

3,3,4,4-Tetracyanoalkanones as expedient reagents for utilization of *N,N*-dimethylhydrazine

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EXPERIMENTAL SECTION

Caution! Syntheses involving the release of hydrogen cyanide (prussic acid) should be conducted with the provision of a gas vent and an absorption flask, and performed under properly functioned fume hood. It is essential to wear protective eyewear and latex gloves during the process.

All reagents were procured from commercial vendors and employed without additional purification. The progress of reactions and the purity of products were monitored *via* thin-layer chromatography (TLC) on Sorbfil plates. Visualization of spots was achieved under ultraviolet (UV) light, upon treatment with iodine vapor, or through heating. Melting and decomposition points were determined using the Optimelt MPA100 apparatus. Infrared (IR) spectra were obtained using the FSM-1202 spectrometer equipped with Fourier transform technology, with samples dispersed in Nujol. Proton nuclear magnetic resonance (^1H NMR) and carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were acquired in DMSO- d_6 solvent, utilizing the TMS internal standard. The measurements were conducted on a Bruker AVANCE400 WB spectrometer operating at frequencies of 400.13 MHz for ^1H and 100.61 MHz for ^{13}C .

Mass spectra were acquired using the AB Sciex Triple TOF 5600 mass spectrometer (AB SCIEX PTE. Ltd., Singapore) equipped with a quadrupole time-of-flight (t, qTOF) analyzer. The turbo-ion spray source was employed, utilizing nitrogen as the nebulizer gas. Positive ionization polarity was applied, and the needle voltage was set to 5,500 V. The spectra were recorded in the TOF MS mode with a collision energy of 10 eV, declustering potential of 100 eV, and a resolution exceeding 30,000 full-width half-maximum. To prepare the samples for analysis, the test compounds were dissolved in hypergrade methanol for LC-MS (Merck) to achieve an analyte concentration of 5 $\mu\text{mol/L}$.

***N,N*-Dimethyl-2-methylenehydrazone (2)** was synthesized using the previously described procedure^{S1}, resulting in a yield of 90%.

5-Amino-1-dimethylamino-1,2-dihydro-3H-pyrrole-3,3,4-tricarbonitrile 6.

1,1-Dimethyl-2-methylenehydrazine (1.1 mmol) was added to a solution containing ethane-1,1,2,2-tetracarbonitrile (1 mmol) in ethyl acetate (2 ml). The resulting mixture was maintained at room temperature for 14 h (TLC monitoring). Afterward, the mixture was cooled, and the precipitate that formed was filtered and washed with cold ethyl acetate (2 ml). The yield obtained was 81%. The elemental analysis yielded the following results: C 53.61%; H 4.72%; N 41.67%. The calculated values for the compound $\text{C}_9\text{H}_{10}\text{N}_6$ were: C 53.46%; H 4.98%; N 41.56%.

4-Oxopentane-1,1,2,2-tetracarbonitrile (7a), 4-oxohexane-1,1,2,2-tetracarbonitrile (7b), 3-methyl-4-oxopentane-1,1,2,2-tetracarbonitrile (7c) were obtained according to the general procedure^{S2} with the yields of 72%, 69%, 65% respectively.

Synthesis of compounds 8a-c. *N,N*-Dimethyl-*N'*-methylenedihydrazine **2** (8 mmol), catalytic amount of sodium hydroxide, and 3,3,4,4-tetracyanoalkaneone **7a-c** (9 mmol), were separately dissolved in ethyl acetate. The resulting solutions were combined, thoroughly mixed and kept at room temperature. The reaction progress was monitored using TLC, with *N,N*-dimethyl-*N'*-methylenedihydrazine **2** serving as the reference. After an hour, sand-colored crystals precipitated from the reaction mixture. The product was separated by filtration through a Schott filter, followed by washing with cold ethyl acetate. Subsequently, recrystallization was performed using propan-2-ol as the solvent.

In the specified quantities, the liberation of hydrogen cyanide does not present any danger. However, when dealing with larger quantities, it is imperative to utilize the aforementioned apparatus.

3-Amino-5-dimethylamino-6-methyl-1-oxo-4,5-dihydro-1H-pyrrolo[3,4-c]pyridine-3a,7a-dicarbonitrile (9a), yield 57%. Found: C 56.01; H 5.33; N 32.75. C₁₂H₁₄N₆O. Calculated %: C 55.80; H 5.46; N 32.54.

