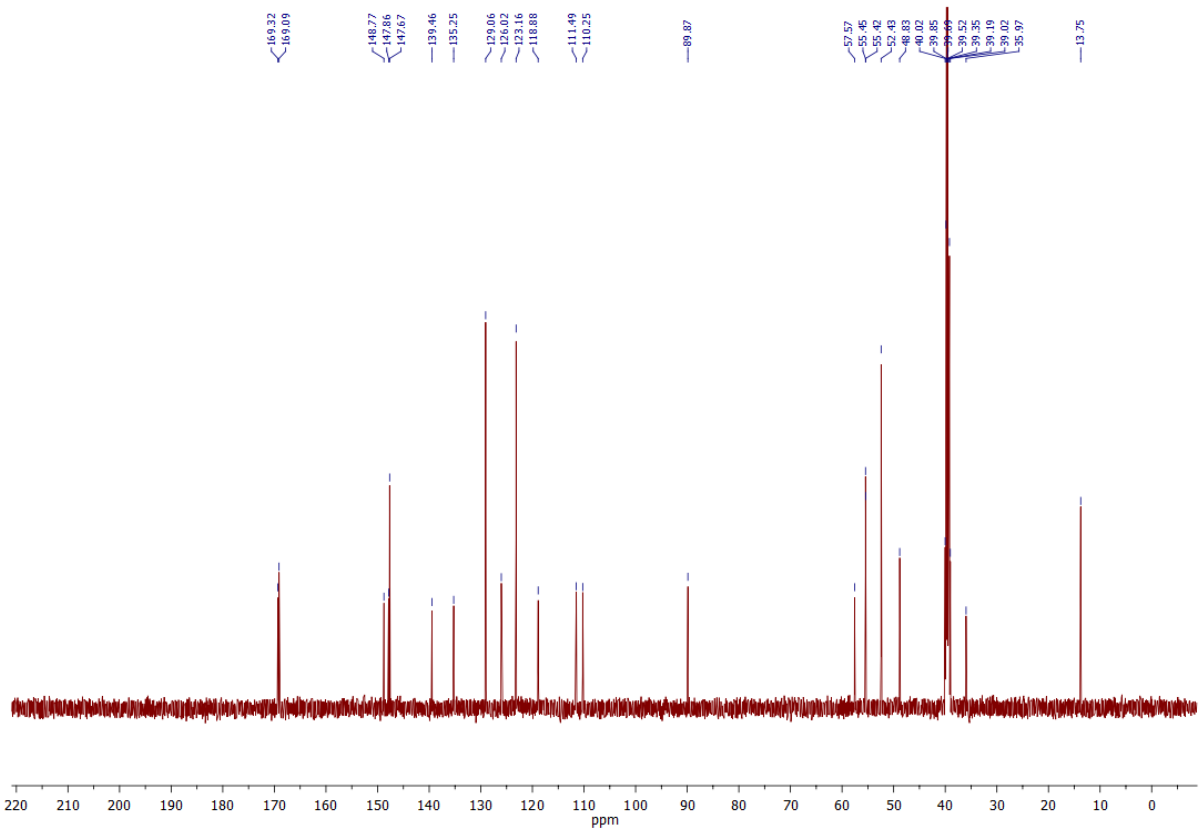


Dimethyl 2-{2-(3,4-dimethoxyphenyl)-2-[(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)amino]ethyl}malonate (3g)

^{1}H NMR (500 MHz, DMSO-d_6)

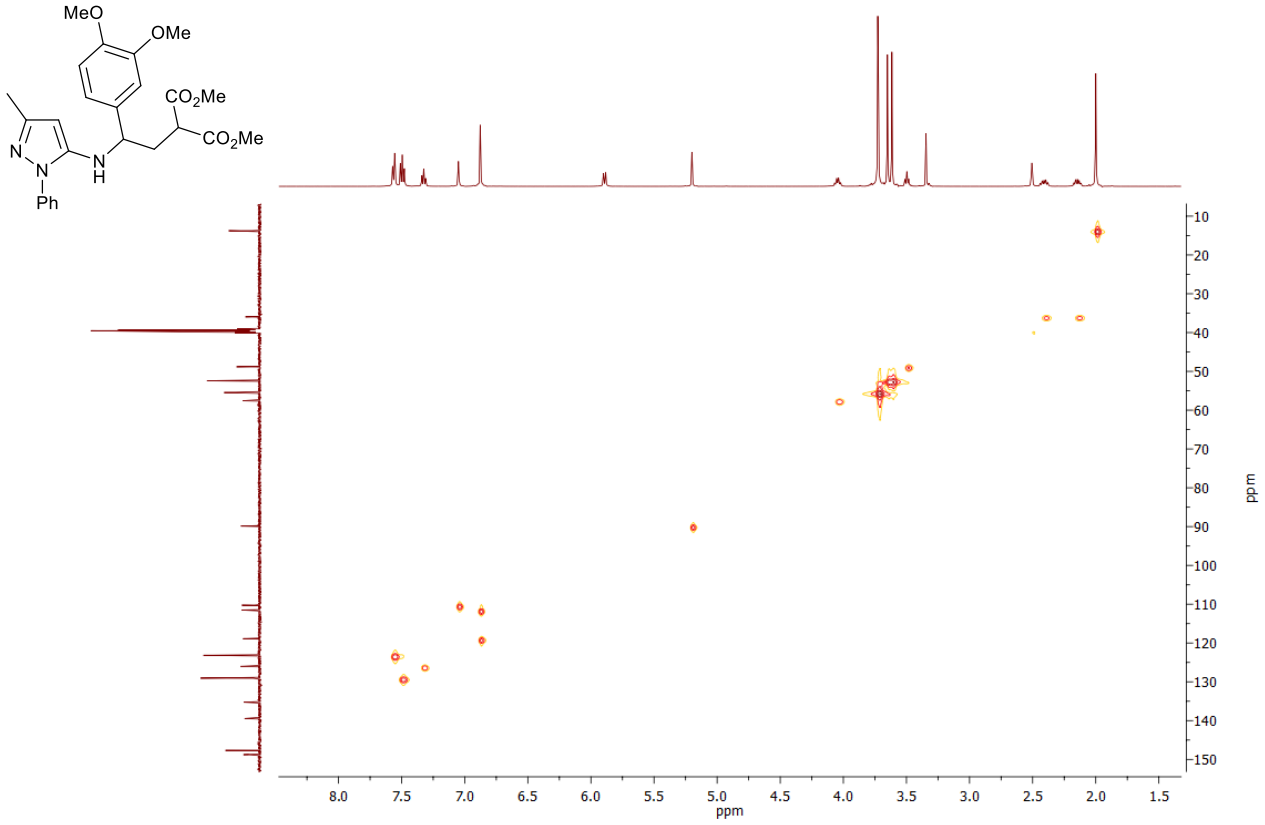


^{13}C NMR (126 MHz, DMSO-d_6)

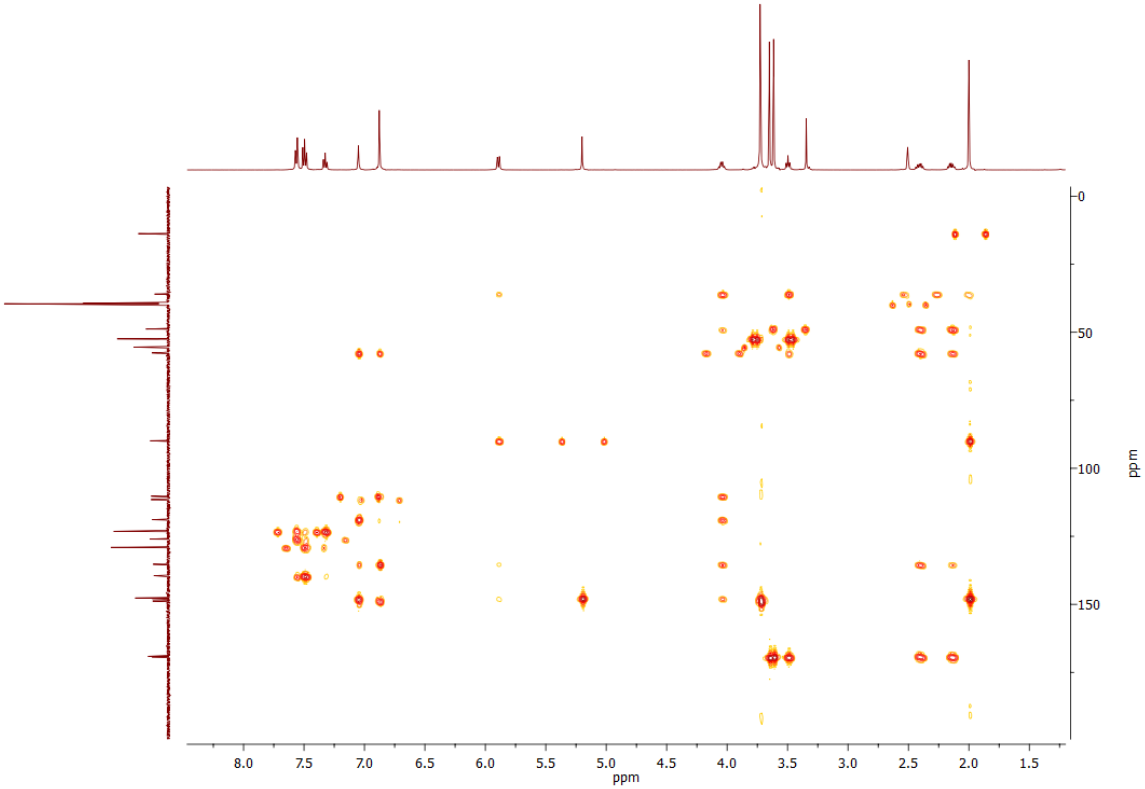


Dimethyl 2-{2-(3,4-dimethoxyphenyl)-2-[(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)amino]ethyl}malonate (3g)

HSQC ^{1}H-^{13}C (DMSO-d_6)

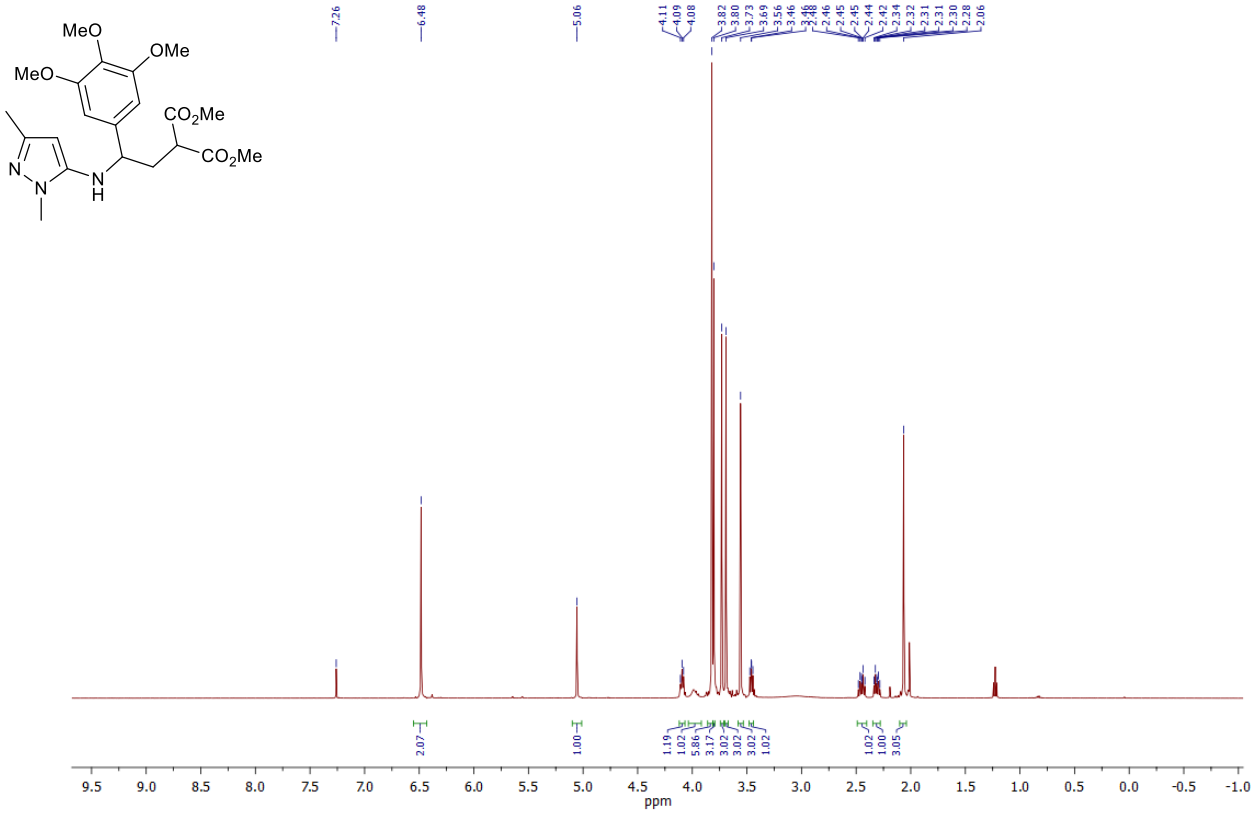


HMBC ^{1}H-^{13}C (DMSO-d_6)

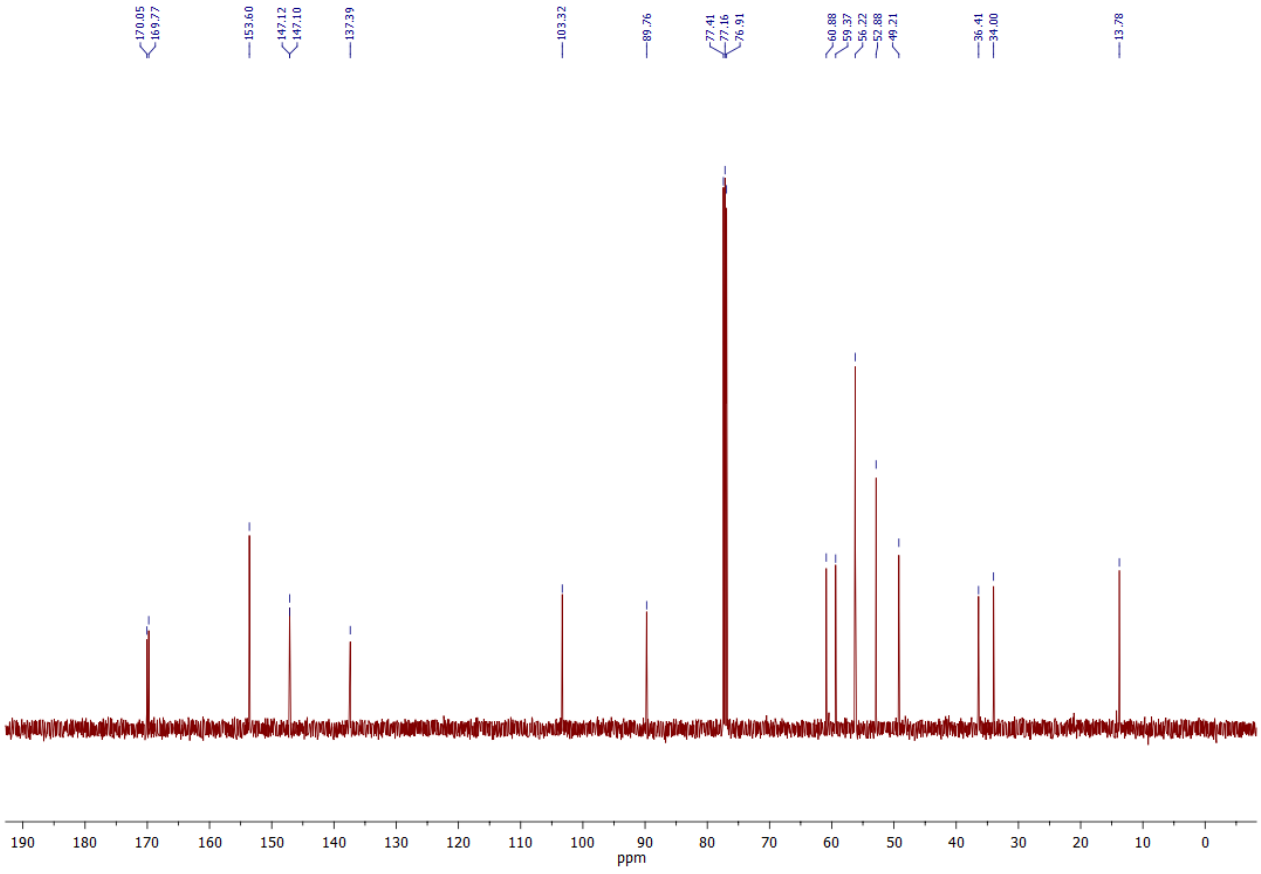


Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(3,4,5-trimethoxyphenyl)ethyl}malonate (3h)

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

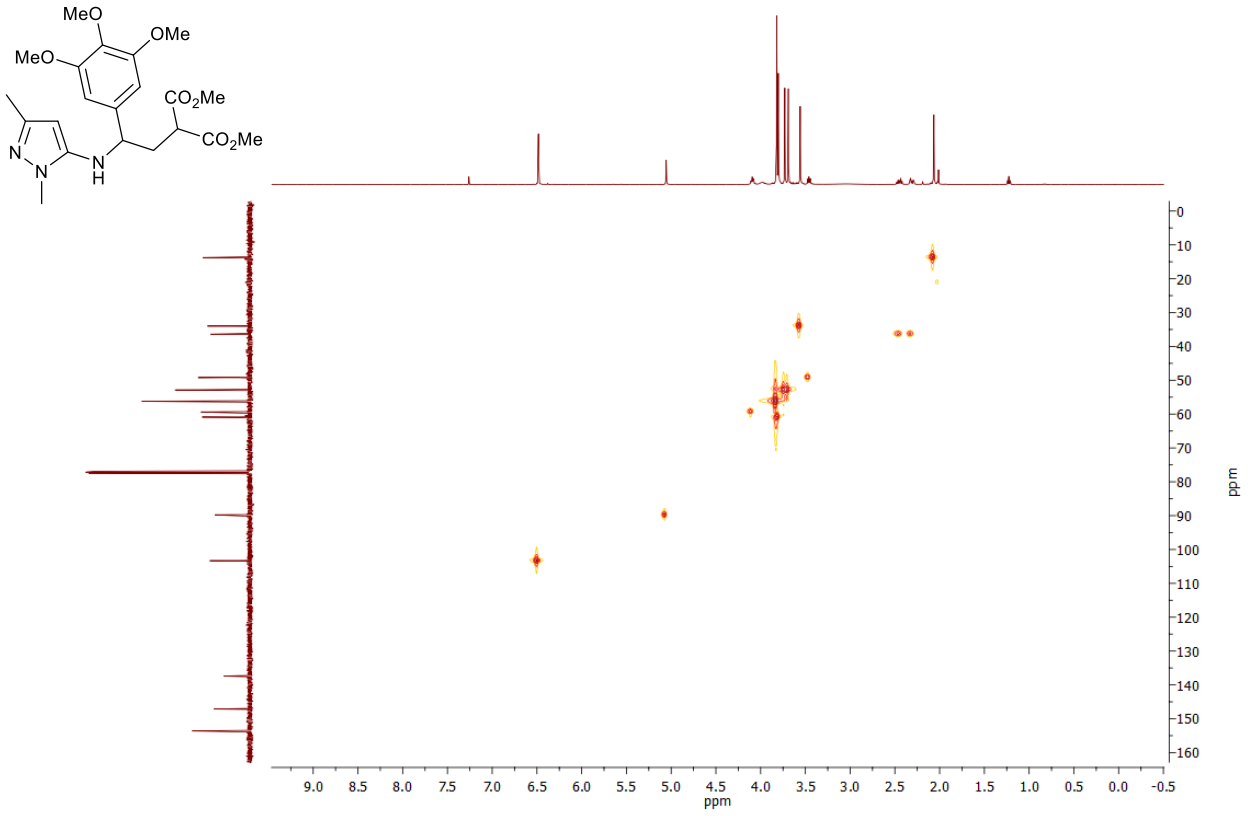


^{13}C NMR (126 MHz, $CDCl_3$)

