Electronic supplementary materials *Mendeleev Commun.*, 2026, **36**, 335–337

Synthesis of oxo dihydro pyrrolo[1,2-*a*]quinazoline and benzo[*e*]pyrrolo[1,2-*b*][1,2,4]triazepine carboxylic acids

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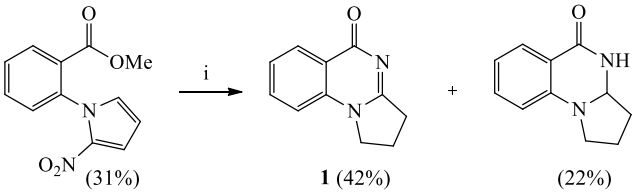

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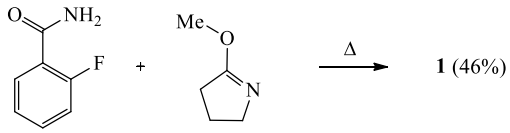

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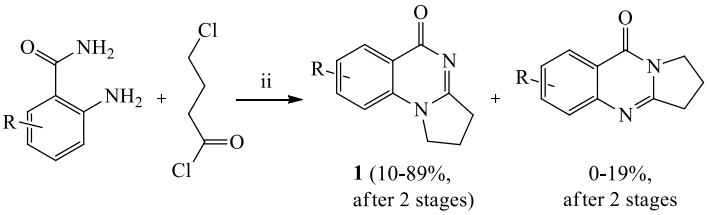

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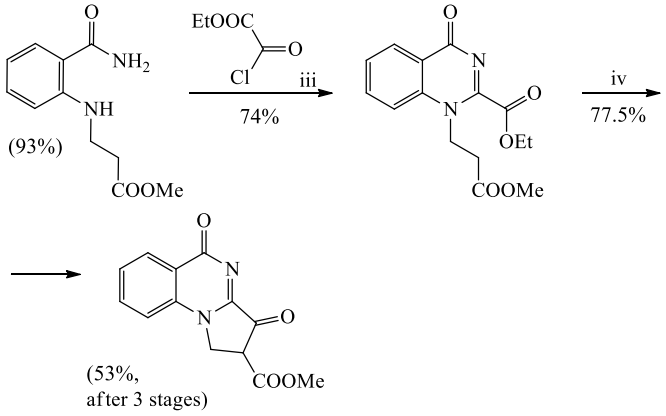

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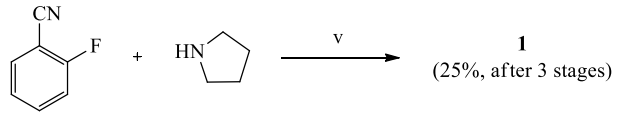


Scheme S1 Reported synthetic strategies for 2,3-dihydropyrrolo[1,2-*a*]quinazolin-5(1*H*)-one **1** and its derivatives. *Reagents and conditions*: i, 1) H_2/Pd-C, MeOH, 2) NaOEt, EtOH, Δ; ii, 1) Et_3N, THF, 2) NaOMe, MeOH or Bu^tOK, THF; iii, $CHCl_3$, rt; iv, NaOMe, MeOH, rt; v, 1) K_2CO_3, DMF, Δ, 2) H_2SO_4, AcOH, Δ, 3) $[Cp^*IrCl_2]_2$, 2-HOPy (Py – pyridyl), CF_3CH_2OH, Δ.

Table S1. The molar ratio of components **2:3:4** of the reaction mixture depending on the temperature (*T*) and time (*t*) of fusion of anthranilamide **2** and itaconic acid.*

t/ h	The **2:3:4** molar ratio				
	115 °C	125 °C	135 °C	145 °C	155 °C
0.5	82 : 17 : 1	53 : 44 : 3	12 : 64 : 24	7 : 31 : 62	3 : 15 : 82
1	61 : 37 : 2	38 : 52 : 10	3 : 31 : 66	2 : 17 : 81	0 : 5 : 95
2	36 : 57 : 7	13 : 57 : 30	2 : 10 : 90	0 : 3 : 97	
3	25 : 60 : 15	5 : 28 : 67	1 : 5 : 95		
4	15 : 60 : 25		0 : 2 : 98		
6	9 : 43 : 48				
7	7 : 39 : 54				

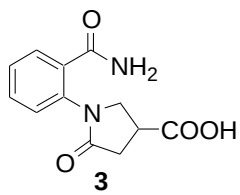
* According to the data of ^{1}H NMR spectra. The calculation of the relative content of compounds **2**, **3** and **4** was carried out on the basis of a comparison of the integral intensities of the aromatic protons of compounds **2** and **3** and the protons of the N-CH_2 group of compounds **3** and **4**, based on the total content of all three components of 100%.

Experimental section

All standard reagents and methanol were purchased from Aldrich or Acros Organics and used without further purification. Melting points were determined on a Boetius microblock. IR spectra were recorded on a Bruker "Alpha" spectrophotometer in the range 400–4000 cm^{-1} (resolution: 2 cm^{-1}). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300 (300.13 and 75.47 MHz, respectively) spectrometer and referenced to the residual solvent peak (δ_H 2.50, δ_C 39.50). The chemical shifts are reported in ppm (δ); multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). Coupling constants, *J*, are reported in Hertz. High-resolution mass spectra (HRMS) were measured on the Bruker micrOTOF II instrument using electrospray ionization (ESI). The measurements were done in a positive ion mode (interface capillary voltage: 4500 V); mass range from *m/z* 50 to 3000 Da; external or internal calibration was done with Electrospray Calibrant Solution (Fluka). A syringe injection was used for solutions in MeCN or MeOH (flow rate 3 μL/min). N_2 was applied as a dry gas; interface temperature was set at 180 °C.

Anthranilic acid methyl ester and amide are commercially available reagents (Sigma-Aldrich).

Synthesis of 1-(2-carbamoylphenyl)-5-oxopyrrolidine-3-carboxylic acid (3).

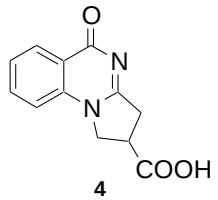


3

A suspension of anthranilic acid amide **2** (4.08 g, 0.03 mol) and itaconic acid (4.68 g, 0.036 mol) in water (50 ml) was refluxed for 12 h, cooled to room temperature, filtered off and dried. Acetonitrile (15 ml) was added to the precipitate, and the mixture stirred under reflux for 1 h. Then it was cooled to room temperature, the precipitate of acid **3** was filtered off and dried in air. Yield 4.53 g (61%), cream-colored powder, mp 186-189 °C (decomp.). IR (KBr, *ν*/cm^{-1}): 3307, 3139 (OH,

NH_2), 2927 (CH), 1701, 1674 (C=O), 1606, 1562, 1502, 1416 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.56 (d, 2H, CH_2, J = 5.8 Hz); 3.30-3.40 (m, 1H, CH); 3.85-3.99 (m, 2H, NCH_2); 7.27-7.37 (m, 3H, Ar); 7.47-7.54 (m, 2H, Ar, NH); 7.70 (s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 34.0, 36.4 (CH, CH_2CO); 52.3 (CH_2N); 126.9, 127.4, 128.6, 130.6 (CH_{Ar}); 134.3, 136.3 (C_{Ar}); 168.8, 172.0, 174.1 (C=O, COOH). HRMS (ESI), *m*/*z*: 249.0876 $[M + H]^+$; calc. for $C_{12}H_{13}N_2O_4^+$ 249.0870; 271.0698 $[M + Na]^+$; calc. for $C_{12}H_{12}N_2NaO_4^+$ 271.0689.

Synthesis of 5-oxo-1,2,3,5-tetrahydropyrrolo[1,2-*a*]quinazoline-2-carboxylic acid (4). *Method A.*



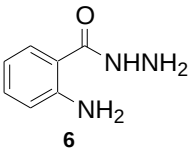
4

Anthranilic acid amide **2** (1.0 g, 7.4 mmol) and itaconic acid (1.06 g, 8.1 mmol) were thoroughly mixed and placed in a 50 ml round-bottomed flask. The reaction mixture was heated in an oil bath at 135 °C for 4 hours (or at 145 °C for 2 hours, or at 155 °C for 1 hour) and cooled to room temperature. Then acetonitrile (600 ml) was added. The resulting mixture was heated several times to a boil and cooled to room temperature until the melt completely dissolved. Then the solution was kept at room temperature, the precipitate formed was filtered off and dried in air. Yield 0.9 g (49%), light yellow powder, mp 208-210 °C (decomp.). IR (KBr, ν/cm^{-1}): 3433 (OH), 3045 (CH_{Ar}), 2957, 2925, 2854 (CH_{Alk}), 1725, 1645 (C=O), 1607, 1546, 1506, 1465 (C=N, C=C). ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.19-3.36 (m, 2 H, CH_2); 3.56-3.66 (m, 1 H, CH); 4.37-4.51 (m, 2 H, NCH_2); 7.46-7.55 (m, 2 H, Ar); 7.80 (t, 1 H, Ar, J = 7.3 Hz); 8.05 (d, 1 H, Ar, J = 7.9 Hz), 12.81 (br.s, COOH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 35.3, 36.4 (CH, CH_2CO); 50.6 (CH_2N); 115.8 (CH_{Ar}); 118.2 (C_{Ar}); 125.6, 127.3, 133.7 (CH_{Ar}); 138.5 (C_{Ar}); 165.2, 173.5 (C=O); the signal of the C=N atom is not observed. HRMS (ESI), *m*/*z*: 231.0768 $[M + H]^+$; calc. for $C_{12}H_{11}N_2O_3^+$ 231.0764; 253.0577 $[M + Na]^+$; calc. for $C_{12}H_{10}N_2NaO_3^+$ 253.0584.