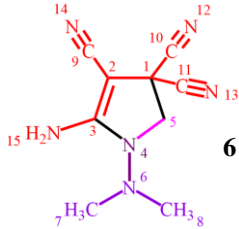
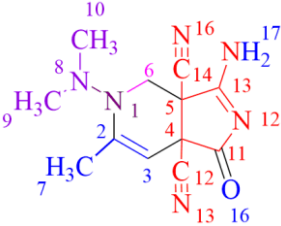
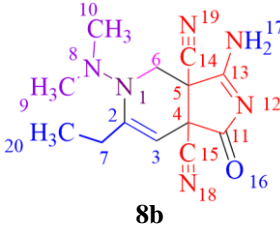
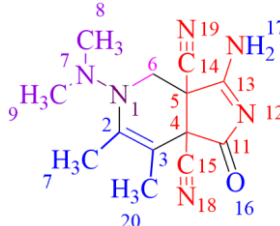
3-Amino-5-dimethylamino-6-ethyl-1-oxo-4,5-dihydro-1H-pyrrolo[3,4-c]pyridine-3a,7a-dicarbonitrile (7b), yield 54%. Found: C 57.21; H 6.08; N 30.56. C₁₃H₁₆N₆O. Calculated %: C 57.34; H 5.92; N 30.86.

3-Amino-5-dimethylamino-6,7-dimethyl-1-oxo-4,5-dihydro-1H-pyrrolo[3,4-c]pyridine-3a,7a-dicarbonitrile (7c), yield 52%. Found: C 57.30; H 6.01; N 30.63 C₁₃H₁₆N₆O. Calculated %: C 57.34; H 5.92; N 30.86

In the ¹H and ¹³C NMR spectra, the chemical shifts of the pivotal atoms in structures **8a-c** closely resembled those of the analogous compounds reported in the publication SSRN^{S3}. In that work, the structures of some analogues were established by the X-Ray Diffraction Analysis method^{S3}.

The data on yield, melting point, IR, MNR ¹H, ¹³C, mass-spectra of the compounds obtained are presented in Table S1.

Table S1. Yields, melting points, IR, ¹H, ¹³C NMR and mass spectral data.

Structural number	Yield, %	Melting point, °C	IR(Nujol), ν _{max} /cm ⁻¹	¹ H NMR δ, ppm, J, Hz (DMSO-d ₆)	¹³ C NMR ppm, (DMSO-d ₆)	HMRS(ESI), m/z
 <p>6</p>	81%	163-165	1646 (vs) (C=C), 2112 (vs), 2165 (s) (C≡N), 3177 (w, br), 3240 (w, br), 3362 (w, br), 3386 (w, br) (NH ₂)	7.56 (s, 2H, NH ₂), 4.05 (s, 2H, CH ₂ ⁵), 2.43 (s, 6H, N(CH ₃) ₂).	161.85 (C ³), 117.70 (C≡N ⁹), 115.14 ((C≡N ^{11,10}) ₂), 48.42 (CH ₂ ⁵), 46.42 (C ²), 42.24 (N(CH ₃) ₂), 34.59 (C ¹)	Calcd. C ₉ H ₁₀ N ₆ : 202.1000 [M] ⁺ , Found: 203.1047
 <p>8a</p>	57	160-161	1651 (s) (C=C), 1750 (s) (C=O), 2257 (vs) (C≡N), 3480 (vs, br) (NH ₂)	9.63 (d, J = 30.6 Hz, 2H, NH ₂ ¹⁷), 3.73 (d, J = 11.7 Hz, 1H, CH ₃), 3.35 (d, J = 9.2 Hz, 2H, CH ₂ ⁶), 2.33 (s, 6H, N(CH ₃) ₂), 2.10 – 1.80 (m, 3H, CH ₃ ⁷).	178.27 (C=O), 177.07 (C ⁹), 144.94 (C ²), 116.16 (CN ¹³), 115.24 (CN ¹³), 95.07 (CH ³), 59.76 (C ⁵), 52.94 (C ⁴), 51.08 (CH ₂ ⁶), 40.15 (N(CH ₃) ₂), 21.88 (CH ₃ ¹⁶)	C ₁₂ H ₁₄ N ₆ O 258.12 (100.0%)
 <p>8b</p>	54	165-166	1639 (s) (C=C), 1745 (s) (C=O), 2260 (s) (C≡N), 3395 (vs, br) (NH ₂)	9.61 (d, J = 15.2 Hz, 2H, NH ₂ ¹⁷), 4.35 (d, J = 4.2 Hz, 1H, CH ₃), 3.96 (d, J = 11.7 Hz, 1H, CH ₂ ⁶), 3.20 (d, J = 11.7 Hz, 1H, CH ₂ ⁶), 1.37 – 1.17 (m, 2H, CH ₂ ⁷), 1.03 (d, J = 6.2 Hz, 6H, N(CH ₃) ₂), 0.88 (t, J = 7.1 Hz, 3H, CH ₃ ²⁰).	178.07 (C=O), 177.15 (C ⁹), 145.03 (C ²), 116.19 (CN ¹³), 115.30 (CN ¹³), 94.70 (CH ³), 62.07 (C ⁵), 53.33 (C ⁴), 51.57 (CH ₂ ⁶), 40.17 (N(CH ₃) ₂), 19.63 (CH ₃ ¹⁶), 14.18 (CH ₃ ²⁰)	C ₁₃ H ₁₆ N ₆ O 272.14 (100.0%)
 <p>8c</p>	52	167-169	1624 (s) (C=C), 1736 (s) (C=O), 2243 (s) (C≡N), 3457 (vs, br) (NH ₂)	5.27 (s, 3H, NH ₂), 4.02 (q, J = 7.0 Hz, 2H, CH ₂ ⁶), 2.61 (s, 6H, N(CH ₃) ₂), 2.19 (s, 3H, CH ₃ ⁷), 1.49 (s, 3H, CH ₃ ²⁰)	178.07 (C=O), 177.15 (C ⁹), 145.03 (C ²), 116.19 (CN ¹³), 115.30 (CN ¹³), 94.70 (C ⁵), 62.07 (C ⁴), 51.57 (C ⁵), 41.14 (CH ₂ ⁶), 39.96 (N(CH ₃) ₂), 19.63 (CH ₃ ¹⁶), 14.18 (CH ₃ ²⁰)	C ₁₃ H ₁₆ N ₆ O 272.14 (100.0%)

