Supporting Information

Synthesis, structure and biological activity of 3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazides

Natal'ya V. Gorodnicheva[1], Olga S. Vasil'eva[1], Evgeny S. Ostroglyadov[1], Ruslan I. Baichurin[1], Alina V. Fel'gendler[2], Igor A. Litvinov[3], Sergey V. Makarenko[1*], Dmitry A. Bakulin[4], Nikita S. Bolokhov[4], Vladislav E. Pustynnikov[4], Ivan N. Tyurenkov[4]

[1] *Herzen State Pedagogical University of Russia,*
48 Moyka River Embankment, Saint Petersburg 191186, Russia; e-mail: kohrgpu@yandex.ru
[2] *Kirov Military Medical Academy,*
6 Akademika Lebedeva St., Saint Petersburg 194044, Russia
[3] *Federal Research Center "Kazan Scientific Center of the Russian Academy of Sciences", Arbuzov Institute of Organic and Physical Chemistry,*
8 Akademika Arbuzova St., Kazan 420088, Russia; e-mail: litvinov@iopc.ru
[4] *Volgograd State Medical University,*
1 Pavshikh Bortsov Sq., Volgograd 400131, Russia; e-mail: fibfuv@mail.ru

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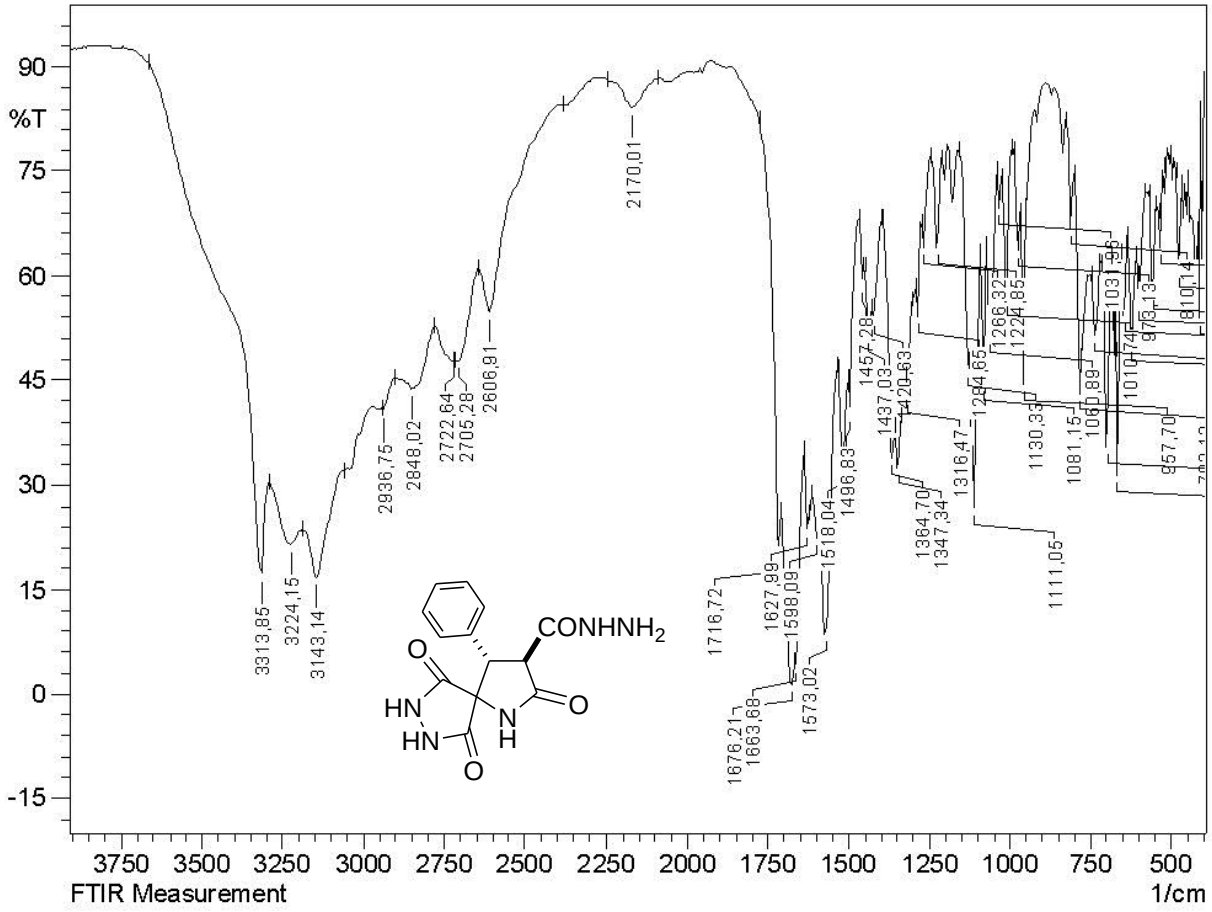

Fig. 1. IR spectrum of (*3′S*,4′R**)-3′-phenyl-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2a)** in KBr.

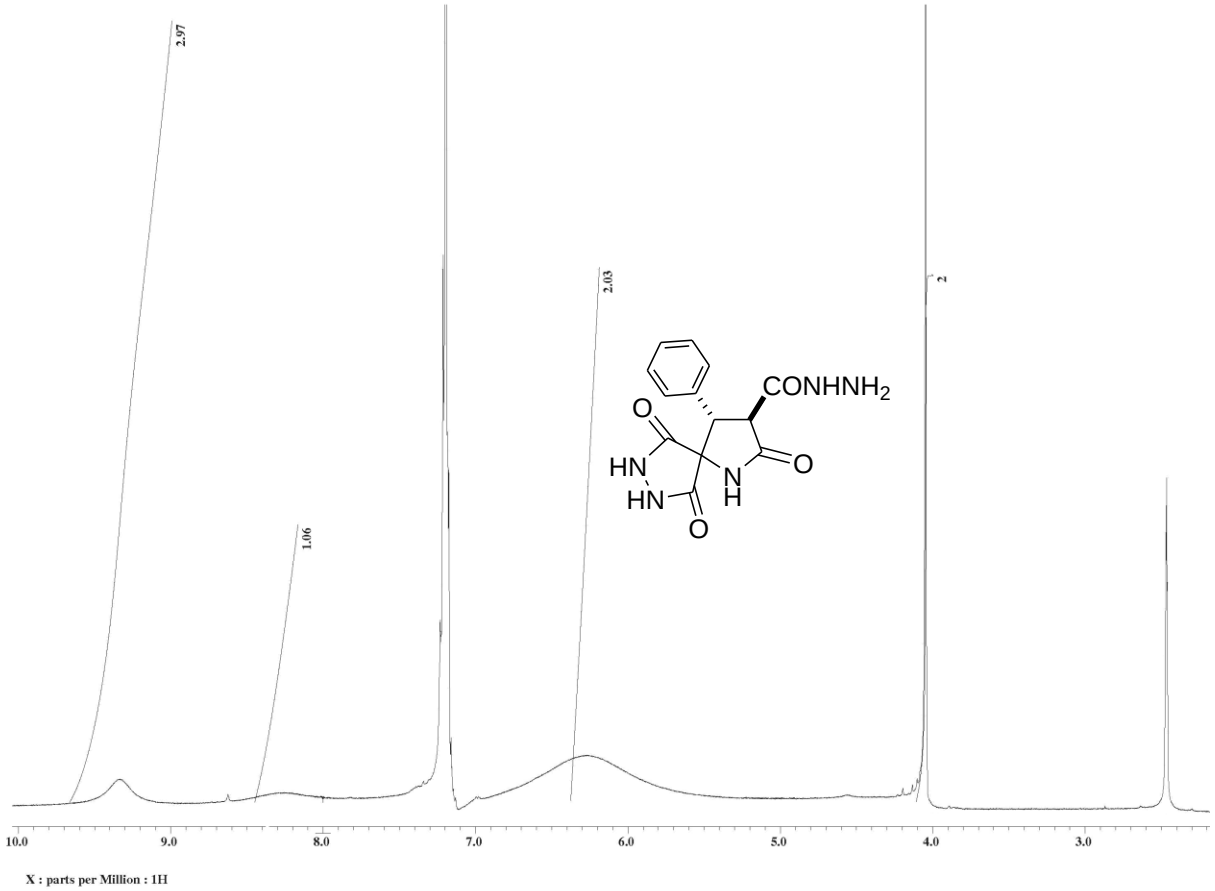

Fig. 2. ^{1}H NMR spectrum of (*3′S**,*4′R**)-3′-phenyl-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2a)** in DMSO-d_6.

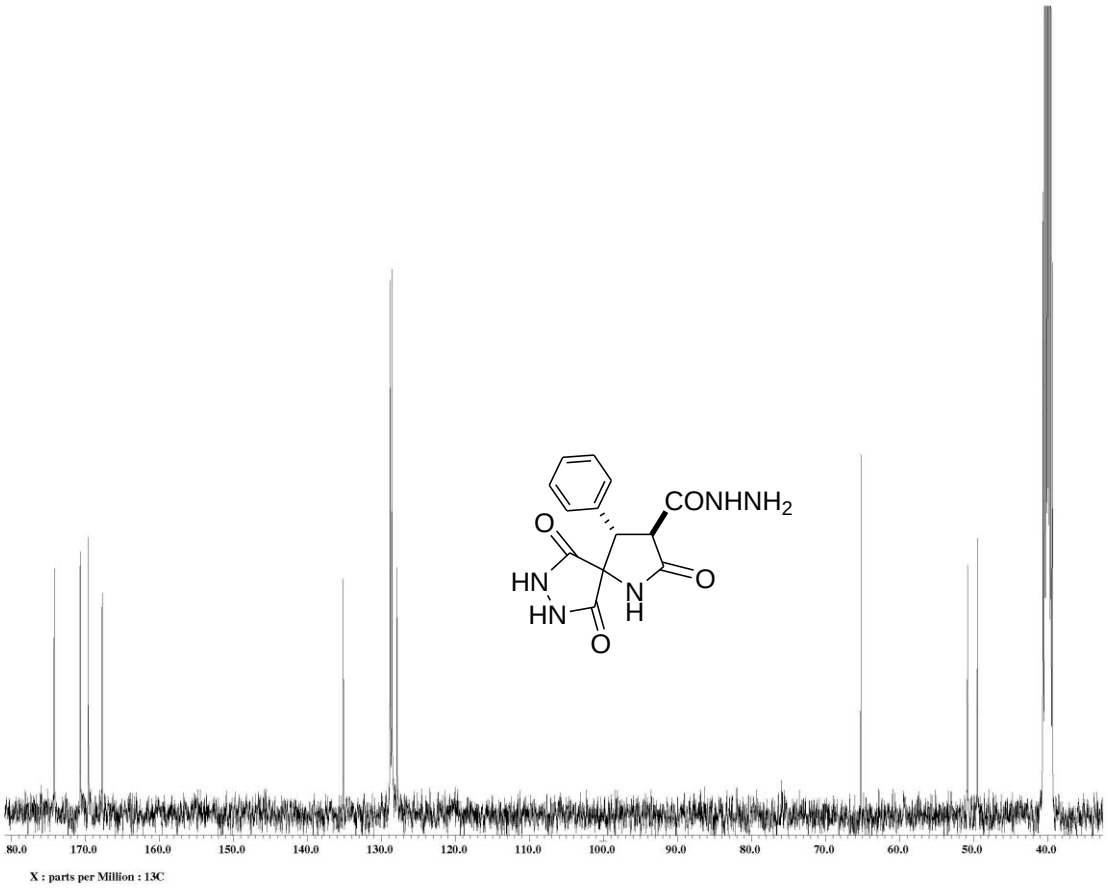

Fig. 3. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′S*,4′R**)-3′-phenylspyro-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2a)** in DMSO-d_6.

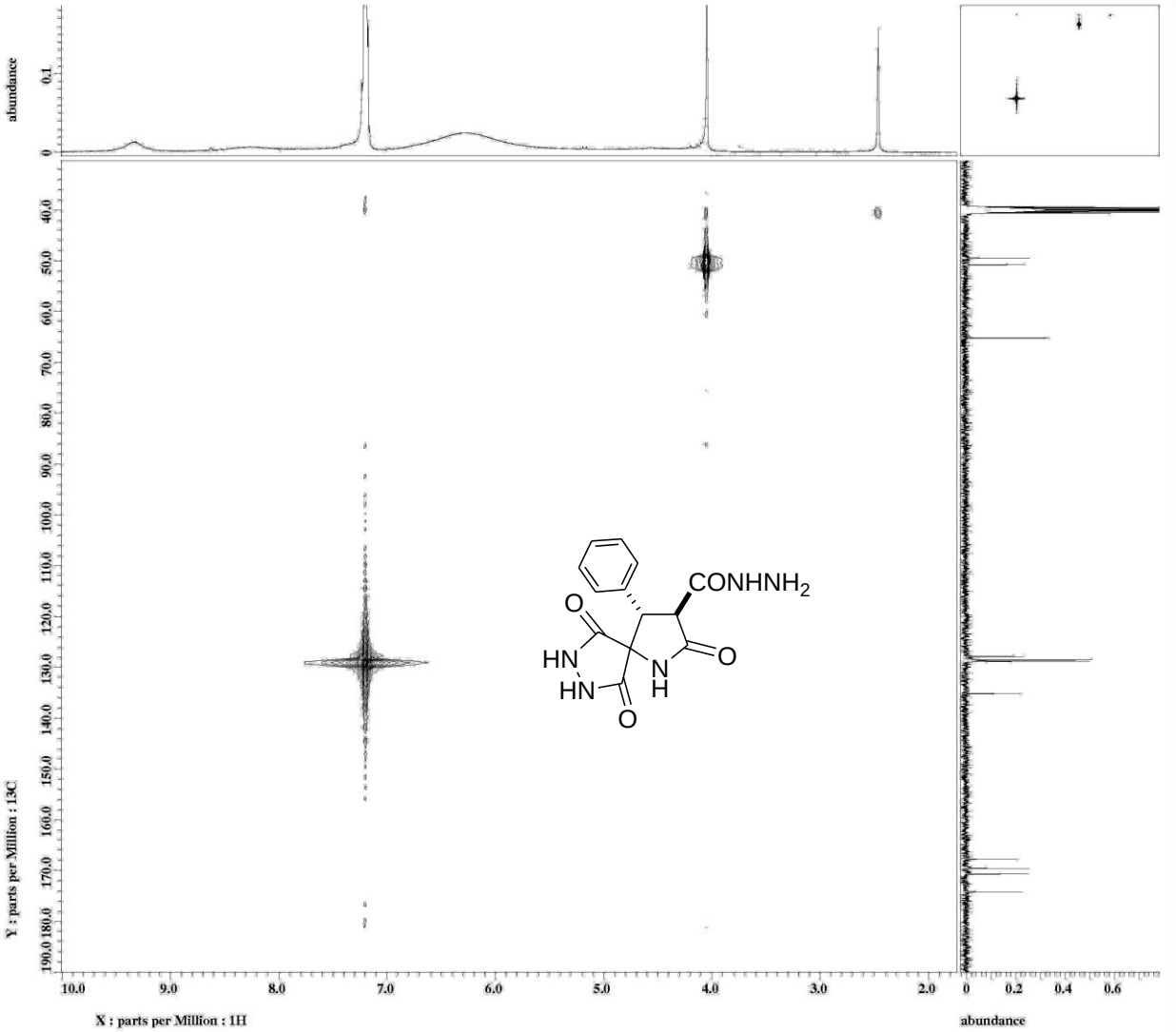

Fig. 4. ^{1}H-^{13}C HMQC spectrum of (*3′S*,4′R**)-3′-phenyl-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2a)** in DMSO-d_6.

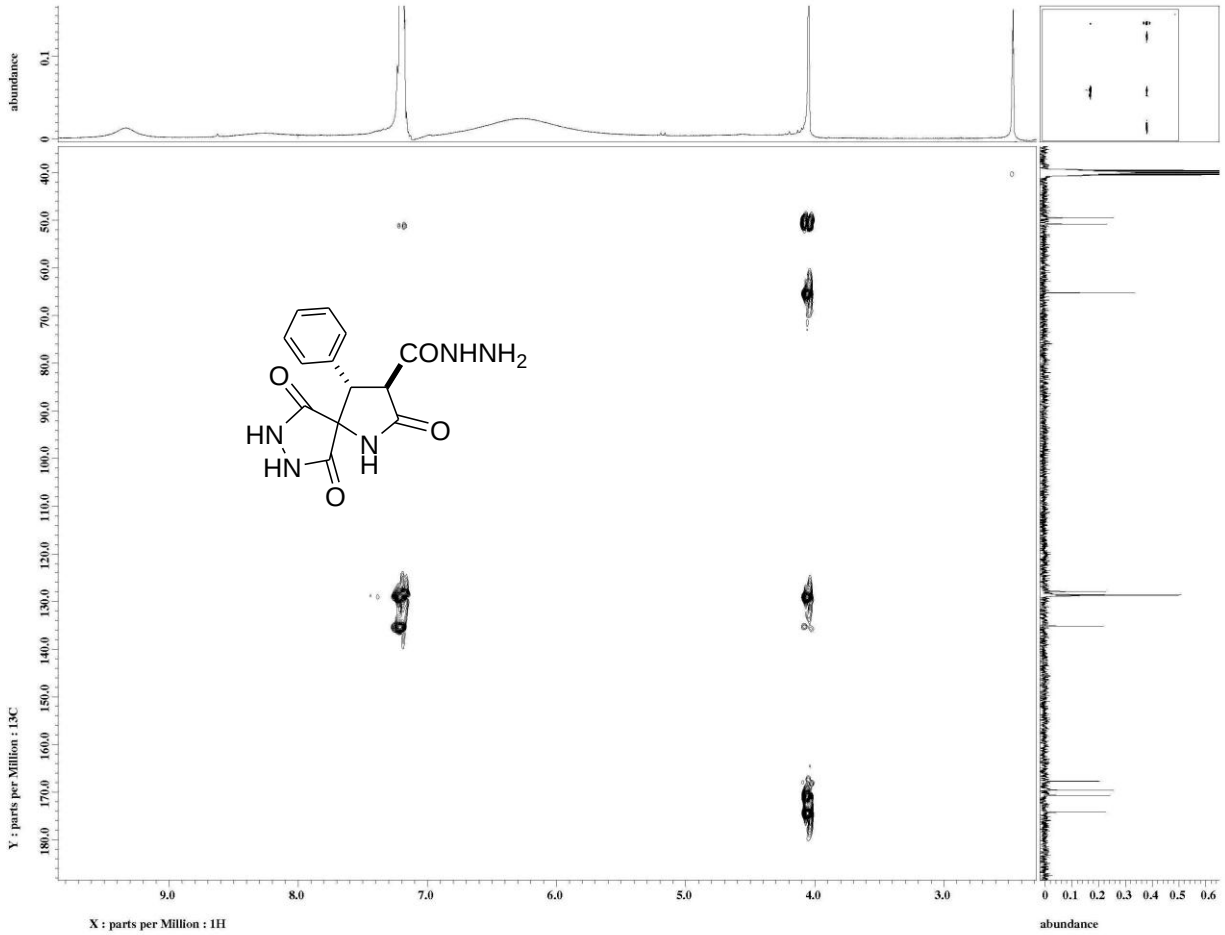

Fig. 5. ^{1}H-^{13}C HMBC spectrum of (*3′S**,*4′R**)-3′-phenyl-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2a)** in DMSO-d_6.

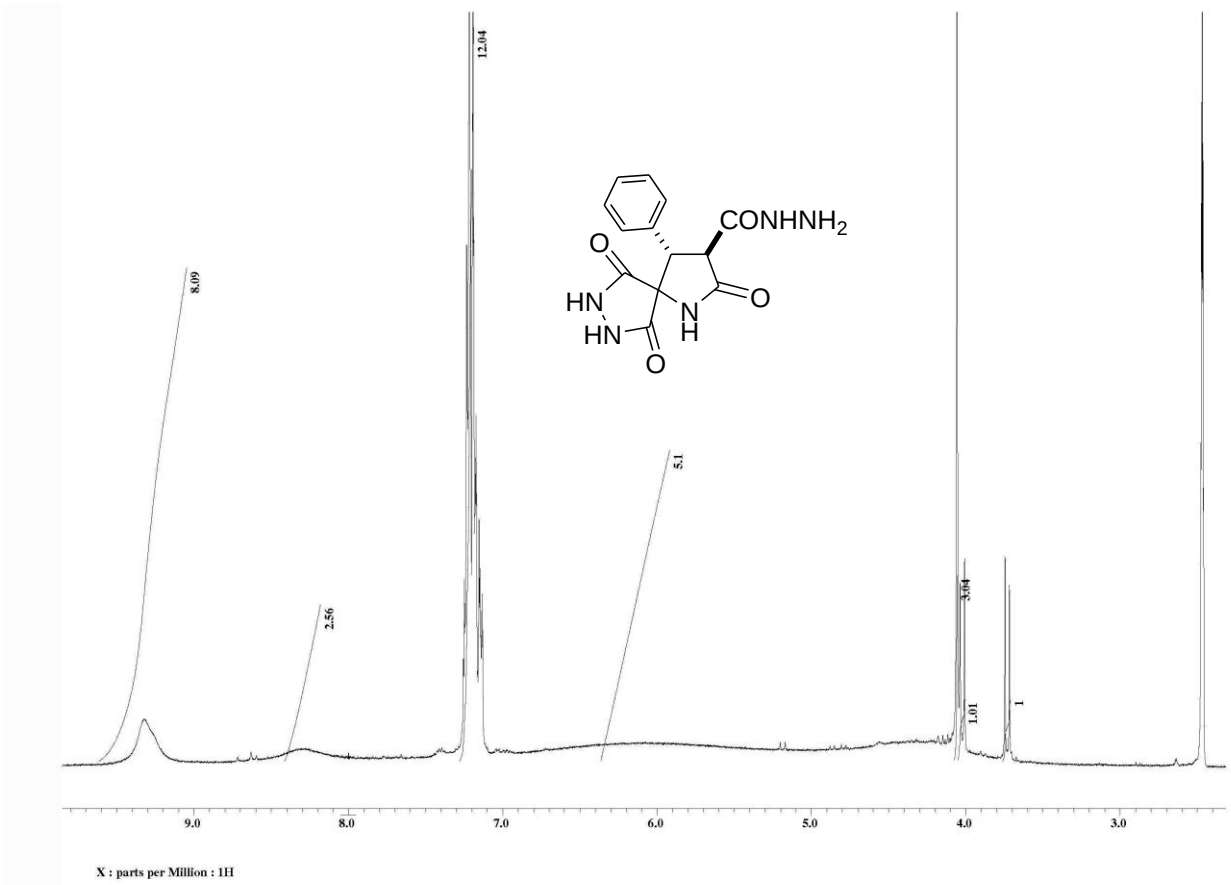

Fig. 6. ^{1}H NMR spectrum of (*3′S**,*4′R**)-3′-phenyl-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2a)** in DMSO-d_6.(exposition 72 h).