Method B. A mixture of anthranilic acid amide **2** (3.0 g, 22.2 mmol) and itaconic acid (2.87 g, 22.2 mmol) was refluxed in *m*-xylene (40 ml) for 7 h and cooled to room temperature. The precipitate formed was filtered off and then refluxed in ethyl acetate (40 ml) for 3 h and left overnight at room temperature. The precipitate was filtered, dried in air, mixed with ether (20 ml), and stirred at room temperature for 1 h. The precipitate was filtered again and dried in air. Yield 3.04 g (60%).

Method C. A 50 ml round-bottomed flask was charged with 1.0 g (4 mmol) of compound **3** and the flask was placed in an oil bath preheated to 80 °C. The reaction mixture was heated at a rate of 4-5 K min^{-1} to reach 153-155 °C (the content of the flask began to melt at 140 °C) and maintained at this temperature for 1 h until the mixture completely solidified. According to the ^{1}H NMR spectrum, the product does not require further purification. Yield 0.921 g (100%).

Method D. Compound **3** (0.5 g, 2 mmol) was refluxed in *m*-xylene (15 ml) for 7 h. Then the reaction mixture was cooled, the resulting light yellow precipitate of compound **4** was filtered and dried at 80-90 °C for 6 h. Yield 0.313 g (67%).

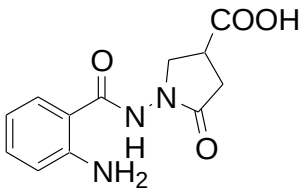


6

2-Aminobenzohydrazide (6). Methyl 2-aminobenzoate **5** (4.91 g, 32.5 mmol) was refluxed in hydrazine hydrate (8.13 g, 162 mmol) for 4 h, cooled and left overnight in the refrigerator. The precipitated compound **6** was filtered off, washed with water (4 ml), and dried in air. Yield 3.95 g (83%), mp 119-121 °C (*cf.* lit. mp 118-120 °C, M. K. Kathiravan, N. Vidyasagar, R. Khiste, A. Chote, K. Jain, *Arabian J. Chem.*, 2016, **9**, (Suppl._1), S395; https://doi.org/10.1016/j.arabjc.2011.05.009.).

Synthesis of 1-(2-aminobenzamido)-5-oxopyrrolidine-3-carboxylic acid (8). *Method A.* Anthranilic acid hydrazide **6** (11.78 g, 80.0 mmol) and itaconic acid (11.44 g, 88.0 mmol) were thoroughly mixed and placed in a 150 ml round-bottomed flask. The reaction mixture was heated in an oil bath at a rate of 4-5 K min^{-1}. The mixture began to melt at 70 °C and completely melted at 90 ° C. The rate of

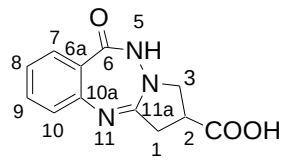
temperature raising was reduced to 1-2 K min^{-1} before the spontaneous rising the temperature began. The heating of the flask was stopped. The reaction mass foamed, and its temperature rose to 120 °C. After 5 minutes, the foaming stopped and the melt turned into a hard brittle mass. The reaction mixture was heated in an oil bath at 100-105 °C for 1 h. After cooling the reaction mixture to room temperature, acetonitrile (500 ml) was added. The resulting mixture was stirred under reflux for 10-15 min and cooled to room temperature. The precipitate formed was filtered off and dried in air. Yield 16.46 g (84%), white powder, mp 232-234 °C (decomp.). IR (KBr, ν/cm^{-1}): 3486, 3376, 3258, 3230 (OH, NH, NH_2), 3049, 3012 (CH_{Ar}), 2952, 2910 (CH_{Alk}), 1744, 1700, 1635 (C=O), 1580, 1534, 1493, 1450 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.50-2.68 (m, 2 H, CH_2, overlaps with solvent signal); 3.32-3.36 (m, 1 H, CH, overlaps with water signal); 3.63-3.77 (m, 2 H, NCH_2); 6.49-6.54 (m, 3 H, Ar, NH_2); 6.73 (d, 1 H, Ar, J = 8.2), 7.19 (t, 1 H, Ar, , J = 7.5); 7.53 (d, 1 H, Ar, J = 7.9), 10.32 (s, 1 H, NH), 12.69 (br.s, COOH). Спектр ЯМР ^{13}C (δ, м.д.): 31.4, 34.1 (CH, CH_2CO); 49.8 (CH_2N); 111.2 (C_{Ar}); 114.6, 116.6, 128.2, 132.8 (CH_{Ar}); 150.3 (C_{Ar}); 167.4, 171.2, 174.1 (C=O). MS (ESI): found m/z 279.0979 $[M + H]^+$; calcd. for $C_{12}H_{14}N_3O_4^+$ 279.0979; found m/z 286.0792 $[M + Na]^+$; calcd. for $C_{12}H_{13}N_3NaO_4^+$ 286.0798.



8

Method B. A mixture of anthranilic acid hydrazide **11** (0.430 g, 2.85 mmol) and itaconic acid (0.403 g, 3.1 mmol) was refluxed in *m*-xylene (5 ml) for 0.5 h. Then the reaction mixture was cooled, the resulting precipitate was filtered off and dried. Then acetonitrile (10 ml) was added to the dry precipitate, the mixture refluxed for 1 h and cooled to room temperature. The precipitate was filtered off and dried in air. Yield 0.44 g (59%).

Synthesis of 6-oxo-2,3,5,6-tetrahydro-1*H*-benzo[*e*]pyrrolo[1,2-*b*][1,2,4]triazepine-2-carboxylic acid (7). *Method A.* Anthranilic acid hydrazide **6** (1.0 g, 6.8 mmol) and itaconic acid (1.15 g, 8.8 mmol) were placed in a 50 ml round-bottomed flask and thoroughly mixed. The flask was placed in an oil bath preheated to 70 °C and heated at a rate of 4-5 K min^{-1}. The mixture began to melt at 75-80 ° C and completely melted at 105-110 °C. A violent release of gas continued for several minutes, then the mixture solidified. At 145-150 °C, the mixture melted again, and gas was released again at 165-170 °C. The reaction mixture was heated at 178-182 °C for 1 h and cooled to room temperature. To a solid dark cherry mass obtained, acetonitrile (100 ml) was added. The resulting mixture was stirred under reflux for 3 h, cooled to room temperature and filtered. The filtrate is evaporated to 1/3 of the volume (≈ 30-35 ml) and left at room temperature for 1 h. The precipitate formed was filtered off and dried in air. Yield 0.33 g (21%), white powder, mp 223-225 °C. IR (KBr, ν/cm^{-1}): 3271 (OH, NH), 3016 (CH_{Ar}), 2914 (CH_{Alk}), 1709, 1675 (C=O), 1606, 1567, 1497, 1465 (C=N, C=C). ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.11-3.28 (m, 3 H, CH_2, CH); 3.30-3.39 (m, 2 H, NCH_2, overlaps with water signal); 7.40 (s, 1 H, NH), 7.49 (t, 1 H, C(8)H, J = 7.6), 7.63 (d, 1 H, C(10)H, J = 8.1), 7.78 (m, 1 H, C(9)H); 8.11 (d, 1 H, C(7)H, J = 8.0), 12.71 (br.s, COOH). Спектр ЯМР ^{13}C (δ, м.д.): 30.4 ($C(1)H_2$); 37.9 (C(2)H); 46.9 ($NC(3)H_2$); 119.6 (C(6a)); 125.7 (C(7)H), 126.0 (C(8)H), 126.7 (C(10)H), 133.7 (C(9)H); 146.3 (C(10a)); 151.5 (C(11a), 156.8 (C=O), 174.3 (COOH). Масс-спектр (ESI): найдено m/z 246.0878 $[M + H]^+$; вычислено для $C_{12}H_{12}N_3O_3^+$ 246.0873; найдено m/z 268.0690 $[M + Na]^+$; вычислено для $C_{12}H_{11}N_3NaO_3^+$ 268.0693.