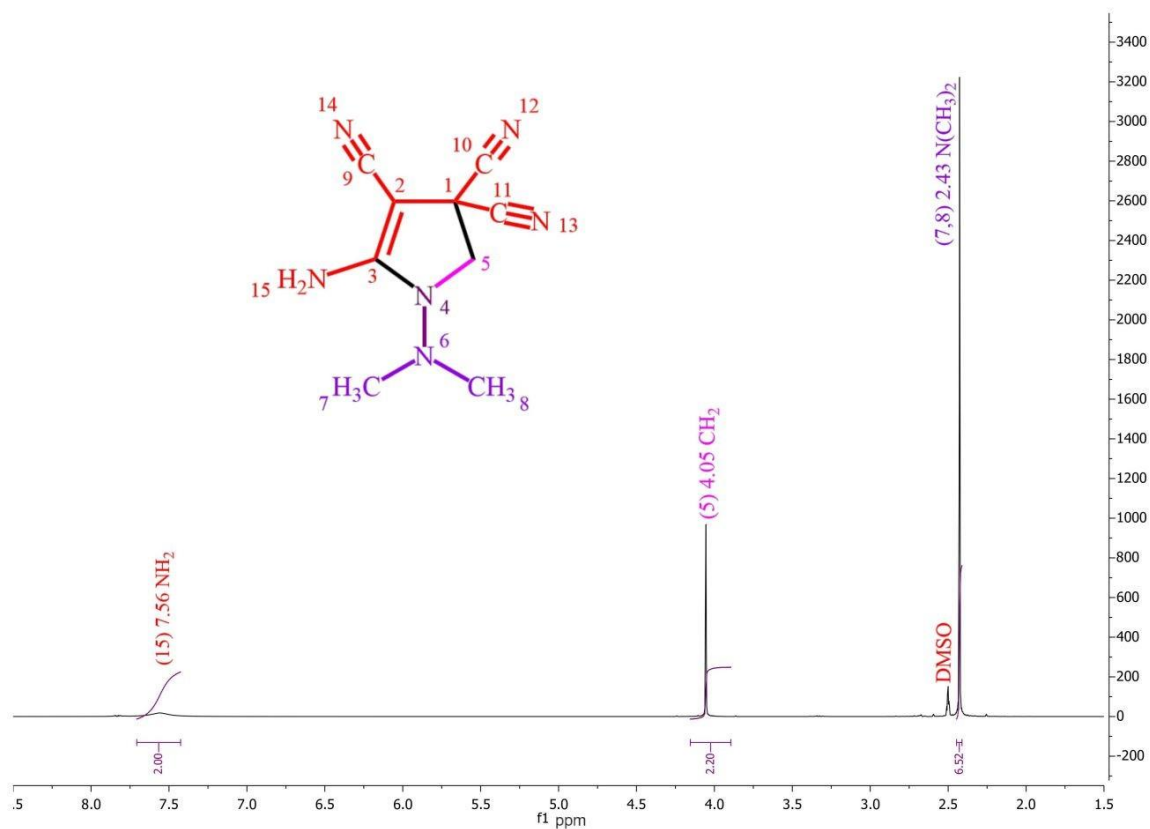


Figure S1. ¹H NMR-spectrum of **6** (500.13 MHz, DMSO-d₆, 297 K)

