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Graphical Abstract

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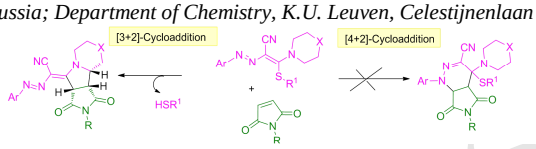

1,3-Dipolar cycloaddition of 3-alkylsulfanyl-2-arylazo-3-(*tert*-cycloalkylamino)acrylonitriles with *N*-methyl- and *N*-phenylmaleimides

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ABSTRACT

A series of 1,2-diaza-1,3-butadienes with terminal *S,N*-acetal function were obtained and reacted with *N*-methyl- and *N*-phenylmaleimides. As a result of the 1,3-dipolar cycloaddition, a range of new functionalized nonaromatic heterocyclic compounds including: octahydro-1*H*-pyrrolo[3,4-*a*]indolizine, octahydropyrrolo[3',4':3,4]pyrrolo[1,2-*a*]azepine, hexahydropyrrolo [3',4':3,4]pyrrolo[2,1-*c*][1,4]oxazine and -thiazine, were obtained with good yields in mild conditions. Experimental and theoretic results allowed establishment of a relationship between the structures of the *tert*-cycloalkylamine group and the activity of the azomethine ylides generated.

Keywords:
Diazadiene
S,N-acetal
Cycloaddition
Maleimide
Azomethine ylide

1. Introduction

It is known that intramolecular [3+2]-cycloaddition of azomethine ylides is a powerful tool to construct various nitrogen-containing cyclic systems from relatively simple precursors.[1] Among the heterocycles targeted by azomethine ylide cycloaddition methods the most popular are substituted pyrrolidines, dihydropyrroles and pyrroles.[1d,2]

To construct the heterocyclic systems with more complicated ring frameworks it is necessary to select precursors containing various functional groups, and enriched with double bonds and cyclic fragments.[3] A direct strategy to achieve this purpose is the employment of cyclic azomethine ylide moieties. The most known and widely described examples of azomethine ylides of this type were generated from nitrogen-containing five-membered saturated heterocycles, such as proline and 1,3-thiazolidin-4-carboxylic acid. Six-membered *tert*-cycloalkylamines most commonly utilized as substrates for the formation of this type of 1,3-dipole are oxazin-2-one and 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid. Piperidine-2-carboxylic acid is a less applied reagent. However, not every route available for generation of linear azomethine ylides is also suitable for their cyclic analogues.

A traditional and widely spread method for the generation of azomethine ylides is the reaction of aldehydes and ketones with *tert*-cycloalkylamines, first proposed by R. Grigg.[4] Electron withdrawing groups usually are included into the structure of the starting amines for the stabilization of the formed 1,3-dipole, such as: esters, carboxy- and carbonyl groups at the 2-position of morpholine and at the 2-position of pyrrolidine.[3e] This approach to cycloaddition was characterized by moderate yields and showed little *exo/endo* selectivity.[3e,4b,5] On the other hand, examples of the azomethine ylides obtained from unsubstituted pyrrolidine, piperidine, morpholine and, especially, azepine and thiomorpholine are more rare. The all abovementioned limitations of the known method for the formation of azomethine ylides prompted a search for new sources and new methods to generate the cyclic analogs. An important reason to develop new convenient routes to azomethine ylides, especially from *tert*-cycloalkyl amines, is the synthesis of nitrogen-containing nonaromatic heterocycles, that composed the key core motif of natural alkaloids.[6] New synthetic strategies for the construction of pyrrolizidines, indolizidines and their structural analogous scaffolds are of importance to many areas of pharmaceutical and biological research.

In this way, F. Laduron and H. G. Viehe have reported[7] on the generation of trifluoromethyl azomethine ylides either by heating α-trifluoromethyl thioaminals or by deprotonating trifluoromethyl thioamidium salts.

An original method for the generation of the azomethine ylides, is based on simultaneous formation of a cyclic fragment and a dipolar moiety.[8] Nonstabilized azomethine ylides have been formed from (2-azaallyl)stannanes and (2-azaallyl)silanes through an intramolecular *N*-alkylation/demetallation cascade. The resulting ylides undergo intramolecular [3+2]-cycloaddition with dipolarophiles to afford bicyclic or tricyclic products in good yield as 1:1 mixtures of *exo*- and *endo*-diastereomeres.

O-Methylation of α-hydroxy lactams, followed by treatment with cesium fluoride in the presence of methyl acrylate gave a bicyclic adduct intermediate in the synthesis of (±)-retronecine and (±)-indicine.[9] However, other imidate ylide cycloadditions were proved to be inconsistent, and exhibited low yields.[10]

In preliminary communications,[11] we have shown that 1,2-diaza-1,4-butadienes **1** with alkylthio- and *tert*-aminogroups at the terminal carbon atom are new convenient and available reagents, that rather easily and in mild conditions are able to generate azomethine ylides. As a result of [3+2]-cycloaddition reactions between these compounds and *N*-methyl- and *N*-phenylmaleimides **2a**,**b** we have synthesized a new tricyclic derivatives **3**,**4** which can be considered as a synthetic analogues of natural alkaloids of the pyrrolizidine type (Scheme 1).

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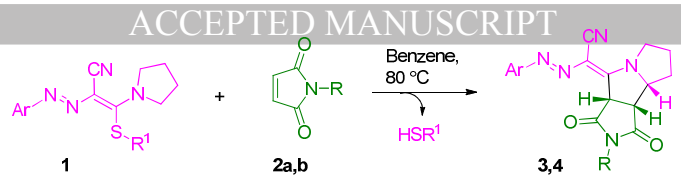


R^1 = Me, Allyl, Propargyl R = Me (**a**), Ph (**b**)

Ar = 4-$NO_2C_6H_4$, 4-$CF_3C_6H_4$, 4-$EtO_2CC_6H_4$, 4-$CF_3C_6H_4$, 2,4-$Cl_2C_6H_3$, 4-ClC_6H_4, 2-Cl-4-MeC_6H_3, Ph, 4-MeC_6H_4, 4-$EtOC_6H_4$, 4-$MeOC_6H_4$

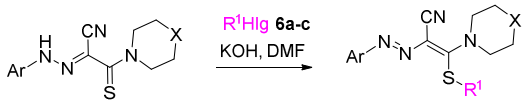
Scheme 1. Reaction of 3-alkylsulfanyl-2-arylazo-(3-pyrrolidin-1-yl)-acrylonitriles **1** with *N*-methyl- and *N*-phenylmaleimides **2a**,**b**.

The aim of the current work was to estimate the scope and limitations of the transformation of 1,2-diaza-1,3-butadienes, containing a terminal *S*,*N*-acetal function, to 1,3-dipoles, and to establish the relationship between the structure of the *tert*-cycloalkylaminogroup (ring size and amount or nature of the heteroatoms) and the reactivity of the azomethine ylide formed.

2. Results and discussion

Interaction of 3-alkylsulfanyl-2-arylazoacrylonitriles with N-methyl- and N-phenylmaleimides

The required 3-alkylsulfanylarylazoacrylonitriles **7-9** were synthesized by the *S*-alkylation of the arylhydrazonothioacetamides **5** according to a previously published method[11] in excellent yields (Scheme 2, Table 1). All compounds **7-9** were satisfactorily characterized by ^{1}H NMR spectroscopy and EI-MS spectrometry (see the Supplementary data for synthetic details and full analytical and spectroscopic characterization).



5 X = CH_2 Ar = 4-$NO_2C_6H_4$ (**a**), 4-ClC_6H_4 (**b**), Ph (**c**), 4-$MeOC_6H_4$ (**d**);
X = O Ar = 4-$NO_2C_6H_4$ (**e**), 4-$MeOC_6H_4$ (**f**), 3,5-$(CF_3)_2C_6H_3$ (**g**);
X = $(CH_2)_2$ Ar = 4-$NO_2C_6H_4$ (**h**), 4-ClC_6H_4 (**i**);
X = S Ar = 4-$NO_2C_6H_4$ (**j**), 4-$CF_3C_6H_4$ (**k**), 4-ClC_6H_4 (**l**)
6 R^1 = Me Hlg = I (**a**), R^1 = Allyl Hlg = Br (**b**), R^1 = Propargyl Hlg = Br (**c**)

Scheme 2. Synthesis of 3-methyl-, 3-allyl- and 3-propargylsulfanyl-2-arylazoacrylonitriles **7-9**.

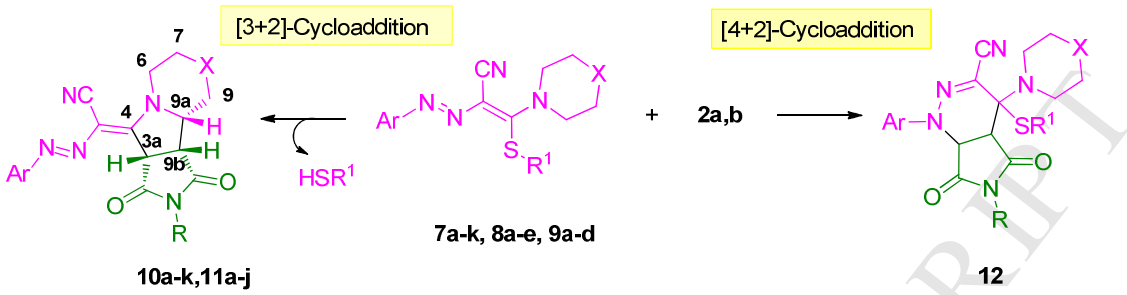
Table 1
The yields of the methyl-, allyl-, propargylsulfanylarylazoacrylonitriles **7a-k**, **8a-e** and **9a-d**

Entry	Compd, №	X	Ar	R	Yield[a] **7-9**, (%)
1	**7a**	CH_2	4-$NO_2C_6H_4$	Me	66
2	**8a**	CH_2	4-$NO_2C_6H_4$	Allyl	82
3	**9a**	CH_2	4-$NO_2C_6H_4$	Propargyl	91
4	**7b**	CH_2	4-ClC_6H_4	Me	90
5	**8b**	CH_2	4-ClC_6H_4	Allyl	91
6	**9b**	CH_2	4-ClC_6H_4	Propargyl	84
7	**7c**	CH_2	Ph	Me	83
8	**8c**	CH_2	Ph	Allyl	89
9	**9c**	CH_2	Ph	Propargyl	72
10	**7d**	CH_2	4-$MeOC_6H_4$	Me	82
11	**8d**	CH_2	4-$MeOC_6H_4$	Allyl	74
12	**9d**	CH_2	4-$MeOC_6H_4$	Propargyl	67
13	**7e**	O	4-$NO_2C_6H_4$	Me	64
14	**7f**	O	4-$MeOC_6H_4$	Me	86
15	**8e**	O	3,5-$(CF_3)_2C_6H_3$	Allyl	73
16	**7g**	$(CH_2)_2$	4-$NO_2C_6H_4$	Me	70
17	**7h**	$(CH_2)_2$	4-ClC_6H_4	Me	92
18	**7i**	S	4-$NO_2C_6H_4$	Me	58
19	**7j**	S	4-ClC_6H_4	Me	85
20	**7k**	S	4-$CF_3C_6H_4$	Me	67

[a] The isolated yield.

The reaction of 3-alkylsulfanylarylazoacrylonitriles **7a-k**, **8a-e** and **9a-d** with *N*-methyl- and *N*-phenylmaleimides **2a**,**b** was performed at reflux in dry benzene with excess of the dipolarophiles **2** (Scheme 3, Table 2). Compounds **10a-k** and **11a-j** were isolated by filtration and further purified by column liquid chromatography. The structures of tricyclic products **10-11** were confirmed by elemental analysis, EI-MS, and ^{1}H and ^{13}C NMR spectra as well as 2D ^{1}H-^{13}C HMQC, HMBC, ^{1}H-^{1}H NOESY experiments and X-ray data. The molecular ions of compounds **10a-k** and **11a-j** confirmed the addition of the reagents and the elimination of methyl-, allyl- or propargylthiol. The IR spectra exhibited absorption bands of the C-H bonds with ν wavenumber at 2800-3000 cm^{-1}, the CN-bond ν at 2200 cm^{-1} and the two carbonyl bonds ν in the region 1700-1720 cm^{-1}. The ^{1}H NMR spectra of cycloadducts **10a-k** and **11a-j** in DMSO-d_6 contain characteristic signals including: doublets for the H3a proton at δ 5.2-5.5 ppm, doublets of triplets or multiplets at δ 4.2-4.6 ppm for H6 proton, and two doublet of doublets or triplets at δ 3.7-4.1 ppm (J = 9.2-10.0

and J = 10.0-10.4 Hz) for H9b. A main feature of the NMR spectra of compounds **10-11** were the downfield shift of the *tert*-cycloalkylamine group protons. Registered chemical shift of the protons of this group and their multiplicity confirmed that they have participated in the process. It should be mentioned that ^{1}H and ^{13}C NMR spectra octahydro-1*H*-pyrrolo[3,4-*a*]indolizine **10** and **11a-d**, octahydropyrrolo[3',4':3,4]pyrrolo[1,2-*a*]azepine **10h**,**i** and **11g**,**h** and hexahydropyrrolo[3',4':3,4]pyrrolo[2,1-*c*][1,4]thiazine **10j**,**k** and **11i**,**j**, showed two sets of signals. Such spectral behavior was observed earlier for hexahydropyrrolo[3,4-*a*]pyrrolizines **3** and **4** (Scheme 1). This fact demonstrates that a mixture of two stereoisomers for compounds **10a-d**,**h-k** and **11a-d**,**g-j** was obtained (Table 3). Only the ^{1}H, ^{13}C spectra of pyrrolo[3,5-*a*][1,4]oxazines **10e-g** and **11e-f**, exhibited the presence of four isomers, although the predominance for the one of isomers was also observed.

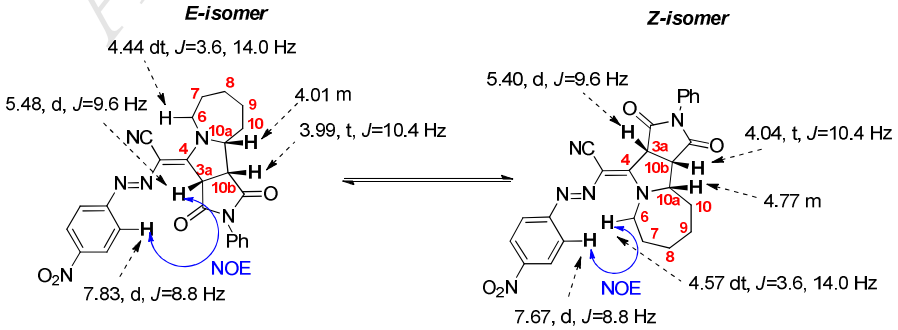


Scheme 3. 1,3-Dipolar cycloaddition of *S*,*N*-acetals **7a-k**, **8a-e**, and **9a-d** vs. hetero-Diels-Alder reaction of the 1,2-diazo-1,3-butadiene system.

Table 2
The time of conversion of the starting materials and yields of cycloadducts **10** for the reactions of **7-9** with *N*-methyl- and *N*-phenylmaleimides **2a,b**

Entry	Compounds **7-9**				Reaction with **2a** (R=Me)			Reaction with **2b** (R=Ph)		
	№	X	Ar	R^1	№	Time of conversion, (h)	Yield **10a-m**, (%)	№	Time of conversion, (h)	Yield **11a-m**, (%)
1	**7a**	CH_2	4-$NO_2C_6H_4$	Me	**10a**	2.5	90	**11a**	4.5	63
2	**8a**	CH_2	4-$NO_2C_6H_4$	Allyl	**10a**	1.5	97	**11a**	2.0	66
3	**9a**	CH_2	4-$NO_2C_6H_4$	Propargyl	**10a**	1.0	70	**11a**	1.0	70
4	**7b**	CH_2	4-ClC_6H_4	Me	**10b**	43	90	**11b**	12	90
5	**8b**	CH_2	4-ClC_6H_4	Allyl	**10b**	21	86	**11b**	8	97
6	**9b**	CH_2	4-ClC_6H_4	Propargyl	**10b**	21	83	**11b**	5	81
7	**7c**	CH_2	Ph	Me	**10c**	30	70	**11c**	16	89
8	**8c**	CH_2	Ph	Allyl	**10c**	10	71	**11c**	11	78
9	**9c**	CH_2	Ph	Propargyl	**10c**	6	83	**11c**	7	84
10	**7d**	CH_2	4-$MeOC_6H_4$	Me	**10d**	40	91	**11d**	50	64
11	**8d**	CH_2	4-$MeOC_6H_4$	Allyl	**10d**	70	62	**11d**	50	68
12	**9d**	CH_2	4-$MeOC_6H_4$	Propargyl	**10d**	20	44	**11d**	90	58
13	**7e**	O	4-$NO_2C_6H_4$	Me	**10e**	9	61	**11e**	8	92
14	**7f**	O	4-$MeOC_6H_4$	Me	**10f**	25	45	**11f**	20	67
15	**8e**	O	3,5-$(CF_3)_2C_6H_3$	Allyl	**10g**	20	60	-	-	-
16	**7g**	$(CH_2)_2$	4-$NO_2C_6H_4$	Me	**10h**	2.5	98	**11g**	0.5	86
17	**7h**	$(CH_2)_2$	4-ClC_6H_4	Me	**10i**	-	75	**11h**	1.5	78
19	**7i**	S	4-$NO_2C_6H_4$	Me	**10j**	46	45	**11i**	40	67
20	**7j**	S	4-ClC_6H_4	Me	**10k**	90	50	-	-	-
20	**7k**	S	4-$CF_3C_6H_4$	Me	-	-	-	**11j**	45	60

The stereochemistry of tricyclic compounds **7-8** was assigned in accordance to ^{1}H-^{1}H NOESY experiments. In the case of the *Z*-isomer there is a cross-peak for the H-*ortho* with H6 proton of tricyclic fragment (Scheme 4), while a strong NOESY cross-peak was observed between H-*ortho* and H3a in *E*-isomer. Signal of the nodal proton H3a in ^{1}H NMR spectra *Z*-isomer compounds **7-8** was deshielded in comparison to the same signal of *E*-isomers.

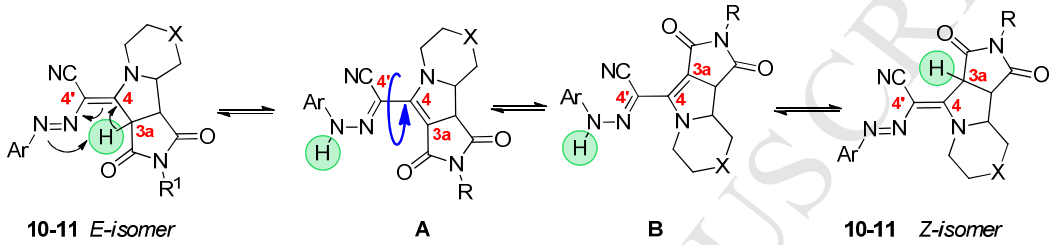


Scheme 4. Selected NMR spectra data for compound **11g** (in DMSO-d_6)

Table 3
The ratio of *Z*- and *E*-isomers for compounds **10** and **11a-d** in DMSO-d_6 in according the ^{1}H NMR data

Entry	Compound, №	R^1	R = Me		Compound, №	R = Ph	
			E-isomer, %	*Z*-isomer, %		*E*-isomer, %	*Z*-isomer, %
1	**10a**	4-$NO_2C_6H_4$	74	26	**11a**	74	26
2	**10b**	4-ClC_6H_4	70	30	**11b**	-	-
3	**10c**	Ph	65	35	**11c**	81	19
4	**10d**	4-$MeOC_6H_4$	60	40	**11d**	54	36

As can be concluded from the NMR spectral data for products **7-8** (Scheme 4), the *E*-isomer is the major one in contrast to hexahydropyrrolo[3,4-*a*]pyrrolizines[4,5] where both stereoisomers are present in equal ratio. All attempts to separate *Z*- and *E*-isomers of compounds **10-11** with column chromatography have failed. This may be explained by the existence of dynamic equilibrium between two stereo configurations generated from the nodal H3a proton due to the influence of electron-withdrawing group.[11] The 1,6-H shift to the nitrogen atom of the azo group leads to the formation of a tautomer A with a single C4-C4′ bond, then followed by the rotation around this bond (Scheme 5).



Scheme 5 Proposed mechanism of dynamic equilibrium between the *E*- and *Z*-isomers compounds **10-11**

Single-crystal X-ray determination was performed, confirming the formation of the *endo*-adduct of the 1,3-dipolar cycloaddition of the major stereoisomer – namely *E*-isomer hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]oxazine **10g** (Fig. 1).

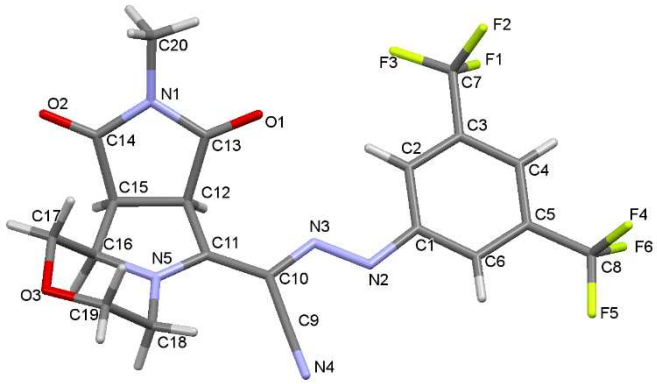
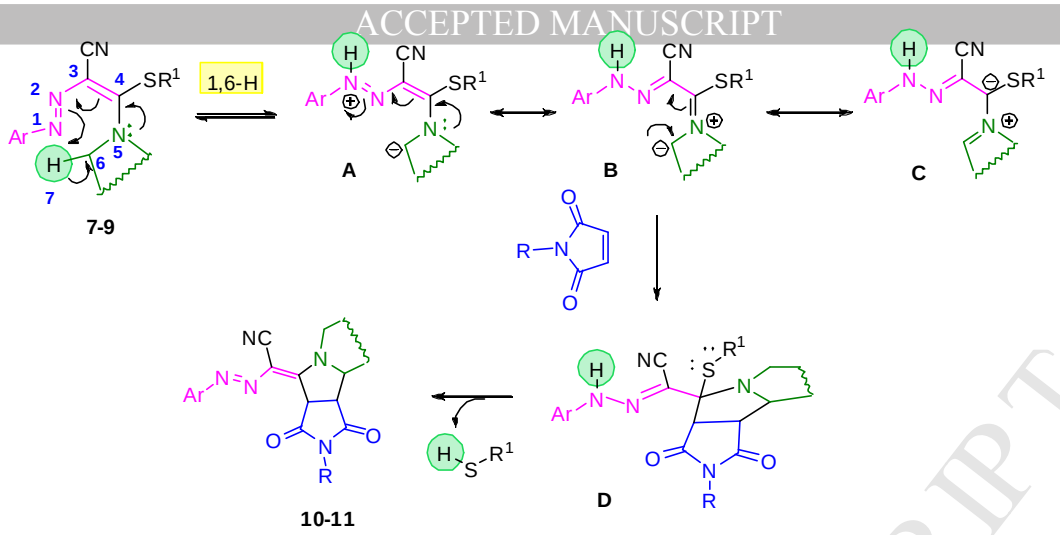


Fig. 1. Structure of hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]oxazine **10g** (X-ray data)

Mechanistic investigation

As discussed above, the 1,2-diaza-1,3-butadiene system did not take part in a [4+2]-cycloaddition reaction with *N*-methyl- or *N*-phenylmaleimides **2a**,**b**,[11] instead the [3+2]-cycloaddition occurred (Scheme 6). Previously we have elucidated that this is possibly due to a 1,6-hydrogen shift that proceeds with relative ease. The nature of this 1,6-shift is a pericyclic reaction assisted by a secondary orbital interaction rather than a pseudopericyclic one. This was confirmed by NBO[12] and ACID[13] methods. The spatial distortion of the π-system framework from planar geometry led to a weaker involvement of the lone pair of electrons located on N1 and a stronger involvement of the π-electrons. The activation barrier for the respective transition state was higher than the activation energy for the following cycloaddition. It is well known that relatively high activation barriers in pericyclic reactions are arising from electron-electron repulsion,[14] while in the course of a pseudopericyclic reaction this factor is avoided because of planar geometry and favorable interaction between nucleophilic/electrophilic centers located on the π-system.[15] By varying types of *N*-cycloalkyl groups in the 1,2-diaza-1,3-butadiene system, one can achieve a stronger planarity of transition state and thus, the mode of reaction mechanism can be controlled. Moreover, the change in planarity can also lead to a change in delocalization within the π-system and change the energies of the frontier orbitals. Thus, indirectly, [4+2]- vs. [3+2]-cycloaddition can be controlled via a change of the character of the frontier orbitals.



Scheme 6. Proposed mechanism of azomethine ylide generation and cycloaddition to *N*-methyl- and *N*-phenylmaleimides **2a**,**b**

To address the unresolved question of "structure-mechanism" relationship for this reaction we have performed density functionalcalculations at the B3LYP/6-31G** level using Gaussian 09 RevC.01[16] to connect the geometrical features of *S*,*N*-acetals[11] with their reactivity. In the first step, we have fully optimized substrates **1a**,**b** and **7a**,**d-g**,**i**,**l**,**m**. The true character of the minima for all structures was confirmed by calculation of the Hessian matrix. Geometric parameters of compounds **1** and **7** were collected in Table 4.

Table 4
Optimized geometry parameters of compounds **1a**,**b** and **7a**,**d-g**,**i**,**l**,**m** (B3LYP/6-31+G**)

Entry	Compounds			Optimized geometry parameters				
	№	Ar	X	rH7-C6, Å	rN1···H7, Å	tN1N2C3C4, °	tN2C3C4N5, °	tC3C4N5C6, °
1	**1a**	4-$NO_2C_6H_4$	CH_2	1.096	2.186	6.2	42.6	16.7
2	**1b**	4-$MeOC_6H_4$	CH_2	1.096	2.164	-10.1	-36.7	-20.2
3	**7a**	4-$NO_2C_6H_4$	$(CH_2)_2$	1.086	2.473	-3.6	40.4	31.6
4	**7d**	4-$MeOC_6H_4$	$(CH_2)_2$	1.097	2.483	-6.6	-34.4	-27.6
5	**7e**	4-$NO_2C_6H_4$	O	1.089	2.523	-2.5	35.6	30.5
6	**7f**	4-$MeOC_6H_4$	O	1.095	2.448	7.6	33.6	27.3
7	**7g**	4-$NO_2C_6H_4$	$(CH_2)_3$	1.086	2.386	-3.5	42.4	26.2
8	**7l**	4-$MeOC_6H_4$	$(CH_2)_3$	1.087	2.426	-1.4	36.7	30.0
9	**7i**	4-$NO_2C_6H_4$	S	1.089	2.577	1.1	38.3	27.0
10	**7m**	4-$MeOC_6H_4$	S	1.094	2.590	1.5	33.4	32.1

In the second step, the obtained electron density was analyzed by means of the Natural Bond Orbitals (NBO) localization scheme[12] and Atoms in Molecules (AIM) analysis.[17] Results of NBO and AIM analyses were listed in Table 5.

Assuming that the transition state (TS) is a superposition of the starting and final states for the process, the TS for a 1,6-H transfer in compounds **7** is expected to have a non-planar geometry. A non-planar atomic arrangement of the π-system of compounds **7** (see torsion angles' values at Table 4) is consistent with the assumption of a pericyclic mechanism. In addition, one can stipulate that the shorter non-covalent interaction N···H should enhance reaction rates. The values of bond lengths, r(H···N) and r(CH), depend on the type of *tert*-cycloalkylamino fragment and the nature of the substituent in the aromatic ring. As it follows from the results of calculations (Table 4) the closest N···H contact was observed for arylazoacrylonitriles containing pyrrolidine (**1a**,**b**), piperidine (**7a**) and azepine (**7g**,**h**) residues. Thus, a higher probability should be expected for the 1,6-H shift to occur. Indeed, the insertion of an azepine or piperidine fragment led to the acceleration of the 1,3-cycloaddition reaction. According to experimentally observed values of time vs. conversion (Table 2), the cycloaddition goes at a faster rate (2.5-4.5 h) for compounds **7a** against 8-9 h for compounds **7e** or 40-46 h for compounds **7i**. To estimate the nature and the strength of the N···H interaction we have performed NBO and AIM analysis to obtain the electron density. According to the NBO data presented in the Table 5, a very weak bonding was registered between N1 and H7, as a result of the overlapping of the π(N1-N2) or/and LP(N1) orbitals with the σ*(C6-H7) orbital. This interaction was observed for the compounds **1a**,**b**,**7f**. Interestingly, these alkylsulfanylarylazoacrylonitriles exhibited higher rates of conversion (Table 5). The stabilization energy values for this interaction were between 0.6 and 2.8 kcal/mol.

The value of electron density ρ(BCPN···H) at the bond critical points, BCP (3,-1), can provide information about the strength of this interaction. Topological AIM analysis of electron density for compounds **7** supported the existence of an interaction between N1 and H7 atoms in all compounds (except *S*,*N*-acetals **7e**,**j**,**n**), since N···H bond critical point was located. According to hydrogen bond classification by AIM descriptors,[18] the value of electron density, ρ(BCPNH), which was calculated to be in range between $2.000 \cdot 10^{-3}$ a.u. and $3.500 \cdot 10^{-2}$ a.u. (Table 5), suggests that the N···H hydrogen bond is moderately strong.

The degree of electron density expansion from the lone pair of electrons on the N1 atom to the vacant σ*(C6-H7) bond may be quantitatively characterized by the covalence ratio factor (χ) for the formed N···H bond via equation (eq. 1), as previously introduced by F. Weinhold and coworkers.[19]

$$\chi = \frac{(R_N+R_H)-d_{NH}}{(R_N+R_H)-(r_N+r_H)} \leq 1 \quad (1)$$

where R_N and R_H stand for the van der Waals radii and r_N и r_H for the covalent radii of the interacting atoms; d_{NH} is experimentally determined (or calculated) contact.

Table 5

The data of the electron density analysis between C-H and N···H atoms during 1,6-H shift by the NBO and AIM (B3LYP/6-31+G**) methods and the X-ray data

Entry	Compd., N	NBO (B3LYP/6-31+G**) $E(2)$n → σ*, kcal/mol	AIM (B3LYP/6-31+G**) $E(2)$ π → σ*, kcal/mol	ρ(BCPN···H), $^{x}10^{-2}$ a.u.	ρ (BCPC-H), $^{x}10^{-1}$ a.u.	Covalence ratio factor, χ
1	**1a**	2.64	0.65	2.1198	2.8524	0.31
2	**1b**	2.80	0.65	2.1928	2.8506	0.32
3	**7a**	-	0.74	1.2352	2.9162	0.14
4	**7d**	-	-	1.3733	2.8268	0.13
5	**7e**	-	-	-	2.7826	0.13
6	**7f**	0.58	-	1.4882	2.7741	0.15
7	**7g**	-	0.69	1.4846	2.8533	0.19
8	**7m**	-	0.53	1.3822	2.9143	0.16
9	**7j**	-	-	-	2.8223	0.07
10	**7n**	-	-	-	2.7882	0.07

The covalence ratio for these compounds were ~7-32% and this was decreasing in the series:

1b > 1a > 7g > 7 m > 7f > 7a > 7d ≈ 7e > 7j ≈ 7n

The canonical orbital diagram (Fig. 2) constructed with the help of B3LYP/6-31G** level using the Gaussian 09 RevC.0116 method suggests that the cycloaddition reaction is driven by the interaction between the HOMO of the dipole (*S*,*N*-acetal **7g**) and the LUMO located on the dipolarophile **2a**.

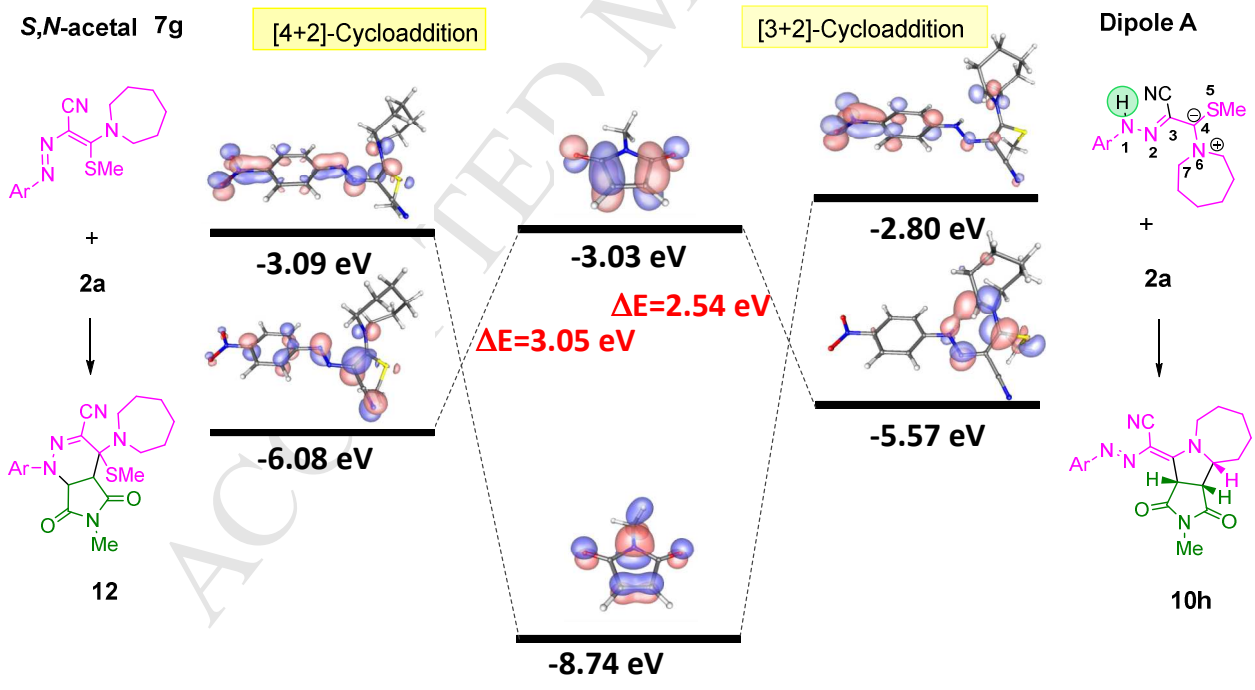


Fig. 2. Orbital diagram for the two directions of the *S*,*N*–acetals **7g** reaction with *N*-methylmaleimides **2a**

We suggested that the cycloaddition could proceed through two following reaction pathways:

(a) The first one includes reaction of dienophile **2a** with *S*,*N*-acetal **7** as the diene. This mechanism i.e. [4+2]-cycloaddition is shown on the left side of the Fig. 2.

(b) The second one starts with a 1,6-shift yielding **dipole A**. Then, the newly generated dipole reacts with dipolarophile **2a**. This process is depicted on the right half of the Fig. 2.

A comparison of the energy gap between the frontier orbitals for both pathways favors the [3+2]-cycloaddition. Its gap Δ*E* was calculated to be 2.54 kcal/mole, while for [4+2]-cycloaddition (pathway a) the energy gap was 3.05 kcal/mol.

According to NBO calculations the HOMO of dipole for **7g** can be represented as a following combination of NBOs:

$$\Psi^{HOMO}\text{ (Dipole A)} = 0.481\,\chi^{LP(C7)} + 0.387\chi^{\pi(C4N6)} - 0.383\,\chi^{\pi^*(C4N6)} + 0.327\chi^{\pi(N2C3)} - 0.281\chi^{LP(S5)} + 0.241\chi^{LP(N1)} + 0.239\chi^{\pi^*(N2C3)} \quad (2)$$

Higher coefficients for NBOs localized on C7, N6 and C4 atoms are in line with the involvement of the 1,3-dipole in cycloaddition rather than the involvement of the diazadiene system.

Conclusion

In this paper, we describe the reactivity of azomethine ylides generated from alkylsulphanylarylazoacrylonitriles **7-9** toward substituted maleimides **2a**,**b**, which led to a [3+2]-cycloaddition reaction independent of the type of *tert*-cycloalkylaminogroup, substituents at the aromatic ring and thio fragment. A variety of *N*- cycloalkyl groups, such as piperidine, morpholine, thiomorpholine and azepine, may be introduced in structure of alkylsulfanylarylazoacrylonitriles without change in the reaction outcome. Thus we have extended the scope of this new method for the generation of azomethine ylides from available diazadienes with terminal *S,N*-acetal group.

A quantum chemistry study has shown that simultaneous 1,6-H shift occurs to generate reactive ylide species and this mechanism distinguishes this method considerably from other well-known routes. Extended conjugation of the 1,2-diaza-1,3-butadiene π-system linked with aromatic and *tert*-cycloalkylamino groups in the terminal positions is a key features in this approach.

Ylides lacking stabilizing groups in cycloalkylamine fragment underwent cycloaddition with *N*-methyl- and *N*-phenylmaleimides resulting in non-aromatic heterocyclic *endo*-adducts with high yields. The observed high stereoselectivity of the reaction occurring in mild conditions has allowed us to develop a facile synthesis of functionalized - dioxohexahydro-1*H*-pyrrolo[3,4-*a*]indolizine, hexahydropyrrolo[3',4':3,4]pyrrolo[2,1-*c*][1,4]oxazine, hexahydropyrrolo[3',4':3,4]pyrrolo[2,1-*c*][1,4]thiazine and octahydropyrrolo[3',4':3,4]pyrrolo[1,2-*a*]azepine. This protocol can be incorporated in new routes toward piperidine, or indolizidine natural alkaloids and their analogs, since these heterocycles are the main cyclic fragments in their structure.

Experimental section

4.1. General

Melting points were determined with a Stuart SMP3 apparatus. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance II (400 MHz for ^{1}H and 100.6 MHz for ^{13}C) spectrometer using DMSO-d_6 and $CDCl_3$ as solvents. Chemical shifts (δ) have been reported in parts per million (ppm) relative to TMS in ^{1}H and ^{13}C spectra. Coupling constants (*J*) values given in Hertz. Mass spectra were performed on a «SHIMADZU GCMS-QP2010 Ultra» mass spectrometer using the electron impact ionization technique (40-200 ^{o}C, 70 eV). The IR data have been recorded on a Bruker Alpha (NPVO, ZnSe) IR-Fur spectrometer. Elemental analyses were carried out using a CHNS/O analyzer Perkin-Elmer 2400 Series II instrument. Single crystal X-ray diffraction analyses have been performed on an Xcalibur S CCD area-detector diffractometer (MoKα irradiation, ω-scanning with step 1o, 295(2) K). Absorption correction was not performed. Solution and refinement of structures were accomplished with the SHELXTL program package.[20]

For **10g**, the crystal system is triclinic, a = 8.289(2) Å, b = 8.6627(12) Å, c = 13.0570(14) Å, α = 94.191(12)^o, β = 93.649(16)o, γ = 99.640(16)^o, space group P-1, Volume 919.1(3) Å3, Z = 2, μ = 0.216 mm^{-1}. Reflections collected/independent/with [I > 2σ(I)].038/5775/2453, R_{int} = 0.0315, completeness to θ = 26.00^o 98.5 %. S = 1.001, final R indices: R^1 = 0.0487, wR^2 = 0.0806 [I > 2σ(I)], R^1 = 0.1296, wR^2 = 0.0888 (all data). Largest diff. peak and hole: 0.461 and –0.419 ēÅ-3.

CCDC 902766 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via link www.ccdc.cam.ac.uk/data_request/cif.

Chromatographic purification of compounds **10-11** was done using silica gel (0.035–0.070, 60 Å). The reactions were monitored on silica gel plates (Sorbfil UV–254) and visualization was effected by short wavelength UV light (254 nm). Solvents were dried and distilled according to the common procedure.

All calculations have been done with a help of G09 2 suit.[16] Structures were initially optimized at the B3LYP/6-31G* level of theory. All located points had a minima character according to Hessian calculation. NBO analysis was performed at the same level of theory by using the appropriate module, implemented in G09.[21] The obtained B3LYP/6-31G* wave functions were studied by the AIM method with the help of AIMAll software.[22]

Arylhydrazonoethanethioamides **5** and *S,N*-acetals **7-9** were prepared by the procedure reported in our previous articles.[11,23]

*4.2. Reaction S,N-acetals **7-9** with N-methyl- and N-phenylmaleimides **2a**,**b**.*

General procedure: A solution of 0.3 mmol of *S,N*-acetals **7-9** and 1.5 mmol dipolarophiles **2a**,**b** was heated at reflux in 10 ml of benzene (TLC). Products were filtered and purified by liquid column chromatography (eluent: chloroform-acetone 20:1)

*4.2.1. 2-(2-Methyl-1,3-dioxo-6,7,8,9,9a,9b-hexahydro-3aH-pyrrolo[3,4-a]indolizin-4-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**10a**).* From **7a** and **2a** (0.105 g, 90%), **8a** and **2a** (0.114 g, 97%), **9a** and **2a** (0.083 g, 70%) as an orange solid, m.p. 269-270 ^{o}C; Mixture of isomers (1:3); [Found: C, 57.8; H, 4.47; N, 21.5. $C_{19}H_{18}N_6O_4$ requires C, 57.86; H, 4.60; N, 21.3%]; ν_{max} 3100, 3030, 2950, 2860, 2200, 1720 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.28 and 7.84, 8.28 and 7.65 (4H, two AA'XX', *J* 8.6 Hz, Ar), 5.22 and 4.72 (1H, two d, *J* 9.2 Hz, CH), 5.22 and 4.83 (1H, two d, *J* 12.2 Hz, CH), 4.29 (1H, dt, *J* 10.2, 2.6 Hz, CH), 3.83 and 3.78 (1H, t, *J* 9.7 Hz, CH), 3.41-3.33 (m, 1H, CH), 2.89 (3H, s, NMe), 2.09-1.95 (1H, m, CH), 1.90-1.76 (2H, m, CH_2), 1.63-1.49 (2H, m, CH_2), 1.35-1.19 (1H, m, CH); δ_c (100.6 MHz, DMSO-d_6) 174.5 (CO), 172.6 (CO), 160.5 (C), 146.2 (C), 125.2 (CH), 122.4 (CH), 117.1 (C),

114.4 (C), 100.1 (C), 67.2 (CH), 53.8 (CH), 47.0 (CH_2), 42.9 (CH), 29.1 (CH_2), 25.6 (NCH_3), 24.4 (CH_2), 23.2 (CH_2); m/z (I, %): 394 (25, M^+).

*4.2.2. 2-[(4-Chlorophenyl)azo]-2-(2-methyl-1,3-dioxo-6,7,8,9,9a,9b-hexahydro-3aH-pyrrolo[3,4-a]indolizin-4-ylidene)acetonitrile (**10b**).* From **7b** and **2a** (0.103 g, 90%), **8b** and **2a** (0.100 g, 86%), from **9b** and **2a** (0.98 g, 83%) as a yellow solid, m.p. 273-274 °C; Mixture of isomers (1:2); [Found: C, 59.5; H, 4.5; N, 18.1. $C_{19}H_{18}ClN_5O_2$ requires C, 59.45; H, 4.73; N, 18.25%]; ν_{max} 1710, 2190, 2860, 2920, 2955 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 7.68 and 7.49, (4H, AA'XX', *J* 8.8 Hz, Ar), 5.21 and 4.75 (1H, two d, *J* 9.2 Hz, CH) 5.20 and 4.64 (1H, d, *J* 11.9 Hz, CH), 4.21 (1H, dt, *J* 10.0, 3.2 Hz, CH), 3.82 and 3.78 (1H, two dd, *J* 9.2, 10.4 Hz, CH_2), 3.42-3.34 (1H, m, CH_2), 2.89 and 2.87 (3H, two s, NMe), 2.07-1.94 (1H, m, CH_2), 1.90-1.72 (2H, m, CH_2), 1.59-1.45 (2H, m, CH_2), 1.27-1.12 (1H, m, CH_2); δ_c (100.6 MHz, DMSO-d_6) 174.8 (CO), 173.1 and 172.9 (C), 160.9 and 155.6 (C), 152.1 and 151.7 (C), 132.9 and 132.4 (C), 129.8 and 129.4 (CH), 123.6 and 123.2 (CH), 115.9 and 115.0 (C), 104.3 and 101.4 (C), 66.8 and 66.3 (CH), 53.9 and 52.9 (CH), 49.3 and 46.5 (CH_2), 43.9 and 43.0 (CH), 29.2 and 29.0 (CH_2), 25.7 and 25.6 (NCH_3), 24.6 and 24.2 (CH_2), 23.3 and 23.2 (CH_2); m/z (I, %): 383 (20, M^+).

