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New β-[*o*-(5-oxopyrazol-3-yl)aryl]ethylamines and their unusual metastable betaine form

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General Information

NMR spectra of new compounds were recorded on a spectrometer Bruker Avance 600 (600 MHz) or Varian XL 300 (300 MHz) (compound **2b**) in DMSO-d_6. Chemical shifts of nuclei ^{1}H and ^{13}C were measured relatively the residual signals of deuterated solvent (see δ values in ref. [S1]). Coupling constants (*J*) are reported in Hz. Melting points were determined by using Fisher-Johns Melting Point Apparatus (Fisher Scientific) and are uncorrected. Elemental analysis was performed using a EuroEA 3000 analyzer by burning a portion of the sample in an oxygen flow followed by chromatography of the combustion gases. The reaction and purity of the obtained compounds were monitored by TLC (plates with Al_2O_3 III activity grade, eluent $CHCl_3$, development of TLC plates by exposition to iodine vapors in iodine chamber).

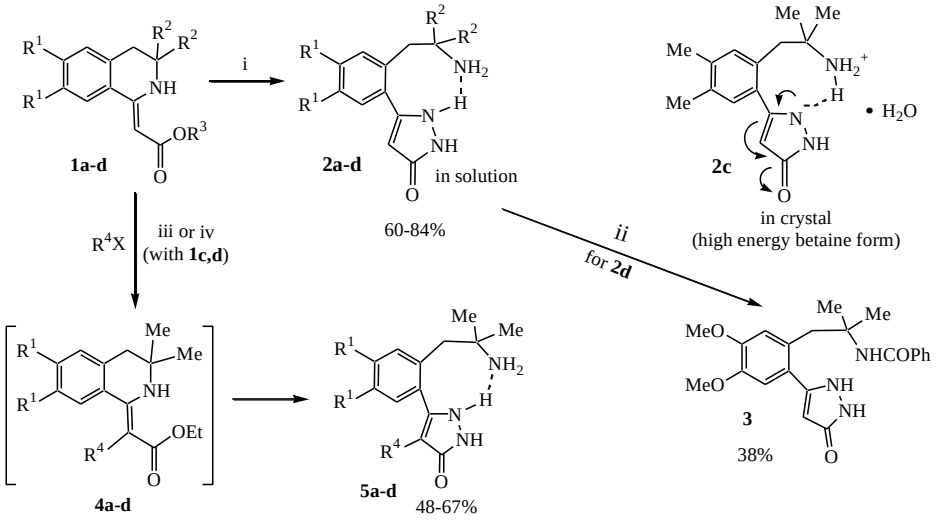
The crystallographic data for structure **2c** were obtained on an Agilent SuperNova diffractometer by using a microfocus X-ray source with copper anode and an Atlas S2 two-dimensional CCD detector. The reflections were collected, unit cell parameters determined and refined by using the specialized CrysAlisPro 1.171.41.93a (Rigaku OD, 2020) [S2]. The structures were solved by using the ShelXT 2018/2 program (Sheldrick, 2018) [S3] and refined with the ShelXL 2018/3 program (Sheldrick, 2015) [S4].

Molecular graphics for structure **2c** were performed with the Olex software suite (ver 1.5) [S5]. CCDC 2193910 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk.

Quantum-chemical calculations were performed using quantum chemical program package Firefly 8.0 [S6], which is partially based on the GAMESS (US) [S7] source code at the DFT level of theory (B3LYP/6-311G**).

Starting compounds **1a,c** [S8], **1b,d [S**9], were synthesized as described previously.

Synthesis and characterization of compounds 2, 3, 5.



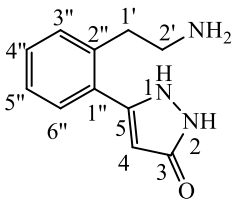
1a $R^1 = R^2 = H$, $R^3 = Me$ | **2a** $R^1 = R^2 = H$ | **4a,5a** $R^1 = OMe$, $R^4 = Me$

1b $R^1 = OMe$, $R^2 = H$, $R^3 = Me$ | **2b** $R^1 = OMe$, $R^2 = H$ | **4b,5b** $R^1 = OMe$, $R^4 = Bn$

1c $R^1 = R^2 = Me$, $R^3 = Et$ | **2c** $R^1 = R^2 = Me$ | **4c,5c** $R^1 = R^4 = Me$

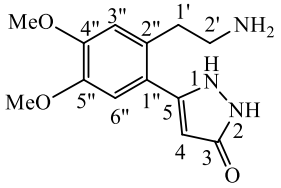
1d $R^1 = OMe$, $R^2 = Me$, $R^3 = Et$ | **2d** $R^1 = OMe$, $R^2 = Me$ | **4d,5d** $R^1 = Me$, $R^4 = Bn$

5-[2-(2-Aminoethyl)phenyl]-1,2-dihydro-3*H*-pyrazol-3-one (2a).



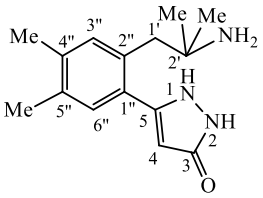
A mixture of methyl 2-(3,4-dihydroisoquinolin-1(2*H*)-ylidene)acetate (**1a**) [S8] (2.03 g, 0.01 mol) and hydrazine hydrate (2 mL) in EtOH (7 mL) was boiled for 6 h. The precipitate formed was filtered off from the hot solution, washed with hot EtOH (3×3 mL) and dried at 100 ºC in air. Yield was 1.22 g (60%). Colourless crystals from EtOH, mp 220-221ºC (dec.). ^{1}H NMR (600 MHz), δ: 2.77 (s, 4H, C(1')H_2, C(2')), 5.57 (s, 1H, H-4), 6.39 (br. s, 4H, NH_2, 2NH), 7.21-7.25 (m, 1H, H-5''), 7.26-7.31 (m, 2H, H-3'', H-6''), 7.33 (d, *J* 7.5, 1H, H-6''). ^{13}C NMR (150 MHz), δ: 36.4, 42.6, 89.3, 125.9, 127.9, 129.1, 130.1, 131.1, 137.8, 143.0 160.6. Found (%): C, 65.31; H, 6.71; N, 20.54. Calc. for $C_{11}H_{13}N_3O$. (%): C, 65.01; H, 6.45; N, 20.68.

5-[2-(2-Aminoethyl)-4,5-dimethoxyphenyl]-1*H*-pyrazol-3(2*H*)-one (2b).



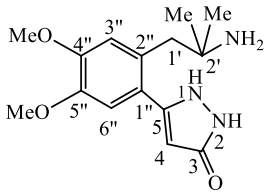
The compound was obtained analogously to the **2a** from methyl 2-(6,7-dimethoxy-3,4-dihydroisoquinolin-1-yl)acetate **1b** and hydrazine hydrate. Yield was 1.22 g (68%). Colourless crystals with mp 239-241ºC (EtOH). ^{1}H NMR (600 MHz), δ: 2.72 (t, *J* 6.9, 2H, C(1')H_2), 2.78 (t, *J* 6.9, 2H, C(2')H_2), 3.74 (s, 3H, OMe), 3.76 (s, 3H, OMe), 5.52 (s, 1H, H-4), 6.61 (br. s, 3H, NH_2, NH), 6.85 (s, 1H, H-6"), 6.90 (s, 1H, H-3").^{13}C NMR (150 MHz), δ: 35.9, 42.7, 55.5, 83.8, 112.7, 113.7, 123.4, 130.1, 143.2, 146.7, 148.4, 161.0. Found (%): C, 59.11; H, 6.30; N, 16.72. Calc. for $C_{13}H_{17}N_3O_3$ (%): C, 59.30; H, 6.51; N, 15.96.

5-[2-(2-Amino-2-methylpropyl)-4,5-dimethylphenyl]-1,2-dihydro-3*H*-pyrazol-3-one (2c).



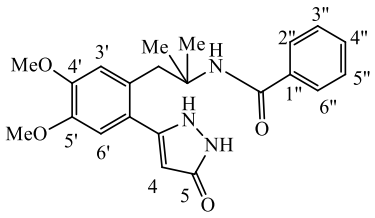
A mixture of ethyl 2-(3,3,6,7-tetramethyl-3,4-dihydroisoquinolin-1-yl)acetate **1c** (1.64 g, 0.006 mol) and hydrazine hydrate (3 mL) in methylcellosolve (10 mL) was boiled for 6 h, cooled, the precipitate was filtered off, washed with methylcellosolve (2×3 mL) and EtOH (3×3 mL) and dried at 100 ºC in air. Yield was 1.31 g (84%). Colourless crystals with mp 205-206 ºC (methylcellosolve) (dec.). ^{1}H NMR (600 MHz), δ: 1.10 s (6H, 2Me-2'), 2.21 2s (6H, Me-4", Me-5"), 2.68 s (2H, CH_2), 5.46 s (1H, H-4), 6.66 br.s (3H, NH_2, NH), 7.04 s (1H, H-3"), 7.13 s (1H, H-6"). ^{13}C NMR (150 MHz), δ: 18.8, 19.1, 30.57, 45.2, 50.2, 88.8, 129.9, 130.5, 132.5, 133.4, 134.2, 135.1, 143.8, 161.1. Found (%): C, 61.70; H, 7.09; N, 14.26. Calc. for $C_{15}H_{21}N_3O$ (%): C, 61.84; H, 7.27; N, 14.42.

5-[2-(2-Amino-2-methylpropyl)-4,5-dimethoxyphenyl]-1,2-dihydro-3*H*-pyrazol-3-one (2d).



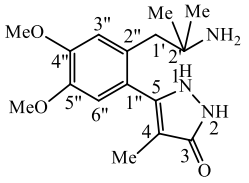
The compound was obtained analogously to the **2c** from ethyl 2-(6,7-dimethoxy-3,3-dimethyl-3,4-dihydroisoquinolin-1-yl)acetate **1d** and hydrazine hydrate. Yield was 1.19 g (68%). Colorless crystals with mp 249-251°C (methylcellosolve). ^{1}H NMR (600 MHz), δ: 1.11 s (6H, 2Me-2'), 2.68 s (2H, C(1')H_2), 3.75 (s, 3H, OMe), 3.76 (s, 3H, OMe), 5.51s (1H, H-4), 5.59-7.28 (m, 5H, NH_2, NH, H-3", 6"). ^{13}C NMR (150 MHz), δ: 30.5, 45.2, 50.3, 55.4, 55.5, 88.8, 112.9, 115.7, 124.7, 127.8, 143.6, 147.1, 147.7, 161.2. Found (%): C, 61.59; H, 7.12; N, 14.18. Calc. for $C_{15}H_{21}N_3O_3$. (%): C, 61.84; H, 7.27; N, 14.42.

***N*-{1-[4,5-Dimethoxy-2-(5-oxo-2,5-dihydro-1*H*-pyrazol-3-yl)phenyl]-2-methylprop-2-yl}benzamide (3).**



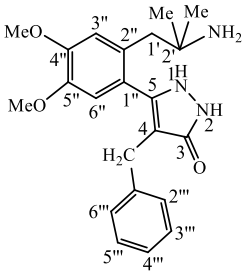
The mixture of 5-[2-(2-amino-2-methylpropyl)-4,5-dimethoxyphenyl]-1,2-dihydro-3H-pyrazol-3-one **2d** (0.29 g, 0.001 mol), benzoyl chloride (0.23 mL, 0.28 g, 0.002 mol), Et_3N (0.42 mL, 0.30 g, 0.003 mol) in $CHCl_3$ (10 mL) was boiled 5 h. Then H_2O (10 mL) was added, and the mixture was stirred for 5 h, hydrazine hydrate (2 mL) was added, stirring was continued for 6 h. The organic layer was separated and kept at 5-8°C for 12 h. The precipitate formed was filtered off, washed with $CHCl_3$ (2×2 mL). Yield was 0.15 g (38%), mp 168-171°C. ^{1}H NMR (600 MHz), δ: 1.18 s (6H, 2Me), 3.31 s (2H, CH_2), 3.45 (s, 3H, OMe), 3.75 (s, 3H, OMe), 5.59 s (1H, H-4), 6.71 s (1H, H-3'), 6.87 (s, 1H, H-6'), 7.39-7.44 m (2H, H-3", H-5"), 7.47-7.54 m (1H, H-4"), 7.74-7.81 m (2H, H-2", H-6"), 9.97 s (1H, NH), 11.60 s (1H, NH). ^{13}C NMR (150 MHz), δ: 27.3, 43.3, 55.1, 55.3, 55.9, 89.9, 113.4, 115.2, 124.9, 127.8, 128.5, 129.1, 131.4, 136.1, 147.3, 148.2, 150.8, 160.3, 167.1. Found (%): C, 66.58; H, 6.12; N, 10.39. Calc. for $C_{22}H_{25}N_3O_4$. (%): C, 66.82; H, 6.37; N, 10.63.

5-[2-(2-Amino-2-methylpropyl)-4,5-dimethoxyphenyl]-4-methyl-1*H*-pyrazol-3(2*H*)-one (5a).



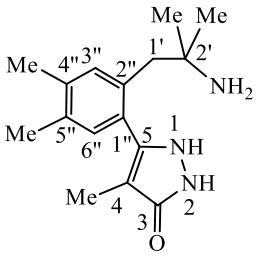
A mixture of ethyl 2-(6,7-dimethoxy-3,3-dimethyl-3,4-dihydroisoquinolin-1-yl)acetate **1d** (0.61 g, 0.002 mol), iodomethane (0.19 mL, 0.43 g, 0.003 mol) and methylcellosolve (7 mL) was boiled for 10 h. The excess of MeI was pumped off in a water jet vacuum for 4 h at room temperature. Hydrazine hydrate (2 mL) was added, and this was boiled for 5 h. The mixture was cooled, kept at 5-8°C for 24 h, the precipitate formed was filtered off, washed with methylcellosolve (2 × 1 mL) and ethanol (2 × 2 mL). Yield was 0.41 g (67%), m.p. 237-238°C (PrOH) (dec.). ^{1}H NMR (600 MHz), δ: 1.01 (s, 6H, 2Me-2'), 1.77 (s, 3H, Me), 2.54 (2H, CH_2), 3.74 (s, 3H, OMe), 3.77 (s, 3H, OMe), 4.34-6.62 (m, 4H, 2NH, NH_2), 6.76 (s, 1H, H-3''), 6.89 (s, 1H, H-6''). ^{13}C NMR (150 MHz), δ: 7.1, 27.9, 30.7, 45.5, 50.0, 55.5, 55.5, 95.9, 113.4, 115.4, 124.0, 129.3, 140.0, 146.8, 147.7, 160.0. Found (%): C 62.68; H 7.34; N 13.46. Calc. for $C_{16}H_{23}N_3O_3$ (%): C 62.93; H 7.59; N 13.76.