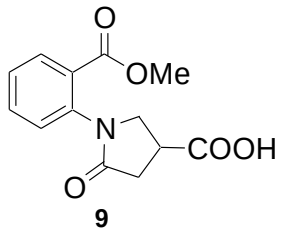
7

Method B. A mixture of anthranilic acid hydrazide **6** (1.0 g, 6.6 mmol) and itaconic acid (0.86 g, 6.6 mmol) was refluxed in water (15 ml) for 36 h. The resulting precipitate was filtered off from hot suspension and dried in air. Yield 0.68 g (45%).

Method C. 1-(2-Aminobenzamido)-5-oxopyrrolidine-3-carboxylic acid **8** (1.23 g, 4.7 mmol) was placed in a 50 ml round-bottomed flask. The flask was placed in an oil bath preheated to 70 °C and heated at a rate of 4-5 K min^{-1} to 180 °C. During the heating, the mass melted, foamed, and solidified. The reaction mass was heated at 178-182 °C for 1 h and cooled to room temperature. To a solid mass obtained, acetonitrile (100 ml) was added. The resulting mixture was stirred under reflux for 3 h, cooled to room temperature and filtered. The filtrate was evaporated to 1/3 of the volume (≈ 30-35 ml) and left at room temperature for 1 h. The precipitate formed was filtered off and dried in air. Yield 0.57 g (50%).

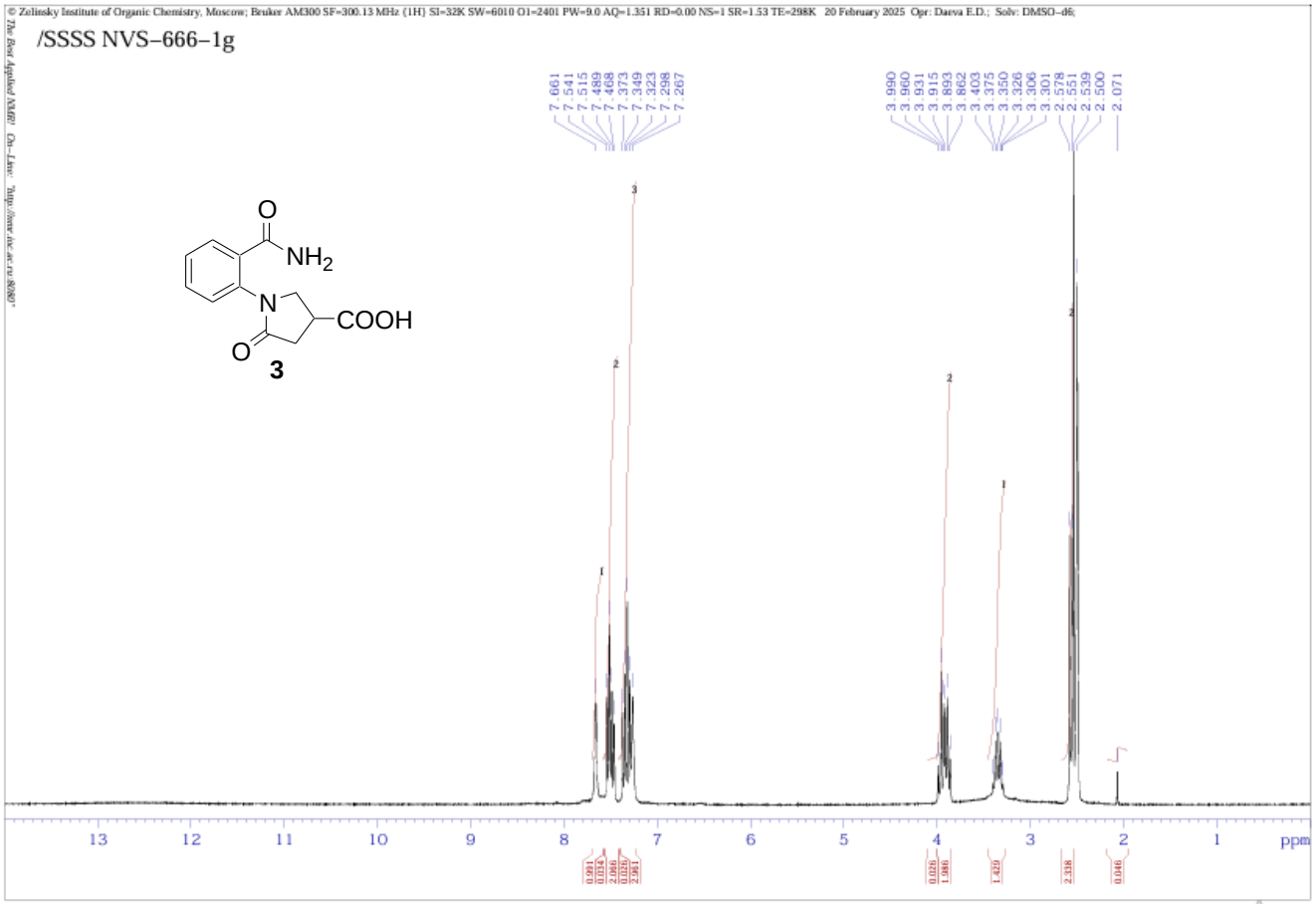
Method D. 1-(2-Aminobenzamido)-5-oxopyrrolidine-3-carboxylic acid **8** (1.0 g, 3.8 mmol) was refluxed in water (15 ml) for 48 h. The resulting precipitate was filtered off from hot suspension and dried in air. Yield 0.336 g (52%).

Synthesis of 1-[2-(methoxycarbonyl)phenyl]-5-oxopyrrolidine-3-carboxylic acid (9). A mixture of methyl 2-aminobenzoate **5** (20.0 g, 132.0 mmol) and itaconic acid (17.22 g, 132.0 mmol) was placed in a 250 ml round-bottomed flask, heated at 140 °C for 3 h and cooled to 60 °C. Then the mixture was poured into 10% solution of hydrochloric acid (60 ml) preheated to 60 °C, stirred for several minutes and cooled to room temperature. The precipitated compound **9** was filtered, washed with water, diethyl ether, and dried in air. Yield 18.0 g (53%), cream powder, mp 90-92 °C. IR (KBr, ν/cm^{-1}): 3435, 3248 (OH), 3004 (CH_{Ar}), 2955, 2901 (CH_{Alk}), 1718, 1671 (C=O), 1601, 1576, 1492, 1461 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.62-2.66 (m, 2 H, CH_2); 3.33-3.40 (m, 1 H, CH, overlaps with water signal); 3.95 (dd, 1 H, NCH_2, J = 5.8, 9.4 Hz); 4.01-4.07 (m, 1 H, NCH_2); 7.37-7.44 (m, 2 H, Ar), 7.64 (dd, 1 H, Ar, J = 7.6, 6.7 Hz), 7.78 (d, 1 H, Ar, J = 7.77 Hz); 12.78 (br.s, COOH). Спектр ЯМР ^{13}C (δ, м.д.): 33.9, 36.1 (CH_2,CH); 51.8, 52.1 (OMe, NCH_2); 126.4 (CH_{Ar}); 126.9 (CH_{Ar}), 127.9 (C_{Ar}), 130.3 (CH_{Ar}), 132.9 (CH_{Ar}); 137.3 (C_{Ar}); 166.2, 172.1 174.0 (C=O, COOH). MS (ESI): found m/z 264.0862 $[M + H]^+$; calcd. for $C_{13}H_{14}NO_5^+$ 264.0866; found m/z 286.0676 $[M + Na]^+$; calcd. for $C_{13}H_{13}NNaO_5^+$ 286.0686.