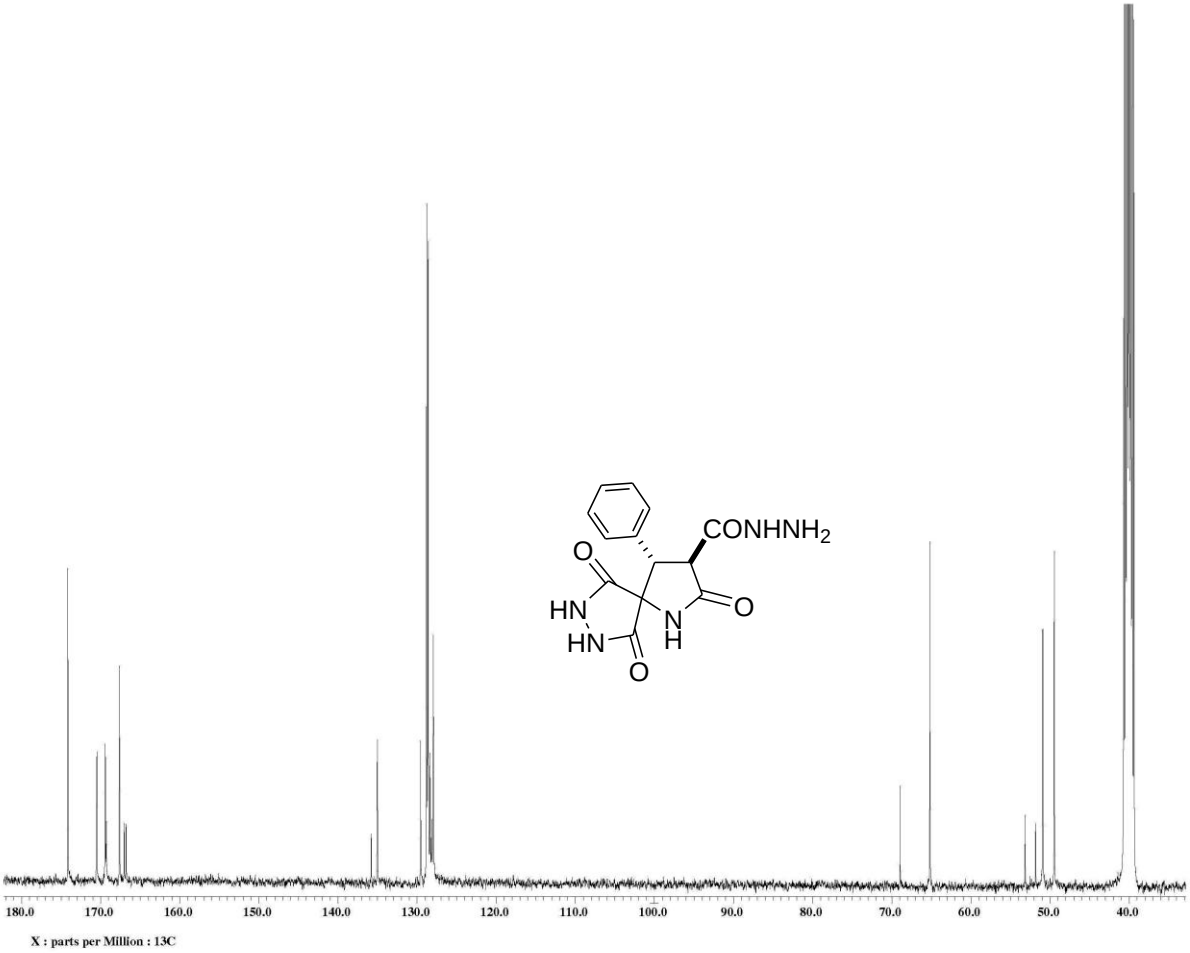

Fig. 7. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′S*,4′R**)-3′-phenyl-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2a)** in DMSO-d_6 (exposition 72 h).

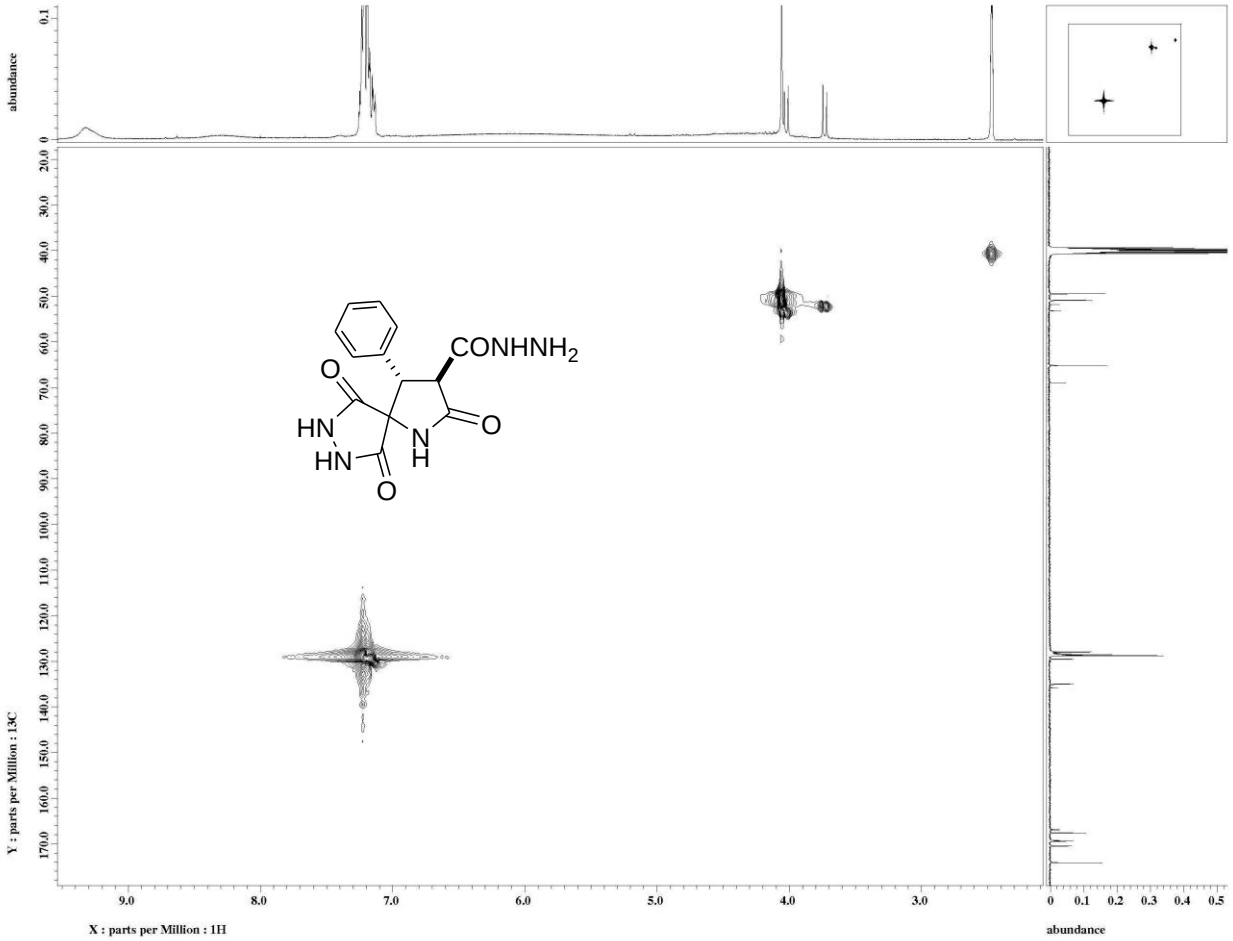

Fig. 8. ^{1}H-^{13}C HMQC spectrum of (*3′S*,4′R**)-3′-phenyl-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2a)** in DMSO-d_6 (exposition 72 h).

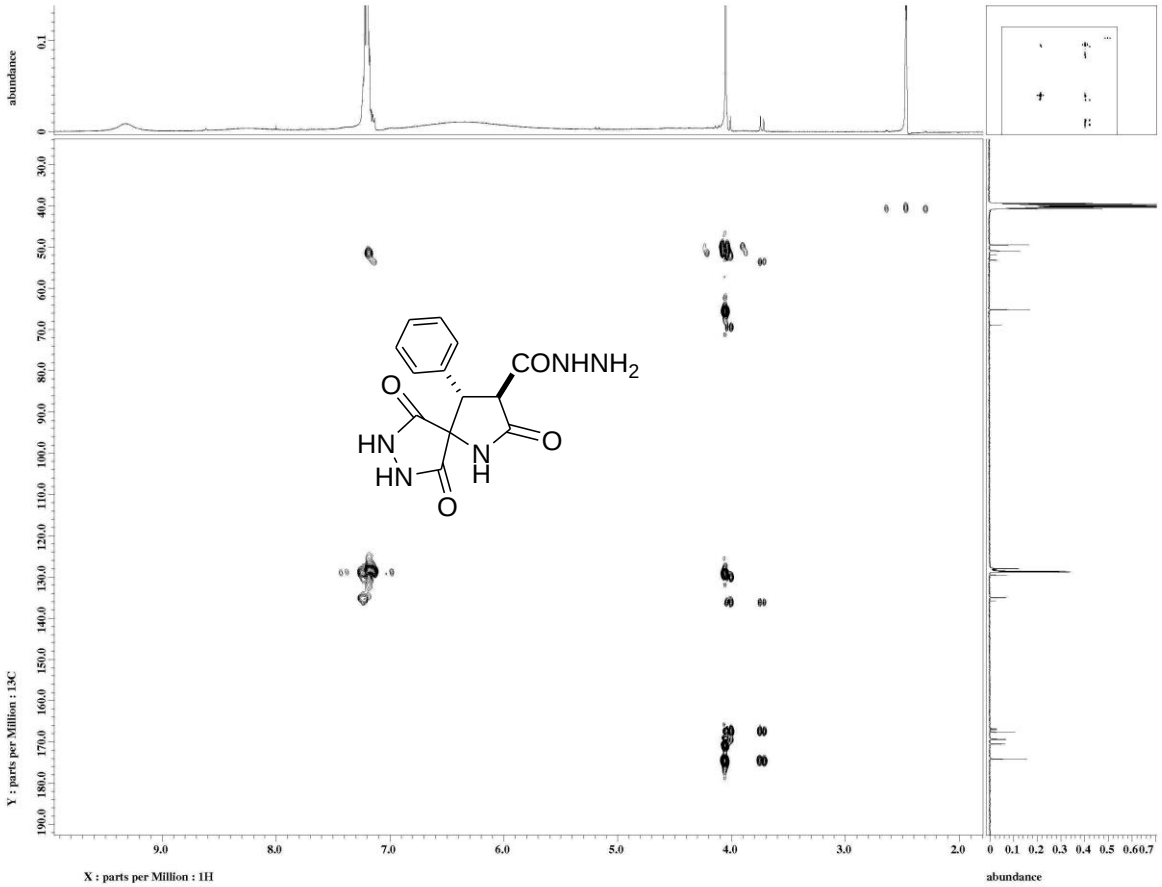

Fig. 9. ^{1}H-^{13}C HMBC spectrum of (*3′S*,4′R**)-3′-phenyl-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2a)** in DMSO-d_6 (exposition 72 h).

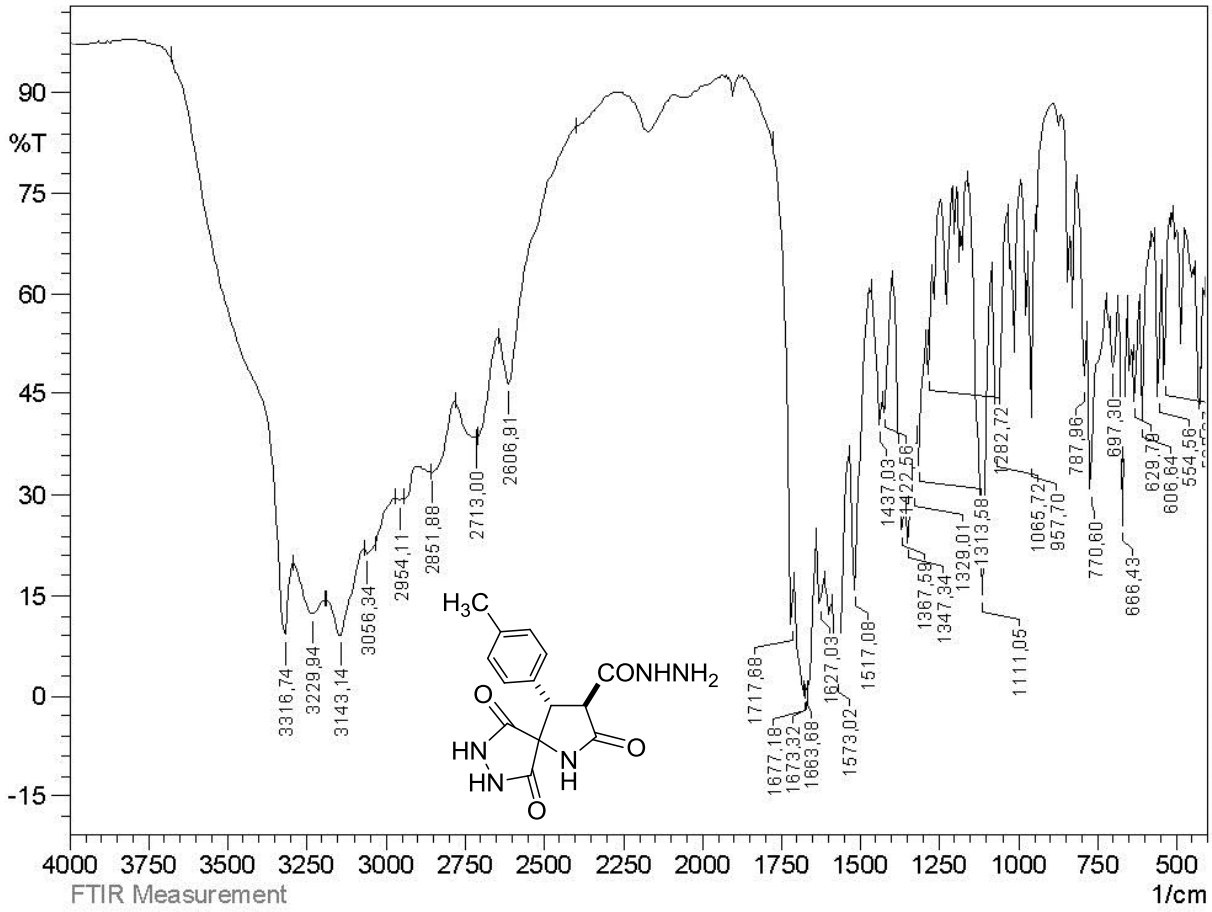

Fig. 10. IR spectrum of (*3′S*,4′R**)-3′-(4-methylphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2b)** in KBr.

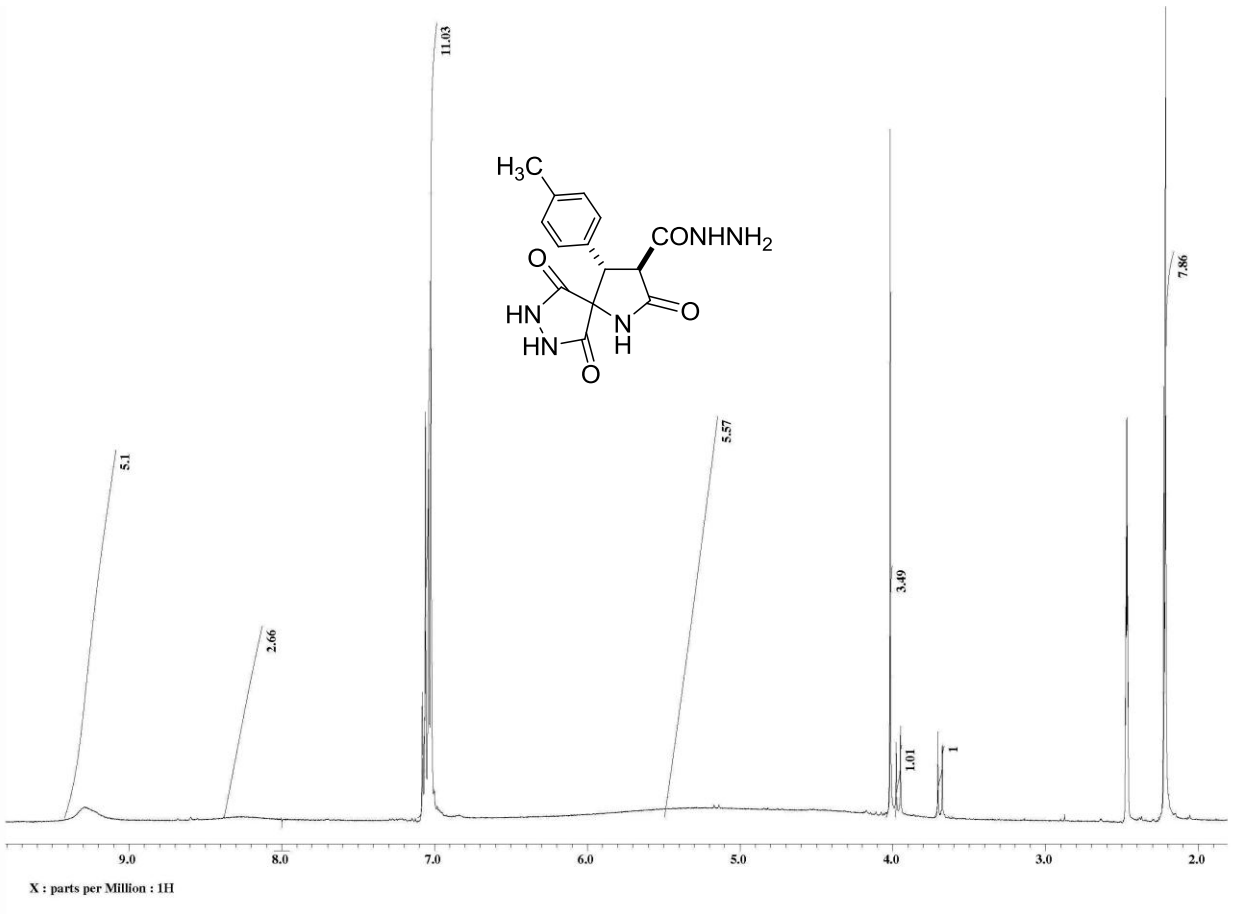

Fig. 11. ^{1}H NMR spectrum of (*3′S*,4′R**)-3′-(4-methylphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2b)** in DMSO-d_6.

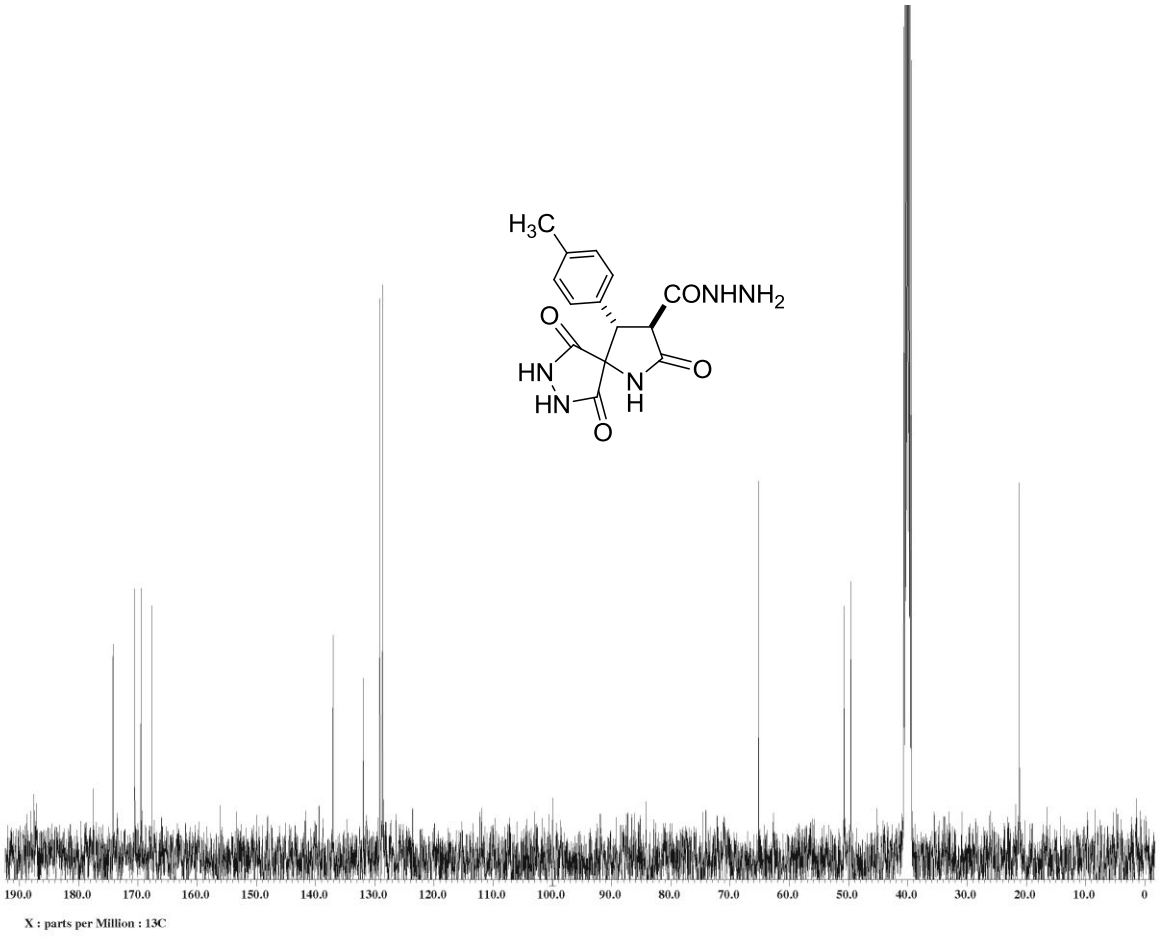

Fig. 12. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′S*,4′R**)-3′-(4-methylphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2b)** in DMSO-d_6.

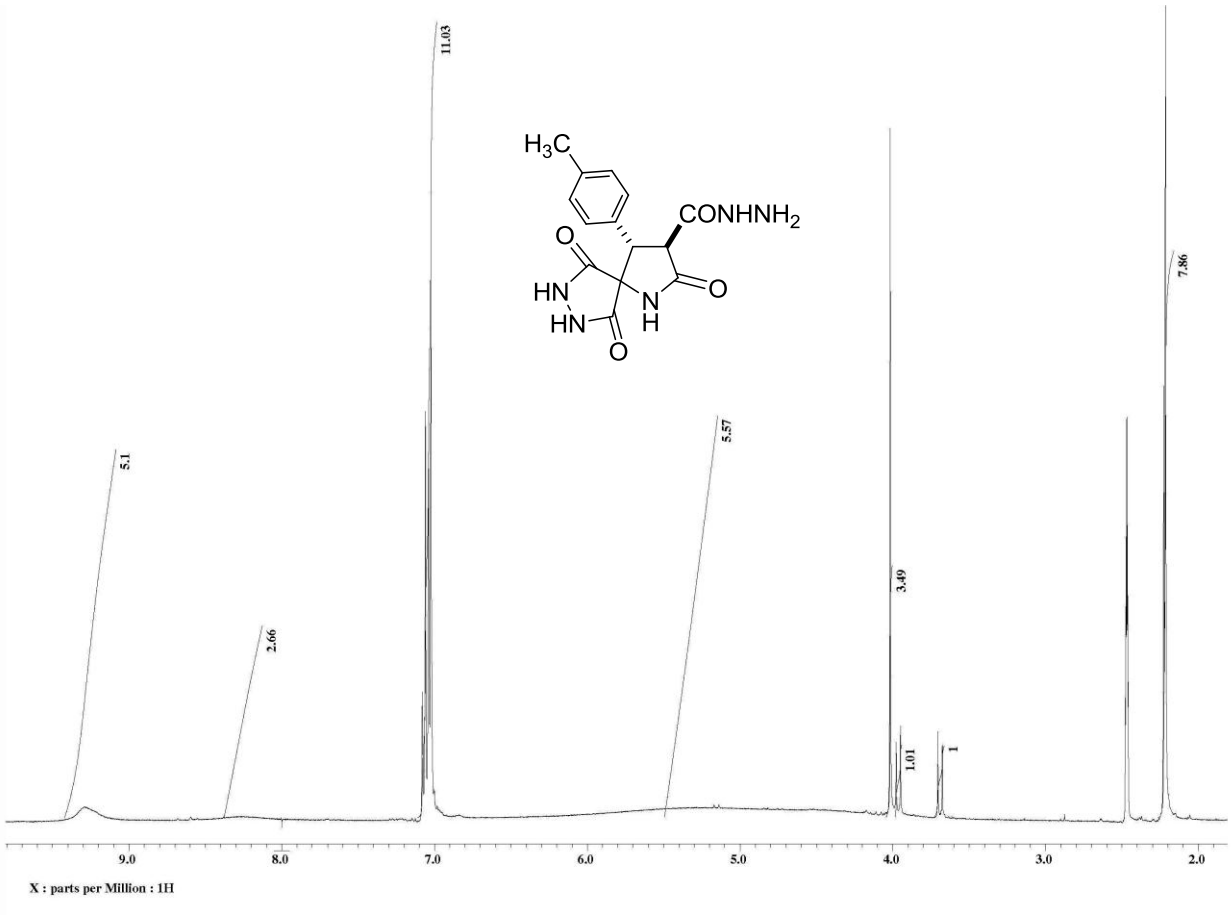

Fig. 13. ^{1}H NMR spectrum of (*3′S*,4′R**)-3′-(4-methylphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2b)** in DMSO-d_6 (exposition 72 h).