4.2.3. *2-(2-Methyl-1,3-dioxo-6,7,8,9,9a,9b-hexahydro-3aH-pyrrolo[3,4-a]indolizin-4-ylidene)-2-(phenylazo)acetonitrile (**10c**).* From **7c** and **2a** (74 g, 70%), from **8c** and **2a** (75 g, 71%), from **9c** and **2a** (87 g, 83%) as a yellow solid, m.p. 286-287 °C; Mixture of two isomers (4:7); [Found: C, 65.2; H, 5.4; N, 20.1. $C_{19}H_{19}N_5O_2$ requires C, 65.32; H, 5.48; N, 20.04%]; ν_{max} 1710, 2200, 2860, 2920, 2960, 3000, 3030, 3060 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 7.68 (1H, d, *J* 7.2 Hz, Ar), 7.55-7.18 (4H, m, Ar), 5.25 and 4.77 (1H, two d, *J* 12.6 Hz, CH), 5.20 and 4.63 (1H, two d, *J* 9.0 Hz, CH), 4.18 (1H, dt, *J* 12.6, 9.0 Hz, CH), 3.82 and 3.76 (1H, two t, *J* 10.2 Hz, CH_2), 3.43-3.18 (1H, m, CH_2), 2.92 and 2.90 (3H, two s, NMe), 2.16-1.98 (1H, m, CH_2), 1.97-1.70 (2H, m, CH_2), 1.67-1.38 (2H, m, CH_2), 1.26-1.03 (1H, m, CH_2); δ_c (100.6 MHz, DMSO-d_6) 173.6 (CO), 171.9 and 171.6 (CO), 160.0 and 154.6 (C), 152.8 and 152.5 (C), 132.2 and 132.0 (C), 129.3 and 129.0 (CH), 128.9 and 128.8 (CH), 121.4 and 121.1 (C), 115.6 and 114.8 (C), 103.7 and 101.0 (C), 66.5 and 65.9 (CH), 53.69 and 52.6 (CH), 48.7 and 46.0 (CH_2), 43.7 and 42.7 (CH), 28.9 and 28.6 (CH_2), 24.1 and 23.7 (CH_2), 23.0 and 22.8 (CH_2); m/z (I, %): 349 (25, M^+).

*4.2.4. 2-[(4-Methoxyphenyl)azo]-2-(2-methyl-1,3-dioxo-6,7,8,9,9a,9b-hexahydro-3aH-pyrrolo[3,4-a]indolizin-4-ylidene)acetonitrile (**10d**).* From **7d** and **2a** (0.103 g, 91%), from **8d** and **2a** (0.070 g, 62%), from **9d** and **2a** (0.50 g, 44%) as a yellow solid, m.p. 223-224 °C; Mixture of isomers (2:3); [Found: C, 63.2; H, 5.7; N, 18.4. $C_{20}H_{21}N_5O_3$ requires C, 63.31; H, 5.58; N, 18.46%]; ν_{max} 1710, 2190, 2850, 2920, 2960, 3070 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 7.65, 7.49, 6.96, (4H, two AA'XX', *J* 9.0 Hz, Ar), 5.24 and 4.77 (1H, two d, *J* 11.6 Hz, CH), 5.14 and 4.57 (1H, two d, *J* 9.0 Hz, CH), 4.11 (1H, dt, *J* 11.6, 2.4 Hz, CH), 3.83 (3H, s, OMe), 3.80-3.72 (m, 1H, CH_2), 3.30-3.20 (1H, m, CH_2), 2.93 and 2.92 (3H, two s, NMe), 2.06 (1H, t, *J* 12.2 Hz, CH_2), 2.00-1.89 (1H, m, CH_2), 1.85-1.80 (1H, m, CH_2), 1.65-1.50 (2H, m, CH_2), 1.35-1.10 (1H, m, CH_2); δ_c (100.6 MHz, DMSO-d_6) 175.0 (CO), 173.5 and 173.2 (CO), 160.2 and 154.2 (C), 159.8 and 159.7 (C), 147.5 and 147.1 (C), 123.5 and 123.2 (CH), 116.3 and 115.4 (C), 115.0 and 114.6 (C), 103.9 and 101.0 (C), 66.2 and 65.7 (CH), 55.9 and 55.8 (OCH_3), 53.6 and 52.6 (CH), 49.1 and 46.3 (CH_2), 44.0 and 43.0 (CH), 29.3 and 29.0 (CH_2), 25.6 and 25.2 (NCH_3), 24.6 and 24.3 (CH_2), 23.4 and 23.2 (CH_2); m/z (I, %): 379 (46, M^+).

*4.2.5. 2-(8-Methyl-7,9-dioxo-1,3,4,6a,9a,9b-hexahydropyrrolo[1,2]pyrrolo[3,5-a][1,4]oxazin-6-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**10e**).* From **7e** and **2a** (0.072 g, 61%) as an orange solid, m.p. 326-327 °C; Mixture of isomers (2:12:1:6); [Found: C, 54.7; H, 4.1; N, 21.3. $C_{18}H_{16}N_6O_5$ requires C, 54.55; H, 4.07; N, 21.20%]; ν_{max} 1710, 2200, 2855, 2950, 3090 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.30, 7.89, 7.83, 7.69 (4H, four AA'XX', *J* 9.2 Hz, Ar), 5.31, 5.19, 5.07, 4.98 (1H, four d, *J* 9.2 Hz, CH), 4.77, 4.68, 4.65, 4.59 (1H, four d, *J* 8.8 Hz, CH), 4.36 (1H, dt, *J* 10.8, 3.6 Hz, CH), 4.11 (1H, dt, *J* 12.0, 3.6 Hz, CH), 4.02-3.80 (2H, m, CH_2), 3.71-3.53 (2H, m, CH_2), 3.39-3.28 (1H, m, CH_2), 2.88 and 2.86 (3H, two s, Me); δ_c (100.6 MHz, DMSO-d_6) 175.4 and 175.3 and 174.1 (CO), 173.7 and 172.6 and 172.3 (CO), 162.7 and 162.2 (C), 158.0 and 157.4 and 157.0 (C), 146.5 and 146.4 (C), 125.4 and 125.2 (CH), 122.7 and 122.5 and 122.3 (CH), 115.3 and 115.0 and 114.4 (C), 106.1 and 103.3 and 102.7 and 100.0 (C), 68.4 and 68.3 (CH_2), 64.8 and 64.3 (CH_2), 64.1 and 67.7 (CH), 54.0 and 53.2 (CH), 46.9 and 46.8 (CH_2), 41.9 and 41.1.6 (CH), 25.9 and 25.8 and 25.7 (NCH_3); m/z (I, %): 396 (39, M^+).

*4.2.6. 2-[(4-Methoxyphenyl)azo]-2-(8-methyl-7,9-dioxo-1,3,4,6a,9a,9b-hexahydropyrrolo[1,2]pyrrolo[3,5-a][1,4]oxazin-6-ylidene)acetonitrile (**10f**).* From **7f** and **2a** (0.051 g, 45%) as a yellow solid, m.p. 280-281 °C; Mixture of isomers (1:1); [Found: C, 60.0; H, 4.9; N, 18.4. $C_{19}H_{19}N_5O_4$ requires C, 59.84; H, 5.02; N, 18.36%]; ν_{max} 1700, 2195, 2830, 2965, 2995 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 7.70, 7.54, 7.03, 7.00 (4H, two AA'XX', *J* 9.2 Hz, Ar), 5.11 and 4.56 (1H, two d, *J* 8.9 Hz, CH), 4.88 and 4.46 (1H, two d, *J* 12.3 Hz, CH), 4.22 (1H, dt, *J* 12.3, 3.6 Hz, CH), 4.09 (1H, dt, *J* 12.0, 3.2 Hz, CH), 3.91 (3H, s, OMe), 3.93-3.75 (2H, m, CH_2), 3.63-3.45 (2H, m, CH_2), 2.87 and 2.73 (4H, m, NMe+CH); δ_c (100.6 MHz, DMSO-d_6) 174.7 (CO), 173.4 and 172.8 (CO), 160.4 and 160.1 (C), 159.7 and 155.1 (C), 147.7 and 147.3 (C), 128.8 and 123.6 (CH), 115.1 and 115.0 (C), 114.9 and 114.6 (CH), 102.7 (C), 64.8 and 64.9 (CH_2), 62.5 and 62.4 (CH_2), 59.8 and 59.7 (CH), 55.9 and 55.6 (NMe), 52.6 and 55.3 (CH), 49.4 and 45.6 (CH_2), 4.3 and 40.7 (CH), 25.8 (OMe); *m/z* (I, %): 381 (29, M^+).

*4.2.7. 2-[3,5-Bis(trifluoromethyl)phenyl]azo-2-(8-methyl-7,9-dioxo-1,3,4,6a,9a,9b-hexahydropyrrolo[1,2]pyrrolo[3,5-a][1,4]oxazin-6-ylidene)acetonitrile (**10g**).* From **8e** and **2a** (0.09 g, 60%) as a yellow solid, m.p. 225-226 °C; Mixture of isomers (12:3:2:2); [Found: C, 49.1; H, 2.9; N, 14.4. $C_{20}H_{15}F_6N_5O_3$ requires C, 49.29; H, 3.10; N, 14.37%]; δ_H (400 MHz, DMSO-d_6) δ 8.29, 8.21, 8.16, 7.97, 7.95, 7.88, 7.82, 7.78, 7.53 (3H, all s, Ar), 5.23, 5.11, 5.05 and 4.95 (1H, four d, *J* 9.6 Hz, CH), 4.75, 4.71, 4.68 and 4.63 (1H, four d, *J* 8.8 Hz, CH), 4.33 (1H, dt, *J* 10.8, 3.2 Hz, CH), 4.14 (1H, dd, *J* 11.6, 3.2 Hz, CH_2), 3.96-3.83 (2H, m, CH_2), 3.70-3.53 (2H, m, CH_2), 3.34 (1H, t, *J* 11.6 Hz, CH_2), 2.92 and 2.91 (3H, two s, Me); m/z (I, %): 487 (40, M^+).

*4.2.8. 2-(2-Methyl-1,3-dioxo-3a,6,7,8,9,10,10a,10b-octahydropyrrolo[1,2]pyrrolo[3,5-a]azepin-4-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**10h**).* From **7g** and **2a** (0.120 g, 98%) as an orange solid, m.p. 205-206 °C; Mixture of isomers (3:7); [Found: C, 58.7; H, 4.9; N, 20.39. $C_{20}H_{20}N_6O_4$ requires C, 58.82; H, 4.94; N, 20.58%]; ν_{max} 1720, 2195, 2850, 2925 cm^{-1}; δ_H (400

MHz, DMSO-d_6) 8.28, 7.83, 7.65 (8.28, 7.83, 8.28 and 7.65 (4H, two AA'XX', *J* 9.2 Hz, Ar), 5.33 and 4.82 (1H, two d, *J* 9.2 Hz, CH), 4.77-4.62 (1H, m, CH), 4.46 and 4.33 (1H, two dt, *J* 5.2, 15.2 Hz, CH), 3.76-3.61 (1H, m, CH), 3.45-3.32 (1H, m, CH), 2.88 (3H, s, NMe), 2.10-1.97 (1H, m, CH), 1.93-1.73 (3H, m, CH_2), 1.70-1.49 (3H, m, CH_2), 1.35-1.23 (1H, m, CH); δ_c (100.6 MHz, DMSO-d_6) 175.1 (CO), 172.3 (CO), 163.2 (C), 157.9 and 157.5 (C), 146.0 (C), 123.5 and 123.2 (CH), 116.3 and 115.4 (C), 115.0 and 114.6 (C), 103.9 and 101.0 (C), 66.2 and 65.7 (CH), 55.9 and 55.8 (OCH_3), 53.6 and 52.6 (CH), 49.1 and 46.3 (CH_2), 44.0 and 43.0 (CH), 29.3 and 29.0 (CH_2), 25.6 and 25.2 (NMe), 24.6 and 24.3 (CH_2), 23.4 and 23.2 (CH_2); *m/z* (I, %): 408 (11, M^+).

*4.2.9. 2-[(4-Chlorophenyl)azo]-2-(2-methyl-1,3-dioxo-3a,6,7,8,9,10,10a,10b-octahydropyrrolo[1,2]pyrrolo[3,5-a]azepin-4-ylidene)acetonitrile (**10i**).* From **7h** and **2a** (0.09 g, 75%) as a yellow solid, m.p. 250-251 °C; Mixture of isomers (2:3); [Found: C, 60.5; H, 4.8; N, 17.3. $C_{20}H_{20}ClN_5O_2$ requires C, 60.38; H, 5.07; N, 17.60%]; ν_{max} 1700, 2200, 2860, 2920, 2955, 3050, 3080 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 7.65, 7.37, 7.48 and 7.38 (4H, two AA'XX', *J* 8.8 Hz, Ar), 5.24 and 4.74 (1H, two d, *J* 9.2 Hz, CH), 4.63-4.53 (1H, m, CH), 4.51 and 4.35 (1H, two dt, *J* 5.2, 14.8 Hz, CH), 3.85 and 3.79 (1H, two t, *J* 10.0 Hz, CH_2), 3.63-3.49 (1H, m, CH_2), 2.91 and 2.90 (3H, two s, Me), 2.08-1.95 (1H, m, CH_2), 1.94-1.76 (3H, m, CH_2), 1.71-1.52 (3H, m, CH_2), 1.37-1.19 (1H, m, CH_2); δ_C (100.6 MHz, DMSO-d_6) 175.3 (CO), 172.8 and 172.6 (CO), 161.8 and 156.2 (C), 152.1 and 151.9 (C), 132.6 and 132.4 (C), 129.8 and 129.4 (CH), 123.6 and 123.2 (CH), 116.0 and 115.1 (C), 104.3 and 101.2 (C), 69.8 and 69.0 (CH), 54.5 and 53.5 (CH), 50.3 and 47.9 (CH_2), 44.1 and 43.4 (CH), 30.4 and 30.3 (CH_2), 28.0 and 27.8 (CH_2), 27.1 and 26.4 (CH_2), 25.6 and 25.5 (NCH_3), 24.0 and 23.6 (CH_2); *m/z* (I, %): 397 (15, M^+).

*4.2.10. 2-(8-Methyl-7,9-dioxo-1,3,4,6a,9a,9b-hexahydropyrrolo[1,2]pyrrolo[3,5-a][1,4]thiazin-6-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**10j**).* From **7i** and **2a** (0.055 g, 45%) as an orange solid, m.p. 278-279 °C; Mixture of isomers (1:3); [Found: C, 52.7; H, 3.6; N, 20.2. $C_{18}H_{16}N_6O_4S$ requires C, 52.42; H, 3.91; N, 20.38%]; ν_{max} 1705, 2195, 2920, 2960 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.26, 7.86, 8.25 and 7.67 (4H, two AA'XX', *J* 8.8 Hz, Ar), 5.60 and 5.19 (1H, two dt, *J* 13.2, 2.8 Hz, CH), 5.22 and 4.73 (1H, two d, *J* 9.2 Hz, CH), 4.51-4.41 (1H, m, CH), 3.96 and 3.90 (1H, two t, *J* 10.0 Hz, CH_2), 3.58 (1H, t, *J* 11.6 Hz, CH_2), 3.03-2.95 (1H, m, CH_2), 2.92 and 2.91 (3H, two s, Me), 2.84-2.72 (2H, m, CH_2), 2.71-2.64 (1H, m, CH_2); δ_c (100.6 MHz, DMSO-d_6) 174.2 (CO), 172.3 (CO), 163.2 (C), 157.4 (C), 146.3 (C), 125.5 and 125.2 (CH), 122.6 and 122.4 (CH), 115.3 and 114.6 (C), 103.1 (C), 67.9 and 67.6 (CH), 53.7 and 52.7 (CH), 52.6 and 49.6 (CH_2), 44.4 and 43.5 (CH), 29.5 (CH_2), 25.8 (NCH_3), 25.7 and 25.6 (CH_2), 23.3 and 23.2 (CH_2); *m/z* (I, %): 412 (30, M^+).

*4.2.11. 2-[(4-Chlorophenyl)azo]-2-(8-methyl-7,9-dioxo-1,3,4,6a,9a,9b-hexahydropyrrolo[1,2]pyrrolo[3,5-a][1,4]thiazin-6-ylidene)acetonitrile (**10k**).* From **7j** and **2a** (0.060g, 50%) as a yellow solid, m.p. 240-241 °C; Mixture of isomers (3:5); [Found: C, 53.7; H, 4.1; N, 17.3. $C_{18}H_{16}ClN_5O_2S$ requires C, 53.80; H, 4.01; N, 17.43%]; δ_H (400 MHz, DMSO-d_6) 7.51, 7.40, 7.68 and 7.38 (4H, two AA'XX', *J* 8.4 Hz, Ar), 5.59 and 5.15 (1H, two br. d, *J* 13.6 Hz, CH), 5.17 and 4.65 (1H, two d, *J* 9.2 Hz, CH), 4.38 (1H, dt, *J* 11.2, 3.2 Hz, CH_2), 3.93 and 3.86 (1H, two t, *J* 10.0 Hz, CH_2), 3.63-3.48 (1H, m, CH_2), 2.93 and 2.91 (3H, two s, NMe), 2.98-2.87 (1H, m, CH_2), 2.84-2.61 (3H, m, CH_2);. δ_C (100 MHz DMSO-d_6) 174.4 and 174.3 (CO), 172.7 and 172.5 (CO), 161.9 and 156.2 (C), 152.6 and 151.6 (C), 133.2 and 132.7 (C), 129.4 and 128.8 (CH), 123.7 and 123.4 (CH), 115.7 and 115.0 (C), 104.6 and 101.9 (C), 67.2 and 66.8 (CH), 53.2 and 52.2 (C), 51.9 and 49.2 (CH_2), 44.5 and 43.6 (CH), 29.8 and 28.5 (CH_2), 26.2 and 25.7 (CH_2), 25.8 and 25.7 (NMe); *m/z* (I, %): 401 (34, M^+).

*4.2.12. 2-(1,3-Dioxo-2-phenyl-6,7,8,9,9a,9b-hexahydro-3aH-pyrrolo[3,4-a]indolizin-4-ylidene)-2-[(4-nitrophenyl)azo] acetonitrile (**11a**).* From **7a** and **2b** (0.086 g, 63%), from **8a** and **2b** (0.090 g, 66%), from **9a** and **2b** (0.095 g, 70%) as an orange solid, m.p. 259-260 °C; Mixture of isomers (1:3); [Found: C, 63.1; H, 4.4; N, 18.4. $C_{24}H_{20}N_6O_4$ requires C, 63.15; H, 4.42; N, 18.41%]; ν_{max} 1720, 2200, 2860, 2920, 2950, 3070 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.24, 7.81, 8.24 and 7.66 (4H, two AA'XX', *J* 9.1 Hz, Ar), 7.59-7.38 (3H, m, Ar), 7.37-7.25 (2H, m, Ar), 5.42 and 4.90 (1H, two d, *J* 9.2 Hz, CH), 5.30 and 4.88 (1H, two d, *J* 12.8 Hz, CH), 4.36 (1H, dt, *J* 12.2, 3.2 Hz, CH), 4.03 and 3.98 (1H, two t, *J* 10.0 Hz, CH_2), 3.53-3.34 (1H, m, CH_2), 2.22-2.09 (1H, m, CH_2), 2.05-1.82 (2H, m, CH_2), 1.81-1.56 (2H, m, CH_2), 1.54-1.10 (1H, m, CH_2); δ_C (100.6 MHz, DMSO-d_6) 173.9 (CO), 171.9 and 171.7 (CO), 162.0 (C), 157.6 (C), 154.5 (C), 146.3 and 146.1 (C), 132.7 and 132.5 (C), 129.5 and 129.4 (CH), 129.3 and 129.2 (CH), 127.9 and 127.7 (CH), 125.6 and 125.2 (CH), 122.4 and 122.2 (CH), 116.6 and 114.7 (C), 102.8 and 91.1 (C), 68.0 and 67.4 (CH), 53.7 (CH), 47.8 and 47.1 (CH_2), 44.1 and 43.1 (CH), 29.1 (CH_2), 24.2 and 23.38 and 23.4 (CH_2); m/z (I, %): 456 (19, M^+).

*4.2.13. 2-[(4-Chlorophenyl)azo]-2-(1,3-dioxo-2-phenyl-6,7,8,9,9a,9b-hexahydro-3aH-pyrrolo[3,4-a]indolizin-4-ylidene)acetonitrile (**11b**).* From **7b** and **2b** (0.120 g, 90%), **8b** and **2b** (0.129 g, 97%), **9a** and **2b** (0.108 g, 81%) as an orange solid, m.p. 279-280 °C; Mixture of isomers (3:7); [Found: C, 64.6; H, 4.7; N, 15.7. $C_{24}H_{20}ClN_5O_2$ requires C, 64.65; H, 4.52; N, 15.71%]; ν_{max} 1700, 2200, 2850, 2920, 2950 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 7.64 (1H, d, *J* 8.7 Hz, Ar), 7.58-7.23 (8H, m, Ar), 5.34 and 4.87 (1H, two d, *J* 9.2 Hz, CH), 5.29 and 4.80 (1H, two d, *J* 10.6 Hz, CH), 4.26 (1H, dt, *J* 11.5, 3.2 Hz, CH), 4.07 and 3.94 (1H, dd, *J* 9.6, 9.2 Hz, CH_2), 3.50-3.29 (1H, m, CH_2), 2.22-2.06 (1H, m, CH_2), 2.01-1.78 (2H, m, CH_2), 1.75-1.33 (2H, m, CH_2), 1.27-1.02 (1H, m, CH_2); δ_C (100.6 MHz, DMSO-d_6) 173.5 (CO), 171.7 and 171.5 (CO), 160.2 and 154.9 (C), 151.6 and 151.2 (C), 132.4 and 132.2 (C), 132.0 and 131.9 (C), 129.3 and 129.0 (CH), 128.9 (CH), 128.8 and 128.7 (CH), 127.3 and 127.2 (CH), 123.0 and 122.7 (CH), 115.4 and 114.6 (C), 103.7 and 101.0 (CN), 66.7 and 66.1 (CH), 53.8 and 52.7 (CH), 48.8 and 46.1 (CH_2), 43.6 and 42.7 (CH), 28.9 and 28.6 (CH_2), 24.1 and 23.7 (CH_2), 22.9 and 22.8 (CH_2); m/z (I, %): 445 (34, M^+).

*4.2.14. 2-(1,3-Dioxo-2-phenyl-6,7,8,9,9a,9b-hexahydro-3aH-pyrrolo[3,4-a]indolizin-4-ylidene)-2-(phenylazo)acetonitrile (**11c**).* From **7c** and **2b** (0.110 g, 89%), **8c** and **2b** (0.096 g, 78%), **9c** and **2b** (0.103 g, 84%) as a yellow solid, m.p. 227-228 °C; Mixture of isomers (2:3); [Found: C, 69.9; H, 5.1; N, 16.8%. $C_{24}H_{21}N_5O_2$ requires C, 70.1; H, 5.1; N, 17.0%]; ν_{max} 1720, 2195, 2860, 2930, 2950, 3020, 3060 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 7.62 (1H, d, *J* 9.1 Hz, Ar), 7.58-7.17 (9H, m, Ar), 5.34 and 4.87 (1H, two d, *J* 13.2 Hz, CH), 5.35 and 4.80 (1H, two d, *J* 9.8 Hz, CH), 4.24 (1H, t, *J* 10.4 Hz, CH), 3.98 and 3.92 (1H, dt, *J* 10.2 Hz, CH_2), 3.46-3.24 (1H, m, CH_2), 2.10-1.92 (1H, m, CH_2), 1.90-1.68 (2H, m, CH_2), 1.67-1.35 (2H, m, CH_2), 1.22-1.02 (1H, m, CH_2); δ_C (100.6 MHz, DMSO-d_6)

173.6 (CO), 171.9 and 171.6 (CO), 160.0 and 154.6 (C), 152.8 and 152.5 (C), 132.2 and 132.0 (C), 129.3 and 129.0 (CH), 128.9 and 128.8 (CH), 128.7 and 128.6 (CH), 128.3 and 127.8 (CH), 127.3 and 127.2 (CH), 121.4 and 121.1 (CH), 115.6 and 114.8 (C), 103.7 and 101.0 (CN), 66.5 and 65.9 (CH), 53.7 and 52.6 (CH), 48.7 and 46.0 (CH_2), 43.7 and 42.7 (CH), 28.9 and 28.6 (CH_2), 24.1 and 23.7 (CH_2), 23.0 and 22.8 (CH_2); *m/z* (I, %): 411 (34, M^+).

*4.2.15. 2-(1,3-Dioxo-2-phenyl-6,7,8,9,9a,9b-hexahydro-3aH-pyrrolo[3,4-a]indolizin-4-ylidene)-2-[(4-methoxyphenyl)azo] acetonitrile (**11d**).* From **7d** and **2b** (0.085 g, 64%), from **8d** and **2b** (0.090 g, 68%), from **9d** and **2b** (0.075 g, 58%) as a yellow solid, m.p. 264-265 °C; Mixture of isomers (2:3); [Found: C, 67.9; H, 5.2; N, 15.8. $C_{25}H_{23}N_5O_3$ requires C, 68.01; H, 5.25; N, 15.90%]; ν_{max} 1720, 2200, 2840, 2860, 2930, 2960, 3060 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 7.61 (1H, d, *J* 9.0 Hz, Ar), 7.53-7.48 (4H, m, Ar), 7.37-7.32 (2H, m, Ar), 7.02 and 6.97 (2H, two d, *J* 9.0 Hz, Ar), 5.34 and 4.77 (1H, two d, *J* 12.8 Hz, CH), 5.26 and 4.78 (1H, two d, *J* 8.2 Hz, CH), 4.24 (1H, t, *J* 10.3 Hz, CH), 3.99 and 3.93 (1H, two dd, *J* 9.3, 10.6 Hz, CH_2), 3.80 and 3.78 (3H, two s, OMe), 3.40-3.30 (1H, m, CH_2), 2.07-1.98 (1H, m, CH_2), 1.94-1.85 (1H, m, CH_2), 1.84-1.76 (1H, m, CH_2), 1.68-1.50 (2H, m, CH_2), 1.42-1.30 (1H, m, CH_2); δ_C (100.6 MHz, DMSO-d_6) 173.5 (CO), 172.0 and 171.6 (CO), 159.3 and 159.1 (C), 159.8 and 153.5 (C), 147.1 and 146.7 (C), 132.3 (C) and 132.1, 128.9 and 128.8 (CH), 128.7 and 128.6 (CH), 127.2 and 127.1 (CH), 122.9 and 122.7 (CH), 115.7 and 114.8 (C), 114.5 and 114.1 (CH), 103.6 and 100.9 (C), 66.1 and 65.6 (CH), 55.4 and 55.3 (OMe), 53.4 and 52.3 (CH), 48.7 and 45.9 (CH_2), 43.7 and 42.8 (CH), 28.9 and 28.6 (CH_2), 24.1 and 23.8 (CH_2), 23.0 and 22.9 (CH_2); *m/z* (I, %): 441 (42, M^+).

*4.2.16. 2-(7,9-Dioxo-8-phenyl-1,3,4,6a,9a,9b-hexahydropyrrolo[1,2]pyrrolo[3,5-a][1,4]oxazin-6-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**11e**).* From **7e** and **2b** (0.125 g, 92%) as an orange solid, m.p. 306-307 °C; The mixture of four isomers in ratio 10:4:2:1; [Found: C, 60.3; H, 4.0; N, 18.2. $C_{23}H_{18}N_6O_5$ requires C, 60.26; H, 3.96; N, 18.33%]; ν_{max} 1720, 2200, 2850, 2920, 2960, 3070 cm^{-1}; δ_H (400 MHz DMSO-d_6) 8.23, 7.87, 8.23, 7.82, 8.23, 7.70, 8.23 and 7.41 (4H, four AA'XX', *J* 8.7 Hz, Ar), 7.55-7.25 (5H, m, Ar), 5.42 and 5.31 and 5.16 and 5.06 (four d, 1H, *J* 9.3 Hz, CH), 4.93 and 4.85 and 4.76 and 4.70 (1H, four d, *J* 9.0 Hz, CH), 4.43 (1H, dt, *J* 9.5, 4.3 Hz, CH), 4.27-4.11 (1H, m, CH_2), 4.10-3.88 (2H, m, CH_2), 3.82-3.56 (2H, m, CH_2), 3.55-3.39 (m, 1H, CH_2); δ_C (100.6 MHz, DMSO-d_6) 174.3 (CO), 172.6 and 171.9 (CO), 161.4 and 156.4 (CH), 152.0 and 151.6 (CH), 132.8 (C), 132.6 and 132.6 (C), 132.4 and 132.3 (C), 129.8 and 129.6 (CH), 129.5 and 129.4 (CH), 129.3 and 129.2 (CH), 127.6 and 127.5 (CH), 123.5 and 123.3 (CH), 116.1 and 115.2 (C), 104.5 and 101.5 (C), 70.1 and 69.3 (CH_2), 54.8 and 53.7 (CH_2), 50.4 and 48.0 (CH), 44.4 and 43.7 (CH), 30.6 and 30.5 (CH_2), 28.2 and 28.0 (CH). *m/z* (I, %): 458 (40, M^+).

*4.2.17. 2-(7,9-Dioxo-8-phenyl-1,3,4,6a,9a,9b-hexahydropyrrolo[1,2]pyrrolo[3,5-a][1,4]oxazin-6-ylidene)-2-[(4-methoxyphenyl) azo]acetonitrile (**11f**).* From **7f** and **2b** (0.89 g, 67%**)** as a yellow solid, m.p. 249-250 °C; Mixture of isomers (7:3); [Found: C, 65.1; H, 4.8; N, 15.6. $C_{24}H_{21}N_5O_4$ requires C, 65.00; H, 4.77; N, 15.79%]; δ_H (400 MHz, DMSO-d_6) 7.70-7.57, 7.55-7.45 and 7.20-7.10 (9H, three m, Ar), 5.20 and 4.87 (1H, two d, *J* 9.8 Hz, CH), 4.56 and 4.00 (1H, two d, *J* 11.4 Hz, CH), 4.28 (1H, dt, *J* 11.2, 3.2 Hz, CH), 4.17-4.09 (1H, m, CH_2), 3.94-3.86 (2H, m, CH_2), 3.80 (3H, s, OMe), 3.64-3.50 (2H, m, CH_2), 3.35-3.28 (1H, m, CH_2); *m/z* (I, %): 443 (30, M^+).

*4.2.18. 2-(1,3-Dioxo-2-phenyl-3a,6,7,8,9,10,10a,10b-octahydropyrrolo[1,2]pyrrolo[3,5-a]azepin-4-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**11g**).* From **7g** and **2b** (0.120 g, 86%) as an orange solid, mp 258-259 °C; Mixture of two isomers (1:2); [Found: C, 63.6; H, 4.5; N, 18.1. $C_{25}H_{22}N_6O_4$ requires C, 63.82; H, 4.71; N, 17.86%]; ν_{max} 1720, 2200, 2850, 2910, 2970 cm^{-1}; δ_H (400 MHz DMSO-d_6) 8.27, 7.67, 8.25 and 7.83 (4H, two AA'XX', *J* 8.8 Hz, Ar), 7.54-7.40 (3H, m, Ar), 7.33-7.26 (2H, m, Ar), 5.48 and 5.00 (1H, two d, *J* 9.6 Hz, CH), 4.83-4.71 (1H, m, CH), 4.57 and 4.44 (1H, two dt, *J* 3.6, 14.0 Hz, CH), 4.04 and 3.99 (1H, two t, *J* 10.4 Hz, CH), 3.77-3.64 (1H, m, CH_2), 2.19-2.09 (1H, m, CH_2), 2.08-1.85 (3H, m, CH_2), 1.81-1.62 (3H, m, CH_2), 1.55-1.34 (1H, m, CH_2); δ_c (100.6 MHz, DMSO-d_6) 173.8 (CO), 171.2 and 171.0 (CO), 162.6 and 157.3 (C), 157.0 and 156.9 (C), 145.7 and 145.6 (C),132.9 and 132.1 (C), 129.1 and 129.0 (CH), 128.9 and 128.8 (CH), 127.1 and 127.0 (CH), 127.1 and 124.8 (CH), 121.7 and 122.0 (CH), 115.1 and 114.2 (C), 105.3 and 102.3 (C), 70.2 and 69.5 (CH), 54.7 and 53.5 (CH), 50.4 and 47.9 (CH_2), 43.7 and 43.0 (CH), 29.7 and 29.5 (CH_2), 27.7 and 27.5 (CH_2), 26.6 and 25.9 (CH_2), 23.8 and 23.5 (CH_2); *m/z* (I, %): 470 (12, M^+).

*4.2.19. 2-[(4-Chlorophenyl)azo]-2-(1,3-dioxo-2-phenyl-3a,6,7,8,9,10,10a,10b-octahydropyrrolo[1,2]pyrrolo[3,5-a]azepin-4-ylidene)acetonitrile (**11h**).* From **7h** and **2b** (0.107 g, 78%) as a yellow solid, m.p. 166-167 °C; Mixture of isomers (2:3); [Found: C, 65.0; H, 4.8; N, 15.4. $C_{25}H_{22}ClN_5O_2$ requires C, 65.29; H, 4.82; N, 15.23%]; ν_{max} 1720, 2200, 2850, 2920 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 7.65-7.16, 7.56-7.42, 7.32-7.27 (9H, m, Ar), 5.47 and 4.94 (1H, two d, *J* 9.6 Hz, CH), 4.76-4.66 (1H, m, CH), 4.51 and 4.34 (1H, two dt, *J* 4.4, 13.6 Hz, CH), 4.08-3.85 (1H, m, CH_2), 3.70-3.57 (1H, m, CH_2), 2.10-2.07 (1H, m, CH_2), 2.00-1.77 (3H, m, CH_2), 1.72-1.55 (3H, m, CH_2), 1.45-1.22 (1H, m, CH_2); δ_C (100.6 MHz, DMSO-d_6) 174.4 (CO), 172.0 and 171.8 (CO), 161.7 and 156.1 (C), 152.1 and 151.9 (C), 132.7 and 132.6 (C), 132.4 and 132.3 (C), 129.8 and 129.6 (CH), 129.5 and 129.4 (CH), 129.3 and 129.2 (CH), 127.6 and 127.5 (CH), 123.5 and 123.2 (CH), 116.1 and 115.2 (CN), 104.5 and 101.4 (C), 70.0 and 69.3 (CH), 54.8 and 53.7 (CH), 50.4 and 48.0 (CH_2), 44.4 and 43.7 (CH), 30.5 and 30.4 (CH_2), 28.2 and 28.0 (CH_2), 27.1 and 26.4 (CH_2), 24.4 and 24.0 (CH_2); *m/z* (I, %): 459 (13, M^+).

*4.2.20. 2-(7,9-Dioxo-8-phenyl-1,3,4,6a,9a,9b-hexahydropyrrolo[1,2]pyrrolo[3,5-a][1,4]thiazin-6-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**11i**).* From **7i** and **2b** (0.095 g, 67%) as an orange solid, m.p. 299-300 °C; Mixture of isomers (3:7); [Found: C, 58.3; H, 3.7; N, 17.5. $C_{23}H_{18}N_6O_4S$ requires C, 58.22; H, 3.82; N, 17.71%]; ν_{max} 1715, 2200, 2915 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.26, 8.23, 7.83 and 7.69 (4H, two AA'XX', *J* 8.8 Hz, Ar), 7.51-7.33 (5H, m, Ar), 5.57 (1H, dt, *J* 10.8, 2.8 Hz, CH), 5.65 and 5.26 (1H, two dt, *J* 3.2, 13.6 Hz, CH), 5.40 and 4.92 (1H, two d, *J* 9.2 Hz, CH), 4.12 and 4.06 (1H, two t, *J* 10.0 Hz, CH_2), 3.63 (1H, t, *J* 12.8 Hz, CH_2), 3.18-3.06 (1H, m, CH_2), 3.00 (1H, t, *J* 12.0 Hz, CH_2), 2.90-2.83 (1H, m, CH_2), 2.76-2.66 (1H, m, CH_2); δ_c (100.6 MHz, DMSO-d_6) 174.2 (CO), 172.7 and 172.6 (CO), 161.9 and 156.2 (C), 152.0 and 151.6 (C), 133.2 and 132.7 (C), 129.4 and 129.3 (CH), 128.1 (CH), 127.9 and 127.8 (CH), 127.0 and 126.9 (CH), 126.7 and 126.6 (CH), 122.5 and 122.2 (CH), 114.9 (C),

105.0 and 102.5 (C), 67.2 and 66.8 (CH), 53.2 and 52.2 (CH), 49.2 and 43.6 (CH_2), 40.7 and 40.5 (CH), 29.8 and 29.5 (CH_2), 25.7 and 25.6 (CH); *m/z* (I, %): 474 (41, M^+).

*4.2.21. 2-(7,9-Dioxo-8-phenyl-1,3,4,6a,9a,9b-hexahydropyrrolo[1,2]pyrrolo[3,5-a][1,4]thiazin-6-ylidene)-2-[4-(trifluoromethyl)phenylazo]acetonitrile (**11j**).* From **7k** and **2b** (0.090 g, 60%) as a yellow solid; mp 272-273 ^oC; Mixture of isomers (7:3); [Found: C, 58.0; H, 3.5; N, 14.1. $C_{24}H_{18}F_3N_5O_2S$ requires C, 57.94; H, 3.65; N, 14.08%]; δ_H (400 MHz DMSO-d_6) 8.50-7.64 (4H, m, Ar), 7.53-7.35 (5H, m, Ar), 5.68 and 5.23 (1H, two dt, *J* 2.0, 12.4 Hz, CH), 5.37 and 4.88 (1H, two d, *J* 9.6 Hz, CH), 4.53 (1H, dt, *J* 10.6, 2.8 Hz, CH), 4.10 and 4.04 (1H, two t, *J* 10.4 Hz, CH_2), 3.60 (1H, t, *J* 12.8 Hz, CH_2), 3.18-3.06 (1H, m, CH_2), 3.02-2.92 (1H, m, CH_2), 2.88-2.81 (1H, m,CH_2), 2.75-2.65 (1H, m, CH_2); δ_c (100.6 MHz, DMSO-d_6) 173.5 (CO), 171.6 and 171.4 (CO), 162.4 and 157.0 (C), 155.8 (C),132.8 and 129.2 (C), 129.4 and 129.3 (CH), 128.1 (CH), 127.9 and 127.8 (CH), 127.0 and 126.9 (CH), 126.7 and 126.6 (CH), 122.5 and 122.2 (CH), 114.9 (C), 105.0 and 102.5 (C), 68.1 and 67.6 (CH), 53.8 and 52.7 (CH), 52.1 and 49.5 (CH_2), 44.7 and 43.9 (CH), 29.8 and 29.6 (CH_2), 26.1 and 25.6 (CH); δ_F (100 MHz, DMSO-d_6): -61.80 and -61.65 (two s, 3F, CF_3); MS *m/z* (I, %): 497 (M^+, 35).

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Supplementary Data

Supplementary Data related to this article can be found at http://

1. References and notes

1. (a) Padwa, A.; Pearson, W. H. Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry toward Heterocycles and Natural Products, John Wiley & Sons, Inc., New York, 2002. (b) Adrio, J.; Carretero, J. C. *Chem. Commun*., **2011**, *47*, 6784-6794. (c) Stanley, L. M.; Sibi, M. P. *Chem. Rev*., **2008**, *108*, 2887. (d) Nair, V.; Suja, T. D. *Tetrahedron*, **2007**, *63*, 12247-12275. (e) Pellissier, H. *Tetrahedron*, **2007**, *63*, 3235-3285.
2. (a) Garner, P.; Kanishkan, H. U. *J. Org. Chem*., **2005**, *70*, 10868-10871. (b) Komatsu, M.; Kasano, Y.; Yonemori, J.-I.; Oderaotoshi, Y.; Minakata, S. *Chem. Commun*., **2006**, 526-528.
3. (a) Kathiravan, S.; Raghunathan, R. *Synthetic Comm*., **2013**, *43*, 147-155. (b) Sarrafi, Y.; Hamzehloueian, M.; Alimohammadi, K.; Yeganegi, S. *J. Mol. Structure*, **2012**, *1030*, 168-176. (c) Nayak, M.; Rastogi, N.; Batra, S. *Tetrahedron*, **2013**, *69*, 5029-5043. (d) Dingce, Y.; Qinghua, L.; Chunjiang, W. *Chin. J. Chem*, **2012**, *30*, 2714-2720. (e) Cardoso, A. L.; Kaczor, A.; Silva, A. M. S.; Fausto, R.; Pinho e Melo, T. M. V. D.; d'A. Rocha Gonsales A. M. *Tetrahedron*, **2006**, *62*, 9861-9871. (f) Chandraprakash, K.; Sankaran, M.; Uvarani, C.; Shankar, R.; Ata, A.; Dallemer, F.; Mohan, P. S. *Tetrahedron Lett*., **2013**, *54*, 3896-3948. (g) Arun, A.; Bhaskar, G.; Balachandran, C.; Ignacimuthu, S.; Perumal, P. T. *Bioorg. Med. Chem. Lett*., **2013**, *23*, 1839-1845. (h) Zhang, W.; Lu, Y.; Geib, S. *Org. Lett*., **2005**, *7*, 11, 2269-2272.
4. (a) Grigg, R.; Surendrakumar, S.; Tianpatanagul, S.; Vipond, D. *J. Chem. Perkin. Trans I*, **1988**, 2693-2701. (b) Grigg, R.; Idle, J.; McMeekin, P.; Surendrakumar, S.; Vipond, D. *J. Chem. Perkin. Trans I*, **1988**, 2703-2713. (c) Grigg, R.; Savic, V.; Thornton-Pett, M. *Tetrahedron*, **1997**, *53*, 10633-10642. (d) Grigg, R.; Jones, M. F.; McTiernan, M.; Sridharan, V. *Tetrahedron*, **2001**, *57*, 7979-7989. (e) Chinchilla, R.; Falvello, L. R.; Galindo, N.; Najera, C. *Eur. J. Org. Chem*., **2001**, 3133-3140. (f) Dondas, H. A.; Durust, Y.; Grigg, R.; Slatera, M. J.; Sarkera, M. A. B. *Tetrahedron*, **2005**, 10667-10682. (g) Poornachandran, M.; Raghavachary, R. *Tetrahedron Lett*., **2005**, *46*, 7197-7200. (h) Brome, V. A.; Harwood, L. M.; Osborn, H. M. I. *Can. J. Chem*., **2006**, *84*, 1448-1455. (i) Draffin, W. N.; Harwood, L. M. *Synlett*, **2006**, *6*, 857-860. (j) Kumar, R. R.; Perumal, S. Manju, S. C.; Bhatt, P.; Yogeeswari, P.; Sriram, D. *Bioorg. Med. Chem. Lett.*, **2009**, *45*, 3461-65. (k) Zhang, Z.; Giampa, G. M.; Draghici, C.; Huang, Q.; Brewer, M. *Org. Lett*., **2013**, *15*, 2100-2103.
5. (a) Moshkin V. S.; Sosnovskikh, V. Ya.; Roschenthaler, G.-V. *Tetrahedron*, **2013**, *69*, 5884-5892. (b) Epperson, M. T.; Gin, D. Y. *Angew. Chem. Int. Ed*., **2002**, *41*, 1778-1780.
6. (a) Jordan, A.M.; Roughly, S. D. *J. Med. Chem*., **2011**, *54*, 3451-3479. (b) Pandey, G.; Banerjee, P.; Gadre, S. R. *Chem. Rev*., **2006**, *106*, 4484-4517. (c) Salonen, L. M.; Bucher, C.; Banner, D. W.; Haap, W.; Mary, J.-L.; Benz, J.; Kuster, O.; Seiler, P.; Schweizer, W. B.; Diederich, F. *Angew. Chem. Int. Ed*., **2009**, *48*, 811-814. (d) Schweizer, E.; Hoffmann-Roder, A.; Olsen, J. A.; Seiler, P.; Obst-Sander, U.; Wagner, B.; Kansy, M.; Banner D. W.; Diederich F. *Org. Biomol. Chem*., **2006**, *4*, 2364-2375. (e) Pinho, V. D.; Procter, D. J.; Burtoloso, A. C. B. *Org. Lett*., **2013**, *15*, 2434-2437. (f) Murray, W.V.; Francois, D.; Maden A.; Turchi, I. *J. Org. Chem*., **2007**, *72*, 3097-3099.
7. (a) Laduron, F.; Viehe, H. G. *Tetrahedron*, **2002**, *58*, 3543-3451. (b) Laduron, F.; Ates, C.; Viehe, H. G. *Tetrahedron Lett*., **1996**, *37*, 31, 5515-5518.
8. (a) Pearson, W. H.; Stoy, P.; Mi, Y. *J. Org. Chem*., **2004**, *69*, 1919-1939. (b) Coldham, I.; Burrell, A. J. M.; Guerrand, H. D. S.; Watson, L., Martin, N. G.; Oram, N. *Beilstein J. Org. Chem*. **2012**, *8*, 107-111. (c) Burrell, A. J. M.; Watson, L.; Martin, N. G.; Oram, N.; Coldham, I. *Org. Biomol. Chem*. **2010**, *8*, 4530-4532. (d) Coldham, I.; Jana, S.; Watson L.; Martin N. G. *Org. Biomol. Chem*. **2009**, *7*, 1674-2679. (e) Burrell, A. J. M.; Coldham, I.; Oram, N. *Org. Lett*. **2009**, *11*, 1515-1518. (f) Coldham, I.; Jana, S.; Watson, L.; Pilgram, C. D. *Tetrahedron Lett*., **2008**, *49*, 5408-5410. (g) Coldham, I.; Burrell, A. J. M.; White, L. E.; Adams, H.; Oram, N. *Angew. Chem. Int. Ed*. **2007**, *46*, 6159-6162.
9. Vedejs, E.; Martines, G. R. *J. Am. Chem. Soc*., **1980**, *102*, 7993-7994.
10. (a) Vedejs, E.; Larsen, S.; West, F. G. *J. Org. Chem*. **1985**, *50*, 2170-2174.
    (b) Vedejs, E.; West, F. G. *J. Org. Chem*., **1983**, *48*, 4773-4774.
11. (a) Deryabina, T. G.; Belskaya, N. P.; Kodess, M. I.; Dehaen, W.; Toppet, S.; Bakulev, V. A. *Tetrahedron Lett*., **2006**, *47*, 1853-1855. (b) Belskaya, N. P.; Bakulev, V. A.; Deryabina, T. G.; Subbotina, J. O.; Kodess, M. I.; Dehaen, W.; Toppet, S.; Robeyns, K.; Van Meervelt, L. *Tetrahedron*, **2009**, *65*, 7662-7672.
12. Weinhold, F. *J. Comput. Chem*., **2012**, *33*, 2363-2379.
13. Geuenich, D.; Hess, K.; Koehler, F.; Herges, R. *Chem. Rev*., **2005**, *105*, 3758-3772.
14. (a) Houk, K. N.; Gandour, R. W.; Robert, W.; Strozier, R. W.; Rondan, N. G.; Paquette, L. A. *J. Am. Chem. Soc*., **1979**, *101*, 6797-6802. (b) Bach, R. D.; Wolber, G. J.; Schlegel, H. B. *J. Am. Chem. Soc*., **1985**, *107*, 10, 2837-2841.
15. Birney, D. M. *J. Org. Chem*., **1996**, 61, 1, 243-251.
16. Gaussian 09, Revision A.02, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.;

Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.