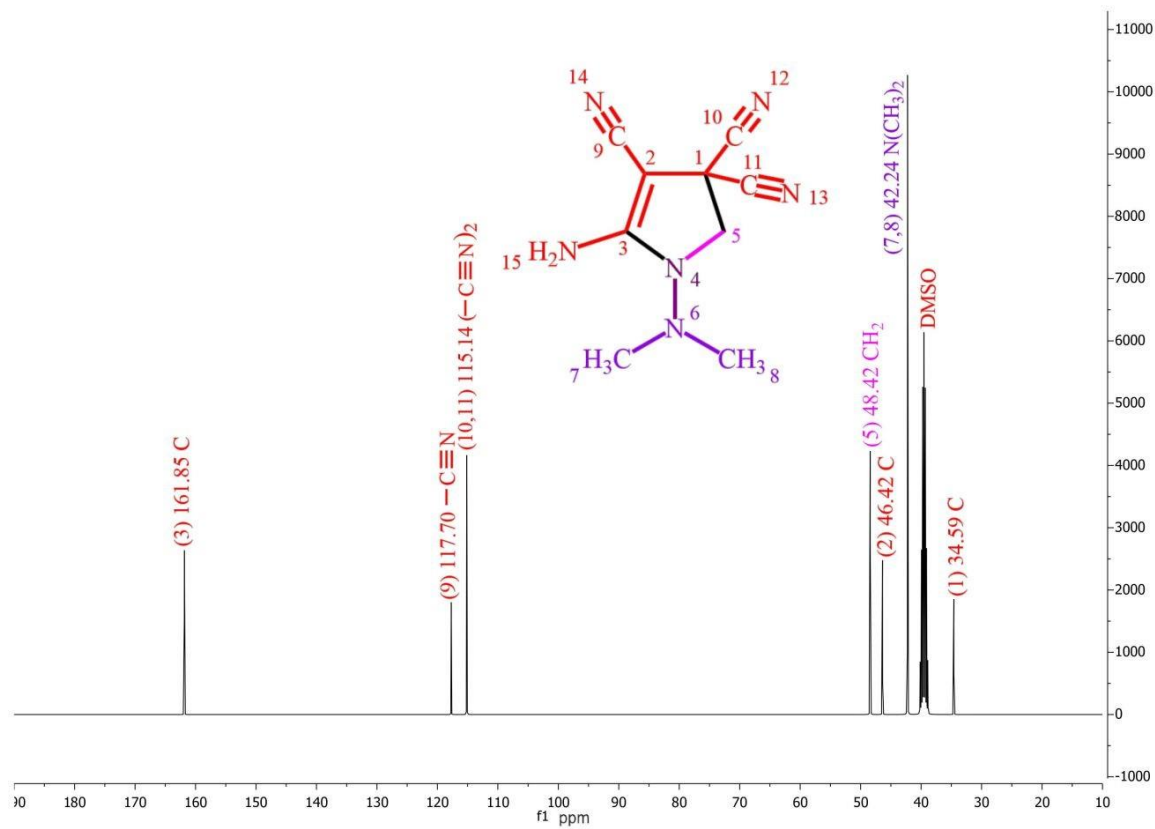


Figure S2. ¹³C NMR-spectrum of **6** (125.76 MHz, DMSO-d₆, 297 K)