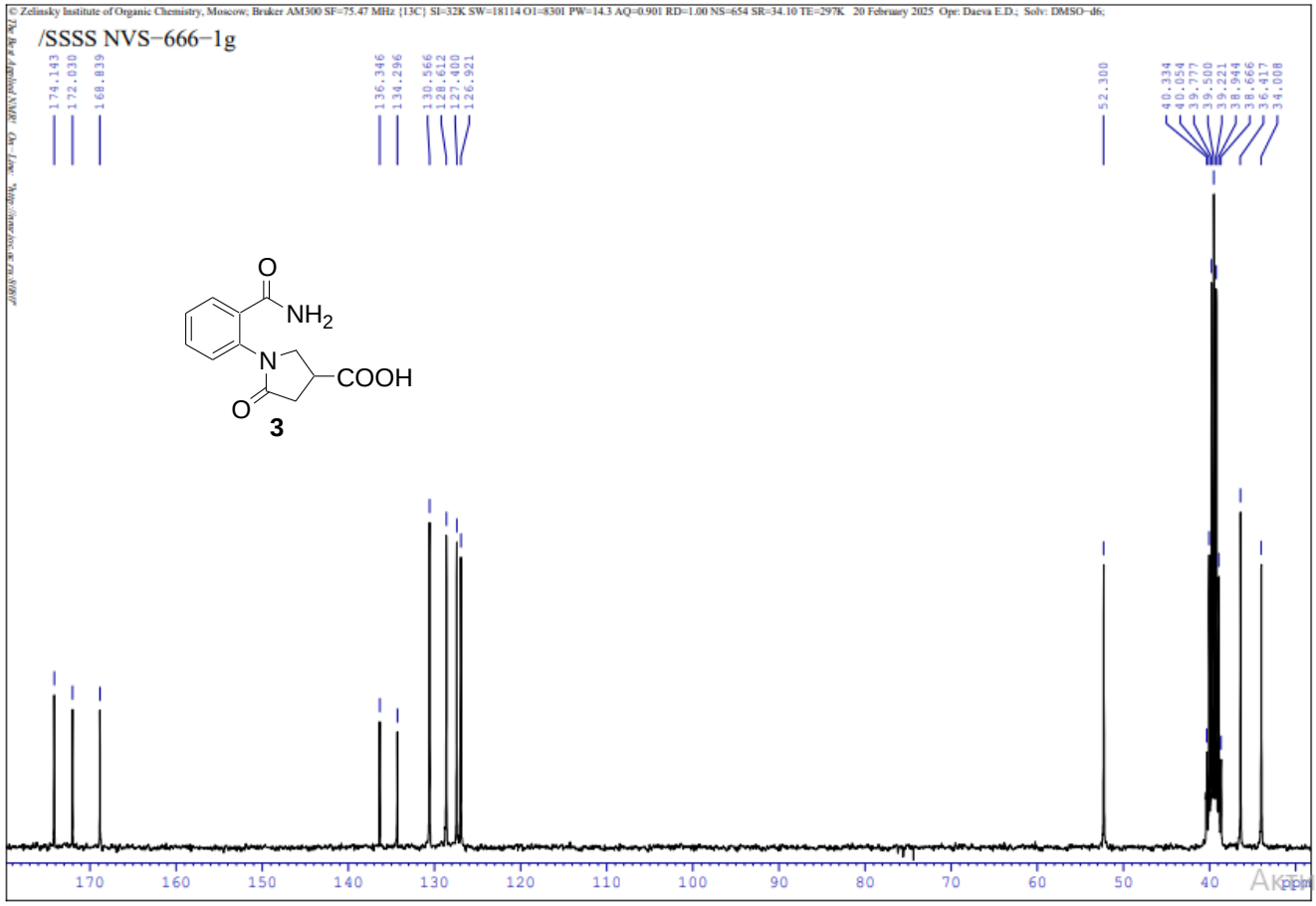


9

^{1}H NMR spectrum of compound **3**



^{13}C NMR spectrum of compound **3**