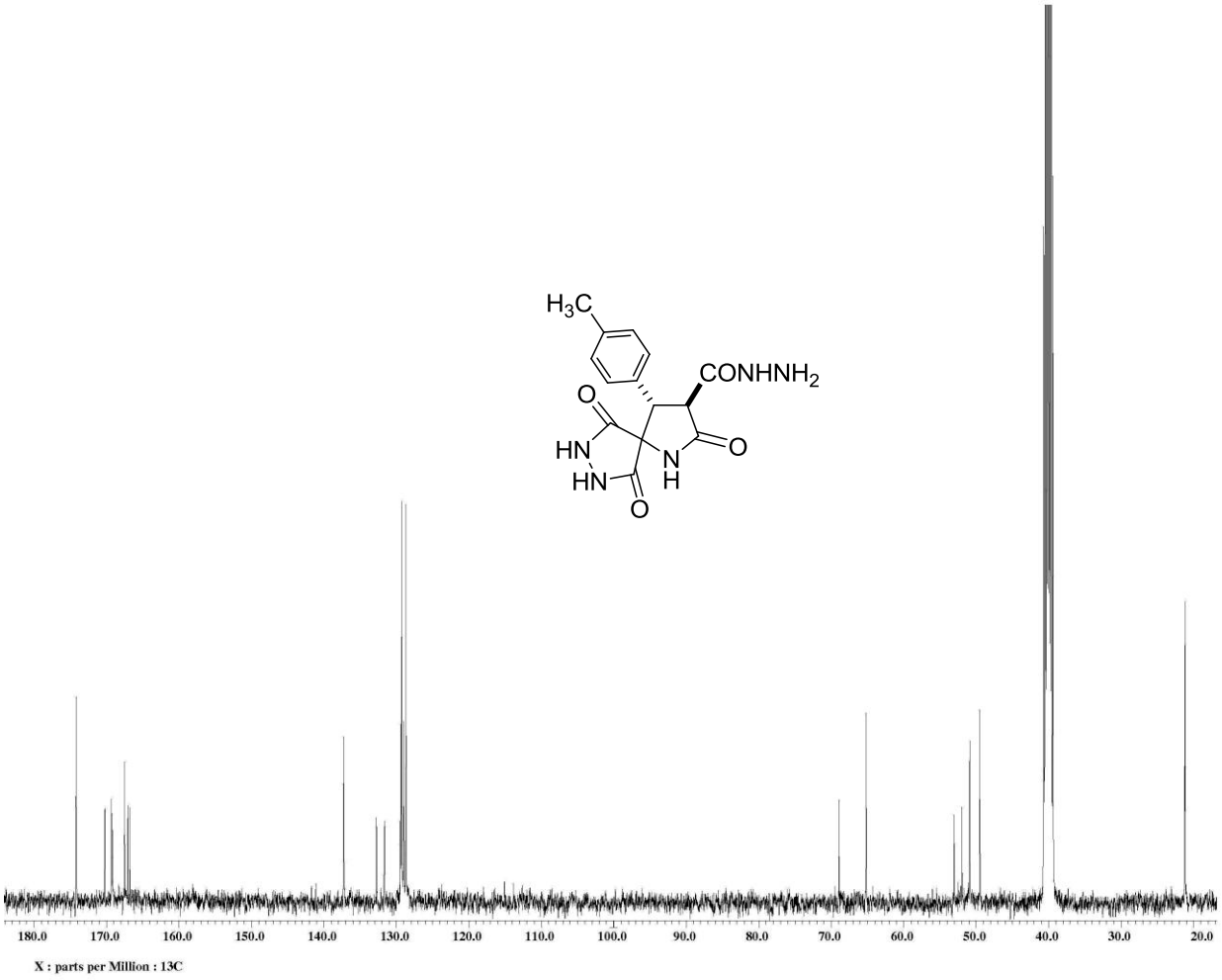

Fig. 14. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′S*,4′R**)-3′-(4-methylphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2b)** in DMSO-d_6 (exposition 72 h).

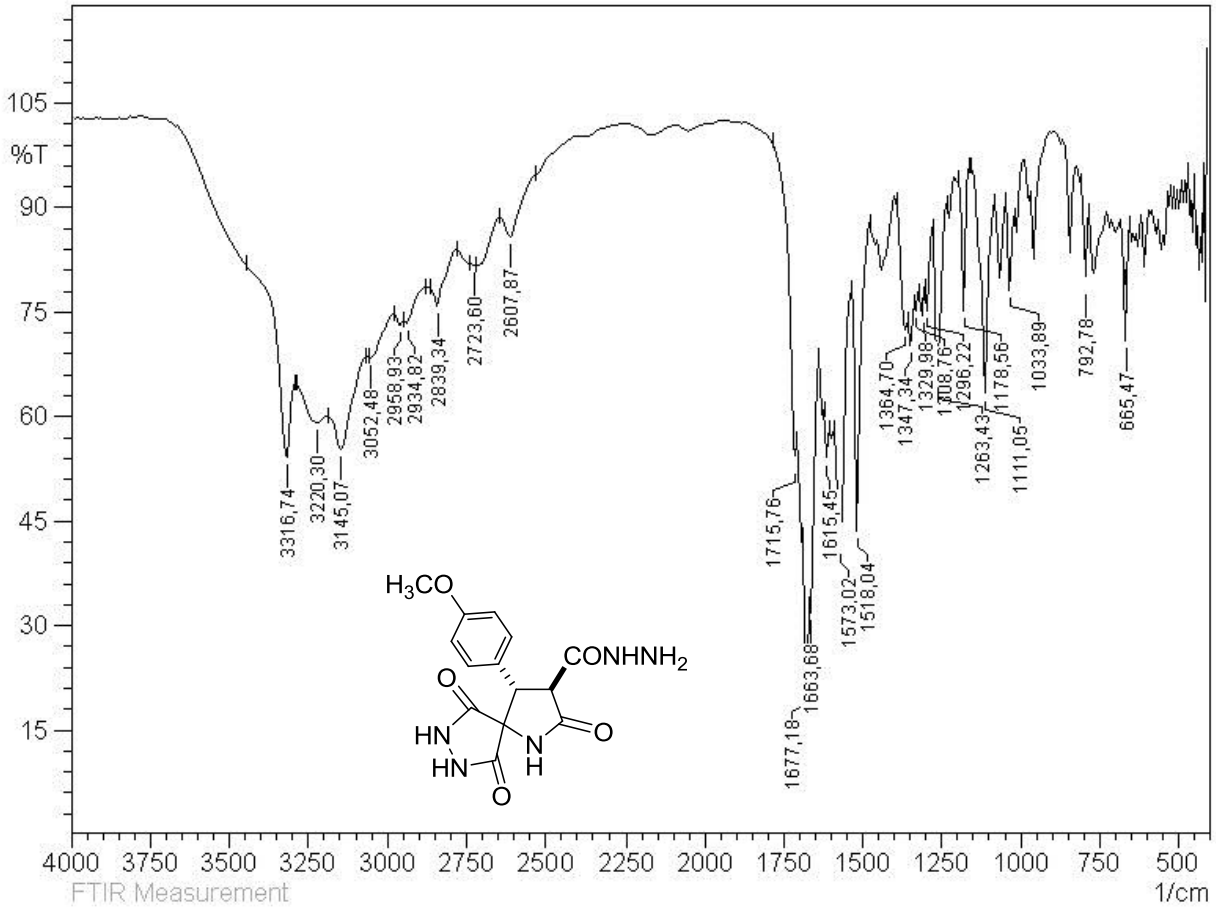

Fig. 15. IR spectrum of (*3′S**,*4′R**)-3′-(4-methoxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2c)** in KBr.

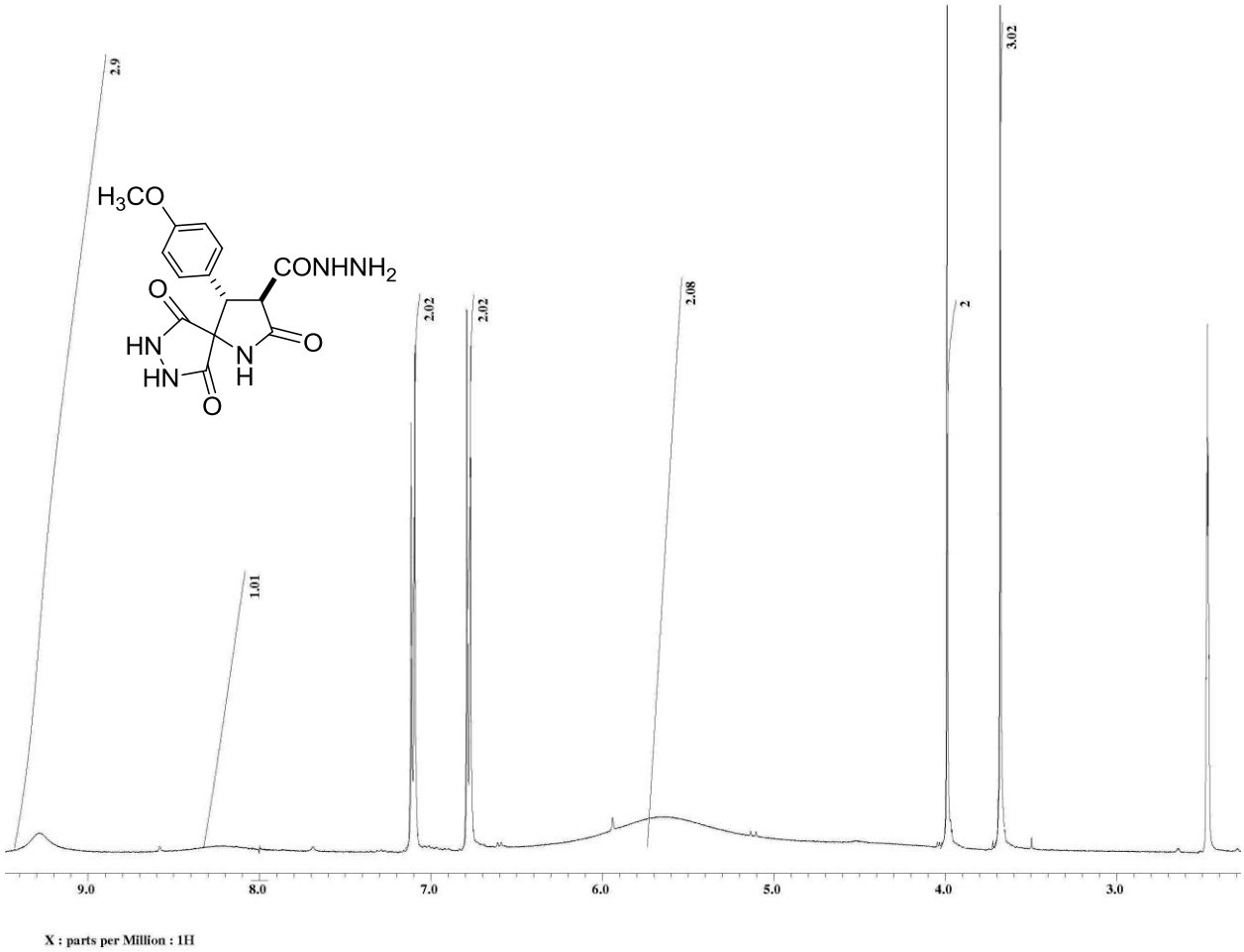

Fig. 16. ^{1}H NMR spectrum of (*3′S*,4′R**)-3′-(4-methoxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2c)** in DMSO-d_6.

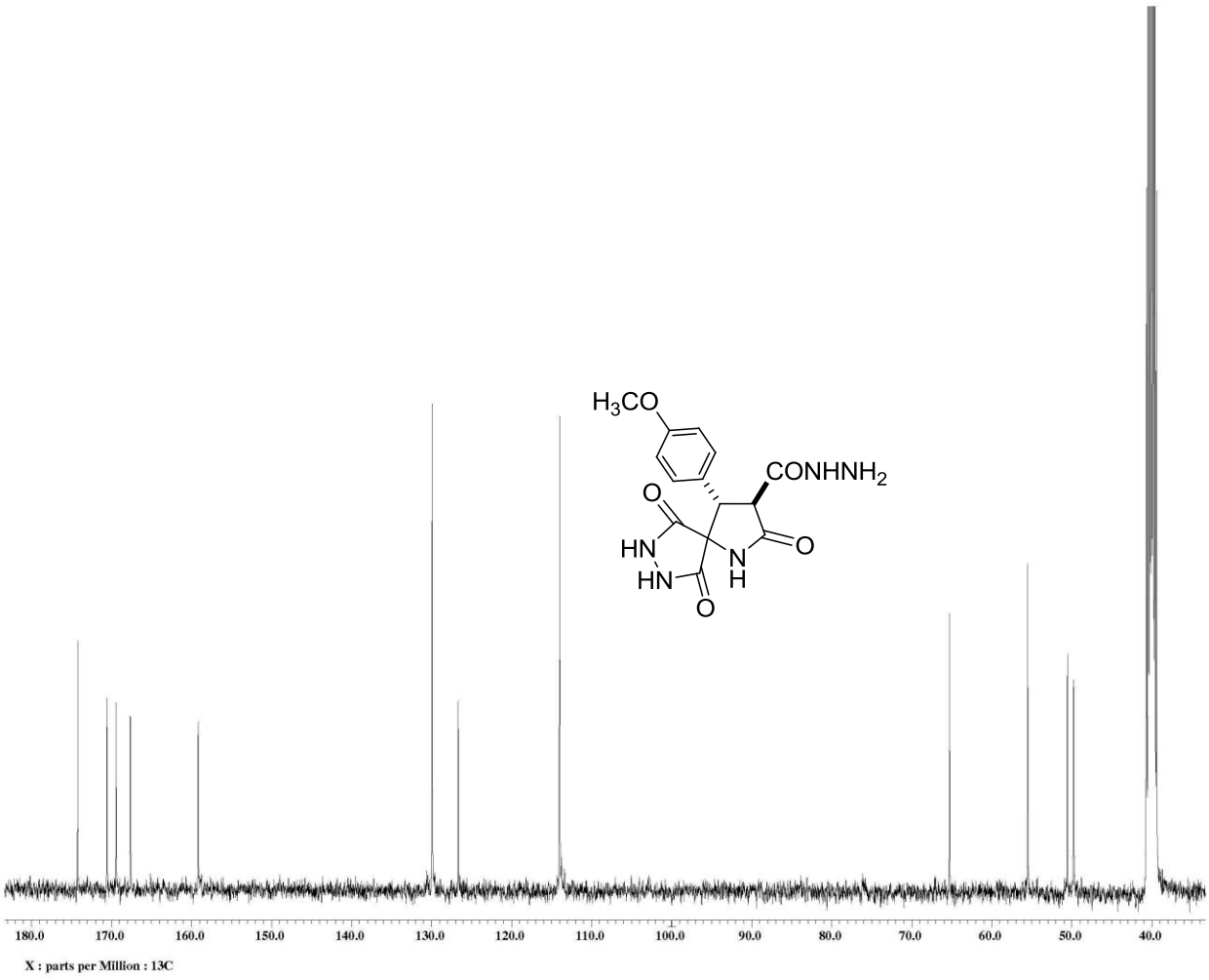

Fig. 17. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′S*,4′R**)-3′-(4-methoxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2c)** in DMSO-d_6.

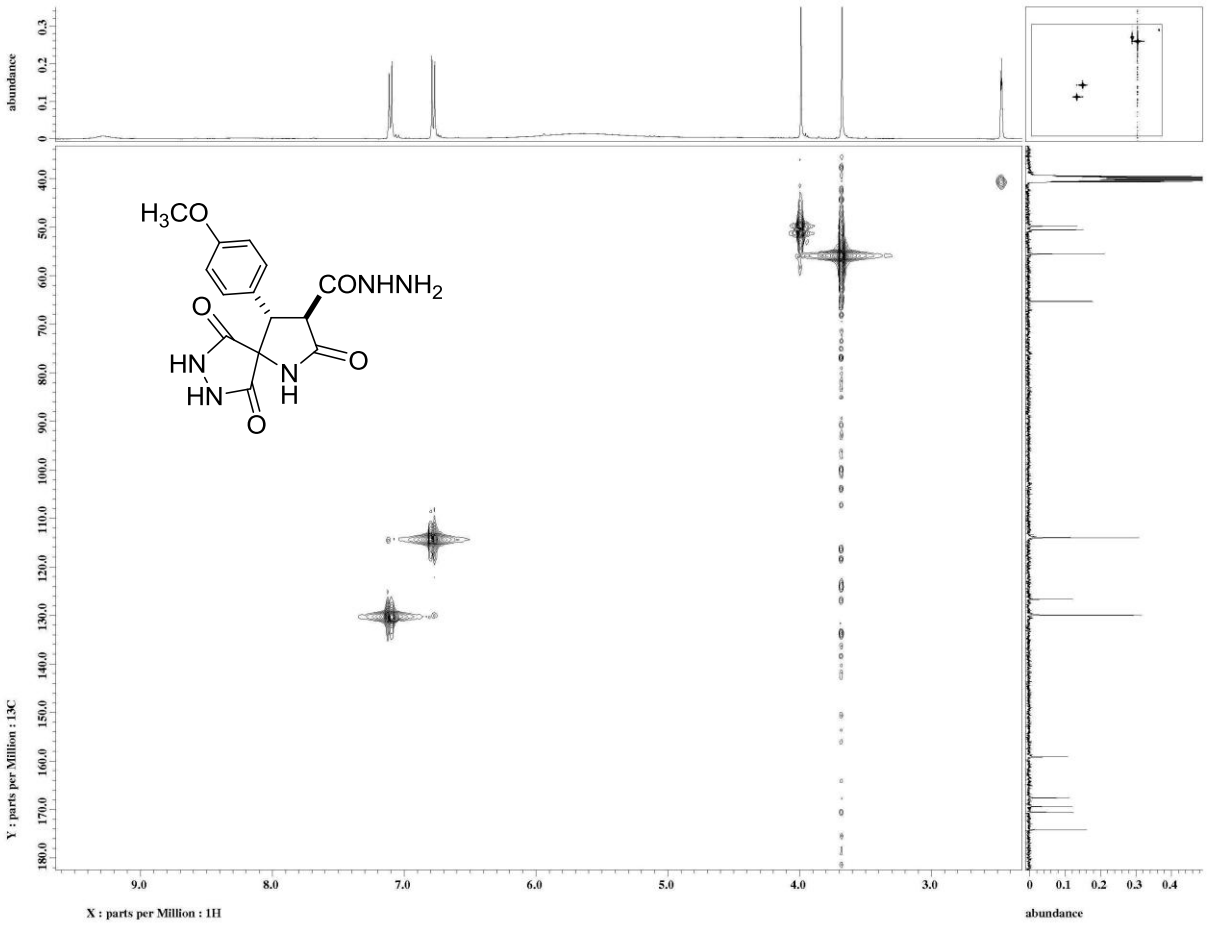

Fig. 18. ^{1}H-^{13}C HMQC spectrum of (*3′S*,4′R**)-3′-(4-methoxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2c)** in DMSO-d_6.

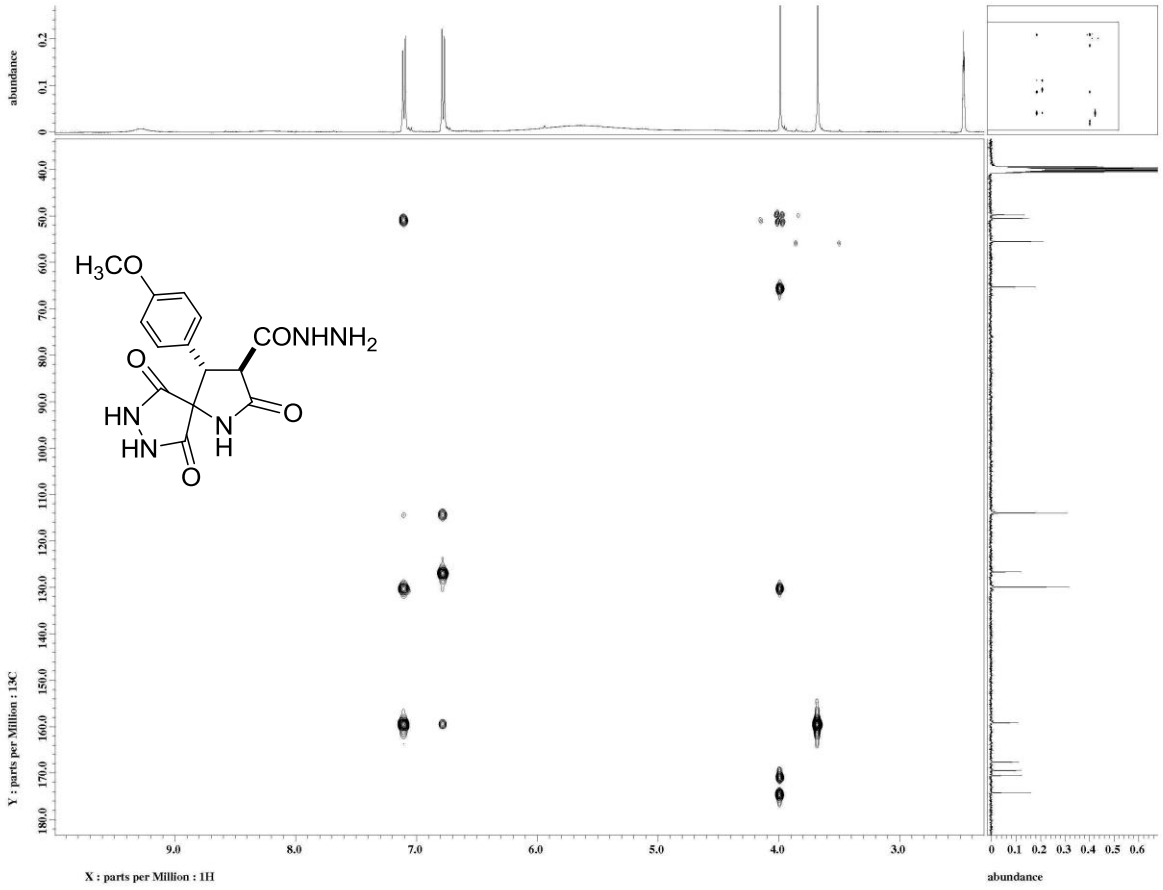

Fig. 19. ^{1}H-^{13}C HMBC spectrum of (*3′S*,4′R**)-3′-(4-methoxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2c)** in DMSO-d_6.