5-[2-(2-Amino-2-methylpropyl)-4,5-dimethoxyphenyl]-4-benzyl-1,2-dihydro-3*H*-pyrazol-3-one (5b).



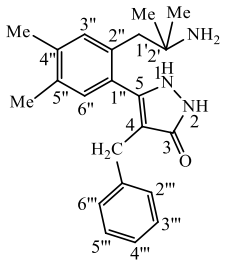
A mixture of ethyl 2-(6,7-dimethoxy-3,3-dimethyl-3,4-dihydroisoquinolin-1-yl)acetate **1d** (0.92 g, 0.003mol), benzyl chloride (0.35 mL, 0.38 g, 0.003 mol) and EtOH (8 mL) was boiled for 10 h. Then hydrazine hydrate (3 mL) was added, and this was boiled for 8 h, cooled and kept at room temperature for 24 h. The precipitate was filtered off and washed with ethanol (2 x 2 mL). Yield was 0.59 g (52%), m.p. 208-209°C (EtOH) (dec.). ^{1}H NMR (600 MHz), δ: 1.07 (s, 6H, 2Me-2'), 2.53 (s, 2H, CH_2), 3.36 (3H, OMe), 3.58 (s, 2H, CH_2), 3.75 (3H, OMe), 4.15-6.43 (m, 3H, NH_3^+), 6.51 (1H, H-3''), 6.86 (s, 1H, H-6''), 7.09-7.11 (m, 3H, H-2''', H-4''', H-6'''), 7.20-7.22 (m, 2H, H-3''', H-5'''). ^{13}C NMR (150 MHz), δ: 27.6, 30.8, 45.3, 49.9, 54.8, 55.4, 99.2, 113.1, 115.3, 123.9, 125.3, 127.8, 127.9, 129.0, 140.5, 142.0, 146.6, 147.6, 160.35. Found (%): C 69.00; H 7.11; N 11.40.Calc. for $C_{22}H_{27}N_3O_3$ (%): C 69.27; H 7.13; N 11.02.

5-[2-(2-Amino-2-methylpropyl)-4,5-dimethylphenyl]-4-methyl-1*H*-pyrazol-3(2*H*)-one (5c).



The compound was obtained analogously to the compound **5a** from ethyl 2-(3,3,6,7-tetramethyl-3,4-dihydroisoquinolin-1-yl)acetate **1c**, iodomethane and hydrazine hydrate. Yield was 0.33 g (60%), m.p. 231-233ºC (EtOH) (dec.). ^{1}H NMR (600 MHz), δ: 0.99 (s, 6H, 2Me-2'), 1.74 (s, 3H, Me), 2.21 (3H, Me), 2.23 (3H, Me), 2.53 (s, 2H, CH_2), 5.98-7.354 (m, 5H, H-3", H-6", NH_2, NH). ^{13}C NMR (150 MHz), δ: 7.1, 18.8, 19.1, 30.7, 30.7, 45.5, 49.9, 95.8, 129.3, 130.4, 130.9, 132.9, 133.8, 133.9, 135.1, 140.0, 159.7. Found (%): C 69.92; H 8.11; N 15.41. Calc. for $C_{16}H_{23}N_3O$ (%): C 70.30; H 8.48; N 15.37.

5-[2-(2-Amino-2-methylpropyl)-4,5-dimethylphenyl]-4-benzyl-1*H*-pyrazol-3(2*H*)-one (5d).



The compound was obtained analogously to compound **5b** from ethyl 2-(3,3,6,7-tetramethyl-3,4-dihydroisoquinolin-1-yl)acetate **1c**, benzyl iodide and hydrazine hydrate. Yield was 0.50 g (48%), m.p. 191-193ºC (EtOH) (dec.) ^{1}H NMR (600 MHz), δ: 1.04 (s, 6H, 2Me-2'), 2.09 (s, 3H, Me), 2.21 (s, 3H, Me), 2.52 (s, 2H, CH_2), 3.54 (s, 2H, CH_2), 4.35-6.75 (m, 3H, NH_2, NH), 6.83 (s, 1H, H-3"), 7.08-7.11 (m, 4H, H-6", H-3'" – H-5'"), 7.19-7.21 (m, 2H, H-2'", H-6'"). ^{13}C NMR (150 MHz), δ: 18.7, 19.1, 27.7, 30.7, 45.2, 49.9, 99.7, 125.3, 127.9, 127.9, 129.1, 131.0, 132.9, 133.6, 133.7, 135.2, 140.6, 142.1, 160.1. Found (%): C 75.31; H 7.41; N 11.85. Calc. for $C_{22}H_{27}N_3O_3$ (%): C 75.61; H 7.79; N 12.02.

Structure and crystal data for compound 2c.

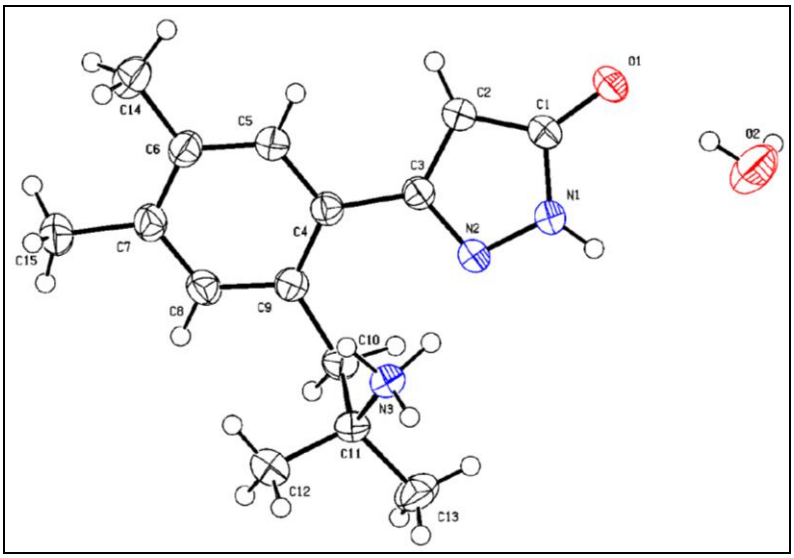
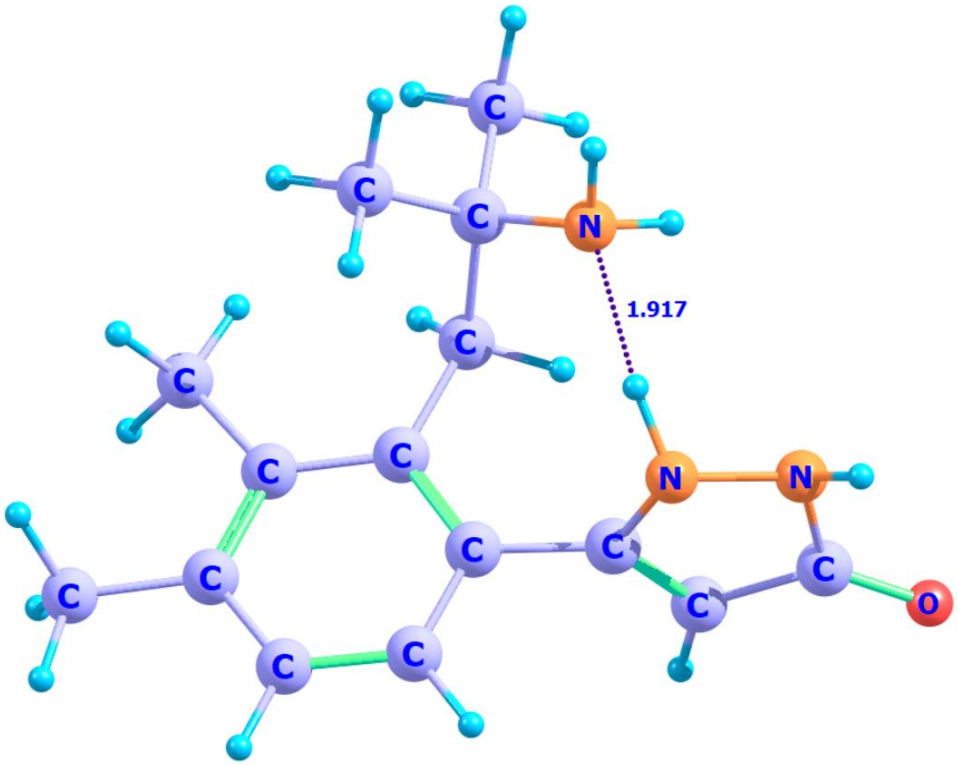


Table S1 Crystal data and structure refinement for	**2c**
CDC Number	2193910
Empirical formula	$C_{15}H_{23}N_3O_2$
Formula weight	277.36
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	13.0630(3)
b/Å	9.6899(2)
c/Å	12.6477(3)
α/°	90
β/°	108.487(3)
γ/°	90
Volume/Å^3	1518.32(6)
Z	4
ρ_{calc}g/cm^3	1.213
μ/mm^{-1}	0.656
F(000)	600.0
Crystal size/mm^3	0.4 × 0.303 × 0.159
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.136 to 152.378
Index ranges	$-16 \le h \le 16$, $-12 \le k \le 11$, $-13 \le l \le 15$
Reflections collected	16441
Independent reflections	3167 [R_{int} = 0.0249, R_{sigma} = 0.0163]
Data/restraints/parameters	3167/0/208
Goodness-of-fit on F^2	1.047
Final R indexes [I>=2σ (I)]	R_1 = 0.0391, wR_2 = 0.1117
Final R indexes [all data]	R_1 = 0.0416, wR_2 = 0.1148
Largest diff. peak/hole / e Å^{-3}	0.27/-0.17

Quantum chemical data

(B3LYP/6-311G**)

Compound **2c**, 1*H*,2*H*-tautomeric non-betaine form



E_{tot} = -863.2811342 a.u.

Cartesian coordinates, Å

O	-4.086481739700	0.320293028400	-0.550843608200	C	3.050190908500	0.019338163900	-0.583665038400
N	0.073605919100	-3.048342597800	0.618260705500	C	3.480920970800	1.233192796400	-0.009569200000
H	-0.757293653300	-3.222334828800	0.056826108700	H	2.887558349400	2.993041342200	1.062001168200
H	-0.672050801800	-1.417331275900	1.296606851000	H	-1.573132076200	1.399048972000	-1.478831529600
H	0.157993422900	-3.833161482600	1.257759011900	C	2.493212380000	-3.060024198900	0.662691080000
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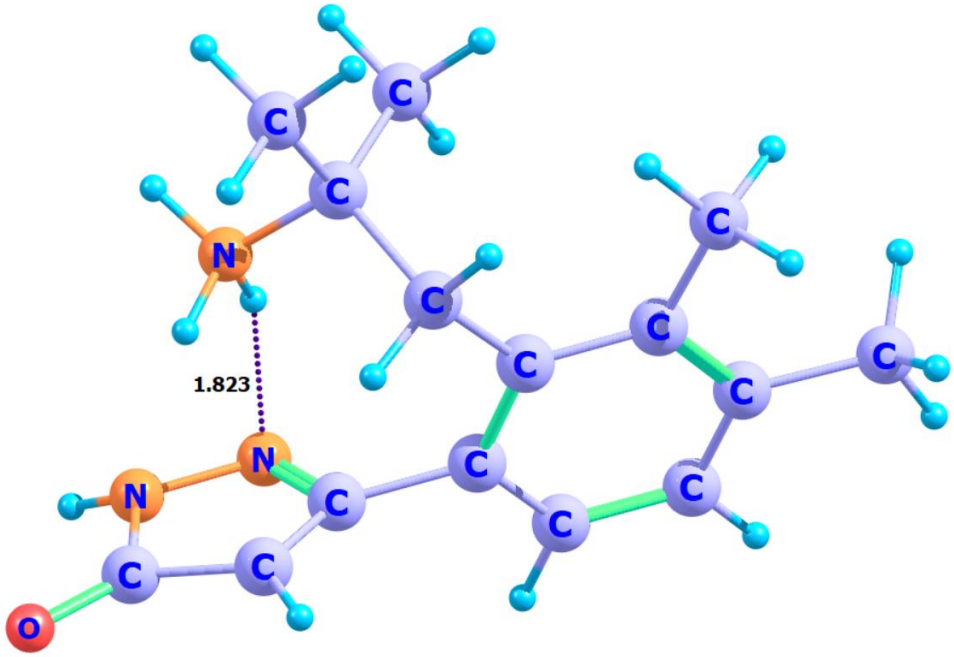
N	-2.549200819400	-0.767537345300	0.821215801700	H	3.421237643700	-3.051376580400	0.095170573700
H	-3.178318840600	-0.847187741400	1.608283579400	H	2.506101800200	-2.226159137900	1.363311261200
C	-0.684462809400	0.255841246100	0.155850754500	C	1.280698482300	-4.182596872900	-1.232549395900
C	-2.931199025300	0.133130475800	-0.207271024400	H	2.183293286400	-4.193702117600	-1.847411199800
C	0.775663833700	0.518313204500	0.108593226700	H	1.236765179200	-5.125289910200	-0.682592385100
C	2.556317465900	2.061816812600	0.619478700000	H	0.419293642400	-4.142575245600	-1.903980014400
C	1.692587403500	-0.366114972700	-0.500344000700	C	4.928490462300	1.658030388600	-0.075526668800
C	1.271099361000	-2.988033715200	-0.258494092600	H	5.594427578000	0.906917729500	0.356137177000
C	1.216120983300	1.716965192000	0.666895995500	H	5.257902451000	1.818734912600	-1.105644776000
H	0.497577783100	2.376950998600	1.133848453600	H	5.080670613000	2.589500182700	0.468116020700
C	-1.670295947100	0.706973975700	-0.661614711800	C	4.092630339900	-0.809111169100	-1.304317331200
C	1.201242169000	-1.670742619100	-1.111231641000	H	4.859484025600	-1.172051963100	-0.614817065800
H	1.748152655300	-1.853672686700	-2.034938331500	H	3.679286290400	-1.673687342300	-1.812894226900
H	0.160349309900	-1.544718124800	-1.416260479400	H	4.608736471400	-0.206977309800	-2.055477945000