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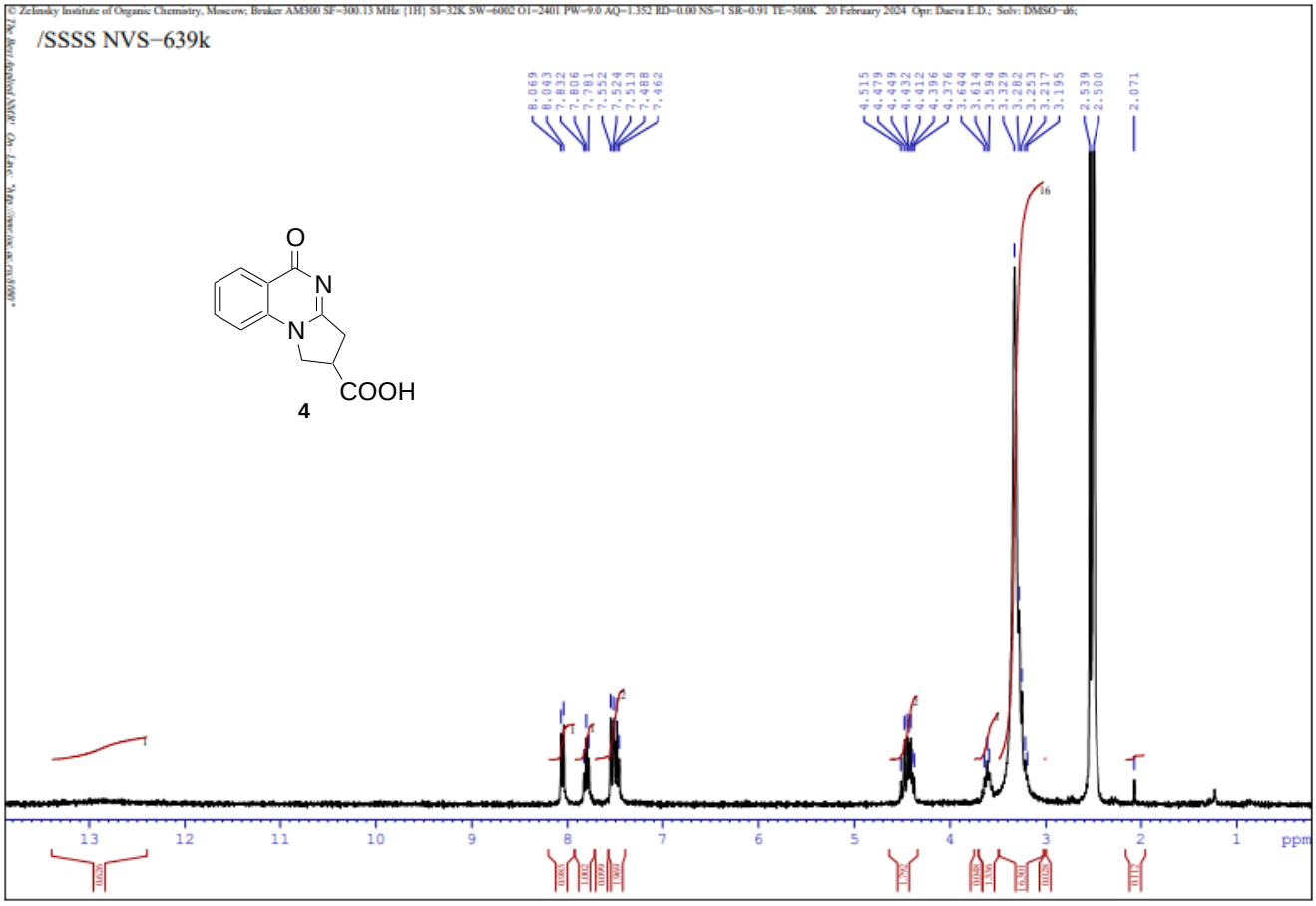
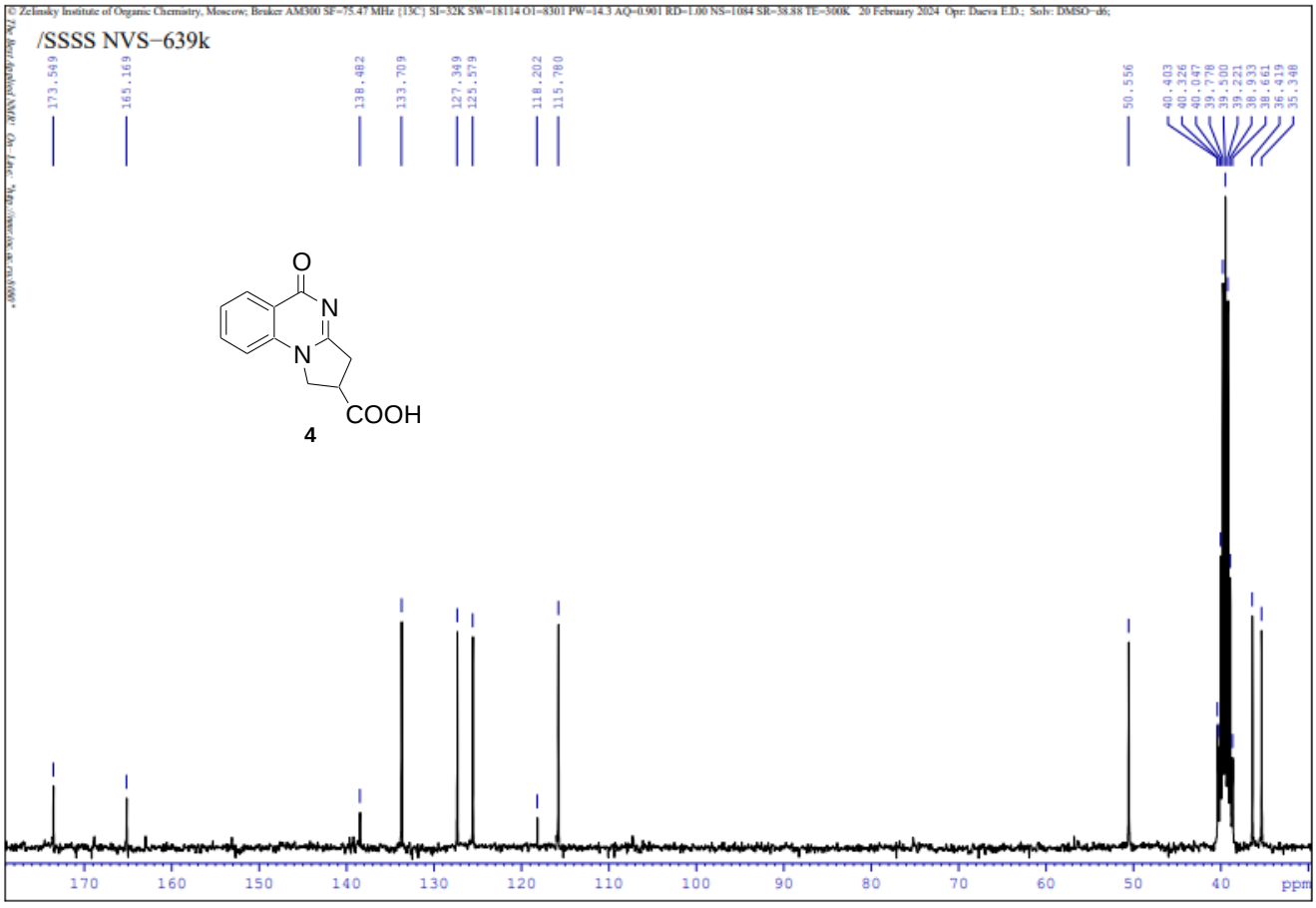
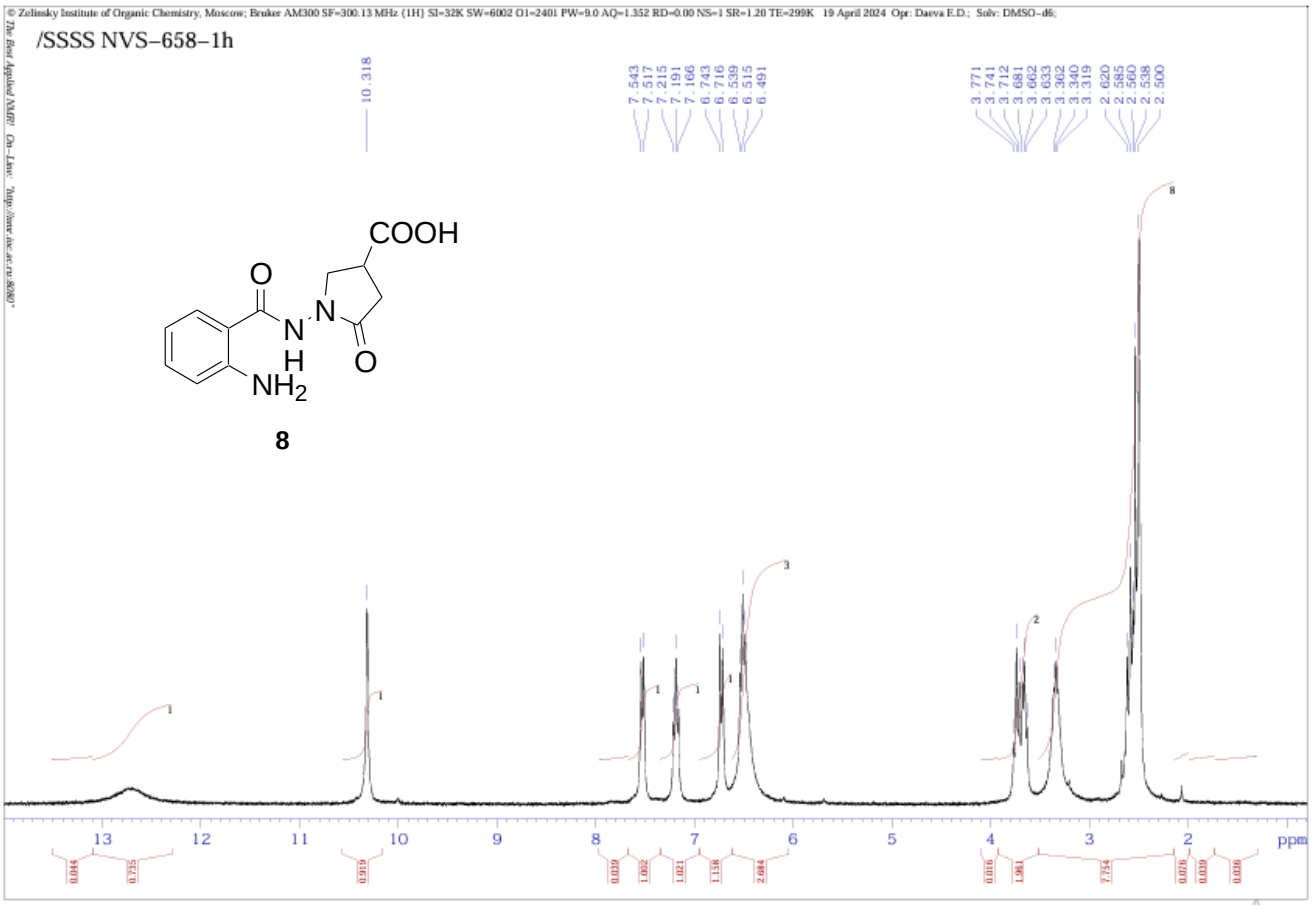