17. (a) Bader, R. F W. *Chem. Rev*., **1991**, *91*, 893-928. (b) Poater, J; Casanovas, J.; Sola, M.; Aleman, C. *J. Phys. Chem*., A. **2010**, *114*, 1023-1028.
18. Koch, U.; Popelier, P.L.A. *J. Phys. Chem*., **1995**, *99*, 9747-9754.
19. Reed, A. E.; Curtiss, L. A., Weinhold, F. *Chem. Rev*. **1988**, *88*, 899-926.
20. Sheldrick, G. M. *Acta Cryst*., **2008**, *A64*, 112-122.
21. NBO Version 3.1, Glendening, E. D.; Reed, A. E.; Carpenter, J. E. and Weinhold, F.
22. AIM All (Version 13.02.26), Todd A. Keith, TK Gristmill Software, Overland Park KS, USA, 2012 (aim.tkgristmill.com).
23. Belskaya, N.P.; Koksharov, A.V.; Eliseeva, A.I.; Fan, Z.; Bakulev, V.A. *Chem. Heterocycl. Comp.*, **2011**, *47*, 564-570.

Supplementary Data

1,3-Dipolar Cycloaddition of 3-Alkylsulfanyl-2-arylazo-3-(*tert*-cycloalkylamino)acrylonitriles with *N*-Methyl- and *N*-Phenylmaleimides

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Contents

General

Melting points were determined with a Stuart SMP3 apparatus. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance II (400 MHz for ^{1}H and 100.6 MHz for ^{13}C) spectrometer using DMSO-d_6 and $CDCl_3$ as solvents. Chemical shifts (δ) have been reported in parts per million (ppm) relative to TMS in ^{1}H and ^{13}C spectra. Coupling constants (*J*) values given in Hertz. Mass spectra were performed on a «SHIMADZU GCMS-QP2010 Ultra» mass spectrometer using the electron impact ionization technique (40-200 ^{o}C, 70 eV). The IR data have been recorded on a Bruker Alpha (NPVO, ZnSe) IR-Fur spectrometer. Elemental analyses were carried out using a CHNS/O analyzer Perkin-Elmer 2400 Series II instrument.

S,*N*-acetals **7-9** were prepared by the procedure reported in our previous articles.[1-3]

*3-Methylsulfanyl-2-[(4-nitrophenyl)azo]-3-(1-piperidyl)prop-2-enenitrile (**7a**)*. Red solid (218 mg, 66%), m.p. 147-148 ºC; [Found: C, 54.53, H, 5.31, N, 20.9. $C_{15}H_{17}N_5O_2S$ requires C, 54.37, H, 5.17, N, 21.13%]; δ_H (400 MHz, $CDCl_3$) 8.28 and 7.69 (4H, AA'XX', *J* 9.2 Hz, Ar), 3.99-3.81 (4H, m, CH_2), 2.60 (3H, s, SMe), 1.81-1.59 (6H, m, CH_2); m/z (I, %): 331 (6, M^+).

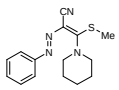
*3-Allylsulfanyl-2-[(4-nitrophenyl)azo]-3-(1-piperidyl)prop-2-enenitrile (**8a**)*. Red solid (293 mg, 82%), m.p. 141-142 ºC; [Found: C, 57.11, H, 5.12, N, 19.41. $C_{17}H_{19}N_5O_2S$ requires C, 57.13, H, 5.36, N, 19.59%]; δ_H (400 MHz, $CDCl_3$) 8.29 and 7.70 (4H, AA'XX', *J* 9.0 Hz, Ar), 5.95-5.82 (1H, m, CH), 5.21 (1H, d, *J* 16.8 Hz, CH$\underline{CH_2}$), 5.16 (1H, d, *J* 9.2 Hz, CH$\underline{CH_2}$), 3.99-3.91 (4H, m, CH_2), 3.74 (2H, d, *J* 7.2 Hz, SCH_2), 1.81-1.69 (6H, m, CH_2); m/z (I, %): 357 (3, M^+).

*2-[(4-Nitrophenyl)azo]-3-(1-piperidyl)-3-prop-2-ynylsulfanyl-prop-2-enenitrile (**9a**)*. Red solid (323 mg, 91%), m.p. 140-141 ºC; [Found: C, 57.33, H, 4.75, N, 19.55. $C_{17}H_{17}N_5O_2S$ requires C, 57.45, H, 4.82, N, 19.70%]; δ_H (400 MHz, $CDCl_3$) 8.29 and 7.71 (4H, AA'XX', *J* 9.2 Hz, Ar), 3.96 (2H, d, *J* 2.5 Hz, SCH_2), 3.94-3.81 (4H, m, CH_2), 3.44 (1H, t, *J* 2.8 Hz, CH), 1.84-1.65 (6H, m, CH_2); m/z (I, %): 355 (17, M^+).
*2-[(4-Chlorophenyl)azo]-3-methylsulfanyl-3-(1-piperidyl)prop-2-enenitrile (**7b**)*. Yellow solid (288 mg, 90%), m.p. 141-142 ºC; [Found: C, 56.00, H, 5.15, N, 17.65. $C_{15}H_{17}ClN_4S$ requires C, 56.15, H, 5.34, N, 17.46%]; δ_H (400 MHz, $CDCl_3$) 7.55 and 7.49 (4H, AA'XX', *J* 8.9 Hz, Ar), 3.89-3.80 (4H, m, CH_2), 2.55 (3H, s, SMe), 1.80-1.65 (6H, m, CH_2); m/z (I, %): 320 (17, M^+).

*3-Allylsulfanyl-2-[(4-chlorophenyl)azo]-3-(1-piperidyl)prop-2-enenitrile (**8b**)*. Orange solid (315 mg, 91%), m.p. 126-127 ºC; [Found: C, 58.61, H, 5.34, N, 16.11. $C_{17}H_{19}ClN_4S$ requires C, 58.86, H, 5.52, N, 16.15%]; δ_H (400 MHz, $CDCl_3$) 7.55 and 7.50 (4H, AA'BB', *J* 8.8 Hz, Ar), 5.95-5.79 (1H, m, CH), 5.19 (1H, d, *J* 16.8 Hz, CH$\underline{CH_2}$), 5.15 (1H, d, *J* 10.0 Hz, CH$\underline{CH_2}$), 3.93-3.81 (4H, m, CH_2), 3.68 (2H, d, *J* 7.2 Hz, SCH_2), 1.82-1.67 (6H, m, CH_2); m/z (I, %): 346 (10, M^+).

*2-[(4-Chlorophenyl)azo]-3-(1-piperidyl)-3-prop-2-ynylsulfanyl-prop-2-enenitrile (**9b**)*. Orange solid (289 mg, 84%), m.p. 125-126 ºC; [Found: C, 59.15, H, 5.11, N, 16.29. $C_{17}H_{17}ClN_4S$ requires C, 59.21, H, 4.97, N, 16.25%]; δ_H (400 MHz, $CDCl_3$) 7.53 and 7.49 (4H, AA'BB', *J* 8.9 Hz, Ar), 3.82 (2H, d, *J* 2.7 Hz, SCH_2), 3.81-3.72 (4H, m, CH_2), 3.27 (1H, t, *J* 2.7 Hz, CH), 1.79-1.63 (6H, m, CH_2); m/z (I, %): 344 (8, M^+).

*3-Methylsulfanyl-2-(phenylazo)-3-(1-piperidyl)prop-2-enenitrile (**7c**)*. Yellow solid (237 mg, 83%), m.p. 123-124 ºC; [Found: C, 62.78, H, 6.53, N, 19.66. $C_{15}H_{18}N_4S$ requires C, 62.91, H, 6.33, N, 19.56%]; δ_H (400 MHz, $CDCl_3$) 7.56 (2H, d, *J* 7.2 Hz, Ph), 7.45 (2H, t, *J* 7.6 Hz, Ph), 7.34 (1H, t, *J* 7.6 Hz, Ph), 4.00-3.85 (4H, m, CH_2), 2.63 (3H, s, SMe), 1.85-1.59 (6H, m, CH_2); m/z (I, %): 286 (9, M^+).



*3-Allylsulfanyl-2-(phenylazo)-3-(1-piperidyl)prop-2-enenitrile (**8c**)*. Orange solid (278 mg, 89%), m.p. 124-125 º; [Found: C, 65.23, H, 6.57, N, 18.02. $C_{17}H_{20}N_4S$ requires C, 65.35, H, 6.45, N, 17.93%]; δ_H (400 MHz, $CDCl_3$) 7.56 (2H, d, *J* 7.2 Hz, Ph), 7.45 (2H, t, *J* 7.6 , Ph), 7.34 (1H, t, *J* 7.6 Hz, Ph), 5.96-5.80 (1H, m, CH), 5.21 (1H, d, *J* 16.7 Hz, CH$\underline{CH_2}$), 5.15 (1H, d, *J* 10.0 Hz, CH$\underline{CH_2}$), 3.95-3.78 (4H, m, CH_2), 3.67 (2H, d, *J* 7.2 Hz, SCH_2), 1.85-1.65 (6H, m, CH_2); m/z (I, %): 312 (9, M^+).

*2-(Phenylazo)-3-(1-piperidyl)-3-prop-2-ynylsulfanyl-prop-2-enenitrile (**9c**)*. Orange solid (223 mg, 72%), m.p. 124-125 ºC; [Found: C, 65.62, H, 5.75, N, 18.14. $C_{17}H_{18}N_4S$ requires C, 65.78, H, 5.84, N, 18.05%]; δ_H (400 MHz, $CDCl_3$) 7.57 (2H, d, *J* 8.8 Hz, Ar), 7.47 (2H, t, *J* 7.2 Hz, Ph), 7.37 (1H, t, *J* 7.2 Hz, Ph), 3.90 (2H, d, *J* 2.6 Hz, SCH_2), 3.88-3.81 (4H, m, CH_2), 3.41 (1H, t, *J* 2.6 Hz, CH), 1.81-1.68 (6H, m, CH_2);m/z (I, %): 310 (13, M^+).

*2-[(4-Methoxyphenyl)azo]-3-methylsulfanyl-3-(1-piperidyl)prop-2-enenitrile (**7d**)*. Yellow solid (259 mg, 82%), m.p. 125-126 ºC; [Found: C, 60.48, H, 6.34, N, 17.59. $C_{16}H_{20}N_4OS$ requires C, 60.73, H, 6.37, N, 17.71%]; δ_H (400 MHz, $CDCl_3$) 7.54 and 7.01 (4H, AA'XX', *J* 9.2 Hz, Ar), 3.80 (3H, s, OMe), 3.81-3.74 (4H, m, CH_2), 2.52 (3H, s, SMe), 1.77-1.66 (6H, m, CH_2); m/z (I, %): 316 (12, M^+).

*3-Allylsulfanyl-2-[(4-methoxyphenyl)azo]-3-(1-piperidyl)prop-2-enenitrile (**8d**)*. Orange solid (253 mg, 74%), m.p. 106-107 ºC; [Found: C, 63.05, H, 6.65, N, 16.39. $C_{18}H_{22}N_4OS$ requires C, 63.13, H, 6.48, N, 16.36%]; δ_H (400 MHz, $CDCl_3$) 7.54 and 7.02 (4H, AA'XX', *J* 8.9 Hz, Ar), 5.94-5.80 (1H, m, CH), 5.21 (1H, d, *J* 16.6 Hz, CH$\underline{CH_2}$), 5.15 (1H, d, *J* 10.0 Hz, CH$\underline{CH_2}$), 3.80 (3H, s, OMe), 3.79-3.76 (4H, m, CH_2), 3.64 (2H, d, *J* 7.1 Hz, SCH_2), 1.77-1.65 (6H, m, CH_2); m/z (I, %): 342 (7, M^+).

*(2-[(4-Methoxyphenyl)azo]-3-(1-piperidyl)-3-prop-2-ynylsulfanyl-prop-2-enenitrile (**9d**)*. Orange solid (229 mg, 67%), m.p. 106-107 ºC; [Found: C, 63.36, H, 6.02, N, 16.58. $C_{18}H_{20}N_4OS$ requires C, 63.50, H, 5.92, N, 16.46%]; δ_H (400 MHz, $CDCl_3$) 7.56 and 7.02 (4H, AA'XX', *J* 8.8 Hz, Ar), 3.81 (2H, d, *J* 2.5 Hz, SCH_2), 3.79-3.76 (4H, m, CH_2), 3.64 (1H, t, *J* 2.5 Hz, CH), 1.79-1.67 (6H, m, CH_2); m/z (I, %): 340 (5, M^+).

*3-Methylsulfanyl-3-morpholino-2-[(4-nitrophenyl)azo]prop-2-enenitrile (**7e**)*. Red solid (213 mg, 64%), m.p. 202-203 ºC; [Found: C, 50.65, H, 4.27, N, 21.22. $C_{14}H_{15}N_5O_3S$ requires C, 50.44, H, 4.54, N 21.01%]; δ_H (400 MHz, $CDCl_3$) 8.25 and 7.71 (4H, AA'XX', *J* 9.2 Hz, Ar), 3.98-3.91 (4H, m, CH_2), 3.86-3.79 (4H, m, CH_2), 2.62 (3H, s, SMe); m/z (I, %): 333 (14, M^+).

*(2-[(4-Methoxyphenyl)azo]-3-methylsulfanyl-3-morpholino-prop-2-enenitrile (**7f**)*. Yellow solid (273 mg, 86%), m.p. 118-119 ºC; [Found: C, 56.76, H, 5.84, N, 17.40. $C_{15}H_{18}N_4O_2S$ requires C, 56.59, H, 5.70, N, 17.60%]; δ_H (400 MHz, $CDCl_3$) 7.54 and 6.94 (4H, AA'XX', *J* 8.8 Hz, Ar), 3.82 (3H, s, OMe), 3.90-3.75 (8H, m, CH_2), 2.53 (3H, s, SMe); m/z (I, %): 318 (23, M^+).

*3-Allylsulfanyl-2-[(3,5-dimethylphenyl)azo]-3-morpholino-prop-2-enenitrile (**8e**)*. Orange solid (329 mg, 73%), m.p. 115-116 ºC; [Found: C, 48.11, H, 3.39, N, 12.36. $C_{18}H_{16}F_6N_4OS$ requires C, 48.00, H, 3.58, N, 12.44%]; δ_H (400 MHz, $CDCl_3$) 8.05 (1H, s, Ar), 7.70 (1H, s, Ar), 7.30 (1H, s, Ar), 5.95-5.85 (1H, m, CH), 5.27 (1H, dd, *J* 16.2, 1.6 , $CH\underline{CH_2}$), 5.20 (1H, d, *J* 9.6 Hz, $CH\underline{CH_2}$), 4.28-4.20 (4H, m, CH_2), 3.90-3.82 (4H, m, CH_2), 3.78 (2H, d, *J* 7.2 Hz, SCH_2); m/z (I, %): 450 (23, M^+).

*(3-(Azepan-1-yl)-3-methylsulfanyl-2-[(4-nitrophenyl)azo]prop-2-enenitrile (**7g**)*. Red solid (242 mg, 70%), m.p. 160-161 ºC; [Found: 55.58, H, 5.71, N, 20.02. $C_{16}H_{19}N_5O_2S$ requires C, 55.64, H, 5.54, N, 20.27%]; δ_H (400 MHz, $CDCl_3$) 8.26 and 7.68 (4H, AA'XX', *J* 9.2 Hz, Ar), 3.99-3.89 (4H, m, CH_2), 2.61 (3H, s, SMe), 1.90-1.82 (4H, m, CH_2), 1.61-1.54 (4H, m, CH_2); m/z (I, %): 345 (2, M^+).

*3-(Azepan-1-yl)-2-[(4-chlorophenyl)azo]-3-methylsulfanyl-prop-2-enenitrile (**7h**)*. Yellow solid (301 mg, 92%), m.p. 108-109 ºC; [Found: C, 57.27, H, 5.81, N,16.51. $C_{16}H_{19}ClN_4S$ requires C, 57.39, H, 5.72, N, 16.73%]; δ_H (400 MHz, $CDCl_3$) 7.52 and 7.48 (4H, AA'BB', *J* 8.8 Hz, Ar), 3.92-3.87 (4H, m, CH_2), 2.57 (3H, s, SMe), 1.90-1.80 (4H, m, CH_2), 1.62-1.50 (4H, m, CH_2); m/z (I, %): 334 (2, M^+).

*3-Methylthio-2-(4-nitrophenylazo)-3-thiomorpholinoacrylonitrile (**7i**)*. Red solid (202 mg, 58%), m.p. 177-178 ºC; [Found: C, 47.97, H, 4.12, N, 19.75. $C_{14}H_{15}N_5O_2S_2$ requires C, 48.12, H, 4.33, N, 20.04%]; δ_H (400 MHz, $CDCl_3$) 8.26 and 7.70 (4H, AA'XX', *J* 9.0 Hz, Ar), 4.20-4.15 (4H, m, CH_2), 2.90-2.80 (4H, m, CH_2), 2.61 (3H, s, SMe); m/z (I, %): 349 (4, M^+).

*3-Methylsulfanyl-2-[(4-nitrophenyl)azo]-3-thiomorpholino-prop-2-enenitrile (**7j**)*. Yellow solid (287 mg, 85%), m.p. 166-167 ºC; [Found: C, 49.43, H, 4.57, N, 16.27. $C_{14}H_{15}ClN_4S_2$ requires C, 49.62, H, 4.46, N, 16.53%]; δ_H (400 MHz, $CDCl_3$) 7.57 and 7.51 (4H, AA'BB', *J* 8.8 Hz, Ar), 4.09-4.05 (4H, m, CH_2), 2.87-2.82 (4H, m, CH_2), 2.56 (3H, s, SMe); m/z (I, %): 338 (4, M^+).

*3-Methylsulfanyl-2-[p-tolylazo]-3-thiomorpholino-prop-2-enenitrile (**7k**)*. Yellow solid (249 mg, 67%), m.p. 95-96 ºC; [Found: C, 48.11, H, 4.15, N, 14.83. $C_{15}H_{15}F_3N_4S_2$ requires C, 48.38, H, 4.06, N, 15.04%]; δ_H (400 MHz, $CDCl_3$) 7.71 (4H, s, Ar), 4.18-4.11 (4H, m, CH_2), 2.91-2.83 (4H, m, CH_2), 2.59 (3H, s, SMe); m/z (I, %): 372 (10, M^+).

References

1. Belskaya, N.P.; Koksharov, A.V.; Eliseeva, A.I.; Fan, Z.; Bakulev, V.A. *Chem. Heterocycl. Comp.*, **2011**, *47*, 564-570.
2. Deryabina, T. G.; Belskaya, N. P.; Kodess, M. I.; Dehaen, W.; Toppet, S.; Bakulev, V. A. *Tetrahedron Lett*., **2006**, *47*, 1853-1855.
3. Belskaya, N. P.; Bakulev, V. A.; Deryabina, T. G.; Subbotina, J. O.; Kodess, M. I.; Dehaen, W.; Toppet, S.; Robeyns, K.; Van Meervelt, L. *Tetrahedron*, **2009**, *65*, 7662-7672.

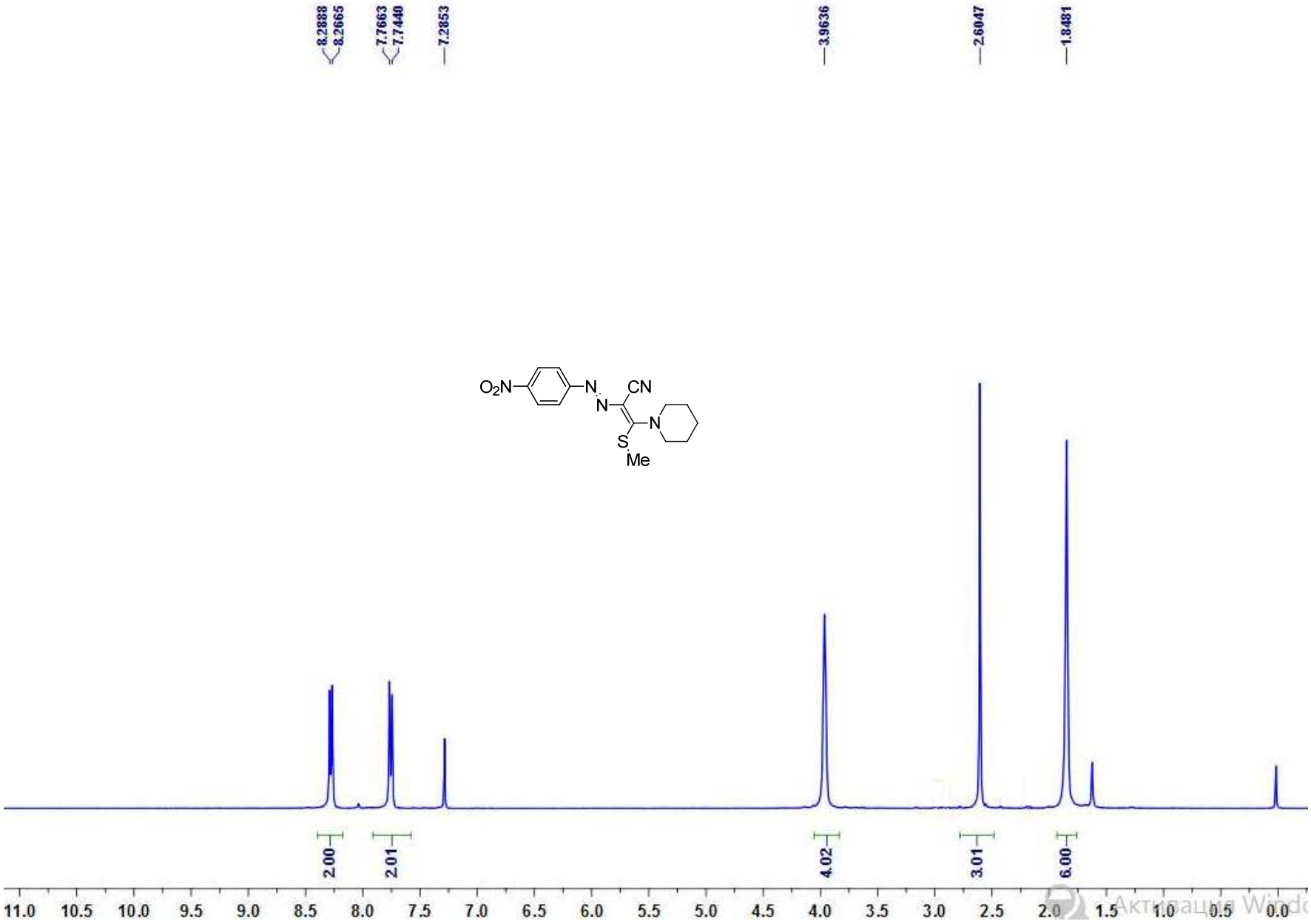


Fig. S1. Spectrum ^{1}H NMR 3-methylsulfanyl-2-[(4-nitrophenyl)azo]-3-(1-piperidyl)prop-2-enenitrile (**7a**) ($CDCl_3$)

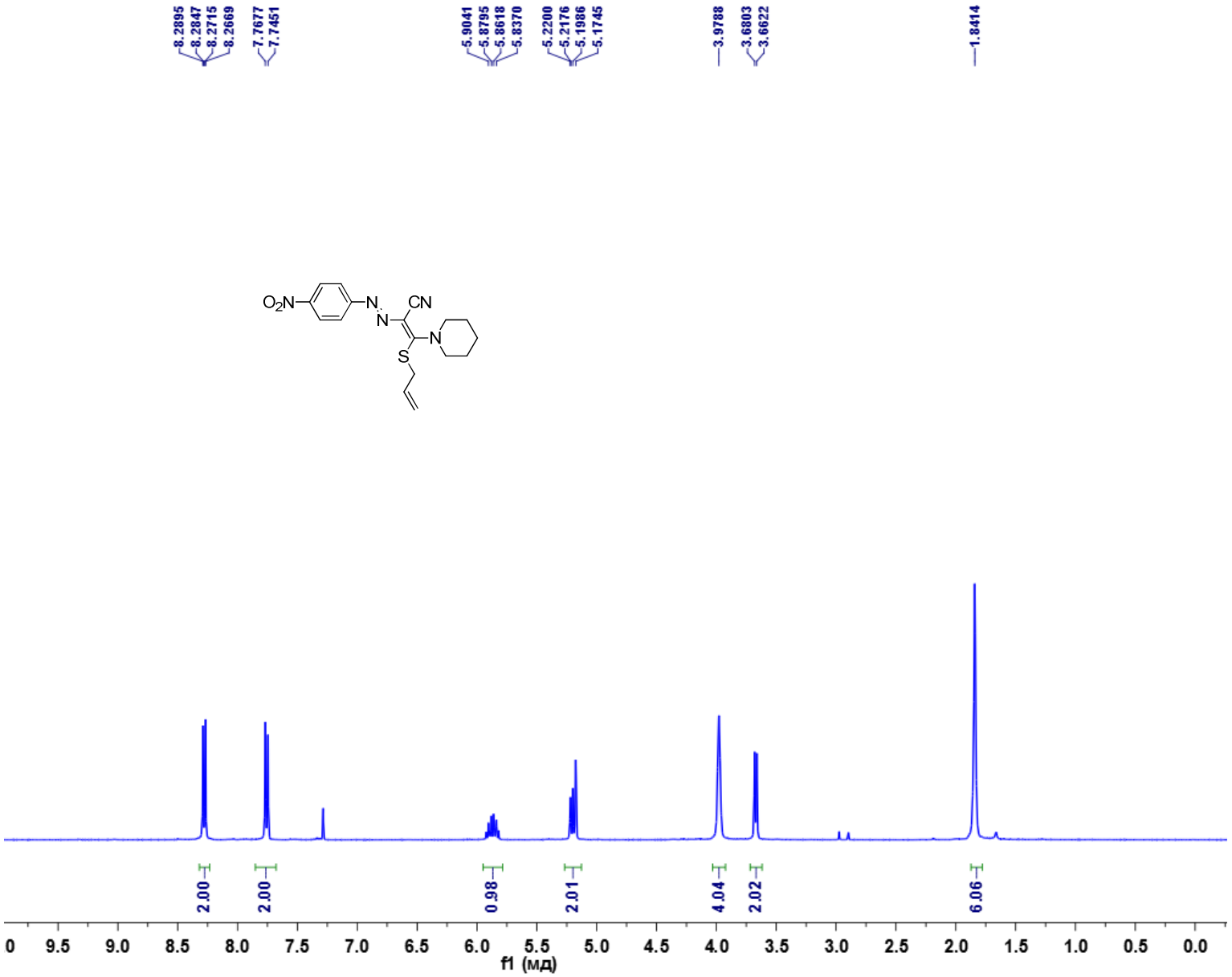


Fig. S2. Spectrum ^{1}H NMR 3-allylsulfanyl-2-[(4-nitrophenyl)azo]-3-(1-piperidyl)prop-2-enenitrile (**8a**) ($CDCl_3$)

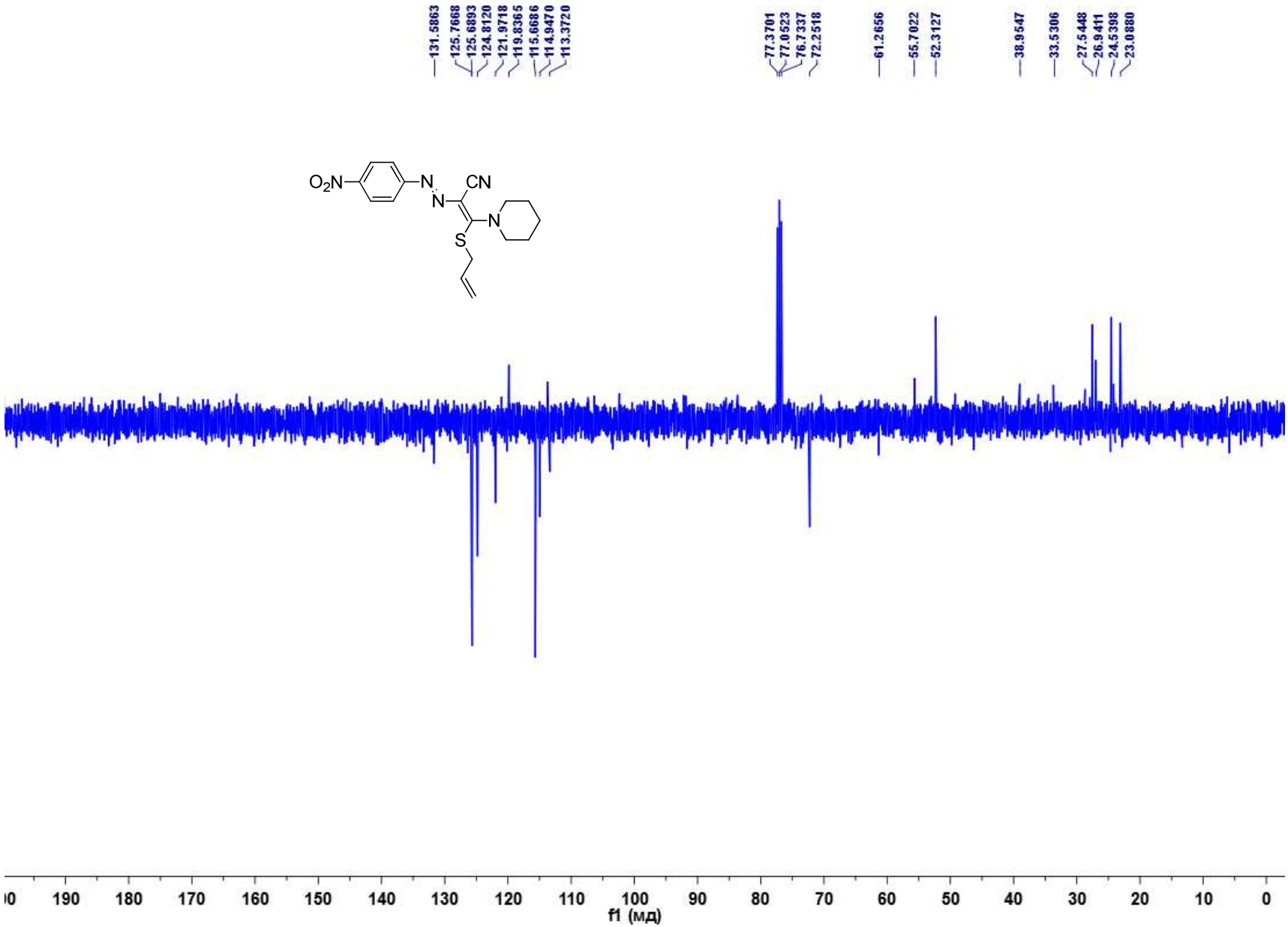


Fig. S3. Spectrum ^{13}C NMR 3-allylsulfanyl-2-[(4-nitrophenyl)azo]-3-(1-piperidyl)prop-2-enenitrile (**8a**) ($CDCl_3$)

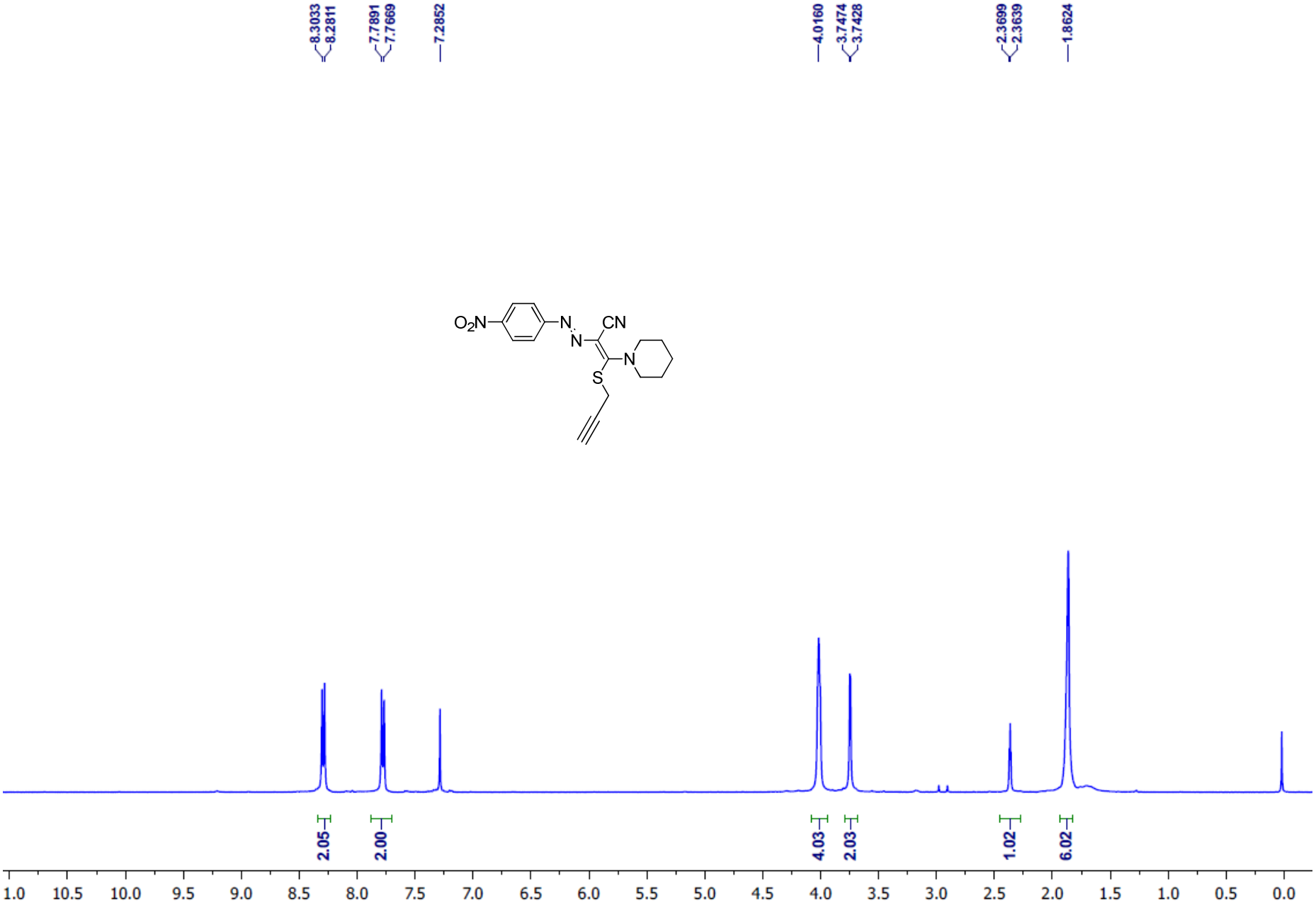


Fig. S4. Spectrum ^{1}H NMR 2-[(4-nitrophenyl)azo]-3-(1-piperidyl)-3-prop-2-ynylsulfanyl-prop-2-enenitrile (**9a**) ($CDCl_3$)

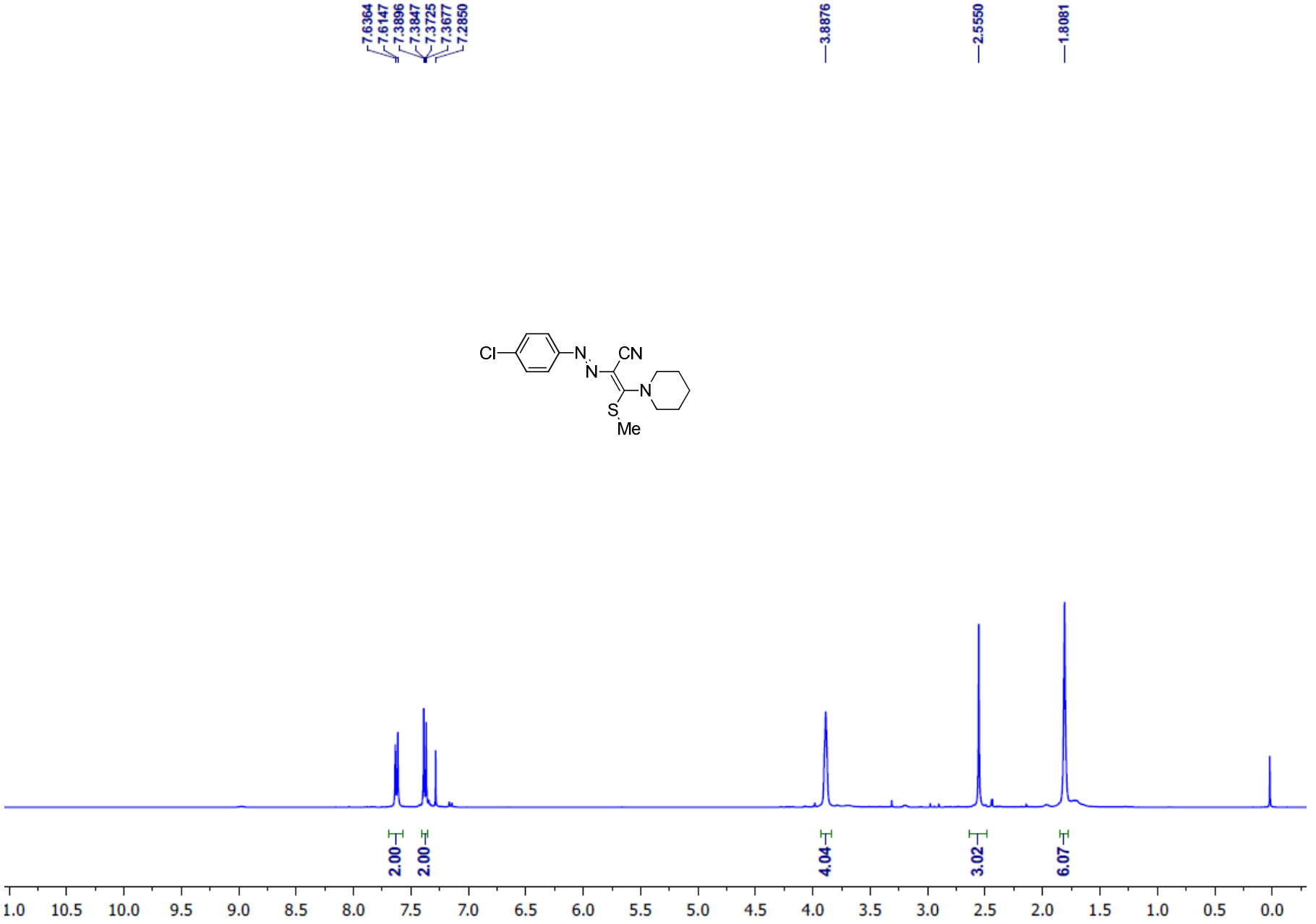


Fig. S5. Spectrum ^{1}H NMR 2-[(4-chlorophenyl)azo]-3-methylsulfanyl-3-(1-piperidyl)prop-2-enenitrile (**7b**) ($CDCl_3$)

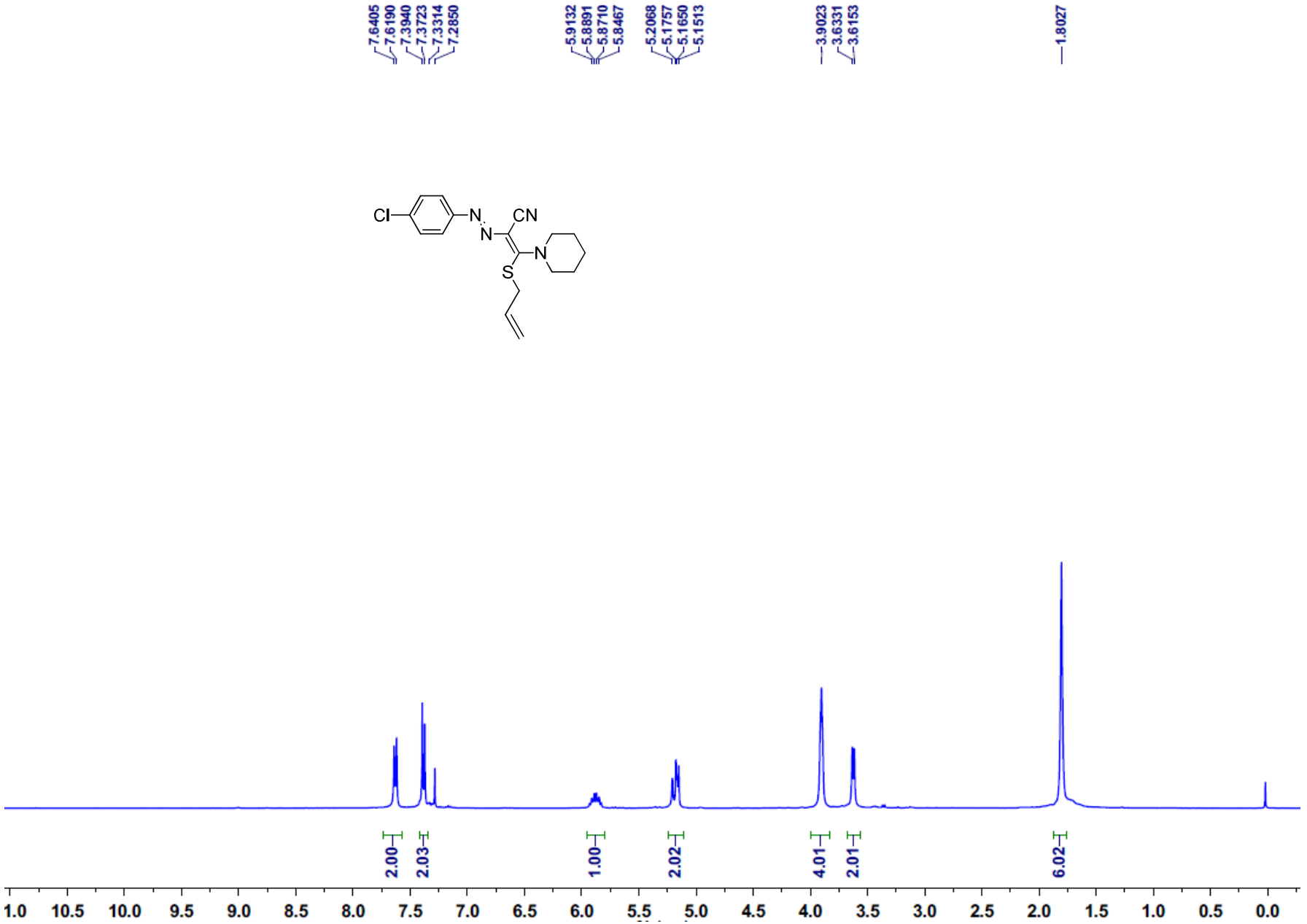


Fig. S6. Spectrum ^{1}H NMR 3-allylsulfanyl-2-[(4-chlorophenyl)azo]-3-(1-piperidyl)prop-2-enenitrile (**8b**) ($CDCl_3$)