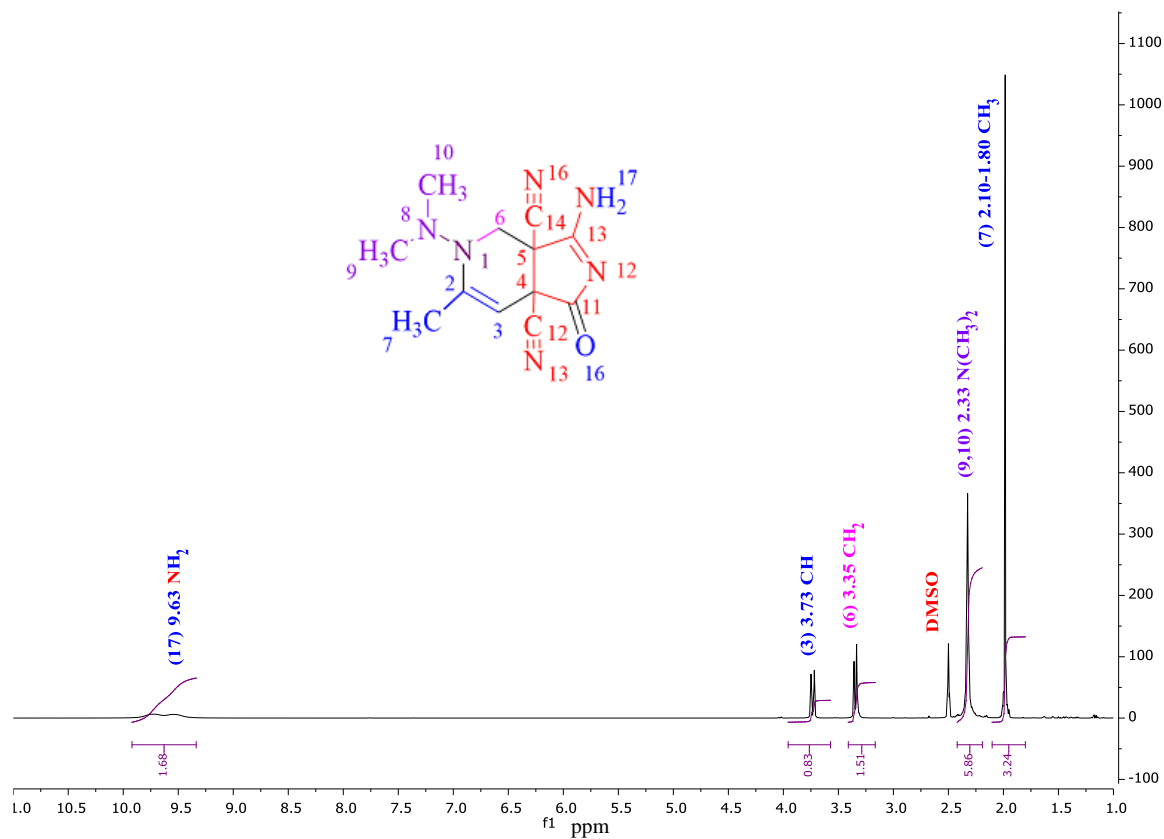


Figure S3. ¹H NMR-spectrum of **8a** (500.13 MHz, DMSO-d₆, 299 K)