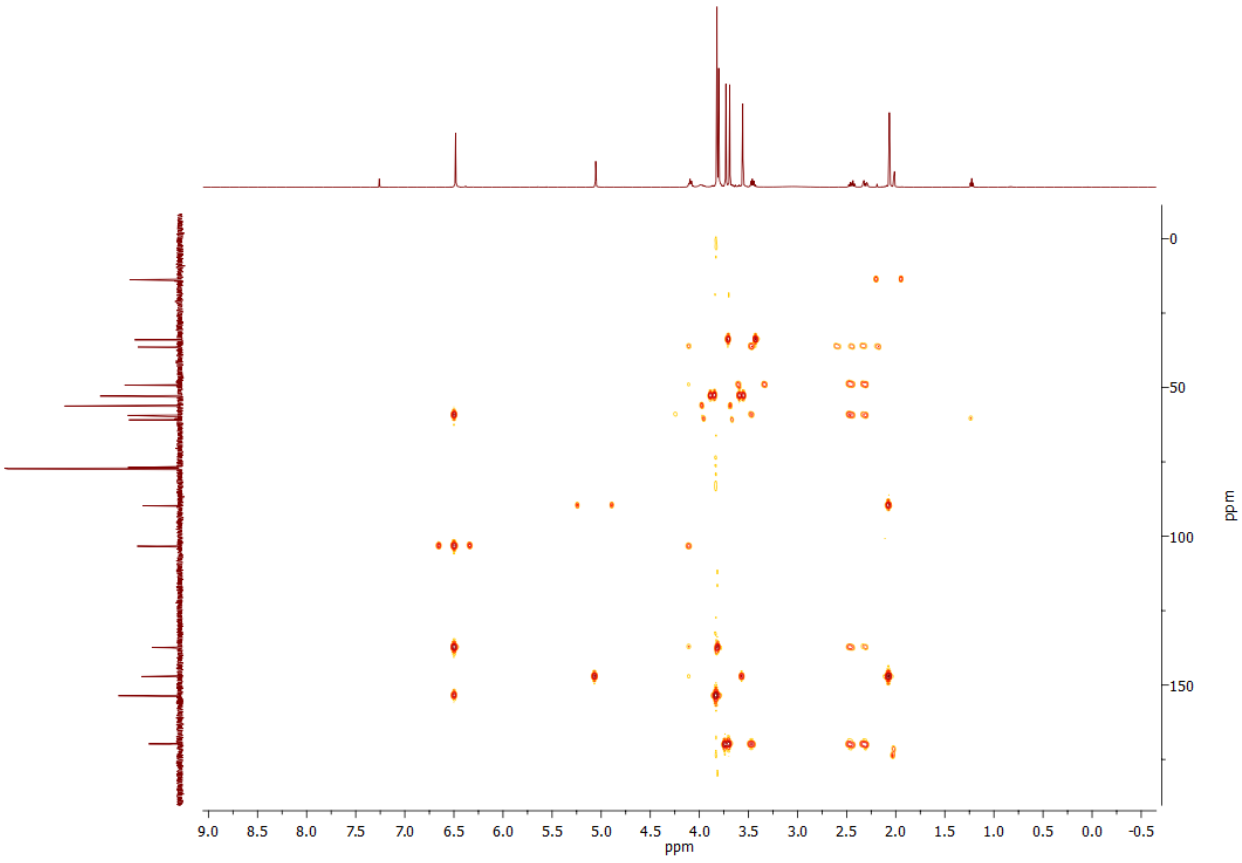


Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(3,4,5-trimethoxyphenyl)ethyl}malonate (3h)

HSQC ^{1}H-^{13}C ($CDCl_3$)

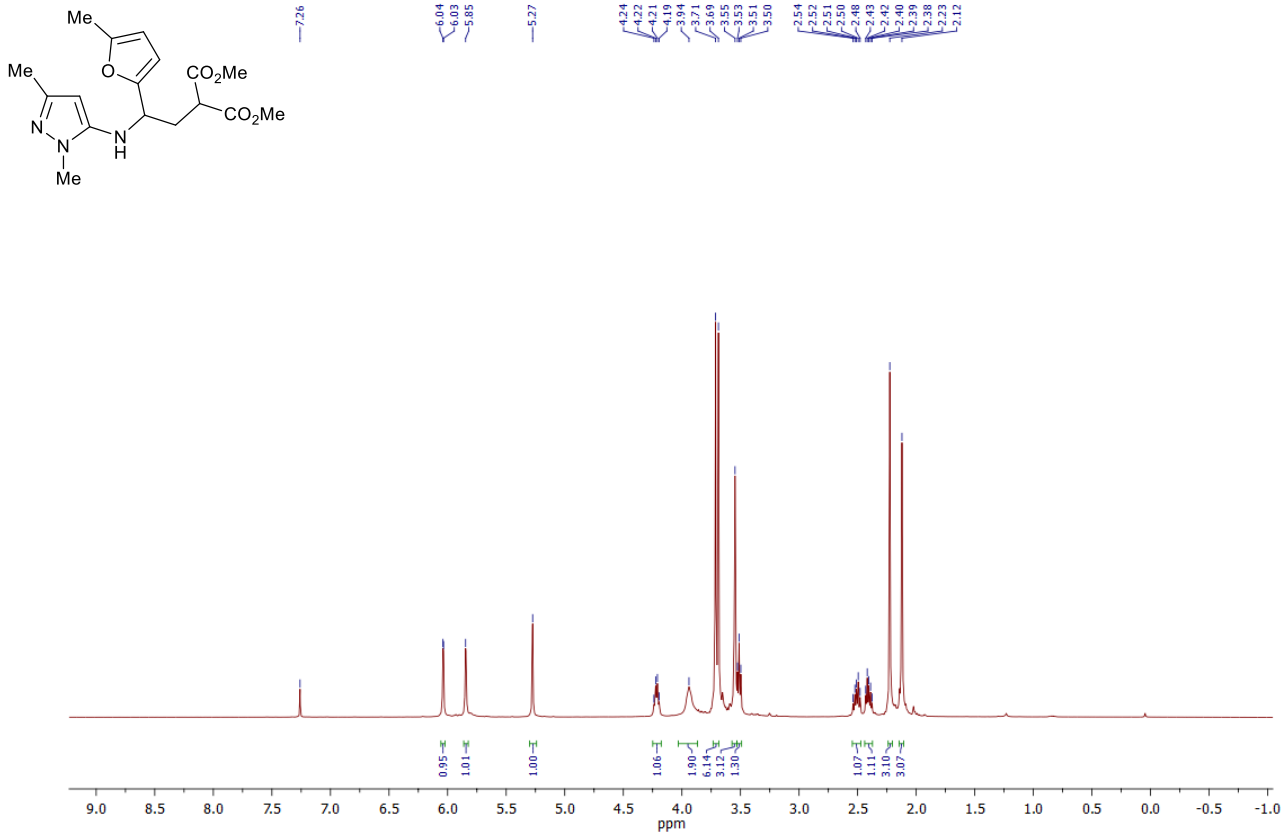


HMBC ^{1}H-^{13}C ($CDCl_3$)

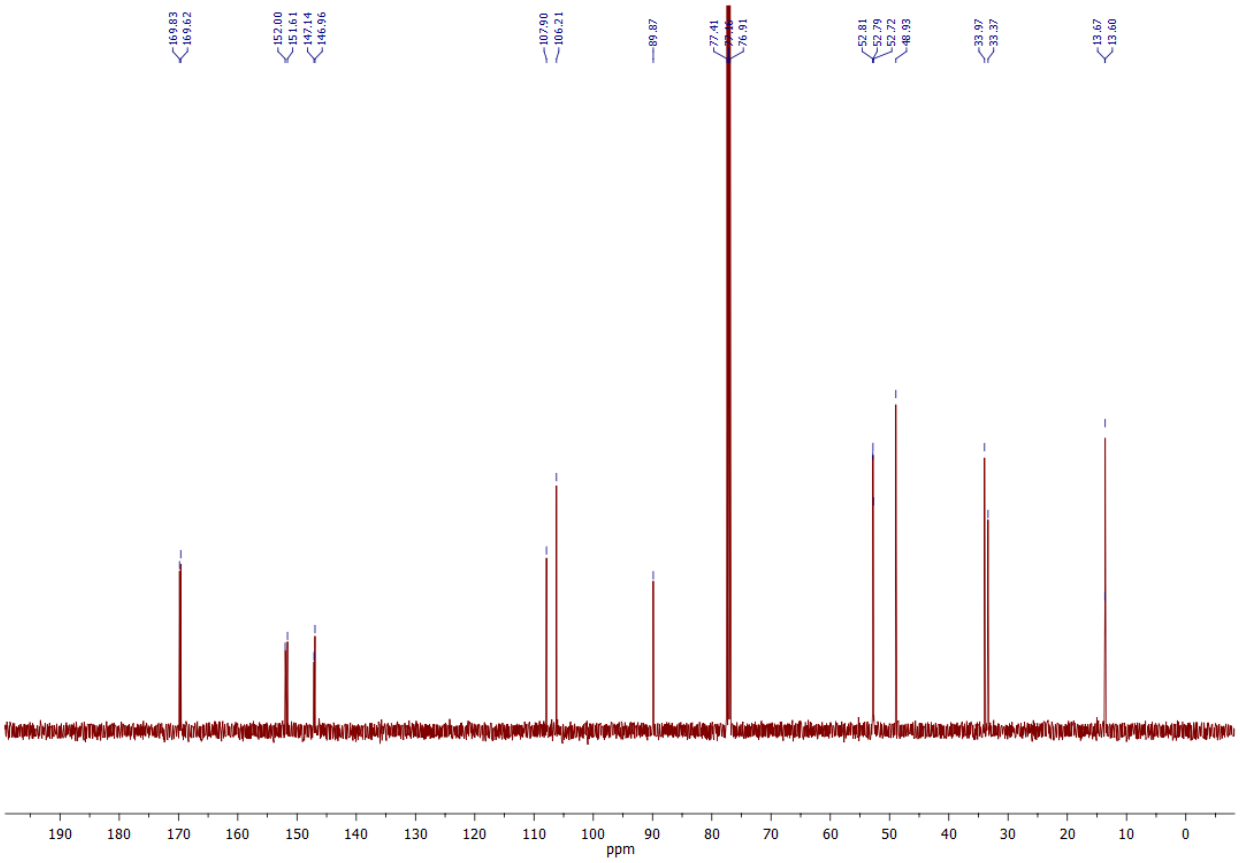


Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(5-methylfuran-2-yl)ethyl}malonate (3i)

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

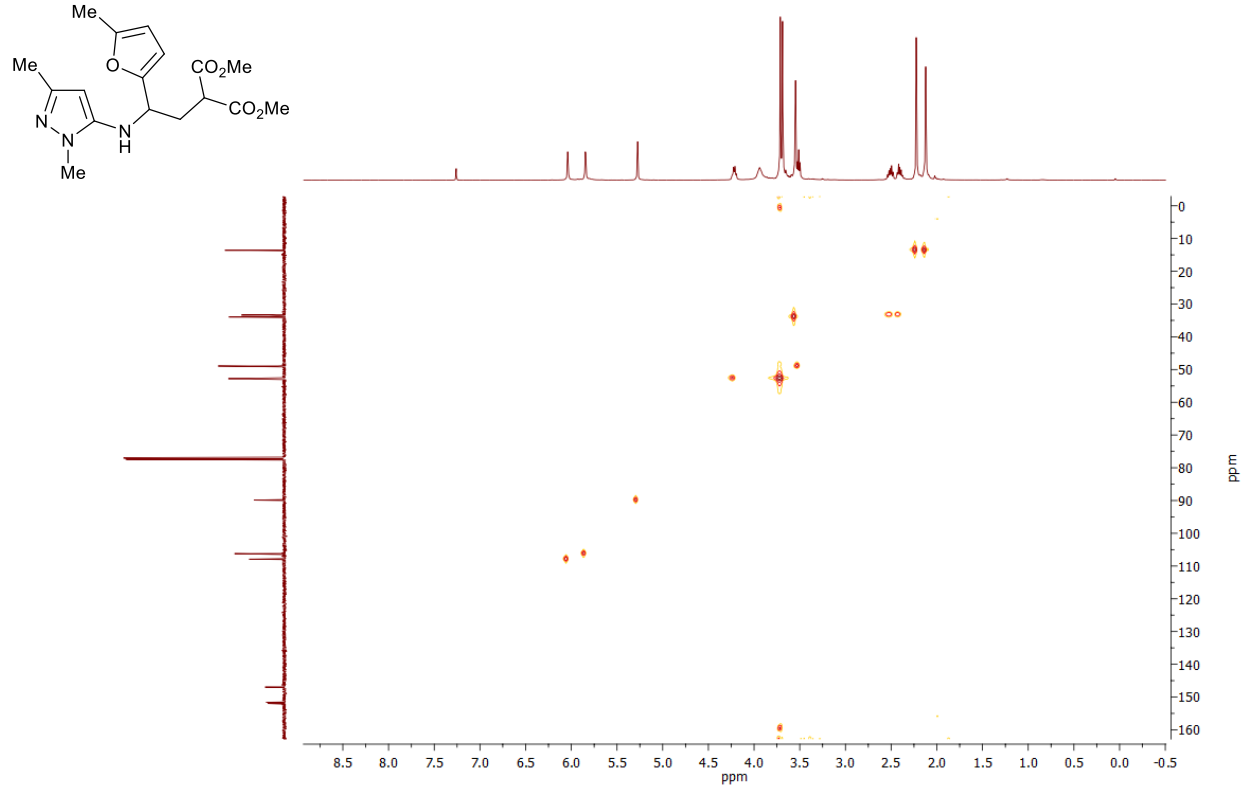


^{13}C NMR (126 MHz, $CDCl_3$)

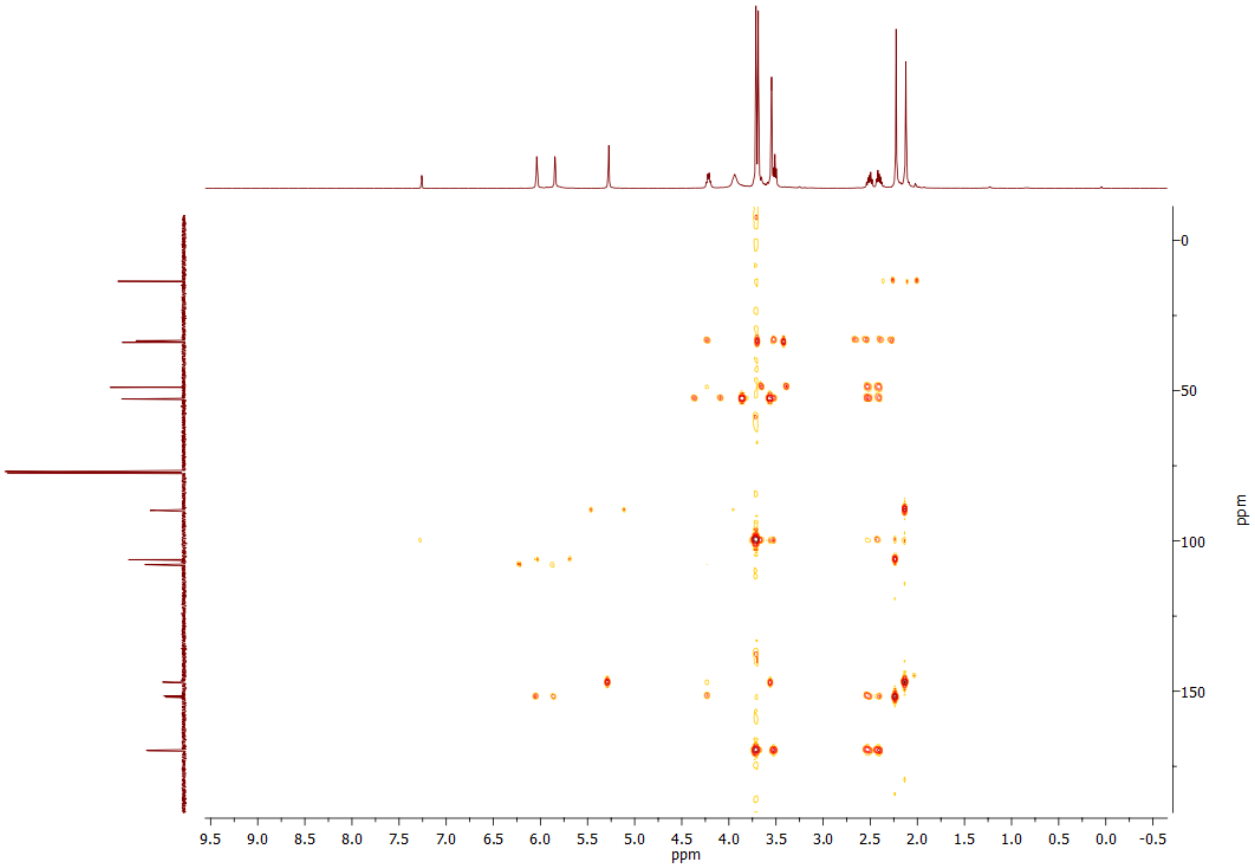


Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(5-methylfuran-2-yl)ethyl}malonate (3i)

HSQC ^{1}H-^{13}C ($CDCl_3$)

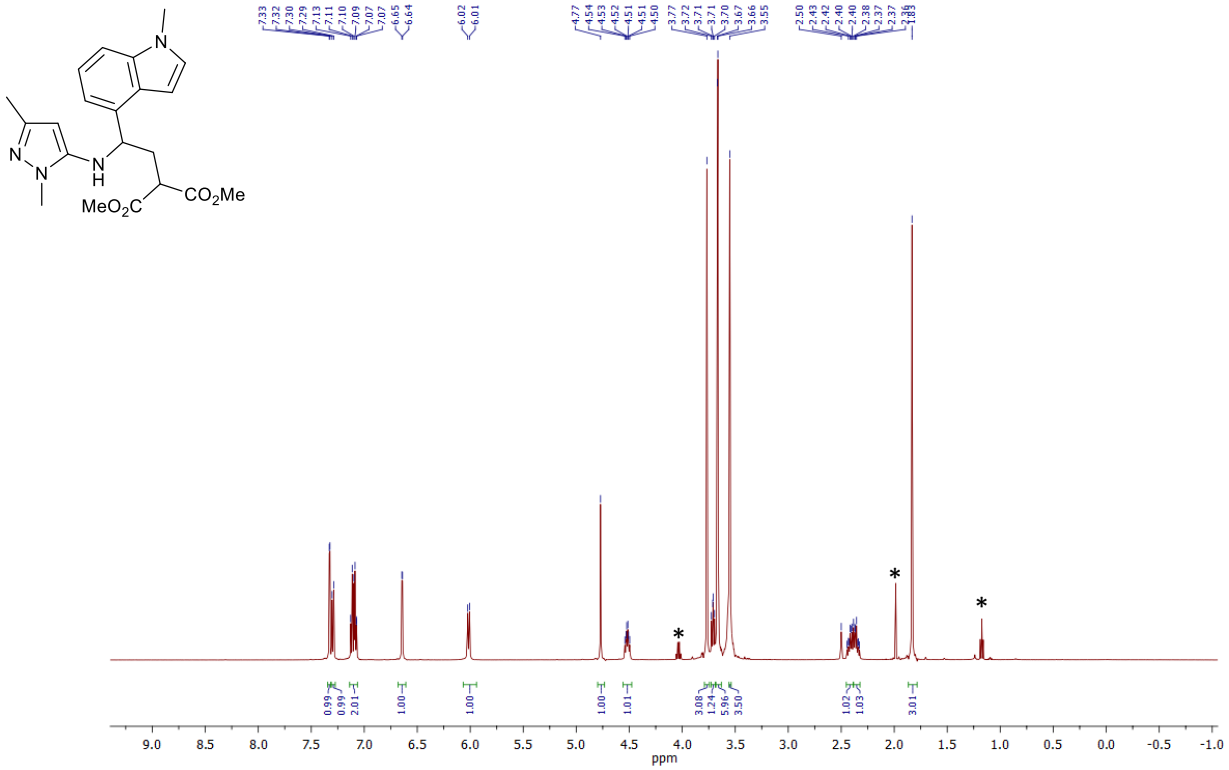


HMBC ^{1}H-^{13}C ($CDCl_3$)

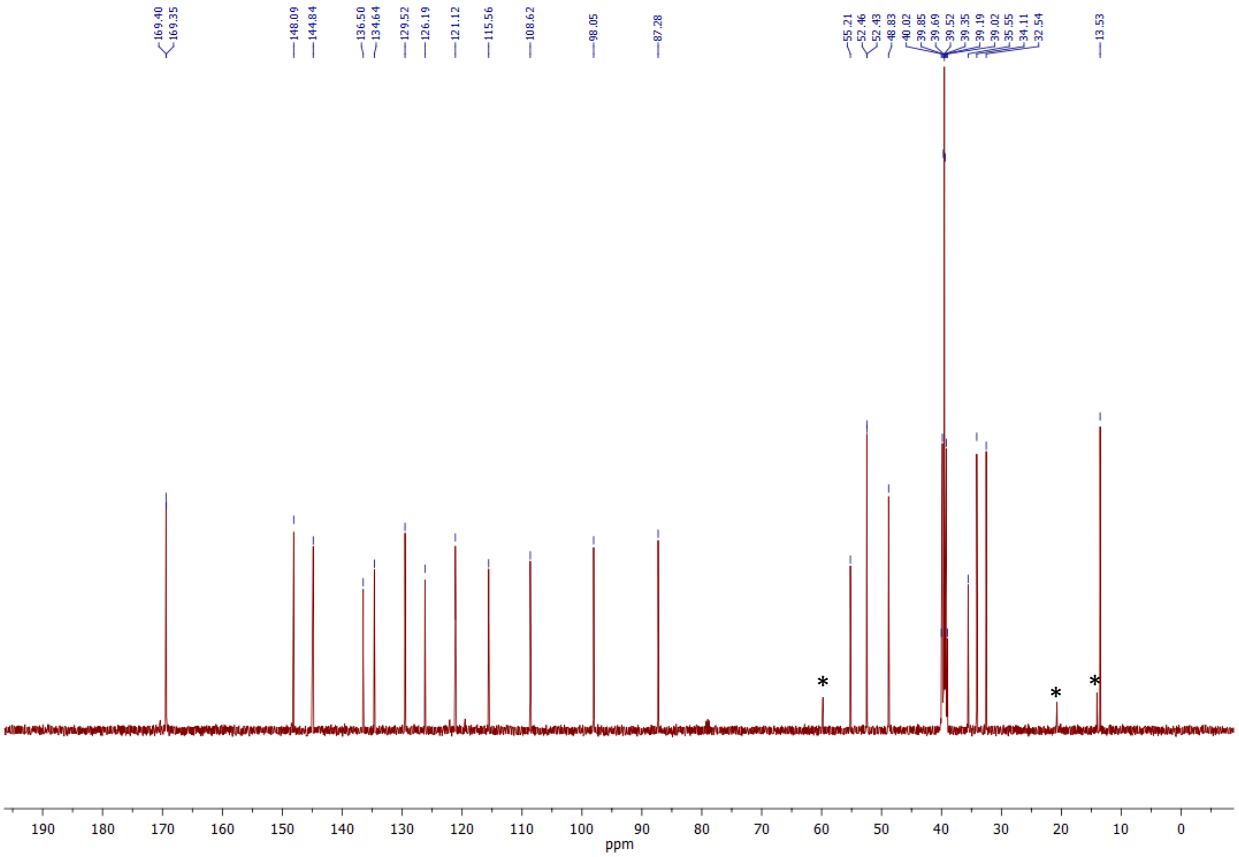


Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(1-methyl-1*H*-indol-4-yl)ethyl}malonate (3j)