Partly optimized betaine form of compound **2c** ($d^{N—H}$ = 1.00 Å)

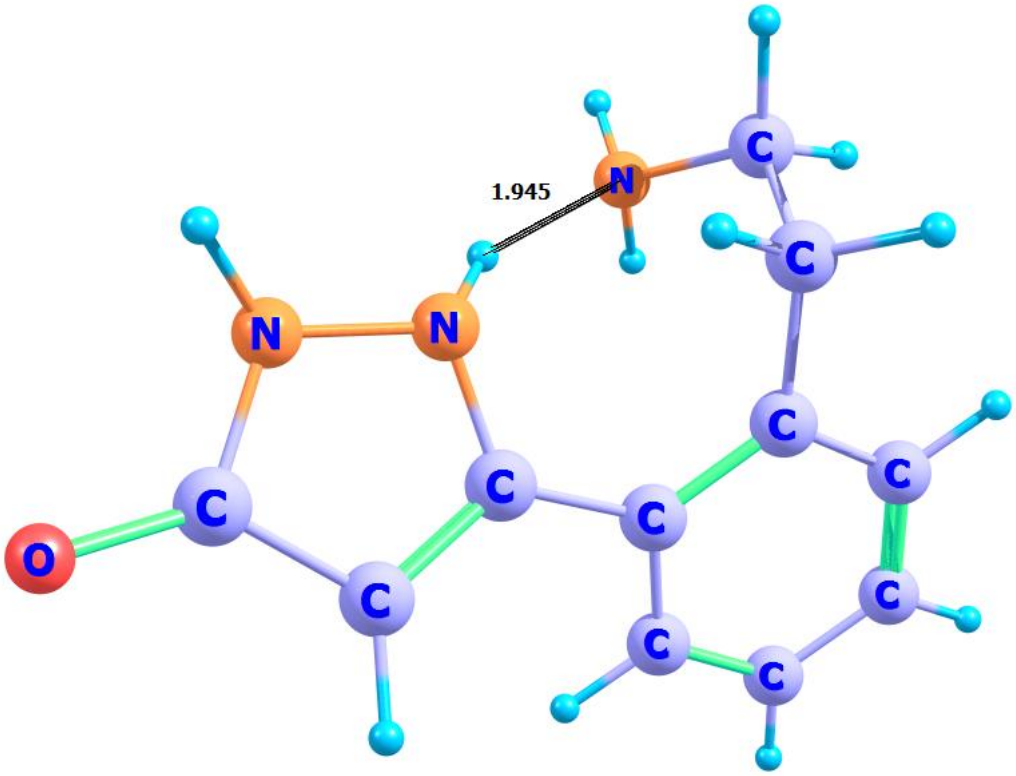


E_{tot} = -863.2415810 a.u.

Cartesian coordinates, Å

O	-4.101775770000	-0.061010713800	-0.440034493700	C	4.041405568100	-0.445187175500	-1.194263599200
N	-0.506856250700	-2.256644721700	0.410344346300	H	4.879574797400	-0.651437535800	-0.525434449600
H	-1.249688286900	-1.924346411400	-0.225441065800	H	3.669614185600	-1.403505680600	-1.543263545300
H	-0.474373403600	-1.520006923700	1.085851282400	H	4.456045401400	0.075690217400	-2.062078340900
H	-0.818669418000	-3.117243302600	0.856813831800				
N	-1.166272269400	0.113920871900	1.502327636800				
N	-2.487420542500	-0.274358974200	1.246099074700				
H	-3.122054586800	-0.305716119800	2.028575516200				
C	-0.738800579300	0.563777074800	0.308615293200				
C	-2.938481543600	0.070502325400	-0.055609168500				
C	0.704849014000	0.903011253000	0.192241037100				
C	2.508351617200	2.394408125500	0.780654627300				
C	1.622404588200	0.058623709700	-0.472818867800				
C	0.808571771200	-2.460317919800	-0.331525943600				
C	1.164418446100	2.056856428300	0.820305866600				
H	0.454002430000	2.685416181400	1.338980885400				
C	-1.718221055900	0.513467368100	-0.687837841600				
C	1.103597396300	-1.188293693800	-1.179456356100				
H	1.809051503400	-1.501120810400	-1.944816316000				
H	0.184033370800	-0.933833200800	-1.708001991400				
C	2.991870953600	0.400494345300	-0.502072476600				
C	3.431667836500	1.585528485600	0.124896029600				
H	2.848204000600	3.300538715300	1.267383944200				
H	-1.652761367800	0.898200731800	-1.691343805100				
C	1.871780343500	-2.752315319000	0.726636811500				
H	1.616464574400	-3.643005475000	1.306094730000				
H	2.832454258500	-2.934365309700	0.246965073500				
H	1.989762567900	-1.909795464200	1.407218686000				
C	0.596438694000	-3.657347365900	-1.264637785500				
H	1.519851360400	-3.881755609300	-1.797138130400				
H	0.310796915300	-4.553184560800	-0.707818770800				
H	-0.176389972800	-3.448793480500	-2.006944165600				
C	4.885949470600	1.992680043600	0.097737130700				
H	5.526539918700	1.256252040800	0.590734443800				
H	5.260256093000	2.105304014600	-0.923069456600				
H	5.026386700100	2.944779170600	0.607781811400				

Analogue of **2c** without methyl groups



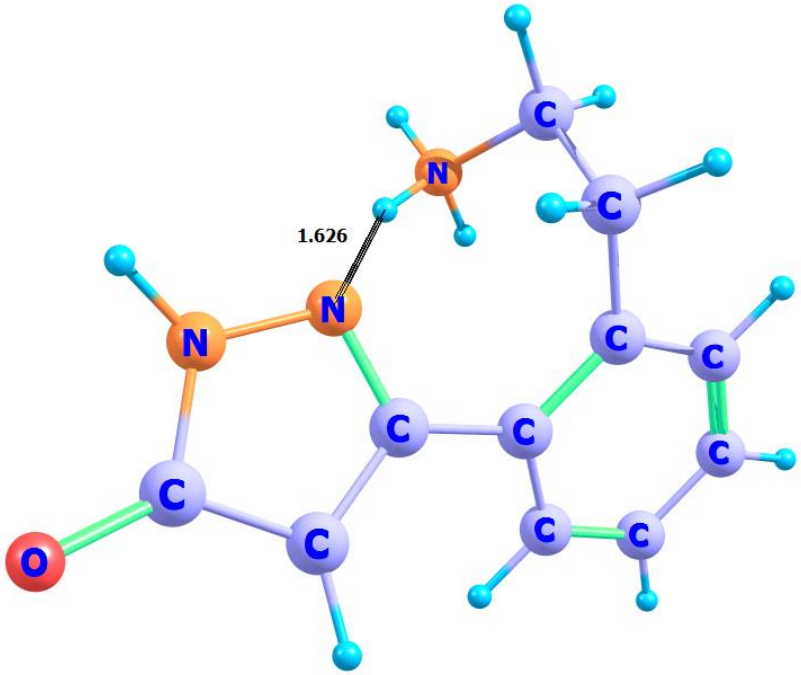
E_{tot} = -666.6476120 a.u.

Cartesian coordinates, Å

	28		
	symmetry c1		
O	-4.316486555	0.878540858	-0.215457913
N	0.747740604	-2.479348532	1.211755749
H	-0.857233757	-1.562949947	0.606228618
H	1.174041526	-1.769806234	1.799494710
H	0.694519587	-3.327250465	1.764443123
N	-1.358248813	-0.903050547	-0.005584715
N	-2.744705243	-0.790920420	0.194529656
H	-3.297886413	-1.536464978	-0.204650135
C	-0.867786948	0.384497548	-0.102398340
C	-3.151095177	0.538280183	-0.088913669
C	0.580507592	0.679321694	-0.058367786
C	2.272911586	2.344932200	0.504464788
C	1.597220872	-0.195209434	-0.508152190
C	1.566685175	-2.696456043	0.003611330
C	0.949767687	1.938054752	0.448952485
H	0.174632821	2.594011040	0.819046233
C	-1.902179972	1.272074294	-0.191752630
H	-1.842879939	2.326919122	-0.388679731
C	1.343487673	-1.589518495	-1.047093210
H	2.033542892	-1.777156497	-1.873109484
H	0.334162055	-1.671276378	-1.443109037
C	2.926439282	0.241731439	-0.446185513
H	3.704821390	-0.418514460	-0.810376722
C	3.272931174	1.490460632	0.049908485
H	1.271722808	-3.651990789	-0.433626127
H	2.635812623	-2.764508231	0.237797141
H	2.521305325	3.320086019	0.901904067
H	4.311262071	1.794060555	0.079617234

Partly optimized analogue of betaine form of compound **2c** without methyl groups

($d^{N—H}$ = 1.00 Å)



E_{tot} = -666.6069560 a.u.

Cartesian coordinates, Å

28

symmetry c1

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N	0.237603572	-2.082857647	1.033247797
H	-0.633415896	-1.685188351	0.744831054
H	0.728481969	-1.338595434	1.531766780
H	0.107810477	-2.869556423	1.666442103
N	-1.670898004	-0.706141130	-0.035374938
N	-3.045959862	-0.587591290	-0.001485178
H	-3.619841018	-1.408492123	-0.092870913
C	-1.238488420	0.570553120	-0.210315244
C	-3.516446078	0.715007359	-0.260402619
C	0.204077980	0.897061157	-0.186847883
C	1.911077086	2.558201614	0.363264735
C	1.230364051	0.038161408	-0.654300540
C	1.012302365	-2.461918510	-0.203937969
C	0.585505772	2.154740748	0.316770065
H	-0.190207755	2.811463846	0.684680691
C	-2.291710909	1.467563637	-0.342655098
H	-2.237738582	2.520522566	-0.554167373
C	0.936031044	-1.329688349	-1.239925238
H	1.665581032	-1.565604922	-2.017313217
H	-0.056267205	-1.333959034	-1.685082259
C	2.563973585	0.462295619	-0.597245751
H	3.337755407	-0.192748791	-0.982651130
C	2.914725608	1.707441095	-0.093838222
H	0.566065585	-3.377454349	-0.589498805
H	2.037655043	-2.667495884	0.100964920
H	2.161435742	3.534807224	0.757161083
H	3.952215242	2.013804299	-0.069606666

References

S1 http://chem.ch.huji.ac.il/nmr/software/solvent.html.

S2 *CrysAlisPro, version 1.171.38.41, Rigaku Oxford Diffraction*, Oxford, 2015.

S3 G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Adv*., 2015, **71**, 3.

S4 G. M. Sheldrick, *Acta Crystallogr., Sect. C: Struct. Chem.*, 2015, **71**, 3.

S5 O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. J. Puschmann, *Appl. Crystallogr.*, 2009, **42**, 339.

S6 A. A. Granovsky, *Firefly, version 8*, http://classic.chem.msu.su/gran/firefly/index.html.