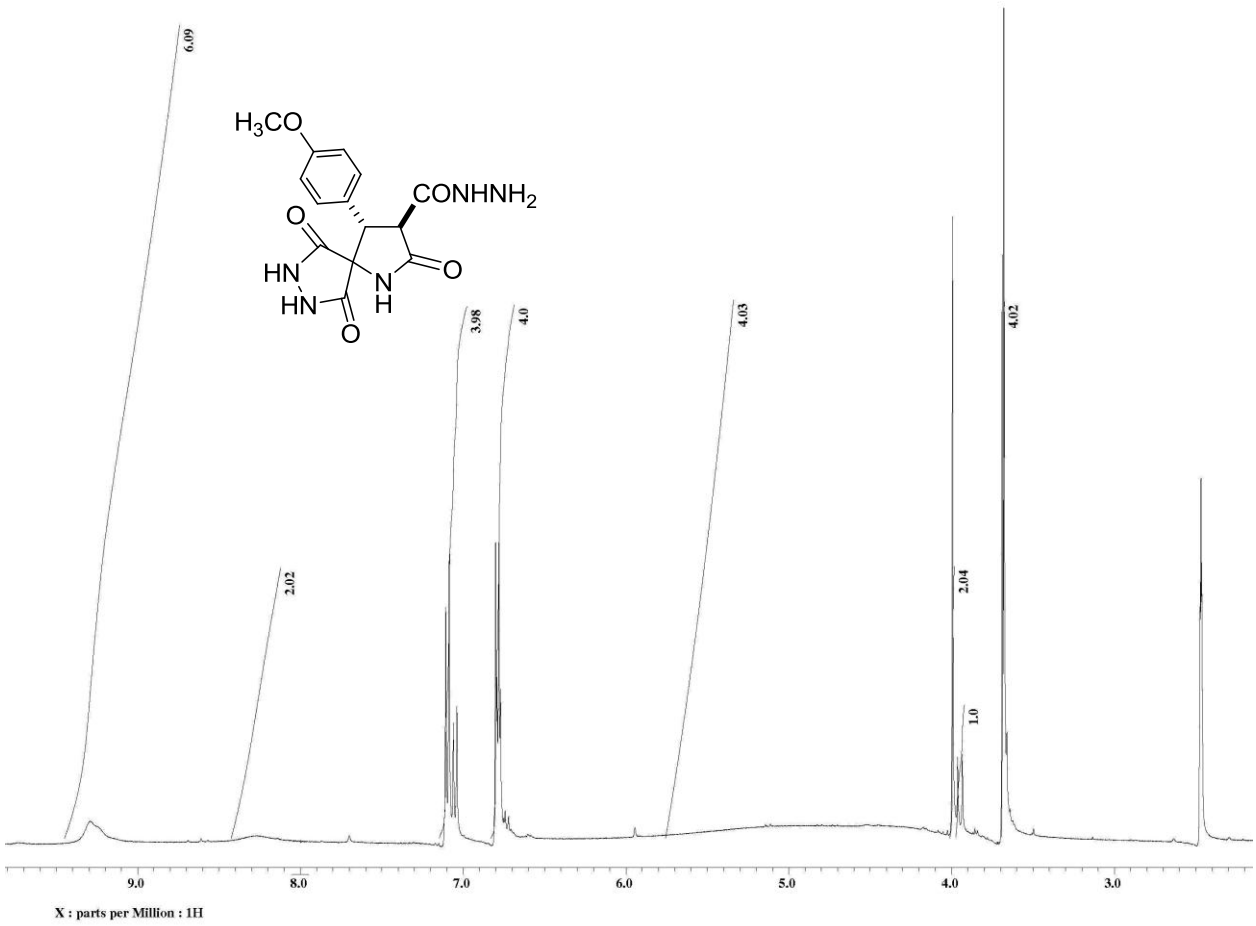

Fig. 20. ^{1}H NMR spectrum of (*3′S*,4′R**)-3′-(4-methoxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2c)** in DMSO-d_6 (exposition 72 h).

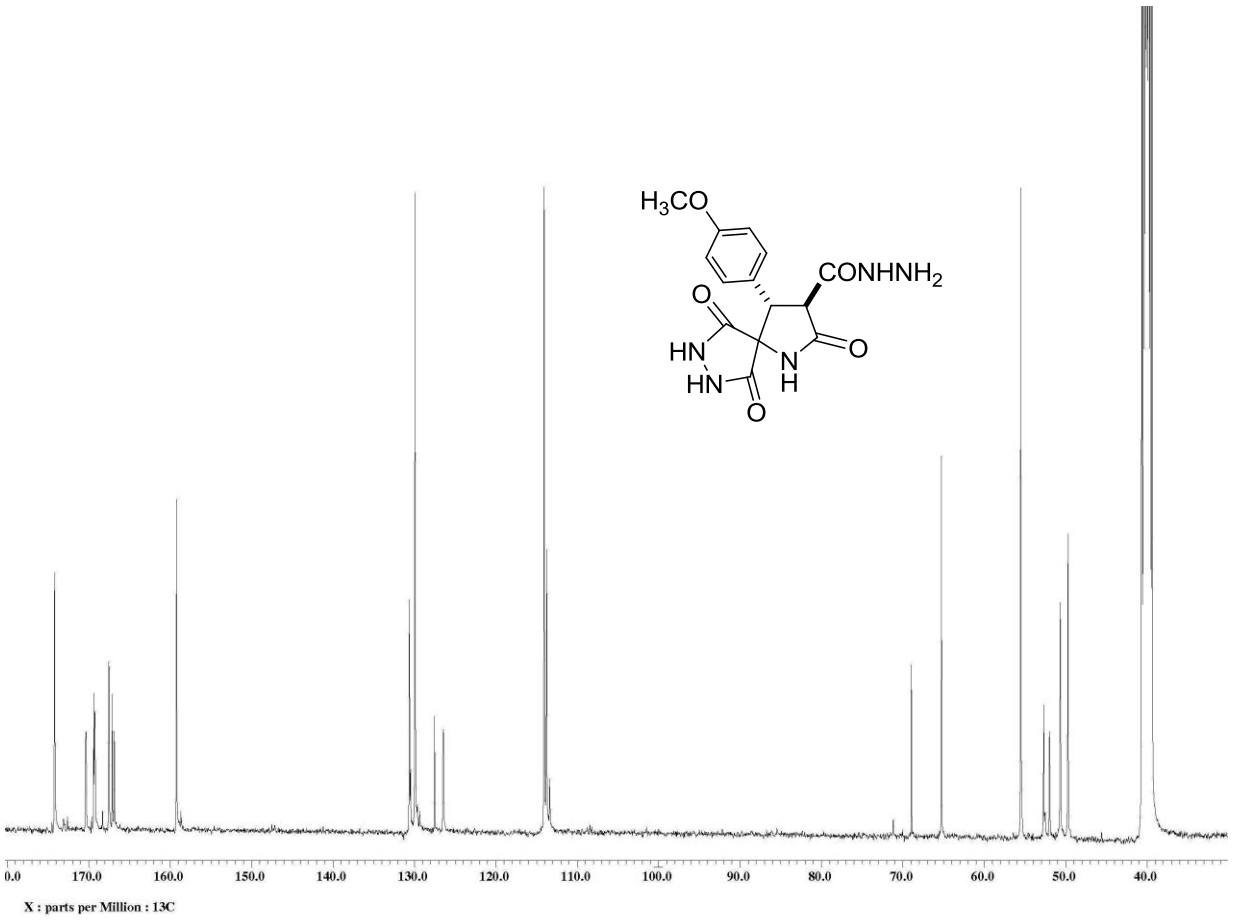

Fig. 21. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′S*,4′R**)-3′-(4-methoxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2c)** in DMSO-d_6 (exposition 72 h).

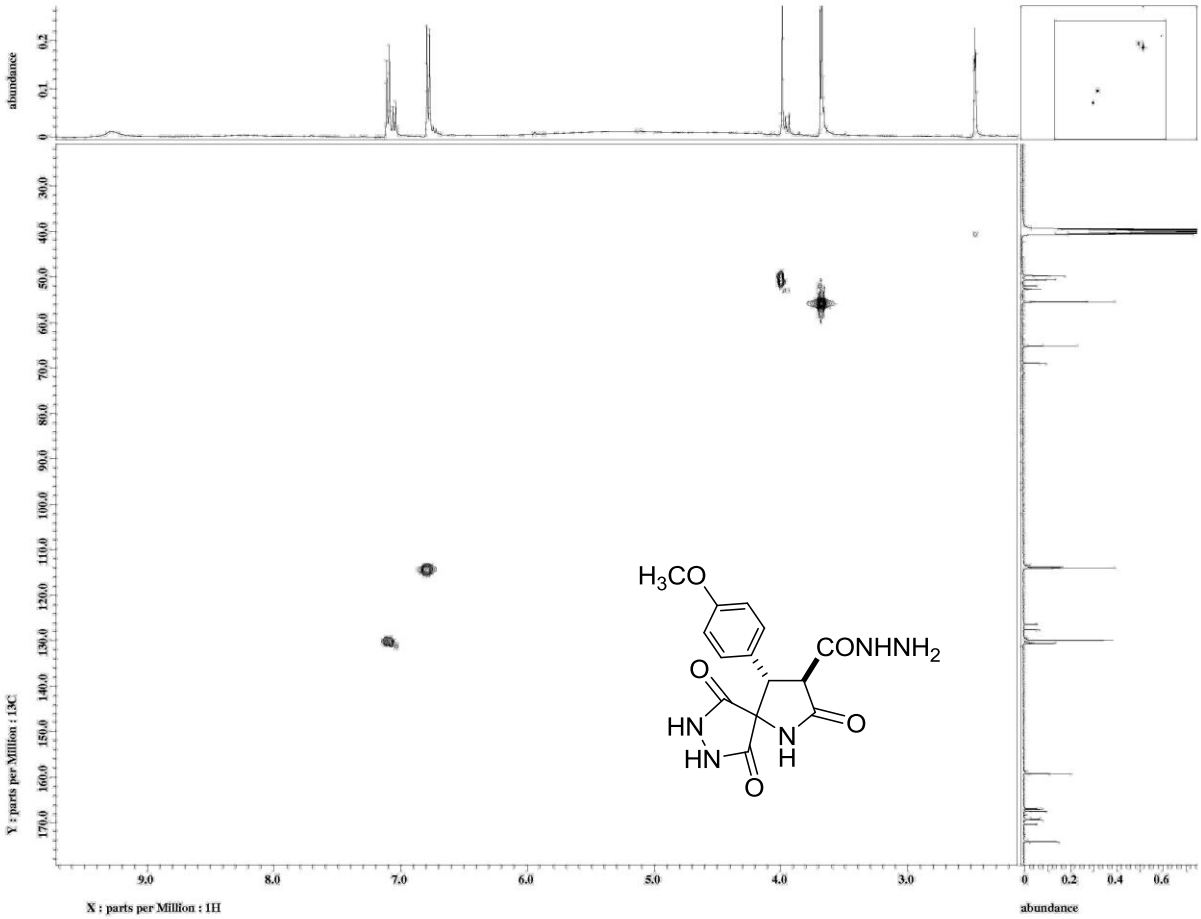

Fig. 22. ^{1}H-^{13}C HMQC spectrum of (*3′S*,4′R**)-3′-(4-methoxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2c)** in DMSO-d_6 (exposition 72 h).

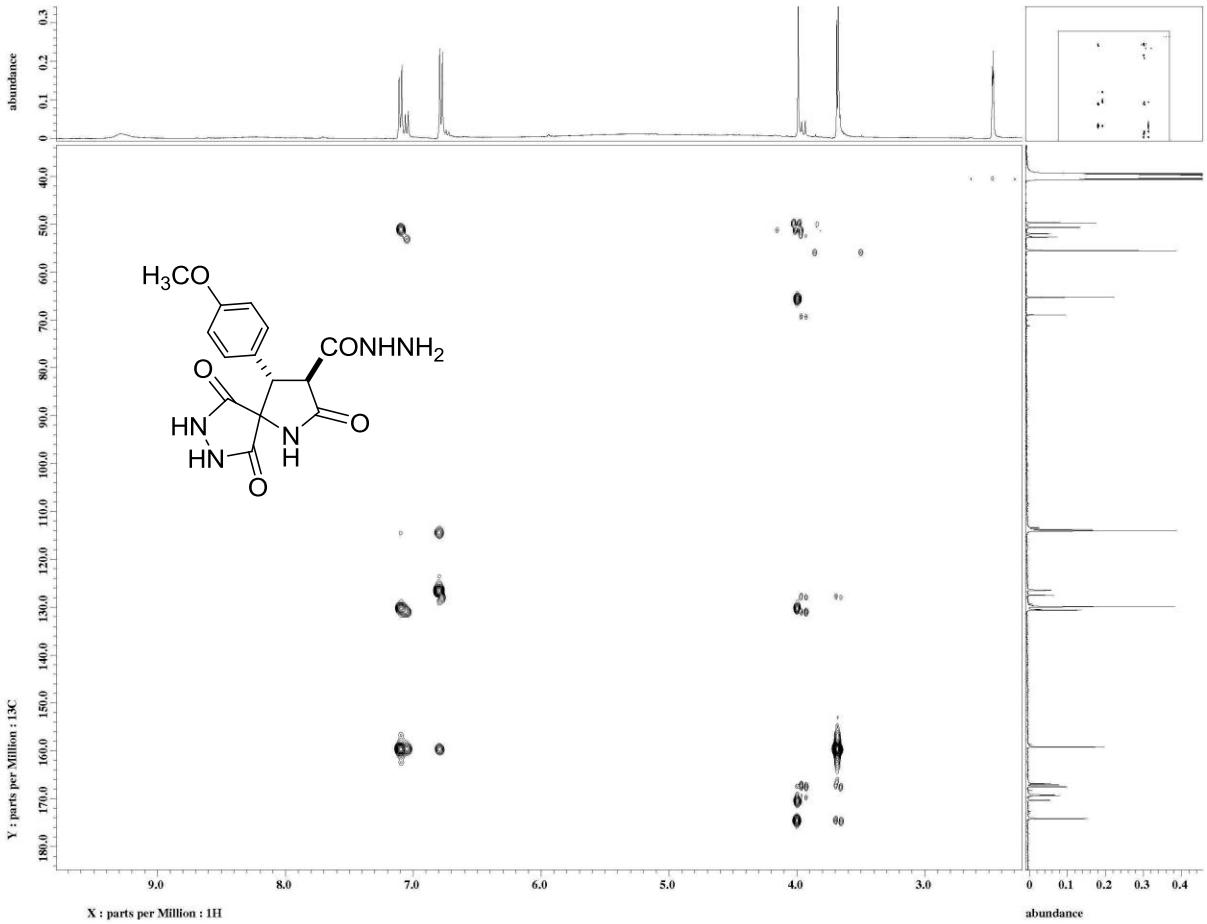

Fig. 23. ^{1}H-^{13}C HMBC spectrum of (*3′S*,4′R**)-3′-(4-methoxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2c)** in DMSO-d_6 (exposition 72 h).

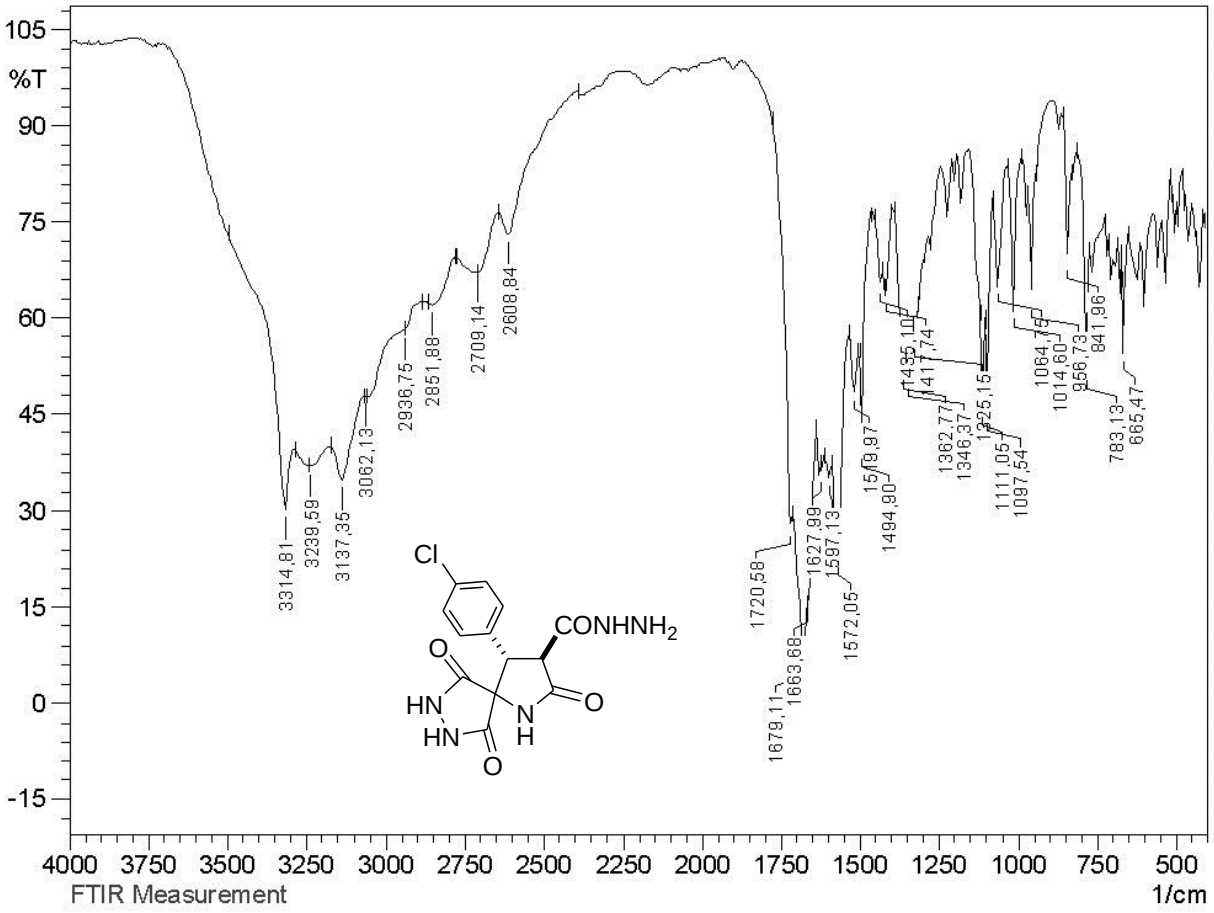

Fig. 24. IR spectrum of (*3′S*,4′R**)-3′-(4-chlorophenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2d)** in KBr.

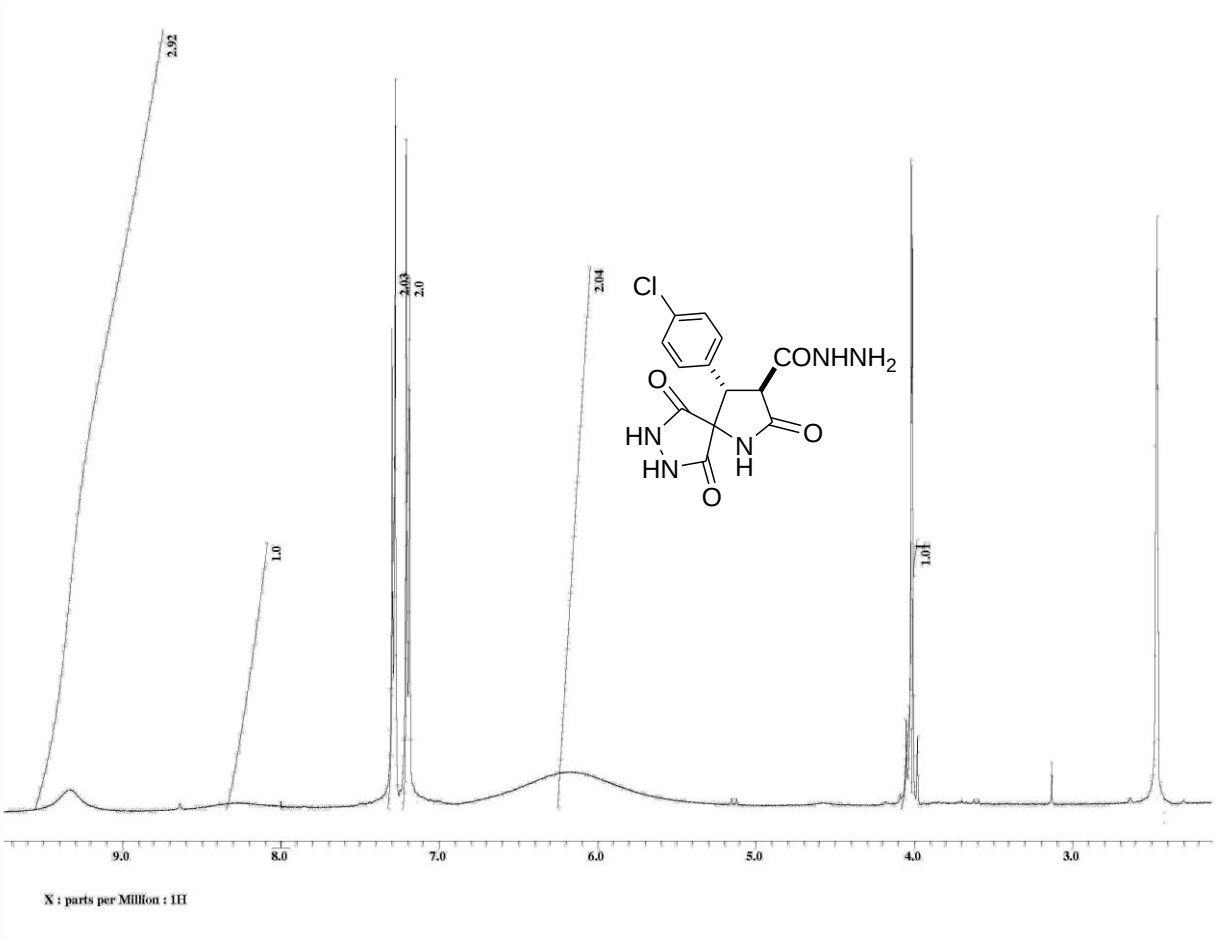

Fig. 25. ^{1}H NMR spectrum of (*3′S*,4′R**)-3′-(4-chlorophenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2d)** in DMSO-d_6.

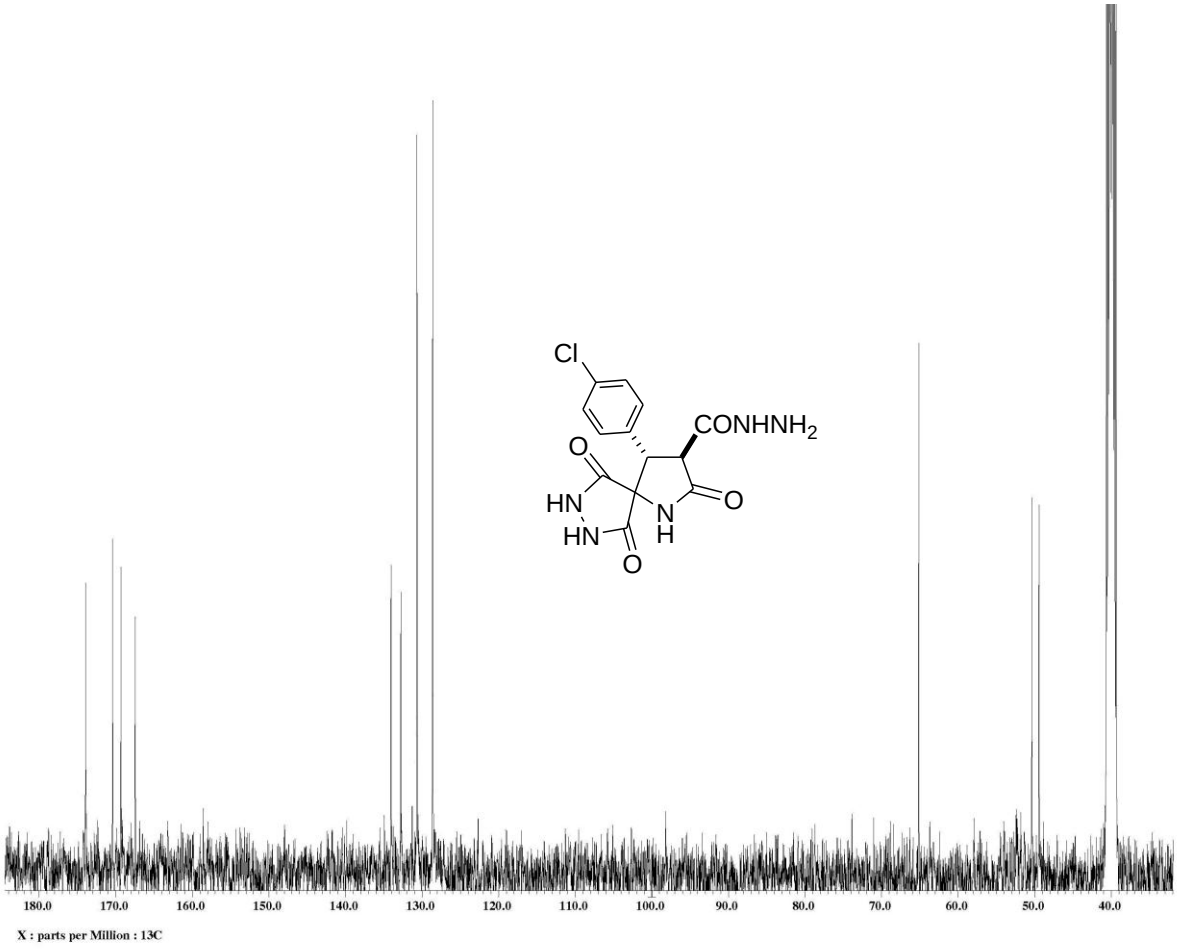

Fig. 26. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′S*,4′R**)-3′-(4-chlorophenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2d)** in DMSO-d_6.