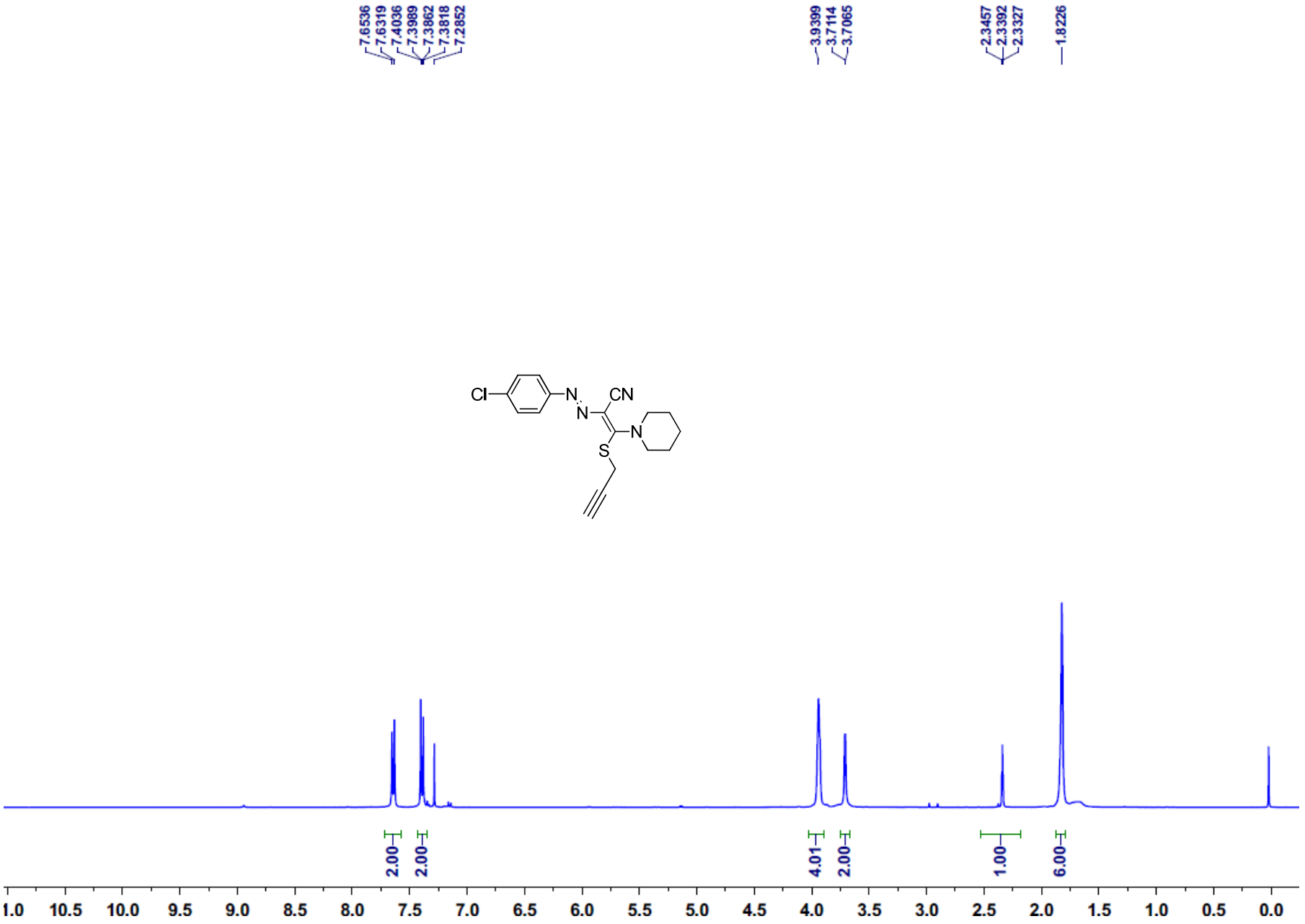


Fig. S7. Spectrum ^{1}H NMR 2-[(4-chlorophenyl)azo]-3-(1-piperidyl)-3-prop-2-ynylsulfanyl-prop-2-enenitrile (**9b**) ($CDCl_3$)

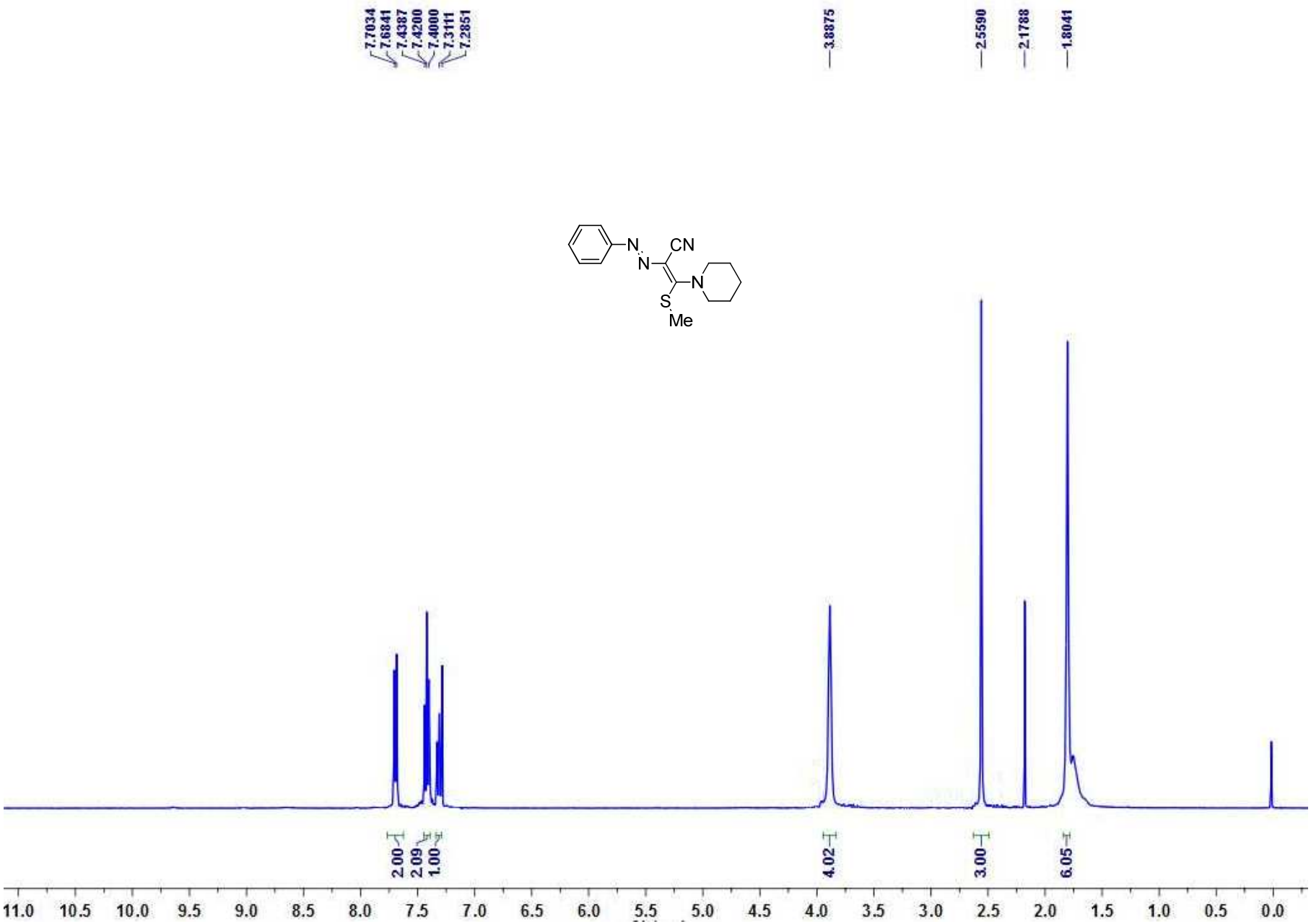


Fig. S8. Spectrum ^{1}H NMR 3-methylsulfanyl-2-(phenylazo)-3-(1-piperidyl)prop-2-enenitrile (**7c**) ($CDCl_3$)

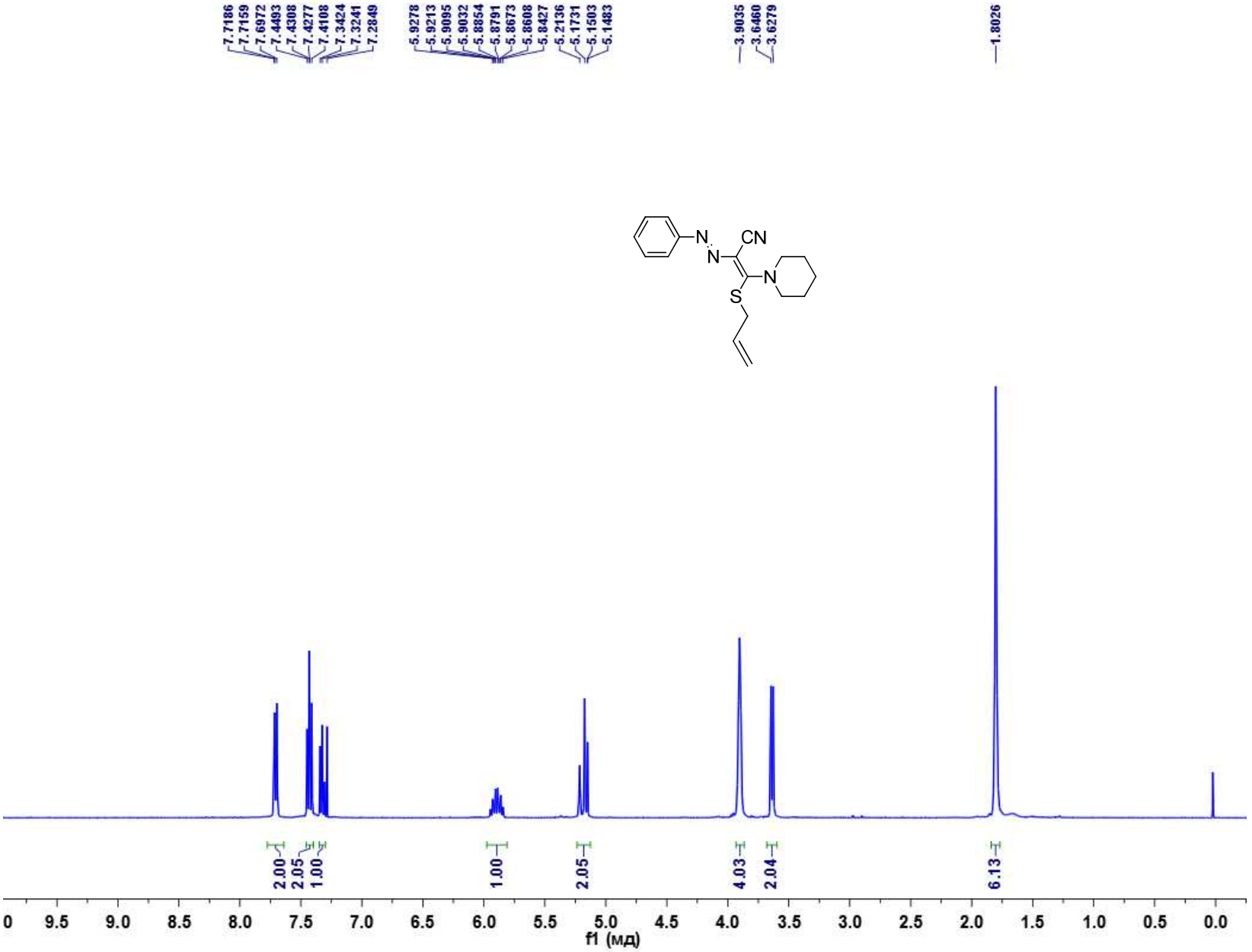


Fig. S9. Spectrum ^{1}H NMR 3-allylsulfanyl-2-(phenylazo)-3-(1-piperidyl)prop-2-enenitrile (**8c**) ($CDCl_3$)

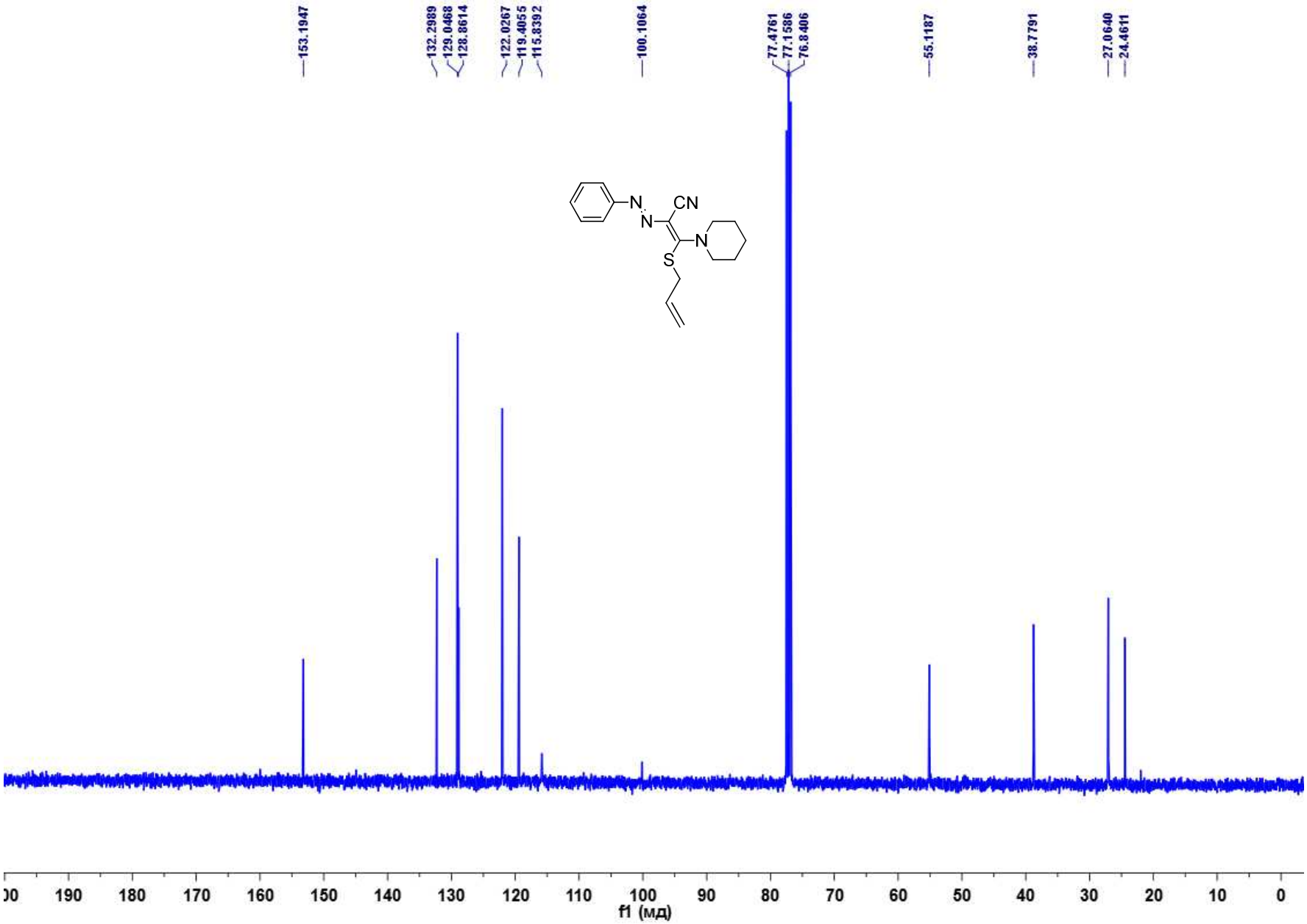


Fig. S10. Spectrum ^{13}C NMR 3-allylsulfanyl-2-(phenylazo)-3-(1-piperidyl)prop-2-enenitrile (**8c**) ($CDCl_3$)

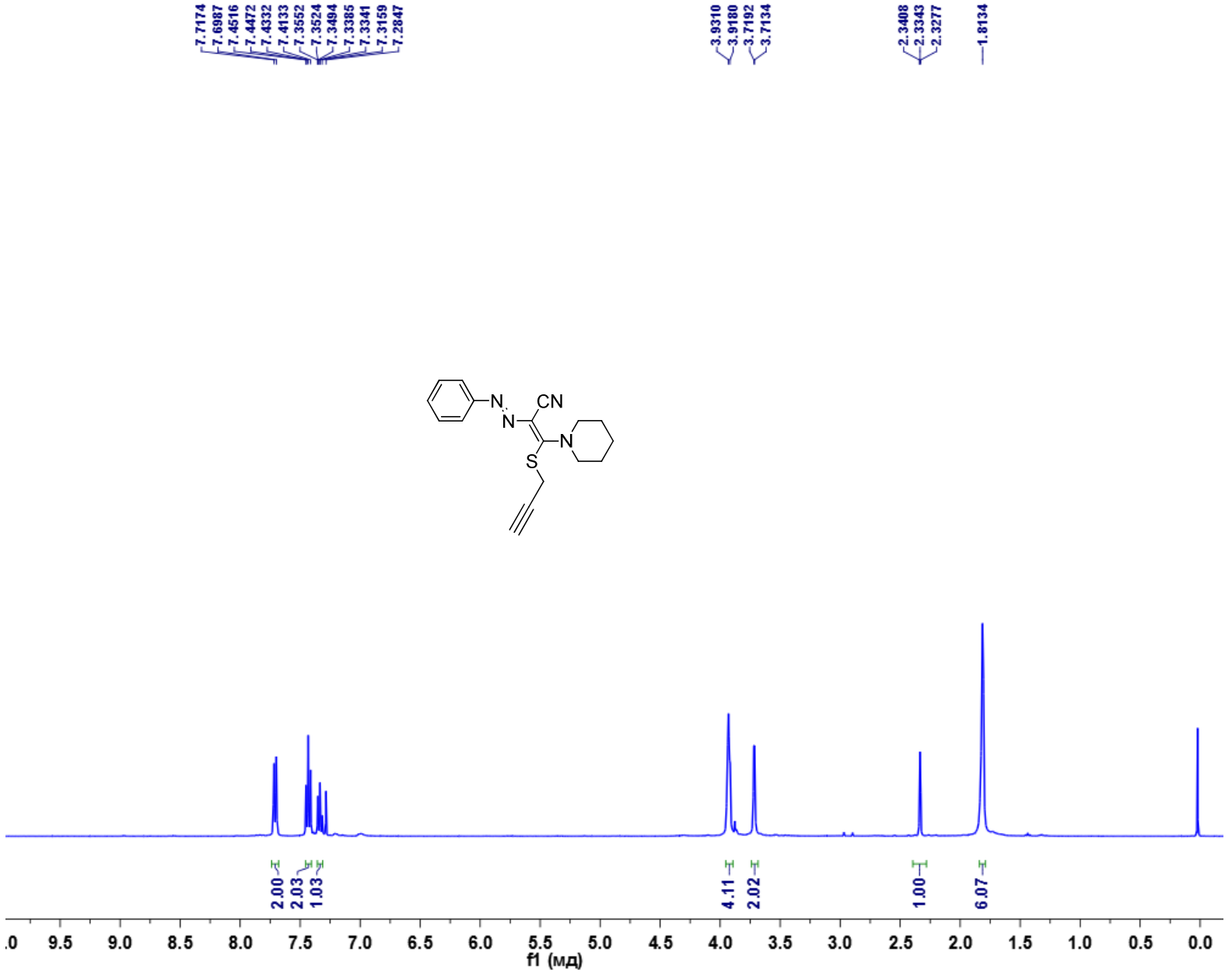


Fig. S11. Spectrum ^{1}H NMR 2-(phenylazo)-3-(1-piperidyl)-3-prop-2-ynylsulfanyl-prop-2-enenitrile (**9c**) (DMSO-d_6)

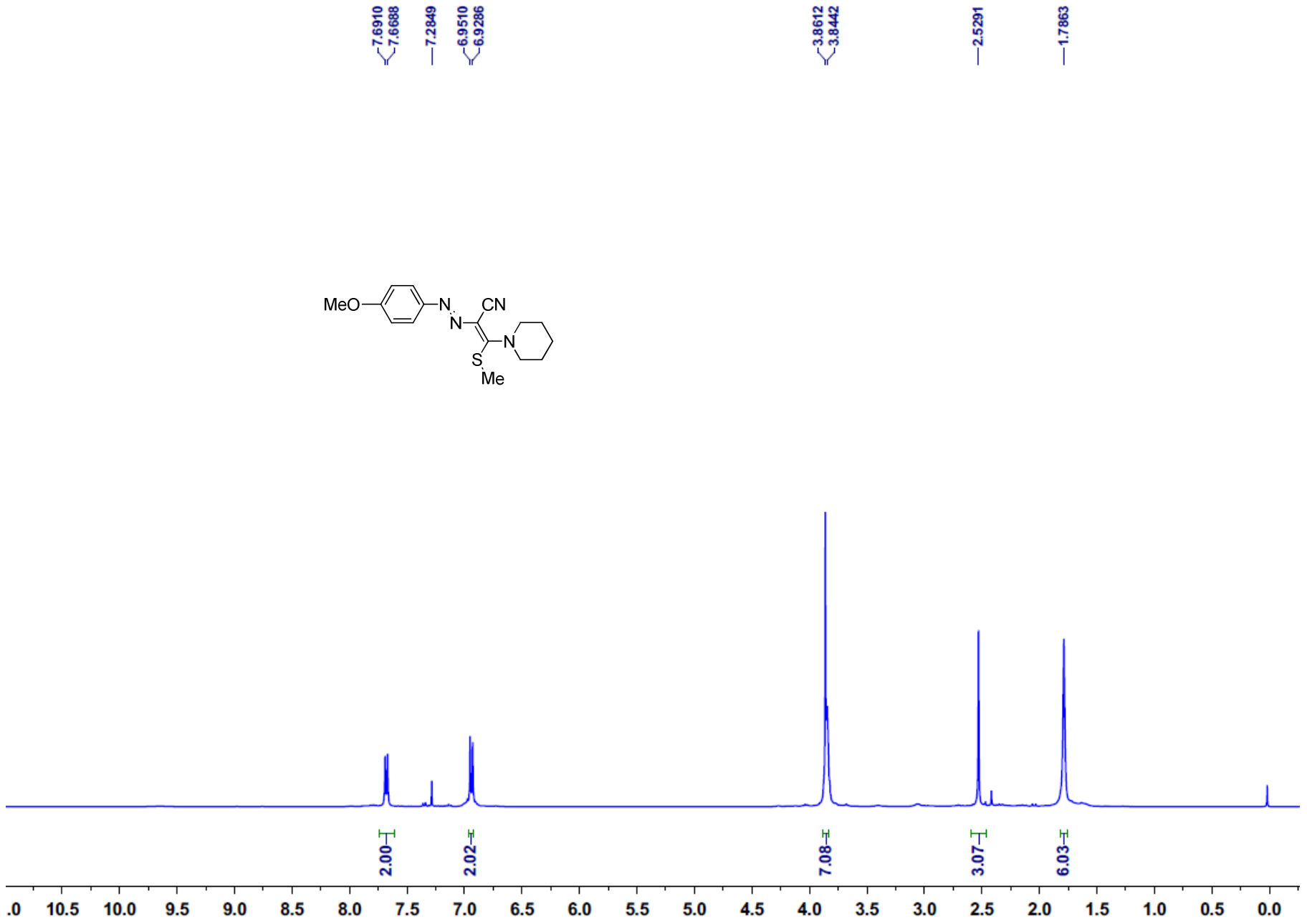


Fig. S12. Spectrum ^{1}H NMR 2-[(4-methoxyphenyl)azo]-3-methylsulfanyl-3-(1-piperidyl)prop-2-enenitrile (**7d**) ($CDCl_3$)

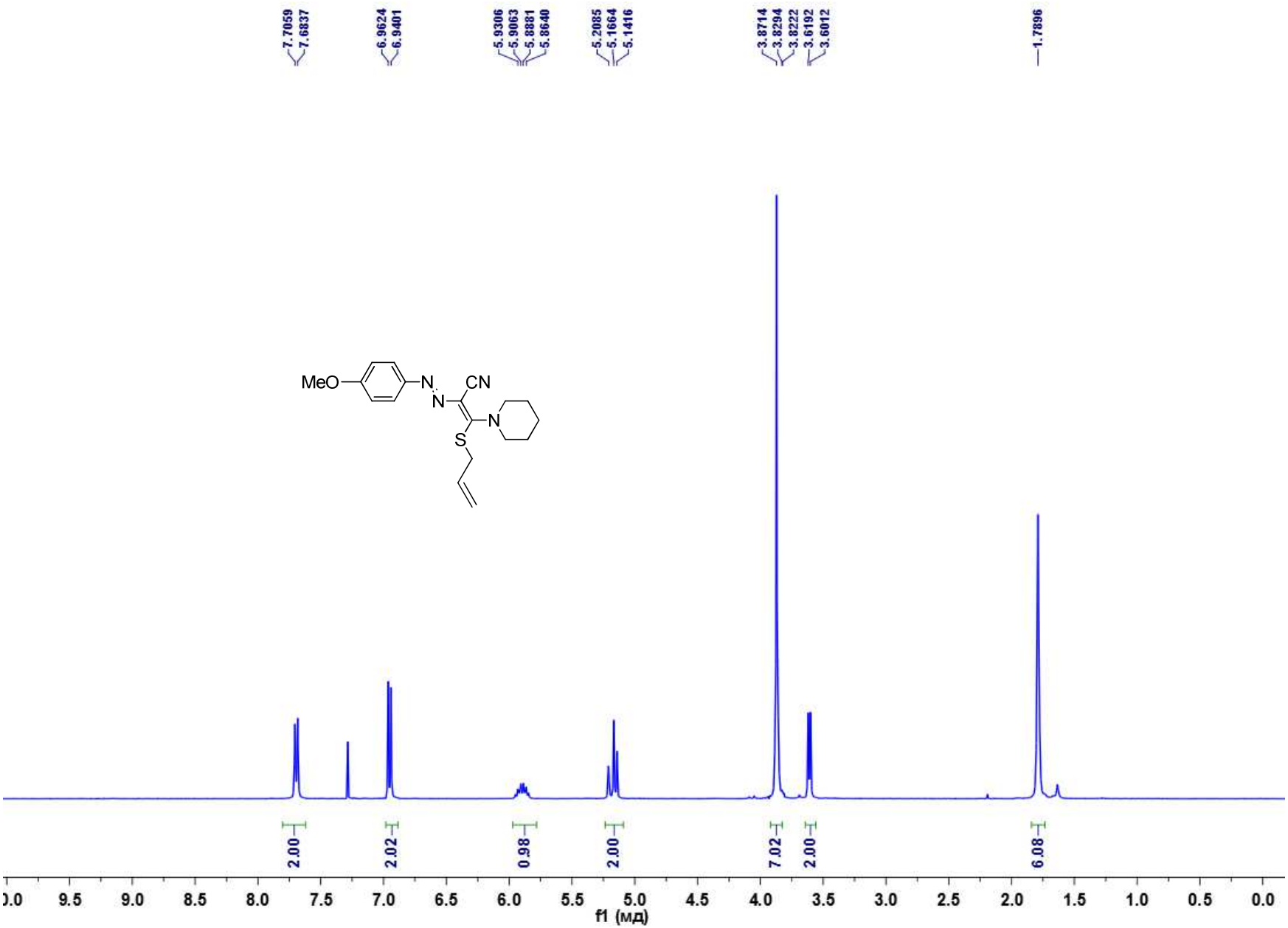


Fig. S13. Spectrum ^{1}H NMR 3-allylsulfanyl-2-[(4-methoxyphenyl)azo]-3-(1-piperidyl)prop-2-enenitrile (**8d**) ($CDCl_3$)

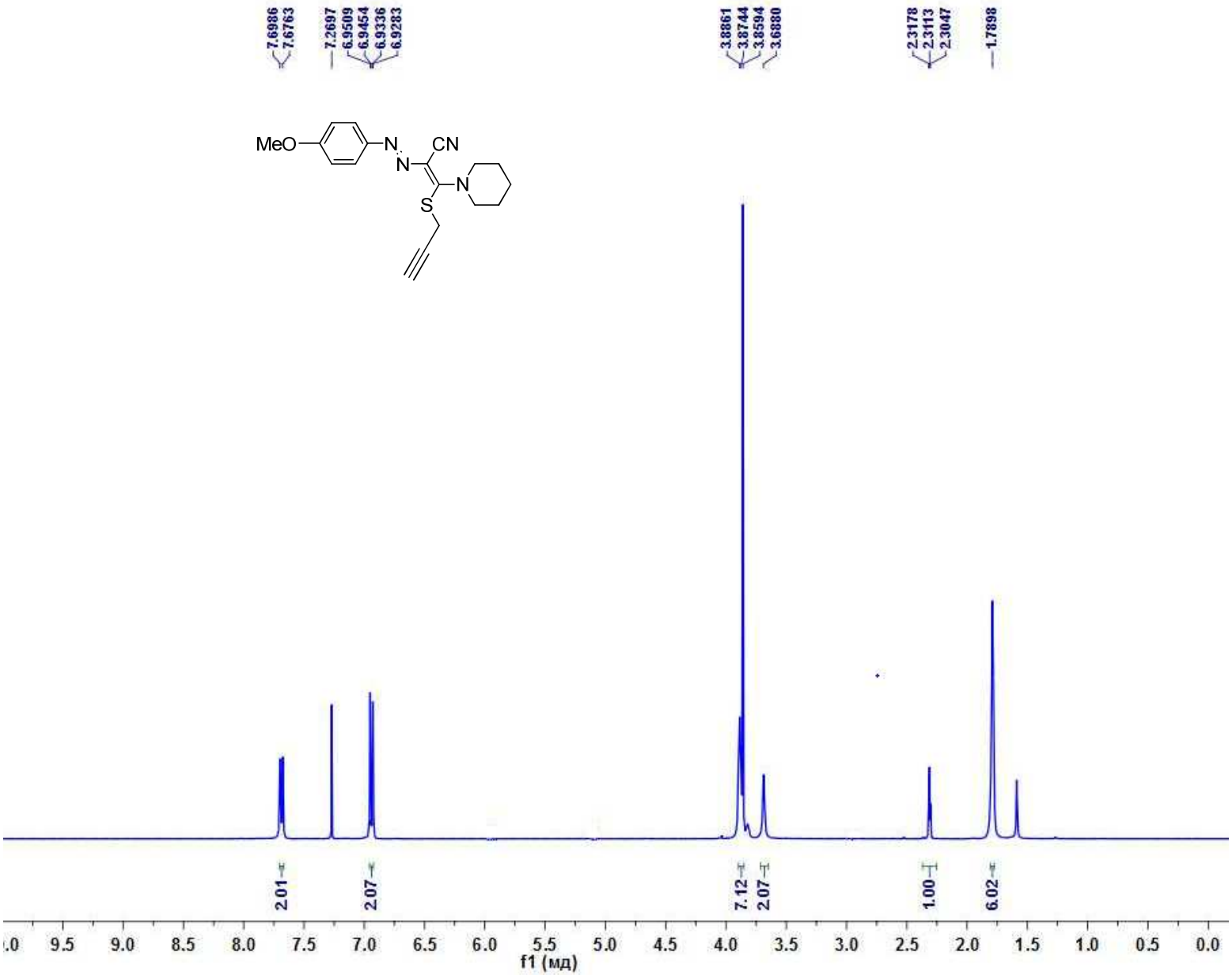


Fig. S14. Spectrum ^{1}H NMR (2-[(4-methoxyphenyl)azo]-3-(1-piperidyl)-3-prop-2-ynylsulfanyl-prop-2-enenitrile (**9d**) ($CDCl_3$)

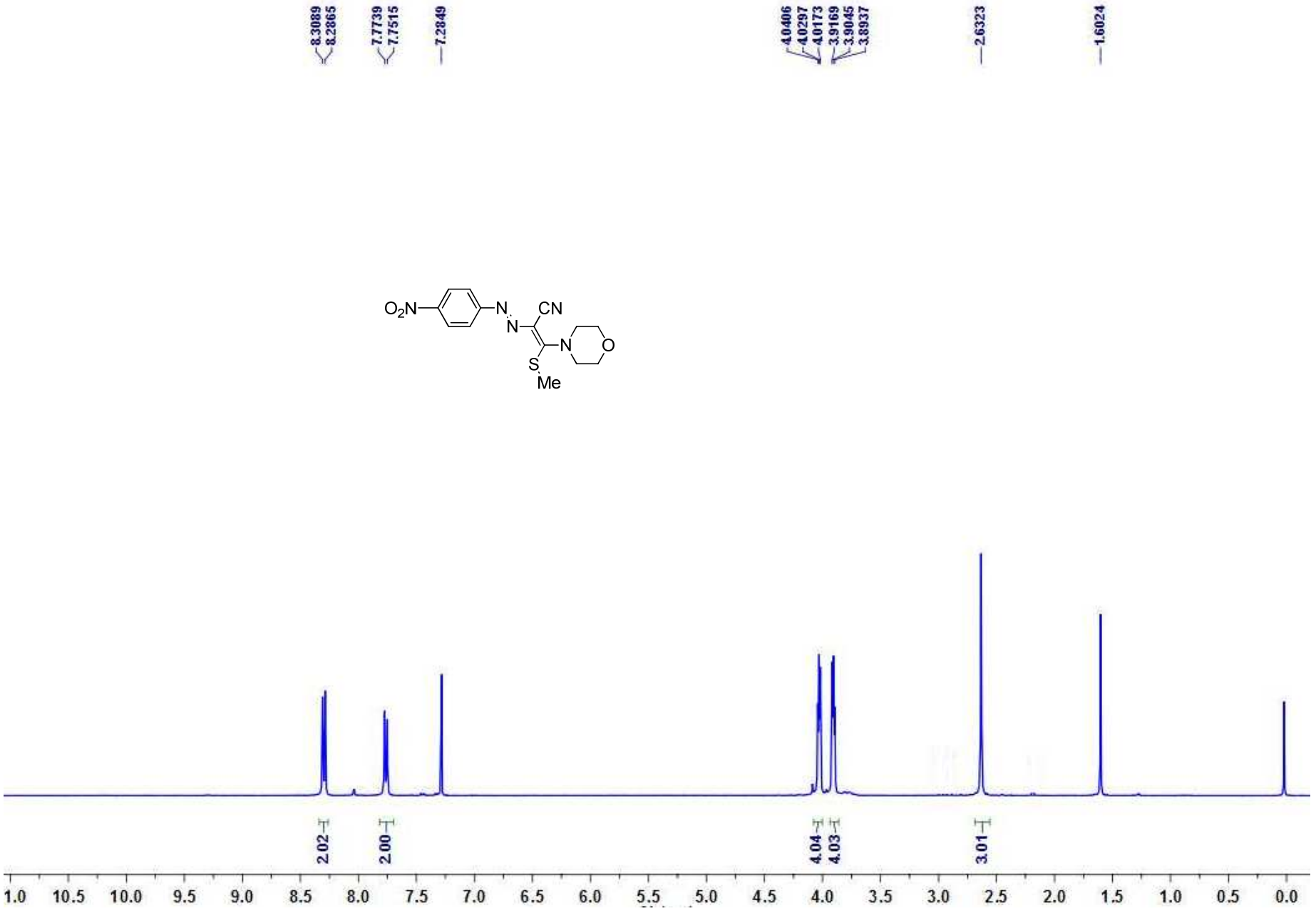


Fig. S15. Spectrum ^{1}H NMR 3-methylthio-3-morpholino-2-(4-nitrophenylazol)acrylonitrile (**7e)** ($CDCl_3$)

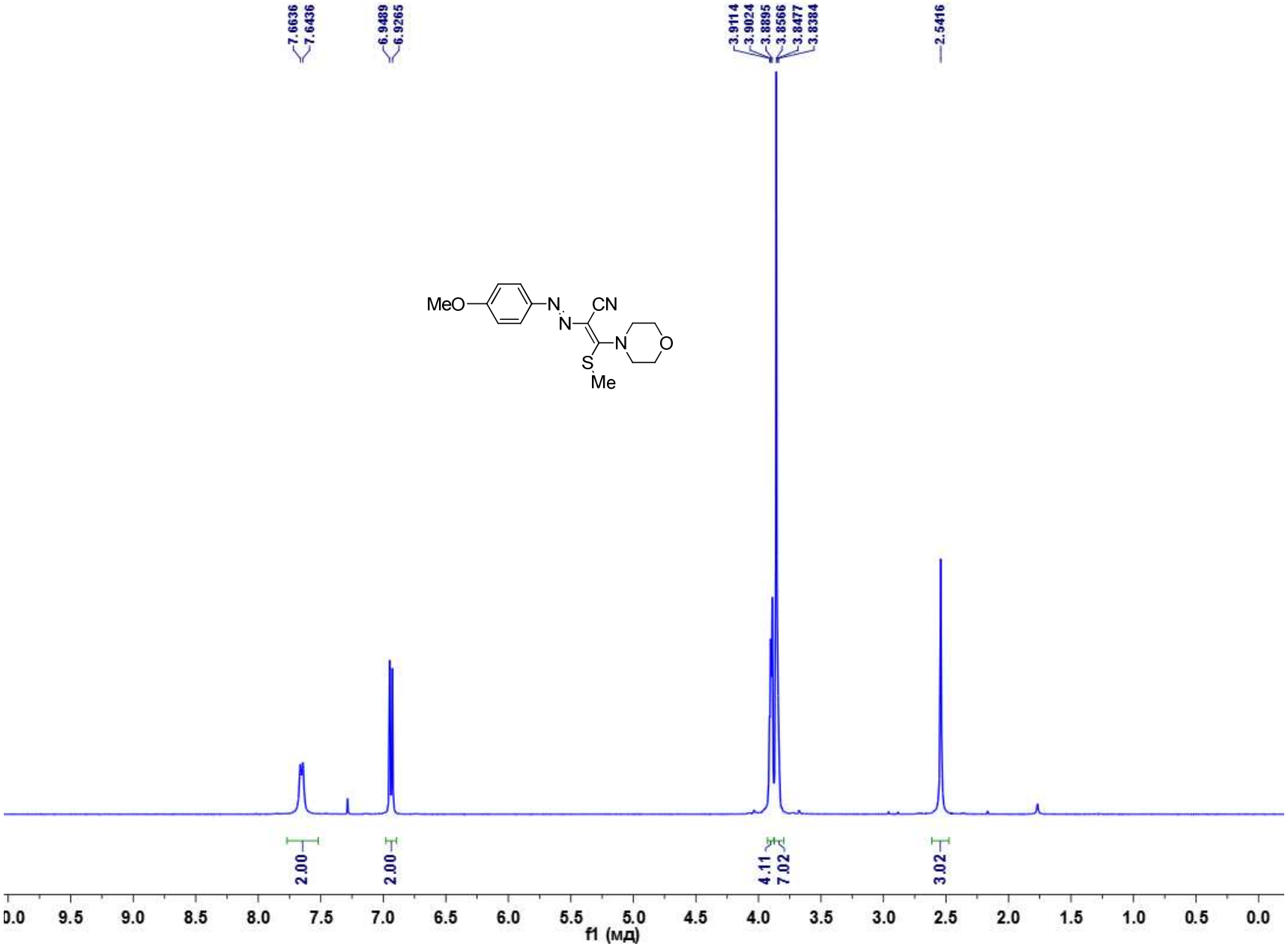


Fig. S16. Spectrum ^{1}H NMR 3-methylsulfanyl-3-morpholino-2-[(4-nitrophenyl)azo]prop-2-enenitrile (**7f**) ($CDCl_3$)

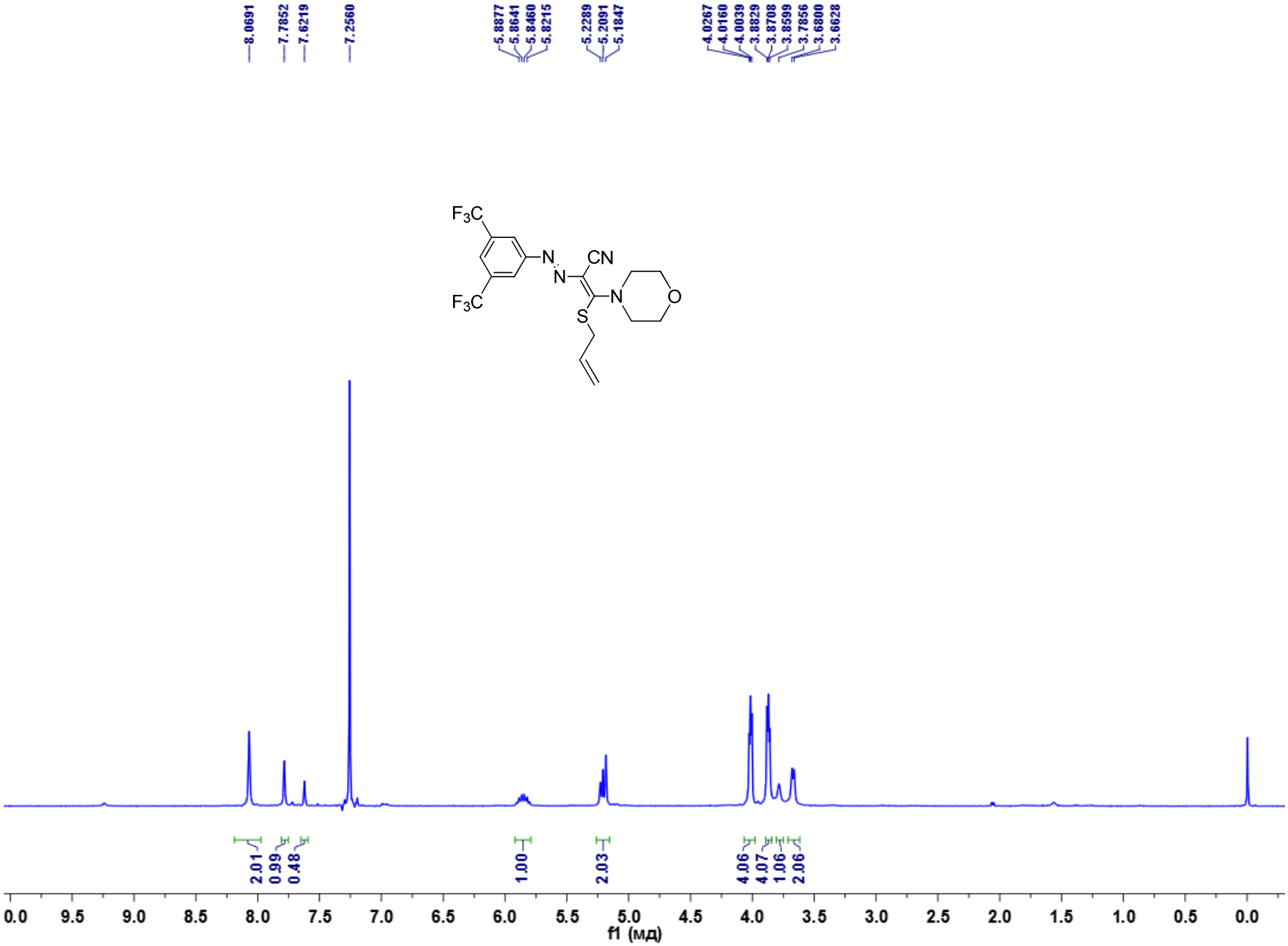


Fig. S17. Spectrum ^{1}H NMR 3-allylsulfanyl-2-[(3,5-dimethylphenyl)azo]-3-morpholino-prop-2-enenitrile (**8e**) ($CDCl_3$)

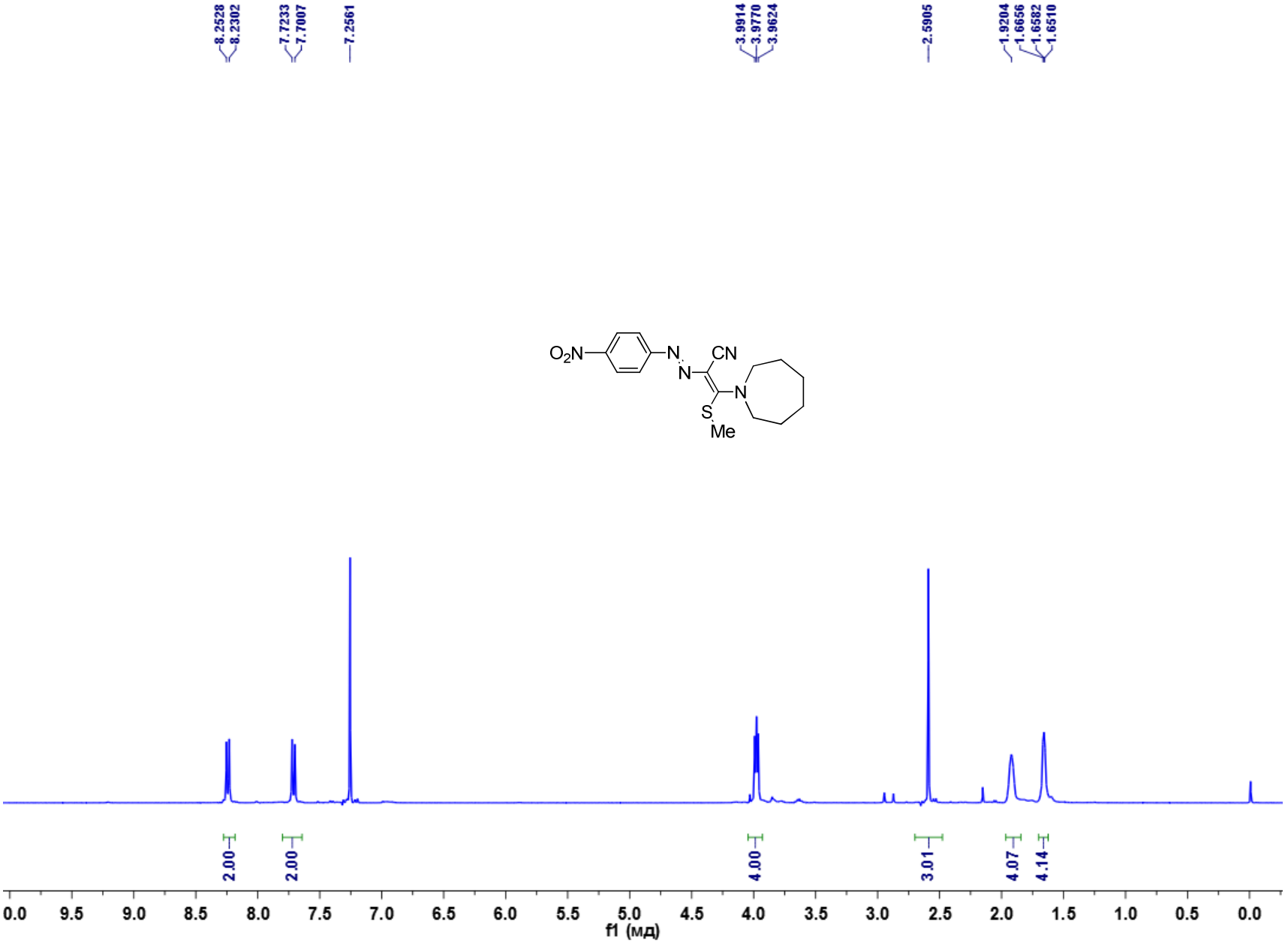


Fig. S18. Spectrum ^{1}H NMR (3-(azepan-1-yl)-3-methylsulfanyl-2-[(4-nitrophenyl)azo]prop-2-enenitrile (**7g**) ($CDCl_3$)