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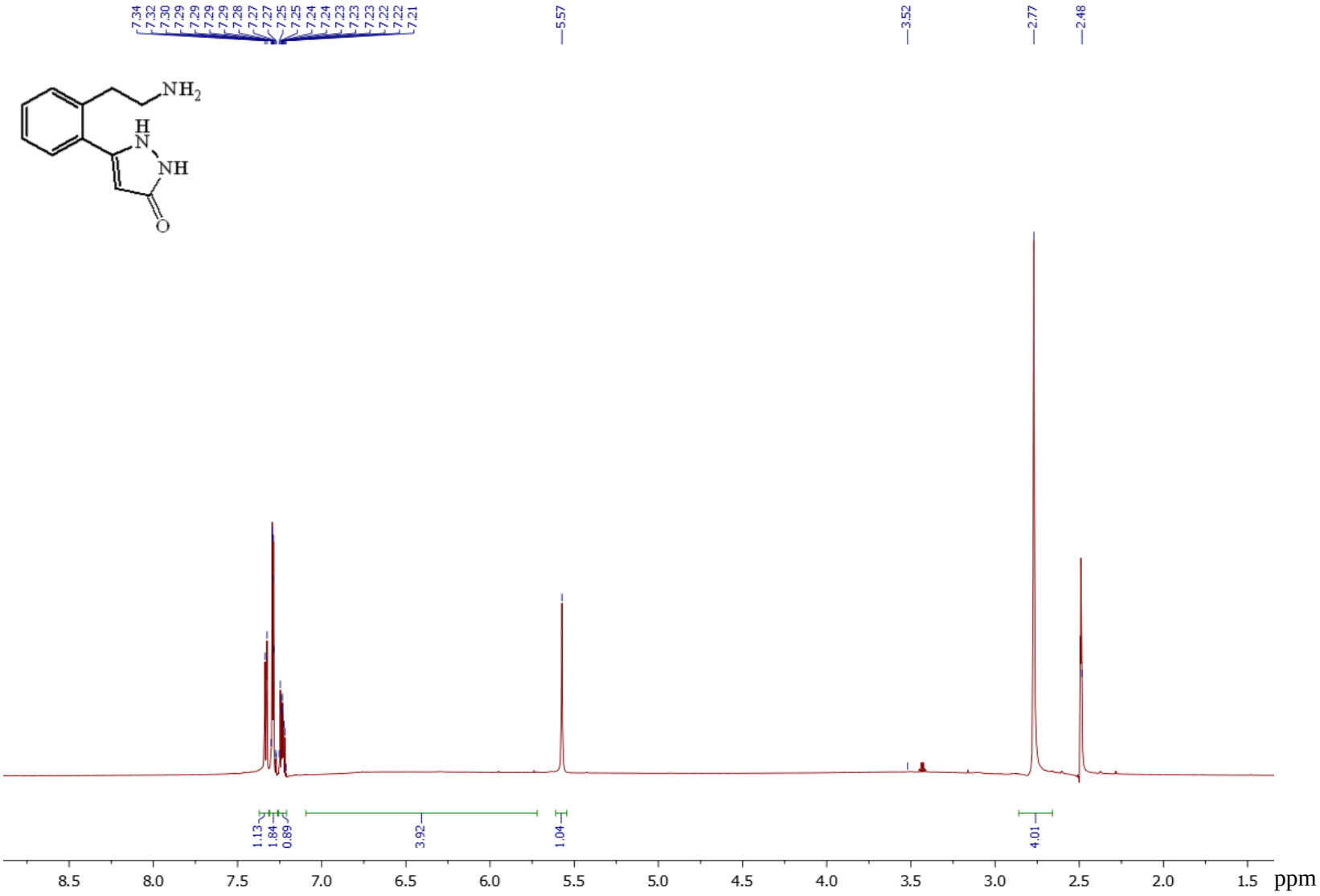
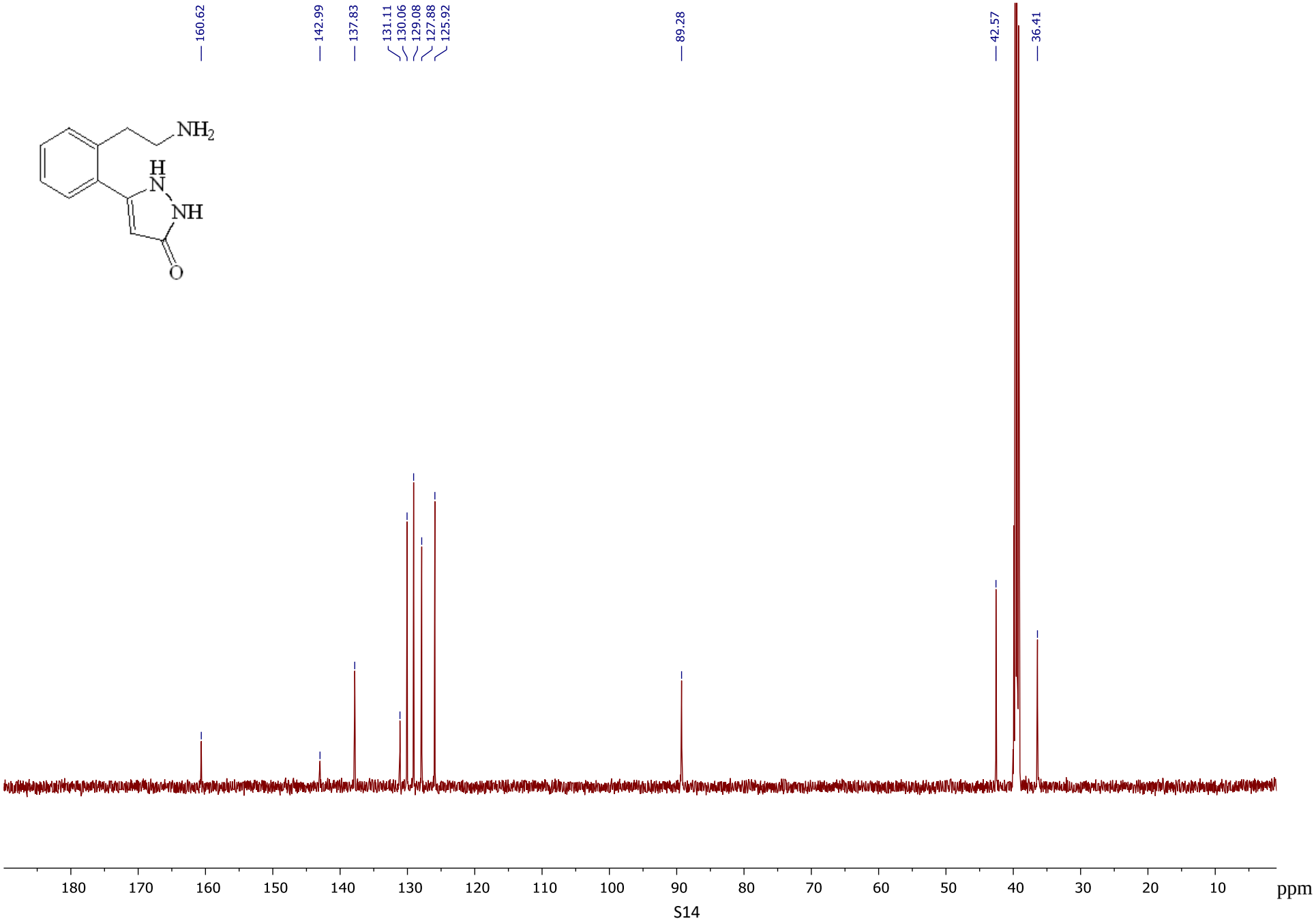
S8 T. Sano, J. Toda, N. Kashiwaba, T. Ohsima and V. Tsuda, *Chem. Pharm. Bull*., 1987, **35**, 479.

S9 B. B. Aleksandrov, M .S. Gavrilov, M. I. Vakhrin and V. S. Shklyaev, *Chem. Heterocycl. Compd*., 1985, **21**, 662 (*Khim. Geterotsikl. Soedin*., 1985, **21**,794).

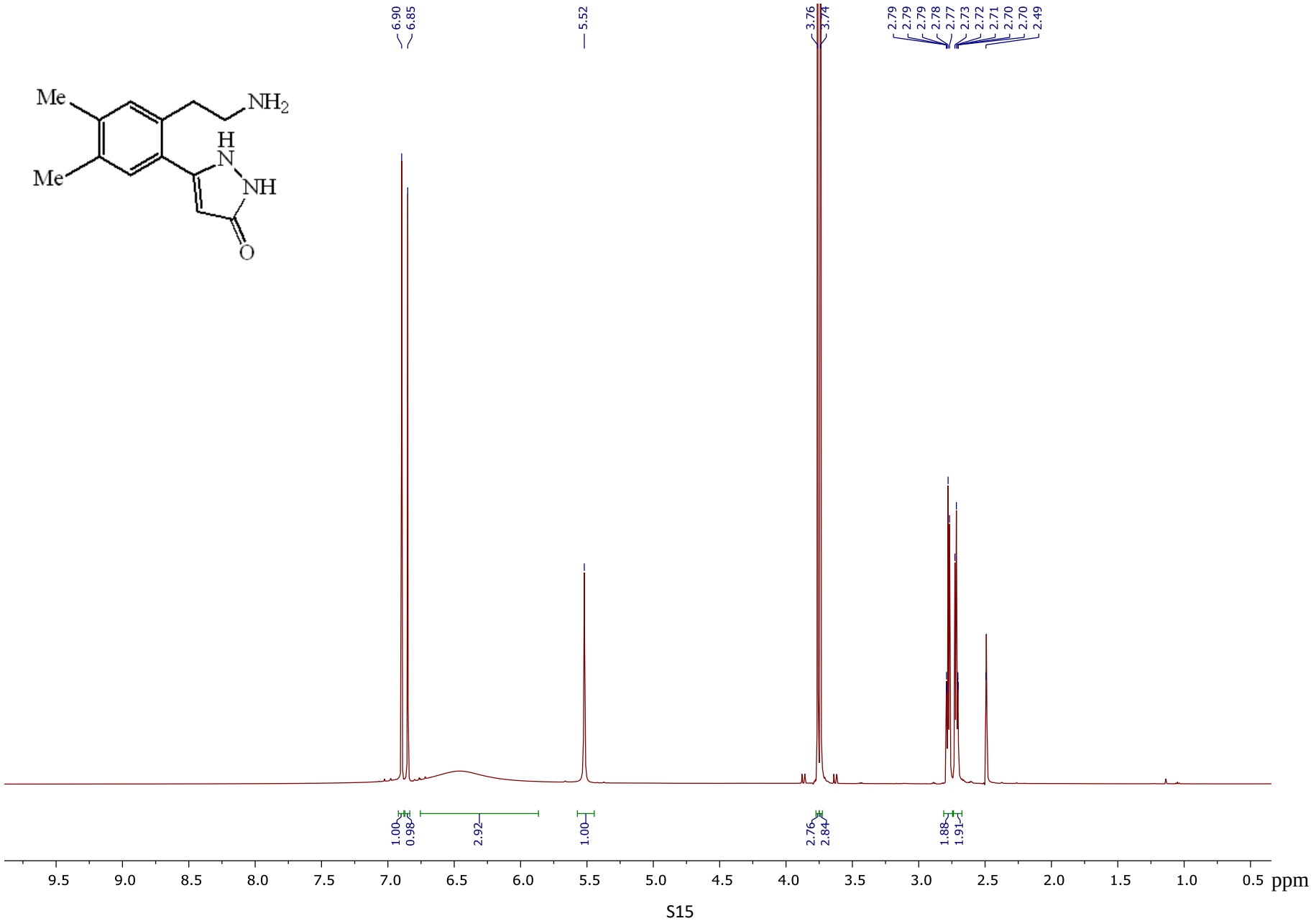
NMR Spectra of compounds 2a-d, 3, 5a-d.

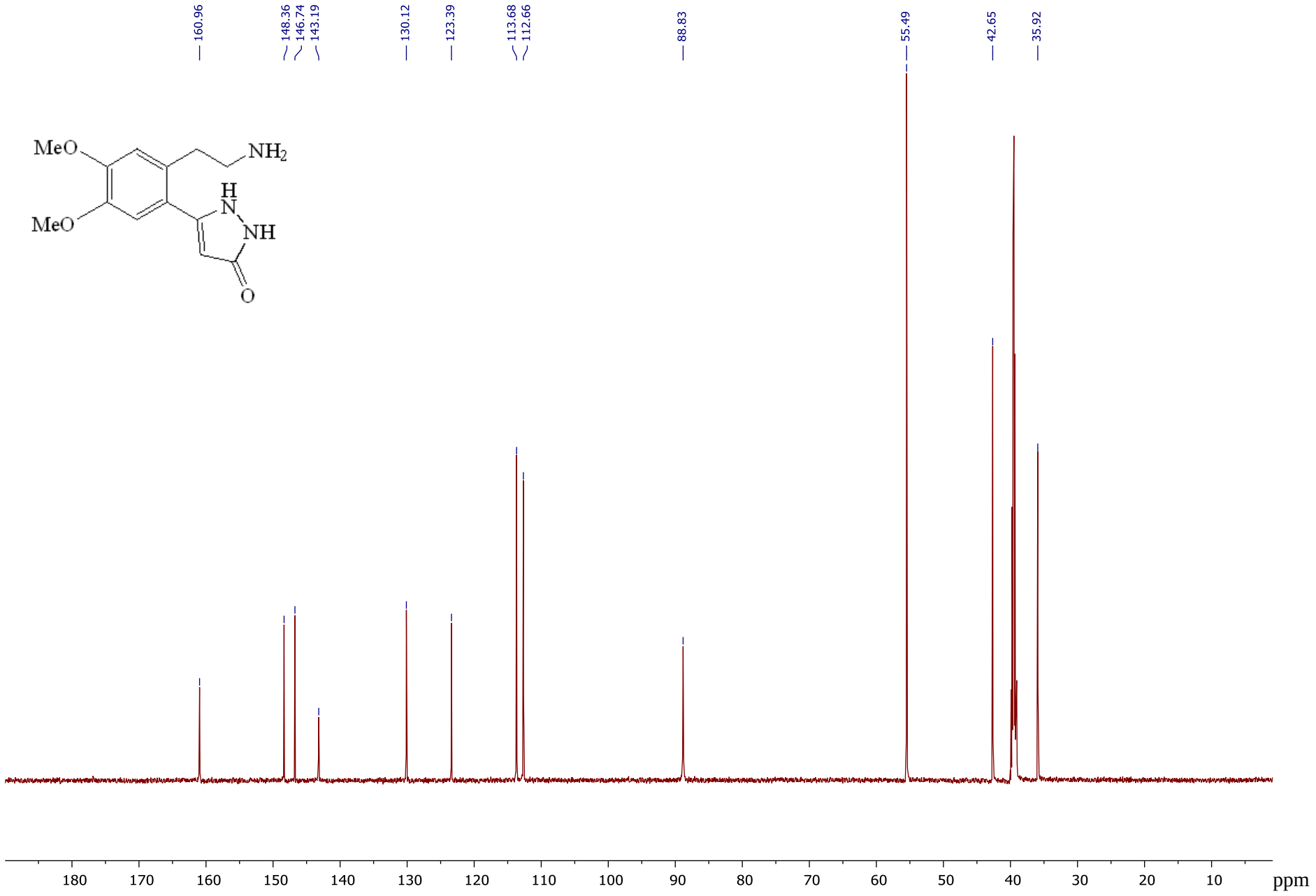
5-[2-(2-Aminoethyl)phenyl]-1,2-dihydro-3*H*-pyrazol-3-one (**2a**).