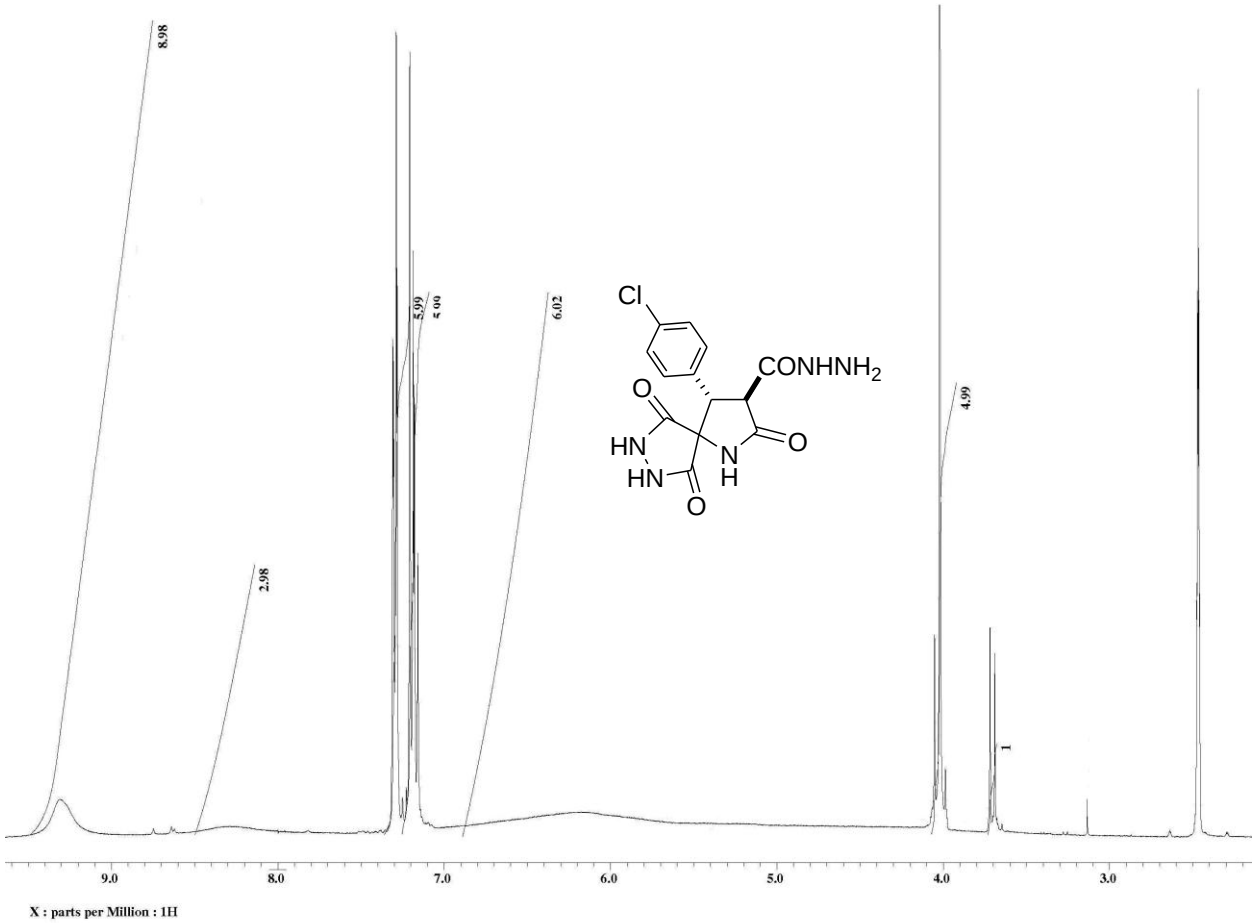

Fig. 27. ^{1}H NMR spectrum of (*3′S*,4′R**)-3′-(4-chlorophenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2d)** in DMSO-d_6 (exposition 72 h).

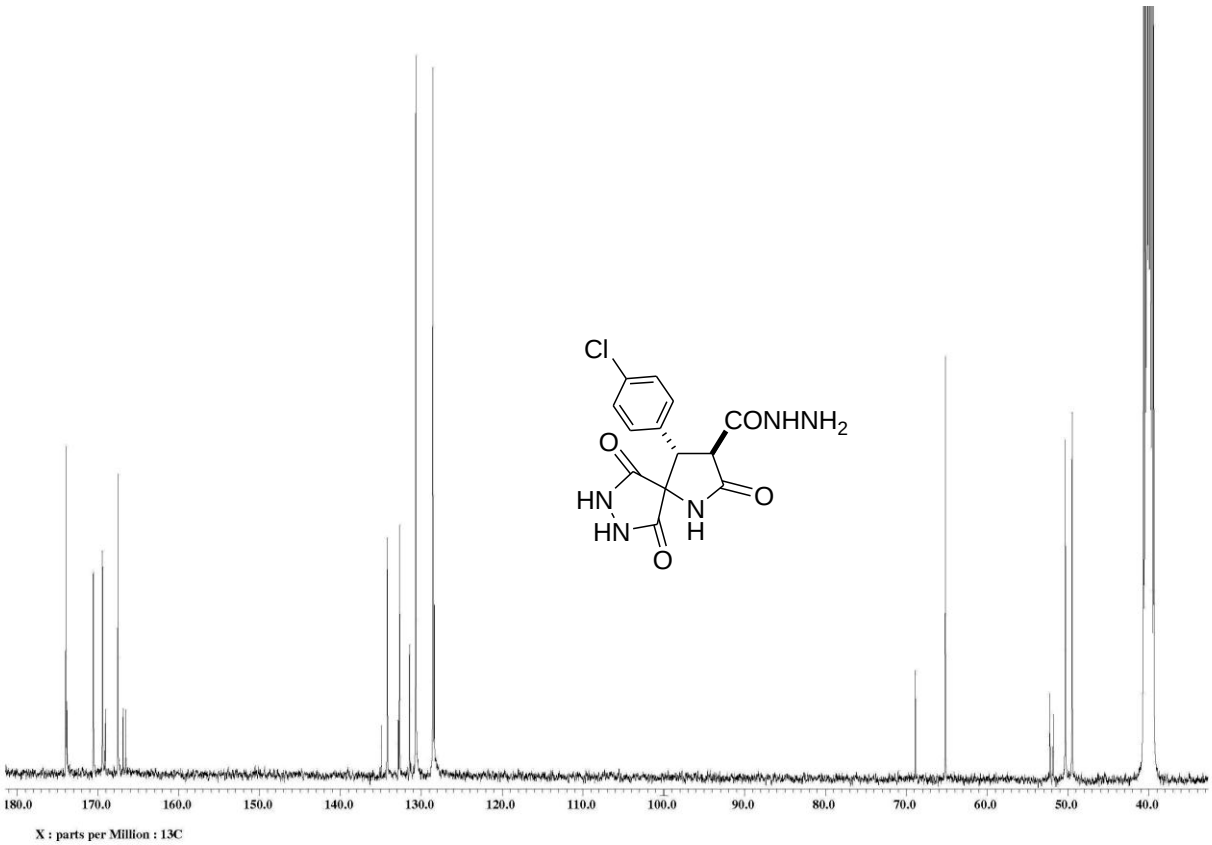

Fig. 28. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′S*,4′R**)-3′-(4-chlorophenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **2d** in DMSO-d_6 (exposition 72 h).

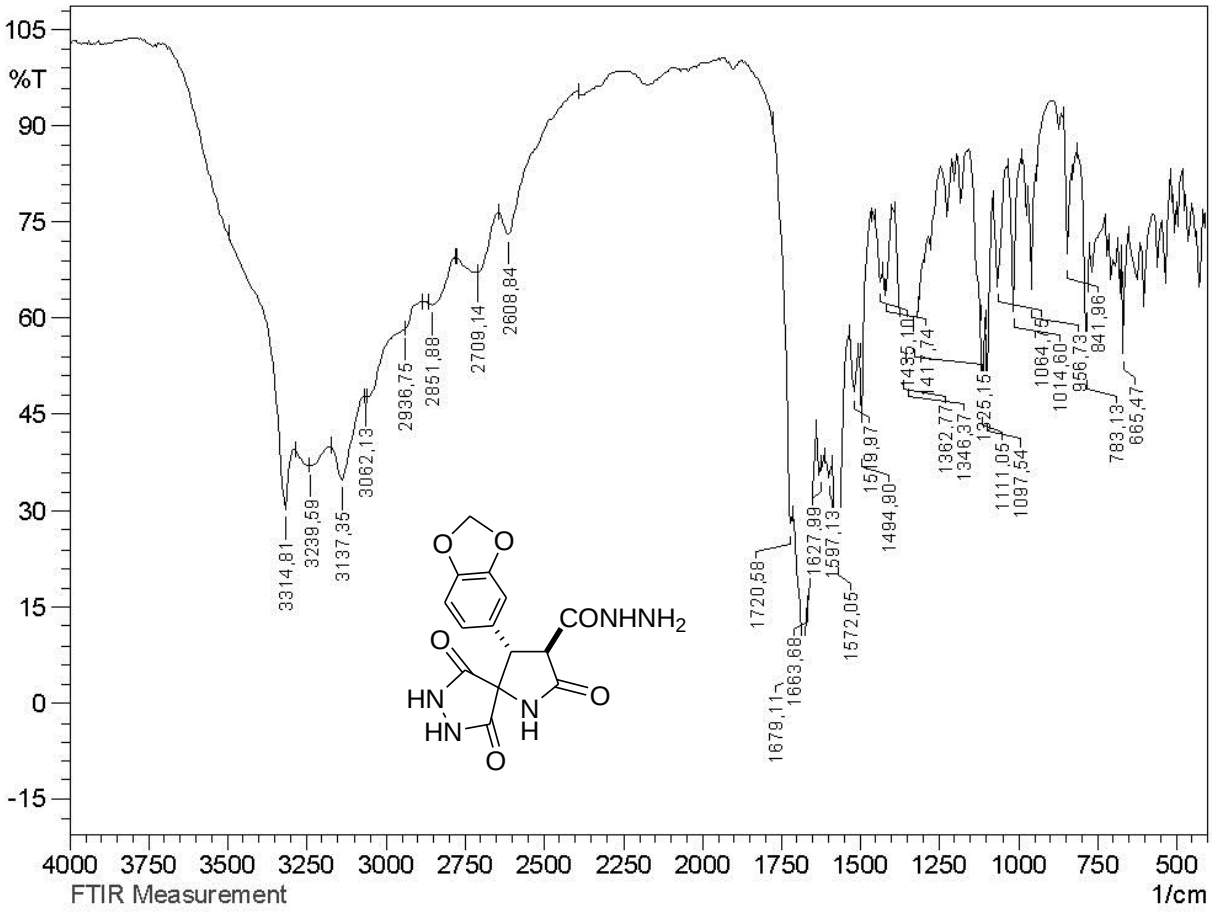

Fig. 29. IR spectrum of (*3′S*,4′R**)-3′-(3,4-methylenedioxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2e)** in KBr.

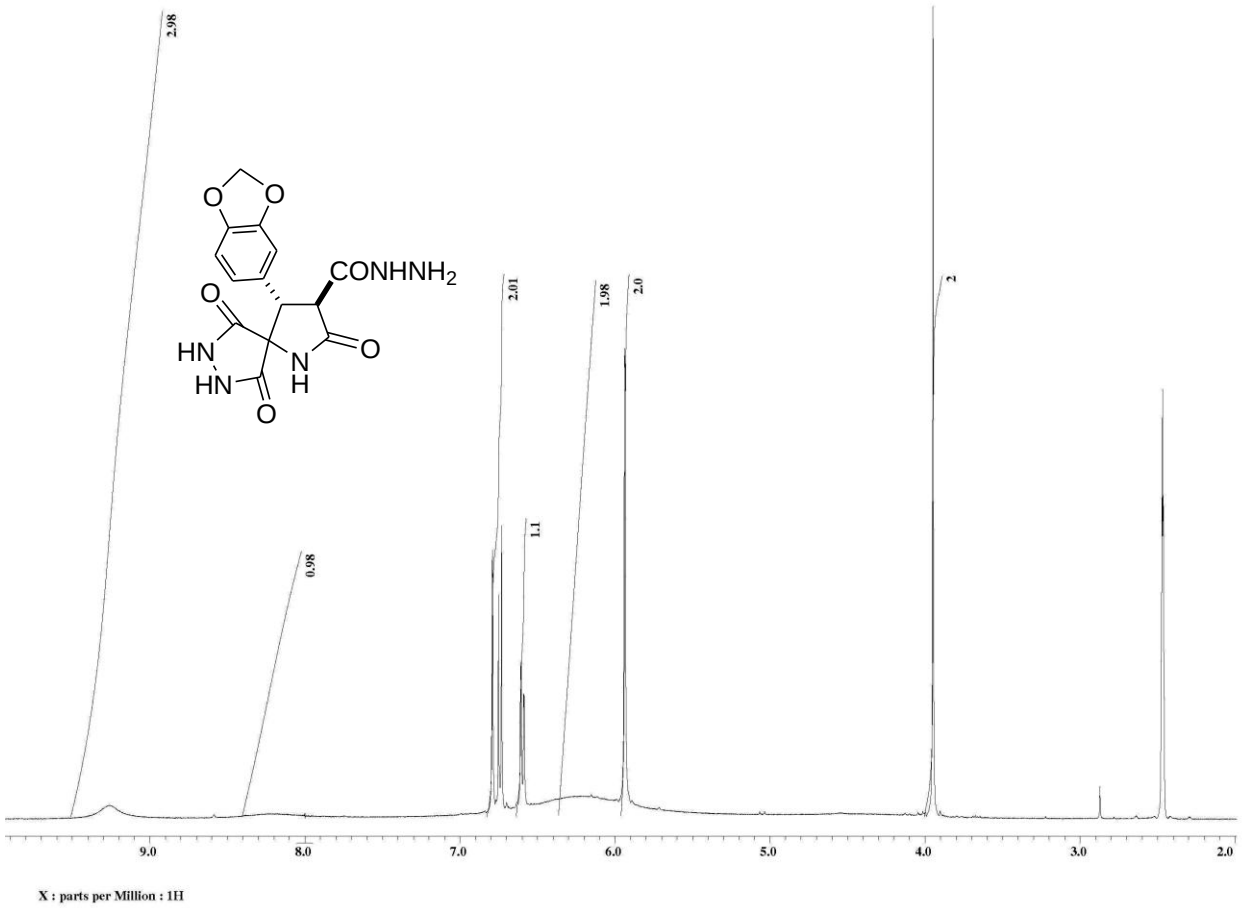

Fig. 30. ^{1}H NMR spectrum of (*3′S*,4′R**)-3′-(3,4-methylenedioxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2e)** in DMSO-d_6.

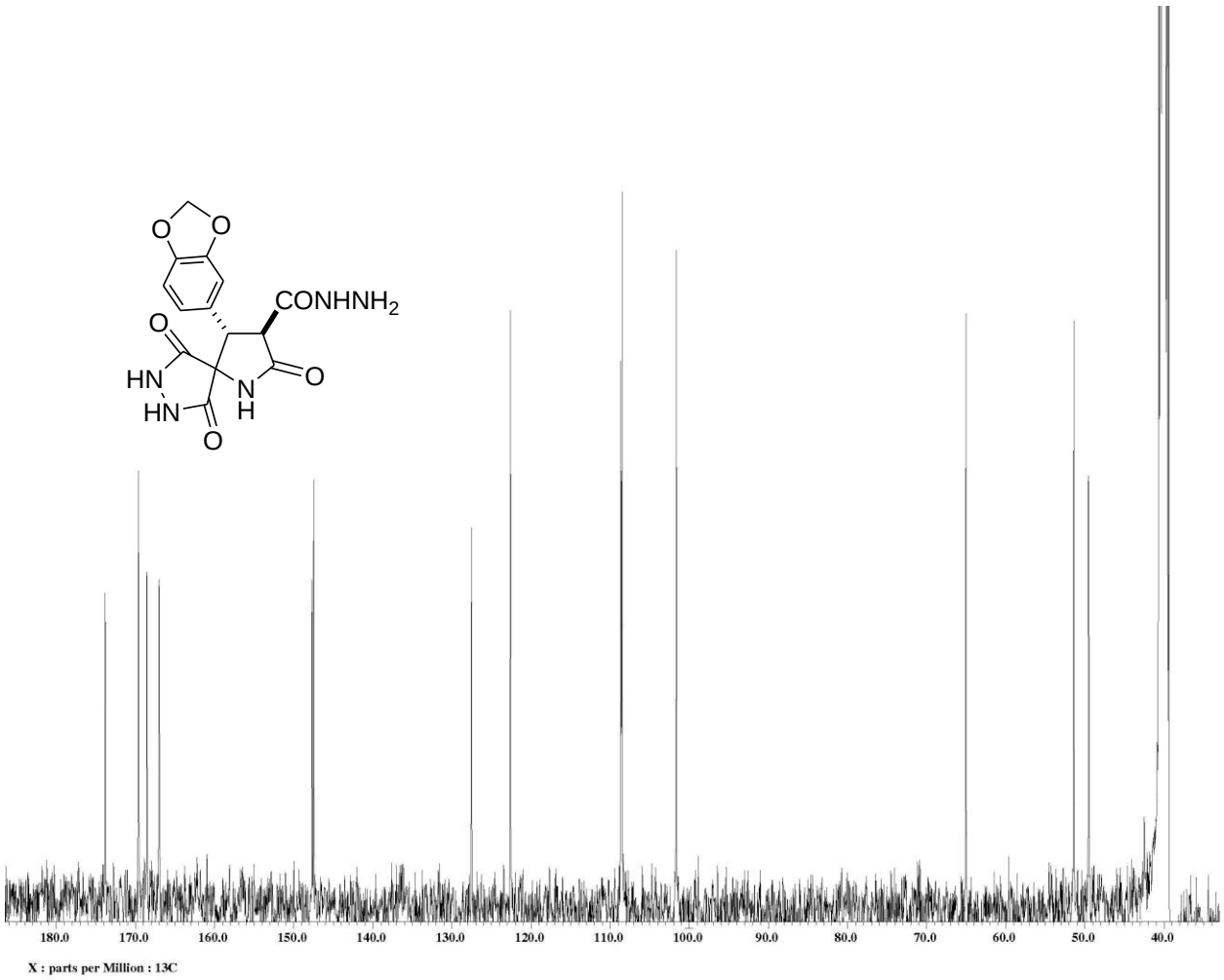

Fig. 31. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′S*,4′R**)-3′-(3,4-methylenedioxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2e)** in DMSO-d_6.

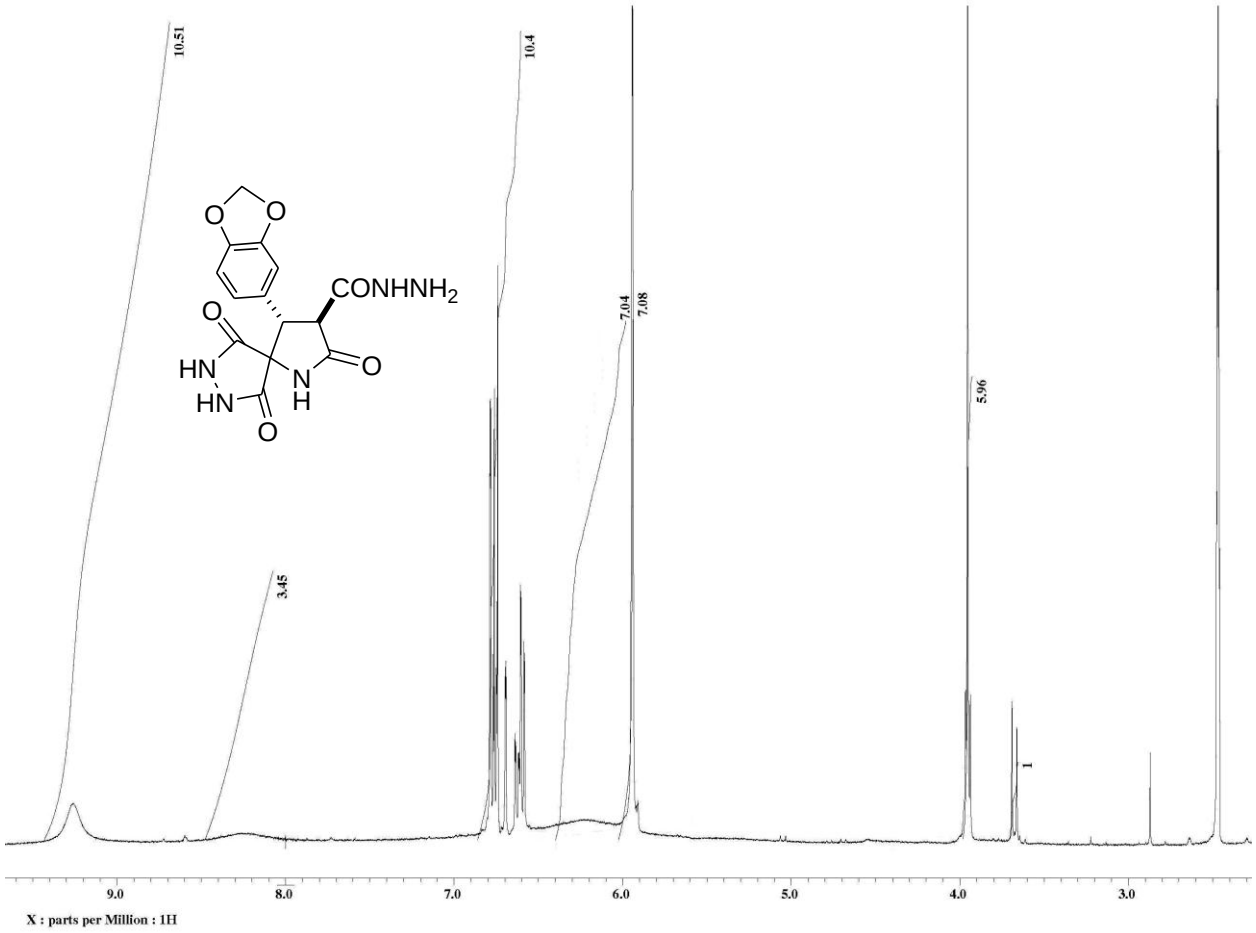

Fig. 32. ^{1}H NMR spectrum of (*3′S*,4′R**)-3′-(3,4-methylenedioxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2e)** in DMSO-d_6 (exposition 72 h).