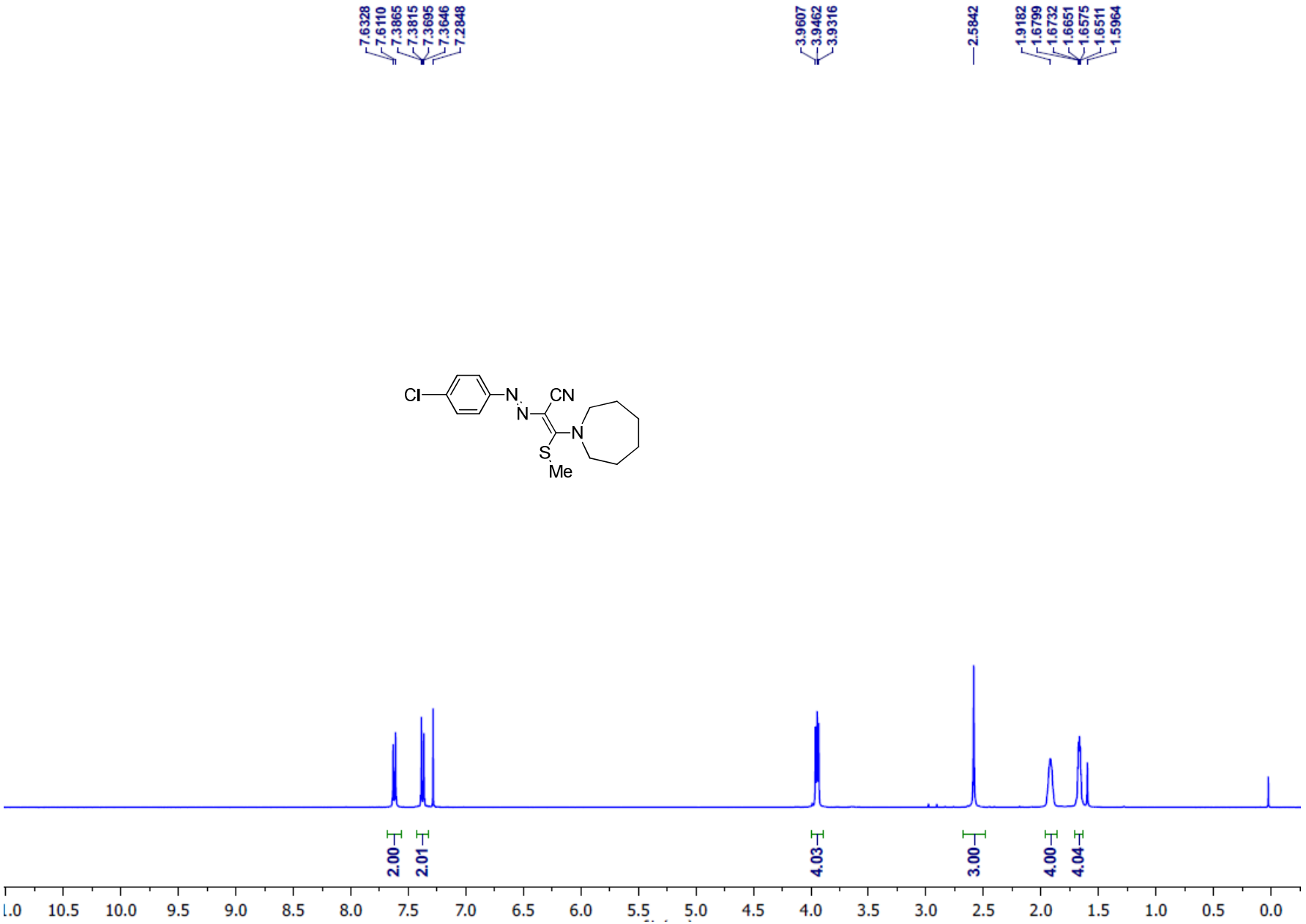


Fig. S19. Spectrum ^{1}H NMR 3-(azepan-1-yl)-2-[(4-chlorophenyl)azo]-3-methylsulfanyl-prop-2-enenitrile (**7h**) ($CDCl_3$)

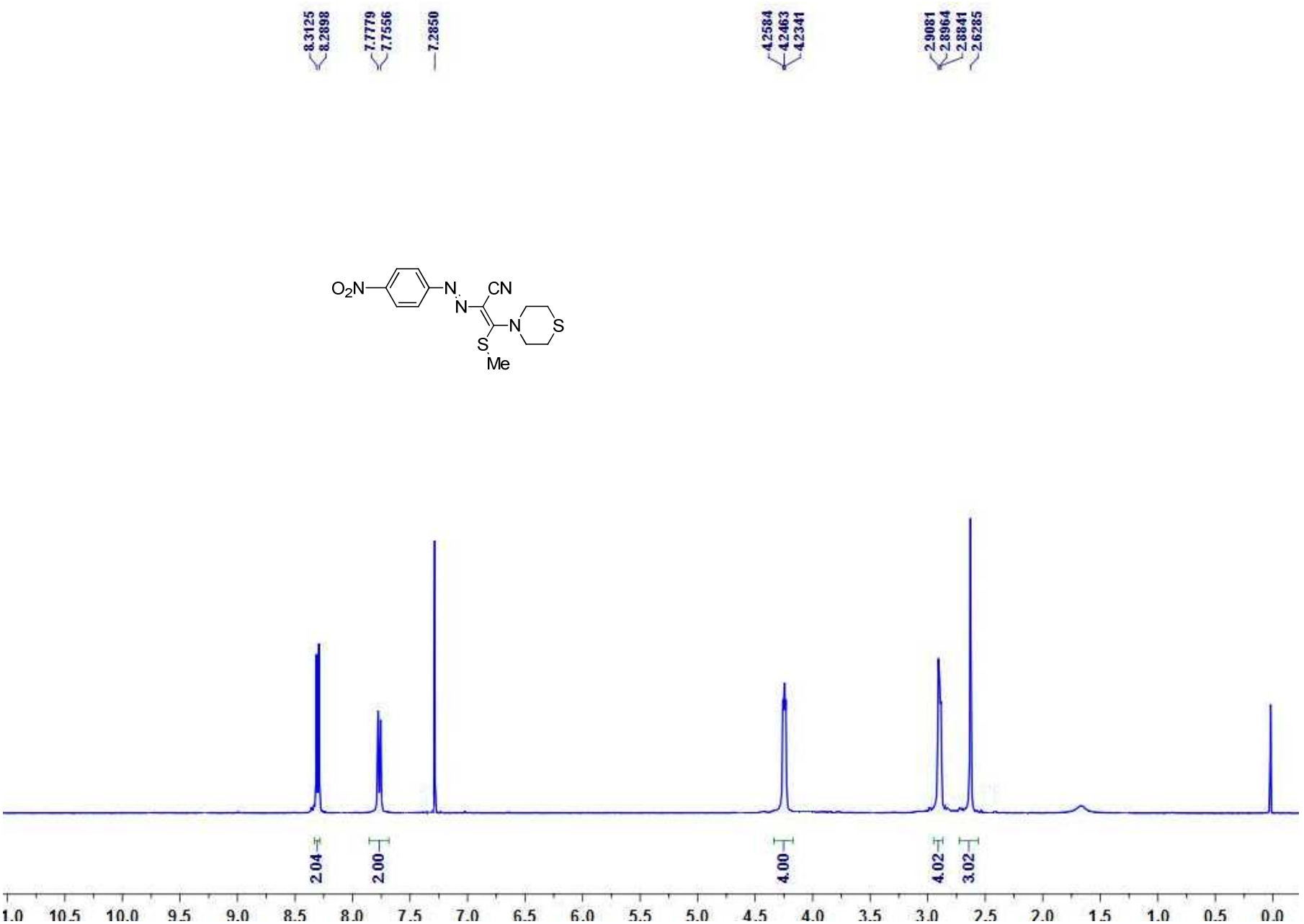


Fig. S20. Spectrum ^{1}H NMR 3-methylthio-2-(4-nitrophenylazo)-3-thiomorpholinoacrylonitrile (**7i**) ($CDCl_3$)

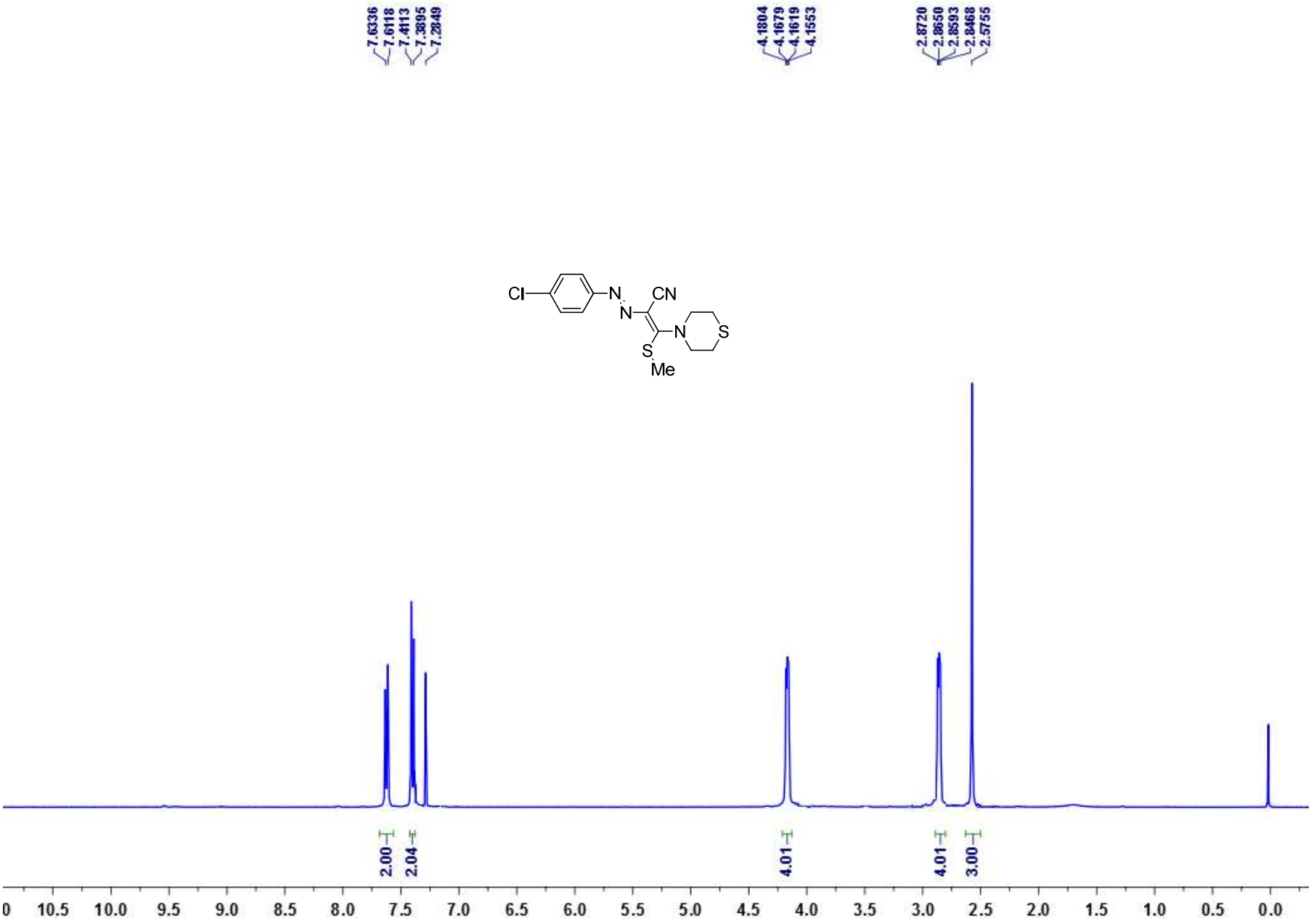


Fig. S21. Spectrum ^{1}H NMR 3-methylsulfanyl-2-[(4-nitrophenyl)azo]-3-thiomorpholino-prop-2-enenitrile (**7j**) ($CDCl_3$)

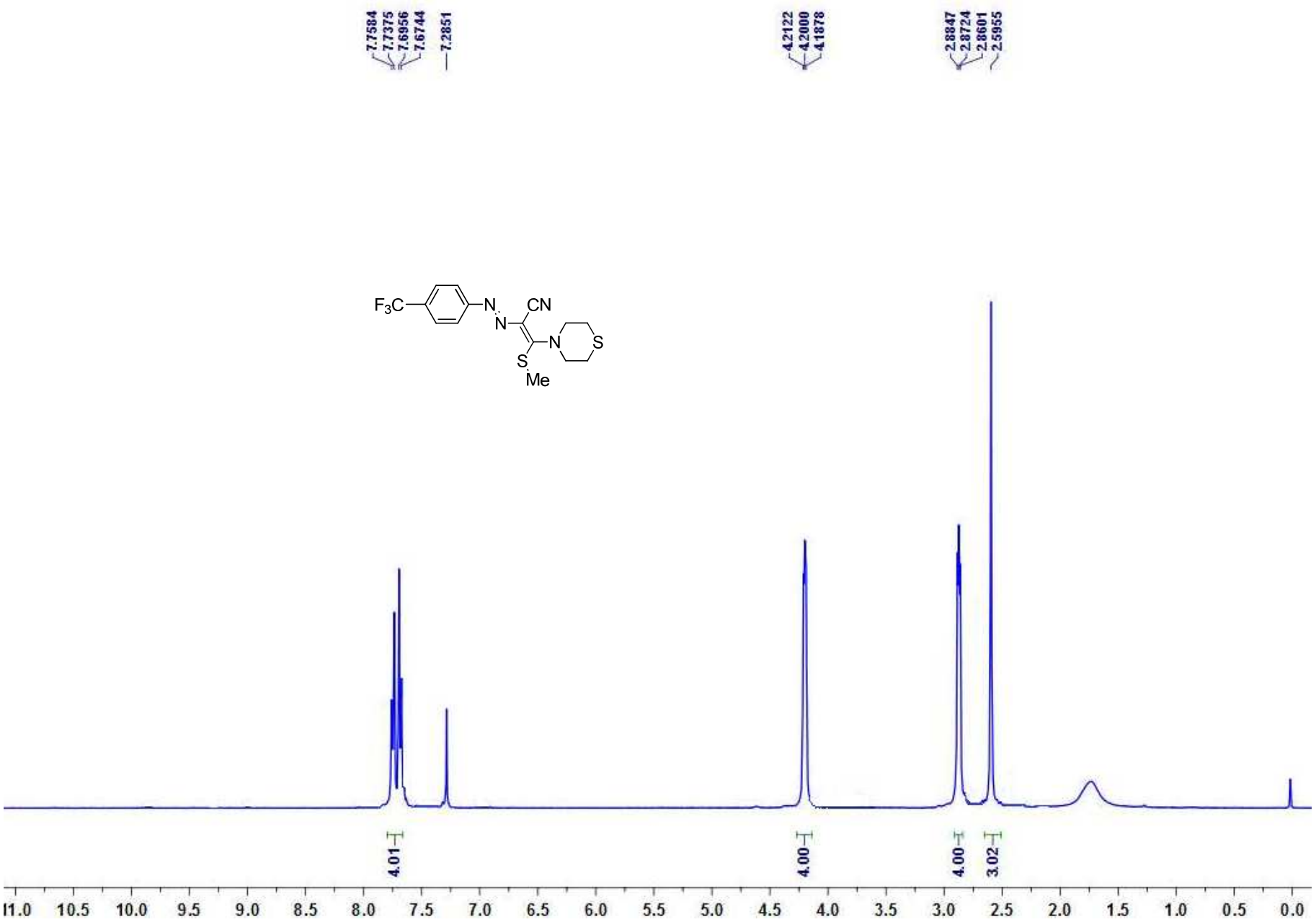


Fig. S22. Spectrum ^{1}H NMR 3-methylsulfanyl-2-[*p*-tolylazo]-3-thiomorpholino-prop-2-enenitrile (**7k**) ($CDCl_3$)

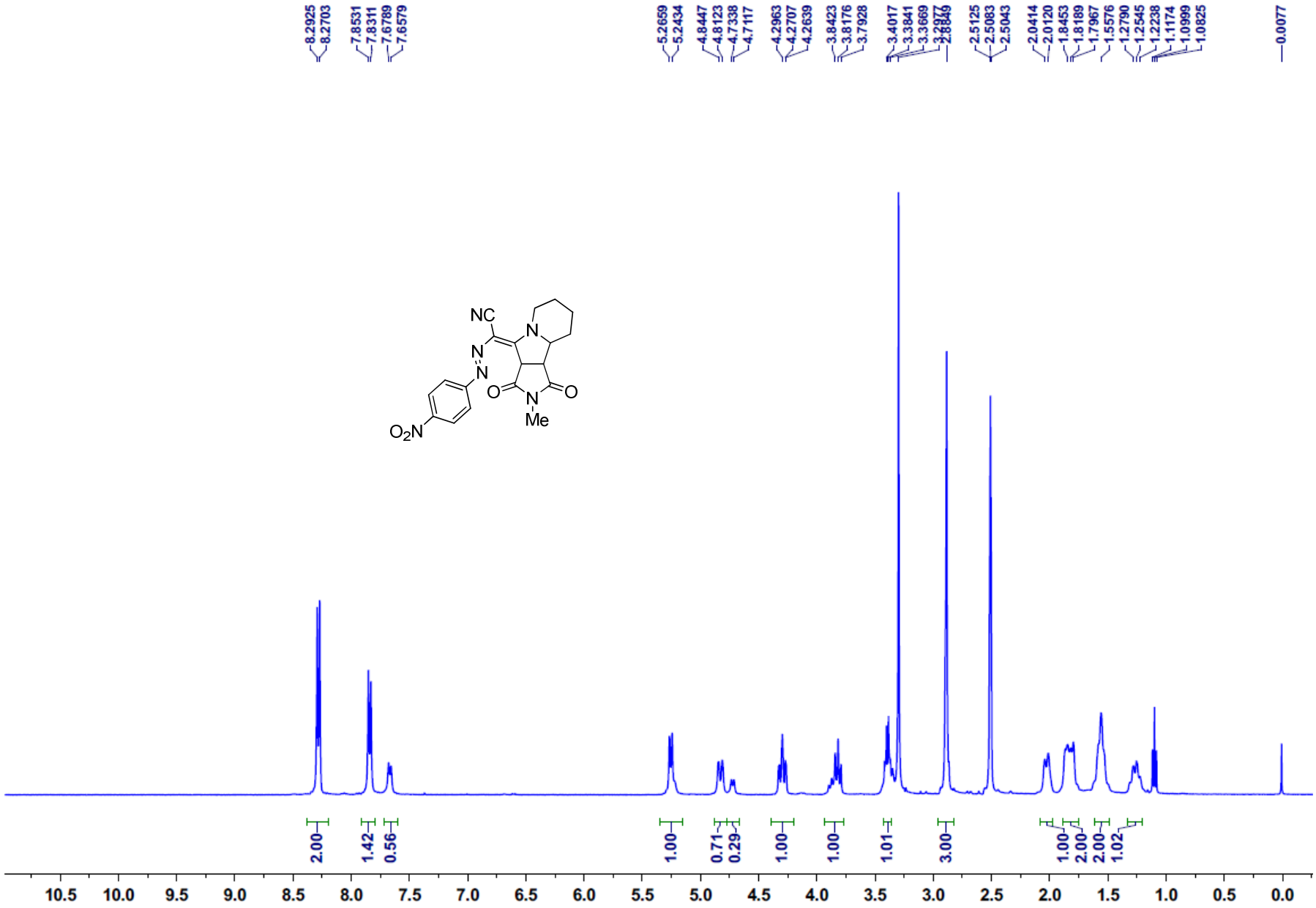


Fig. S23. Spectrum ^{1}H NMR 2-(2-methyl-1,3-dioxo-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)-2-[(4-nitrophenyl)azo] acetonitrile (**10a**) (DMSO-d_6)

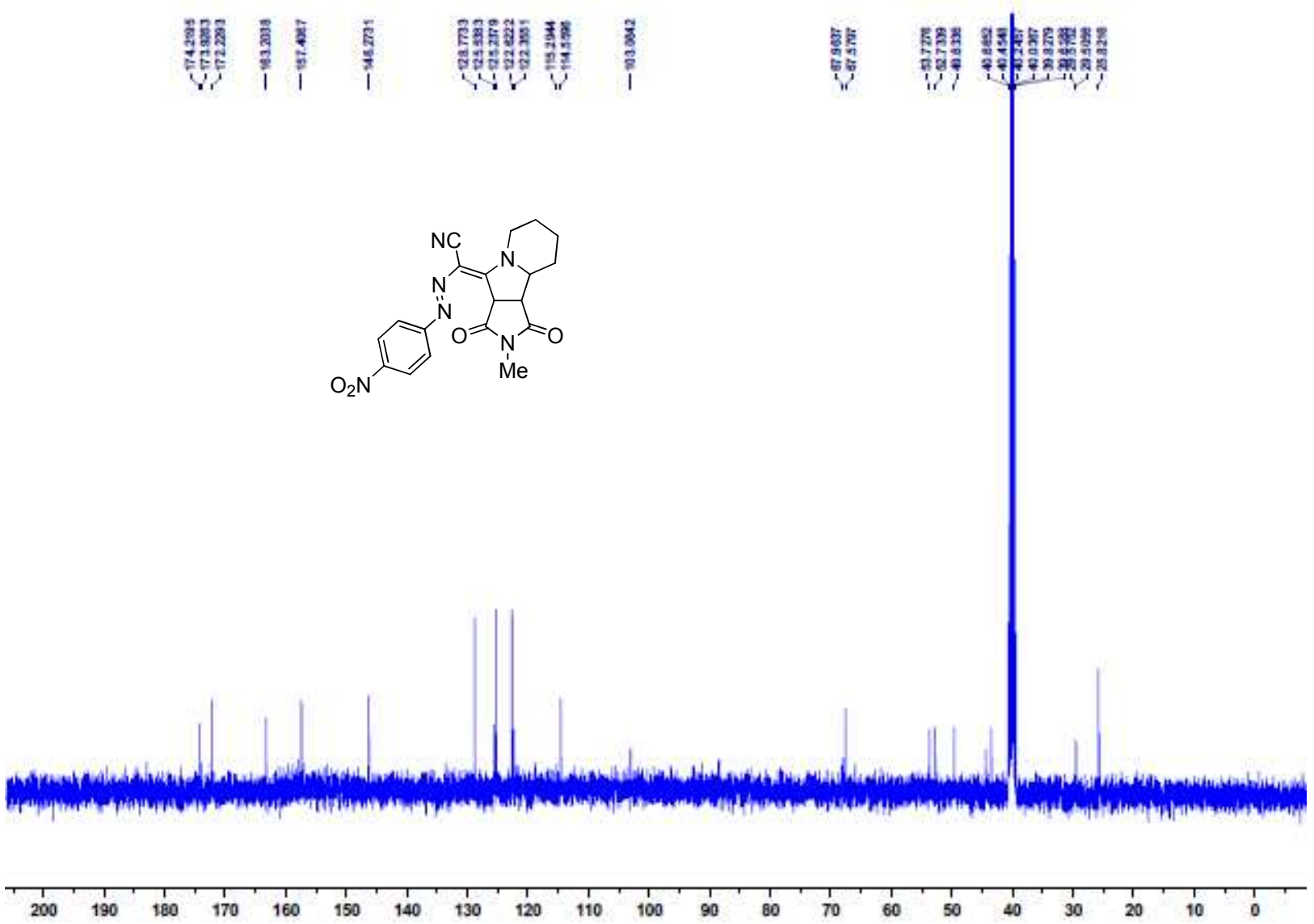


Fig. S24. Spectrum ^{13}C NMR 2-(2-methyl-1,3-dioxo-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)-2-[(4-nitrophenyl)azo] acetonitrile (**10a**) (DMSO-d_6)

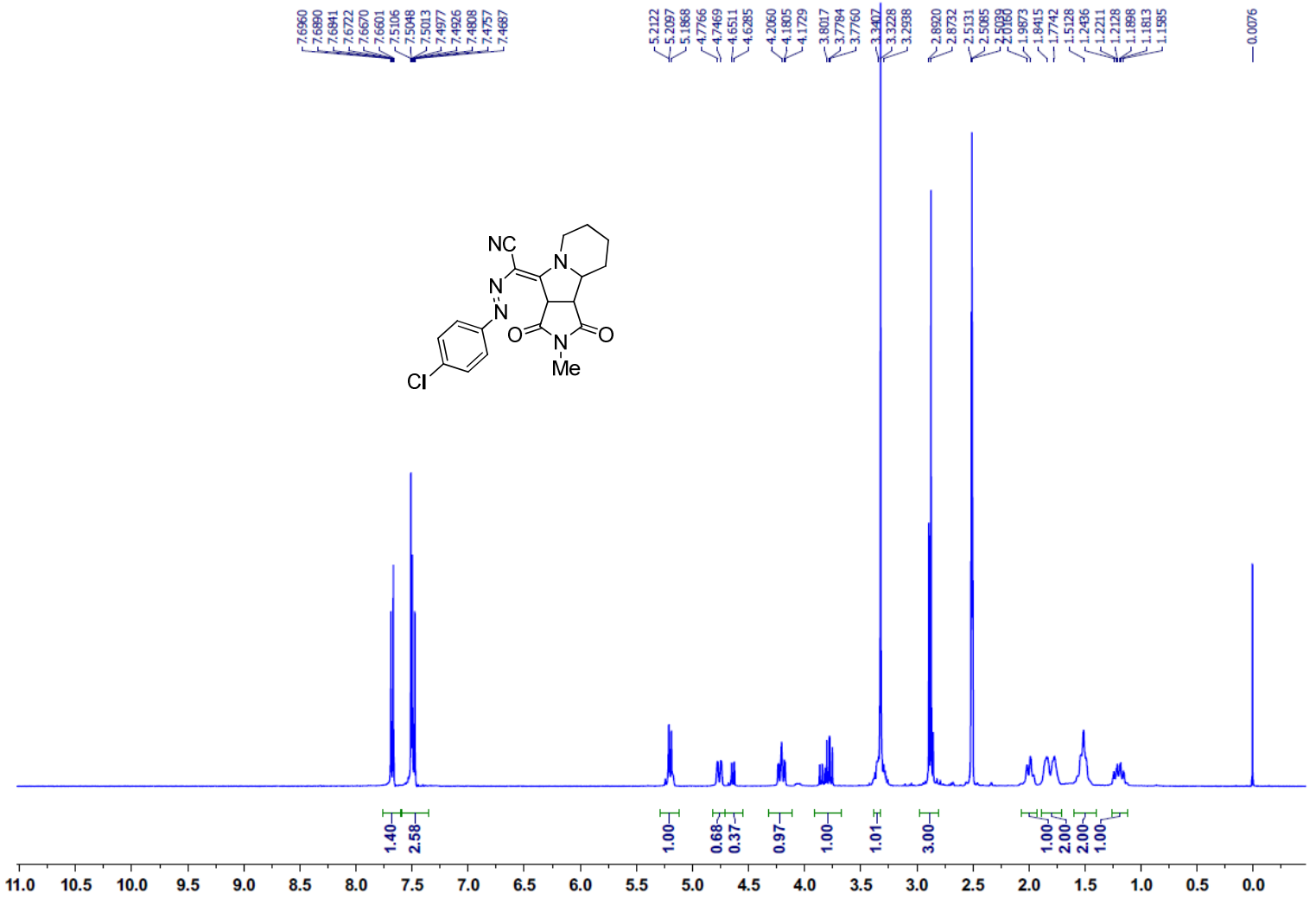


Fig. S25. Spectrum ^{1}H NMR 2-[(4-chlorophenyl)azo]-2-(2-methyl-1,3-dioxo-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)acetonitrile (**10b**)

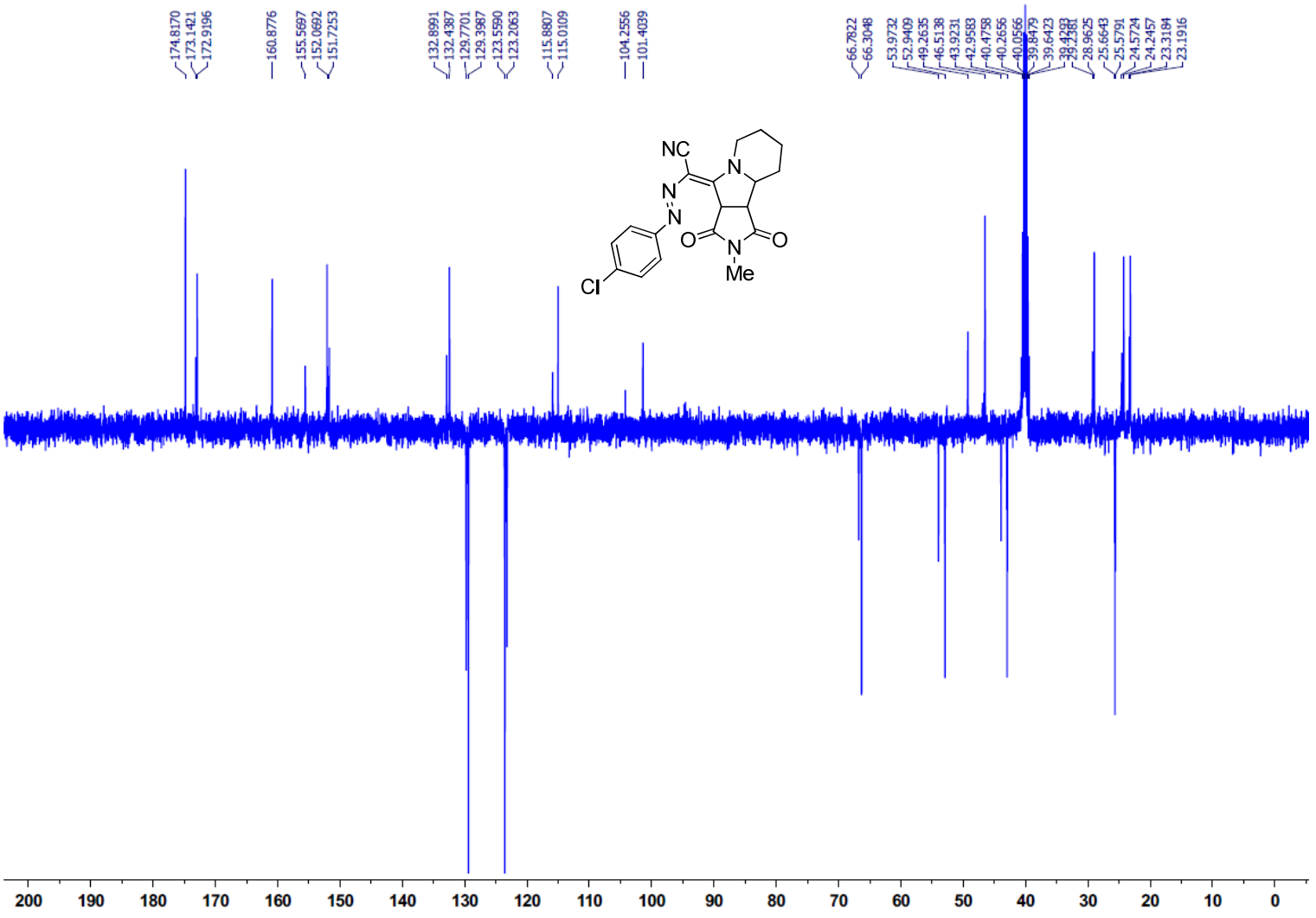


Fig. S26. Spectrum ^{13}C NMR 2-[(4-chlorophenyl)azo]-2-(2-methyl-1,3-dioxo-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)acetonitrile (**10b**)

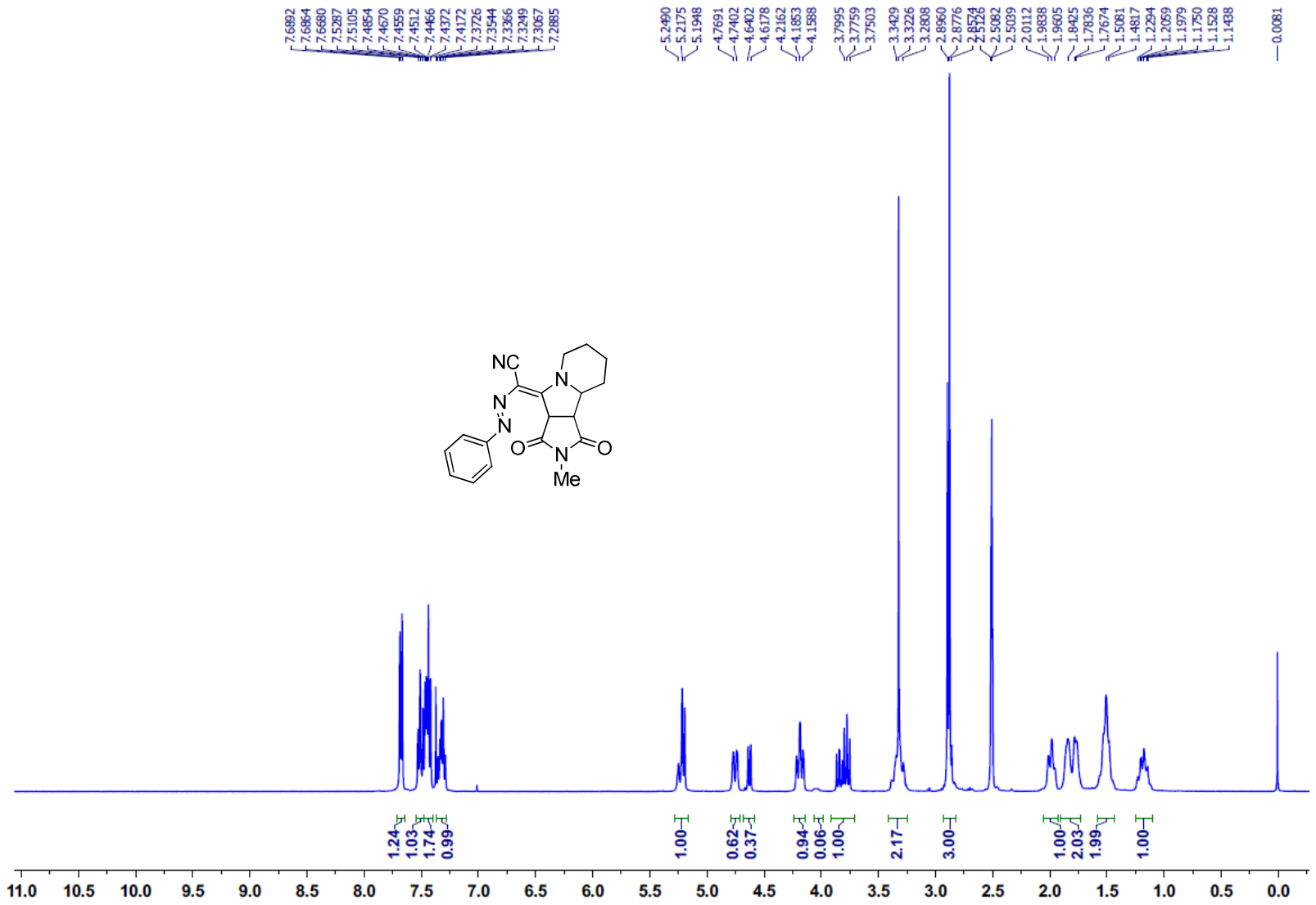


Fig. S27. Spectrum ^{1}H NMR 2-(2-methyl-1,3-dioxo-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)-2-(phenylazo)acetonitrile (**10c**) (DMSO-d_6)

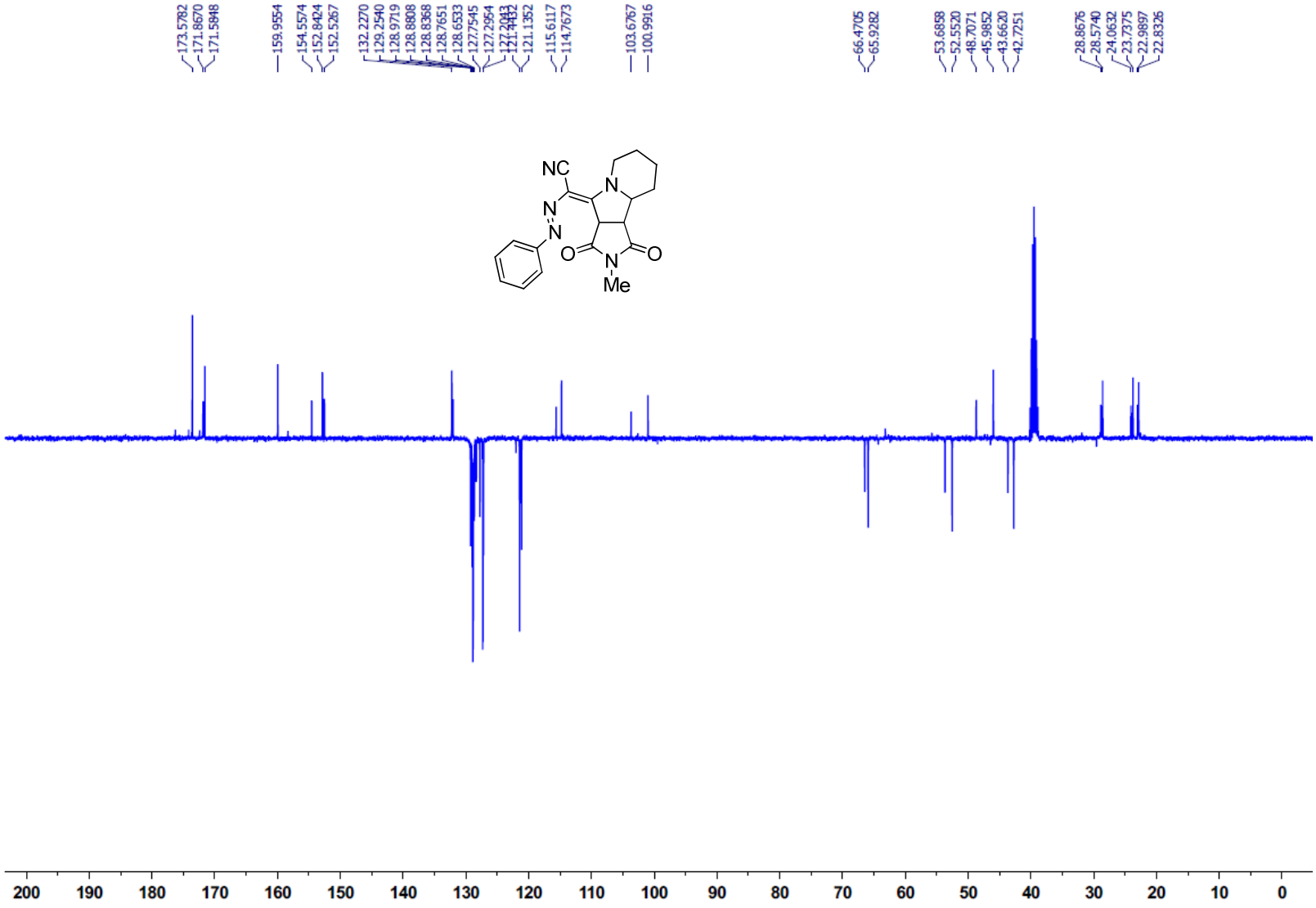


Fig. S28. Spectrum ^{13}C NMR 22-(2-methyl-1,3-dioxo-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)-2-(phenylazo)acetonitrile (**10c**) (DMSO-d_6)

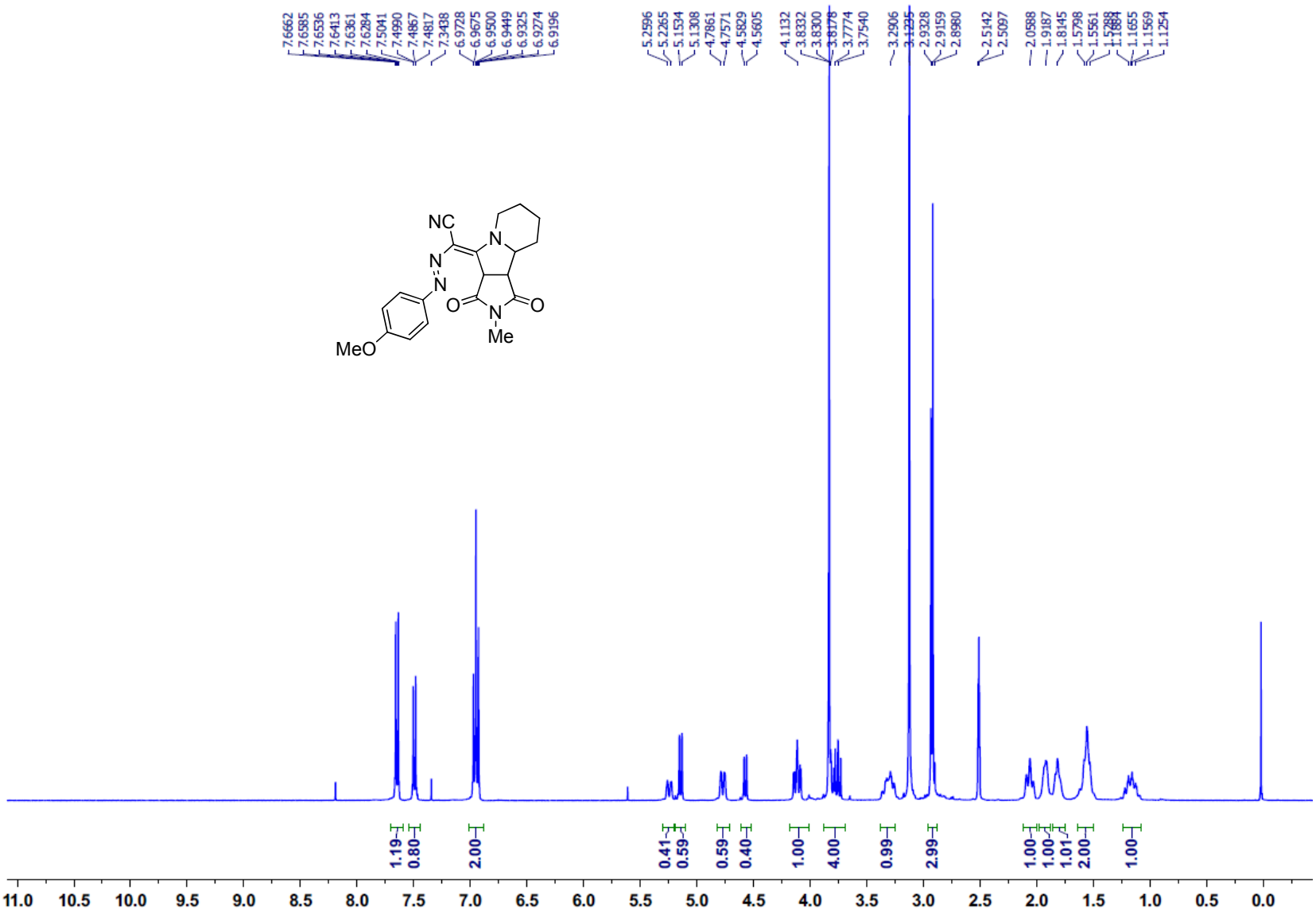


Fig. S29. Spectrum ^{1}H NMR 2-[(4-methoxyphenyl)azo]-2-(2-methyl-1,3-dioxo-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)acetonitrile (**10d**) (DMSO-d_6)