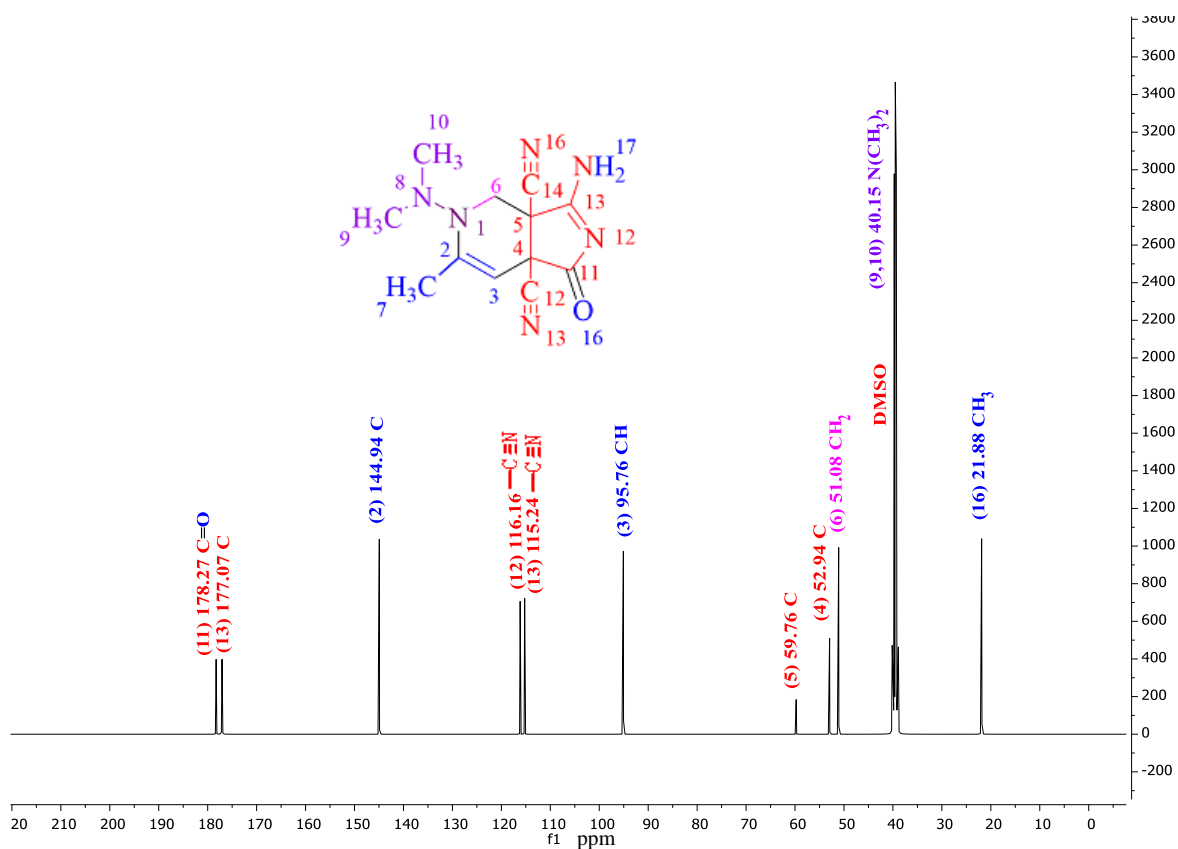
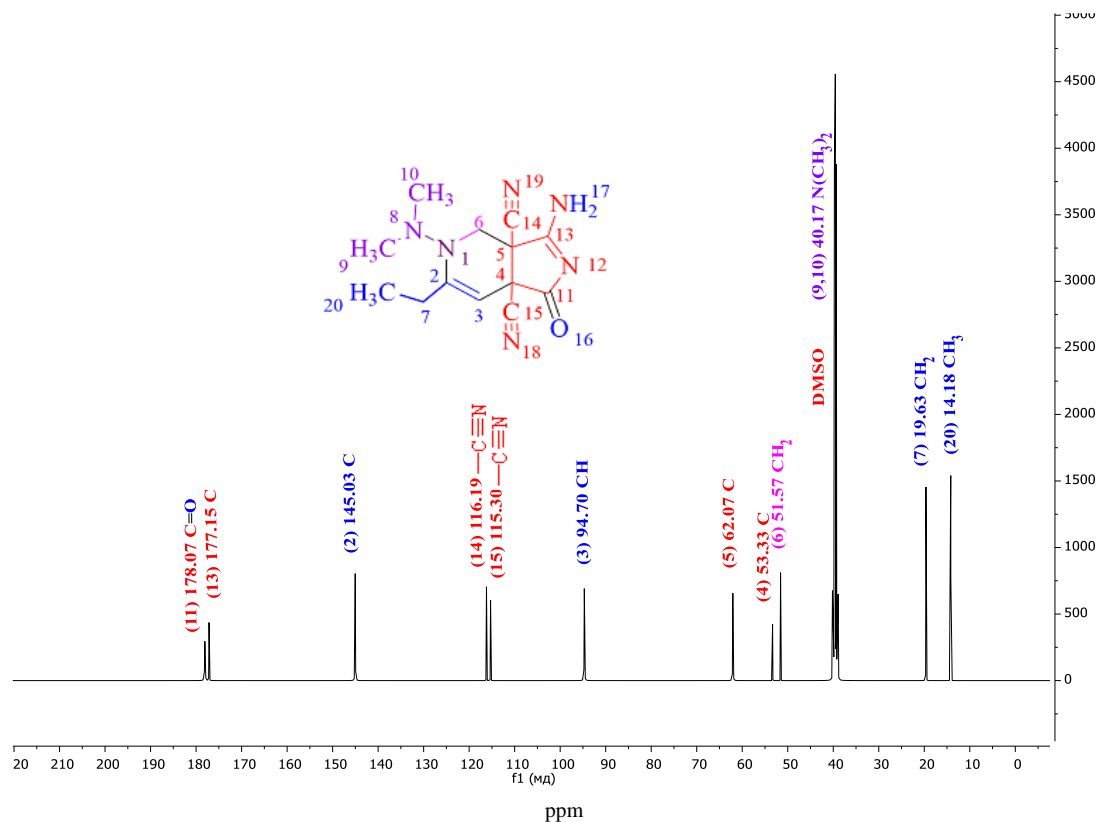