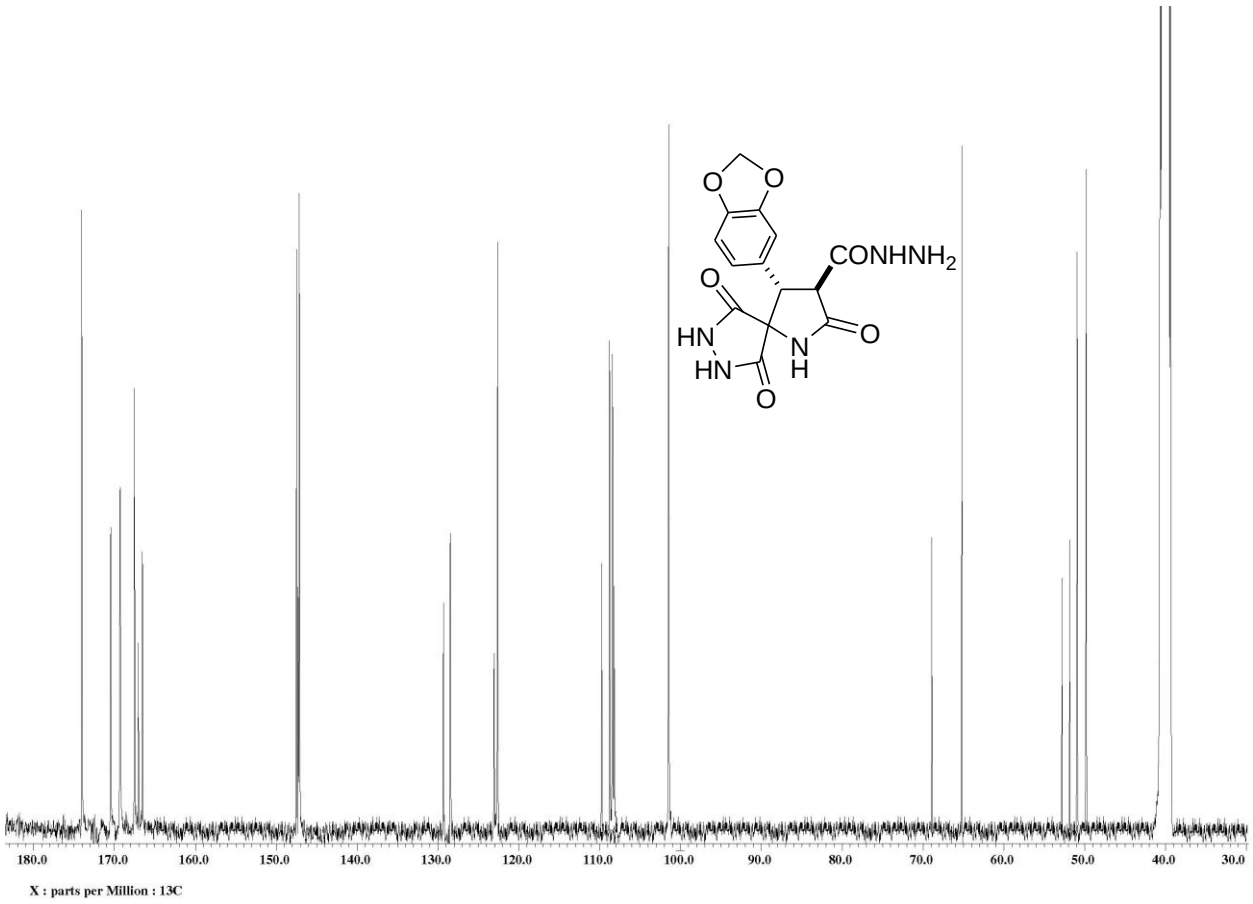

Fig. 33. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′S*,4′R**)-3′-(3,4-methylenedioxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **2e** in DMSO-d_6 (exposition 72 h).

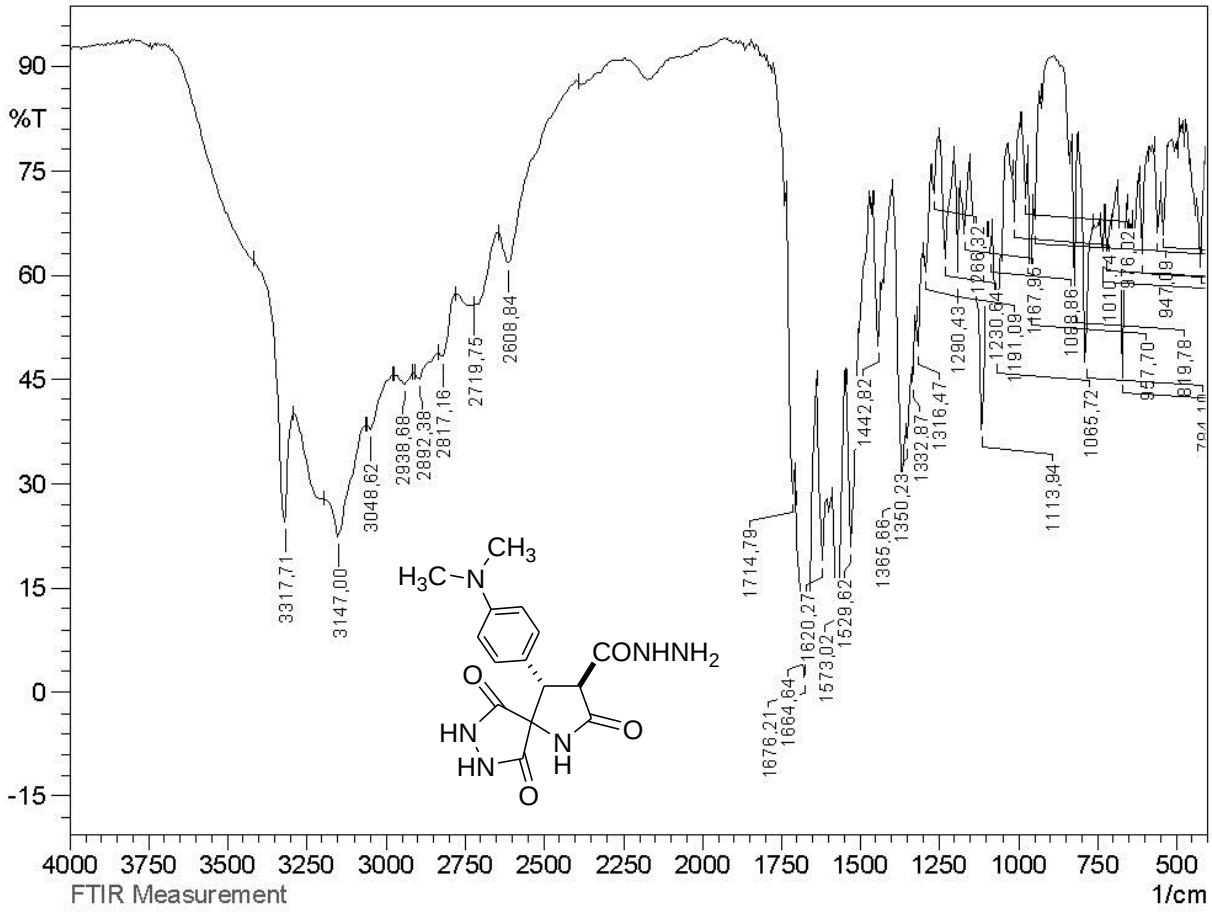

Fig. 34. IR spectrum of (*3′S*,4′R**)-3′-(4-dimethylaminophenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2f)** in KBr.

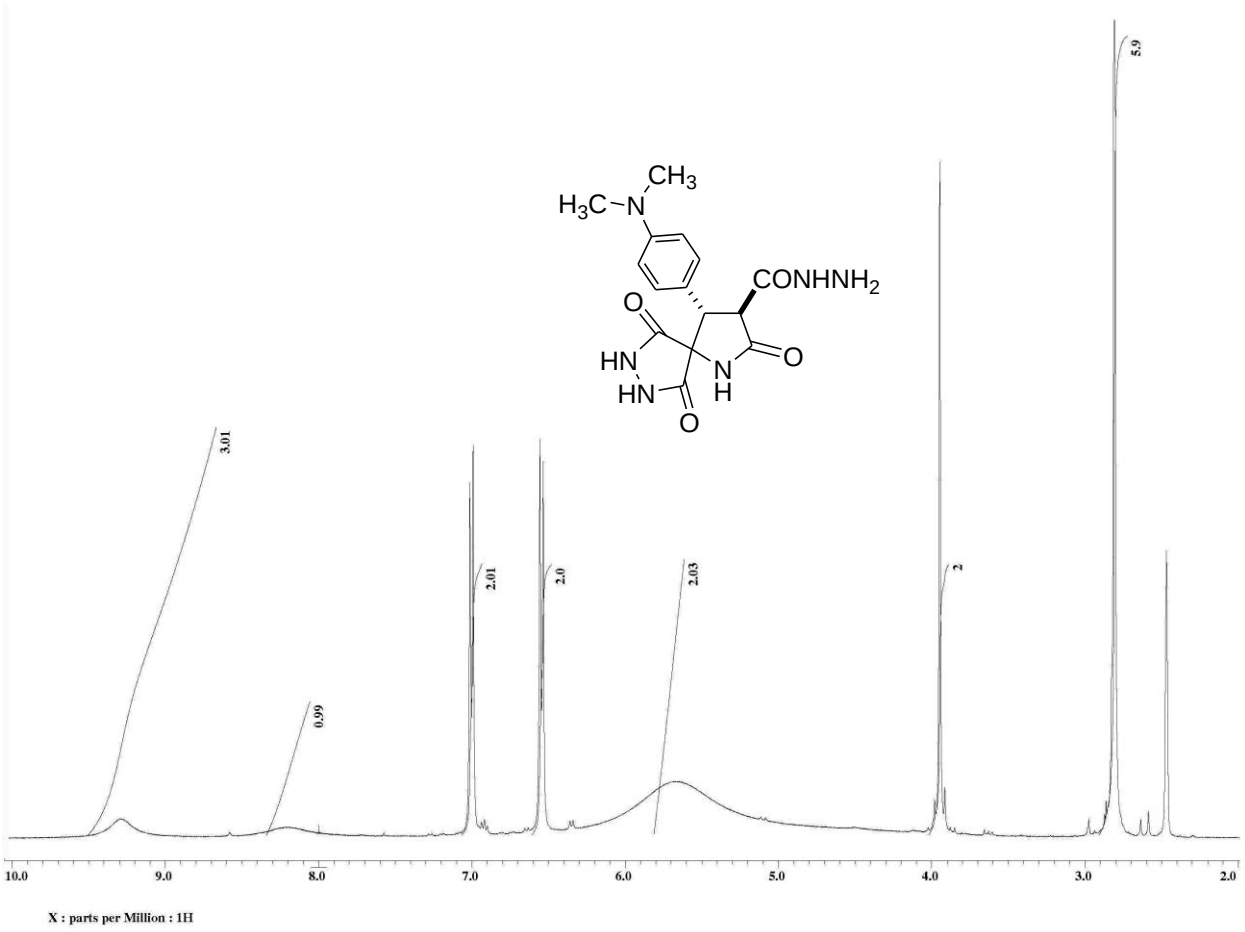

Fig. 35. ^{1}H NMR spectrum of (*3′S*,4′R**)-3′-(4-dimethylaminophenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2f)** in DMSO-d_6.

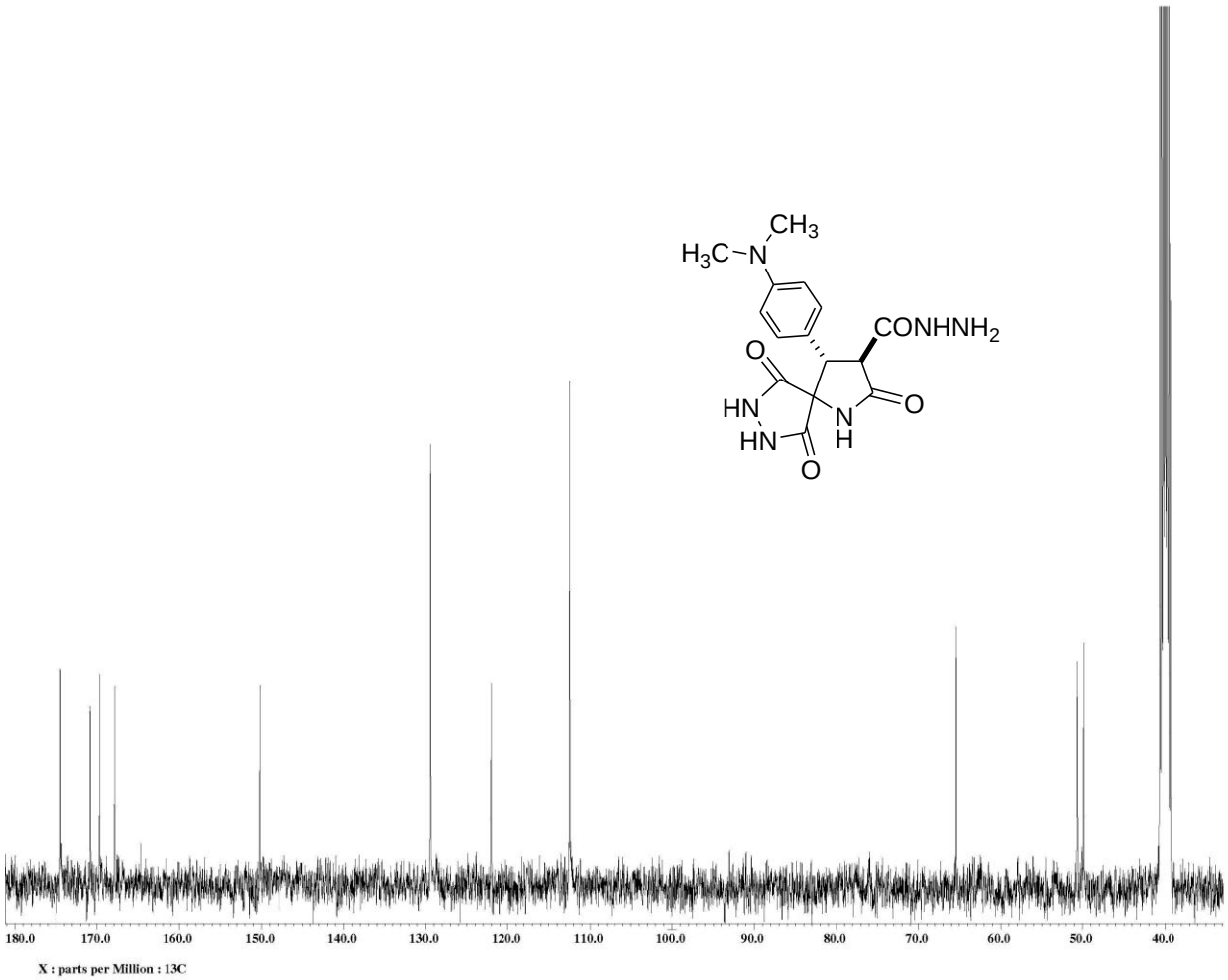

Fig. 36. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′S*,4′R**)-3′-(4-dimethylaminophenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2f)** in DMSO-d_6.

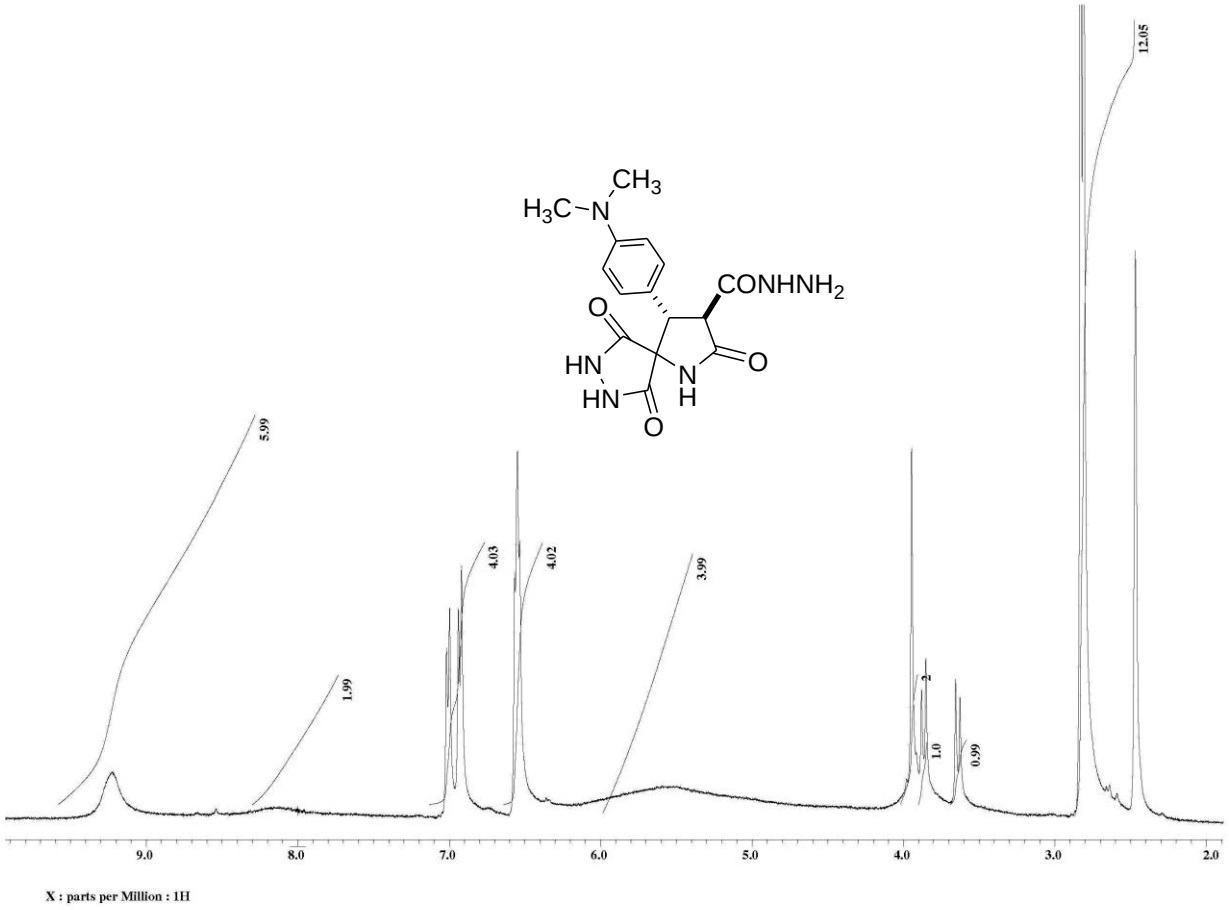

Fig. 37. ^{1}H NMR spectrum of (*3′S*,4′R**)-3′-(4-dimethylaminophenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2f)** in DMSO-d_6 (exposition 72 h).

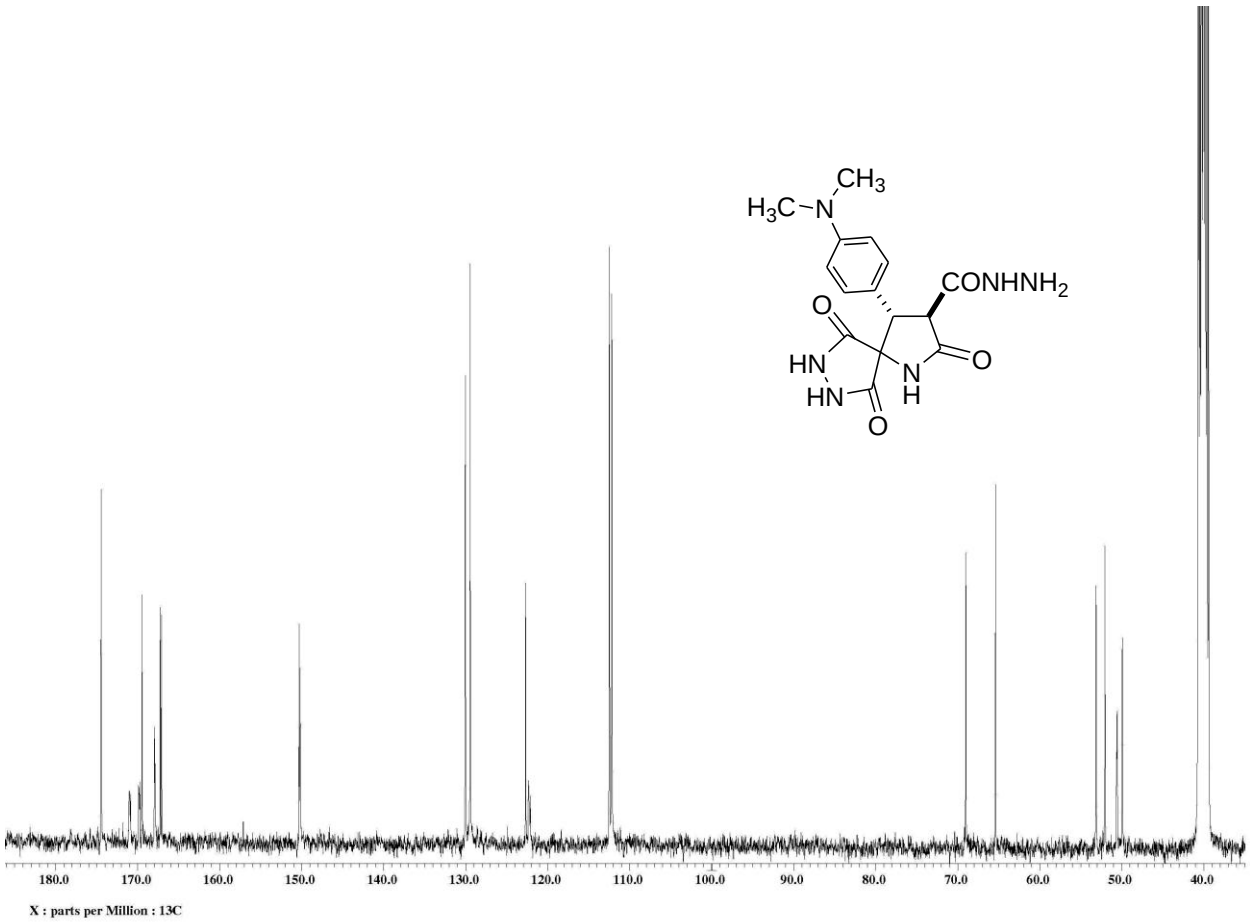

Fig. 38. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′S*,4′R**)-3′-(4-dimethylaminophenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2f)** in DMSO-d_6 (exposition 72 h).

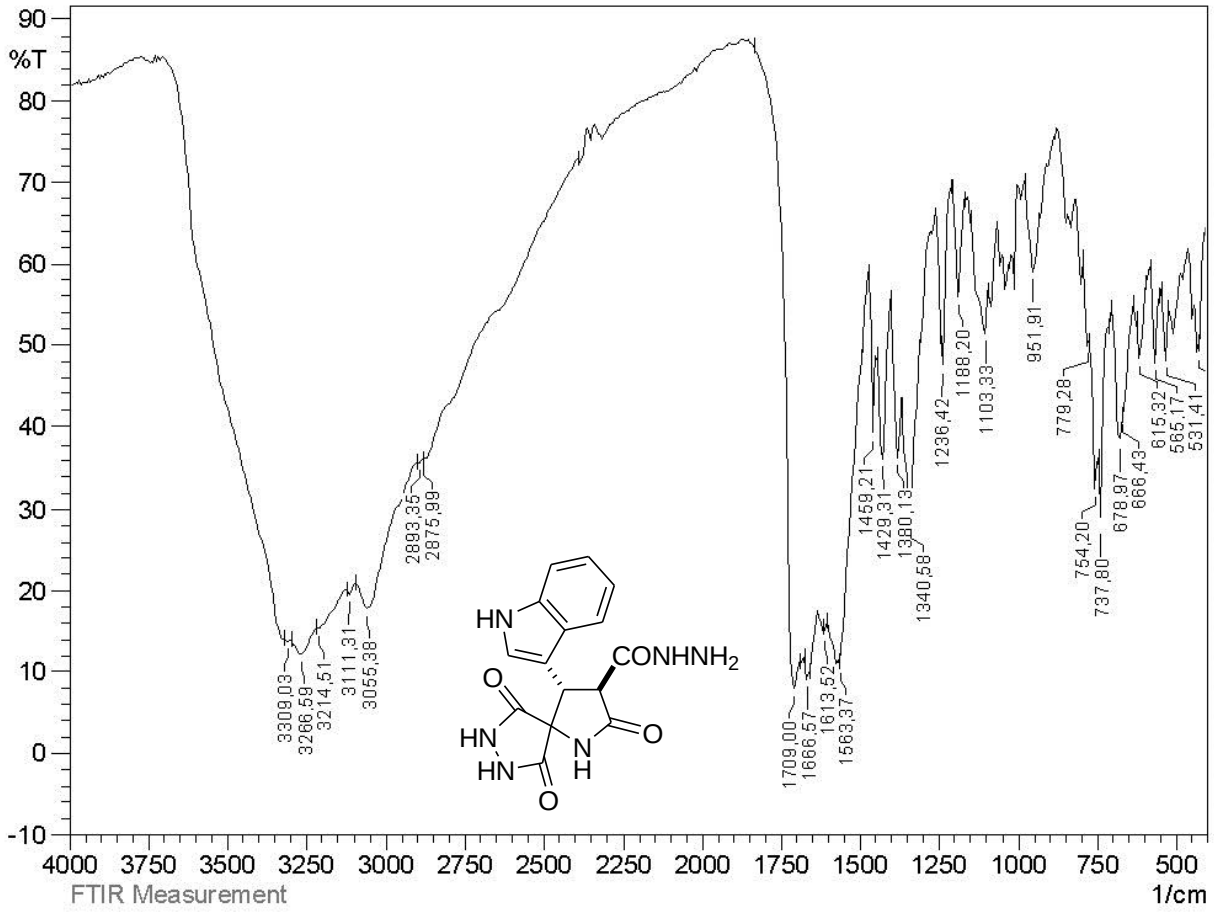

Fig. 39. IR spectrum of (*3′S*,4′R**)-3′-(indol-3-yl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2g)** in KBr.