^{1}H NMR (500 MHz, DMSO-d_6)

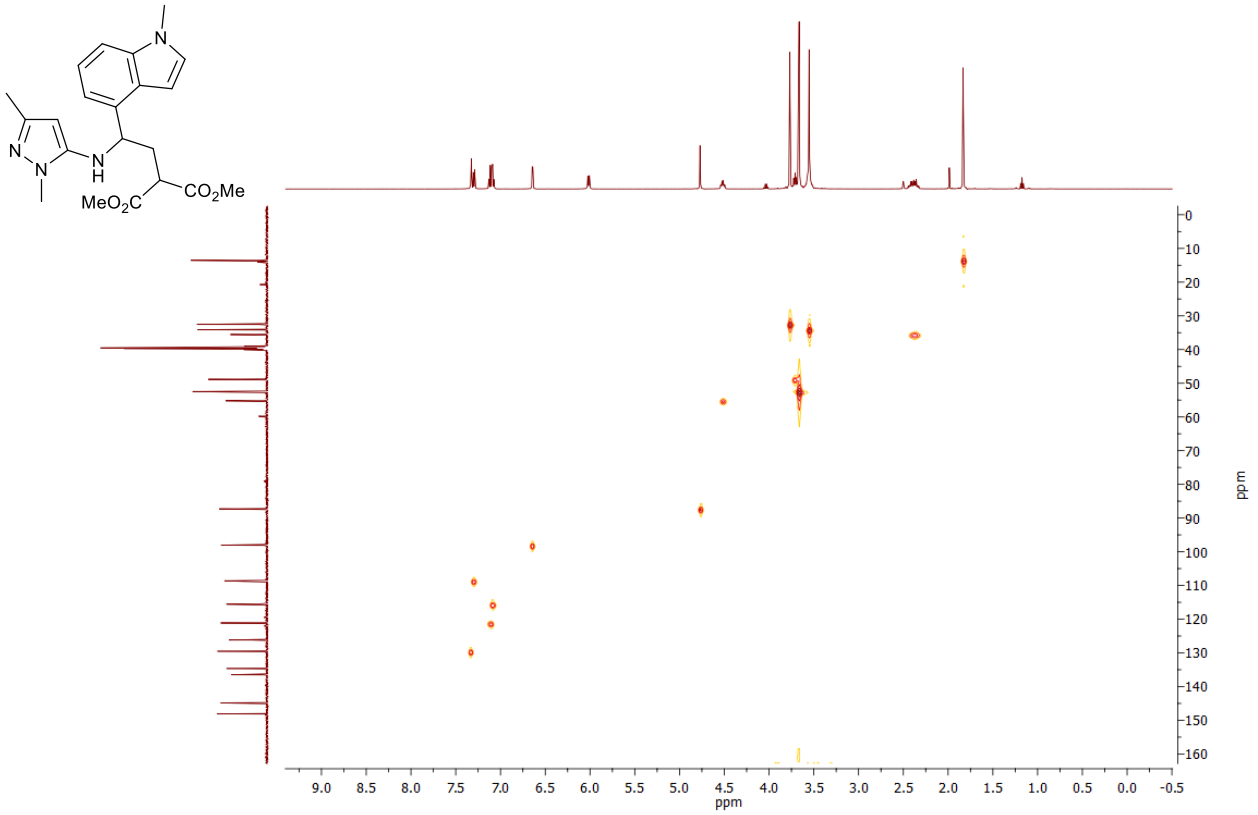


^{13}C NMR (126 MHz, DMSO-d_6)

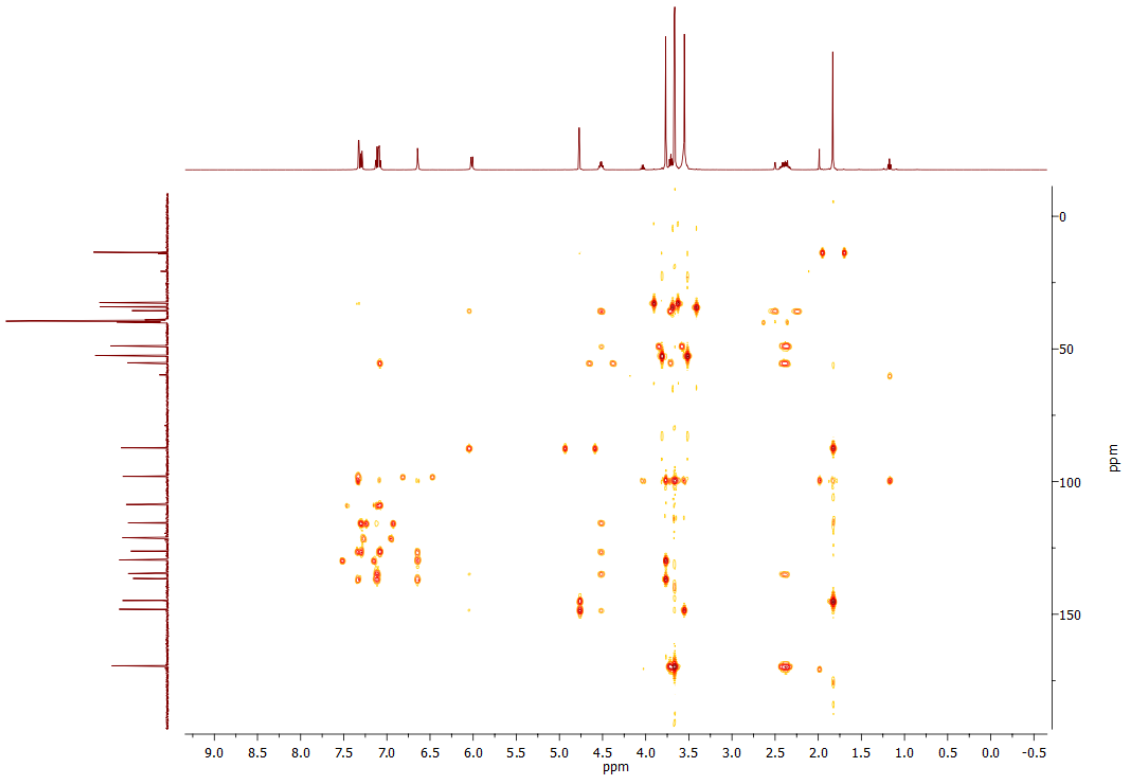


Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(1-methyl-1*H*-indol-4-yl)ethyl}malonate (3j)

HSQC ^{1}H-^{13}C (DMSO-d_6)

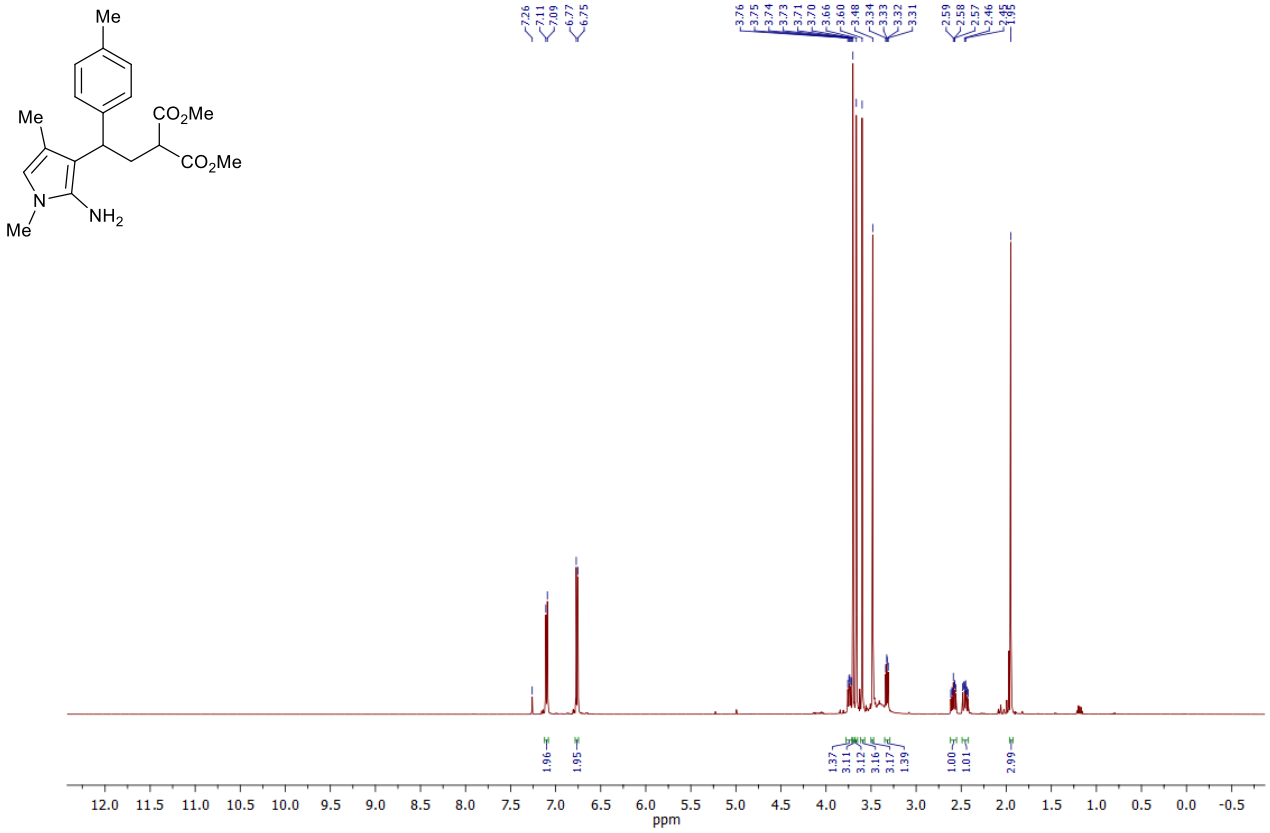


HMBC ^{1}H-^{13}C (DMSO-d_6)

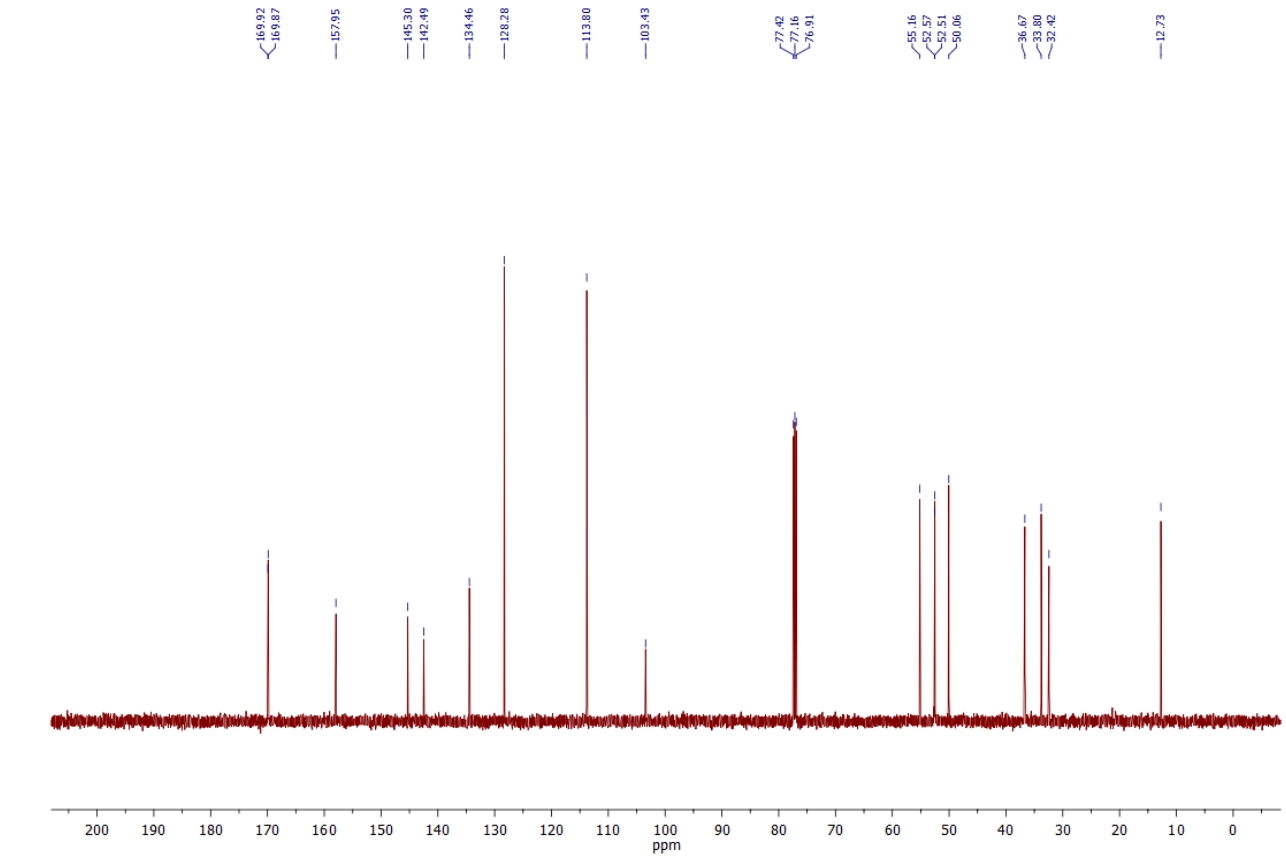


Dimethyl 2-[2-(5-amino-1,3-dimethyl-1*H*-pyrazol-4-yl)-2-(*p*-tolyl)ethyl]malonate (4a)

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

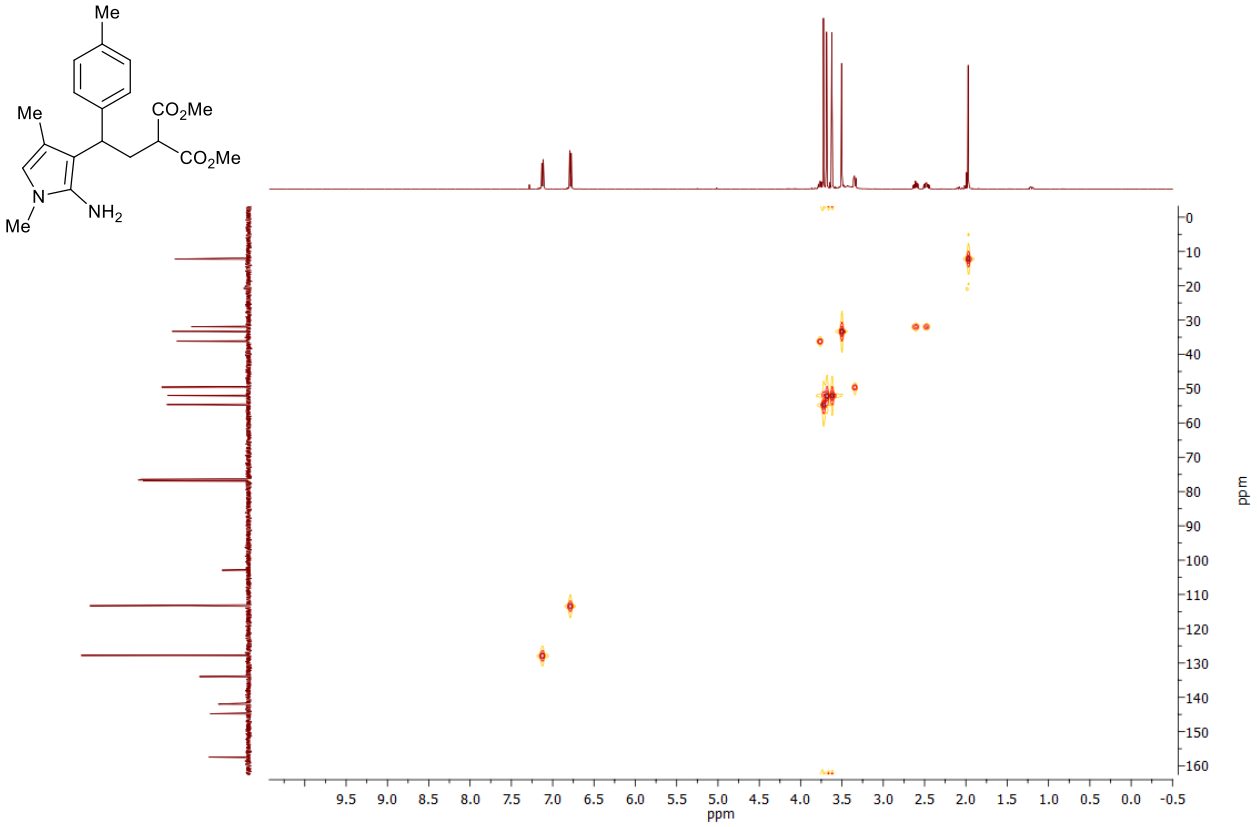


^{13}C NMR (126 MHz, $CDCl_3$)

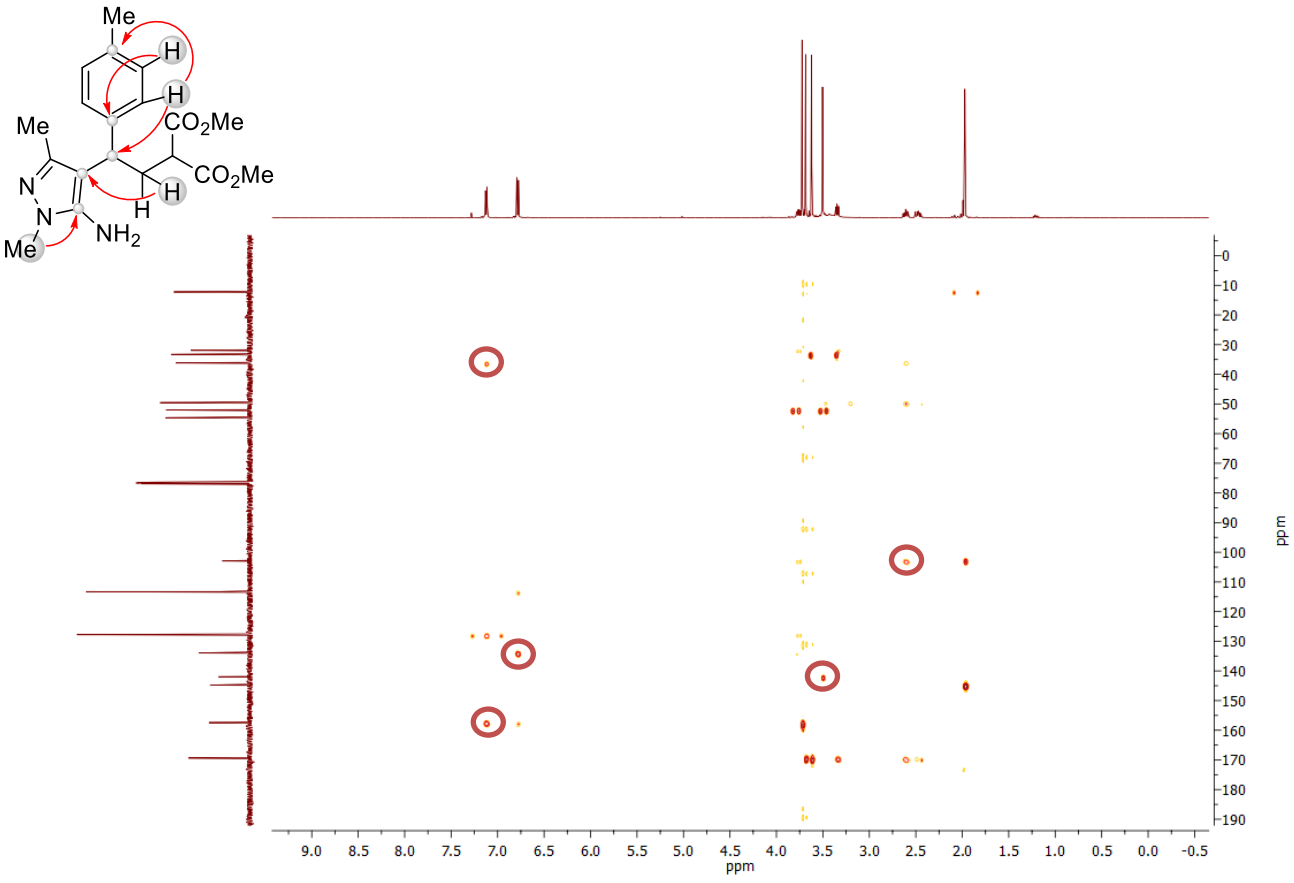


Dimethyl 2-[2-(5-amino-1,3-dimethyl-1*H*-pyrazol-4-yl)-2-(*p*-tolyl)ethyl]malonate (4a)