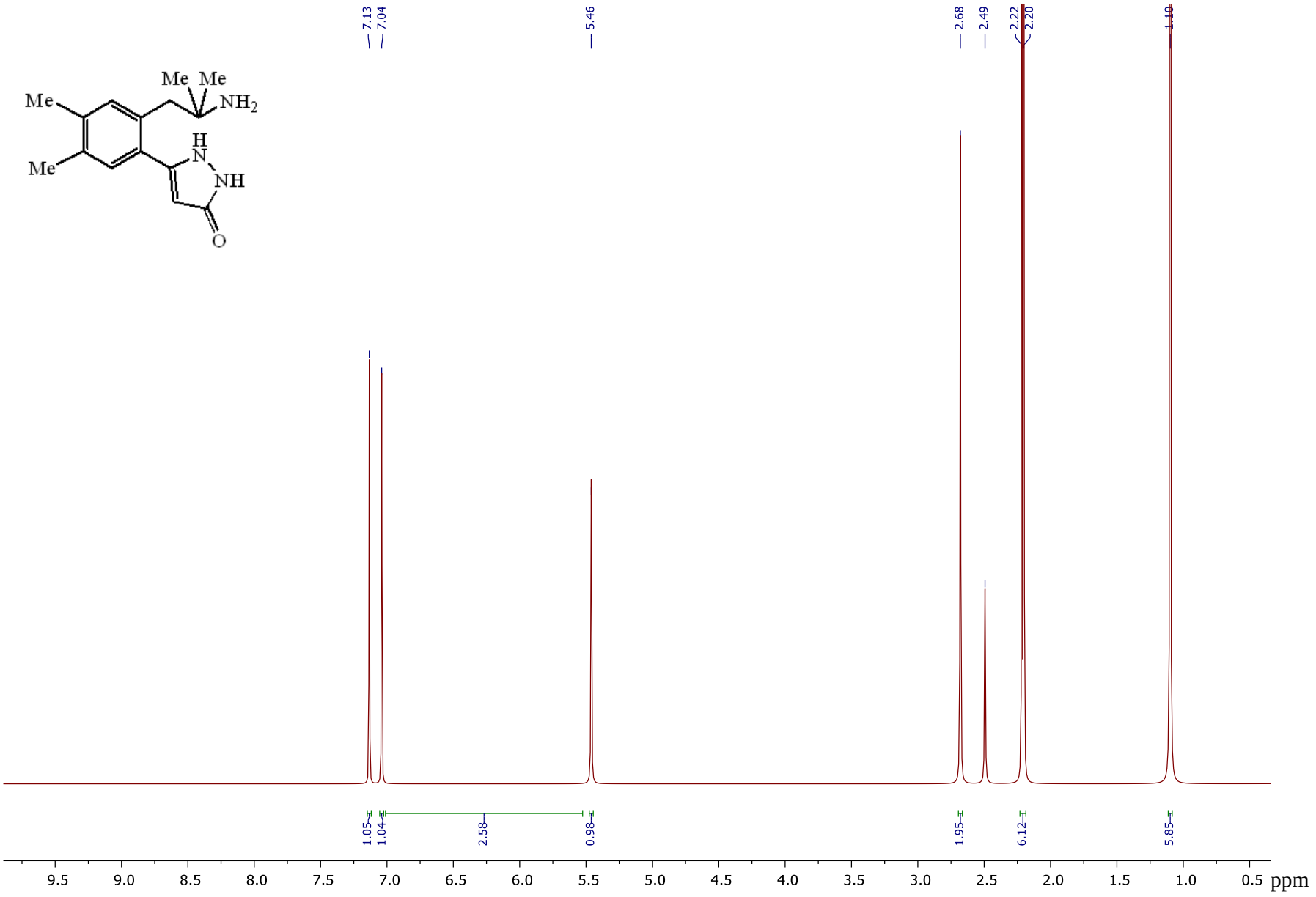

160.62
142.99
137.83
131.11
130.06
129.08
127.88
125.92
89.28
42.57
36.41
NH2
H
N
NH
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

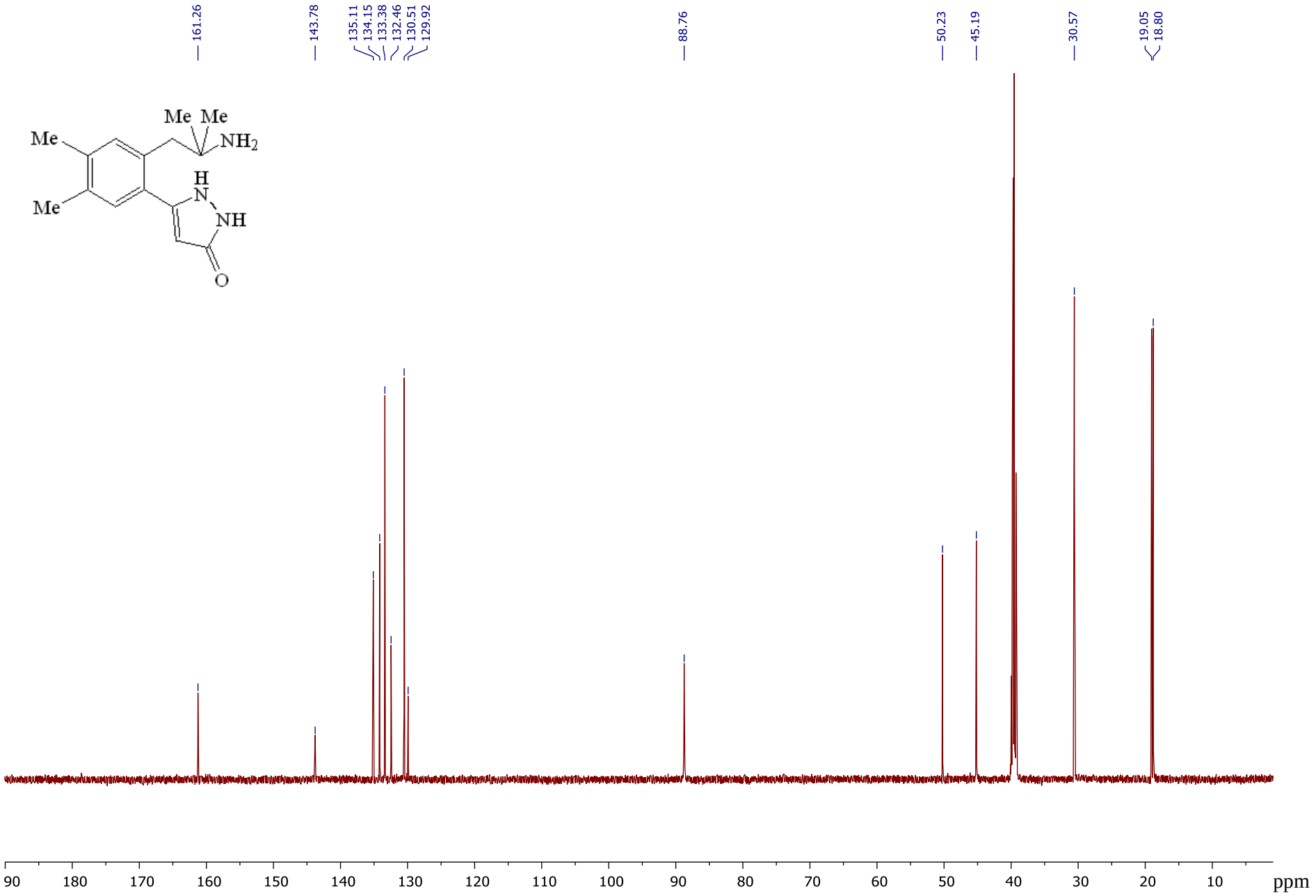
5-[2-(2-Aminoethyl)-4,5-dimethylphenyl]-1*H*-pyrazol-3(2*H*)-one (**2b**).



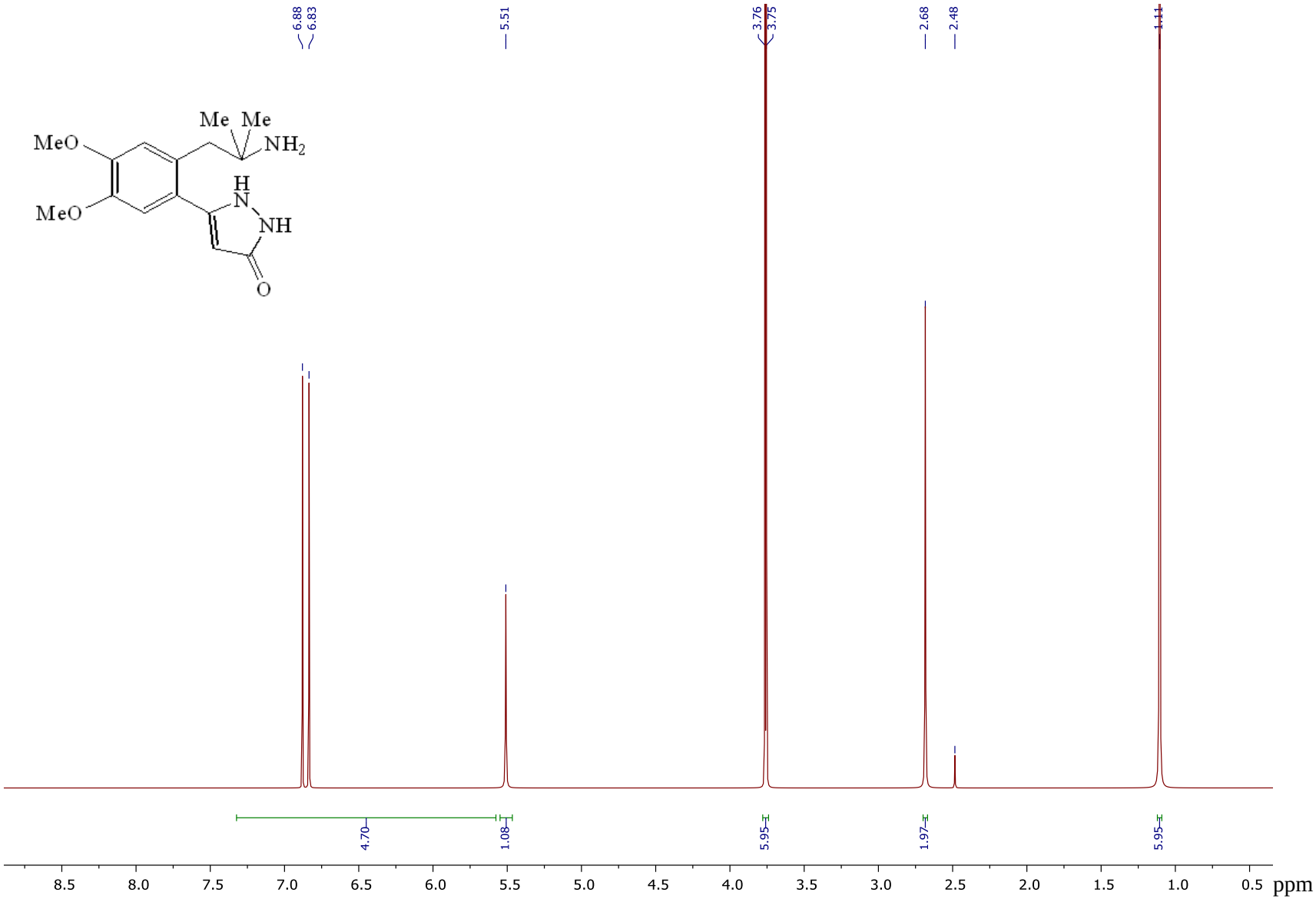

160.96
148.36
146.74
143.19
130.12
123.39
113.68
112.66
88.83
55.49
42.65
35.92
MeO
MeO
NH2
H
N
NH
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

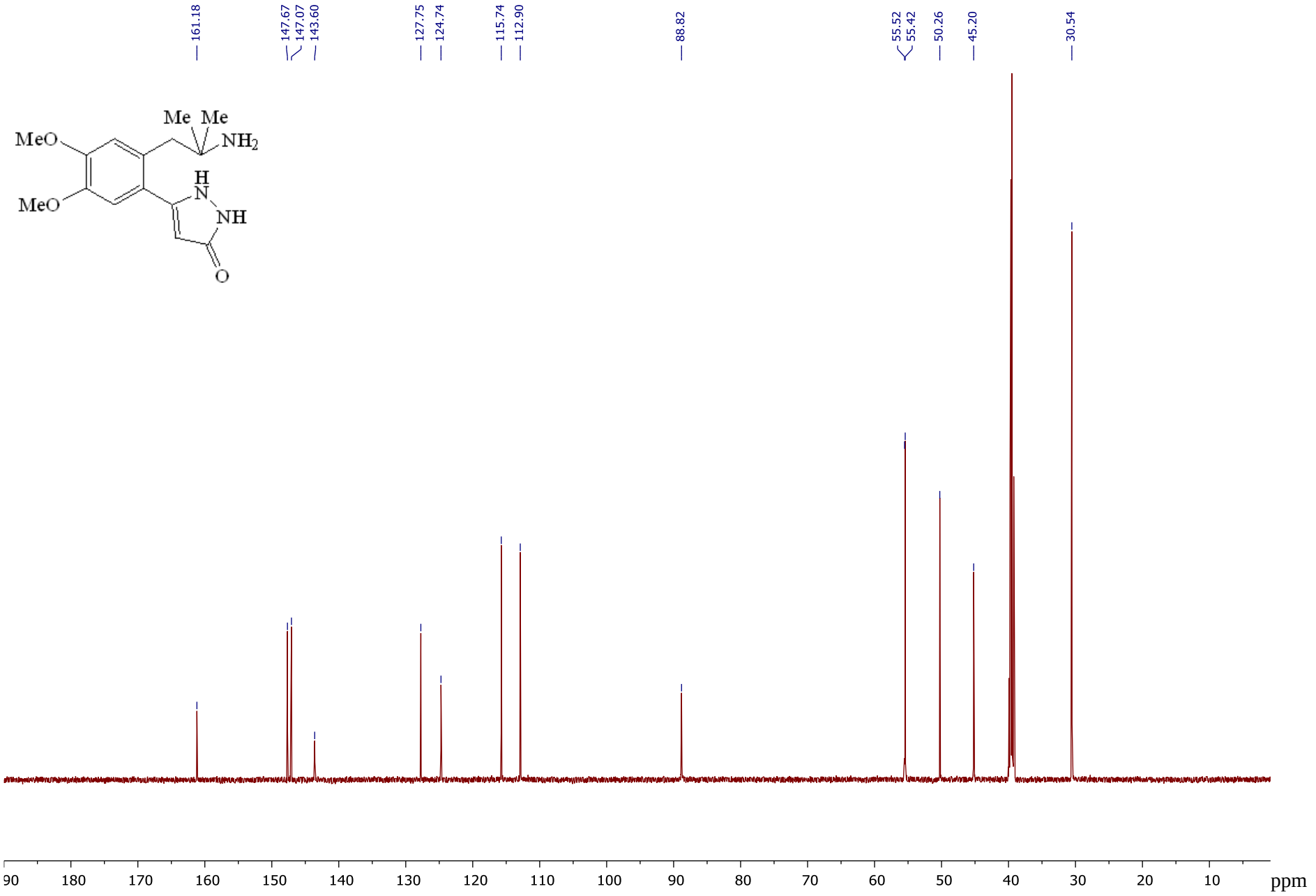
5-[2-(2-Amino-2-methylpropyl)-4,5-dimethylphenyl]-1,2-dihydro-3*H*-pyrazol-3-one (**2c**).