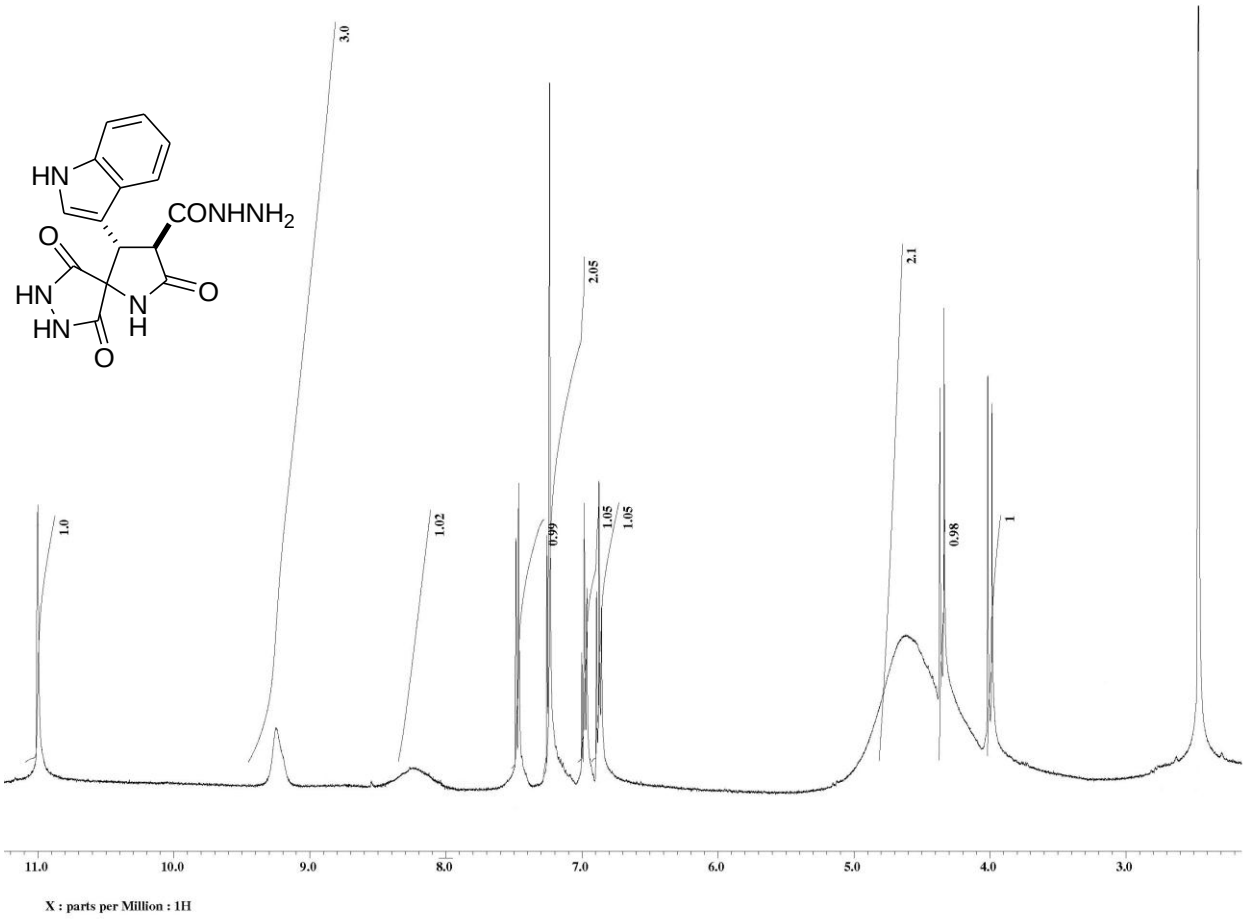

Fig. 40. ^{1}H NMR spectrum of (*3′S*,4′R**)-3′-(indol-3-yl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2g)** in DMSO-d_6.

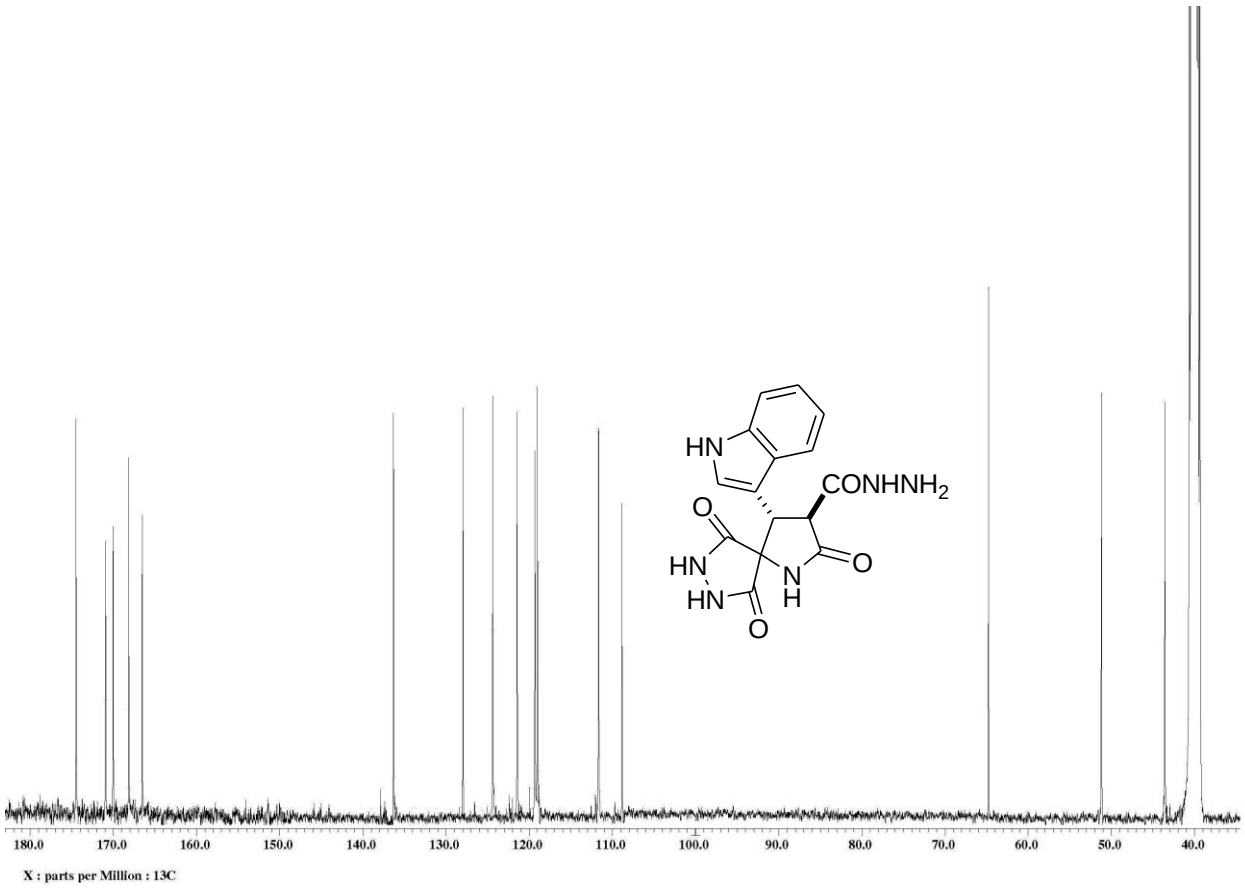

Fig. 41. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′S*,4′R**)-3′-(indol-3-yl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2g)** in DMSO-d_6.

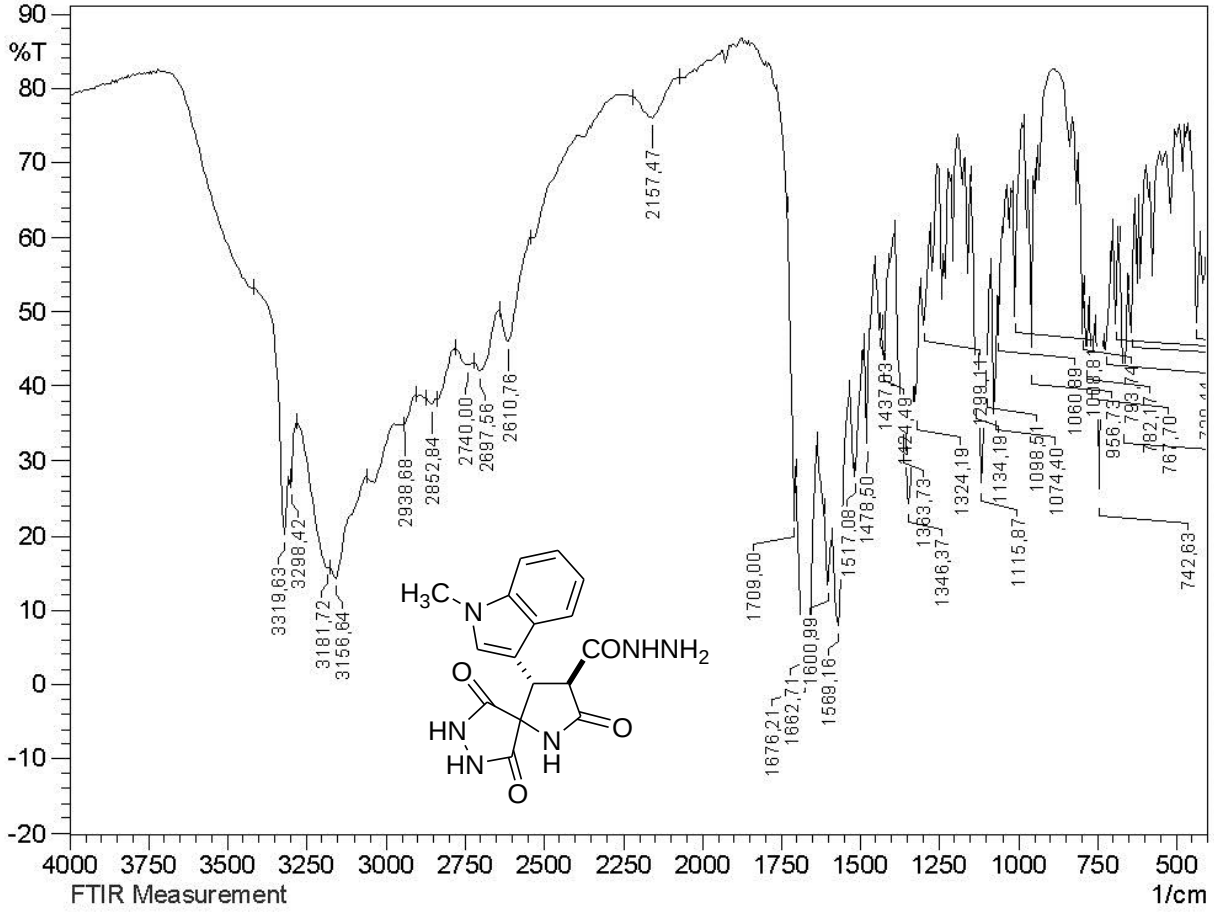

Fig. 42. IR spectrum of (*3′S*,4′R**)-3′-(indol-3-yl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2g)** in KBr

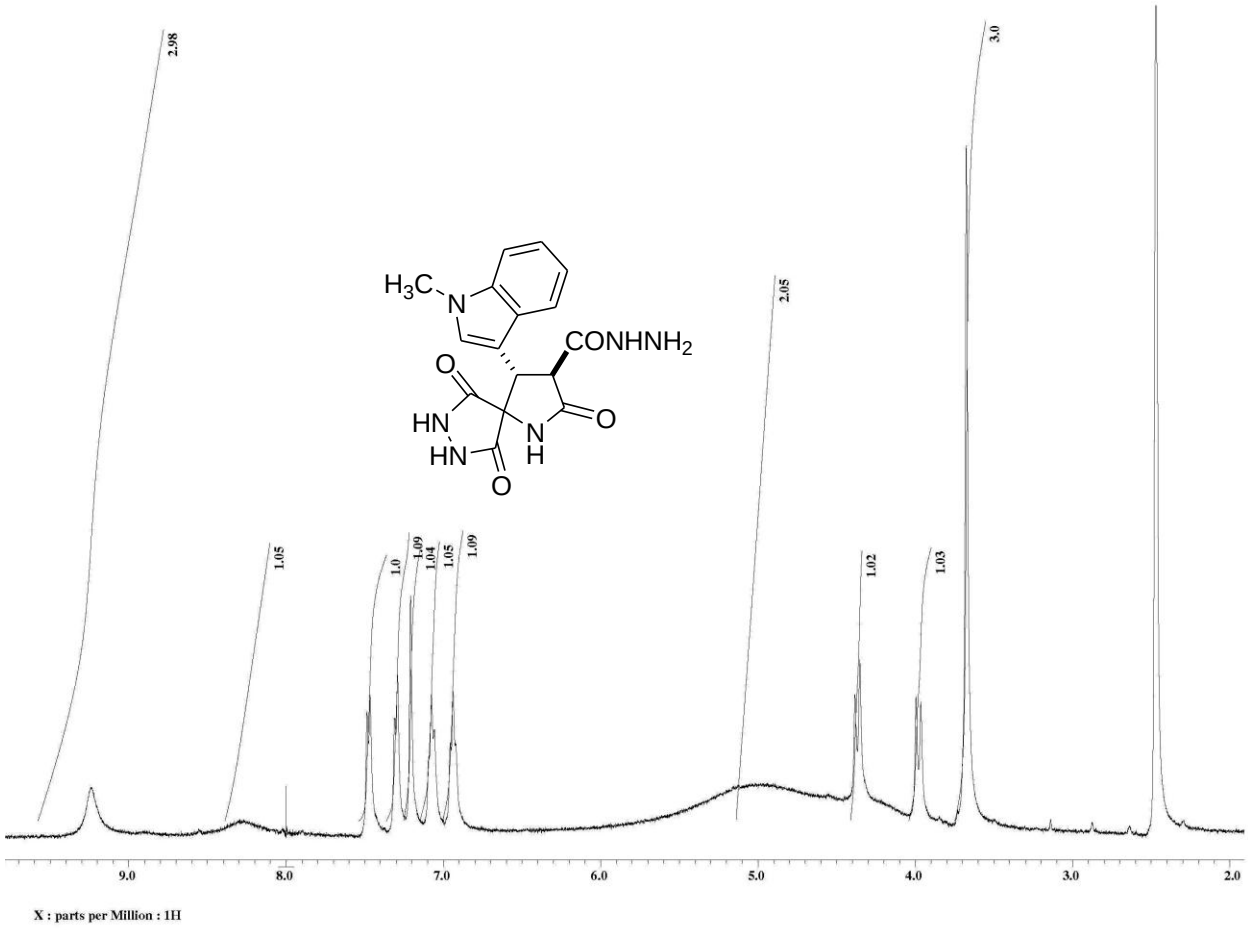

Fig. 43. ^{1}H NMR spectrum of (*3′R*,4′R**)-3′-(1-methylindol-3-yl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2h)** in DMSO-d_6.

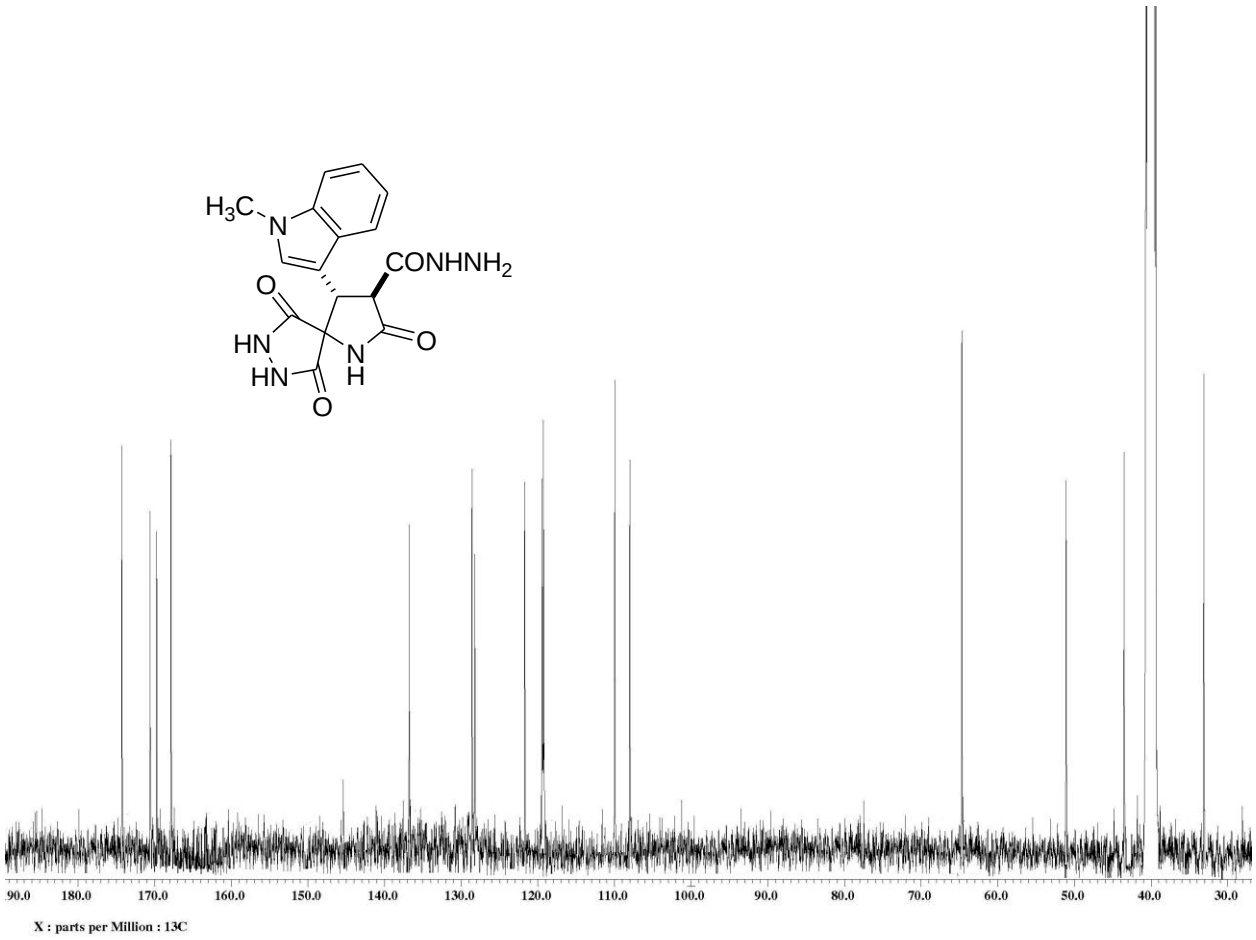

Fig. 44. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′R*,4′R**)-3′-(1-methylindol-3-yl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2h)** in DMSO-d_6.

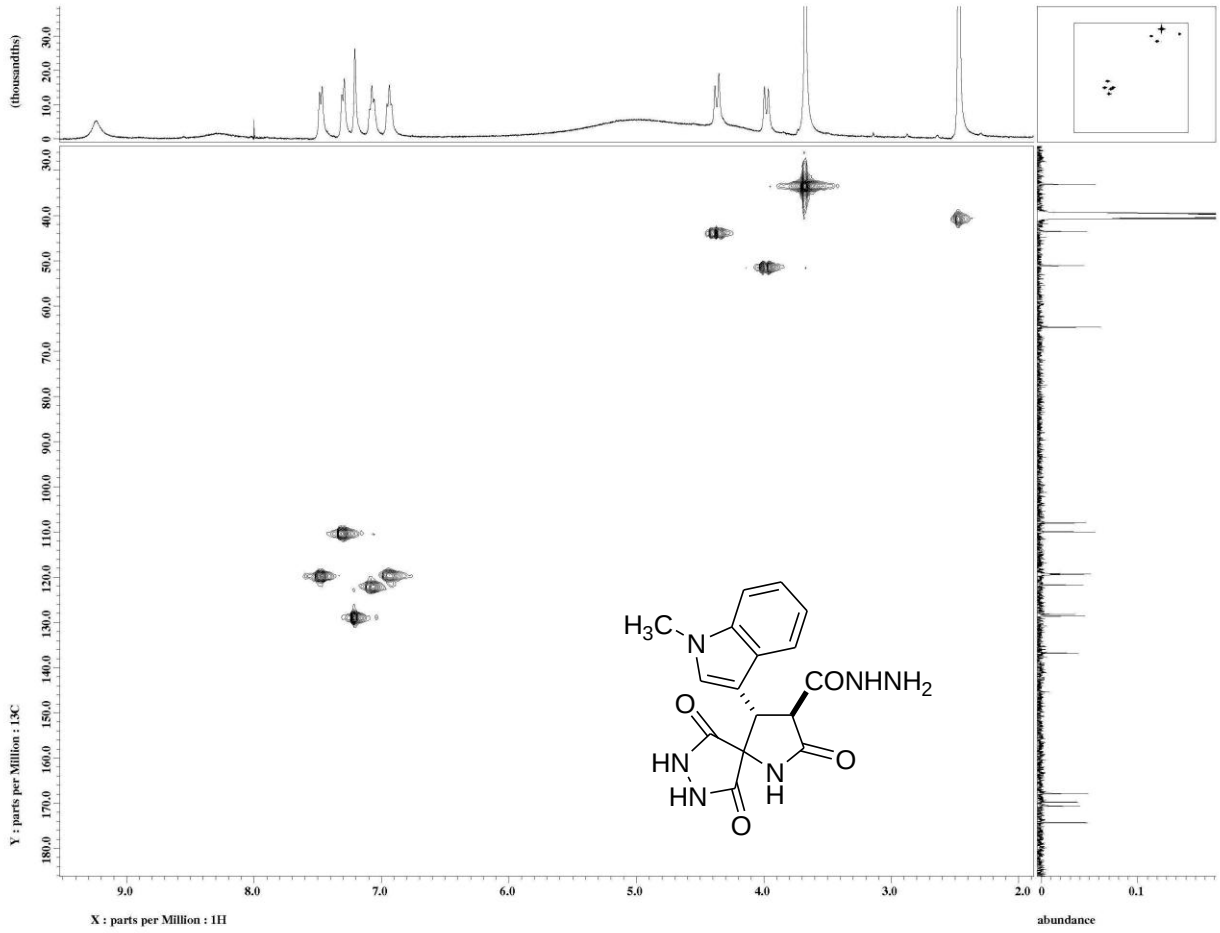

Fig. 45. ^{1}H-^{13}C HMQC spectrum of (*3′R*,4′R**)-3′-(1-methylindol-3-yl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2h)** in DMSO-d_6.