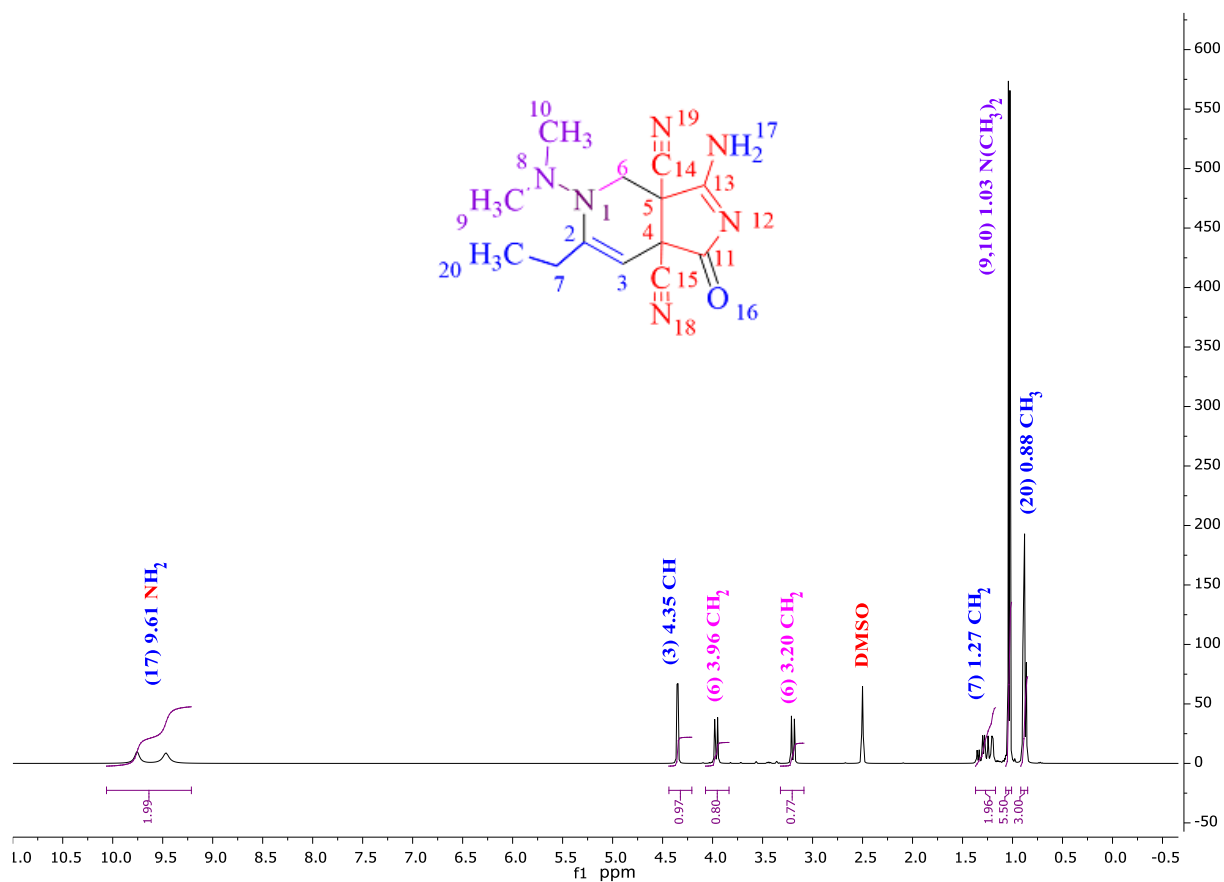