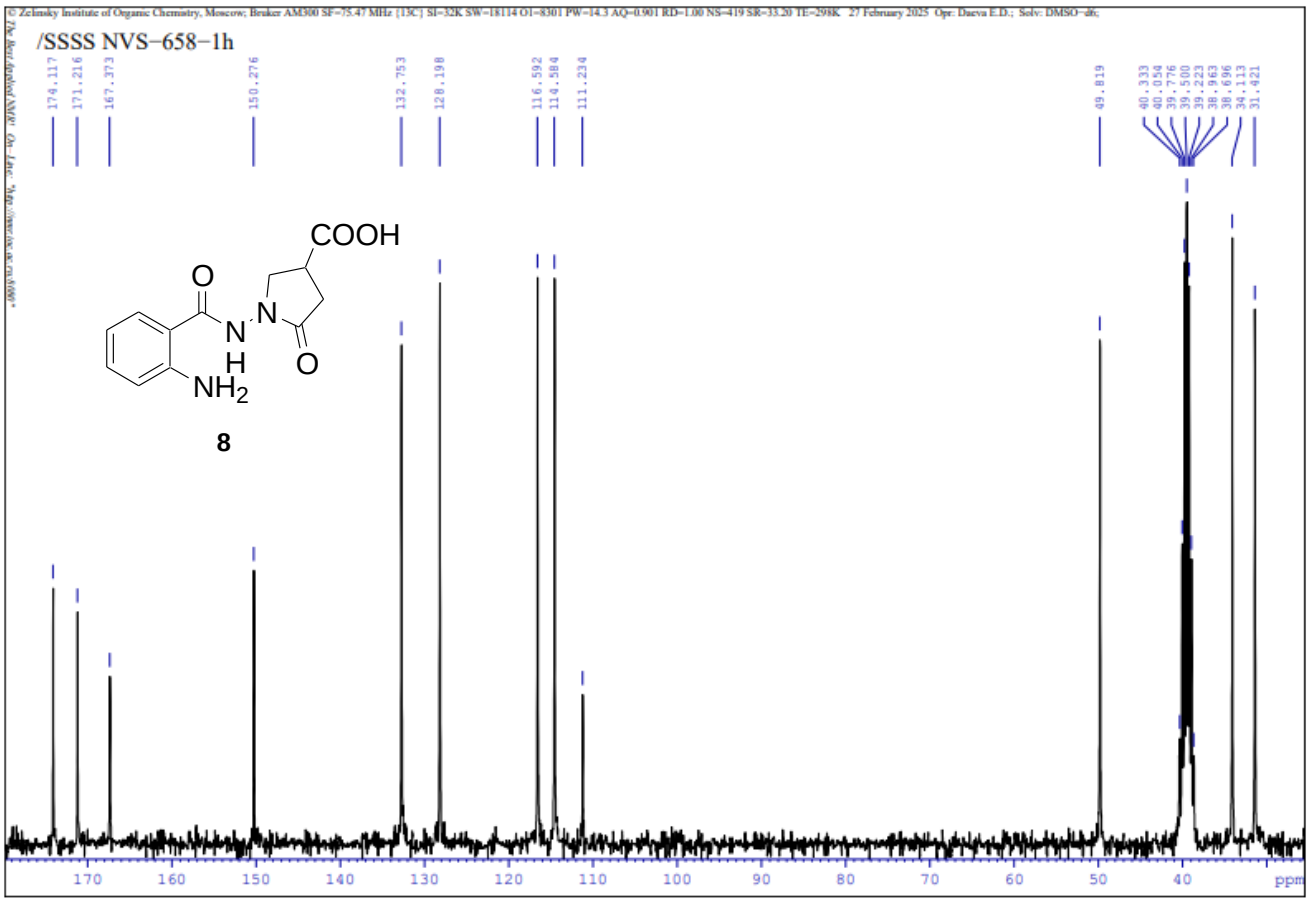
^{13}C NMR spectrum of compound **4**



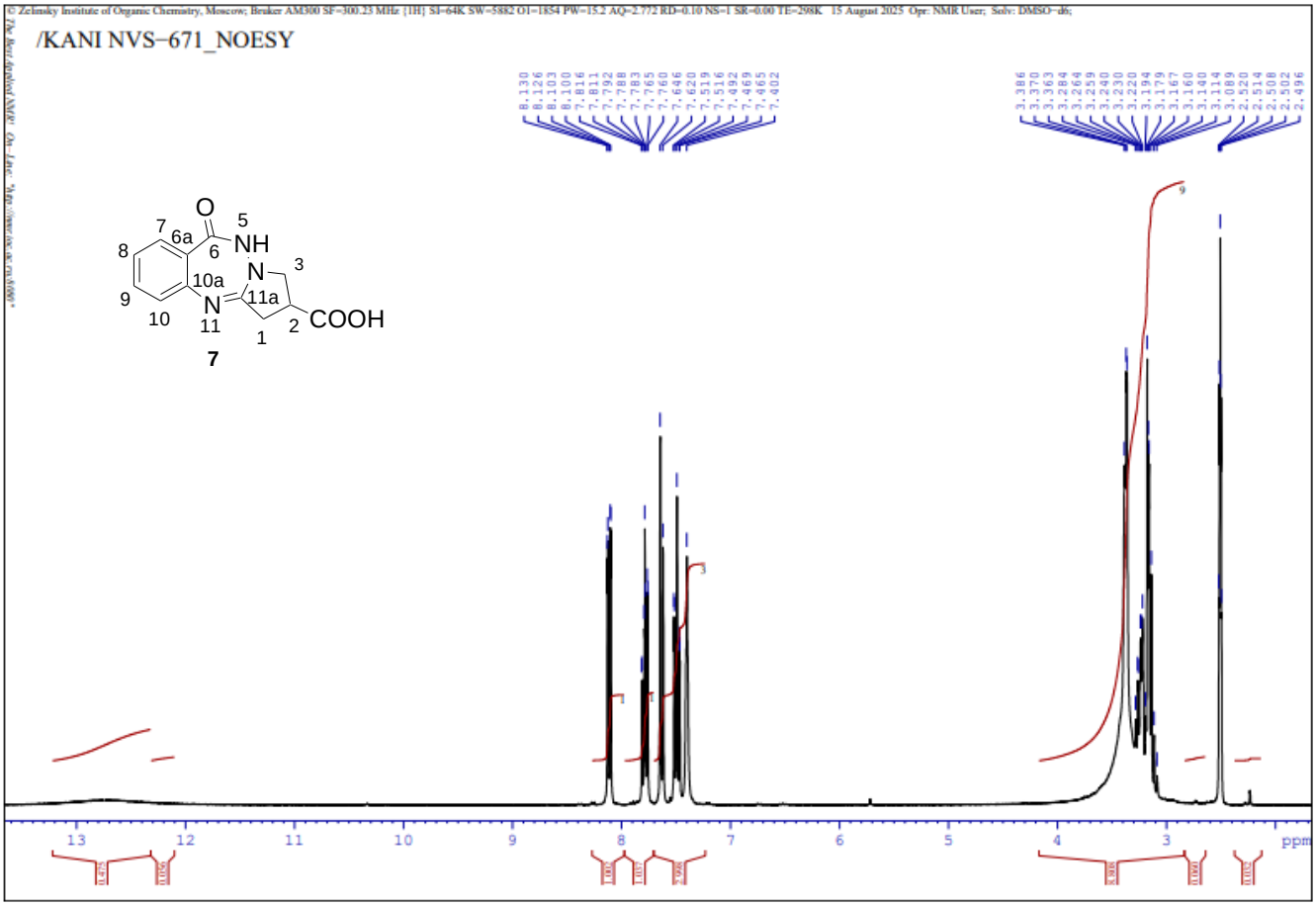
^{1}H NMR spectrum of compound **8**



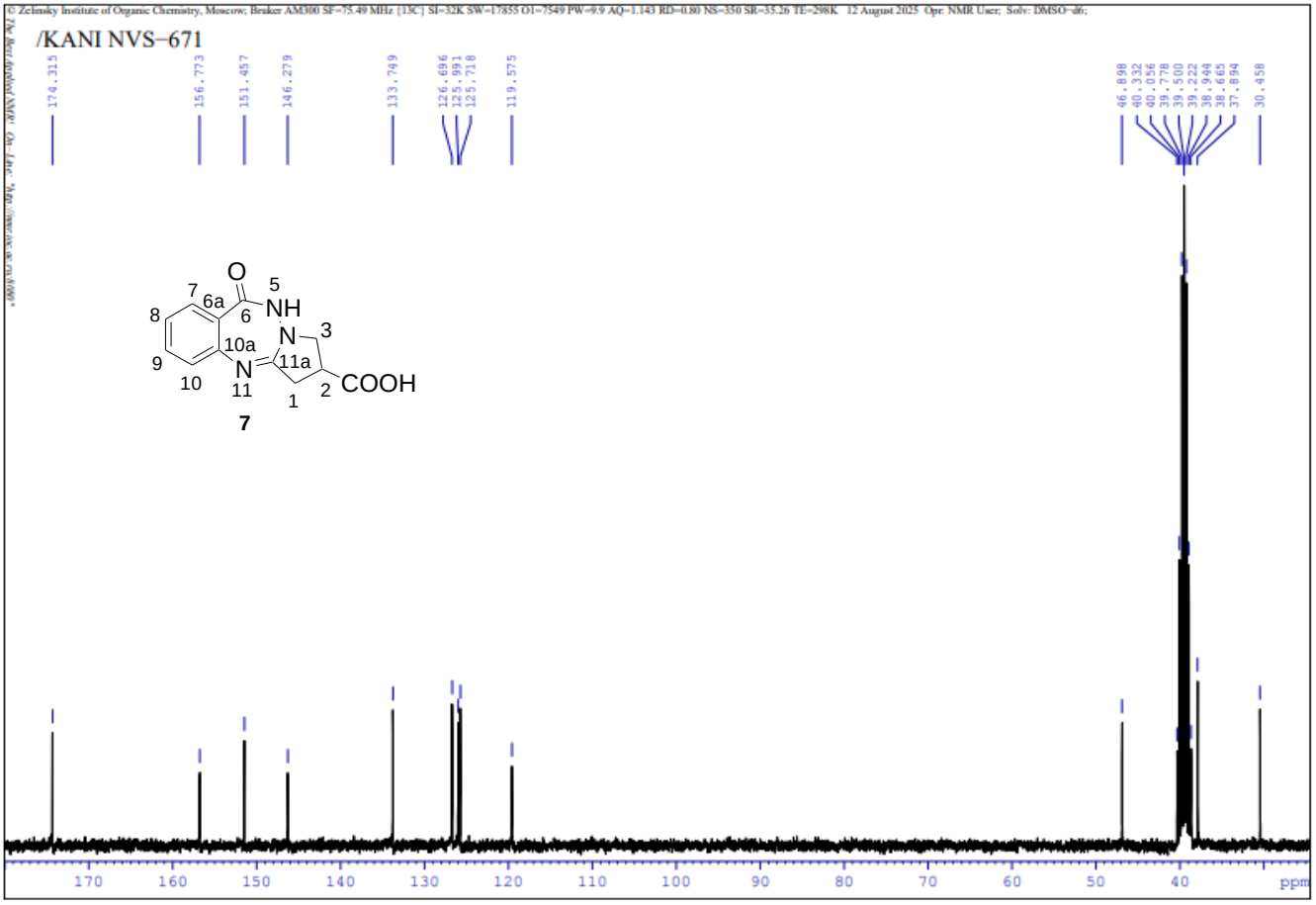
^{13}C NMR spectrum of compound **8**