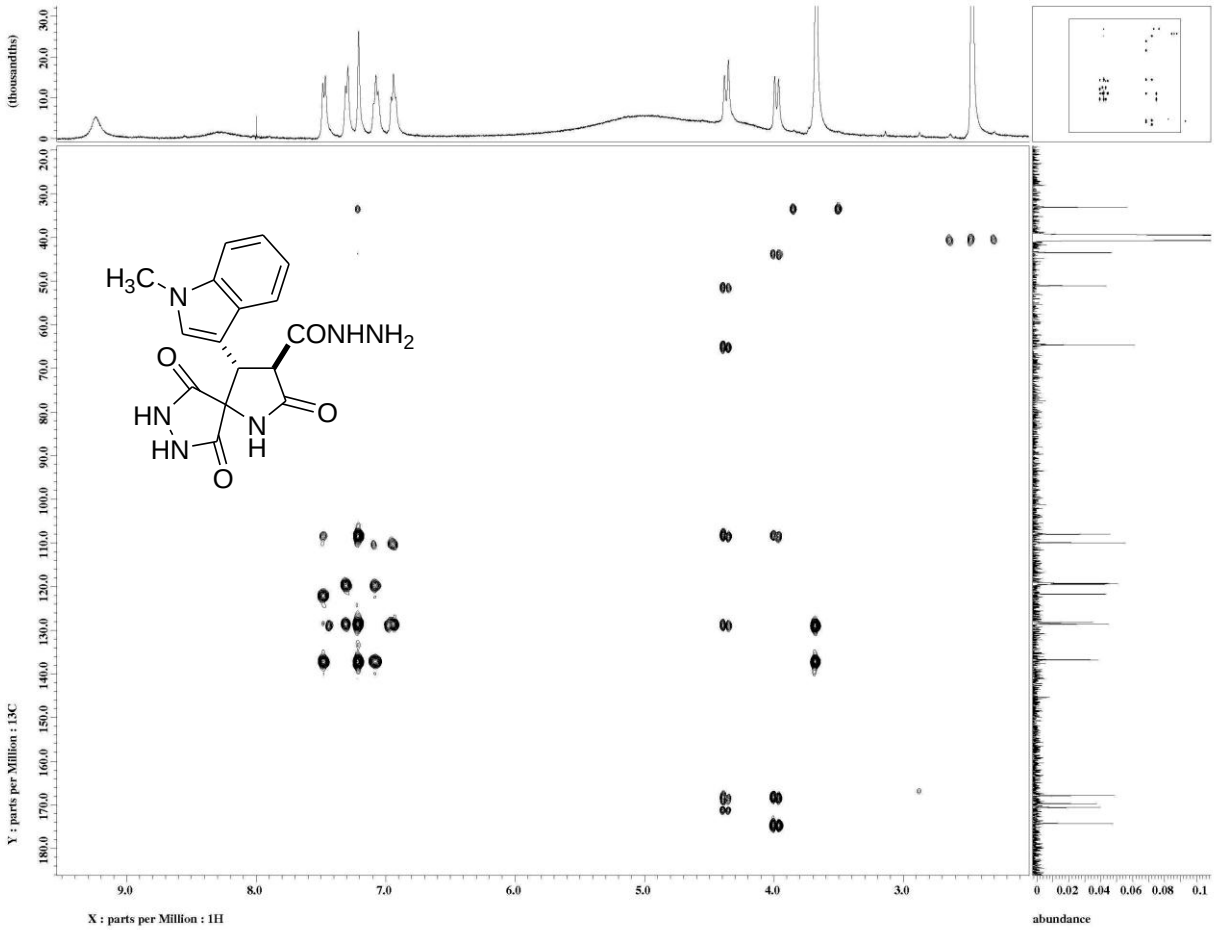

Fig. 46. ^{1}H-^{13}C HMBC spectrum of (*3′R*,4′R**)-3′-(1-methylindol-3-yl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2h)** in DMSO-d_6.

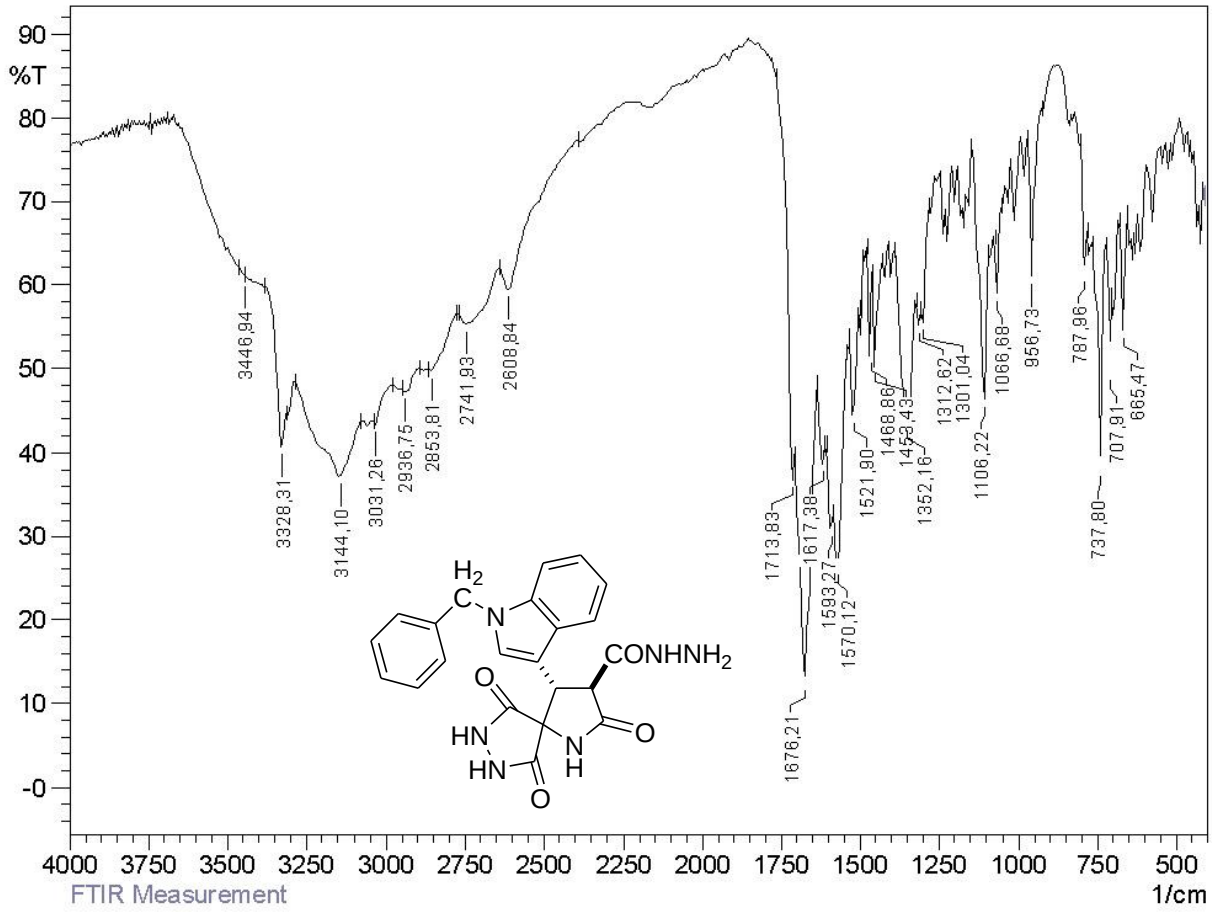

Fig. 47. IR spectrum of (*3′R*,4′R**)-3′-(1-benzylindol-3-yl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2i)** in KBr.

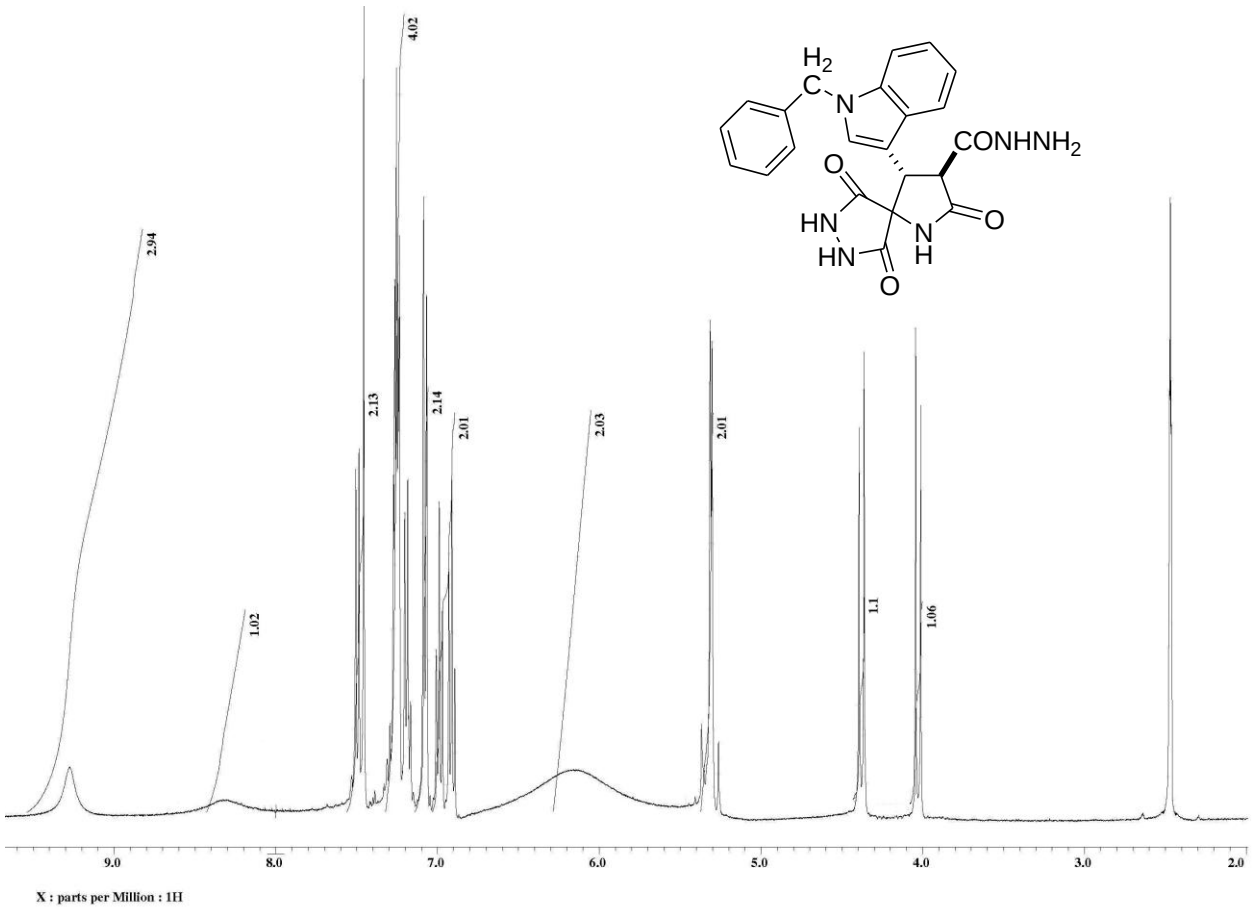

Fig. 48. ^{1}H NMR spectrum of (*3′R*,4′R**)-3′-(1-benzylindol-3-yl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2i)** in DMSO-d_6.

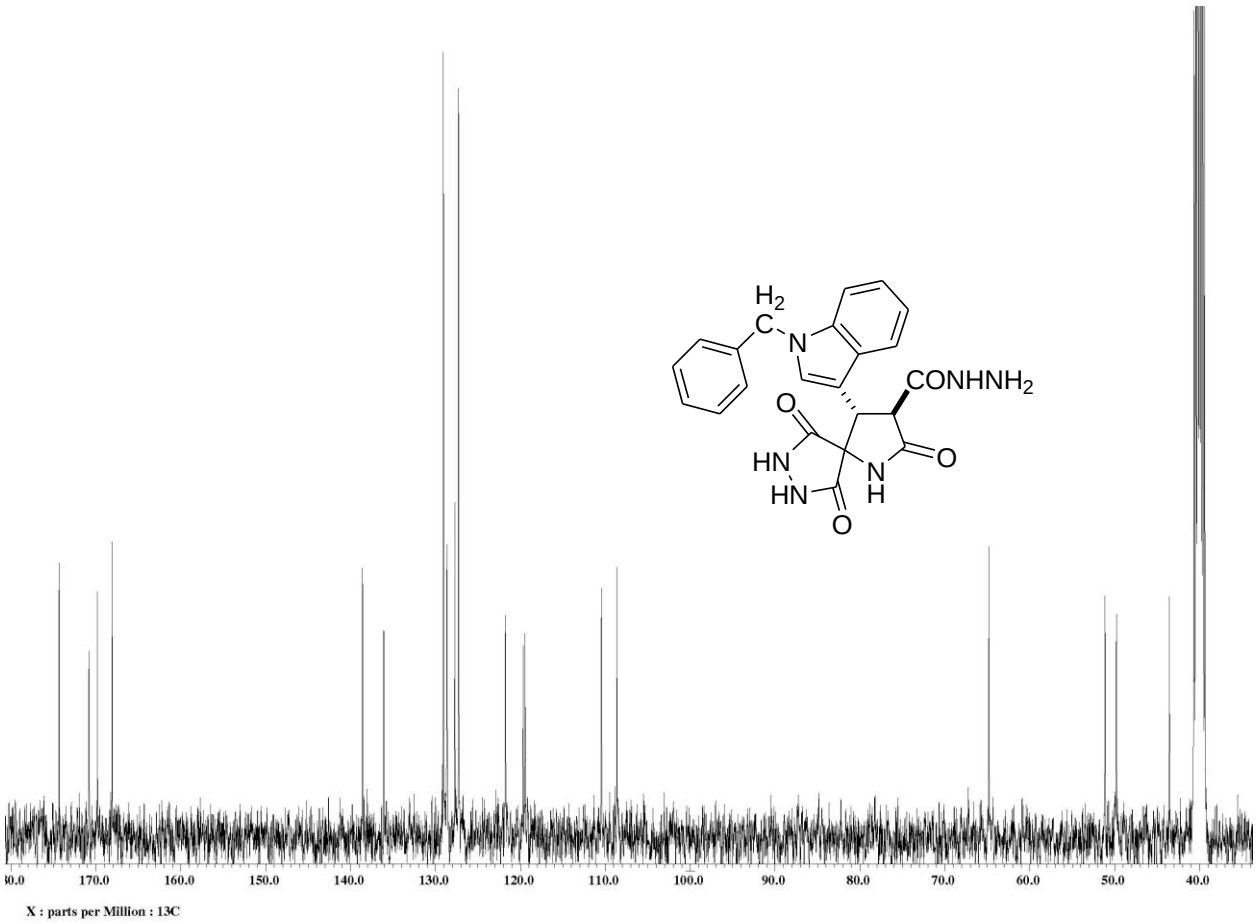

Fig. 49. $^{13}C\{^{1}H\}$ NMR spectrum of (*3′R*,4′R**)-3′-(1-benzylindol-3-yl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2i)** in DMSO-d_6.

X-ray analysis of (*3′S*,4′R**)-3′-(3,4-methylenedioxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2e)**

X-ray diffraction analysis of the structure **2e** was performed on a Bruker D8 QUEST automatic three-circle diffractometer with a PHOTON III two-dimensional detector and an IμS DIAMOND microfocus X-ray tube (λ [Mo Kα] = 0.71073 Å) at cooling conditions (100 K). Data collection and processing of diffraction data were performed using an APEX3 software package. All of the structures were solved by the direct method using the SHELXT program[1] and refined by the full-matrix least squares method over F^2 using the SHELXL program.[2] All of the calculations were performed in the WinGX software package[3], the calculation of the geometry of the molecules and the intermolecular interactions in the crystals was carried out using the PLATON program[4] and the drawings of the molecules were performed using the MERCURY[5] programs. The non-hydrogen atoms were refined in the anisotropic approximation. The hydrogen atoms were placed in geometrically calculated positions and included in the refinement in the "riding" model. The crystallographic data of structure were deposited at the Cambridge Crystallographic Data Center, registration number 2410736.

Crystal **2e**, $C_{14}H_{13}N_5$, M = 347.29, monoclinic, space group *P2₁*, at 100(2) K: a = 8.0704(17), b = 7.0926(17), c = 13.071(3) Å, β = 104.902(7)°, V = 723.0(3) $Å^3$, Z = 2, d_{calc} = 1.595 g cm^{-3}, μ(MoKα) 0.128 mm^{-1}, F(000) = 360. A total of 16152 reflections were collected (3491 independent reflections, R_{int} = 0.143, 1988 observed with $I \geq 2\sigma(I)$), GOOF 1.047, final R indexes (observed reflections) R_1 = 0.0736, wR_2 = 0.1548, all data R_1 = 0.1471, wR_2 = 0.1904, 250 refined parameters.

The X-ray diffraction study was performed at the Department of X-ray Diffraction Research of the Multiple-Access Center on the basis of the Laboratory of Diffraction Research Methods of the A. E. Arbuzov Institute of Organic and Physical Chemistry, the Kazan Scientific Center of the Russian Academy of Sciences.

1. Sheldrick, G.M. *Acta Crystallogr. Sect. A Found. Adv.* **2015**, *71*, 3.
2. Sheldrick, G.M. *Acta Crystallogr. Sect. C* **2015**, *71*, 3.
3. Farrugia, L.J. *J. Appl. Crystallogr.* **2012**, *45*, 849.
4. Spek, A.L. *Acta Crystallogr. Sect. D Biol. Crystallogr.* **2009**, *65*, 148.
5. Macrae, C.F.; Edgington, P.R.; McCabe, P.; Pidcock, E.; Shields, G.P.; Taylor, R.; Towler, M.; Streek, J.V.D. *J. Appl. Crystallogr.* **2006**, *39*, 453.

Table 1. Principal crystallographic parameters of (*3′S*,4′R**)-3′-(3,4-methylenedioxyphenyl)-3,5,5′-trioxospyro[pyrazolidine-4,2′-pyrrolidine]-4′-carbohydrazide **(2e)**
based on X-ray diffraction data

Parameter	**2e**
Molecular formula	$C_{14}H_{13}N_5O_6$
Molecular weight	347.29
Crystal system	monoclinic
Space group	$P2_1$
Z	2
Unit cell parameters	
a/Å	8.0704(17)
b/Å	7.0926(17)
c/Å	13.071(3)
α/deg	90
β/deg	104.902(7)
γ/deg	90
V/Å^3	723.0(3)
d_{calc}/g cm^3	1.595
Absorption coeffi cient, μ/mm^{-1}	0.128
F(000)	360
2Θ (min, max)/deg	3.20, 56.0
Ranges of indices,	
h	$-10 \le h \le 10$
k	$-9 \le k \le 9$
l	$-17 \le l \le 17$
Number of reflections	
total	16152,
unique	3491
R_{int}	0.143
$T_{max/min}$	0.7959/0.9281
Number of observed reflections (I > 2σ(I))	1988
Number of reflections/of constraints/number of parameters	3491/7/250
GOOF	1.047
R [*I* > 2σ(*I*)]	
R_1	0.0736
wR_2	0.1548
R (based on all reflections)	
R_1	0.1471
wR_2	0.1904
Residual electron density (ρ_{max}/ρ_{min})/*e Å*$^{-3}$	0.34/-0.31
CCDC	2410736

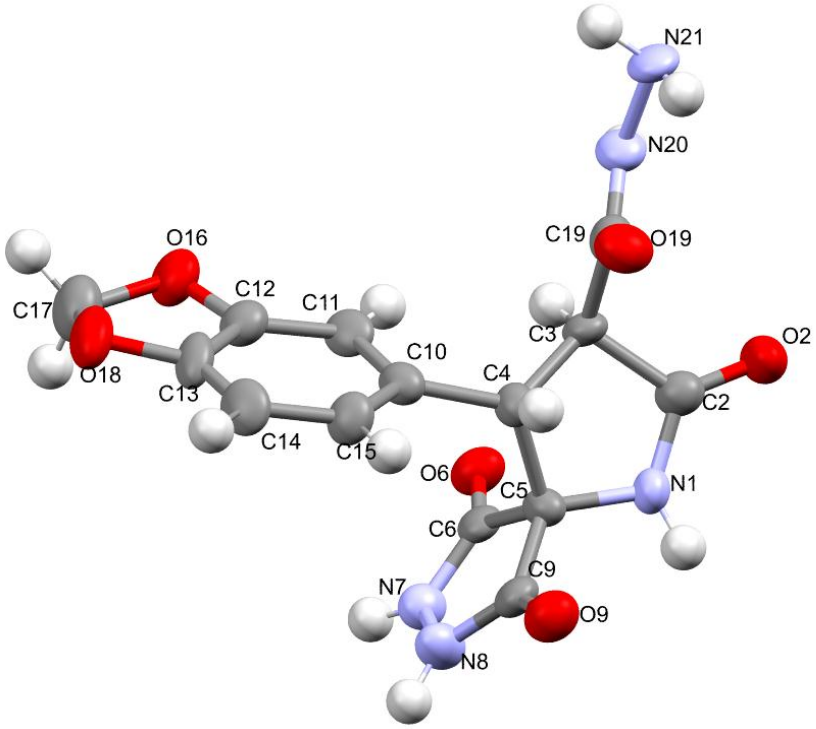

Fig. 50. Geometry of the molecule **2e** in a crystal, and the atomic numbering scheme. Anisotropic displacement ellipsoids are shown with a probability of 50%.

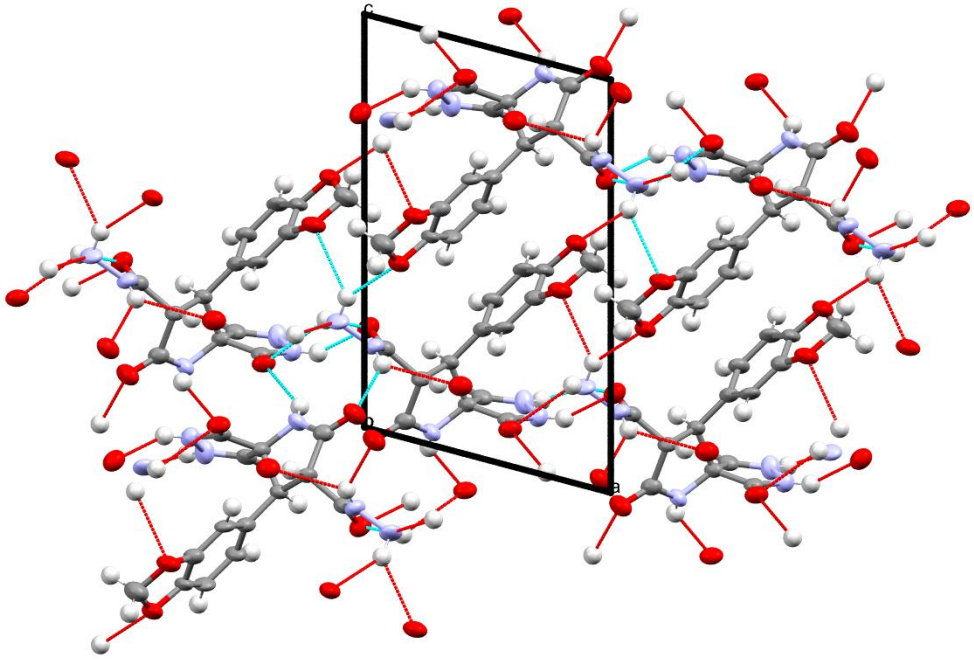

Fig. 51. Hydrogen bond system in crystal **2e** (shown by dotted line). Projection along b-axis.

Hydrogen bond parameters:

1. N1-H1...O6’ (1-x,1/2+y,-z): N1-H 0.87(7), H…O6’ 2.09(9), N1...O6’ 2.802(8) Å, angle N1-H1...O6’ 138(9)^{o};
2. N7-H7...O19’ (1+x,y,z): N7-H7 0.87(5), H7...O19’ 2.04(6), N7...O19’ 2.833(8) Å, angle N7-H7...O19’ 151(6)^{o};
3. N8-H8...N21’ (1+x,1+y,z): N8-H8 0.87(5), H8...N21’ 1.97(5), N8...N21’ 2.835(9), Å, angle N8-H8...N21’ 170(6)^{o};
4. N20-H20...O2’: (-x,-1/2+y,-z): N20-H20 0.87(8), H20...O2’ 2.18(8), N20...O2’ 2.874(8) Å, angle N20-H20...O2’ 137(8)^{o};
5. N21-H21A...O16’ (-1+x,y,z): N21-H21A 0.87(5), H21A...O16’ 2.59(7), N21...O16’ 3.156(8) Å, angle N21-H21A...O16’ 124(8)^{o};
6. N21-H21A...O18’ (1-x,-1/2+y,1-z): N21-H21A 0.87(5), H21A...O18’ 2.34(8), H21A...O18’ 3.097(9) Å, angle N21-H21A...O18’ 146(8)^{o};
7. N21-H21B...O6’ (-1+x,y,z): N21-H21B 0.87(4), H21B...O6’ 2.59(8), N21...O6’ 3.216(8) Å, angle N21-H21B...O6’ 129(7)^{o};
8. N21-H21B...O19 (intra): N21-H21B 0.87(4), H21B...O19 2.21(5), N21...O19 2.700(9) Å, angle N21-H21B...O19 116(6)^{o}