HSQC ^{1}H-^{13}C ($CDCl_3$)

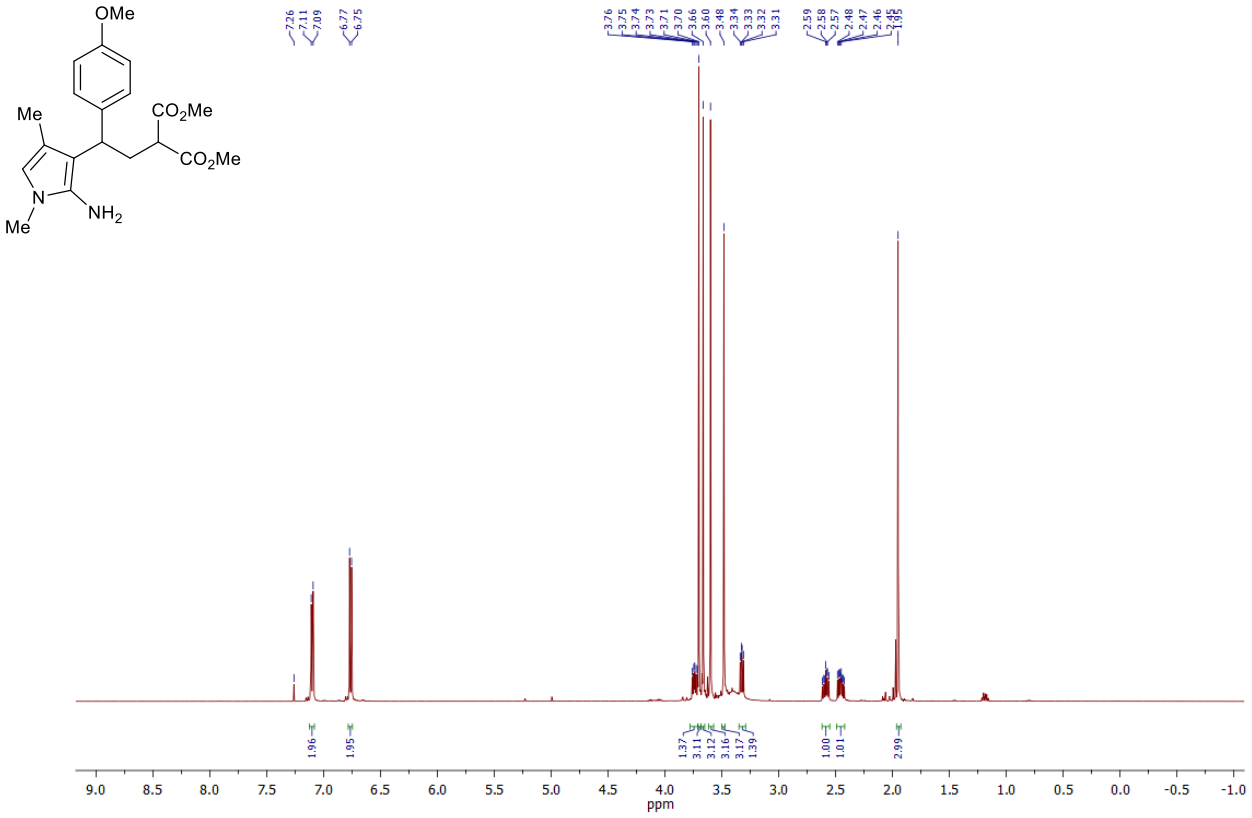


HMBC ^{1}H-^{13}C ($CDCl_3$)

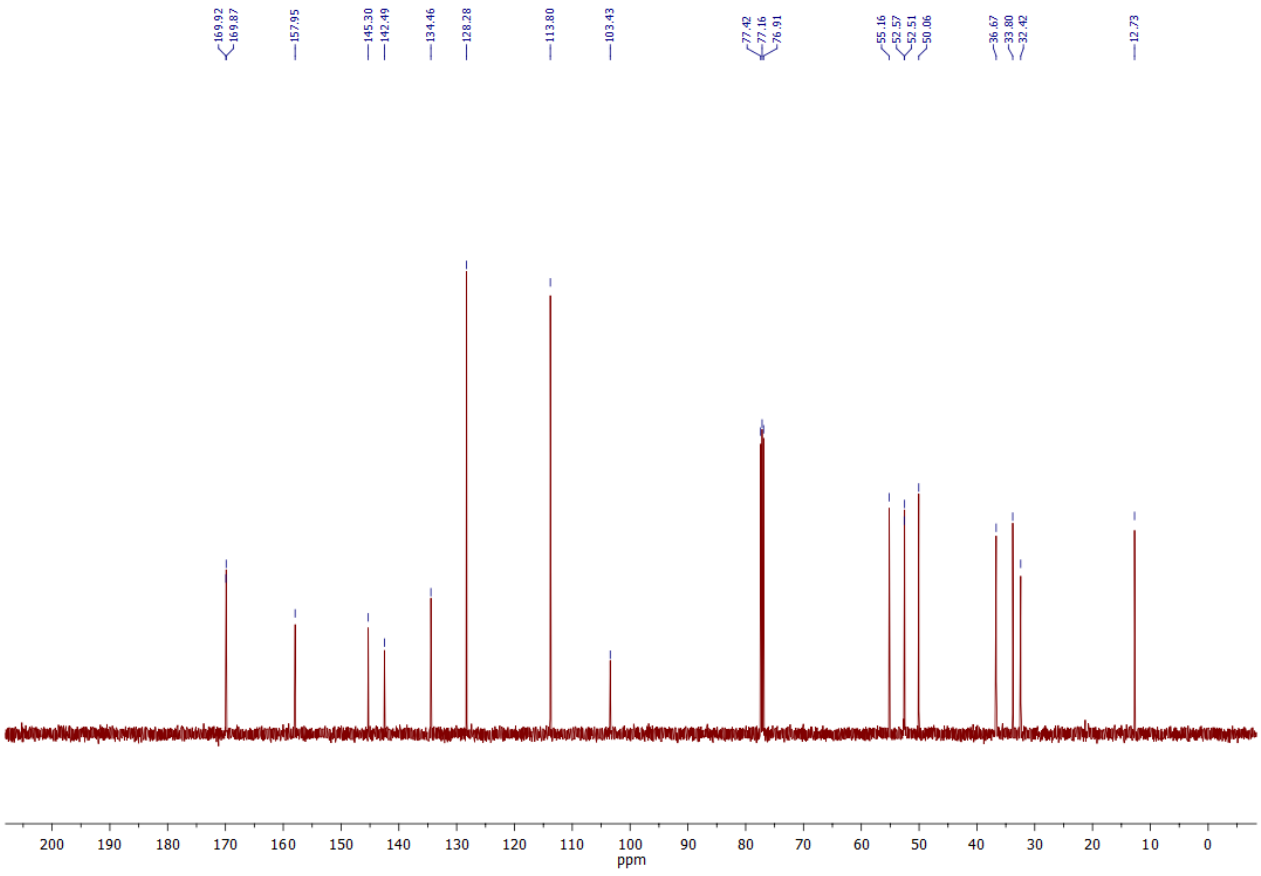


Dimethyl 2-[2-(5-amino-1,3-dimethyl-1*H*-pyrazol-4-yl)-2-(*p*-methoxyphenyl)ethyl]malonate (4b)

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

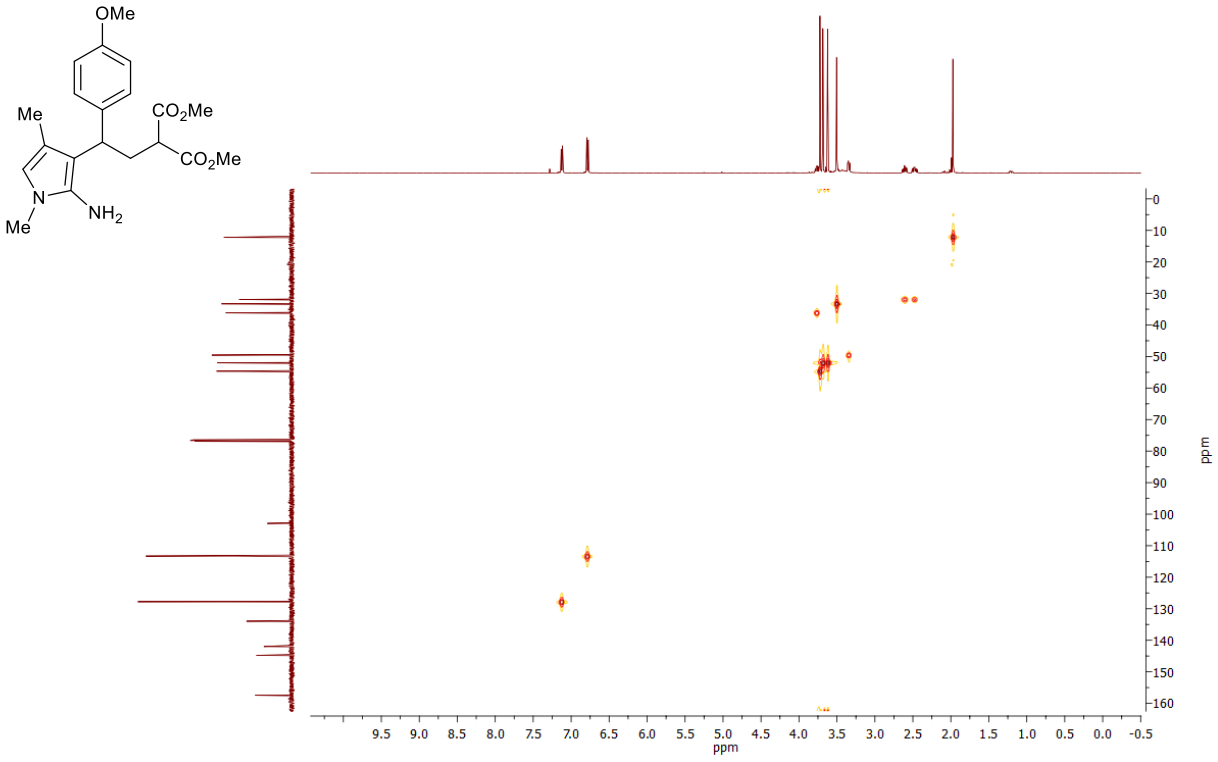


^{13}C NMR (126 MHz, $CDCl_3$)

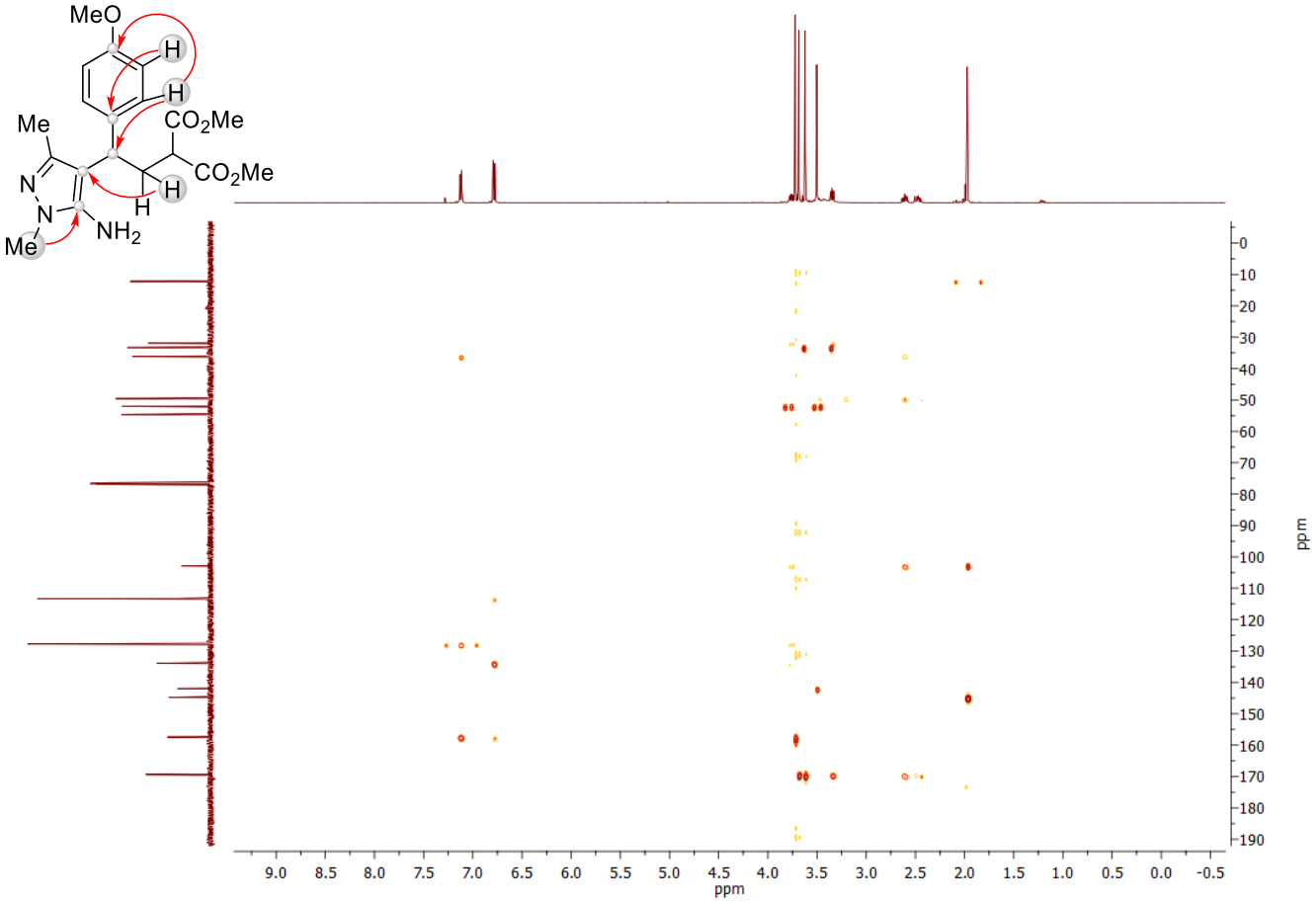


Dimethyl 2-[2-(5-amino-1,3-dimethyl-1*H*-pyrazol-4-yl)-2-(*p*-methoxyphenyl)ethyl]malonate (4b)

HSQC ^{1}H-^{13}C ($CDCl_3$)

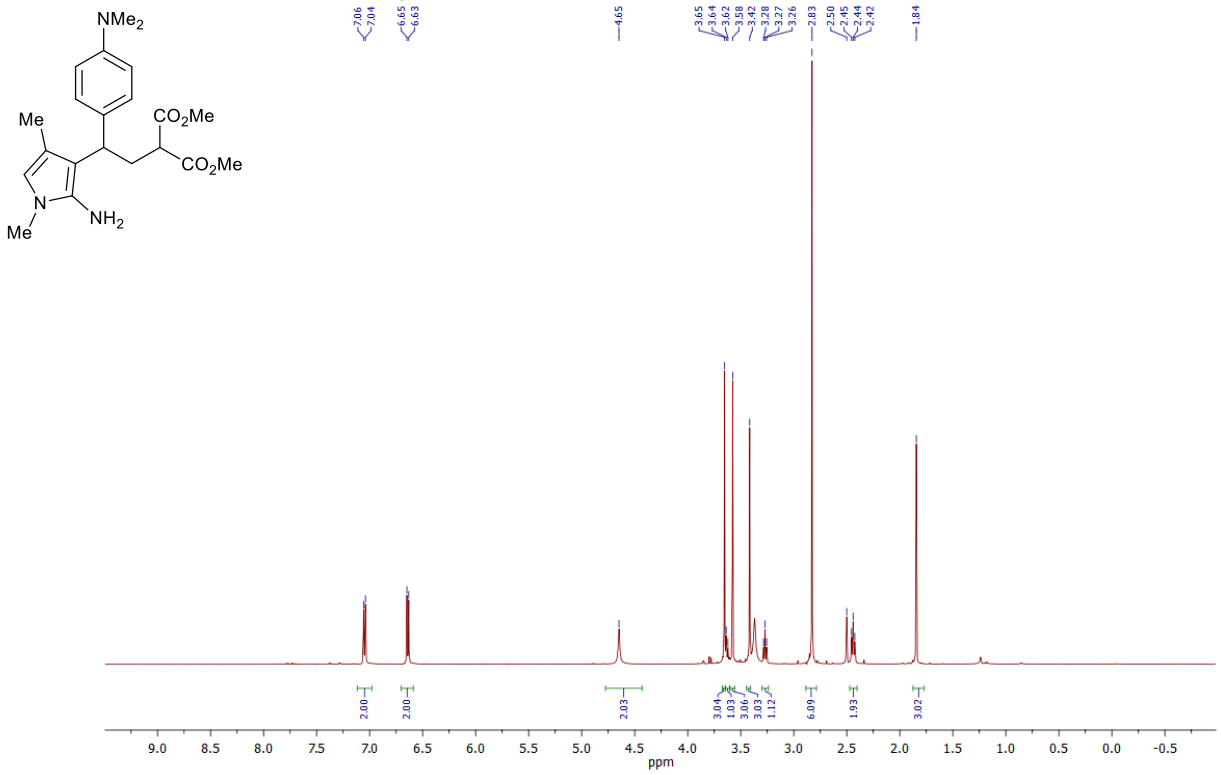


HMBC ^{1}H-^{13}C ($CDCl_3$)

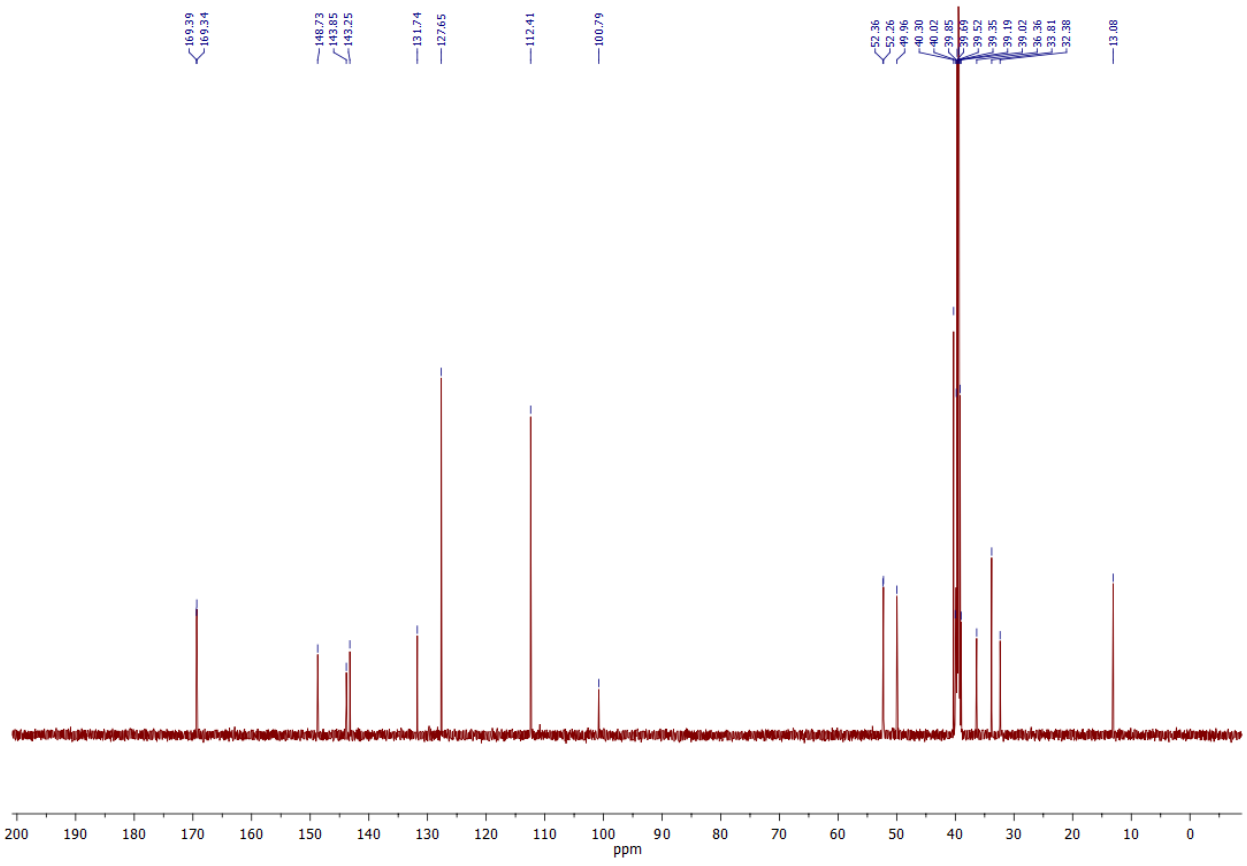


Dimethyl 2-{2-(5-amino-1,3-dimethyl-1*H*-pyrazol-4-yl)-2-[4-(dimethylamino)phenyl]ethyl}malonate (4c)

^{1}H NMR (500 MHz, DMSO-d_6)

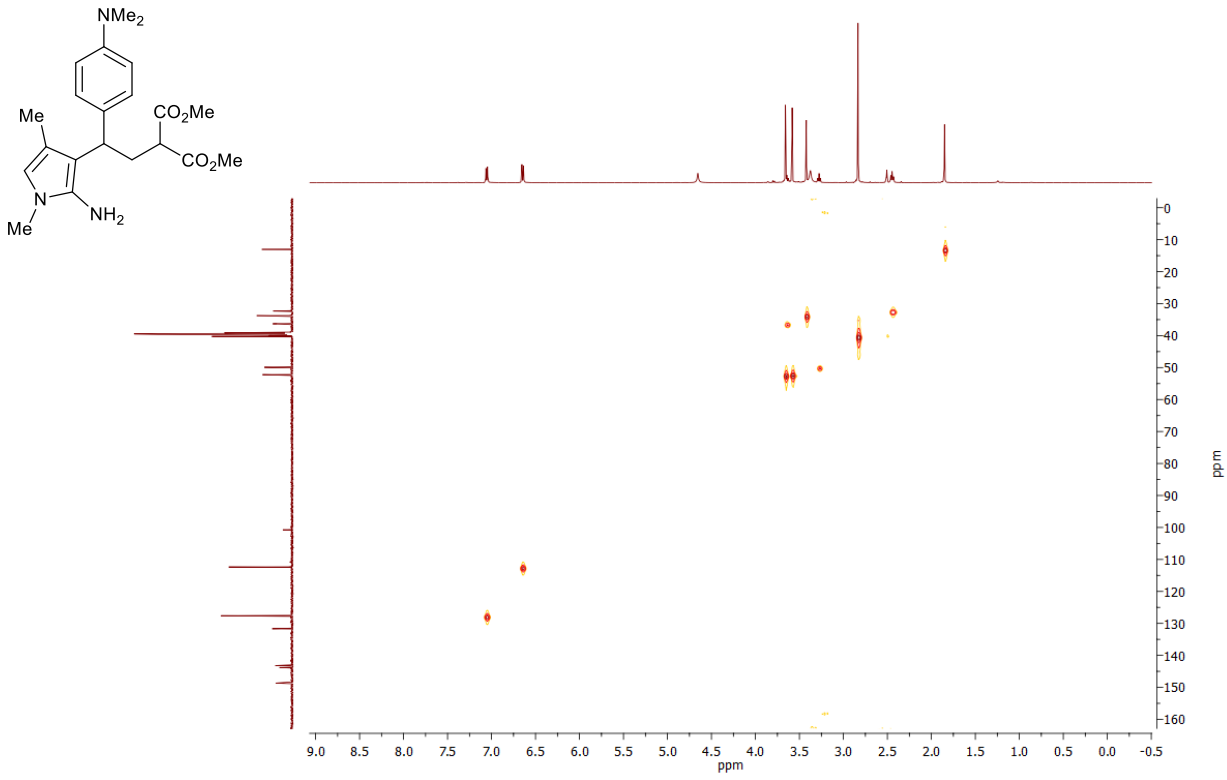


^{13}C NMR (126 MHz, DMSO-d_6)

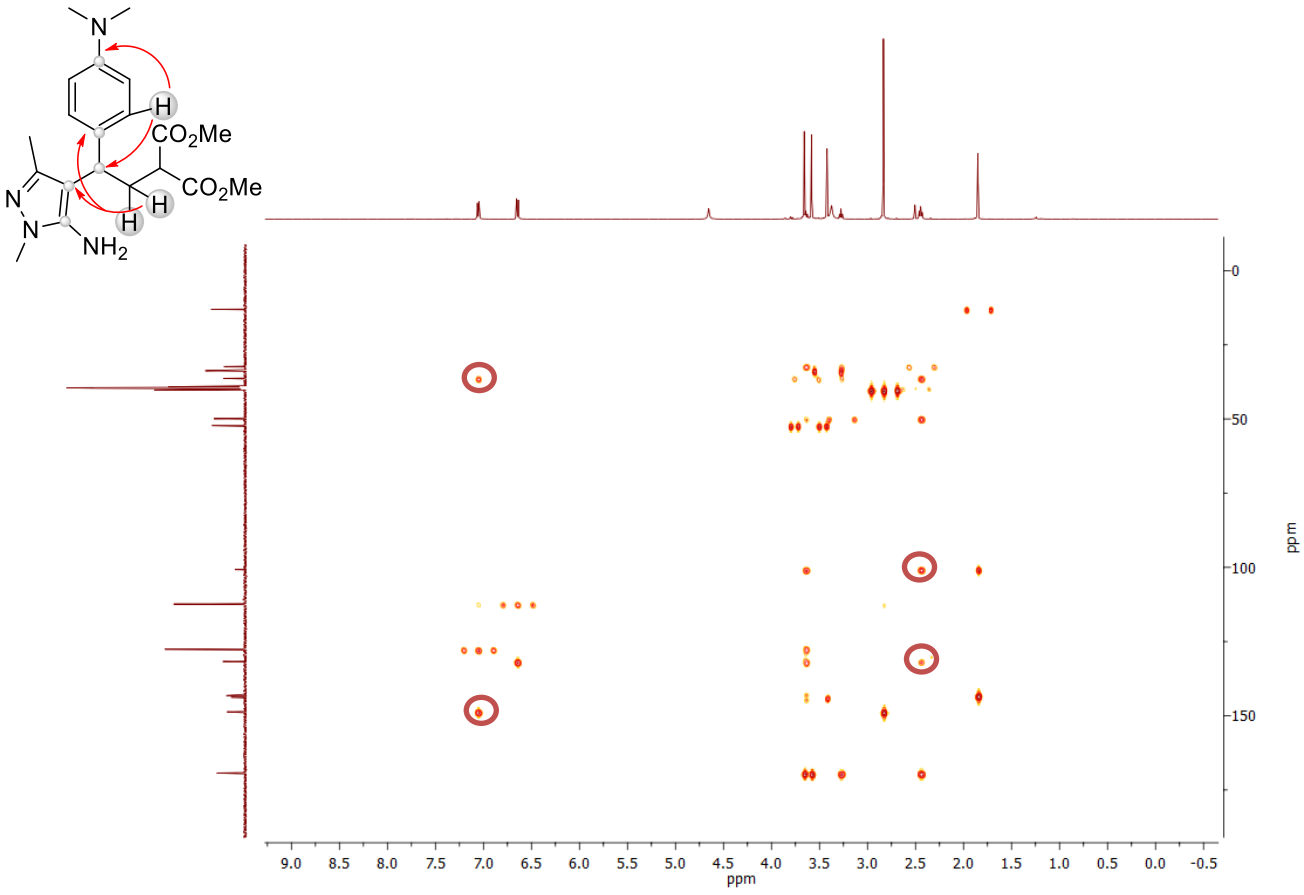


Dimethyl 2-{2-(5-amino-1,3-dimethyl-1*H*-pyrazol-4-yl)-2-[4-(dimethylamino)phenyl]ethyl}malonate (4c)

HSQC ^{1}H-^{13}C (DMSO-d_6)

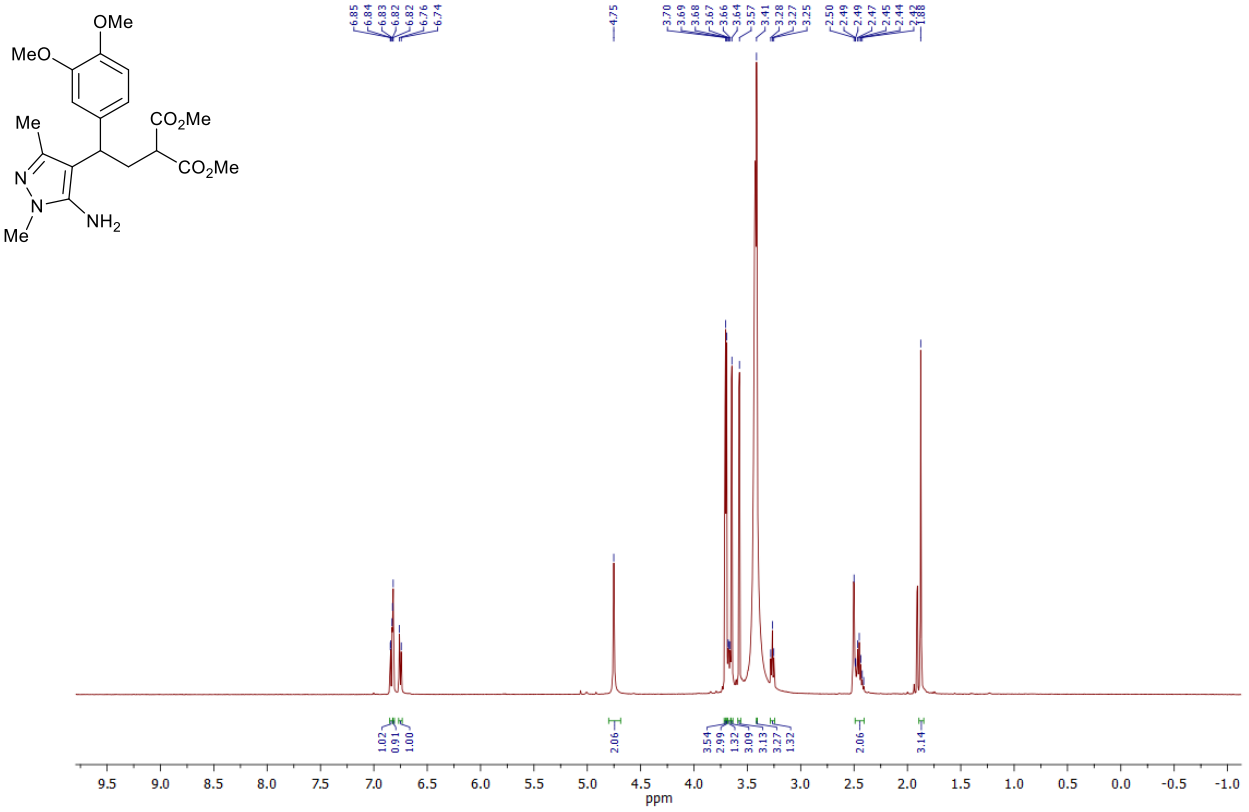


HMBC ^{1}H-^{13}C (DMSO-d_6)

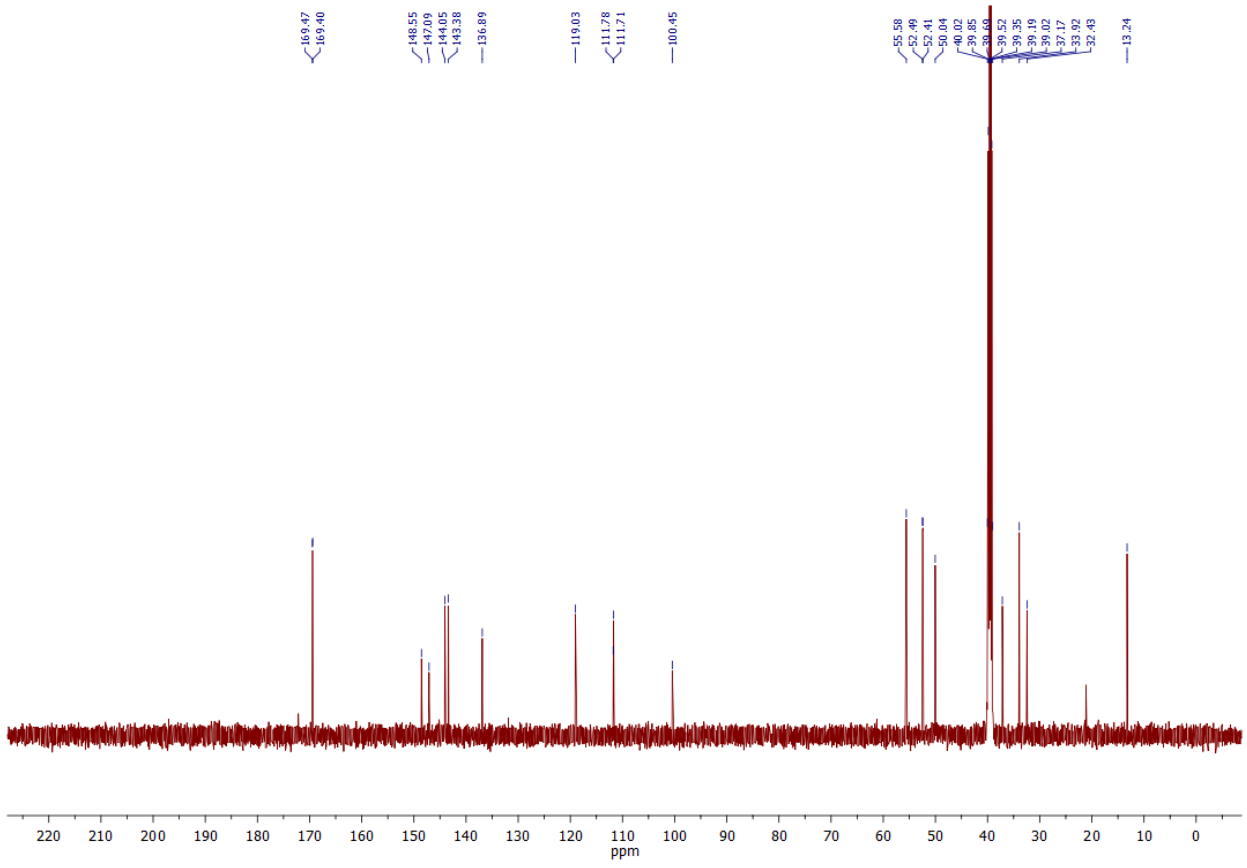


Dimethyl 2-[2-(5-amino-1,3-dimethyl-1*H*-pyrazol-4-yl)-2-(3,4-dimethoxyphenyl)ethyl]malonate (4f)

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

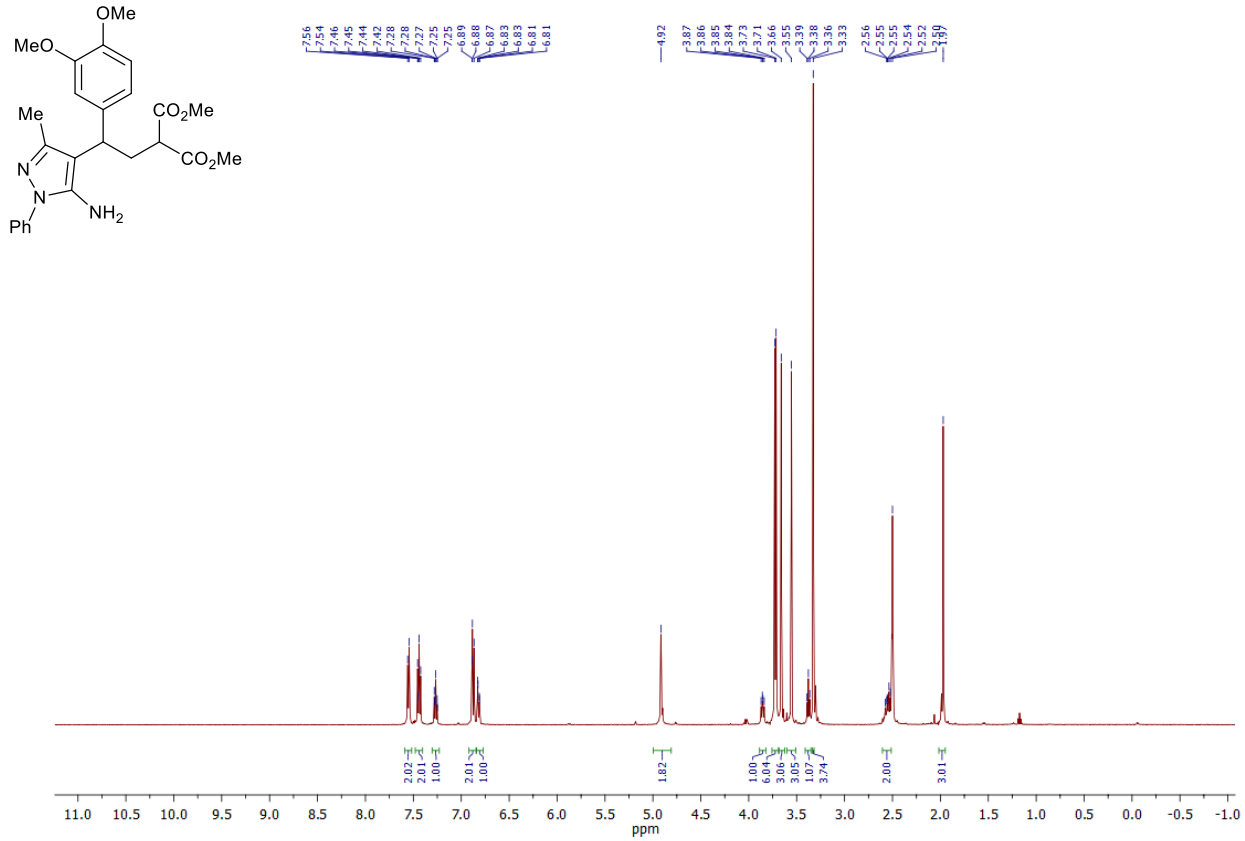


^{13}C NMR (126 MHz, $CDCl_3$)

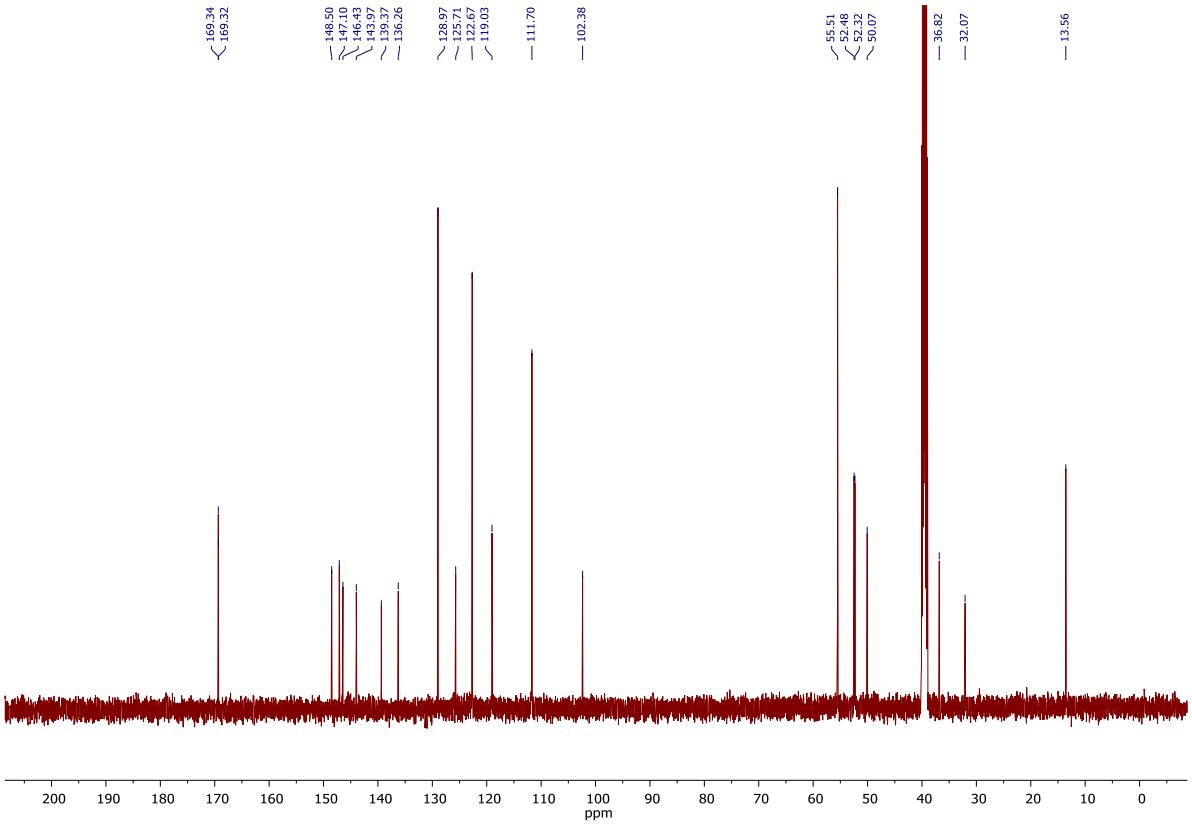


[Dimethyl 2-[2-(5-amino-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-2-(3,4-dimethoxyphenyl)ethyl]-malonate (4g)