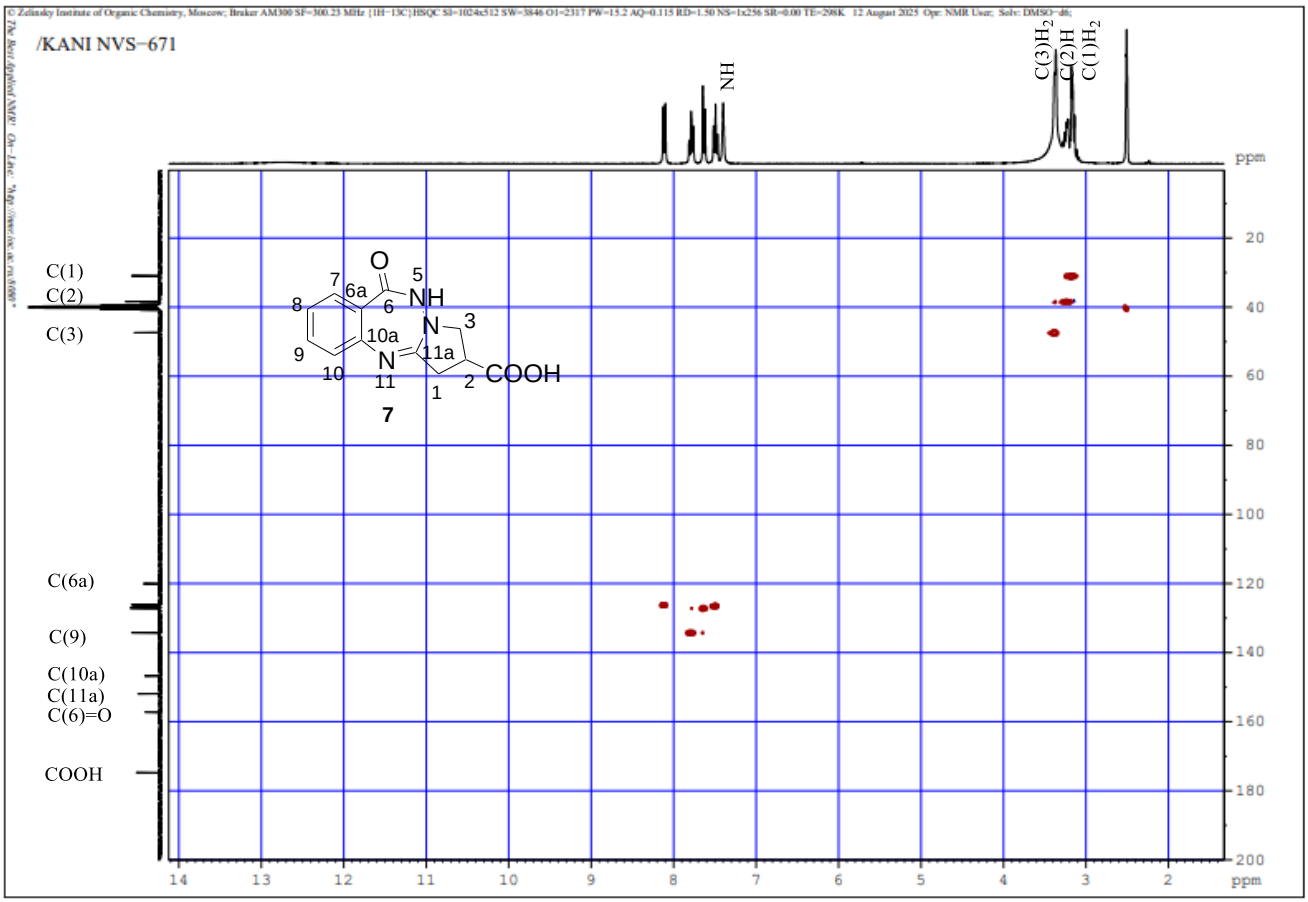
^{1}H NMR spectrum of compound **7**



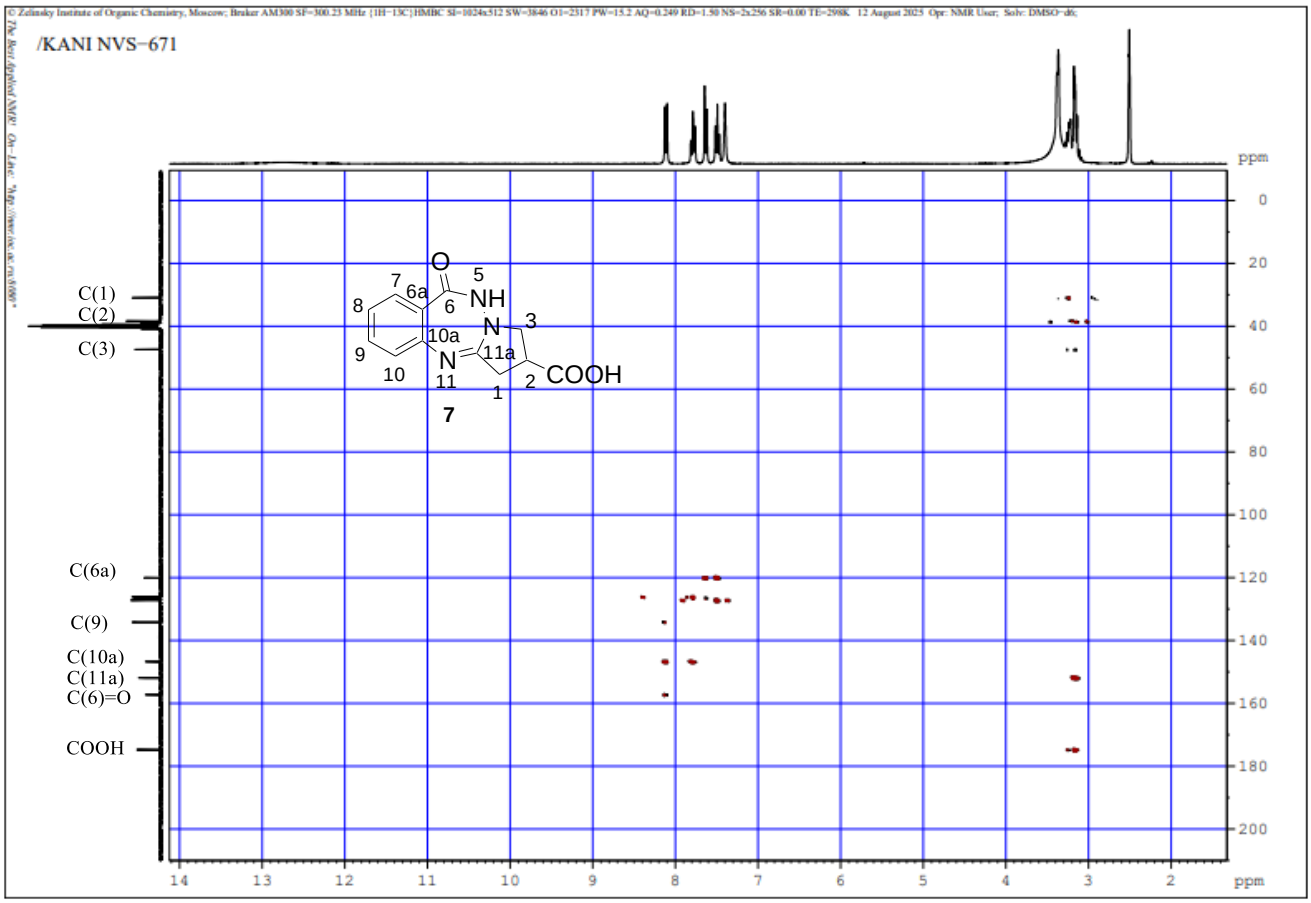
^{13}C NMR spectrum of compound **7**



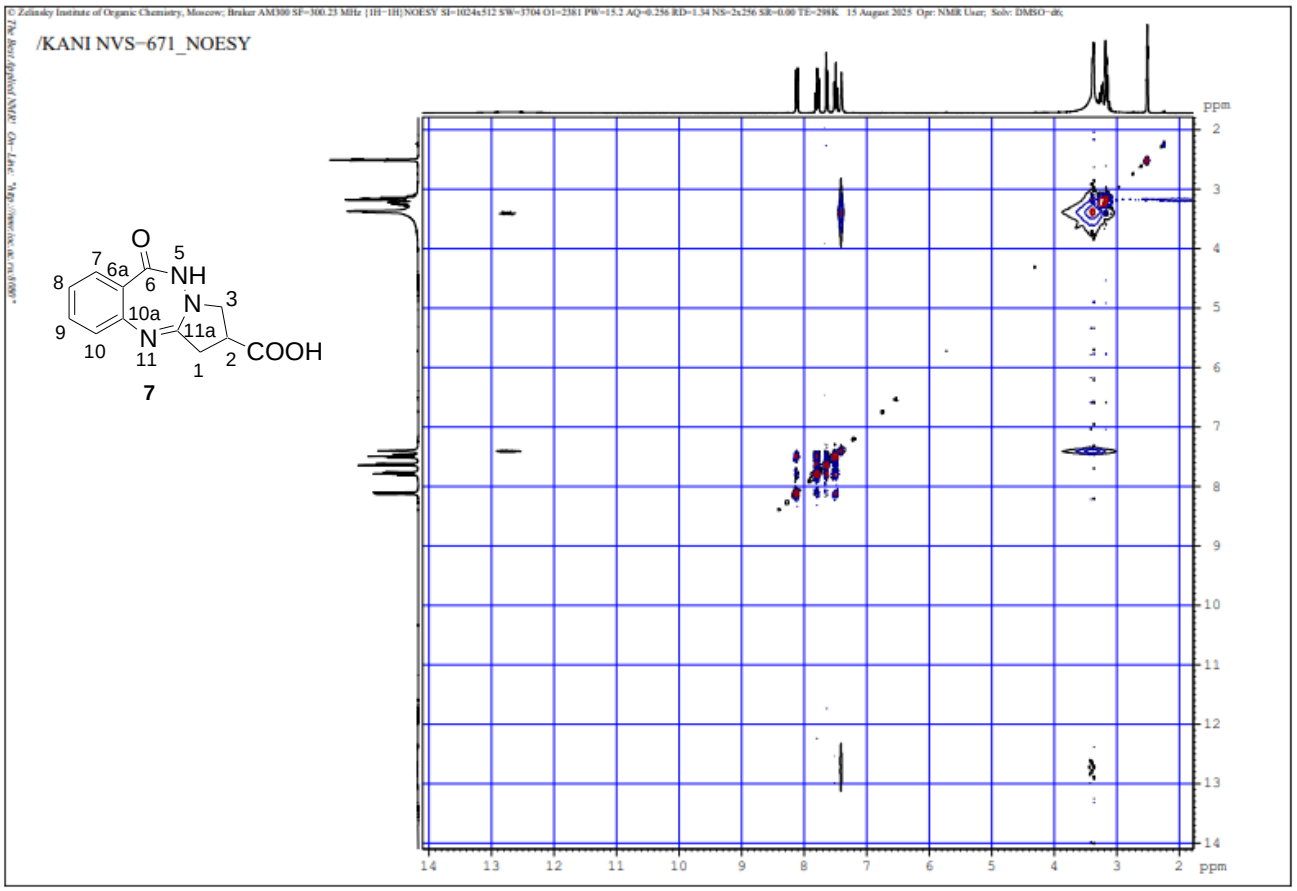
{^{1}H–^{13}C} HSQC spectrum of compound **7**