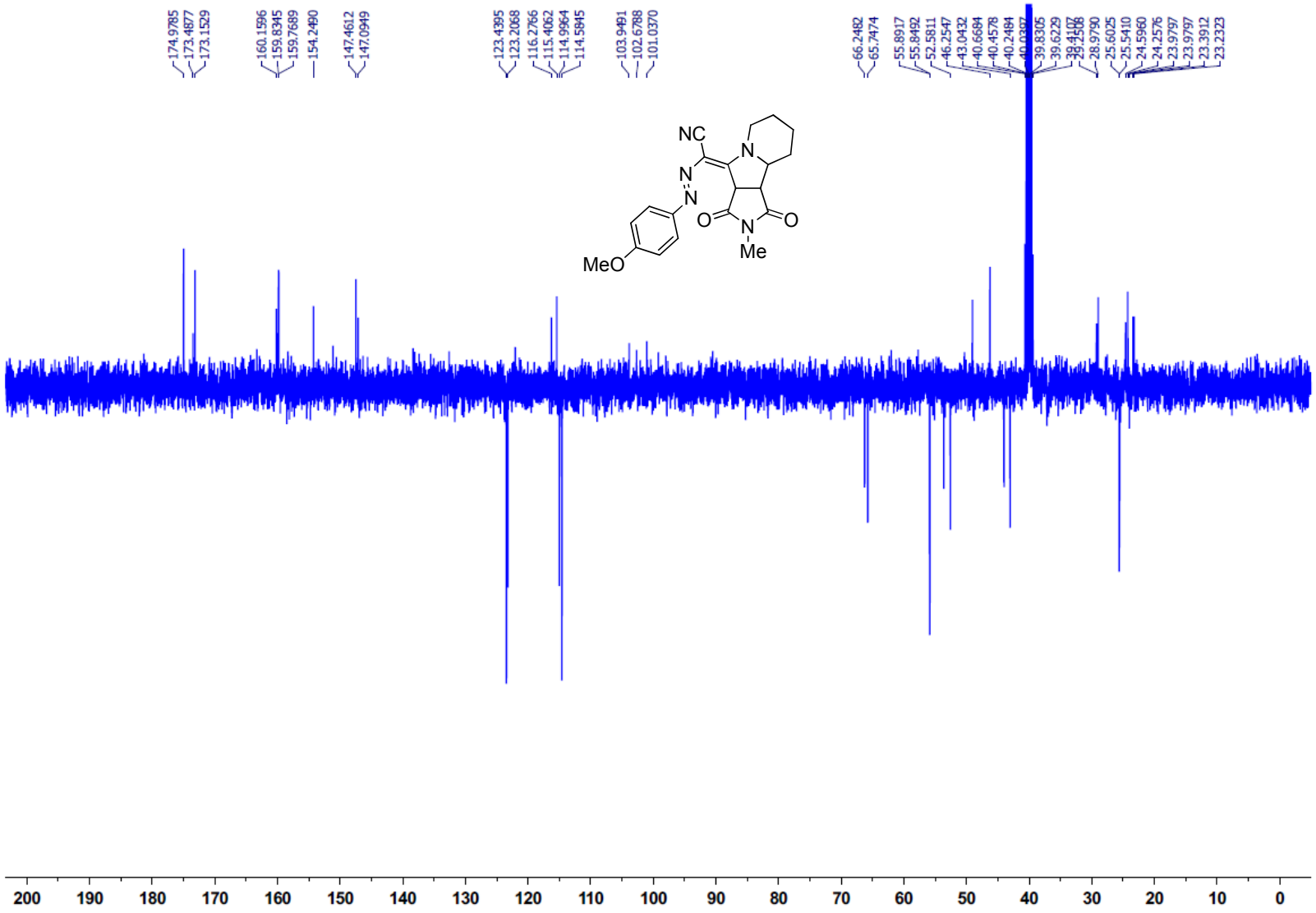


Fig. S30. Spectrum ^{13}C NMR 2-[(4-methoxyphenyl)azo]-2-(2-methyl-1,3-dioxo-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)acetonitrile (**10d**) (DMSO-d_6)

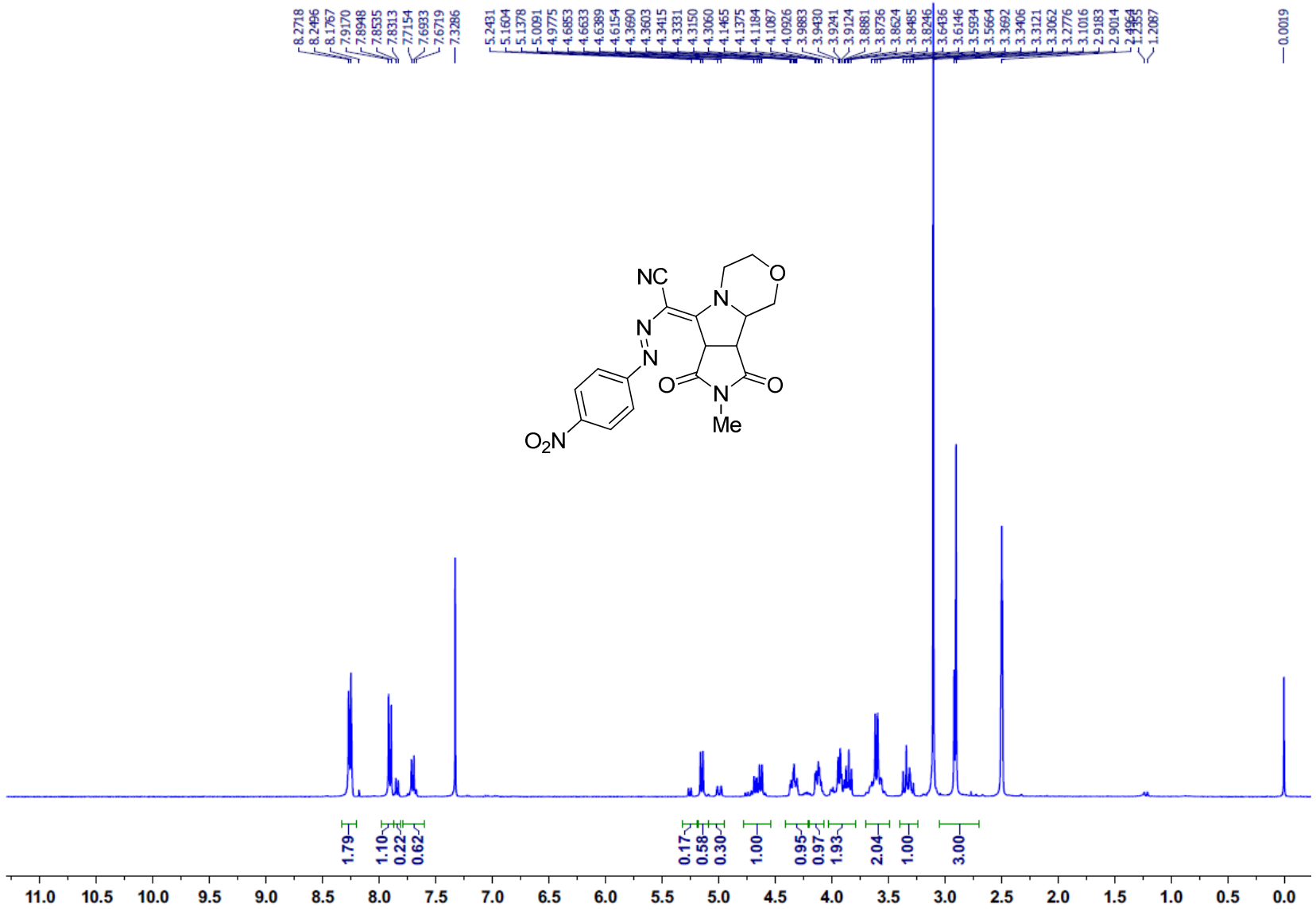


Fig. S31. Spectrum ^{1}H NMR 2-(8-methyl-7,9-dioxo-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]oxazin-6-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**10e**) (DMSO-d_6)

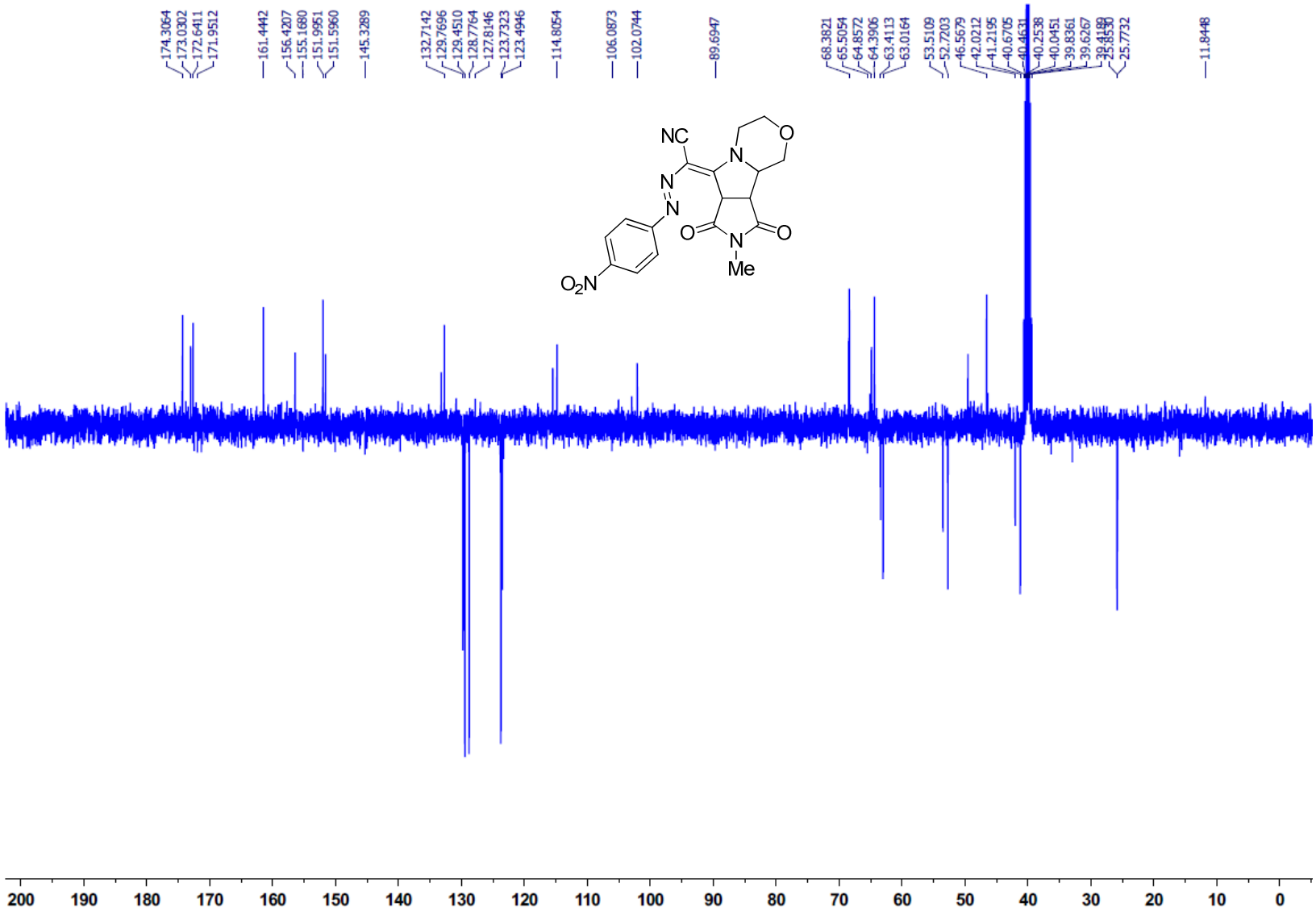


Fig S32. Spectrum ^{13}C NMR 2-(8-methyl-7,9-dioxo-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]oxazin-6-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**10e**) (DMSO-d_6)

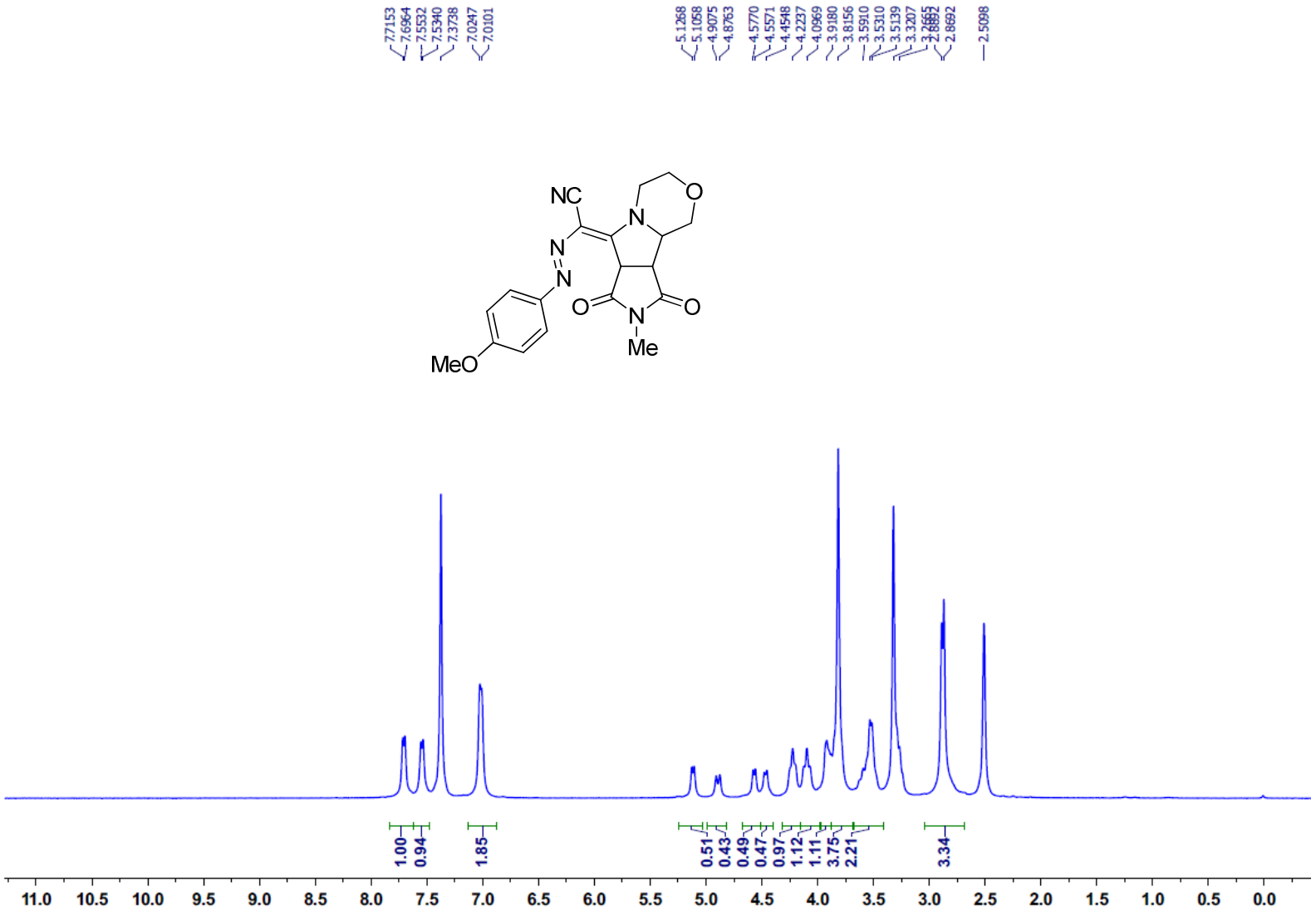


Fig S33. Spectrum ^{1}H NMR 2-[(4-methoxyphenyl)azo]-2-(8-methyl-7,9-dioxo-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]oxazin-6-ylidene)acetonitrile (**10f**) (DMSO-d_6)

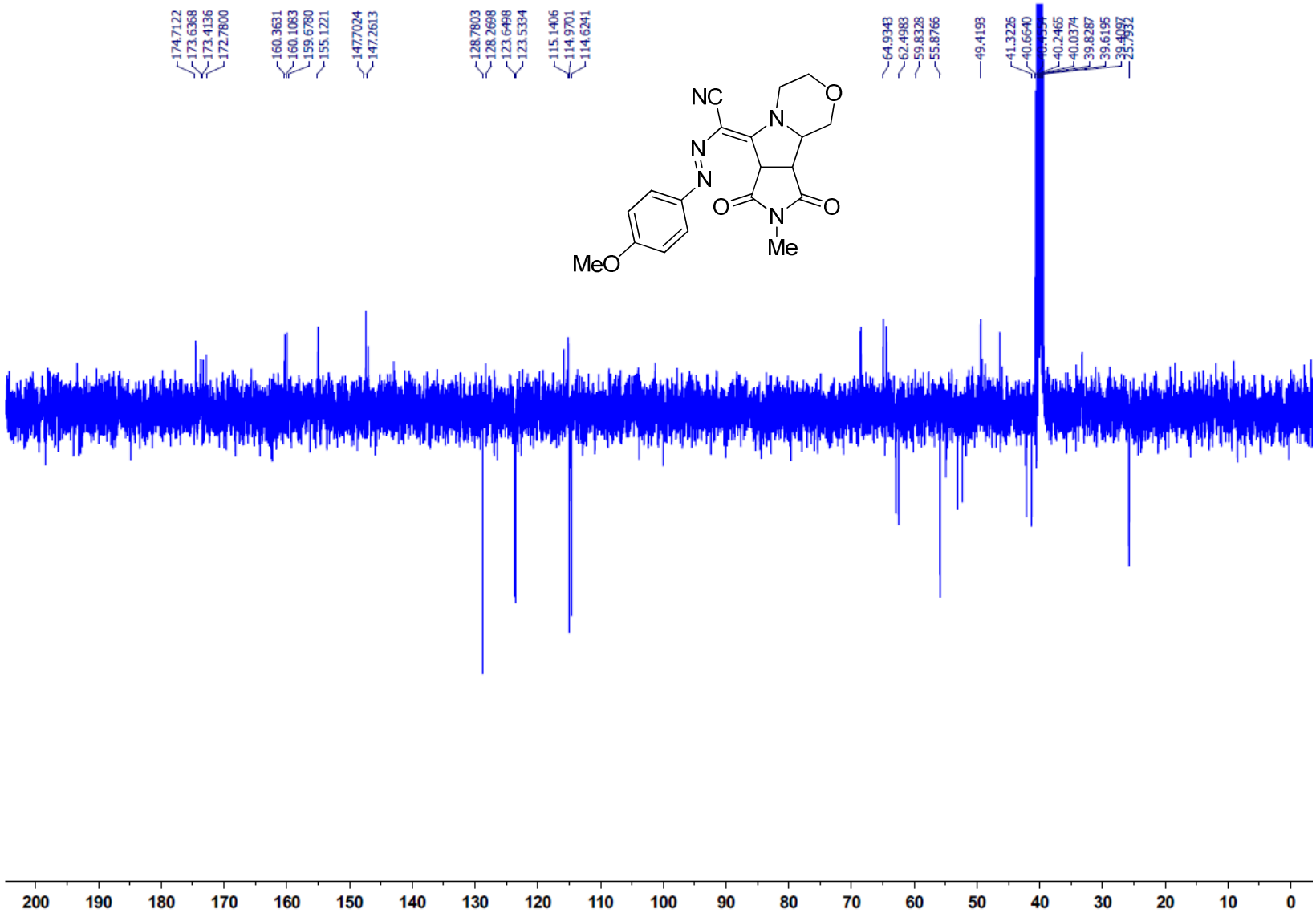


Fig S34. Spectrum ^{13}C NMR 2-[(4-methoxyphenyl)azo]-2-(8-methyl-7,9-dioxo-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]oxazin-6-ylidene)acetonitrile (**10f**) (DMSO-d_6)

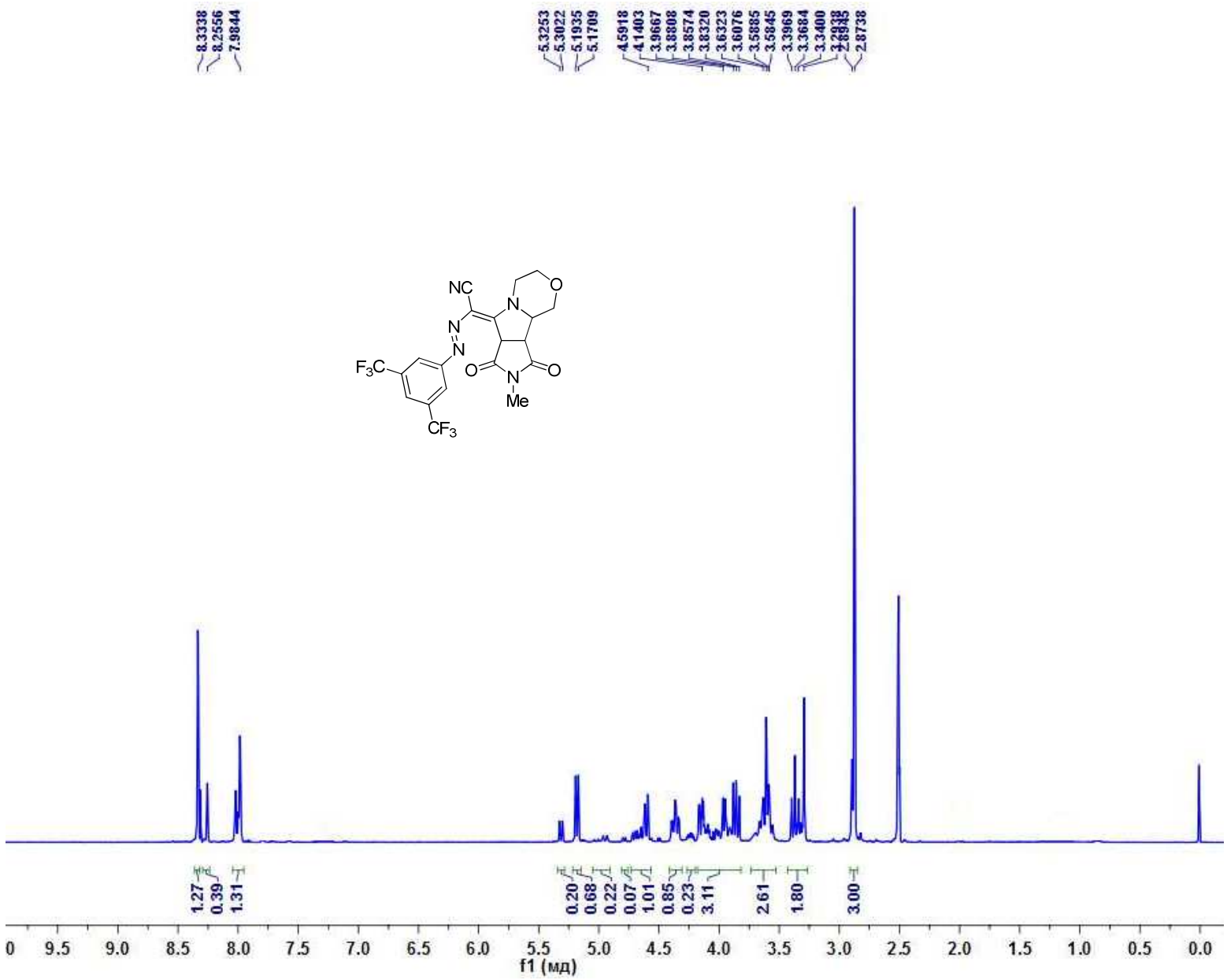


Fig S35. Spectrum ^{1}H 2-[3,5-bis(trifluoromethyl)phenyl]azo-2-(8-methyl-7,9-dioxo-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]oxazin-6-ylidene)acetonitrile (**10g**) (DMSO-d_6)

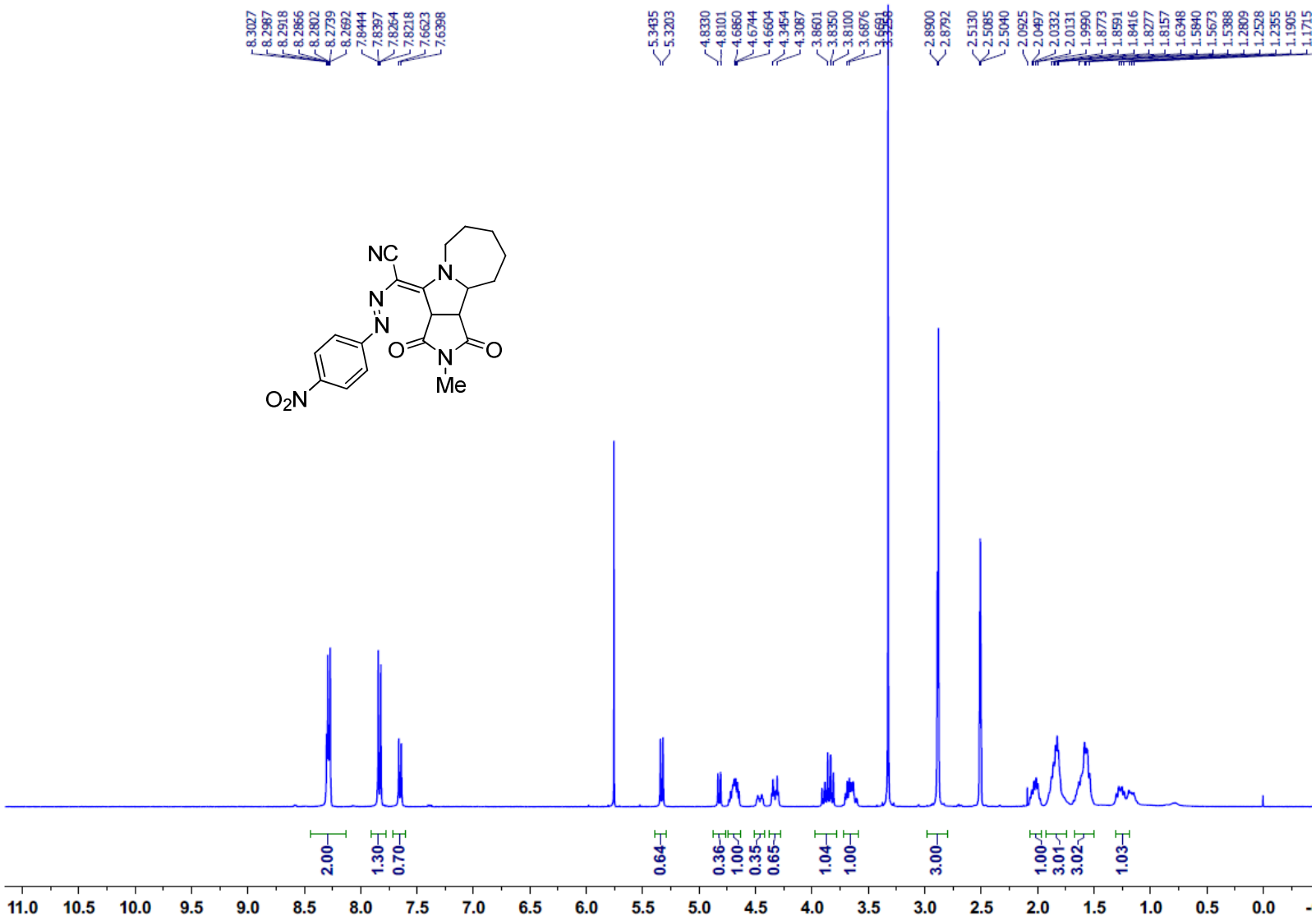


Fig 36. Spectrum ^{1}H NMR 2-(2-methyl-1,3-dioxo-3a,6,7,8,9,10,10*a*,10*b*-octahydropyrrolo[1,2]pyrrolo[3,5-*a*]azepin-4-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**10h**) (DMSO-d_6)

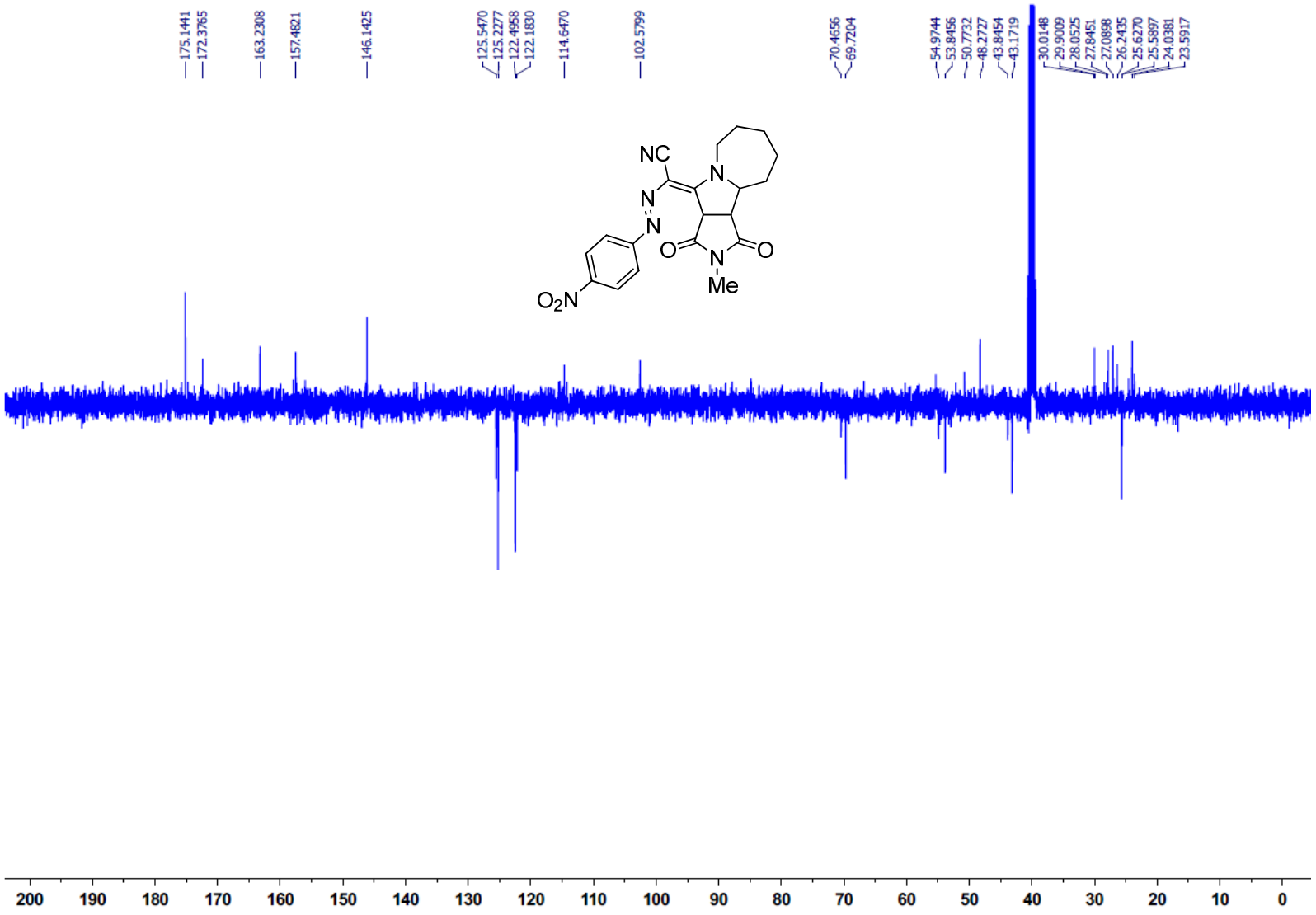


Fig S37. Spectrum ^{13}C NMR 2-(2-methyl-1,3-dioxo-3*a*,6,7,8,9,10,10*a*,10*b*-octahydropyrrolo[1,2]pyrrolo[3,5-*a*]azepin-4-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**10h**) (DMSO-d_6)

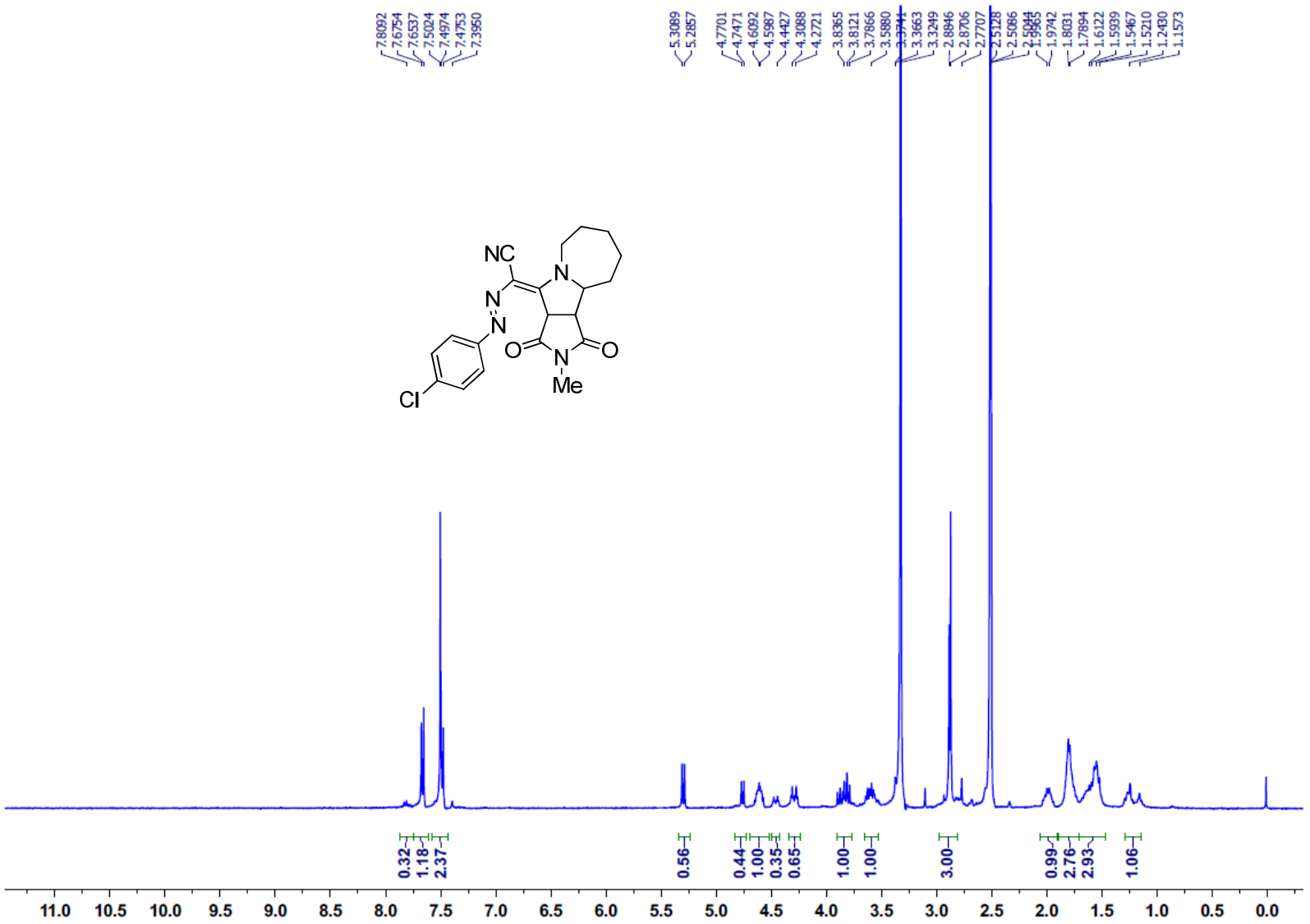


Fig S38. Spectrum ^{1}H NMR 2-[(4-chlorophenyl)azo]-2-(2-methyl-1,3-dioxo-3a,6,7,8,9,10,10*a*,10*b*-octahydropyrrolo[1,2]pyrrolo[3,5-*a*]azepin-4-ylidene)acetonitrile (**10i**) (DMSO-d_6)

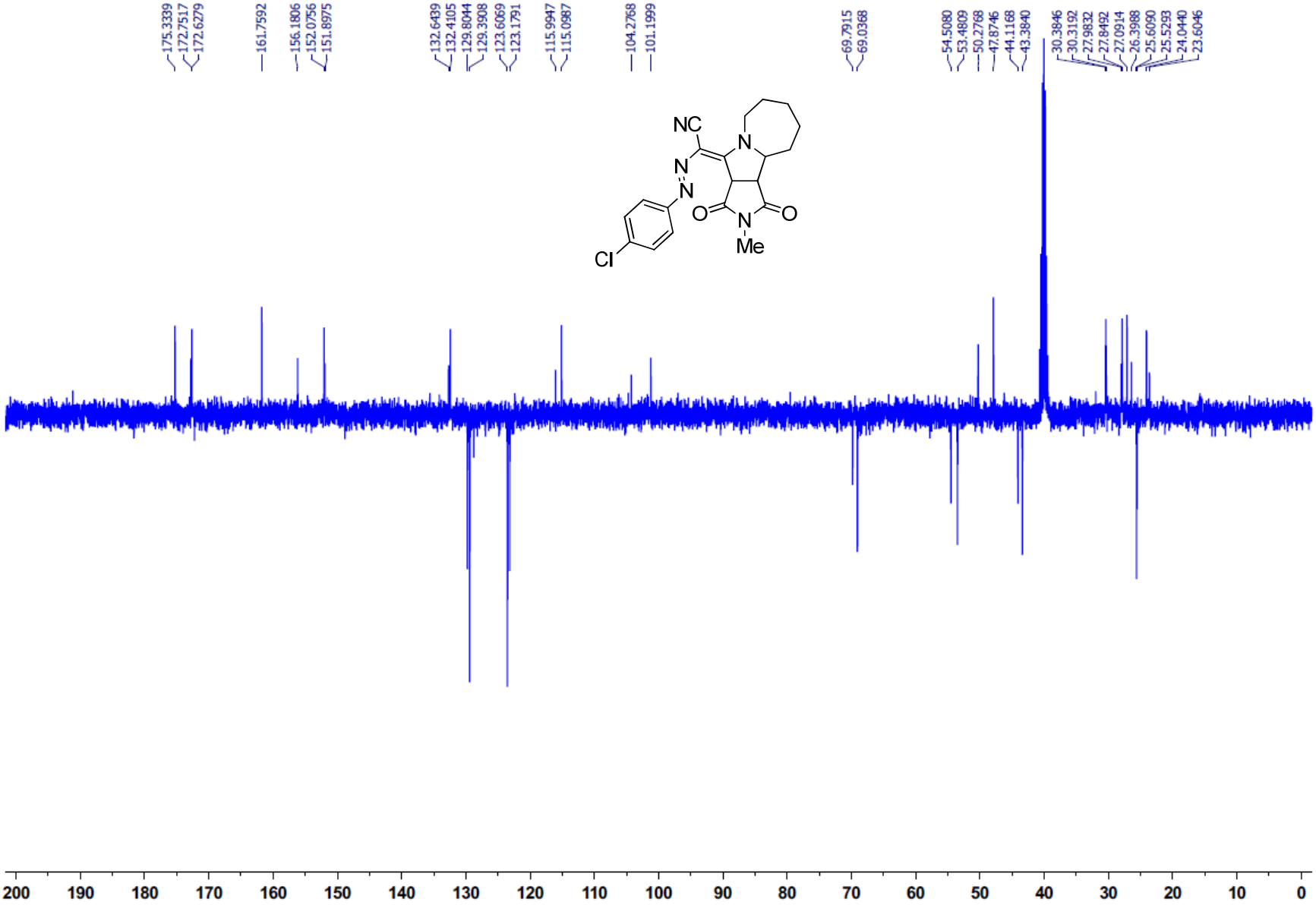


Fig S39. Spectrum ^{13}C NMR 2-[(4-chlorophenyl)azo]-2-(2-methyl-1,3-dioxo-3a,6,7,8,9,10,10*a*,10*b*-octahydropyrrolo[1,2]pyrrolo[3,5-*a*]azepin-4-ylidene)acetonitrile (**10i**) (DMSO-d_6)

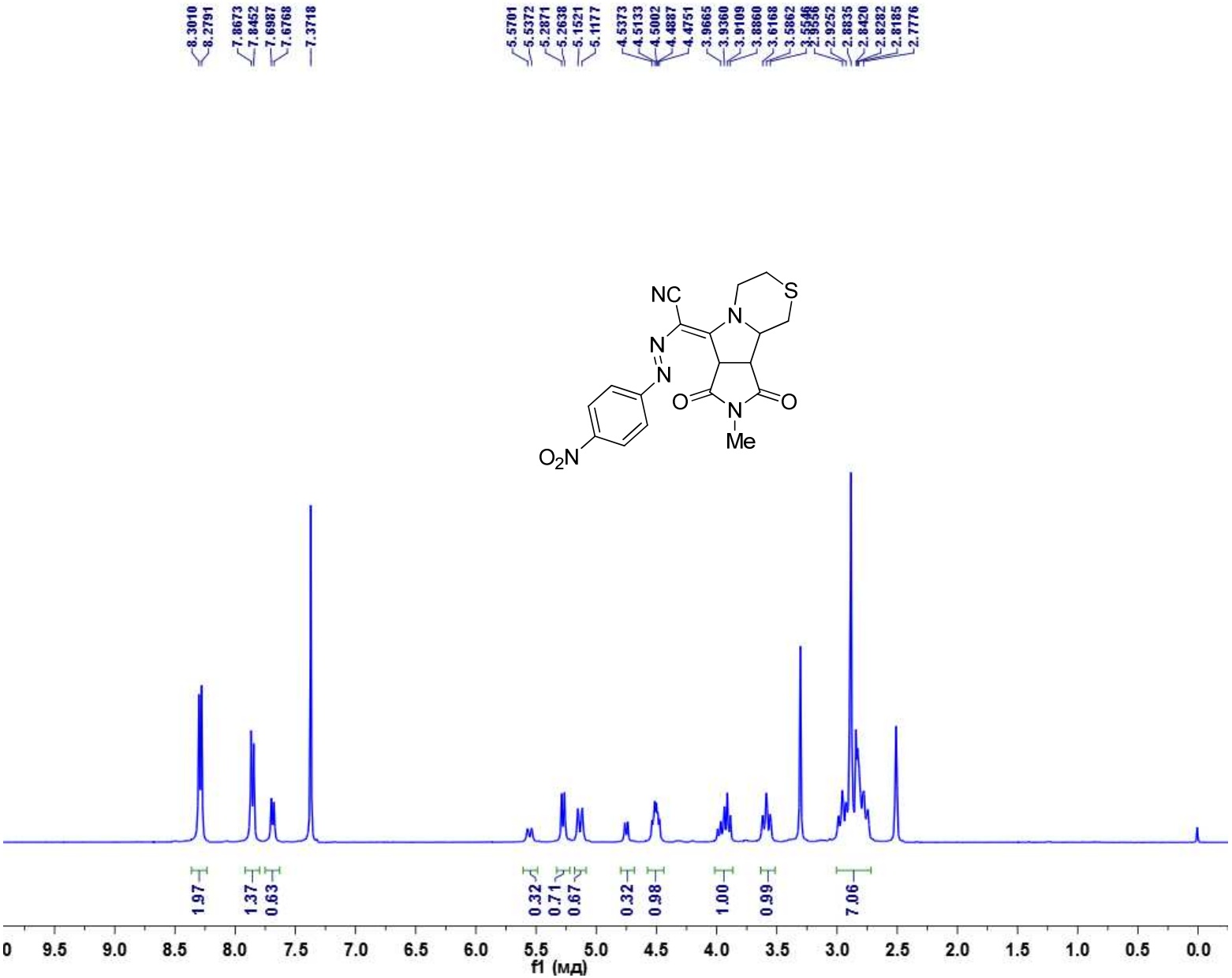


Fig S40. Spectrum ^{1}H NMR 2-(8-methyl-7,9-dioxo-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]thiazin-6-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**10j**) (DMSO-d_6)