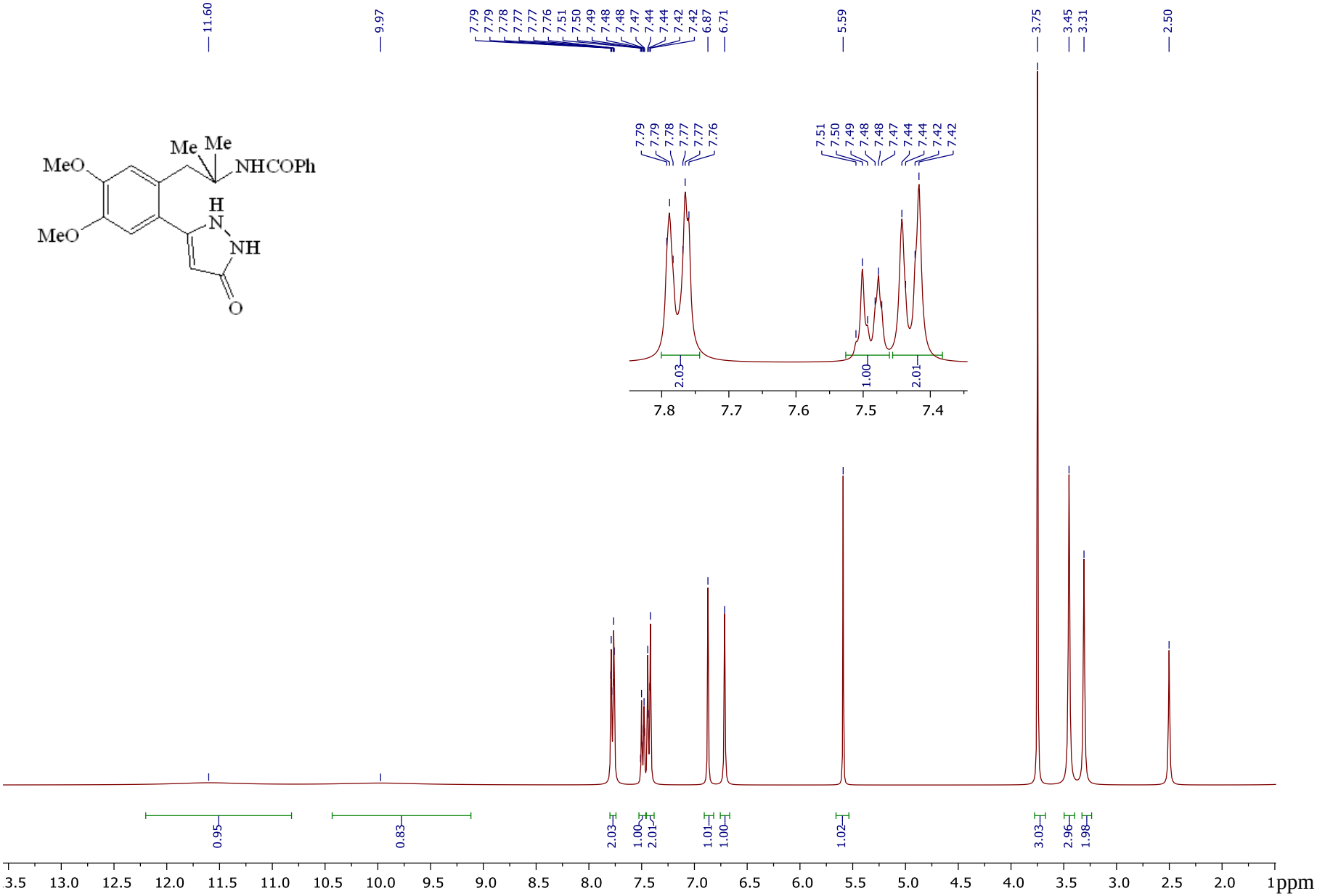

161.26
143.78
135.11
134.15
133.38
132.46
130.51
129.92
88.76
50.23
45.19
30.57
19.05
18.80
Me
Me
Me
Me
NH2
H
N
NH
O
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

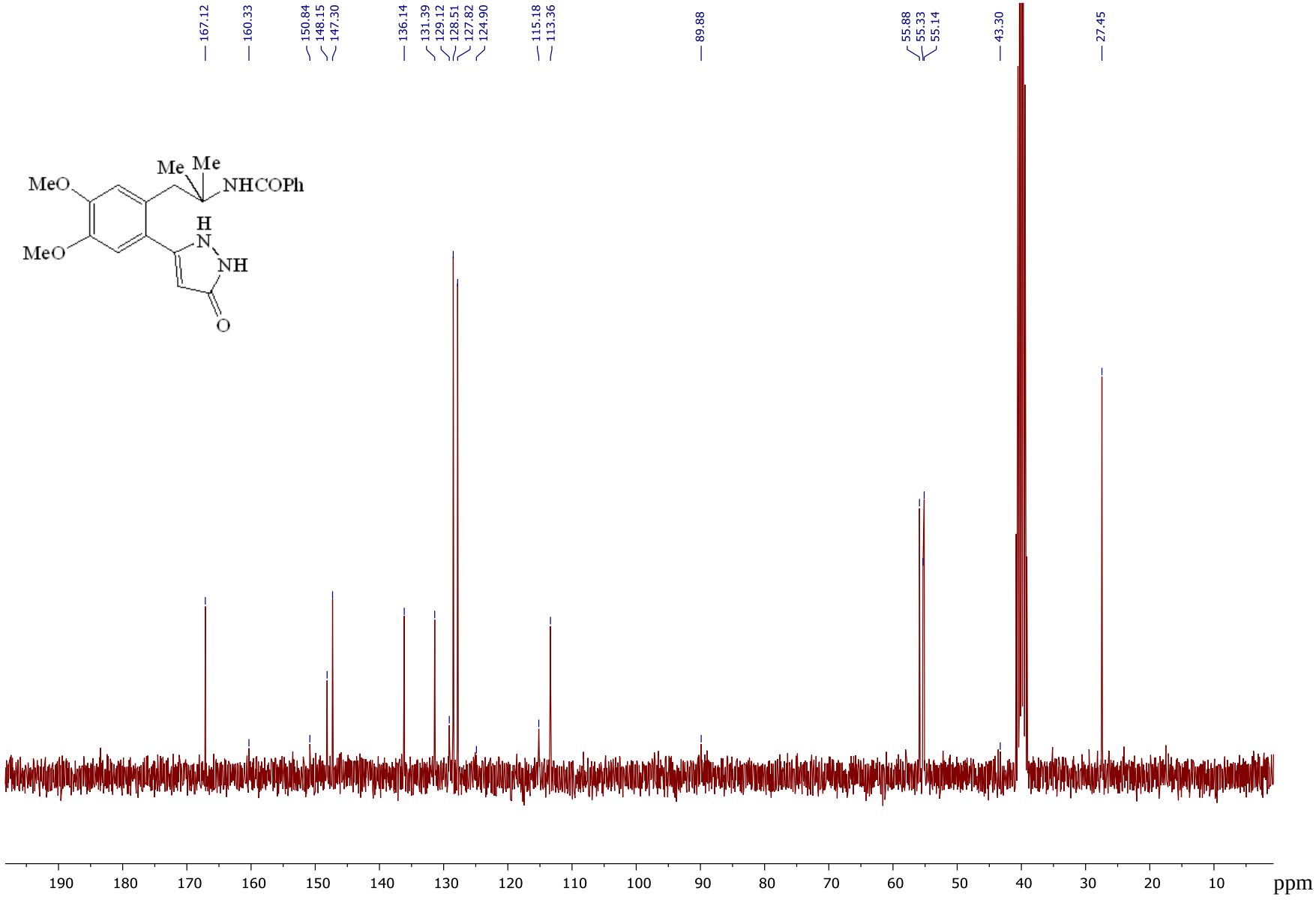
5-[2-(2-Amino-2-methylpropyl)-4,5-dimethoxyphenyl]-1,2-dihydro-3*H*-pyrazol-3-one (**2d**).



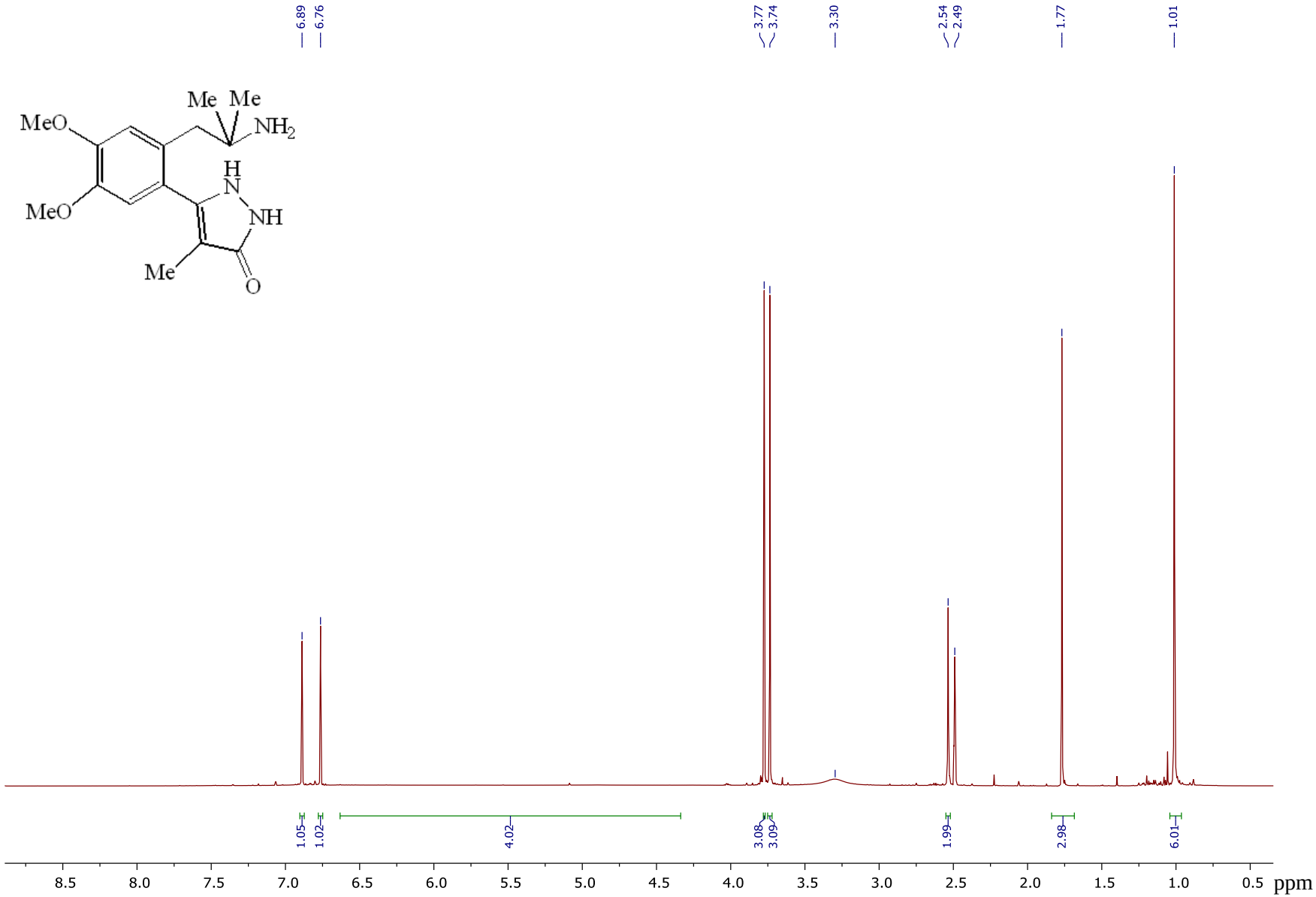

161.18
147.67
147.07
143.60
127.75
124.74
115.74
112.90
88.82
55.52
55.42
50.26
45.20
30.54
MeO
MeO
Me Me
NH2
H
N
NH
O
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