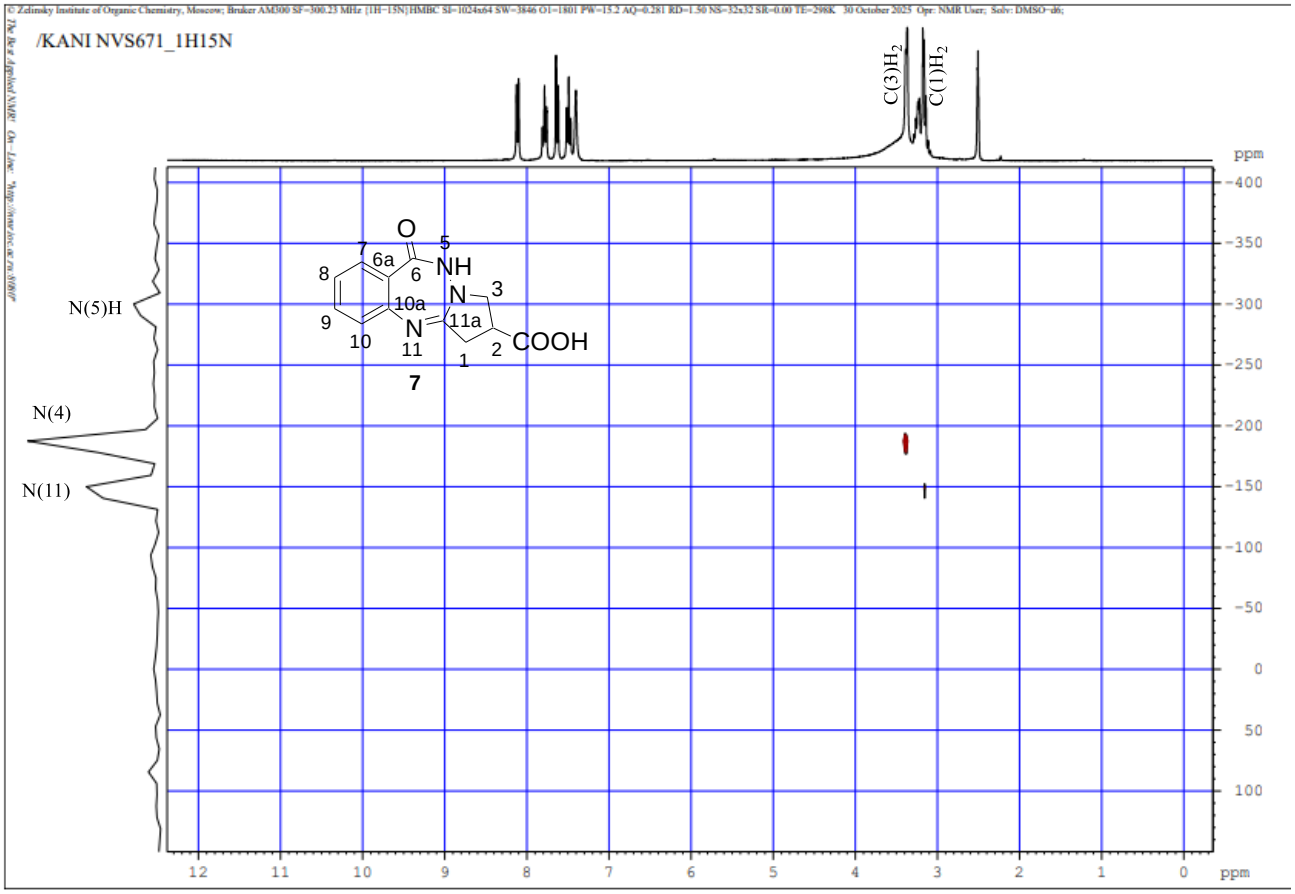
{^{1}H–^{13}C} HMBC spectrum of compound **7**



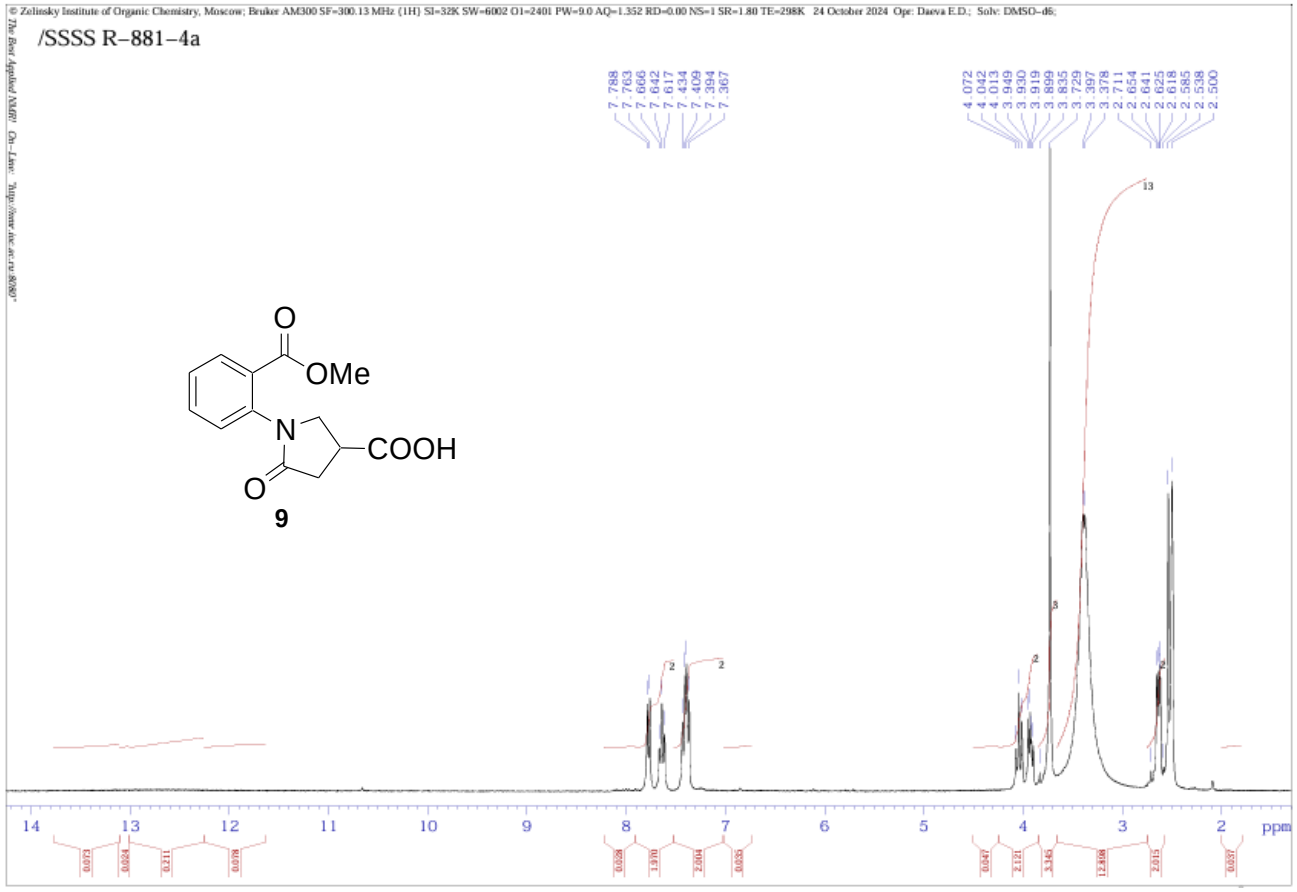
{^{1}H–^{1}H} NOESY spectrum of compound **7**



{^{1}H–^{15}N} HMBC spectrum of compound **7**



^{1}H NMR spectrum of compound **9**



^{13}C NMR spectrum of compound **9**