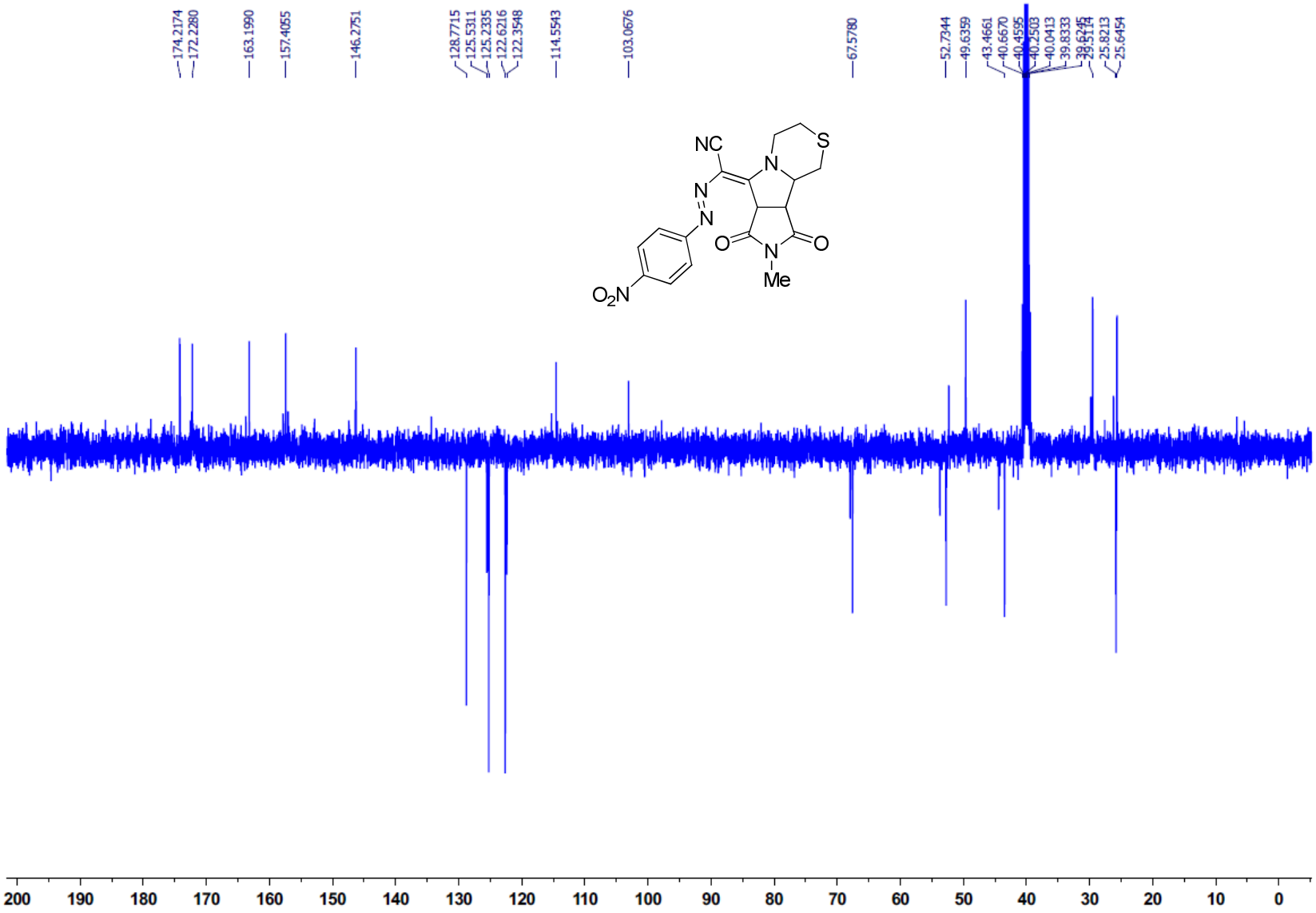


Fig S41. Spectrum ^{13}C NMR 2-(8-methyl-7,9-dioxo-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]thiazin-6-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**10j**) (DMSO-d_6)

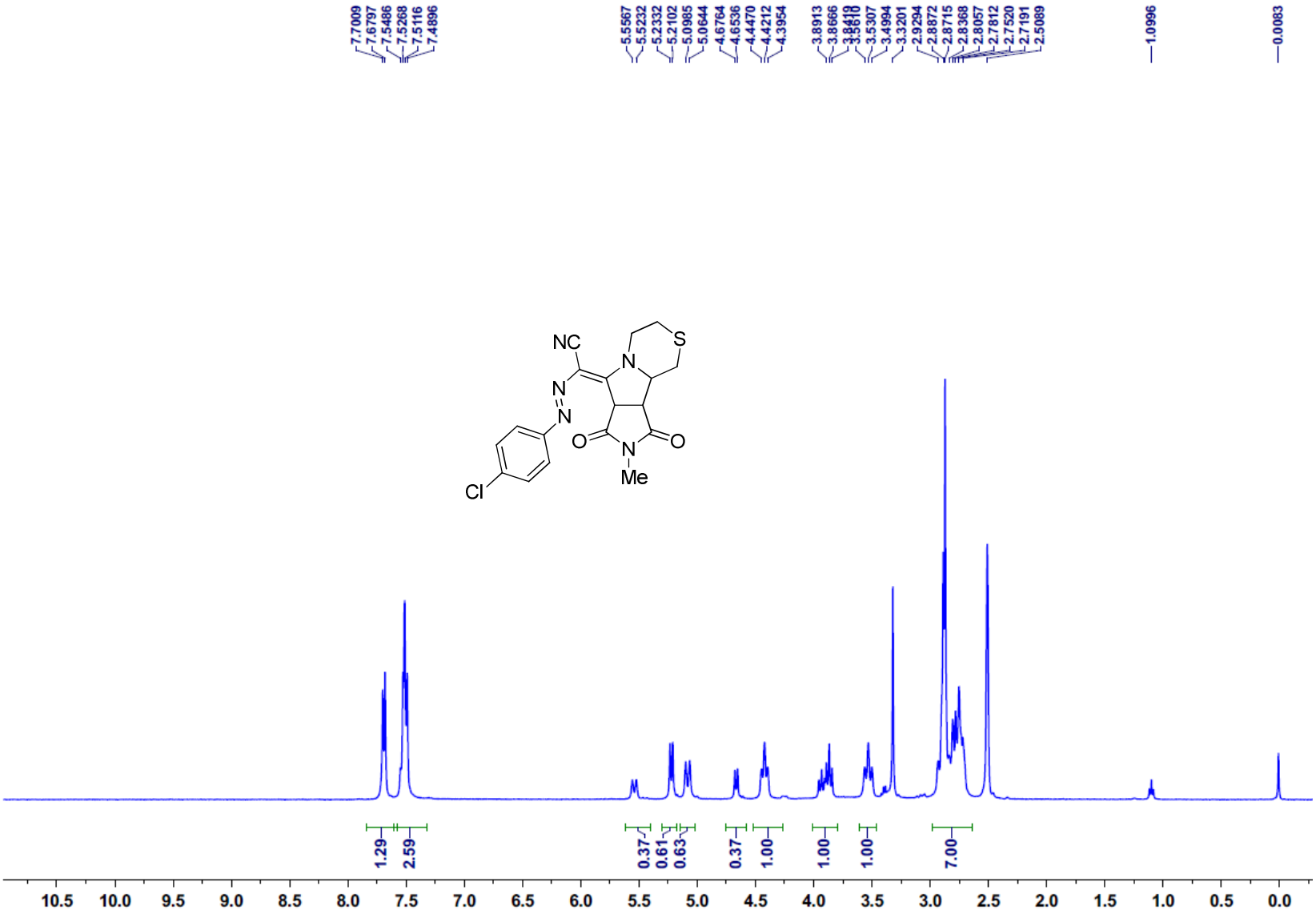


Fig S42. Spectrum ^{1}H NMR 2-[(4-chlorophenyl)azo]-2-(8-methyl-7,9-dioxo-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]thiazin-6-ylidene)acetonitrile (**10k**) (DMSO-d_6)

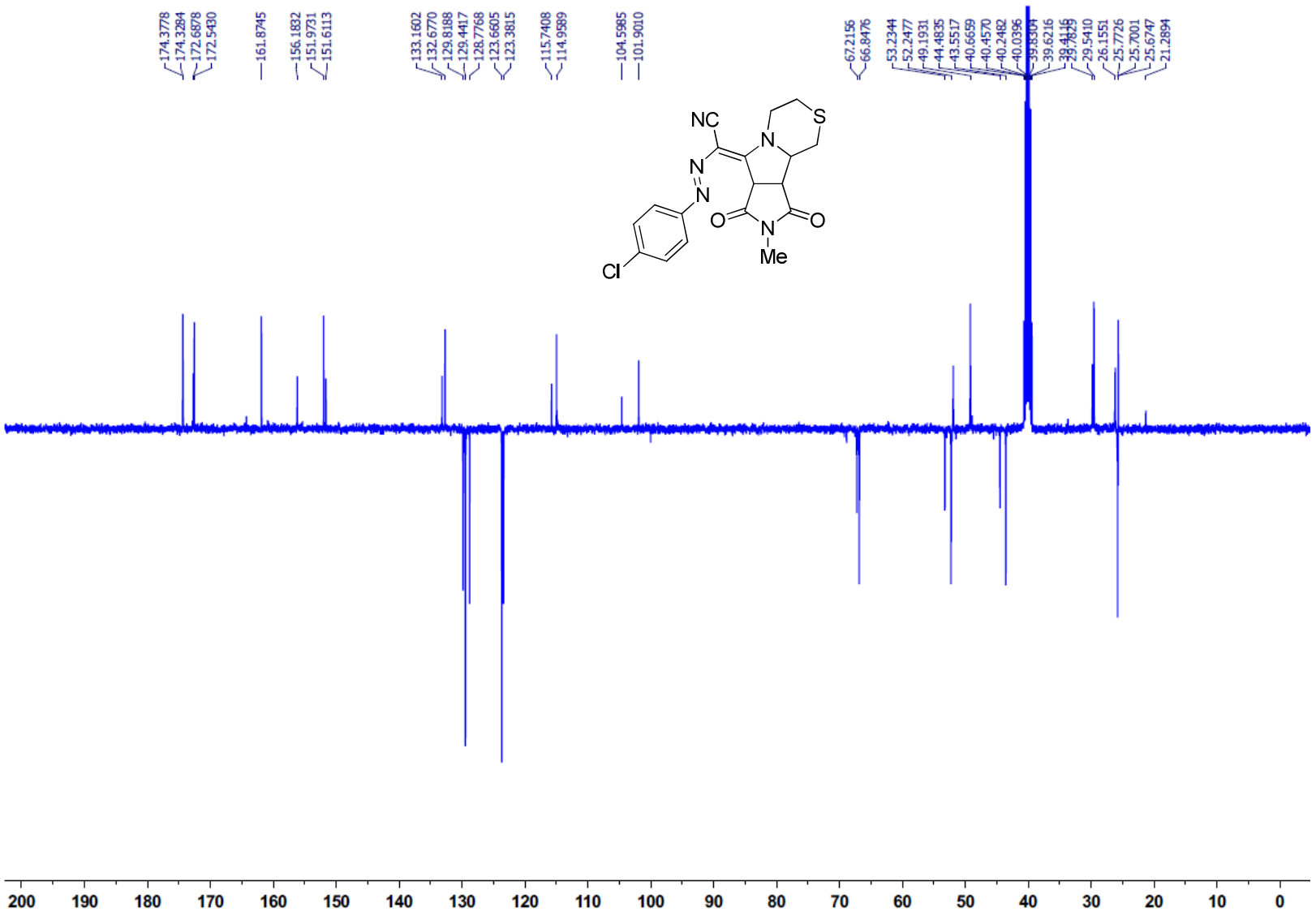


Fig S43. Spectrum ^{13}C NMR 2-[(4-chlorophenyl)azo]-2-(8-methyl-7,9-dioxo-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]thiazin-6-ylidene)acetonitrile (**10k**) (DMSO-d_6)

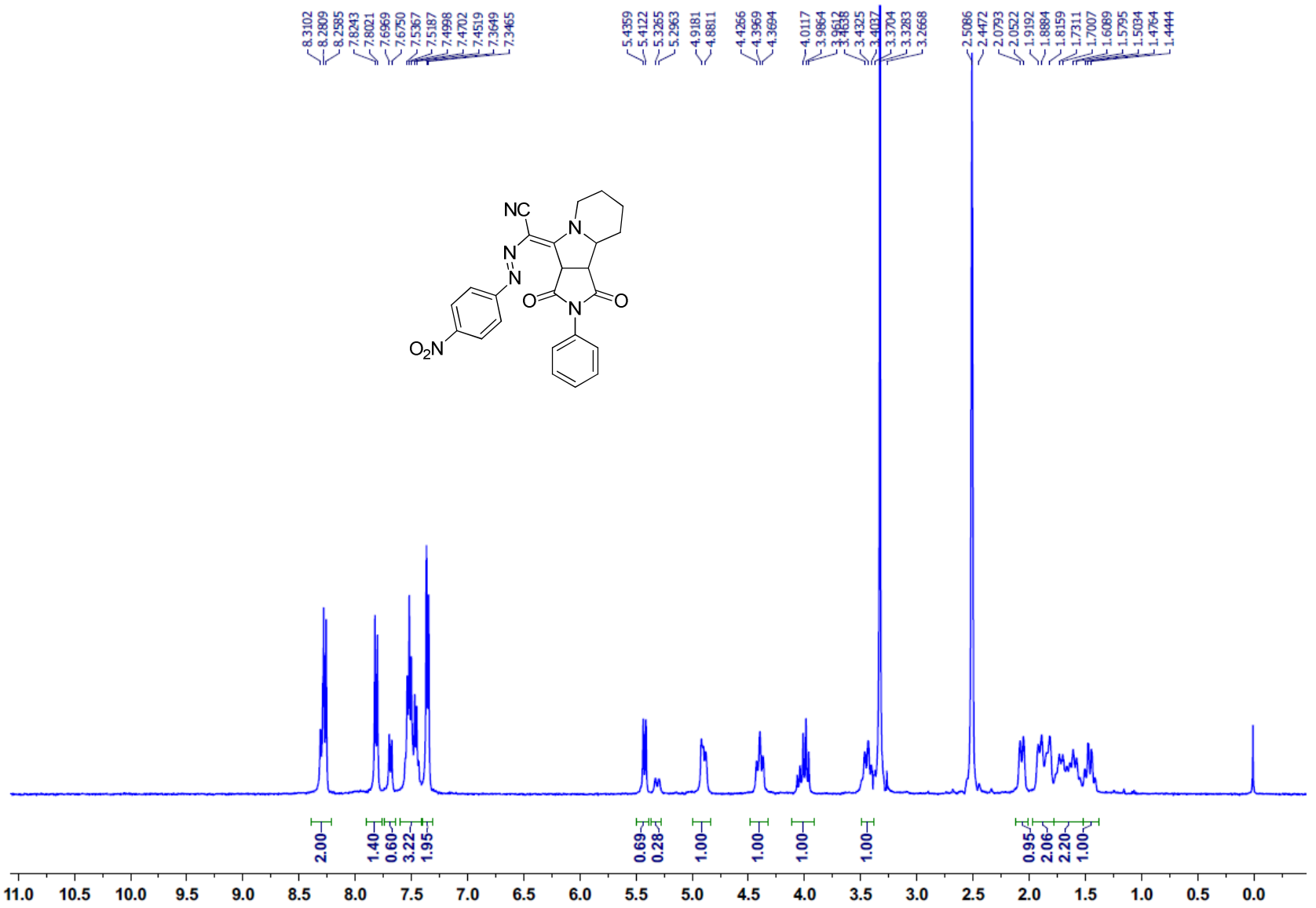


Fig S44. Spectrum ^{1}H NMR 2-(1,3-dioxo-2-phenyl-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**11a**) (DMSO-d_6)

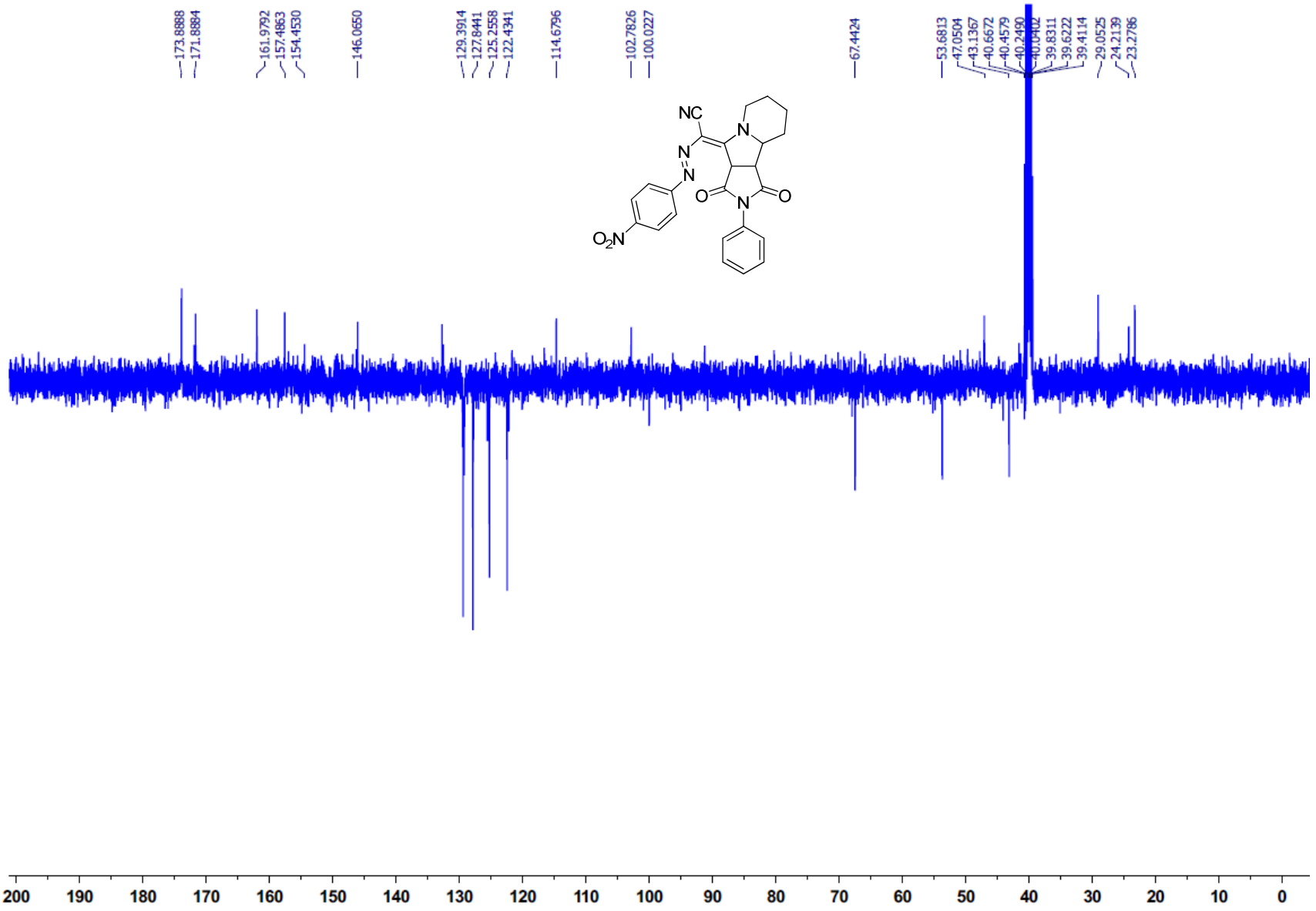


Fig S45. Spectrum ^{13}C NMR 2-(1,3-dioxo-2-phenyl-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**11a**) (DMSO-d_6)

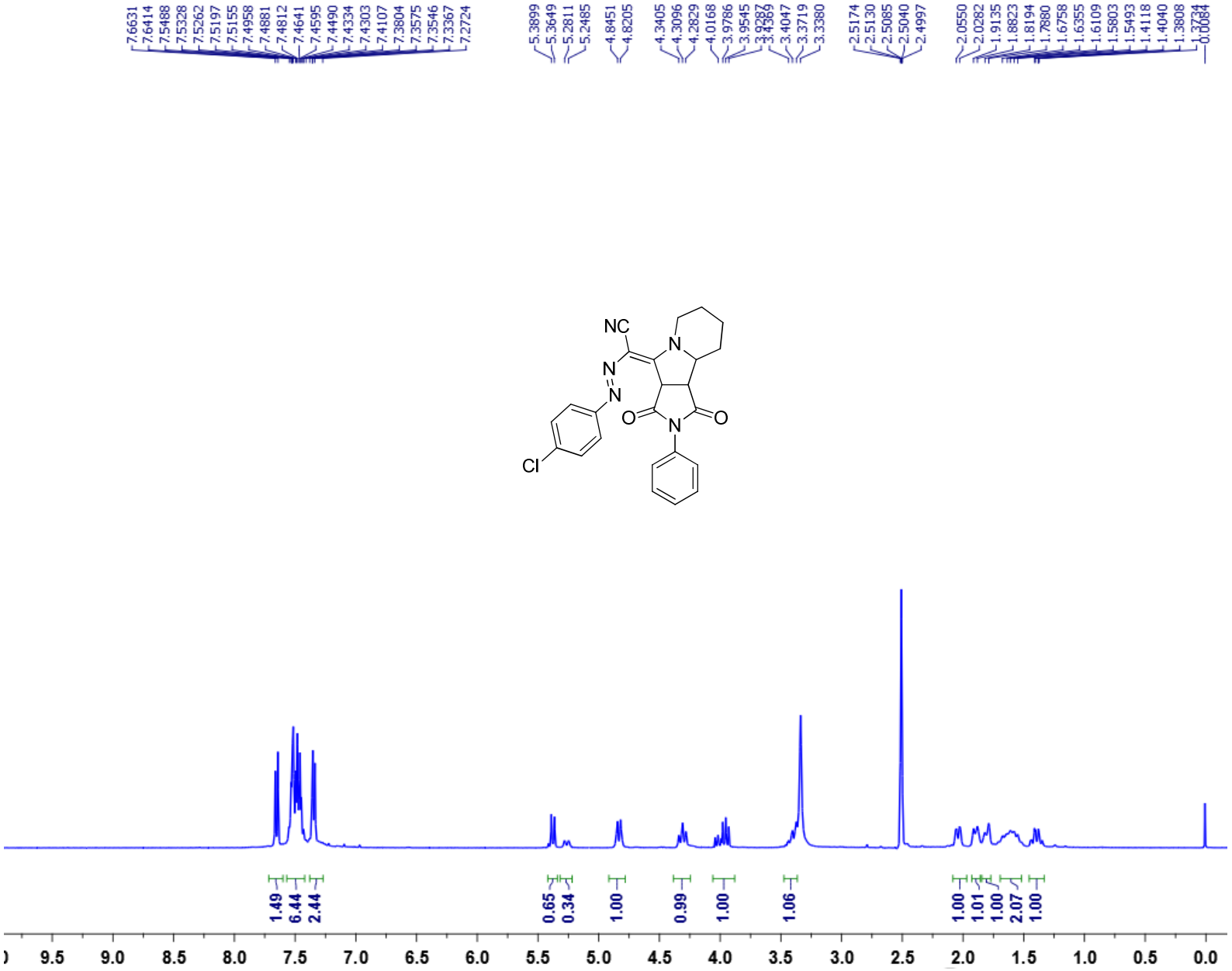


Fig S46. Spectrum ^{1}H NMR 2-[(4-chlorophenyl)azo]-2-(1,3-dioxo-2-phenyl-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)acetonitrile (**11b**) (DMSO-d_6)

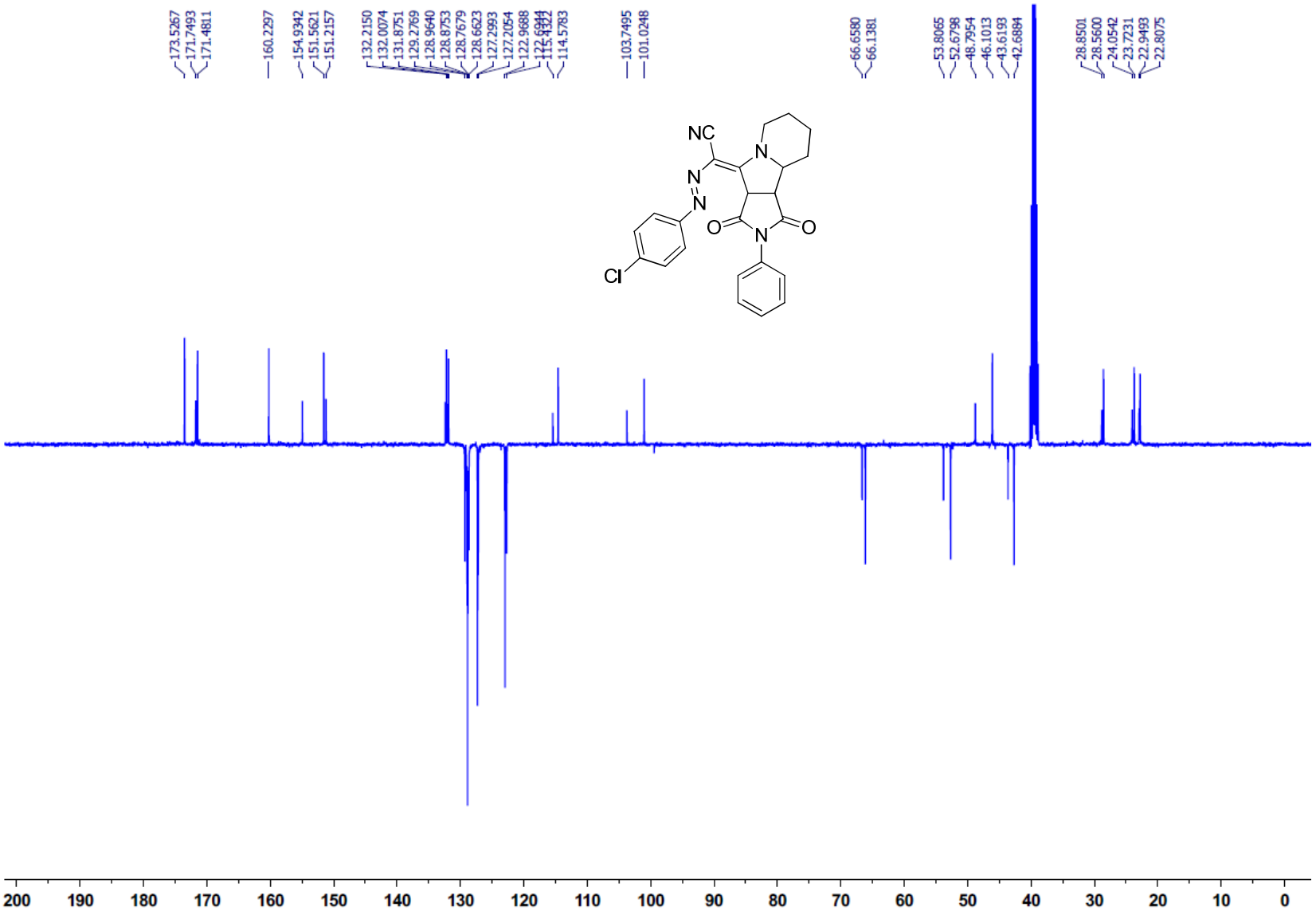


Fig S47. Spectrum ^{13}C 2-[(4-chlorophenyl)azo]-2-(1,3-dioxo-2-phenyl-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)acetonitrile (**11b**) (DMSO-d_6)

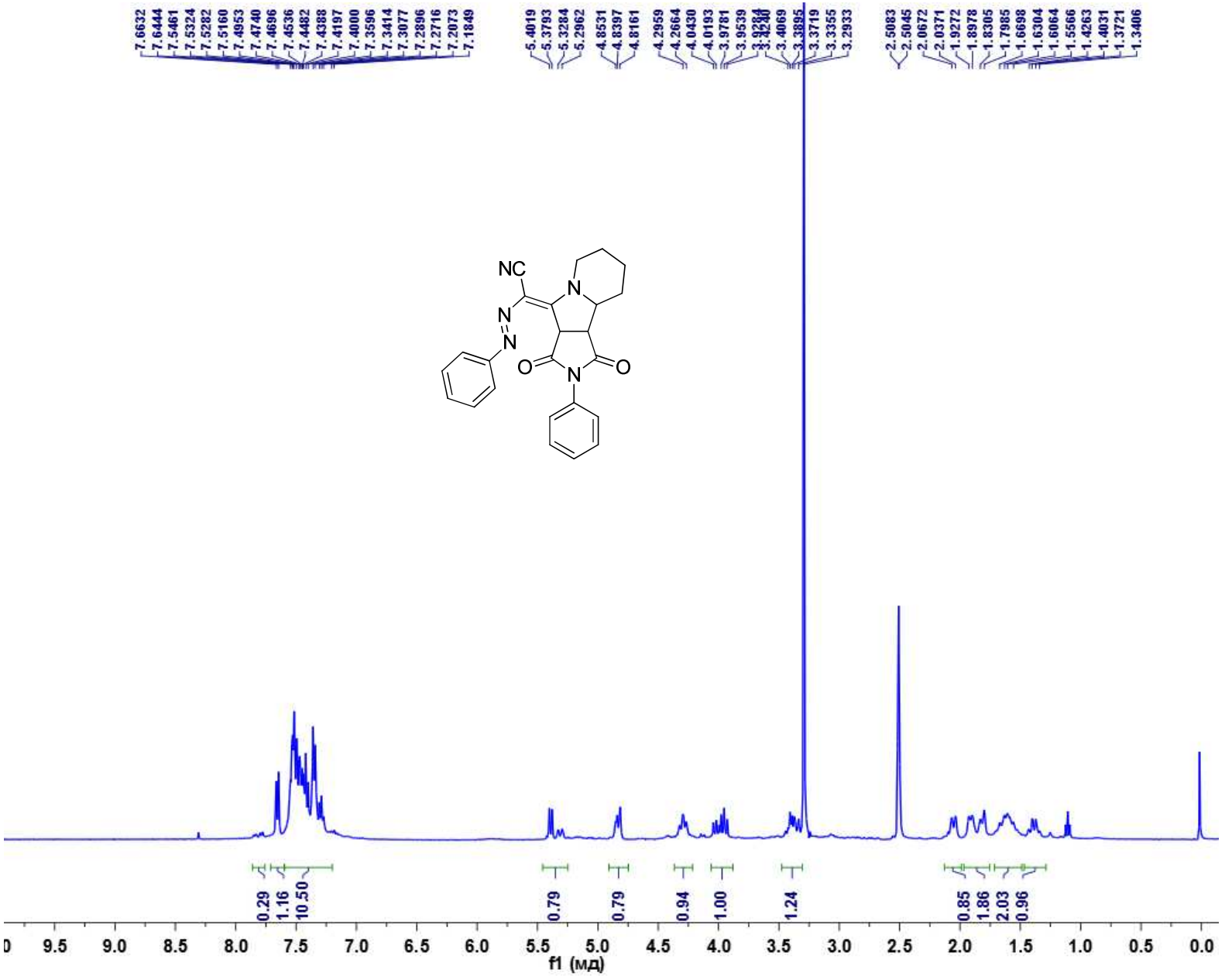


Fig S48. Spectrum ^{1}H NMR 2-(1,3-dioxo-2-phenyl-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)-2-[phenylazo]acetonitrile (**11c**) (DMSO-d_6)

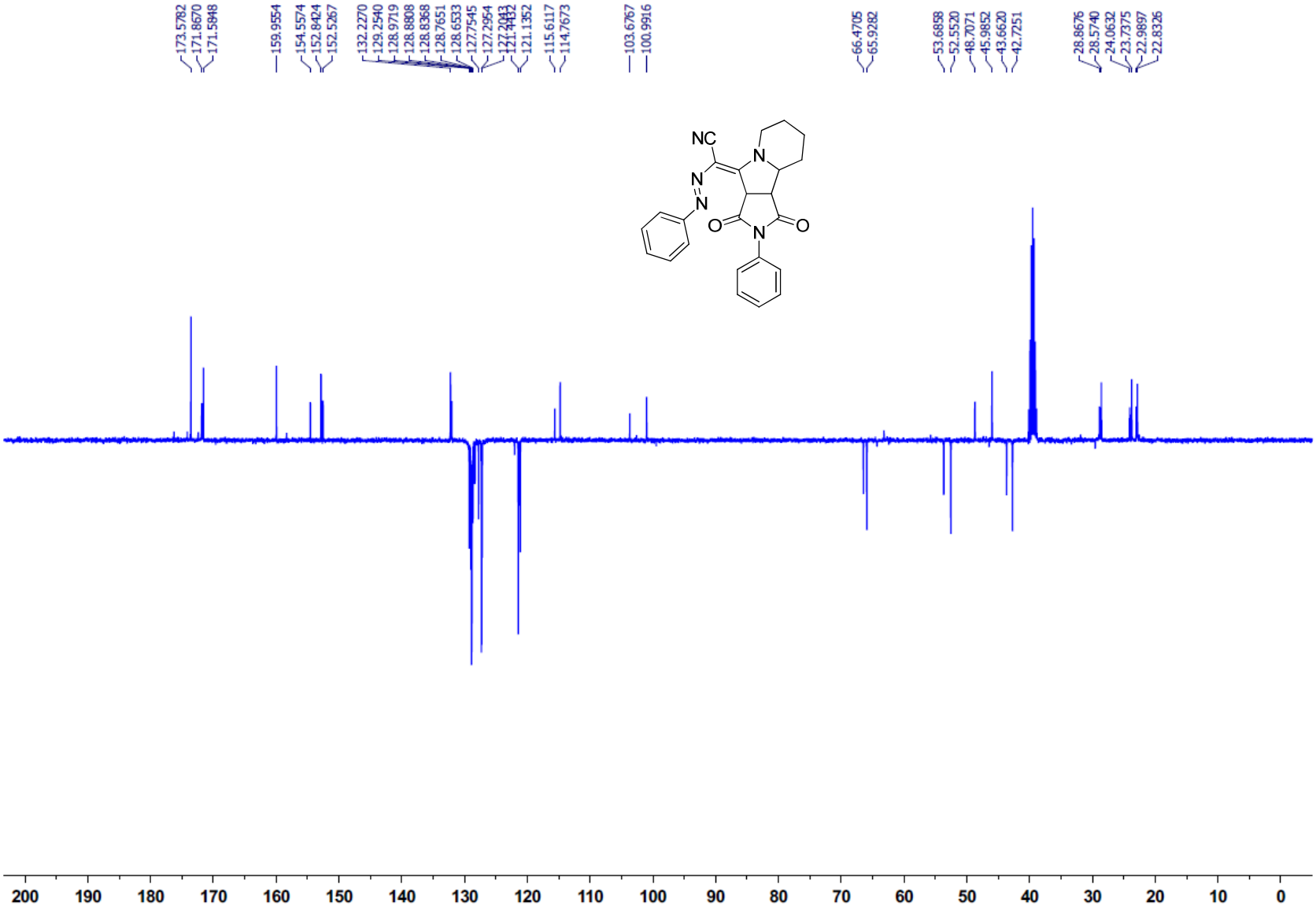


Fig S49. Spectrum ^{13}C NMR 2-(1,3-dioxo-2-phenyl-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)-2-[phenylazo]acetonitrile (**11c**) (DMSO-d_6)

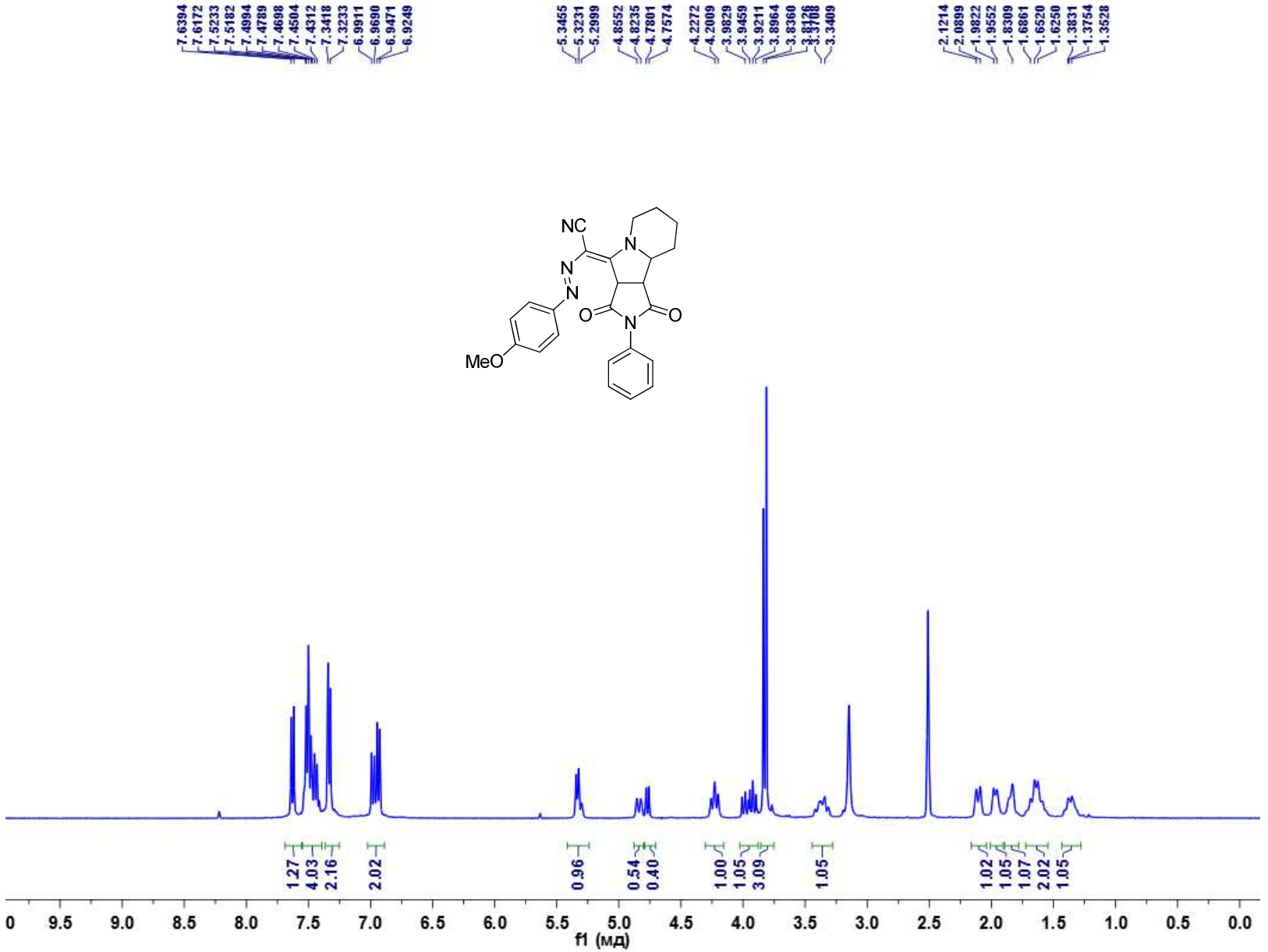


Fig S50. Spectrum ^{1}H NMR 2-(1,3-dioxo-2-phenyl-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)-2-[(4-methoxyphenyl)azo]acetonitrile (**11d**) (DMSO-d_6)

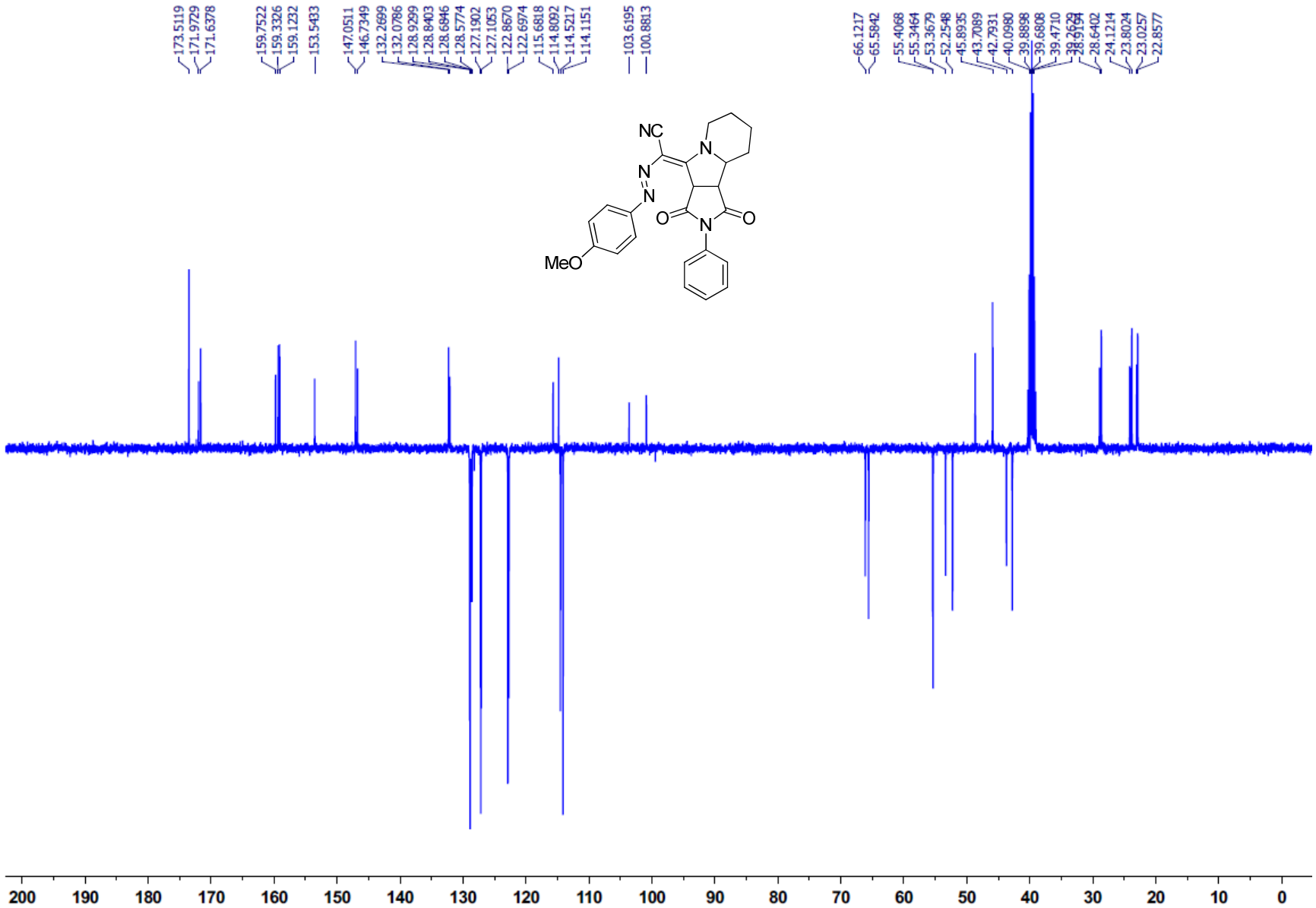


Fig S51. Spectrum ^{13}C NMR 2-(1,3-dioxo-2-phenyl-6,7,8,9,9*a*,9*b*-hexahydro-3*aH*-pyrrolo[3,4-*a*]indolizin-4-ylidene)-2-[(4-methoxyphenyl)azo]acetonitrile (**11d**) (DMSO-d_6)

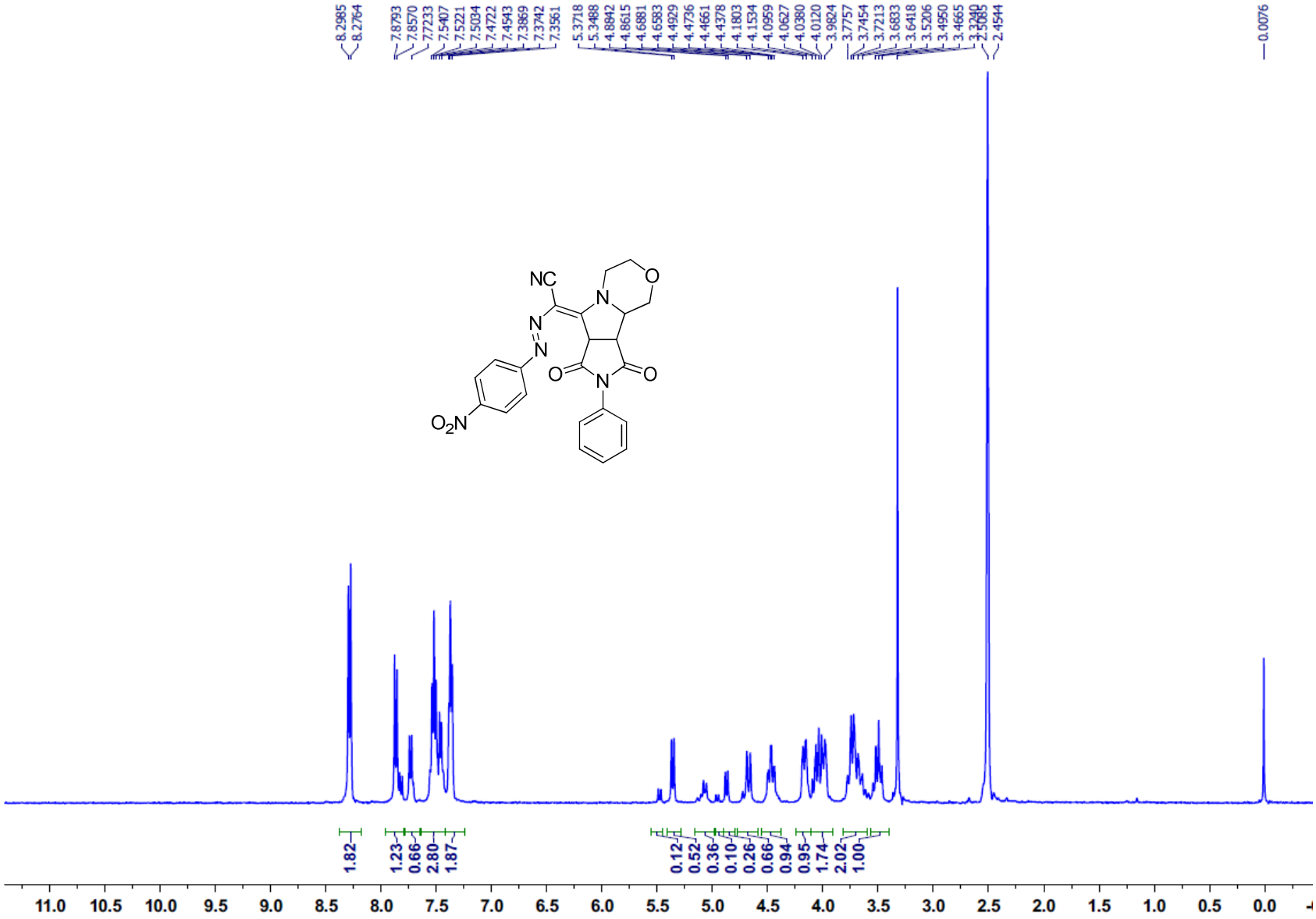


Fig S52. Spectrum ^{1}H NMR 2-(7,9-dioxo-8-phenyl-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]oxazin-6-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**11e**) (DMSO-d_6)