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

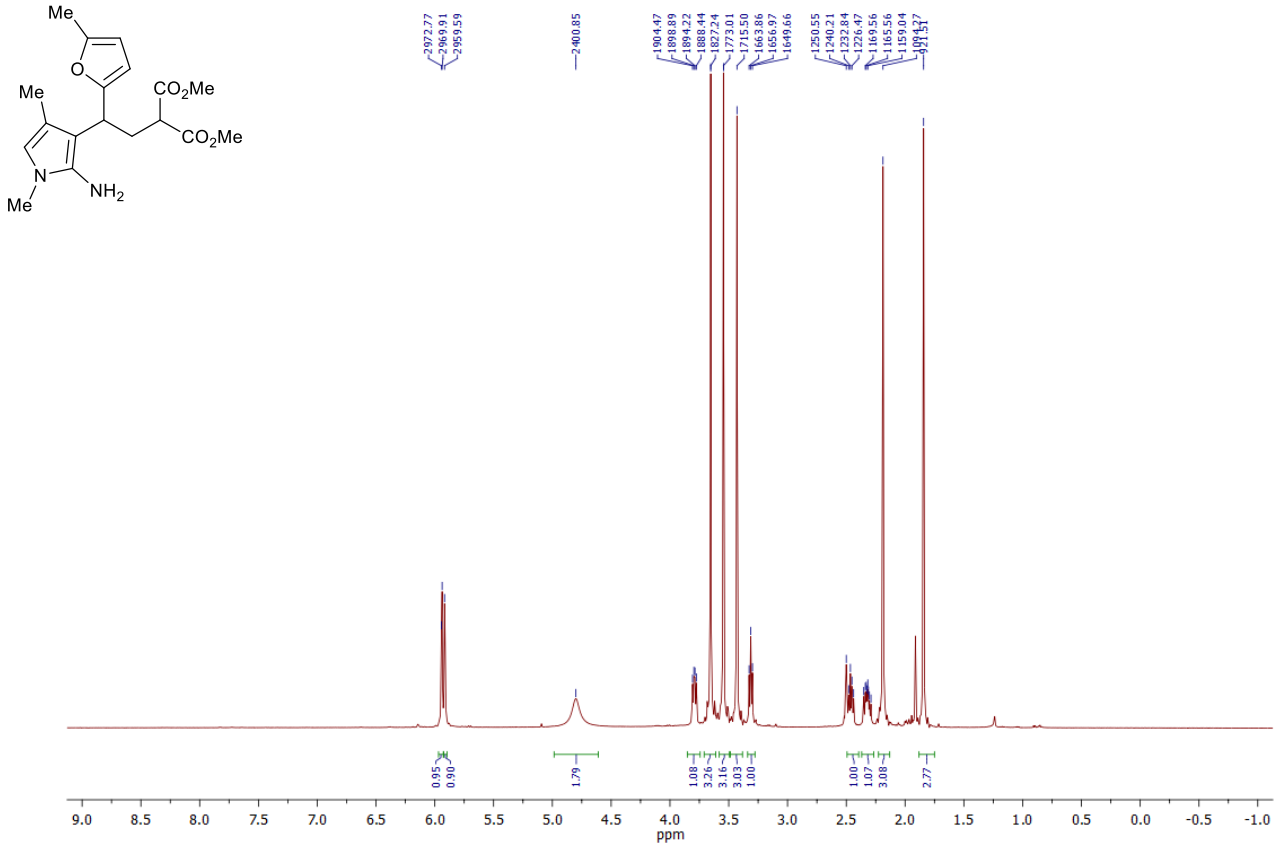


^{13}C NMR (126 MHz, $CDCl_3$)

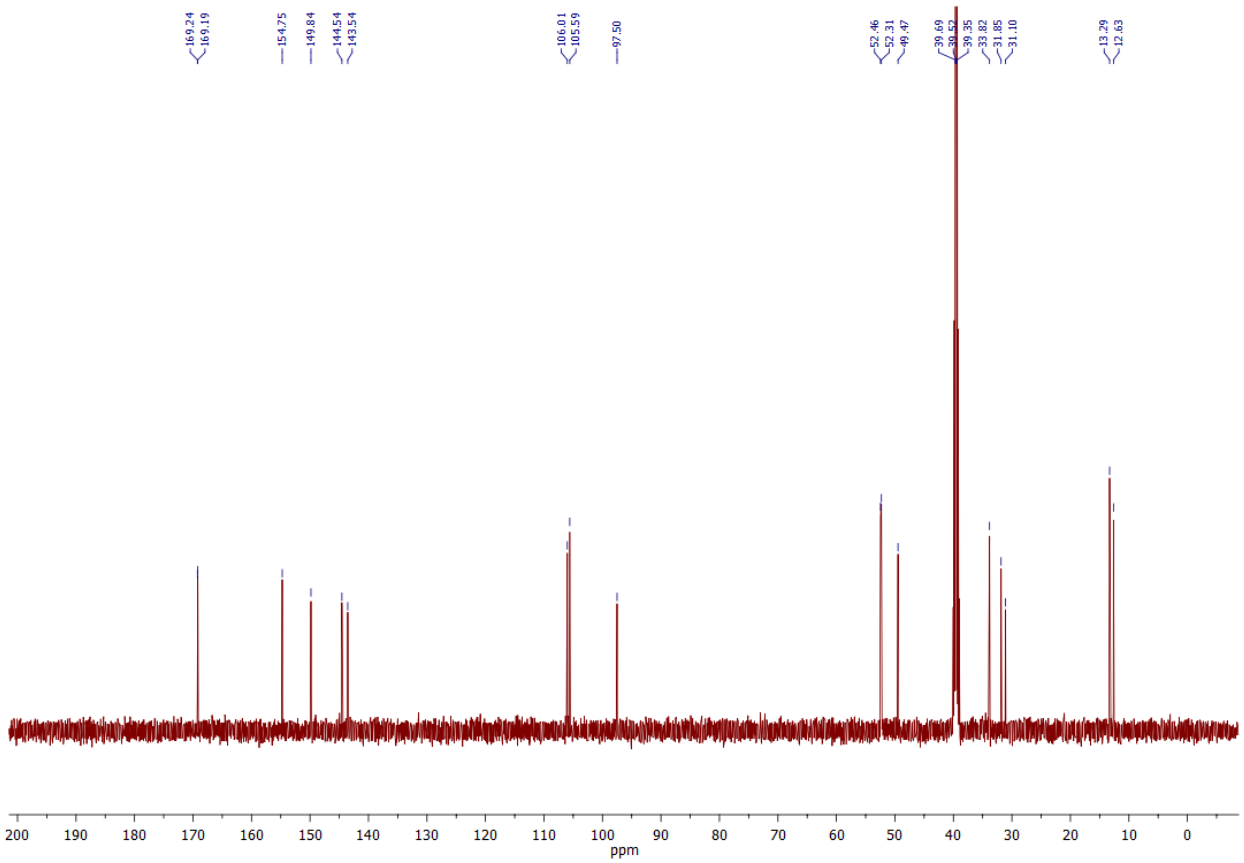


Dimethyl 2-[2-(5-amino-1,3-dimethyl-1*H*-pyrazol-4-yl)-2-(5-methylfuran-2-yl)ethyl]malonate (4i)

^{1}H NMR (500 MHz, DMSO-d_6)

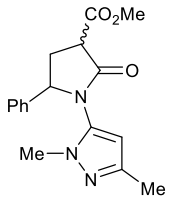


^{13}C NMR (126 MHz, DMSO-d_6)

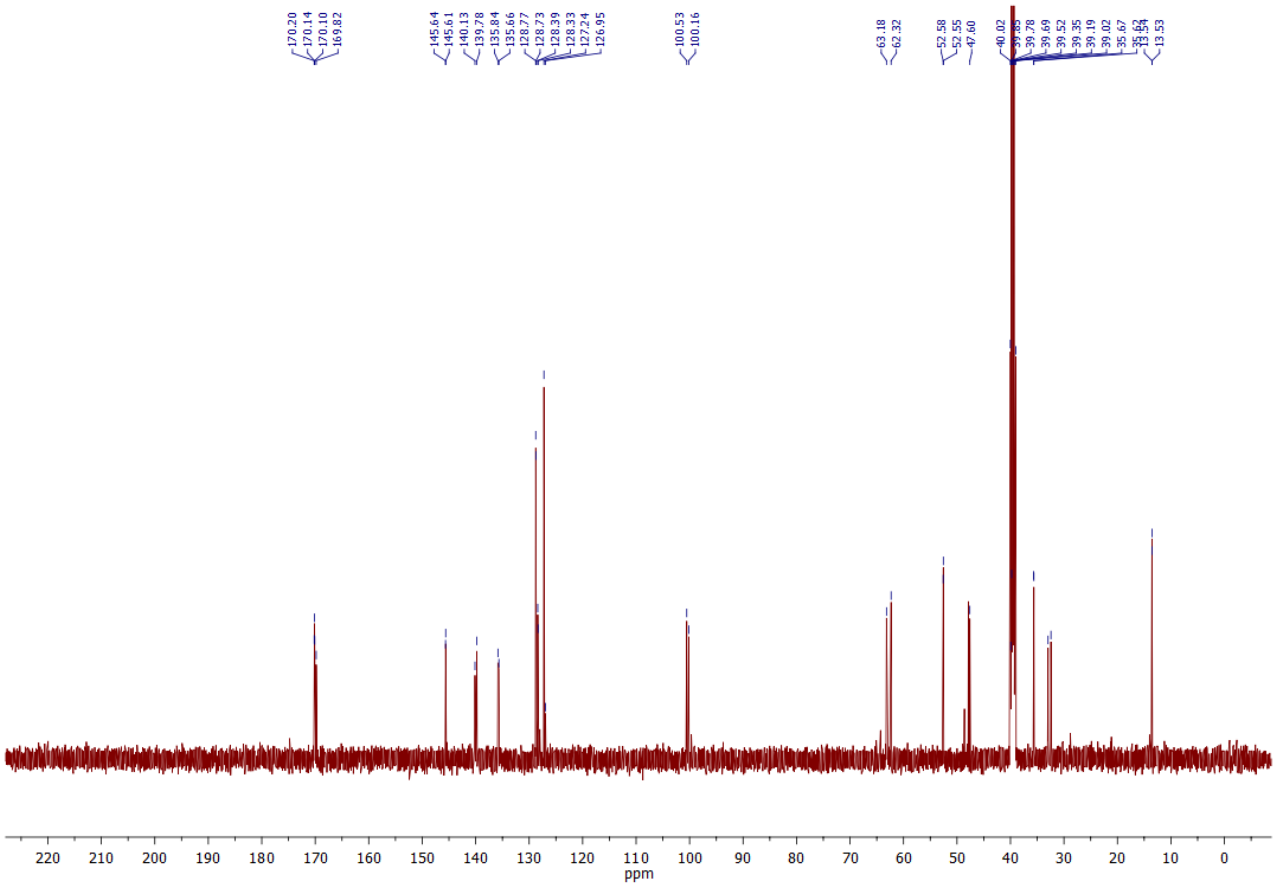


Methyl 1-(1,3-dimethyl-1*H*-pyrazol-5-yl)-2-oxo-5-phenylpyrrolidine-3-carboxylate (5)

^{1}H NMR (500 MHz, DMSO-d_6)

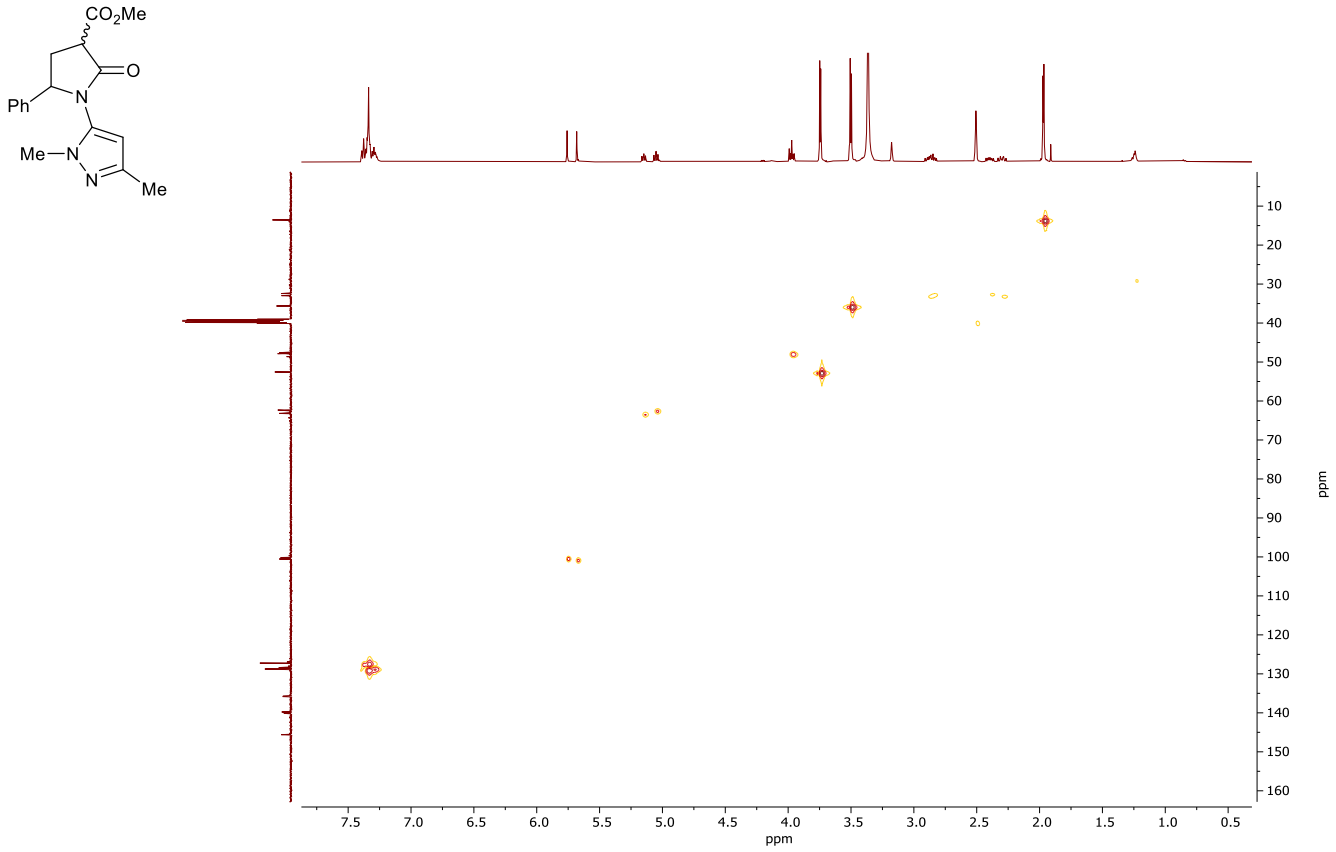


^{13}C NMR (126 MHz, DMSO)

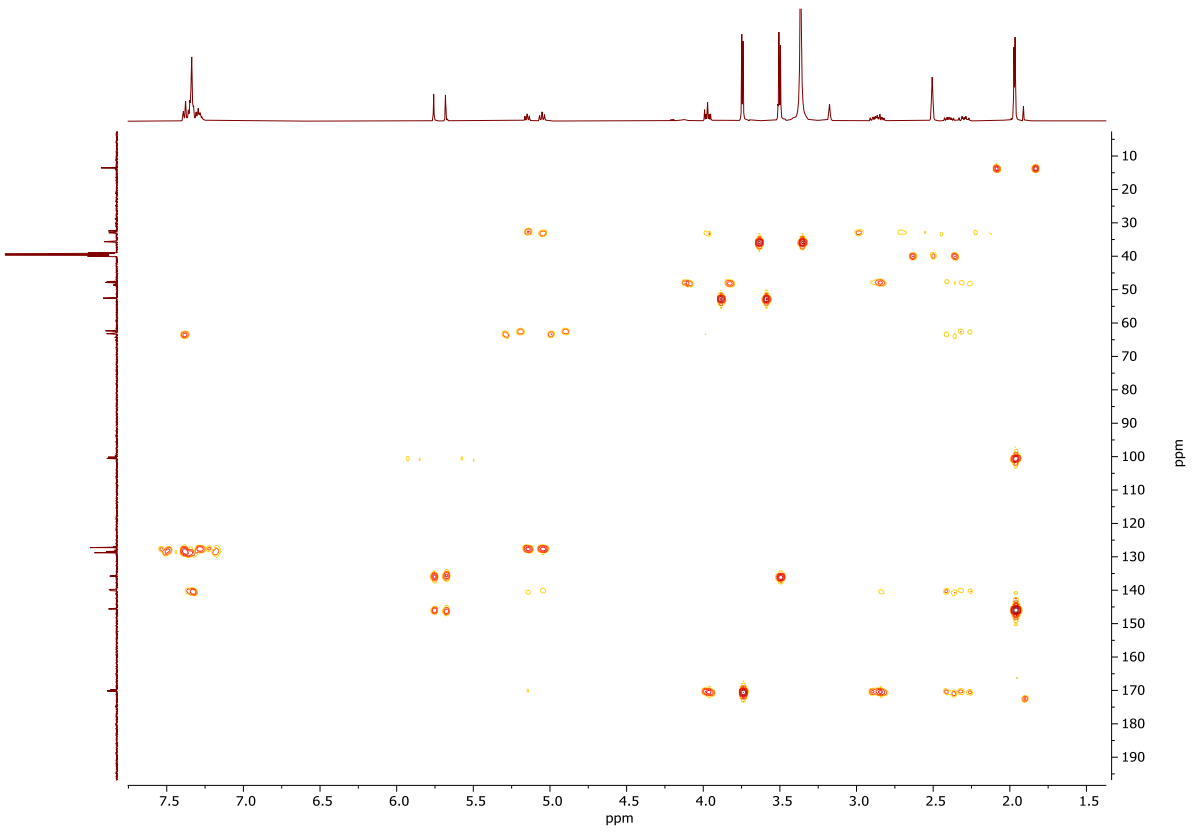


Methyl 1-(1,3-dimethyl-1*H*-pyrazol-5-yl)-2-oxo-5-phenylpyrrolidine-3-carboxylate (5)

HSQC ^{1}H-^{13}C (DMSO-d_6)

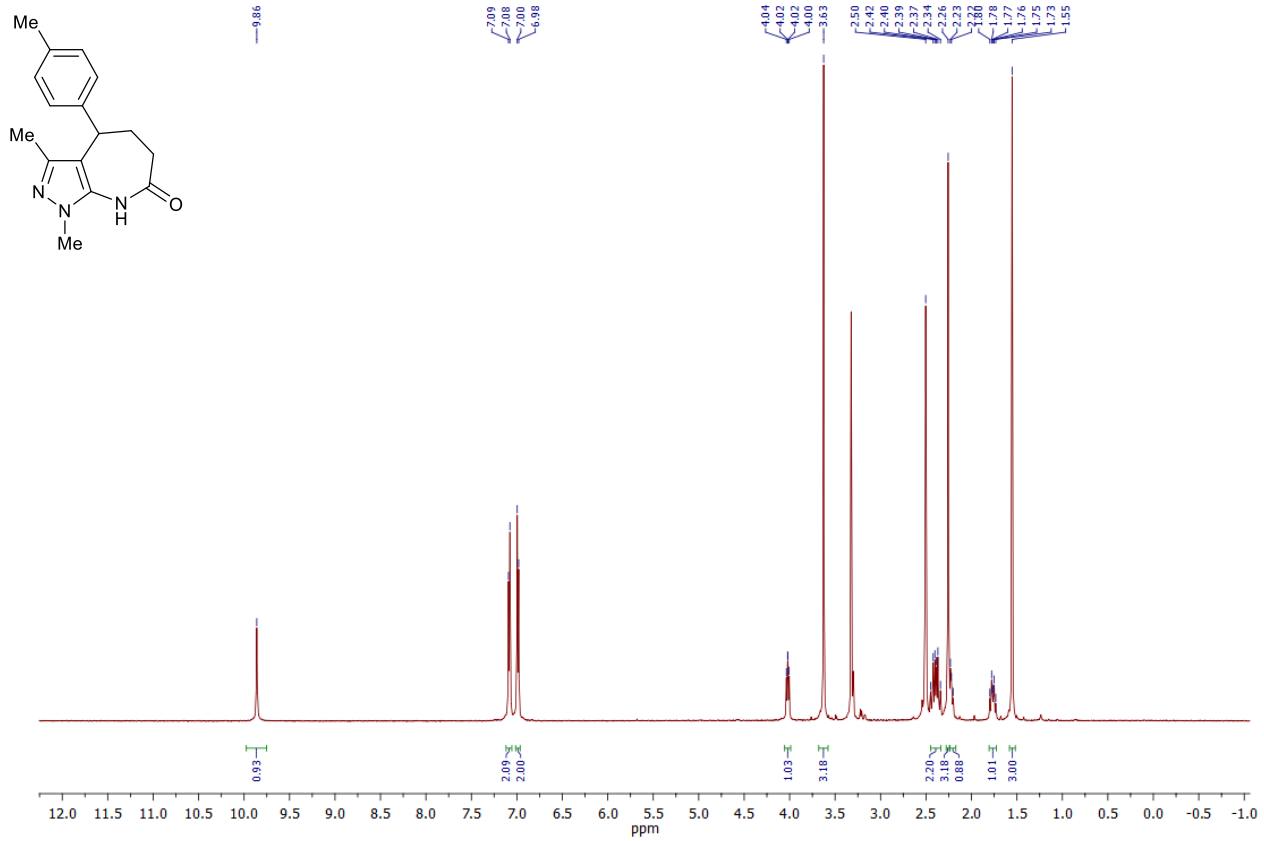


HMBC ^{1}H-^{13}C (DMSO-d_6)

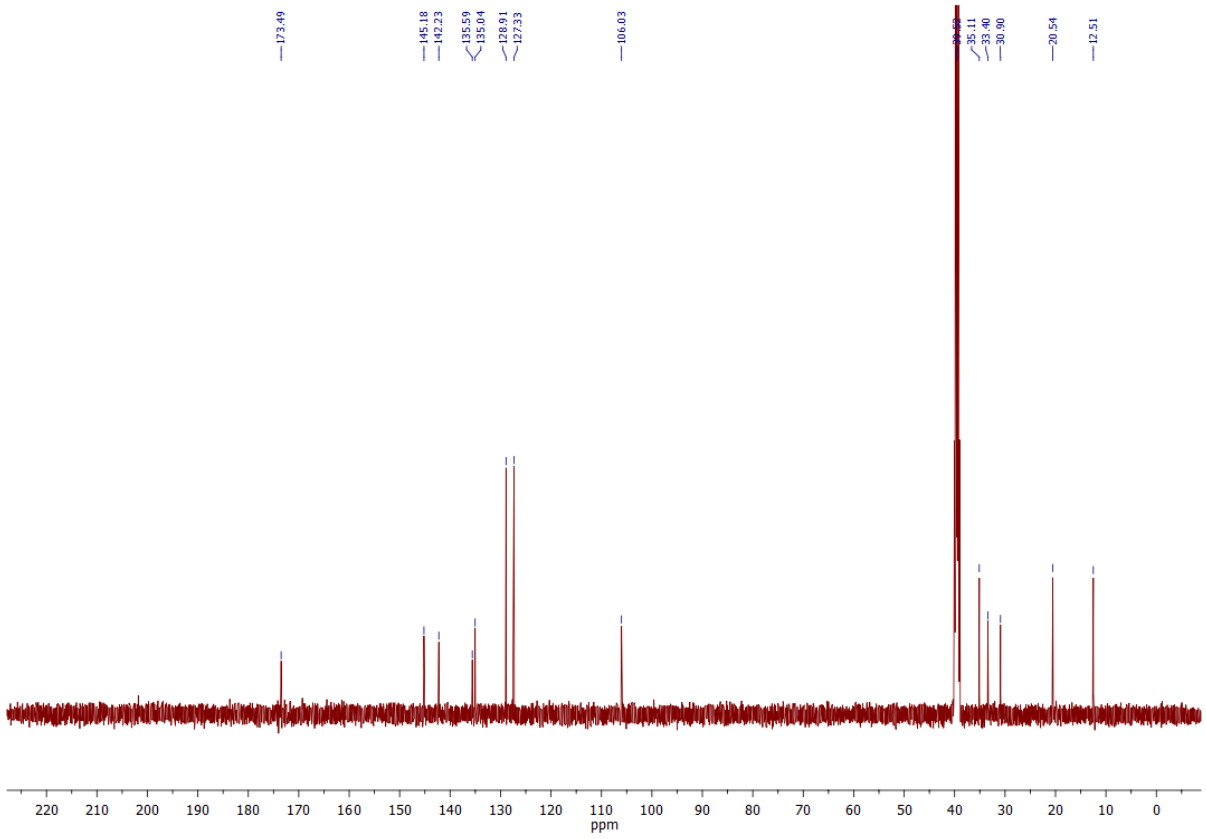


1,3-Dimethyl-4-(*p*-tolyl)-4,5,6,8-tetrahydropyrazolo[3,4-*b*]azepin-7(1*H*)-one (6a)

^{1}H NMR (500 MHz, DMSO-d_6)

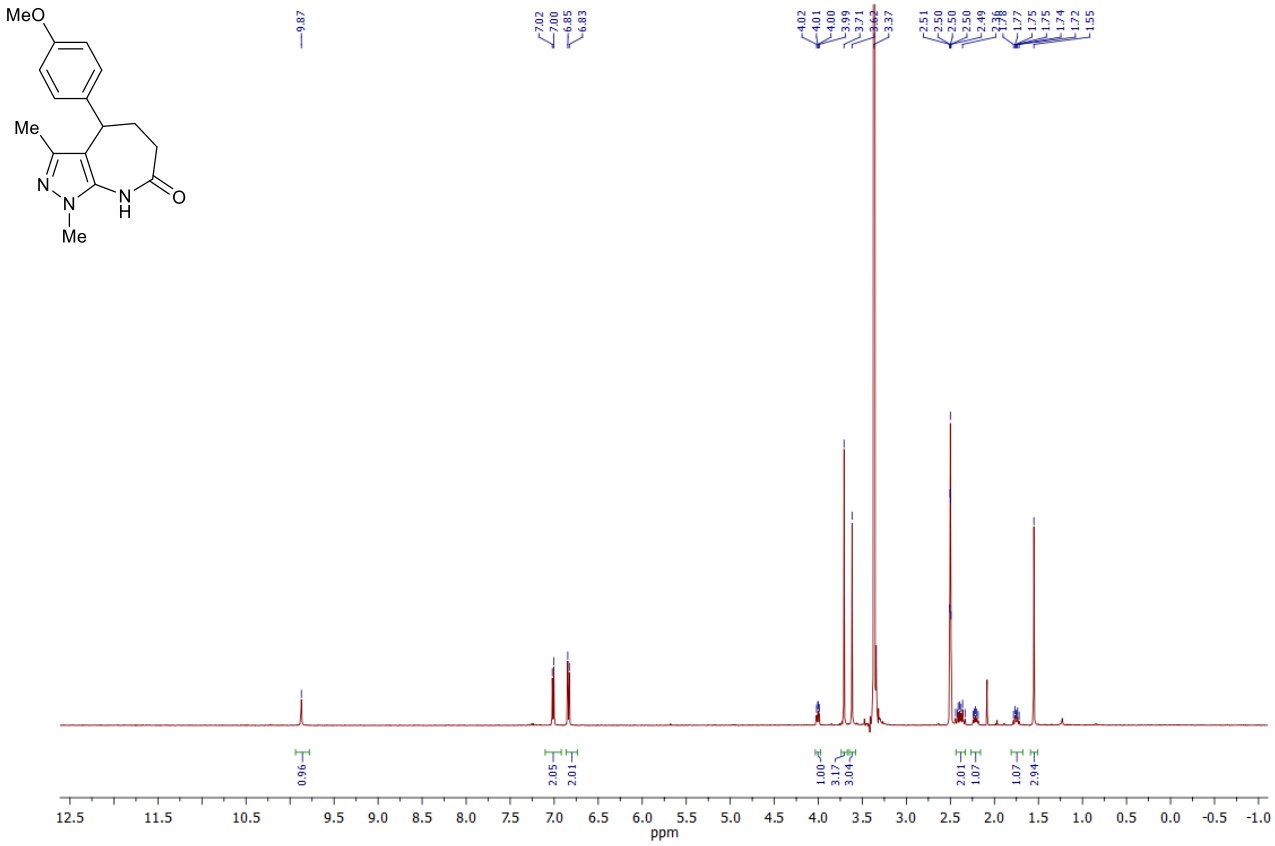


^{13}C NMR (126 MHz, DMSO-d_6)

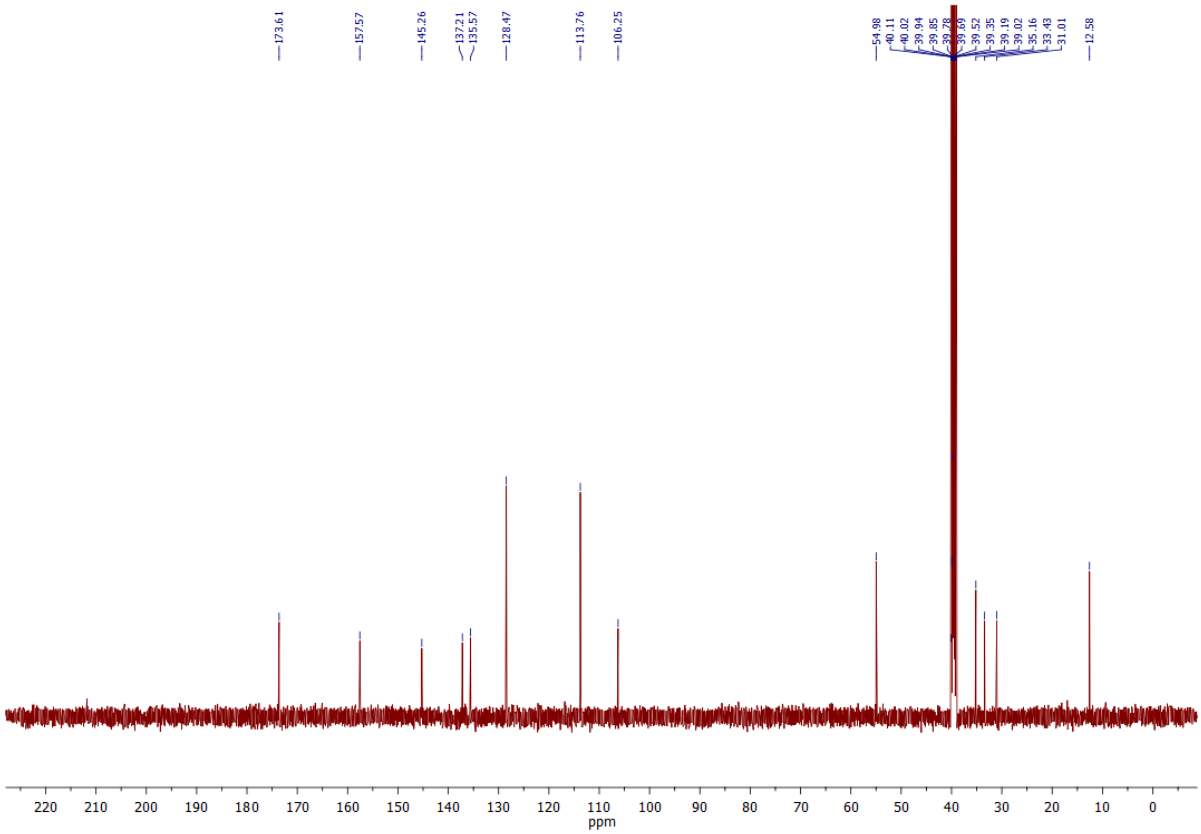


4-(4-Methoxyphenyl)-1,3-dimethyl-4,5,6,8-tetrahydropyrazolo[3,4-*b*]azepin-7(1*H*)-one (6b)

^{1}H NMR (500 MHz, DMSO-d_6)

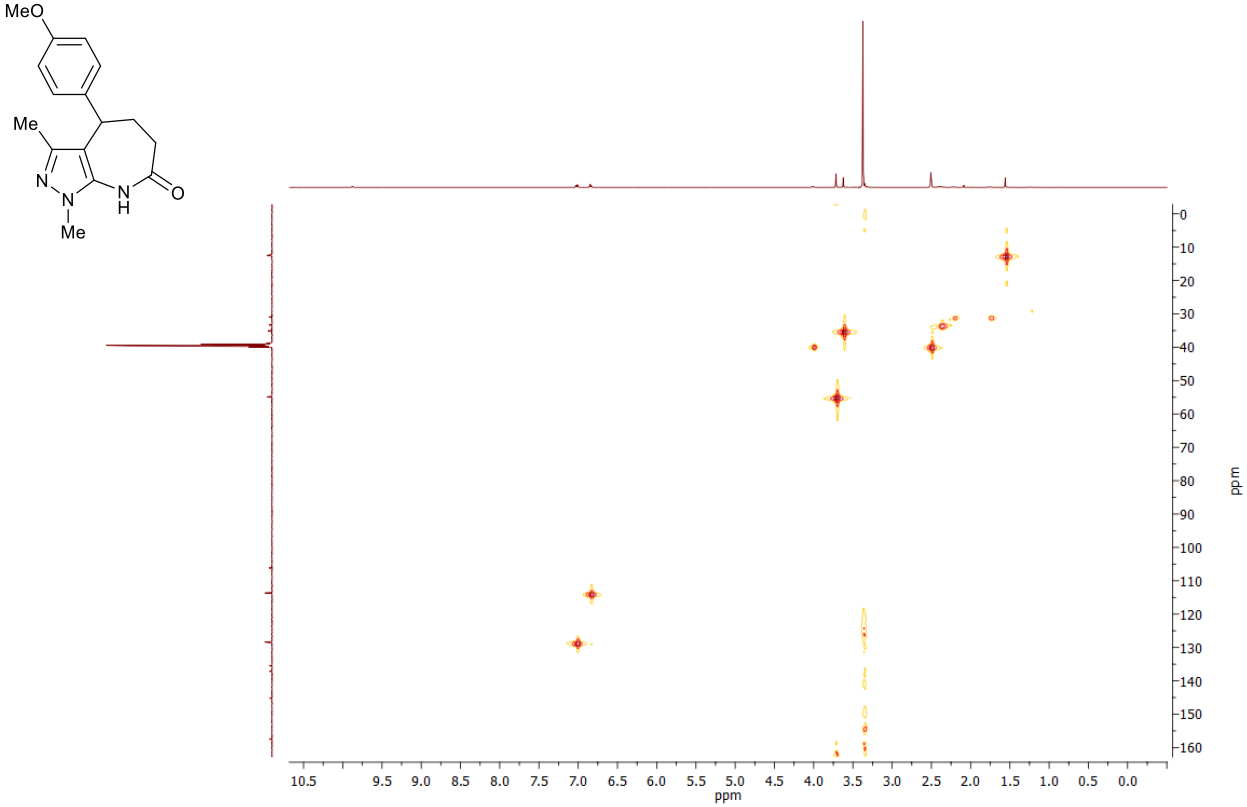


^{13}C NMR (126 MHz, DMSO-d_6)

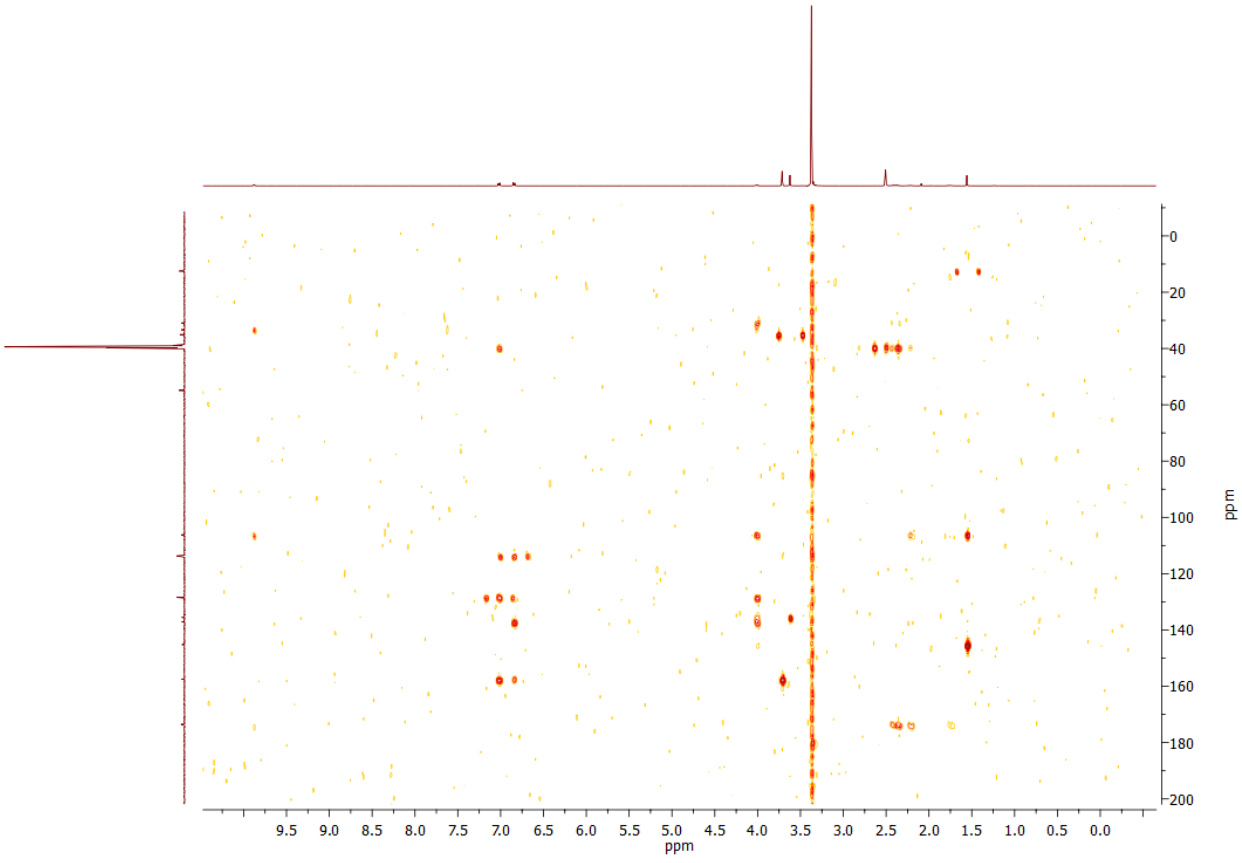


4-(4-Methoxyphenyl)-1,3-dimethyl-4,5,6,8-tetrahydropyrazolo[3,4-*b*]azepin-7(1*H*)-one (6b)

HSQC ^{1}H-^{13}C (DMSO-d_6)

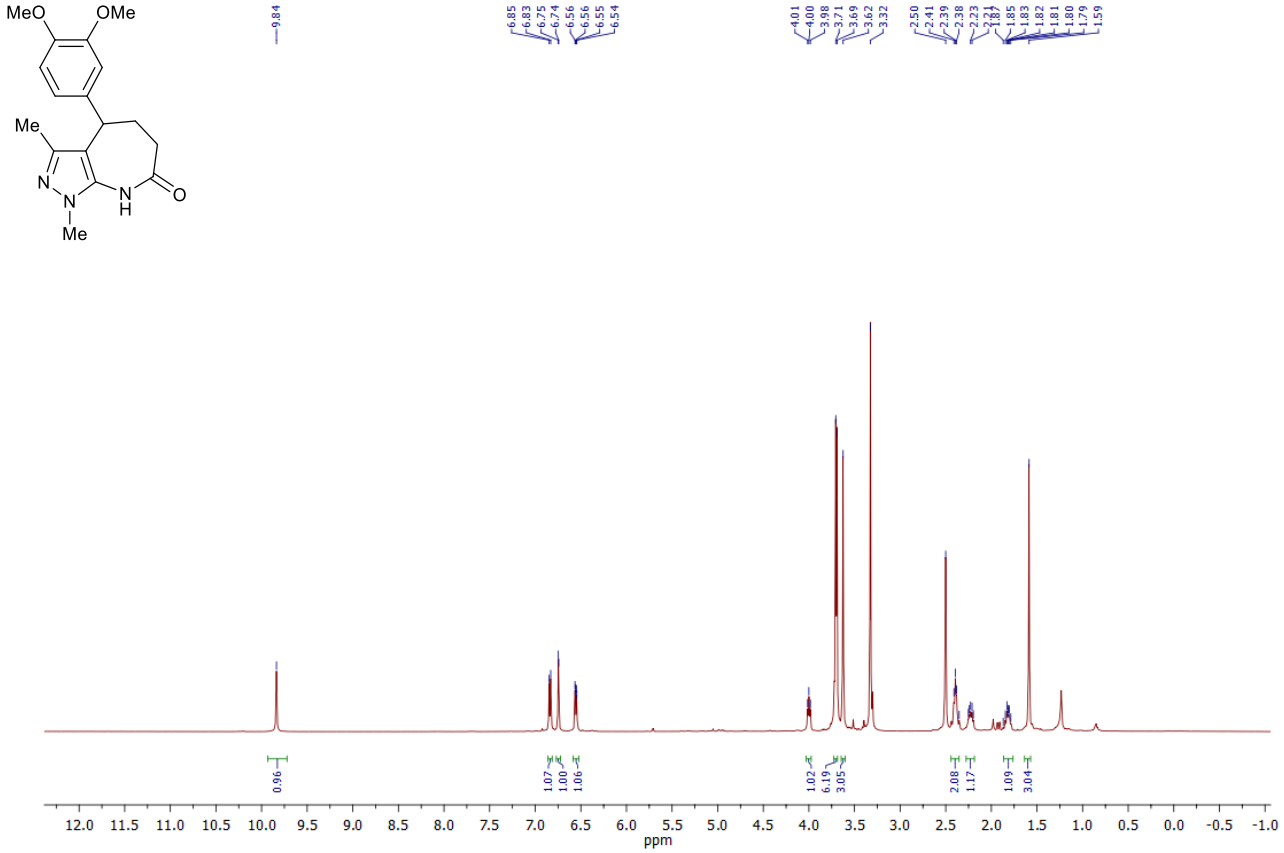


HMBC ^{1}H-^{13}C (DMSO-d_6)