Figure S4. ¹³C NMR-spectrum of **8a** (500.13 MHz, DMSO-d₆, 299 K)



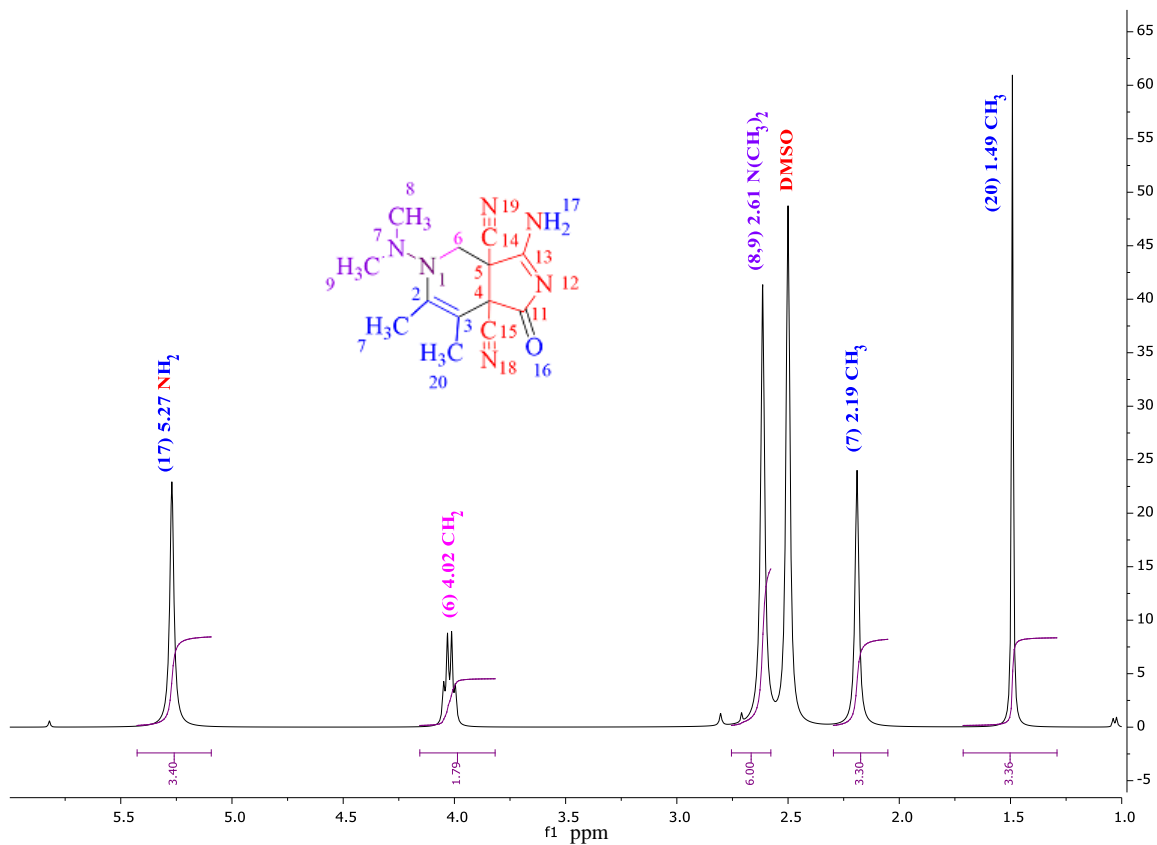


Figure S7. ^1H NMR-spectrum of **8c** (500.13 MHz, DMSO- d_6 , 299 K)

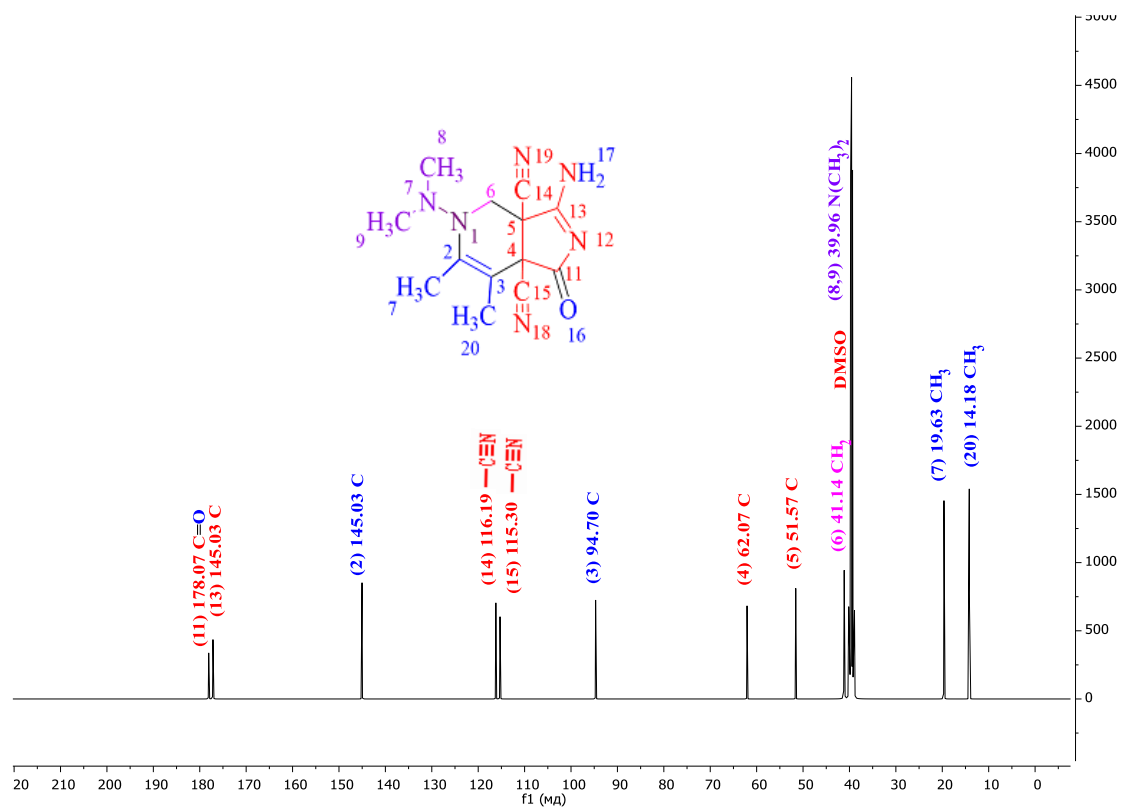


Figure S8. ^{13}C NMR-spectrum of **8c** (125.76 MHz, DMSO- d_6 , 299 K)

References

- S1.** Y. Kamitori, M. Hojo, R. Masuda, T. Fujitani, S. Ohara and T. Yokohama, *J. Org. Chem.*, 1988, **53**, 129.
- S2.** F. Micheli, A. Pasquarello, G. Tedesco, D. Hamprecht, G. Bonanomi, A. Checchia, A. Jaxa-Chamiec, F. Damiani, S. Davalli, D. Donati, C. Gallotti, M. Petrone, M. Rinaldi, G. Riley, S. Terreni and M. Wood, *Bioorg. Med. Chem. Lett.*, 2006, **16**, 3906.
- S3.** O. E. Nasakin, E. S. Ivanova, M. A. Maryasov, V. V. Andreeva, O. A. Lodochnikova and D. U. Grishaev, 2022, *Soc. Sci. Res. Network*, 2022, DOI:[10.2139/ssrn.4272817](https://doi.org/10.2139/ssrn.4272817).