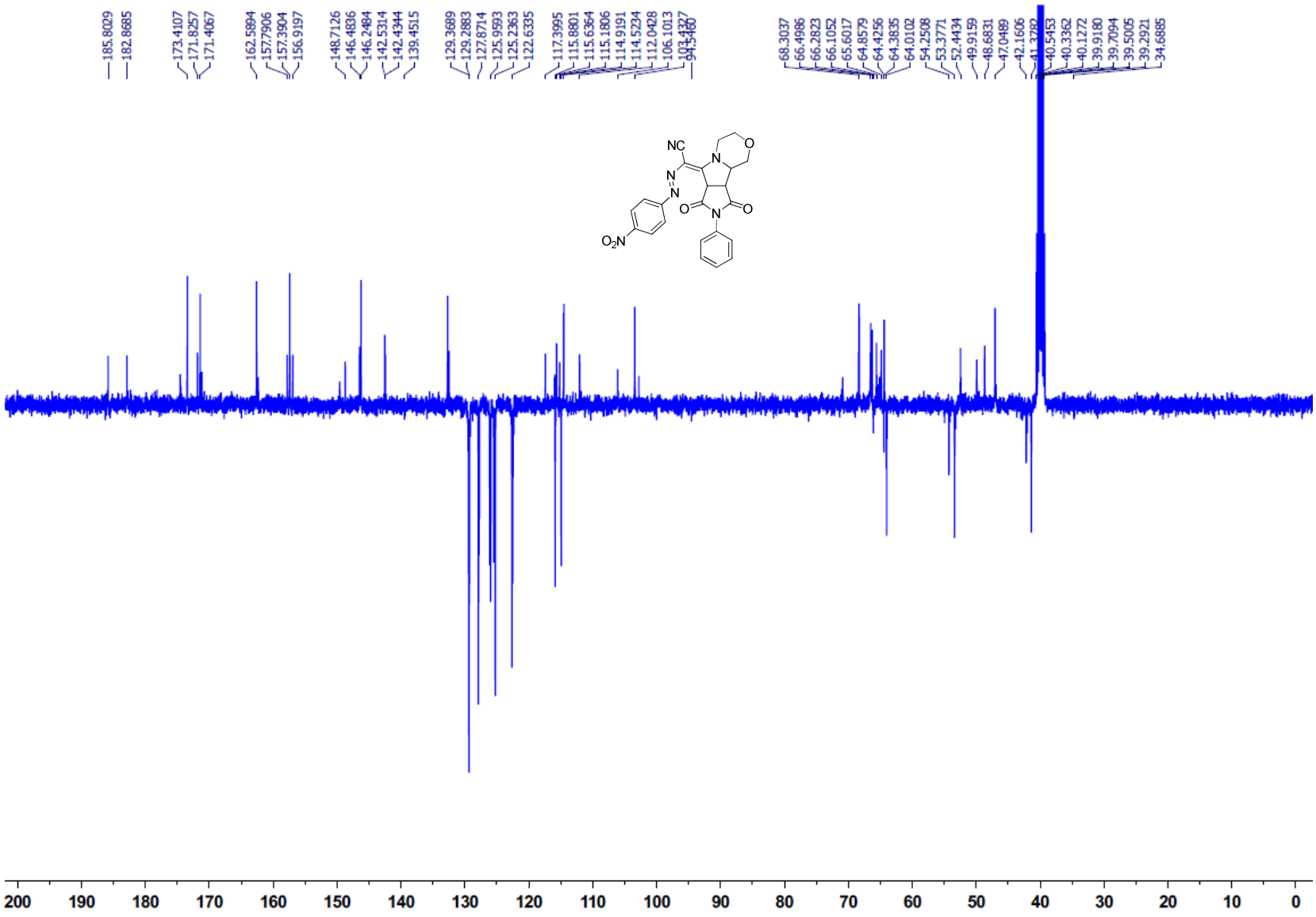


Fig S53. Spectrum ^{13}C NMR 2-(7,9-dioxo-8-phenyl-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]oxazin-6-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**11e**) (DMSO-d_6)

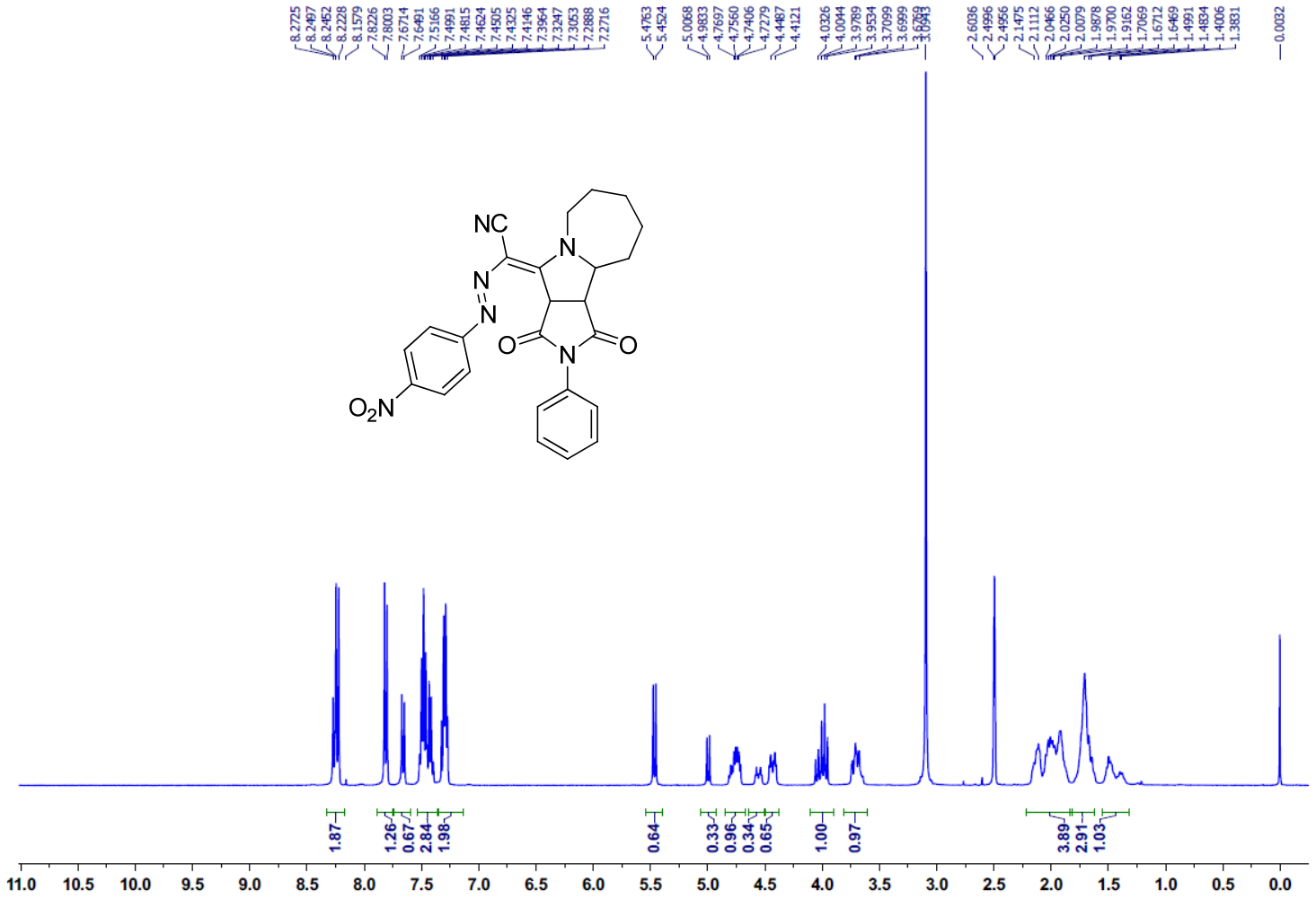


Fig S54. Spectrum ^{1}H NMR 2-(1,3-dioxo-2-phenyl-3*a*,6,7,8,9,10,10*a*,10*b*-octahydropyrrolo[1,2]pyrrolo[3,5-*a*]azepin-4-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**11g**) (DMSO-d_6)

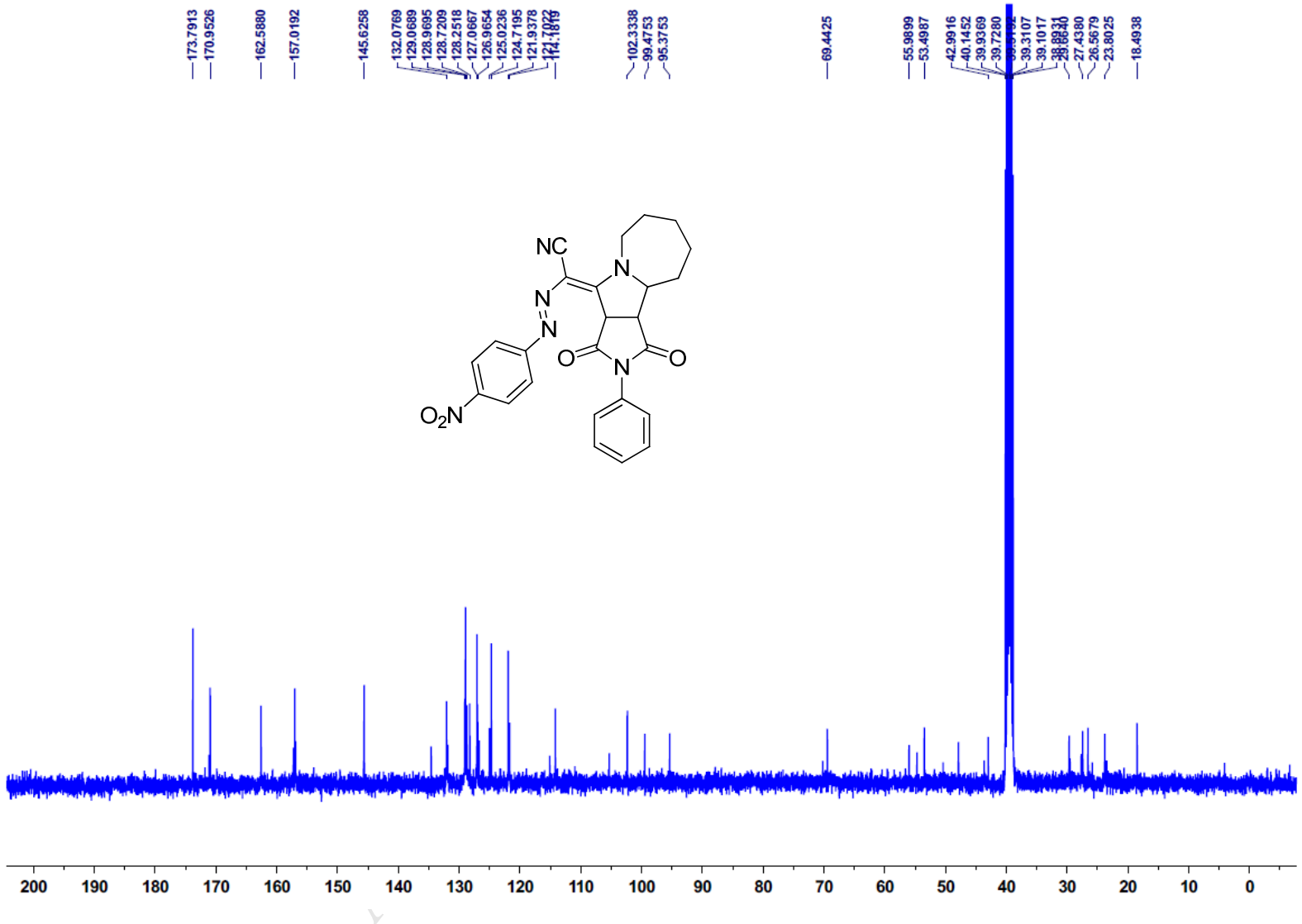


Fig S55. Spectrum ^{13}C NMR 2-(1,3-dioxo-2-phenyl-3*a*,6,7,8,9,10,10*a*,10*b*-octahydropyrrolo[1,2]pyrrolo[3,5-*a*]azepin-4-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**11g**) (DMSO-d_6)

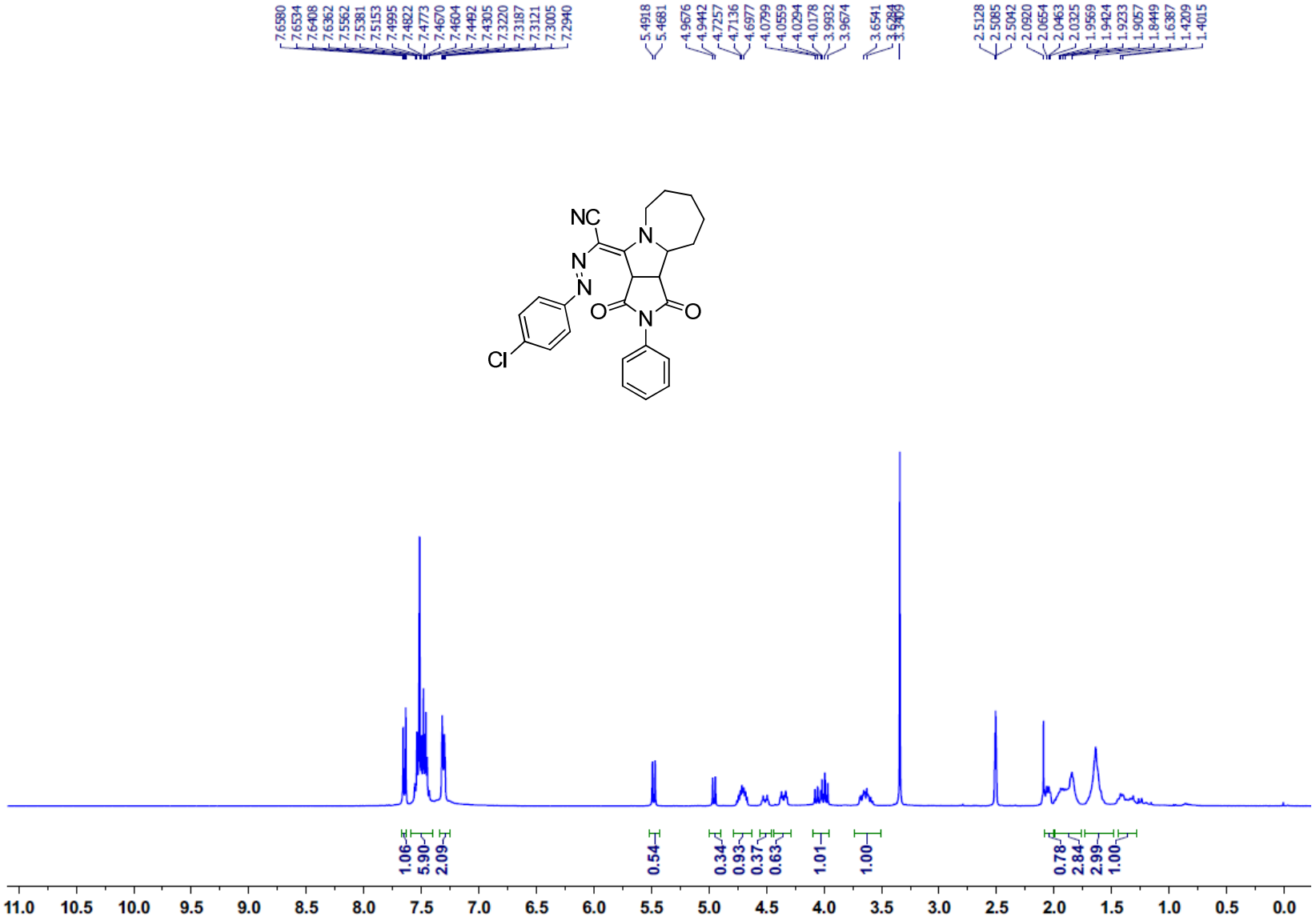


Fig S56. Spectrum ^{1}H NMR 2-[(4-chlorophenyl)azo]-2-(1,3-dioxo-2-phenyl-3*a*,6,7,8,9,10,10*a*,10*b*-octahydropyrrolo[1,2]pyrrolo[3,5-*a*]azepin-4-ylidene)acetonitrile (**11h**) (DMSO-d_6)

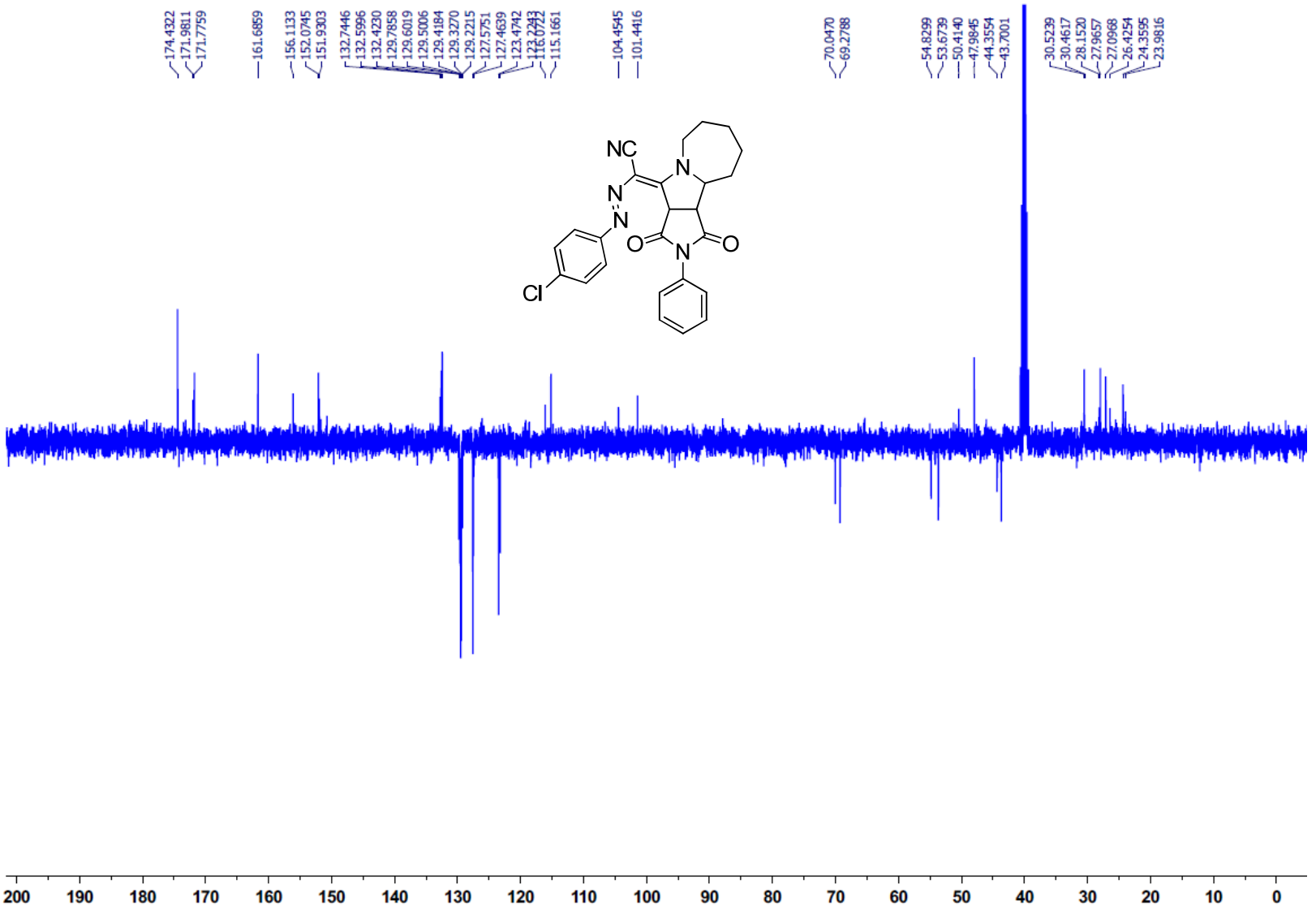


Fig S57. Spectrum ^{13}C NMR 2-[(4-chlorophenyl)azo]-2-(1,3-dioxo-2-phenyl-3*a*,6,7,8,9,10,10*a*,10*b*-octahydropyrrolo[1,2]pyrrolo[3,5-*a*]azepin-4-ylidene)acetonitrile (**11h**) (DMSO-d_6)

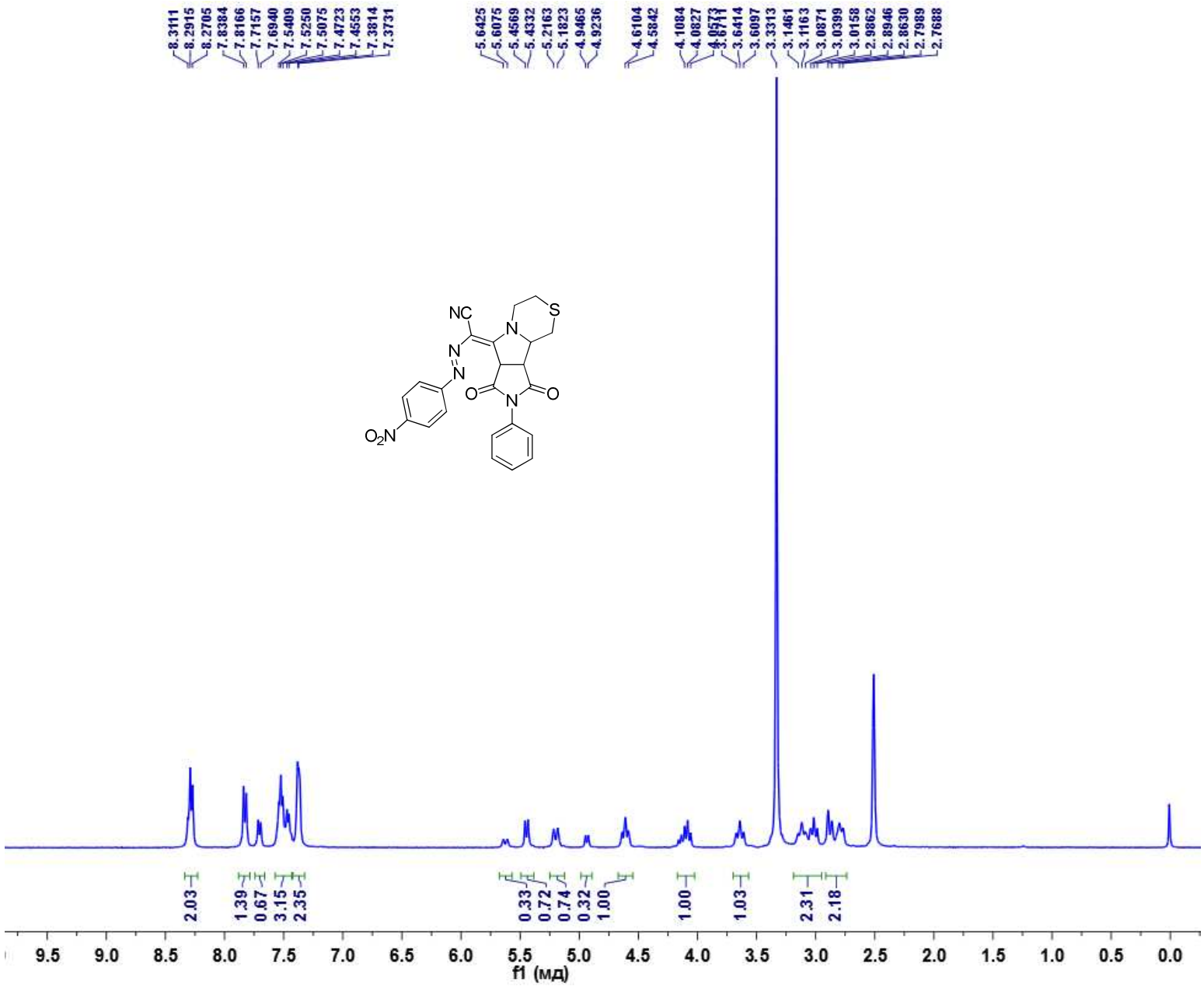


Fig S58. Spectrum ^{1}H NMR 2-(7,9-dioxo-8-phenyl-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]thiazin-6-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**11k**) (DMSO-d_6)

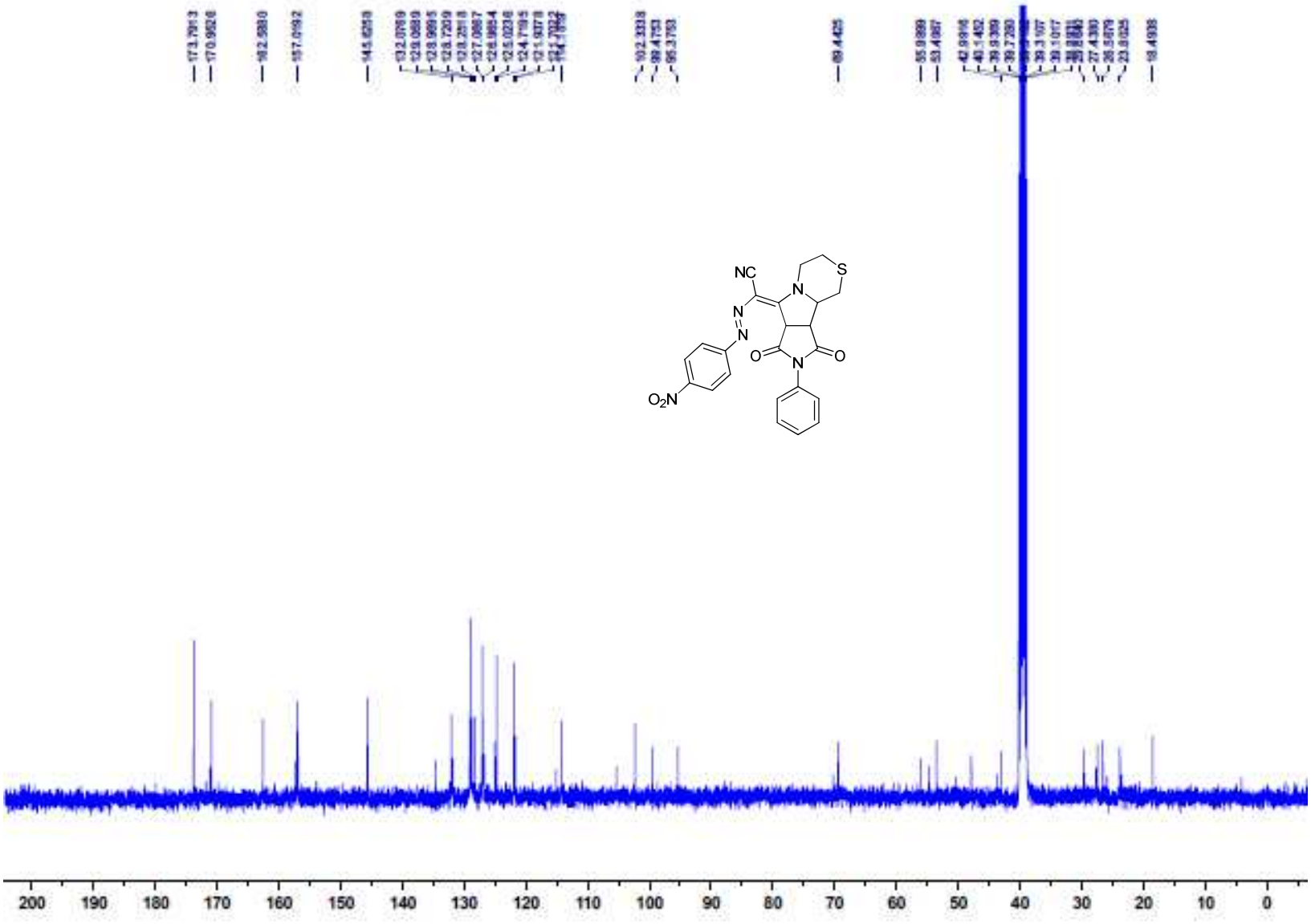


Fig S59. Spectrum ^{13}C NMR 2-(7,9-dioxo-8-phenyl-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]thiazin-6-ylidene)-2-[(4-nitrophenyl)azo]acetonitrile (**11k**) (DMSO-d_6)

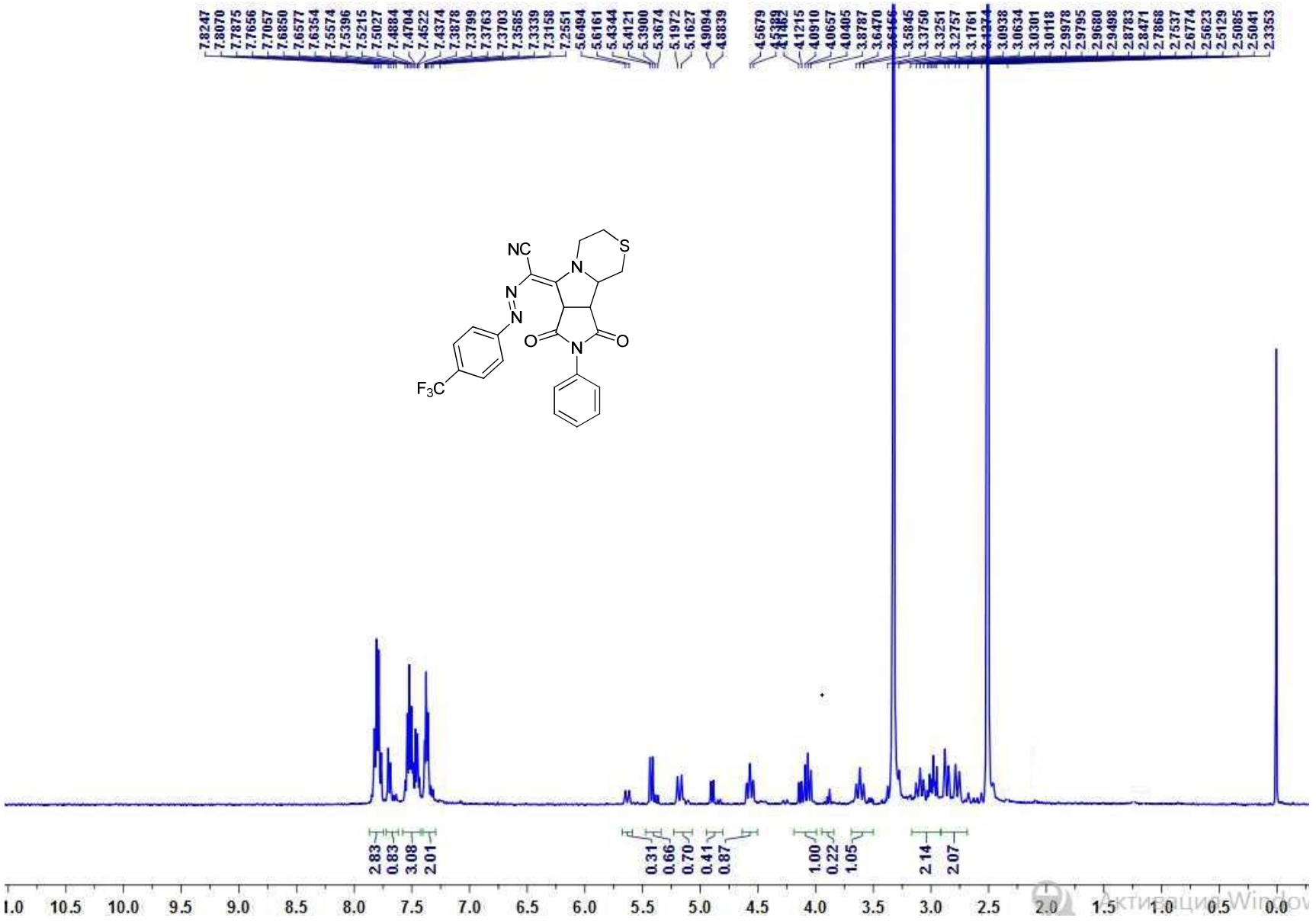


Fig S60. Spectrum ^{1}H NMR 2-(7,9-dioxo-8-phenyl-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]thiazin-6-ylidene)-2-[4-(trifluoromethyl)phenylazo]acetonitrile (**11l**) (DMSO-d_6)

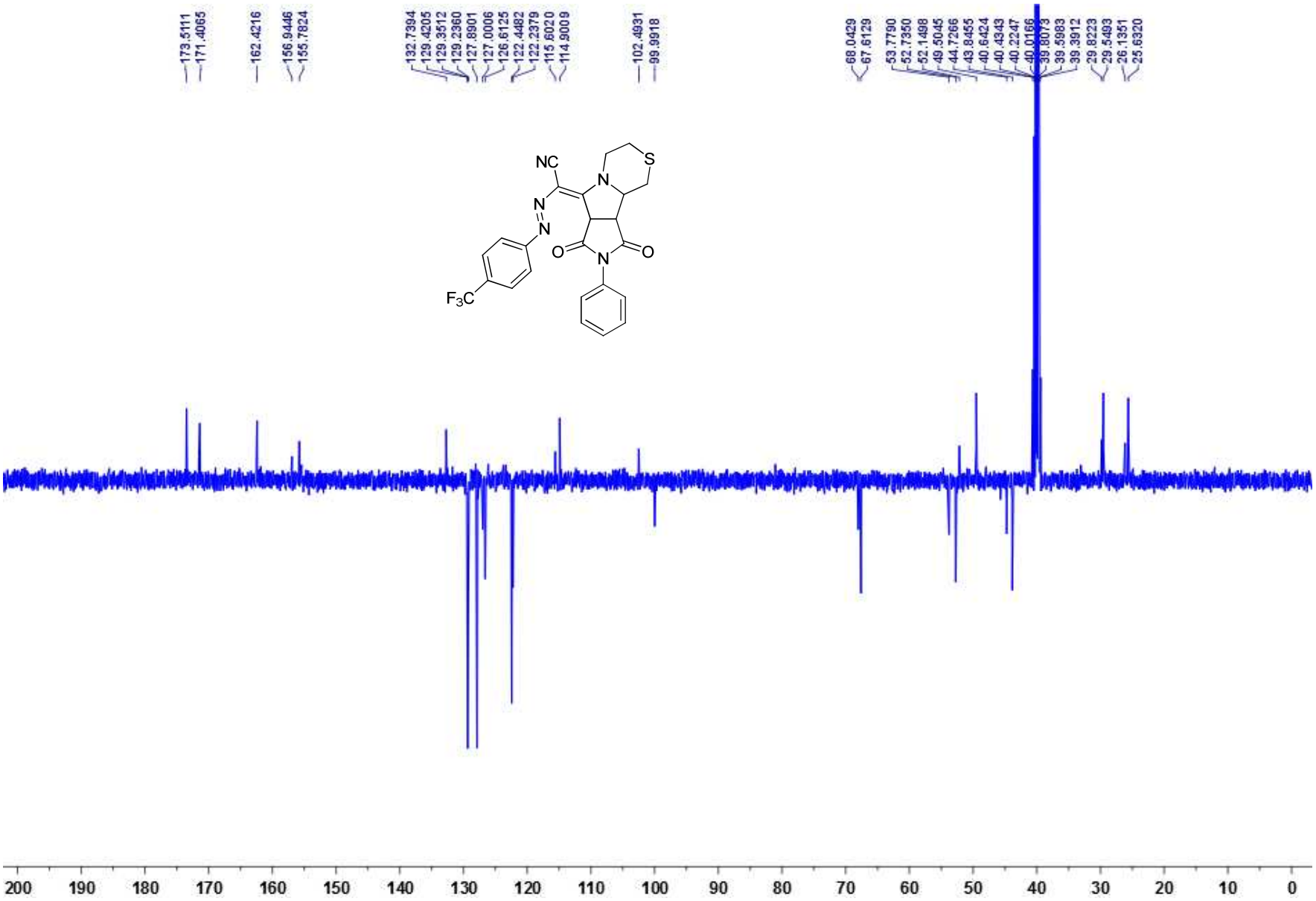


Fig S61. Spectrum ^{13}C NMR 2-(7,9-dioxo-8-phenyl-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]thiazin-6-ylidene)-2-[4-(trifluoromethyl)phenylazo]acetonitrile (**11l**) (DMSO-d_6)

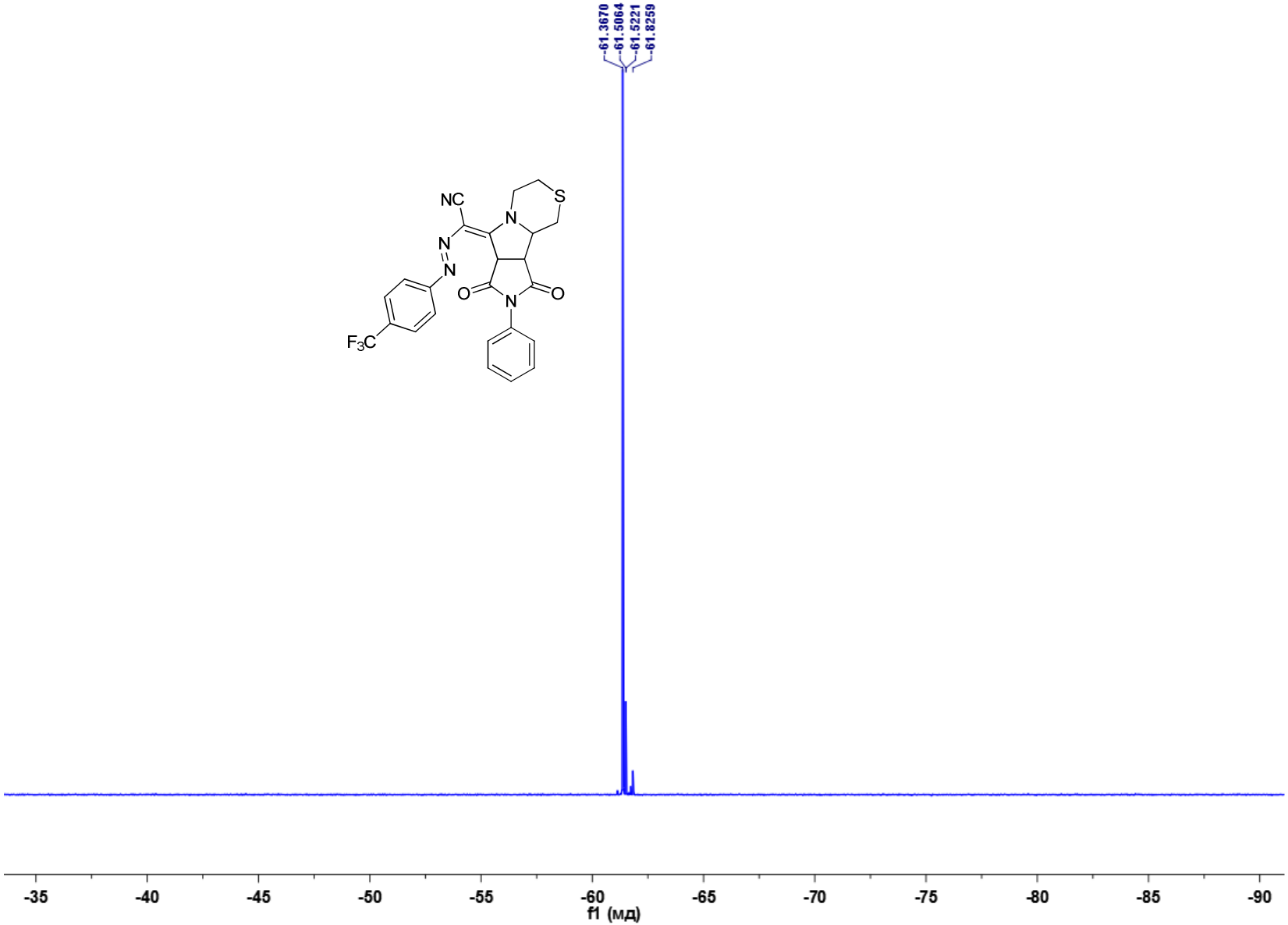


Fig S62. Spectrum ^{19}F NMR 2-(7,9-dioxo-8-phenyl-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]thiazin-6-ylidene)-2-[4-(trifluoromethyl)phenylazo]acetonitrile (**11l**) (DMSO-d_6)

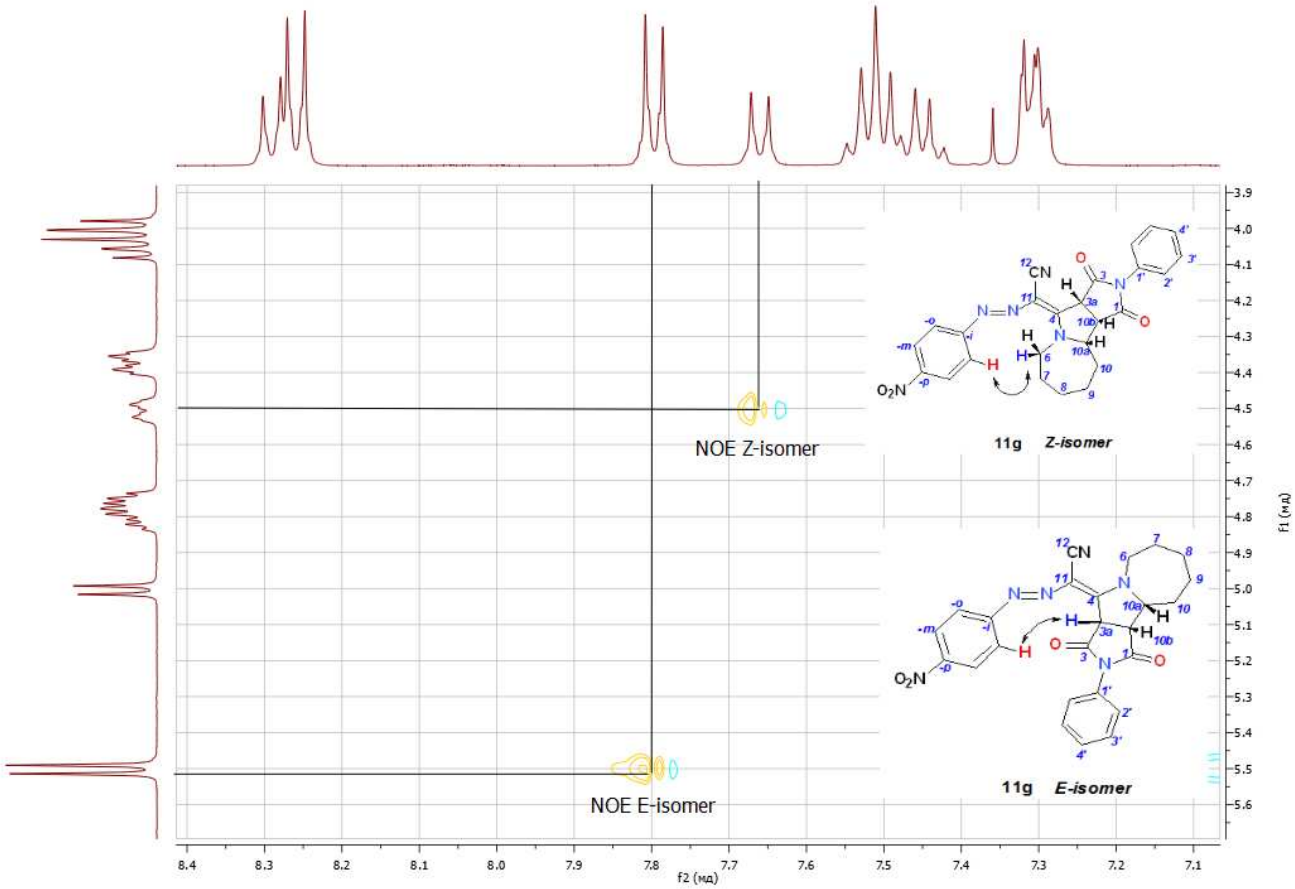


Fig S63. Fragment of the NOE spectrum for 2-(7,9-dioxo-8-phenyl-1,3,4,6*a*,9*a*,9*b*-hexahydropyrrolo[1,2]pyrrolo[3,5-*a*][1,4]thiazin-6-ylidene)-2-[4-(trifluoromethyl)phenylazo]acetonitrile (**11g**) (DMSO-d_6)