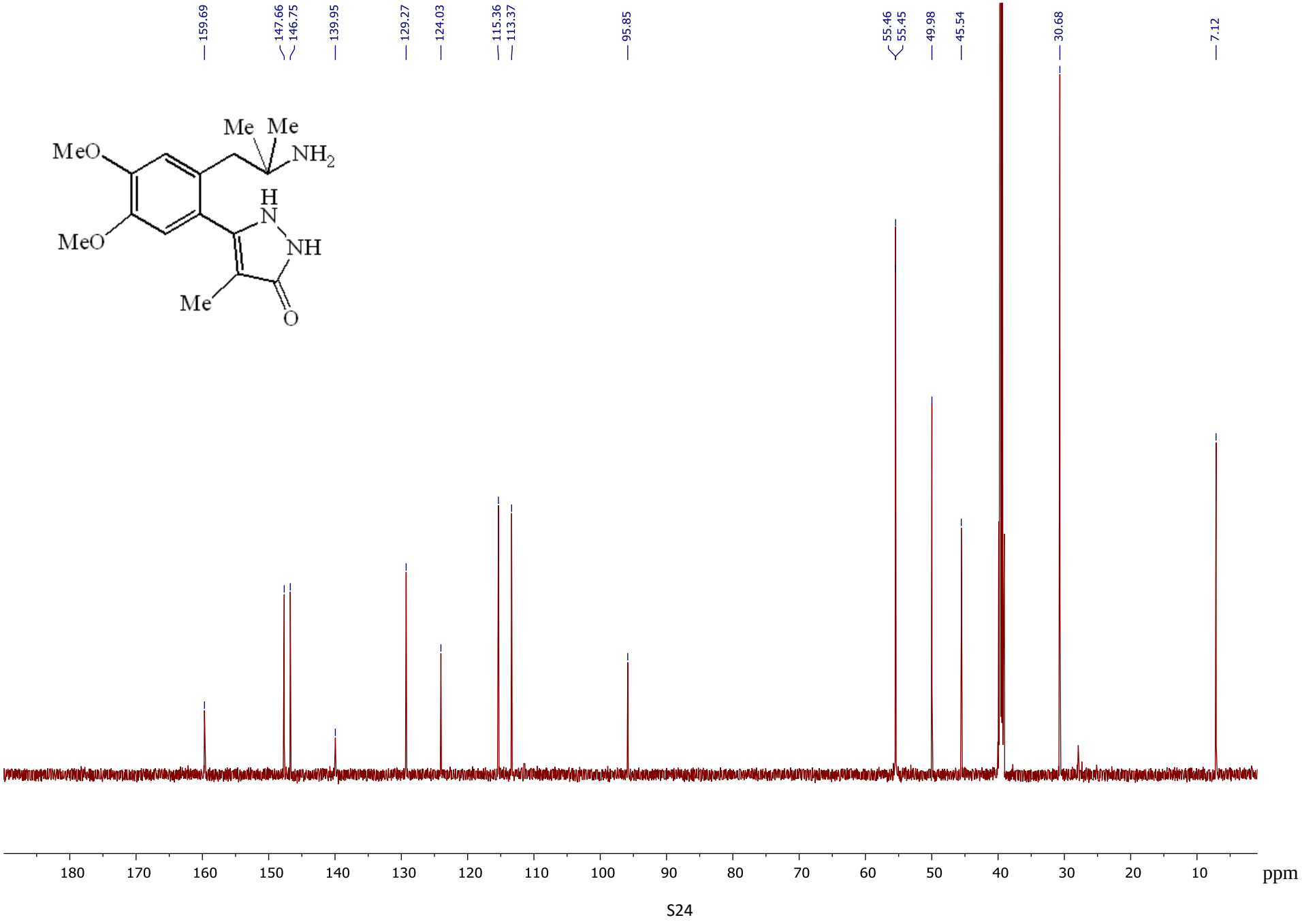
N-{1-[4,5-Dimethoxy-2-(5-oxo-2,5-dihydro-1*H*-pyrazol-3-yl)phenyl]-2-methylprop-2-yl}benzamide (**3**).



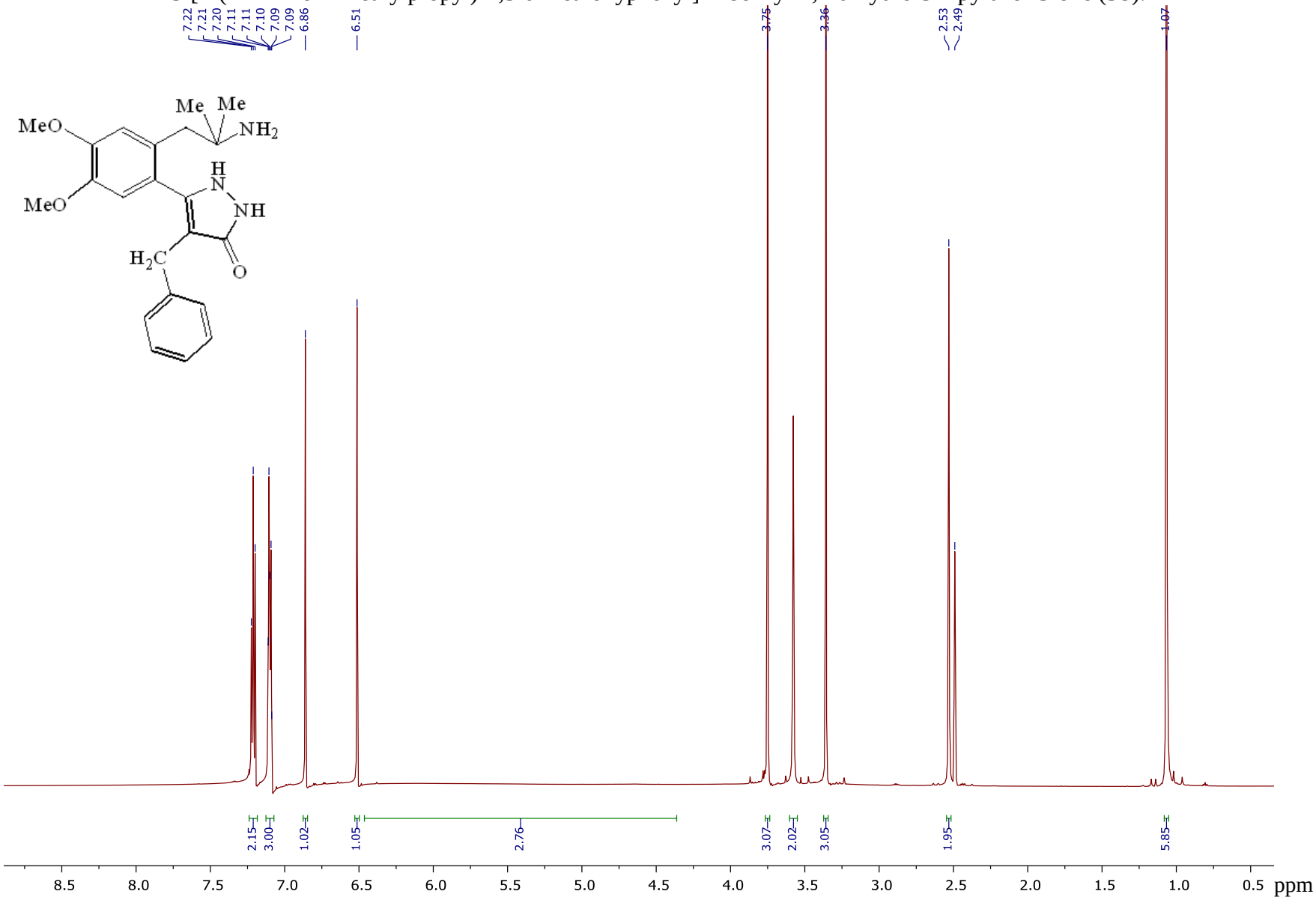

167.12
160.33
150.84
148.15
147.30
136.14
131.39
129.12
128.51
127.82
124.90
115.18
113.36
89.88
55.88
55.33
55.14
43.30
27.45
MeO
MeO
Me
Me
NHCOPh
H
N
NH
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

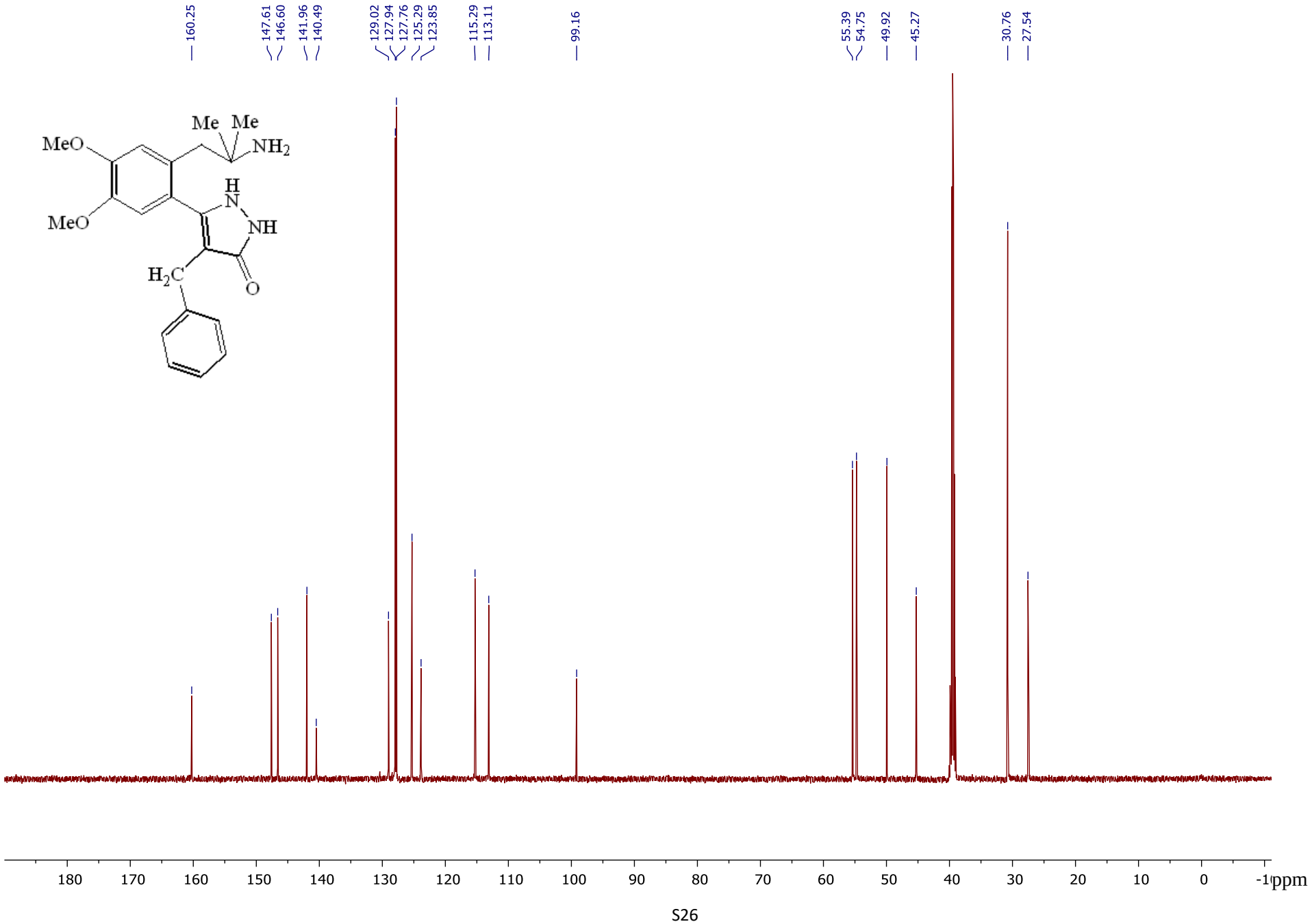
5-[2-(2-Amino-2-methylpropyl)-4,5-dimethoxyphenyl]-4-methyl-1*H*-pyrazol-3(2*H*)-one (**5a**).



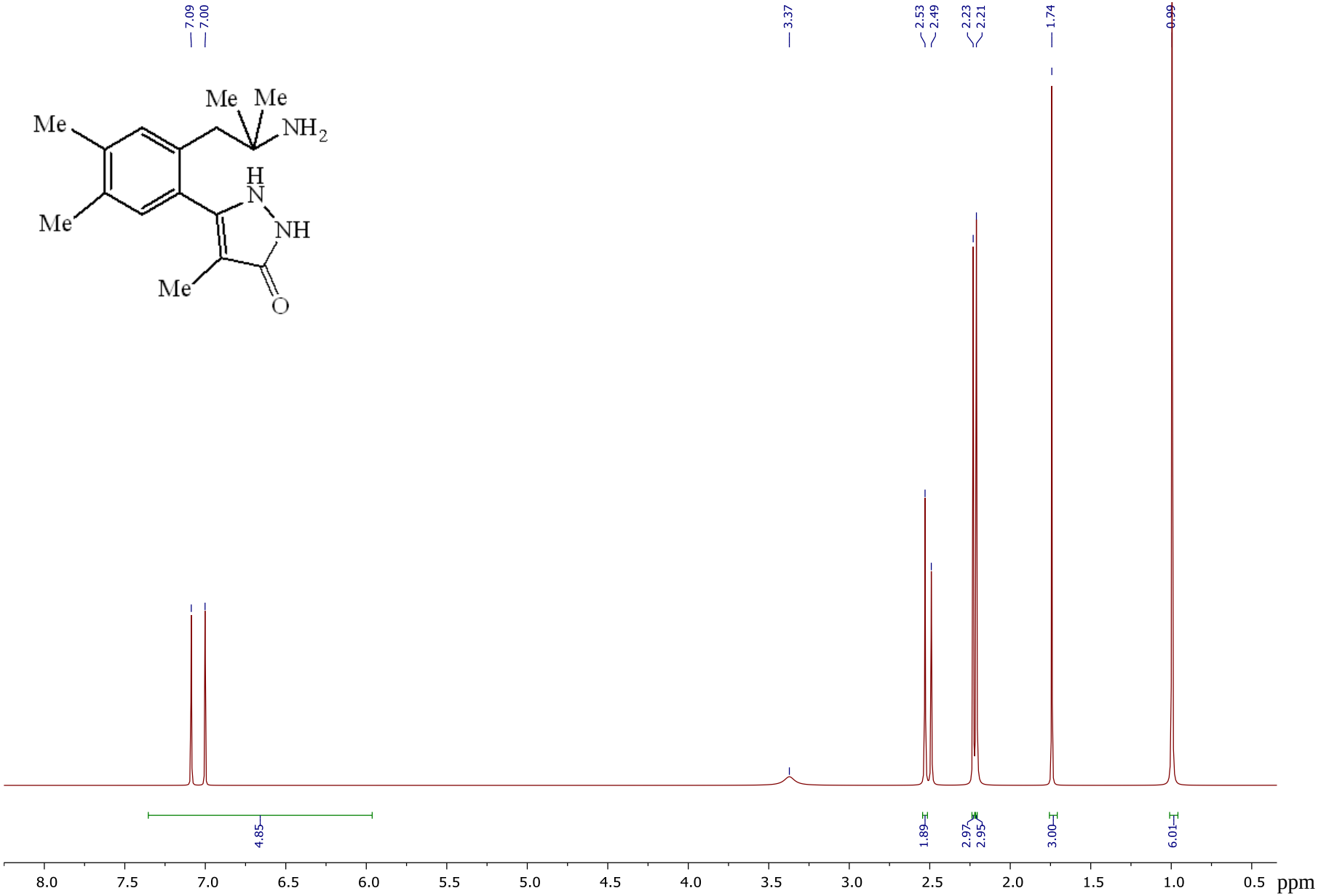

159.69
147.66
146.75
139.95
129.27
124.03
115.36
113.37
95.85
55.46
55.45
49.98
45.54
30.68
7.12
MeO
MeO
Me
Me
NH2
H
N
NH
Me
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