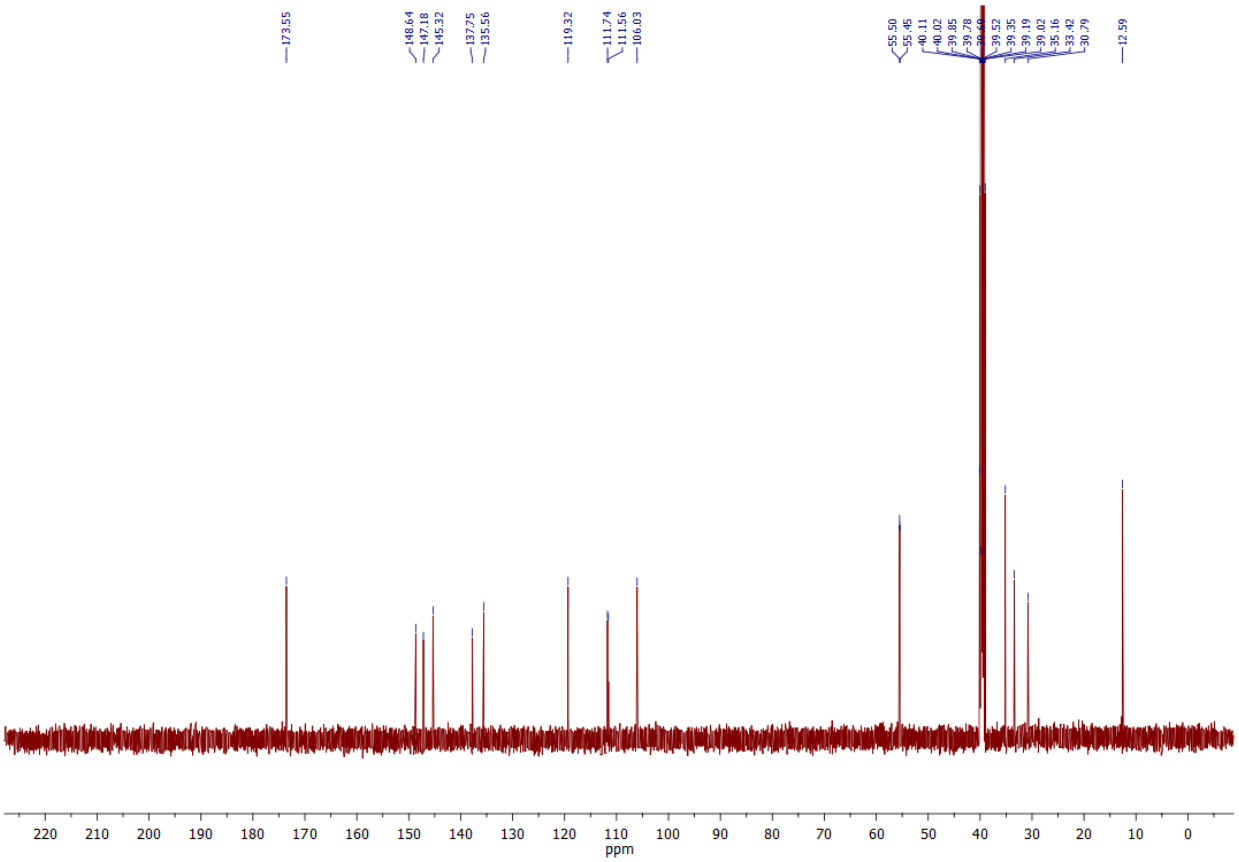


4-(3,4-Dimethoxyphenyl)-1,3-dimethyl-4,5,6,8-tetrahydropyrazolo[3,4-*b*]azepin-7(1*H*)-one (6c)

^{1}H NMR (500 MHz, DMSO-d_6)

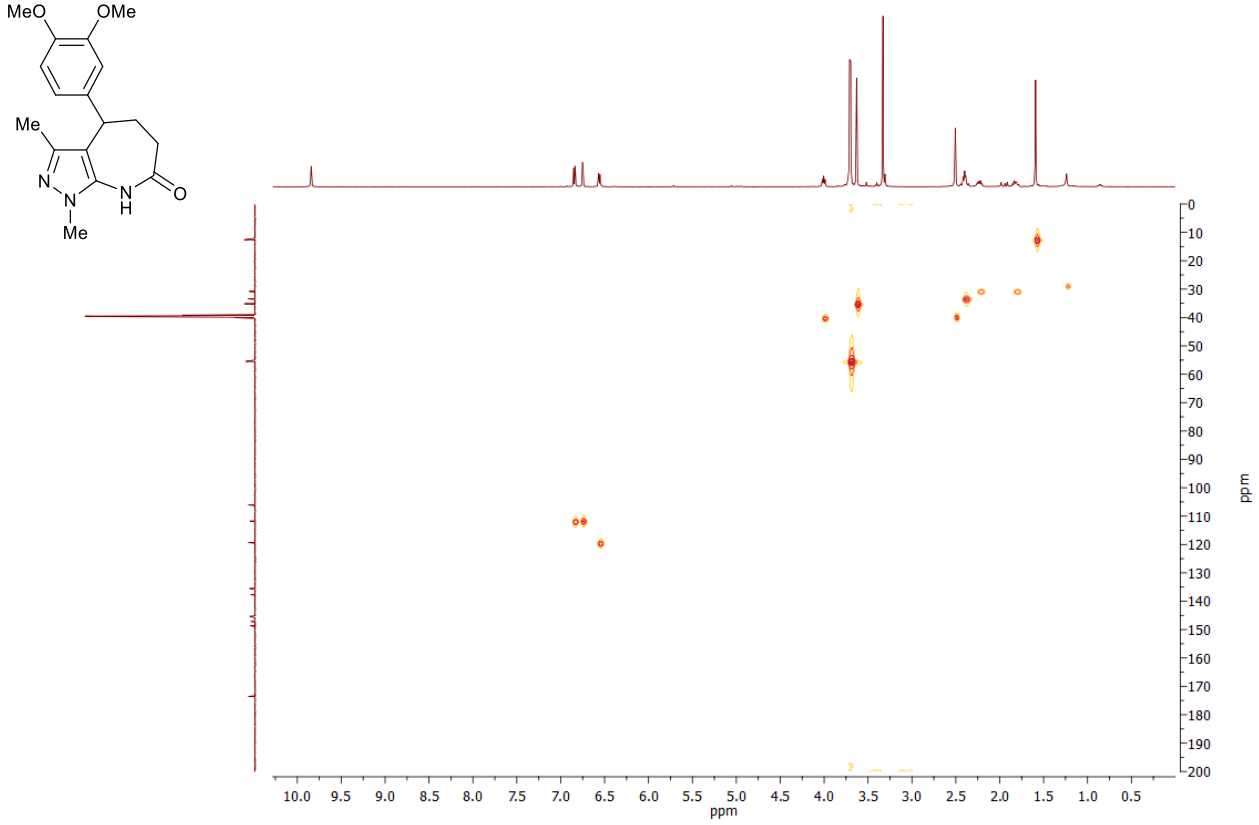


^{13}C NMR (126 MHz, DMSO-d_6)

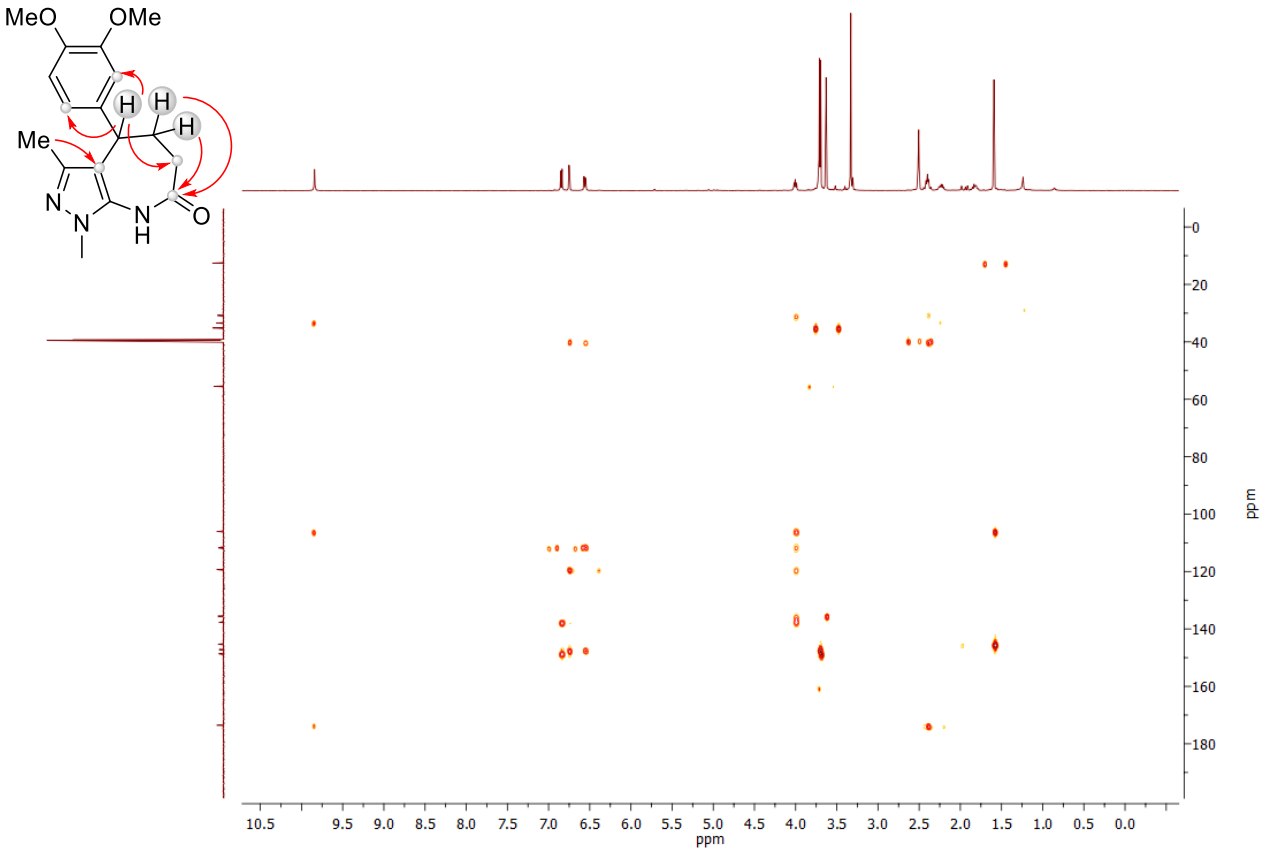


4-(3,4-Dimethoxyphenyl)-1,3-dimethyl-4,5,6,8-tetrahydropyrazolo[3,4-*b*]azepin-7(1*H*)-one (6c)

HSQC ^{1}H-^{13}C (DMSO-d_6)

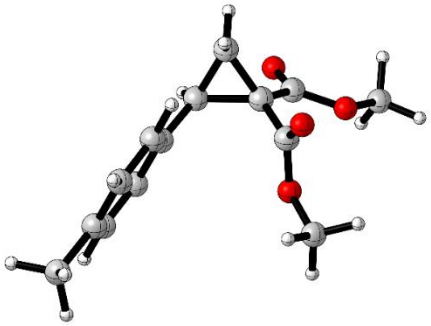


HMBC ^{1}H-^{13}C (DMSO-d_6)



Cartesian coordinates and energetic parameters of starting compounds and products calculated at B3LYP-D3/6-311++G/SMD(MeCN) level**

Dimethyl 2-(*p*-tolyl)cyclopropane-1,1-dicarboxylate (1a)



E_0^{298} = –844.032014 a.u.

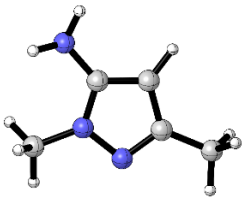
G^{298} = –844.080762 a.u.

0 1

O	-0.7135440	1.5501810	-0.5218480
O	-0.8393800	1.5710870	1.7256020
O	-3.3931940	0.3696150	-0.3384710
O	-2.9821910	-1.8321970	-0.5864020
C	-0.9606060	0.9934560	0.6680750
C	-2.6419840	-0.7316660	-0.2067960
C	1.1857340	-1.0131330	0.1435850
C	1.7706620	-1.1226800	-1.1265970
H	1.1988760	-1.5607480	-1.9387270
C	-1.3621490	-0.4485900	0.5099060
C	3.0656710	-0.6723840	-1.3613230
H	3.4924630	-0.7680230	-2.3551520
C	-0.2215920	-1.4784880	0.3216550
H	-0.5143010	-2.2756810	-0.3528070
C	-0.9742530	-1.4203270	1.6081000
H	-0.5027700	-0.9779570	2.4764010
H	-1.6766330	-2.2176050	1.8163990
C	1.9459710	-0.4437770	1.1700290
H	1.5353330	-0.3487380	2.1682270
C	3.2436240	0.0103860	0.9294820
H	3.8102760	0.4506890	1.7440100
C	-0.3110610	2.9397710	-0.5142070
H	-1.0931380	3.5588710	-0.0714330
H	-0.1632550	3.2037940	-1.5592120
H	0.6189350	3.0592380	0.0439310
C	-4.6699430	0.2100190	-1.0030920
H	-5.1167680	1.2018980	-1.0089650
H	-5.2998240	-0.4889570	-0.4509200
H	-4.5226530	-0.1473850	-2.0233240

C	3.8276710	-0.0940210	-0.3365460
C	5.2397930	0.3698150	-0.5917350
H	5.9292490	-0.4815260	-0.6207770
H	5.3207420	0.8838340	-1.5536410
H	5.5847130	1.0485300	0.1917210

1,3-Dimethyl-1*H*-pyrazol-5-amine (2a)



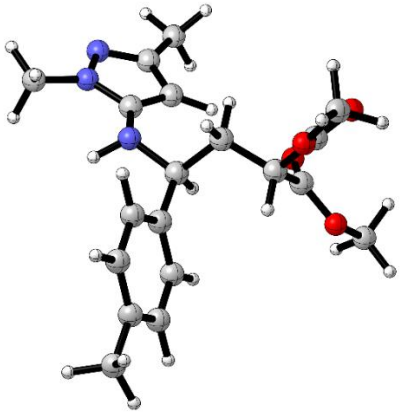
E_0^{298} = –360.178679 a.u.

G^{298} = –360.211869 a.u.

0 1

C	1.3784890	0.0223300	0.0041050
C	0.5856610	1.1922400	0.0017000
C	-0.7282930	0.7337770	-0.0094530
N	-0.6726630	-0.6211420	-0.0274800
N	0.6224850	-1.0762310	-0.0025500
N	-1.9324170	1.4188700	-0.0794910
C	2.8726410	-0.0717760	0.0117380
C	-1.7888310	-1.5476730	0.0083470
H	-2.6937820	1.0024910	0.4449390
H	-1.8409140	2.4024180	0.1429730
H	3.2963800	0.4561680	0.8716130
H	3.3008620	0.3782160	-0.8896290
H	3.1910250	-1.1155790	0.0579440
H	-2.5629630	-1.2252210	-0.6912090
H	-2.2170460	-1.6145540	1.0131650
H	-1.4248850	-2.5285460	-0.2928700
H	0.9114920	2.2207420	0.0111040

Dimethyl 2-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-(*p*-tolyl)ethyl}malonate 3a



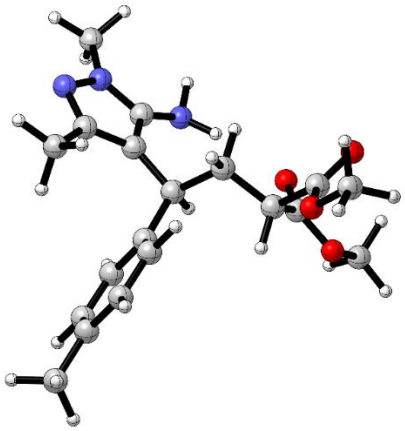
E_0^{298} = –1204.237919 a.u.
G^{298} = –1204.301699 a.u.

0 1

C	4.5350470	-0.2979050	-0.2808700
C	3.1233580	-0.3537040	-0.3420430
C	2.6950810	0.8367370	0.2425940
N	3.8110300	1.5140200	0.6214630
N	4.9548630	0.8314940	0.2889600
N	1.4283530	1.3318620	0.4947540
C	0.2711380	0.6288480	-0.0901330
C	-0.8936340	1.5867300	-0.2452060
C	-0.0937930	-0.5791680	0.8010600
C	-1.1977710	-1.4580340	0.1863160
C	-1.5321800	1.7286600	-1.4781280
C	-2.6304420	2.5789020	-1.6214720
C	-3.1171690	3.3164710	-0.5382330
C	-2.4720130	3.1703360	0.6985740
C	-1.3820550	2.3178060	0.8459940
C	-4.2877560	4.2557190	-0.6876870
C	5.5098460	-1.3269790	-0.7627400
C	-0.7299300	-2.1861730	-1.0666470
O	0.4237280	-2.4120530	-1.3525340
O	-1.7738590	-2.5567760	-1.8169220
C	-1.4725220	-3.3075660	-3.0189950
C	-1.6587460	-2.4876340	1.2089330
O	-1.2866450	-3.6391440	1.2553910
O	-2.5095480	-1.9374560	2.0817340
C	-2.9699770	-2.7866780	3.1626200
H	2.5052580	-1.1414100	-0.7416040
H	1.3586540	2.3398210	0.4257340
H	0.5365510	0.2596040	-1.0867250
H	0.7944760	-1.1897620	0.9708630
H	-0.4339840	-0.2065270	1.7691740
H	-2.0610270	-0.8426450	-0.0744230
H	-1.1734420	1.1654950	-2.3339390
H	-3.1128960	2.6688430	-2.5896630
H	-2.8340140	3.7277830	1.5572050
H	-0.9099480	2.2157570	1.8175380
H	-4.8099370	4.0956480	-1.6336630
H	-5.0053260	4.1262630	0.1277650
H	-3.9547330	5.2991710	-0.6618070
H	5.3927040	-2.2676790	-0.2151210
H	5.3571740	-1.5478110	-1.8236720
H	6.5358800	-0.9773960	-0.6278450
H	-2.4361430	-3.5180850	-3.4778210
H	-0.8522680	-2.7119410	-3.6904390

H	-0.9598920	-4.2365620	-2.7645810
H	-3.6351240	-2.1626330	3.7555320
H	-3.5088070	-3.6472060	2.7636890
H	-2.1245320	-3.1226010	3.7647420
C	3.8766320	2.8311570	1.2252280
H	3.6498540	3.6149640	0.4956610
H	3.1680650	2.8978130	2.0541430
H	4.8856420	2.9777490	1.6066850

Dimethyl 2-(2-(5-amino-1,3-dimethyl-1*H*-pyrazol-4-yl)-2-(*p*-tolyl)ethyl)malonate 4a



E_0^{298} = –1204.247020 a.u.
G^{298} = –1204.307843 a.u.

0 1

C	-2.8163010	-0.8123220	-1.0131470
C	-1.6815970	-1.0705500	-0.2034640
C	-1.8217370	-2.4087070	0.1709090
N	-2.9677990	-2.8675010	-0.3837010
N	-3.5956220	-1.8934530	-1.1179920
N	-1.0286290	-3.1768530	1.0096780
C	-0.5056590	-0.2123690	0.2053180
C	0.7103440	-0.4880010	-0.7085610
C	-0.8691750	1.2618880	0.3608300
C	2.0451720	-0.0470930	-0.0777110
C	-0.4795940	2.2578210	-0.5348500
C	-0.8792850	3.5856290	-0.3550840
C	-1.6799870	3.9631940	0.7247260
C	-2.0666300	2.9618430	1.6283510
C	-1.6655640	1.6424330	1.4506950
C	-2.1050950	5.3954520	0.9338410
C	2.4401300	-0.9450830	1.0893490
O	1.9276310	-2.0095800	1.3625270
O	3.4436460	-0.4053970	1.7841830
C	3.9494580	-1.1740490	2.9049950
C	-3.2084610	0.4543750	-1.7108820
C	3.1429440	-0.0980960	-1.1288930

O	3.8002660	-1.0816040	-1.3911850
O	3.2537140	1.0714100	-1.7676660
C	4.2030310	1.1248700	-2.8620720
C	-3.5396630	-4.1941170	-0.2489610
H	-1.0854460	-4.1768260	0.8563550
H	-0.0608820	-2.8705170	1.0497860
H	-0.2246970	-0.5480770	1.2104160
H	0.5785890	0.0033590	-1.6743850
H	0.7670790	-1.5588980	-0.9092220
H	1.9707170	0.9774710	0.2911670
H	0.1336510	2.0150550	-1.3940280
H	-0.5617800	4.3360420	-1.0727170
H	-2.6878520	3.2226230	2.4802340
H	-1.9842600	0.8864360	2.1622420
H	-1.5986150	5.8315940	1.8019850
H	-3.1809590	5.4653040	1.1210300
H	-1.8687880	6.0131390	0.0643230
H	4.3256310	-2.1381140	2.5599520
H	3.1617340	-1.3230280	3.6447100
H	4.7567010	-0.5766550	3.3228830
H	-2.4262120	0.7922370	-2.3958400
H	-3.3827760	1.2652080	-0.9983430
H	-4.1241820	0.2940110	-2.2846310
H	4.1399700	2.1399990	-3.2479520
H	3.9288610	0.4050870	-3.6347520
H	5.2103530	0.9166410	-2.4987430
H	-3.7802520	-4.4083160	0.7961020
H	-2.8461450	-4.9539430	-0.6204210
H	-4.4521460	-4.2265210	-0.8412490