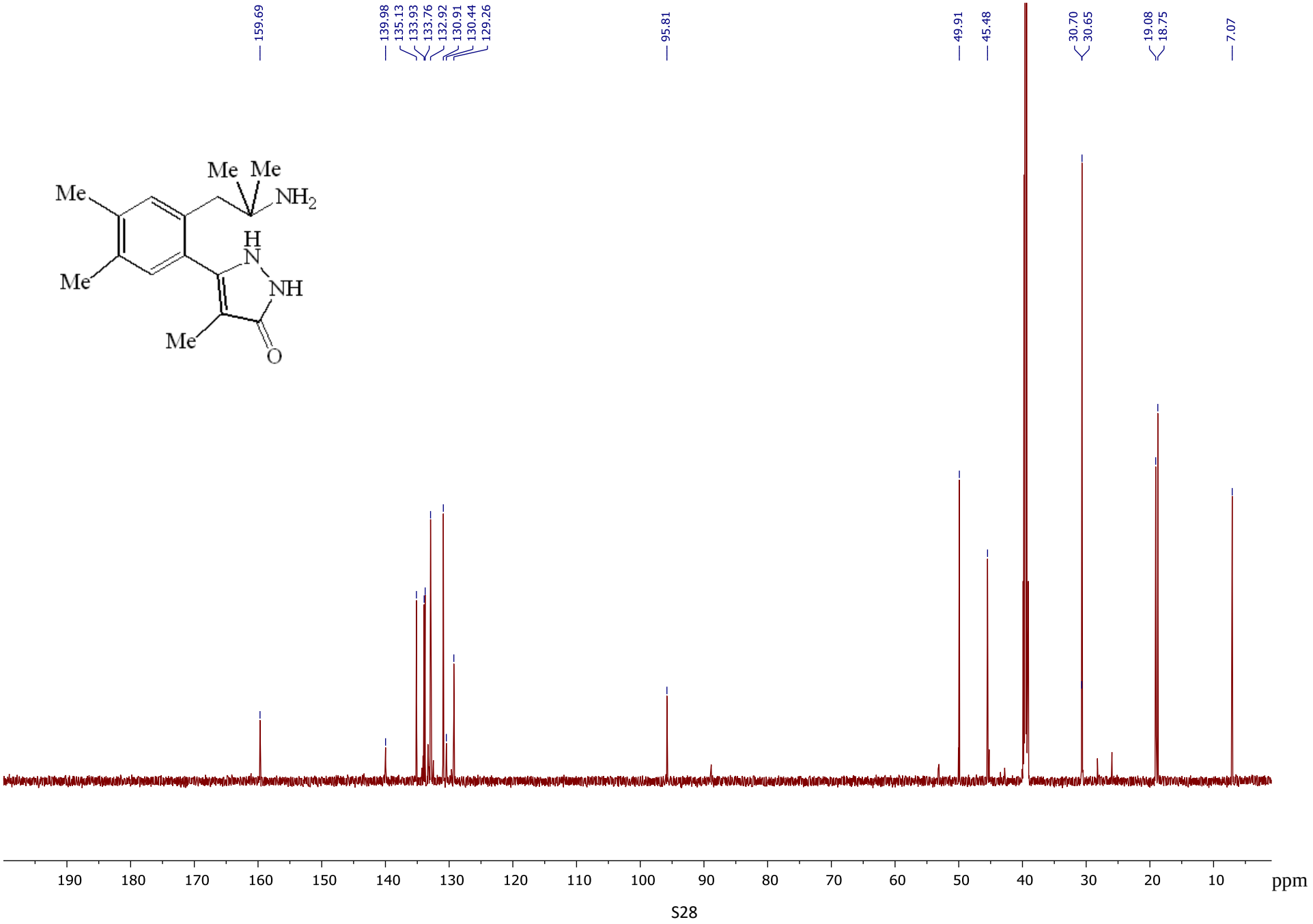
5-[2-(2-Amino-2-methylpropyl)-4,5-dimethoxyphenyl]-4-benzyl-1,2-dihydro-3*H*-pyrazol-3-one (**5b**).



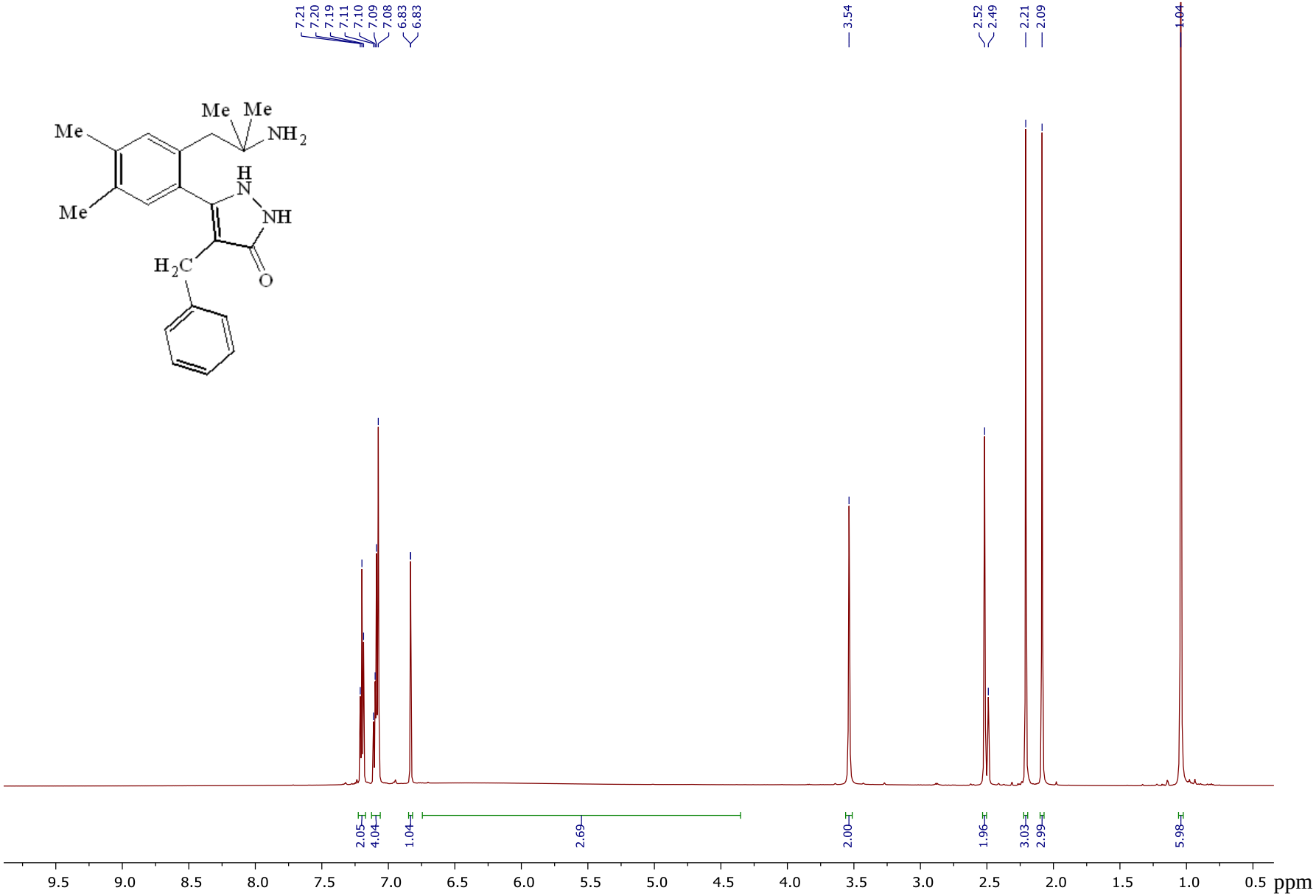

160.25
147.61
146.60
141.96
140.49
129.02
127.94
127.76
125.29
123.85
115.29
113.11
99.16
55.39
54.75
49.92
45.27
30.76
27.54
MeO
MeO
Me
Me
NH2
H
N
NH
H2C
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

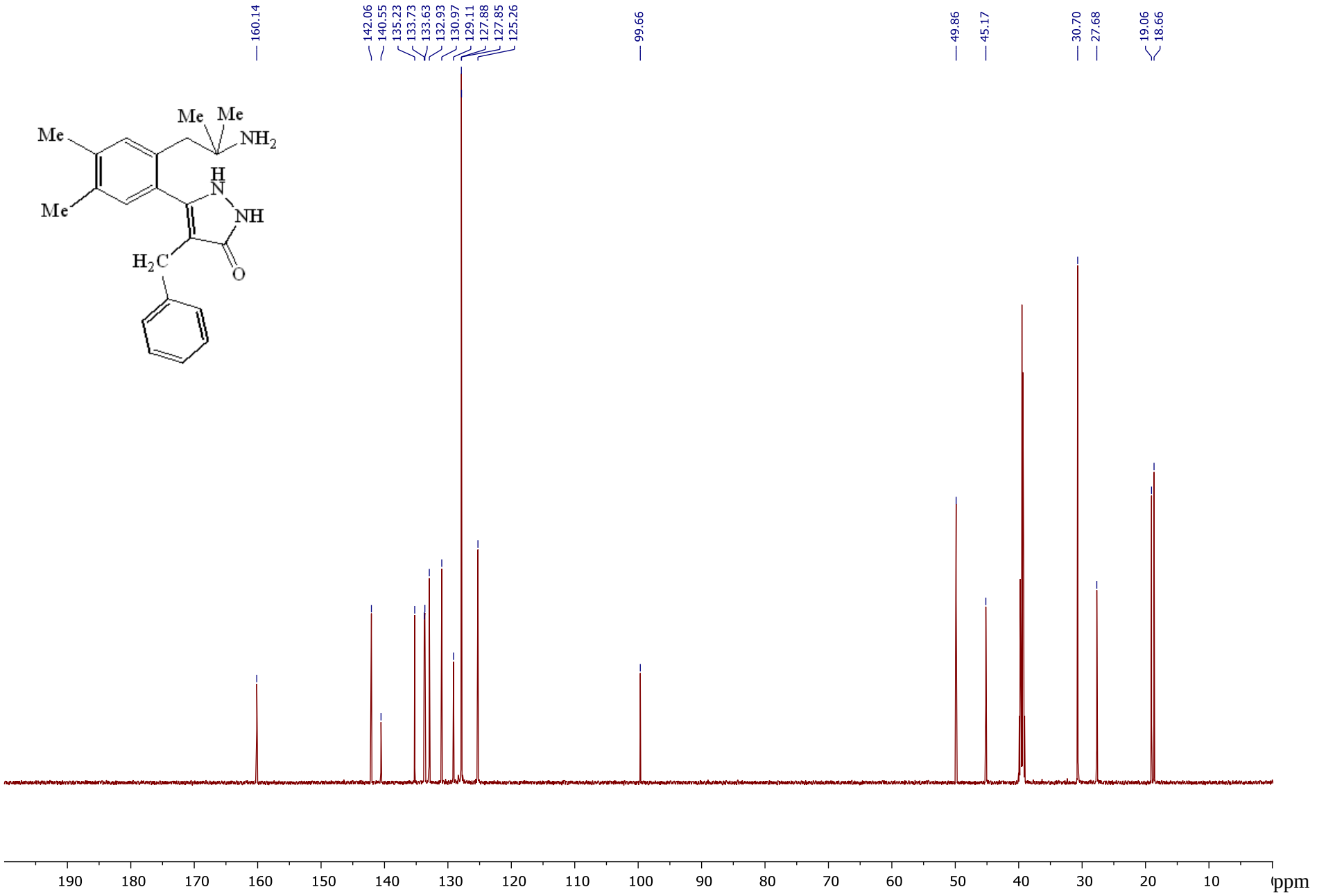
5-[2-(2-Amino-2-methylpropyl)-4,5-dimethylphenyl]-4-methyl-1*H*-pyrazol-3(2*H*)-one (**5c**).




159.69
139.98
135.13
133.93
133.76
132.92
130.91
130.44
129.26
95.81
49.91
45.48
30.70
30.65
19.08
18.75
7.07
Me
Me
Me
Me
NH2
H
N
NH
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

5-[2-(2-Amino-2-methylpropyl)-4,5-dimethylphenyl]-4-benzyl-1*H*-pyrazol-3(2*H*)-one (**5d**).




160.14
142.06
140.55
135.23
133.73
133.63
132.93
130.97
129.11
127.88
127.85
125.26
99.66
49.86
45.17
30.70
27.68
19.06
18.66
Me
Me
Me
NH2
H
N
NH
O
H2C
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm