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Graphical Abstract

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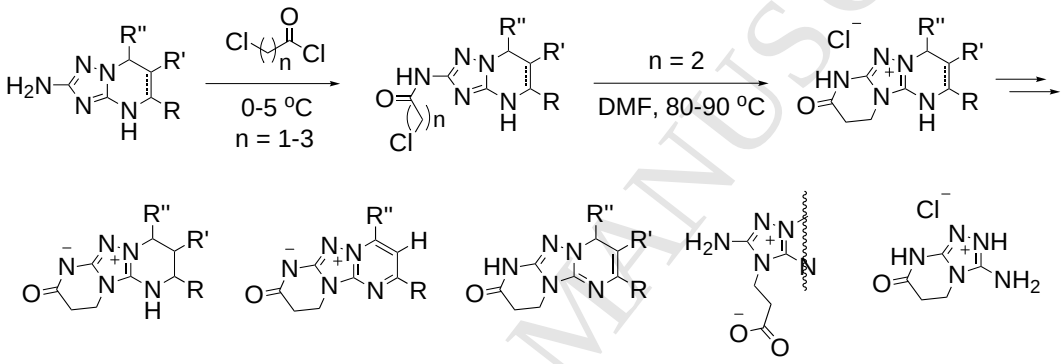
[a] *South-Russia State Technical University, Prosveschenya 132, 346428 Novocherkassk, Russian Federation*

[b] *State Scientific Institution 'Institute for Single Crystals' of National Academy of Sciences of Ukraine, Lenin Ave. 60, 61001 Kharkiv, Ukraine*



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Partially hydrogenated 2-amino[1,2,4]triazolo[1,5-*a*]pyrimidines as synthons for the preparation of polycondensed heterocycles: reaction with chlorocarboxylic acid chlorides

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[a] *South-Russia State Technical University, Prosveschenya 132, 346428 Novocherkassk, Russian Federation*
[b] *State Scientific Institution 'Institute for Single Crystals' of National Academy of Sciences of Ukraine, Lenin Ave. 60, 61001 Kharkiv, Ukraine*
[c] *V. N. Karazin Kharkiv National University, 4 Svobody sq., Kharkiv 61202, Ukraine*

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ABSTRACT

Partially hydrogenated 2-amino[1,2,4]triazolo[1,5-*a*]pyrimidines and 2-amino[1,2,4]triazolo[5,1-b]quinazolines react with the chlorides of chloroacetic, 3-chloropropanoic and 4-chlorobutanoic acids at 0-5 °C to give amides through acylation of the 2-amino group. Heating the corresponding 3-chloropropanoyl derivatives at 80-90 °C in DMF leads to selective intramolecular alkylation at N-3 to form the chlorides of partially hydrogenated [1,2,4]triazolo[1,5-*a*:4,3-*a'*]dipyrimidin-5-ones and pyrimido[2',1':3,4][1,2,4]triazolo[5,1-*b*]quinazolin-12-ones. It may be more convenient to prepare such compounds through one-pot processes. Some reactions of the synthesized chlorides of polycondensed heterocycles have been studied. Conditions have been found to effect the selective synthesis of free bases, oxidative aromatization or hydrolysis of the dihydropyrimidine cycle, and the selective hydrolytic cleavage or elimination of the pyrimidone ring. Some of the resulting compounds represent new mesoionic heterocycles.

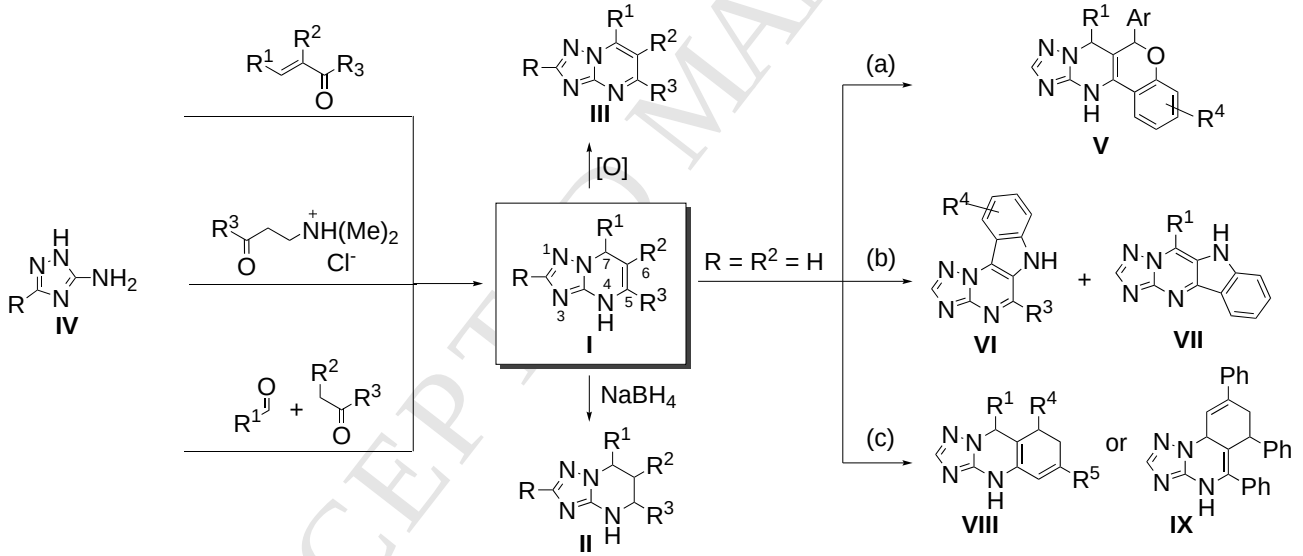
* Corresponding author. Tel.: +7-903-437-24-03; fax: +7-86-352-276-19; e-mail: chern13@yandex.ru.

Introduction

In recent years, much attention has been paid to the development of new methods for the synthesis of [1,2,4]triazolo[1,5-*a*]pyrimidines (**I-III**) with various degrees of saturation of the pyrimidine ring (Scheme 1).[1] Such interest is based on the fact that **I-III** are purine analogs that exhibit various biological properties, including anticancer,[2a-c] antidiabetic,[2d] anticonvulsant,[2e] antihypertensive,[2f] and antiviral activity.[2g] Moreover, the partially hydrogenated [1,2,4]triazolo[1,5-*a*]pyrimidines **I** and **II** are polyfunctional compounds that can react with various electrophiles.[3,4] This versatility allows for design of the triazolopyrimidine scaffold and the construction of more complex heterocyclic systems.[2,3] The 4,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidines **I** (R = H) have been applied to the synthesis of new polycondensed heterocycles (Scheme 1).[2a,b,4] Compounds of type **I** can be obtained readily from the condensation of aminotriazoles **IV** with □,ß-unsaturated carbonyls[1,2a,b,f,g,3a,b,f,g,4e,5] or Mannich bases.[1,3a,6] Such compounds can also be obtained from three-component reactions between aminotriazoles **IV**, methylene-active carbonyl compounds and aldehydes.[1,2d,f,g,3a,4a,5d,7] Compounds of type **I** are especially useful because the dihydropyrimidine motif is amenable to both aromatization by various oxidizing agents[2d,g,3a,b,4c,5a,b,e,6,8] and reduction by sodium borohydride (Scheme 1).[2g,3a-c,e,f,7a] Annelation of new cycles to the molecules of compounds **I** have been realized by various electrophilic reactions through the electron-rich position 6 and a substituent (R^3 or R^1) at position 5 or 6. Some of the polycondensed heterocycles obtained from such reactions are being investigated as promising antitumor agents.[2a,b]

In addition, partially hydrogenated triazolopyrimidines **I** and **II** behave as polydentate *N*-nucleophiles in many reactions with electrophiles,[2a,3a-c,e,f] reactivity that is analogous to that of *C*-amino-1,2,4-triazoles. Compounds **I** and **II** could serve as precursors to polycondensed heterocycles through reactions involving the nitrogen atoms of the triazole fragment, but the potential utility of this approach remains unexplored. We hypothesized that partially hydrogenated [1,2,4]triazolo[1,5-*a*]pyrimidines could be used as novel *N*,*N*□-binucleophilic synthons for the preparation of polycondensed heterocycles. In short preliminary communication we disclosed the reaction of 4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidines (**II**) with 3-chloropropanoic acid chloride.[9] The obtained results demonstrate that it is possible to form a new ring through annelation reactions of the 2-NH_2 and N-3 atom, while alternative ring systems can be formed through atoms N-3 and N-4 of the starting triazolopyrimidine.[9]

Herein we report the results from detailed investigations of the reactions of partially hydrogenated 2-amino[1,2,4]triazolo[1,5-*a*]pyrimidines of type **I** and **II** (R = NH_2) as well as their analogs, partially hydrogenated 2-amino[1,2,4]triazolo[5,1-*b*]quinazolines, with chlorocarboxylic acid chlorides. Finally, we discuss the structural features and chemical properties of the obtained polycondensed heterocycles.



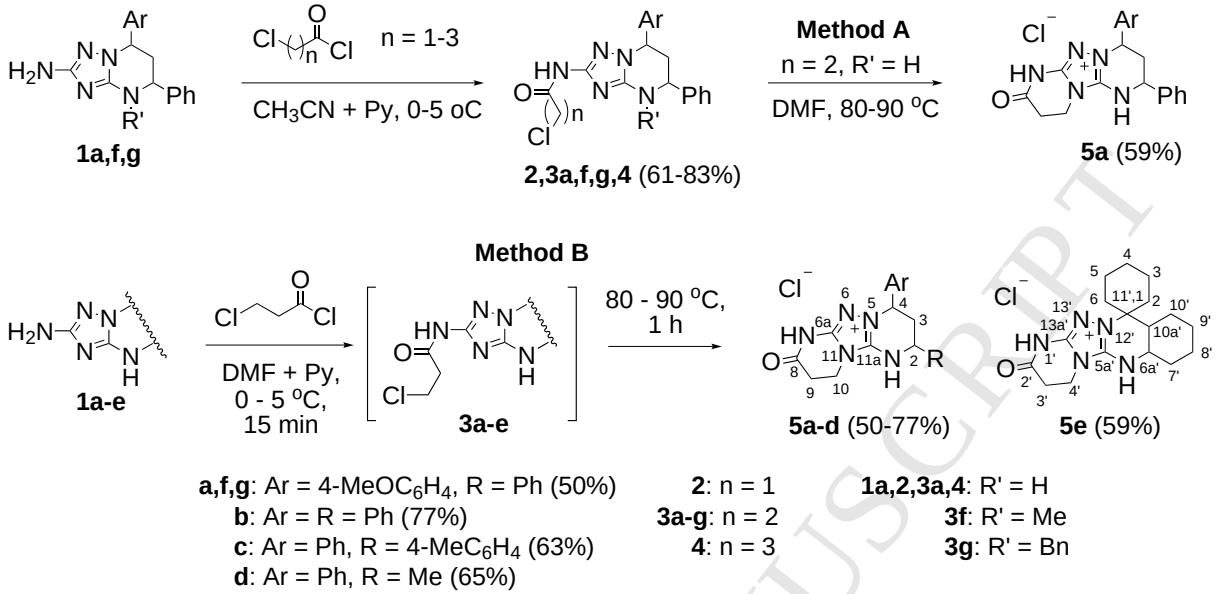
Scheme 1. Synthesis of dihydrotriazolopyrimidines **I** and their use for preparation of triazolopyrimidines **II, III** and polycondensed heterocycles **V-IX**. Reagents: (a) ArCHO, **I** - R^3 = substituted 2-hydroxyphenyl;[2a,b,4a] (b) $NaNO_2$ in AcOH, then heating with polyphosphoric acid or *para*-nitrobenzoyl chloride in pyridine, **I** – R^1 = aryl, R^3 = Me, aryl;[4d] (c) □,ß-unsaturated carbonyls or analogs, **I** – R^1 = aryl, R^3 = Me or R^1 = Me, R^3 = Ph.[4b,c,e,f]

Results and discussion

2.1 Reactions of 2-aminosubstituted triazolopyrimidines and triazoloquinazolines with chlorocarboxylic acid chlorides

Reaction of tetrahydrotriazolopyrimidine **1a** with 2-chloroacetyl, 3-chloropropanoyl or 4-chlorobutanoyl chloride in acetonitrile in the presence of pyridine at 0-5 °C gave amides **2, 3a,** and **4** (Scheme 2), respectively. Attempts to cyclize the chloroacetyl and 4-chlorobutanoyl derivatives **2** and **4** by heating in DMF were unsuccessful. Heating these solutions at temperatures from 80 °C to reflux led only to recovery of the starting materials, even when tetramethylammonium iodide was added as a potential catalyst to enable nucleophilic substitution. However, the 3-chloropropanoyl derivative **3a** cyclized readily upon being heated at 80-90 °C in DMF to give the corresponding 8-oxo-1,2,3,4,7,8,9,10-octahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride **5a** (Scheme 2). We found that it is more convenient to carry out annelation of dihydropyrimidone moiety to 2-aminotriazolopyrimidines in a one-pot procedure, which afforded the polycondensed compounds **5a-e** in yields of 50-77%. Aminoheterocycles **1a-e** were first treated with 3-chloropropanoyl chloride in DMF in the presence of equimolar amounts of pyridine at 0-5 °C. The reaction mixtures were subsequently heated at 80-90 °C (Scheme 2, Method **B**). It should

be noted that the cyclizations of 3-chloropropanoyl derivatives of type **3** are very sensitive to steric factors. For example, compounds **3f** and **3g** did not undergo cyclization even after prolonged heating in DMF; only the starting compounds were isolated from the reaction mixtures (Scheme 2).



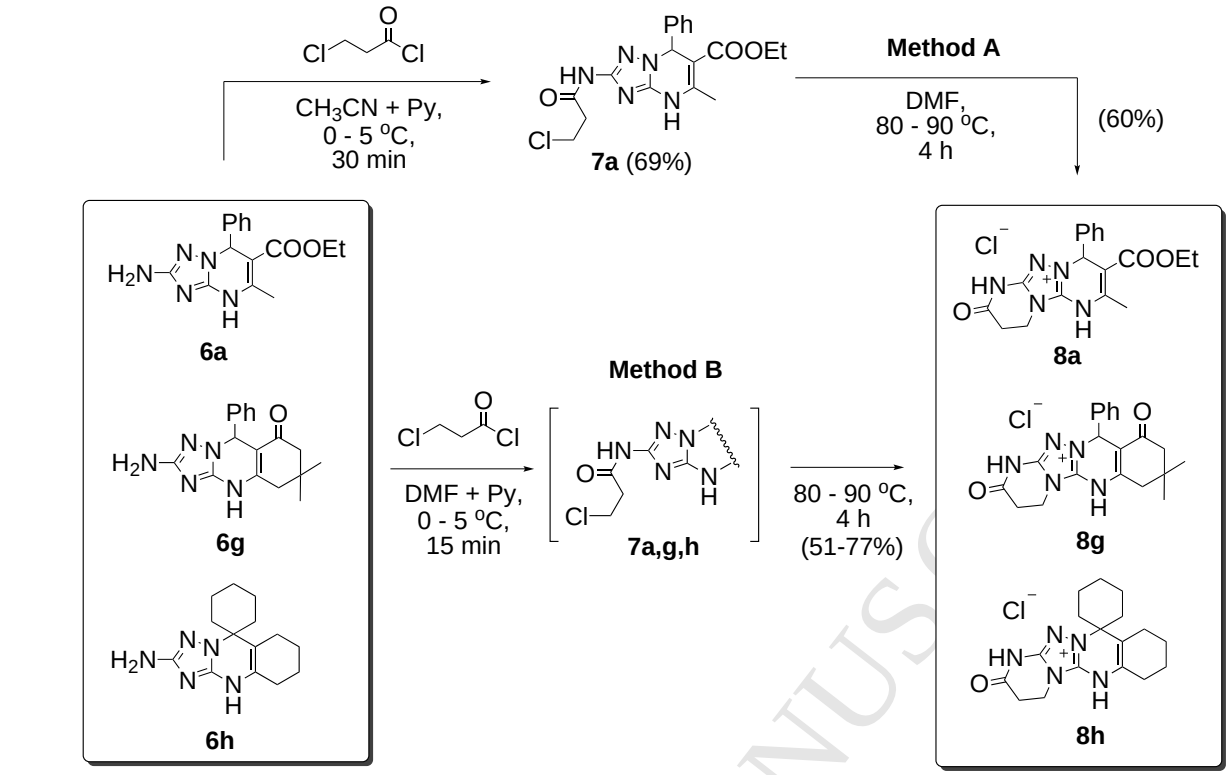
a,f,g: Ar = 4-MeOC$_6$H$_4$, R = Ph (50%)
b: Ar = R = Ph (77%)
c: Ar = Ph, R = 4-MeC$_6$H$_4$ (63%)
d: Ar = Ph, R = Me (65%)

2: n = 1
3a-g: n = 2
4: n = 3

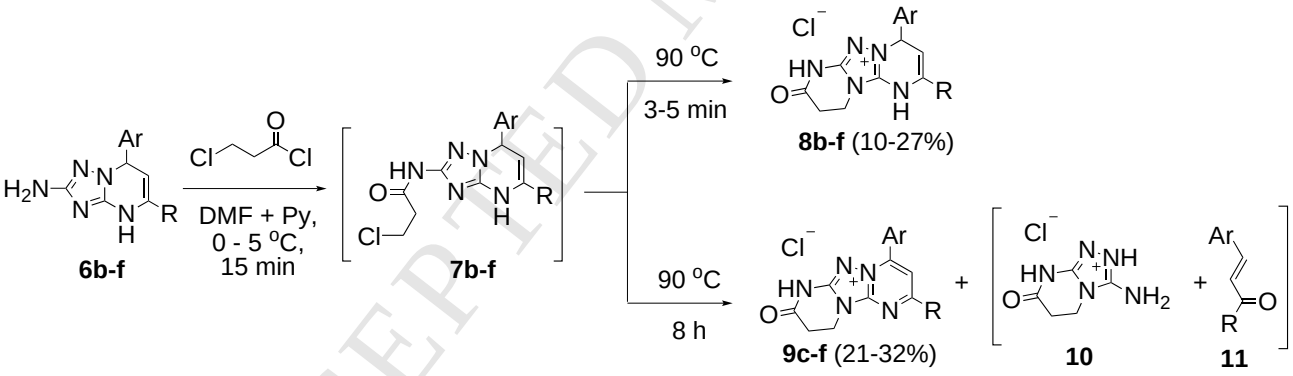
1a,2,3a,4: R' = H
3f: R' = Me
3g: R' = Bn

Scheme 2. Synthesis of amides **2, 3a,f,g,4** and polycondensed compounds **5a-e**.

The reactivity of 2-amino-substituted triazolopyrimidines **6a-f** and triazoloquinazolines **6g,h** towards 3-chloropropanoyl chloride in DMF is generally similar to that of the compounds **1** (Schemes 3-5). Intermediate acylamino compounds **7** formed at 0-5 °C can be converted into the polycondensed heterocycles **8a-h** by heating at 80-90 °C. Isolating and purifying acylamino compounds, for example **7a** (Scheme 3) or **7c** (Scheme 5), showed no significant advantages over the one-pot procedure. Compounds **8b-f,** with hydrogen as the substituent at position 3, are comparatively unstable. It is possible to obtain these compounds with low isolated yields (10-28%), providing that the cyclization reaction time is limited to 3-5 min (Scheme 4). Extending the reaction times to 20 min increased the yields of compounds **8b-f** to 40-60%. However, the ^{1}H NMR spectra of the isolated products showed that they contained 15-20% of compounds **9b-f** as byproducts. These compounds are the products of oxidative aromatization of the dihydropyrimidine rings of compounds **8b-f**. Another side reaction that occurs in addition to oxidative aromatization is hydrolytic cleavage of dihydropyrimidine fragment of compounds **8b-f** during the reaction between compounds **6b-f** and 3-chloropropanoyl chloride. Thus, by prolonging the reaction times up to 8 h, we were able to isolate compounds **9c-f, 10** and chalcon **11c** from the reaction mixtures (Schemes 4 and 5). However, the reaction of compound **6b** (R = CH_3) with 3-chloropropanoyl chloride under these condition gave an inseparable mixture of products in which benzylideneacetone was detected by GC-MS analysis. Compounds **9c**, **10** and **11c** were also obtained by heating pure compounds **7c** (Method A, Scheme 5) or **8c** (Method B, Scheme 5) in DMF for 8 h. Compound **10** was prepared by an alternate method in 50% yield by hydrolysis of compound **8c** in an ethanolic solution of hydrochloric acid.

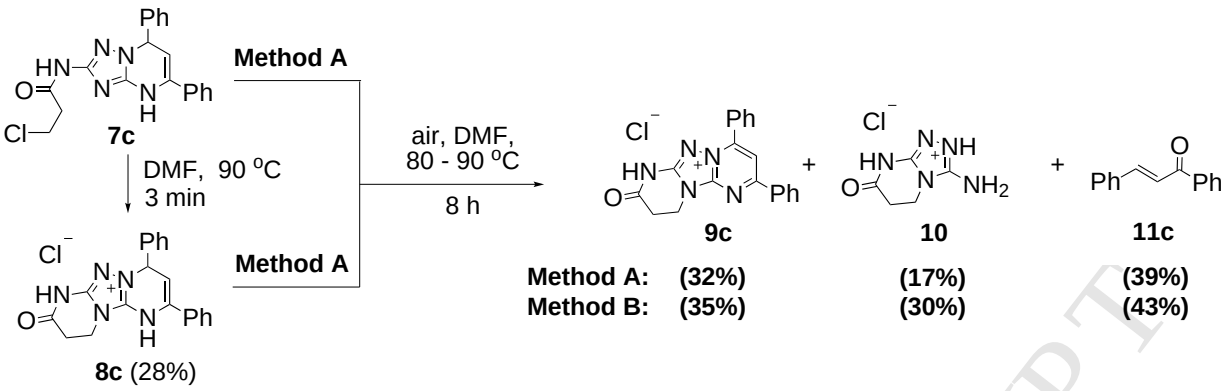


Scheme 3. Synthesis of compounds **7a**, **8a,g,h**.



b: Ar = Ph, R = Me,
c: Ar = R = Ph,
d: Ar = Ph, R = 4-MeC_6H_4,
e: Ar = 4-$MeOC_6H_4$, R = Ph,
f: Ar = R = 4-ClC_6H_4

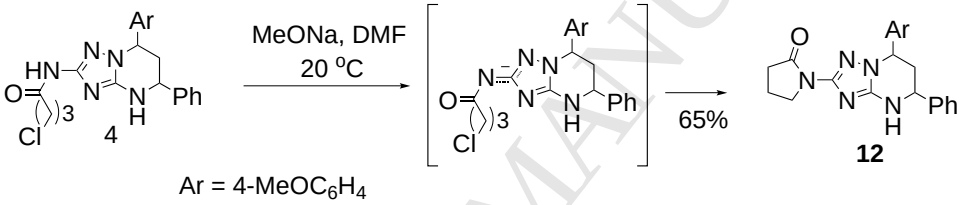
Scheme 4. One-pot synthesis of compounds **8b-f** and **9c-f**.



Scheme 5. Synthesis of compounds **8c, 9c, 10** and **11c**.

Because attempts to effect the thermal cyclization of the chloroacetyl (**2**) and 4-chlorobutanoyl (**4**) derivatives failed, we investigated the behavior of compounds **2, 3a** and **4** in the presence of sodium methoxide. It was anticipated that the highly nucleophilic conjugated N-anions should form via deprotonation of the amide nitrogens in basic media. We were interested to learn whether such anions would cyclize and to determine the direction of such cyclizations.

Treatment of compounds **2** and **3a** with sodium methoxide in DMF or DMSO resulted in the formation of inseparable complex mixtures of products, while compound **4** gave pyrrolidone derivative **12** under these conditions (Scheme 6). The attempts to prepare polycondensed heterocycles from chloroacylated compounds **2, 3a** and **4** through base catalysis were thus unsuccessful.



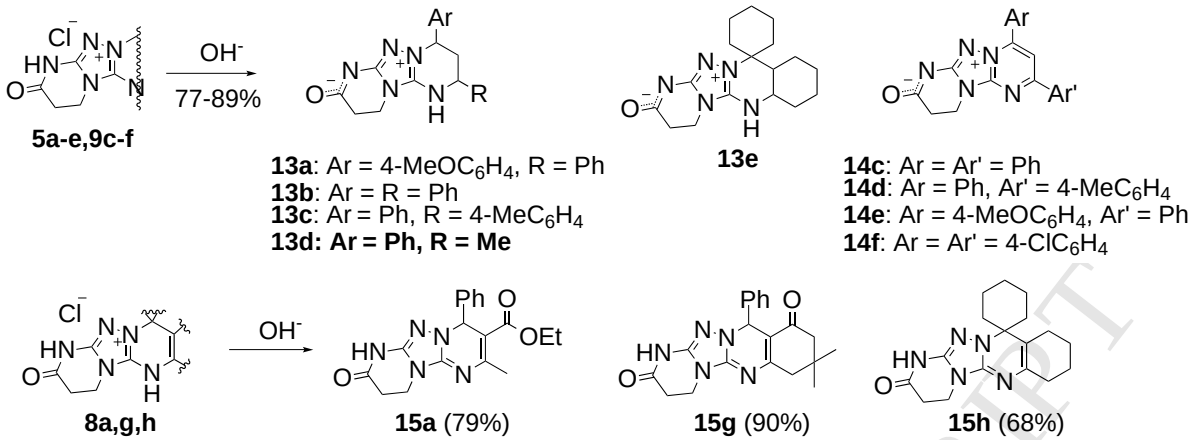
Scheme 6. Synthesis of compound **12**.

2.2 Transformations of polycondensed compounds in basic media

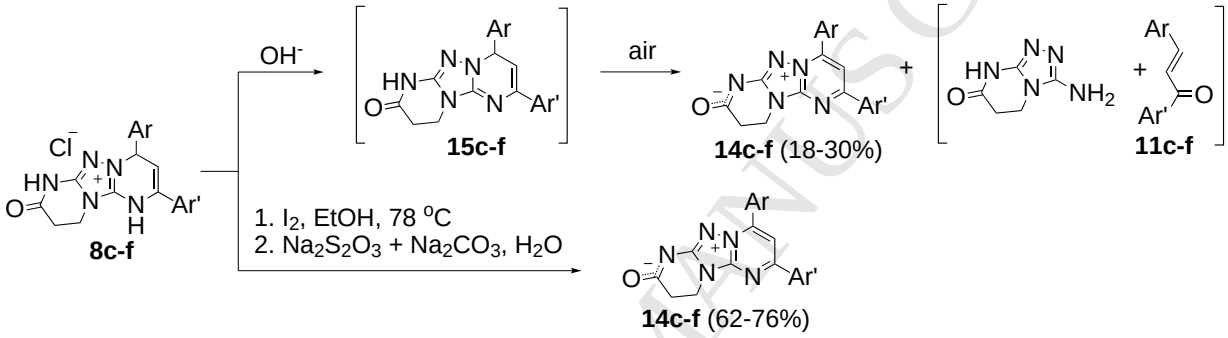
The behavior of the obtained polycondensed heterocycles in the presence of bases was then studied.

In aqueous sodium carbonate solutions at room temperature, cations of compounds **5a-e** and **9c-f** were deprotonated at the amide nitrogen to afford mesoionic compounds **13a-e** and **14c-f**. Cations of compounds **8a,g**,**h** lost the proton from the NH group of the dihydropyrimidine moiety to afford the free bases **15a,g,h**, correspondingly (Scheme 7). Cations of salts **8c-f** in alkaline media were not only deprotonated but also underwent oxidative aromatization to form mesoionic compounds **14c-f** in yields of 18-30% (Scheme 8). Low yields of products **14c-f** from the oxidative aromatization of compounds **8c-f** in basic media were due to concurrent hydrolysis of the dihydropyrimidine ring of the intermediate free bases **15c-f**. This process occurred through enones **11c-f**, which were detected in the reaction mixtures by GC-MS. We have developed an improved, preparative synthesis of compounds **14c-f** employing iodine in ethanol to effect the oxidative aromatization of precursors **8c-f** (Scheme 8). However, all attempts to aromatize compound **8b** were unsuccessful. In alkaline solution the compound **8b** was almost completely hydrolyzed, while treatment with iodine gave an inseparable, complex mixture of products.

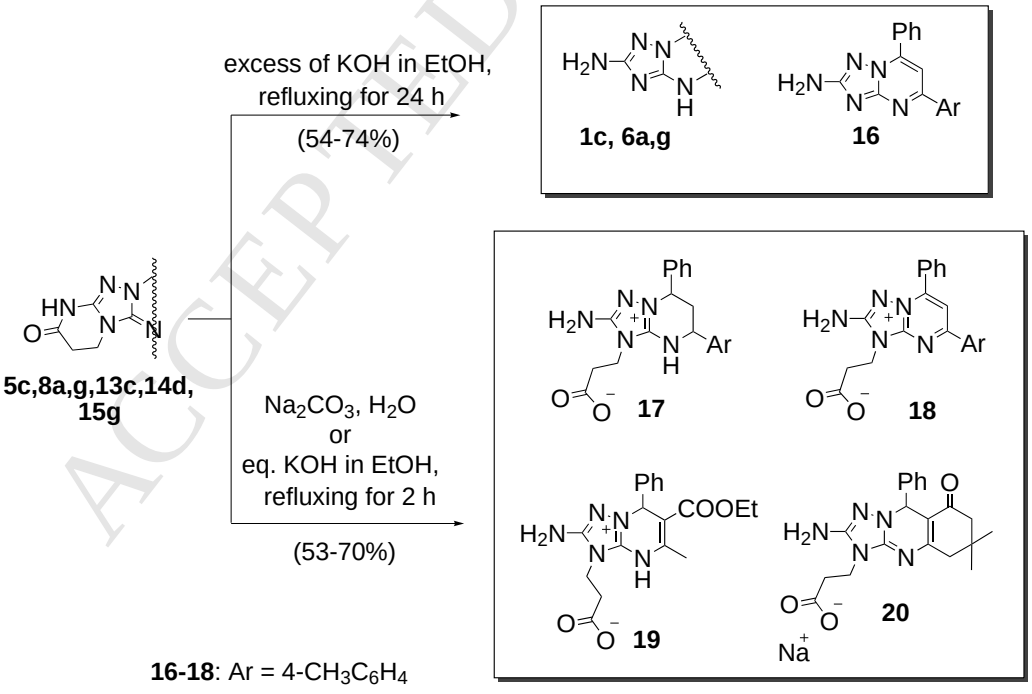
When compounds **5c**, **8a**, **14d** and **15g** were refluxed in ethanol for prolonged periods in the presence of a large excess of KOH, hydrolysis of the amide bond and a retro-Michael reaction in which acrylic acid was eliminated occurred, and aminoheterocycles **1c**, **6a**,**g** and **16** were formed (Scheme 9). However, refluxing compounds **5c**, **8a**,**g** and **14d** in aqueous Na_2CO_3 or with a small excess of KOH in ethanol within 2 h resulted in selective hydrolysis of the lactam and afforded the heterosubstituted propanoic acids **17-20** (Scheme 9).



Scheme 7. Transformations of compounds **5a-e**, **8a,g,h**, **9c-f** in basic media at room temperature.



Scheme 8. Synthesis of compounds **14c-f** by oxidative aromatization of compounds **8c-f**.



Scheme 9. Transformations of polycyclic compounds in basic media with heating.

2.3 Structure determination

The structures of the synthesized compounds were established by elemental analysis, mass-spectrometry and NMR spectral data, including ^{1}H-^{13}C heteronuclear correlation HSQC and HMBC spectra for the majority of compounds (see Supplementary Materials), and X-Ray diffraction studies. p*Ka* measurements, alkylation experiments and quantum chemical calculations were also performed to elucidate the tautomeric structure of free bases **13-15**.

2.3.1 Spectral data, pKa and alkylation

Unfortunately, we were unable to obtain acceptable ^{13}C NMR spectra for compounds **7c** and **8b-f** because they gradually decomposed in solution while the spectra were being recorded. Small signals corresponding to impurities, the integral intensity of which increased over longer recording times, were also observed in the ^{1}H NMR spectra of these compounds. The ^{13}C NMR spectrum of compound **17** was also not obtained due to its insufficient solubility in common NMR solvents.

The ^{1}H and ^{13}C NMR spectra of compounds **2, 3a,f,g, 4, 7a** and 7**c** are analogous to the spectra of the acylated derivatives of partially hydrogenated 2-aminosubstituted [1,2,4]triazolo[1,5-*a*]pyrimidines, which have been described in the literature.[3e,f,8a]

Cyclization of 3-chloropropanoyl derivatives results in an ~8-10 ppm upfield shift in the signal of the triazole carbon bonded to the amide group (Fig. 1). Analogous displacements were observed upon alkylation or protonation of *C*-amino-1,2,4-triazoles at the N-4 atom of the triazole ring (i.e., the atom bonded to two carbons in the triazole ring).[3e,10,11] It should be noted that the signal of the triazole carbon bonded to the amide nitrogen (C-6a in compounds similar to **5a-d**, C-13a in compounds similar to **8g**) is significantly broadened. In the spectra of some compounds, for example **8a** and **13c**, this signal merges into the background due to quadrupole interactions with the neighboring nitrogen atoms. Nevertheless, cross-peaks between the signals from both carbons of the triazole ring and protons of 10-CH_2 (4-CH_2 in pyrimidotriazoloquinazolines) are observed in most of the ^{1}H-^{13}C HMBC spectra of the synthesized polycondensed heterocycles (Fig. 1) that proves the direction of the annelation of pyrimidone cycle. Moreover, well-defined cross-peaks between the signals from the triazole carbons and protons of NC$\underline{H_2}CH_2CO$ in the HMBC spectra of compounds **10**, **19** and **20** serve as additional unambiguous evidence for the assigned annelation (Fig. 1).

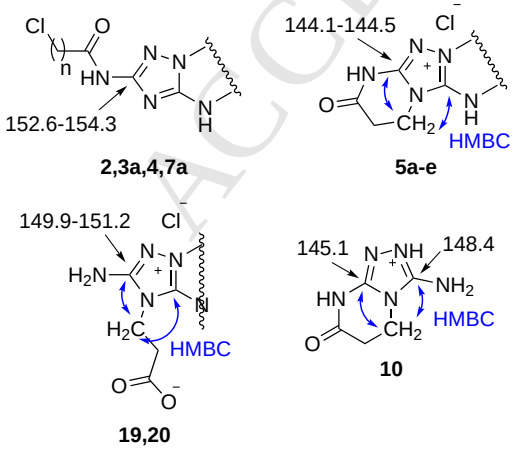
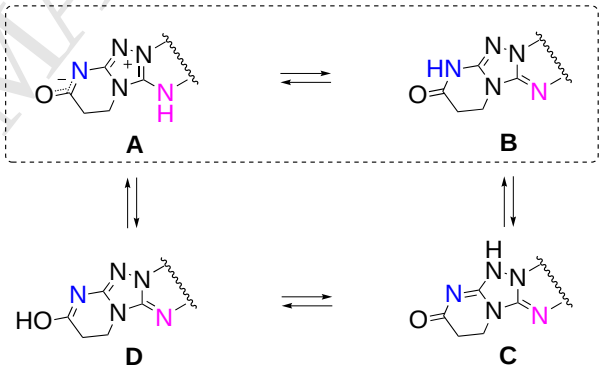


Figure 1. The characteristic ^{13}C NMR signals (ppm) of some compounds (DMSO-d_6) and the key correlations in the ^{1}H-^{13}C HMBC spectra.

A distinctive feature of the ^{1}H NMR spectra of the salts **5a-e** is the sufficient downfield displacement of the NH signal of tetrahydropyrimidine (9.9-10.4 ppm) in relation to the acylated derivatives **2,3a,4** (~7.4 ppm) and amines **1a-e** (6.4-7.0 ppm).[3e,f] The minimal changes between the ^{1}H NMR spectral characteristics of the tetrahydropyrimidine ring in the polycyclic products **5a-e**, **13a-e** and their precursors **3a**, **1a-e** suggests that the spatial configuration of this ring has not undergone significant changes during the annelation of pyrimidone moiety.

The question of the tautomeric structure of compounds **13a-e** and **15a,g,h** deserves a separate discussion (see also Section 2.3.2 below). Deprotonation of cationic salts **5a-e** and **8a,g,h** can occur from the NH groups of any of the pyrimidine rings to afford tautomers **A** and **B** (Scheme 10). A priori, a third possible participant in the prototropic equilibrium is diimino tautomer **C**. However, this tautomer may be present at only very low concentrations because computational results suggest that it should be significantly less stable than the amino-imino form **B**. These computational data are presented in Section 2.3.2, and similar results were obtained for the analogous tautomeric forms of 3,5-diamino[1,2,4]triazole.[12] In light of our computational results (Section 2.3.2) and literature data on the tautomerism of lactams and acylated aminoheterocycles,[13] it can be concluded that hydroxy form **D**, the fourth possible tautomer, is also likely to be present only in minor concentrations. Therefore, in the experimental studies of the tautomerism, the only problem to be addressed is the identification of the two tautomeric forms, **A** and **B**.



Scheme 10. Putative tautomeric forms of free bases **13a-e, 15a,g,h**.

In the ^{1}H NMR spectra of compounds **13a-e** the signal of 1-NH (6□-NH in compound **13e**) is significantly broadened and substantially merged into the background, apparently due to rapid exchange with solvent. Similar broadening was observed for the signals of the NH and NH_2 groups in the spectra of the structurally analogous mesoionic compounds **21**[3e] and **22**[11] (Fig. 2). The predominance of the mesoionic tautomer **A** in solutions of compounds **13a-e** in polar solvents is supported by comparisons of the pK_a values for compounds **13a**, **21**, and **22** with the pK_a values for compounds **23** and **24**, the fixed forms of tautomer **B** (Fig. 2). Compounds **13a**, **21** and **22** (protonation at the nitrogen atom of the ionized amide group, Fig. 2) are 50-80 fold less basic than compounds **23** and **24** (protonation at the imino nitrogen of the tetrahydropyrimidine ring, Fig. 2). Moreover, the mesoionic structures of compounds of type **13** were indirectly supported by selective alkylation of compound **13a** at the amide nitrogen, which gave compound **23** in the absence of strong bases (Scheme 11). The structure of compound **23** was confirmed by its HMBC spectrum, in which cross-peaks between the signals of the benzylic protons (4.63-4.81 ppm) and

carbons C-6a (143.35 ppm) and C-8 (165.73 ppm) were observed (Scheme 11). In their crystalline states, compounds **13a-e** apparently also exist in the mesoionic tautomeric form **A**. This is supported by the fact that their FTIR spectra do not show the C=O bands at 1697-1711 cm^{-1} that are observed in the FTIR spectra of salts **5a-e** (the crystal structure of **5d** was confirmed by X-ray analysis, Section 2.3.3) and compound **23** (representative of the fixed form of tautomer **B)**. The intense bands near 1647-1667 cm^{-1} in the FTIR spectra of compounds **13a-e** were attributed to complex vibrations predominantly involving the valence stretching of C11a—N1 and the antisymmetrical stretching of N6—C6a—N7 based on evidence from quantum chemical calculations on model structure **13A** (Section 2.3.2 below). Unfortunately, we were unable to prepare a crystal suitable for X-ray analysis of the structure of compounds **13a-e**. However, the mesoionic nature of compound **22**, a structural analog of the mesoionic compounds **13a-e**, has been confirmed by X-ray analysis.[11]

Well-defined NH singlets are observed at 11.25-11.53 ppm in the ^{1}H NMR spectra of compounds **15a**,**g**,**h**, in contrast to the spectra of mesoionic compounds **13a-e**. This signal can be attributed to the NH proton of the amide group (tautomer **B**, Scheme 10) as well as the dihydropyrimidine ring (tautomer **A**, Scheme 10). However the very similar pK_a values (Scheme 12) of compounds **15a** and **25**, which is the fixed form of tautomer **B**, suggests that tautomer **B** predominates in solution for compounds **15a**,**g**,**h**. Furthermore, in contrast to the mesoionic compounds **13a-e**, compounds **15a**,**g**,**h** were not amenable to alkylation in DMF in the absence of strong bases. However, in the presence of sodium hydride, which can deprotonate nitrogen, compound **15a** was selectively alkylated at the amide nitrogen to give compound **25** (Scheme 12). The position of the benzyl group in compound **25** was unequivocally confirmed by HMBC spectrum. The close similarity between ν (C=O) in the FTIR spectra of compounds **15a**,**g**,**h** (1685-1706 cm^{-1}) to the corresponding signal in compound **25** (1680-1699 cm^{-1}, combined band of C=O amide and ester) supports the hypothesis that these compounds exist as tautomeric structure **B** in the crystalline state. This has also been confirmed by X-ray analysis of compound **15a** (Section 2.3.3).

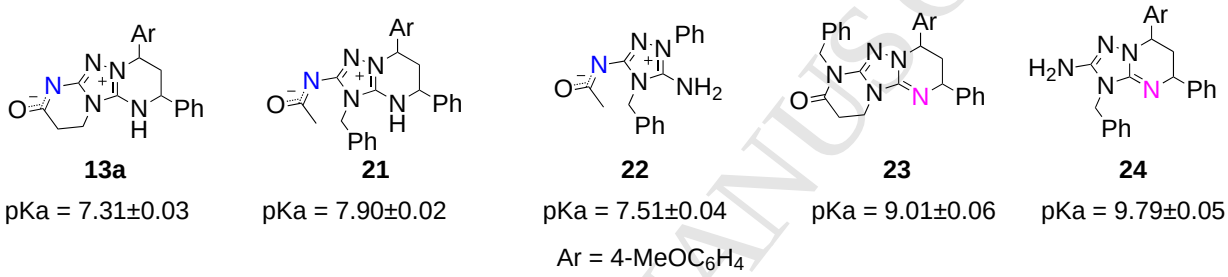
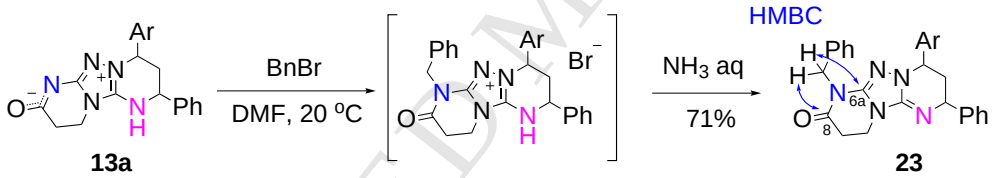
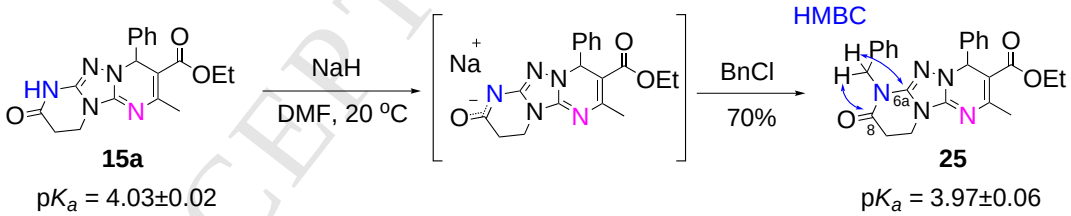


Figure 2. The pK_a values for compounds **13a, 23** and their analogs **21**,[3e] **22**,[11] **24**,[3e] determined by potentiometric titration in 80% ethanol.



Scheme 11. Synthesis of compound **23**.



Scheme 12. Synthesis of compound **25** and the pK_a values for compounds **15a** and **25** (titration by 0.1 M HCl in 80% ethanol).

2.3.2 Theoretical calculations

A computational study on the tautomeric structures of compounds **13a-e** and **15a**,**g**,**h** was performed on model molecules **13A-D** and **15A-D**, which contain only hydrogen atoms as substituents in the partially hydrogenated pyrimidine ring.

Optimized structures of the model molecules for the most stable tautomers of compounds **13** and **15** are presented in Figure 3. Each of the possible tautomers **A-D** (Scheme 10) has multiple stable conformers, but the largest ΔG^{298} between conformers of each tautomer is only 0.6 kcal/mol. A notable exception is that the difference between the conformer energies of tautomers **13D** and **15D** may be 6.1 kcal/mol, depending on the internal rotation around the C8—O bond (see Supplementary Material). The relative Gibbs free energies (ΔG^{298}), dipole moments (μ) and Boltzmann populations (x) of tautomers **A-D** were calculated in a vacuum and in DMSO and aqueous solutions and are presented in Table 1. The calculations were based on the assumption that only most stable conformers were present in the equilibrium mixtures. The Boltzmann populations of tautomeric forms **A-D** were computed from standard Gibbs free energy functions, through the relationship $\Delta G = -RT\ln K$, where ΔG denotes the difference between Gibbs free energy for a given tautomer and that calculated for the lowest energy, and K is the equilibrium constant for these species.

As shown by the values of the dipole moments (Table 1), the mesoionic tautomer **A** should be the most polar molecule. On the other hand, in most cases tautomer **B** should be the least polar molecule in the equilibrium mixtures. According to the computational results determined in vacuo, and consequently in nonpolar solvents, tautomer **B** should predominate for both compounds **13** and **15**. In polar media, compounds of type **13** should exist predominantly in tautomeric form **A**. Compounds of type **15** should remain mostly in tautomeric form **B**, although equilibrium concentrations of tautomer **A** increase significantly with increasing polarity of the medium (Table 1). It should be noted that the computational results are in good agreement with the experimental results discussed in Section 2.3.1.

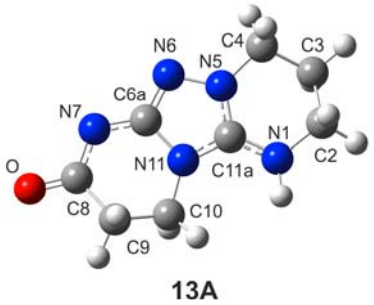


Figure 3. Optimized structures of tautomeres **13A** and **15B** in water.

Table 1. Relative Gibbs Free Energies ΔG^{298} (kcal/mol)[a], dipole moments μ (D) and relative populations *x* (%) of tautomers **A-D** of model compounds **13** and **15** at 25 °C calculated by the B3LYP/6-311++G(2d,2p) method

Tautomer	ΔG^{298}	μ	*x*	Tautomer	ΔG^{298}	μ	*x*
			Vacuum (ε = 1)				
13A	15.63	14.49	0.00	**15A**	18.74	13.41	0.00
13B	0	1.98	100.00	**15B**	0	0.26	100.00
13C	12.22	6.95	0.00	**15C**	14.06	5.31	0.00
13D	9.74	1.53	0.00	**15D**	9.56	3.31	0.00
			Dimethyl sulfoxide (ε = 46.7)				
13A	0	21.21	97.62	**15A**	1.58	19.99	6.46
13B	2.20	2.45	2.38	**15B**	0	0.31	93.54
13C	10.21	10.16	0.00	**15C**	9.98	8.34	0.00
13D	10.82	2.86	0.00	**15D**	8.41	5.21	0.00
			Water (ε = 78.4)				
13A	0	21.37	98.21	**15A**	0.74	20.18	22.42
13B	2.37	2.45	1.79	**15B**	0	0.35	77.58
13C	10.30	10.24	0.00	**15C**	9.87	8.42	0.00
13D	10.96	2.89	0.00	**15D**	8.31	5.24	0.00

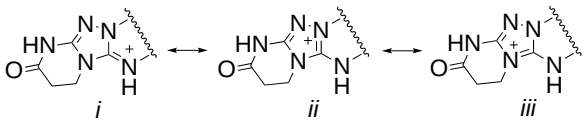
[a]Total Energies, Zero Point Energies, Thermal corrections to Gibbs Free Energies and Relative Energies are presented in Tables S1-S4 of the Supplementary Material.

2.3.3 X-Ray diffraction study

Crystallographic numbering systems will be used for the subsequent discussion of the structures of **5d**, **14c** and **15a** (Fig. 4-6).

Compound **5d** exists in the crystal phase as a cationic organic salt with a chloride counterion (Fig. 4). The asymmetric part of the crystal unit cell contains two organic cations (**5d-A** and **5d-B**), which differ in some geometric parameters, and two chloride anions (Cl1 and Cl2). Analysis of the bond lengths in the tricyclic fragment of **5d** demonstrates that the bonds centered at atom C5 are very similar (the N3-C5 bond is 1.323(6) Å in molecules **5d-A** and **5d-B**; the N4-C5 bond is 1.341(6) Å in **5d-A** and 1.337(6) Å in **5d-B**; the N5-C5 bond is 1.341(6) Å in **5d-A** and 1.338(6) Å in **5d-B**). These bond lengths are longer than the mean value for Csp^2=N(2) bonds (1.313 Å) and shorter than the mean value for Csp^2-N(3) bonds (1.349 Å).[14] In addition, the hydrogen atom at N4 was found from difference Fourier synthesis. Refining this atom in an isotropic approximation revealed the pyramidal configuration of the N4 atom (the sum of the bond angles centered at the nitrogen atom is 355° in **5d-A** and 354° in **5d-B**). Taken together, these facts allow for the assumption that the structure of the organic cation can be described as a superposition of three resonance structures (*i-iii*) with a predominant contribution from structure *ii* (Scheme 13). The tetrahydropyrimidine ring adopts a half-chair conformation (the puckering parameters[15] are: S = 0.74, Θ = 30.9°, and Ψ = 26.5° for **5d-A** and S = 0.75, Θ = 31.0°, and Ψ = 29.2° for **5d-B**). The C3 and C4 atoms deviate from the mean plane of the other atoms in the ring by 0.33 Å and -0.36 Å, respectively, in **5d-A**. The

corresponding atoms in **5d-B** deviate from the plane by -0.36 Å and 0.35 Å, respectively. The phenyl and methyl substituents are oriented equatorially. The C5-N3-C2-C10 torsion angle is 138.3(4)° in **5d-A** and 138.6(4)° in **5d-B**; the C5-N4-C4-C9 torsion angle is -166.2(4)° in **5d-A** and -165.4(4)° in **5d-B**. The tetrahydropyrimidone ring adopts a twist-boat conformation; the puckering parameters are S = 0.59, Θ = 49.9°, and Ψ = 29.2° for **5d-A** and S = 0.60, Θ = 51.1°, and Ψ = 28.8° for **5d-B**. The N5 and C6 atoms deviate from the mean plane of the other atoms of the ring by 0.33 Å and 0.75 Å, respectively, in **5d-A** and by -0.34 Å and -0.76 Å, respectively, in **5d-B**.



Scheme 13. Resonance structures of the cation of compound **5d**.

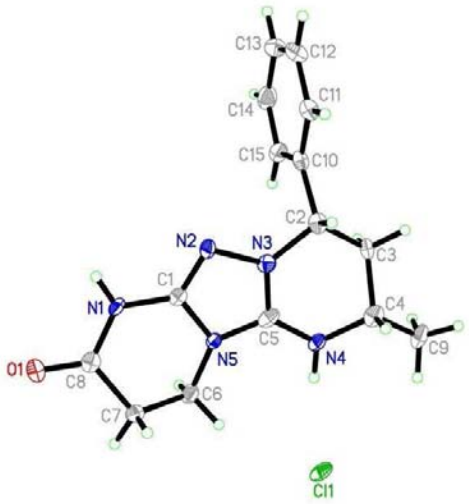


Figure 4. The molecular structure of compound **5d** according to X-ray diffraction data (only one of two crystallographically independent molecules is shown). Thermal ellipsoids are shown at the 50 % probability level.

The triazolopyrimidine fragment in mesoionic compound **14c** (Fig. 5) is planar within 0.02 Å. The absence of hydrogen atoms at N1 and N2 and equalization of the N1-C1 and N2-C1 bonds (1.336(2) Å and 1.334(2) Å, respectively, the mean value for the Csp^2=N(2) bond is 1.313 Å[14]) allows to assume localization of the negative charge within the –N1–C1–N2– fragment. The positive charge is apparently concentrated mainly within the –N4–C5–N5– region, based on the fact that the N4-C5 (1.308(2) Å) and N5-C5 (1.343(2) Å) bonds are shorter than their mean values (1.333 Å and 1.380 Å, respectively).[14] The tetrahydropyrimidone ring adopts a sofa conformation with puckering parameters of S = 0.32, Θ = 35.2°, and Ψ = 6.6°. The C6 atom deviates from the mean plane of the remaining atoms in the ring by 0.27 Å. Benzene rings at the C2 and C4 atoms are almost coplanar to the triazolopyrimidine fragment (the C3-C2-C15-C20 and C3-C4-C9-C10 torsion angles are 15.0(3)° and 10.5(3)°, respectively) resulting in the conjugation between their π-systems.

Figure 5. The molecular structure of compound **14c** according to X-ray diffraction data. Thermal ellipsoids are shown at the 50 % probability level.

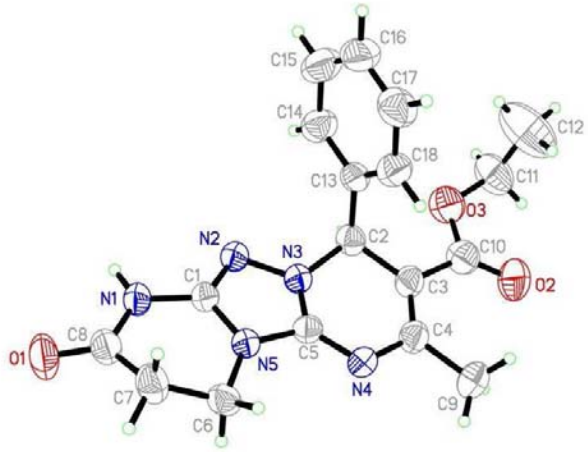


Figure 6. The molecular structure of compound **15a** according to X-ray diffraction data (only one of two crystallographically independent molecules is shown). Thermal ellipsoids are shown at the 50 % probability level.

The asymmetric part of crystal unit cell of compound **15d** contains two molecules (**15a-A** and **15a-B**) differing by conformation of partially saturated rings in the tricyclic fragment. The dihydropyrimidine ring adopts an intermediate conformation between a sofa and a twist-boat in **15a-A** and exhibits a sofa conformation in **15a-B**. The puckering parameters are S = 0.31, Θ = 51.9°, and Ψ = 25.9° in **15a-A** and S = 0.36, Θ = 48.0°, and Ψ = 6.1° in **15a-B**. The C2 and C3 atoms in **15a-A** deviate from the mean plane of the remaining atoms of the ring by 0.40 Å and 0.17 Å, and the C2 atom in **15a-B** shows a deviation of 0.36 Å. An opposite result is observed in the tetrahydropyrimidone ring, which adopts a sofa conformation in **15a-A** (the puckering parameters are S = 0.52, Θ = 42.2°, and Ψ = 1.4° and the C7 atom deviates from the plane by 0.48 Å). In **15a-B** the tetrahydropyrimidone ring adopts an intermediate conformation between a sofa and a twist-boat conformation. The puckering parameters are S = 0.56, Θ = 42.1°, and Ψ = 24.5°, and the C7 and C8 atoms deviate from the plane by -0.63 Å and -0.23 Å,

respectively. The phenyl substituent is almost orthogonal to the dihydropyrimidine ring; the C5-N3-C2-C13 torsion angle is -99.5(3)° in **15a-A** and 95.9(3)° in **15a-B**. The carbonyl functionality of the C3 substituent is coplanar with the endocyclic C3-C4 double bond. The C4-C3-C10-O2 torsion angle is 1.6(5)° in **15a-A** and -8.7(5)° in **15a-B**.

3. Conclusion

In summary, we have demonstrated the applicability of partially hydrogenated 2-amino[1,2,4]triazolo[1,5-*a*]pyrimidines and 2-amino[1,2,4]triazolo[5,1-*b*]quinazolines as novel 1,3-*N*,*N*□-binucleophilic reagents for the synthesis of polycondensed heterocycles. This utility is exemplified by their reactions with chlorocarboxylic acid chlorides. The ability of acylamino derivatives formed in the first stage of the reaction to cyclize is determined primarily by the nature of the chlorocarboxylic acid. All attempts to cyclize chloroacetyl derivatives failed. The 4-chlorobutanoyl derivative did not cyclize upon heating but underwent intramolecular alkylation at the amide nitrogen to form a pyrrolidin-2-one ring. Upon heating to 80-90 °C, only 3-chloropropanoyl derivatives could be converted to polycondensed heterocycles, yielding chlorides of [1,2,4]triazolo[1,5-*a*:4,3-*a*']dipyrimidin-5-ones or decahydropyrimido[2',1':3,4][1,2,4]triazolo[5,1-*b*]quinazolin-12-ones. In most cases, the chlorides of polycondensed heterocycles could be synthesized in a one-pot process starting from the partially hydrogenated aminoheterocycles. Most of the obtained chlorides of polycondensed heterocycles form free bases in alkaline media at room temperature. Some of these compounds exhibit mesoionic structures. Heating the polycondensed compounds to reflux in aqueous sodium carbonate or in the presence of equimolar amounts of potassium hydroxide in ethanol results in cleavage of the dihydropyrimidone ring and formation of 3-heterosubstituted propionic acids. Triazolodipyrimidines containing the 4,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidine motif that are unsubstituted at the position 3 of tricyclic core are unstable in solution. Such compounds undergo oxidative aromatization and hydrolysis of the dihydropyrimidine ring. Preparative methods have been developed to facilitate the selective oxidative aromatization or hydrolytic elimination of the dihypropyrimidine fragment of these compounds.

4. Experimental section

4.1. General

The melting points were determined in open capillary tubes in a Thiele apparatus and are uncorrected. IR spectra were recorded on a Varian 640-IR spectrometer using a single reflection diamond ATR system as a sampling accessory. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX 500 instrument at 500 MHz and 125 MHz, respectively, and a Bruker Avance 600 instrument at 600 MHz (150 MHz for ^{13}C) or Varian Unity 300 at 300 MHz in DMSO-d_6 and using TMS as an internal standard for majority of the compounds synthesized. ^{13}C NMR spectra of compounds **3f**, **8g**, **9e,d**, **13d**, **14e,f**, **18** were recorded in CF_3COOH (TFA) with addition of 5% DMSO-d_6 or TFA-d_1 due to low solubility in DMSO. Mass spectra were recorded in the form of *m/z* (intensity relative to base 100) on a Finnigan MAT INCOS 50 instrument using electron impact ionization. Elemental analyses were performed using a Perkin-Elmer 2400 Elemental Analyzer. The pK_a values of compounds **13a**, **23**, **15a** and **25** were determined by potentiometric titration in 80% ethanol using a Mettler Toledo S40-KS instrument equipped with an InLab®Expert Pro combined electrode. All GC-MS measurements were carried out with an Agilent 7890A GC system, equipped with an Agilent 5975C mass-selective detector (electron impact, 70 eV) and a HP-5-MS column (30 m×0.25 mm × 0.25 μm film) using He as carrier gas at a flow of 1.0 mL/min. The following temperature program was used in all GC-MS measurements: initial temperature 65 °C, hold for 7 min, then 25 °C/min to 190 °C for 1 min, then 10 °C/min to 260 °C for 20 min, then 10 °C/min to 280 °C for 18 min. Retention times of compounds were: 16.9 min for **11c,** 18.07 min for **11d**, 19.6 min for **11e**, 20.3 min for **11f**.

Starting compounds **1a-d,g,**[3e] **1e,**[3f] **6a,**[8c] **6b,**[5c] **6c-f,**[5b] **6g**[5d] and **6h**[5g] were obtained by known methods. All other chemicals are commercially available.

4.2. Quantum-chemical calculations

All calculations were performed with the Gaussian 03 software[16] by using the hybrid Becke three-parameter Lee–Yang–Parr DFT B3LYP functional[17] and 6-311++G(2d,2p) basis set. Solvent effects were modeled by the IEF-PCM method.[18] Geometry optimizations were followed by a frequency calculations in order to prove that the stationary points obtained are true energy minima. The calculated energetic parameters and atomic coordinates of all found conformers of tautomers **13A-D** and **15A-D** are gathered in Supplementary material.

4.3. X-Ray diffraction study

X-Ray diffraction studies were performed on an automatic "Bruker APEX II" diffractometer for compound **5d** and «Xcalibur 3» diffractometer for **14c** and **15a** (graphite monochromated MoK_α radiation, CCD-detector, ω-scanning). The structure was solved by direct method using *SHELXTL* package.[19] The restrains for the bond lengths Csp^3-Csp^3 (1.54 Å) in the ethyl group were applied in the refinement of the structure **15a**. Positions of the hydrogen atoms were located from electron density difference maps and refined by "riding" model with U_{iso} = nU_{eq} of the carrier atom (n = 1.5 for methyl groups and n = 1.2 for other hydrogen atoms). The hydrogen atoms of the NH groups in **5d** and **15a** were refined in isotropic approximation. The crystallographic data and experimental parameters are presented in Supplementary Materials. Final atomic coordinates, geometrical parameters and crystallographic data have been deposited at the Cambridge Crystallographic Data Centre (CCDC), deposition numbers 811047 (compound **5d**), 957615 (compound **14c**), and 957616 (compound **15a**). These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (0044) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk).

4.4. 7-(4-Methoxyphenyl)-4-methyl-5-phenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-a]pyrimidin-2-amine (1f)

Sodium methoxide prepared from sodium (213 mg, 9.3 mmol) and MeOH (1.5 mL) was added to a magnetically stirred suspension of compound **1a** (3 g, 9.3 mmol) in DMSO (30 mL) and the resulted mixture was stirred at room temperature for 20 min, then cooled to 0-5 °C. Iodomethane (1.32 g, 9.3 mmol) was added drop by drop to the reaction mixture, which was then stirred for 1 h at 0-5 °C. Then further portions of sodium methoxide [180 mg (7.8 mmol) of sodium in 1.5 mL of MeOH] and iodomethane (1.11 g, 7.8 mmol) were added gradually to the reaction mixture at 0-5 °C and stirring. The reaction mixture was

stirred at the same temperature for 2 h and then diluted with water (90 mL). The precipitate formed was isolated by filtration and recrystallized from acetonitrile to give compound **1f** as colorless prisms (1.48 g, 52%), mp 207-208 °C. IR ν (cm^{-1}): 3467, 3290, 3147, 3035, 3010, 2955, 2916, 2873, 2836, 2796, 1620, 1580, 1544, 1512, 1478, 1455, 1407, 1365, 1346, 1325, 1301, 1244, 1203, 1175, 1111, 1037. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.25-2.35 (m, 2H, 6-CH_2), 2.65 s (s, 3H, CH_3), 3.75 (s, 3H, CH_3O), 4.39-4.43 (m, 1H, H-5), 4.95 (s, 2H, NH_2), 5.08 (dd, *J*=10.1, 4.8 Hz, 1H, H-7), 6.88 (d, *J*=8.4 Hz, 2H, Ar), 7.21 (d, *J*=8.4 Hz, 2H, Ar), 7.31-7.34 (m, 1H, Ph), 7.38-7.42 (m, 4H, Ph). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 36.3, 43.2, 56.0, 58.1, 61.9, 114.4, 128.0, 128.7, 129.2, 129.6, 133.2, 141.5, 157.4, 159.5, 161.7. MS (EI, 70 eV), *m*/*z* (%): 335 (89) $[M]^+$, 223 (74), 200 (100), 178 (6), 165 (7), 145 (18), 131 (13), 115 (37), 103 (9), 91 (21), 77 (18), 65 (7), 51 (7), 42 (29). Anal. Calcd for $C_{19}H_{21}N_5O$: C, 68.04; H, 6.31; N, 20.88. Found: C 68.33; H 6.21; N 21.07.

4.5. General procedure for the synthesis of compounds 2,3a,f,g, 4, 7a,c

A solution of the corresponding acid chloride (6.6 mmol) in acetonitrile (2 mL) was added drop by drop to a magnetically stirred mixture of compound **1a,f,g, 6a,c** (6.0 mmol), pyridine (0.574 g, 7.3 mmol) and acetonitrile (3 mL) at 0-5 °C. The reaction mixture was stirred at the same temperature for 30 min then diluted with water (5 mL). The precipitate formed was isolated by filtration and recrystallized from appropriate solvent.

*4.5.1. 2-Chloro-N-[7-(4-methoxyphenyl)-5-phenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl]acetamide (**2**)*

Yield 1.89 g (79%) of colorless needles, mp 278-279 °C (from $CHCl_3$/EtOH 1:2). IR ν (cm^{-1}): 3342, 3304, 3141, 3034, 2999, 2939, 2839, 1686, 1611, 1578, 1556, 1515, 1496, 1457, 1406, 1378, 1335, 1313, 1252, 1175. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 2.07-2.13 (m, 1H, 6-CH_2), 2.35-2.38 (m, 1H, 6-CH_2), 3.72 (s, 3H, CH_3O), 4.17 (br s, 2H, C$\underline{H}_2$CO), 4.68-4.70 (m, 1H, H-5), 5.27-5.29 (m, 1H, H-7), 6.88 (d, *J*=8.7 Hz, 2H, Ar), 7.18 (d, *J*=8.7 Hz, 2H, Ar), 7.27-7.30 (m, 1H, Ph), 7.34-7.37 (m, 2H, Ph), 7.44-7.46 (m, 2H, Ph), 7.49 (br s, 1H, NH), 10.38 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 42.1 (C-6), 43.0 ($\underline{C}H_2$CO), 53.8 (C-5), 55.1 (CH_3O), 58.1 (C-7), 113.7, 126.5, 127.6, 128.36, 128.39, 131.7, 141.6 (carbons of benzene rings), 152.6 (C-2), 154.7 (C-3a), 158.8 (C-4 of 4-$CH_3OC_6H_4$), 163.6 (CO). MS (EI, 70 eV), *m*/*z* (%): 397 (1) $[M]^+$, 321 (11), 223 (40), 186 (19), 134 (80), 119 (37), 115 (23), 91 (71), 77 (32), 65 (32), 50 (22), 43 (19), 36 (100). Anal. Calcd for $C_{20}H_{20}ClN_5O_2$: C, 60.38; H, 5.07; N, 17.60. Found: C, 60.52; H, 5.16; N, 17.31.

*4.5.2. 3-Chloro-N-[7-(4-methoxyphenyl)-5-phenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl]propanamide (**3a**)*

Yield 1.88 g (76%) of colorless prisms, mp 238-239 °C (from $CHCl_3$/EtOH 1:2). IR ν (cm^{-1}): 3286, 3138, 3032, 2930, 1671, 1615, 1578, 1562, 1516, 1496, 1457, 1420, 1401, 1313, 1299, 1281, 1259, 1175. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 2.07-2.13 (m, 1H, 6-CH_2), 2.34-2.37 (m, 1H, 6-CH_2), 2.70 (m, 2H, CH_2), 3.72 (s, 3H, CH_3O), 3.77 (t, *J*=6.3 Hz, 2H, CH_2), 4.67-4.69 (m, 1H, H-5), 5.26 (dd, *J*=10.9, 4.6 Hz, 1H, H-7), 6.88 (d, *J*=8.7 Hz, 2H, Ar), 7.17 (d, *J* = 8.7 Hz, 2H, Ar), 7.27-7.29 (m, 1H, Ph), 7.34-7.37 (m, 2H, Ph), 7.43 (br s, 1H, NH), 7.44-7.46 (m, 2H, Ph), 10.13 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 38.4 (CH_2), 40.4 (CH_2), 42.1 (C-6), 53.8 (C-5), 55.1 (CH_3O), 58.0 (C-7), 113.7, 126.5, 127.5, 128.3, 128.4, 131.8, 141.7 (carbons of benzene rings), 152.8 (C-2), 154.7 (C-3a), 158.7 (C-4 of 4-$CH_3OC_6H_4$), 166.9 (CO). MS (EI, 70 eV), *m*/*z* (%): 375 (10) $[M - HCl]^+$, 240 (60), 233 (24), 153 (16), 134 (88), 119 (21), 115 (15), 91 (45), 77 (19), 65 (22), 55 (38), 38 (70), 36 (100). Anal. Calcd for $C_{21}H_{22}ClN_5O_2$: C, 61.24; H, 5.38; N, 17.00. Found: C, 61.47; H, 5.44; N, 16.83.

*4.5.3. 3-Chloro-N-(7-(4-methoxyphenyl)-4-methyl-5-phenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)propanamide (**3f**)*

Yield 1.56 g (61%) of colorless needles, mp 211-212 °C (from AcOH/EtOH 1:3). IR ν (cm^{-1}): 3292, 3262, 3132, 3075, 3009, 2972, 2909, 2870, 2842, 1693, 1613, 1590, 1563, 1510, 1449, 1412, 1393, 1347, 1313, 1244, 1199, 1094, 1027. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.36-2.42 (m, 2H, 6-CH_2), 2.70 (s, 3H, CH_3), 2.71-2.77 (br m, 2H, CH_2CO), 3.75 (s, 3H, CH_3O), 3.80 (t, *J*=6.3 Hz, 2H, CH_2Cl), 4.52 (dd, *J*=9.8, 4.2 Hz, 1H, H-5), 5.27 (dd, *J*=9.7, 5.6 Hz, 1H, H-7), 6.91 (d, *J*=8.7 Hz, 2H, Ar), 7.23 (d, *J*=8.7 Hz, 2H, Ar), 7.33-7.40 (m, 1H, Ph), 7.43-7.45 (m, 4H, Ph), 10.26 (br s, 1H, NH). ^{13}C NMR (125 MHz, TFA + 5% DMSO-d_6) δ: 34.6, 36.6, 38.5, 39.6, 55.2, 59.9, 62.2, 115.3, 126.6, 127.1, 128.7, 129.2, 129.5, 134.4, 143.0, 148.0, 159.3, 172.9. MS (EI, 70 eV), *m*/*z* (%): 425 (37) $[M]^+$, 389 (13), 362 (2), 335 (38), 306 (5), 290 (15), 256 (48), 223 (100), 200 (45), 191 (5), 165 (8), 145 (23), 131 (19), 115 (41), 91 (29), 82 (18), 77 (16), 63 (20), 55 (20), 42 (13), 36 (19). Anal. Calcd for $C_{22}H_{24}ClN_5O_2$: C, 62.04; H, 5.68; N, 16.44. Found: C, 62.28; H, 5.71; N, 16.21.

*4.5.4. N-(4-Benzyl-7-(4-methoxyphenyl)-5-phenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)-3-chloropropanamide (**3g**)*

Yield 1.87 g (62%) of yellowish prisms, mp 165-167 °C (from EtOH). IR ν (cm^{-1}): 3288, 3252, 3120, 3054, 3005, 2962, 2837, 1692, 1613, 1561, 1497, 1452, 1429, 1367, 1336, 1316, 1298, 1253, 1224, 1173, 1224, 1173, 1140, 1034. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 2.34-2.37 (m, 1H, 6-CH_2), 2.42-2.47 (m, 1H, 6-CH_2), 2.73 (br s, 2H, CH_2CO), 3.71 (s, 3H, CH_3O), 3.77 (t, *J*=6.3 Hz, 2H, $ClCH_2$), 3.94 (d, 1H, *J*=15.6 Hz, PhC$\underline{H}_2$), 4.51-4.54 (m, 1H, H-5), 4.86 (d, *J*=15.6 Hz, 1H, PhC$\underline{H}_2$), 5.26 (dd, *J*=10.2, 4.5 Hz, 1H, H-7), 6.86 (d, *J*=8.7 Hz, 2H, Ar), 7.06 (m, 2H, Ar), 7.19 (d, *J*=8.7 Hz, 2H, Ar), 7.22-7.33 (m, 8H, Ar), 10.26 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 38.4 ($\underline{C}H_2$CO), 40.4 (Cl$\underline{C}H_2$), 41.4 (C-6), 50.0 (Ph$\underline{C}H_2$), 55.0 (CH_3O), 57.4 (C-7), 57.9 (C-5), 113.6, 127.1, 127.5, 127.7, 128.0, 128.2, 128.5, 128.6, 131.3, 136.9, 139.2 (carbons of benzne rings), 152.6 (C-2), 155.3 (C-3a), 158.7 (C-4 of 4-$CH_3OC_6H_4$), 166.8 (CO). MS (EI, 70 eV), *m*/*z* (%): 501 (1) $[M]^+$, 223 (26), 134 (20), 116 (16), 91 (100), 65 (16), 55 (25), 36 (41). Anal. Calcd for $C_{28}H_{28}ClN_5O_2$: C, 66.99; H, 5.62; N, 13.95. Found: C 66.90; H 5.78; N 13.71.

*4.5.5. 4-Chloro-N-[7-(4-methoxyphenyl)-5-phenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl]butanamide (**4**)*

Yield 2.12 g (83%) of colorless needles, mp 251-252 °C ($CHCl_3$/EtOH 1:2). IR ν (cm^{-1}): 3323, 3227, 3130, 3037, 2958, 2838, 1659, 1601, 1573, 1551, 1516, 1496, 1465, 1443, 1384, 1348, 1310, 1288, 1249, 1179. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.91-1.94 (m, 2H, CH_2), 2.09-2.12 (m, 1H, 6-CH_2), 2.34-2.41 (m, 3H, 1H of 6-CH_2 + CH_2 of 4-chlorobutanoyl), 3.60 (t, *J*=6.4 Hz, 2H, CH_2), 3.72 (s, 3H, CH_3O), 4.67-4.70 (m, 1H, H-5), 5.26 (dd, *J*=11.0, 4.6 Hz, 1H, H-7), 6.88 (d, 2H, *J*=8.3 Hz, Ar), 7.17 (d, *J*=8.3 Hz, 2H, Ar), 7.24-7.48 (m, 6H, Ph+NH), 10.01 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 27.7 (CH_2), 32.3 (CH_2),

42.1 (C-6), 44.8 (CH_2), 53.8 (C-5), 55.1 (CH_3O), 58.0 (C-7), 113.7, 126.5, 127.5, 128.36, 128.39, 131.8, 141.7 (carbons of benzene rings), 152.9 (C-2), 154.6 (C-3a), 158.8 (C-4 of 4-$CH_3OC_6H_4$), 169.5 (CO). MS (EI, 70 eV), *m*/*z* (%): 425 (3) $[M]^+$, 389 (15), 254 (25), 223 (36), 134 (44), 119 (20), 117 (30), 115 (26), 91 (44), 77 (31), 65 (20), 55 (20), 41 (76), 36 (100). Anal. Calcd for $C_{22}H_{24}ClN_5O_2$: C, 62.04; H, 5.68; N, 16.44. Found: C, 62.31; H, 5.77; N, 16.32.

*4.5.6. Ethyl 2-[(3-chloropropanoyl)amino]-5-methyl-7-phenyl-4,7-dihydro[1,2,4]triazolo[1,5-a]pyrimidine-6-carboxylate (**7a**)*

Yield 1.61 (69%) of colorless prisms, mp 245-246 °C (from EtOH). IR *ν* (cm^{-1}): 3300, 3268, 3225, 3147, 2930, 2823, 1702, 1650, 1597, 1552, 1512, 1412, 1332, 1309, 1270, 1231, 1187, 1161, 1110, 1073, 1019. ^{1}H NMR (600 MHz, DMSO-d_6) *δ*: 1.03 (t, *J*=6.9 Hz, 3H, C<u>H</u>$_3$CH$_2$O), 2.40 (s, 3H, Me), 274 (br s, 2H, ClCH$_2$C<u>H</u>$_2$CO), 3.77 (t, *J*=5.9 Hz, 2H, ClC<u>H</u>$_2$CH$_2$CO), 3.90-3.99 (m, 2H, OC<u>H</u>$_2$CH$_3$), 6.16 (s, 1H, H-7), 7.21-7.31 (m, 5H, Ph), 10.37 (br s, 1H, NH), 10.78 (s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) *δ*: 13.8 (<u>C</u>H$_3$CH$_2$O), 18.3 (CH$_3$), 38.4 (ClCH$_2$<u>C</u>H$_2$CO), 40.3 (Cl<u>C</u>H$_2$CH$_2$CO), 59.2 (C-7), 59.3 (CH$_3$<u>C</u>H$_2$O), 97.7 (C-6), 127.0, 127.8, 128.3, 142.1 (carbons of benzene ring), 146.1 (C-3a), 146.2 (C-5), 154.3 (C-2), 165.0 (<u>C</u>OOEt), 166.9 (ClCH$_2$CH$_2$<u>C</u>O). MS (EI, 70 eV), *m*/*z* (%): 389 (10) $[M]^+$, 353 (10), 326 (27), 312 (34), 276 (51), 248 (21), 222 (47), 194 (47), 155 (14), 128 (34), 115 (12), 91 (15), 77 (27), 63 (46), 55 (49), 36 (100). Anal. Calcd for $C_{18}H_{20}ClN_5O_3$: C, 55.46; H, 5.17; N, 17.96. Found: C, 55.75; H, 5.08; N, 17.81.

*4.5.7. 3-Chloro-N-(5,7-diphenyl-4,7-dihydro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)propanamide (**7c**)*

Yield 1.60 g (70%) of colorless prisms, mp °C ($CHCl_3$/EtOH 1:3). IR *ν* (cm^{-1}): 3284, 3157, 3061, 3030, 2924, 2855, 1665, 1604, 1587, 1561, 1449, 1406, 1340, 1318, 1295, 1221, 1069, 1029, 1001. ^{1}H NMR (300 MHz, DMSO-d_6) *δ*: 2.73 (br s, 2H, CH$_2$), 3.78 (t, *J*=6.3 Hz, 2H, ClCH$_2$), 5.20 (d, *J*=2.3 Hz, 1H, H-5), 6.11 (d, *J*=3.7 Hz, 1H, H-7), 7.27-7.41 (m, 8H, Ar), 7.58-7.61 (m, 2H, Ar), 10.04 (br s, 1H, NH), 10.36 (br s, 1H, NH). MS (EI, 70 eV), *m*/*z* (%): 379 (8) $[M]^+$, 343 (17), 302 (29), 289 (15), 266 (69), 219 (15), 212 (100), 191 (36), 129 (13), 115 (23), 104 (30), 91 (16), 77 (45), 63 (38), 55 (41), 36 (89). Anal. Calcd for $C_{20}H_{18}ClN_5O$: C, 63.24; H, 4.78; N, 18.44. Found: C, 63.48; H, 4.88; N, 18.12.

4.6. General procedure for the synthesis of compounds 5a-e, 8a,g,h

Method A. A solution of 3-chloropropanamide **3a,7a** (2.4 mmol) in DMF (2 mL) was heated at 80-90 °C and stirring for 1 h (4 h in case of compound **7a**), then cooled to 20 °C. The precipitate formed was isolated by filtration, washed with acetone and recrystallized.

Method B. A solution of 3-chloropropanoyl chloride (0.41 g, 3.3 mmol) in acetonitrile (1 mL) was added drop by drop to a magnetically stirred mixture of amine **1a-e, 6a,g,h** (3.0 mmol), pyridine (0.26 g, 3.3 mmol) and dry DMF (3 mL) at 20 °C. The resulted mixture was stirred at the same temperature for 15 min, then heated at 80-90 °C and stirring for 1 h (4 h at the synthesis of compounds **8a,8g,h**) and cooled to 20 °C. The precipitate formed was isolated by filtration, washed with acetone and recrystallized.

*4.6.1. 4-(4-Methoxyphenyl)-8-oxo-2-phenyl-1,2,3,4,7,8,9,10-octahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride (**5a**)*

Yield 0.58 g (59%, *Method A*), 0.61 g (50%, *Method B*), colorless prisms, mp 276-278 °C (from MeOH). IR *ν* (cm^{-1}): 3206, 3038, 2947, 2582, 1711, 1665, 1632, 1614, 1557, 1516, 1484, 1452, 1422, 1376, 1325, 1291, 1251, 1184. ^{1}H NMR (600 MHz, DMSO-d_6) *δ*: 2.27-2.33 (m, 1H, 3-CH$_2$), 2.50-2.51 (m, 1H, 3-CH$_2$), 2.83-2.85 (m, 2H, м, 9-CH$_2$), 3.74 (s, 3H, MeO), 4.18-4.23 (m, 1H, 10-CH$_2$), 4.39-4.43 (m, 1H, 10-CH$_2$), 4.95-4.97 (m, 1H, H-2), 5.37 (dd, *J*=10.6, 4.0 Hz, 1H, H-4), 6.92 (d, *J*=8.5 Hz, 2H, Ar), 7.33–7.42 (m, 5H, Ar), 7.53 (d, *J* = 7.5 Hz, 2H, Ar), 10.12 (br s, 1H, NH), 11.80 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) *δ*: 28.8 (C-9), 38.1 (C-10), 39.5 (C-3), 53.9 (C-2), 55.2 (CH$_3$O), 58.7 (C-4), 113.9, 127.0, 128.2, 128.6, 128.7, 129.1, 139.0 (carbons of benzene rings), 144.5 (C-6a), 146.5 (C-11a), 159.5 (C-4 of 4-CH$_3$OC$_6$H$_4$), 166.6 (C-8). MS (EI, 70 eV), *m*/*z* (%): 376 (3) [M - Cl]$^+$, 375 (8) [M - HCl]$^+$, 315 (26), 272 (18), 240 (100), 134 (90), 119 (14), 91 (7), 55 (7). Anal. Calcd for $C_{21}H_{22}ClN_5O_2$: C, 61.24; H, 5.38; N, 17.00. Found: C, 61.51; H, 5.22; N, 16.73.

*4.6.2. 8-Oxo-2,4-diphenyl-1,2,3,4,7,8,9,10-octahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride hydrate (1:1:1) (**5b**)*

Yield 0.92 g (77%, *Method B*) of colorless prisms, mp 291-292 °C (from MeOH). IR *ν* (cm^{-1}): 3610, 3414, 3196, 3063, 2962, 2908, 2827, 2778, 1710, 1656, 1554, 1492, 1459, 1428, 1365, 1322, 1283, 1262, 1223, 1215, 1102, 1023. ^{1}H NMR (600 MHz, DMSO-d_6) *δ*: 2.27-2.33 (m, 1H, 3-CH$_2$), 2.55-2.57 (m, 1H, 3-CH$_2$), 2.84 (t, *J*=6.7 Hz, 2H, 9-CH$_2$), 4.20-4.22 (m, 1H, 10-CH$_2$), 4.37-4.39 (m, 1H, 10-CH$_2$), 4.97-4.99 (m, 1H, H-2), 5.43 (dd, *J*=10.5, 4.1 Hz, 1H, H-4), 7.31-7.41 (m, 8H, Ar), 7.52-7.53 (m, 2H, Ar), 10.1 (br s, 1H, NH), 11.81 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) *δ*: 28.8 (C-9), 38.1 (C-10), 39.5 (C-3) , 53.8 (C-2), 59.1 (C-4), 127.0, 127.7, 128.3, 128.4, 128.5, 128.6, 137.0, 138.9 (carbons of benzene rings), 144.5 (C-6a), 146.6 (C-11a), 166.5 (C-8). MS (EI, 70 eV), *m*/*z* (%): 346 (5) [M - Cl - H$_2$O]$^+$, 345 (22) [M - HCl - H$_2$O]$^+$, 240 (99), 115 (27), 104 (63), 77 (52), 55 (100), 36 (92). Anal. Calcd for $C_{20}H_{22}ClN_5O_2$: C, 60.07; H, 5.55; N, 17.51. Found: C, 60.31; H, 5.31; N, 17.78.

*4.6.3. 2-(4-Methylphenyl)-8-oxo-4-phenyl-1,2,3,4,7,8,9,10-octahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride (**5c**)*

Yield 0.75 g (63%, *Method B*) of colorless prisms, mp 282-284 °C (from EtOH). IR *ν* (cm^{-1}): 3057, 3001, 2935, 2887, 2818, 2766, 1703, 1684, 1651, 1558, 1496, 1450, 1375, 1340, 1292, 1258, 1220, 1185, 1096, 1025. ^{1}H NMR (600 MHz, DMSO-d_6) *δ*: 2.25-2.27 (m, 1H, 3-CH$_2$), 2.30 (s, 3H, CH$_3$), 2.51-2.53 (m, 1H, 3-CH$_2$), 2.84 (t, *J*=6.9 Hz, 2H, 9-CH$_2$), 4.16-4.19 (m, 1H, 10-CH$_2$), 4.31-4.33 (m, 1H, 10-CH$_2$), 4.90-4.92 (m, 1H, H-2), 5.40 (dd, *J*=10.7, 4.2 Hz, 1H, H-4), 7.22 (d, *J*=7.9 Hz, 2H, Ar), 7.32-7.41 (m, 7H, Ar), 10.93 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) *δ*: 20.7 (CH$_3$), 28.8 (C-9), 37.9 (C-10), 39.6 (C-3), 53.6 (C-2), 59.2 (C-4), 126.9, 127.7, 128.41, 128.45, 129.1, 135.9, 137.0, 137.7 (carbons of benzene rings), 144.5 (C-6a), 146.6 (C-11a), 166.5 (C-8). MS (EI, 70 eV), *m*/*z* (%): 360 (4) [M - HCl]$^+$, 254 (100), 104 (13), 55 (16), 36 (19). Anal. Calcd for $C_{21}H_{22}ClN_5O$: C, 63.71; H, 5.60; N, 17.69. Found: C, 64.01; H, 5.48; N, 17.47.

*4.6.4. 2-Methyl-8-oxo-4-phenyl-1,2,3,4,7,8,9,10-octahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride (**5d**)*

Yield 0.62 g (65%, *Method B*) of colorless needles, mp 289-290 °C (from MeOH). IR ν (cm^{-1}): 3125, 3030, 2964, 2933, 2870, 2754, 1697, 1672, 1639, 1560, 1494, 1458, 1439, 1400, 1380, 1333, 1321, 1262, 1223, 1207, 1158. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.33 (d, J=6.3 Hz, 3H, CH_3), 1.87-1.92 (m, 1H, 3-CH_2), 2.42-2.45 (m, 1H, 3-CH_2), 2.83 (t, J=6.9 Hz, 2H, 9-CH_2), 3.83-3.88 (m, 1H, H-2), 4.23- 4.27 (m, 1H, 10-CH_2), 4.41-4.44 (m, 1H, 10-CH_2), 5.25 (dd, J=11.0, 4.8 Hz, 1H, H-4), 7.33–7.40 (m, 5H, Ph), 10.40 (br s, 1H, NH), 11.71 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 19.4 (CH_3), 28.8 (C-9), 38.1 (C-10), 38.7 (C-3), 46.1 (C-2), 58.8 (C-4), 127.3, 128.3, 128.5, 137.6 (carbons of benzene ring), 144.3 (C-6a), 146.1 (C-11a), 166.5 (C-8). MS (EI, 70 eV), *m/z* (%): 284 (7) [M - Cl]$^+$, 283 (58) [M - HCl]$^+$, 269 (13), 268 (100), 179 (23), 138 (19), 115 (10). Anal. Calcd for $C_{15}H_{18}ClN_5O$: C, 56.34; H, 5.67; N, 21.90. Found: C, 56.48; H, 5.78; N, 21.62.

*4.6.5. 2'-Oxo-1',3',4',6',6a',7',8',9',10',10a'-decahydro-2'H-spiro[cyclohexane-1,11'-pyrimido[2',1':3,4][1,2,4]triazolo[5,1-b]quinazolin[12]ium] chloride (**5e**)*

Yield 0.60 g (59%, *Method B*) of colorless prisms, mp 302-304 °C (from EtOH). IR ν (cm^{-1}): 3132, 3053, 2940, 2890, 2769, 1705, 1676, 1638, 1551, 1494, 1442, 1386, 1364, 1331, 1292, 1263. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 0.96-1.03 (m 1H, CH), 1.24-1.77 (m, 14H, CH), 1.88-2.00 (m, 2H, CH), 2.18-2.26 (m, 2H, CH), 2.81-2.84 (m, 2H, 3-C□H_2), 3.94 (m, 1H, H-6a□), 4.21-4.30 (m, 2H, 4-C□H_2), 9.85 (br s, 1H, NH), 11.71 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 18.8, 19.8, 20.9, 21.1, 24.3, 24.3, 28.1, 28.6 (C-3□), 30.3, 34.5, 36.0, 37.8 (C-4□), 45.9 (C-6a□), 61.5, 144.1 (C-13a□), 144.2 (C-5a□), 166.4 (C-2□). MS (EI, 70 eV), *m/z* (%): 316 (15) [M - Cl]$^+$, 315 (100) [M - HCl]$^+$, 286 (11), 272 (75), 260 (15), 244 (22), 233 (34), 217 (17), 192 (38), 153 (39), 138 (13), 83 (21), 67 (15), 55 (39). Anal. Calcd for $C_{17}H_{26}ClN_5O$: C, 58.03; H, 7.45; N, 19.90. Found: C, 58.34; H, 7.53; N, 19.68.

*4.6.6. 3-(Ethoxycarbonyl)-2-methyl-8-oxo-4-phenyl-1,4,7,8,9,10-hexahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride (**8a**)*

Yield 0.56 g (60%, *Method A*), 0.60 g (51%, *Method B*), colorless prisms, mp 301-302 °C (from EtOH). IR ν (cm^{-1}): 3066, 3028, 2958, 2908, 2769, 2717, 1716, 1663, 1580, 1496, 1475, 1454, 1373, 1322, 1275, 1258, 1232, 1186, 1149, 1103, 1076, 1021. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 0.99 (t, J=7.1 Hz, 3H, C$\underline{H}_3$CH$_2$O), 2.50 (s, 3H, CH_3), 2.83-2.86 (m, 2H, 9-CH_2), 3.91-4.00 (m, 2H, CH$_3$C$\underline{H}_2$O), 4.34-4.37 (m, 2H, 10-CH_2), 6.20 (s, 1H, H-4), 7.32-7.38 (m, 5H, Ph), 11.97 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 13.6 ($\underline{C}$H$_3$CH$_2$O), 18.2 (CH_3), 28.5 (C-9), 38.8 (C-10), 60.0 (2C, CH$_3\underline{C}$H$_2$O and C-4), 101.1 (C-3), 127.9, 128.5, 128.7, 139.6 (carbons of benzene ring), 146.2 (C-11a), 164.1 (C-2), 166.5 (2C, C-8 and $\underline{C}$OOEt). MS (EI, 70 eV), *m/z* (%): 353 (16) [M - HCl]$^+$, 324 (46), 277 (15), 276 (100), 248 (50), 55 (16). Anal. Calcd for $C_{18}H_{20}ClN_5O_3$: C, 55.46; H, 5.17; N, 17.96. Found: C, 55.57; H, 5.11; N, 17.76.

*4.6.7. 8,8-Dimethyl-2,10-dioxo-11-phenyl-1,2,3,4,6,7,8,9,10,11-decahydropyrimido[2',1':3,4][1,2,4]triazolo[5,1-b]quinazolin-12-ium chloride (**8g**)*

Yield 0.92 g (77%, *Method B*) of cream-colored prisms, mp 266-267 °C (from AcOH/EtOH 1:4). IR ν (cm^{-1}): 3075, 3016, 2965, 2881, 2820, 2774, 2647, 1733, 1717, 1668, 1656, 1588, 1492, 1462, 1439, 1367, 1335, 1281, 1249, 1222, 1139. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.03 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 2.18-2.28 (m, 2H, CH_2), 2.67-2.80 (m, 2H, CH_2), 2.88 (t, J=6.9 Hz, 2H, 3-CH_2), 4.42-4.44 (m, 2H, 4-CH_2), 6.18 (s, 1H, CH), 7.32-7.39 (m, 5H, Ph), 11.99 (br s, 1H, NH). ^{13}C NMR (125 MHz, TFA + 5% DMSO-d_6), δ: 25.4, 26.7, 27.9, 32.5, 39.3, 39.4, 48.7, 60.1, 109.9, 127.2, 128.9, 129.8, 135.9, 140.0, 145.5, 150.2, 169.3, 200.0. MS (EI, 70 eV), *m/z* (%): 363 (30) [M - HCl]$^+$, 286 (99), 232 (9), 115 (7), 77 (13), 55 (64), 36 (100). Anal. Calcd for $C_{20}H_{22}ClN_5O_2$: C 60.07; H 5.55; N, 17.51. Found: C, 60.29; H, 5.63; N, 17.30.

*4.6.8. 2'-Oxo-1',3',4',6',7',8',9',10'-octahydro-2'H-spiro[cyclohexane-1,11'-pyrimido[2',1':3,4][1,2,4]triazolo[5,1-b]quinazolin[12]ium] chloride (**8h**)*

Yield 0.66 g (63%, *Method B*) of colorless prisms, mp 277-278 °C (from EtOH). IR ν (cm^{-1}): 3123, 2981, 2939, 2868, 2760, 1703, 1679, 1628, 1559, 1496, 1448, 1386, 1368, 1336, 1313, 1292, 1262, 1223, 1158, 1046, 1011. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.10-2.28 (m, 18H), 2.84 (t, J=6.7 Hz, 2H, 3-CH_2), 4.21 (t, J=6.7 Hz, 2H, 4-CH_2), 11.30 (br s, 1H, NH), 11.96 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 21.2, 21.6, 22.4, 23.5, 23.8, 25.6, 28.6 (C-3□), 33.6, 38.1 (C-4□), 62.7 (C-11□), 111.4 (C-10a□), 126.2 (C-6a□), 141.1, 144.5 (carbons of triazole ring), 166.6 (C-2□). MS (EI, 70 eV), *m/z* (%): 313 (67) [M - HCl]$^+$, 270 (100), 257 (34), 242 (8), 202 (6), 55 (9). Anal. Calcd for $C_{17}H_{24}ClN_5O$: C, 58.36; H, 6.91; N, 20.02. Found: C, 58.56; H, 7.05; N, 20.21.

4.7. General procedure for the synthesis of compounds 8b-f

Method A. A solution of 3-chloropropanoyl chloride (0.41 g, 3.3 mmol) in acetonitrile (1 mL) was added drop by drop to a magnetically stirred mixture of amine **6b-f** (3.0 mmol), pyridine (0.26 g, 3.3 mmol) and dry DMF (2 mL) at 0-5 °C. The resulted mixture was stirred at the same temperature for 15 min, then heated rapidly up to 88-90 °C and stirred at the same temperature for 3-5 min, then cooled to 0-5 °C and diluted with cold acetone (5 mL). The precipitate formed was isolated by filtration, washed with acetone and dried at room temperature. All attempts of crystallization of the substances **8b-f** from various solvents led to their partial destruction and contamination by compounds **9**.

Method B. A solution of 3-chloropropanamide **7c** (3.0 mmol) in DMF (3 mL) was heated rapidly up to 88-90 °C and stirred at the same temperature for 3 min, then cooled to 0-5 °C and diluted with cold acetone (5 mL). The precipitate of compound **8c** was isolated by filtration, washed with acetone and dried at room temperature.

*4.7.1. 2-Methyl-8-oxo-4-phenyl-1,4,7,8,9,10-hexahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride (**8b**)*

Yield 0.18 g (19%, *Method A*) of colorless prisms, mp 278-280 °C. IR ν (cm^{-1}): 3085, 3023, 2893, 2732, 1700, 1661, 1634, 1573, 1497, 1458, 1373, 1319, 1285, 1257, 1226, 1133, 1029. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.00 (s, 3H, CH_3), 2.84 (t, J=6.7 Hz, 2H, 9-CH_2,), 4.28-4.33 (m, 2H, 10-CH_2), 4.95 (d, J=1.3 Hz, 1H, H-3), 6.00 (d, J=1.3 Hz, 1H, H-4), 7.25-7.40 (m, 5H, Ph), 11.94 (br s, 2H, 2NH). MS (EI, 70 eV), *m/z* (%): 281 (9) [M -

HCl]$^+$, 204 (100), 150 (21), 128 (6), 77 (9), 55 (21), 36 (16). Anal. Calcd for $C_{15}H_{16}ClN_5O$: C, 56.69; H, 5.08; N, 22.04. Found: C, 57.11; H, 4.95; N, 22.40.

*4.7.2. 8-Oxo-2,4-diphenyl-1,4,7,8,9,10-hexahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride (**8c**)*

Yield 0.26 g (23%, *Method A*), 0.32 g (28%, *Method B*), colorless needles, mp 283-285 °C. IR ν (cm^{-1}): 3178, 3048, 2994, 2906, 2865, 2711, 1712, 1656, 1622, 1487, 1457, 1374, 1325, 1285, 1254, 1223, 1157, 1108, 1074, 1028. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.88 (t, J=7.3 Hz, 2H, 9-CH$_2$), 4.38-4.42 (m, 2H, 10-CH$_2$), 5.58 (d, J=3.5 Hz, 1H, H-3), 6.21 (d, J=3.5 Hz, 1H, H-4), 7.25-7.60 (m, 10H, Ar), 11.81 (br s, 1H, NH), 12.04 (br s, 1H, NH). MS (EI, 70 eV), m/z (%): 343 (8) [M - HCl]$^+$, 266 (72), 212 (11), 207 (27), 131 (13), 105 (13), 103 (19), 77 (68), 73 (25), 55 (34), 51 (34), 44 (49), 42 (28), 36 (100). Anal. Calcd for $C_{20}H_{18}ClN_5O$: C, 63.24; H, 4.78; N, 18.44. Found: C, 62.87; H, 5.09; N, 18.83.

*4.7.3. 2-(4-Methylphenyl)-8-oxo-4-phenyl-1,4,7,8,9,10-hexahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride (**8d**)*. Yield 0.27 г (23%, *Method A*) of colorless prisms, mp 233-235 °C. IR ν (cm^{-1}): 3143, 3061, 2986, 2942, 2906, 2874, 2746, 1720, 1651, 1614, 1572, 1489, 1458, 1376, 1354, 1322, 1282, 1255, 1200, 1086, 1024, 999. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.34 (s, 3H, CH$_3$), 2.88 (t, J=6.9 Hz, 2H, 9-CH$_2$), 4.19 (t, J=6.9 Hz, 2H, 10-CH$_2$), 5.50 (d, J=3.7 Hz, 1H, H-3), 6.21 (d, J=3.7 Hz, 1H, H-4), 7.28 (d, J=8.2 Hz, 2H, Ar), 7.37-7.48 (m, 5H, Ph), 7.55 (d, J=8.2 Hz, 2H, Ar), 11.75 (br s, 1H, NH), 12.00 (s, 1H, NH). MS (EI, 70 eV), m/z (%): 357 (7) [M - HCl]$^+$, 280 (64), 226 (15), 91 (7), 77 (12), 55 (25), 36 (100). Anal. Calcd for $C_{21}H_{20}ClN_5O$: C, 64.04; H, 5.12; N, 17.78. Found: C, 64.31; H, 4.97; N, 17.49.

*4.7.4. 4-(4-Methoxyphenyl)-8-oxo-2-phenyl-1,4,7,8,9,10-hexahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride (**8e**)*

Yield 0.12 г (10%, *Method A*) of colorless needles, mp 255-257 °C. IR ν (cm^{-1}): 3181, 3006, 2865, 1713, 1651, 1617, 1659, 1514, 1487, 1445, 1377, 1320, 1284, 1246, 1182, 1113, 1068, 1025. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.87 (t, J=6.9 Hz, 2H, 9-CH$_2$), 3.75 (s, 3H, OMe), 4.39 (t, J=6.9 Hz, 2H, 10-CH$_2$), 5.51 (d, J=3.6 Hz, 1H, H-3), 6.17 (d, J=3.6 Hz, 1H, H-4), 6.98 (d, J=8.7 Hz, 2H, Ar), 7.40 (d, J=8.7 Hz, 2H, Ar), 7.48-7.50 (m, 3H, Ar), 7.64-7.67 (m, 2H, Ar), 11.76 (br s, 1H, NH), 12.01 (br s, 1H, NH). MS (EI, 70 eV), m/z (%): 373 (5) [M - HCl]$^+$, 266 (38), 240 (14), 134 (20), 77 (34), 55 (37), 44 (20), 38 (34), 36 (100). Anal. Calcd for $C_{21}H_{20}ClN_5O_2$: C, 61.54; H, 4.92; N, 17.09. Found: C, 61.07; H, 5.18; N, 16.72.

*4.7.5. 2,4-Bis(4-chlorophenyl)-8-oxo-1,4,7,8,9,10-hexahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride (**8f**)*

Yield 0.36 г (27%, *Method A*) of yellowish prisms, mp 279-282 °C. IR ν (cm^{-1}): 3054, 2874, 2757, 1708, 1676, 1658, 1621, 1570, 1490, 1402, 1378, 1288, 1260, 1025, 1091, 1063, 1012. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.87 (t, J=6.7 Hz, 2H, 9-CH$_2$), 4.35-4.41 (m, 2H, 10-CH$_2$), 5.57 (d, J=3.3 Hz, 1H, H-3), 6.26 (d, J=3.3 Hz, 1H, H-4), 7.51-7.70 (m, 8H, Ar), 11.87 (br s, 1H, NH), 12.03 (br s, 1H, NH). MS (EI, 70 eV), m/z (%): 413 (4) [M - HCl]$^+$, 409 (20), 382 (15), 380 (15), 357 (37), 355 (64), 340 (17), 302 (16), 55 (78), 44 (48), 36 (100). Anal. Calcd for $C_{20}H_{16}Cl_3N_5O$: C, 53.70; H, 3.63; N, 15.28. Found: C, 53.53; H, 3.59; N, 15.61.

4.8. General procedure for the synthesis of compounds 9c-f

A solution of 3-chloropropanoyl chloride (0.41 g, 3.3 mmol) in acetonitrile (1 mL) was added drop by drop to a magnetically stirred mixture of amine **6c-f** (3.0 mmol), pyridine (0.26 g, 3.3 mmol) and dry DMF (3 mL) at 0-5 °C. The resulted mixture was stirred at the same temperature for 15 min, then heated at 80-90 °C and stirring for 8 h, cooled to 0-5 °C and diluted with cold acetone (5 mL). The precipitate formed was isolated by filtration, washed successively with acetone, water, again acetone then recrystallized from DMF/EtOH 1:4.

*4.8.1. 8-Oxo-2,4-diphenyl-7,8,9,10-tetrahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride (**9c**)*

Yield 0.24 g (21%) of cream-colored prisms, mp 275-276 °C. IR ν (cm^{-1}): 3126, 3047, 3024, 2948, 2890, 2832, 2770, 2527, 1709, 1633, 1607, 1596, 1555, 1520, 1497, 1413, 1378, 1372, 1354, 1331, 1288, 1274, 1258, 1249, 1225, 1196, 1183, 1162, 1103, 1075, 1043, 1020, 1000. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 3.09 (t, J=7.1 Hz, 2H, 9-CH$_2$), 4.65 (t, J=7.1 Hz, 2H, 10-CH$_2$), 7.67-7.79 (m, 6H, Ar), 8.23-8.24 (m, 2H, Ar), 8.55-8.56 (m, 2H, Ar), 8.67 (s, 1H, H-3), 12.88 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 28.6 (C-9), 37.8 (C-10), 110.9 (C-3), 127.6, 128.6, 128.9, 129.4, 130.2, 133.0, 133.3, 133.8 (carbons of benzene rings), 146.1 (C-6a), 149.7 (C-4), 151.9 (C-11a), 163.6 (C-2), 166.9 (C-8). MS (EI, 70 eV), m/z (%): 341 (51) [M - HCl]$^+$, 313 (98), 285 (84), 272 (41), 232 (40), 218 (11), 204 (19), 189 (59), 165 (14), 129 (35), 115 (15), 102 (28), 77 (77), 55 (100), 44 (21), 36 (55). Anal. Calcd for $C_{20}H_{16}ClN_5O$: C, 63.58; H, 4.27; N, 18.54. Found: C, 63.77; H, 4.34; N, 18.28.

*4.8.2. 2-(4-Methylphenyl)-8-oxo-4-phenyl-7,8,9,10-tetrahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride (**9d**)*

Yield 0.29 g (25%) of colorless prisms, mp 261-263 °C. IR ν (cm^{-1}): 3055, 2887, 2781, 2725, 2695, 1723, 1636, 1604, 1560, 1524, 1449, 1404, 1379, 1354, 1287, 1253, 1227, 1195, 1159, 1129, 1085, 1039, 1013. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.47 (s, 3H, CH$_3$), 3.10 (t, J = 6.5 Hz, 2H, 9-CH$_2$), 4.66 (t, J = 6.5 Hz, 2H, 10-CH$_2$), 7.51-7.52 (m, 2H, Ar), 7.76-7.80 (m, 3H, Ar), 8.23-8.25 (m, 2H, Ar), 8.48-8.50 (m, 2H, Ar), 8.65 s (1H, H-3), 12.89 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6), δ: 21.6, 29.1, 38.2, 111.0, 128.1, 129.0, 129.3, 130.5, 130.6, 131.5, 133.3, 144.5, 146.5, 149.9, 152.2, 163.9, 167.3. MS (EI, 70 eV), m/z (%): 355 (55) [M - HCl]$^+$, 327 (34), 301 (14), 286 (11), 246 (6), 55 (11), 36 (100). Anal. Calcd for $C_{21}H_{18}ClN_5O$: C, 64.37; H, 4.63; N, 17.87. Found: C, 64.29; H, 4.78; N, 17.69.

*4.8.3. 4-(4-Methoxyphenyl)-8-oxo-2-phenyl-7,8,9,10-tetrahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride (**9e**)*

Yield 0.39 g (32%) of colorless prisms, mp 268-269 °C. IR ν (cm^{-1}): 3118, 3054, 3005, 2941, 2882, 2846, 2608, 1717, 1638, 1613, 1599, 1556, 1512, 1412, 1382, 1355, 1307, 1275, 1250, 1183, 1025. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 3.08 (t, J=6.9 Hz, 2H, 9-CH$_2$), 3.96 (s, 3H, OCH$_3$), 4.64 (t, J=6.9 Hz, 2H, 10-CH$_2$), 7.32 (d, J=8.7 Hz, 2H, Ar), 7.71-7.75 (m, 3H, Ar), 8.37 (d, J=8.7 Hz, 2H, Ar), 8.55-8.57 (m, 2H, Ar), 8.63 (s, 1H, H-3), 12.87 (br s, 1H, NH). ^{13}C NMR (125 MHz, TFA-d_1) δ: 18.8, 28.2, 45.4, 100.6, 105.5, 109.9, 118.7, 119.9, 122.5, 123.7, 124.7, 136.8, 140.6, 141.9, 154.4, 157.7, 160.6. MS (EI, 70 eV), m/z (%): 371 (32) [M - HCl]$^+$, 343 (63), 317 (30), 302 (30), 287 (12), 262 (18),

232 (11), 129 (10), 77 (26), 55 (71), 36 (100). Anal. Calcd for $C_{21}H_{18}ClN_5O_2$: C, 61.84; H, 4.45; N, 17.17. Found: C, 61.98; H, 4.56; N, 17.06.

*4.8.4. 2,4-Bis(4-chlorophenyl)-8-oxo-7,8,9,10-tetrahydro[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium chloride (**9f**)*

Yield 0.36 g (27%) of colorless prisms, mp 281-282 °C. IR *v* (cm^{-1}): 3095, 3058, 3022, 2963, 2864, 2565, 1714, 1637, 1611, 1591, 1561, 1523, 1492, 1401, 1369, 1281, 1253, 1228, 1193, 1093, 1009. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 3.05 (t, *J* = 7.0 Hz, 2H, 9-CH_2), 4.68 (t, *J*=7.0 Hz, 2H, 10-CH_2,), 7.76 (d, *J*=7.1 Hz, 2H, Ar), 7.82 (d, *J*=7.1 Hz, 2H, Ar), 8.29 (d, *J*=7.1 Hz, 2H, Ar), 8.60 (d, *J*=7.1 Hz, 2H, Ar), 8.78 (s, 1H, H-3), 13.1 (br s, 1H, NH). ^{13}C NMR (125 MHz, TFA + 5% DMSO-d_6) δ: 28.1, 37.6, 110.5, 124.5, 129.3, 129.4, 129.6, 130.6, 131.3, 141.0, 141.4, 146.0, 150.2, 150.7, 166.1, 169.7. MS (EI, 70 eV), *m*/*z* (%): 410 (0.4) $[M - HCl]^+$, 381 (4), 355 (4), 286 (7), 79 (100), 52 (78), 36 (27). Anal. Calcd for $C_{20}H_{14}Cl_3N_5O$: C, 53.77; H, 3.16; N, 15.68. Found: C, 53.98; H, 3.25; N, 15.32.

4.9. Hydrochloride of 3-amino-5,6-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-7(8*H*)-one (10)

A mixture of compound **8c** (0.5 g, 1.3 mmol), ethanol (5 mL) and concentrated hydrochloric acid (1 mL) was refluxed for 1 h, then evaporated in vacuo. The resulted residue was treated with hot acetonitrile (3 mL). After cooling to 20 °C the precipitate formed was filtered off and recrystallized from water-acetonitrile mixture (1:4) to give compound **10** as colorless prisms. Yield 123 mg (50%), mp 295-296 °C. IR *v* (cm^{-1}): 3467, 3307, 3089, 2918, 2789, 1727, 1705, 1676, 1609, 1553, 1469, 1385, 1305, 1077. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 2.79 (t, *J*=6.9 Hz, 2H, 6-CH_2), 4.13 (t, *J*=6.9 Hz, 2H, 5-CH_2), 8.62 (s, 2H, NH_2), 11.71 (br s, 1H, NH), 13.40 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 28.7 (C-6), 37.4 (C-5), 145.1 (C-8a), 148.4 (C-3), 166.8 (C-7). MS (EI, 70 eV), *m*/*z* (%): 153 (71) $[M - HCl]^+$, 99 (55), 69 (23), 55 (100), 43 (85), 36 (82). Anal. Calcd for $C_5H_8ClN_5O$: C, 31.67; H, 4.25; N, 36.94. Found: C, 31.89; H, 4.33; N, 36.61.

4.10. Synthesis of compounds 9c, 10 and 11

Method A. A magnetically stirred solution of compound **7c** (1.14 g, 3.0 mmol) in DMF (3 mL) was heated at 80-90 °C for 8 h. A precipitate of compound **10**, formed in hot solution, was isolated by filtration and dissolved in hot water (~ 8 mL). Resulted water solution of compound **10** was treated with charcoal (0.2 g), filtered, evaporated to a small volume (~ 0.5 mL), then diluted with acetonitrile (2 mL) and cooled to 0-5 °C. The formed precipitate was isolated by filtration and dried at 120 °C to give 0.097 g (yield 17%) of compound **10**. The reaction mixture after isolation of compound **10** was diluted with water (5 mL). The formed oily precipitate was isolated by filtration and crystallized from DMF-ethanol mixture (1:3) to give compound **9c** (0.36 g, yield 32%). A mother solution after crystallization of **9c** was evaporated to dryness at reduced pressure and the oily residue was diluted in chloroform (8 mL). The resulted solution was washed by water, then dried under sodium sulphate and subjected to a column chromatography (Al_2O_3, $CHCl_3$) to give 0.243 g (yield 39%) of (2*E*)-1,3-diphenylprop-2-en-1-one (**11**), mp 54-56 °C, lit.[20] mp 55-57 °C. GC-MS (EI, 70 eV), *m*/*z* (%): 207 (100) $[M]^+$, 179 (22), 165 (100), 131 (34), 103 (31), 89 (7), 77 (60), 51 (17).

Method B. A magnetically stirred solution of compound **8c** (1.14 g, 3.0 mmol) in DMF (3 mL) was heated at 80-90 °C for 8 h then treated by analogy with *method A* to give 0.39 g (yield 35%) of compound **9c**, 0.17 g (yield 30%) of compound **10** and 0.269 g (43%) of compound **11**.

4.11. 1-[7-(4-Methoxyphenyl)-5-phenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidin-2-yl]pyrrolidin-2-one (12)

A sodium methoxide prepared by dissolution of sodium (56 mg, 2.4 mmol) in MeOH (0.8 mL) was added to a magnetically stirred solution of compound **4** (1 g, 2.3 mmol) in DMF (4 mL). The resulted mixture was stirred at room temperature for 12 h, then neutralized by addition of a few drops of acetic acid and diluted with water (8 mL). The precipitate formed was isolated by filtration and recrystallized from DMF-ethanol mixture (1:3) to give compound **12** (0.58 g, yield 65%) as colorless prisms, mp 242-244 °C. IR *v* (cm^{-1}): 3290, 3061, 3035, 2992, 2960, 2911, 2889, 2836, 1713, 1609, 1584, 1538, 1514, 1483, 1453,1426, 1375, 1350, 1317, 1296, 1254, 1174, 1107, 1053, 1037. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.96-1.99 (m, 2H, CH_2), 2.03-2.09 (m, 1H, 6□-CH_2), 2.34-2.39 (m, 3H, 1H of 6□-CH_2 + CH_2 of pyrrolidin-2-one), 3.60-3.70 (m, 2H, CH_2), 3.72 (s, 3H, CH_3O), 4.68-4.69 (m, 1H, H-5□), 5.29 (dd, *J*=10.6, 4.5 Hz, 1H, H-7□), 6.88 (d, *J*=8.5 Hz, 2H, Ar), 7.15 (d, *J*=8.5 Hz, 2H, Ar), 7.27-7.44 (m, 5H, Ph), 7.52 (s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 17.8 (C-4), 31.7 (C-3), 42.4 (C-6□), 47.6 (C-5), 53.7 (C-5□), 55.1 (CH_3O), 58.1 (C-7□), 113.7, 126.5, 127.6, 128.3, 128.4, 131.8, 141.5 (carbons of benzene rings), 153.6 (C-2□), 154.9 (C-3a□), 158.7 (C-4 of 4-$CH_3OC_6H_4$), 172.4 (C-2). MS (EI, 70 eV), *m*/*z* (%): 389 (11) $[M]^+$, 254 (41), 223 (60), 200 (15), 145 (29), 134 (35), 131 (26), 117 (100), 104 (25), 91 (45), 77 (37), 69 (31), 55 (26), 41 (75). Anal. Calcd for $C_{22}H_{23}N_5O_2$: C, 67.85; H, 5.95; N, 17.98. Found: C, 68.02; H, 6.11; N, 17.63.

4.12. General procedure for the synthesis of compounds 13a-e, 15a,g,h

A suspension of finely ground compound **5a-e, 8a,g,h** (1 mmol) in 10% water solution of Na_2CO_3 (3 mL) was stirred at room temperature for 1 h. The precipitate formed was isolated by filtration, washed with water and recrystallized from ethanol.

*4.12.1. 4-(4-Methoxyphenyl)-8-oxo-2-phenyl-1,2,3,4,9,10-hexahydro-8H-[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium-7-ide (**13a**)*

Yield 0.33 g (86%) of colorless prisms, mp 211-212 °C. IR *v* (cm^{-1}): 3057, 3030, 2977, 2950, 2903, 2833, 1667, 1611, 1525, 1514, 1487, 1450, 1423, 1374, 1324, 1263, 1237, 1173, 1096, 1026. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.83-1.89 (m, 1H, 3-CH_2), 2.34-2.38 (m, 1H, 3-CH_2), 2.55-2.65 (m, 2H, 9-CH_2), 3.72 (s, 3H, CH_3O), 3.75-3.81 (m, 2H, 10-CH_2), 4.68 (dd, *J*=11.0, 2.4 Hz, 1H, H-2), 5.05 (dd, *J* = 10.7, 4.2 Hz, 1H, H-4), 6.87 (d, *J*=8.6 Hz, 2H, Ar), 7.19-7.23 (m, 3H, Ar), 7.30-7.32 (m, 2H, Ar), 7.44 (d, *J*=7.5 Hz, 2H, Ar). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 29.2 (C-9), 35.6 (C-10), 41.9 (C-3), 55.1 (CH_3O), 55.7 (C-2), 58.1 (C-4), 113.6, 126.6 (2C), 128.0, 128.6, 131.7, 144.3 (carbons of benzene rings), 145.6 (C-6a), 147.7 (C-11a), 158.8 (C-4 of 4-$CH_3OC_6H_4$), 168.4 (C-8). MS (EI, 70 eV), *m*/*z* (%): 375 (11) $[M]^+$, 241 (18), 134 (100), 119 (12), 91 (14). Anal. Calcd for $C_{21}H_{21}N_5O_2$: C, 67.18; H, 5.64; N, 18.65. Found: C, 67.36; H, 5.57; N, 18.41.

*4.12.2. 8-Oxo-2,4-diphenyl-1,2,3,4,9,10-hexahydro-8H-[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium-7-ide (**13b**)*

Yield 0.31 g (89%) of colorless needles, mp 219-220 °C. IR *v* (cm^{-1}): 3065, 2980, 2940, 2853, 1647, 1591, 1579, 1520, 1497, 1466, 1441, 1428, 1365, 1333, 1316, 1306, 1256, 1197, 1147, 1020. ^{1}H NMR (600 MHz, DMSO-d_6) *δ*: 1.80-1.86 (m, 1H, 3-CH_2), 2.38-2.42 (m, 1H, 3-CH_2), 2.51-2.61 (m, 2H, 9-CH_2), 3.72-3.80 (m, 2H, 10-CH_2), 4.68-4.69 (m, 1H, H-2), 5.08 (dd, *J*=10.6, 4.5 Hz, 1H, H-4), 7.19-7.32 (m, 8H, Ar), 7.42-7.44 (m, 2H, Ar). ^{13}C NMR (150 MHz, DMSO-d_6) *δ*: 29.2 (C-9), 35.6 (C-10), 42.1 (C-3), 55.7 (C-2), 58.5 (C-4), 126.58, 126.62, 127.3, 127.5, 128.0, 128.2, 140.1, 144.4 (carbons of benzene rings), 146.5 (C-6a), 148.0 (C-11a), 169.1 (C-8). MS (EI, 70 eV), *m*/*z* (%): 345 (22) $[M]^+$, 240 (99), 115 (27), 104 (63), 77 (52), 55 (10), 51 (32), 42 (18). Anal. Calcd for $C_{20}H_{19}N_5O$: C, 69.55; H, 5.54; N, 20.28. Found: C, 69.63; H, 5.65; N, 20.03.

*4.12.3. 2-(4-Methylphenyl)-8-oxo-4-phenyl-1,2,3,4,9,10-hexahydro-8H-[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium-7-ide (**13c**)*

Yield 0.32 g (88%) of colorless needles, mp 245-247 °C. IR *v* (cm^{-1}): 3058, 3028, 2976, 2953, 2908, 2577, 1663, 1601, 1519, 1483, 1457, 1410, 1370, 1333, 1309, 1295, 1257, 1197, 1175, 1153, 1095, 1021. ^{1}H NMR (600 MHz, DMSO-d_6) *δ*: 1.82-1.84 (m, 1H, 3-CH_2), 2.26 (s, 3H, CH_3), 2.37-2.39 (m, 1H, 3-CH_2), 2.59-2.61 (m, 2H, 9-CH_2), 3.74-3.81 (m, 2H, 10-CH_2), 4.63-4.65 (m, 1H, H-2), 5.08-5.09 (m, 1H, H-4), 7.11 (d, *J*=7.5 Hz, 2H, Ar), 7.26–7.32 (m, 7H, Ar). ^{13}C NMR (150 MHz, DMSO-d_6) *δ*: 20.6 (CH_3), 29.2 (C-9), 35.6 (C-10), 42.0 (C-3), 55.4 (C-2), 58.6 (C-4), 126.5, 127.3, 127.5, 128.2, 128.6, 135.6, 140.0, 141.3 (carbons of benzene rings), 147.7 (C-11a), 168.4 (C-8). MS (EI, 70 eV), *m*/*z* (%): 359 (29) $[M]^+$, 254 (100), 240 (15), 200 (20), 130 (10), 117 (10), 115 (16), 104 (34), 91 (21), 77 (22), 55 (48). Anal. Calcd for $C_{21}H_{21}N_5O$: C, 70.17; H, 5.89; N, 19.48. Found: C, 70.05; H, 5.95; N, 19.67.

*4.12.4. 2-Methyl-8-oxo-4-phenyl-1,2,3,4,9,10-hexahydro-8H-[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium-7-ide (**13d**)*

Yield 0.24 g (83%) of colorless needles, mp 223-224 °C. IR *v* (cm^{-1}): 3075, 3036, 2970, 2922, 2795, 2731, 1649, 1612, 1567, 1500, 1459, 1420, 1384, 1335, 1294, 1260, 1263, 1211, 1196, 1149, 1060. ^{1}H NMR (500 MHz, DMSO-d_6) *δ*: 1.18 (d, *J*=6.3 Hz, 3H, CH_3), 1.74 (m, 1H, 3-CH_2), 2.27 (m, 1H, 3-CH_2), 2.42 (m, 2H, 9-CH_2), 3.68 (m, 1H, H-2), 3.80 (t, *J*=7.0 Hz, 2H, 10-CH_2), 5.00 (dd, *J*=11.0, 4.8 Hz, 1H, H-4), 7.24–7.37 (m, 5H, Ph). ^{13}C NMR (125 MHz, TFA + 5% DMSO-d_6) *δ*: 18.1, 27.8, 37.4, 38.1, 47.8, 61.3, 126.8, 129.1, 129.9, 133.4, 143.7, 145.9, 169.5. MS (EI, 70 eV), *m*/*z* (%): 283 (50) $[M]^+$, 268 (100), 179 (53), 151 (18), 138 (51), 115 (24), 104 (33), 91 (23), 77 (27), 55 (99), 42 (25). Anal. Calcd for $C_{15}H_{17}N_5O$: C, 63.59; H, 6.05; N, 24.72. Found: C, 63.76; H, 6.13; N, 24.44.

*4.12.5. 2'-Oxo-3',4',6a',7',8',9',10',10a'-octahydro-2'H,6'H-spiro[cyclohexane-1,11'-pyrimido[2',1':3,4][1,2,4]triazolo[5,1-b]quinazolin[12]ium[1]ide] (**13e**)*

Yield 0.25 g (80%) of colorless prisms, mp 202-204 °C. IR *v* (cm^{-1}): 3219, 2932, 2859, 1658, 1583, 1519, 1513, 1445, 1365, 1328, 1256, 1198, 1104, 1060. ^{1}H NMR (300 MHz, DMSO-d_6) *δ*: 0.85-0.98 (m, 1H, CH), 1.22-2.17 (m, 16H), 2.26-2.35 (m, 2H), 2.41-2.48 (m, 2H, 3□-CH_2), 3.77 (t, *J*=7.2 Hz, 2H, 4□-CH_2), 3.82 (br s, 1H, H-6a□). ^{13}C NMR (150 MHz, DMSO-d_6) *δ*: 20.0, 21.1, 22.1, 22.3, 25.6, 25.7, 29.5, 30.1, 31.4, 35.8, 37.0, 38.2, 46.6, 60.8, 144.3 (C-5a□), 153.5 (C-13a□), 173.0 (C-2). MS (EI, 70 eV), *m*/*z* (%): 315 (62) $[M]^+$, 272 (29), 233 (13), 192 (14), 81 (19), 79 (17), 67 (28), 55 (100), 43 (21), 41 (82). Anal. Calcd for $C_{17}H_{25}N_5O$: C, 64.73; H, 7.99; N, 22.20. Found: C, 64.95; H, 8.15; N, 19.91.

*4.12.6. Ethyl 2-methyl-8-oxo-4-phenyl-7,8,9,10-tetrahydro-4H-[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidine-3-carboxylate (**15a**)*

Yield 0.279 g (79%) of colorless needles, mp 276-277 °C. IR *v* (cm^{-1}): 3158, 3074, 2985, 2933, 2900, 2764, 1713, 1686, 1641, 1603, 1531, 1504, 1457, 1372, 1335, 1272, 1222, 1191, 1149, 1107, 1076. ^{1}H NMR (300 MHz, DMSO-d_6) *δ*: 0.98 (t, *J*=7.0 Hz, 3H, CH_3), 2.33 (s, 3H, CH_3), 2.74 (t, *J*=7.0 Hz, 2H, CH_2), 3.84-3.94 (m, 4H, $2CH_2$), 6.04 (s, 1H, H-4), 7.22-7.29 (m, 5H, Ph), 11.50 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6) *δ*: 14.1 (CH_3), 24.4 (CH_3), 29.0 (CH_2), 35.9 (CH_2), 58.5 ($CH_3\underline{C}H_2O$), 60.1 (C-4), 96.9 (C-3), 127.2, 127.8, 128.2, 143.2 (carbons of benzene ring), 144.8 and 146.7 (C-6a and C-11a), 159.4 (C-2), 165.9 (CO), 167.0 (CO). MS (EI, 70 eV), *m*/*z* (%): 353 (16) $[M]^+$, 324 (46), 276 (100), 248 (50), 194 (6), 128 (4), 55 (16). Anal. Calcd for $C_{18}H_{19}N_5O_3$: C, 61.18; H, 5.42; N, 19.82. Found: C, 61.39; H, 5.51; N, 19.61.

*4.12.7. 8,8-Dimethyl-11-phenyl-3,4,7,11-tetrahydro-8H-pyrimido[2',1':3,4][1,2,4]triazolo[5,1-b]quinazoline-2,10(1H,9H)-dione (**15g**)*

Yield 0.327 g (90%) of yellowish needles, mp 288-289 °C. IR *v* (cm^{-1}): 3097, 3062, 2961, 2947, 2905, 2871, 2781, 1706, 1632, 1619, 1595, 1538, 1515, 1453, 1424, 1382, 1363, 1322, 1282, 1231, 1170, 1132, 1059, 1005. ^{1}H NMR (600 MHz, DMSO-d_6) *δ*: 0.95 (s, 3H, CH_3), 1.01 (s, 3H, CH_3), 2.00 (d, *J*=16.1 Hz, 1H, 9-CH_2), 2.12 (d, *J*=16.1 Hz, 1H, 9-CH_2), 2.38-2.45 (m, 2H, 7-CH_2), 2.77 (t, *J*=7.0 Hz, 2H, 3-CH_2), 3.94-4.03 (m, 2H, 4-CH_2), 6.04 (s, 1H, H-11), 7.19-7.28 (m, 5H, Ph), 11.53 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) *δ*: 27.2 (CH_3), 28.9 (CH_3), 28.9 (C-3), 32.0 (C-8), 36.0 (C-4), 45.5 (C-7), 50.2 (C-8), 58.6 (C-11), 106.3 (C-10a), 127.2, 127.5, 128.0, 142.4 (carbons of benzene ring), 144.8 (C-13a), 147.3 (C-5a), 162.8 (C-6a), 166.9 (C-2), 192.2 (C-10). MS (EI, 70 eV), *m*/*z* (%): 363 (28) $[M]^+$, 286 (100), 232 (13), 202 (9), 115 (9), 77 (18), 55 (69). Anal. Calcd for $C_{20}H_{21}N_5O_2$: C, 66.10; H, 5.82; N, 19.27. Found: C, 65.90; H, 5.65; N, 19.08.

*4.12.8. 3',4',7',8',9',10'-Hexahydrospiro[cyclohexane-1,11'-pyrimido[2',1':3,4][1,2,4]triazolo[5,1-b]quinazolin]-2'(1'H)-one (**15h**)*

Yield 0.213 g (68%) of colorless needles, mp 236-238 °C. IR *v* (cm^{-1}): 2975, 2928, 2858, 2839, 1685, 1605, 1534, 1483, 1449, 1363, 1337, 1316, 1279, 1255, 1232, 1216, 1202, 1186, 1168, 1143, 1120, 1109, 1067, 1007. ^{1}H NMR (600 MHz, DMSO-d_6), *δ*: 1.20-1.26 (m, 1H, CH), 1.47-1.59 (m, 7H), 1.73-1.79 (m, 4H), 1.94-2.06 (m, 6H), 2.69 (t, *J*=7.0 Hz, 2H, CH_2CO), 3.72 (t, *J*=7.0 Hz, 2H, NCH_2), 11.25 (br s, 1H, NH). ^{13}C NMR (150 MHz, DMSO-d_6) *δ*: 22.4, 22.7, 23.5, 24.4, 24.7, 29.3 (C-3□), 30.8, 34.2, 35.0 (C-4□), 60.3 (C-1,11□), 108.0 (C-10a□), 137.3 (C-6a□), 142.4 (C-13a□), 146.3 (C-5a□), 167.1 (CO). MS (EI, 70 eV), *m*/*z* (%): 313 (96) $[M]^+$, 284 (25), 270 (100), 257 (69), 202 (9), 55 (7). Anal. Calcd for $C_{17}H_{23}N_5O$: C, 65.15; H, 7.40; N, 22.35. Found: C, 64.87; H, 7.57; N, 22.07.

4.13. General procedure for the synthesis of compounds 14c-f

Method A. A suspension of finely ground compound **9c-f** (1 mmol) in 10% water solution of Na_2CO_3 (3 mL) was stirred at room temperature for 1 h. The precipitate formed was isolated by

filtration, washed with water and recrystallized from DMF-EtOH mixture (1:3).

Method B. A solution of KOH (0.073 g, 1.3 mmol) in water (1 mL) was added to a magnetically stirred suspension of finely ground compound **8c-f** (1 mmol) in ethanol (3 mL). The resulted mixture was stirred at room temperature for 1 h then diluted with water (5 mL). The precipitate formed was isolated by filtration, washed with water and twice recrystallized from DMF-EtOH mixture (1:3).

Method C. A magnetically stirred mixture of finely ground compound **8c-f** (1 mmol), I_2 (0.76 g, 3.0 mmol) and ethanol (4 mL) was refluxed for 20 min then cooled to room temperature. The precipitate formed was isolated by filtration and suspended in solution of $Na_2S_2O_3 \times 5H_2O$ (1.73 g, 5 mmol) and Na_2CO_3 (0.74 g, 7 mmol) in water (10 mL). The resulted mixture was magnetically stirred within 30 min and then was filtered out to give the solid compound **14c-f**, which was then washed with water and recrystallized from DMF-EtOH mixture (1:3).

*4.13.1. 8-Oxo-2,4-diphenyl-9,10-dihydro-8H-[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium-7-ide (**14c**)*

Yield 0.277 g (81%, *Method A*), 0.103 g (30%, *Method B*), 0.245 g (72%, *Method C*), light-yellow prisms, mp 232-233 °C. IR *ν* (cm^{-1}): 3066, 2986, 2931, 1623, 1600, 1579, 1553, 1523, 1491, 1451, 1424, 1375, 1322, 1292, 1253, 1224, 1193, 1159, 1143, 1104, 1015. ^{1}H NMR (600 MHz, DMSO-d_6) *δ*: 2.58 (t, *J*=7.4 Hz, 2H, 9-CH_2), 4.35 (t, *J*=7.4 Hz, 2H, 10-CH_2), 7.59-7.72 (m, 6H, Ar), 8.25 (s, 1H, H-3), 8.29-8.30 (m, 2H, Ar), 8.39-8.41 (m, 2H, Ar). ^{13}C NMR (150 MHz, DMSO-d_6) *δ*: 28.1 (C-9), 37.6 (C-10), 108.4 (C-3), 127.5, 128.3, 128.6, 128.9, 129.7, 131.7, 131.9, 134.6 (carbons of benzene rings), 146.1 (C-6a), 146.7 (C-2 or C-4), 159.1 (C-2 or C-4), 160.1 (C-11a), 174.0 (C-8). MS (EI, 70 eV), *m*/*z* (%): 341 (38) $[M]^+$, 313 (42), 287 (47), 272 (32), 232 (40), 189 (49), 165 (13), 129 (32), 102 (23), 77 (63), 55 (100), 51 (33), 44 (21). Anal. Calcd for $C_{20}H_{15}N_5O$: C, 70.37; H, 4.43; N, 20.52. Found: C, 70.56; H, 4.51; N, 20.37.

*4.13.2. 2-(4-Methylphenyl)-8-oxo-4-phenyl-1,2,3,4,9,10-hexahydro-8H-[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium-7-ide (**14d**)*

Yield 0.274 g (77%, *Method A*), 0.064 g (18%, *Method B*), 0.270 g (76%, *Method C*), yellow prisms, mp 240-242 °C. IR *ν* (cm^{-1}): 3063, 2917, 2858, 1645, 1624, 1568, 1520, 1496, 1467, 1375, 1336, 1262, 1185, 1168, 1090, 1014. ^{1}H NMR (300 MHz, DMSO-d_6) *δ*: 2.40 (s, 3H, CH_3), 2.53 (t, *J*=7.4 Hz, 2H, 9-CH_2), 4.32 (t, *J*=7.4 Hz, 2H, 10-CH_2), 7.41 (d, *J*=7.1 Hz, 2H, Ar), 7.64-7.70 (m, 3H, Ar), 8.25 (s, 1H, H-3), 8.27-8.34 (m, 4H, Ar). ^{13}C NMR (150 MHz, DMSO-d_6) *δ*: 20.5 (CH_3), 27.9 (C-9), 37.4 (C-10), 108.0 (C-3), 127.4, 128.1, 128.4, 129.3, 129.5, 131.6, 131.8, 142.0 (carbons of benzene rings), 145.9 (C-6a), 146.7 (C-2 or C-4), 159.3 (C-2 or C-4), 159.8 (C-11a), 173.3 (C-8). MS (EI, 70 eV), *m*/*z* (%): 355 (54) $[M]^+$, 327 (45), 301 (35), 286 (26), 246 (22), 202 (10), 77 (14), 55 (100), 44 (25). Anal. Calcd for $C_{21}H_{17}N_5O$: C, 70.97; H, 4.82; N, 19.71. Found: C, 70.65; H, 4.99; N, 19.51.

*4.13.3. 4-(4-Methoxyphenyl)-8-oxo-2-phenyl-9,10-dihydro-8H-[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium-7-ide (**14e**)*

Yield 0.29 g (77%, *Method A*), 0.086 г (23%, *Method B*), 0.230 g (62%, *Method C*), orange prisms, mp 241-242 °C. IR *ν* (cm^{-1}): 3116, 3077, 3062, 3008, 2969, 2933, 2837, 1640, 1619, 1600, 1546, 1510, 1493, 1472, 1446, 1381, 1331, 1299, 1247, 1184, 1162, 1148, 1124, 1093, 1023. ^{1}H NMR (500 MHz, DMSO-d_6) *δ*: 2.52 (t, *J*=7.0 Hz, 2H, 9-CH_2), 3.91 (s, 3H, CH_3O), 4.36 (t, *J*=7.0 Hz, 2H, 10-CH_2), 7.22 (d, *J*=8.2 Hz, 2H, Ar), 7.61-7.70 (m, 3H, Ar), 8.27 (s, 1H, H-3), 8.37-8.46 (m, 4H, Ar). ^{13}C NMR (125 MHz, TFA + 5% DMSO-d_6) *δ*: 28.1, 37.4, 54.8, 109.8, 114.7, 119.0, 128.0, 129.2, 131.7, 133.0, 133.9, 146.0, 149.9, 151.1, 163.7, 166.9, 169.9. MS (EI, 70 eV), *m*/*z* (%): 371 (47) $[M]^+$, 343 (54), 317 (35), 302 (30), 262 (19), 247 (5), 221 (6), 178 (11), 151 (6), 129 (9), 115 (5), 104 (7), 91 (14), 78 (42), 63 (61), 55 (100), 51 (11), 44 (55). Anal. Calcd for $C_{21}H_{17}N_5O_2$: C, 67.91; H, 4.61; N, 18.86. Found: C, 68.13; H, 4.70; N, 18.63.

*4.13.4. 2,4-Bis(4-chlorophenyl)-8-oxo-9,10-dihydro-8H-[1,2,4]triazolo[1,5-a:4,3-a']dipyrimidin-5-ium-7-ide (**14f**)*

Yield 0.324 g (79%, *Method A*), 0.082 g (20%, *Method B*), 0.261 g (64%, *Method C*), yellow prisms, mp 244-245 °C. IR *ν* (cm^{-1}): 3062, 2972, 2927, 1645, 1623, 1590, 1569, 1522, 1493, 1464, 1441, 1409, 1371, 1337, 1259, 1224, 1178, 1167, 1146, 1092, 1048, 1007. ^{1}H NMR (500 MHz, DMSO-d_6) *δ*: 2.56 (t, *J*=6.9 Hz, 2H, 9-CH_2), 4.38 (t, *J*=6.9 Hz, 2H, 10-CH_2), 7.65 (d, *J*=8.2 Hz, 2H, Ar), 7.80 (d, *J*=8.2 Hz, 2H, Ar), 8.38-8.41 (m, 3H, Ar), 8.45 (d, *J*=8.2 Hz, 2H, Ar). ^{13}C NMR (125 MHz, TFA + 5% DMSO-d_6) *δ*: 28.0, 37.6, 110.5, 124.5, 129.3, 129.4, 129.6, 130.6, 131.3, 141.1, 141.5, 146.0, 150.3, 150.8, 166.1, 169.7. MS (EI, 70 eV), *m*/*z* (%): 409 (1) $[M]^+$, 381 (6), 355 (14), 189 (10), 163 (12), 138 (10), 111 (17), 75 (24), 55 (100), 44 (22). Anal. Calcd for $C_{20}H_{13}Cl_2N_5O$: C, 58.55; H, 3.19; N, 17.07. Found: C, 58.78; H, 3.26; N, 17.11.

4.14. General procedure for the synthesis of compounds 1c, 6a, 6g and 16

A finely powdered compound **5c, 8a, 14d** or **15g** (0.5 mmol) was added to a magnetically stirred solution of KOH (0.28 g, 5 mmol) in ethanol (4 mL). The resulted mixture was refluxed for 24 h, then neutralized by addition of acetic acid to pH 8-9 and evaporated to dryness in vacuo. The residue was treated with water (6 mL) giving a precipitate, which was filtered off, washed with water and recrystallized from DMF-ethanol mixture (1:3).

*4.14.1. 5-(4-Methylphenyl)-7-phenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-a]pyrimidin-2-amine (**1c**).* Yield 0.119 g (78%) of colorless plates, mp 223-224 °C, lit.[3e] mp 223-224 °C. The product obtained was identical in both its physical and spectral characteristics with an authentic sample of compound **1c**.

*4.14.2. Ethyl 2-amino-5-methyl-7-phenyl-4,7-dihydro[1,2,4]triazolo[1,5-a]pyrimidine-6-carboxylate (**6a**).* Yield 0.081 g (54%) of colorless plates, mp 228-230 °C, lit.[8c] mp 228-230 °C. The product obtained was identical in both its physical and spectral characteristics with an authentic sample of compound **6a**.

*4.14.3. 2-Amino-6,6-dimethyl-9-phenyl-5,6,7,9-tetrahydro[1,2,4]triazolo[5,1-b]quinazolin-8(4H)-one (**6g**).* Yield 0.080 g (50%) of colorless plates, mp 253-255 °C, lit.[5d] mp 254-256 °C. The product obtained was identical in both its physical and spectral characteristics with an authentic sample of compound **6g**.

*4.14.4. 5-(4-Methylphenyl)-7-phenyl[1,2,4]triazolo[1,5-a]pyrimidin-2-amine (**16**).* Yield 0.111 g (74%) of yellowish plates, mp 219-220 °C, lit.[8a] mp 217-219 °C. The product

obtained was identical in both its physical and spectral characteristics with an authentic sample of compound **16**.

4.15. General procedure for the synthesis of compounds 17-20

Method A. A magnetically stirred mixture of finely powdered compound **5c, 8a** or **8g** (1 mmol), water (6 mL) and Na_2CO_3 (2 g, 18.9 mmol) was refluxed for 2 h. In case of the synthesis of compound **20** the reaction mixture was then cooled to room temperature and the precipitate formed was isolated by filtration, washed with cold water and recrystallized from ethanol. For the preparation of compound **17-19** the reaction mixture was diluted with hot water (6 mL), treated with charcoal (50 mg) and filtered. The filtrate was evaporated to a volume of ~5 mL, cooled to room temperature and acidified by formic acid to pH 4-5. The precipitate formed was isolated by filtration, washed with cold water and recrystallized.

Method B. A 0.5 M solution of KOH (2.3 mL, 1.15 mmol) in ethanol was added to a magnetically stirred suspension of compound **13c** or **14d** (1 mmol) in ethanol (2 mL). The resulted solution was refluxed for 2 h, then evaporated to a volume of ~ 1.5 mL, acidified with formic acid to pH 4-5 and diluted with water (4 mL). After cooling the precipitate formed was isolated by filtration, washed with cold water and recrystallized.

*4.15.1. 3-[2-Amino-5-(4-methylphenyl)-7-phenyl-4,5,6,7-tetrahydro-3H-[1,2,4]triazolo[1,5-a]pyrimidin-8-ium-3-yl]propanoate (**17**)*

Yield 0.245 g (65%, *Method A*), 0.226 g (60%, *Method B*), colorless needles, mp 193-195 °C (from EtOH/CH_3CN 1:5). IR ν (cm^{-1}): 3349, 3156, 3007, 2863, 2775, 2644, 1690, 1658, 1611, 1579, 1514, 1483, 1429, 1387, 1360, 1265, 1251, 1201, 1124, 1059, 1030, 1008. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.12-2.22 (m, 1H, 6-CH_2), 2.24-2.28 (m, 2H, $CH_2C\underline{H}_2COO^-$), 2.30 (s, 3H, CH_3), 2.43-2.46 (m, 1H, 6-CH_2), 3.83-3.99 (m, 2H, $C\underline{H}_2CH_2COO^-$), 4.77-4.82 (m, 1H, H-5), 5.22-5.28 (m, 1H, H-7), 6.89 (s, 2H, NH_2), 7.20 (d, J=8.1 Hz, 2H, Ar), 7.29-7.34 (m, 5H, Ph), 7.38 (d, J=8.1 Hz, 2H, Ar). MS (EI, 70 eV), m/z (%): 305 (100), 186 (27), 207 (5), 200 (6), 131 (5), 115 (6), 104 (6), 72 (7), 55 (5). Anal. Calcd for $C_{21}H_{23}N_5O_2$: C, 66.83; H, 6.14; N, 18.55. Found: C, 66.47; H, 6.34; N, 18.17.

*4.15.2. 3-[2-Amino-5-(4-methylphenyl)-7-phenyl-3H-[1,2,4]triazolo[1,5-a]pyrimidin-8-ium-3-yl]propanoate (**18**)*

Yield 0.198 g (53%, *Method B*) of yellowish prisms, mp 180-182 °C (from EtOH/CH_3CN 1:5). IR ν (cm^{-1}): 3338, 3054, 2957, 2781, 2700, 1668, 1634, 1608, 1561, 1500, 1470, 1379, 1344, 1322, 1264, 1225, 1192, 1126, 1017. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.45 (s, 3H, CH_3), 2.53-2.55 (m, 2H, CH_2), 4.38-4.40 (m, 2H, CH_2), 7.46-7.47 (m, 2H, Ar), 7.67-7.73 (m, 3H, Ar), 8.21-8.22 (m, 2H, Ar), 8.37-8.38 (m, 3H, Ar), 9.29 (br s, 2H, NH_2). ^{13}C NMR (125 MHz, TFA-d_1) δ: 21.9 (2C), 29.4, 101.4, 117.7, 118.6, 119.4, 120.0, 120.8, 121.1, 124.0, 137.0, 137.4, 141.3, 146.5, 156.5, 167.9. MS (EI, 70 eV), m/z (%): 301 (95), 115 (7), 89 (7), 77 (13), 72 (55), 68 (11), 55 (50), 51 (10), 44 (100). Anal. Calcd for $C_{21}H_{19}N_5O_2$: C, 67.55; H, 5.13; N, 18.76. Found: C, 67.69; H, 4.95; N, 18.71.

*4.15.3. 3-[2-Amino-6-(ethoxycarbonyl)-5-methyl-7-phenyl-4,7-dihydro-3H-[1,2,4]triazolo[1,5-a]pyrimidin-8-ium-3-yl]propanoate (**19**)*

Yield 0.260 g (70%, *Method A*) of colorless prisms, mp 200-202 °C (from AcOH/EtOH 1:5). IR ν (cm^{-1}): 3323, 3177, 3037, 2991, 2907, 1705, 1662, 1631, 1547, 1456, 1422, 1382, 1240, 1192, 1154, 1082, 1047. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.00 (t, J=7.1 Hz, 3H, $C\underline{H}_3CH_2O$), 2.32 (s, 3H, CH_3), 2.67 (t, J=7.4 Hz, 2H, $C\underline{H}_2CH_2COO^-$), 3.83-3.92 (m, 4H, $2CH_2$), 5.92 (s, 1H, H-7), 6.30 (s, 2H, NH_2), 7.18-7.27 (m, 5H, Ph). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 14.1 ($\underline{C}H_3CH_2O$), 24.4 (CH_3), 32.1 ($CH_2\underline{C}H_2COO^-$), 36.6 ($\underline{C}H_2CH_2COO^-$), 58.2 ($CH_3\underline{C}H_2O$), 59.7 (C-7), 96.1 (C-6), 127.0, 127.4, 128.0, 143.7 (carbons of benzene ring), 147.4 (C-3a), 150.0 (C-2), 159.4 (C-5), 165.9 ($\underline{C}OOEt$), 172.1 ($CH_2CH_2\underline{C}OO^-$). MS (EI, 70 eV), m/z (%): 371 (0.1) $[M]^+$, 299 (35), 270 (35), 254 (19), 226 (42), 222 (98), 194 (99), 176 (16), 155 (14), 148 (16), 140 (10), 128 (50), 115 (17), 105 (21), 102 (18), 89 (12), 77 (76), 72 (99), 67 (28), 63 (11), 55 (99), 45 (100). Anal. Calcd for $C_{18}H_{21}N_5O_4$: C, 58.21; H, 5.70; N, 18.86. Found: C, 57.89; H, 5.86; N, 18.51.

*4.15.4. Sodium 3-(2-amino-6,6-dimethyl-8-oxo-9-phenyl-5,7,8,9-tetrahydro[1,2,4]triazolo[5,1-b]quinazolin-3(6H)-yl)propanoate (**20**)*

Yield 0.226 g (56%, *Method A*) of colorless needles, mp 213-215 °C (from EtOH). IR ν (cm^{-1}): 3350, 3266, 3164, 2965, 2818, 1674, 1582, 1527, 1487, 1390, 1238, 1190, 1131, 1071, 1029, 1002. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 0.92 (s, 3H, CH_3), 0.99 (s, 3H, CH_3), 1.93 (d, J=16.0 Hz, 1H, 7-CH_2), 2.09 (d, J=16.0 Hz, 1H, 7-CH_2), 2.28-2.31 (m, 2H, CH_2COO^-), 2.38 (s, 2H, 5-CH_2), 3.83 (t, J=5.5 Hz, 2H, NCH_2), 5.90 (s, 1H, H-9), 6.88 (s, 2H, NH_2), 7.15-7.25 (m, 5H, Ph). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 27.1 (CH_3), 29.1 (CH_3), 31.9 (C-6), 36.9 ($\underline{C}H_2COO^-$), 39.3 (NCH_2), 45.7 (C-5), 50.3 (C-7), 58.2 (C-9), 105.9 (C-8a), 127.0, 127.2, 127.9, 143.1 (carbons of benzene ring), 148.0 (C-3a), 151.2 (C-2), 163.3 (C-4a), 174.4 (COO^-), 191.7 (C-8). Anal. Calcd for $C_{20}H_{22}N_5O_3Na$: C, 59.55; H, 5.50; N, 17.36. Found: C, 59.37; H, 5.69; N, 17.56.

4.16. 7-Benzyl-4-(4-methoxyphenyl)-2-phenyl-3,4,9,10-tetrahydro-2*H*-[1,2,4]triazolo[1,5-*a*:4,3-*a'*]dipyrimidin-8(7*H*)-one (23)

Benzylbromide (0.24 g, 1.4 mmol) was added to a solution of compound **13a** (0.5 g, 1.3 mmol) in dry DMF (4 mL) and the resulted mixture was magnetically stirred at room temperature for 4 h then diluted with 5% water solution of NH_3 (15 mL). The precipitate formed was isolated by filtration, washed with water and crystallized from ethanol to give 0.43 g (yield 71%) of compound **23** as colorless prisms, mp 234-235 °C. IR ν (cm^{-1}): 3062, 3029, 2970, 2931, 2869, 2841, 1699, 1661, 1608, 1584, 1516, 1497, 1450, 1419, 1395, 1374, 1338, 1293, 1251, 1225, 1208, 1175, 1112, 1057, 1021. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.55-1.66 (m, 1H, 3-CH_2), 2.36-2.39 (m, 1H, 3-CH_2), 2.91 (t, J = 6.2 Hz, 2H, 9-CH_2), 3.72 (s, 3H, CH_3O), 3.82 (t, J=6.2 Hz, 2H, 10-CH_2,), 4.63-4.81 (m, 3H, H-2+ $PhC\underline{H}_2$), 5.06 (dd, J=10.0, 4.2 Hz, 1H, H-4), 6.83 (d, J=8.5 Hz, 2H, Ar), 7.10–7.42 (m, 12H, Ar). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 29.9, 34.6, 42.9, 44.0, 55.1, 56.4, 58.2, 113.6, 126.2, 126.6, 127.3, 127.8, 127.9, 128.3, 132.4, 136.4, 143.4 (C-6a), 145.9, 149.0 (C-11a), 158.6 (C-4 of 4-$CH_3OC_6H_4$), 165.7 (CO). MS (EI, 70 eV), m/z (%): 465 (16) $[M]^+$, 330 (100), 268 (7), 240 (7), 134 (14), 91 (42), 55 (6). Anal. Calcd for $C_{28}H_{27}N_5O_2$: C, 72.24; H, 5.85; N, 15.04. Found: C, 72.45; H, 5.92; N, 15.13.

4.17. Ethyl 7-benzyl-2-methyl-8-oxo-4-phenyl-7,8,9,10-tetrahydro-4*H*-[1,2,4]triazolo[1,5-*a*:4,3-*a'*]dipyrimidine-3-carboxylate (25)

Sodium hydride (60% dispersion in mineral oil, 0.05 g, 1.1 mmol) was added to a suspension of compound **15a** (0.5 g, 1.1 mmol) in dry DMF (3 mL) and the resulted mixture was stirred at room temperature for 10 min. Benzylchloride (0.16 g, 1.4 mmol) was added and the reaction mixture was stirred for a period of 24 h at room temperature, then diluted with water (10 mL). The precipitate formed was isolated by filtration, washed with water, crystallized from 2-popanol to give 0.32 g (yield 70%) of compound **25** as colorless prisms, mp 276-277 °C. IR ν (cm^{-1}): 3068, 3031, 2978, 2900, 1699, 1621, 1599, 1537, 1511, 1456, 1427, 1376, 1344, 1284, 1263, 1212, 1160, 1090, 1061. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.00 (t, J=7.0 Hz, 3H, $C\underline{H}_3CH_2O$), 2.35 (s, 3H, CH_3), 2.94 (t, J=6.9 Hz, 2H, 9-CH_2), 3.88 (q, J=7.0 Hz, 2H, $CH_3C\underline{H}_2O$), 3.98 (t, J=6.9 Hz, 2H, 10-CH_2), 4.78 (s, 2H, $PhC\underline{H}_2$), 6.11 (s, 1H, H-4), 7.22-7.29 (m, 10H, 2Ph). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 14.0 ($\underline{C}H_3CH_2O$), 24.2 (CH_3), 29.2 (C-9), 35.6 (C-10), 44.5 ($Ph\underline{C}H_2$), 58.5 ($CH_3\underline{C}H_2O$), 59.7 (C-4), 97.0 (C-3), 127.0, 127.3, 127.7, 127.8, 128.1, 128.2, 135.8, 142.5 (carbons of benzene rings), 145.6 (C-6a), 147.4 (C-11a), 159.3 (C-2), 165.3 (C-8), 165.8 ($\underline{C}OOEt$). MS (EI, 70 eV), m/z (%): 443 (9) $[M]^+$, 414 (11), 366 (44), 338 (7), 250 (2), 202 (1), 155 (2), 128 (7), 115 (3), 104 (3), 91 (100), 77 (10), 65 (13), 55 (12). Anal. Calcd for $C_{25}H_{25}N_5O_3$: C, 67.70; H, 5.68; N, 15.79. Found: C, 68.09; H, 5.79; N, 16.14.

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Supplementary Material

Copies of IR, ^{1}H and ^{13}C NMR, HSQC and HMBC spectra of synthesized compounds, MOL files, crystallographic data and X-ray experimental parameters for compounds **5d, 14c**, **15a**, and detailed results of quantum chemical calculations are available. Supplementary data associated with this article can be found in online version.

Partially hydrogenated 2-amino[1,2,4-triazolo[1,5-*a*]pyrimidines as synthons for the preparation of polycondensed heterocycles: reaction with chlorocarboxylic acid chlorides

Victor M. Chernyshev,[a*] Dmitry A. Pyatakov,[a] Andrey N. Sokolov,[a] Alexander V. Astakhov,[a] Eugene S. Gladkov,[b] Svetlana V. Shishkina[b] and Oleg V. Shishkin[b]

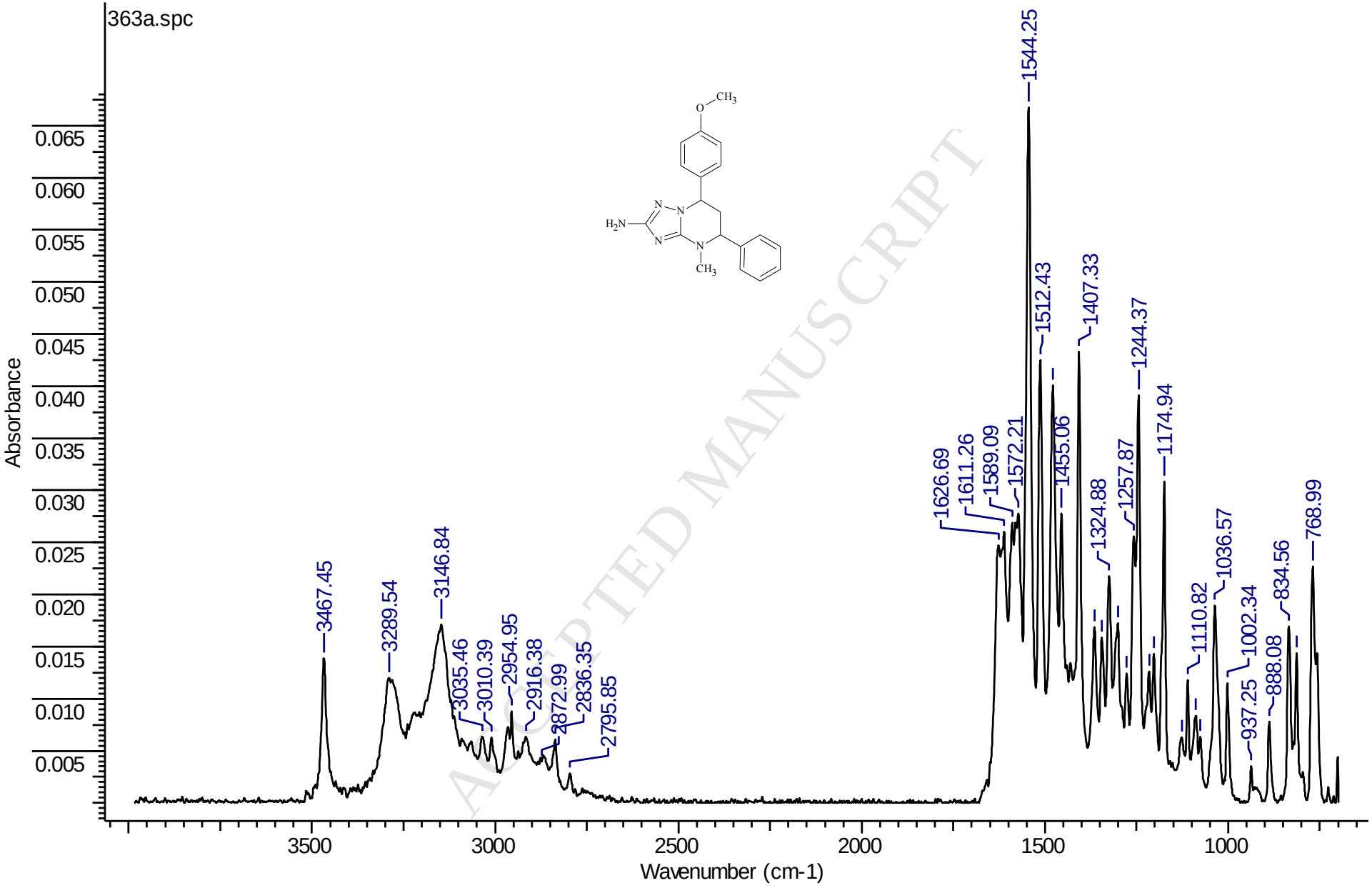
[a] *South-Russia State Technical University, Prosveschenya 132, 346428 Novocherkassk, Russian Federation*
[b] *State Scientific Institution 'Institute for Single Crystals' of National Academy of Sciences of Ukraine, Lenin Ave. 60, 61001 Kharkiv, Ukraine*

Supplementary Material

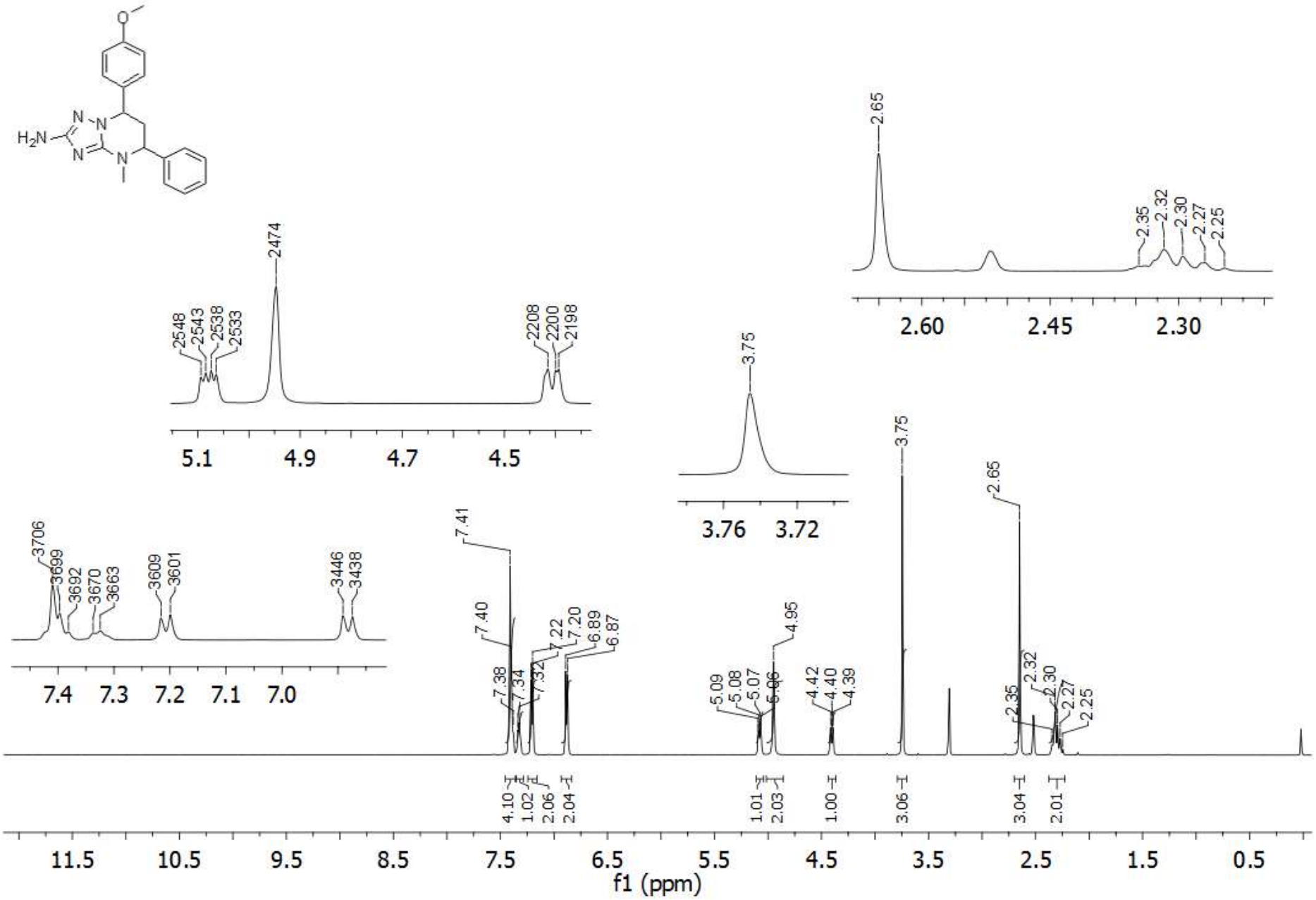
1. IR and NMR spectra of synthesized compounds
2. Detailed results of quantum chemical calculations
3. Crystallographic data and X-ray experimental parameters

[*] Corresponding author. Tel.: +7-903-437-24-03; fax: +7-86-352-276-19; e-mail: chern13@yandex.ru.

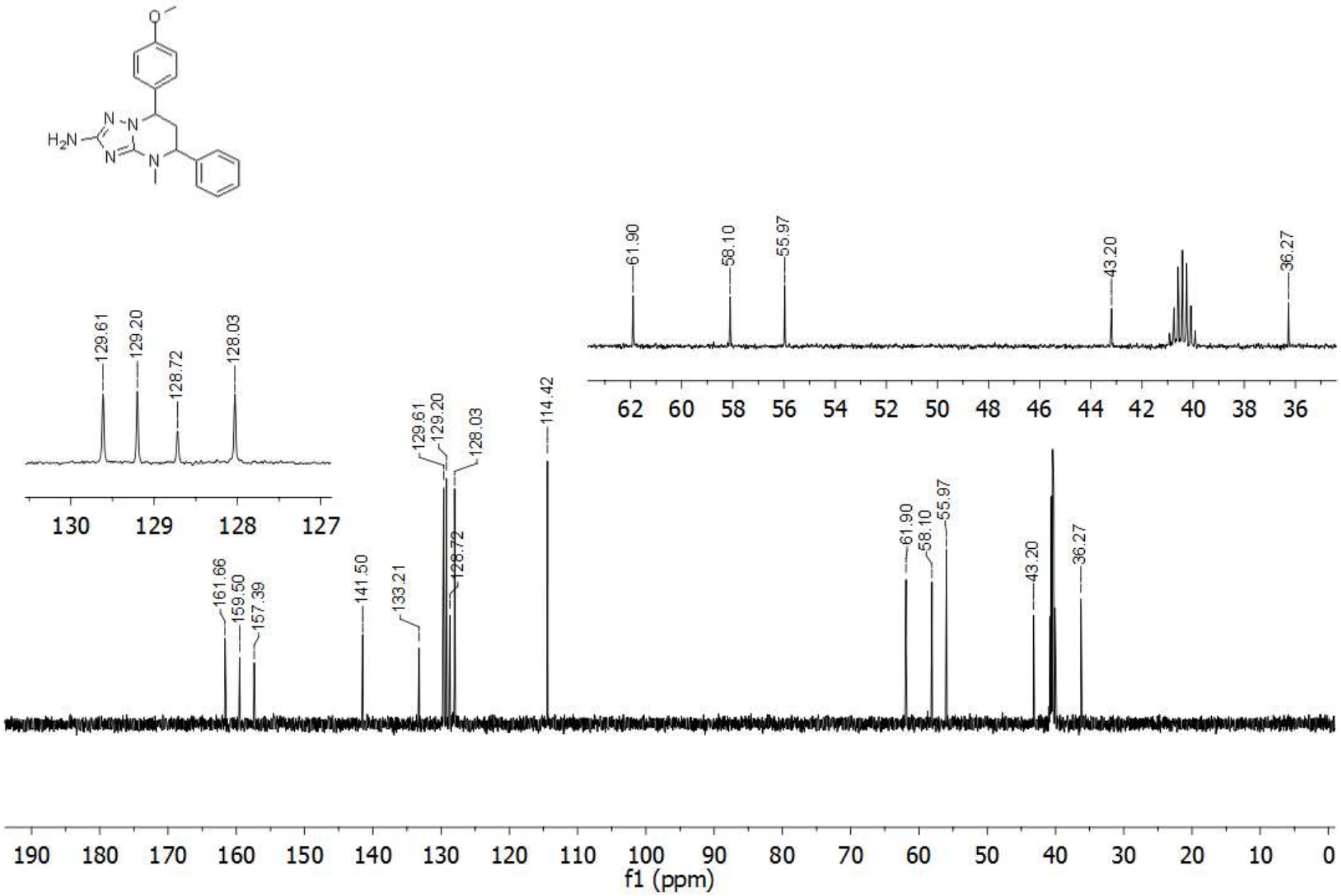
IR and NMR spectra of synthesized compounds



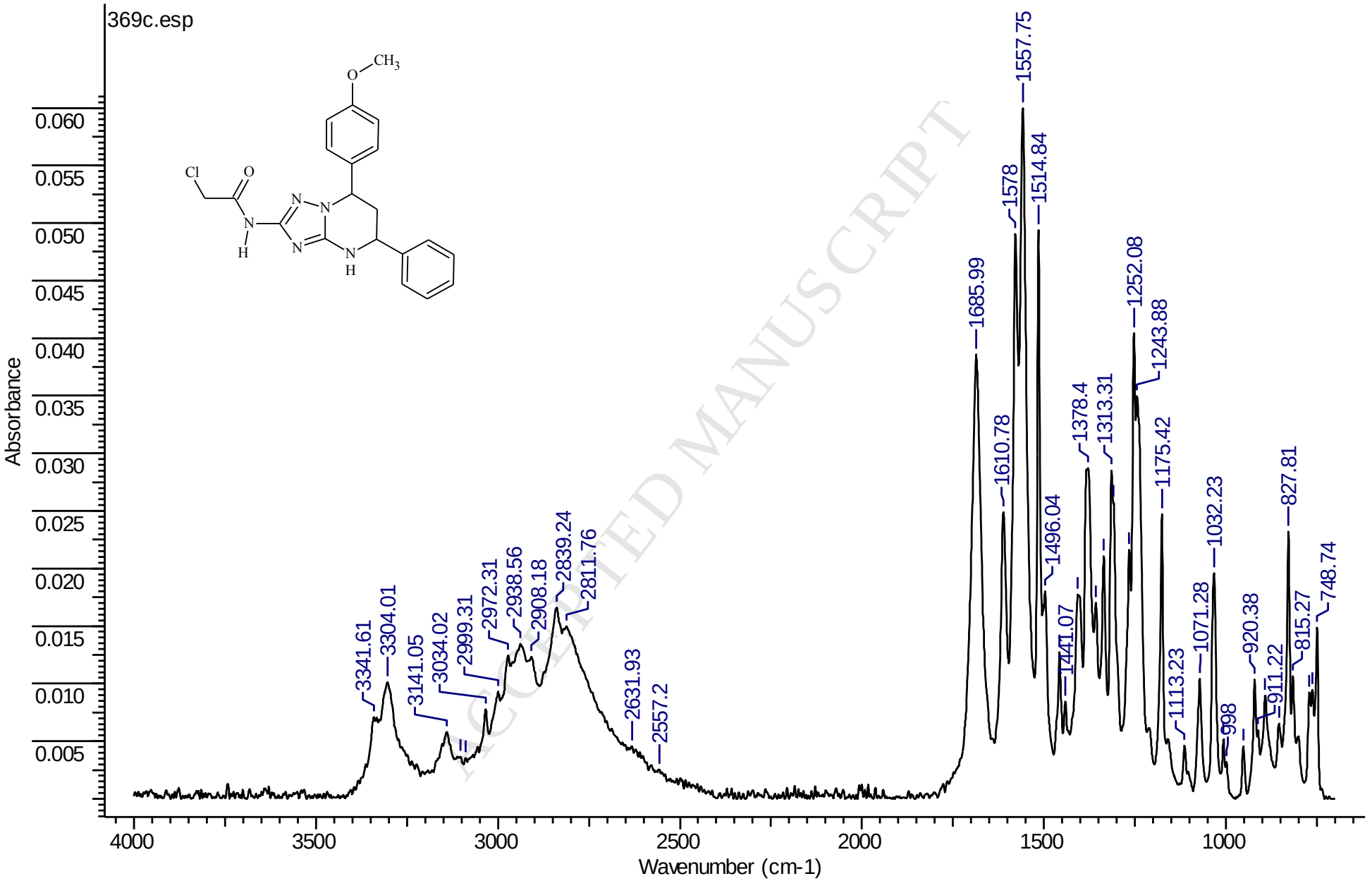
FTIR spectrum of compound **1f** (ATR).



^{1}H NMR spectrum of compound **1f** (DMSO-d_6, 500 MHz).



^{13}C NMR spectrum of compound **1f** (DMSO-d_6, 125 MHz).



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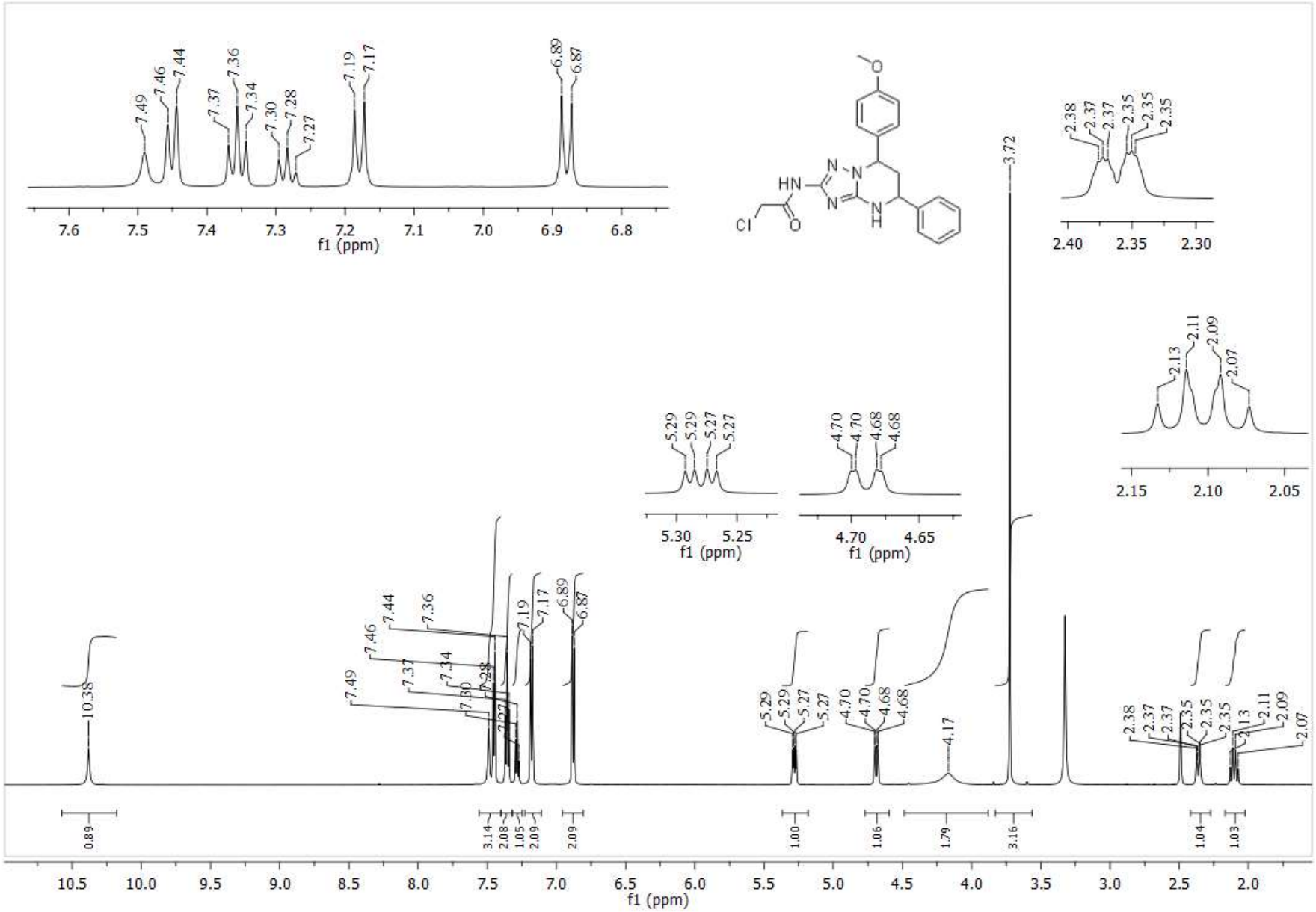

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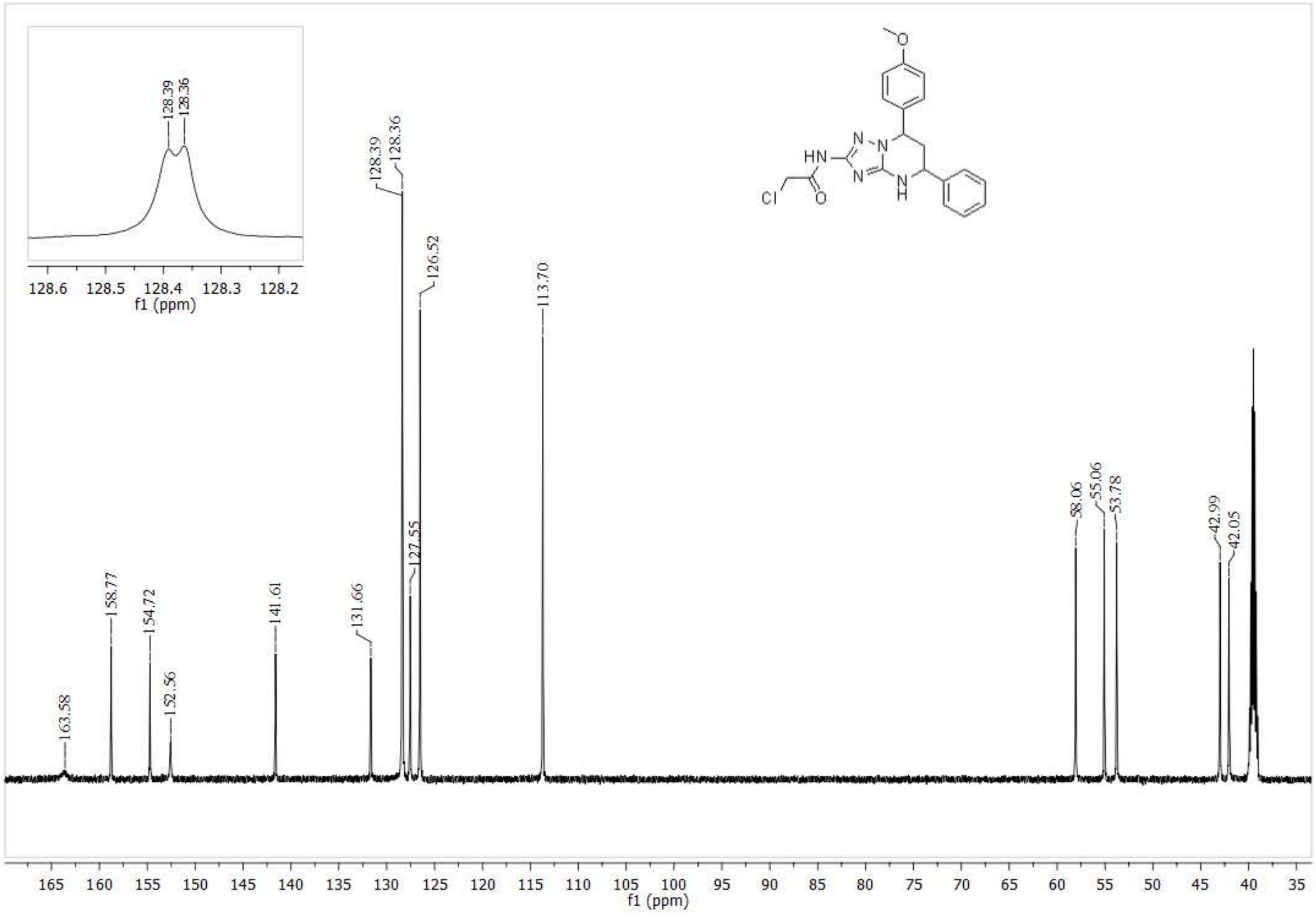

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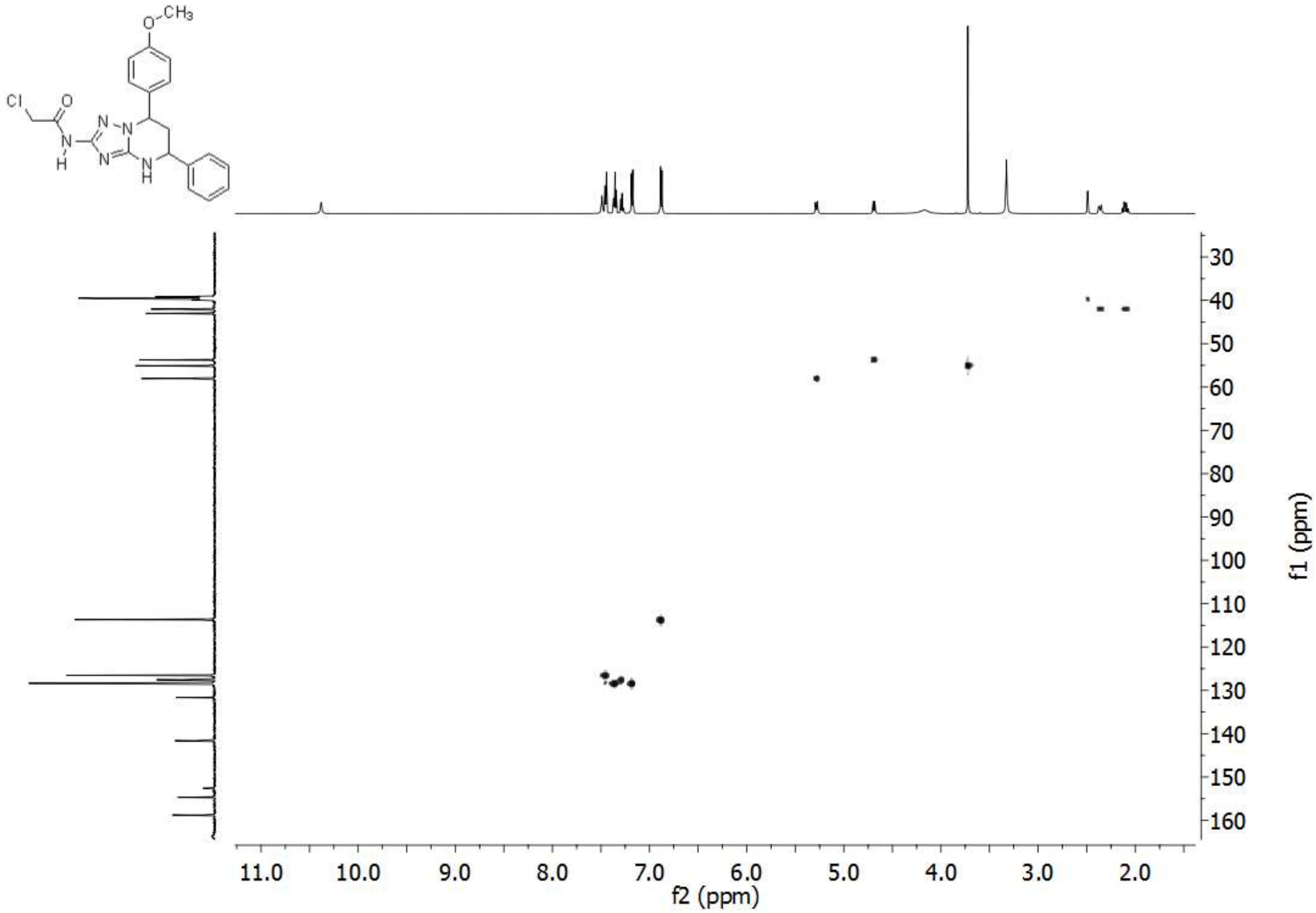

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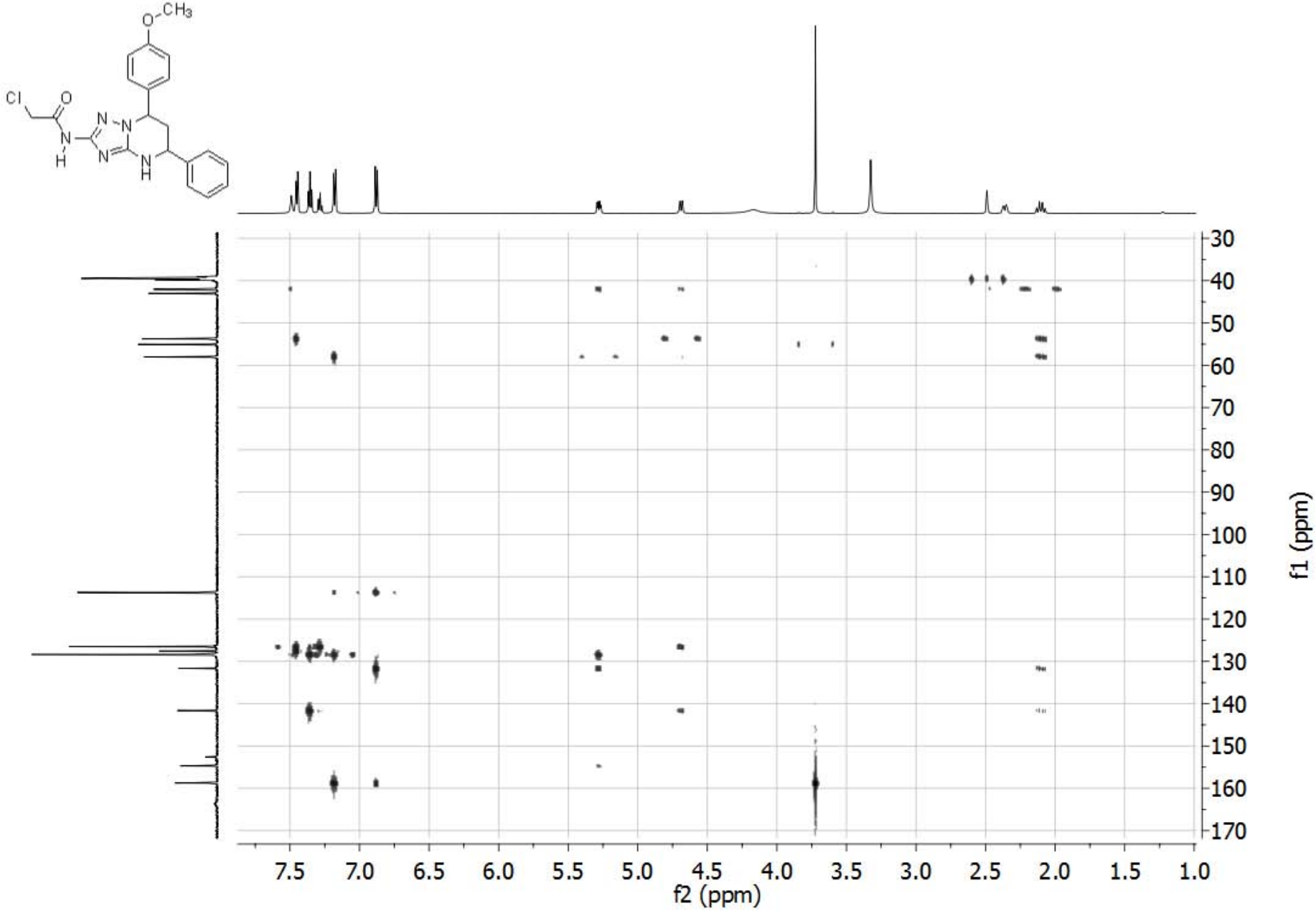

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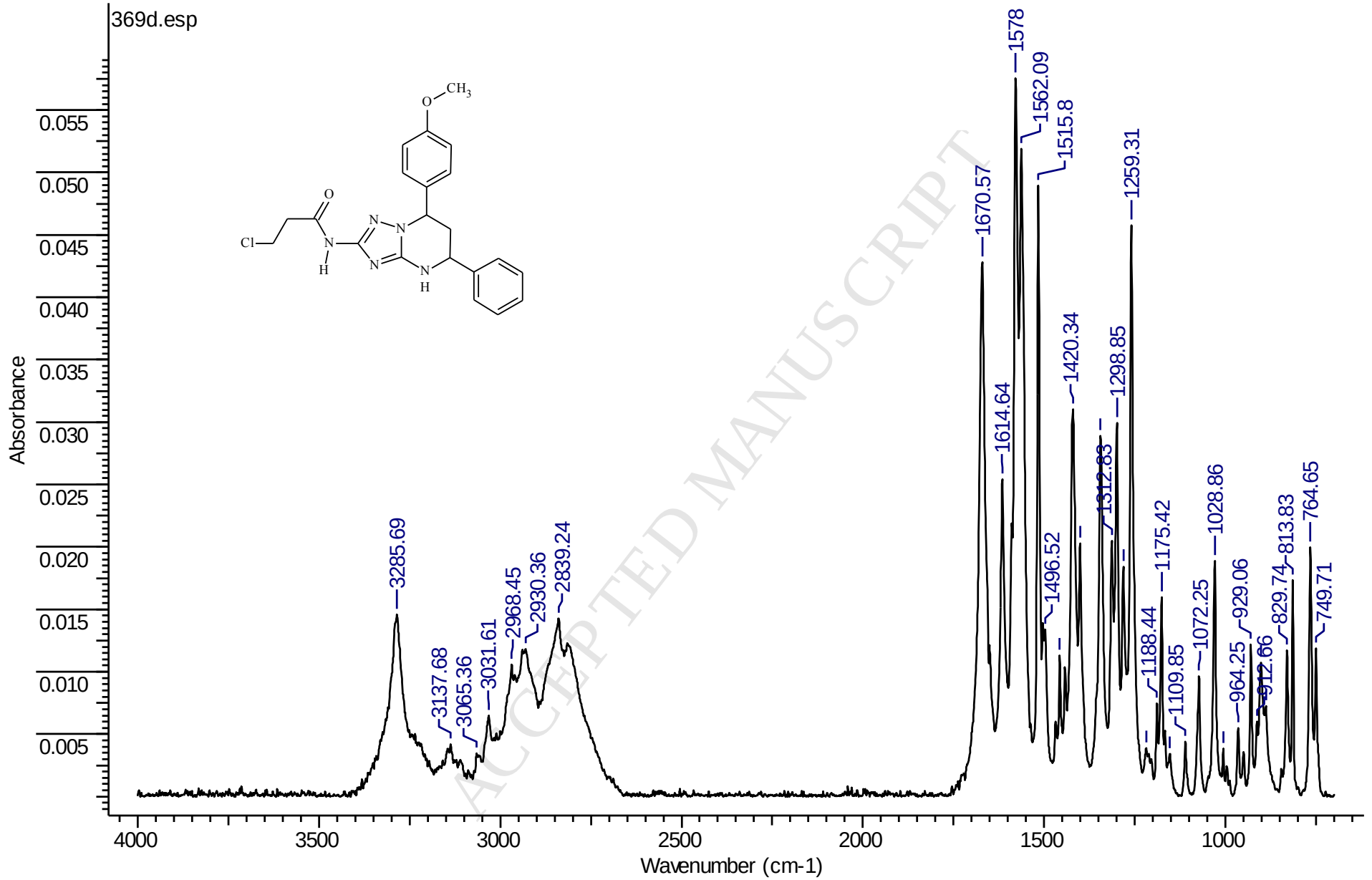
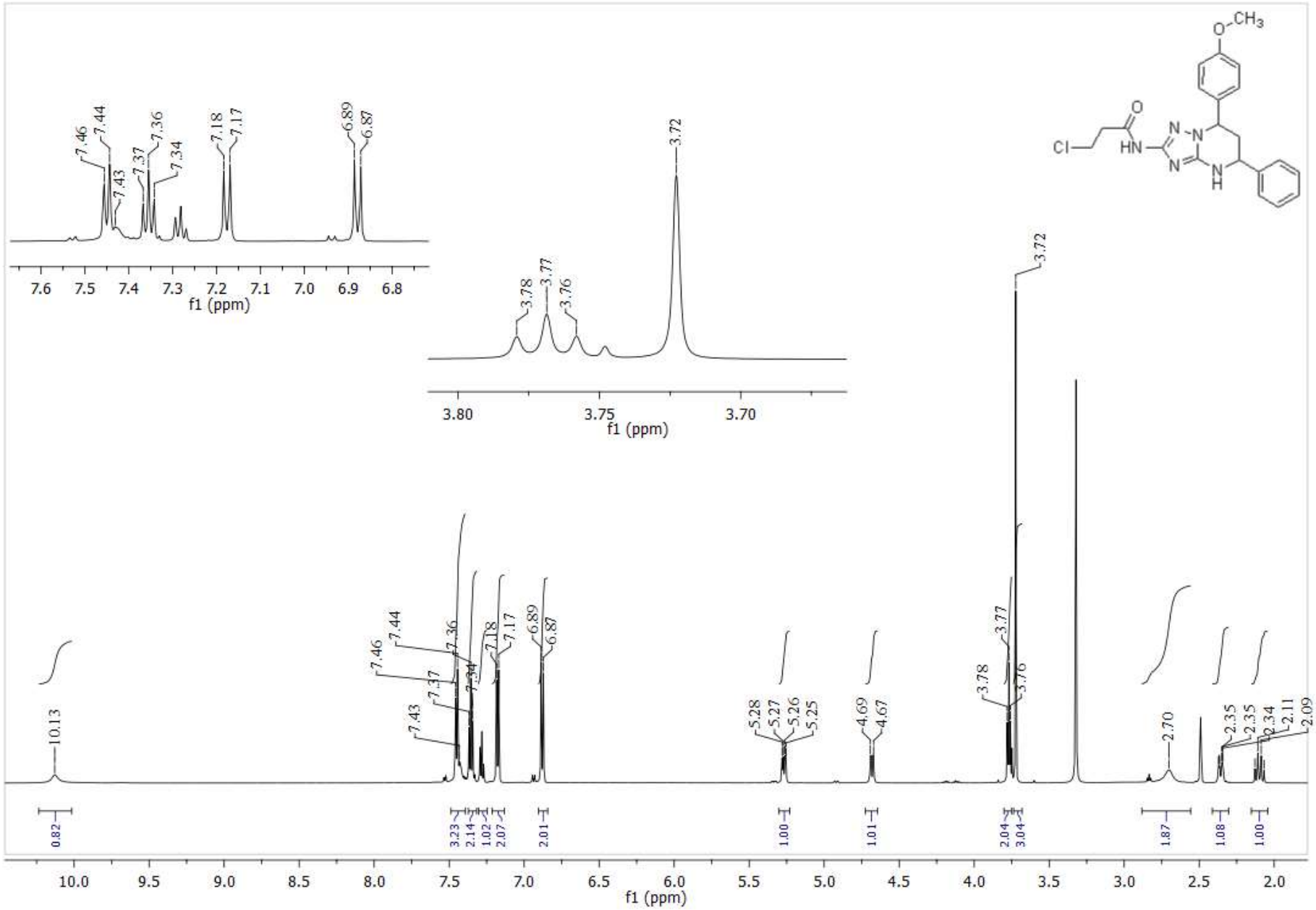


FTIR spectrum of compound **3a** (ATR).



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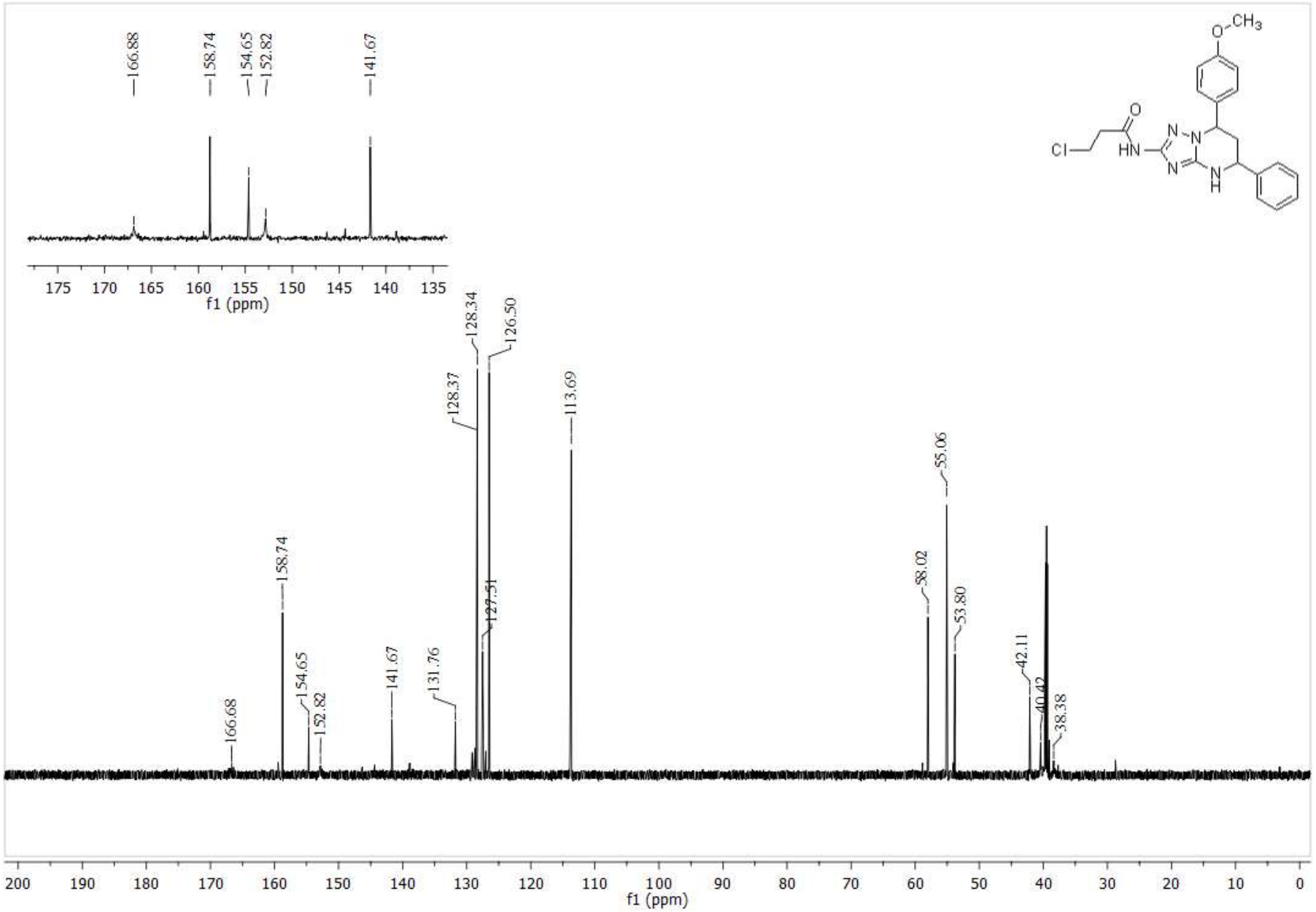

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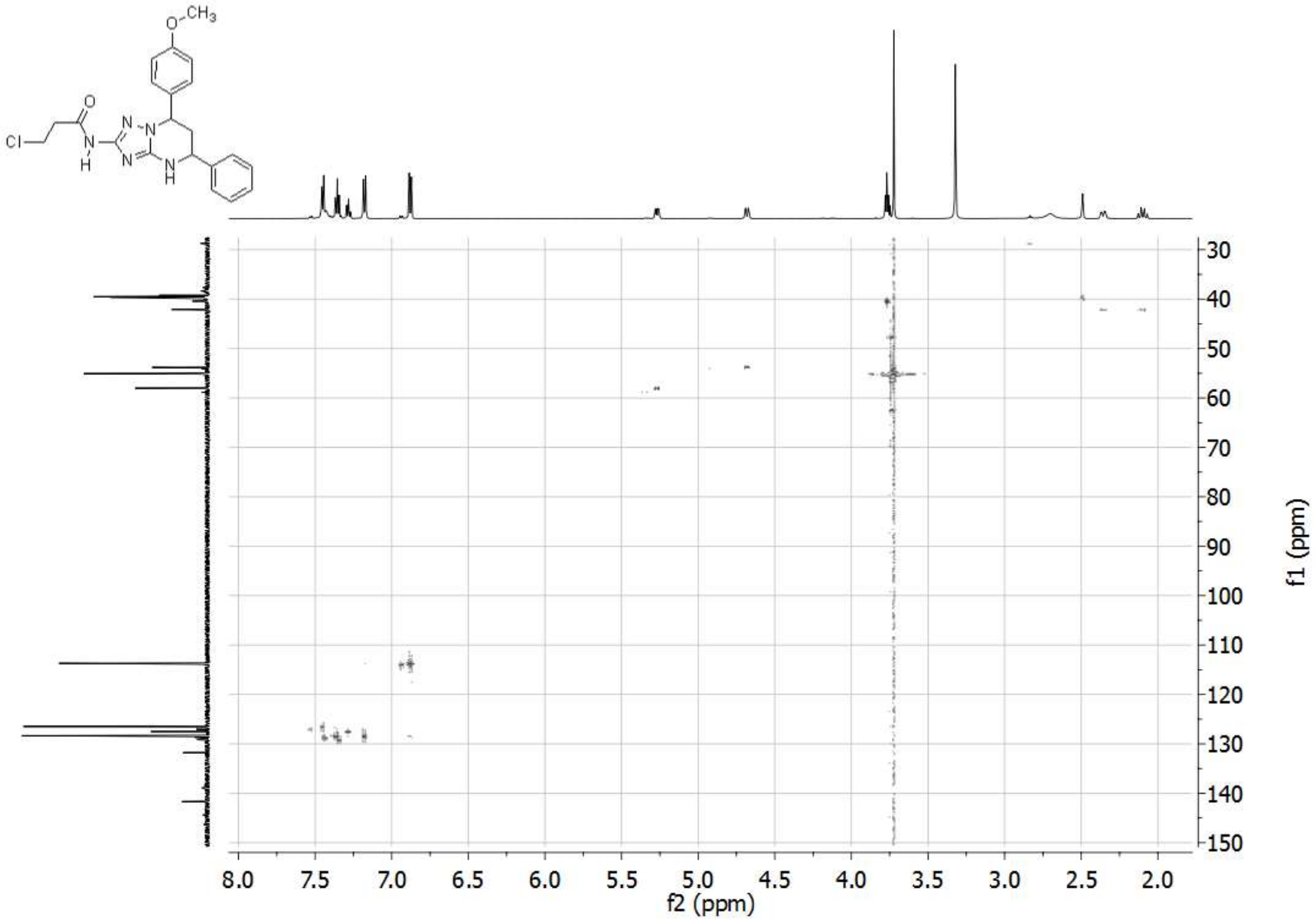

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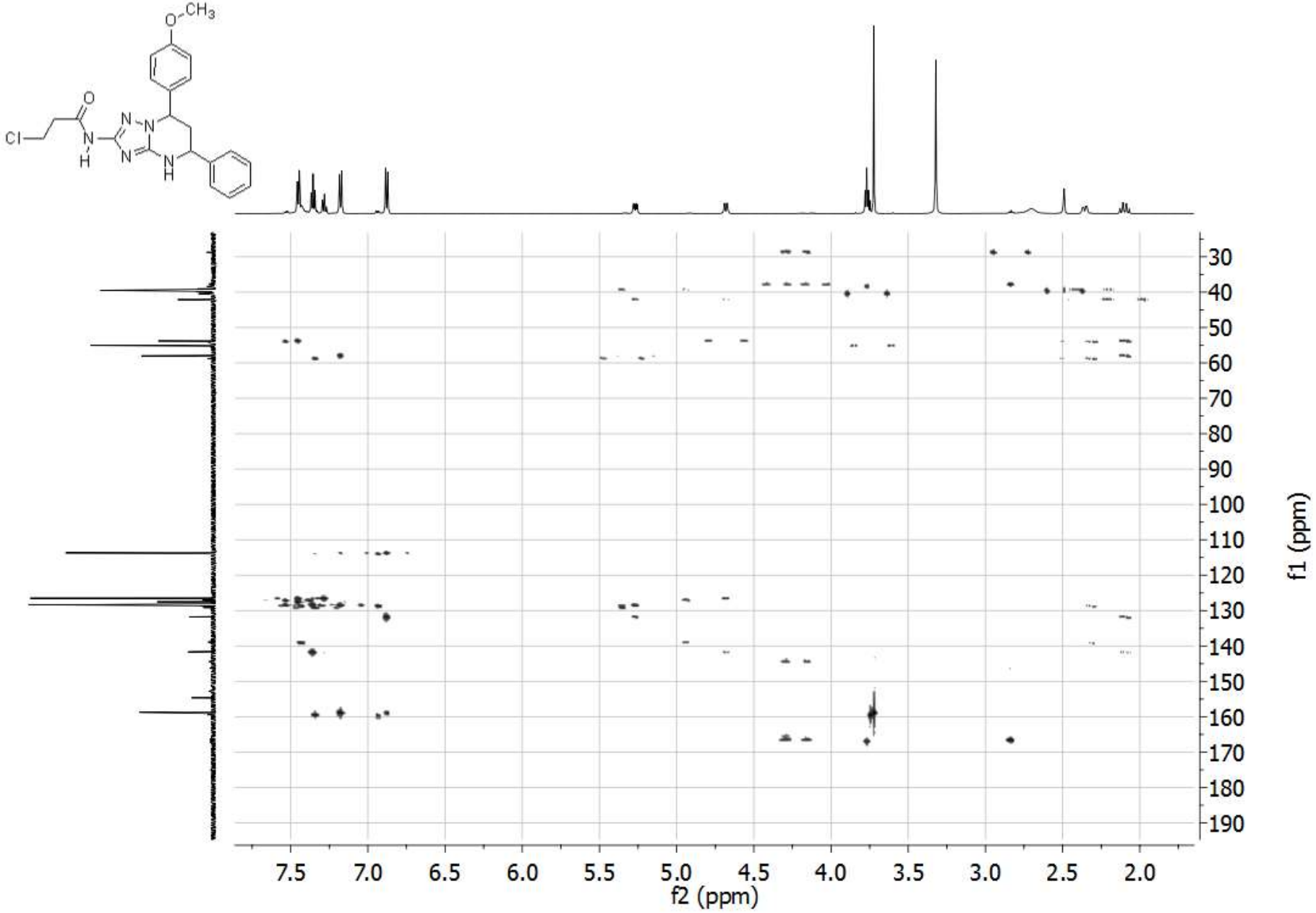

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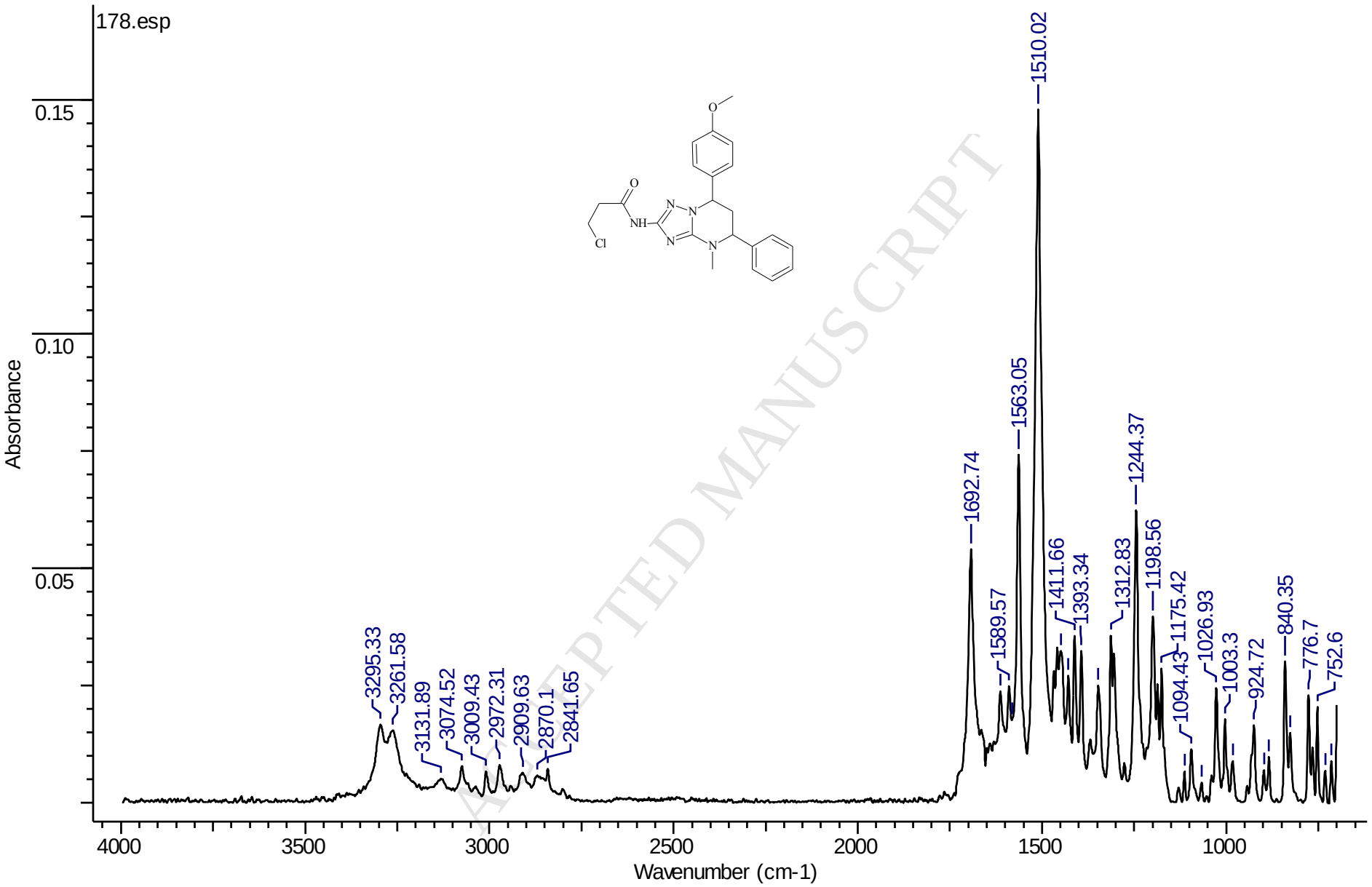

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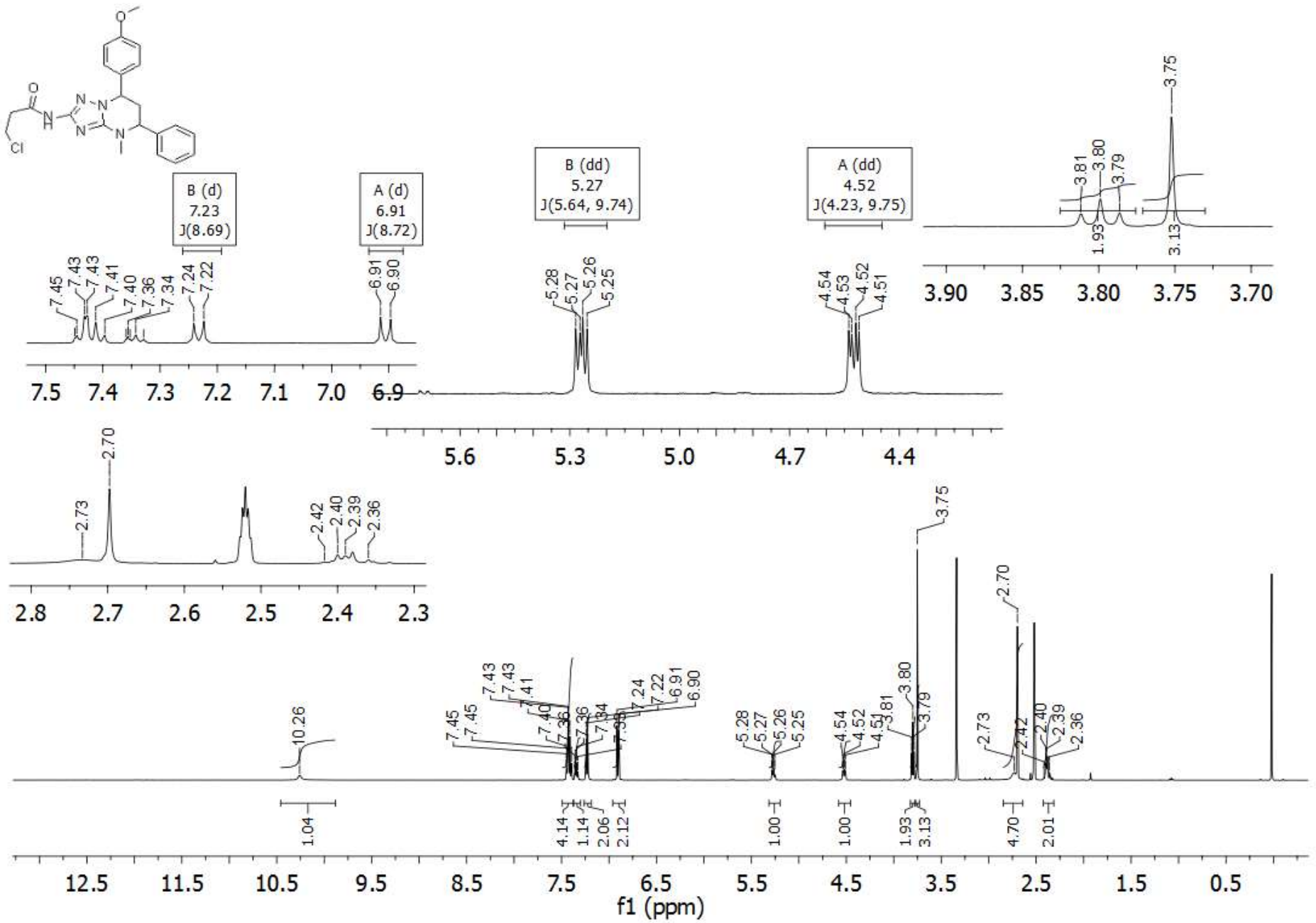
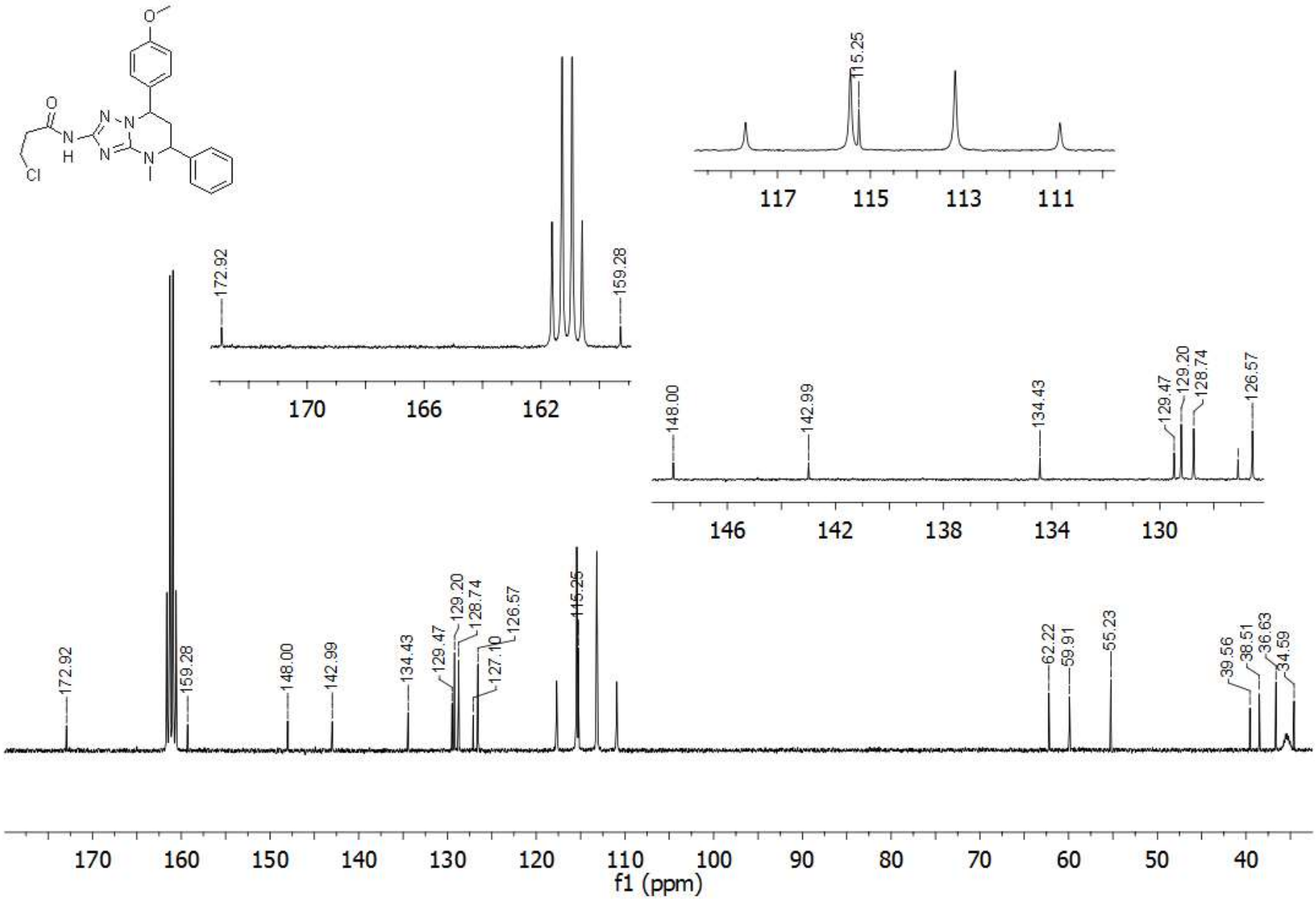


^{1}H NMR spectrum of compound **3f** (DMSO-d_6, 500 MHz).



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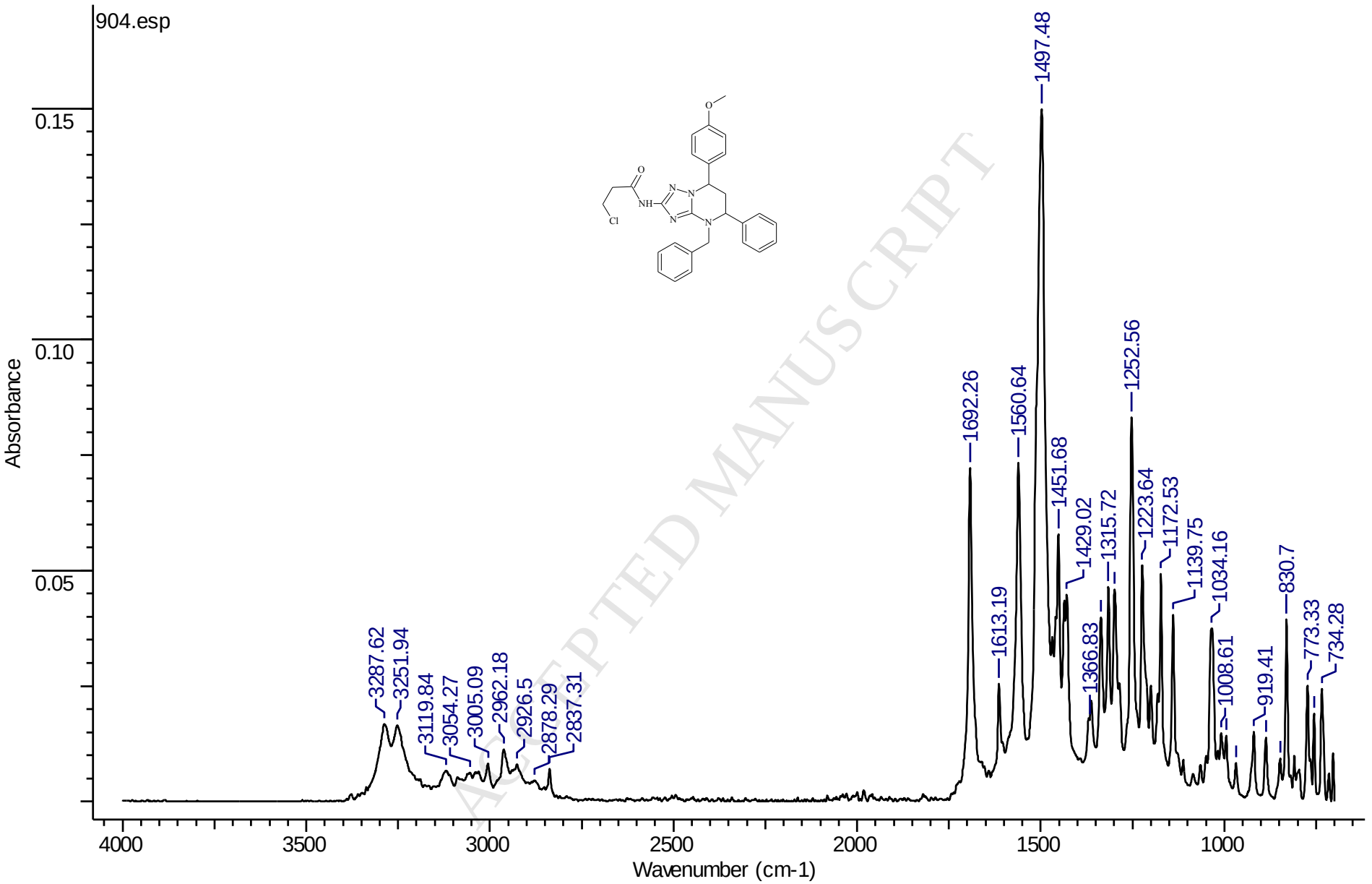

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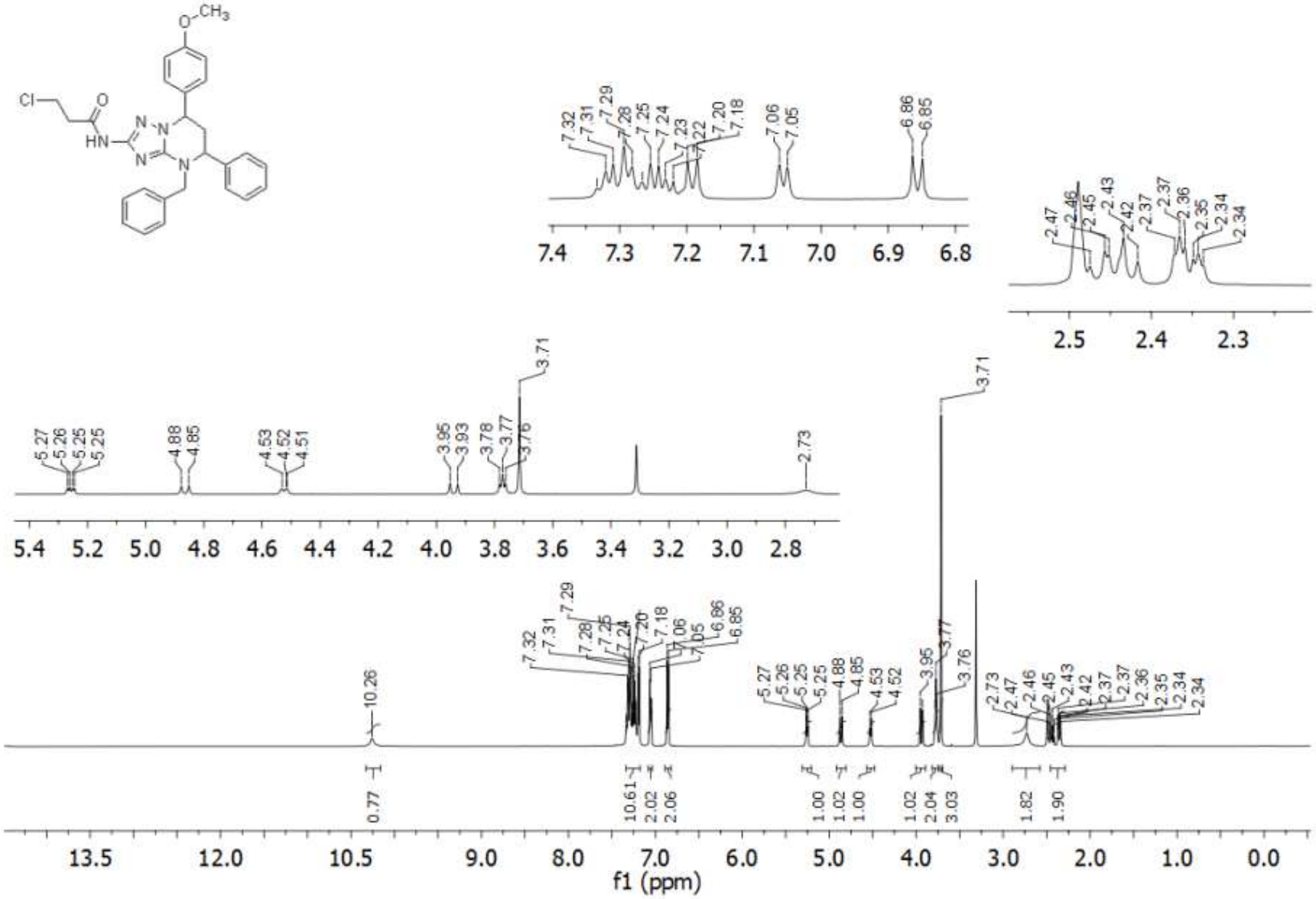

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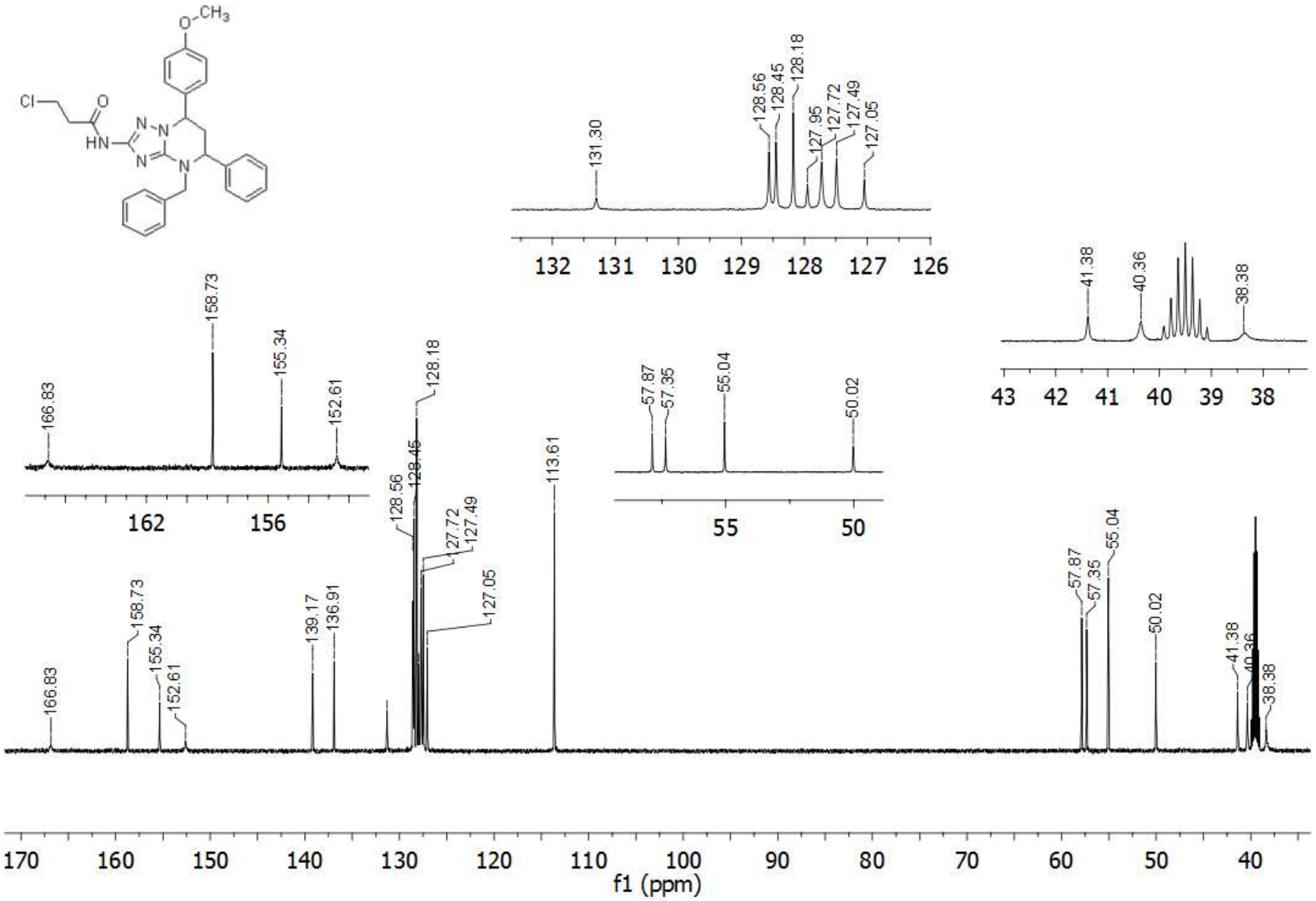
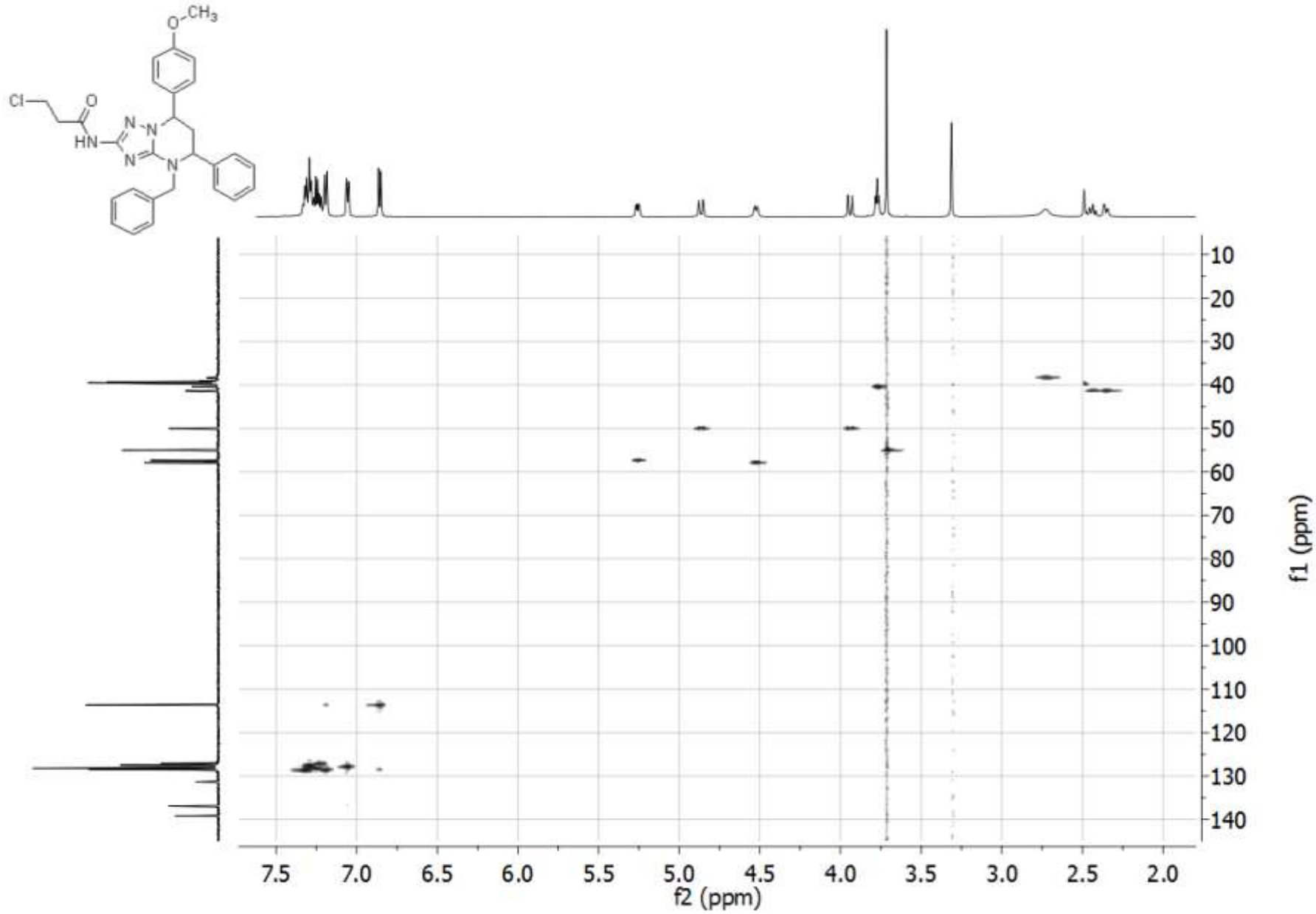


^{13}C NMR spectrum of compound **3g** (DMSO-d_6, 150 MHz).



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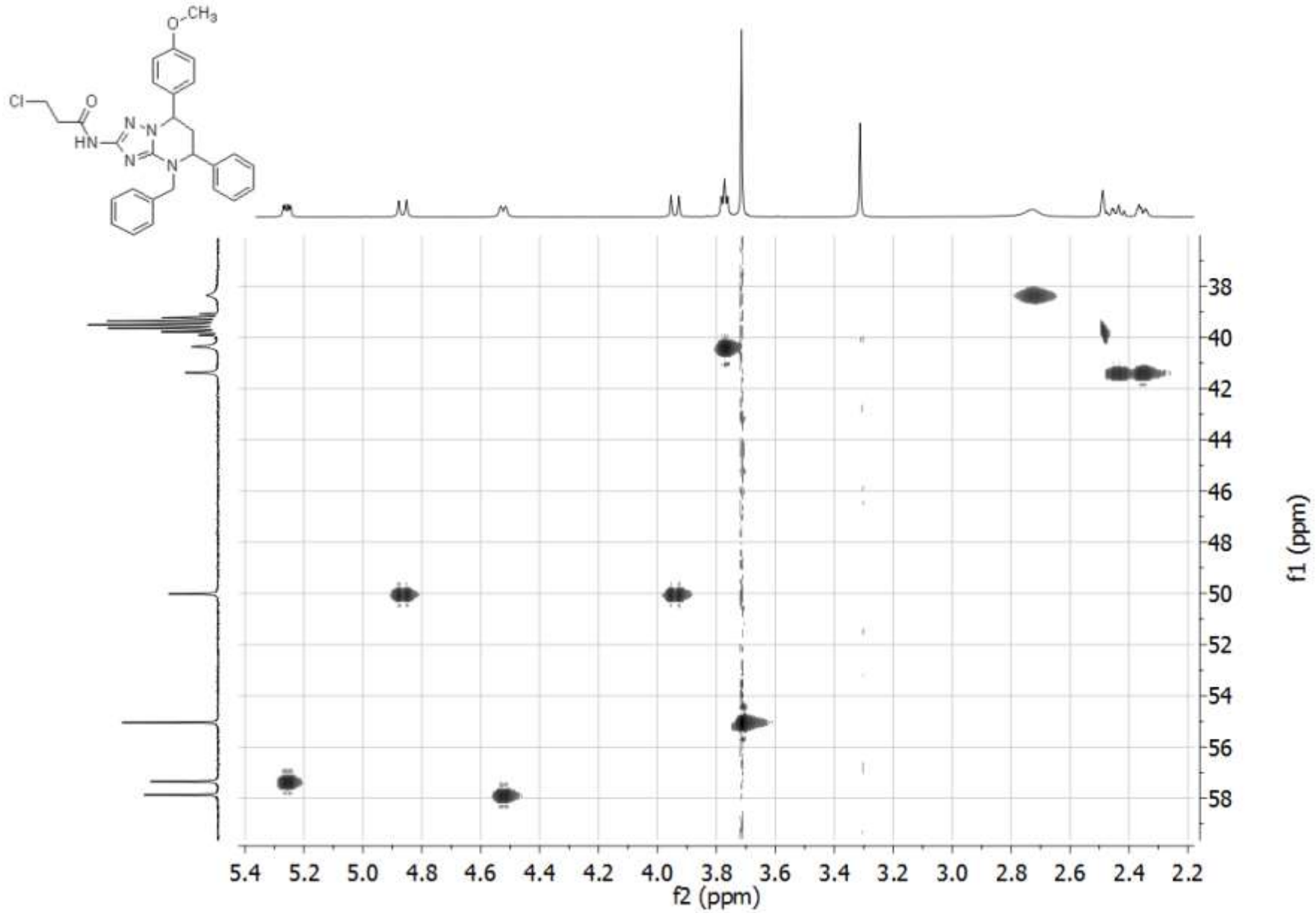
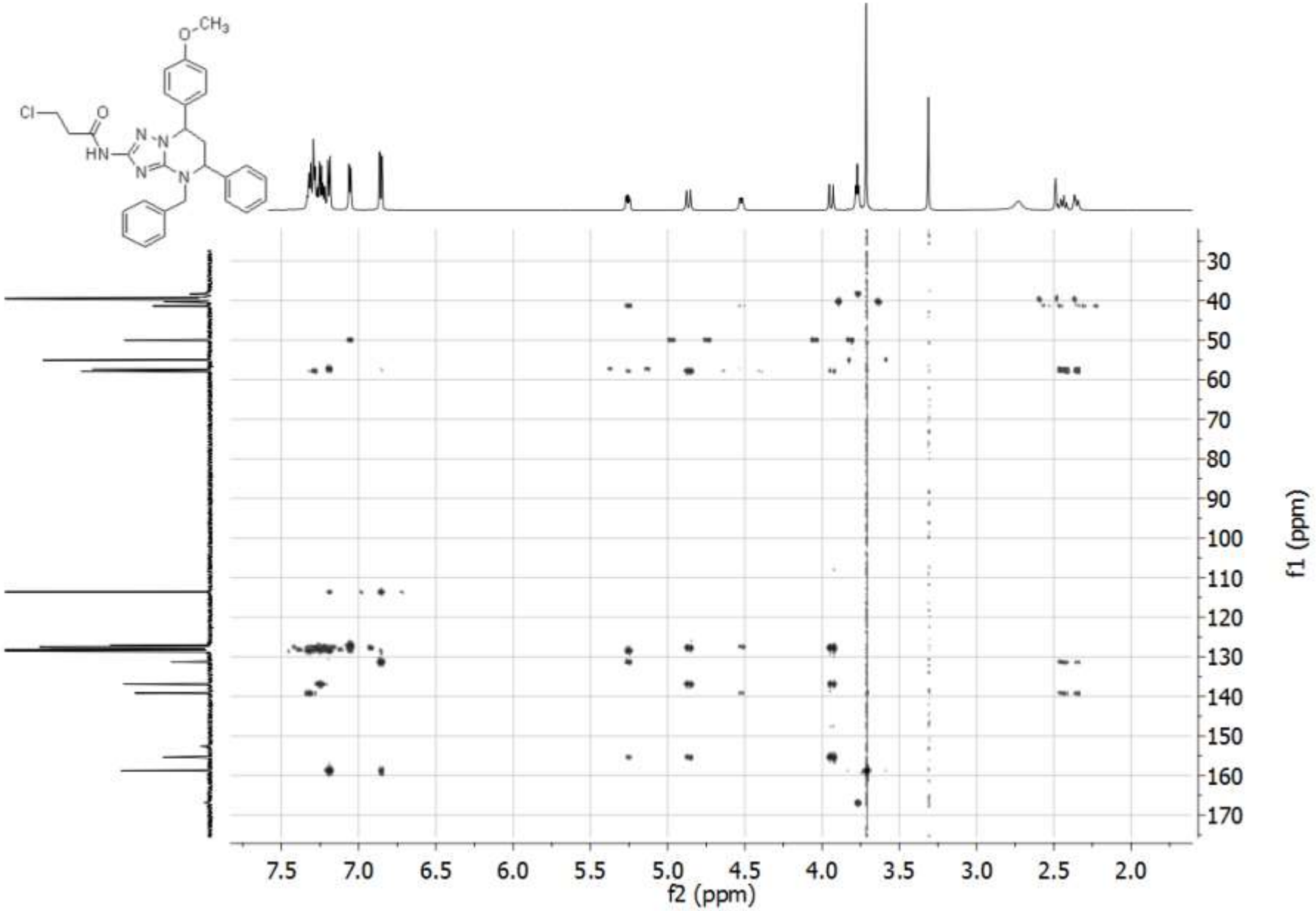


Enlarged fragment of ^{1}H-^{13}C HSQC spectrum of compound **3g** (DMSO-d_6).



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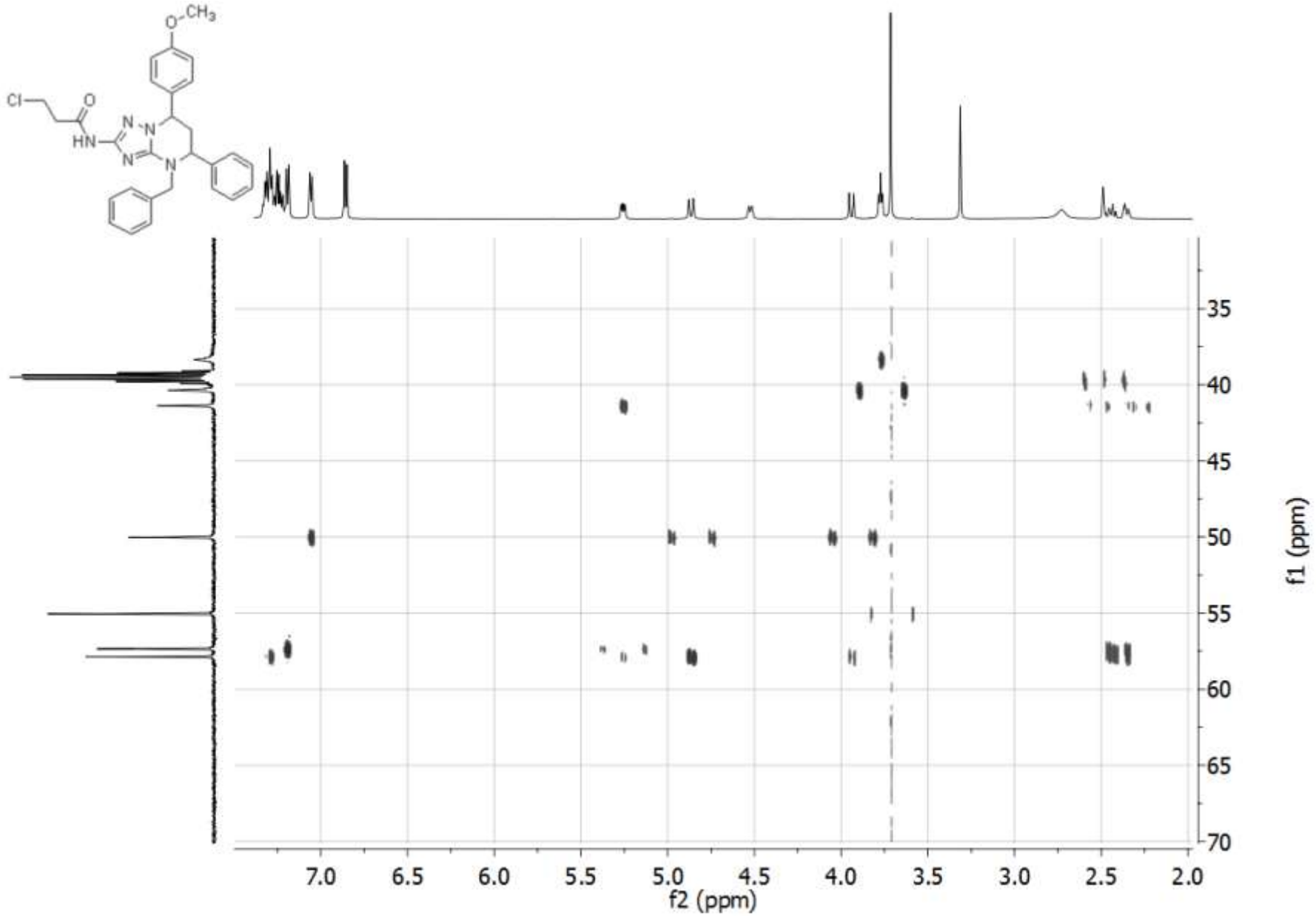

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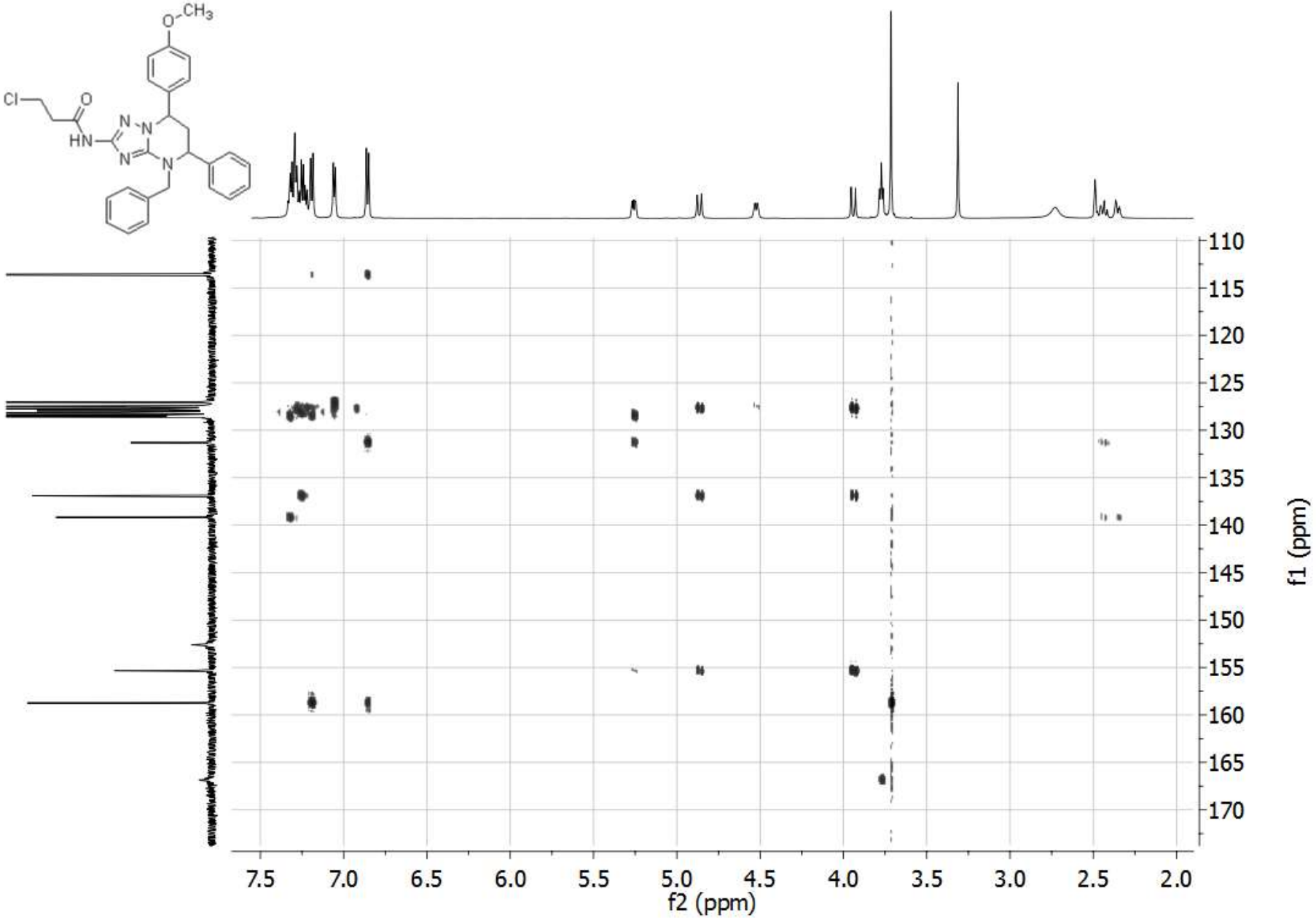
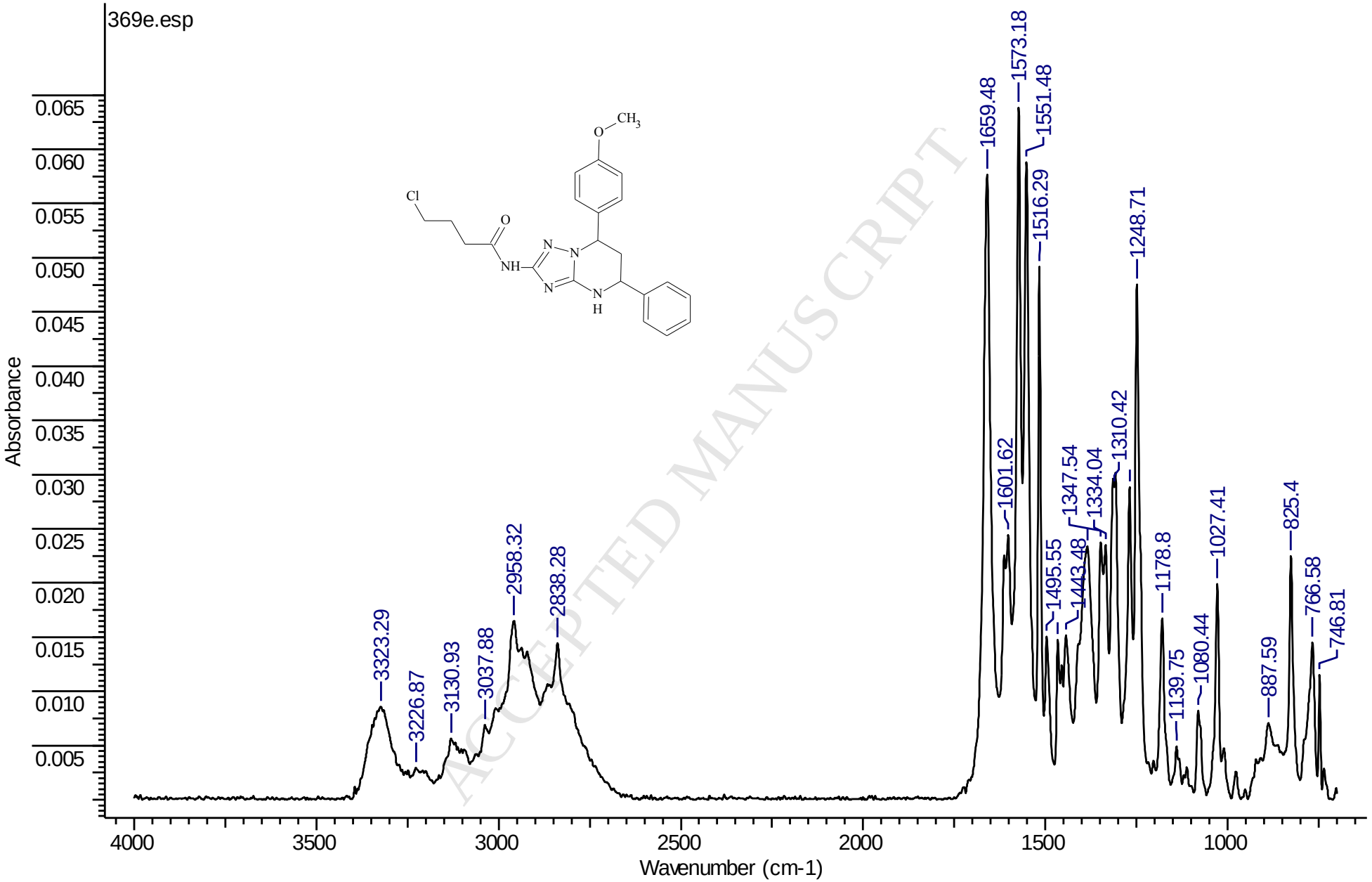
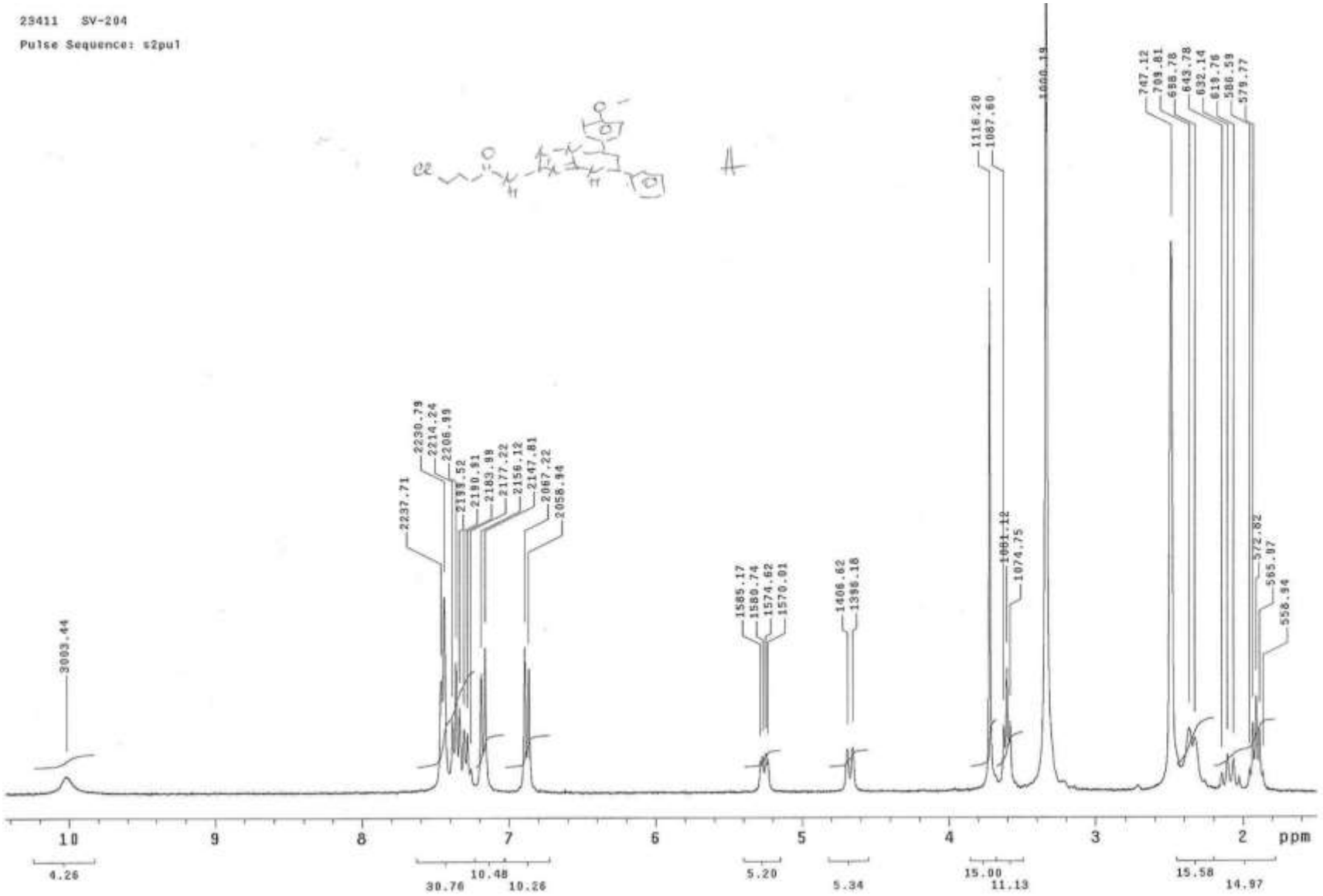


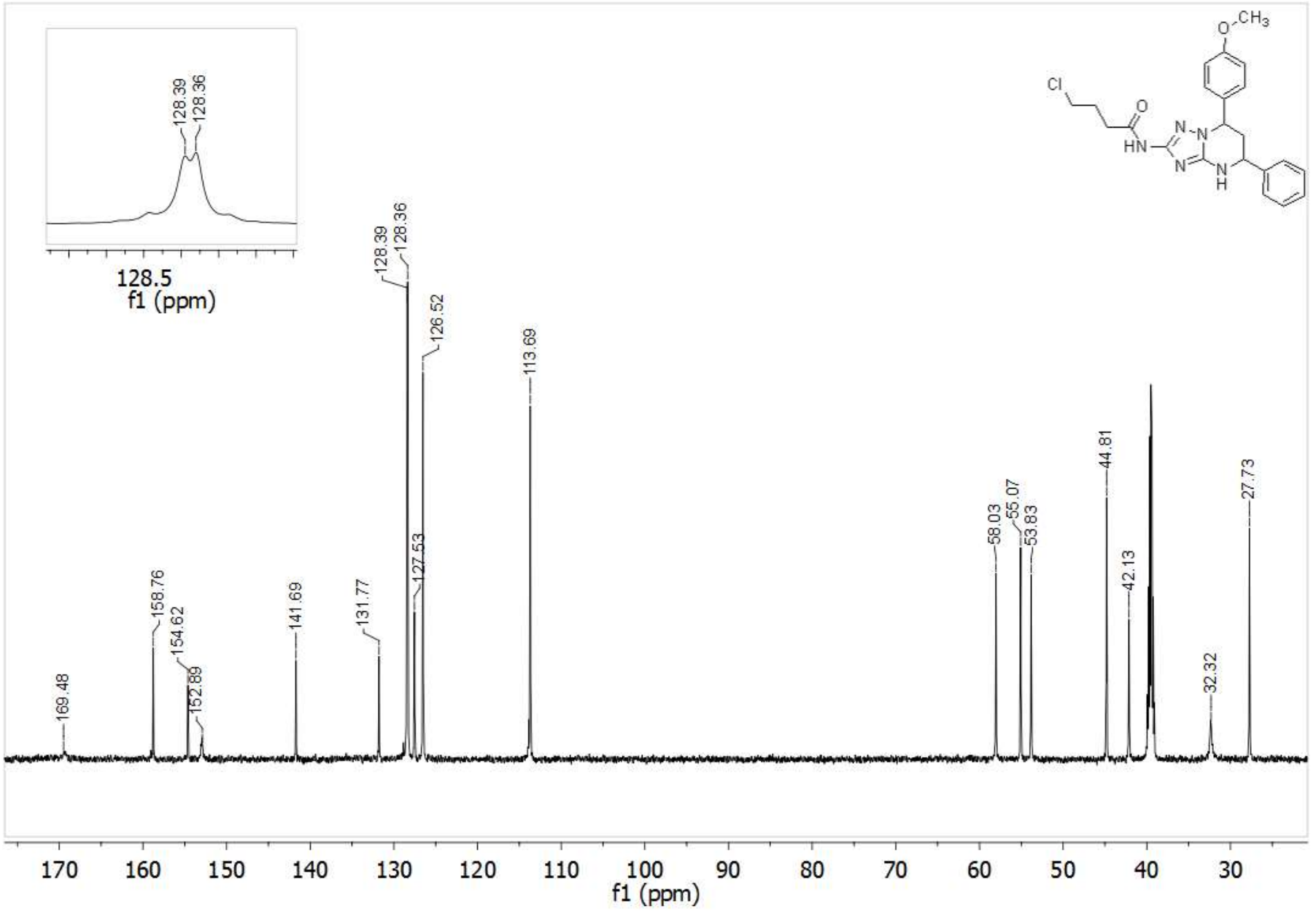
Enlarged fragment of ^{1}H-^{13}C HMBC spectrum of compound **3g** (DMSO-d_6).



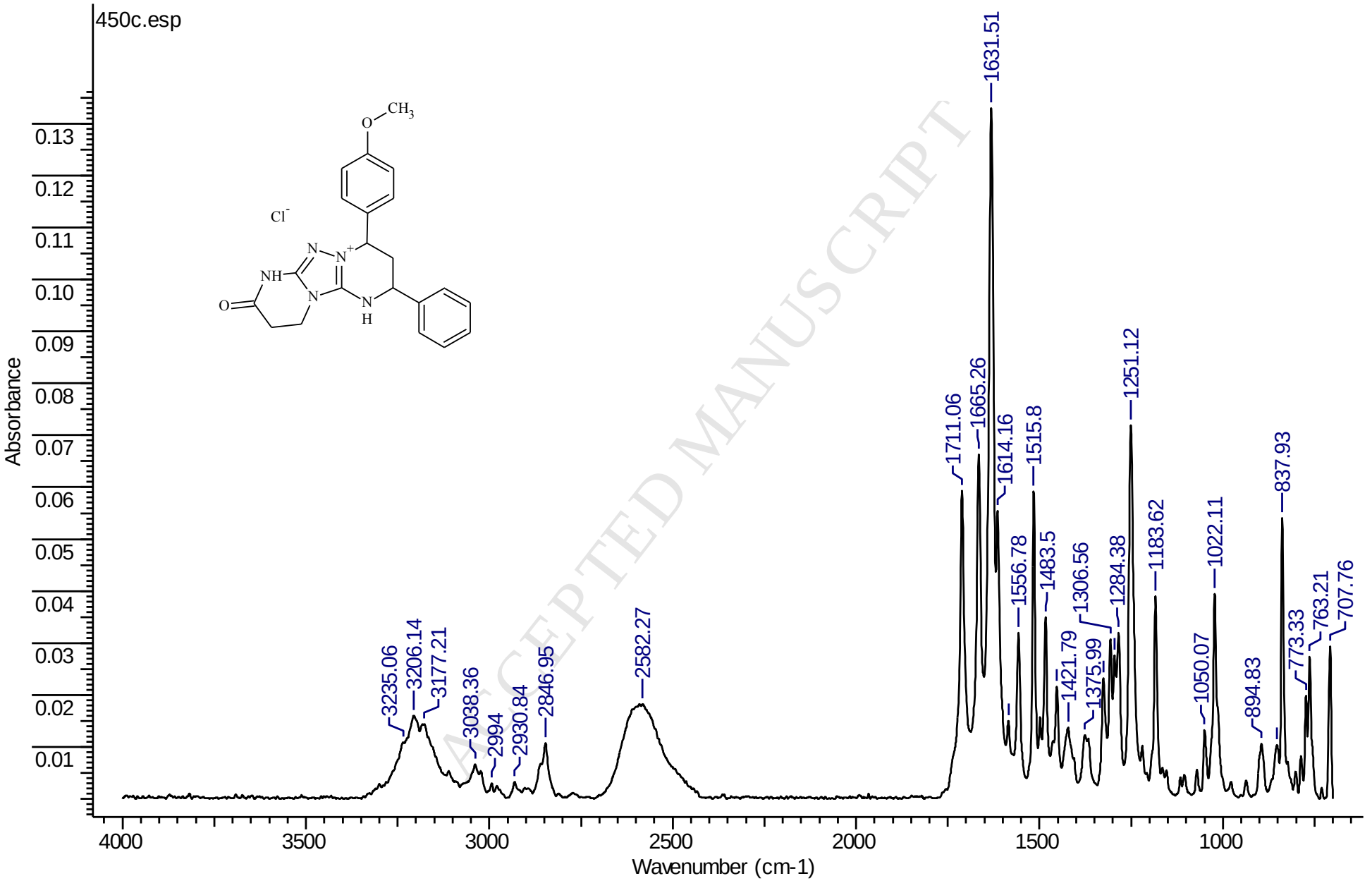
FTIR spectrum of compound **4** (ATR)**.**



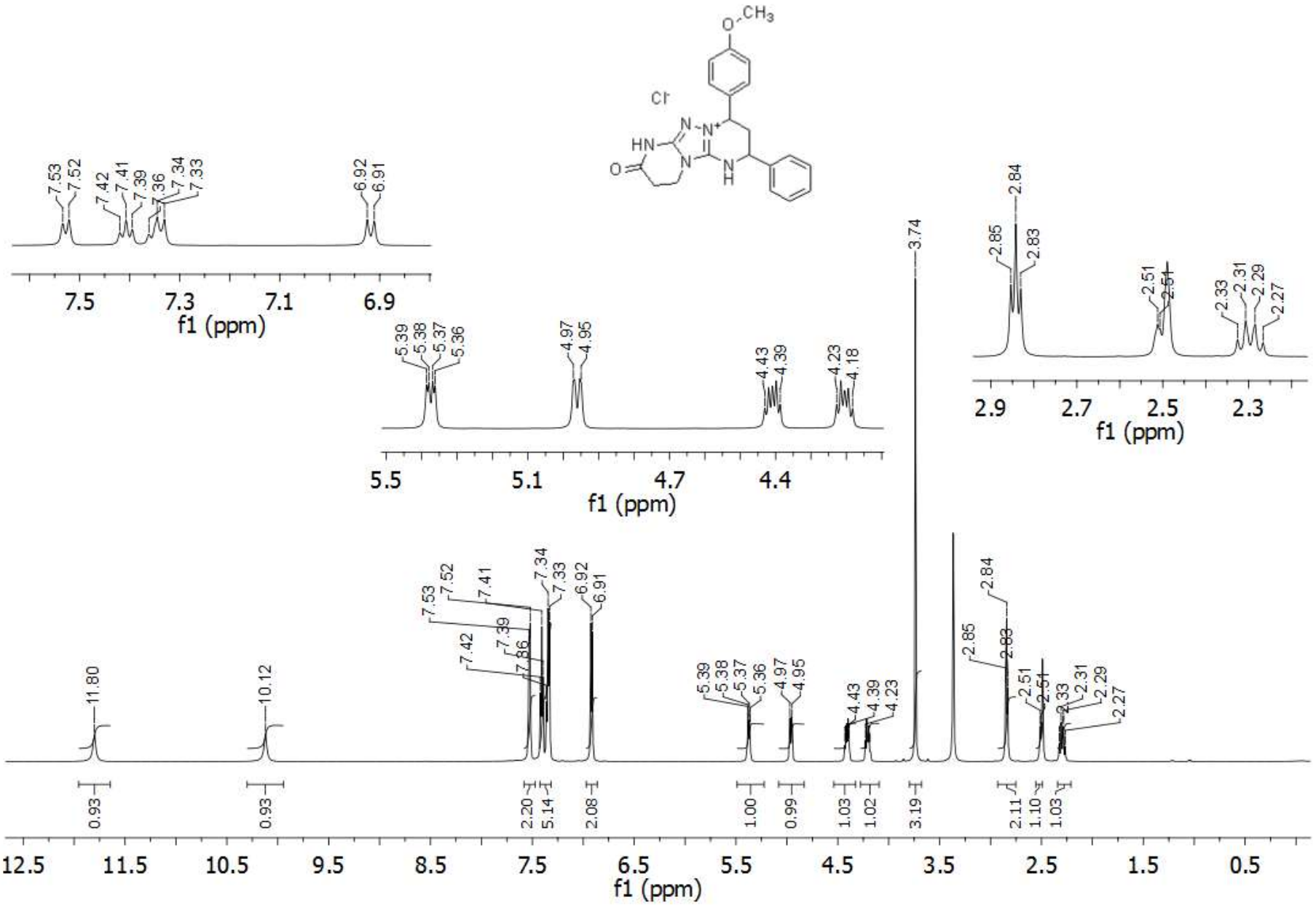
^{1}H NMR spectrum of compound **4** (DMSO-d_6, 300MHz).



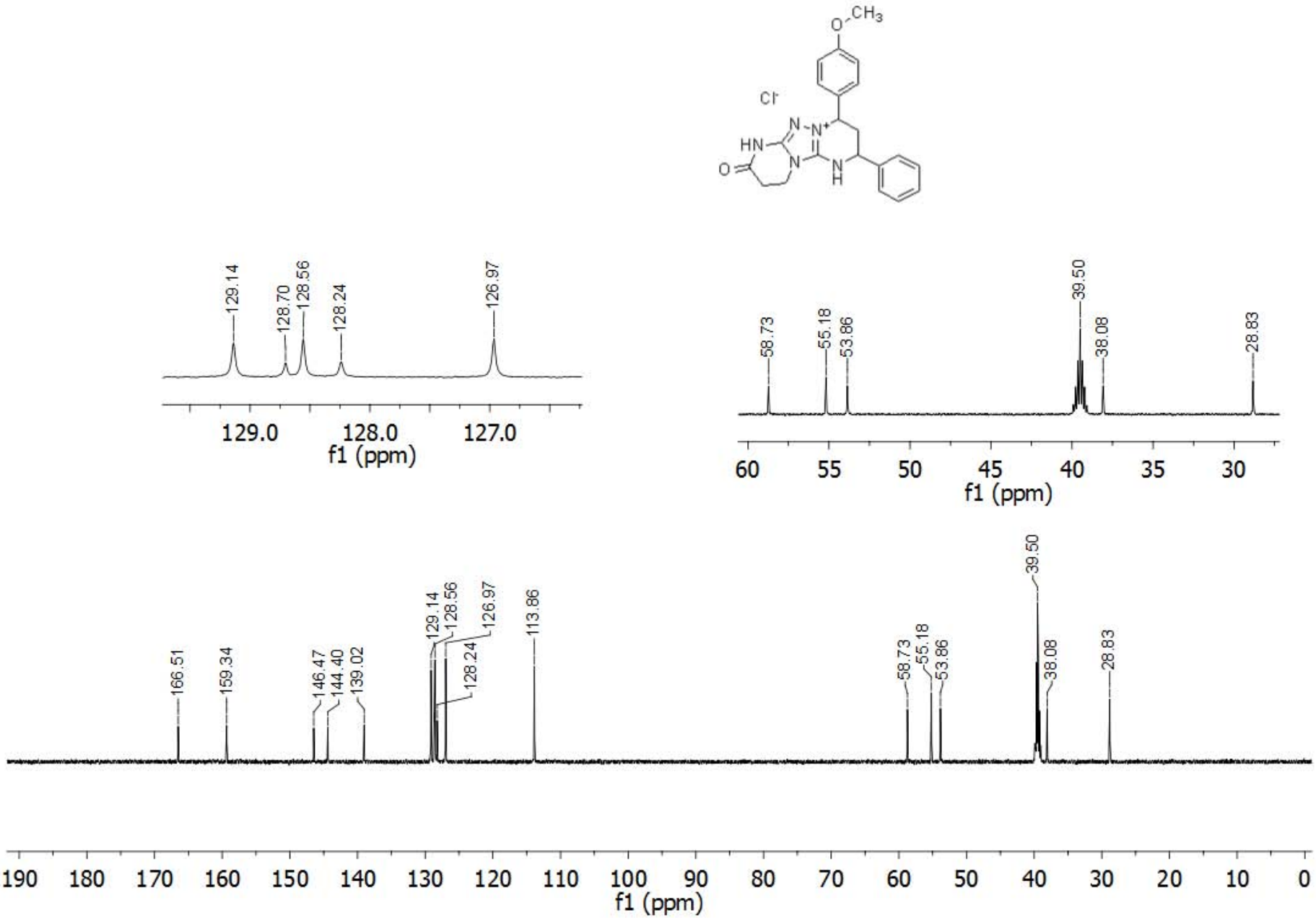
^{13}C NMR spectrum of compound **4** (DMSO-d_6, 150 MHz).



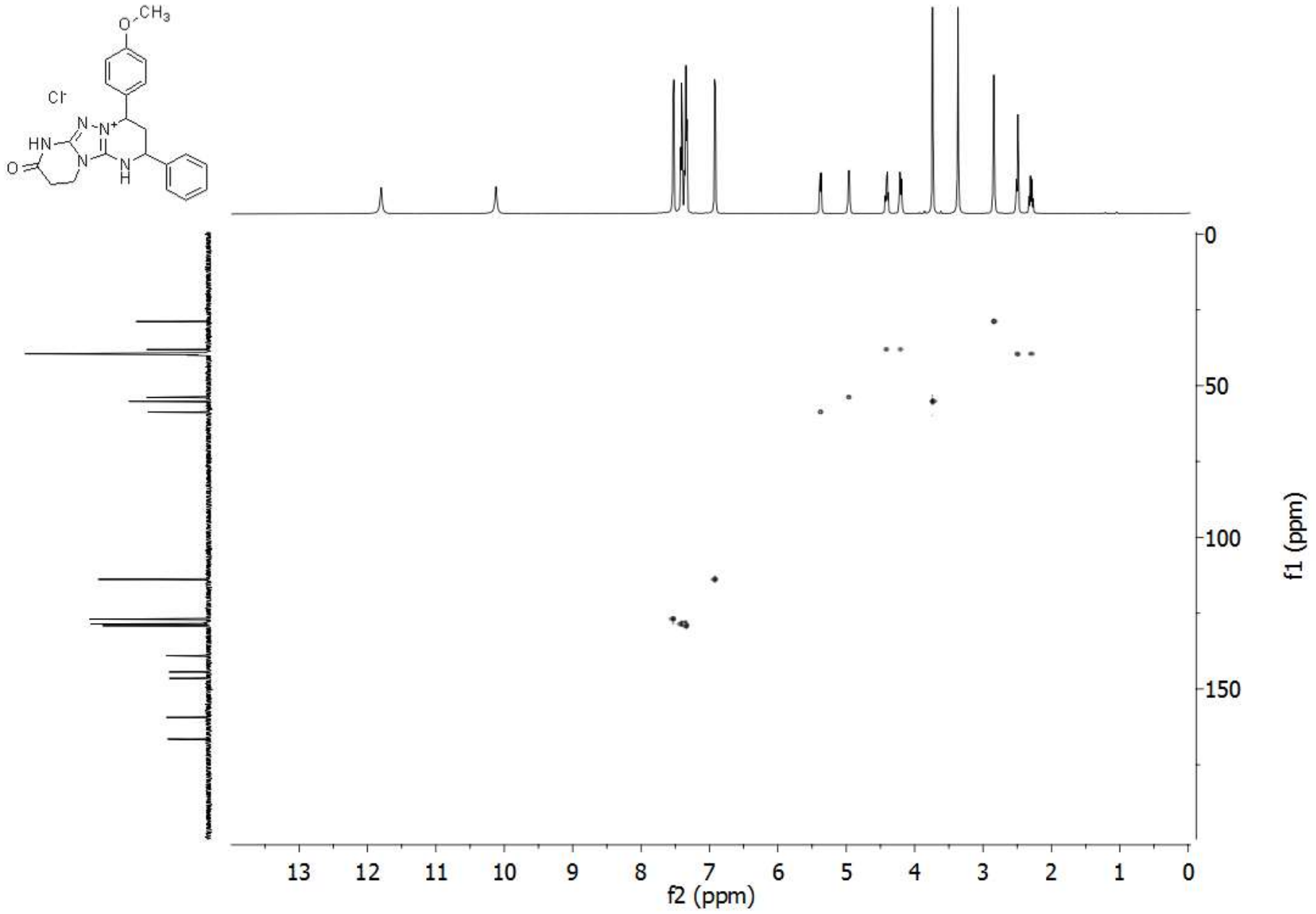
FTIR spectrum of compound **5a** (ATR).



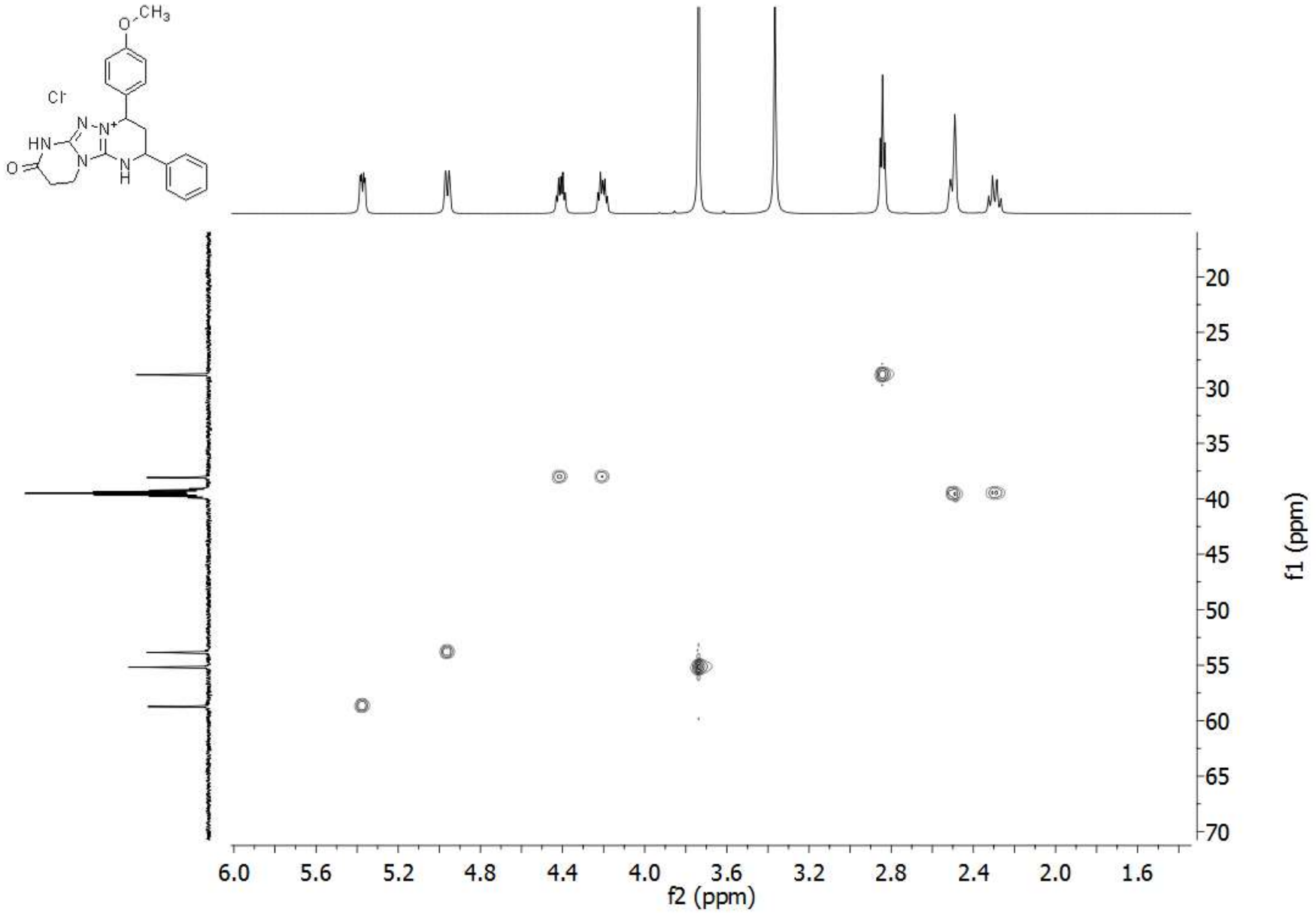
^{1}H NMR spectrum of compound **5a** (DMSO-d_6, 600 MHz).



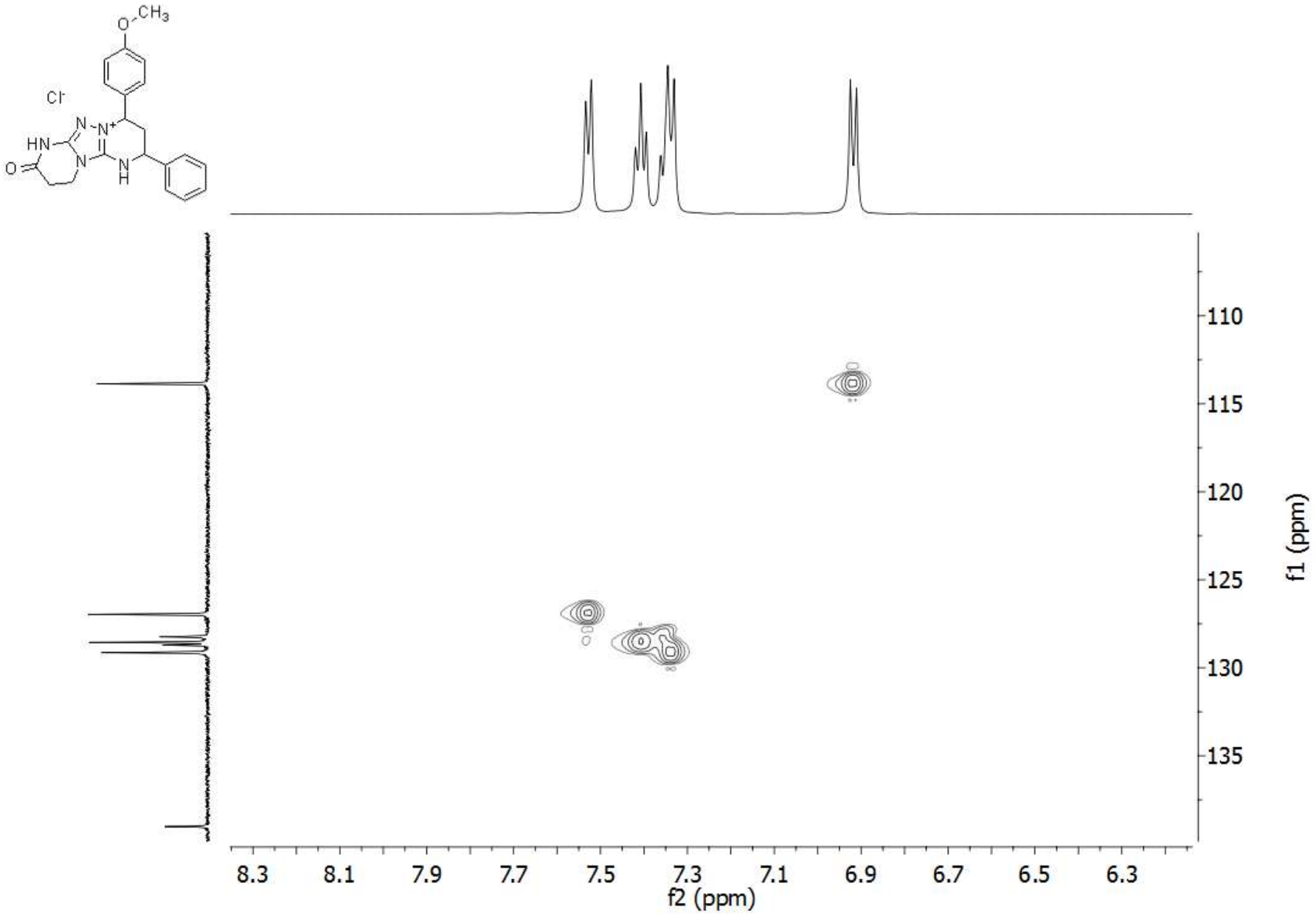
^{13}C NMR spectrum of compound **5a** (DMSO-d_6, 150 MHz).



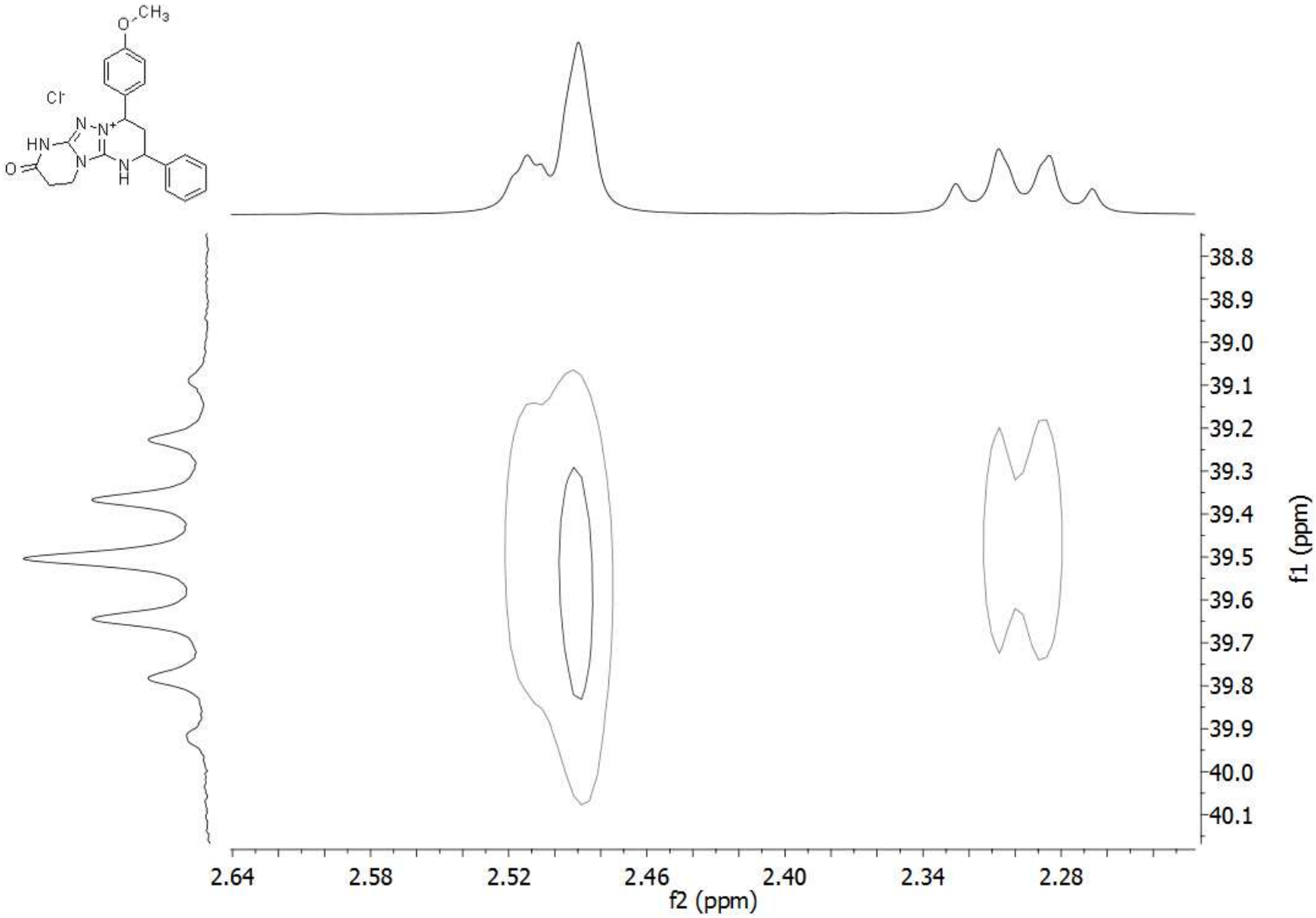
^{1}H-^{13}C HSQC spectrum of compound **5a** (DMSO-d_6).



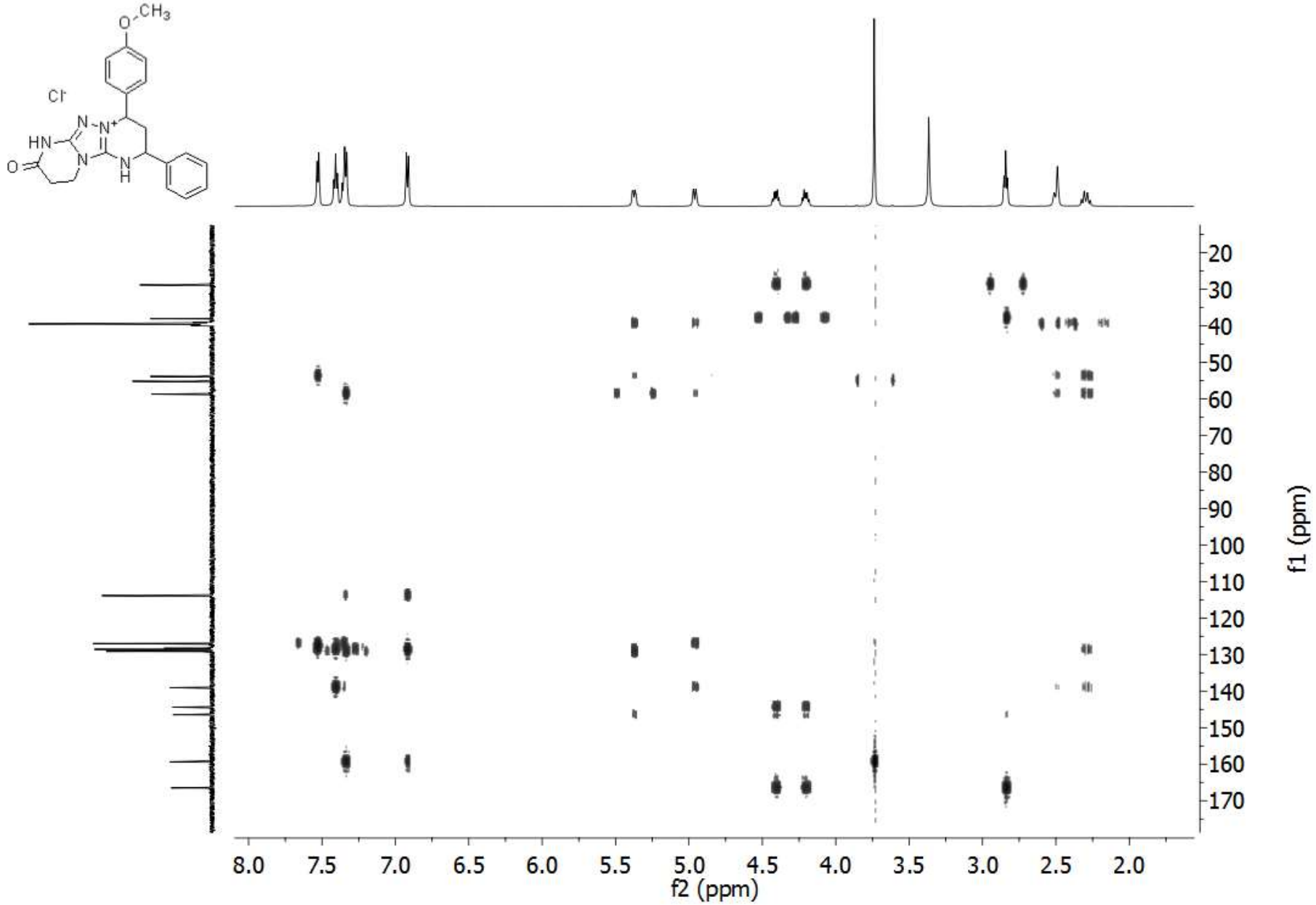
Enlarged fragment of ^{1}H-^{13}C HSQC spectrum of compound **5a** (DMSO-d_6).



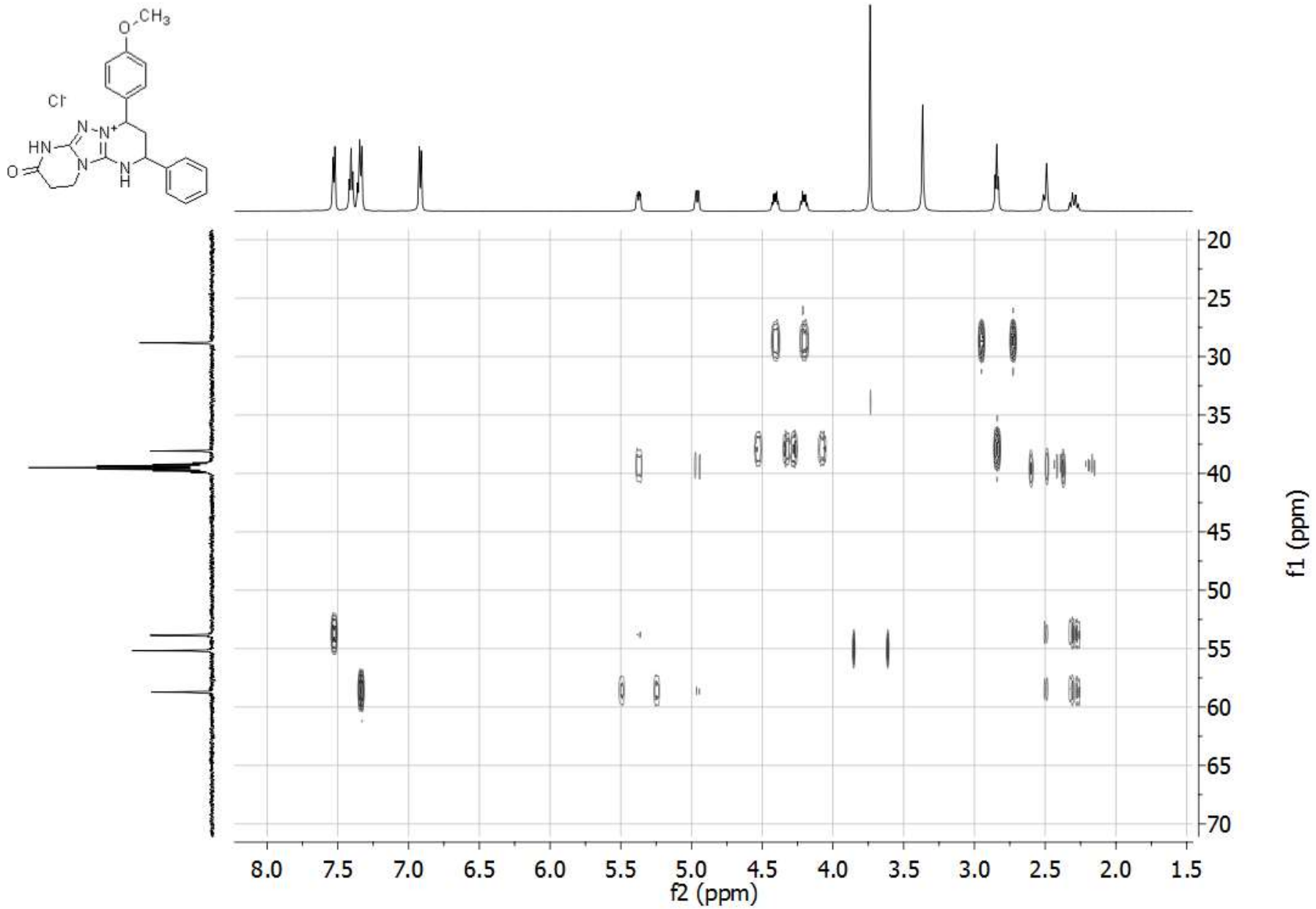
Enlarged fragment of ^{1}H-^{13}C HSQC spectrum of compound **5a** (DMSO-d_6).



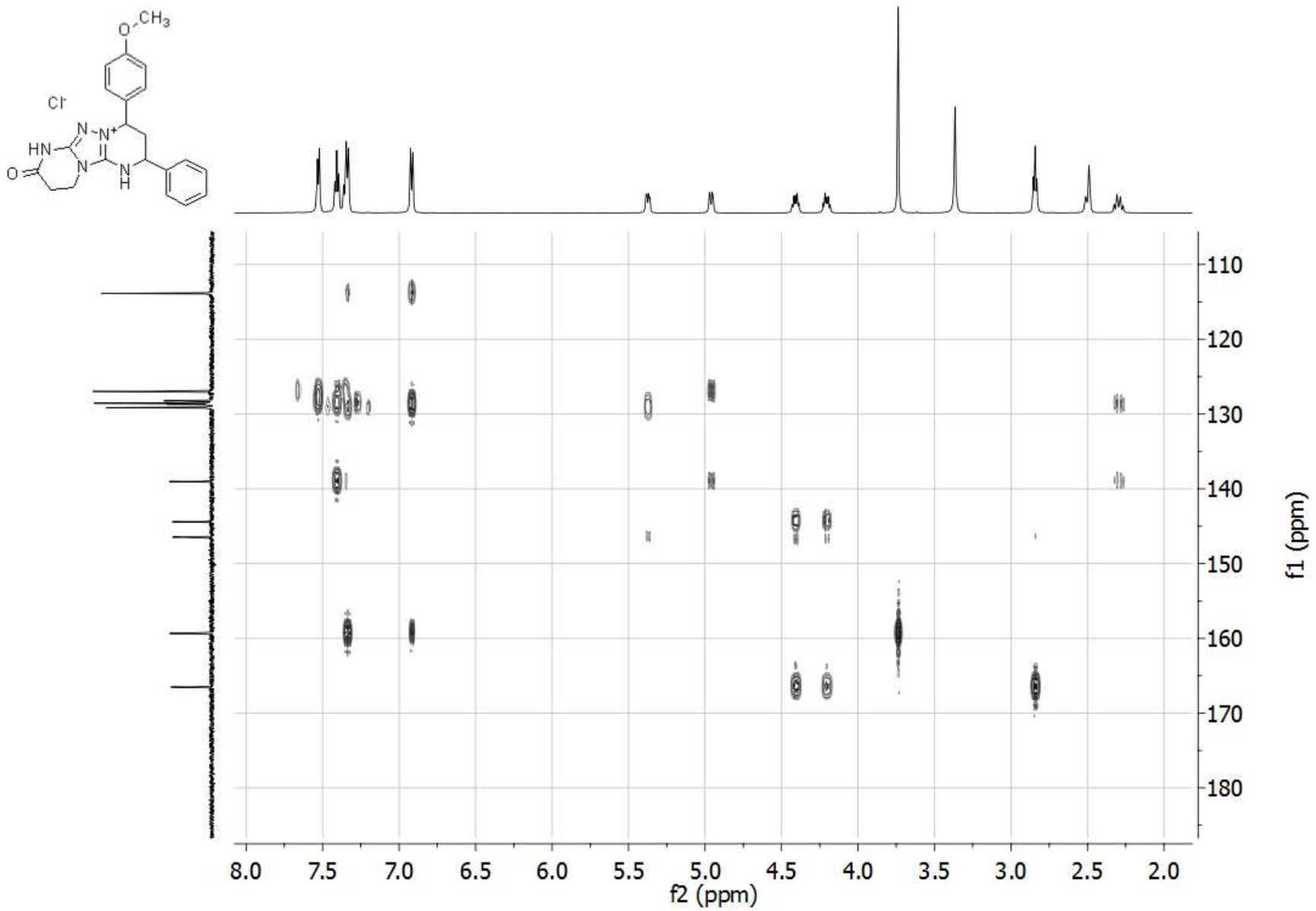
Enlarged fragment of ^{1}H-^{13}C HSQC spectrum of compound **5a** (DMSO-d_6). This figure discloses a position of C3 signal which is masked by the signal of DMSO in ^{13}C NMR spectrum.



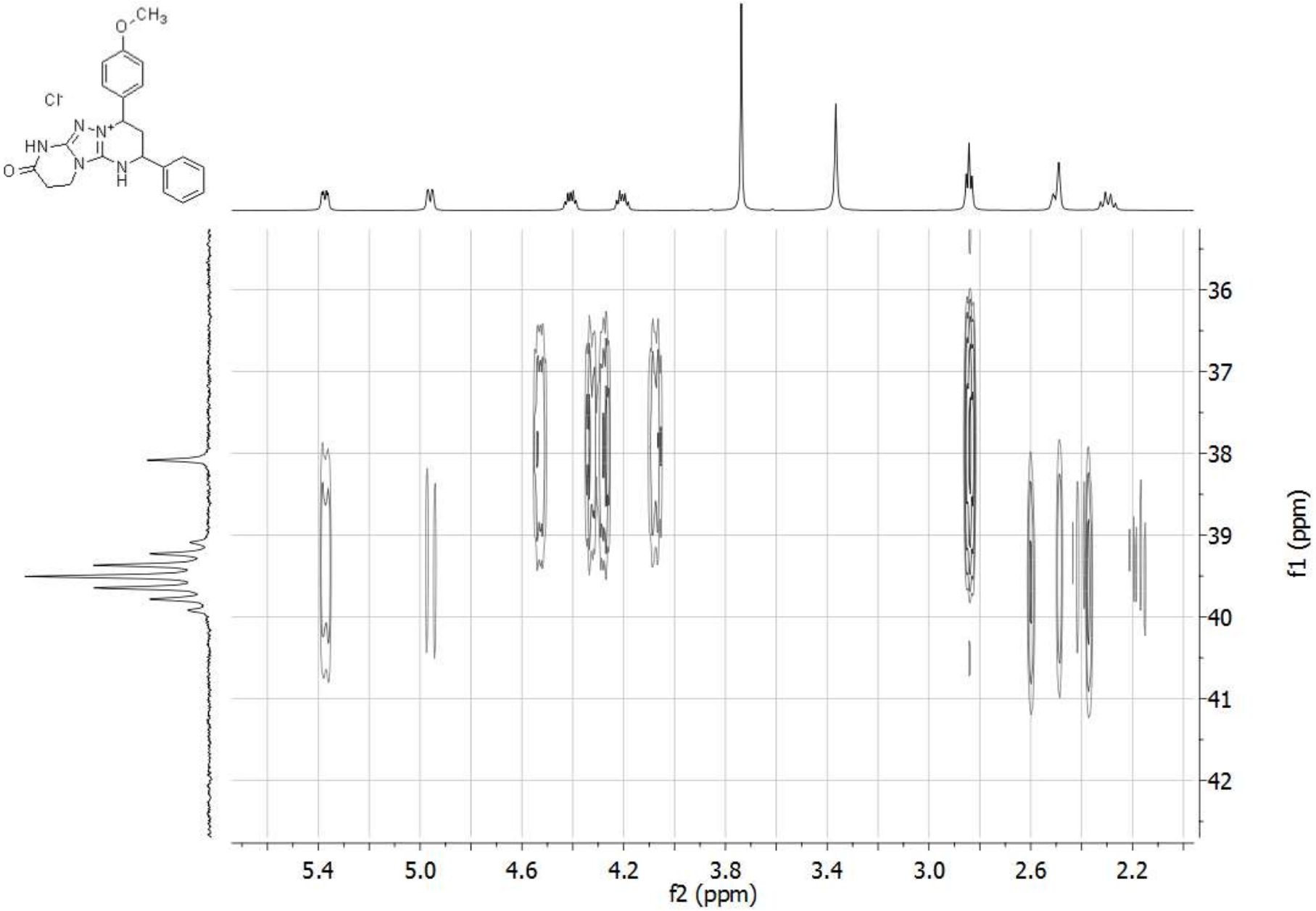
^{1}H-^{13}C HMBC spectrum of compound **5a** (DMSO-d_6).



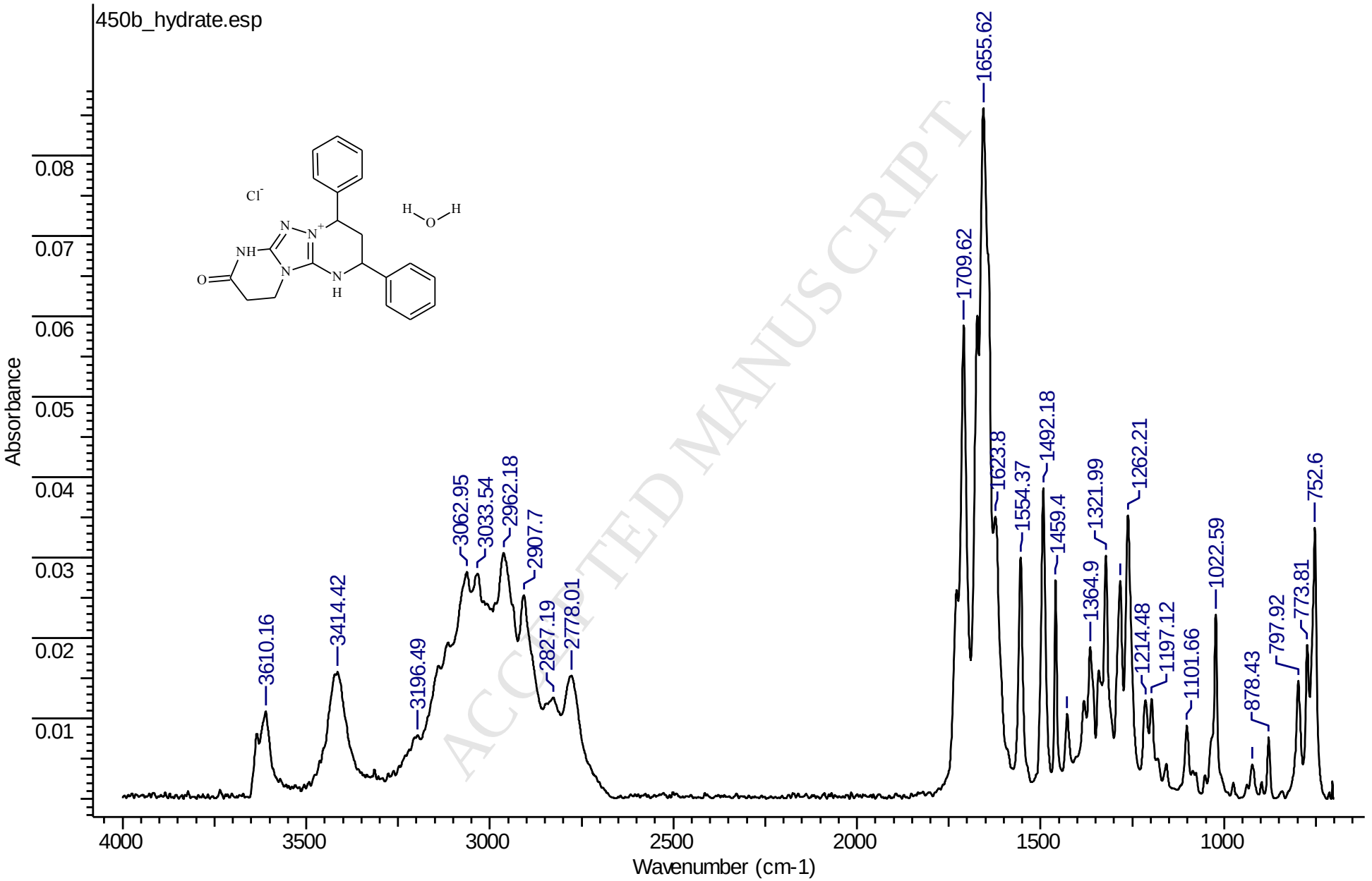
Enlarged fragment of ^{1}H-^{13}C HMBC spectrum of compound **5a** (DMSO-d_6).



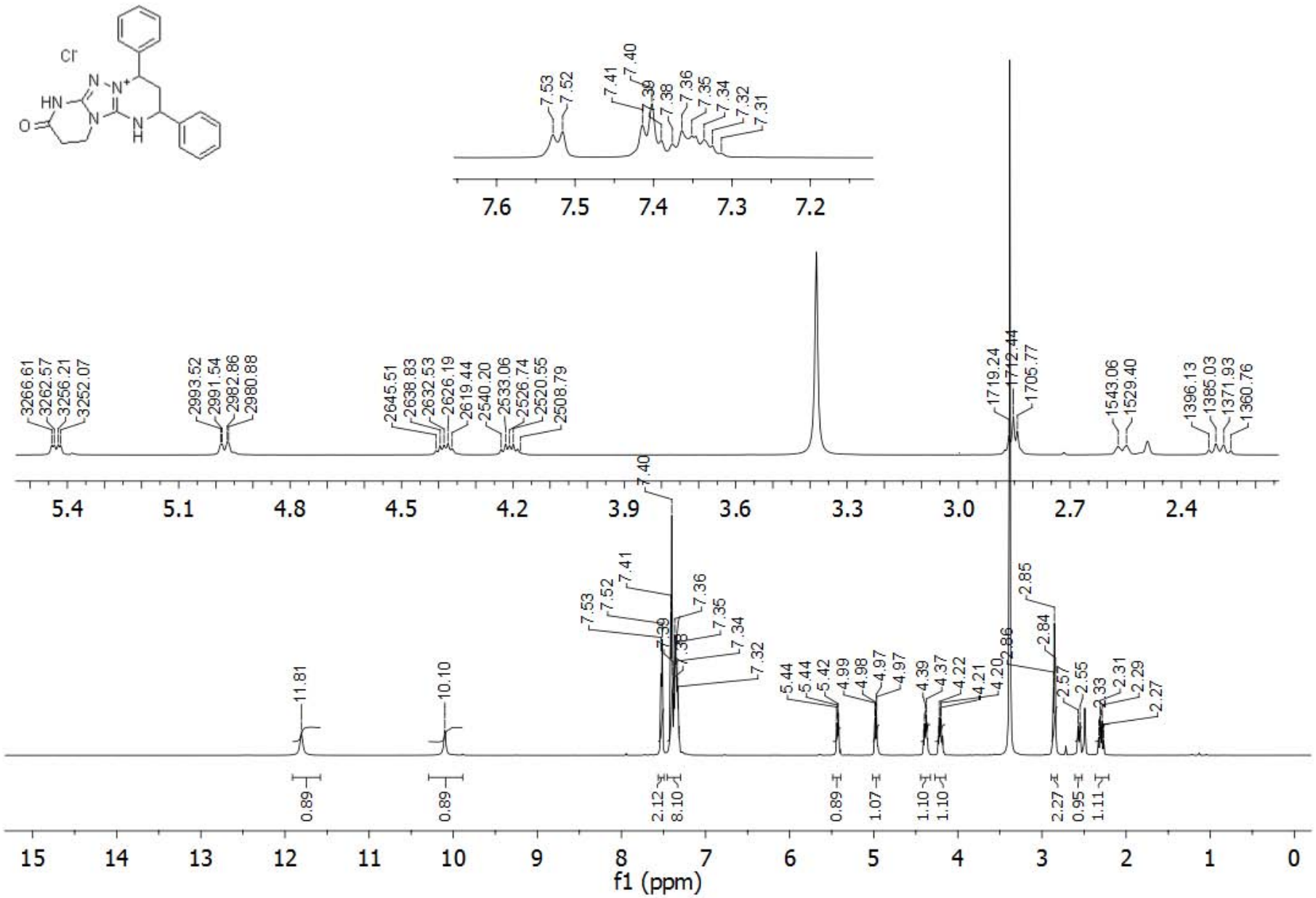
Enlarged fragment of ^{1}H-^{13}C HMBC spectrum of compound **5a** (DMSO-d_6).



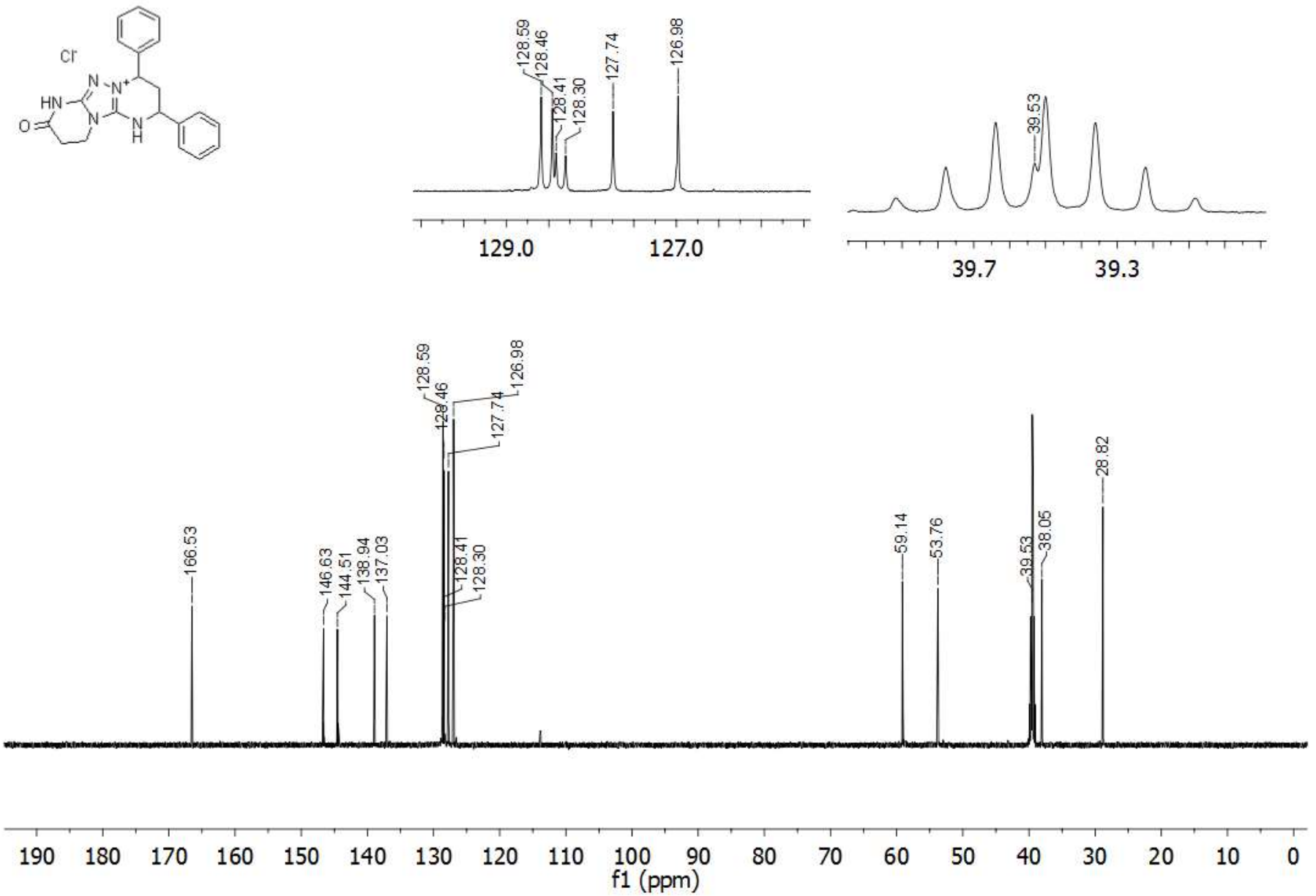
Enlarged fragment of ^{1}H-^{13}C HMBC spectrum of compound **5a** (DMSO-d_6). This figure discloses a position of C3 signal which is masked by the signal of DMSO in ^{13}C NMR spectrum.



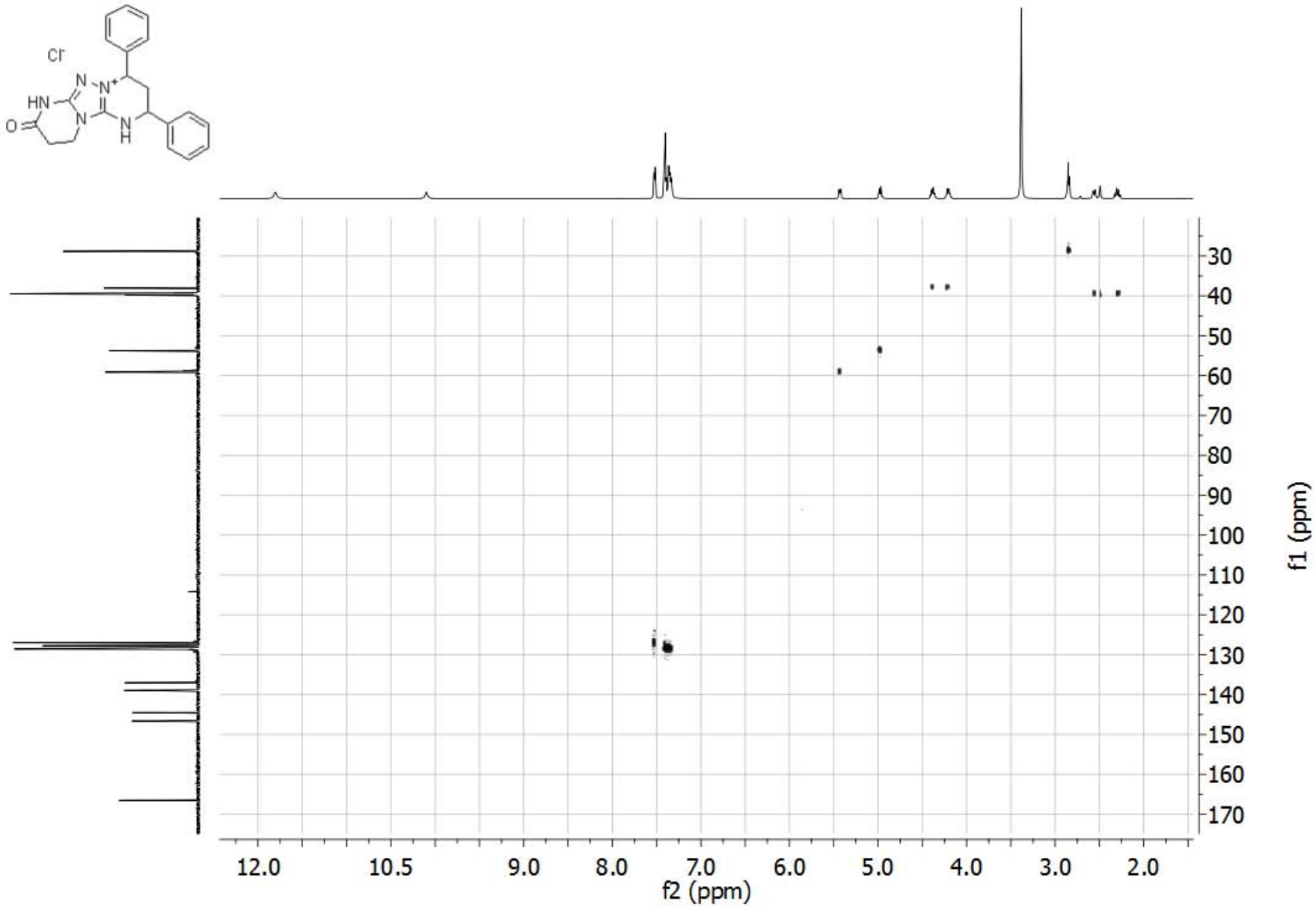
FTIR spectrum of compound **5b** (ATR).



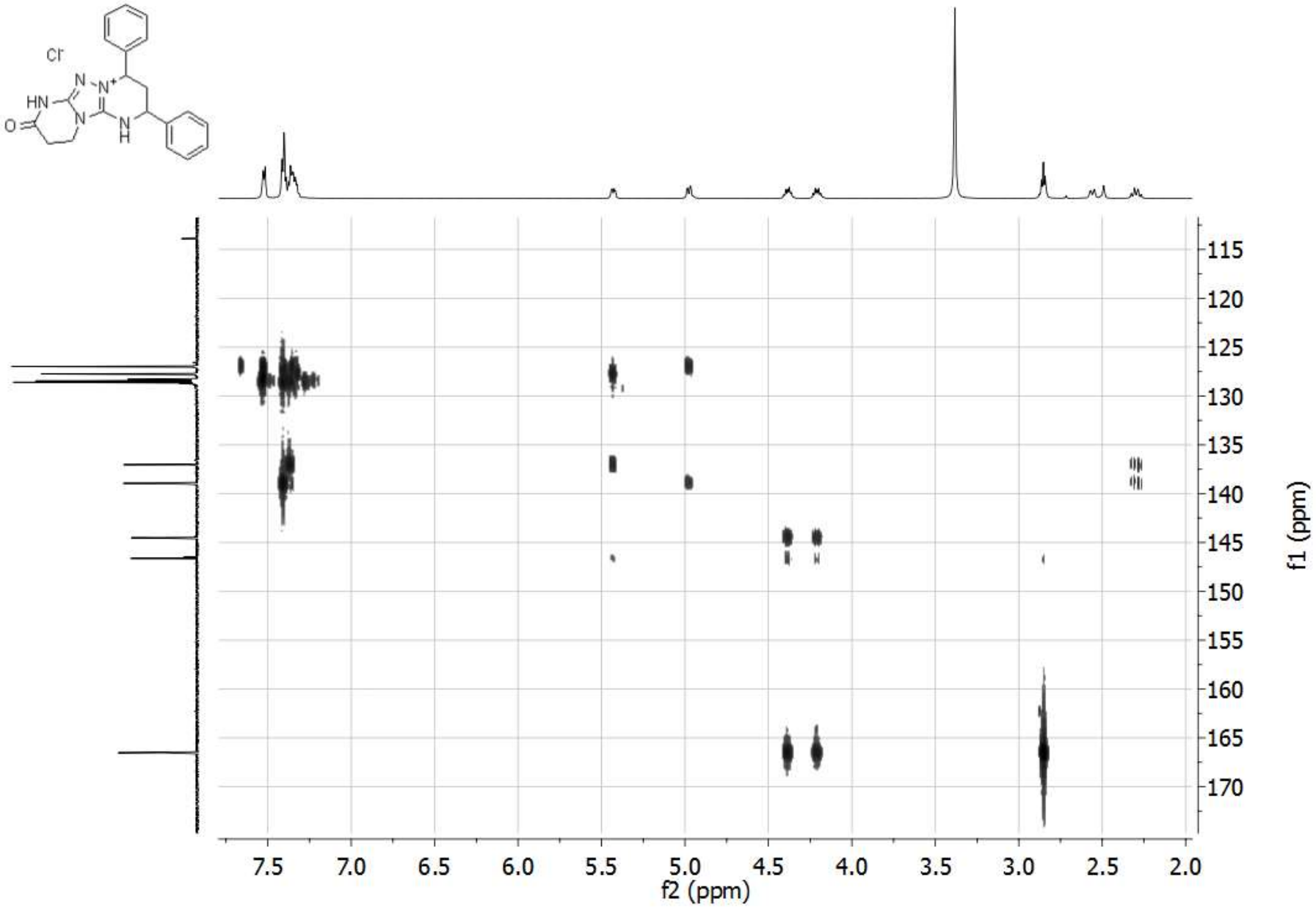
^{1}H NMR spectrum of compound **5b** (DMSO-d_6, 600 MHz).



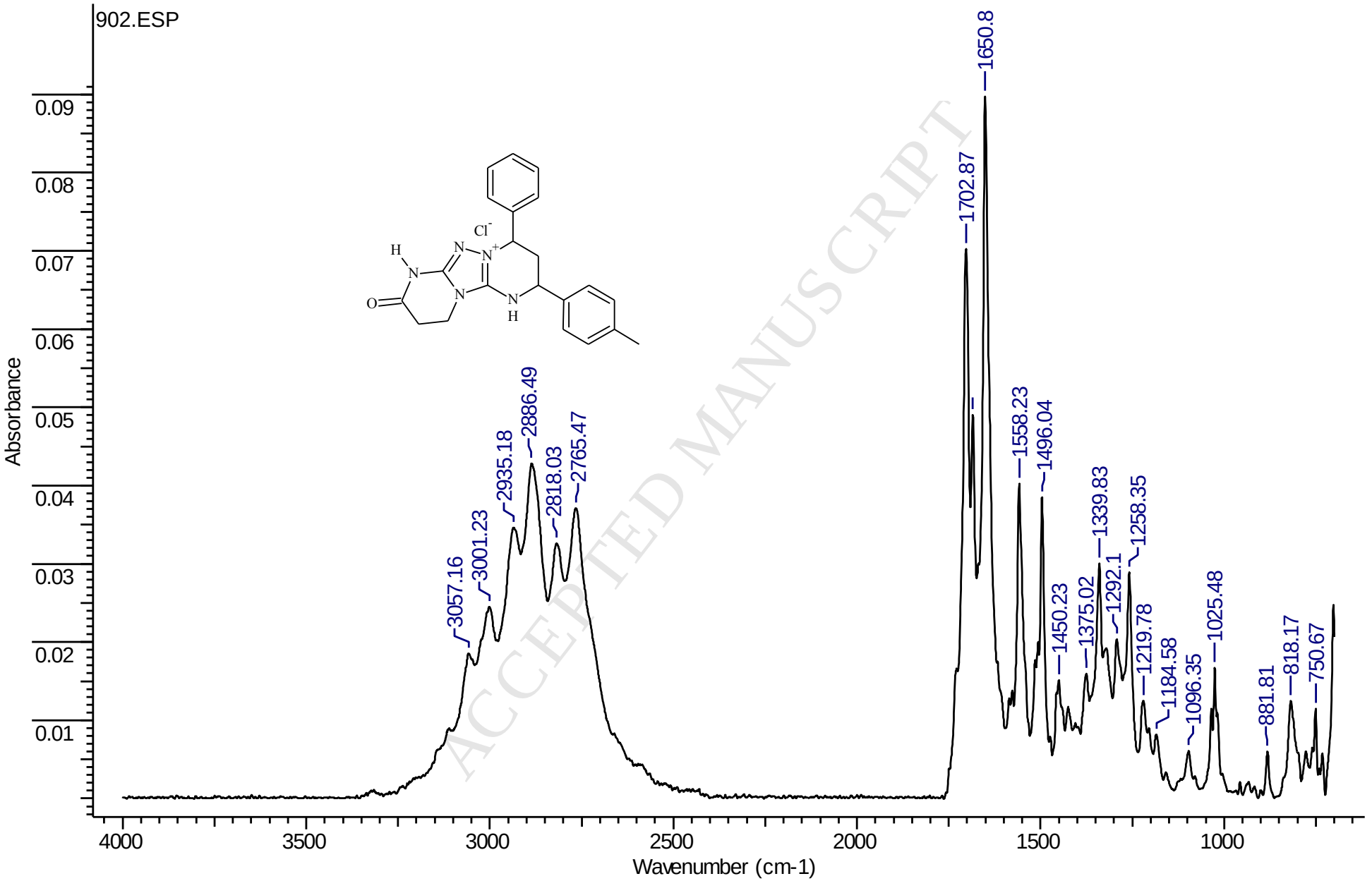
^{13}C NMR spectrum of compound **5b** (DMSO-d_6, 150 MHz).



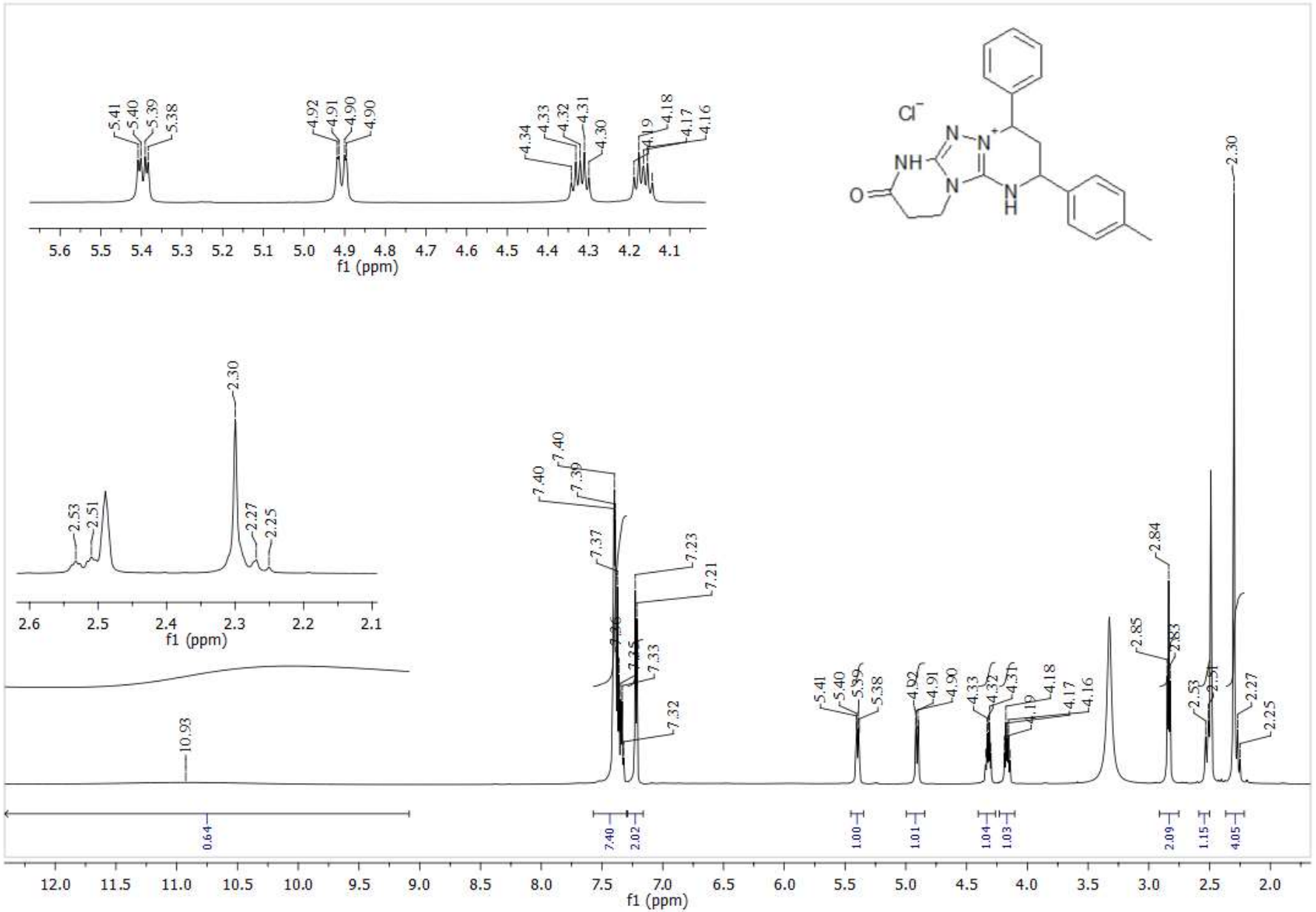
^{1}H-^{13}C HSQC spectrum of compound **5b** (DMSO-d_6).



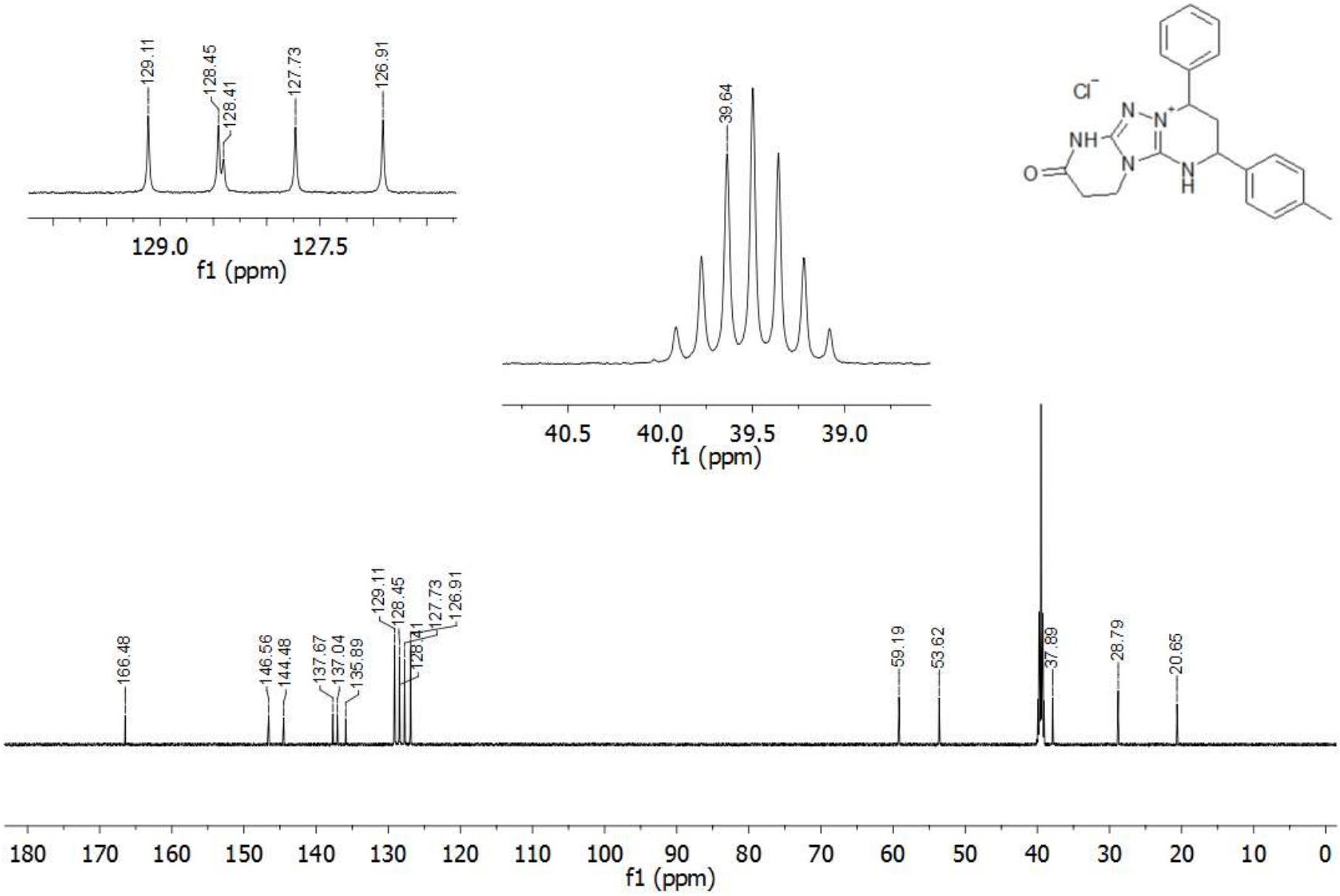
Enlarged fragment of ^{1}H-^{13}C HMBC spectrum of compound **5b** (DMSO-d_6).



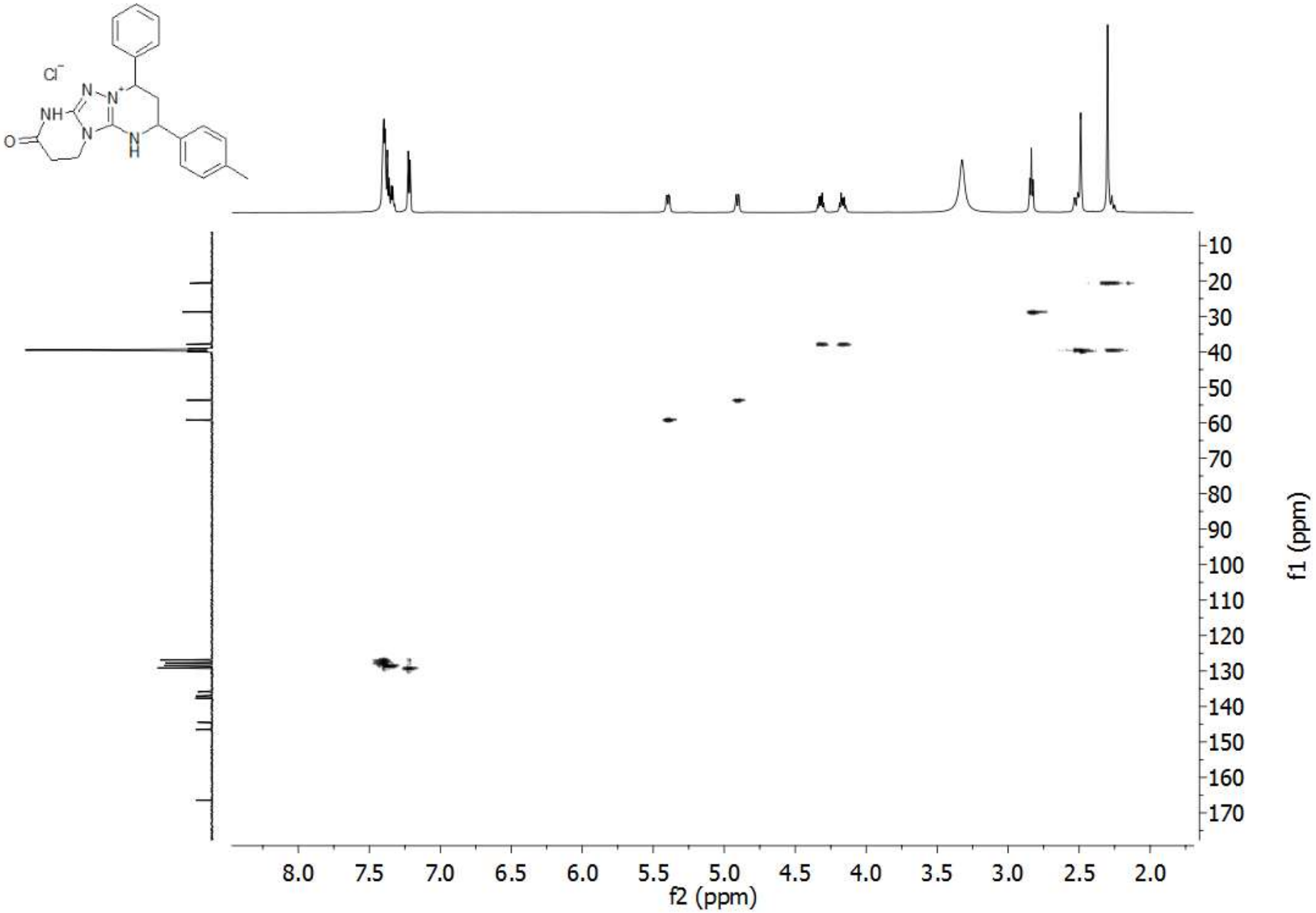
FTIR spectrum of compound **5c** (ATR).



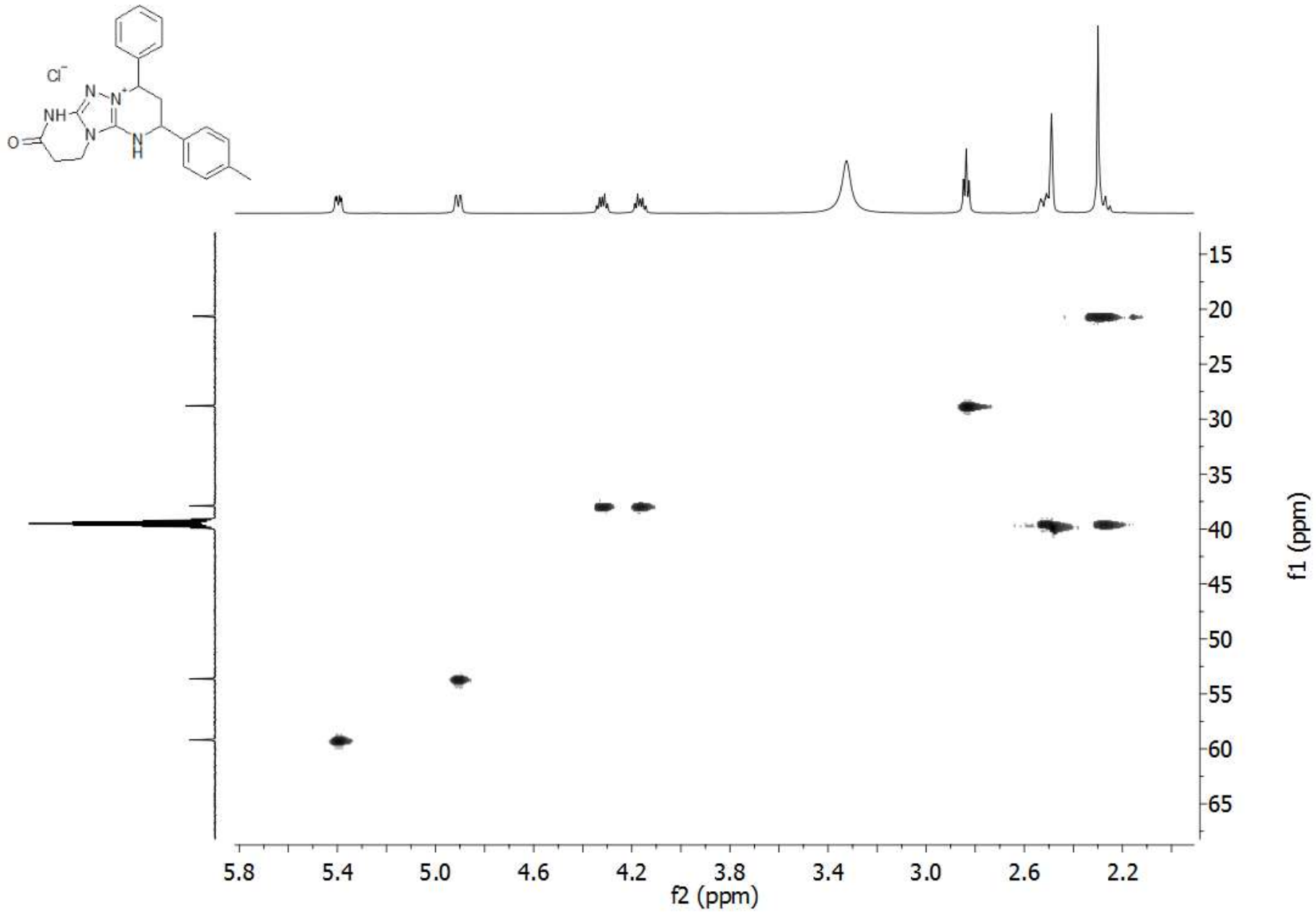
^{1}H NMR spectrum of compound **5c** (DMSO-d_6, 600 MHz).



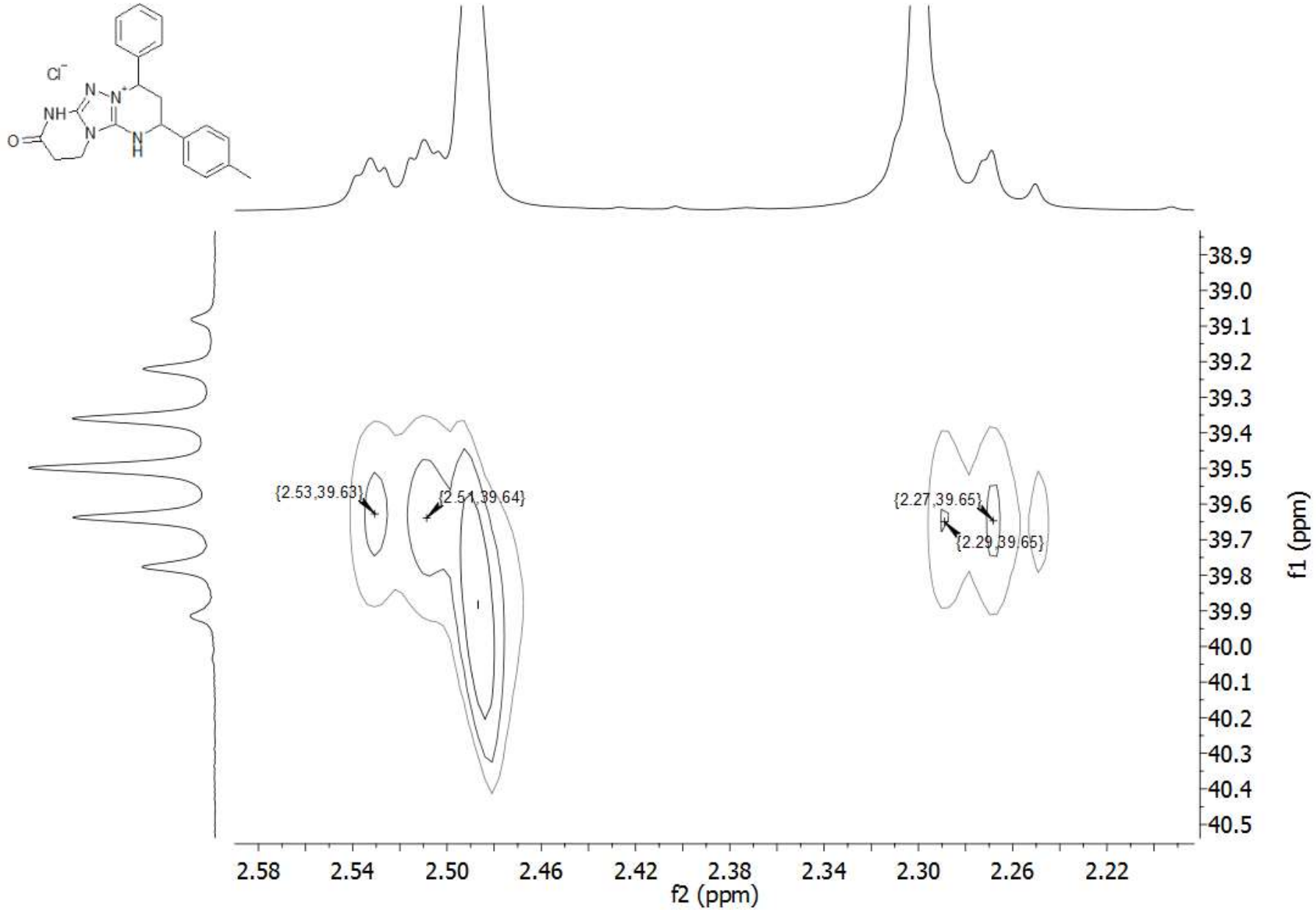
^{13}C NMR spectrum of compound **5c** (DMSO-d_6, 150 MHz).



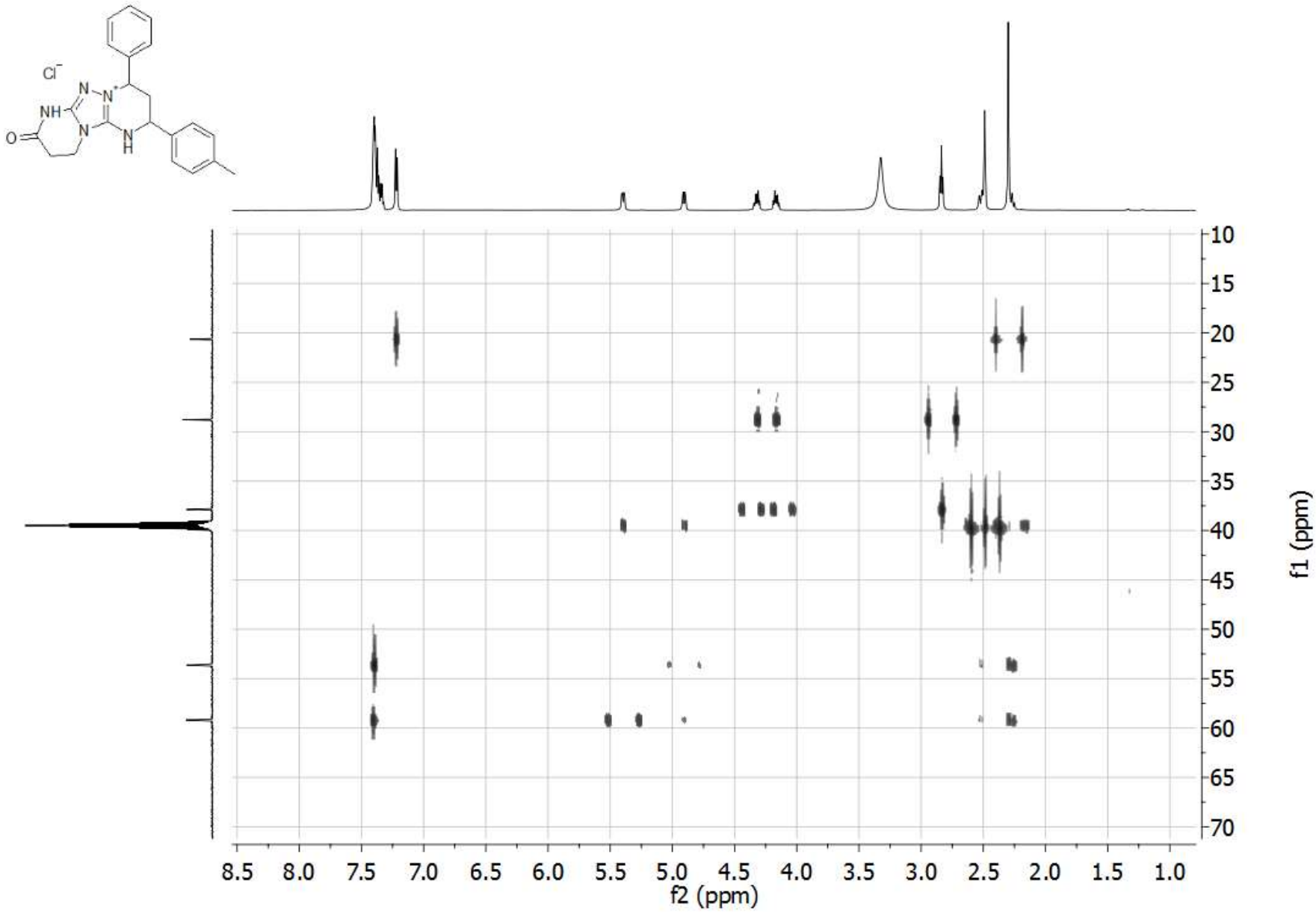
^{1}H-^{13}C HSQC spectrum of compound **5c** (DMSO-d_6).



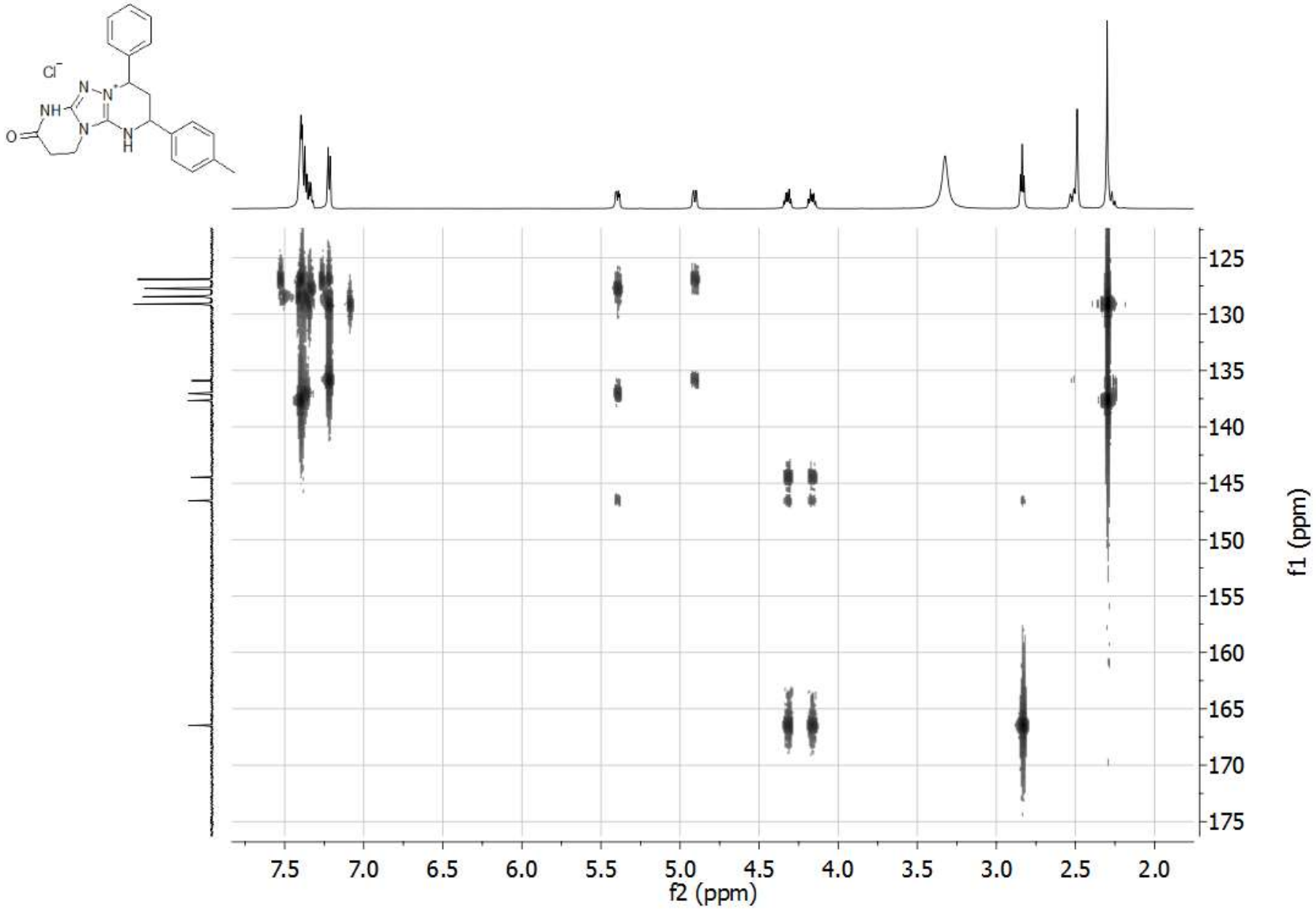
Enlarged fragment of ^{1}H-^{13}C HSQC spectrum of compound **5c** (DMSO-d_6).



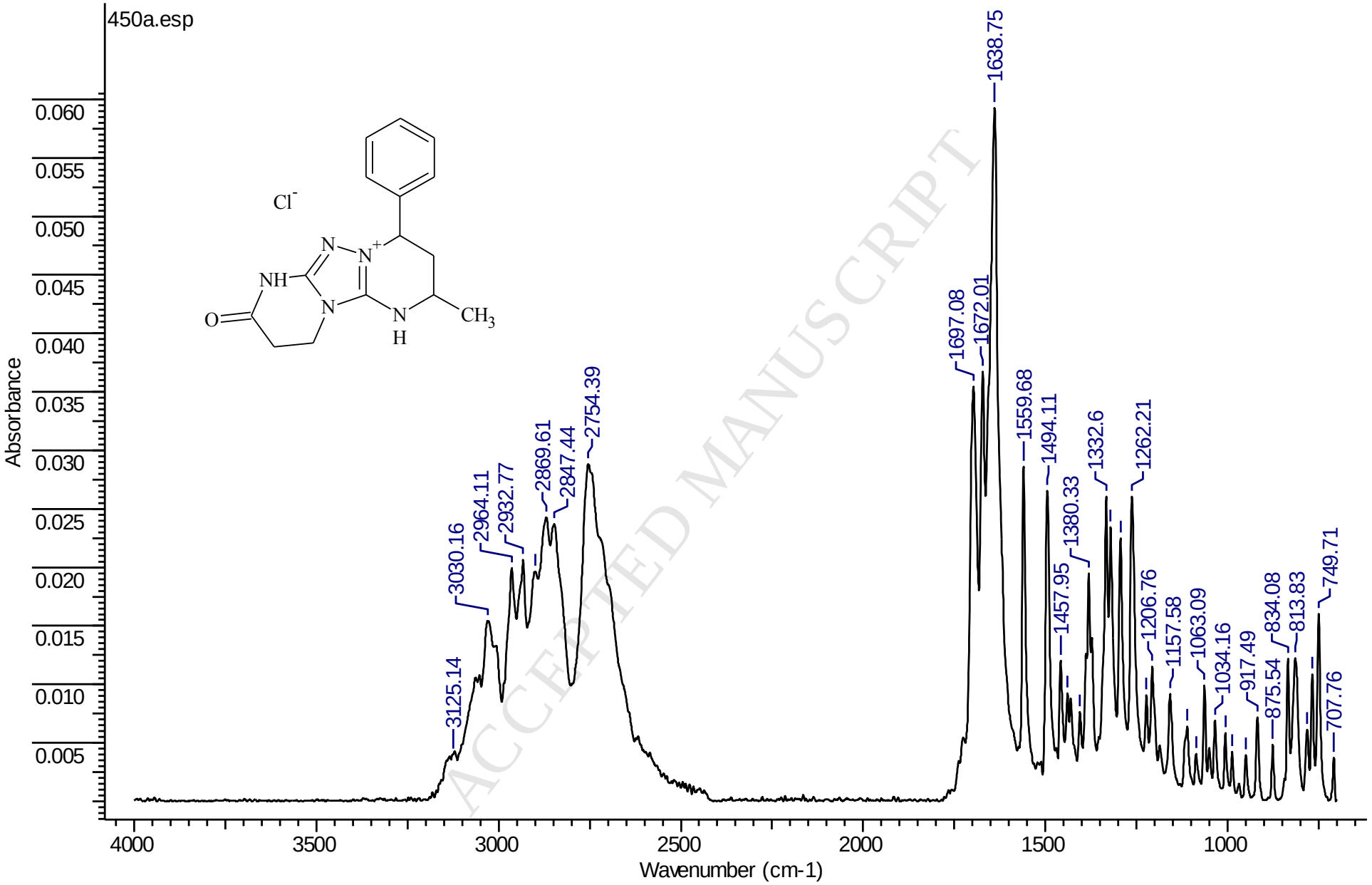
Enlarged fragment of ^{1}H-^{13}C HSQC spectrum of compound **5c** (DMSO-d_6). This figure discloses a position of C3 signal which is masked by the signal of DMSO in ^{13}C NMR spectrum.



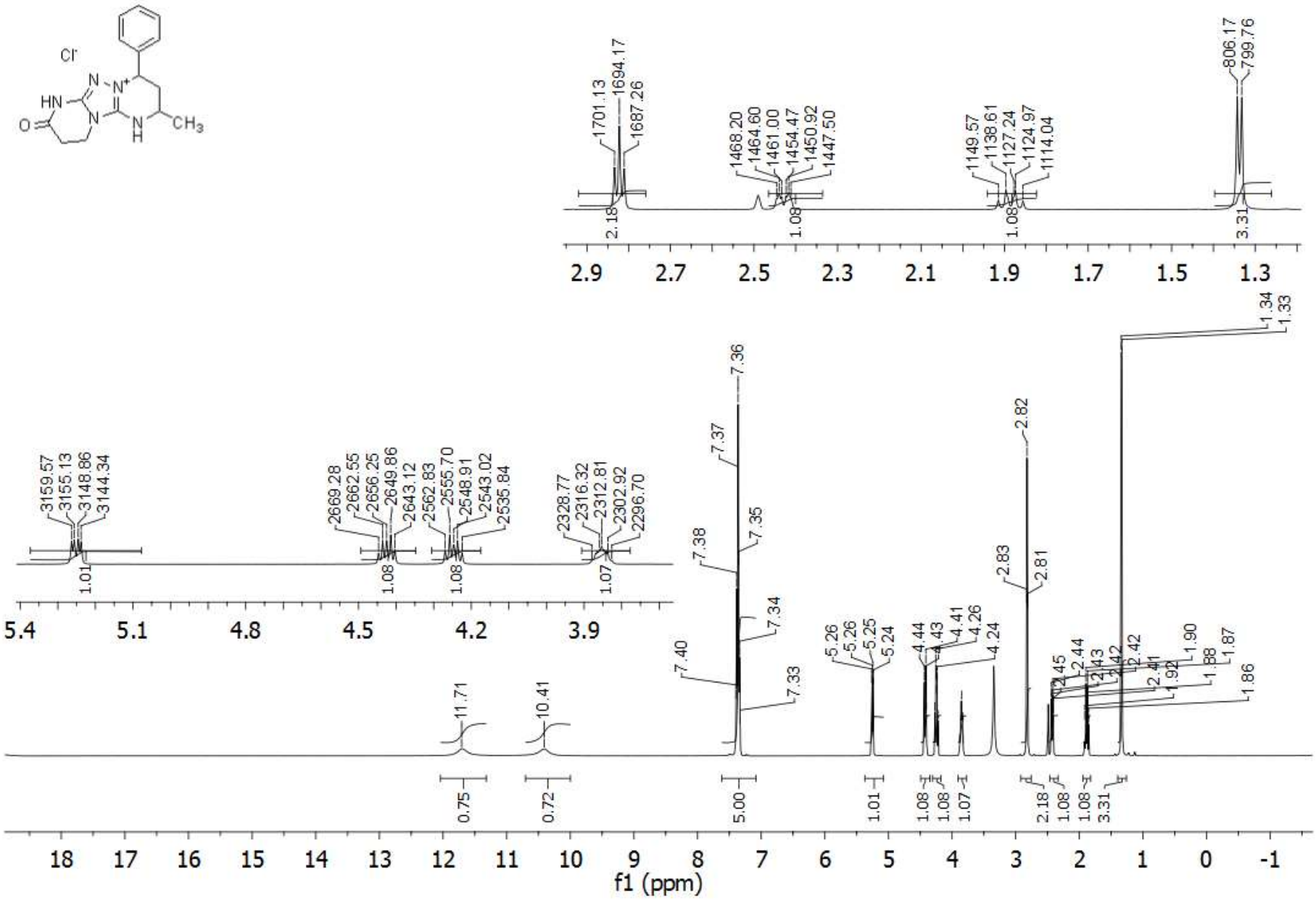
Enlarged fragment (high field) of ^{1}H-^{13}C HMBC spectrum of compound **5c** (DMSO-d_6).



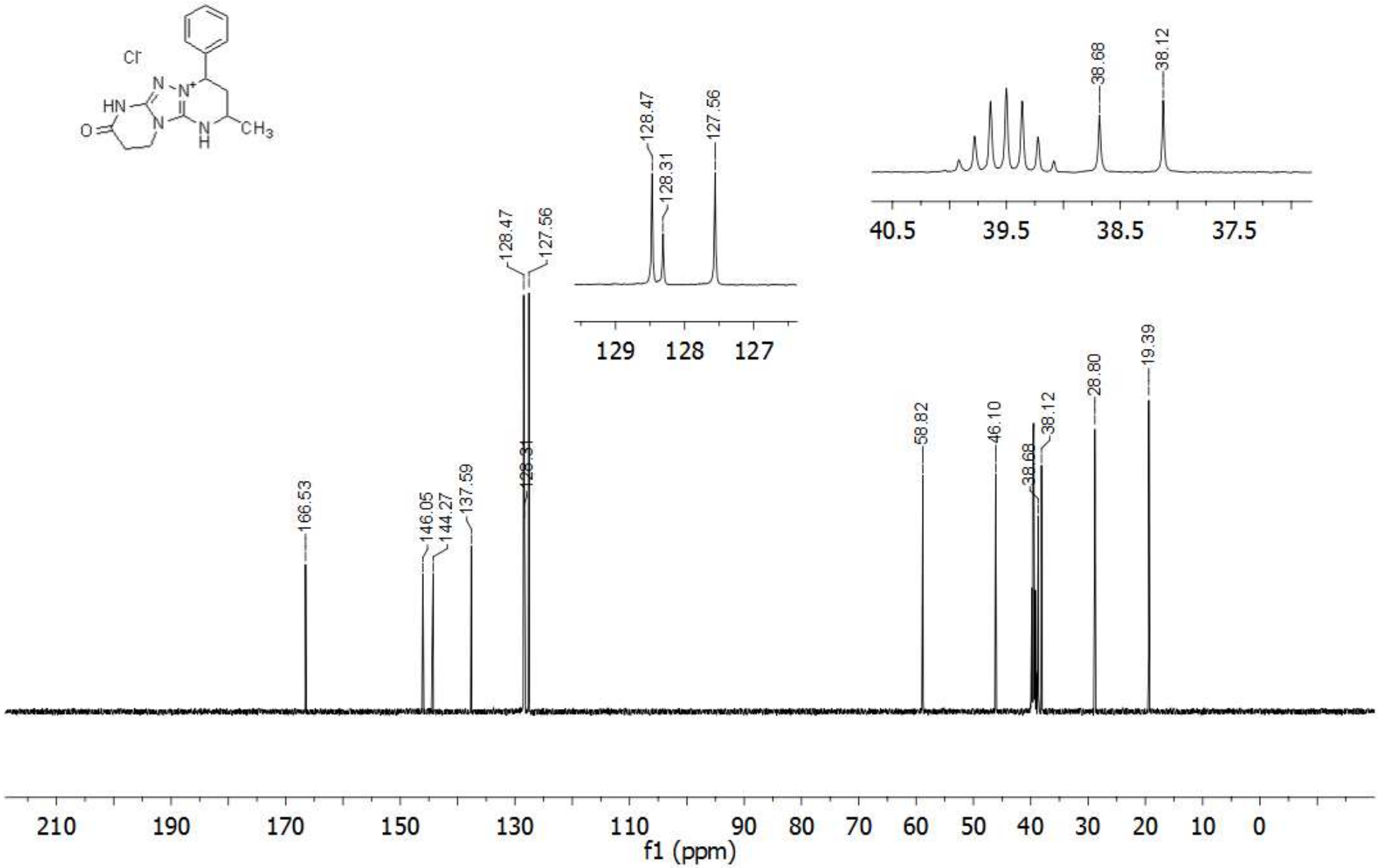
Enlarged fragment (low field) of ^{1}H-^{13}C HMBC spectrum of compound **5c** (DMSO-d_6).



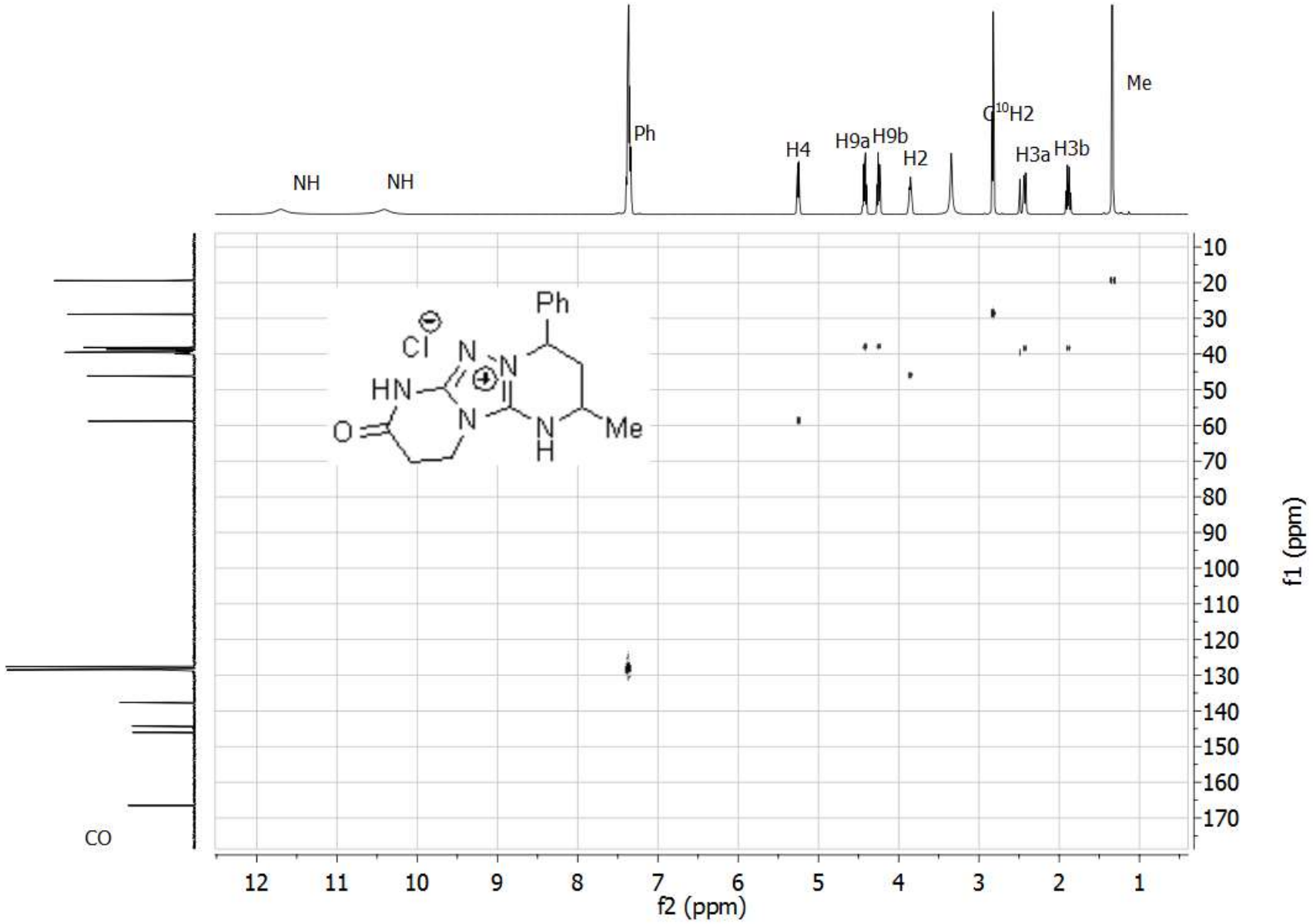
FTIR spectrum of compound **5d** (ATR).



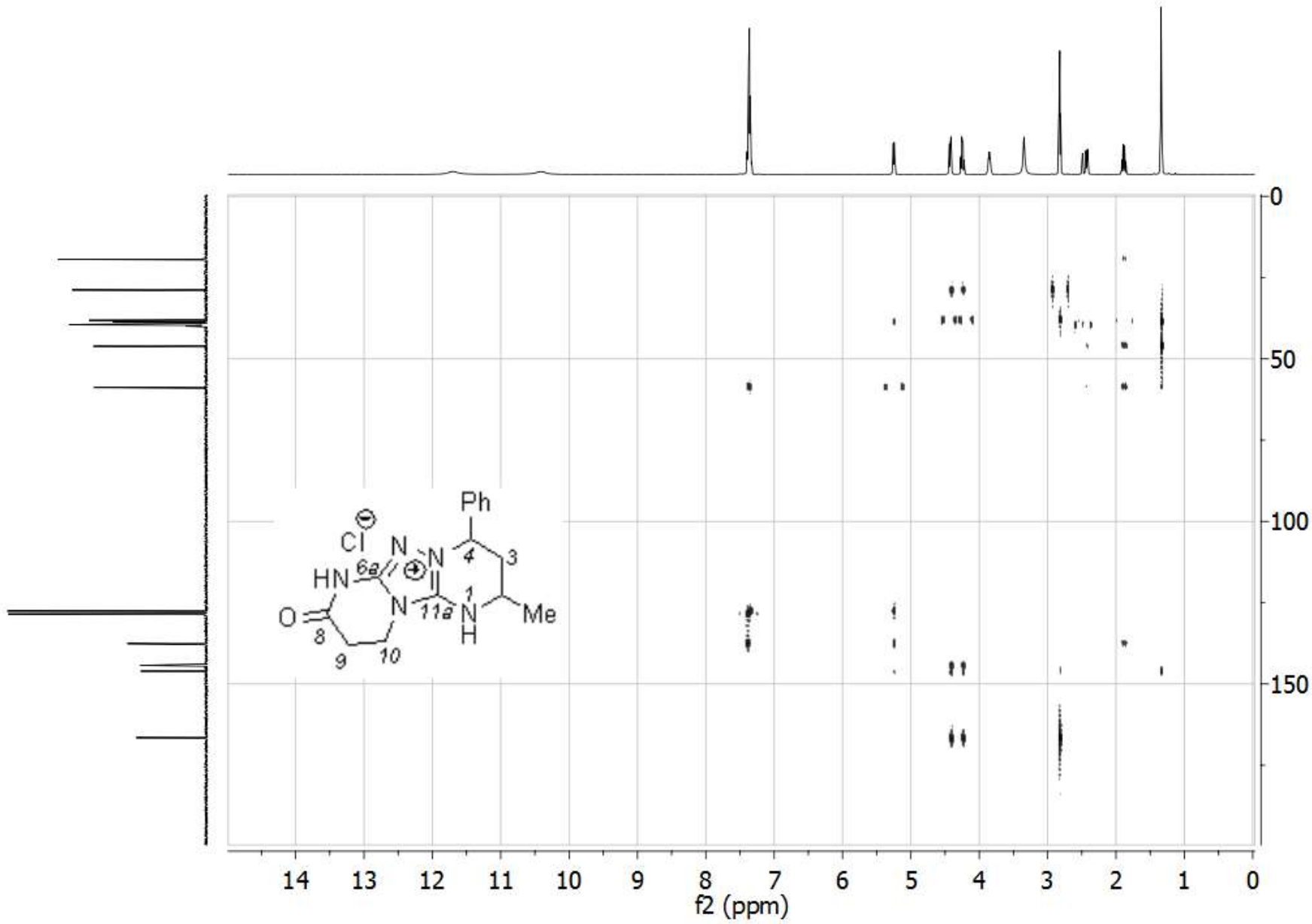
^{1}H NMR spectrum of compound **5d** (DMSO-d_6, 600 MHz).



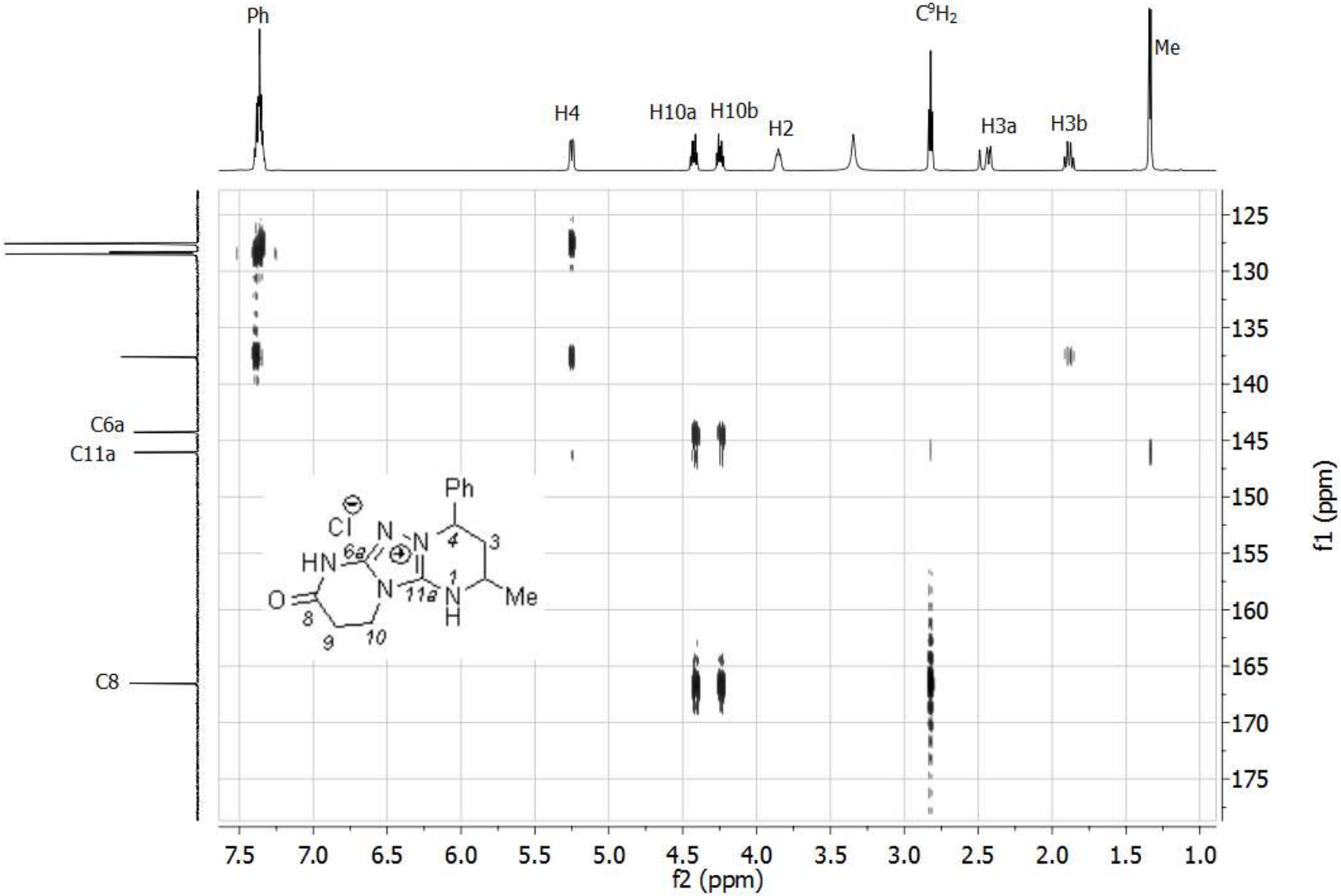
^{13}C NMR spectrum of compound **5d** (DMSO-d_6, 150 MHz).



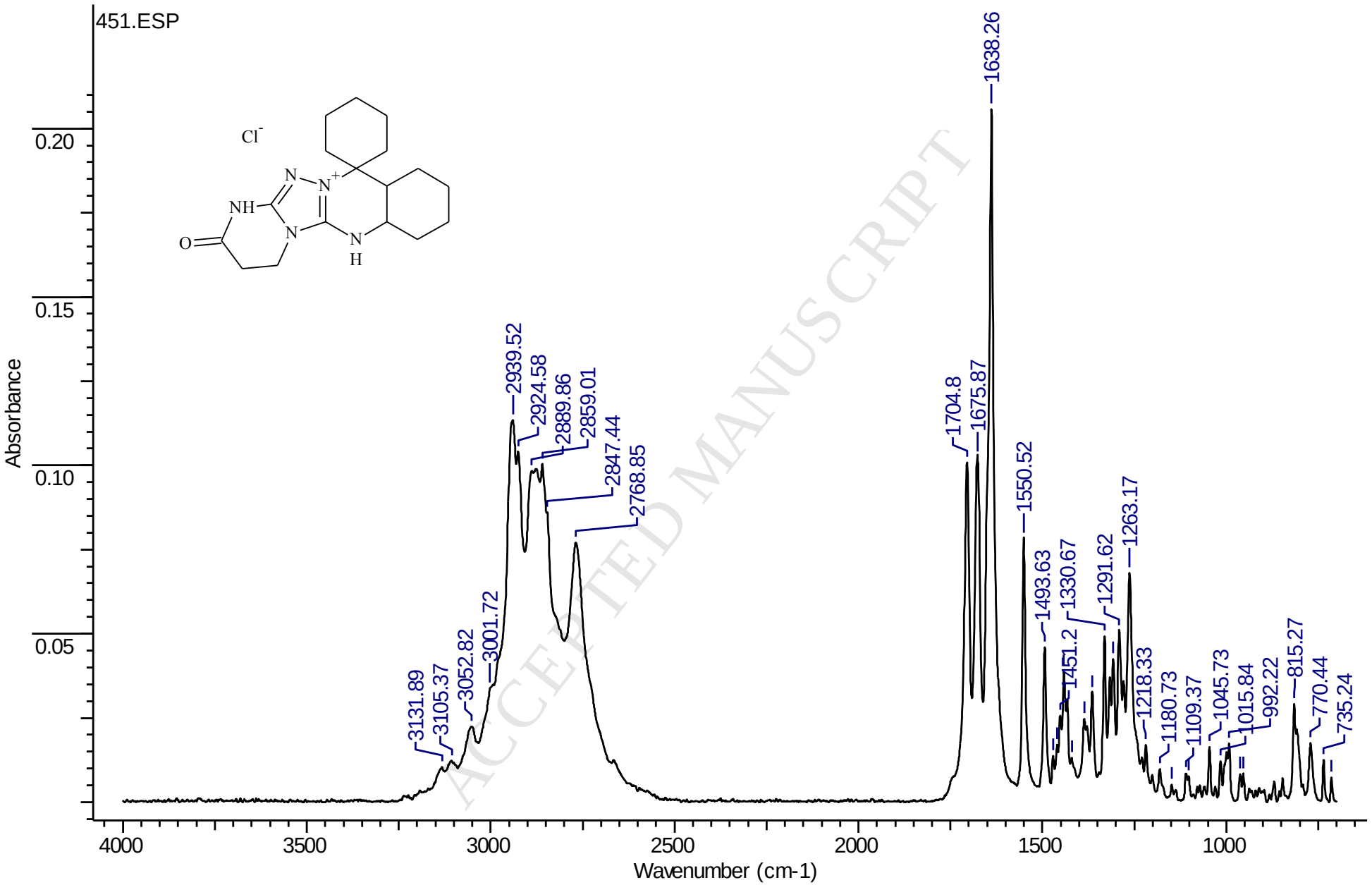
^{1}H-^{13}C HSQC spectrum of compound **5d** (DMSO-d_6).



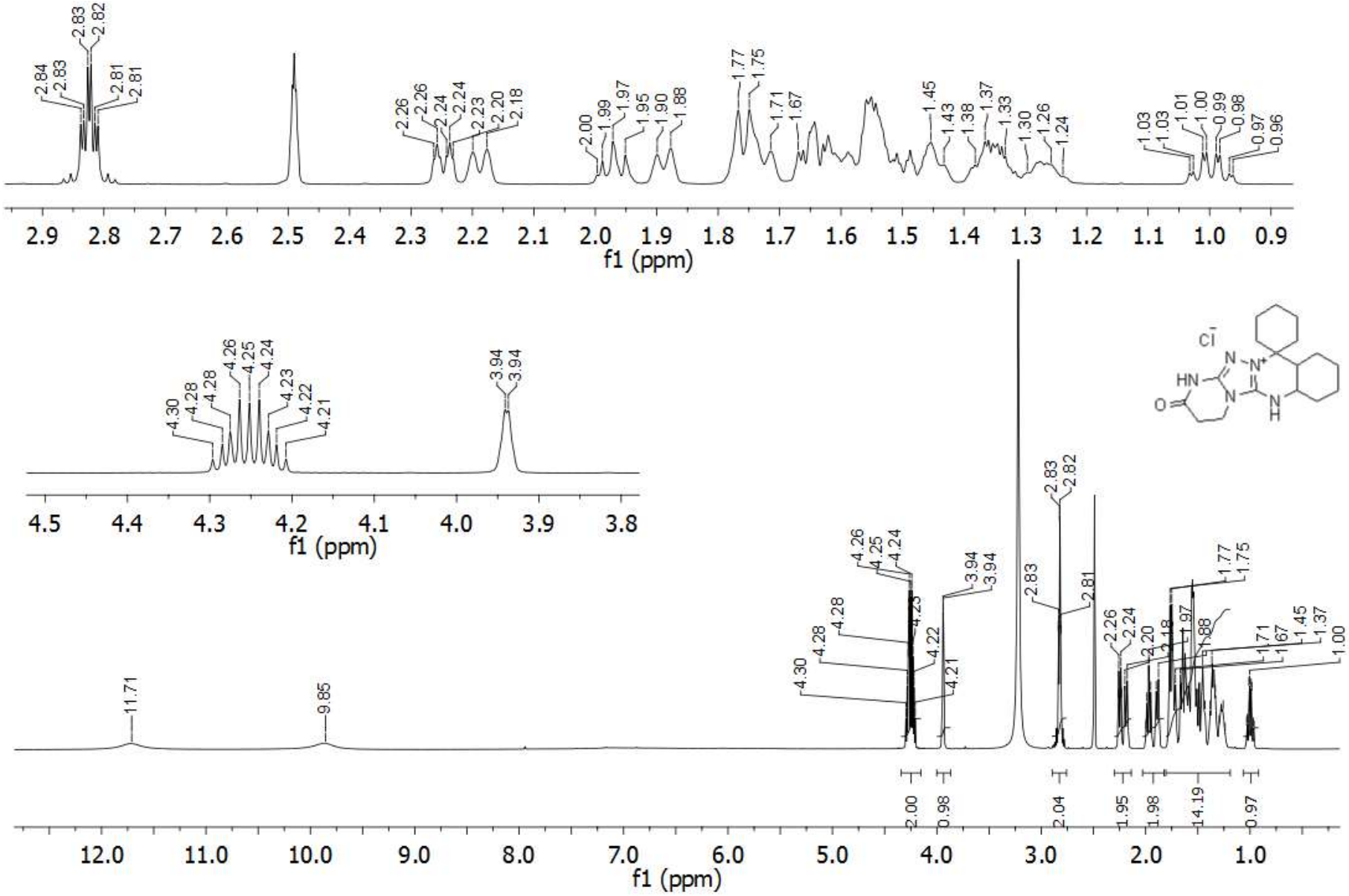
^{1}H-^{13}C HMBC spectrum of compound **5d** (DMSO-d_6).



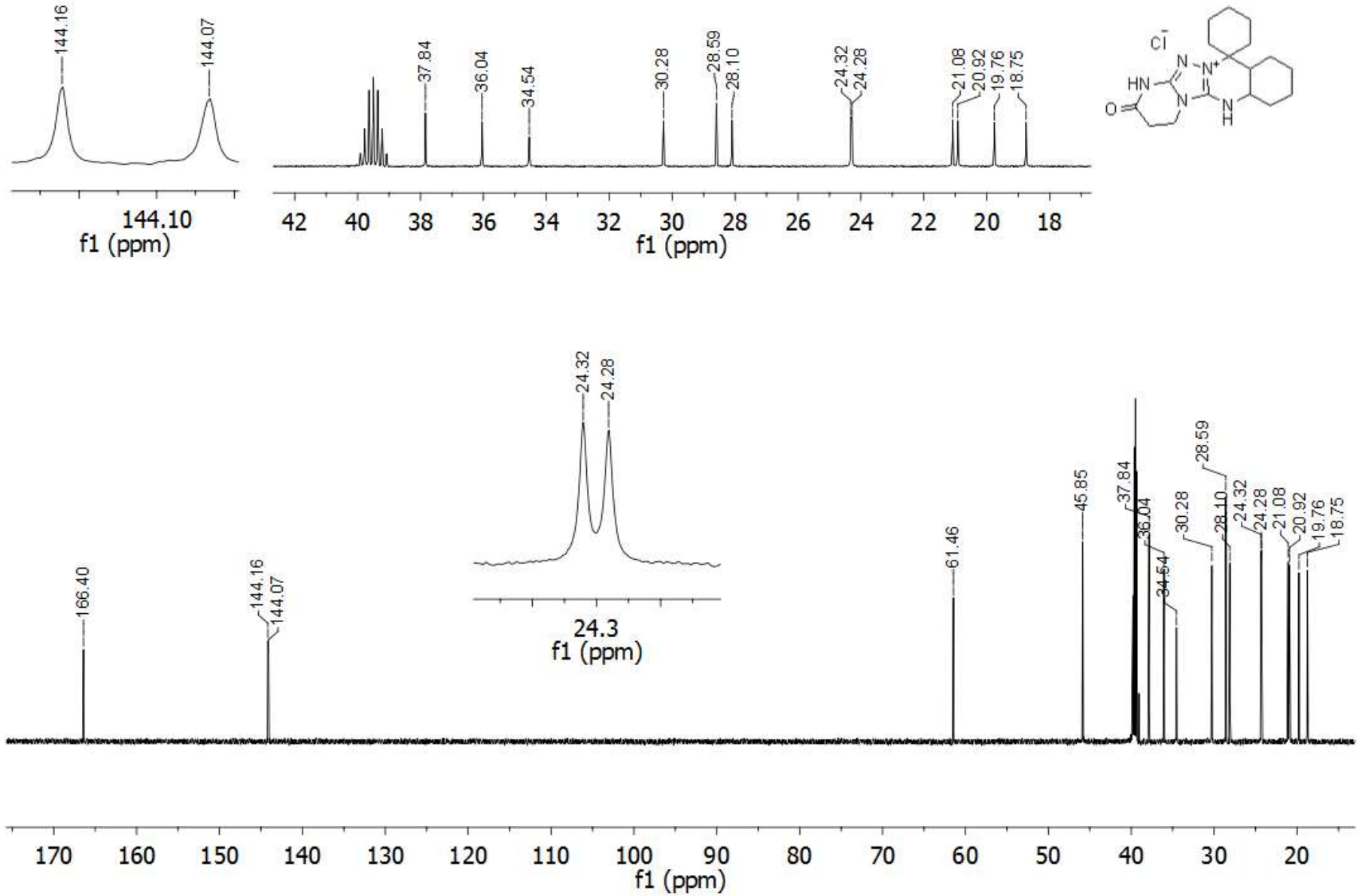
Enlarged fragment of ^{1}H-^{13}C HMBC spectrum of compound **5d** (DMSO-d_6). Correlations between H10a,b and C6a, C11a confirm direction of cyclization.



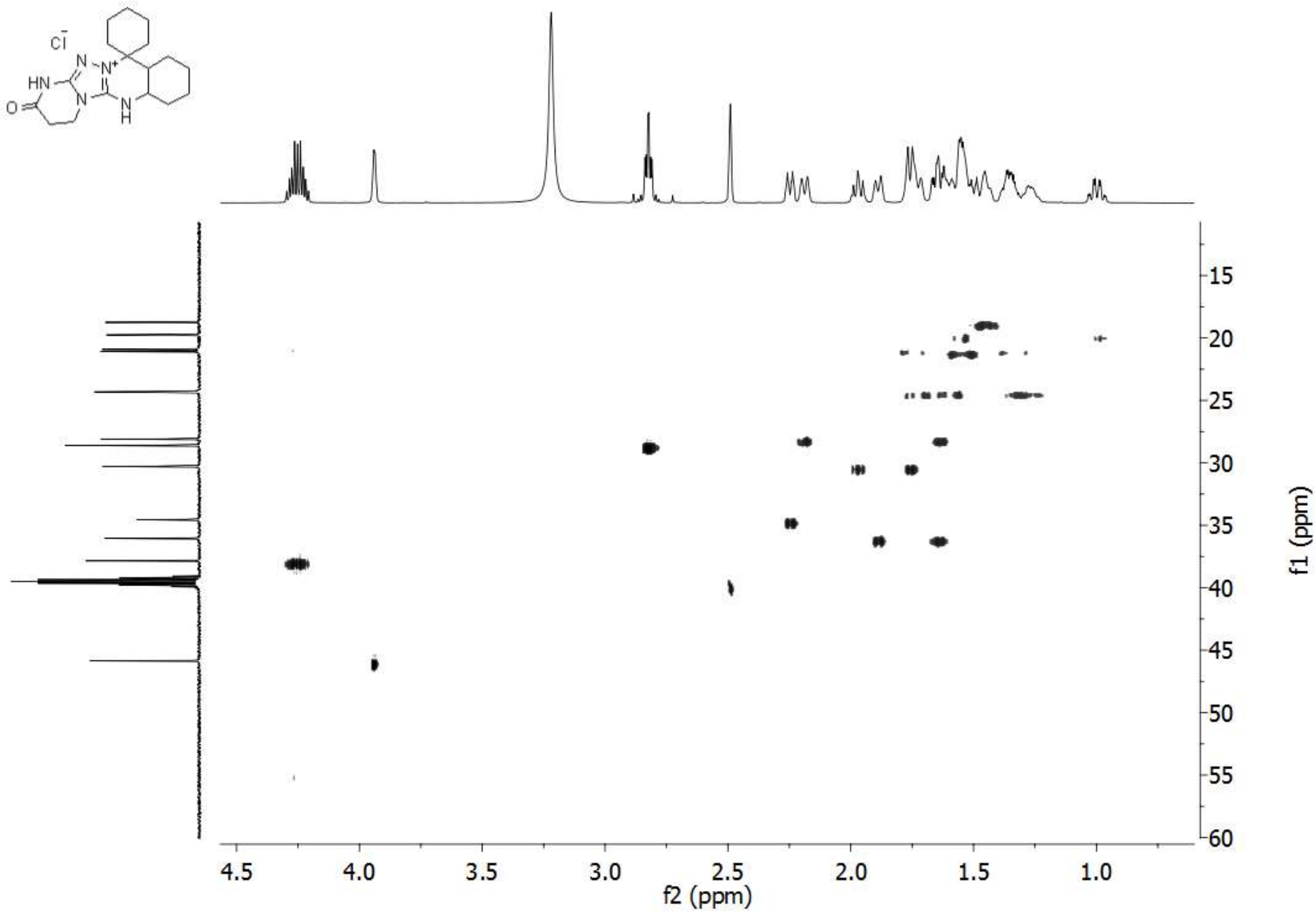
FTIR spectrum of compound **5e** (ATR).



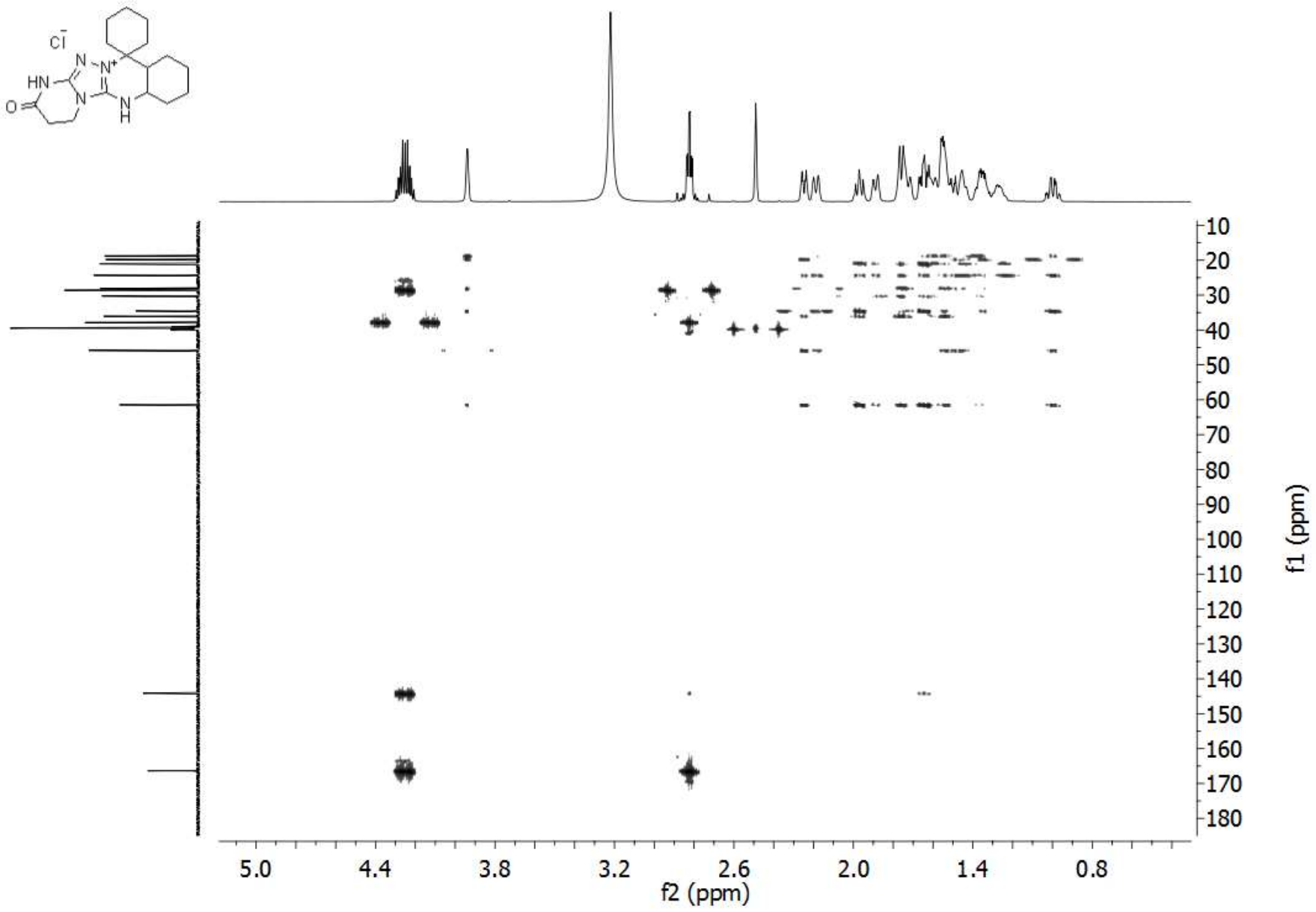
^{1}H NMR spectrum of compound **5e** (DMSO-d_6, 600 MHz).



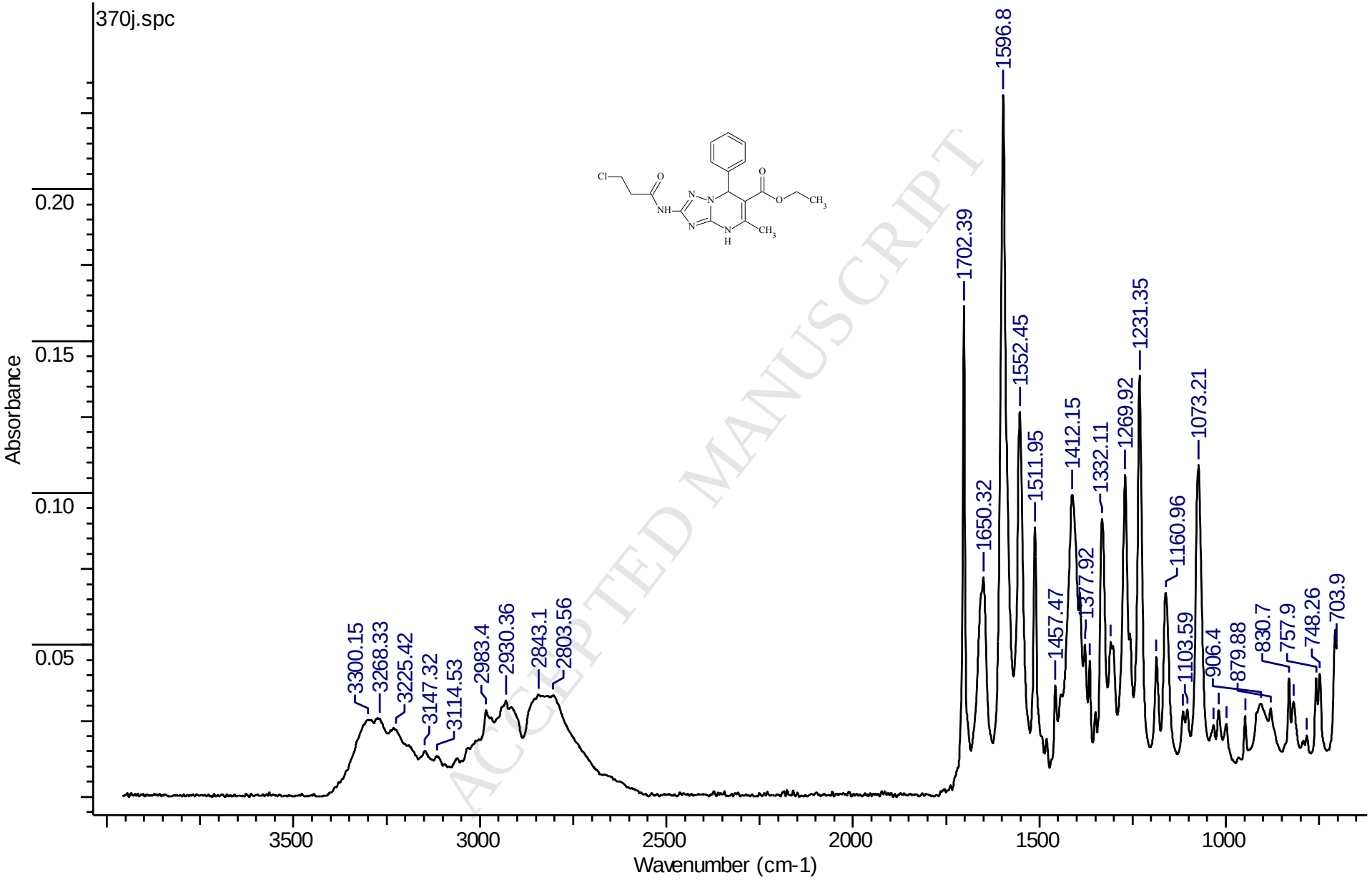
^{13}C NMR spectrum of compound **5e** (DMSO-d_6, 150 MHz).



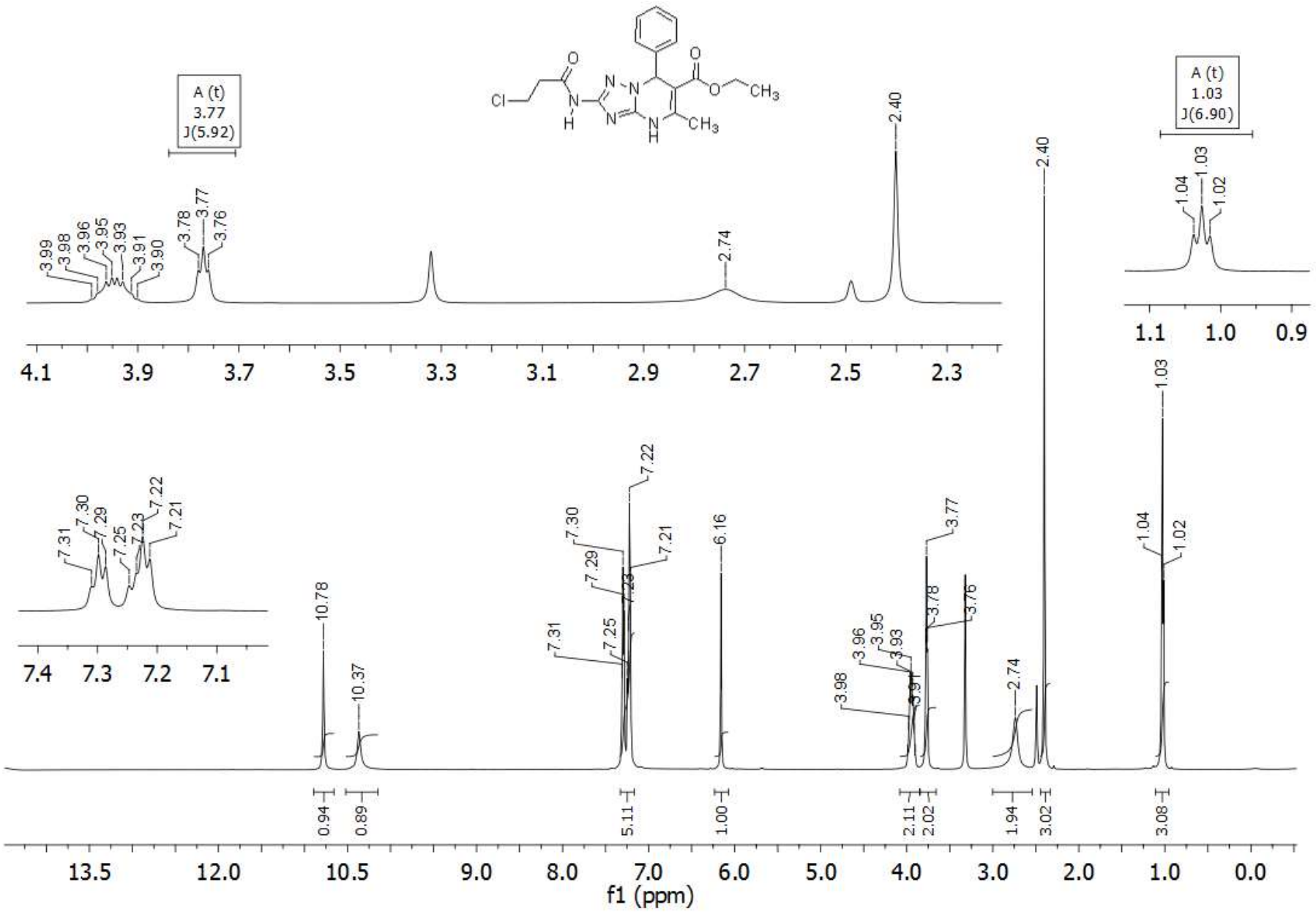
Enlarged fragment (high field) of ^{1}H-^{13}C HSQC spectrum of compound **5e** (DMSO-d_6).



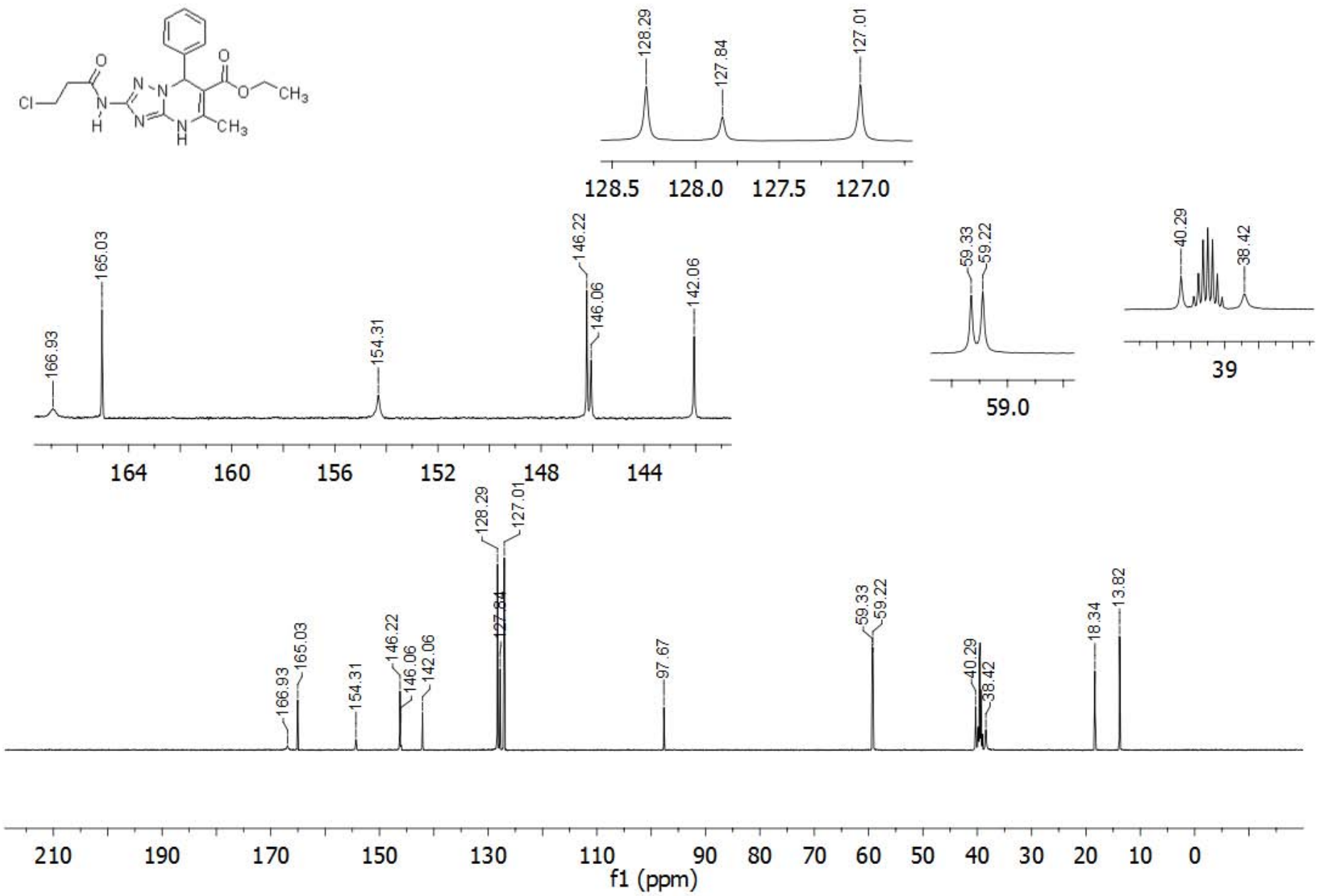
^{1}H-^{13}C HMBC spectrum of compound **5e** (DMSO-d_6).



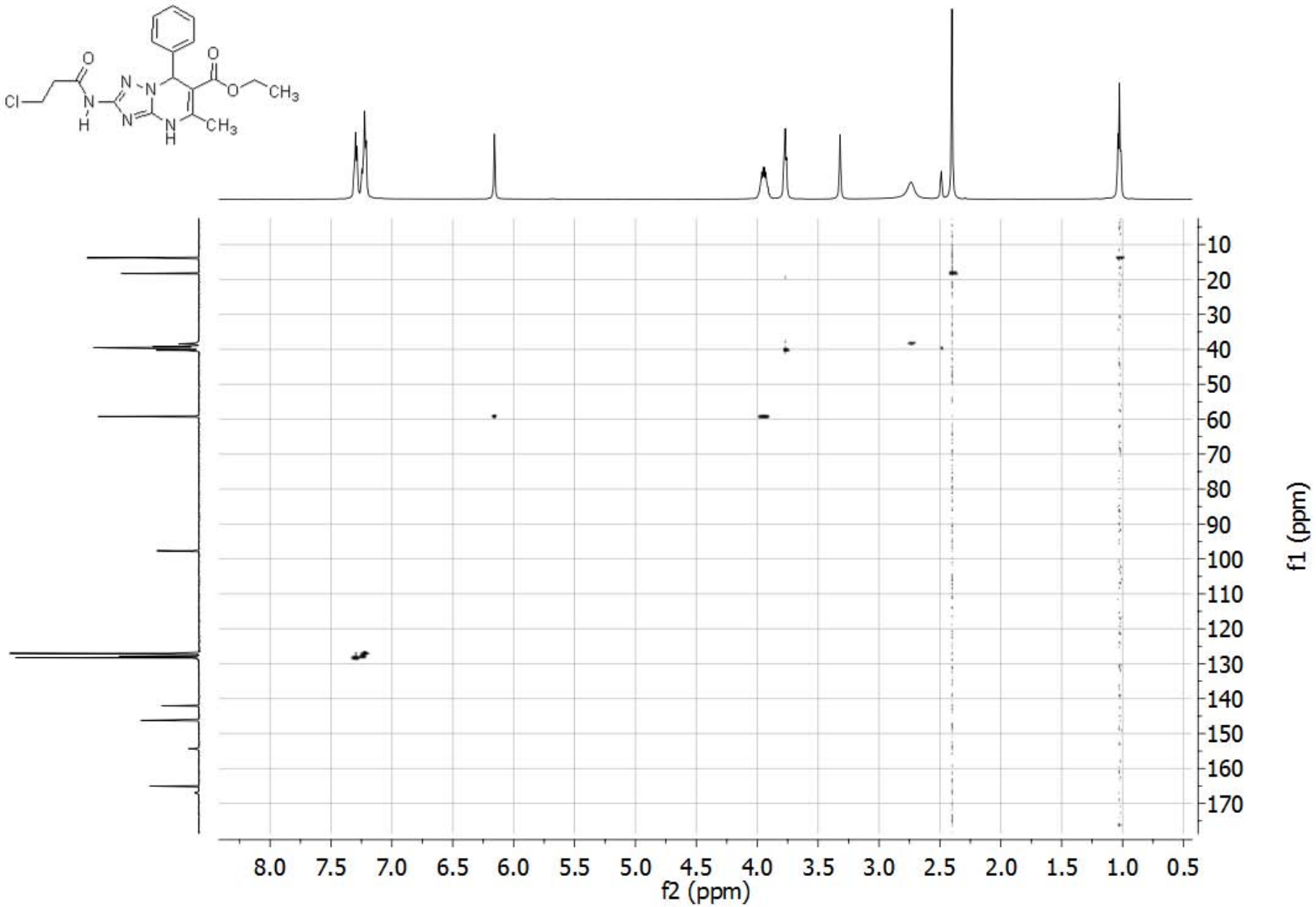
FTIR spectrum of compound **7a** (ATR).



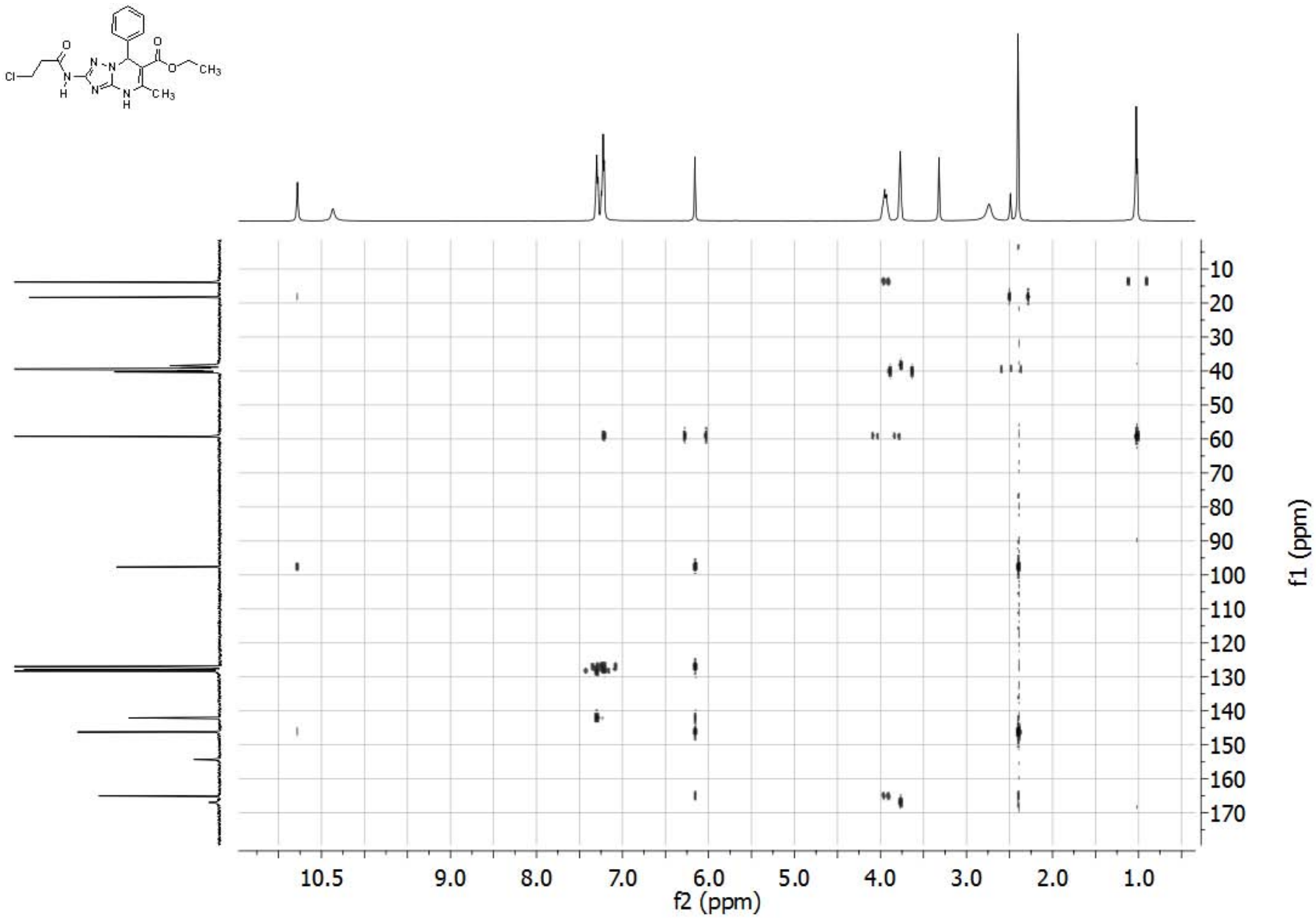
^{1}H NMR spectrum of compound **7a** (DMSO-d_6, 600 MHz).



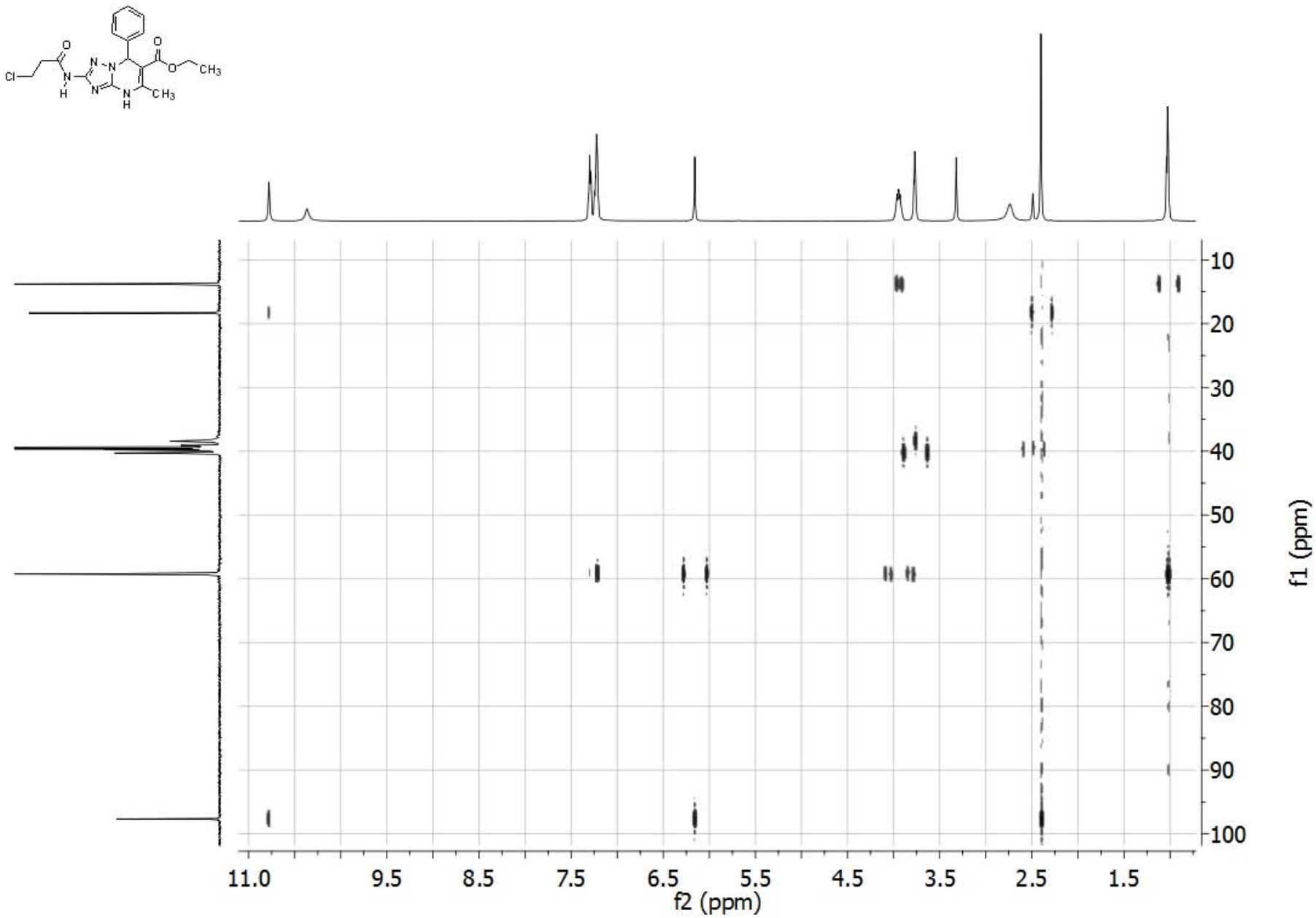
^{13}C NMR spectrum of compound **7a** (DMSO-d_6, 150 MHz).



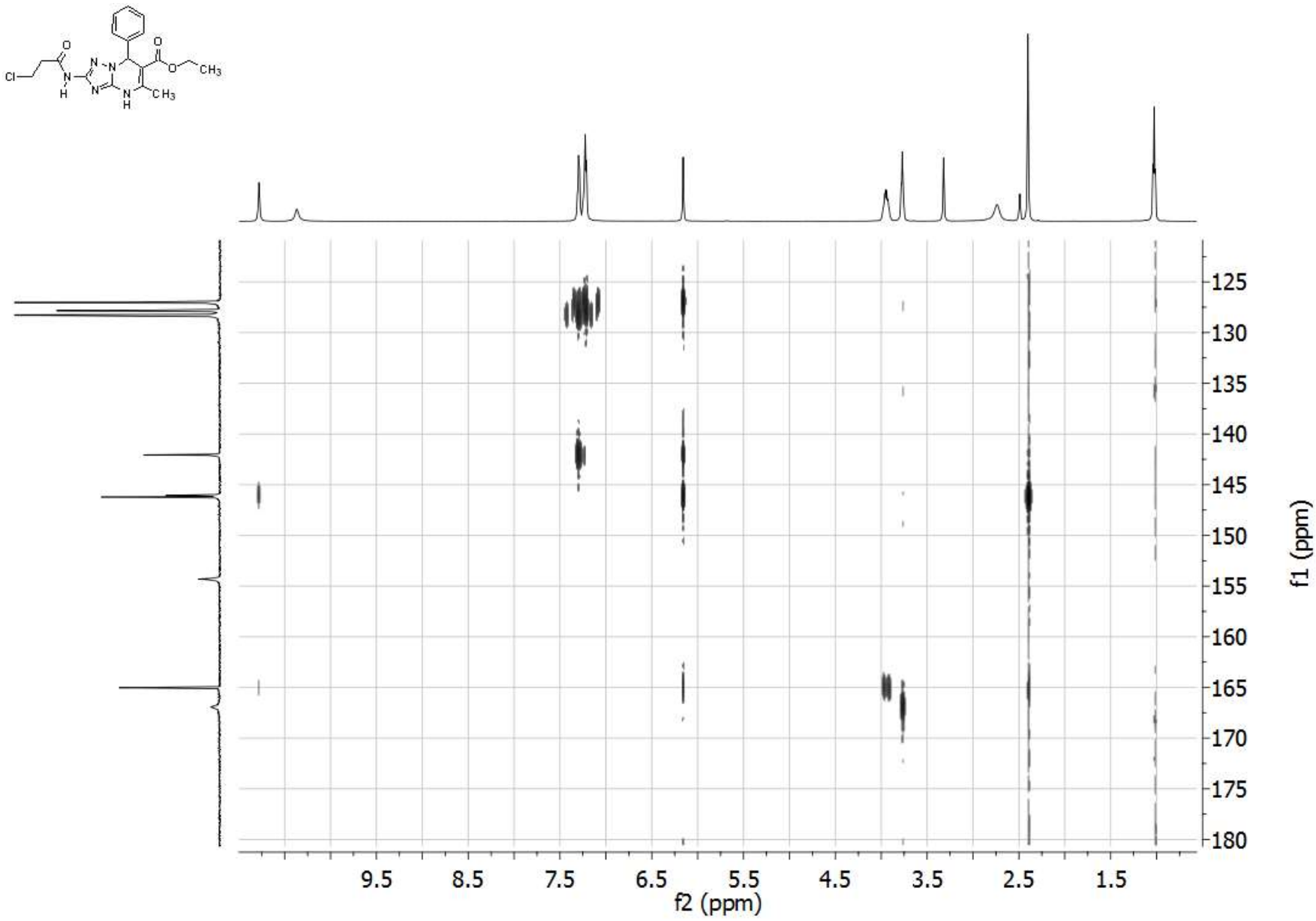
^{1}H-^{13}C HSQC spectrum of compound **7a.**



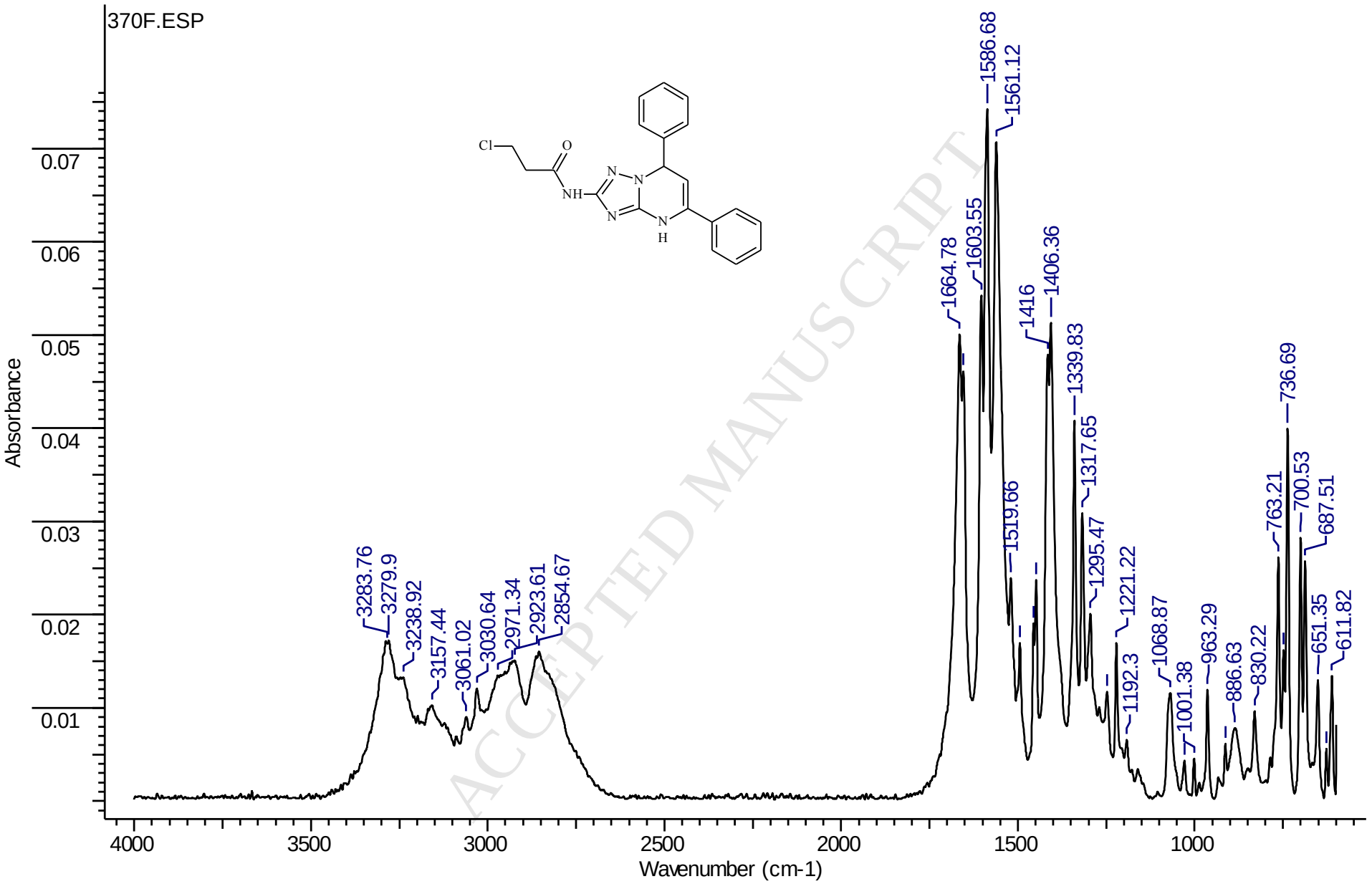
^{1}H-^{13}C HMBC spectrum of compound **7a.**



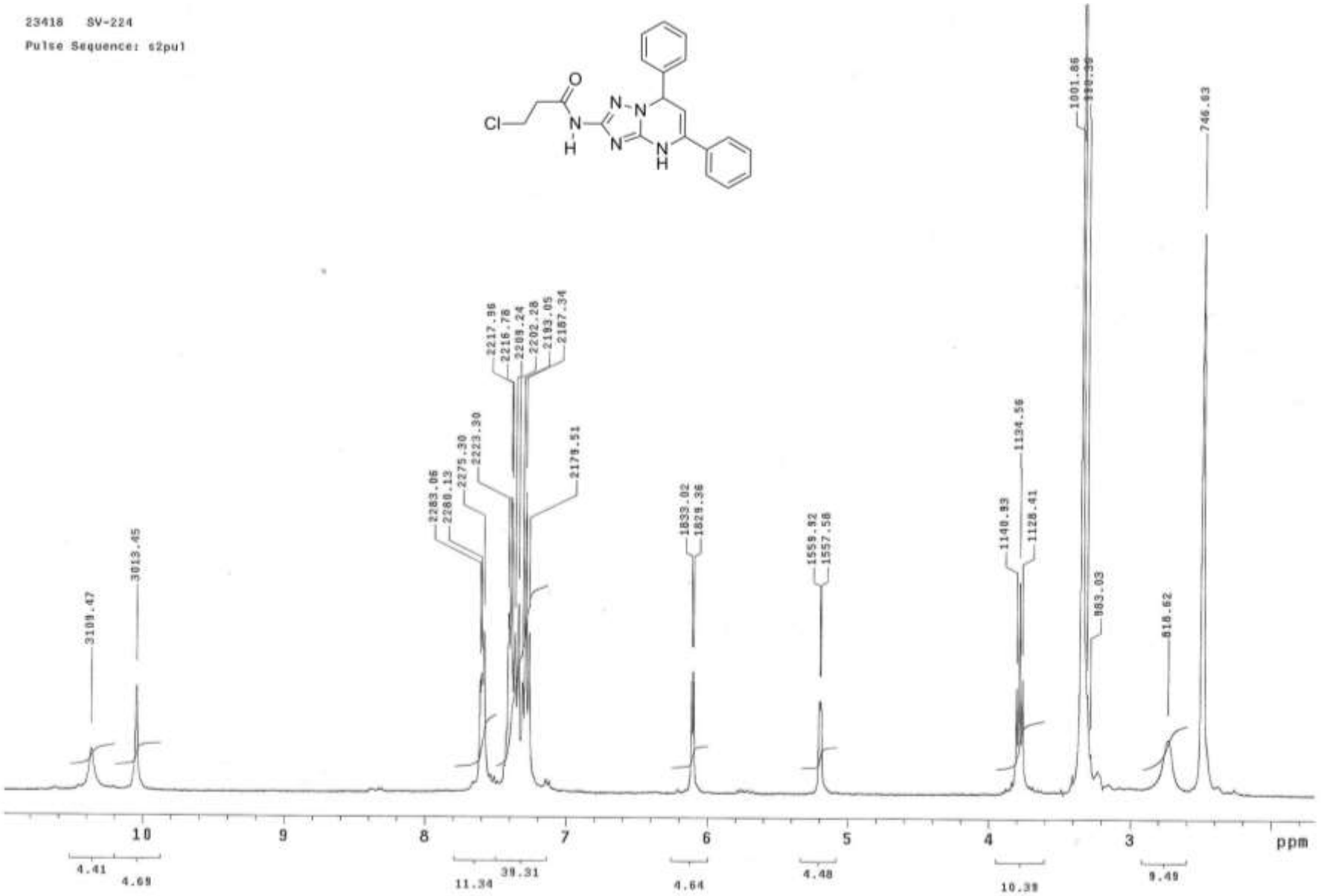
Enlarged fragment of ^{1}H-^{13}C HMBC spectrum of compound **7a.**



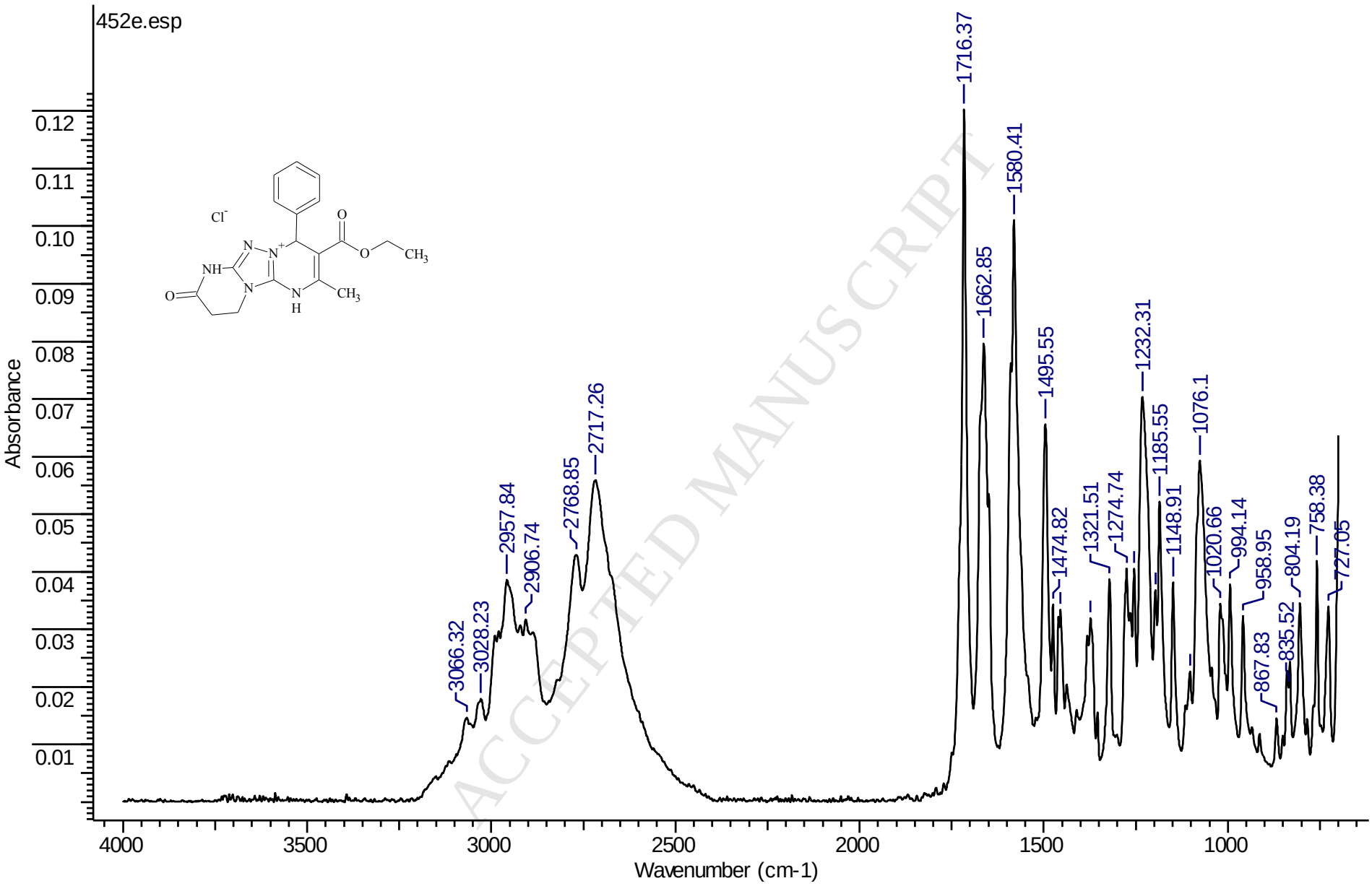
Enlarged fragment of ^{1}H-^{13}C HMBC spectrum of compound **7a.**



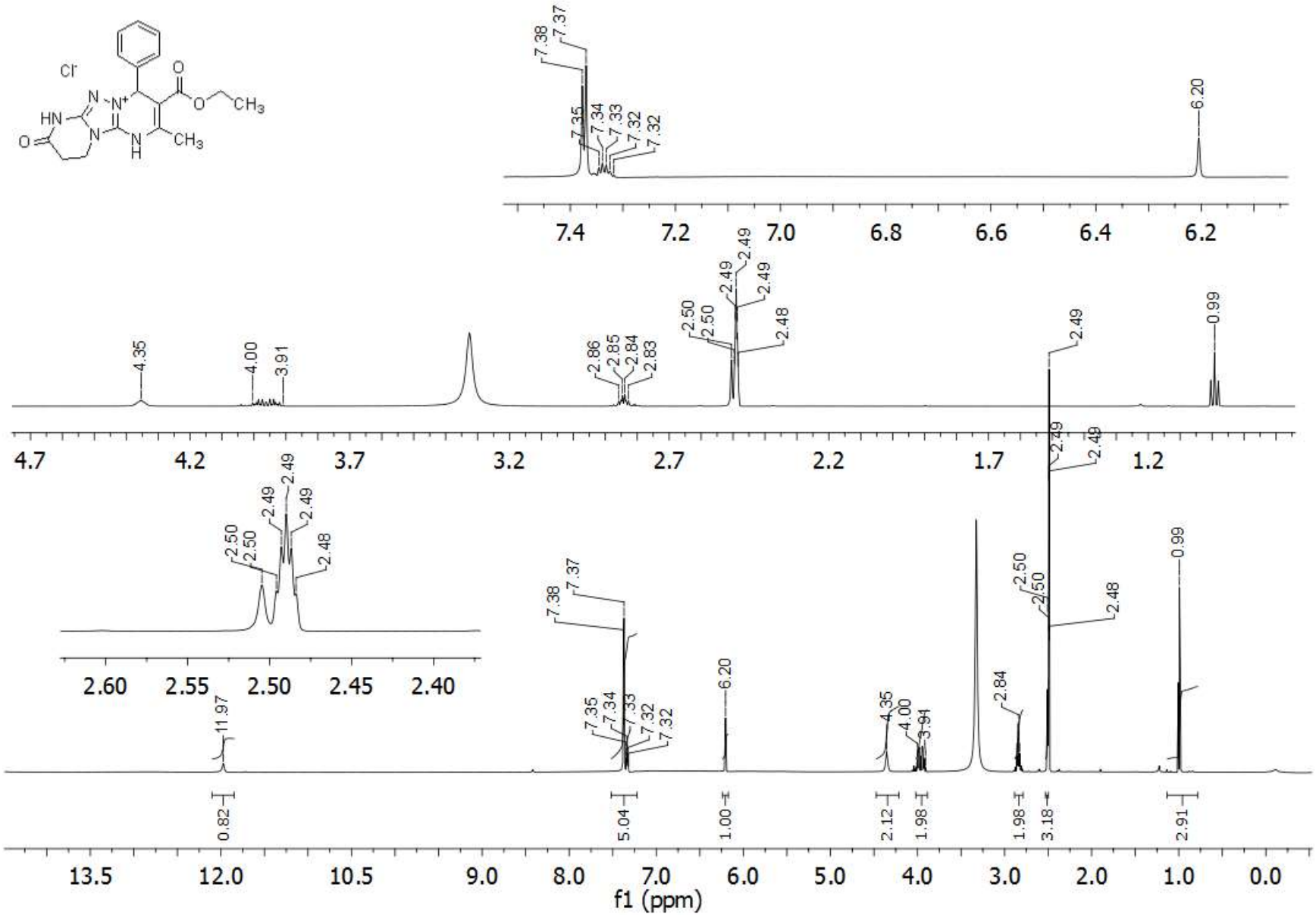
FTIR spectrum of compound **7c** (ATR).



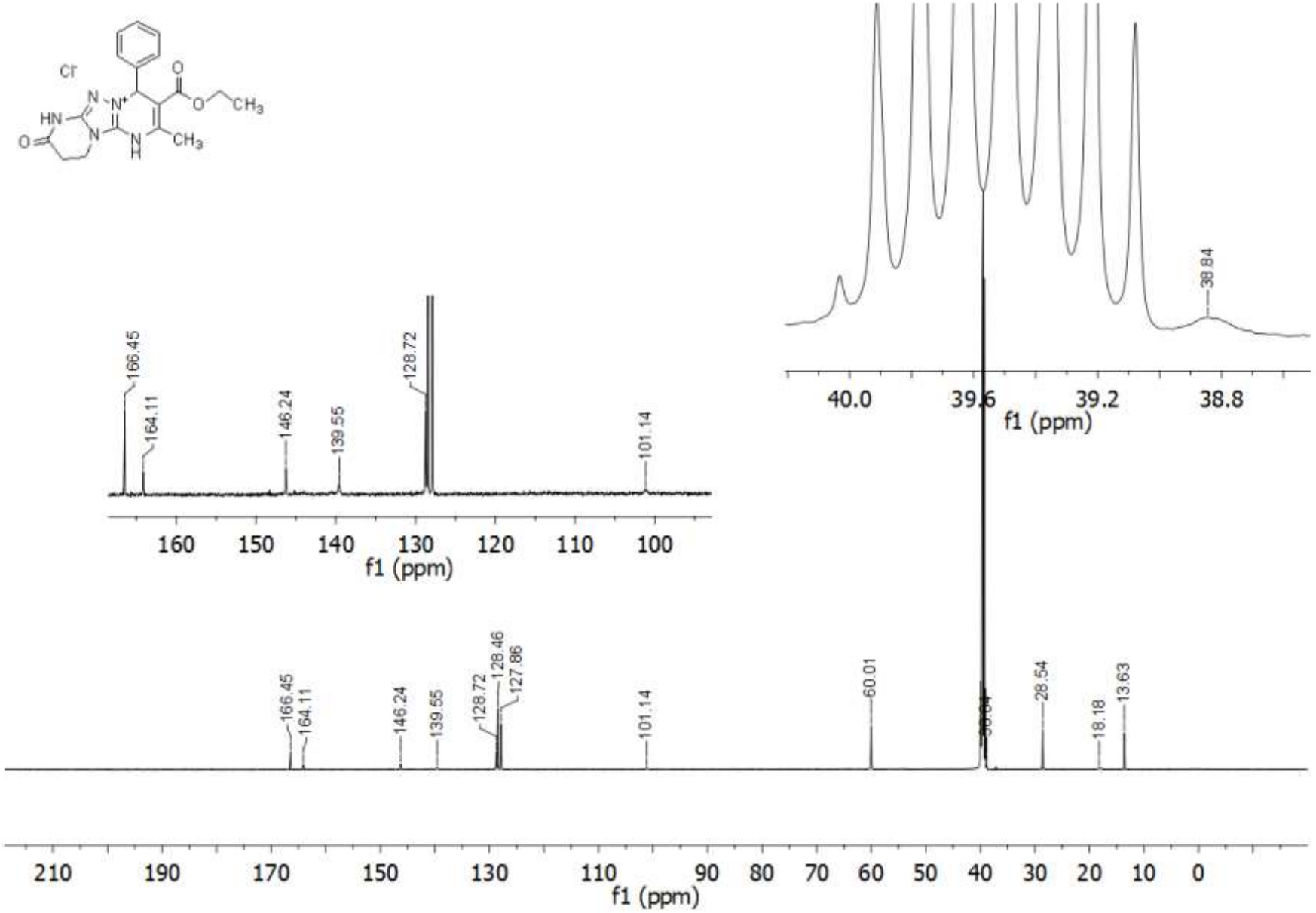
^{1}H NMR spectrum of compound **7c** (DMSO-d_6, 300 MHz).



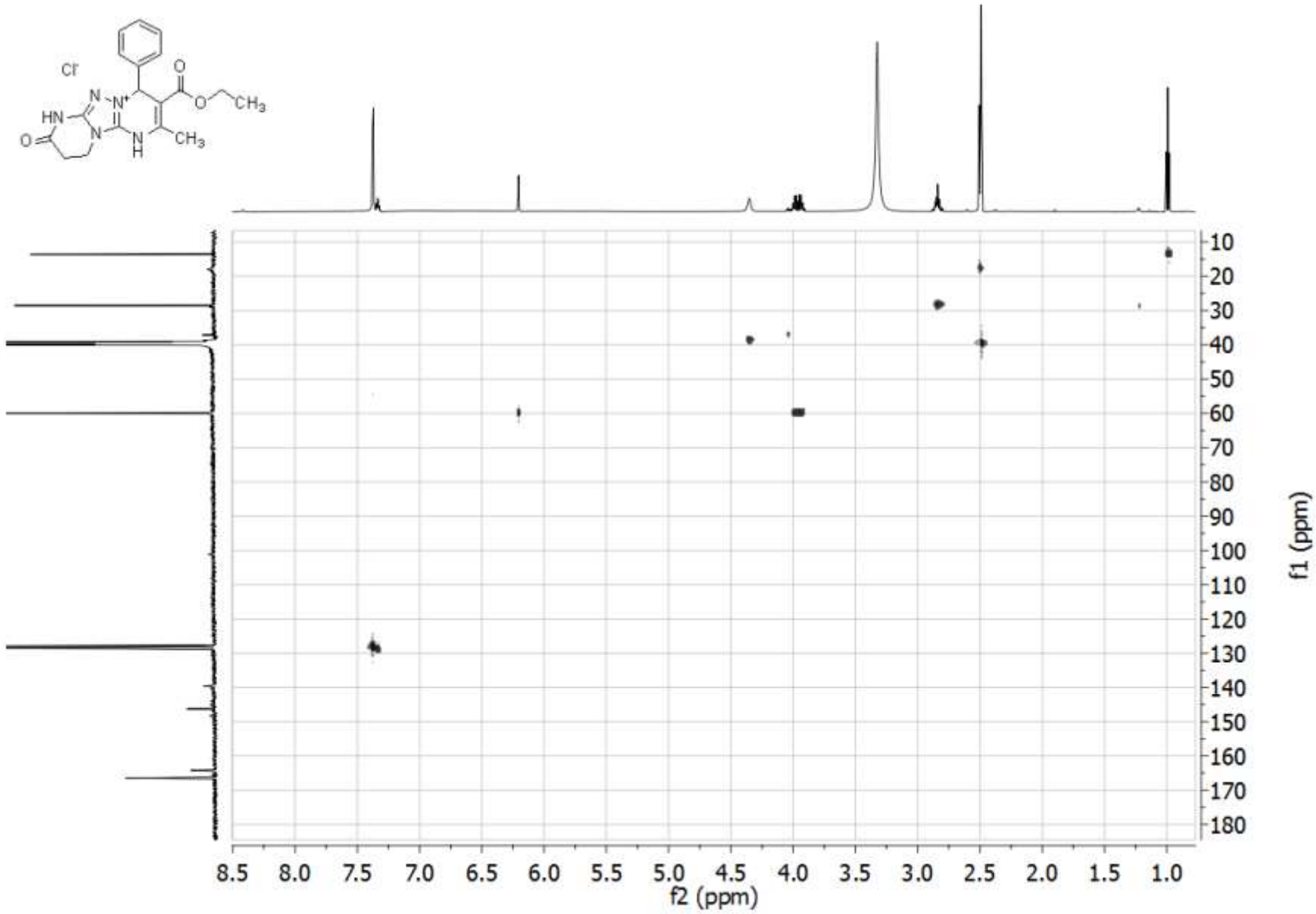
FTIR spectrum of compound **8a** (ATR).



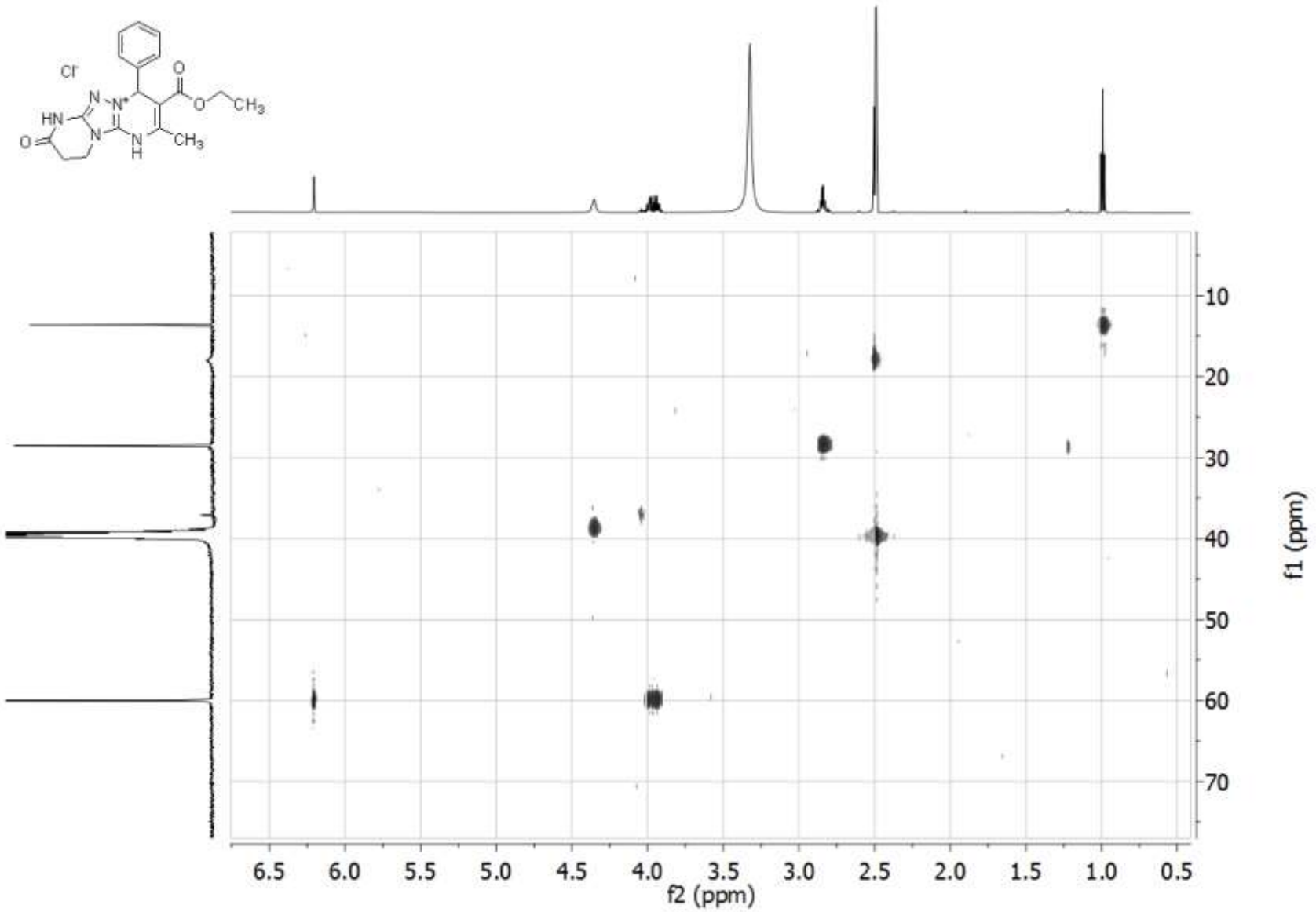
^{1}H NMR spectrum of compound **8a** (DMSO-d_6, 600 MHz).



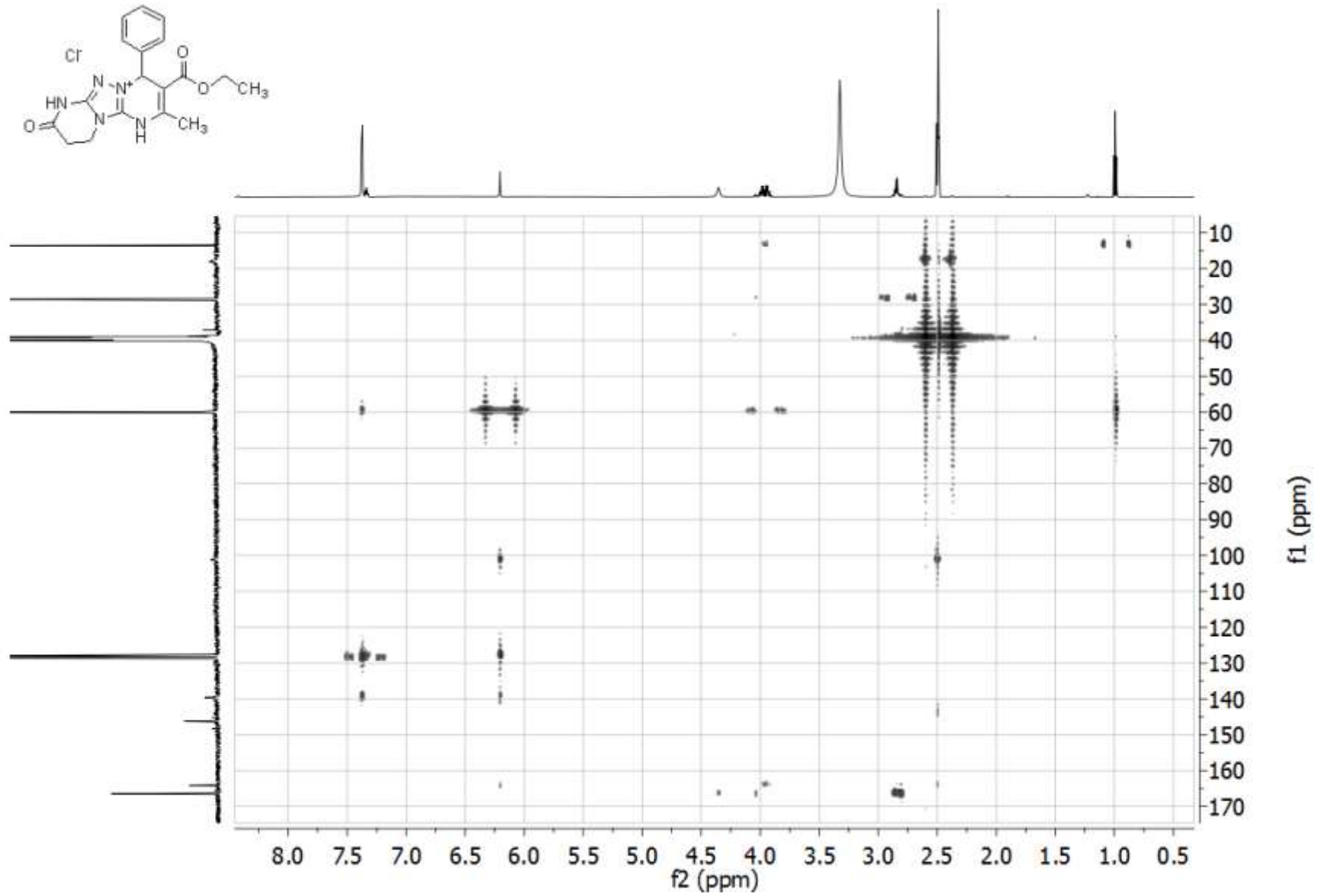
^{13}C NMR spectrum of compound **8a** (DMSO-d_6, 150 MHz).



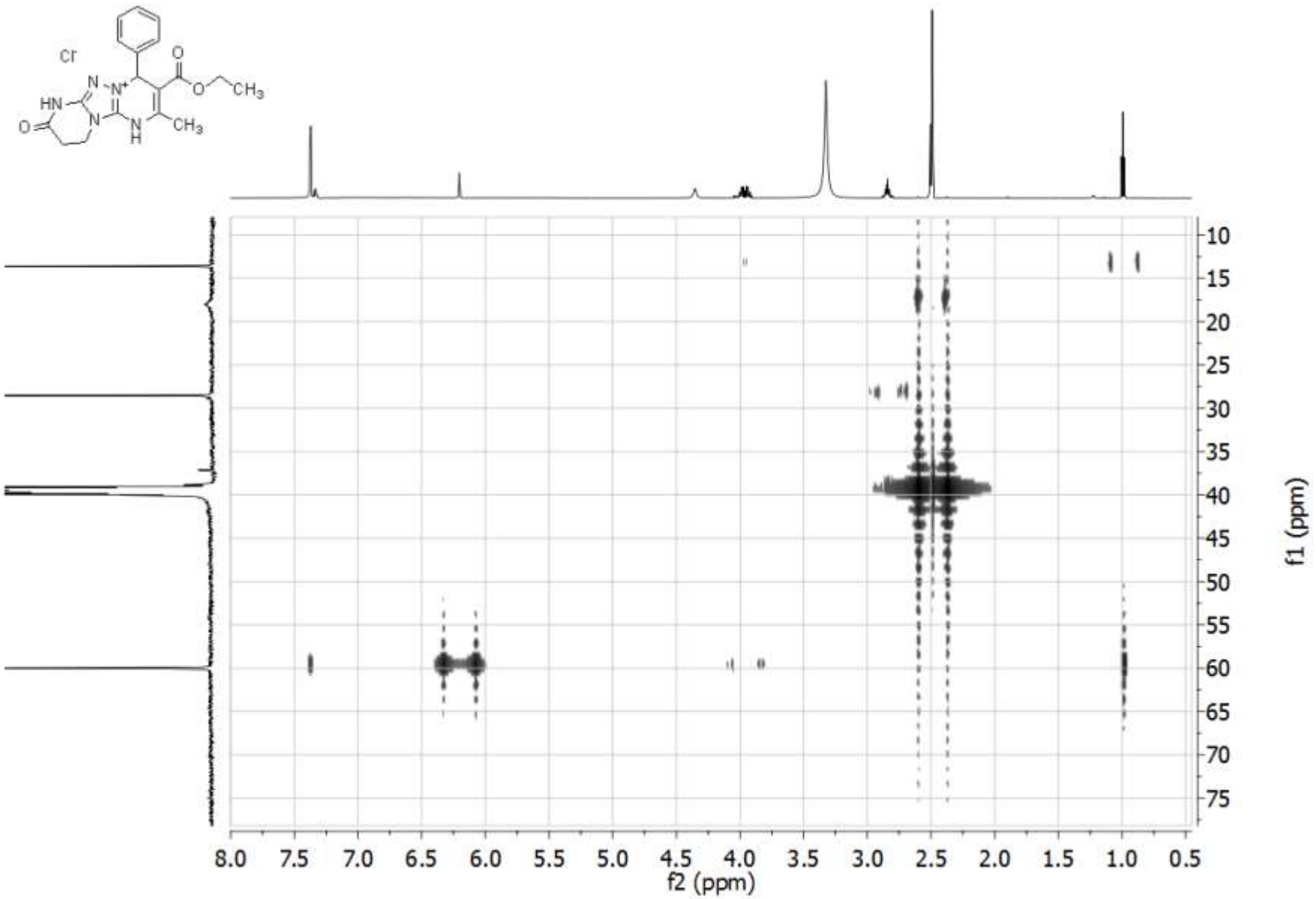
^{1}H-^{13}C HSQC spectrum of compound **8a** (DMSO-d_6).



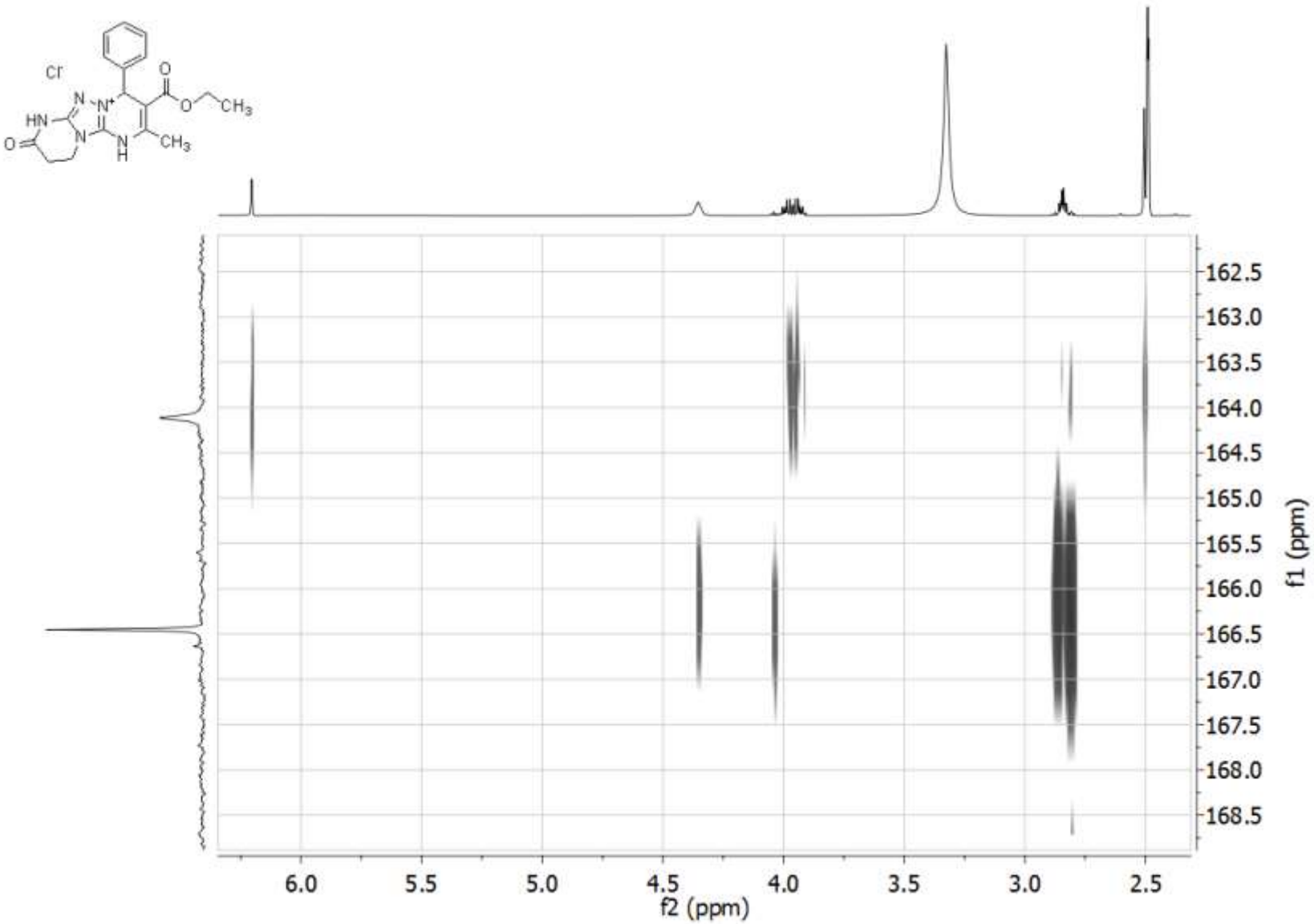
Enlarged fragment of ^{1}H-^{13}C HSQC spectrum of compound **8a** (DMSO-d_6). A peak at 60.01 ppm in ^{13}C NMR spectrum is a combined peak of two carbons because it has two cross-peaks with protons of O$C\underline{H}_2CH_3$ group (3.9 ppm) and C^4H (6.2 ppm).



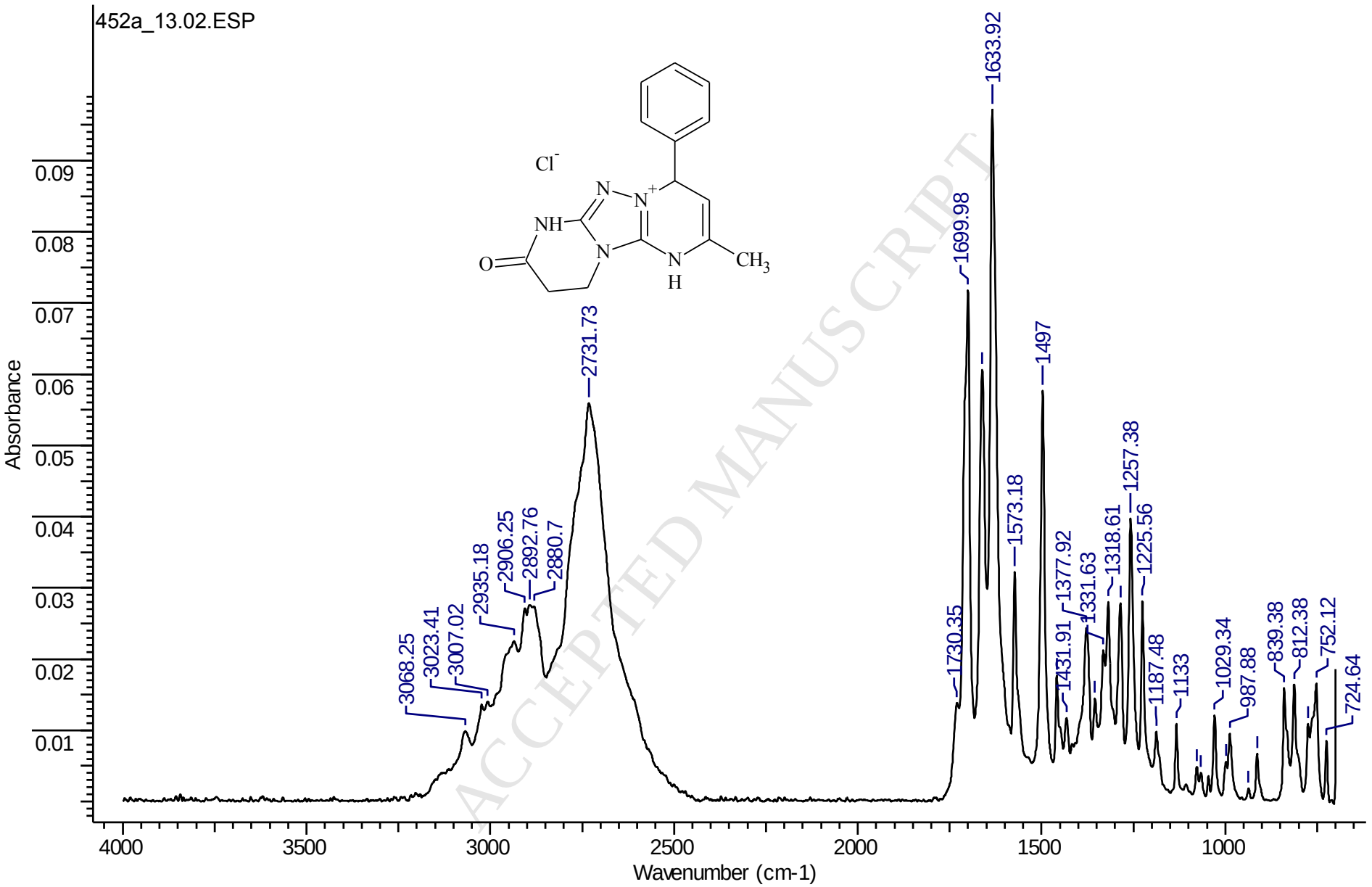
^{1}H-^{13}C HMBC spectrum of compound **8a** (DMSO-d_6).



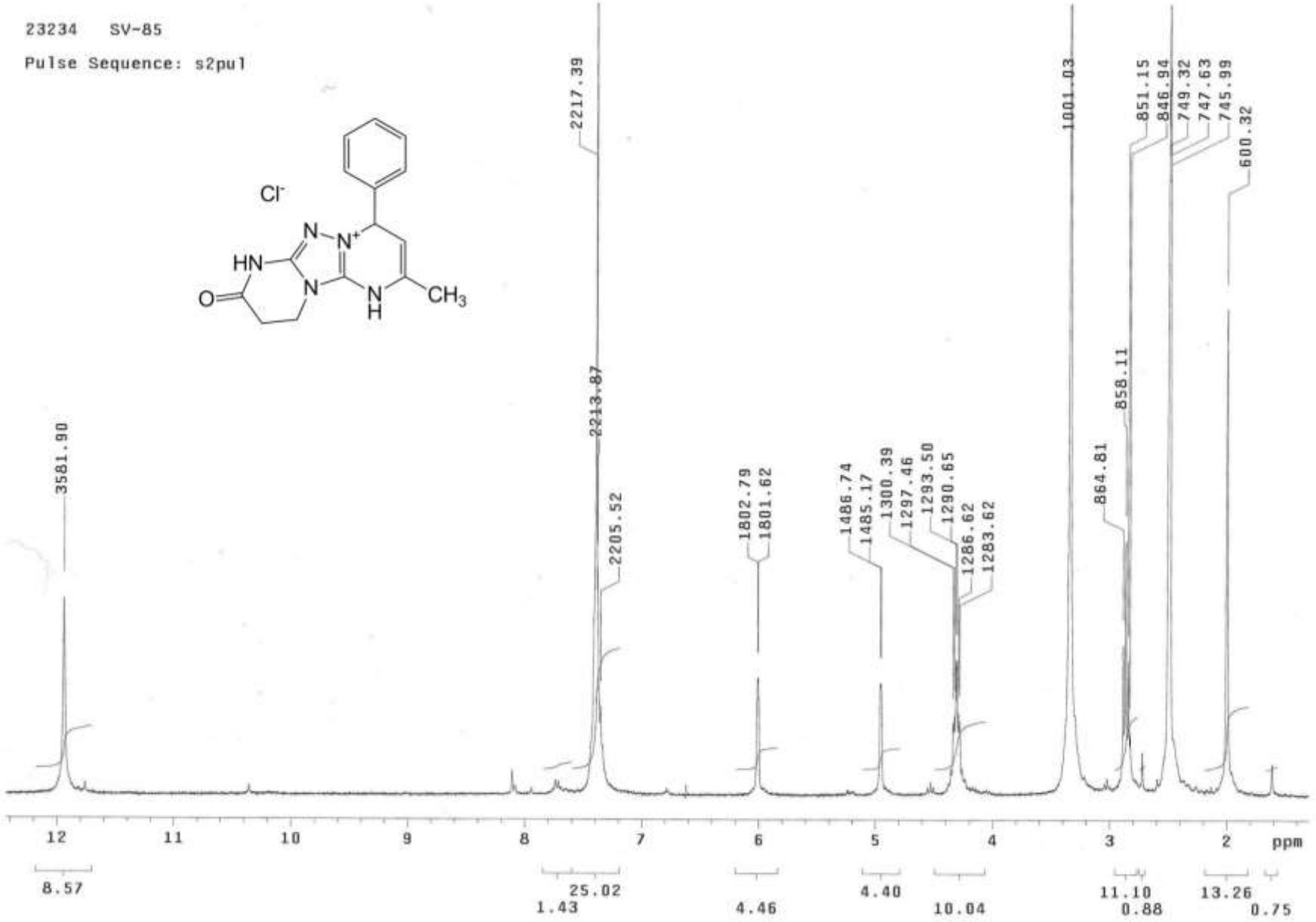
Enlarged fragment of HMBC spectrum of compound **8a** (DMSO-d_6).



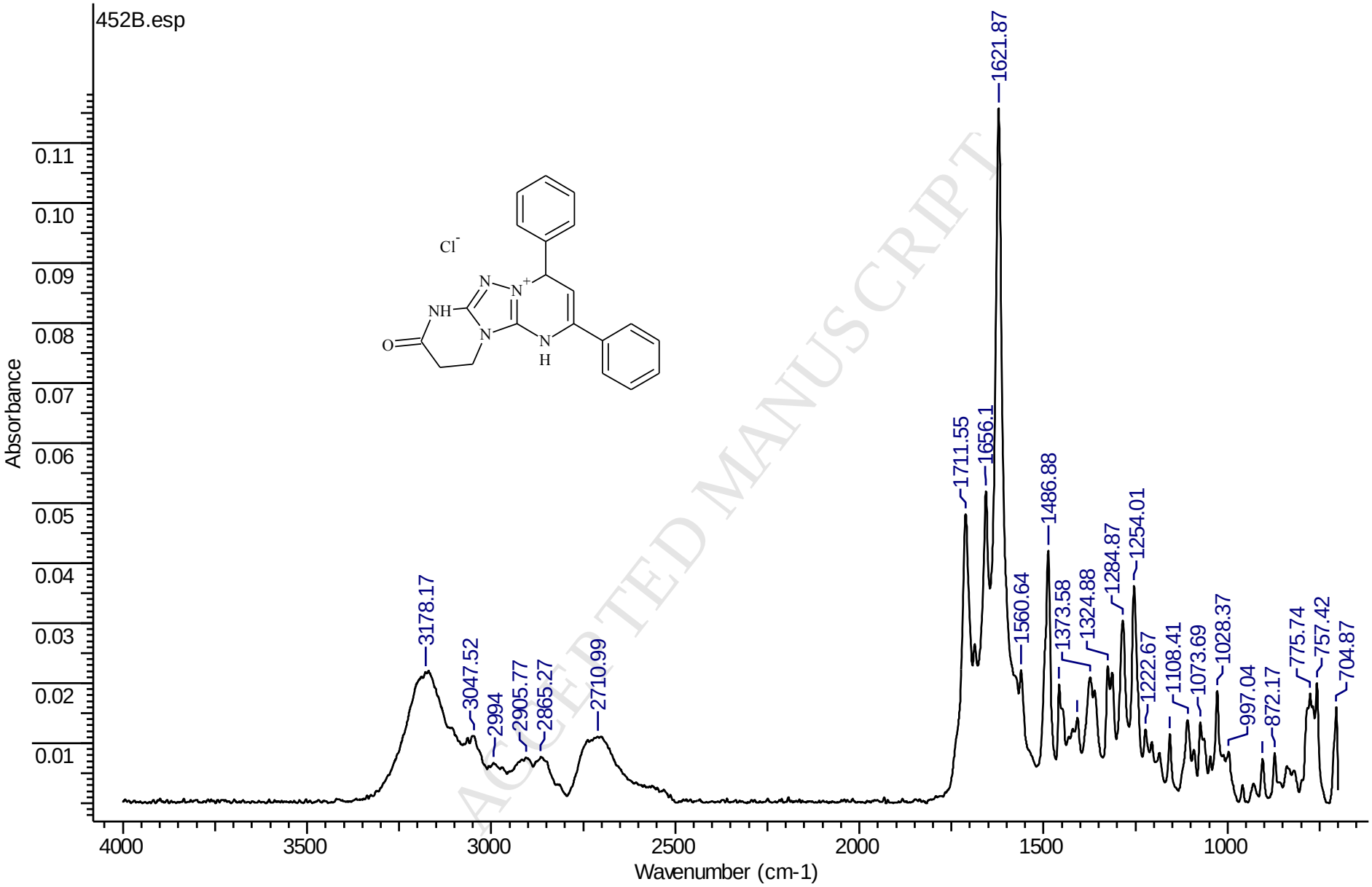
Enlarged fragment of ^{1}H-^{13}C HMBC spectrum of compound **8a** (DMSO-d_6). A peak at 166.45 ppm in ^{13}C NMR spectrum is a combined peak of two carbons of carbonyl groups because it has cross-peaks with signals of protons $C^{9}H_2$, $C^{10}H_2$ and $OC\underline{H}_2CH_3$ groups.



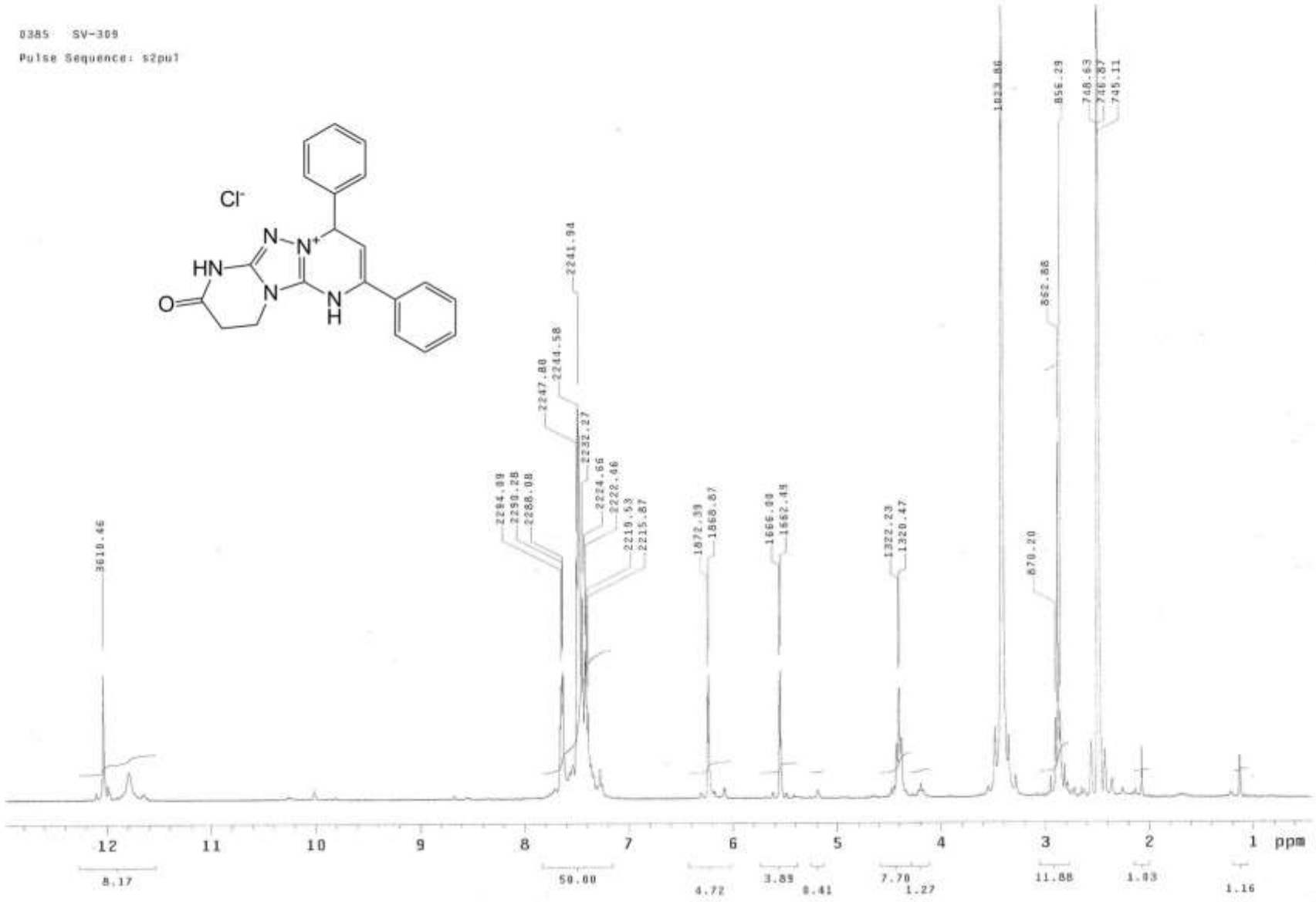
FTIR spectrum of compound **8b** (ATR).



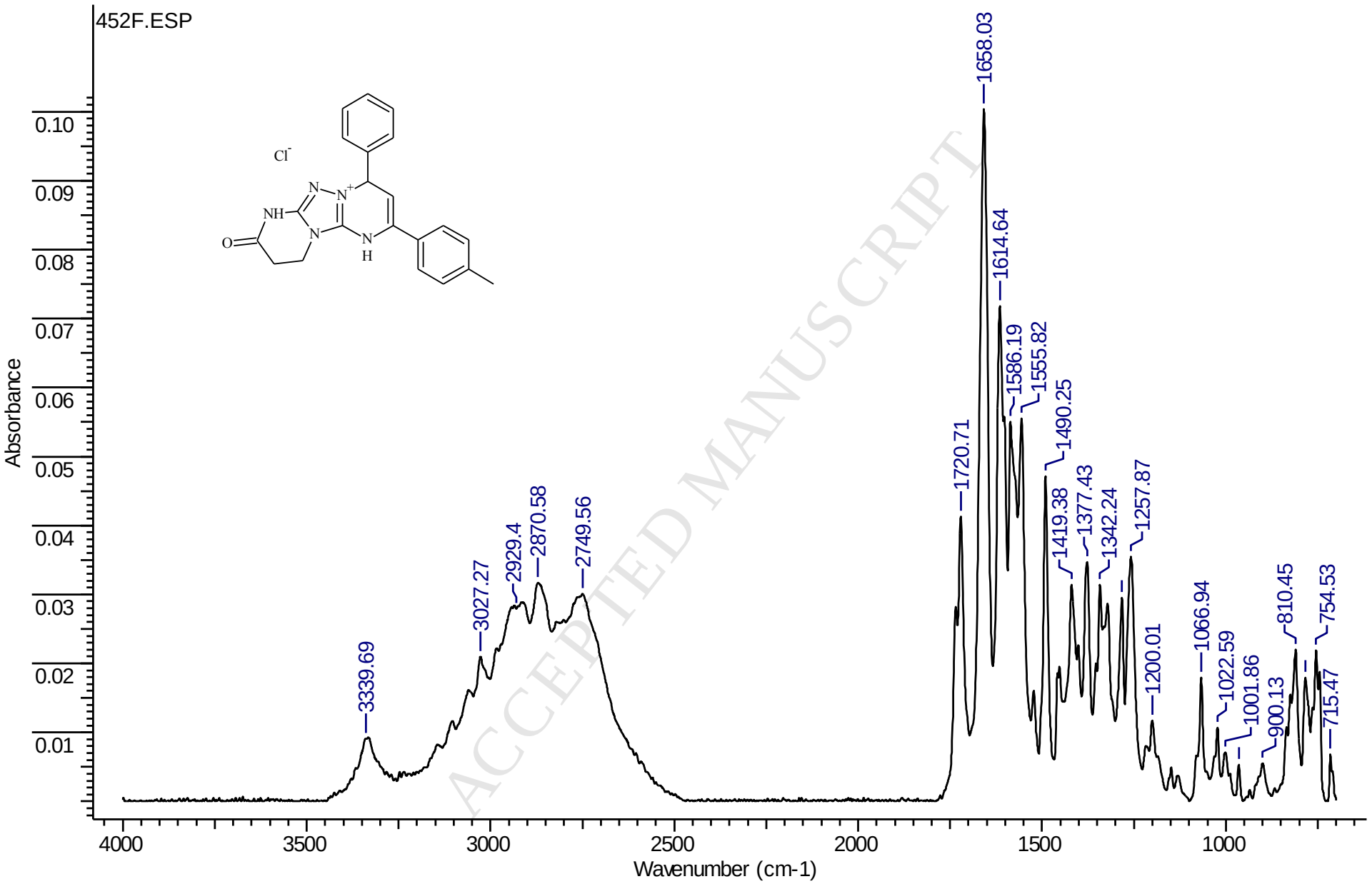
^{1}H NMR spectrum of compound **8b** (300 MHz, DMSO-d_6).



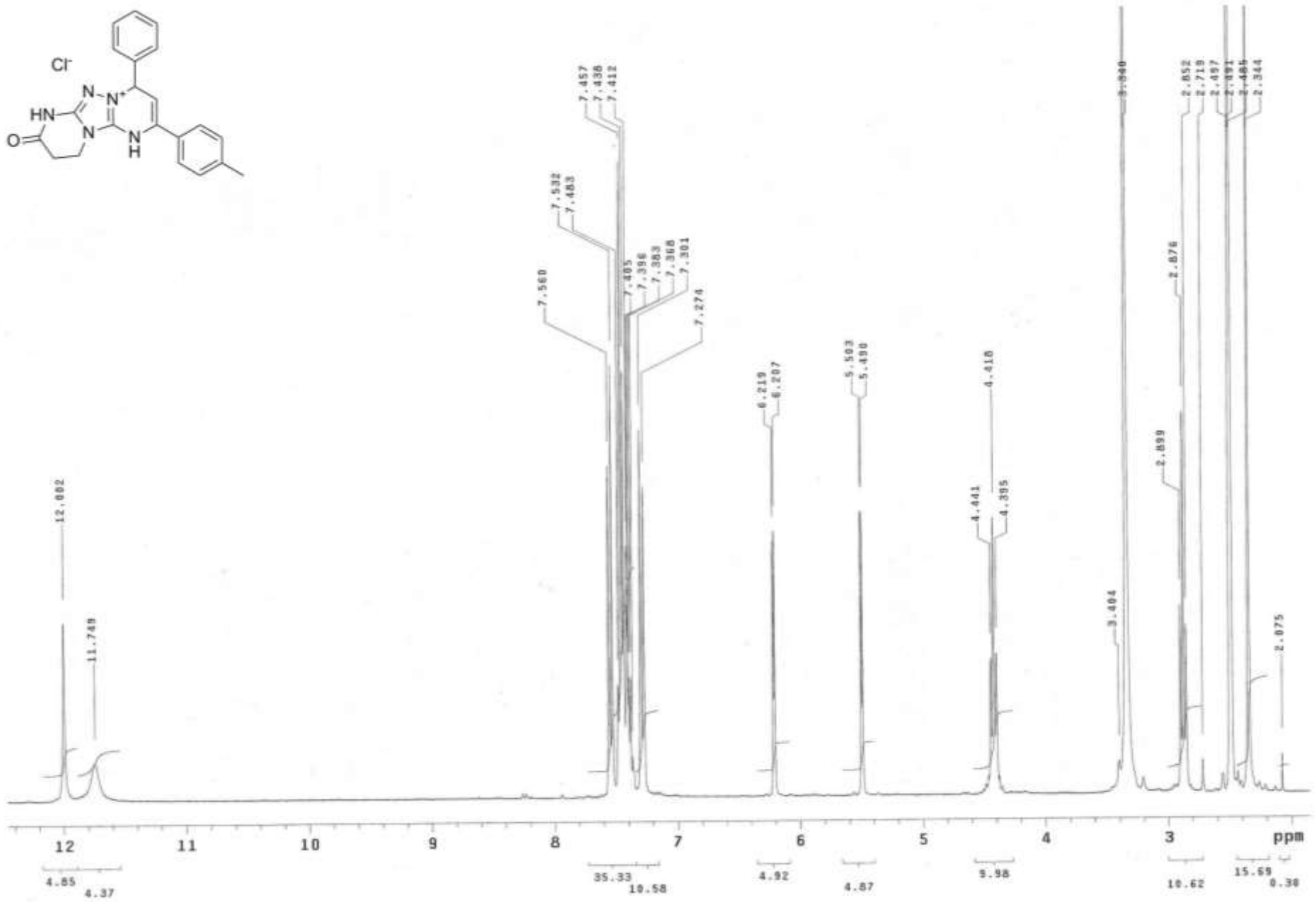
FTIR spectrum of compound **8c** (ATR).



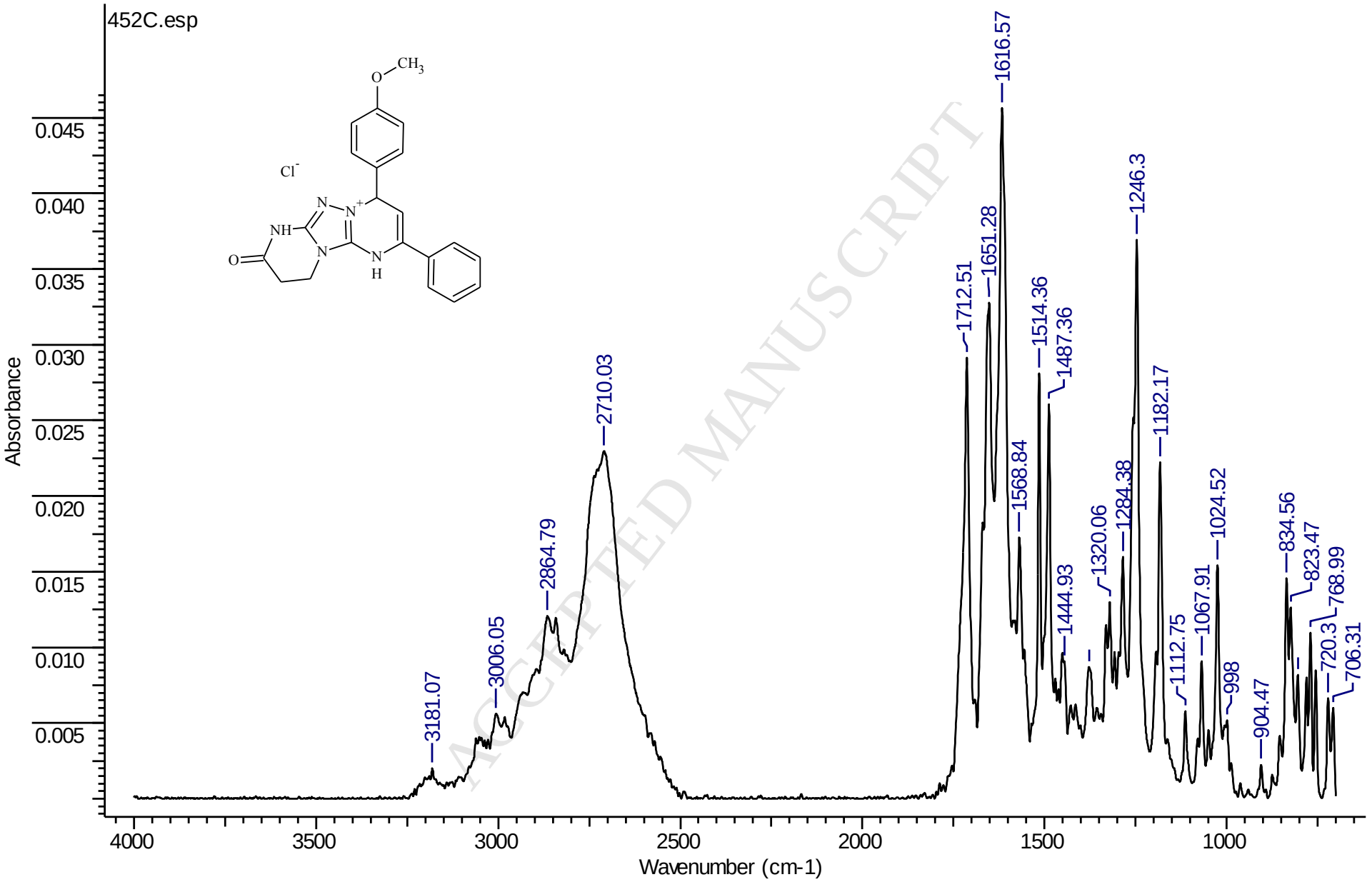
^{1}H NMR spectrum of compound **8c** (300 MHz, DMSO-d_6).



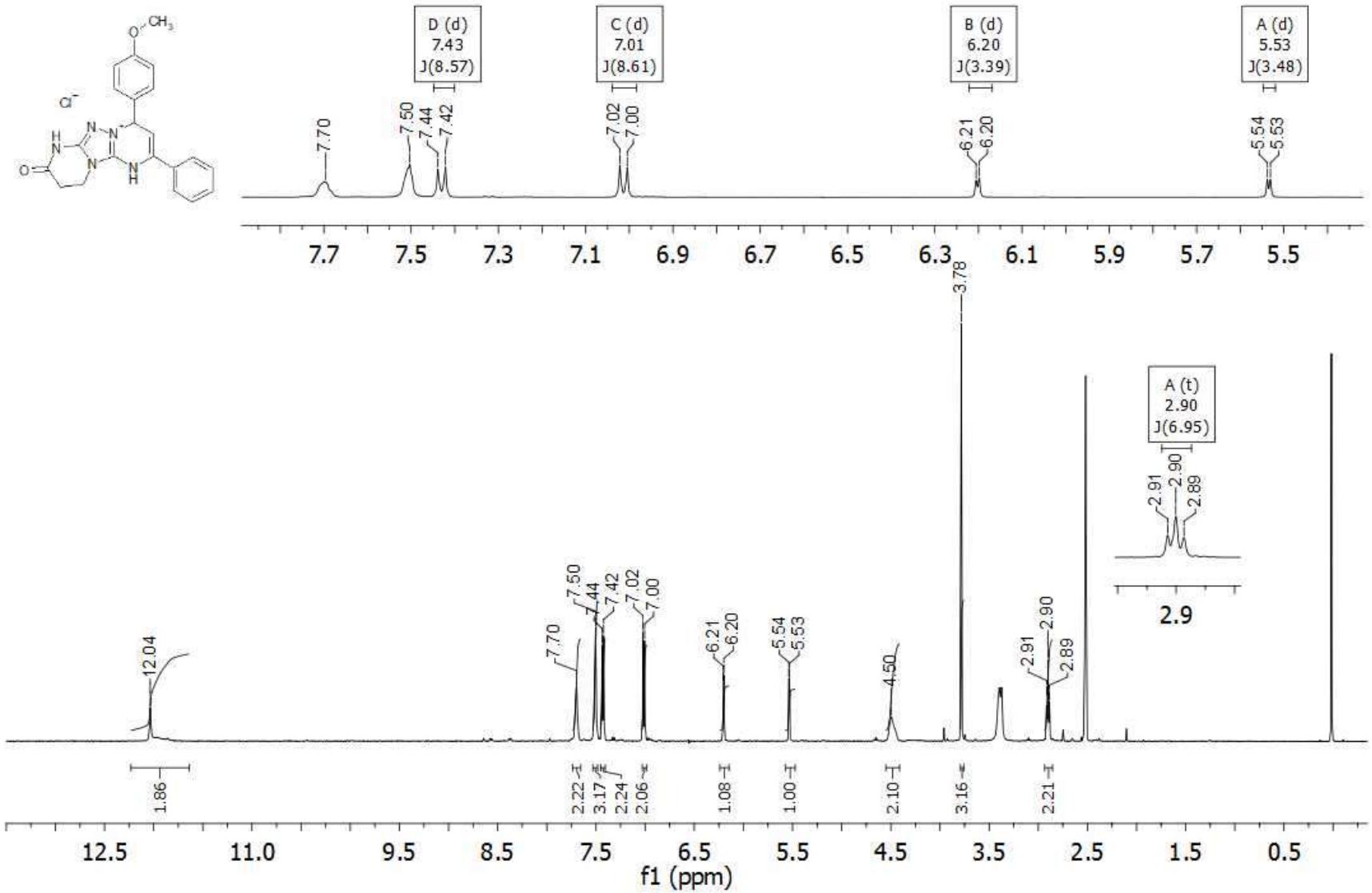
FTIR spectrum of compound **8d** (ATR).



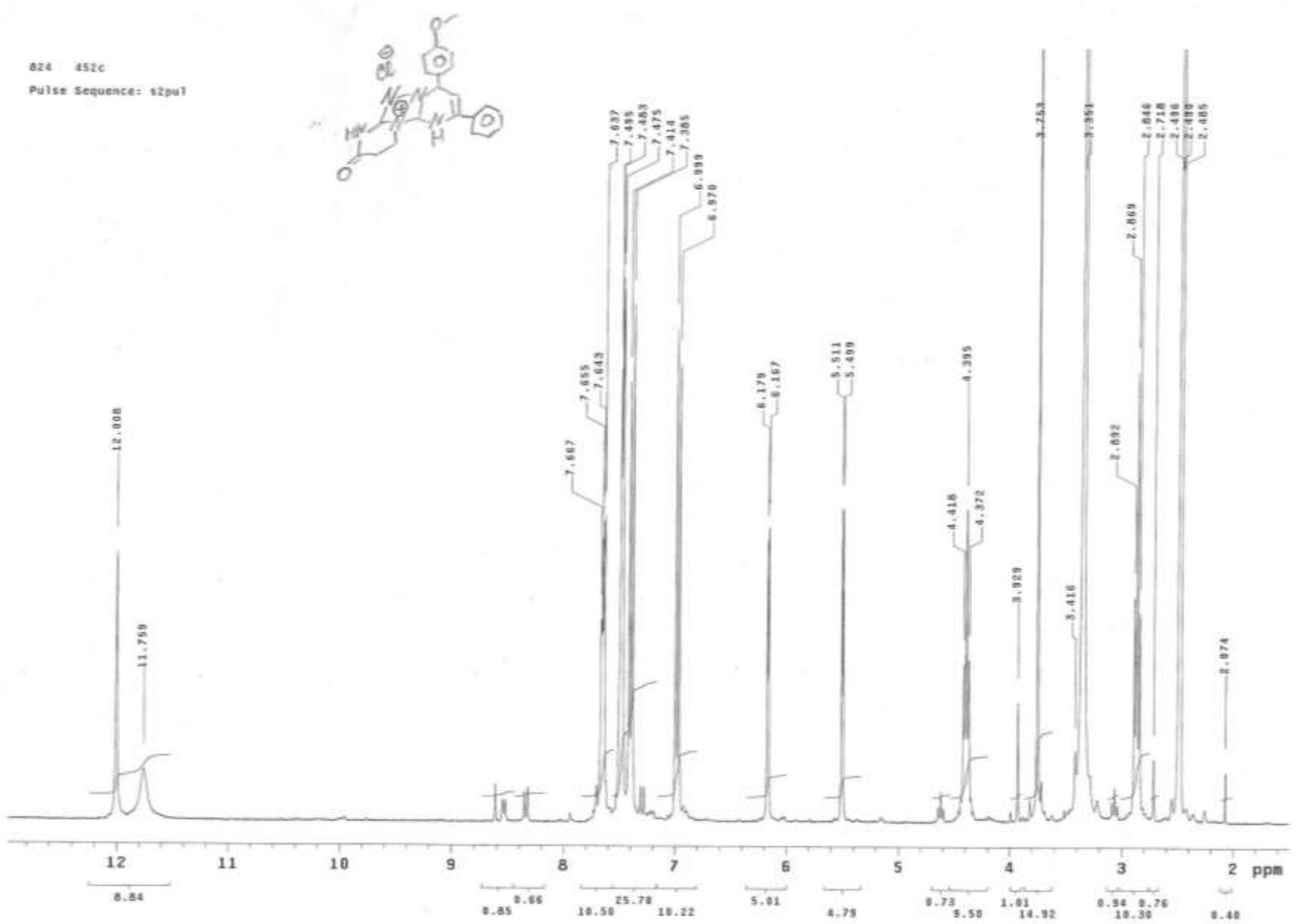
[1]H NMR spectrum of compound **8d** (DMSO-d6, 300 MHz).



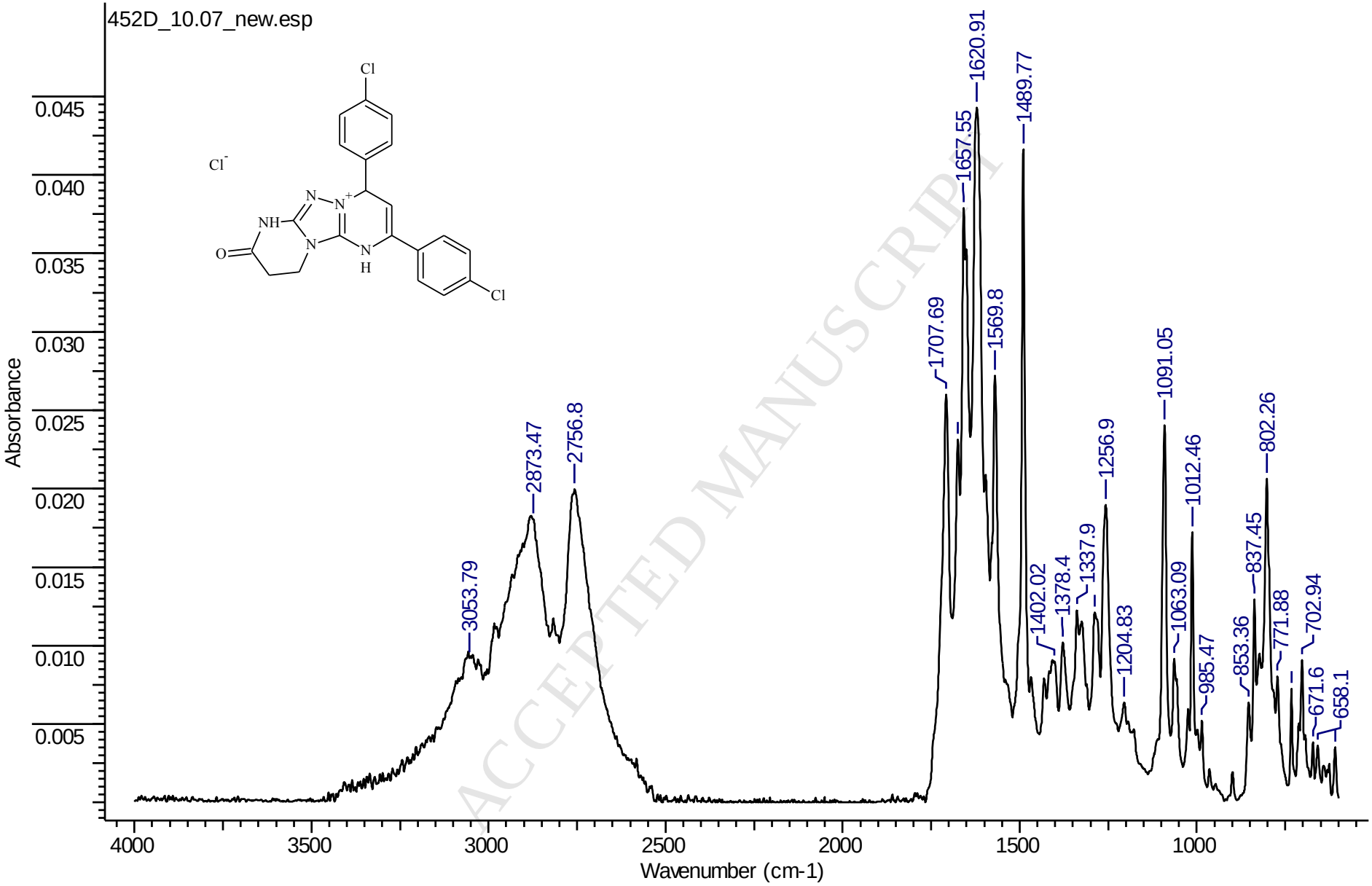
FTIR spectrum of compound **8e** (ATR).



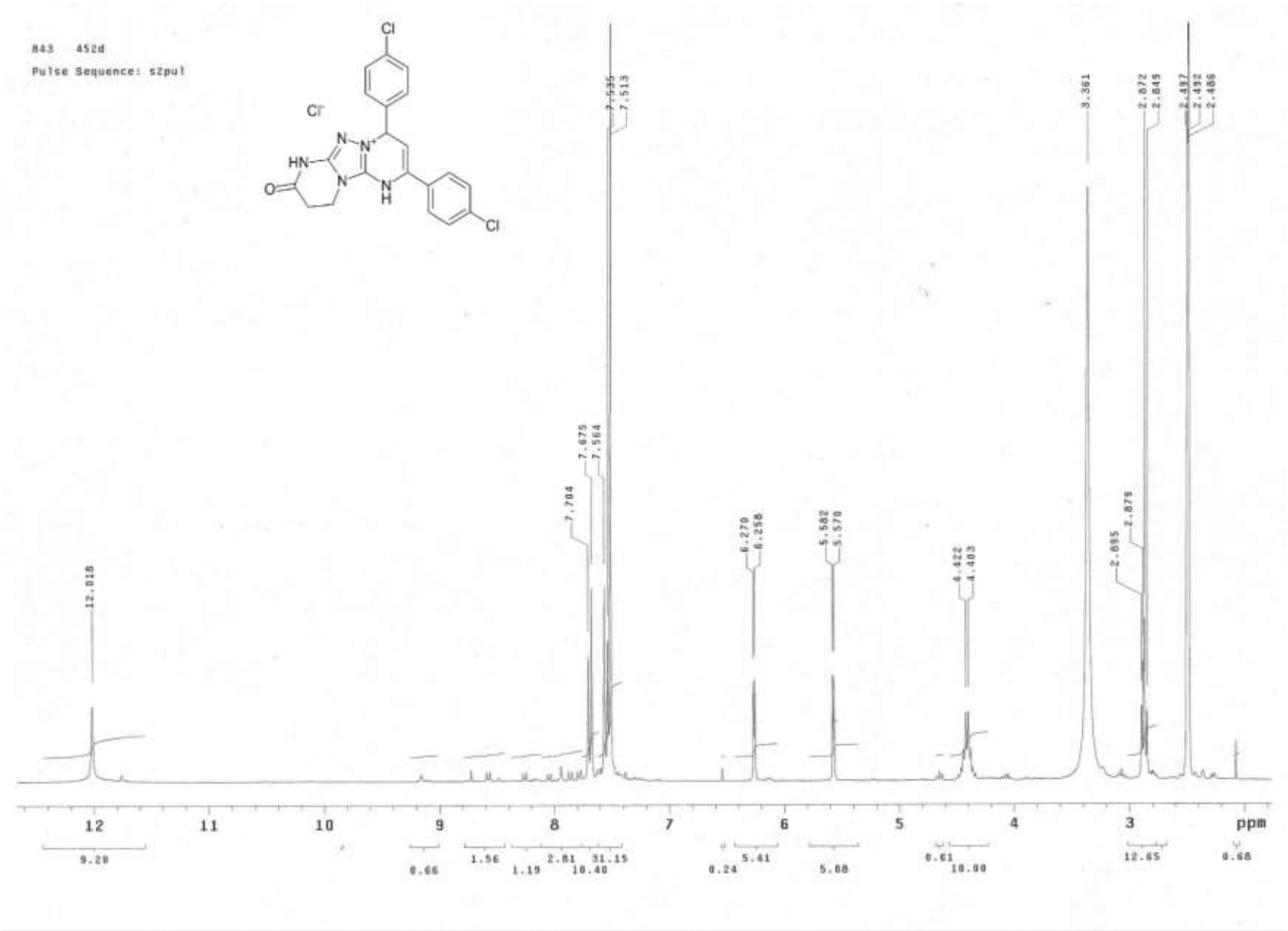
^{1}H NMR spectrum of compound **8e** (DMSO-d_6, 500 MHz). The spectrum was recoded for freshly prepared solution.



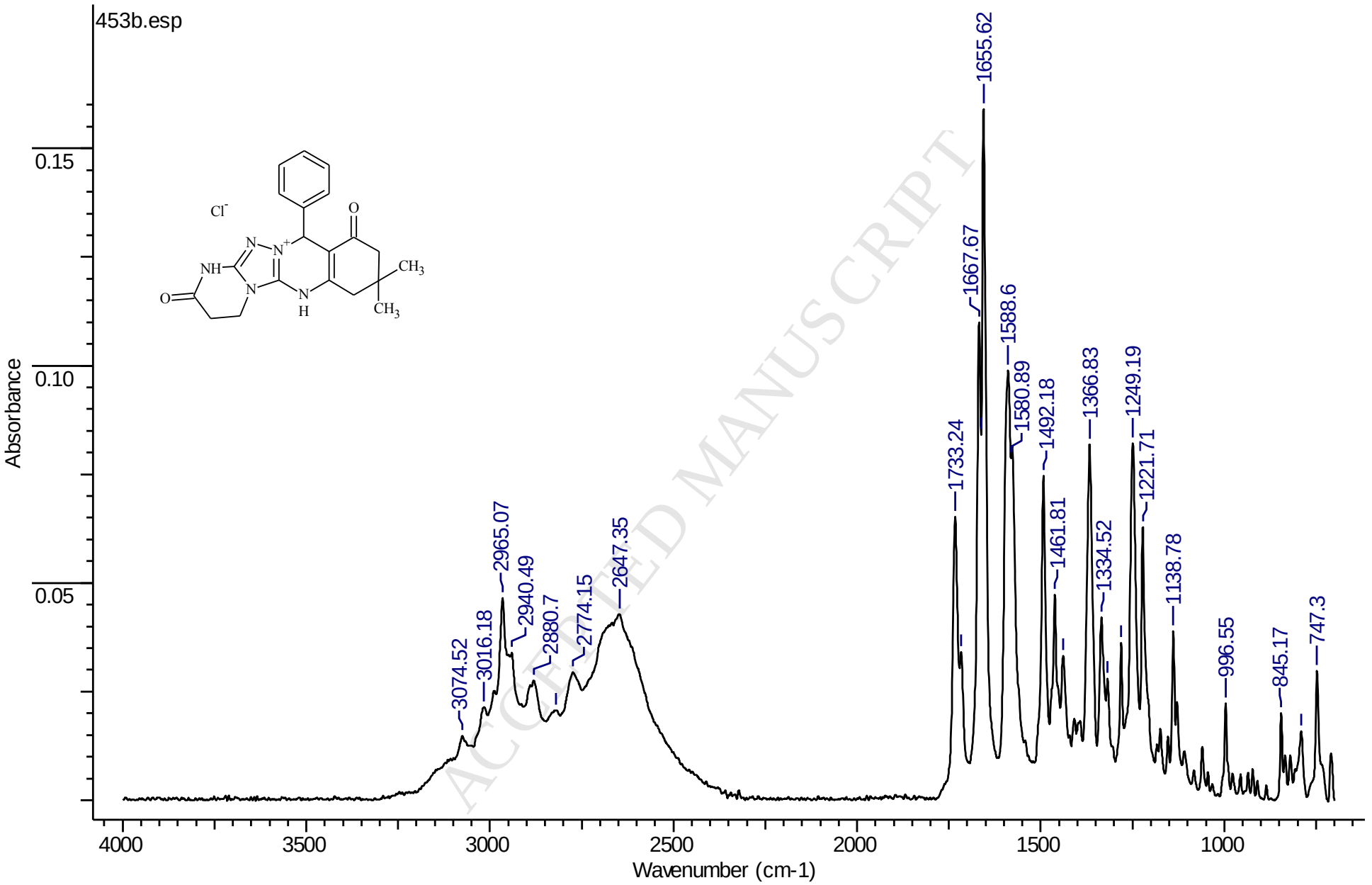
^{1}H NMR spectrum of compound **8e** (DMSO-d_6, 300 MHz). The spectrum was recoded ~ 30 min after sample dissolution in DMSO.



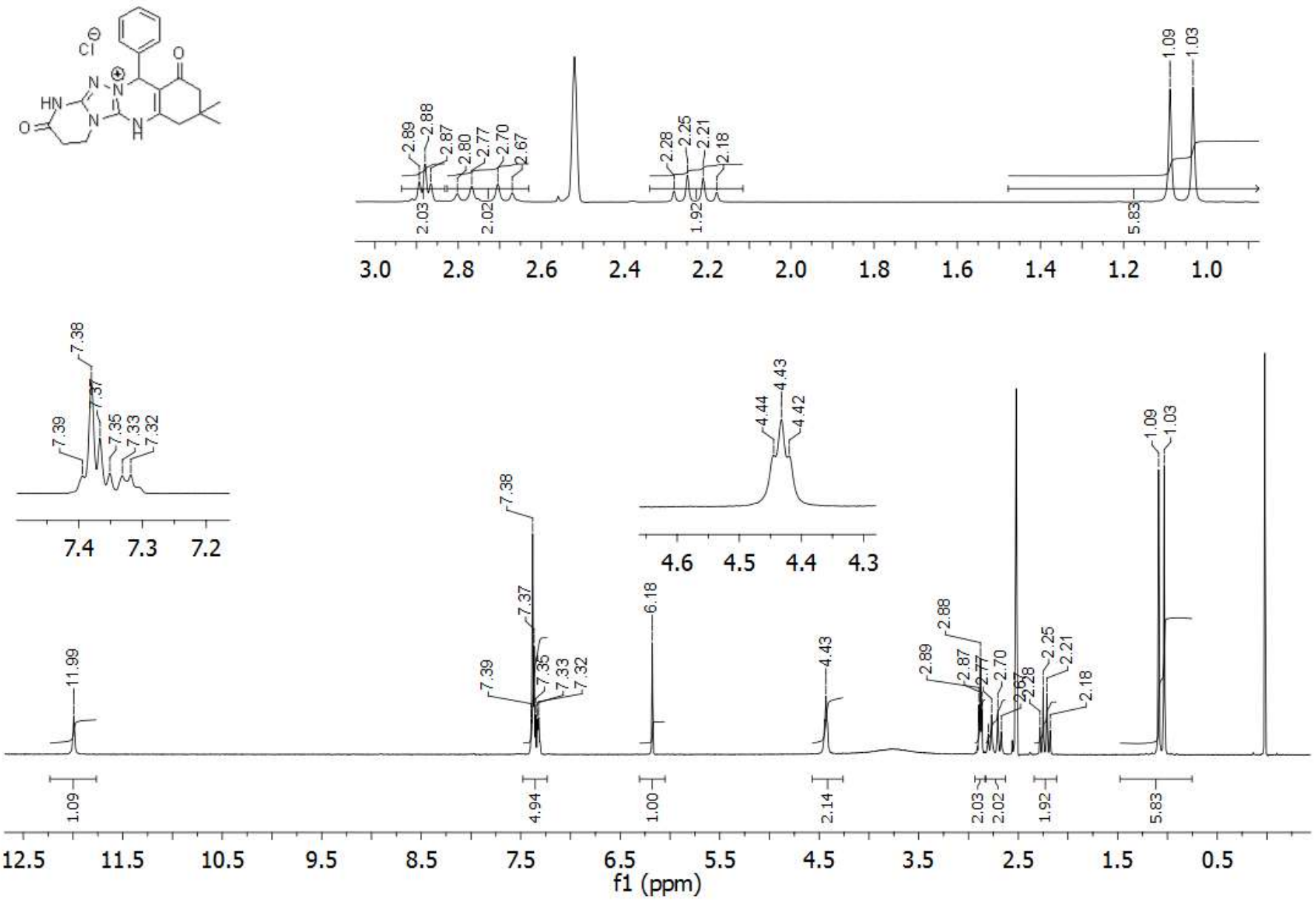
FTIR spectrum of compound **8f** (ATR)**.**



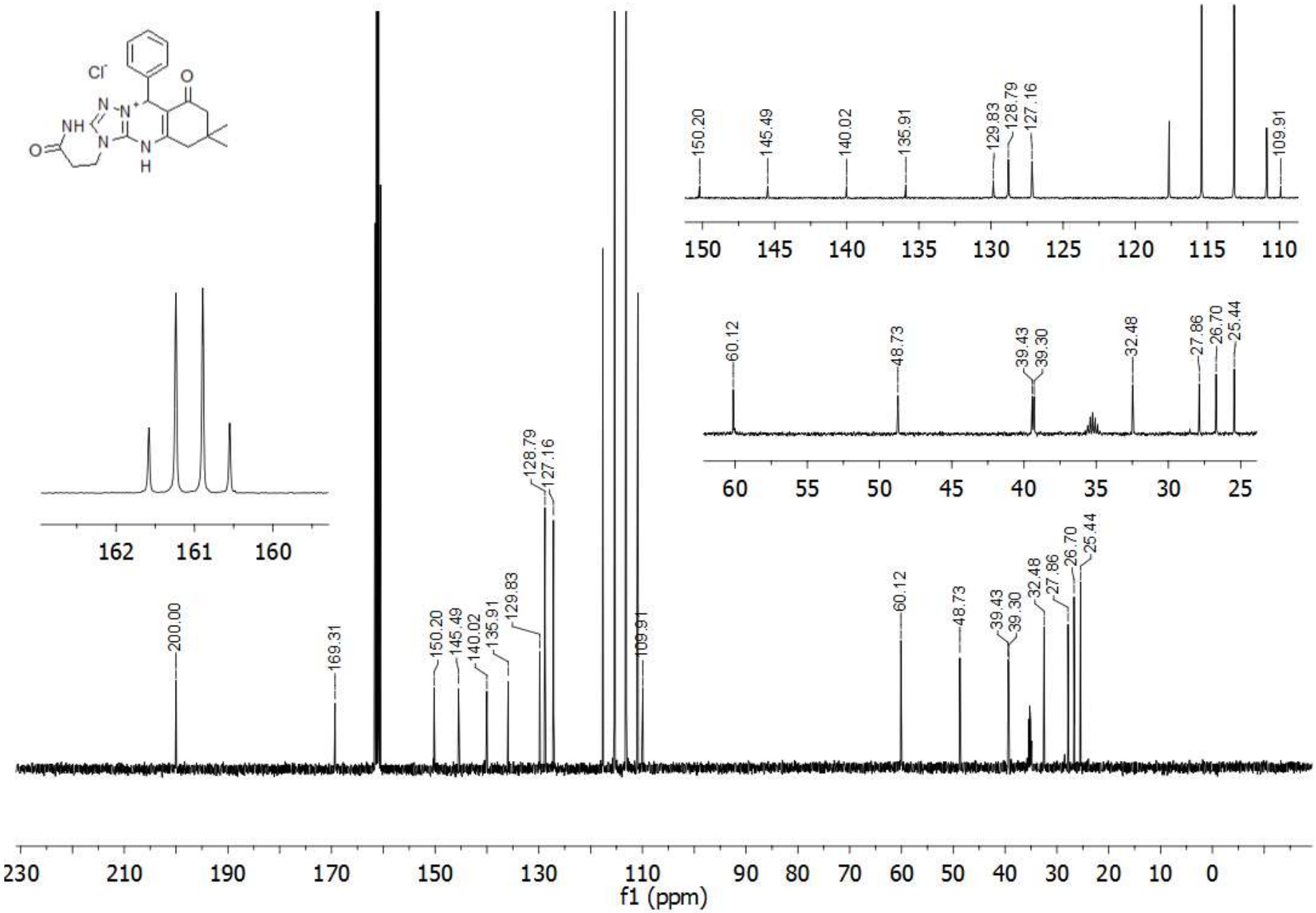
^{1}H NMR spectrum of compound **8f** (DMSO-d_6, 300 MHz).



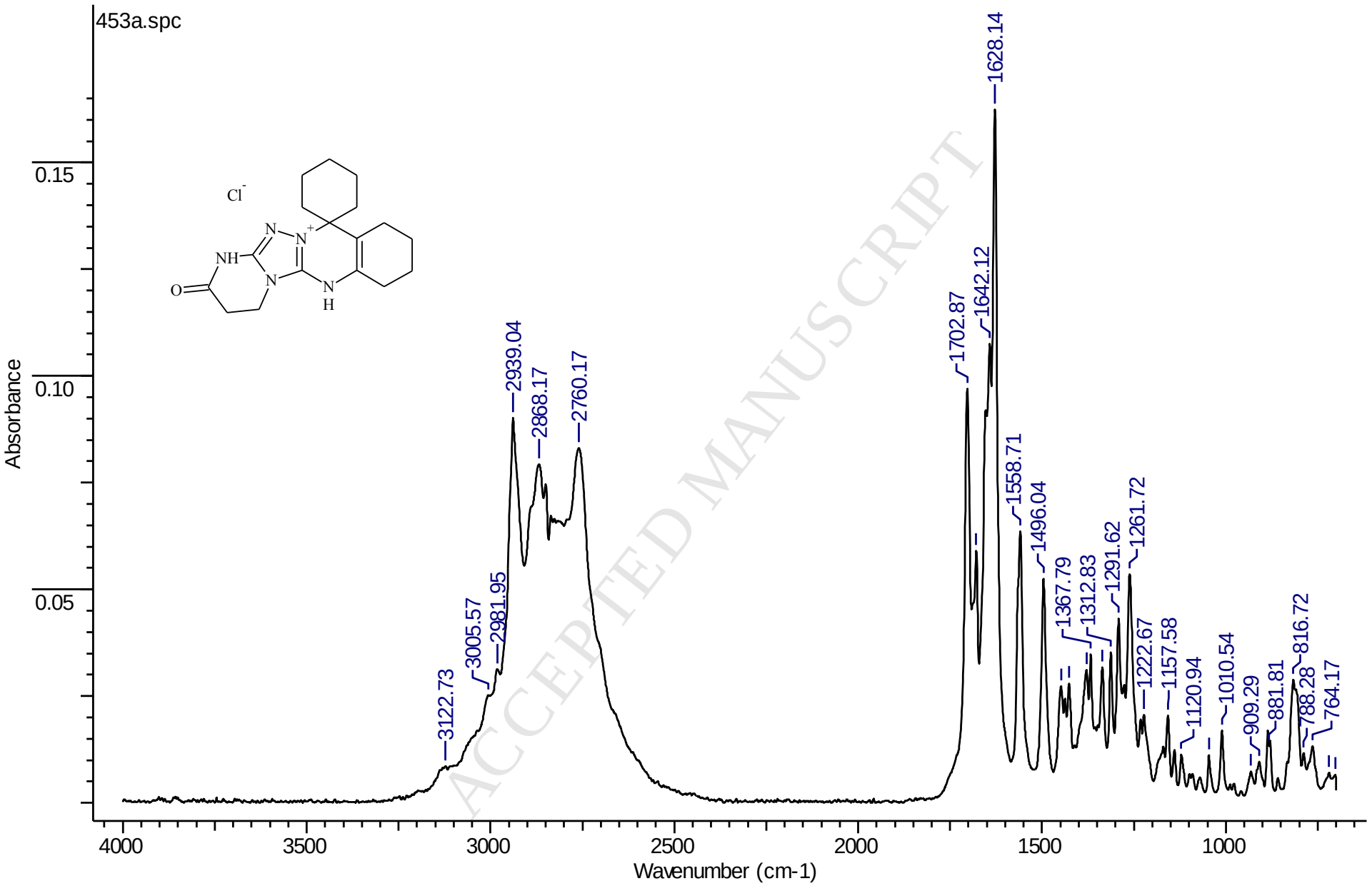
FTIR spectrum of compound **8g**.



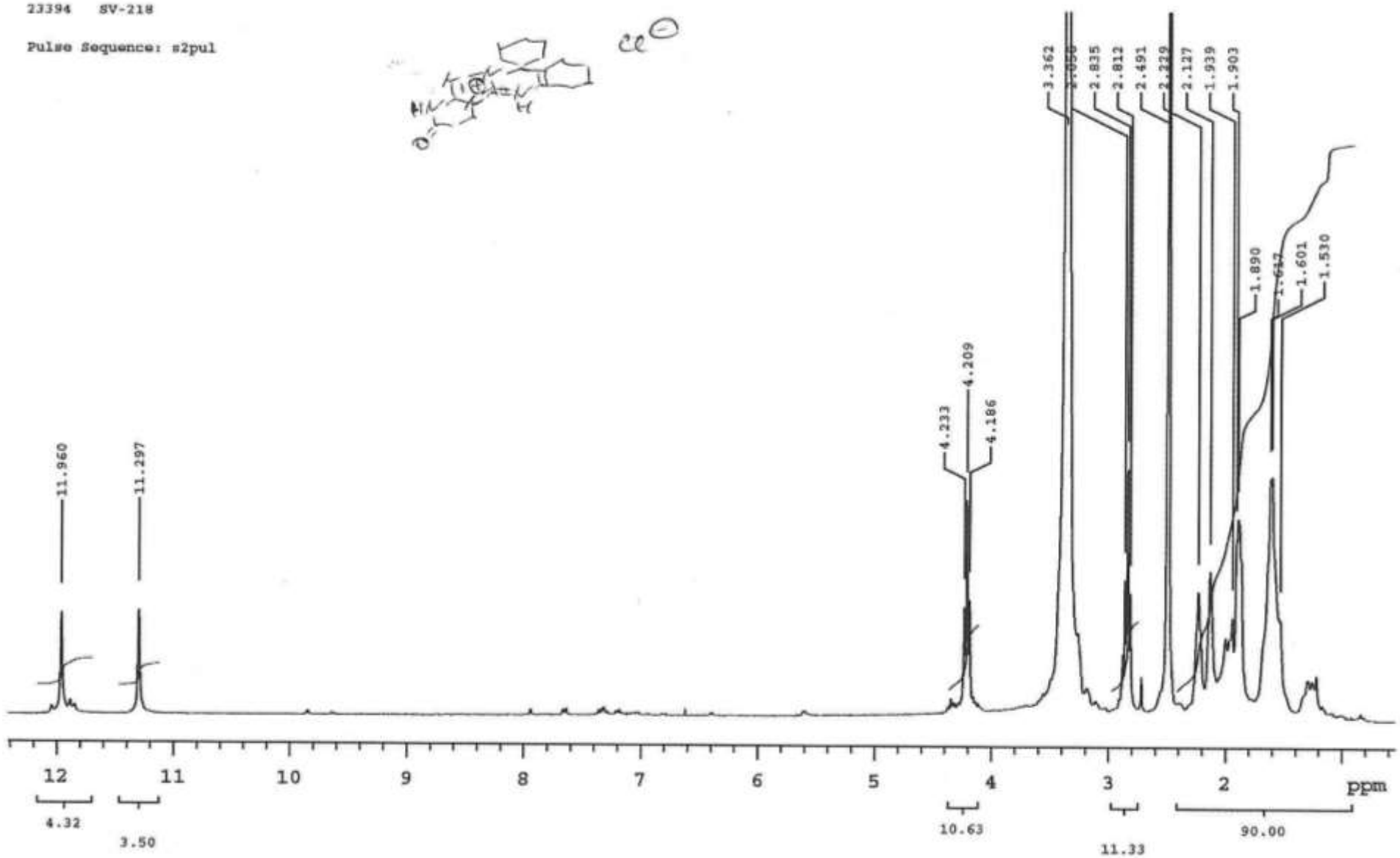
^{1}H NMR spectrum of compound **8g** (DMSO-d_6, 500 MHz).



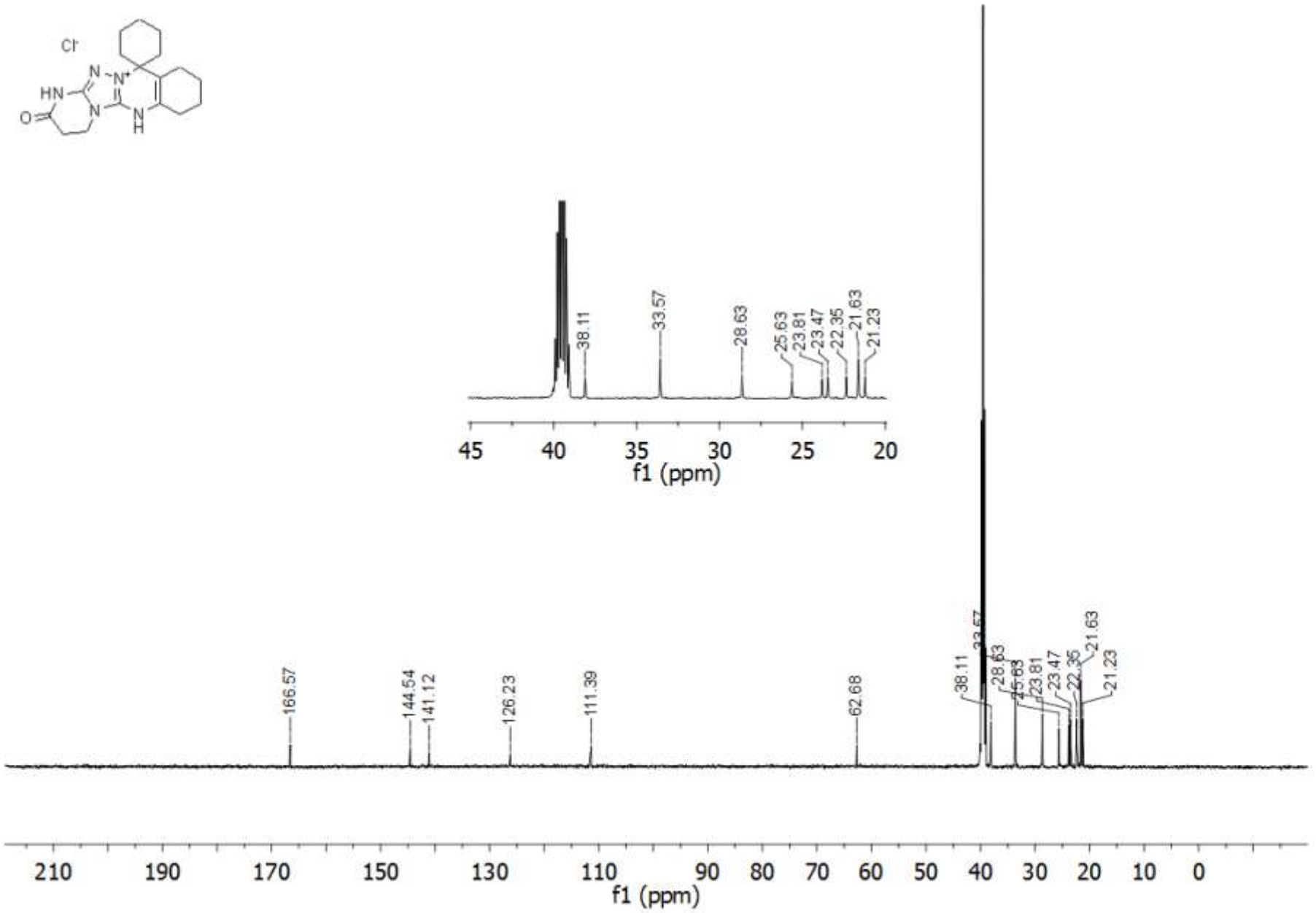
^{13}C NMR spectrum of compound **8g** (CF_3COOH + 5% DMSO-d_6, 125 MHz).



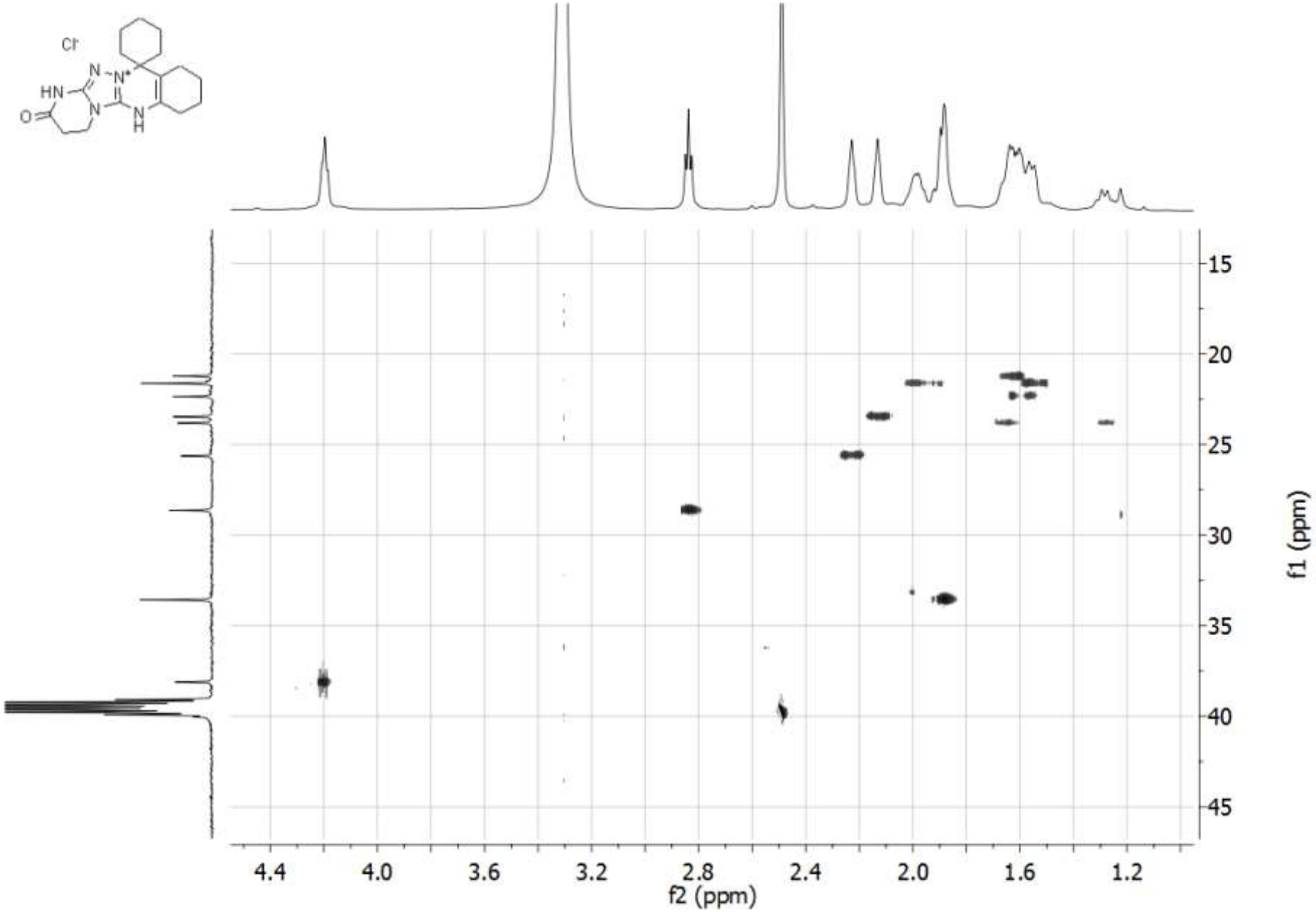
FTIR spectrum of compound **8h** (ATR).



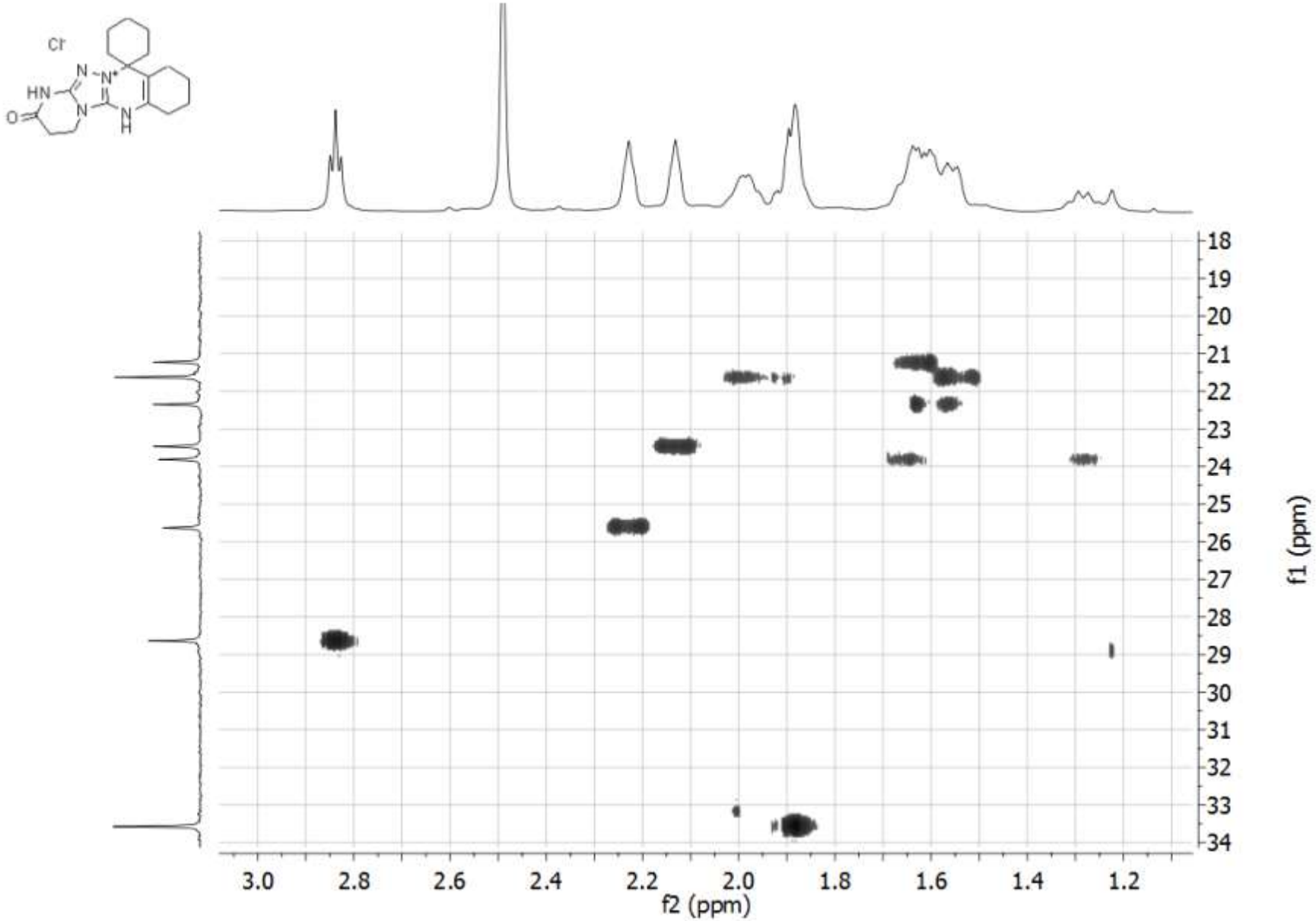
^{1}H NMR spectrum of compound **8h** (DMSO-d_6, 300 MHz).



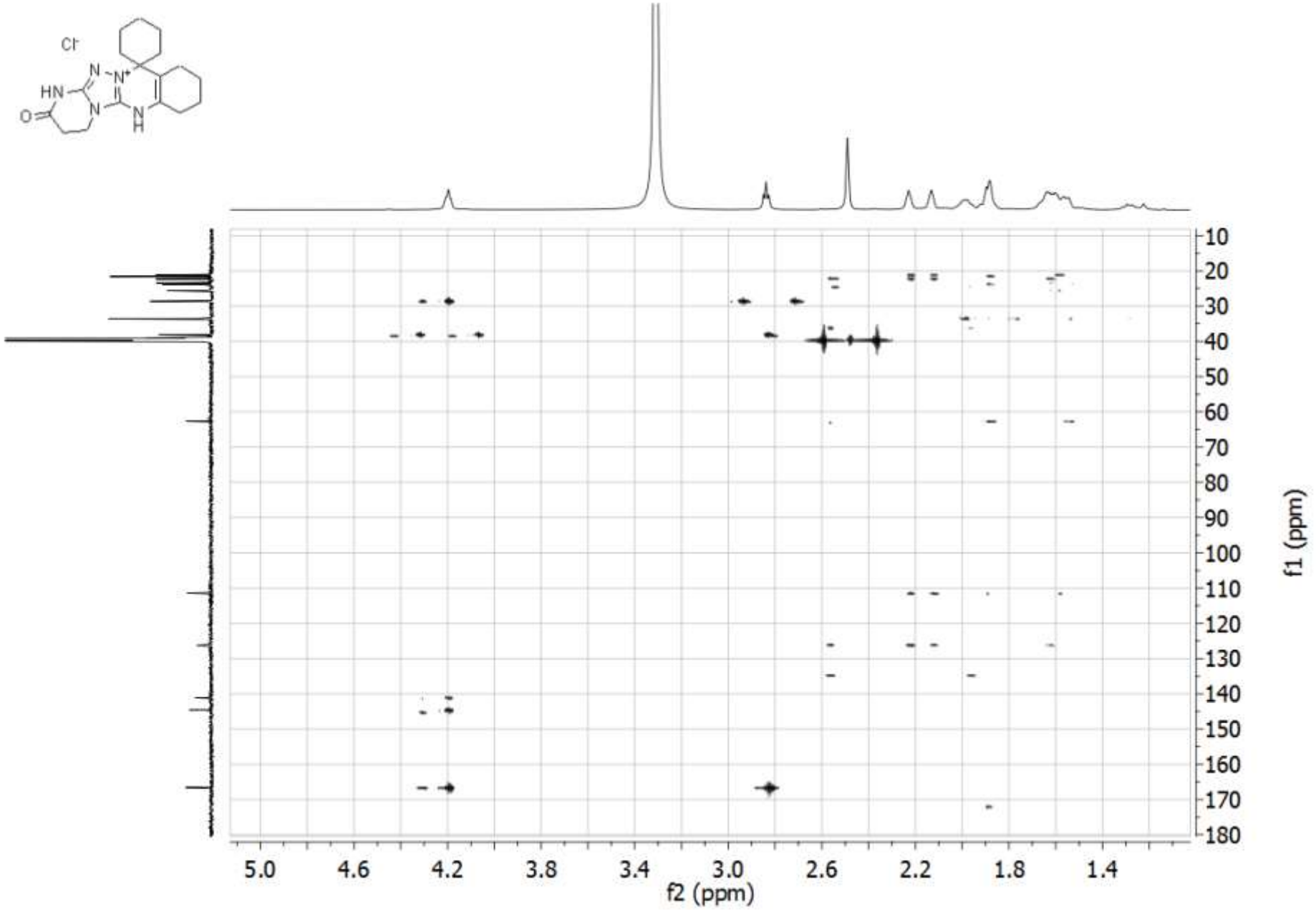
^{13}C NMR spectrum of compound **8h** (DMSO-d_6, 150 MHz).



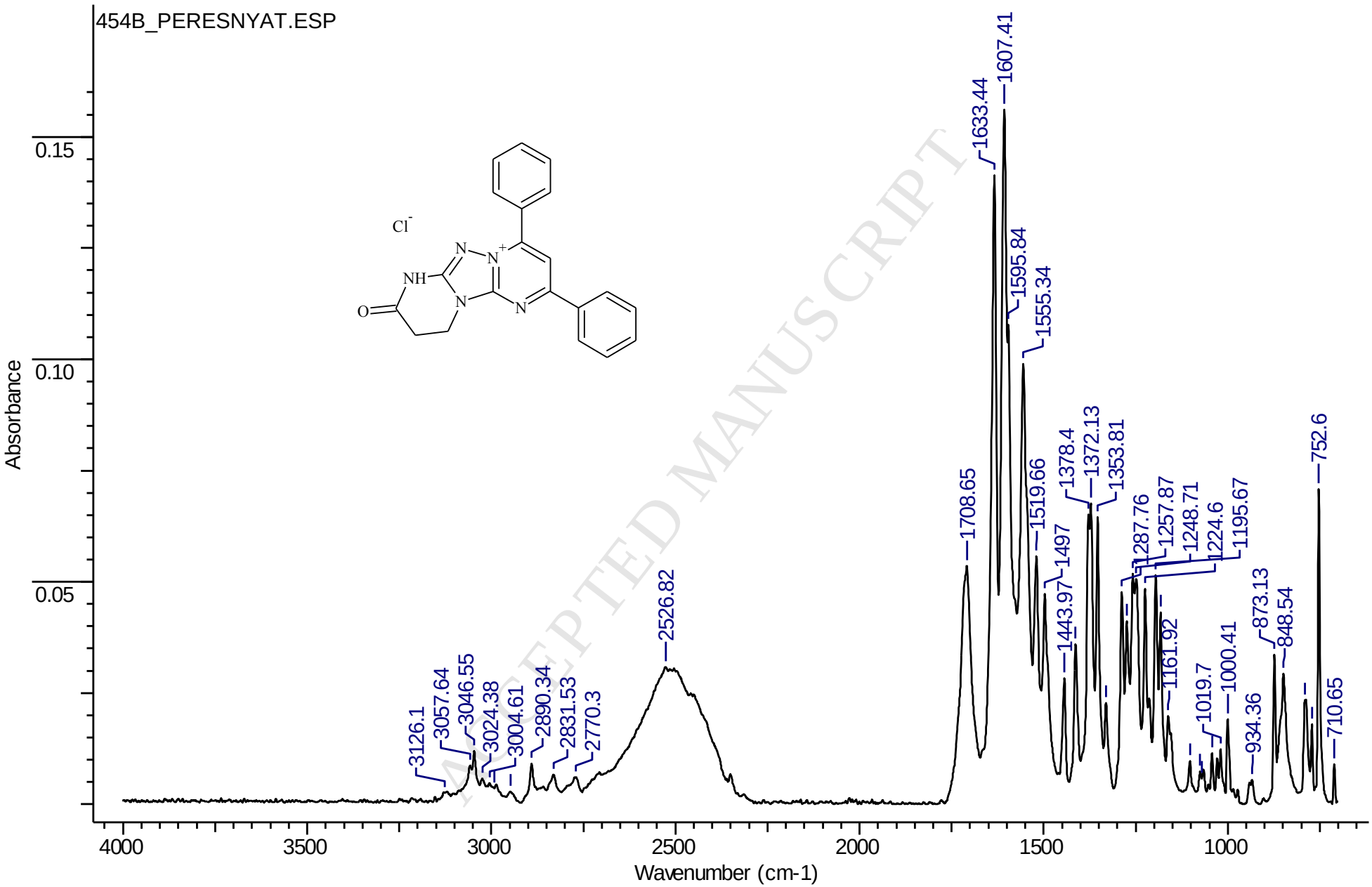
^{1}H-^{13}C HSQC spectrum of compound **8h** (DMSO-d_6).



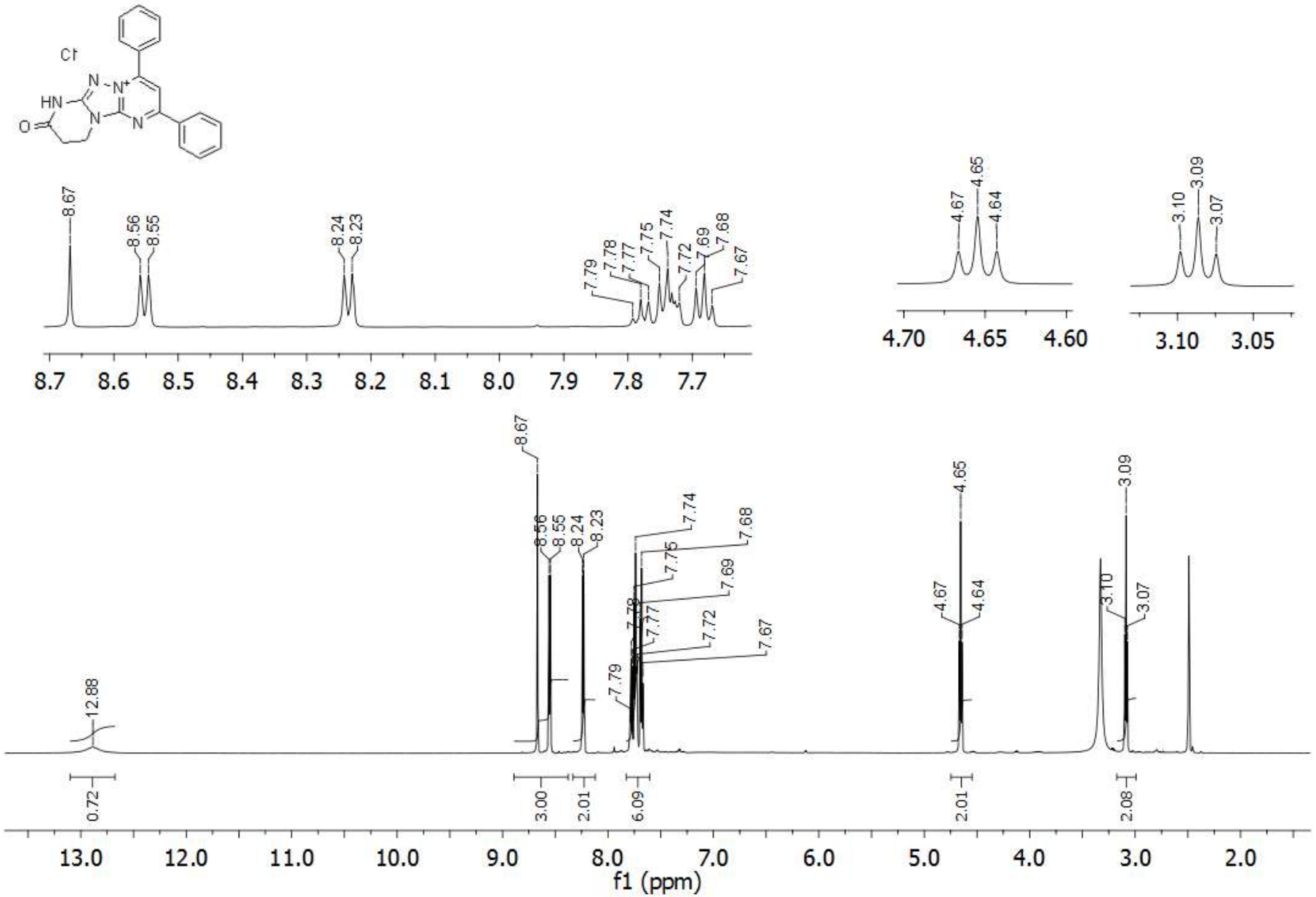
Enlarged fragment of the ^{1}H-^{13}C HSQC spectrum of compound **8h** (DMSO-d_6).



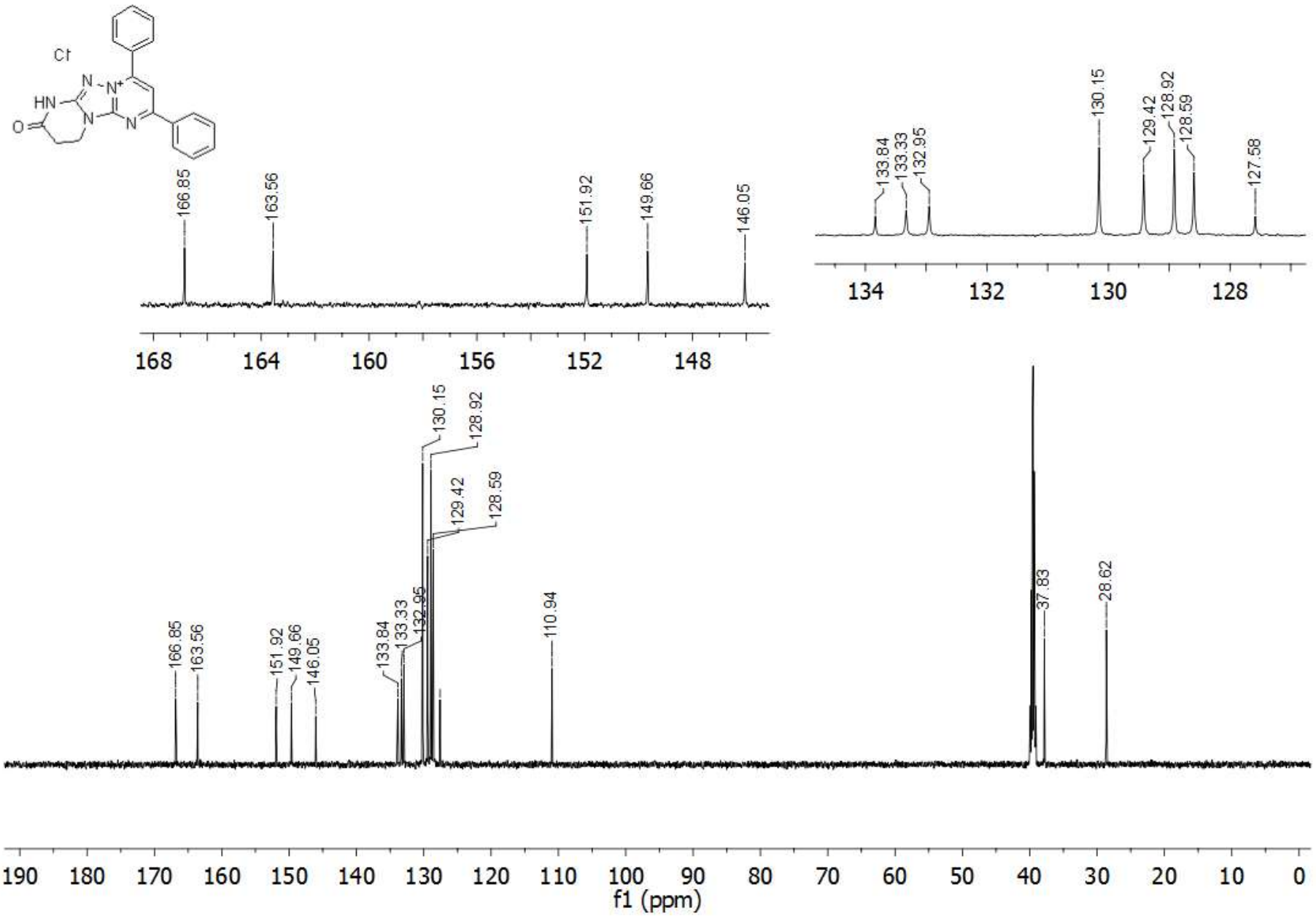
^{1}H-^{13}C HMBC spectrum of compound **8h** (DMSO-d_6).



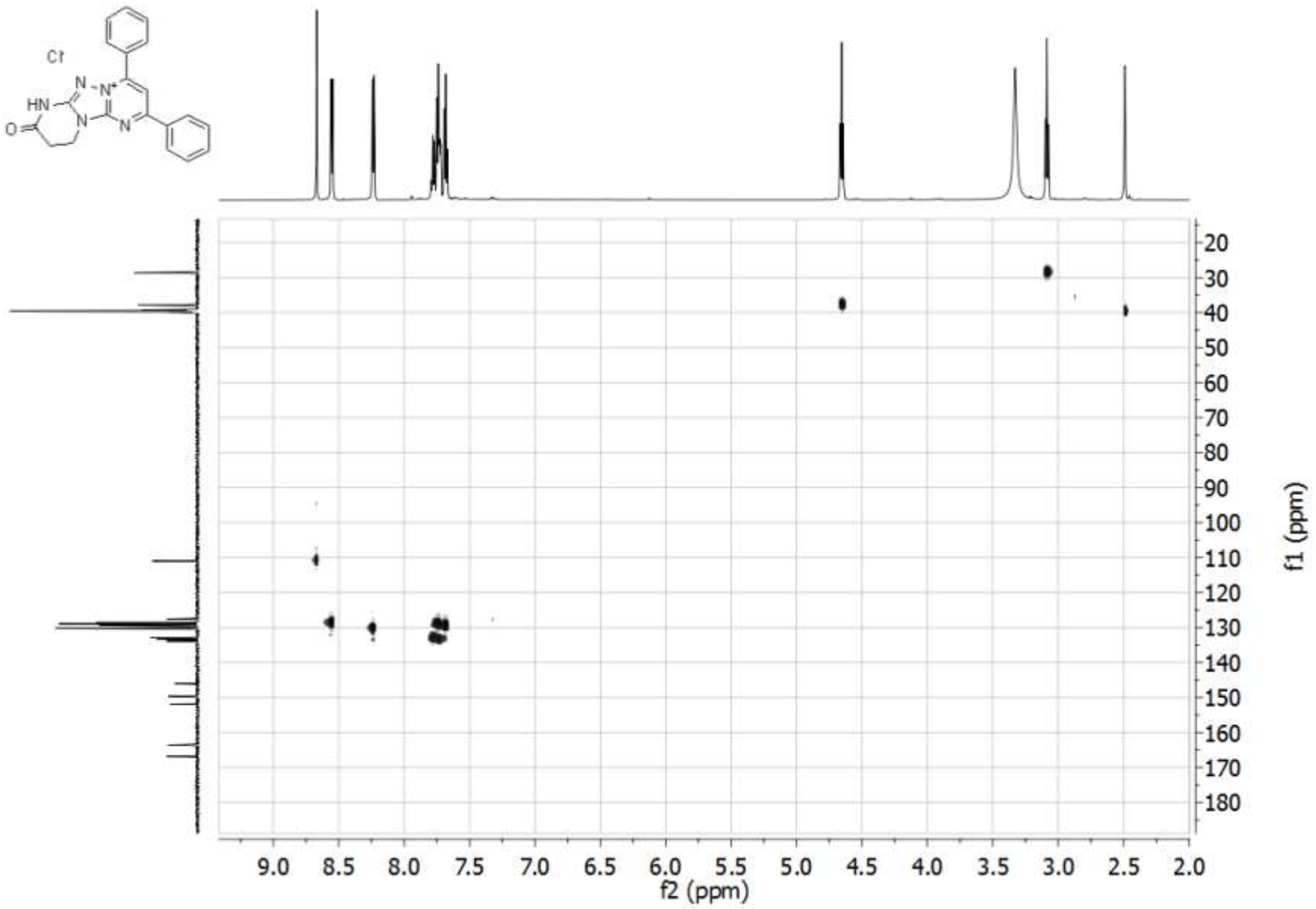
FTIR spectrum of compound **9c** (ATR).



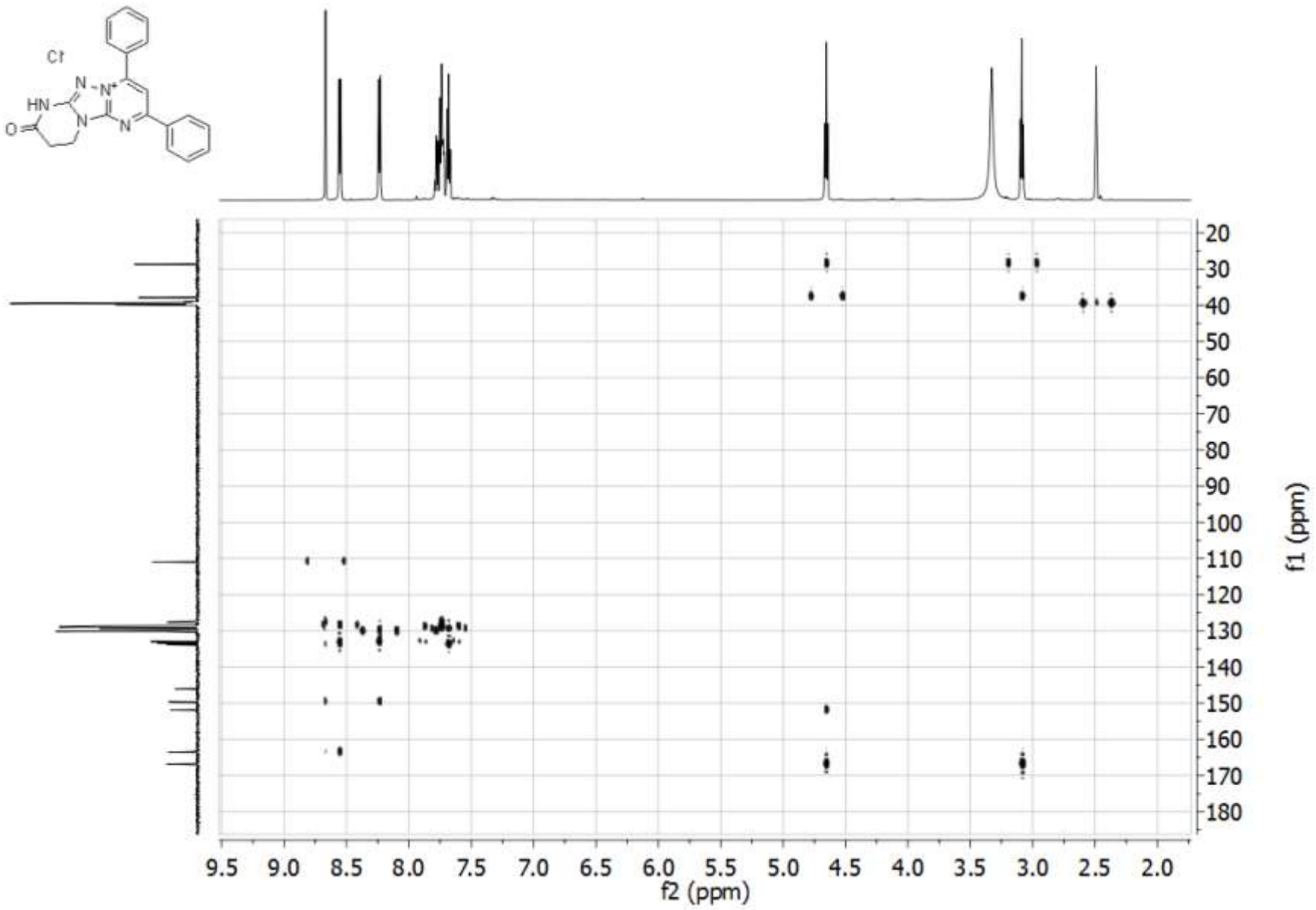
^{1}H NMR spectrum of compound **9c** (DMSO-d_6, 600 MHz).



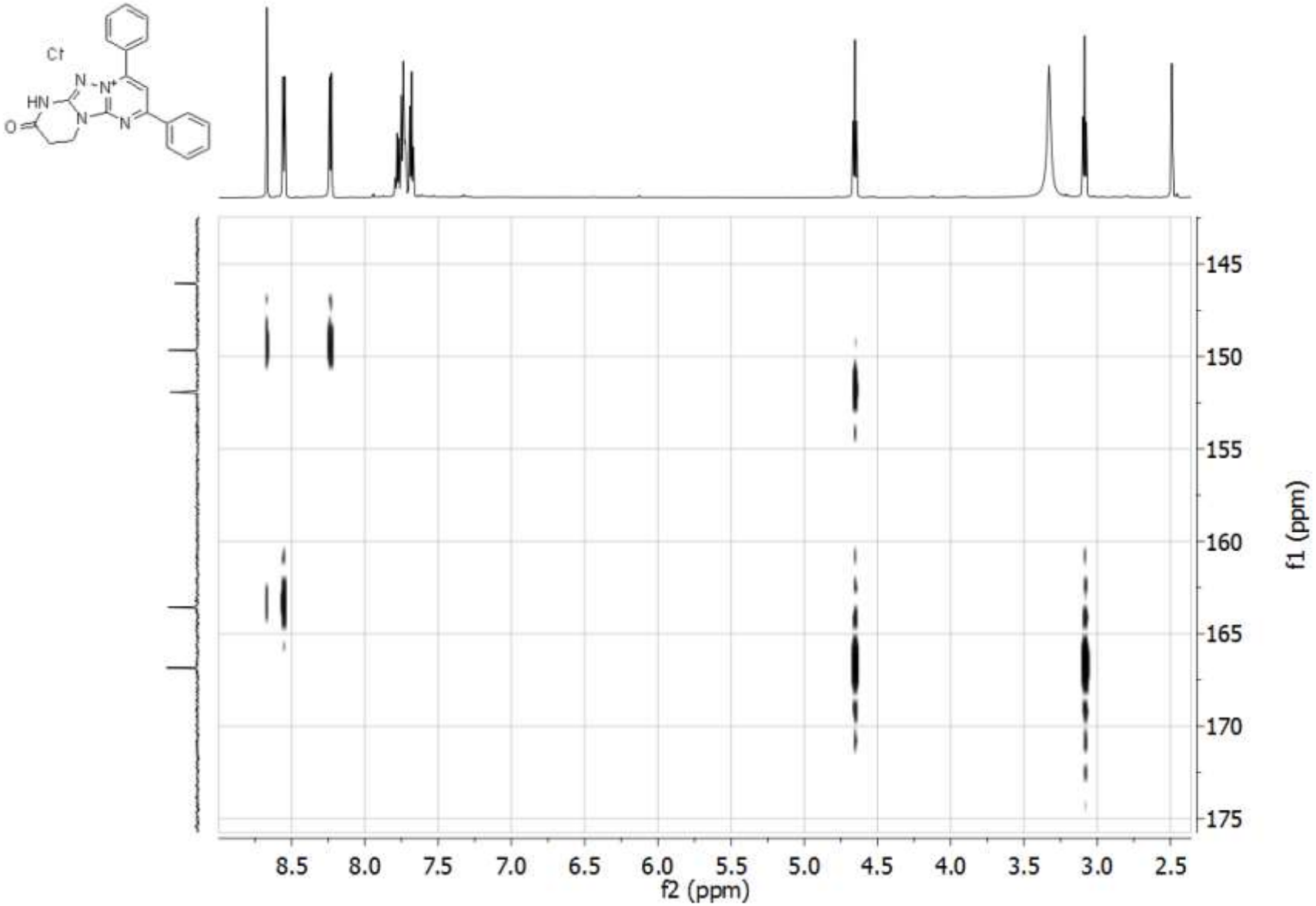
^{13}C NMR spectrum of compound **9c** (DMSO-d_6, 150 MHz).



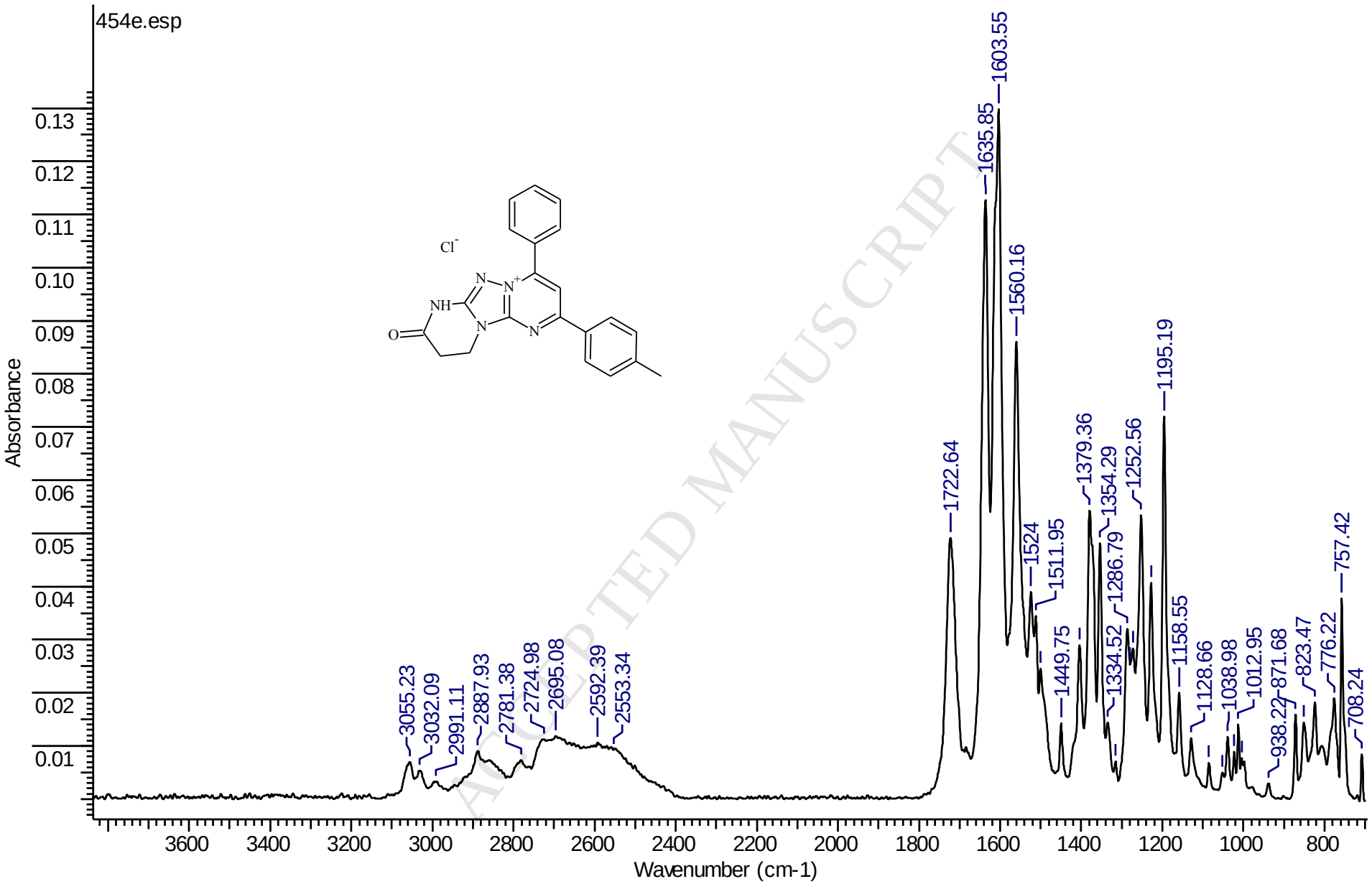
^{1}H-^{13}C HSQC spectrum of compound **9c** (DMSO-d_6).



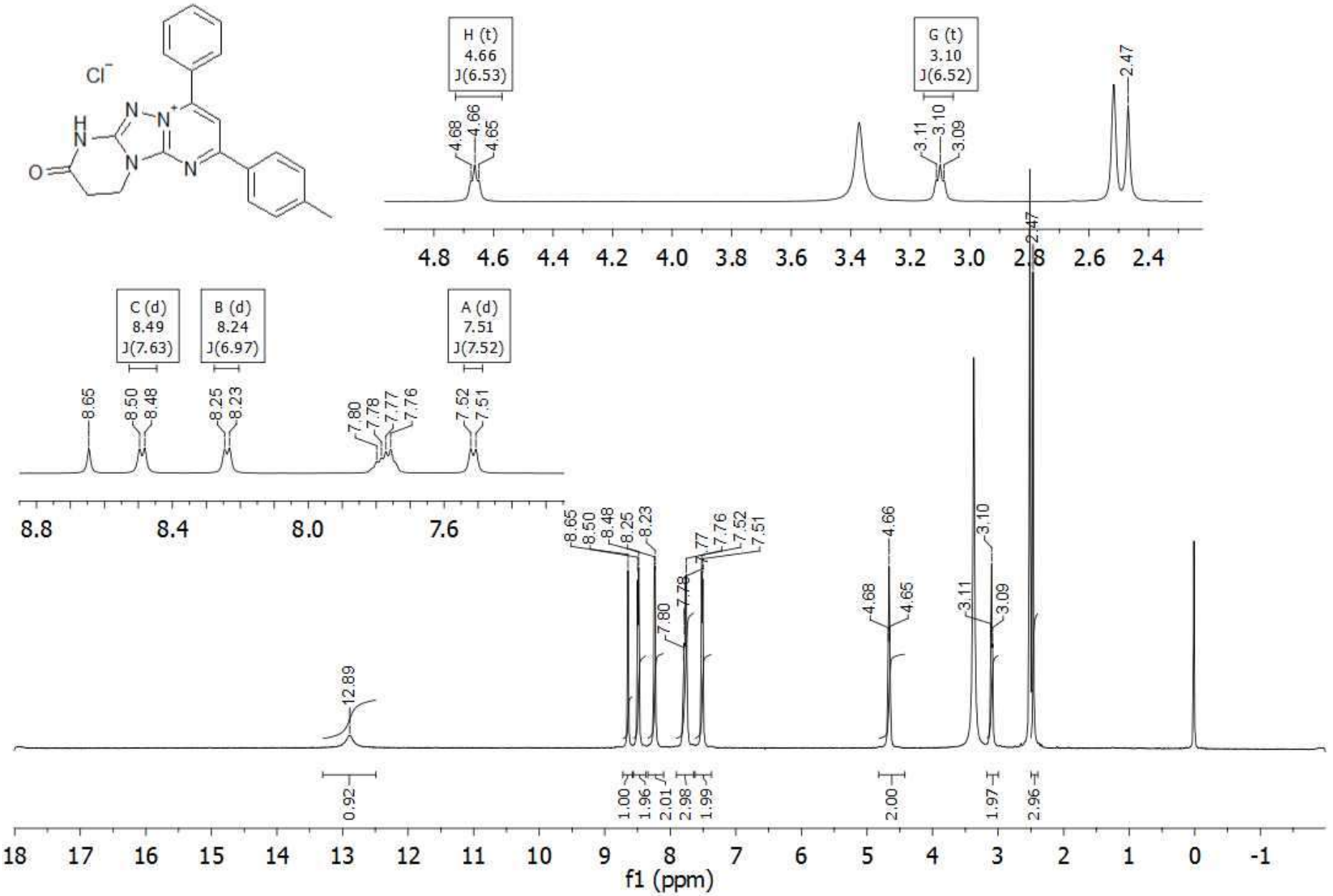
^{1}H-^{13}C HMBC spectrum of compound **9c** (DMSO-d_6).



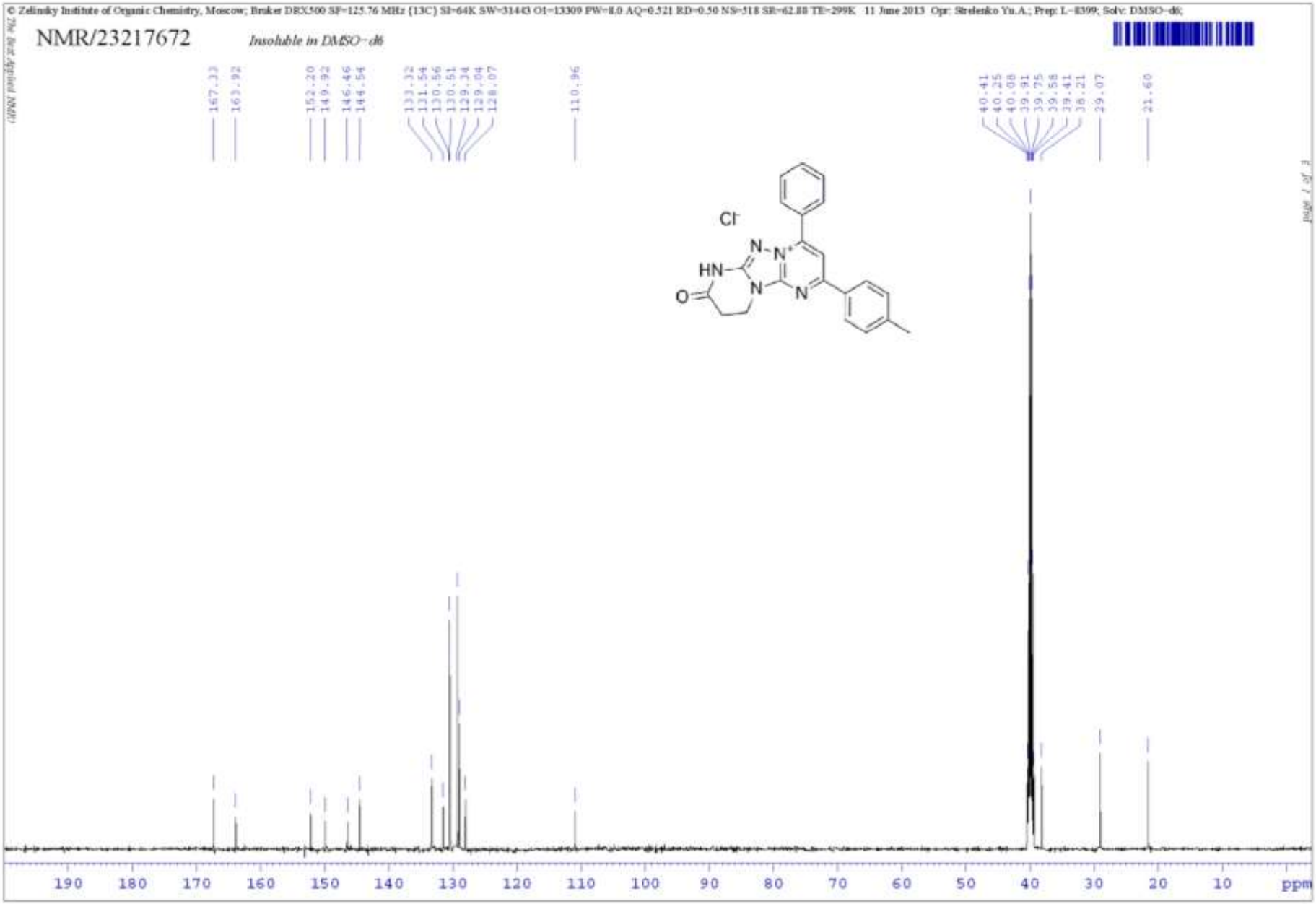
Enlarged fragment of ^{1}H-^{13}C HMBC spectrum of compound **9c** (DMSO-d_6).



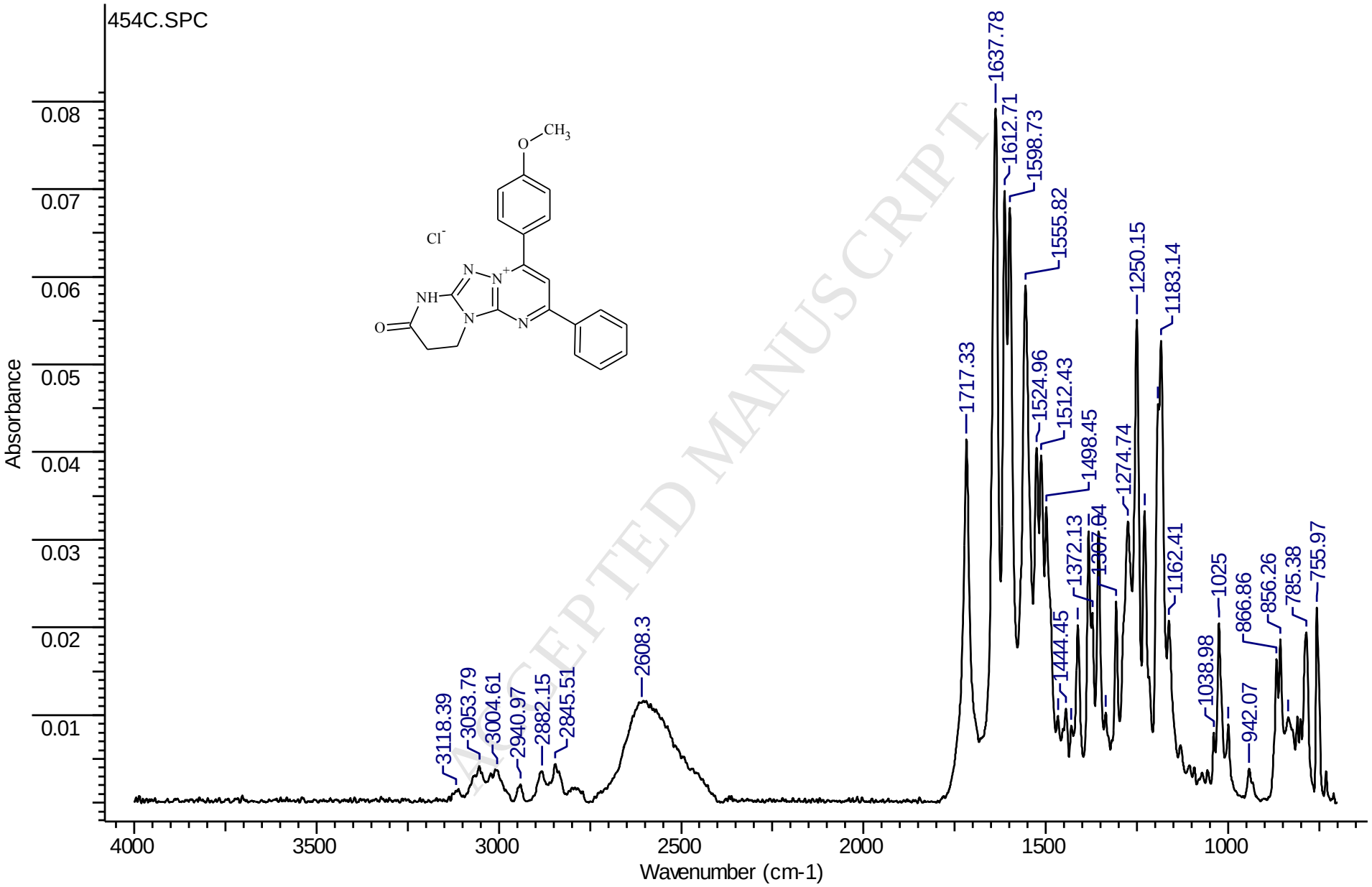
FTIR spectrum of compound **9d** (ATR).



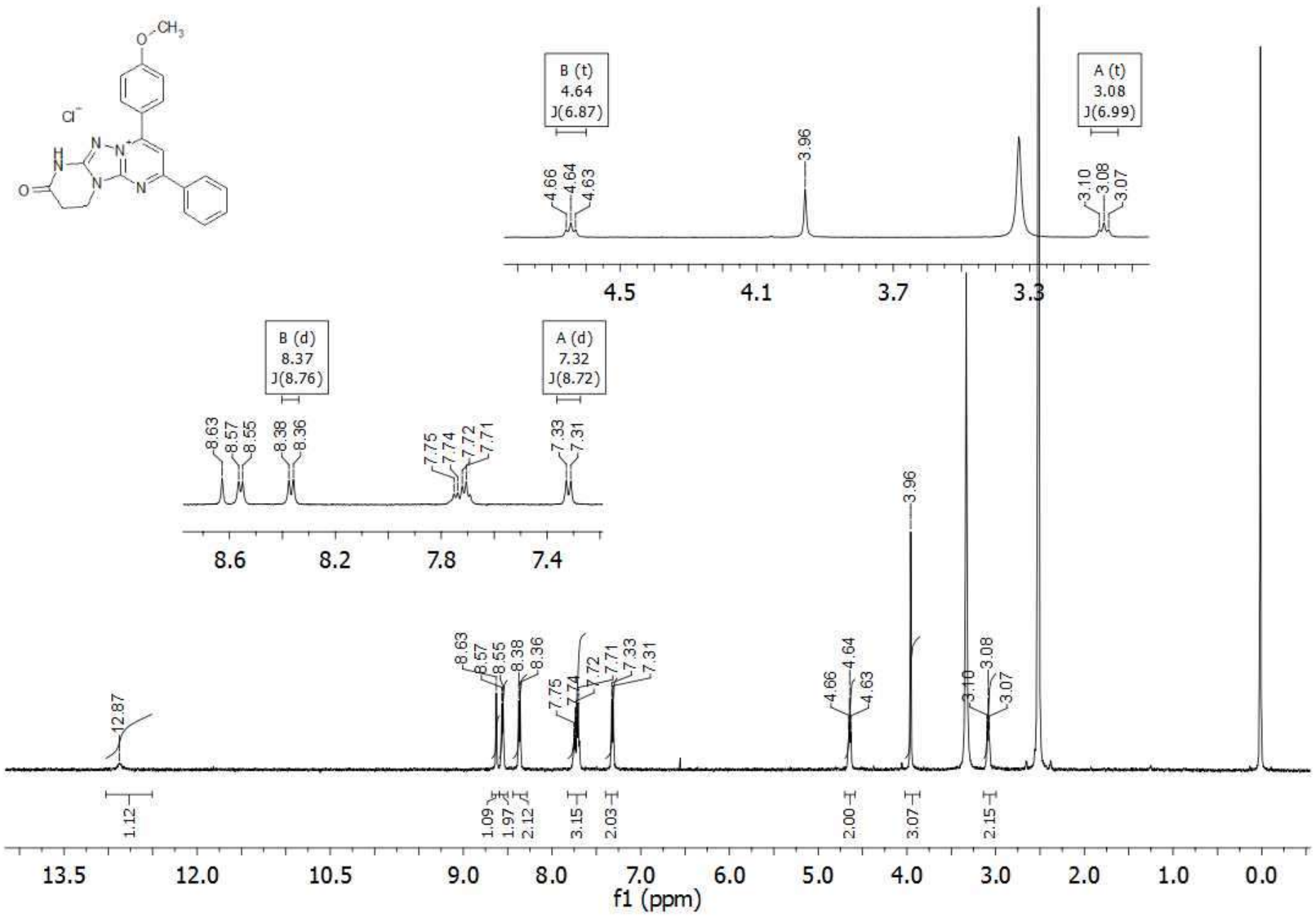
[1]H NMR spectrum of compound **9d** (DMSO-d6, 500 MHz).



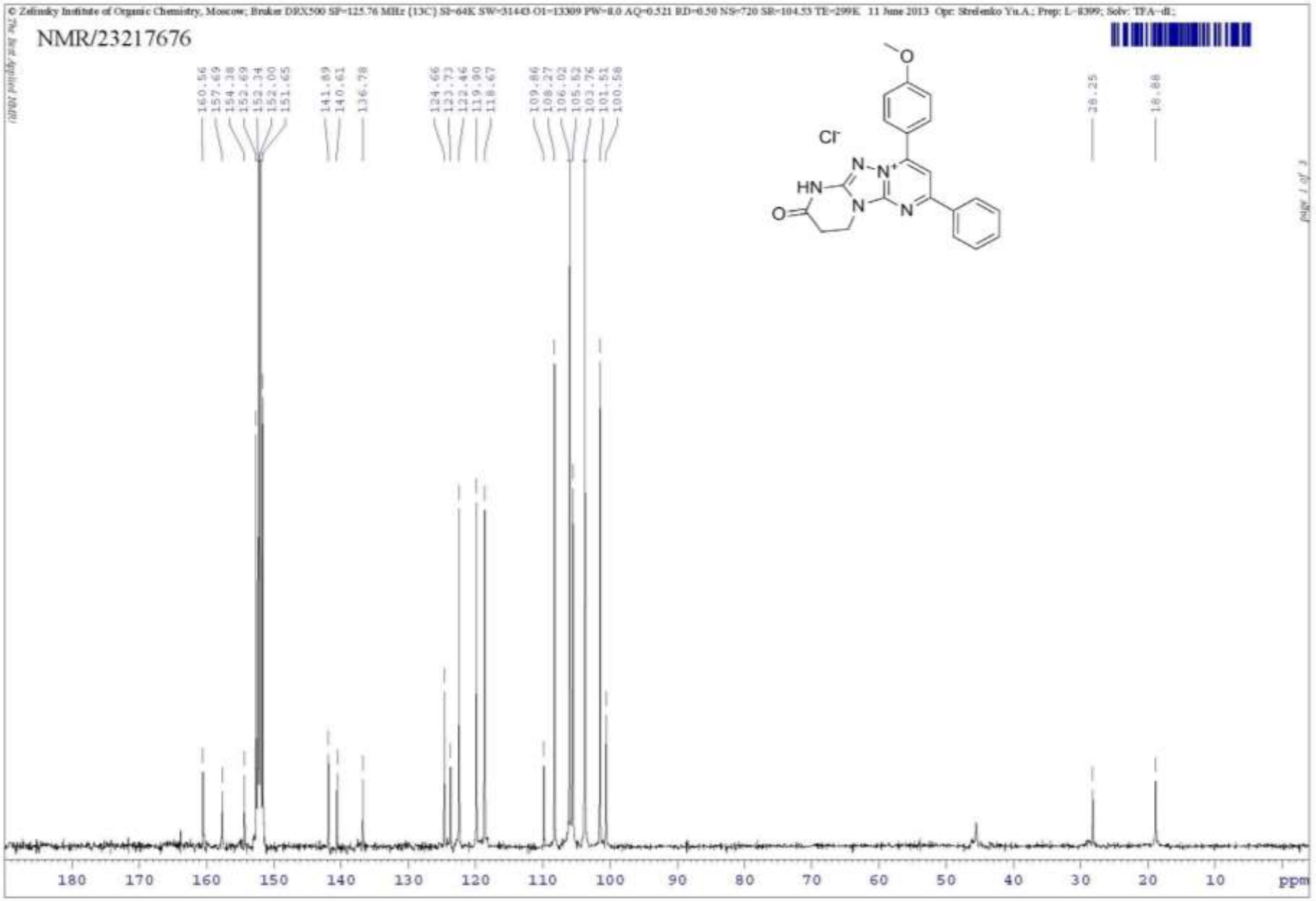
^{13}C NMR spectrum of compound **9d** (DMSO-d6, 125 MHz).



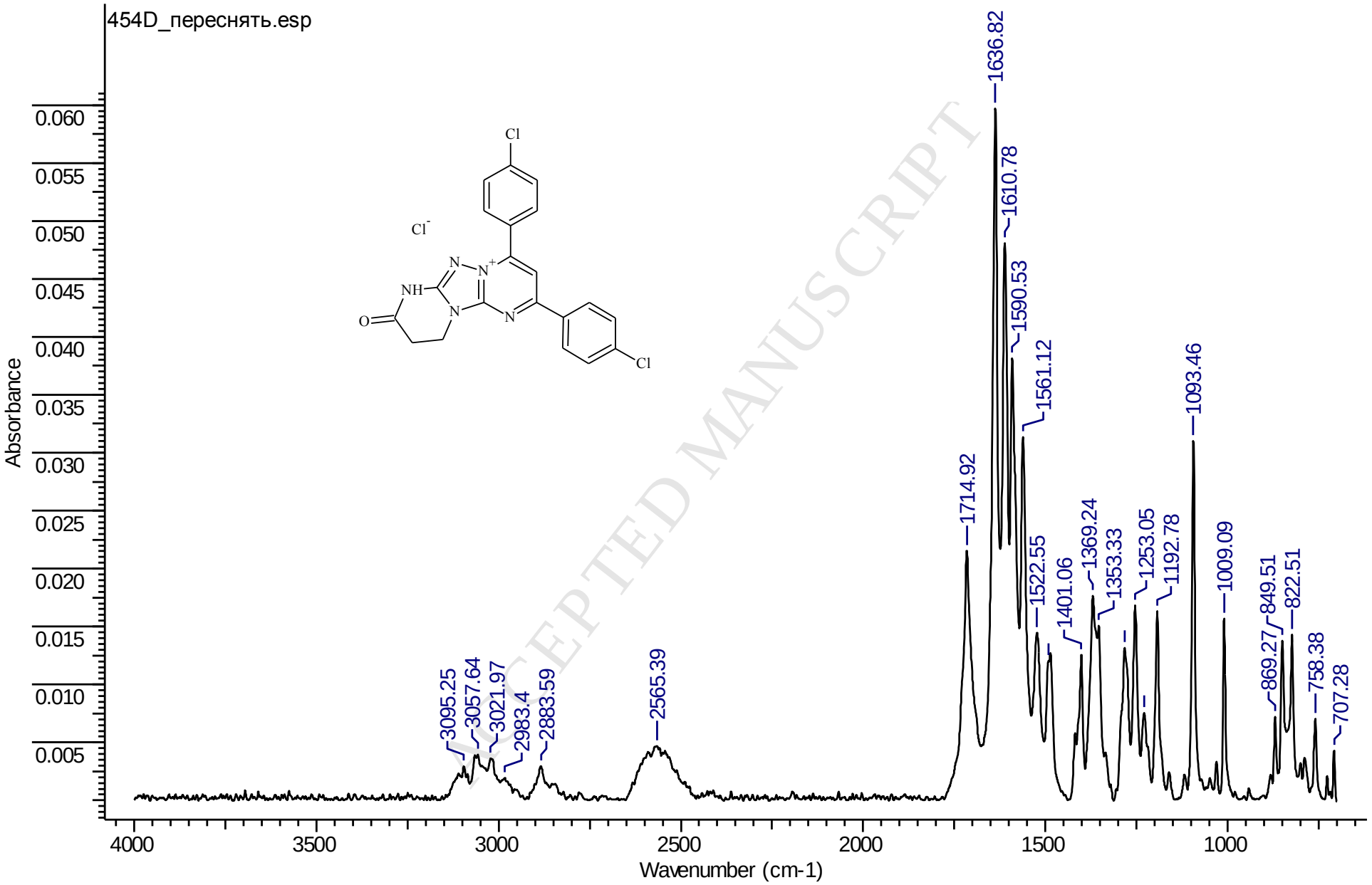
FTIR spectrum of compound **9e** (ATR).



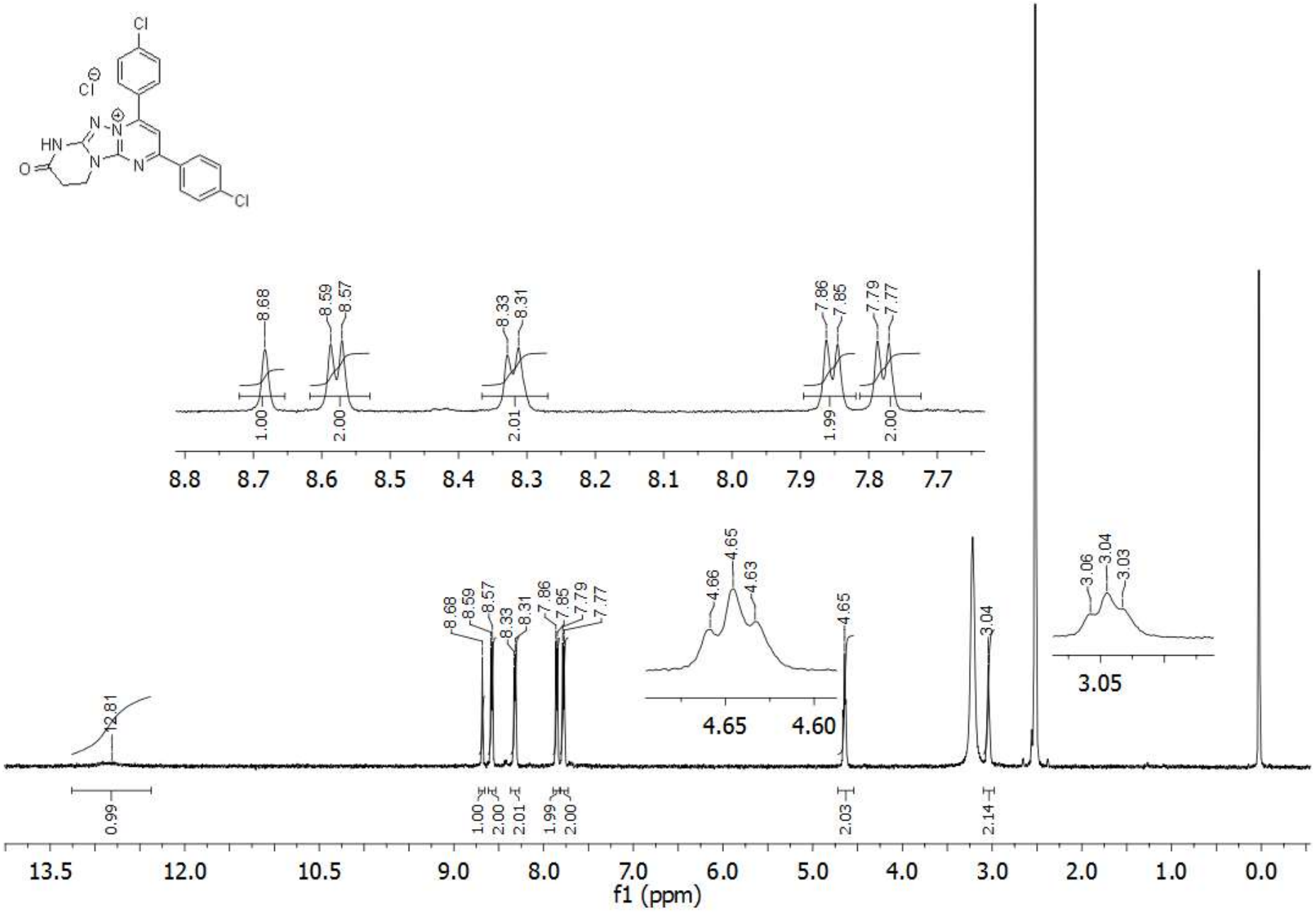
^{1}H NMR spectrum of compound **9e** (DMSO-d_6, 500 MHz).



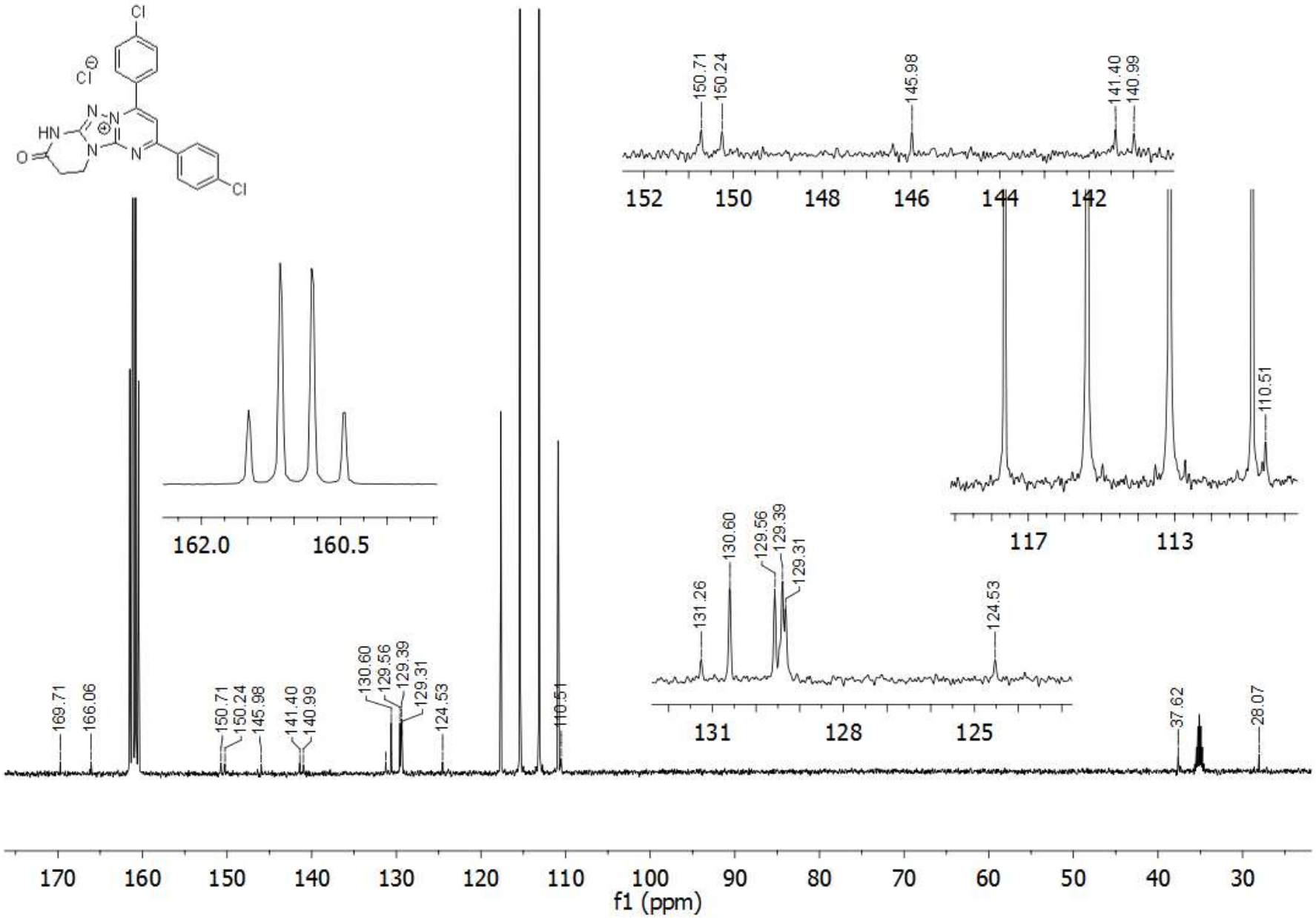
^{13}C NMR spectrum of compound **9e** (TFA-d_1, 125 MHz).



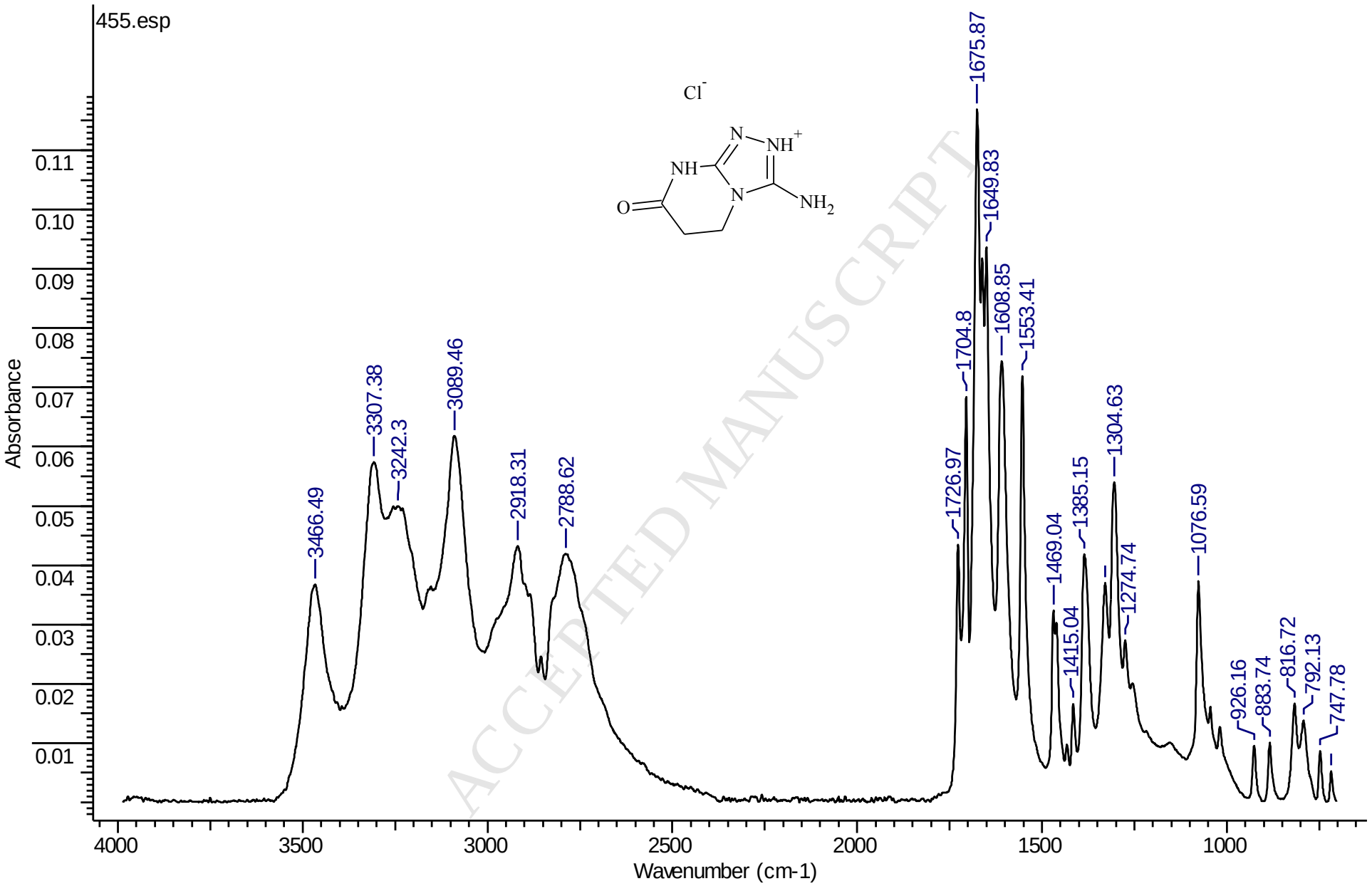
FTIR spectrum of compound **9f** (ATR).



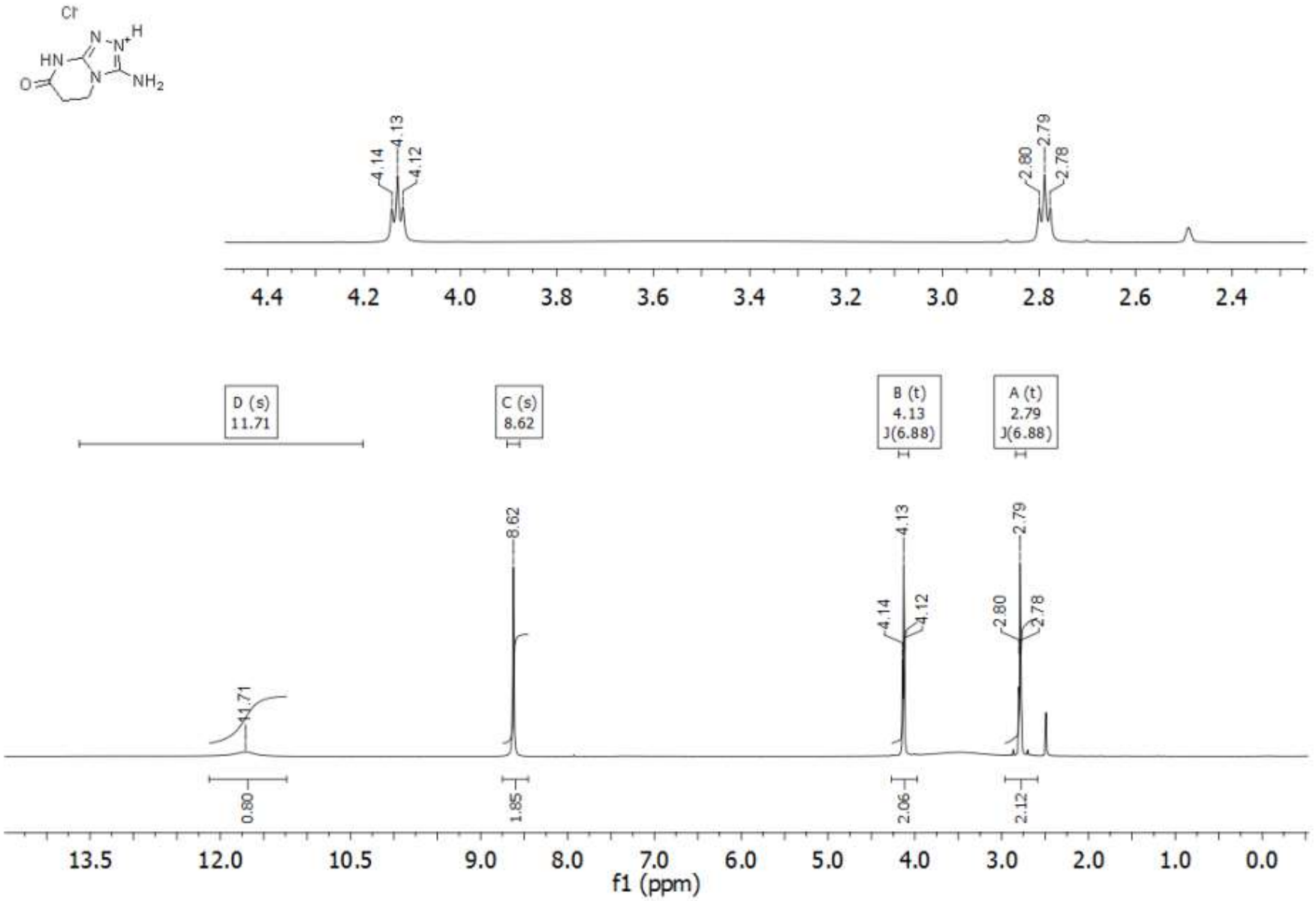
^{1}H NMR spectrum of compound **9f** (DMSO-d_6, 500 MHz).



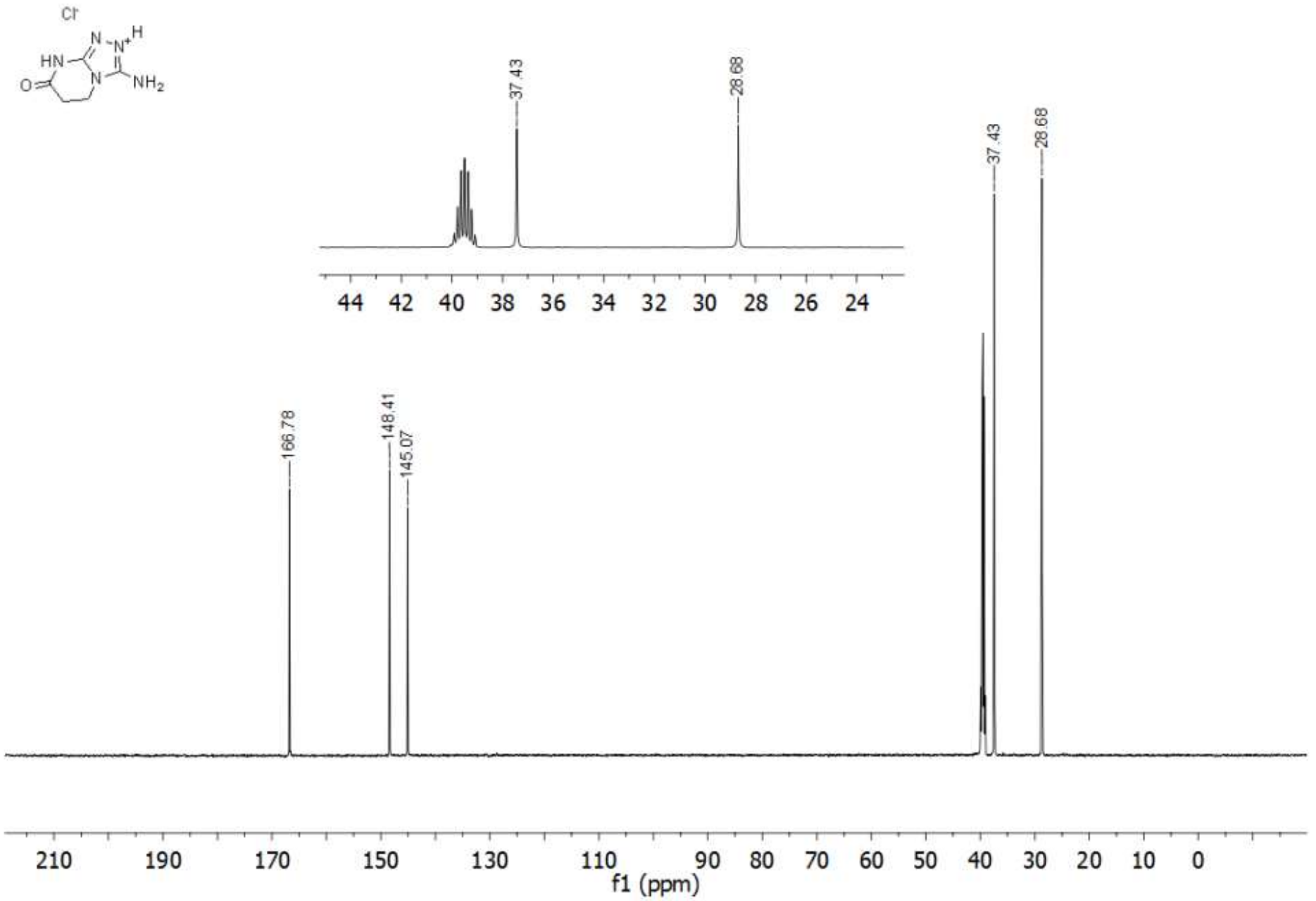
^{13}C NMR spectrum of compound **9f** (CF_3COOH + 5% DMSO-d_6, 125 MHz).



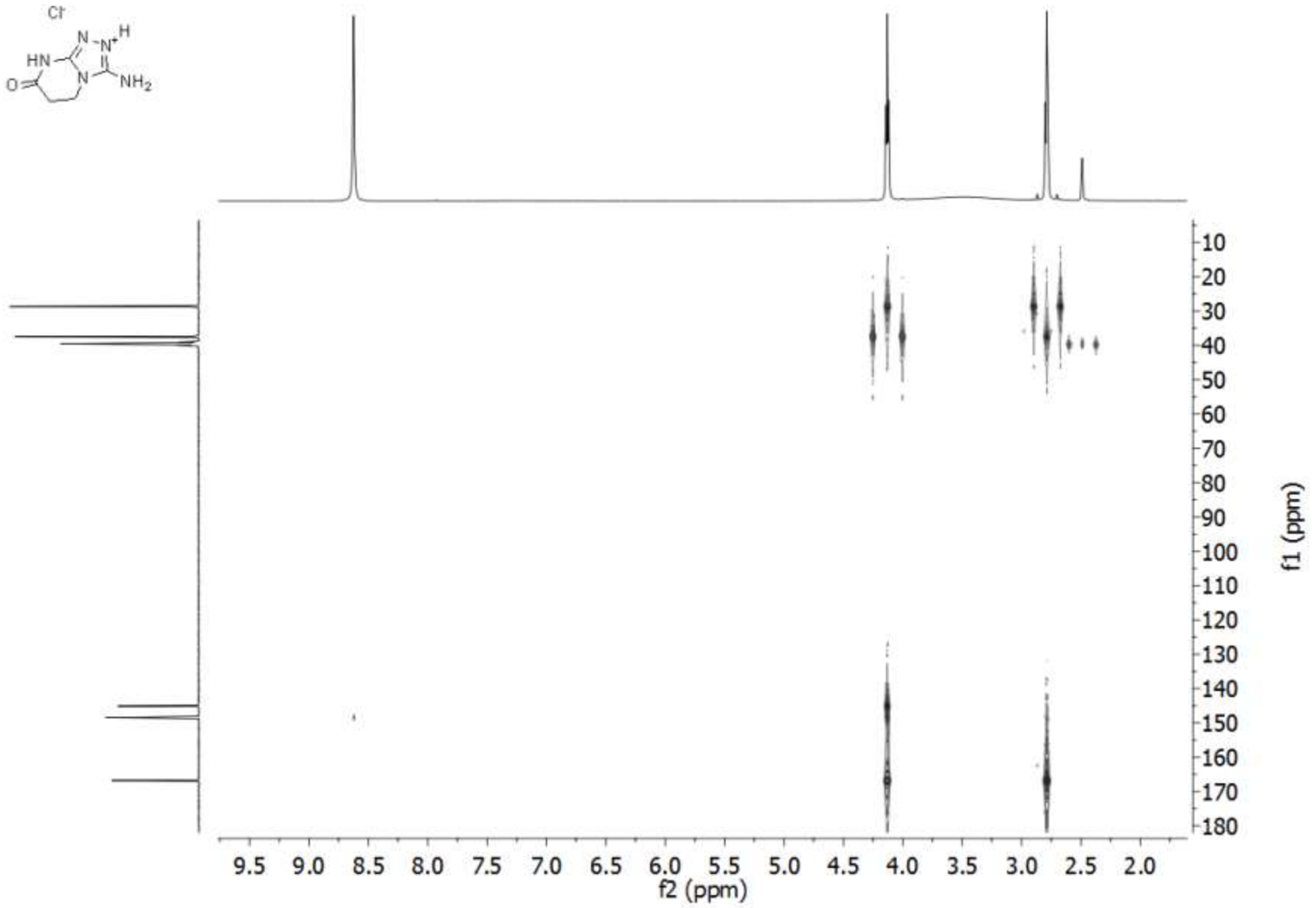
FTIR spectrum of compound **10** (ATR).



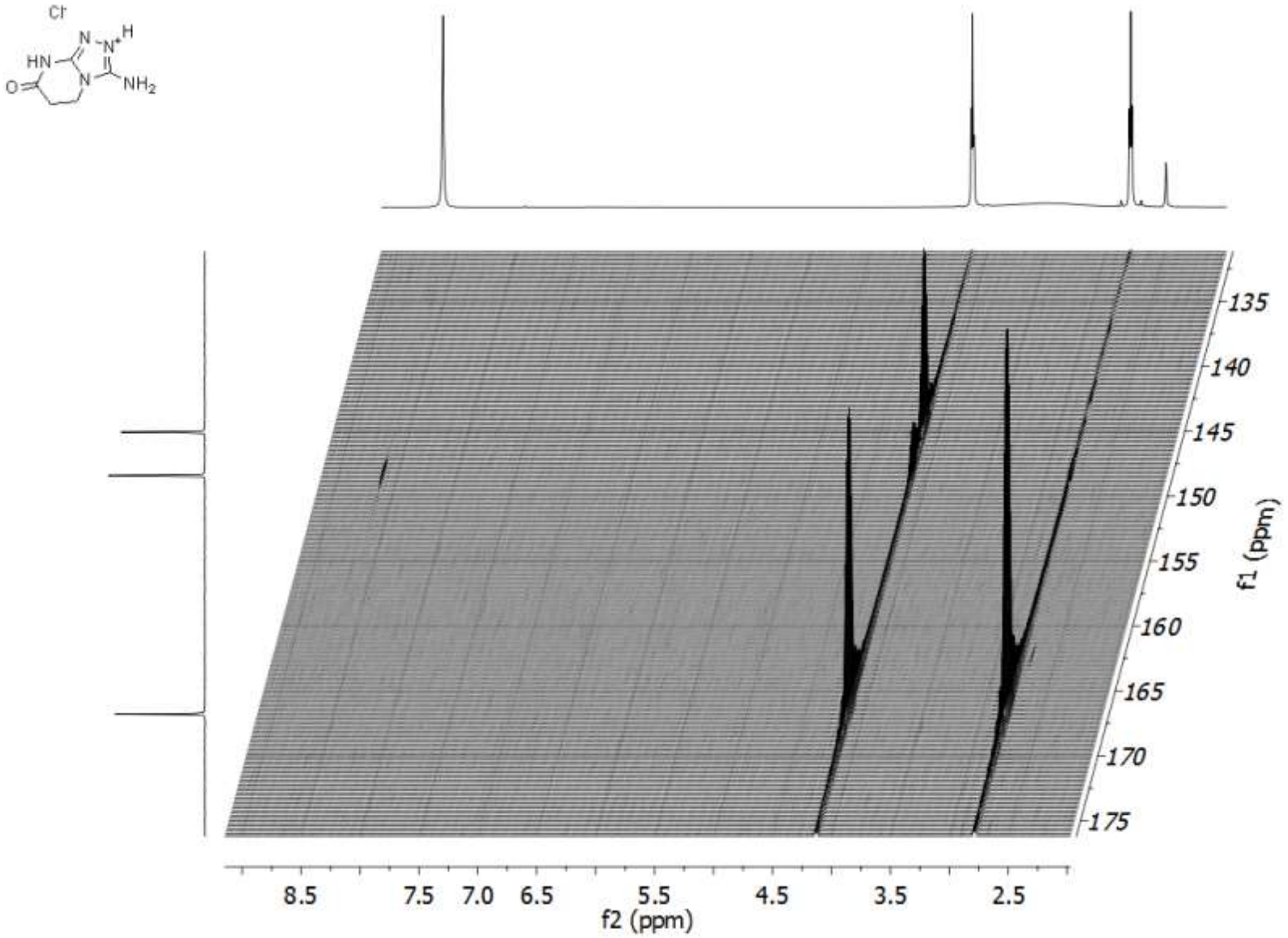
^{1}H NMR spectrum of compound **10** (DMSO-d_6, 600 MHz).



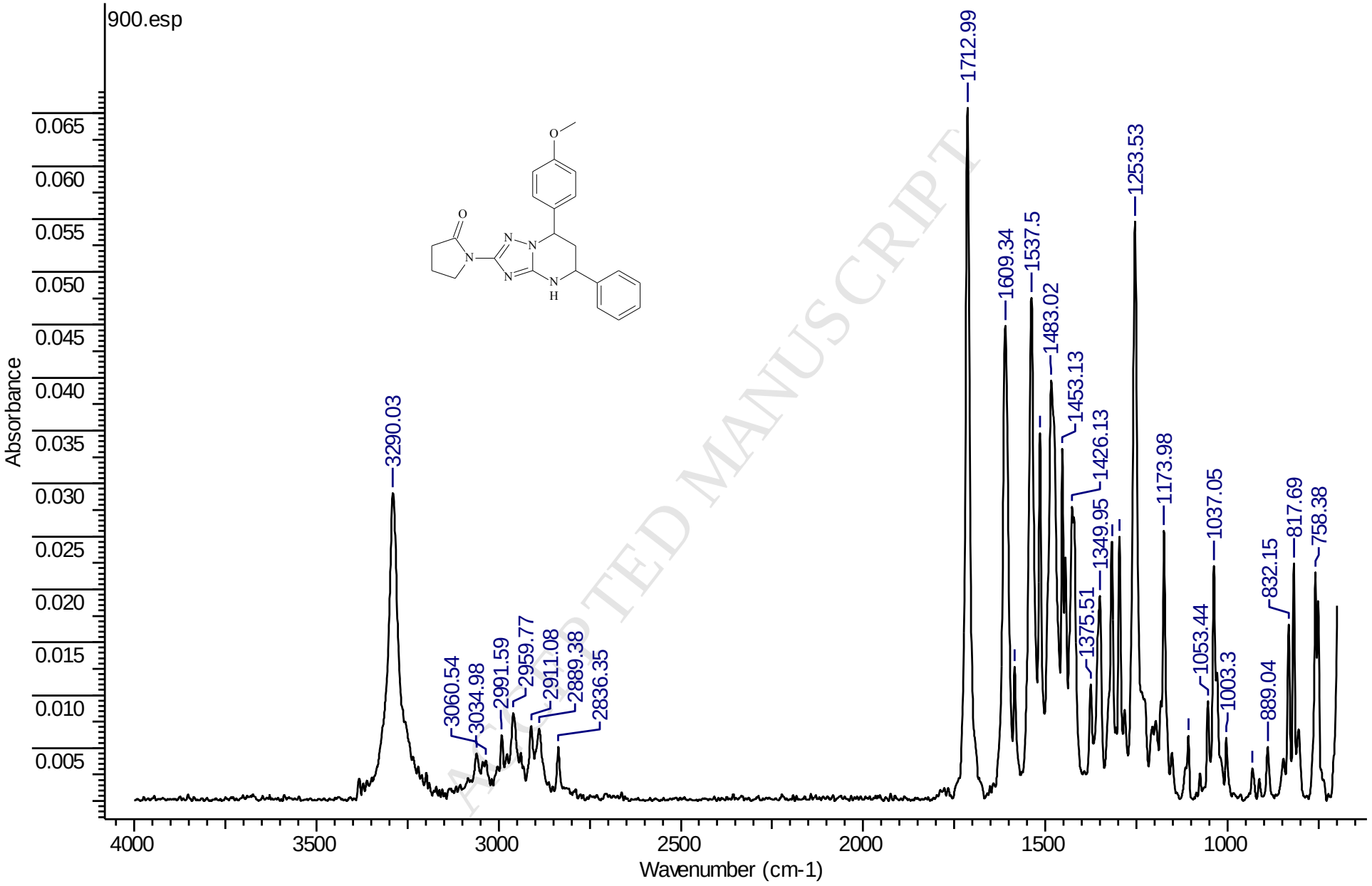
^{13}C NMR spectrum of compound **10** (DMSO-d_6, 150 MHz).



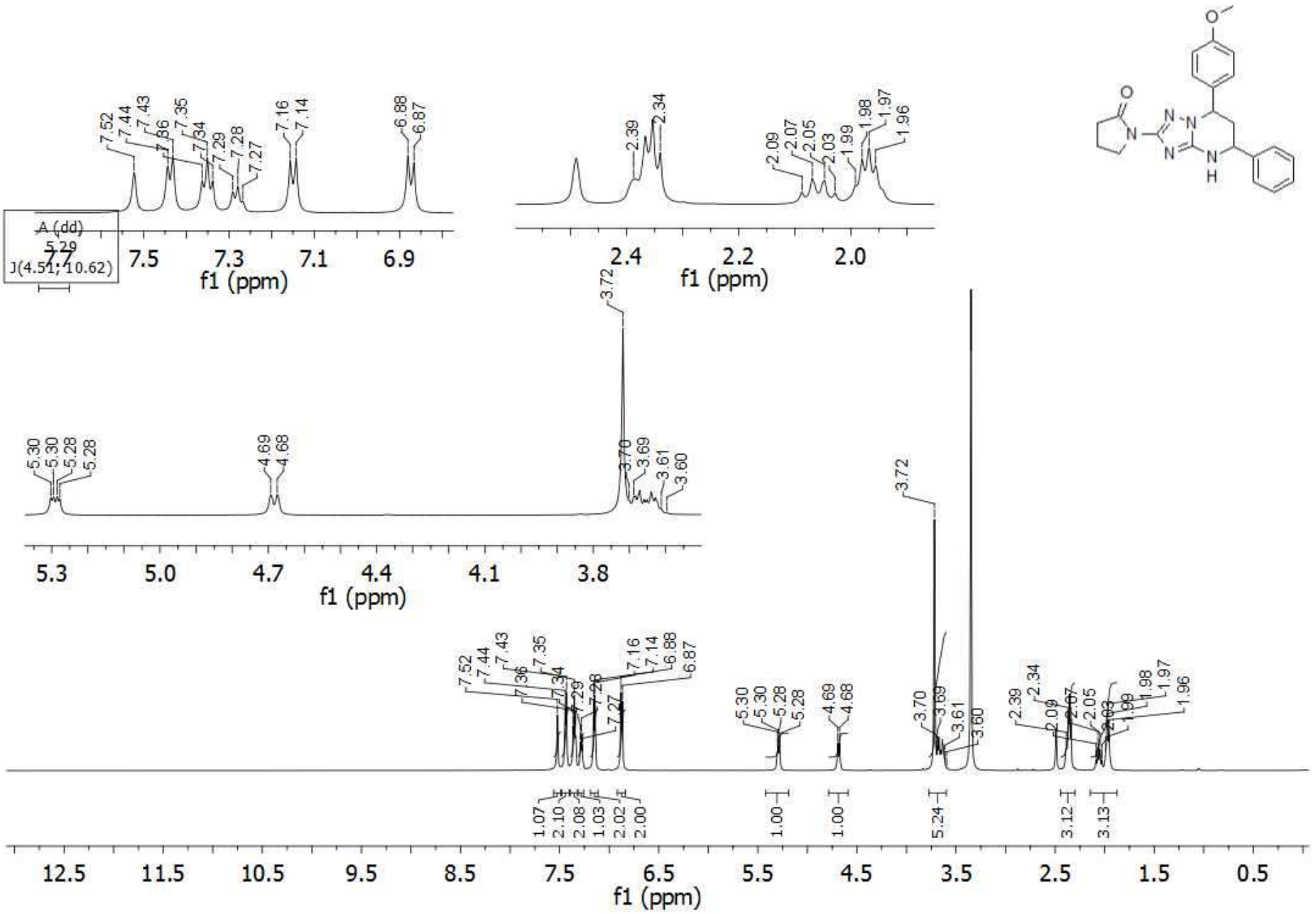
^{1}H-^{13}C HMBC spectrum of compound **10** (DMSO-d_6).



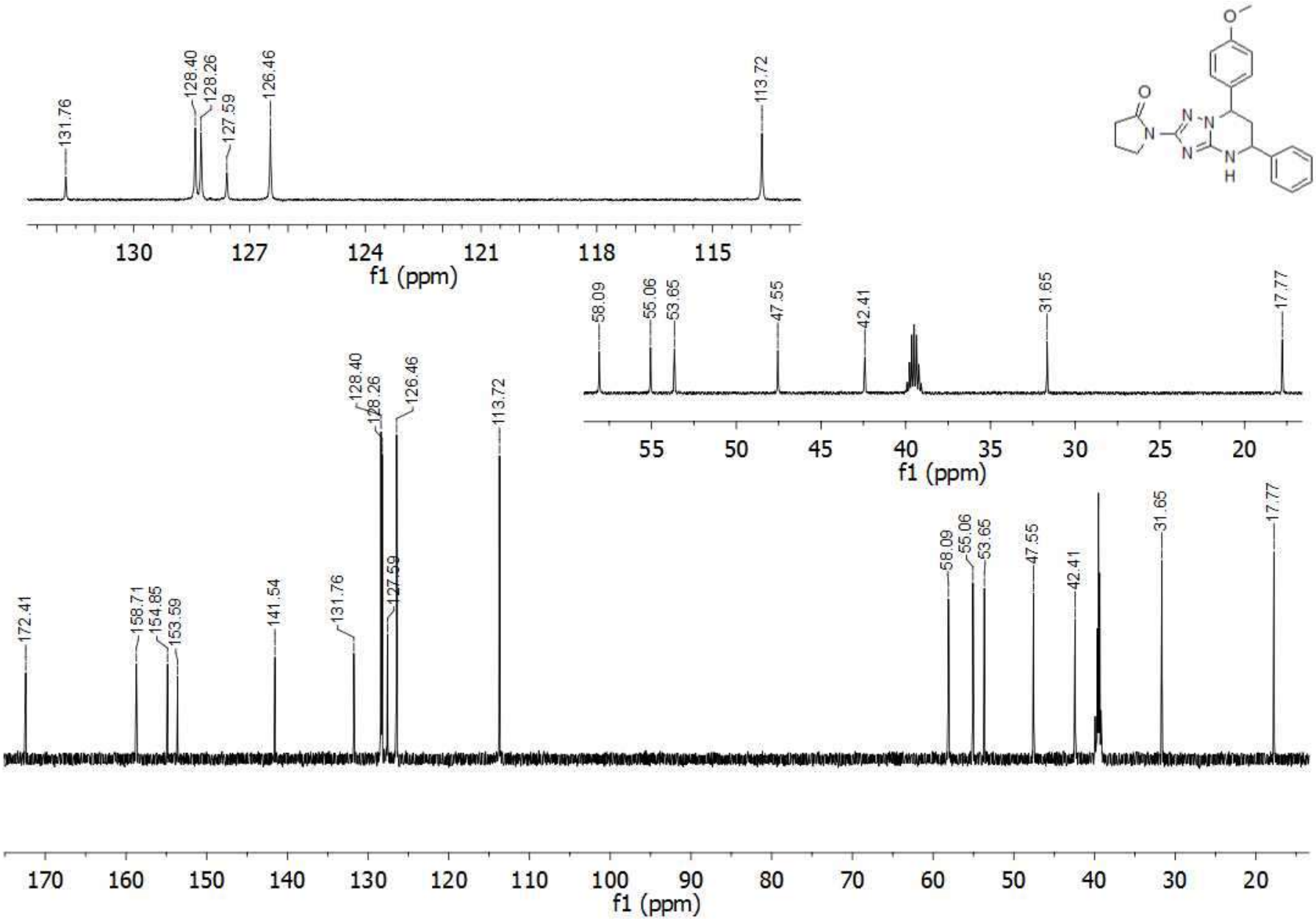
Enlarged fragment of the 3D ^{1}H-^{13}C HMBC spectrum of compound **10.**



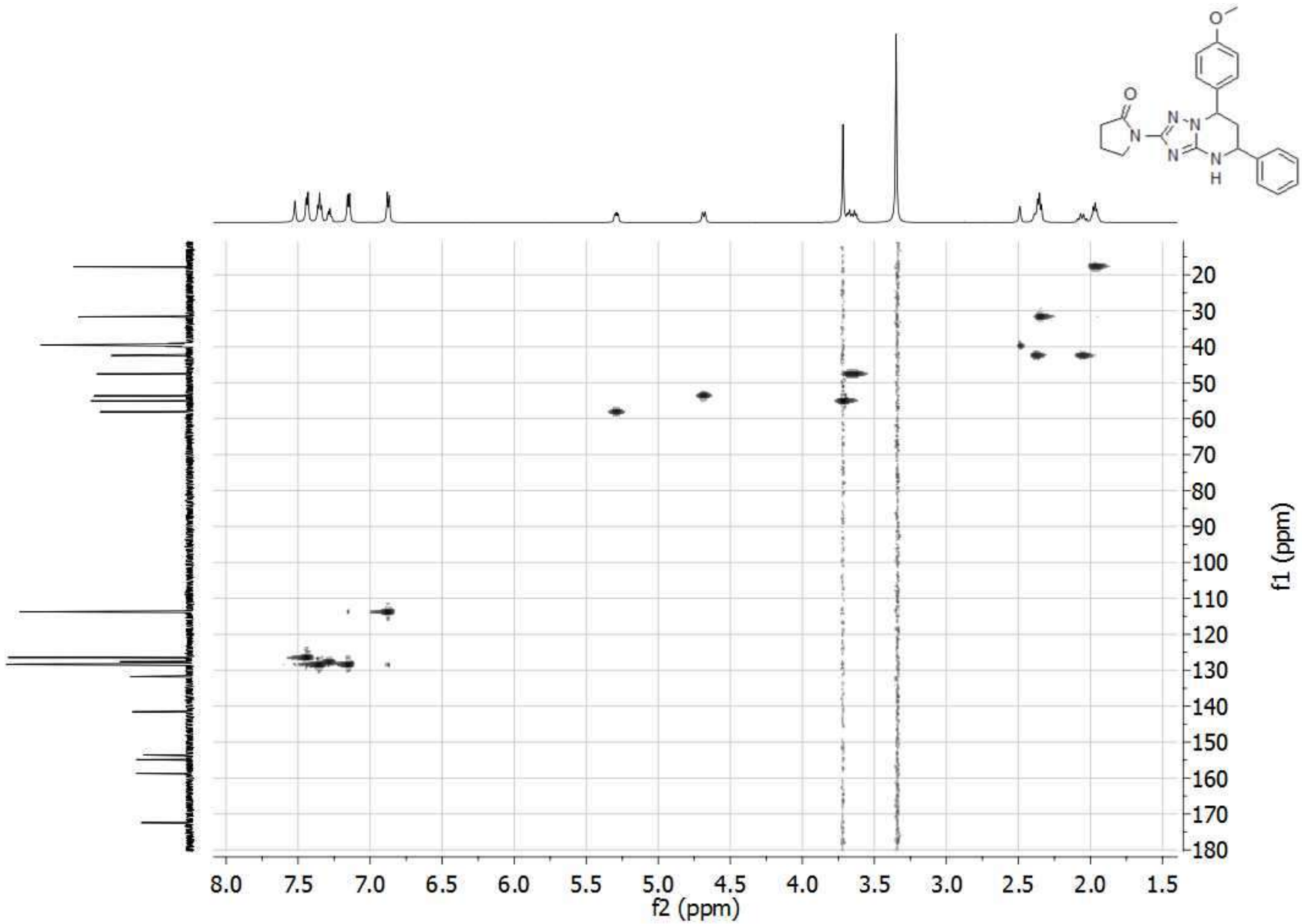
FTIR spectrum of compound **12** (ATR).



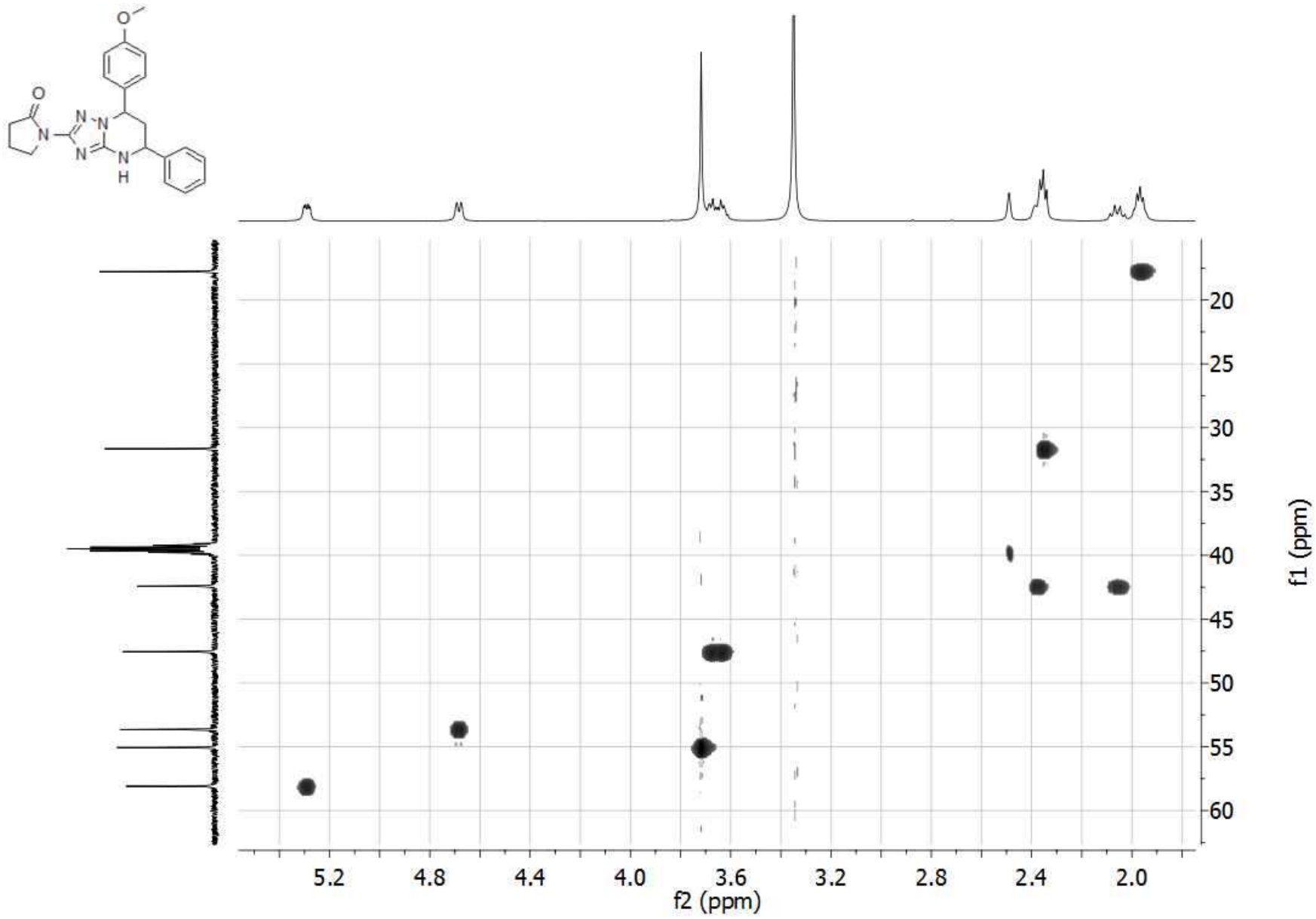
^{1}H NMR spectrum of compound **12** (600 MHz, DMSO-d_6).



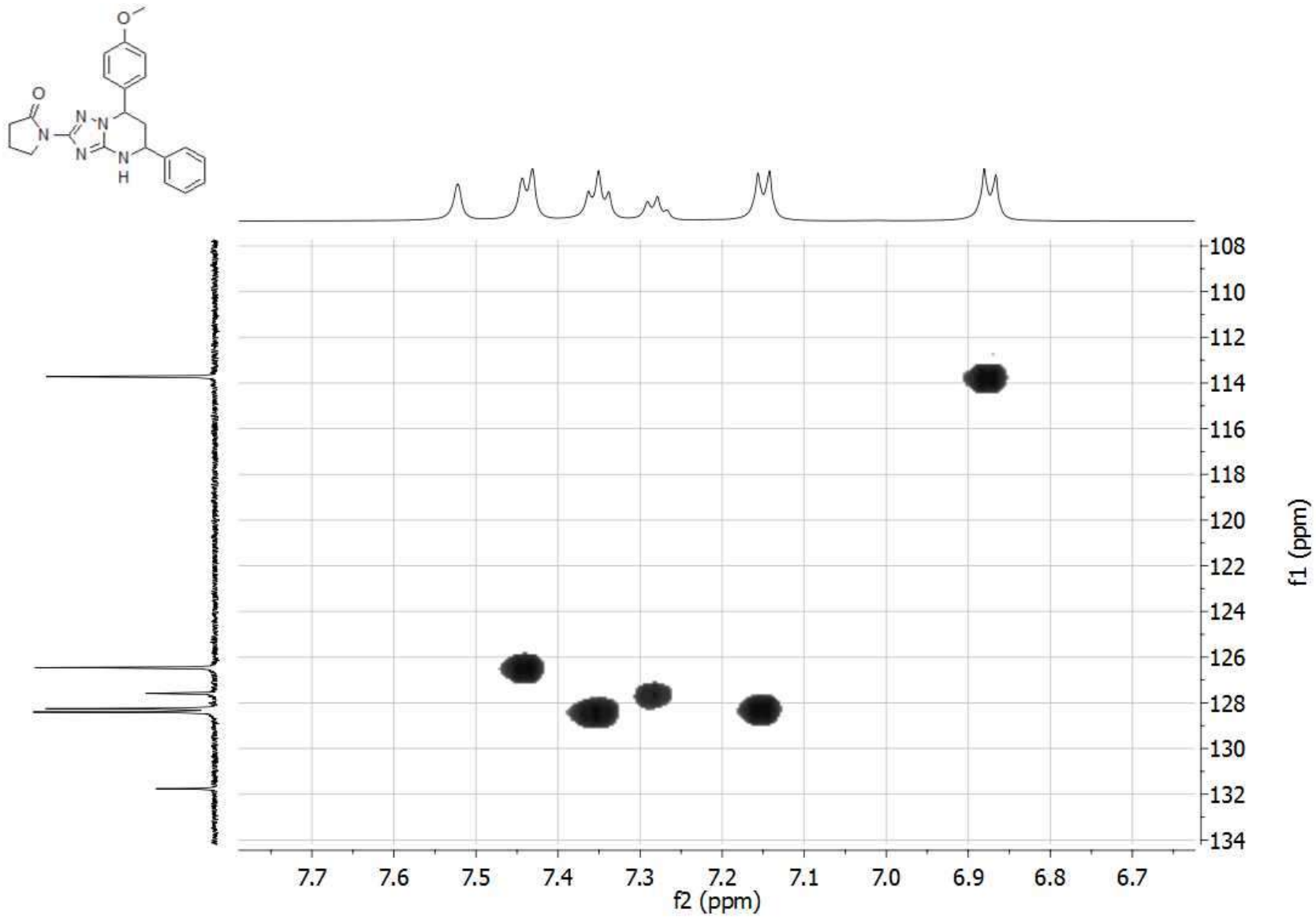
^{13}C NMR spectrum of compound **12** (150 MHz, DMSO-d_6).



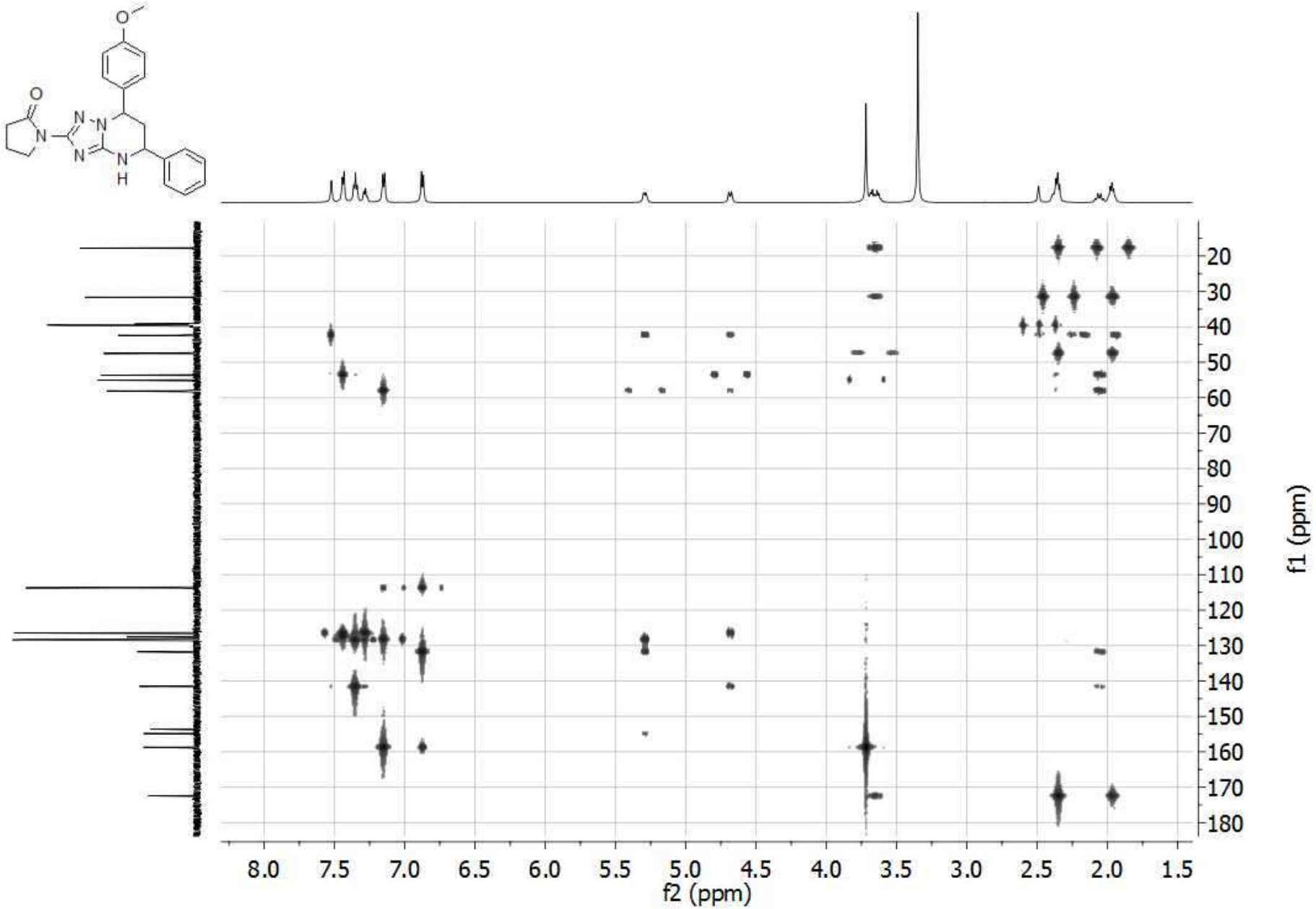
^{1}H-^{13}C HSQC spectrum of compound **12** (DMSO-d_6).



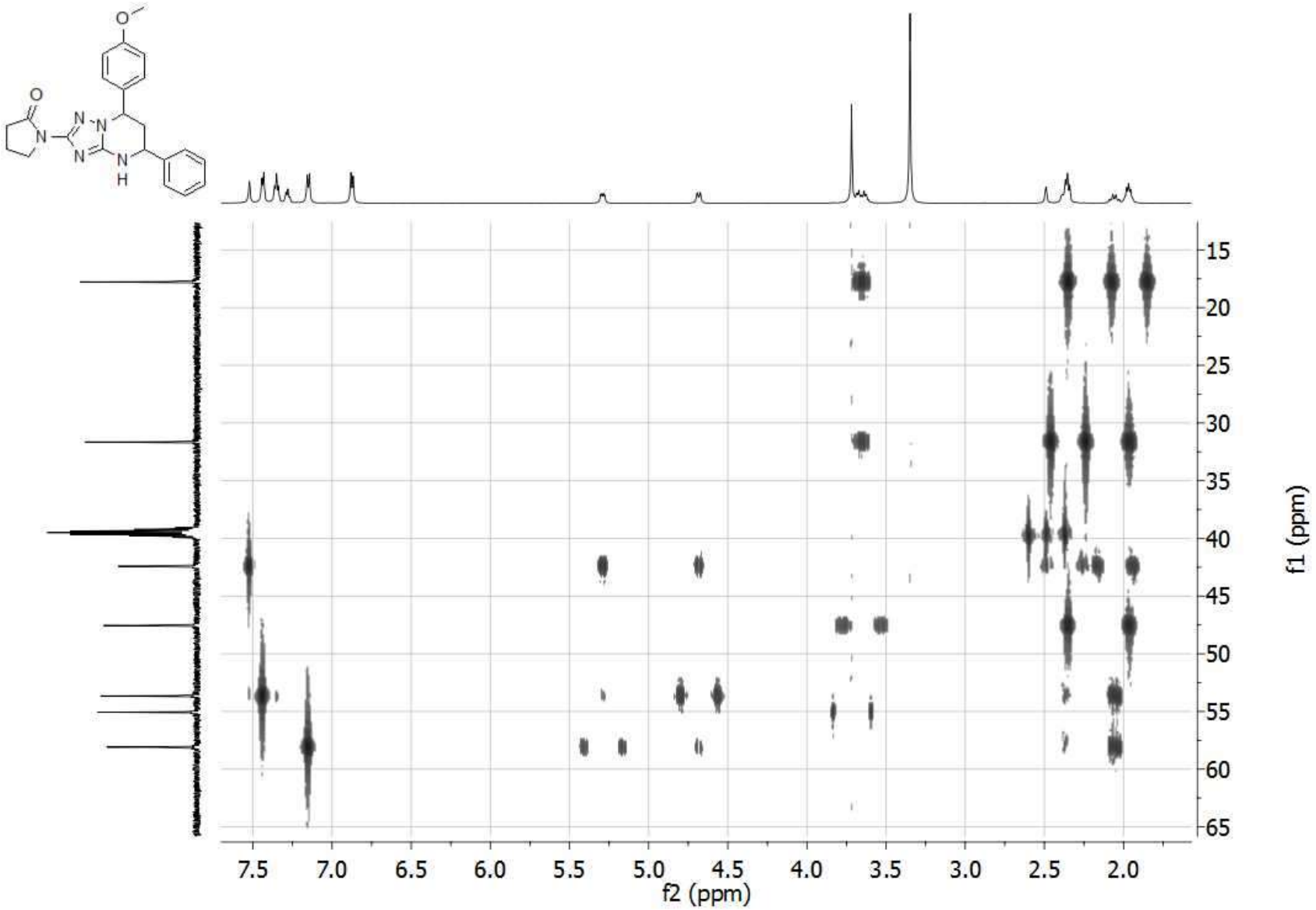
Enlarged high-field fragment of ^{1}H-^{13}C HSQC spectrum of compound **12.**



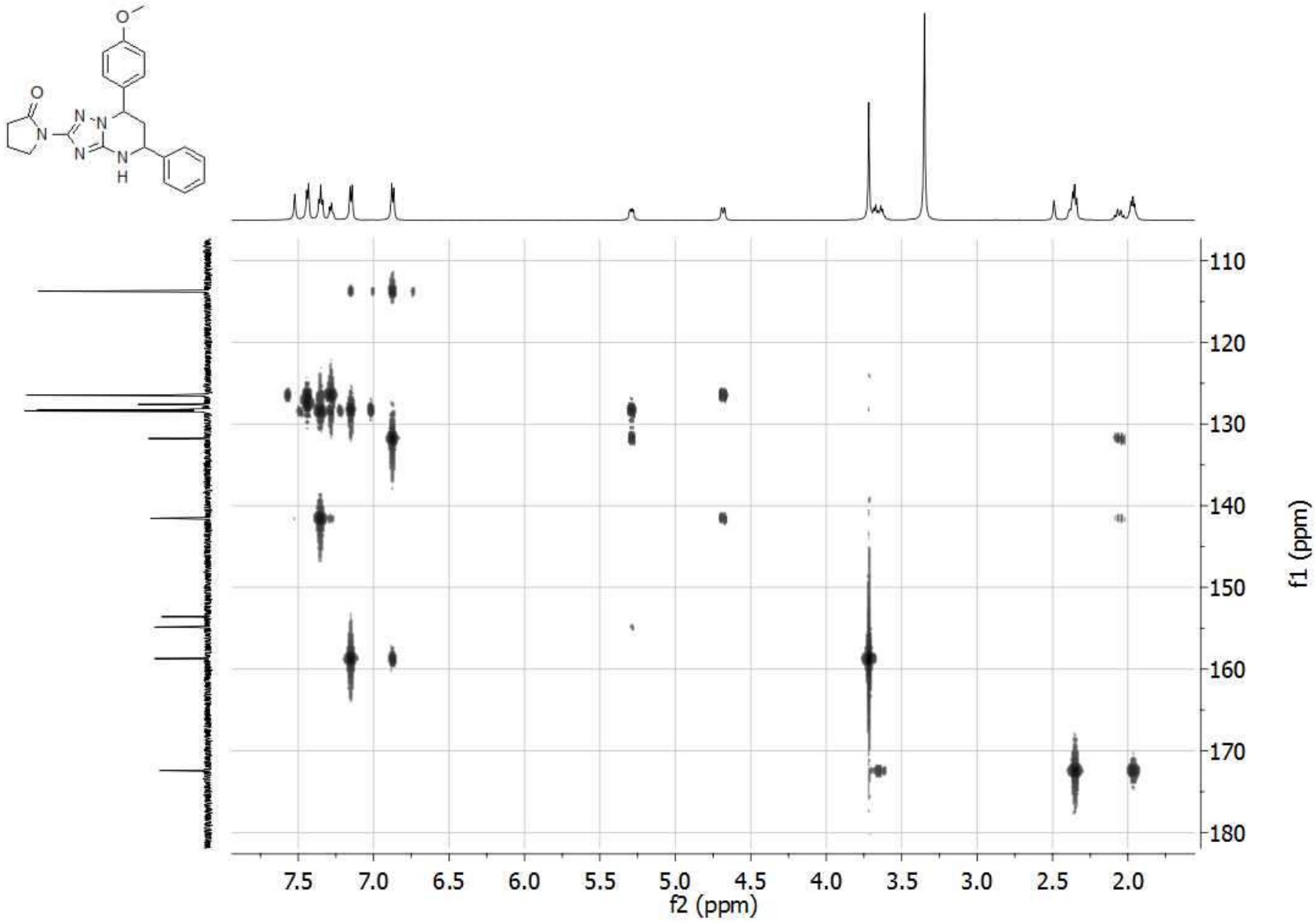
Enlarged low-field fragment of ^{1}H-^{13}C HSQC spectrum of compound **12.**



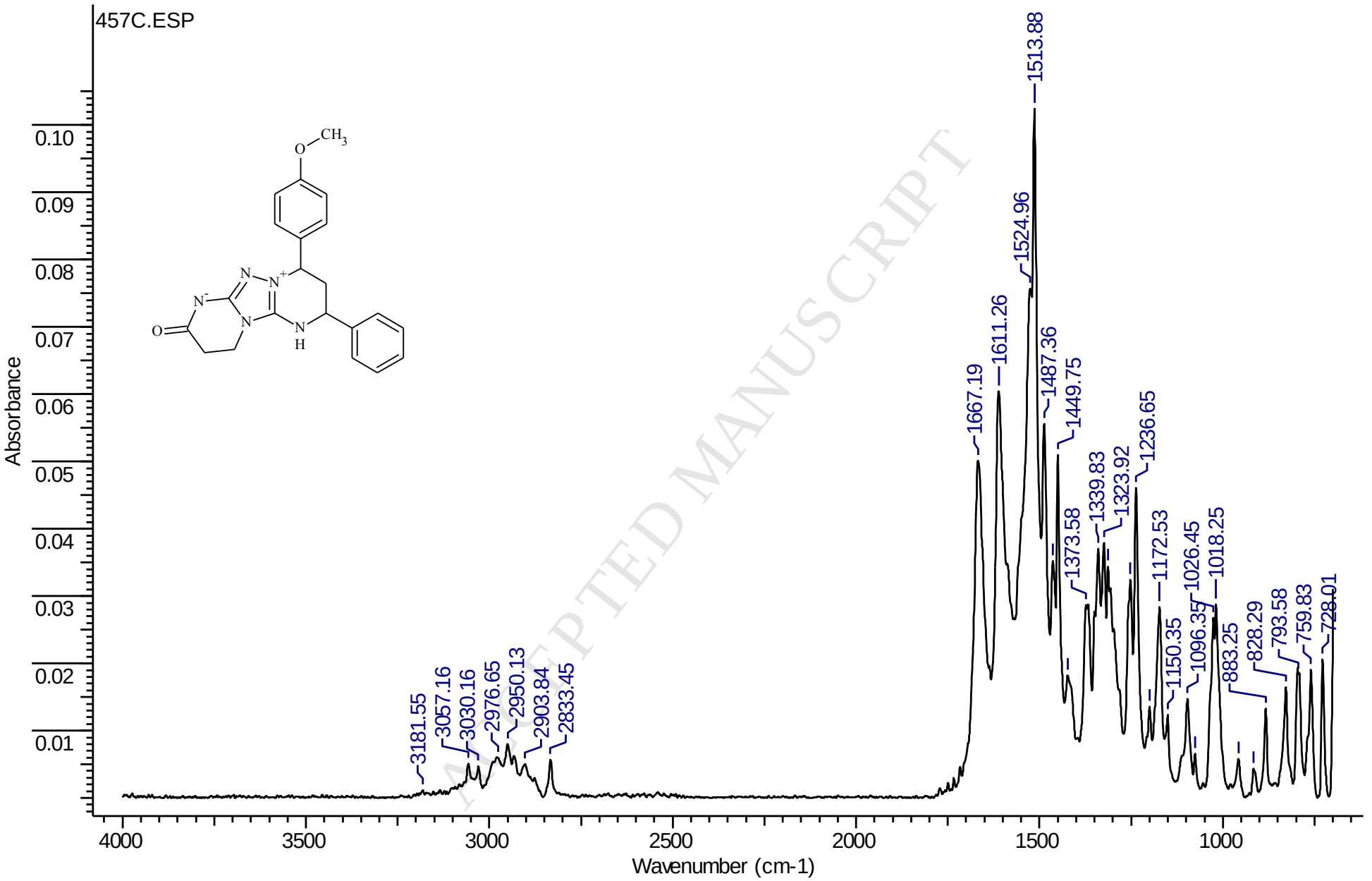
^{1}H-^{13}C HMBC spectrum of compound **12** (DMSO-d_6).



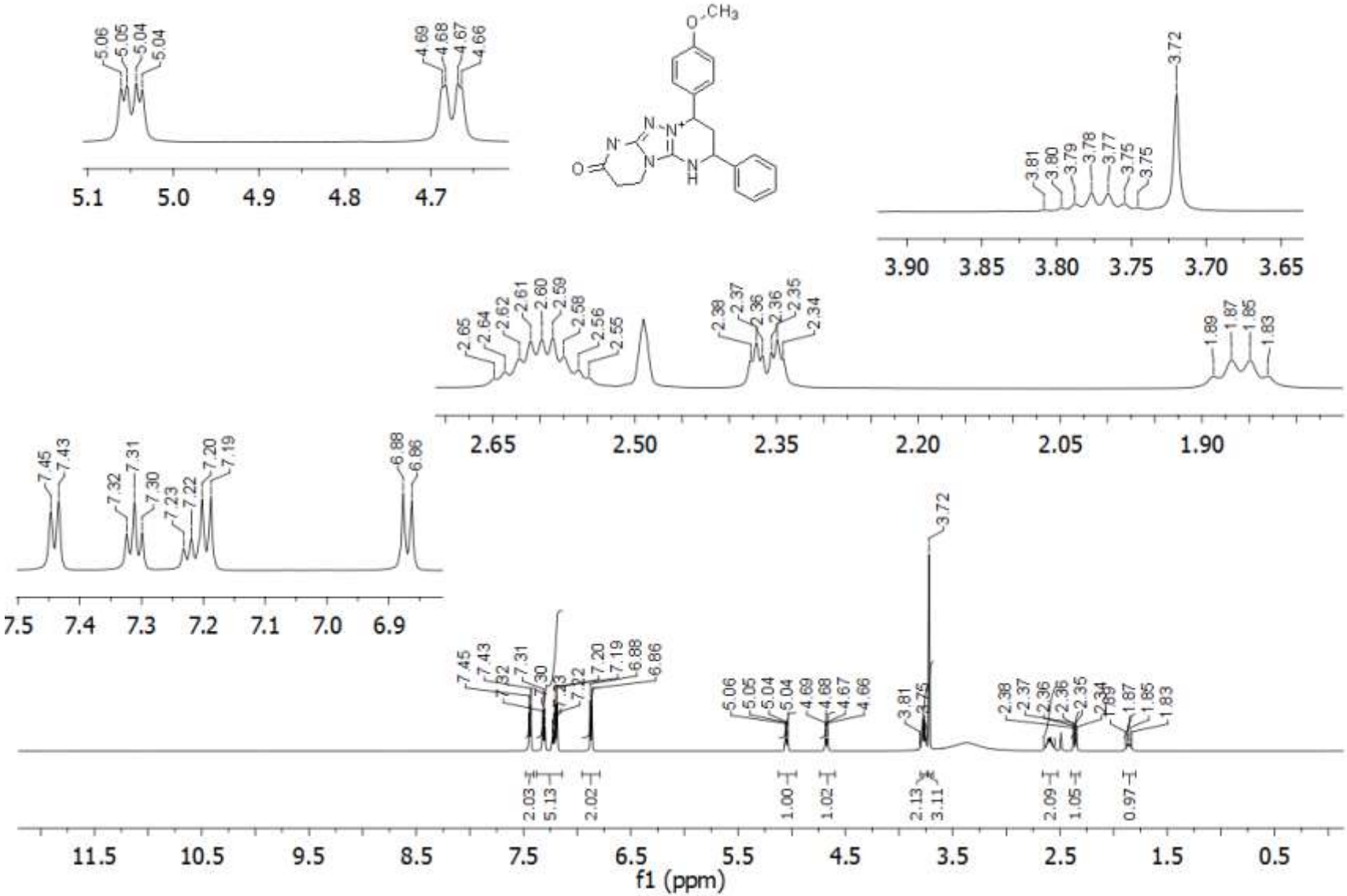
Enlarged high-field fragment of ^{1}H-^{13}C HMBC spectrum of compound **12.**



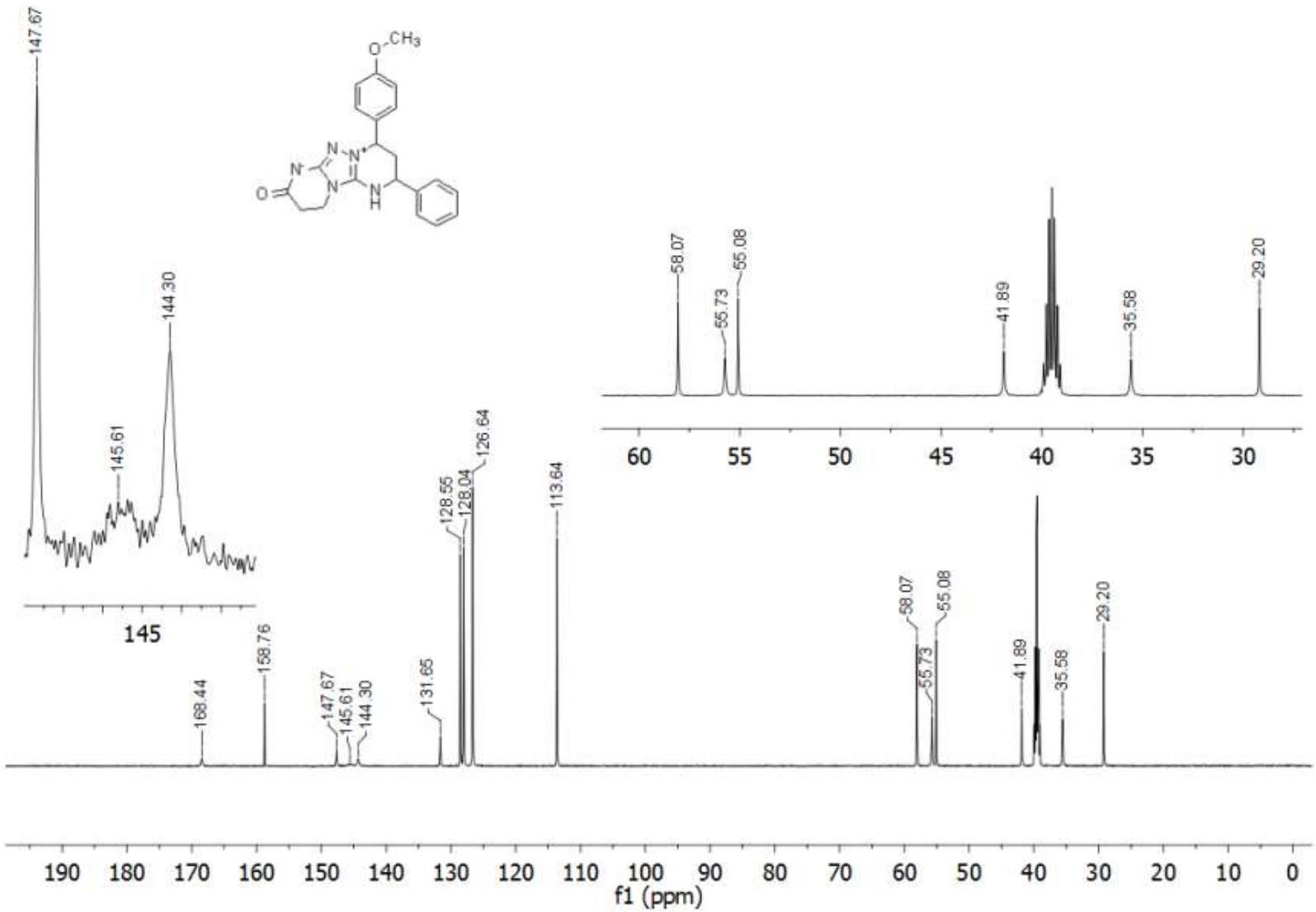
Enlarged low-field fragment of ^{1}H-^{13}C HMBC spectrum of compound **12.**



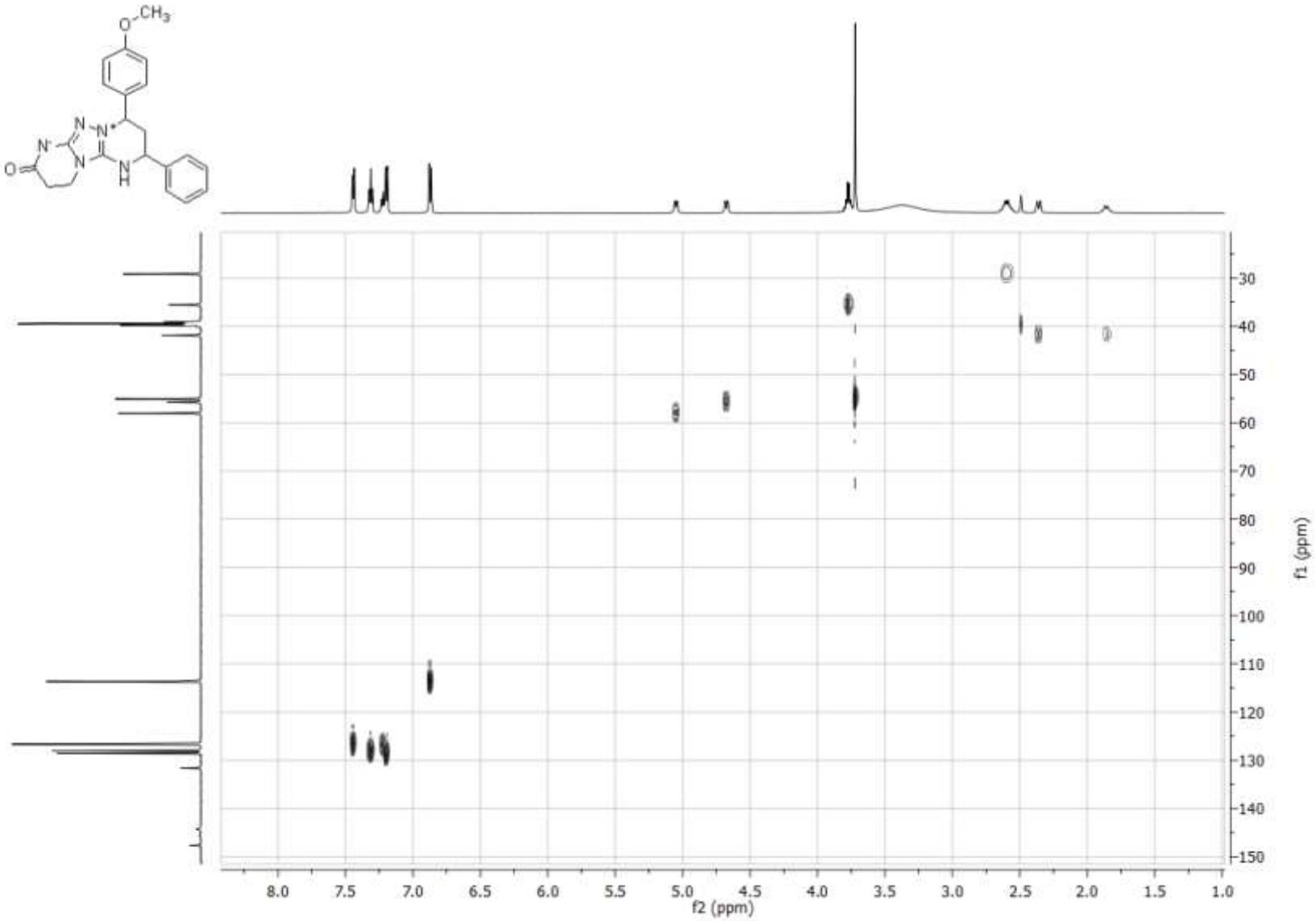
FTIR spectrum of compound **13a** (ATR).



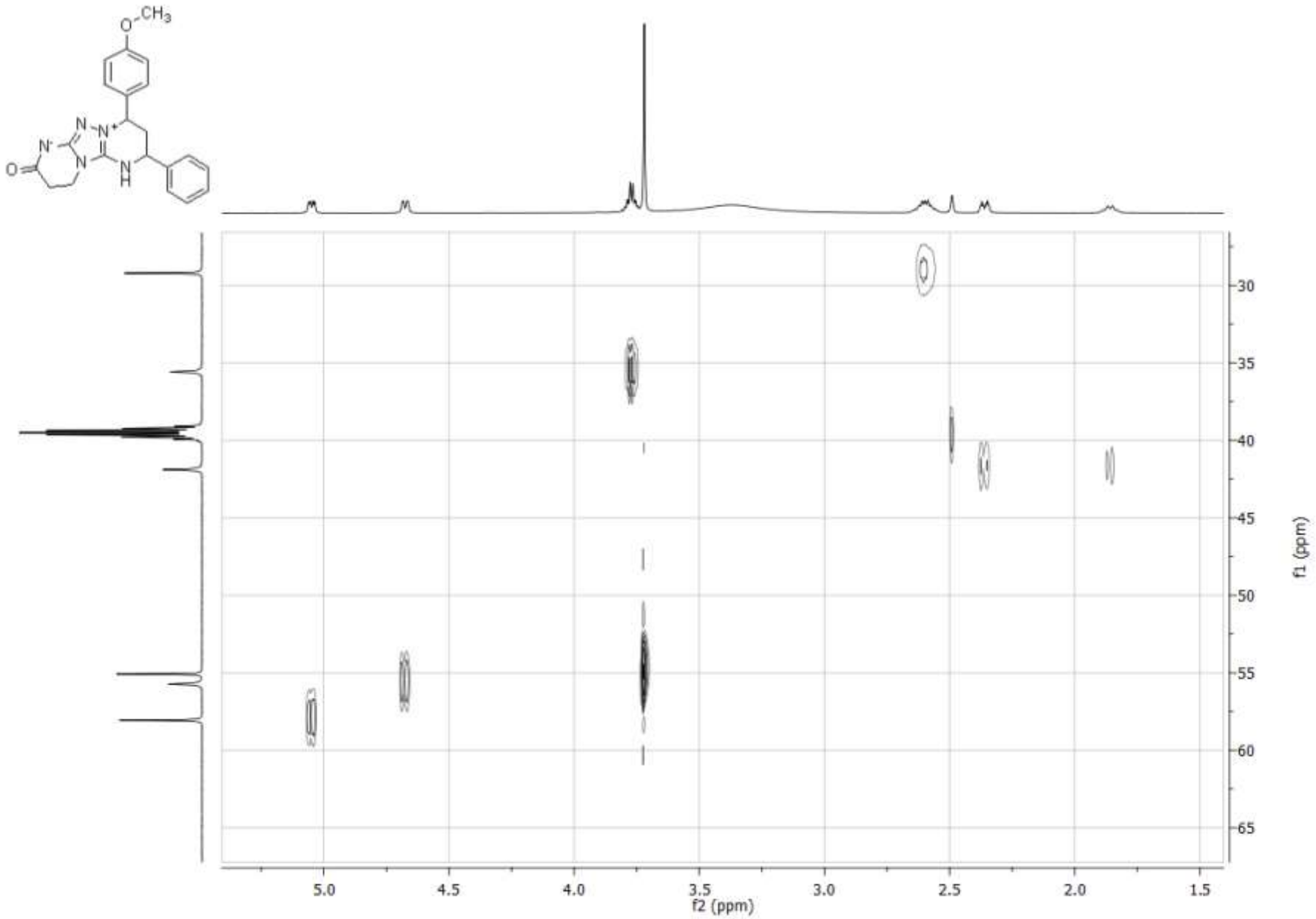
^{1}H NMR spectrum of compound **13a** (DMSO-d_6, 600 MHz).



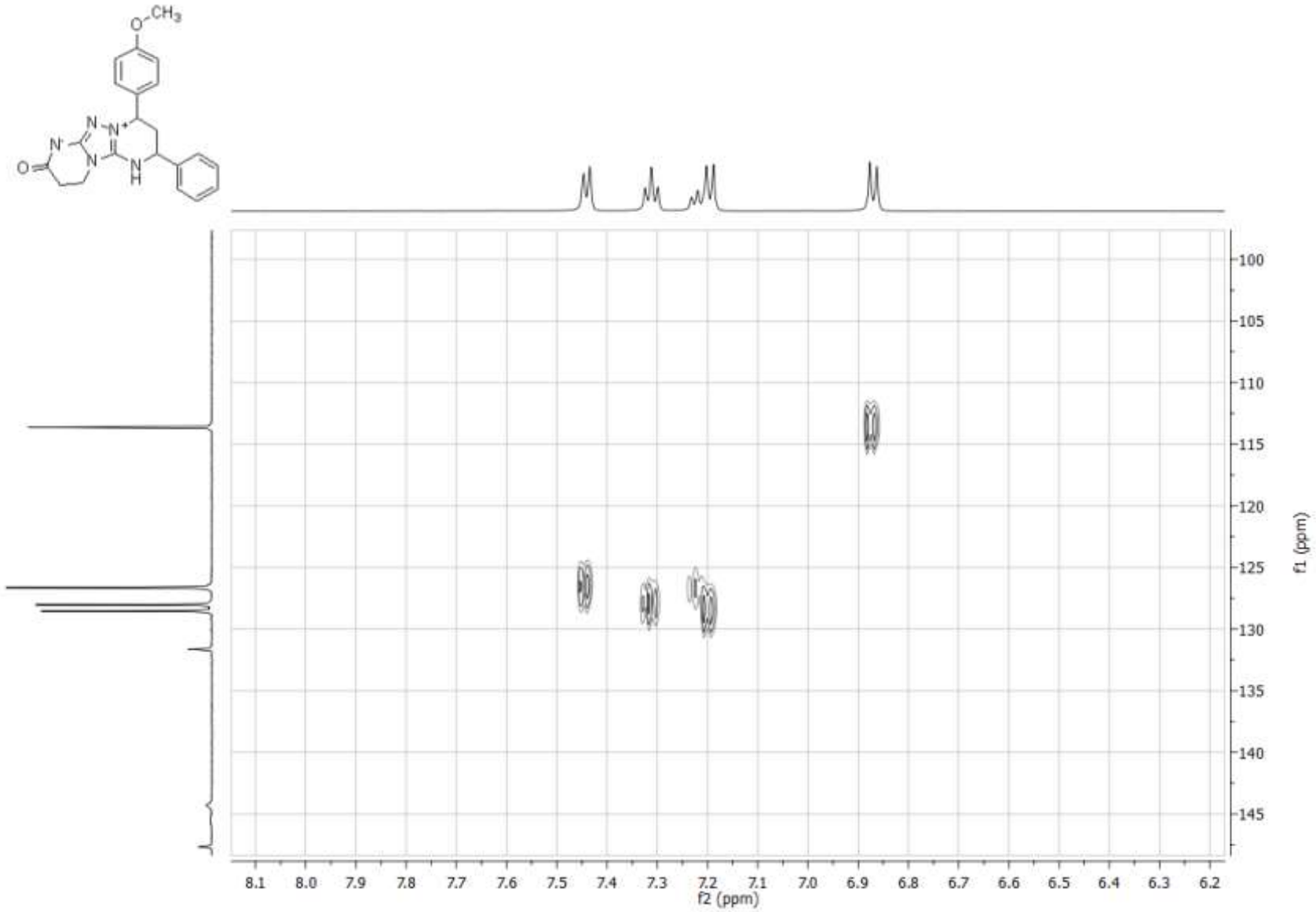
^{13}C NMR spectrum of compound **13a** (DMSO-d_6, 150 MHz).



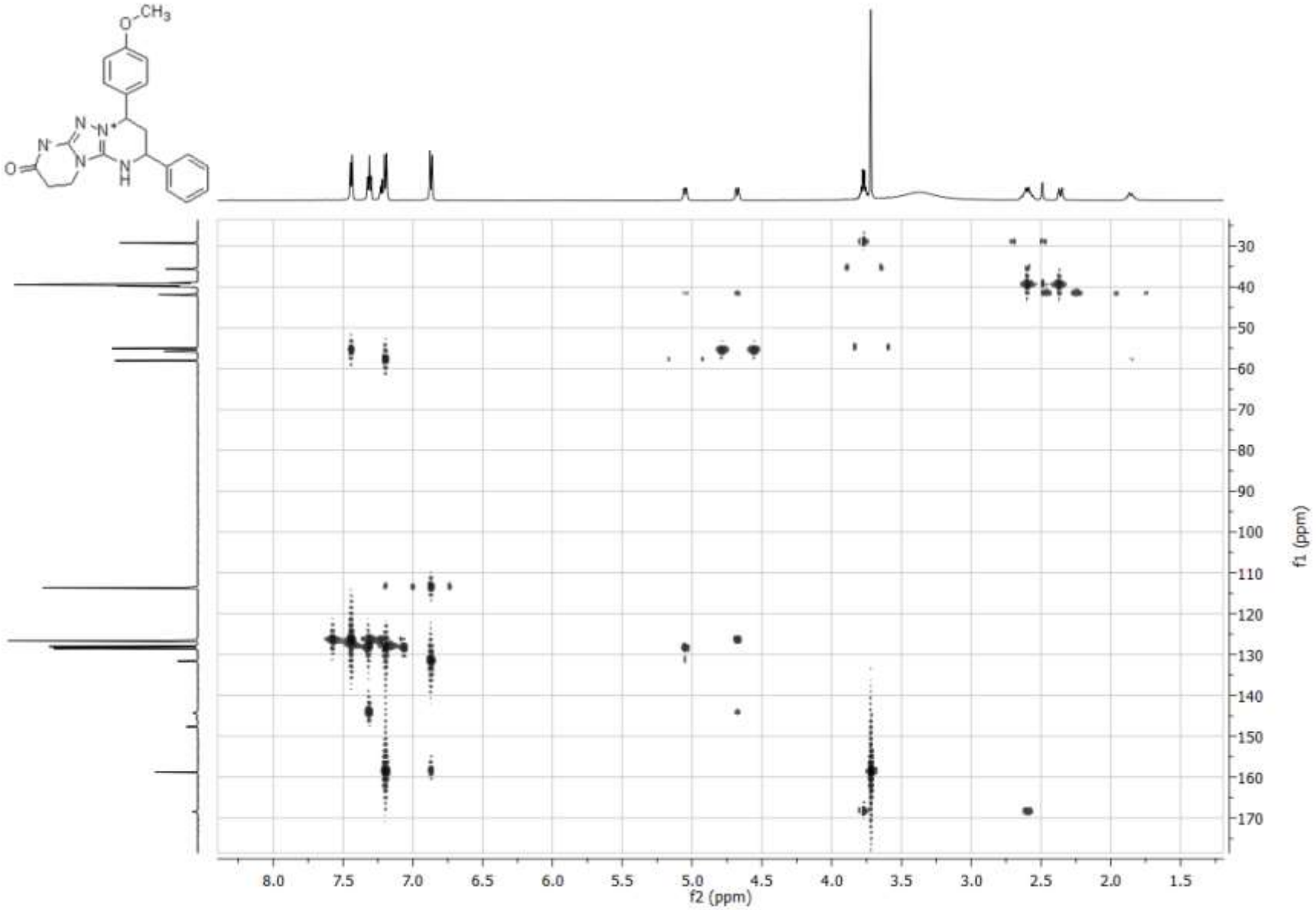
^{1}H-^{13}C HSQC spectrum of compound **13a** (DMSO-d_6).



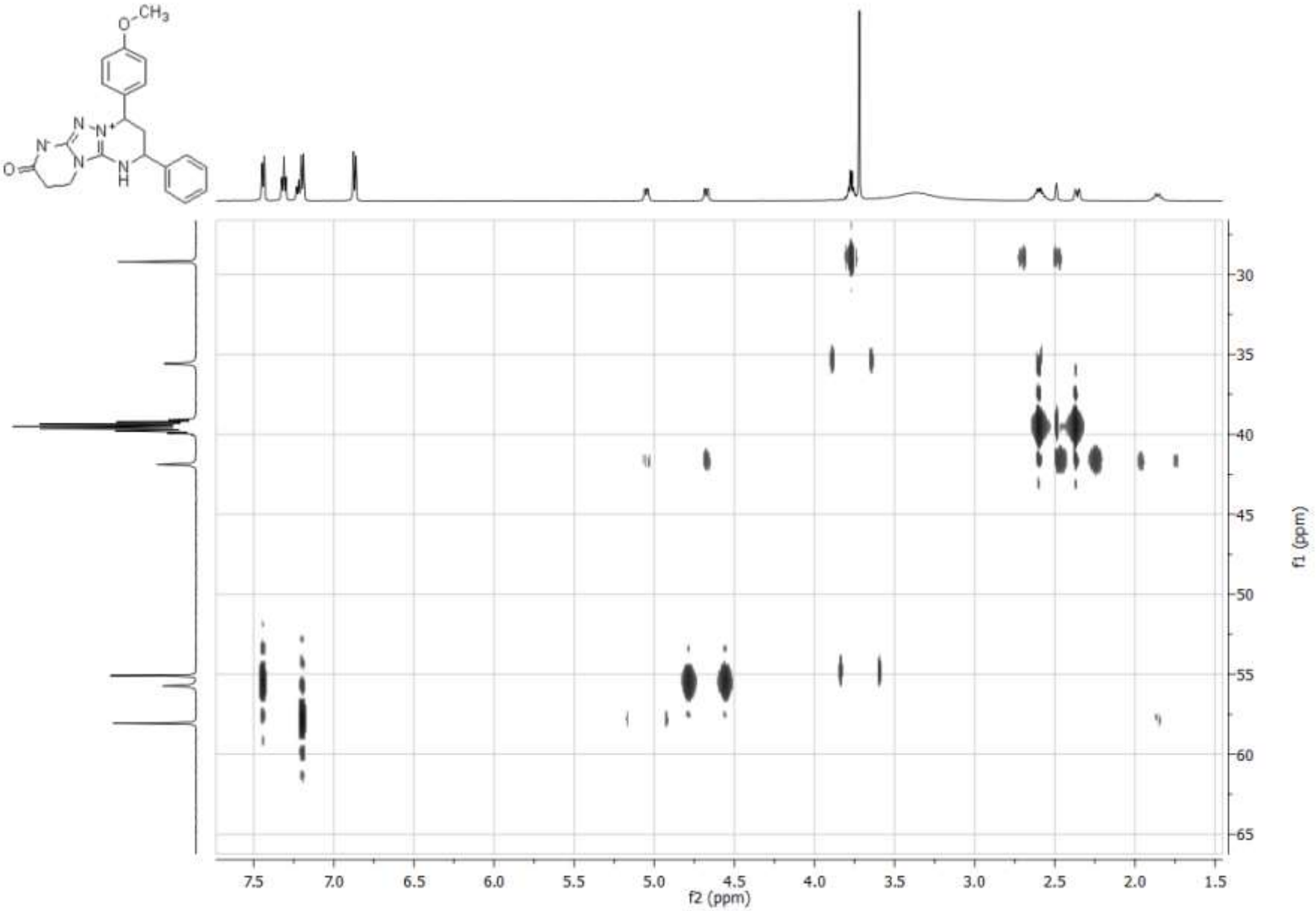
Enlarged fragment of the ^{1}H-^{13}C HSQC spectrum of compound **13a**.



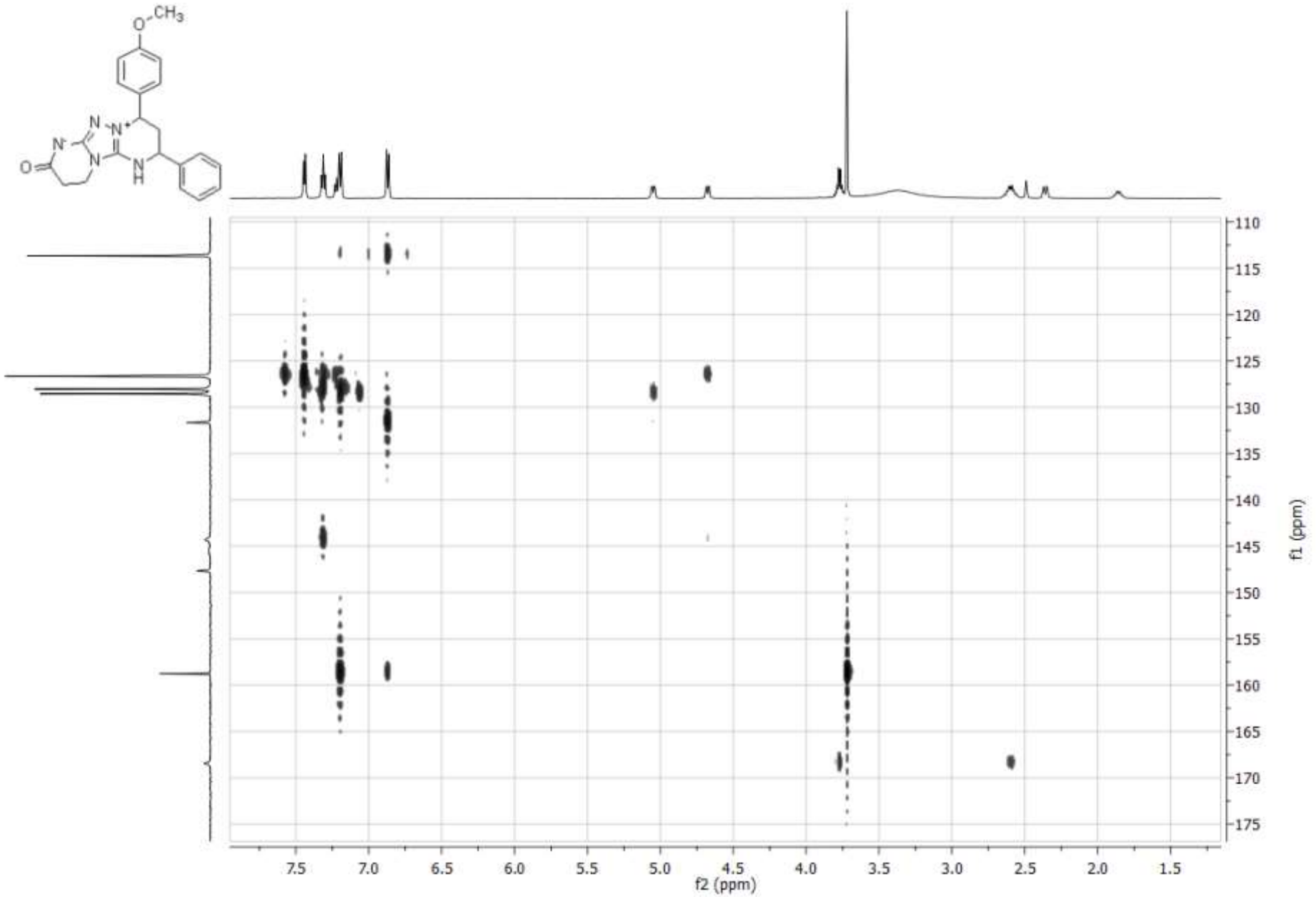
Enlarged fragment of the ^{1}H-^{13}C HSQC spectrum of compound **13a**. A peak at 126.64 ppm in 13C NMR spectrum is a combined peak of two carbons because it has two cross-peaks with protons of benzene rings (7.22 and 7.43 ppm).



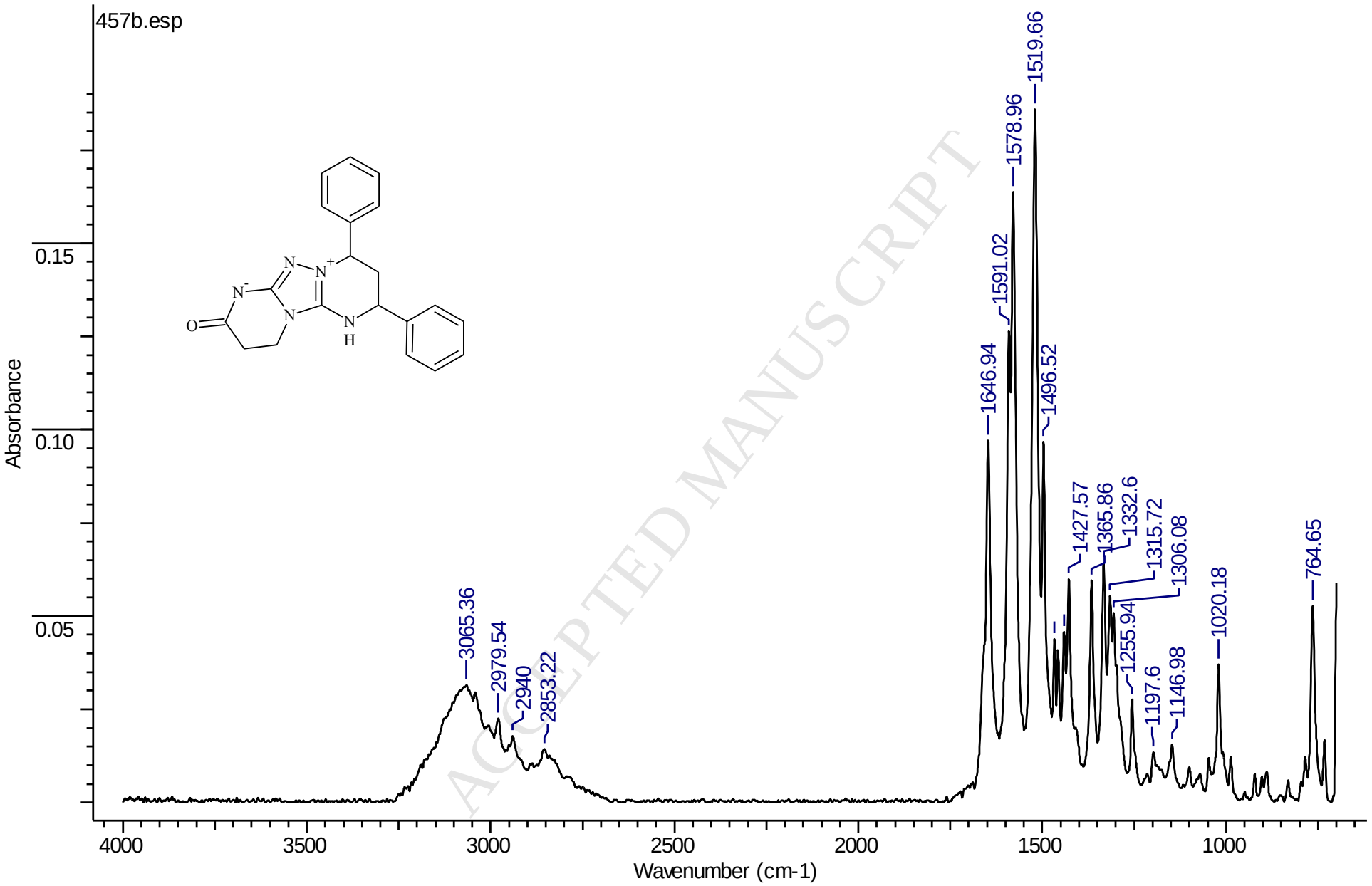
^{1}H-^{13}C HMBC spectrum of compound **13a** (DMSO-d_6).



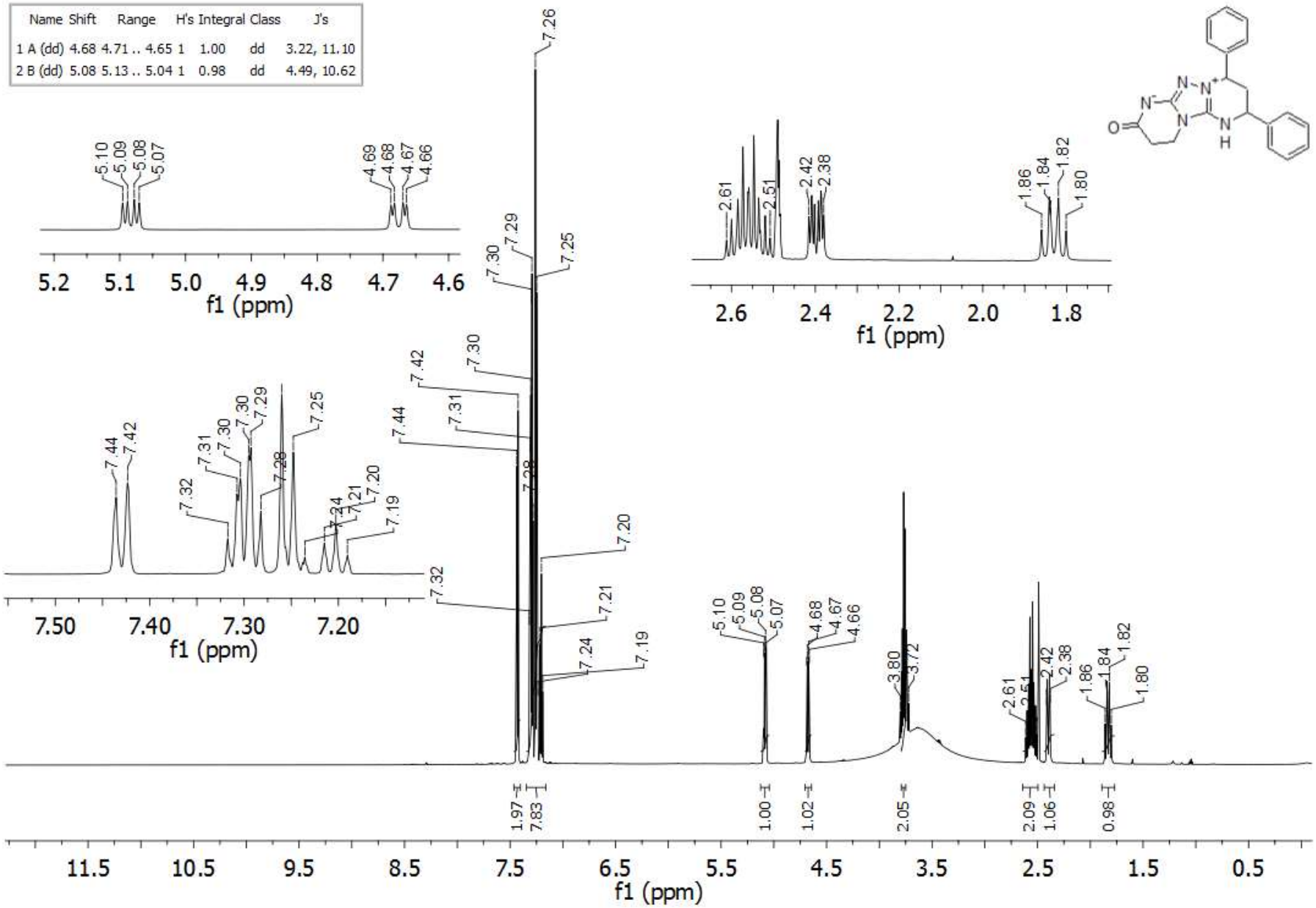
Enlarged fragment of the the ^{1}H-^{13}C HMBC spectrum of compound **13a.**



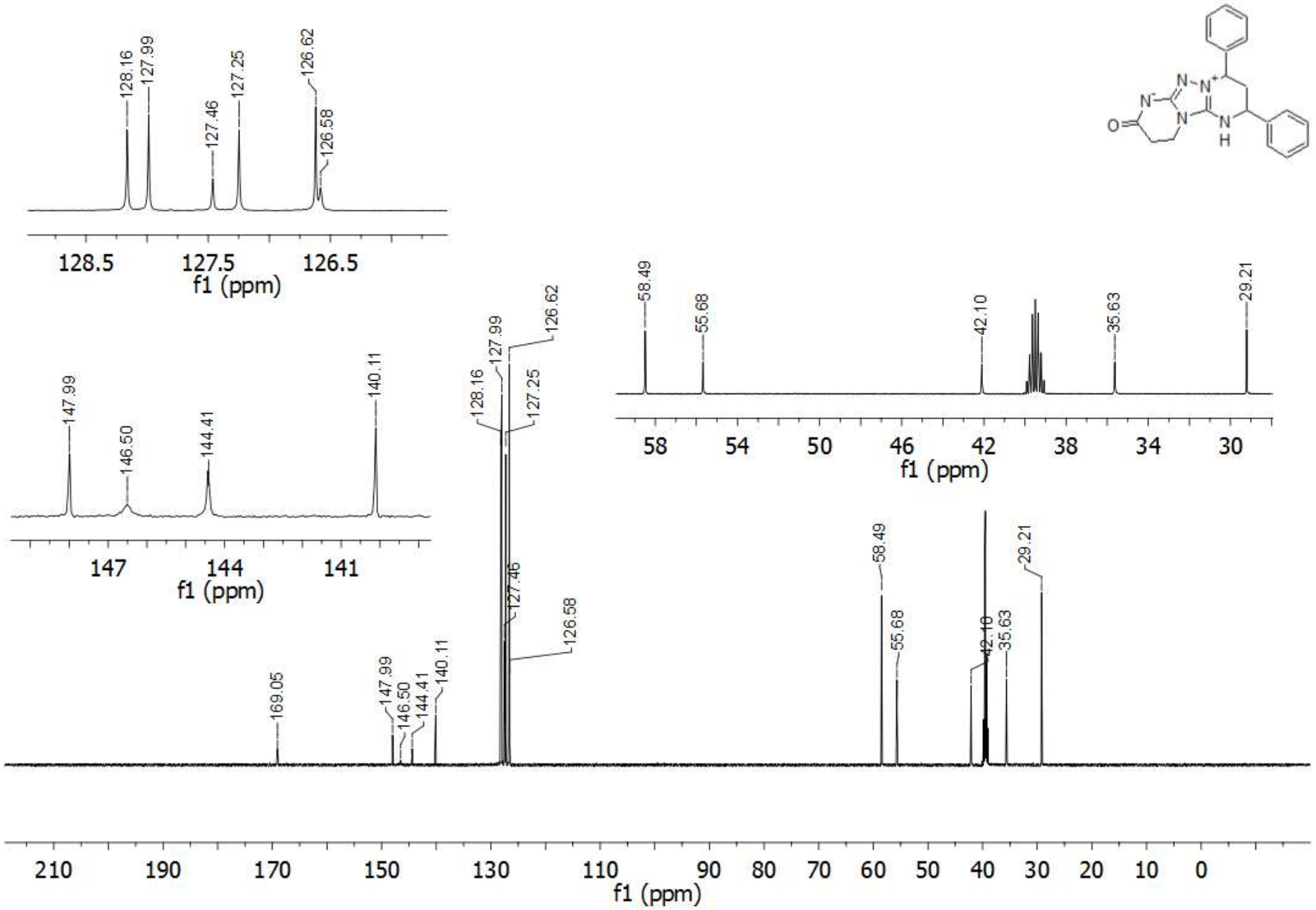
Enlarged fragment of the the ^{1}H-^{13}C HMBC spectrum of compound **13a**.



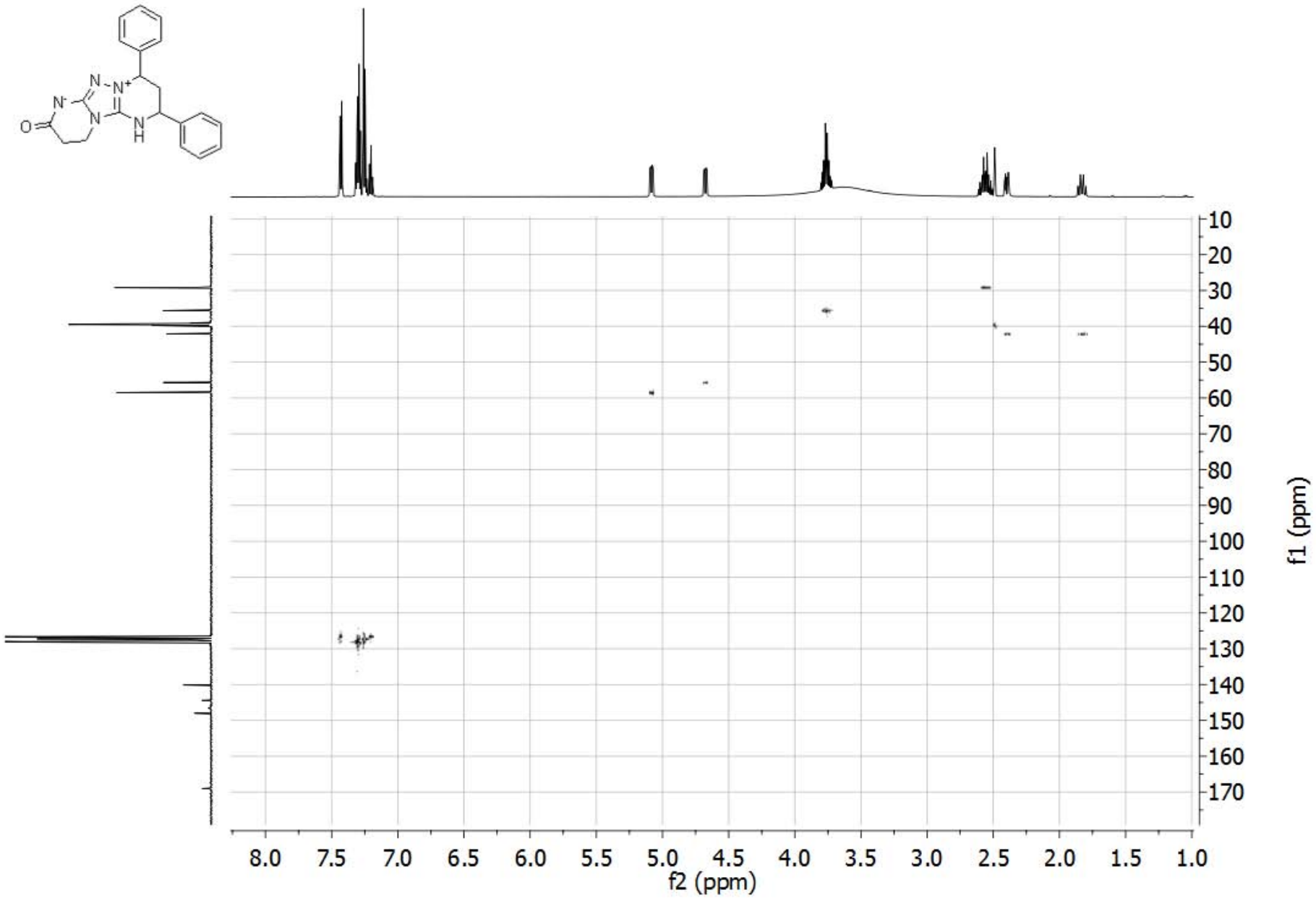
FTIR spectrum of compound **13b** (ATR).



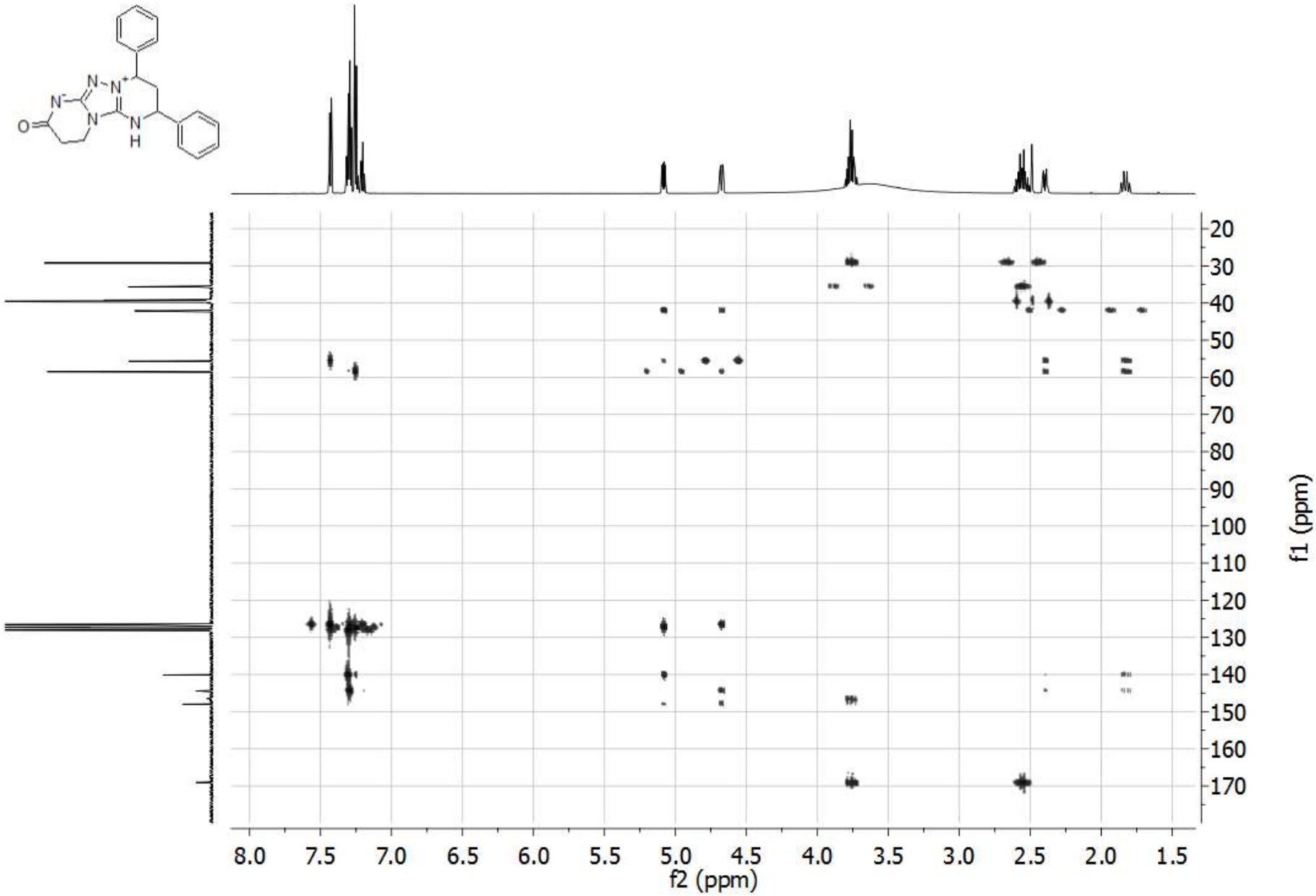
^{1}H NMR spectrum of compound **13b** (DMSO-d_6, 600 MHz).



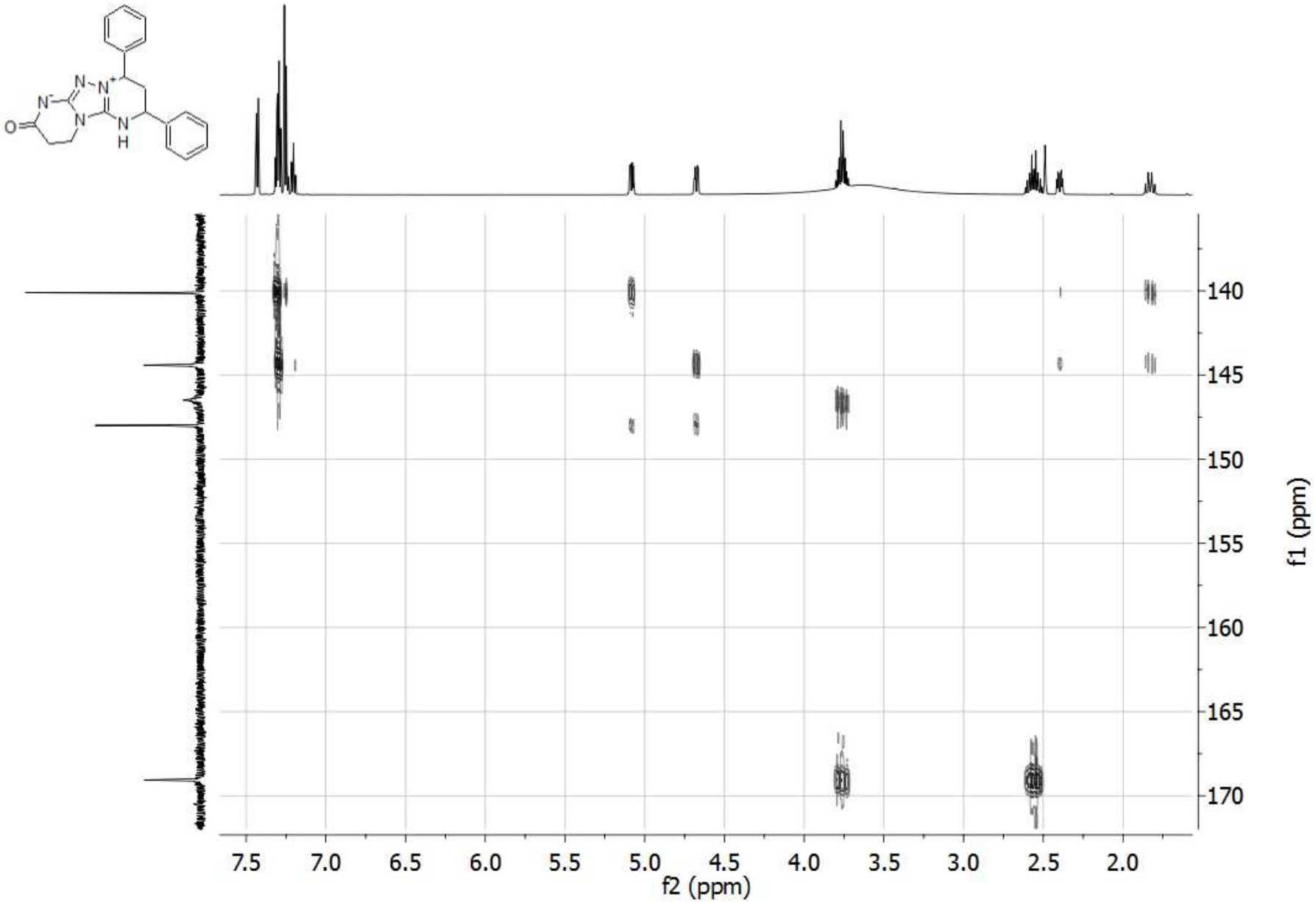
^{13}C NMR spectrum of compound **13b** (DMSO-d_6, 150 MHz).



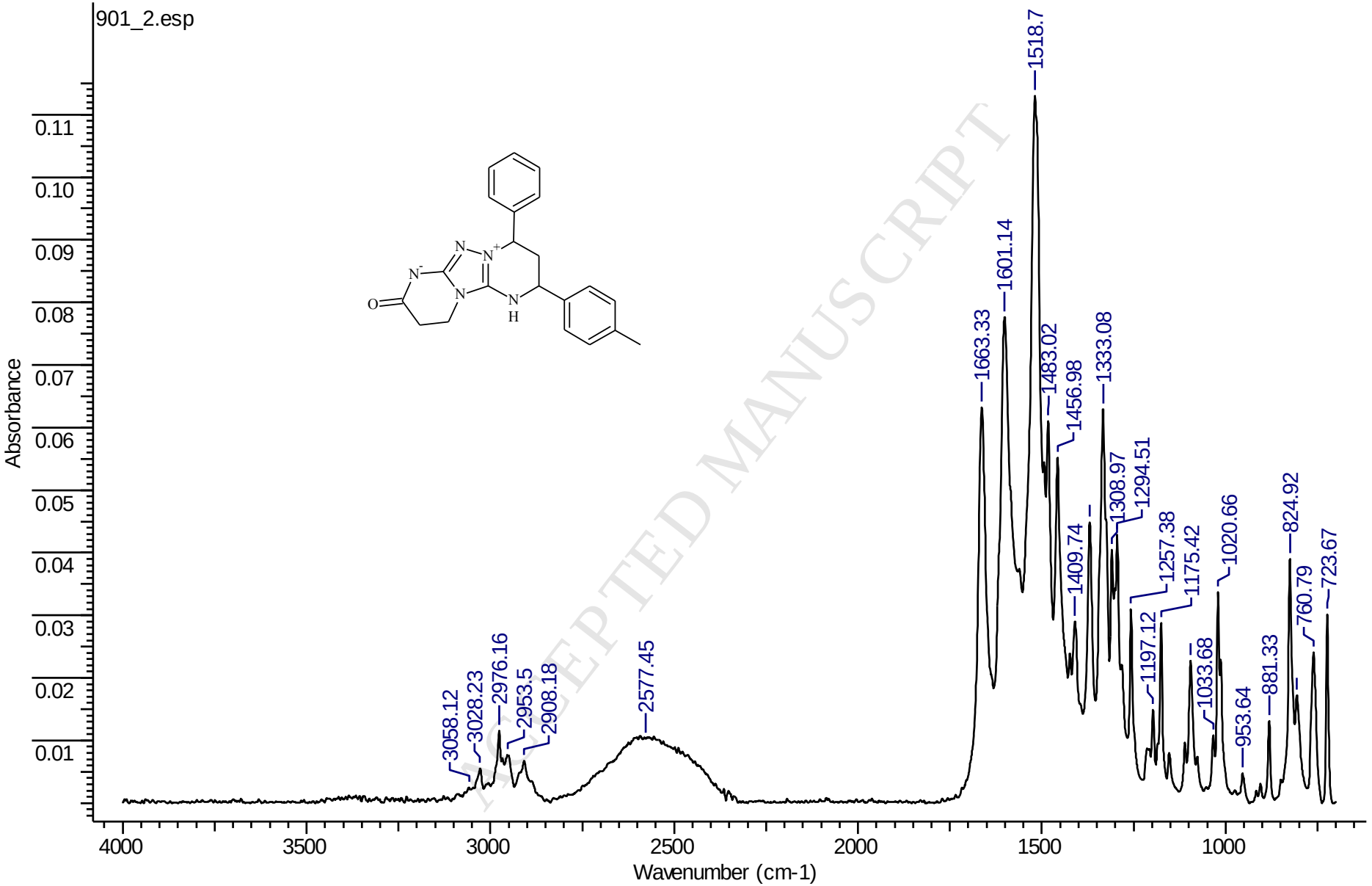
^{1}H-^{13}C HSQC spectrum of compound **13b** (DMSO-d_6).



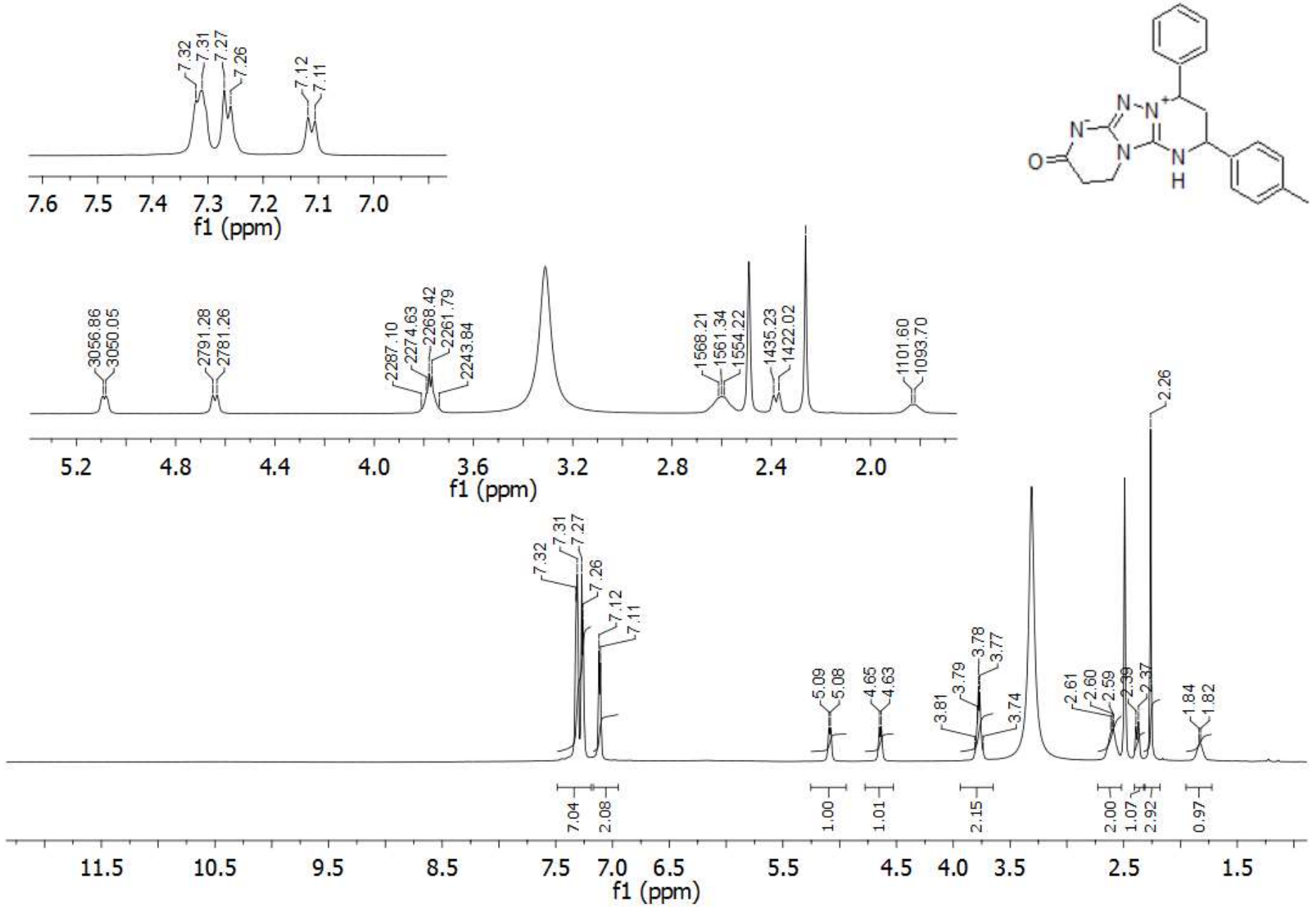
^{1}H-^{13}C HMBC spectrum of compound **13b** (DMSO-d_6).



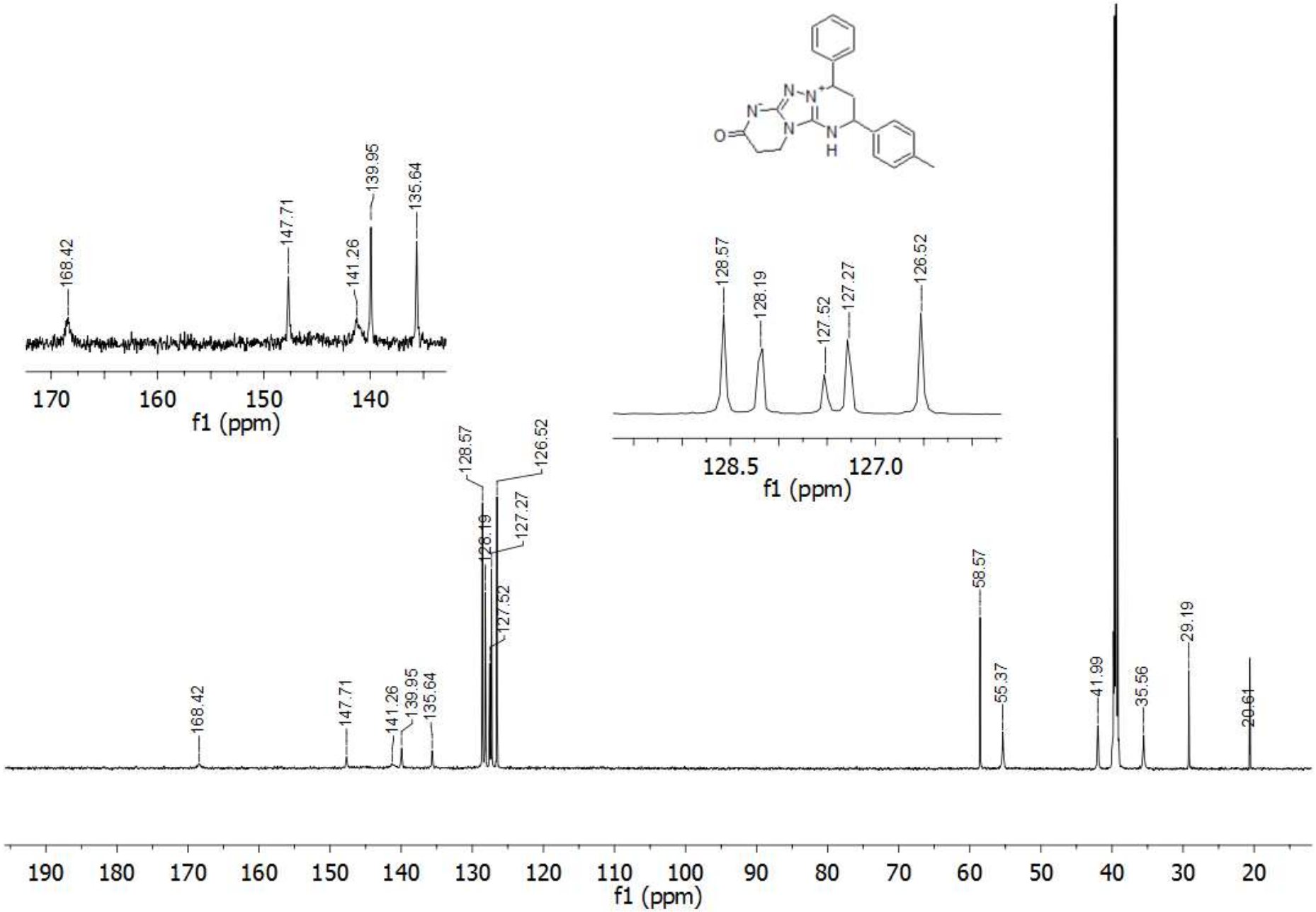
Enlarged fragment of ^{1}H-^{13}C HMBC spectrum of compound **13b** (DMSO-d_6).



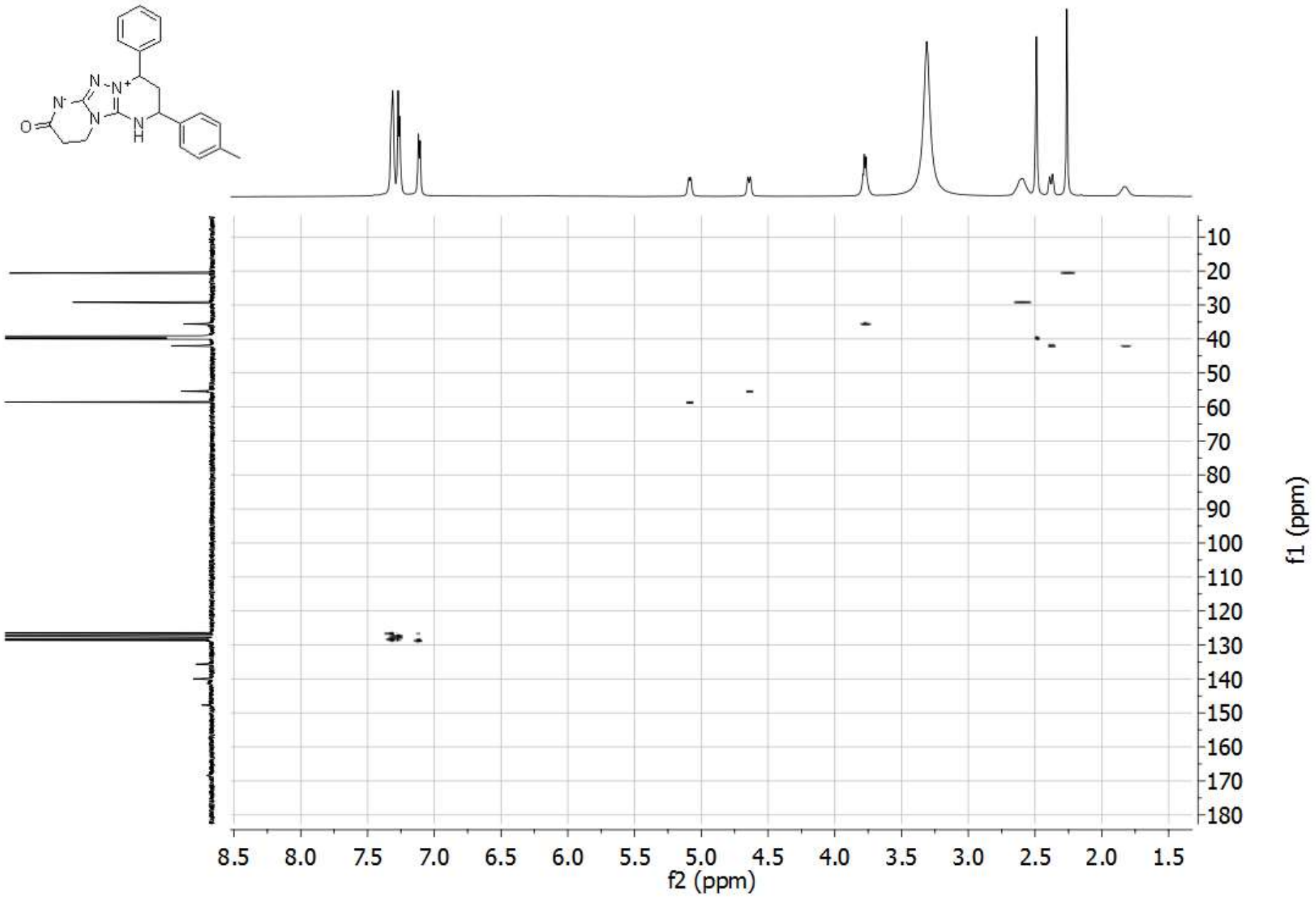
FTIR spectrum of compound **13c** (ATR).



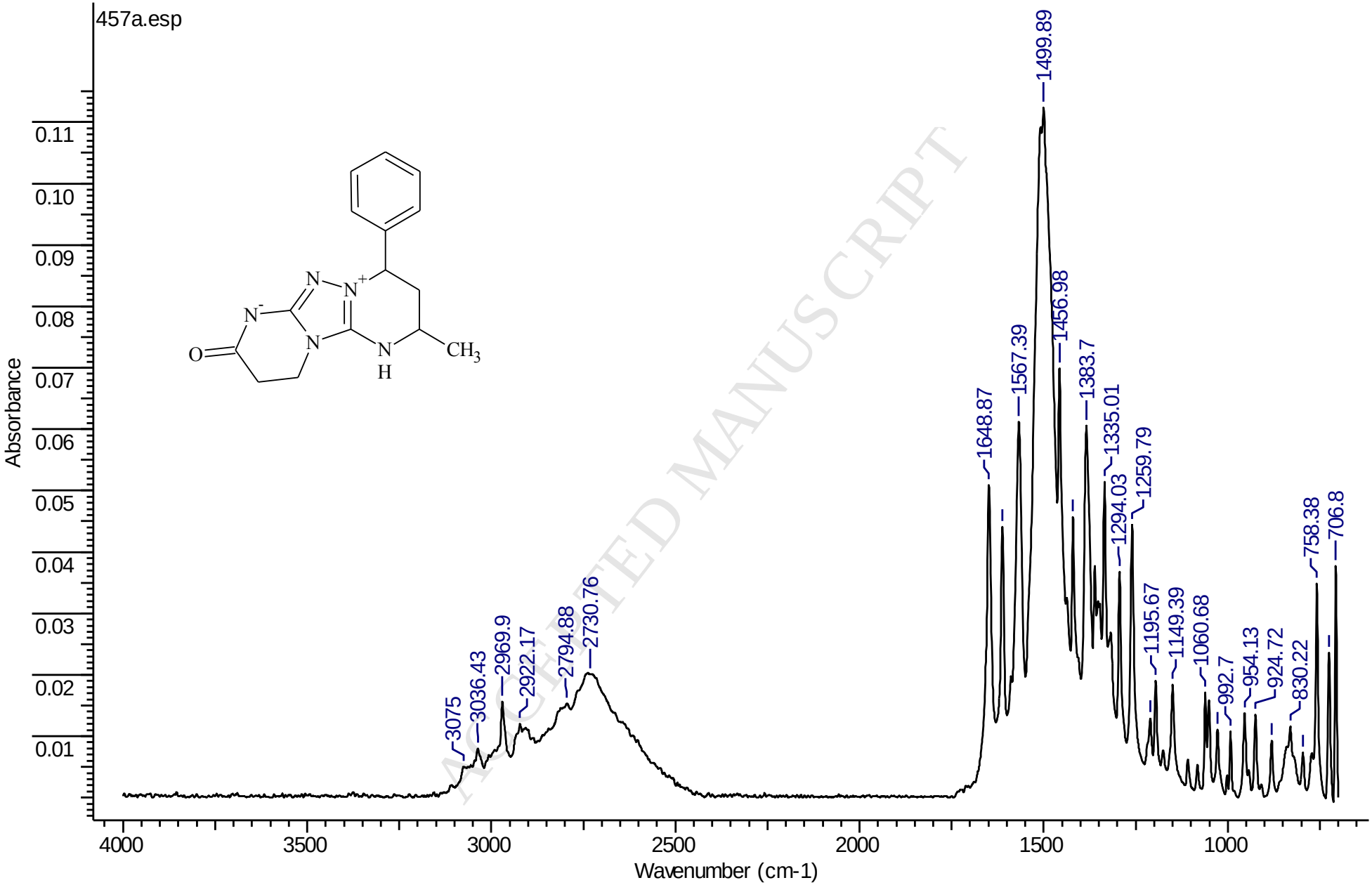
^{1}H NMR spectrum of compound **13c** (DMSO-d_6, 600 MHz).



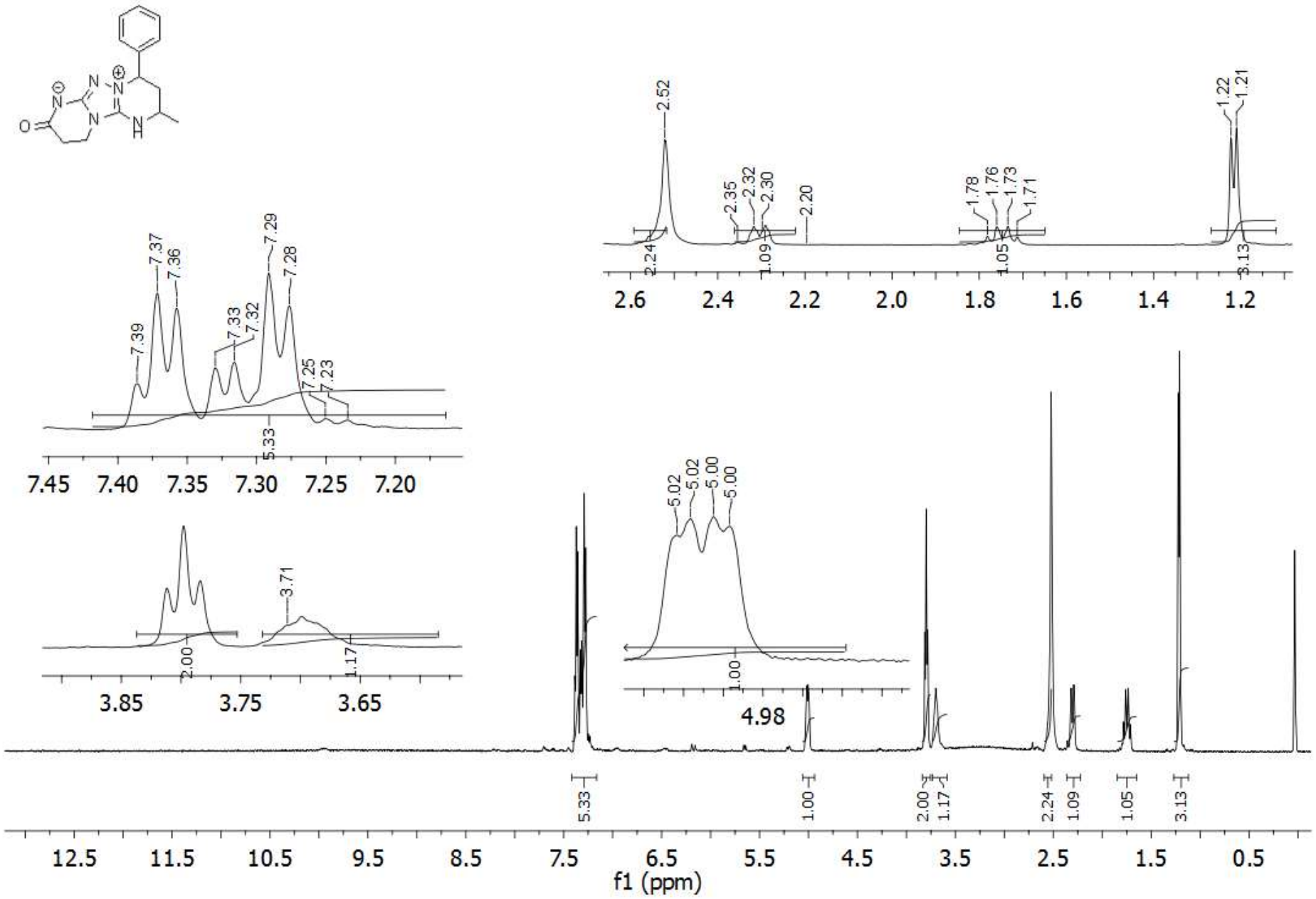
^{13}C NMR spectrum of compound **13c** (DMSO-d_6).



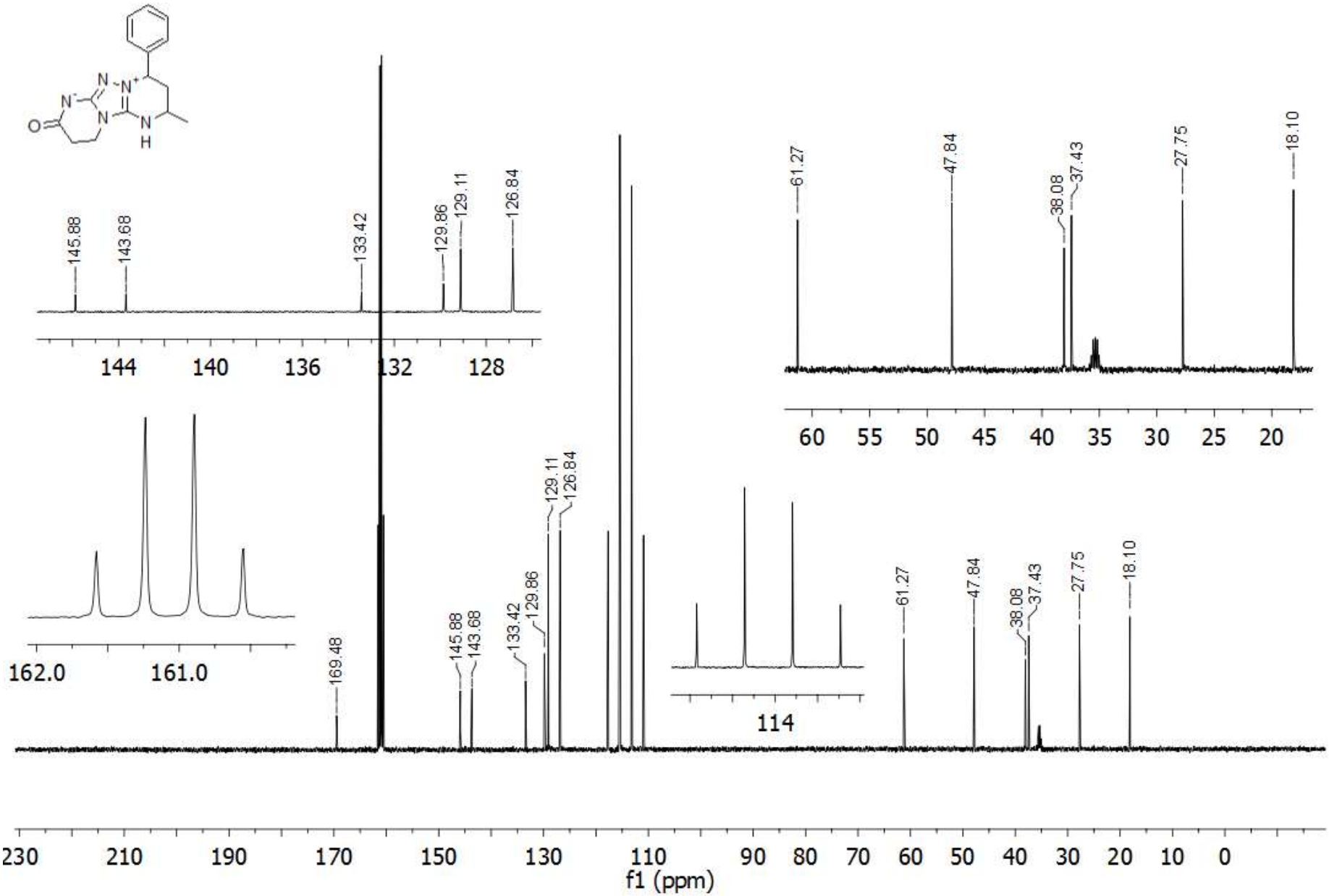
^{1}H-^{13}C HSQC spectrum of compound **13c** (DMSO-d_6).



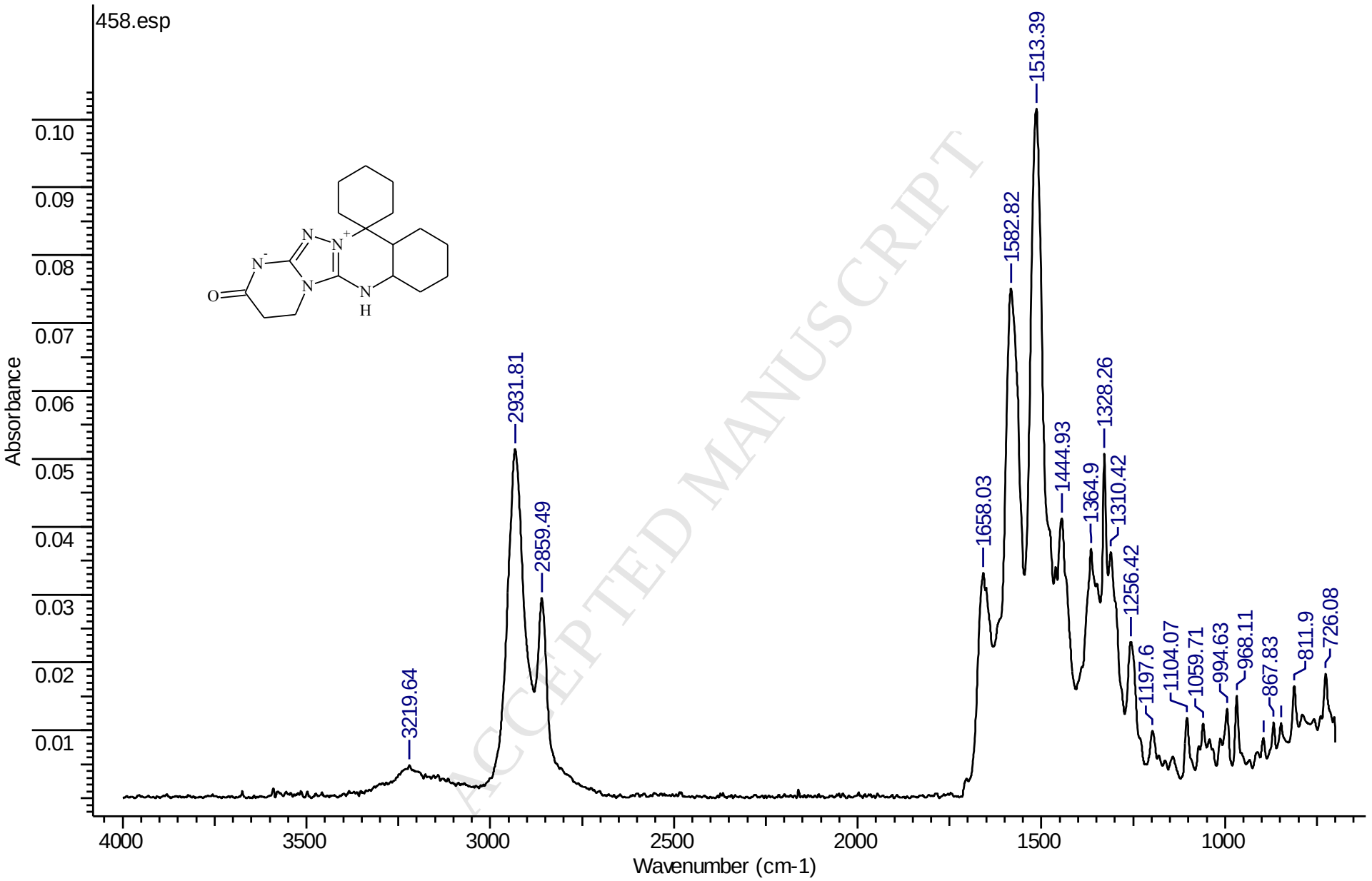
FTIR spectrum of compound **13d**.



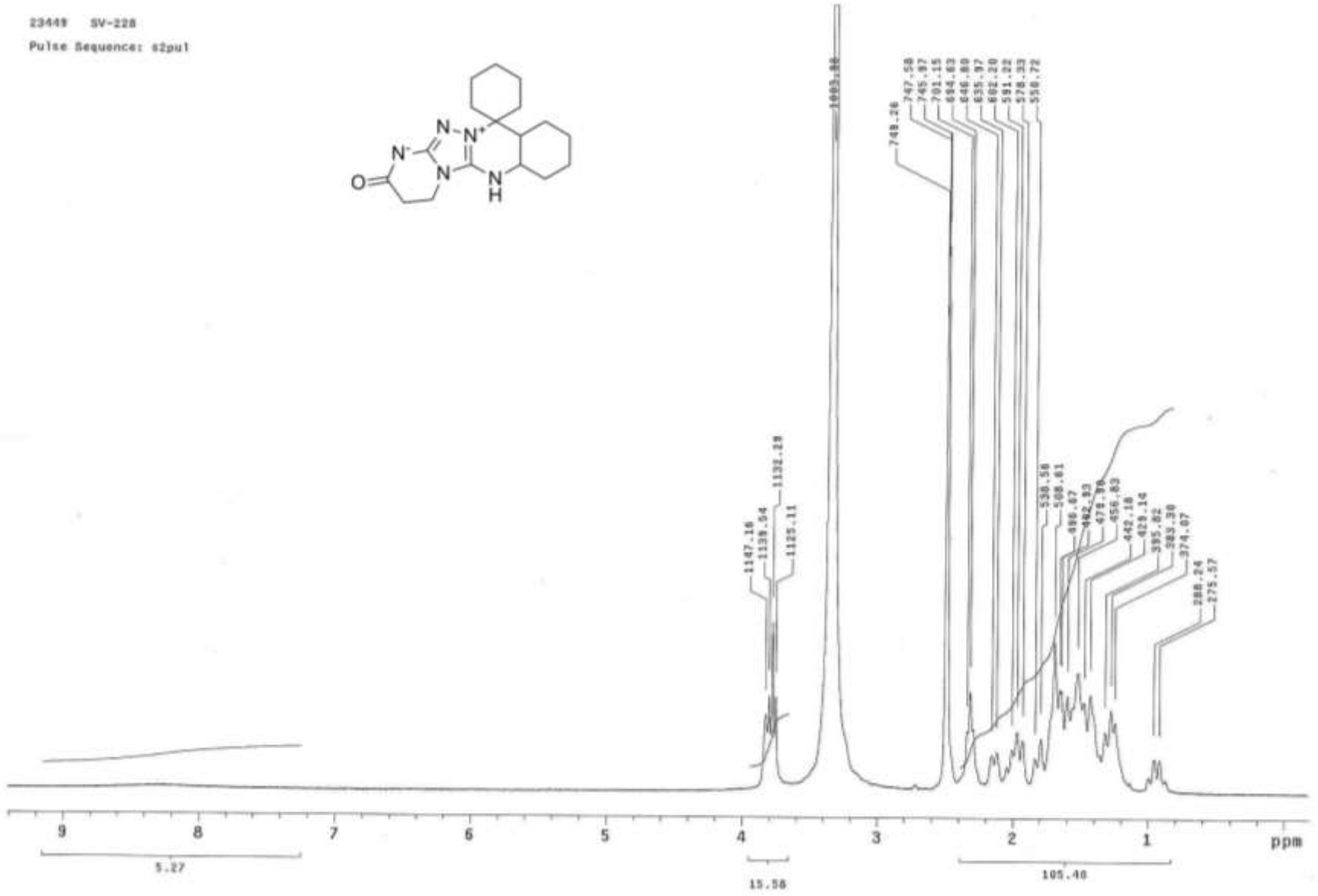
^{1}H NMR spectrum of compound **13d** (DMSO-d_6, 500 MHz).



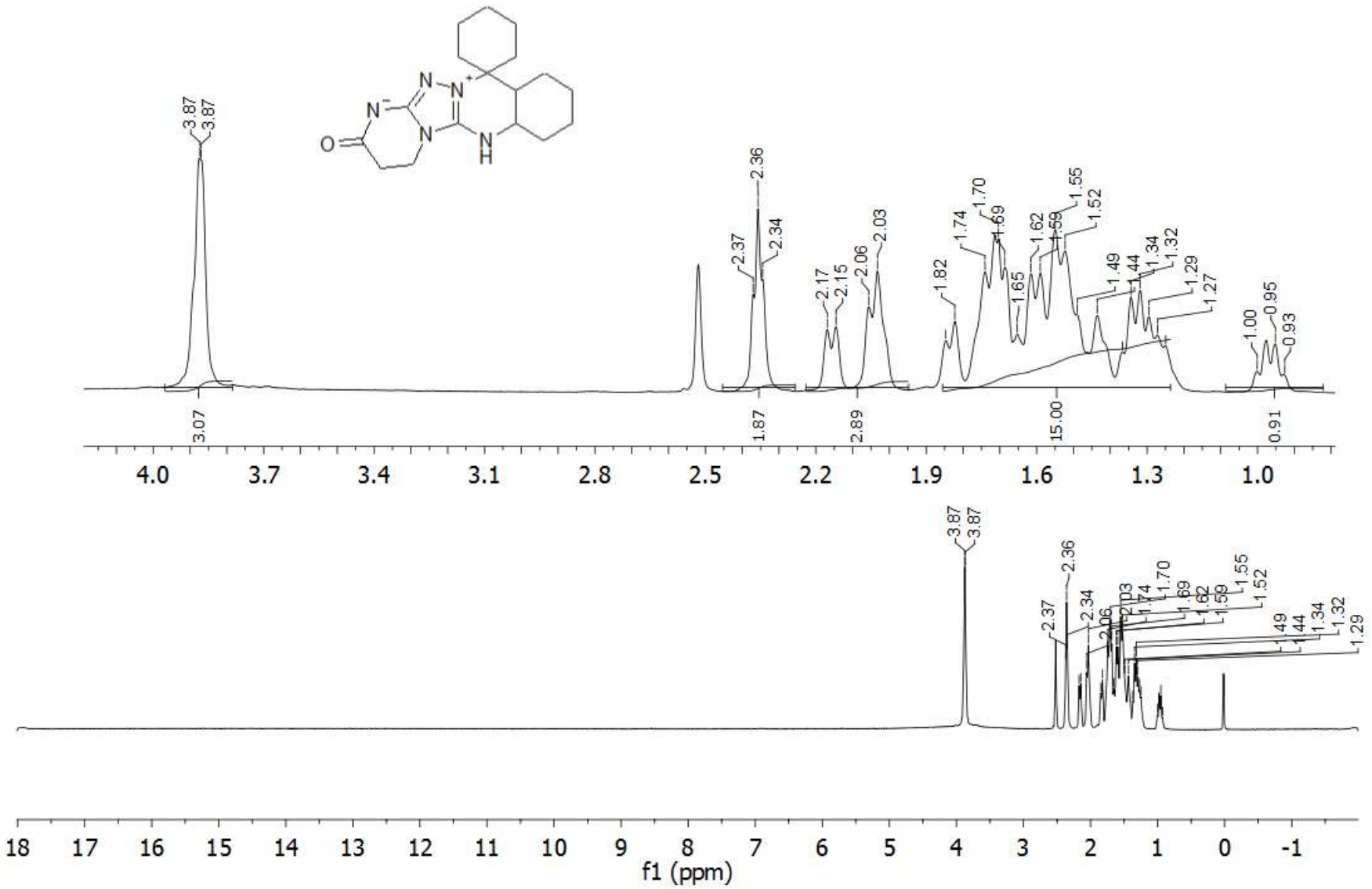
^{13}C NMR spectrum of compound **13d** (CF_3COOH + 5% DMSO-d_6, 125 MHz).



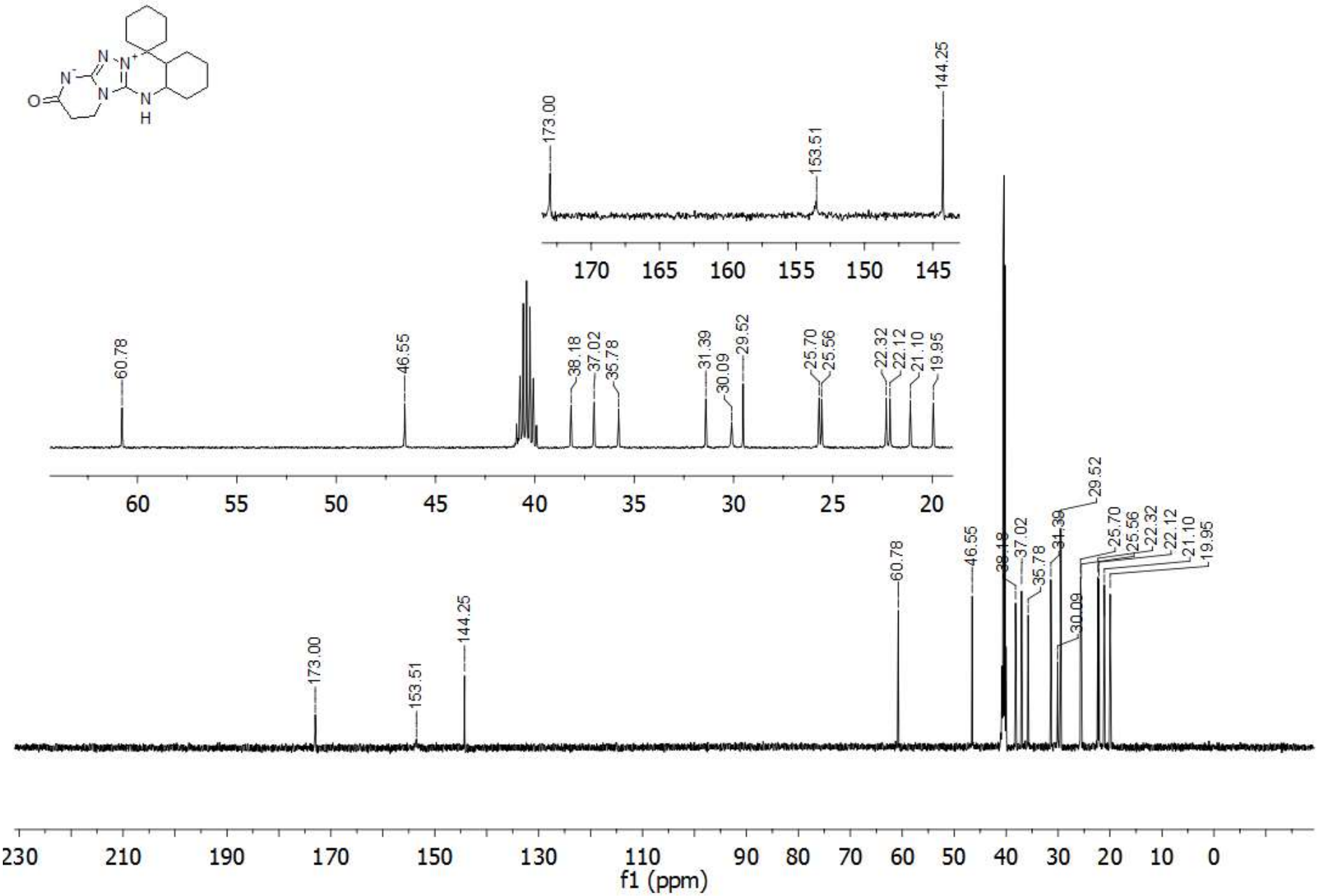
FTIR spectrum of compound **13e** (ATR).



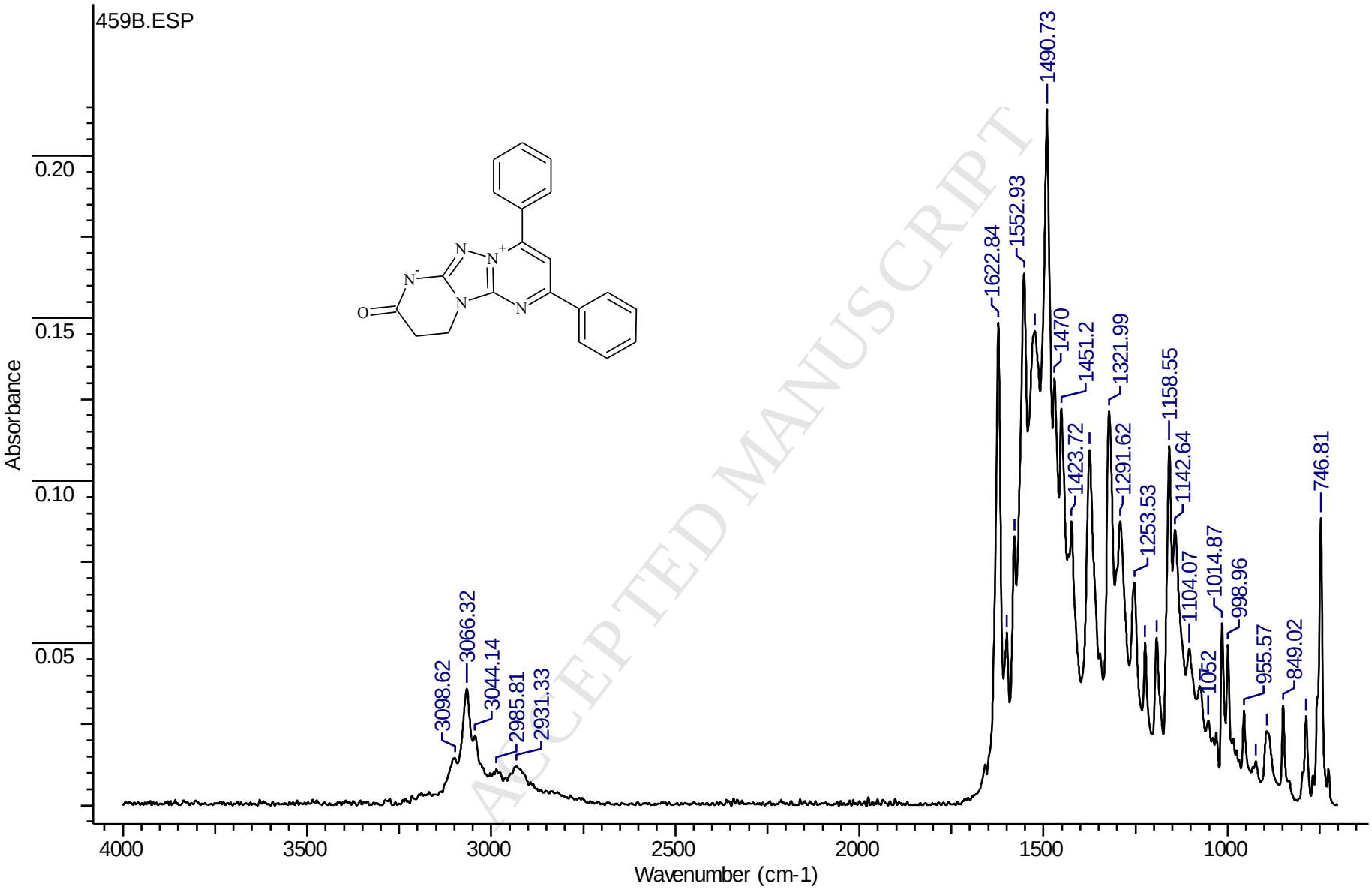
^{1}H NMR spectrum of compound **13e** (300 MHz, DMSO-d_6).



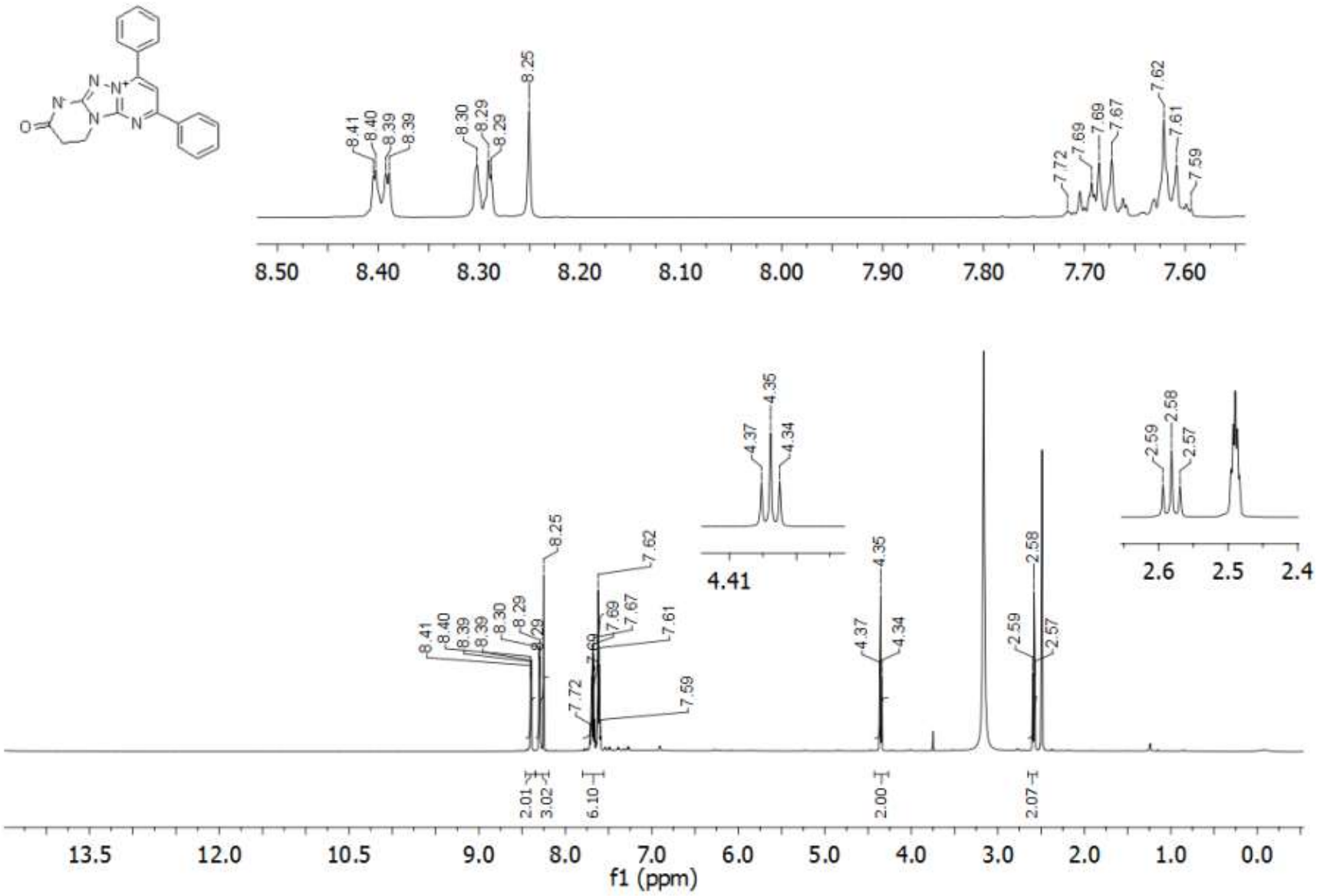
^{1}H NMR spectrum of compound **13e** (500 MHz, DMSO-d_6).



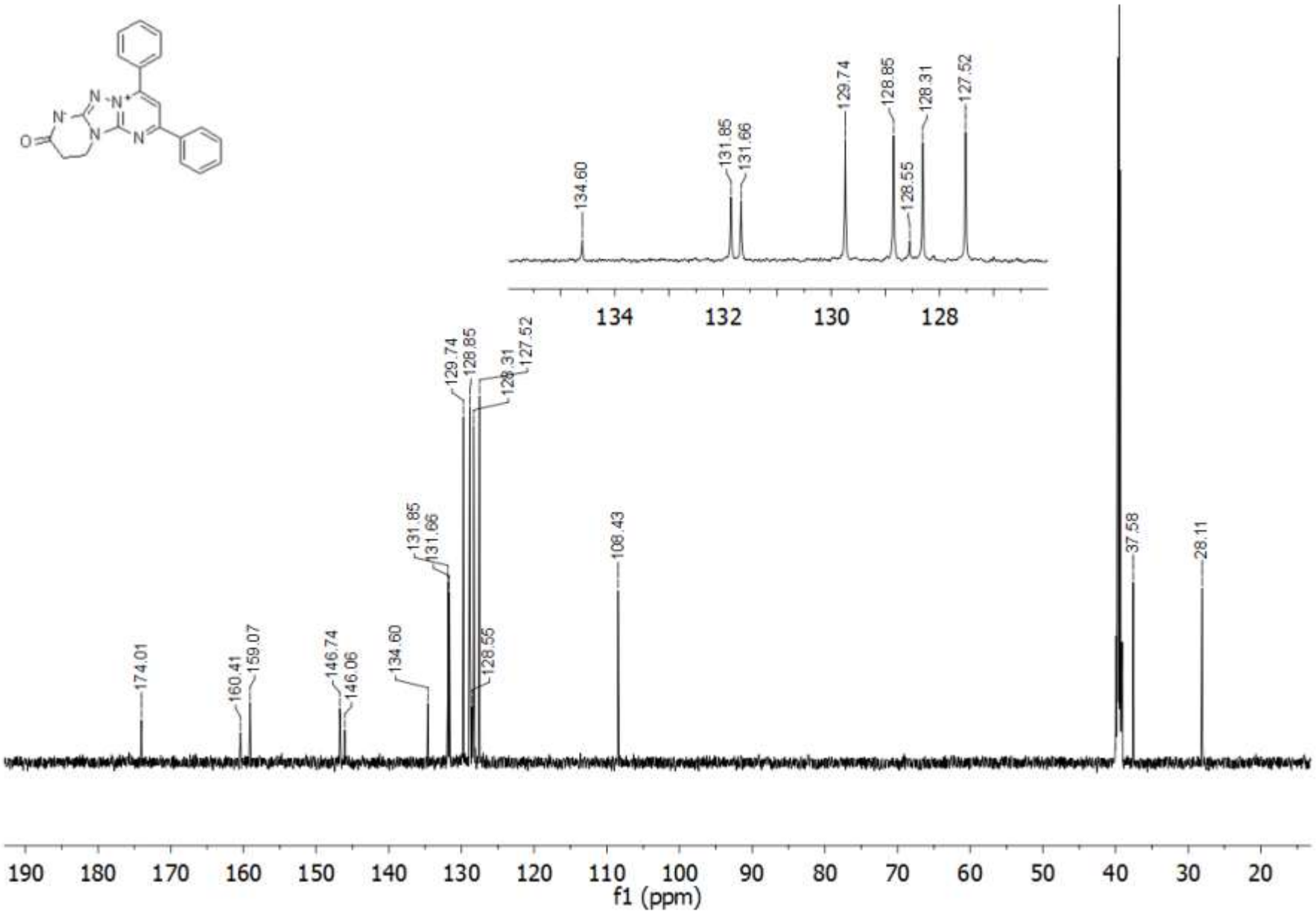
^{13}C NMR spectrum of compound **13e** (DMSO-d_6, 150 MHz).



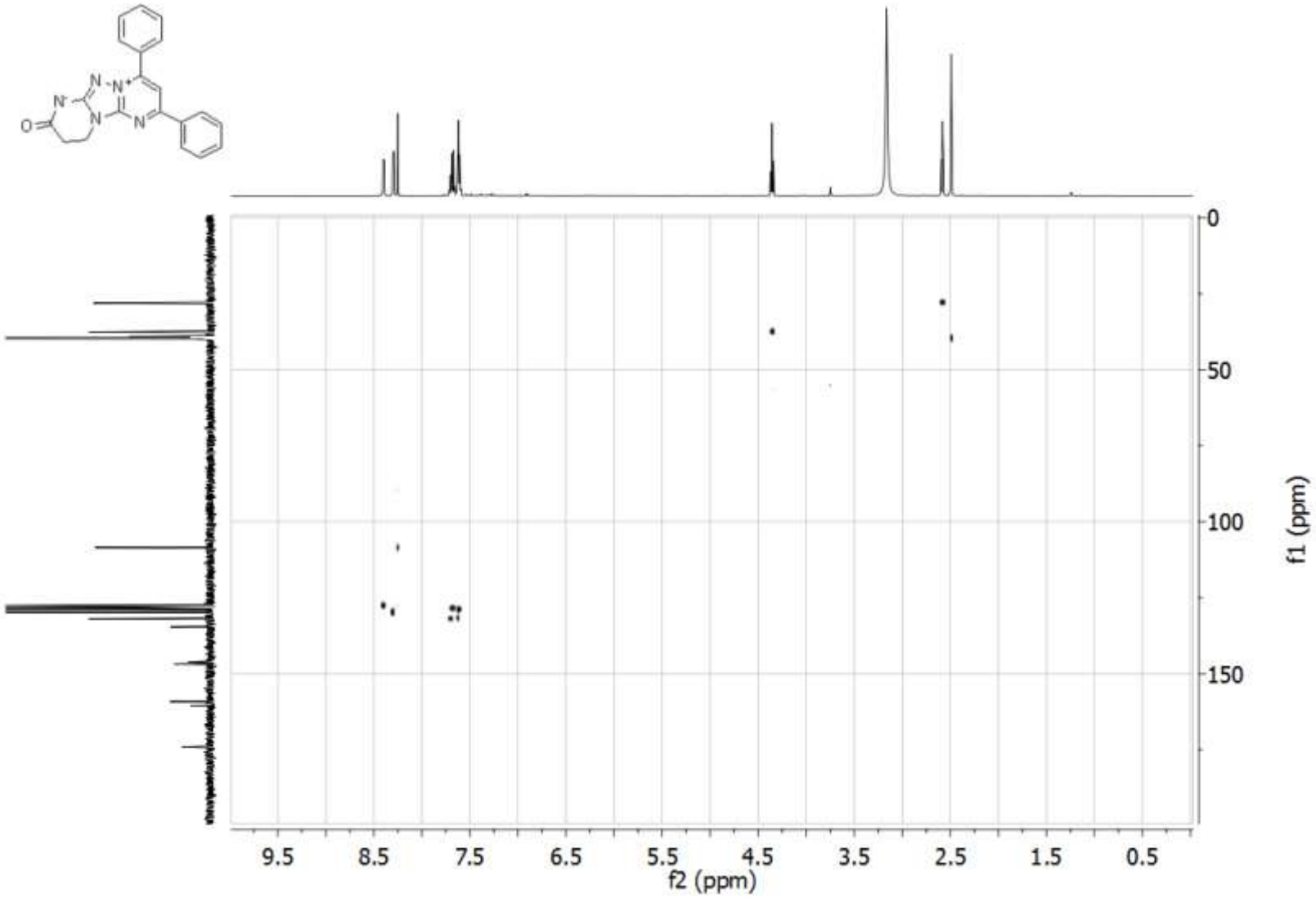
FTIR spectrum of compound **14c** (ATR).



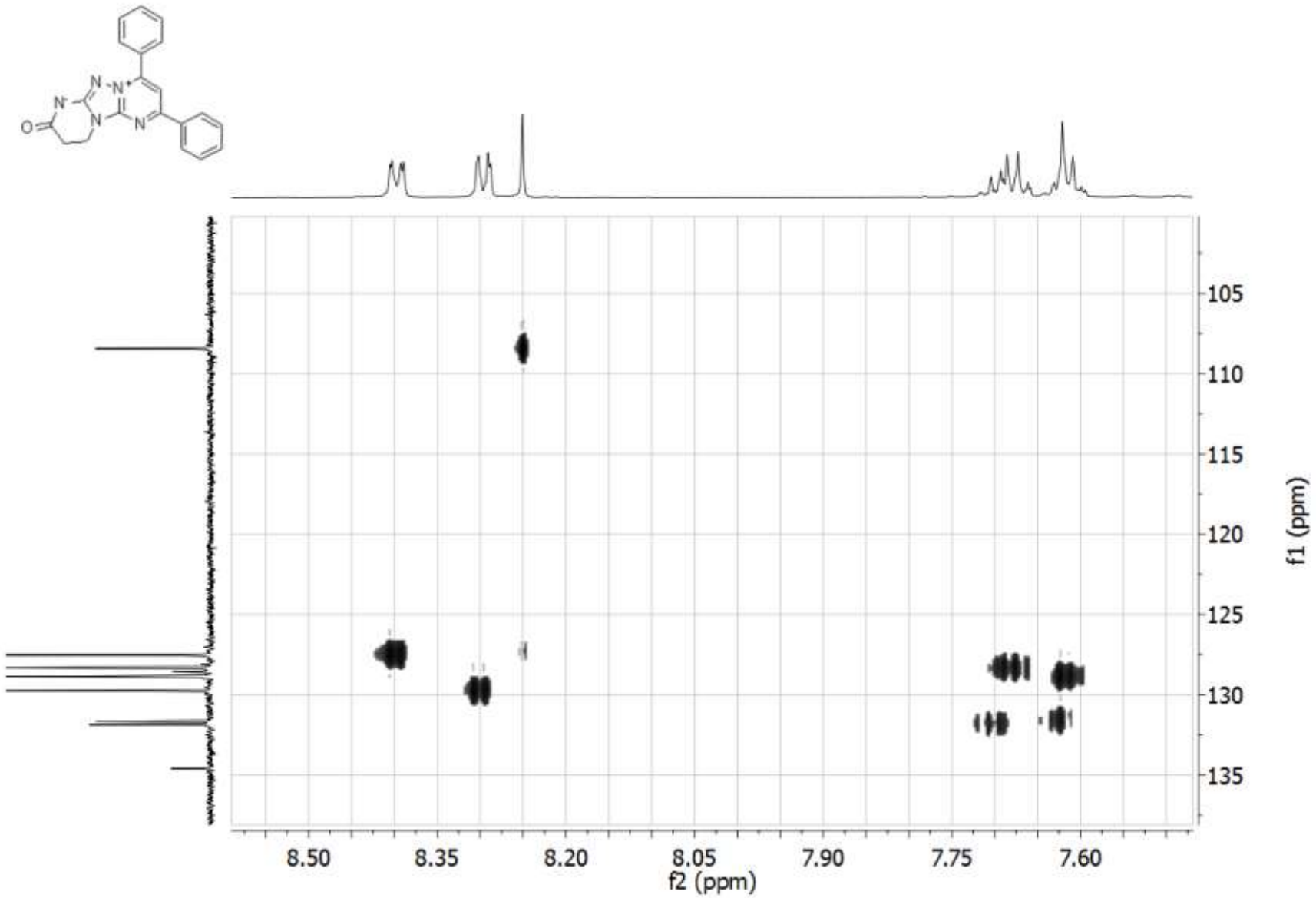
^{1}H NMR spectrum of compound **14c** (DMSO-d_6, 600 MHz).



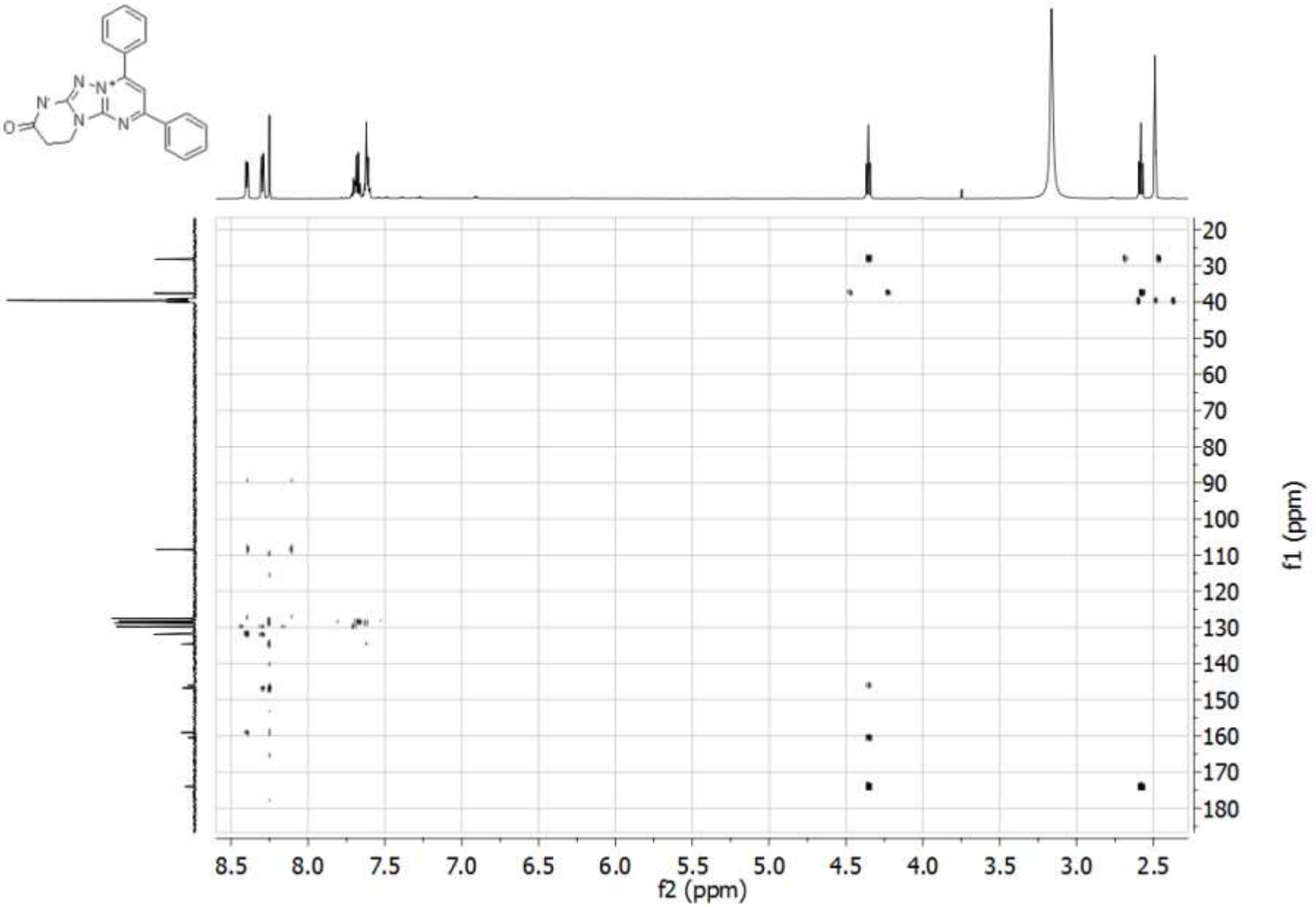
^{13}C NMR spectrum of compound **14c** (DMSO-d_6, 150 MHz).



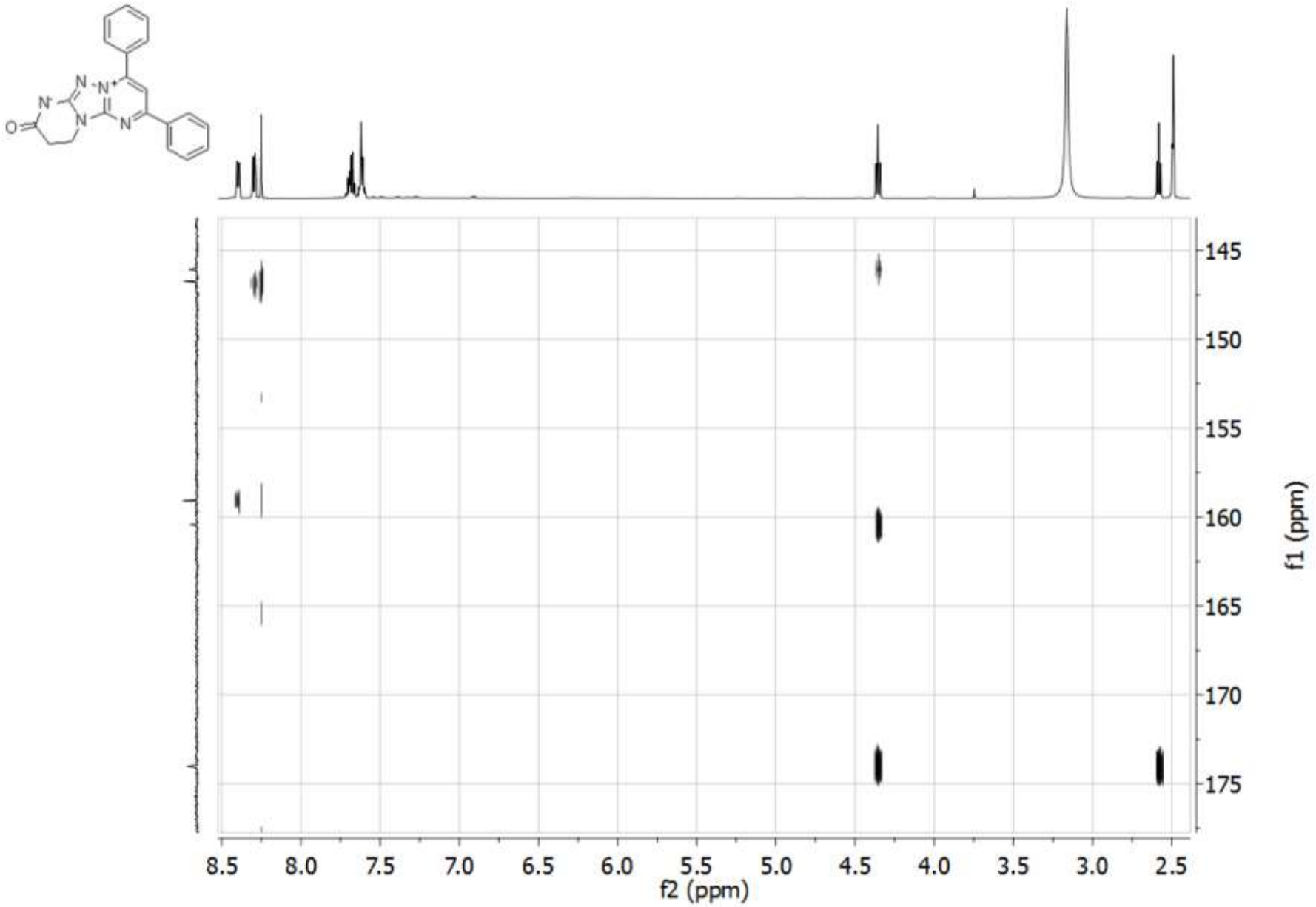
^{1}H-^{13}C HSQC spectrum of compound **14c** (DMSO-d_6).



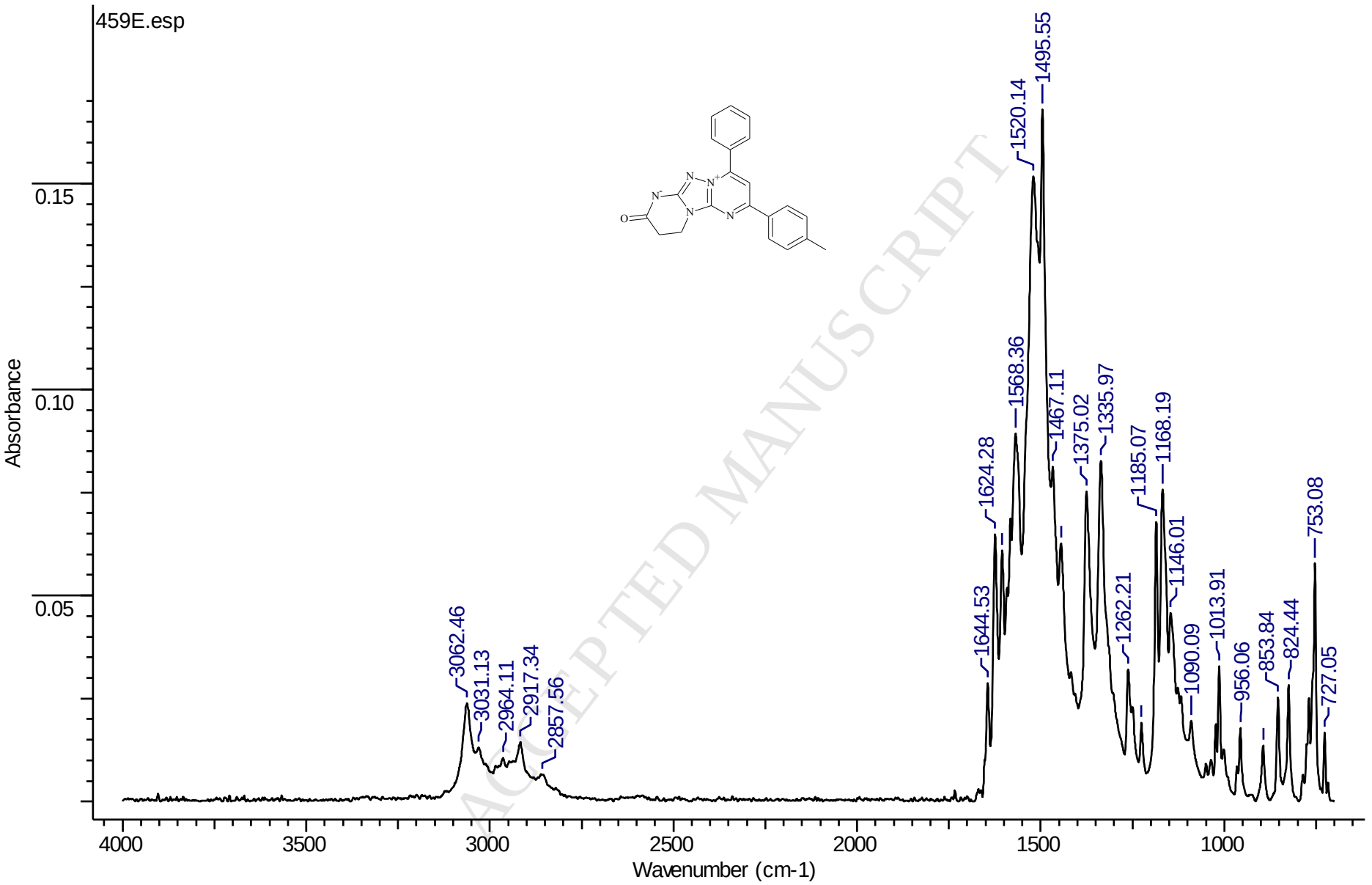
Enlarged fragment of ^{1}H-^{13}C HSQC spectrum of compound **14c**.



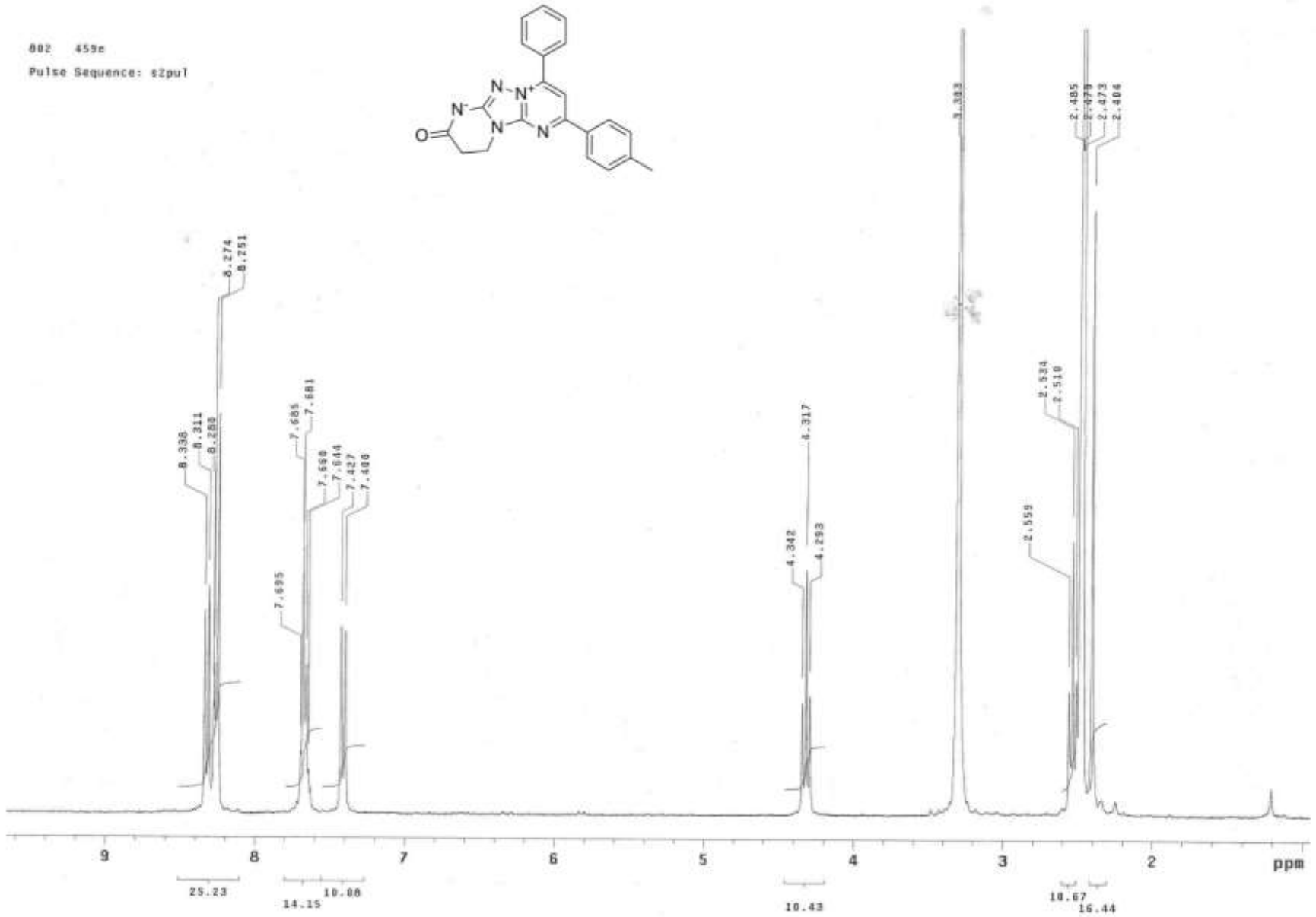
^{1}H-^{13}C HMBC spectrum of compound **14c** (DMSO-d_6).



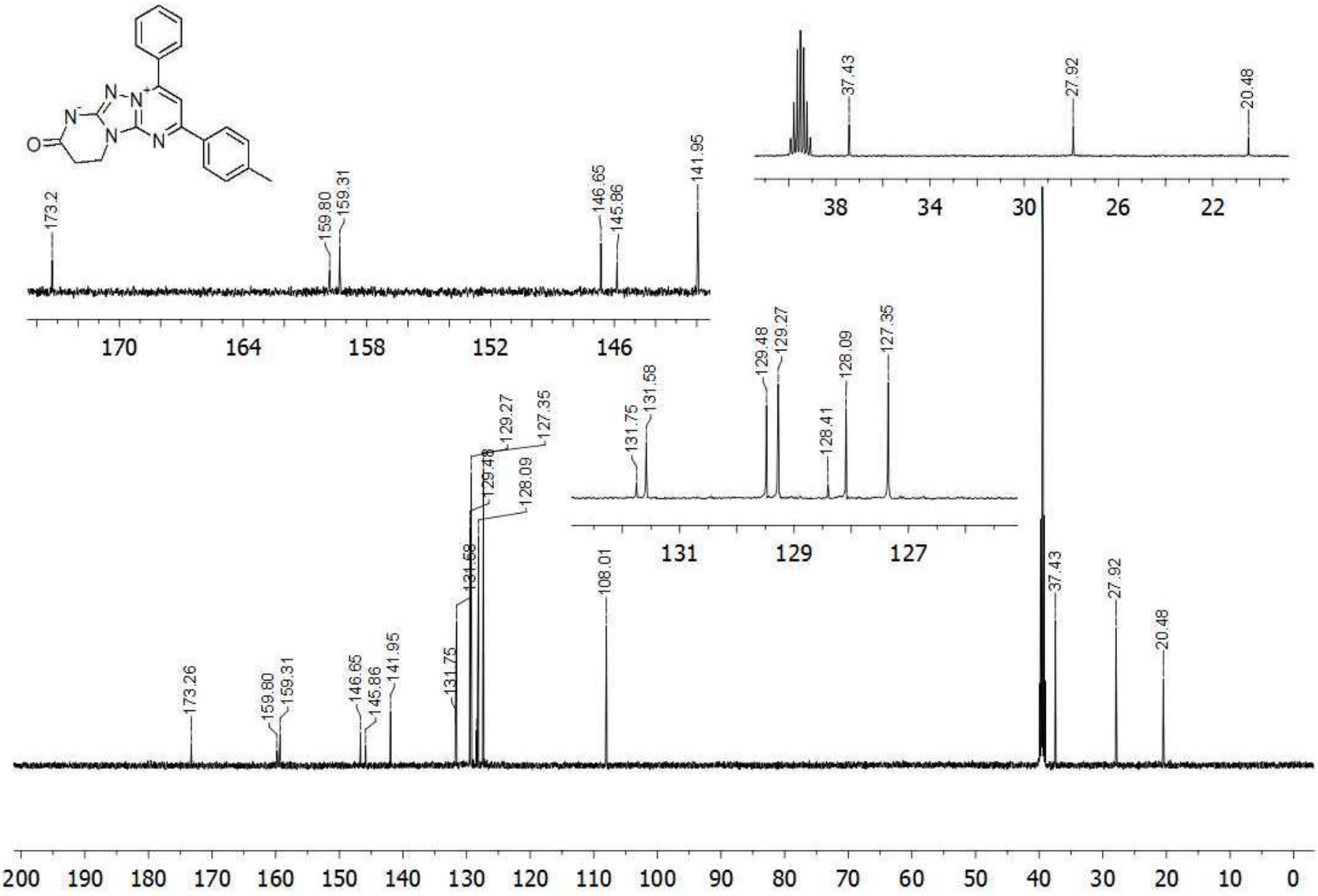
Enlarged fragment of ^{1}H-^{13}C HMBC spectrum of compound **14c**.



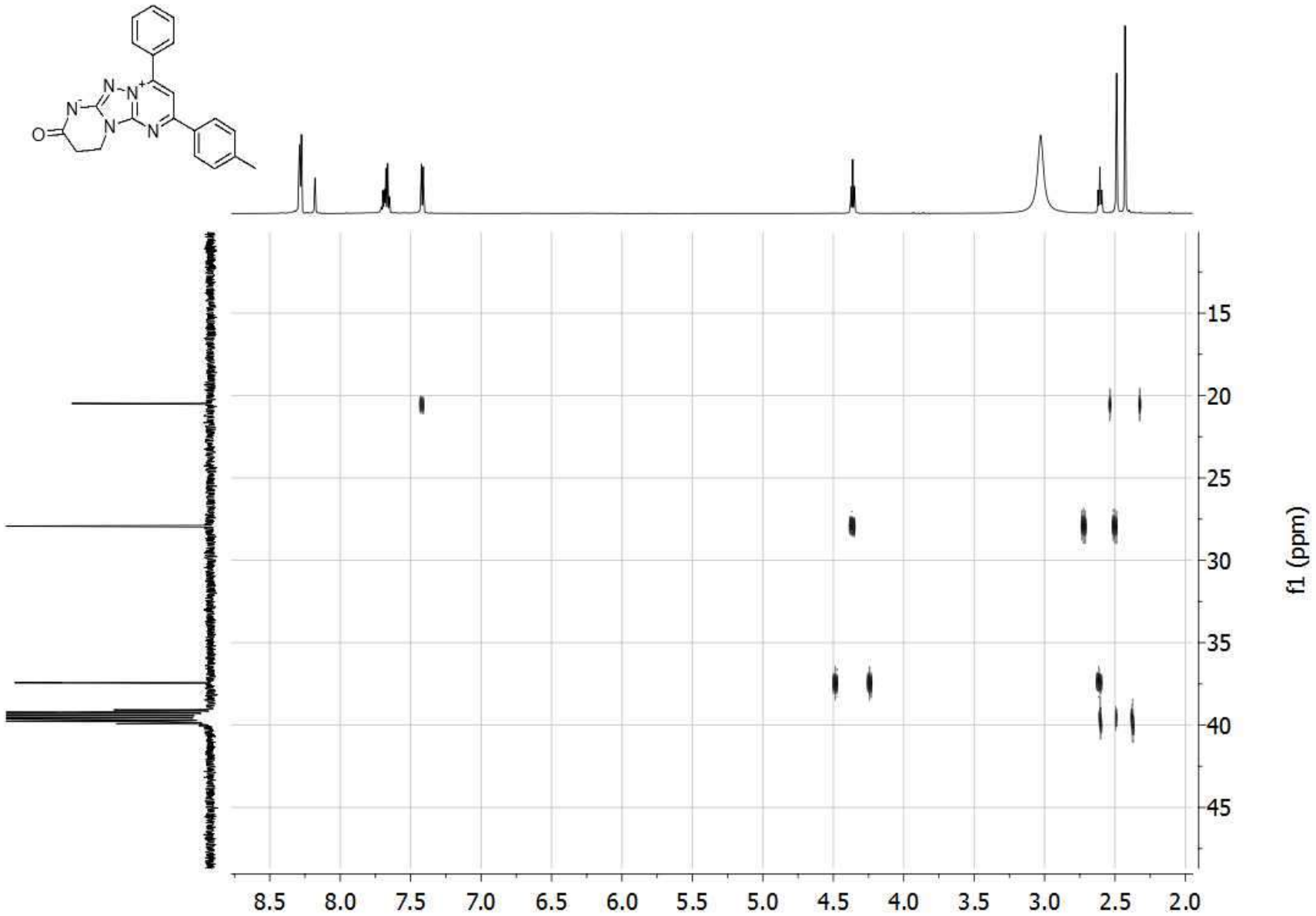
FTIR spectrum of compound **14d** (ATR).



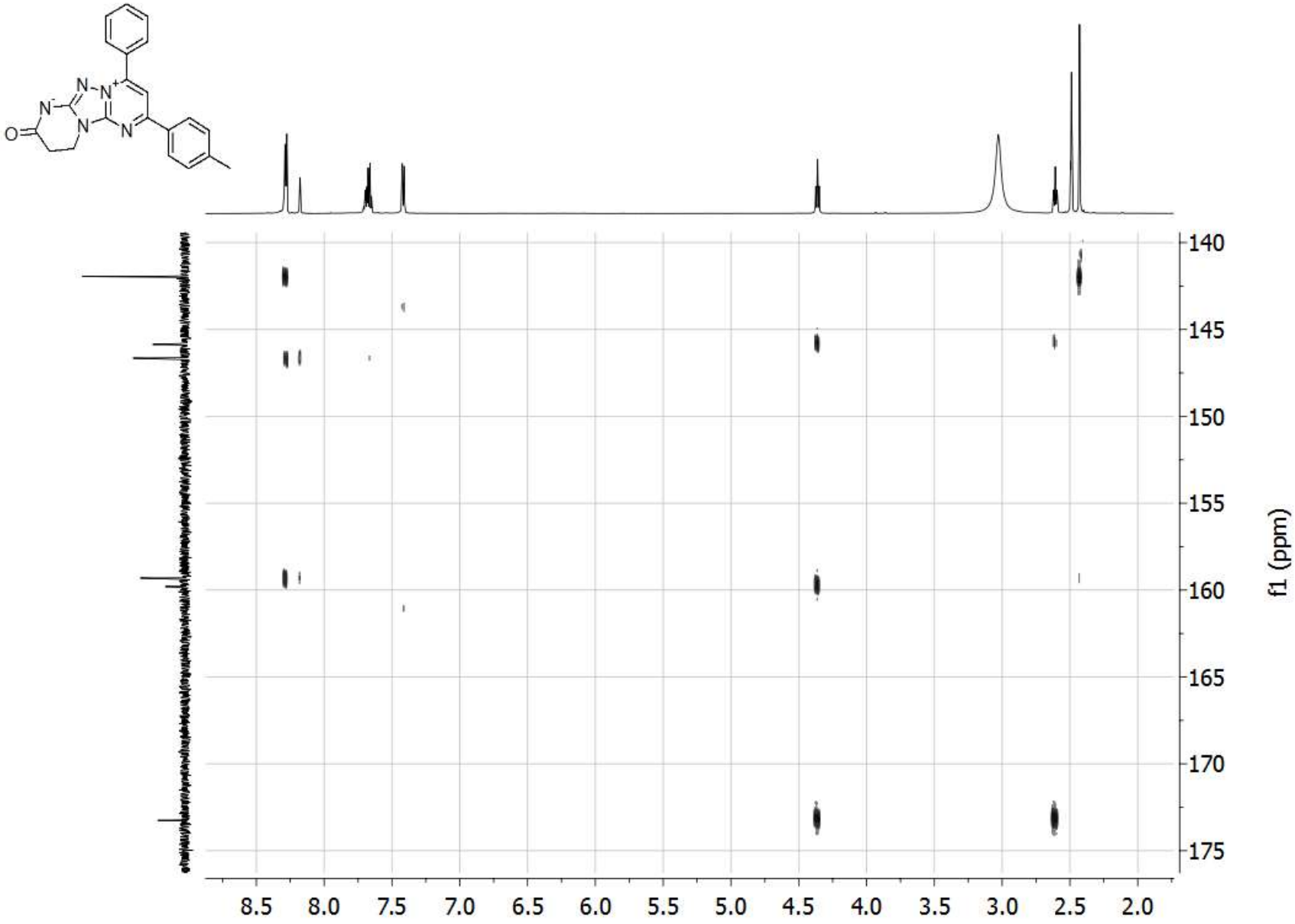
^{1}H NMR spectrum of compound **14d** (DMSO-d_6, 300 MHz).



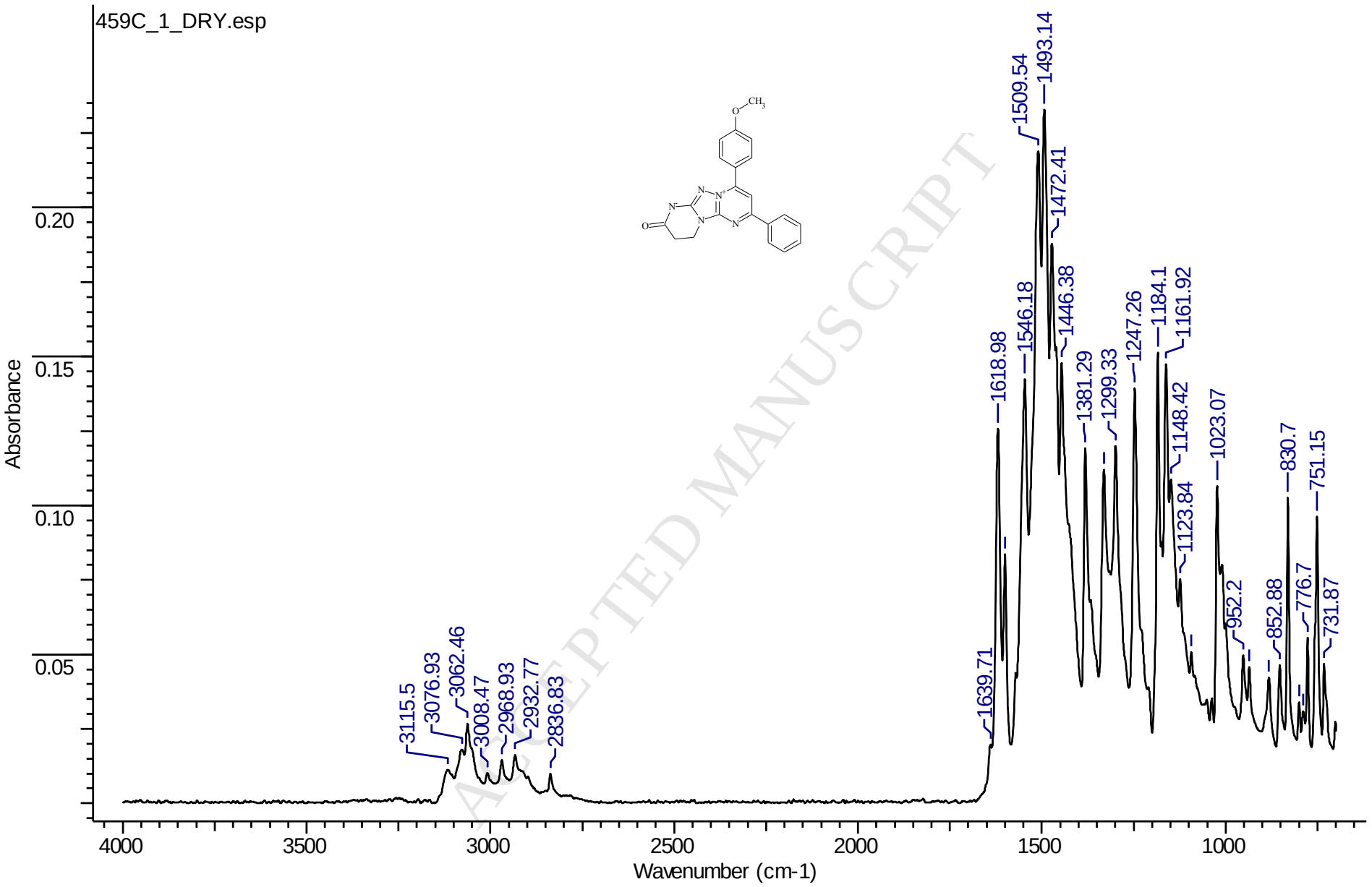
^{13}C NMR spectrum of compound **14d** (DMSO-d_6, 150 MHz).



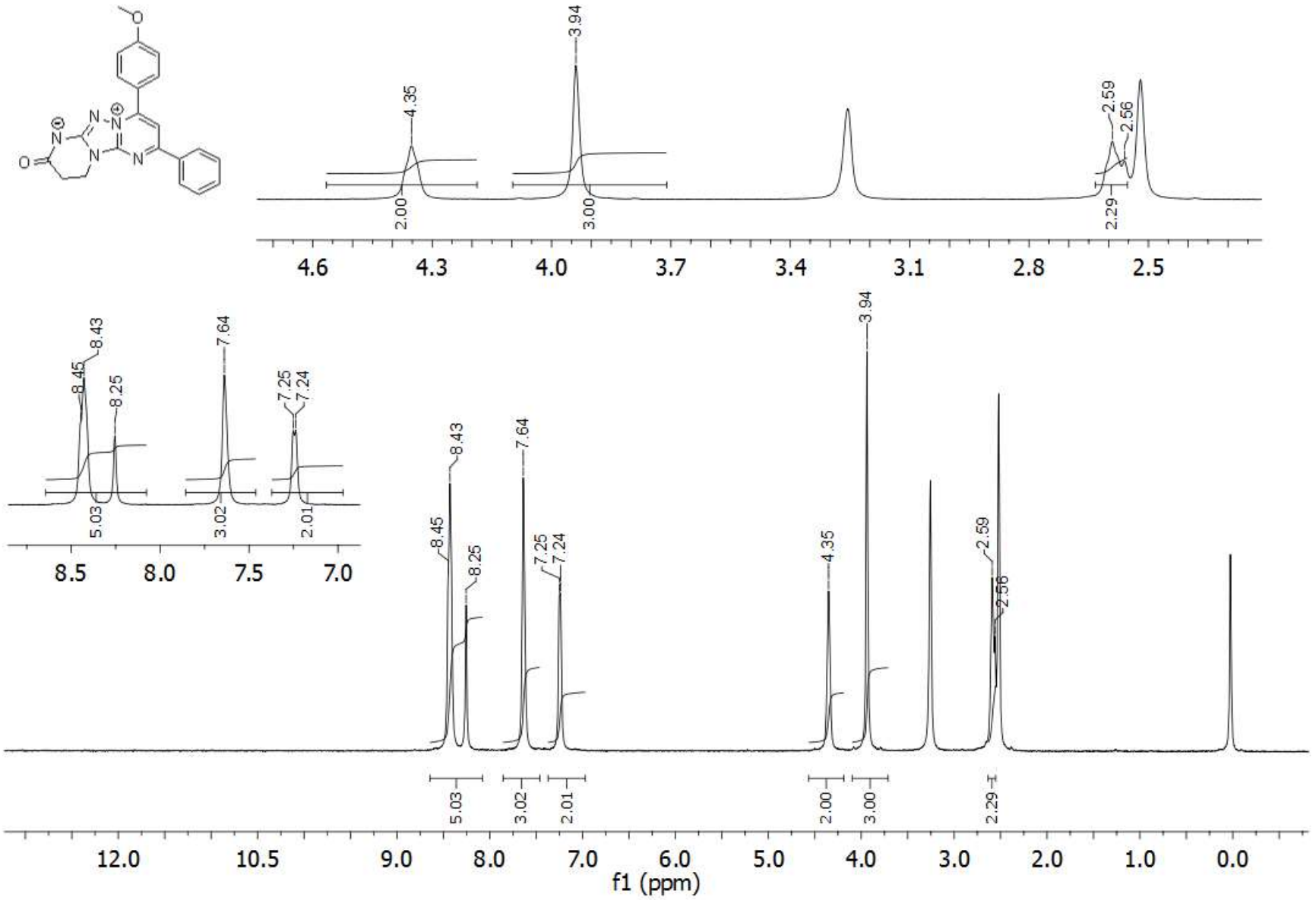
High-field fragment of ^{1}H-^{13}C HMBC spectrum of compound **14d** (DMSO-d_6).



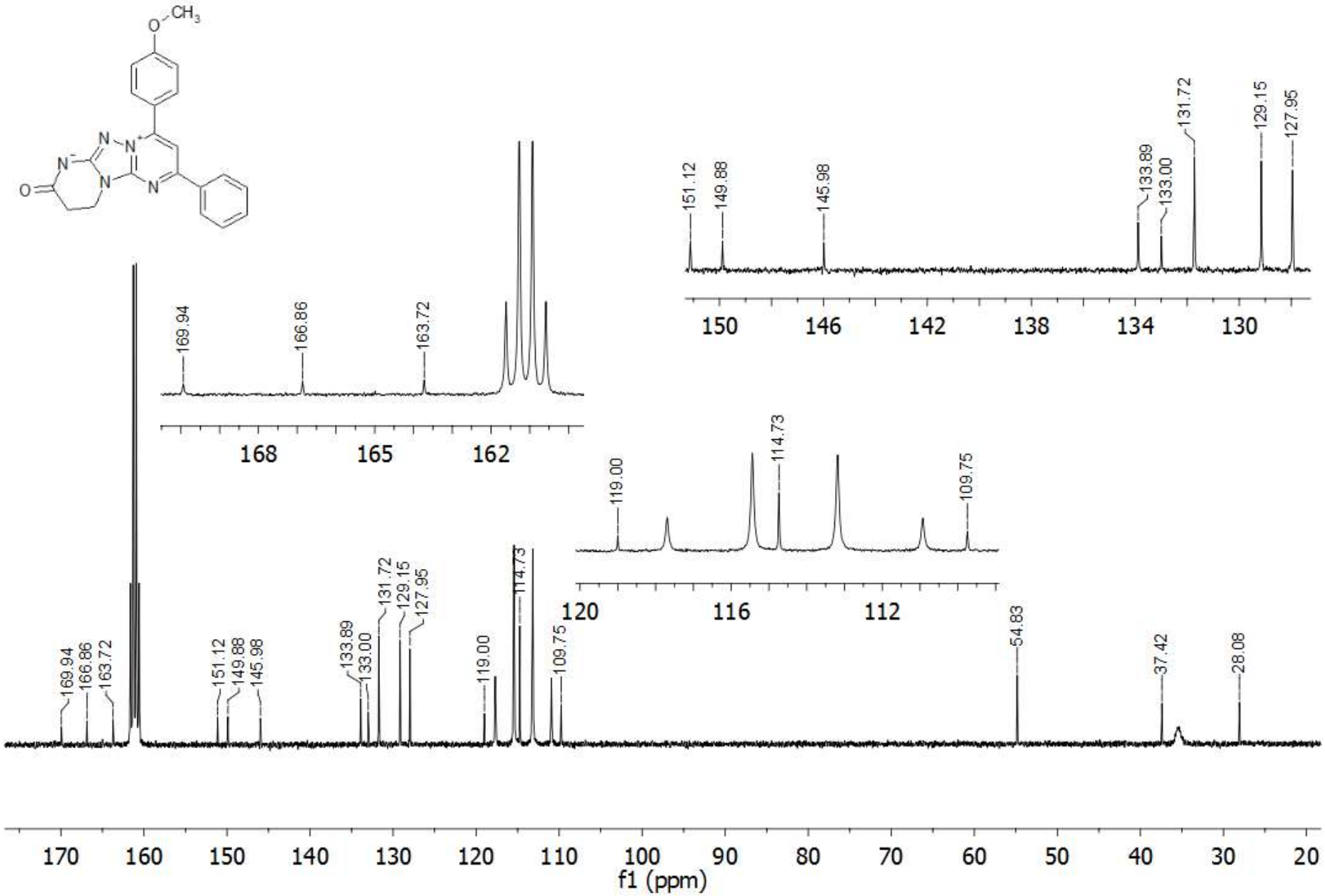
Low-field fragment of ^{1}H-^{13}C HMBC spectrum of compound **14d** (DMSO-d_6).



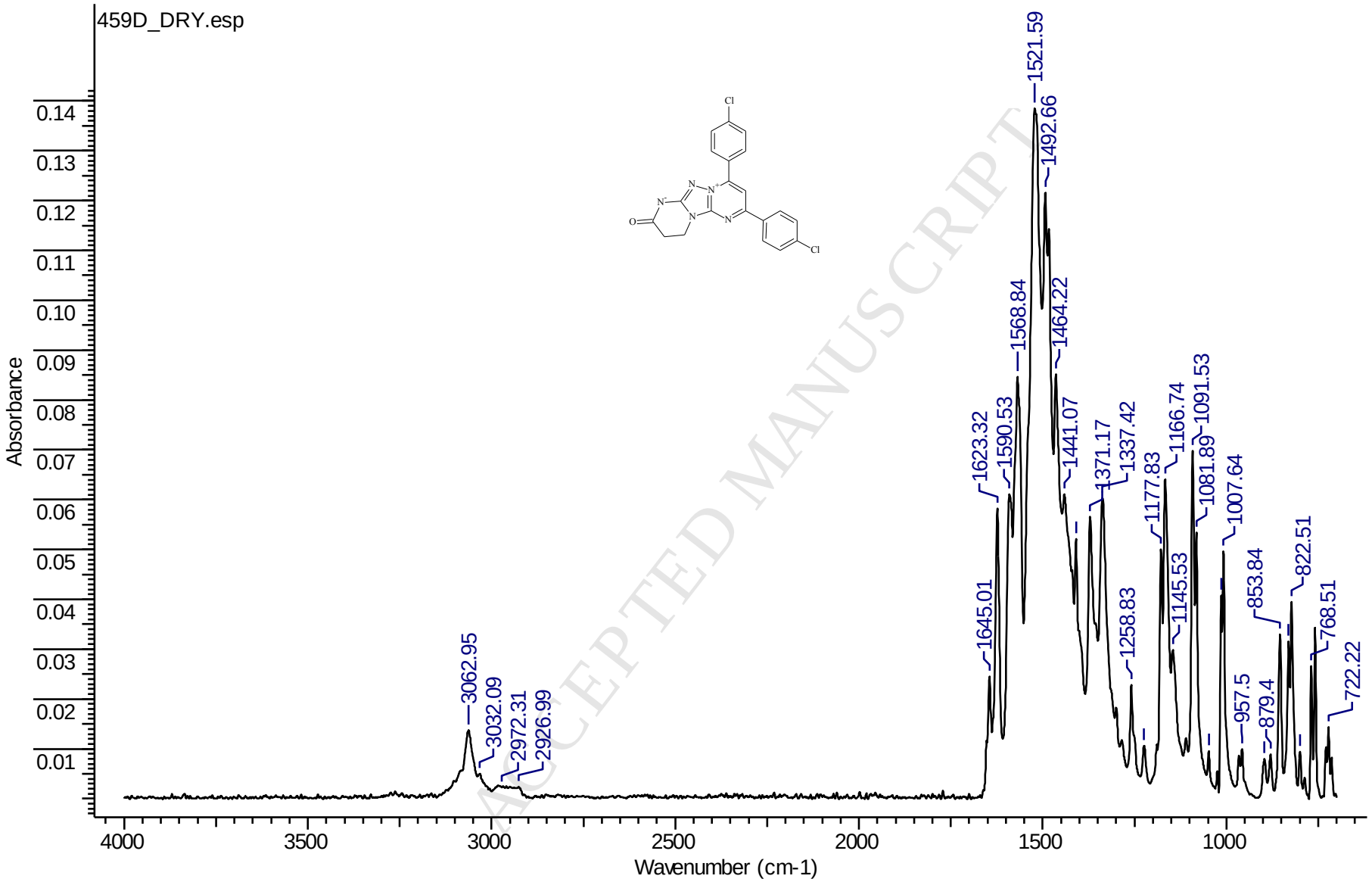
FTIR spectrum of compound **14e** (ATR).



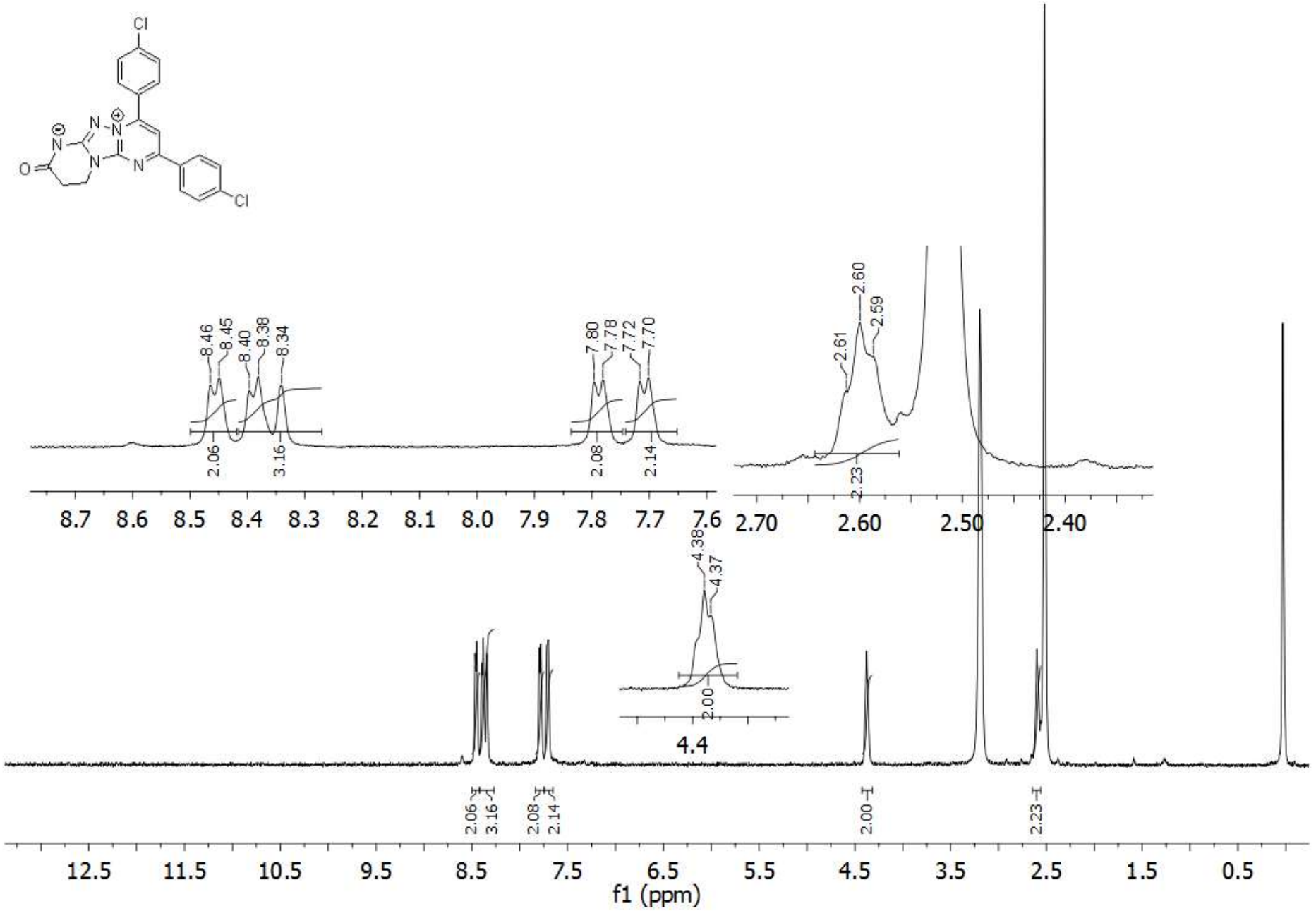
^{1}H NMR spectrum of compound **14e** (DMSO-d_6, 500 MHz).



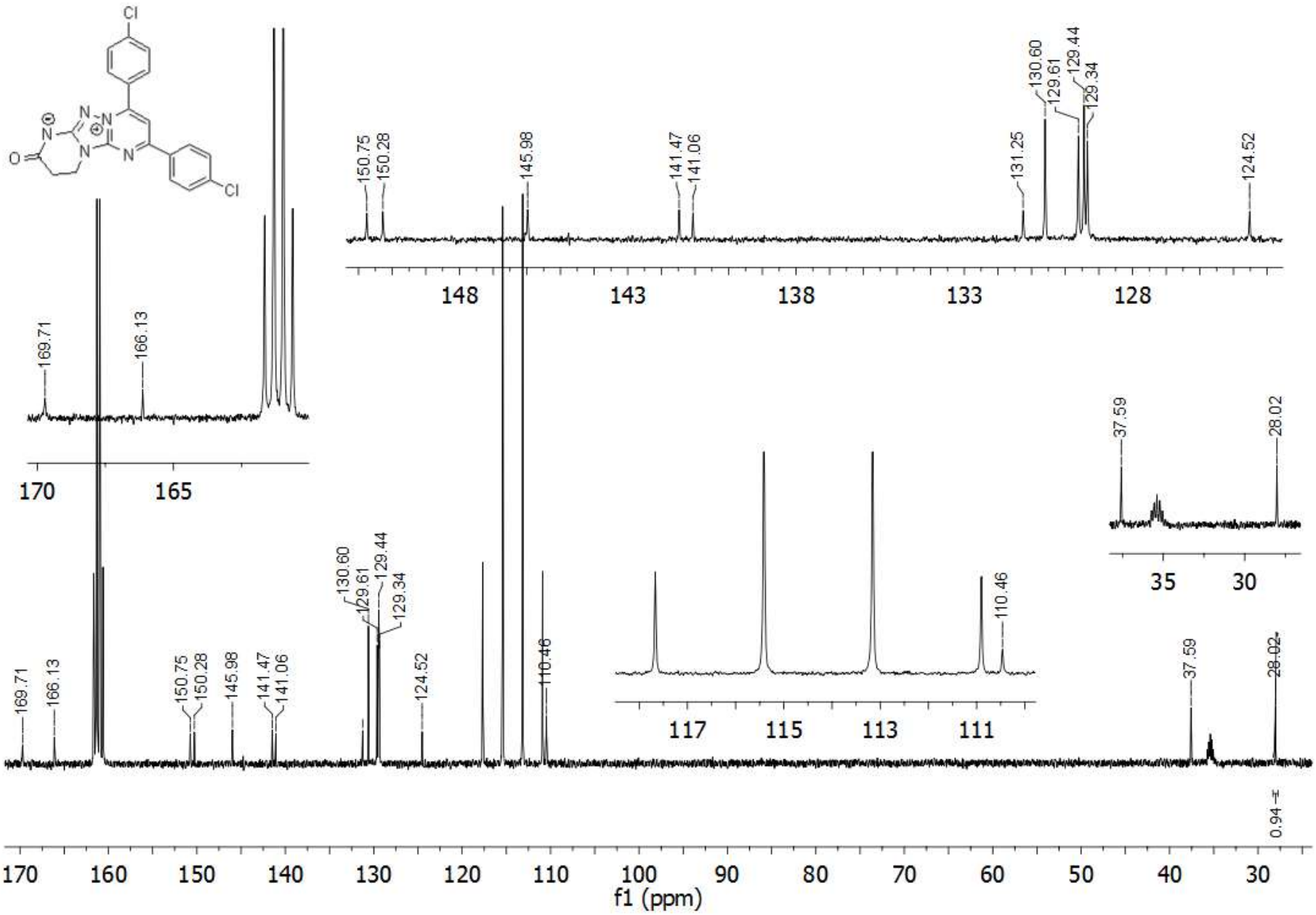
^{13}C NMR spectrum of compound **14e** (CF_3COOH, 5% DMSO-d_6, 125 MHz).



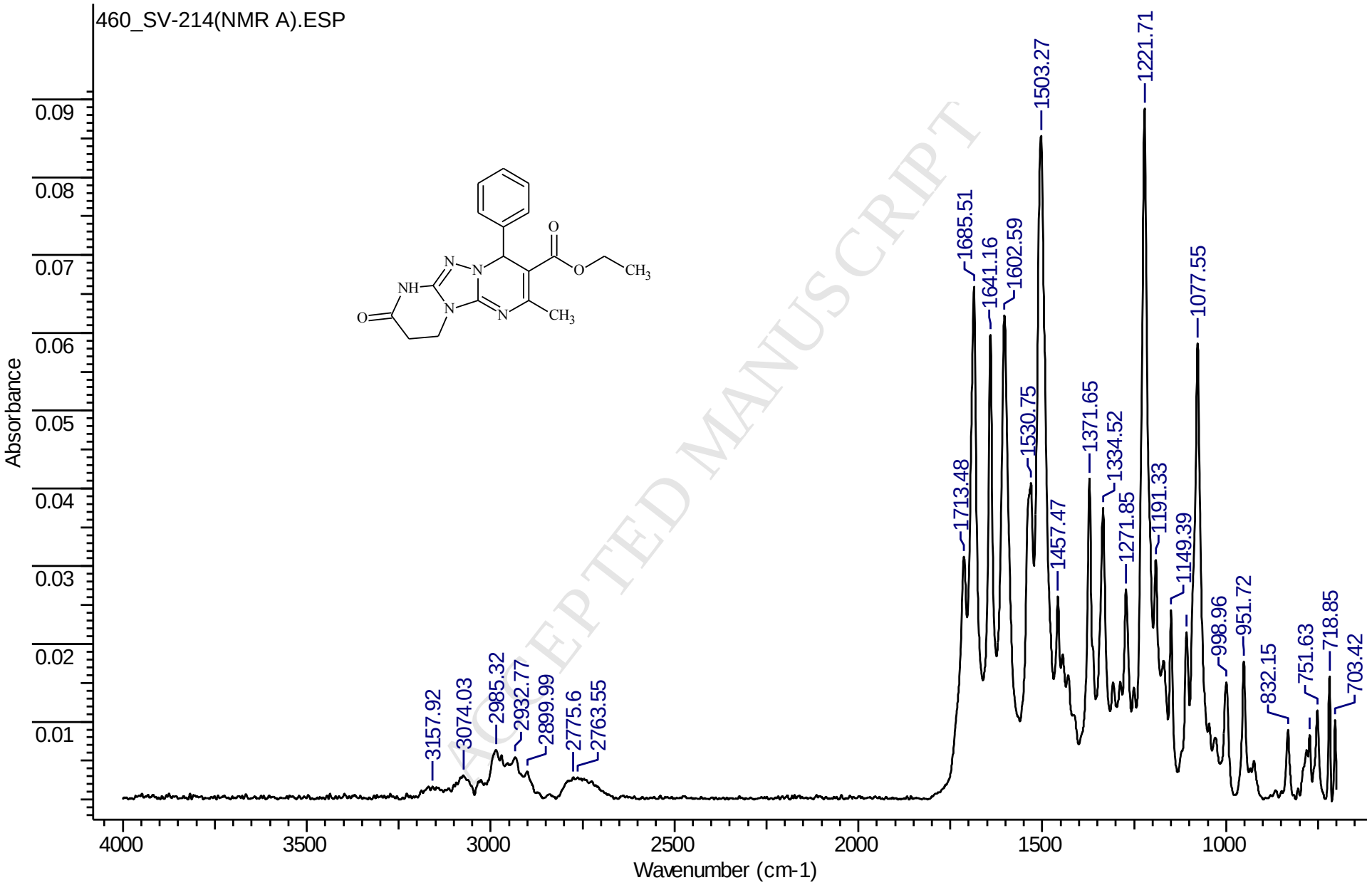
FTIR spectrum of compound **14f** (ATR).



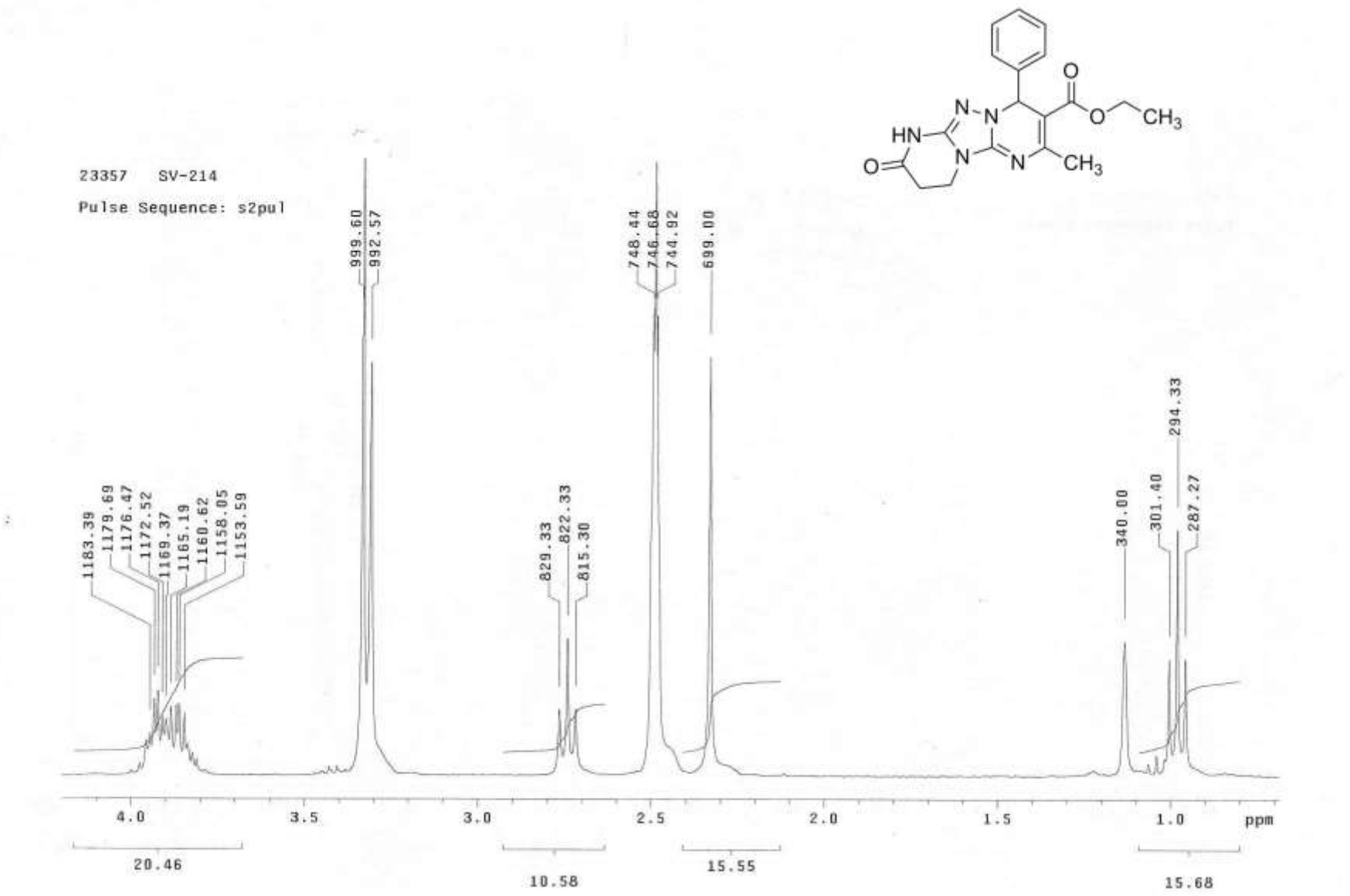
^{1}H NMR spectrum of compound **14f** (DMSO-d_6, 500 MHz).



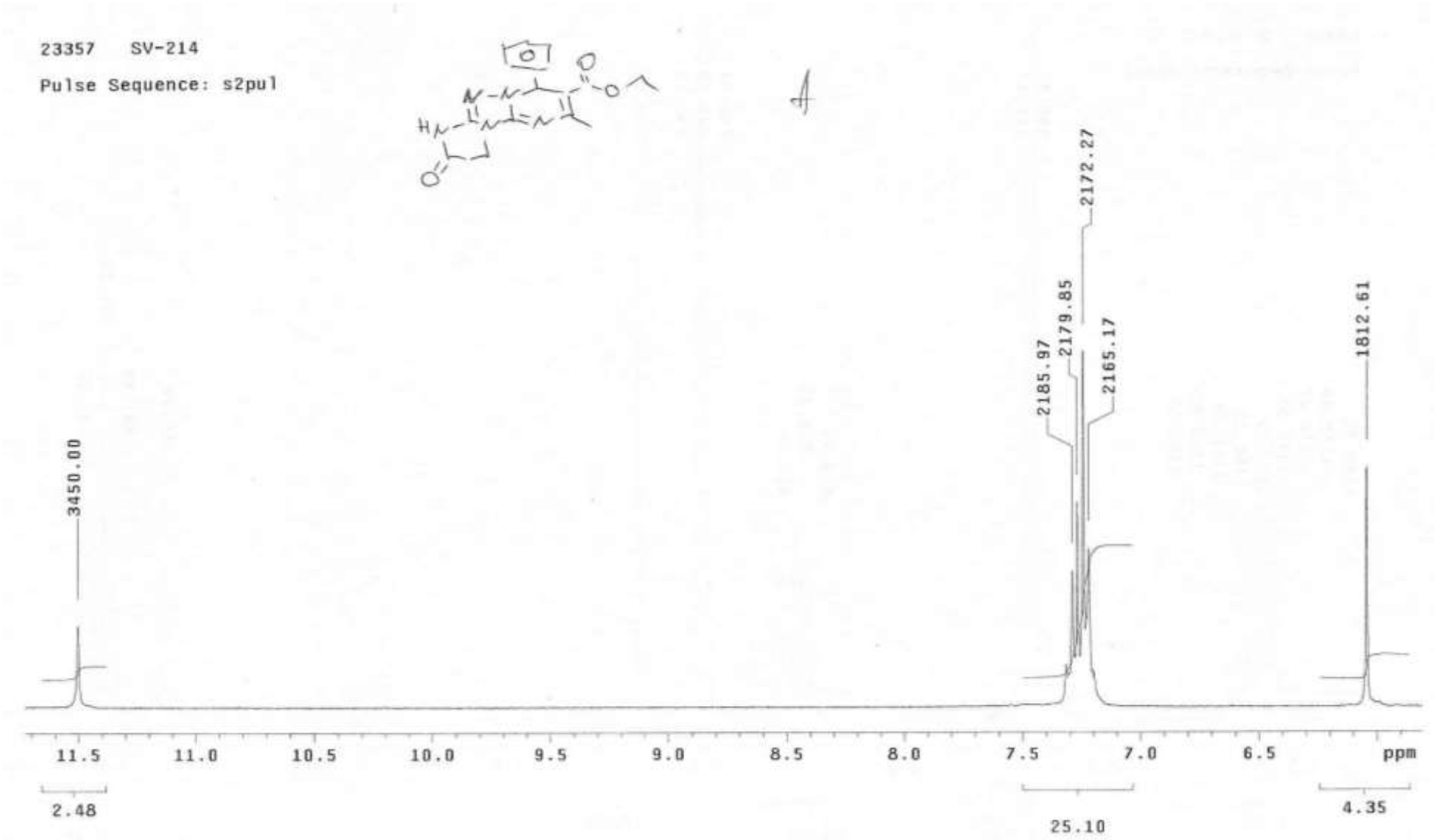
^{13}C NMR spectrum of compound **14f** (CF_3COOH, 5% DMSO-d_6, 125 MHz).



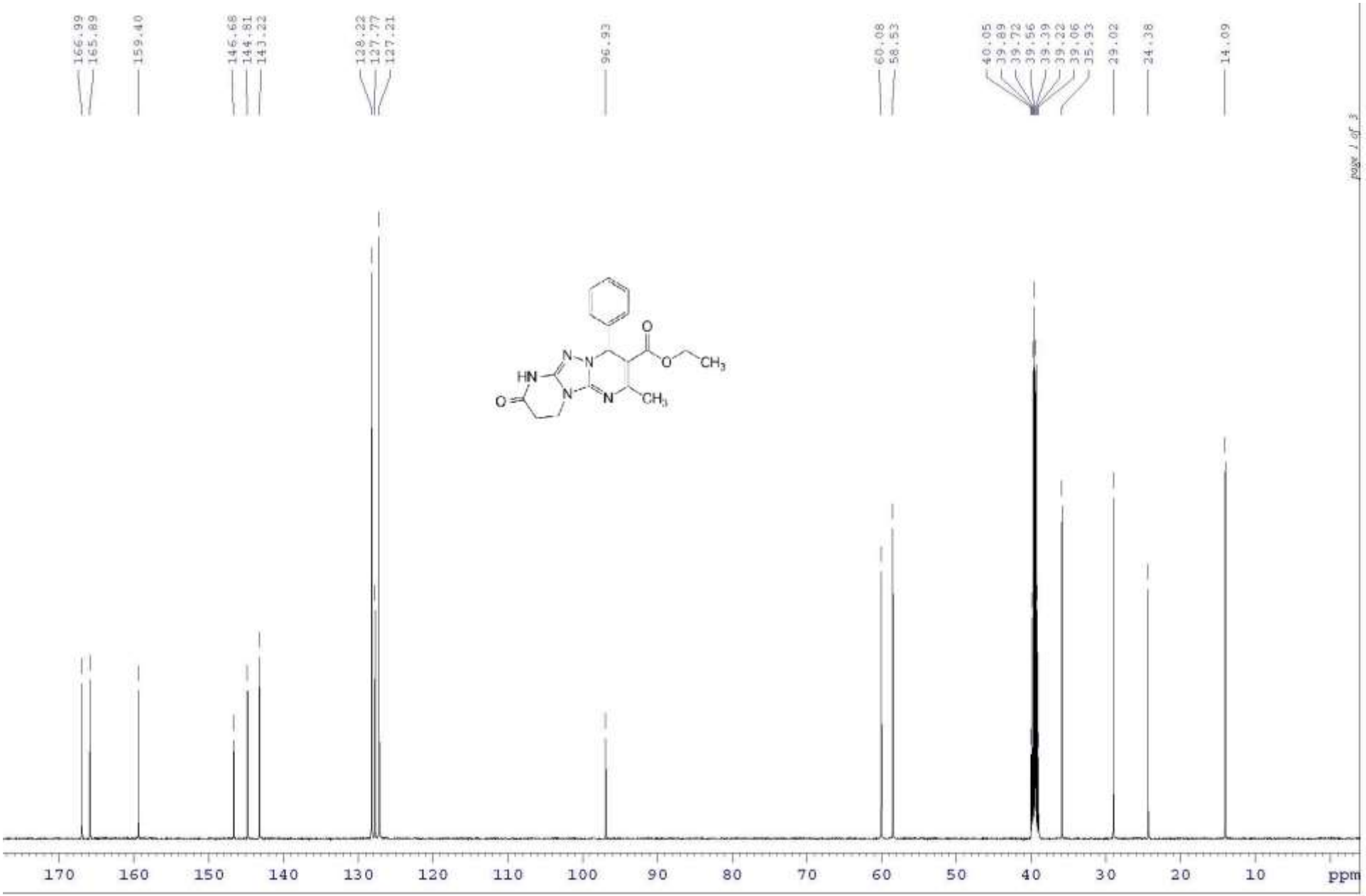
FTIR spectrum of compound **15a** (ATR).



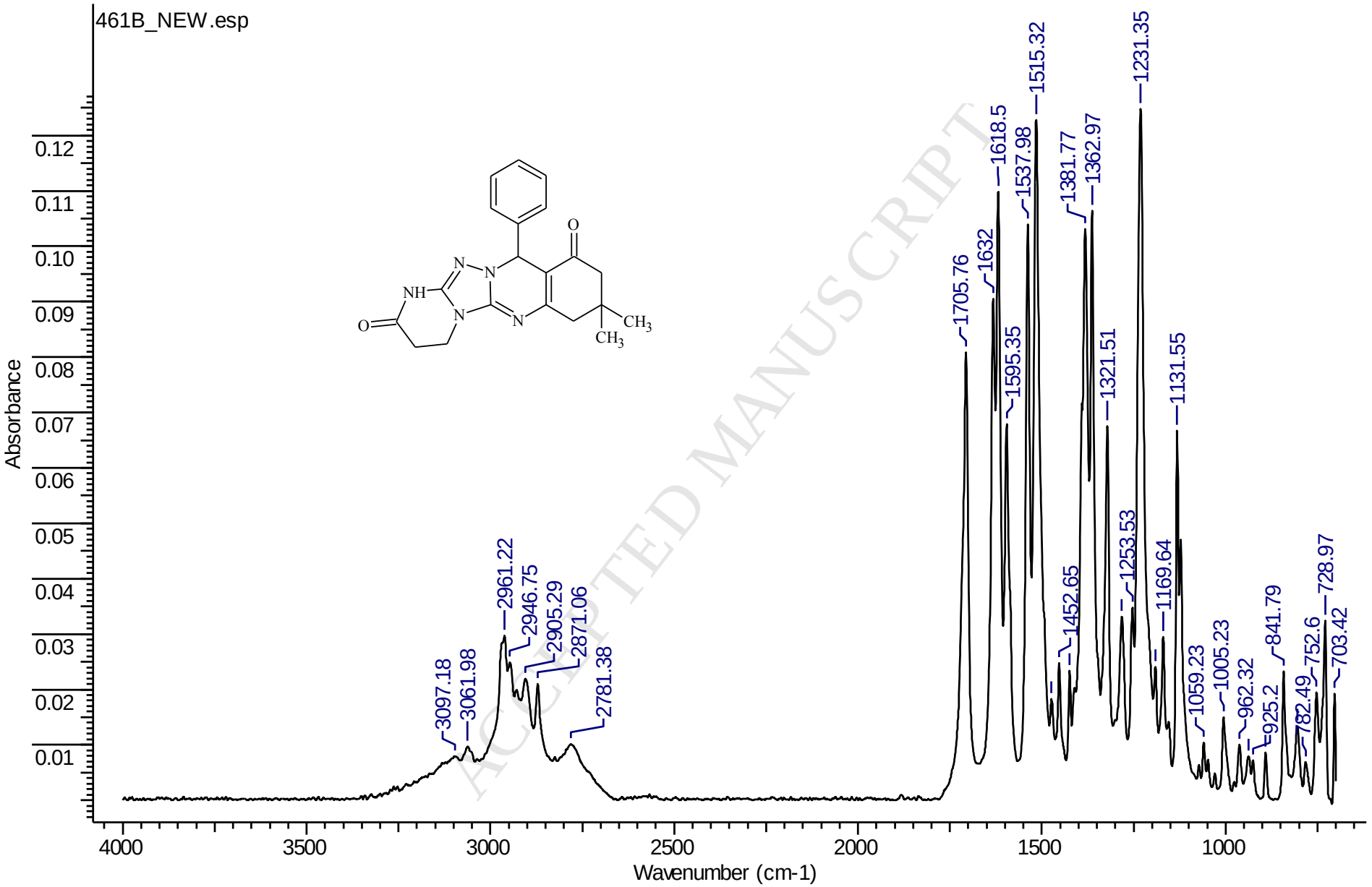
High-field part of ^{1}H NMR spectrum of compound **15a** (300 MHz, DMSO-d_6).



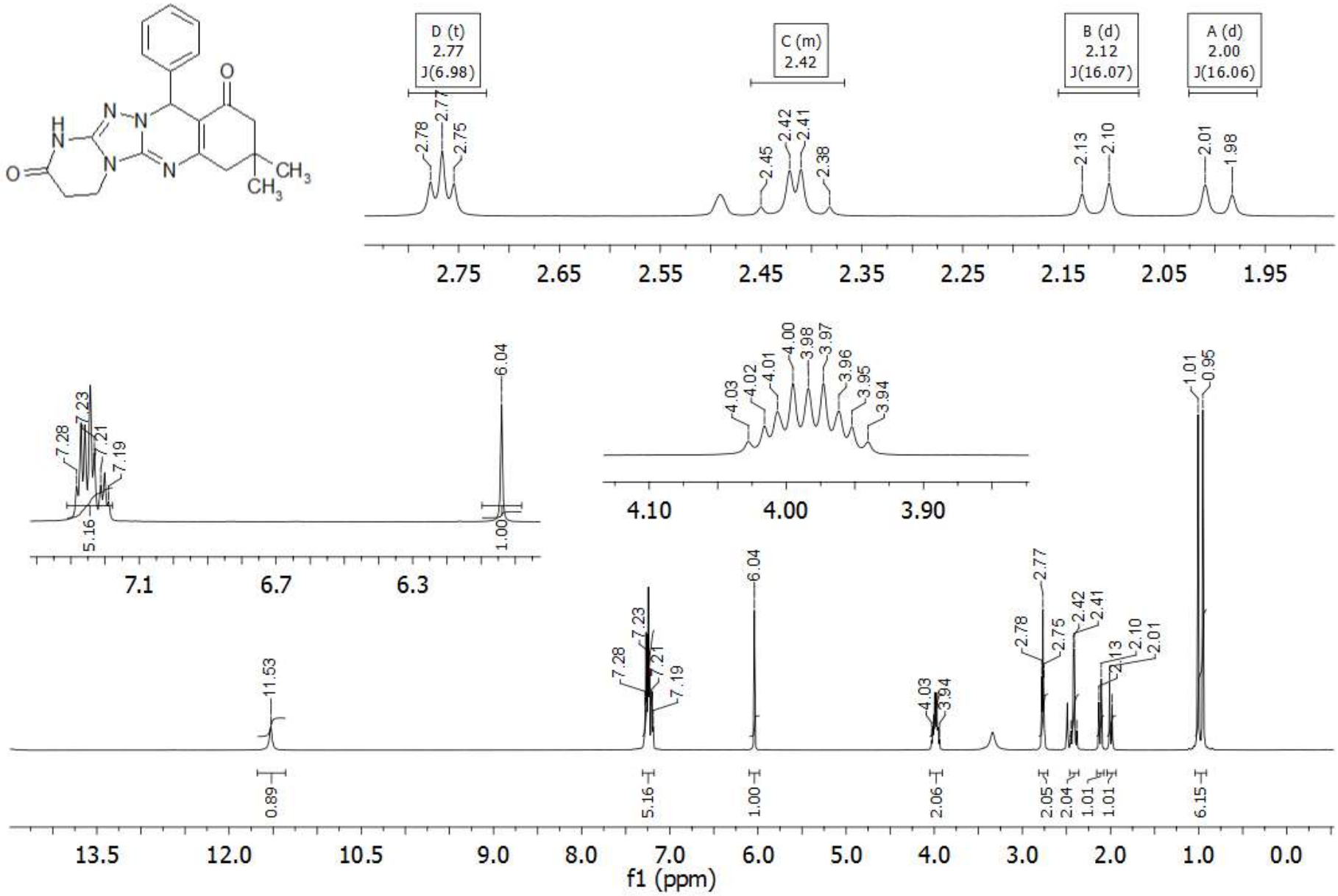
Low-field part of ^{1}H NMR spectrum of compound **15a** (300 MHz, DMSO-d_6).



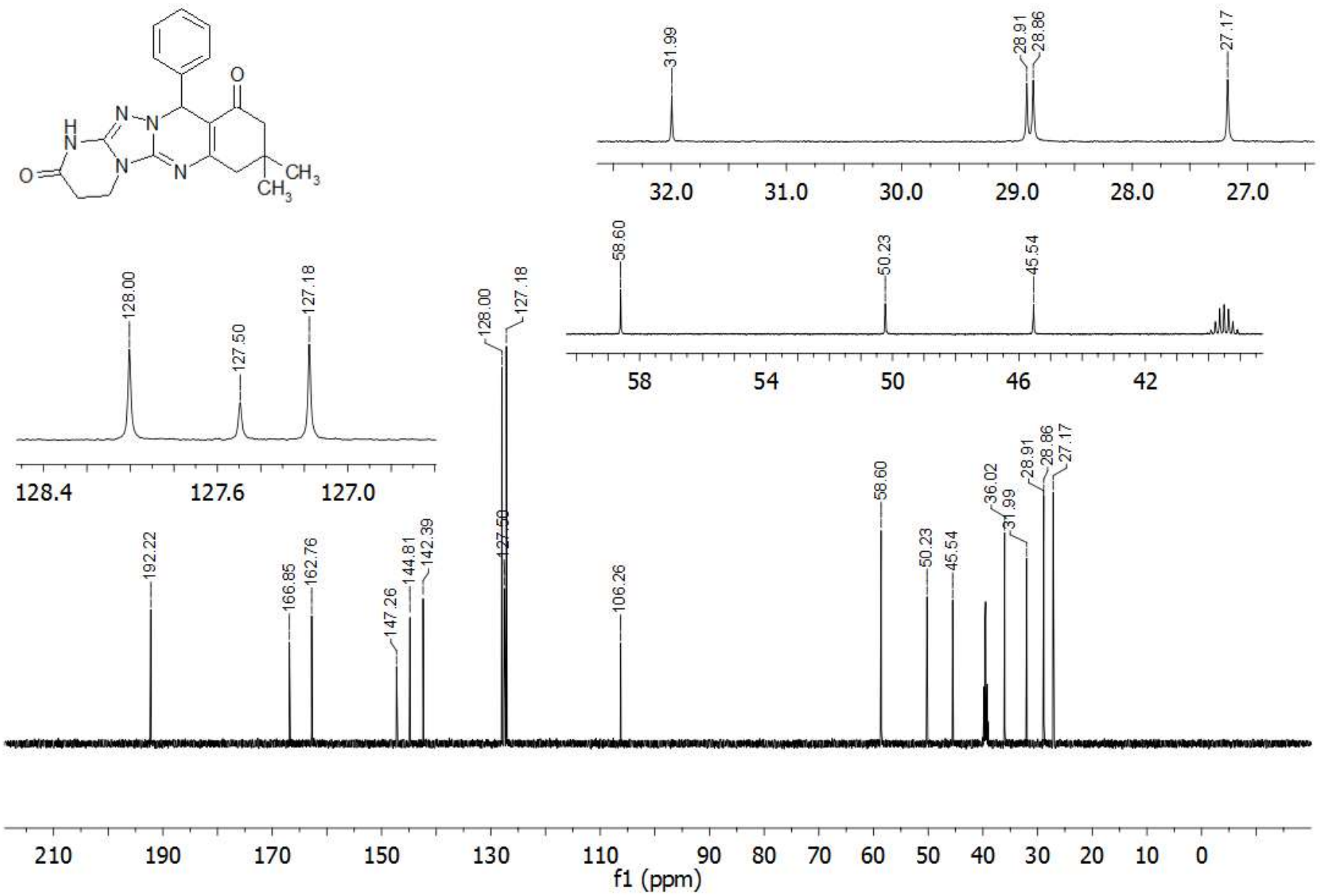
^{13}C NMR spectrum of compound **15a** (125 MHz, DMSO-d_6).



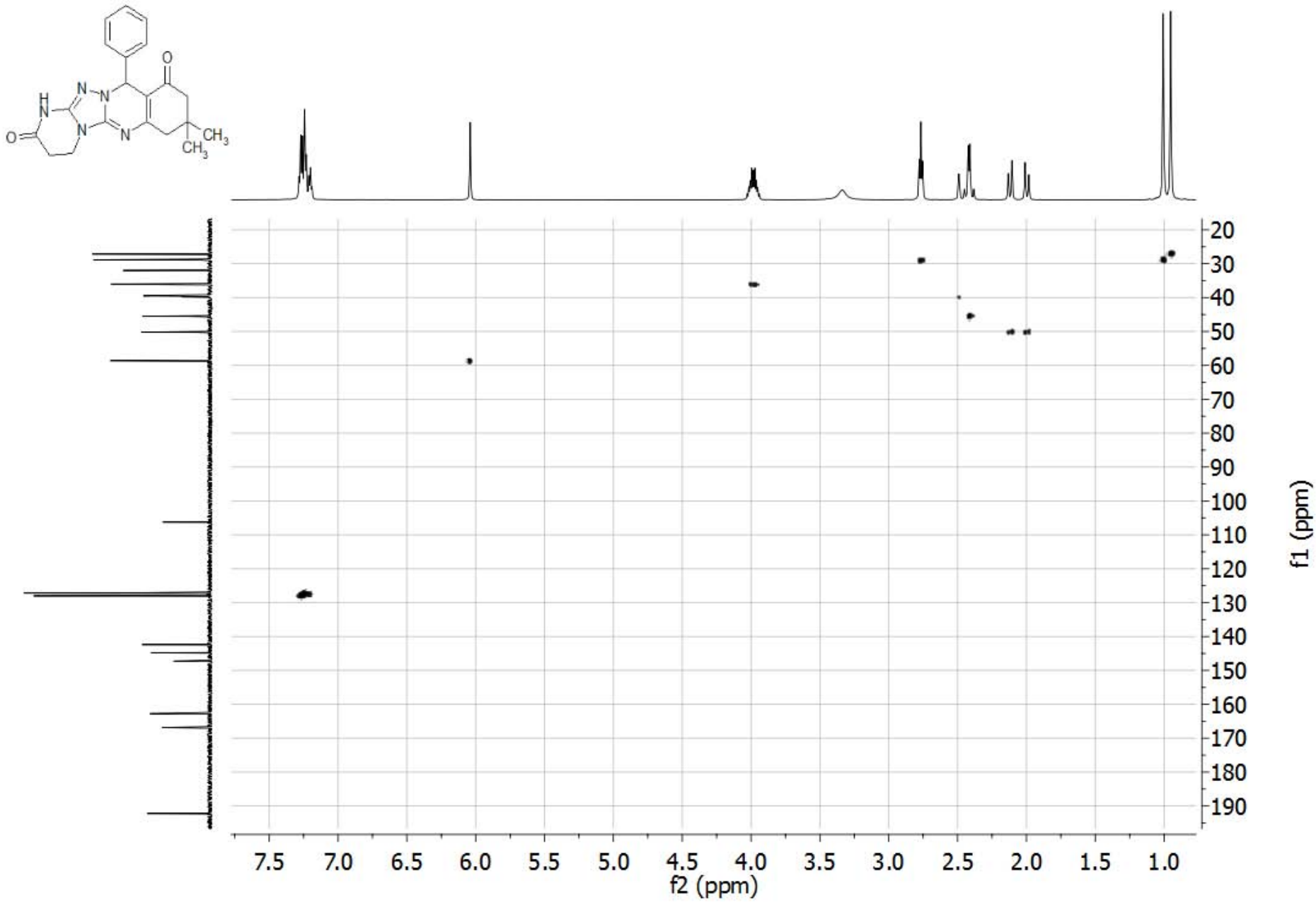
FTIR spectrum of compound **15g** (ATR).



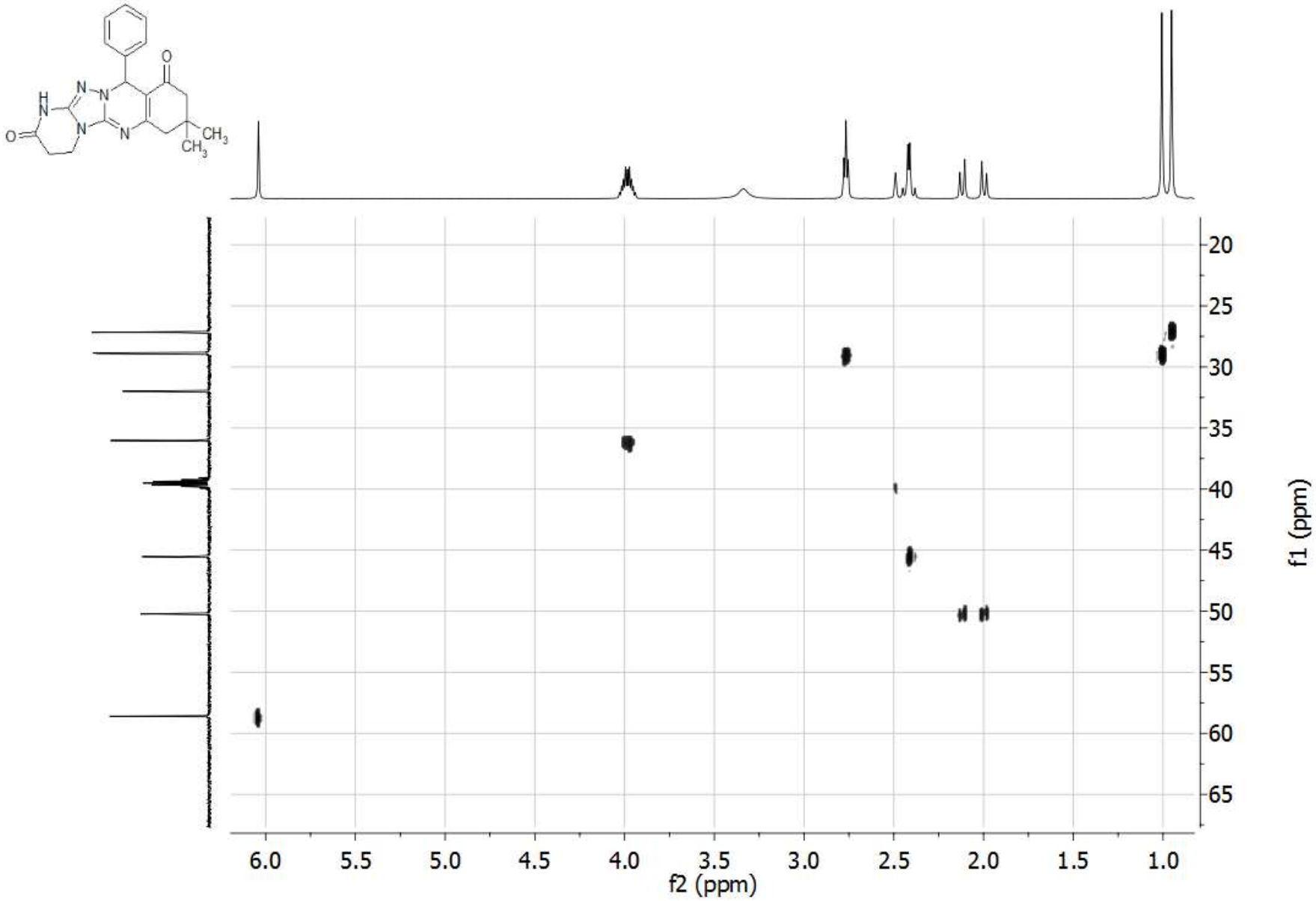
^{1}H NMR spectrum of compound **15g** (600 MHz, DMSO-d_6).



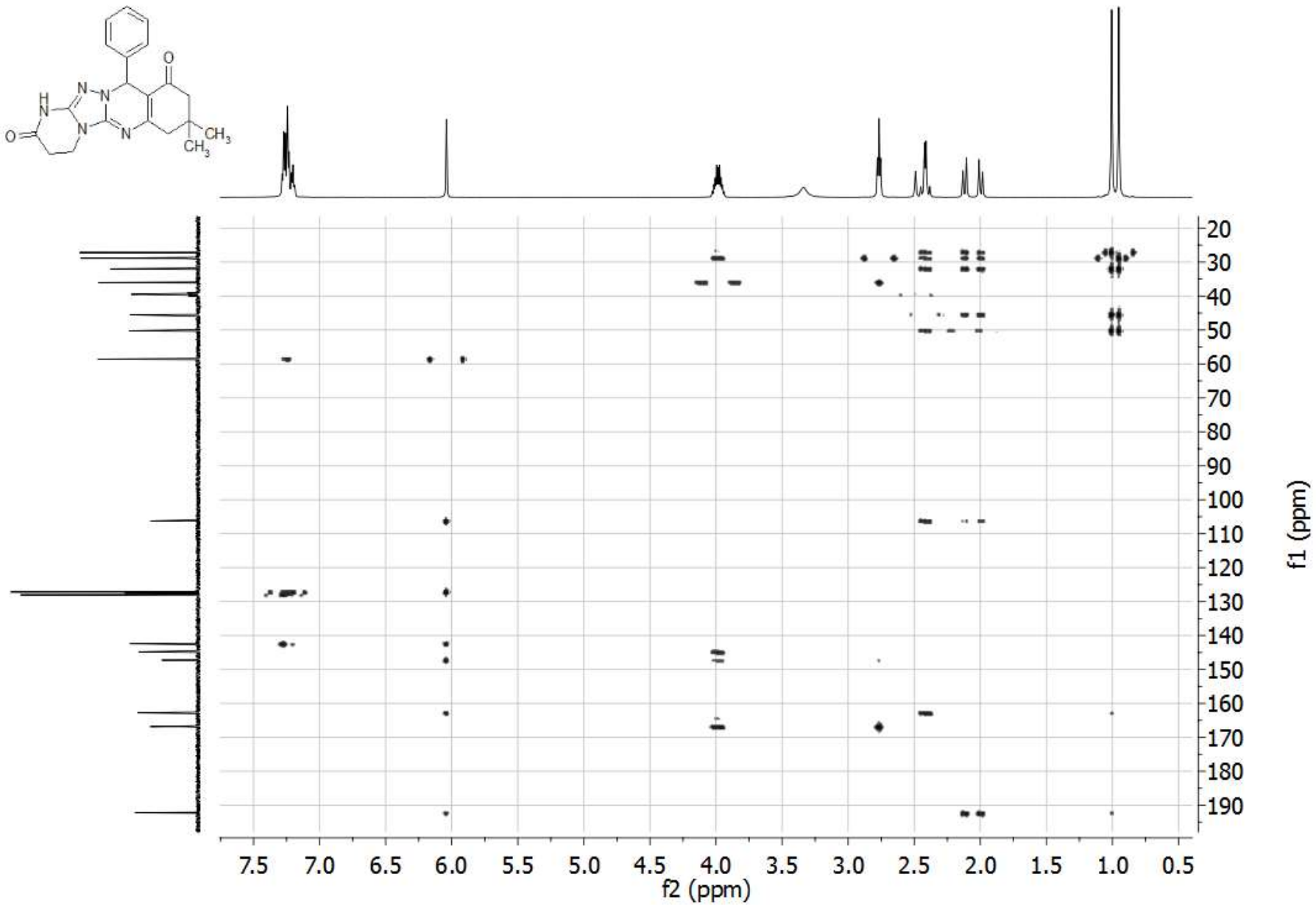
^{13}C NMR spectrum of compound **15g** (150 MHz, DMSO-d_6).



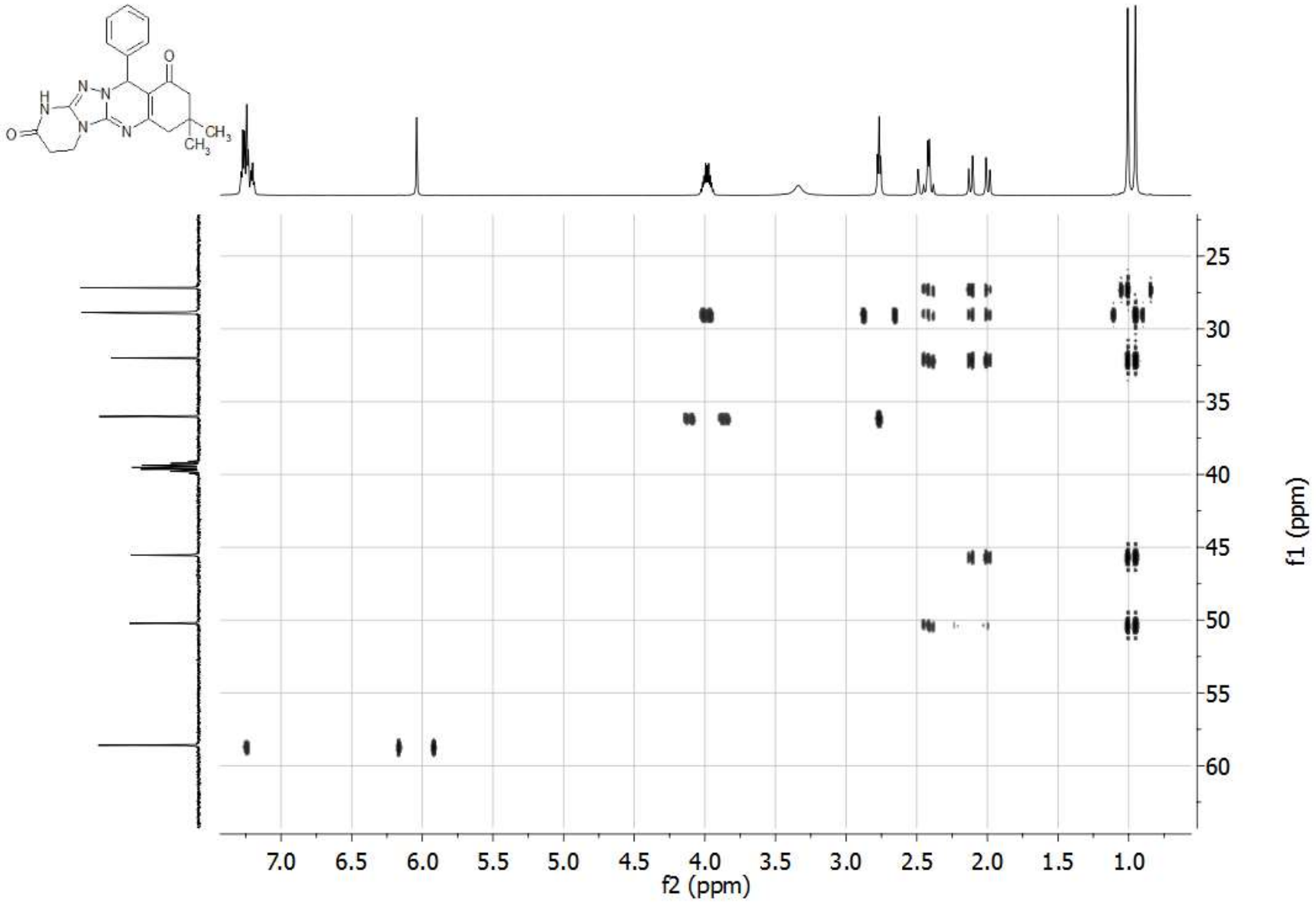
^{1}H-^{13}C HSQC spectrum of compound **15g** (DMSO-d_6).



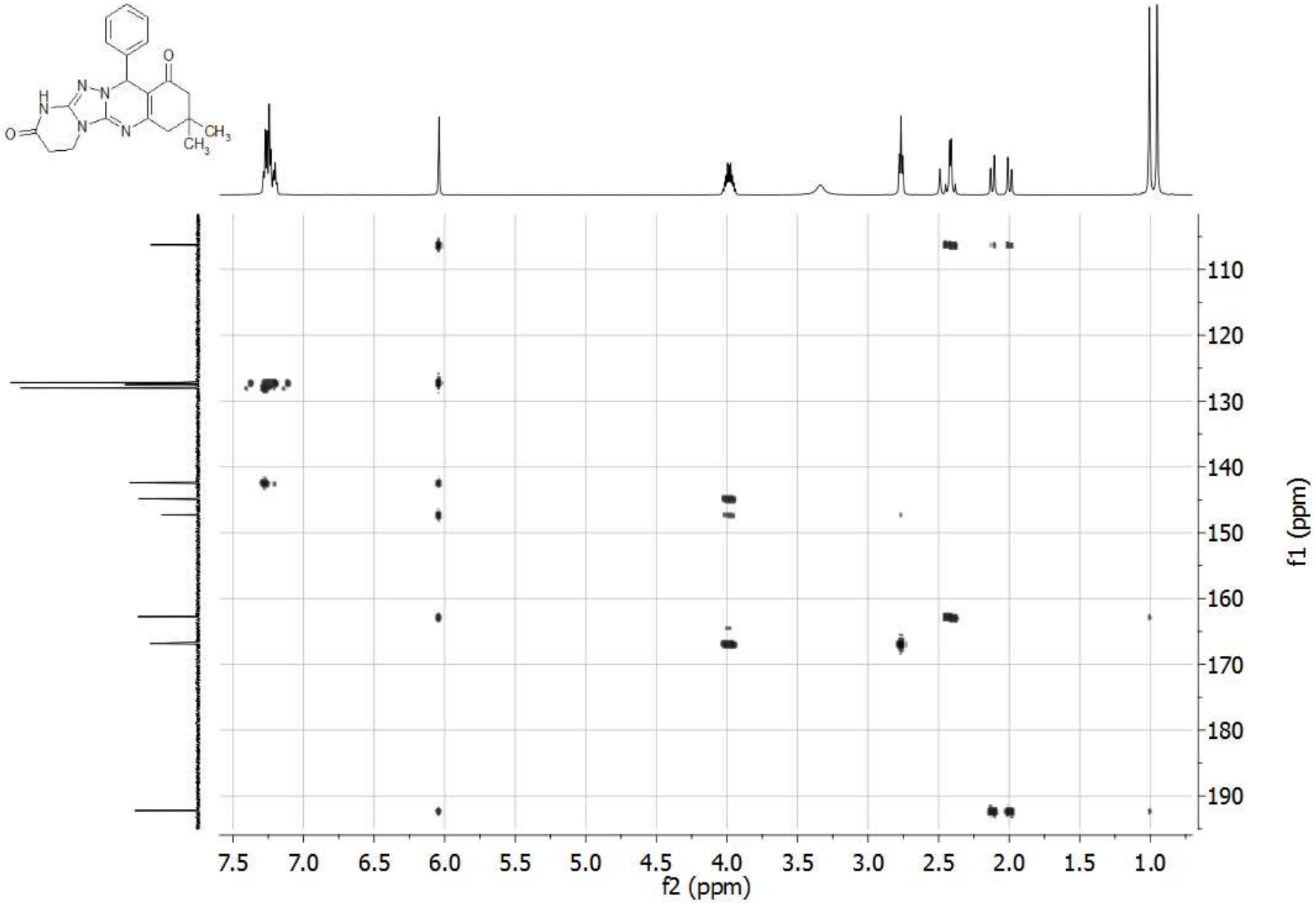
Enlarged fragment of ^{1}H-^{13}C HSQC spectrum of compound **15g**.



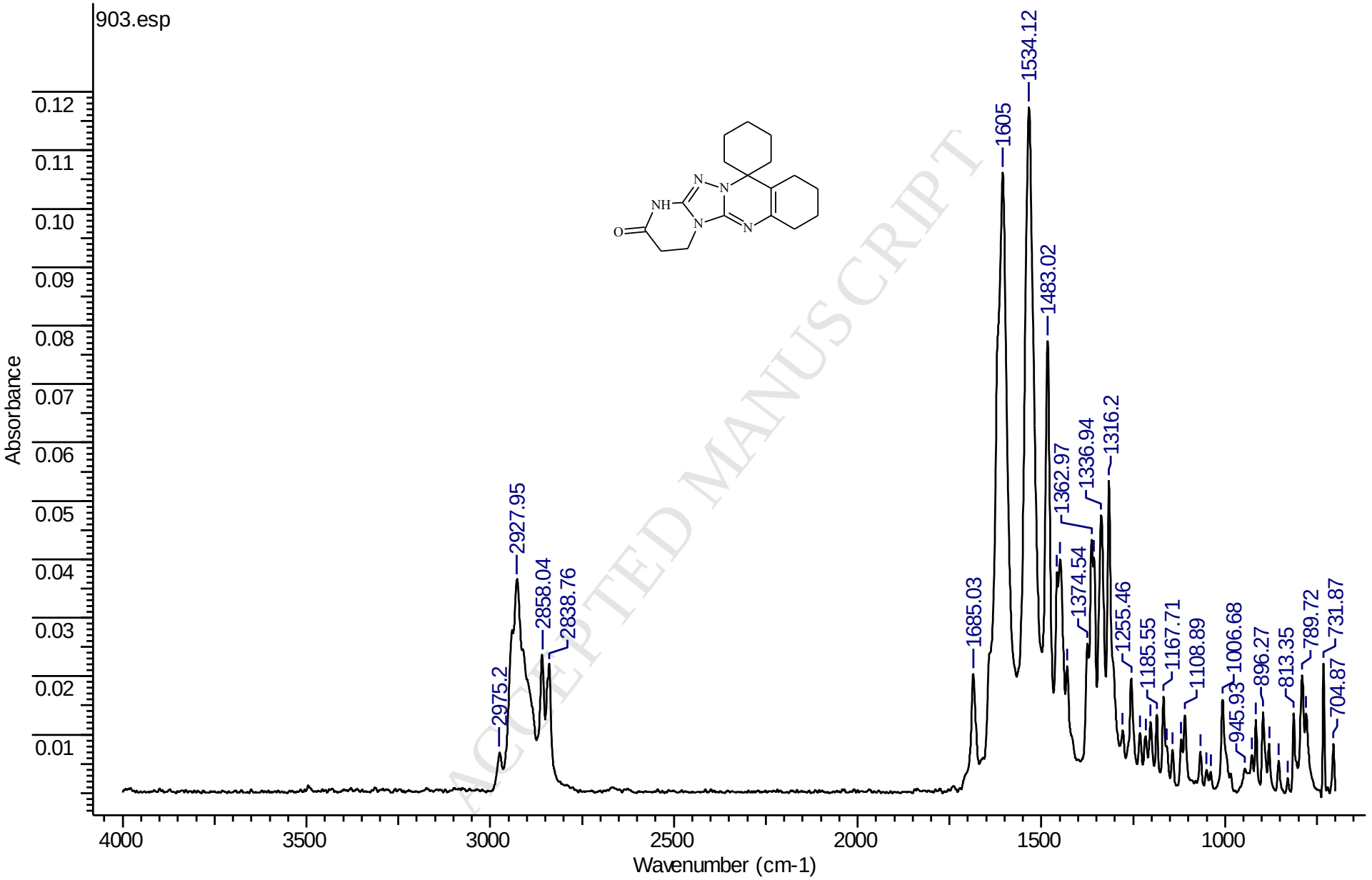
^{1}H-^{13}C HMBC spectrum of compound **15g** (DMSO-d_6).



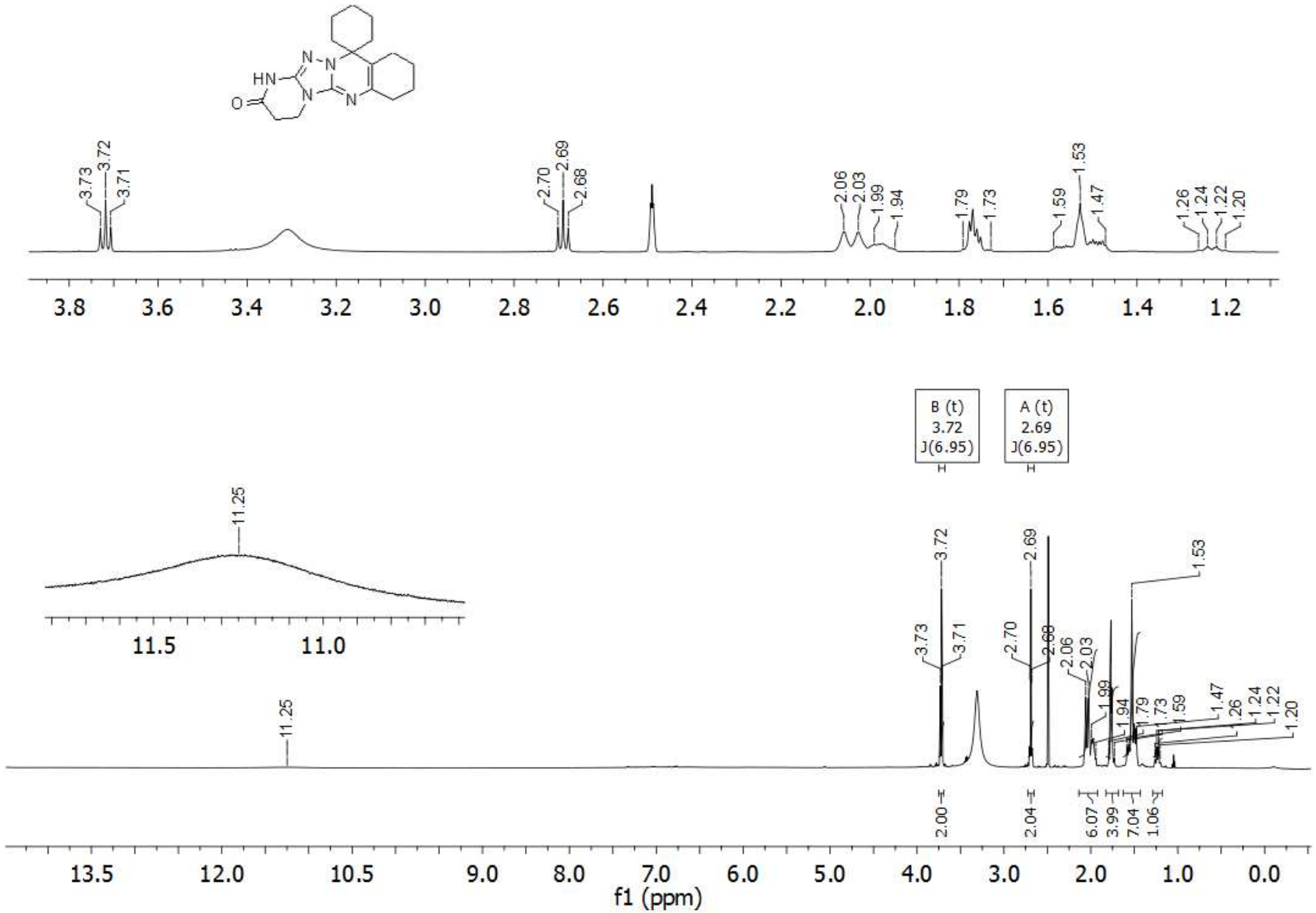
High-field fragment of ^{1}H-^{13}C HMBC spectrum of compound **15g**.



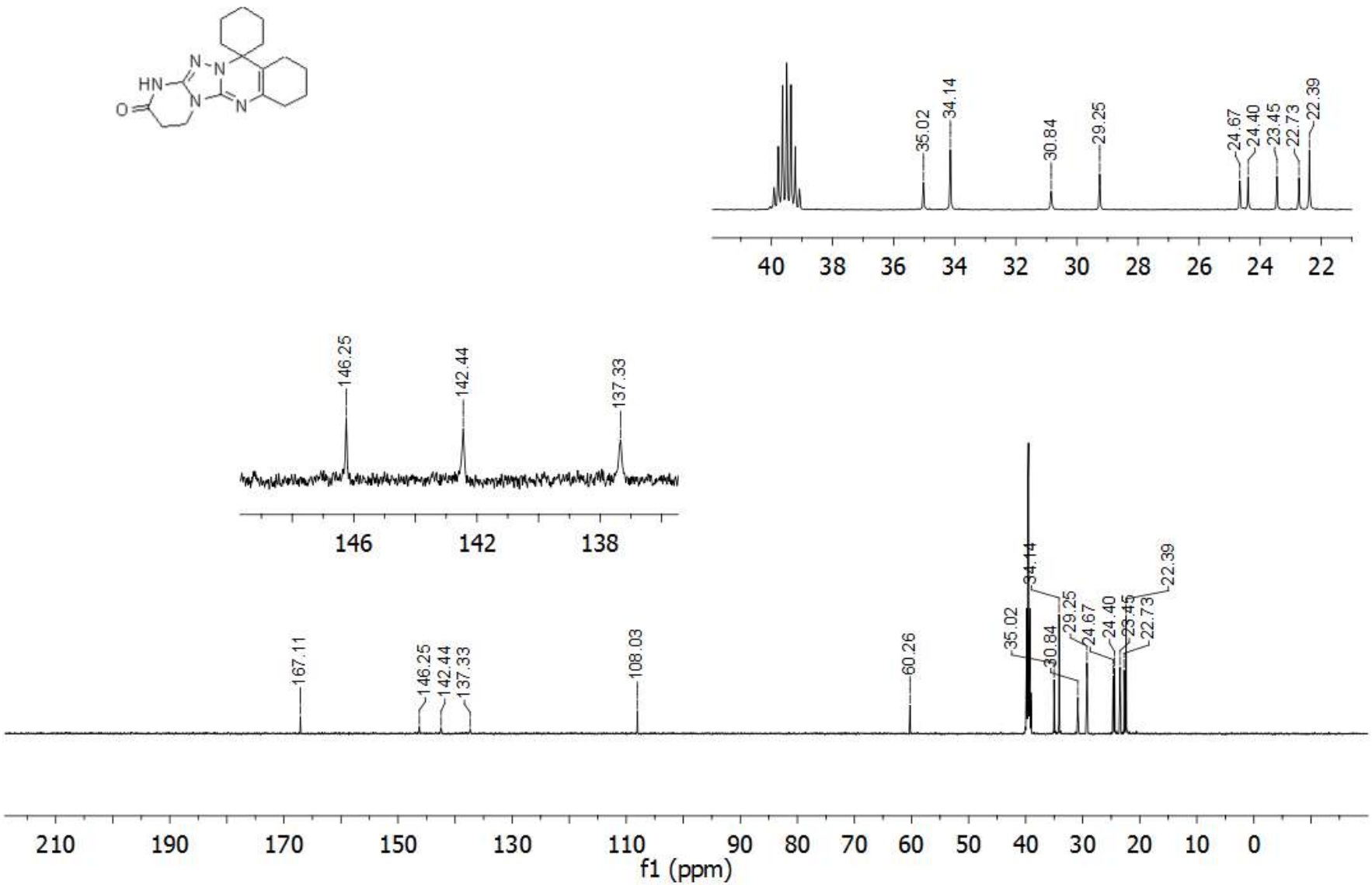
Low-field fragment of ^{1}H-^{13}C HMBC spectrum of compound **15g**.



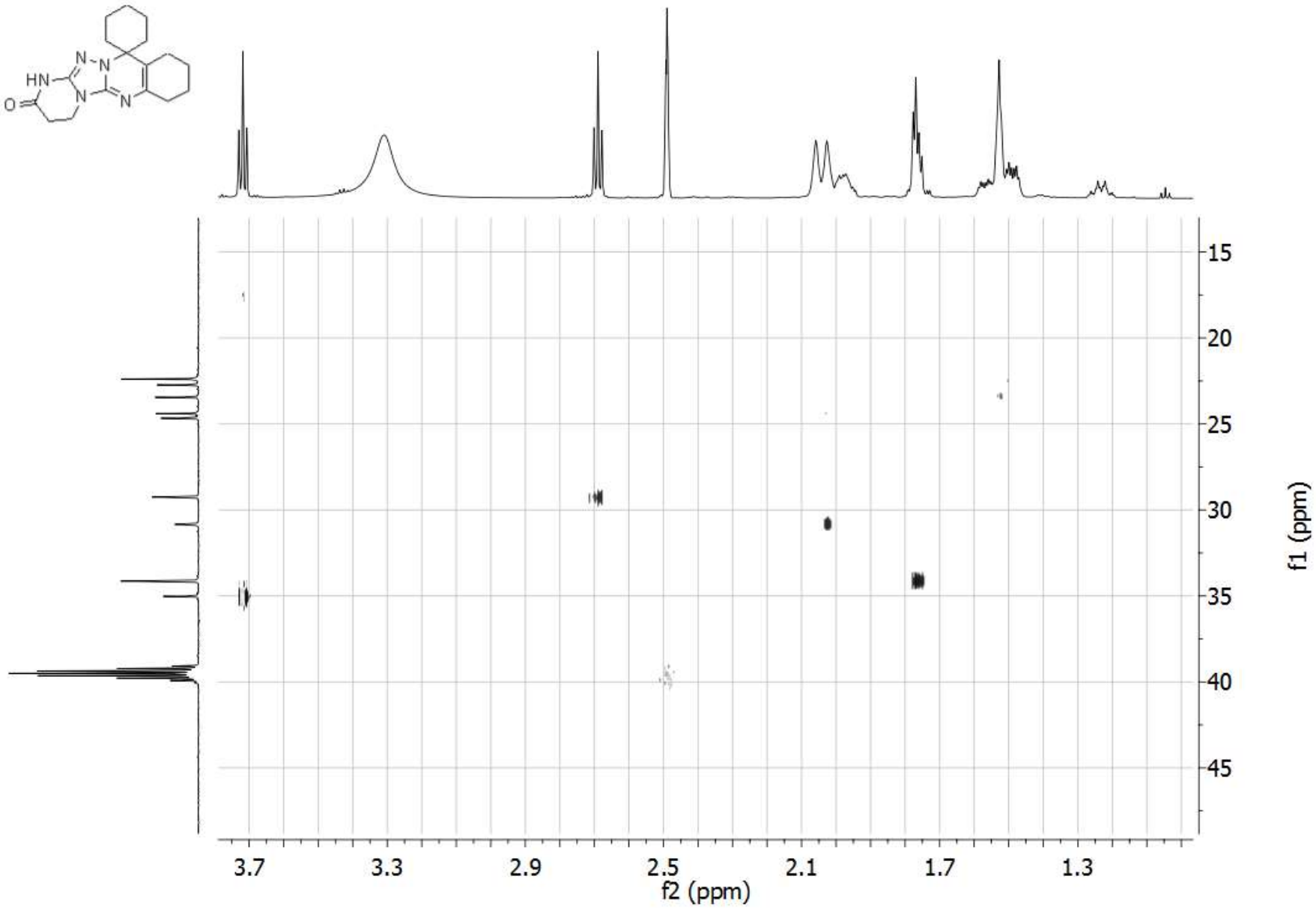
FTIR spectrum of compound **15h** (ATR).



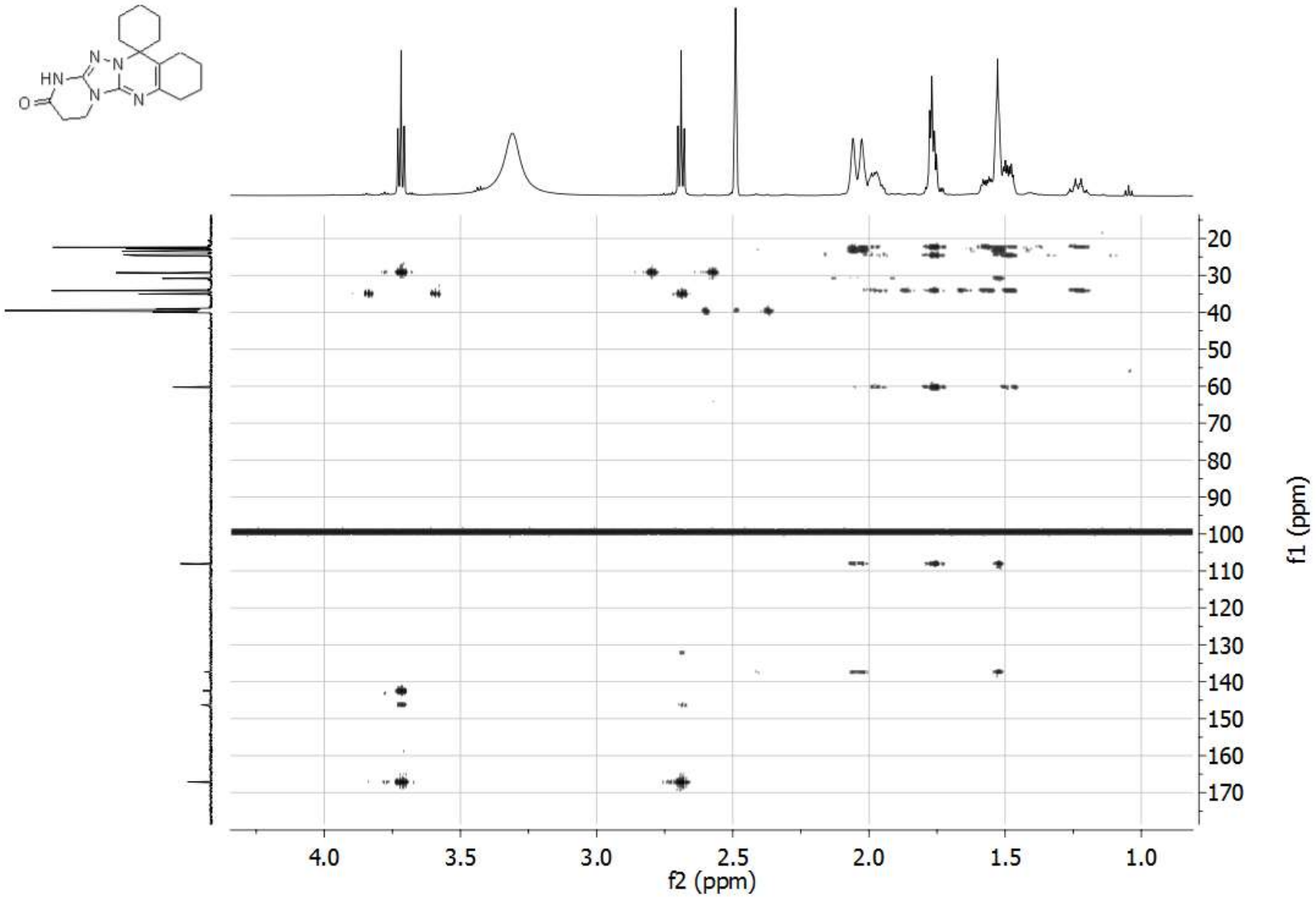
^{1}H NMR spectrum of compound **15h** (DMSO-d_6, 600 MHz).



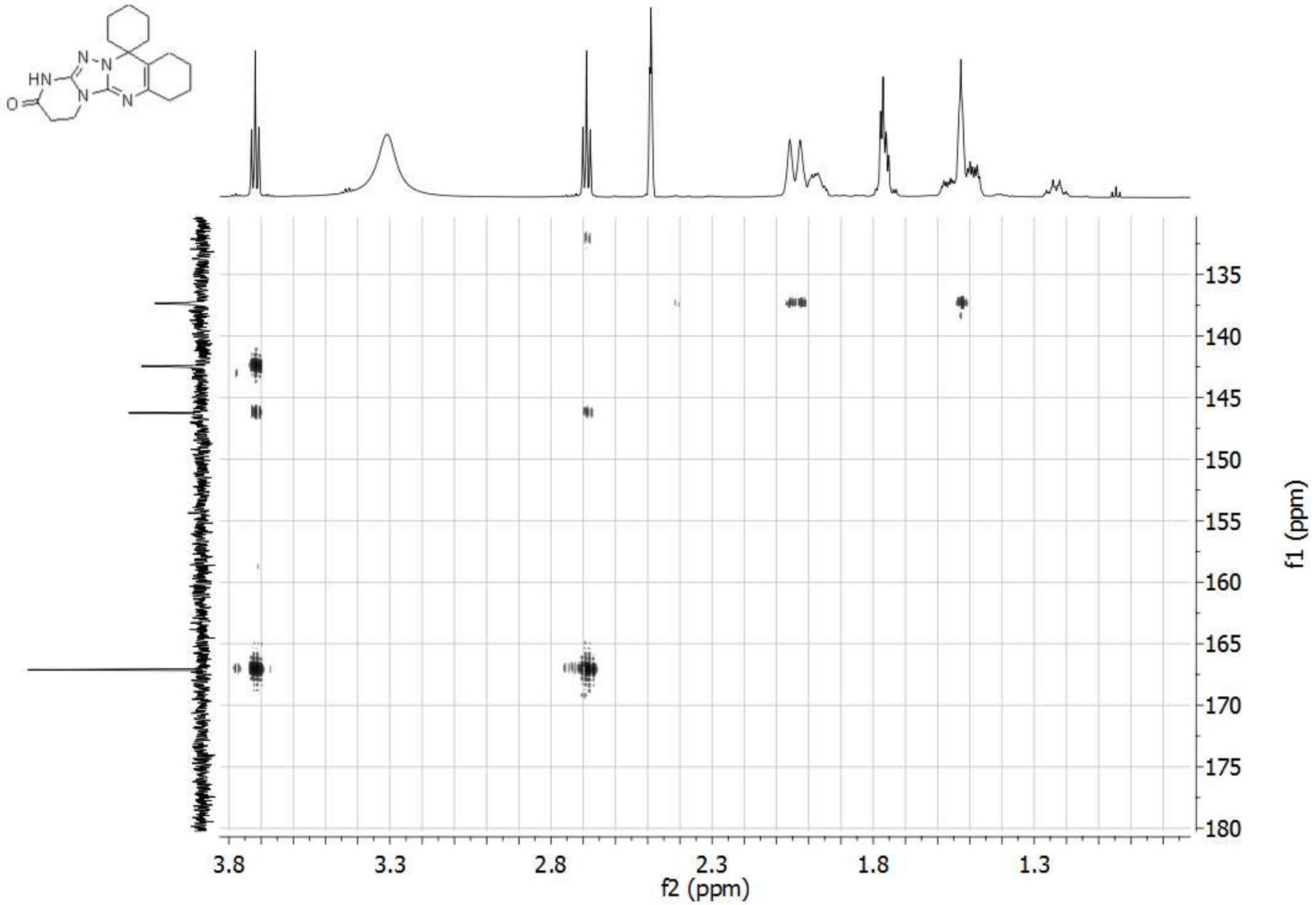
^{13}C NMR spectrum of compound **15h** (DMSO-d_6, 150 MHz).



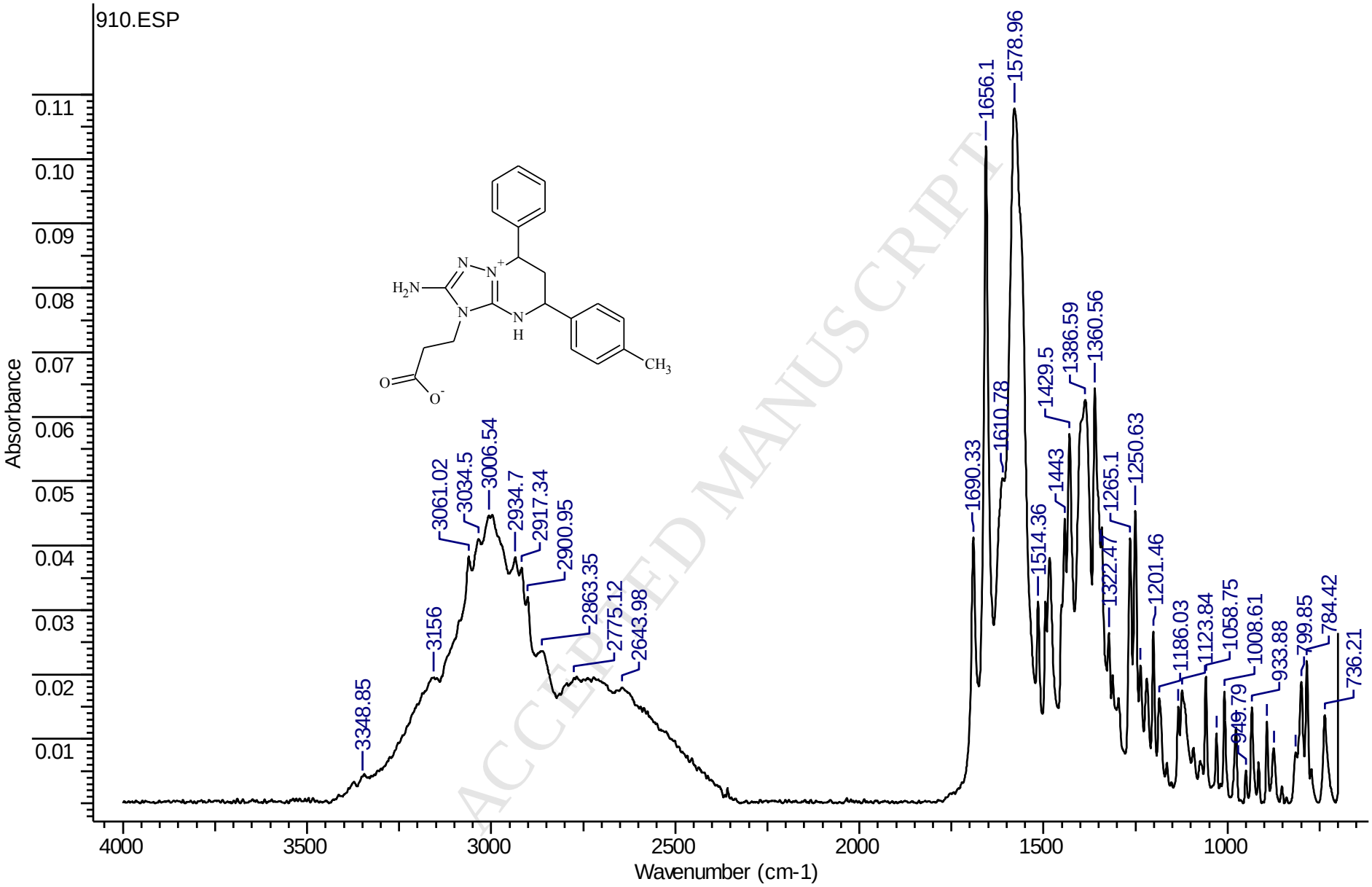
Enlarged fragment of ^{1}H-^{13}C HSQC spectrum of compound **15h.**



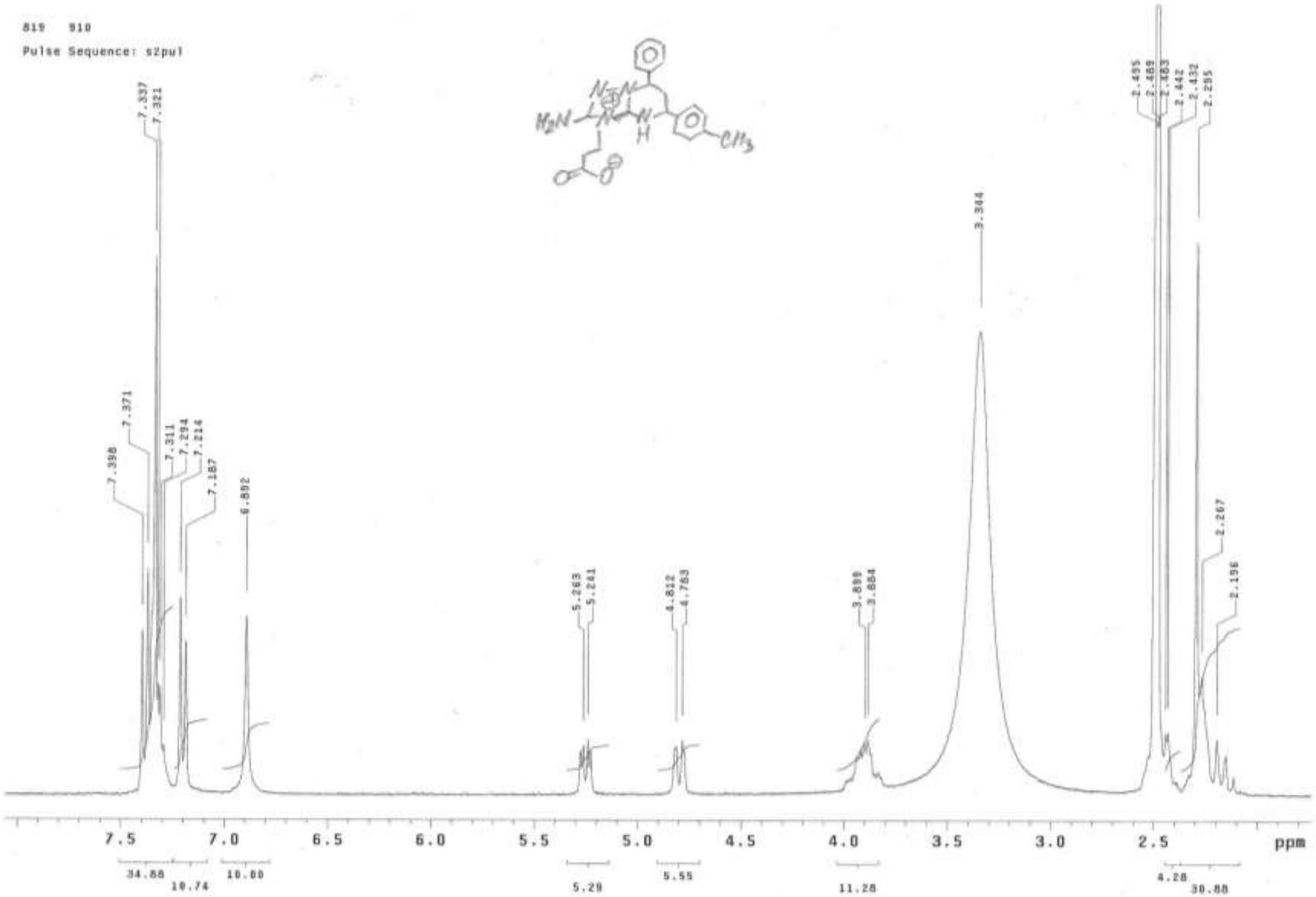
^{1}H-^{13}C HMBC spectrum of compound **15h** (DMSO-d_6).



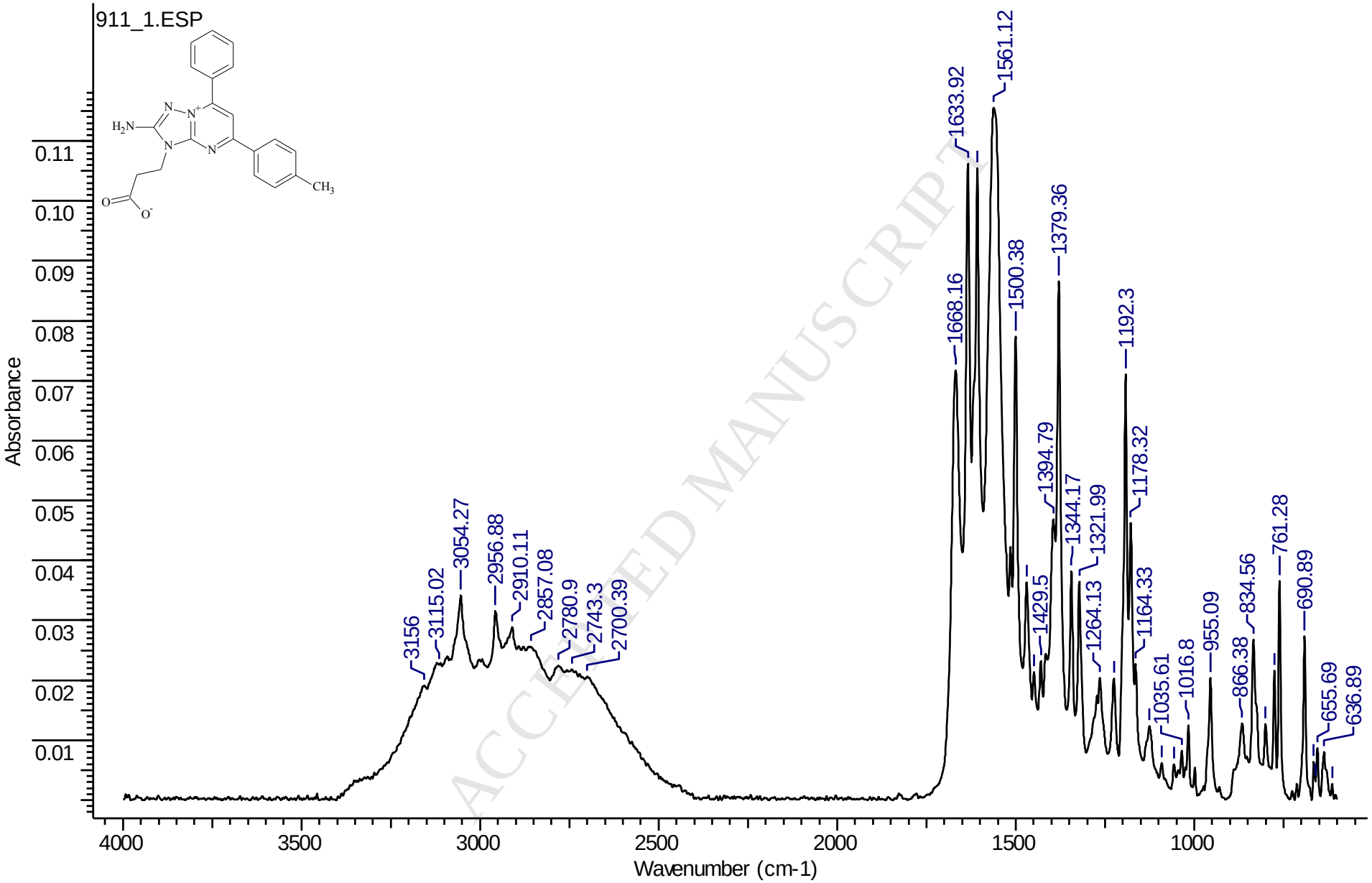
Enlarged fragment of ^{1}H-^{13}C HMBC spectrum of compound **15h.**



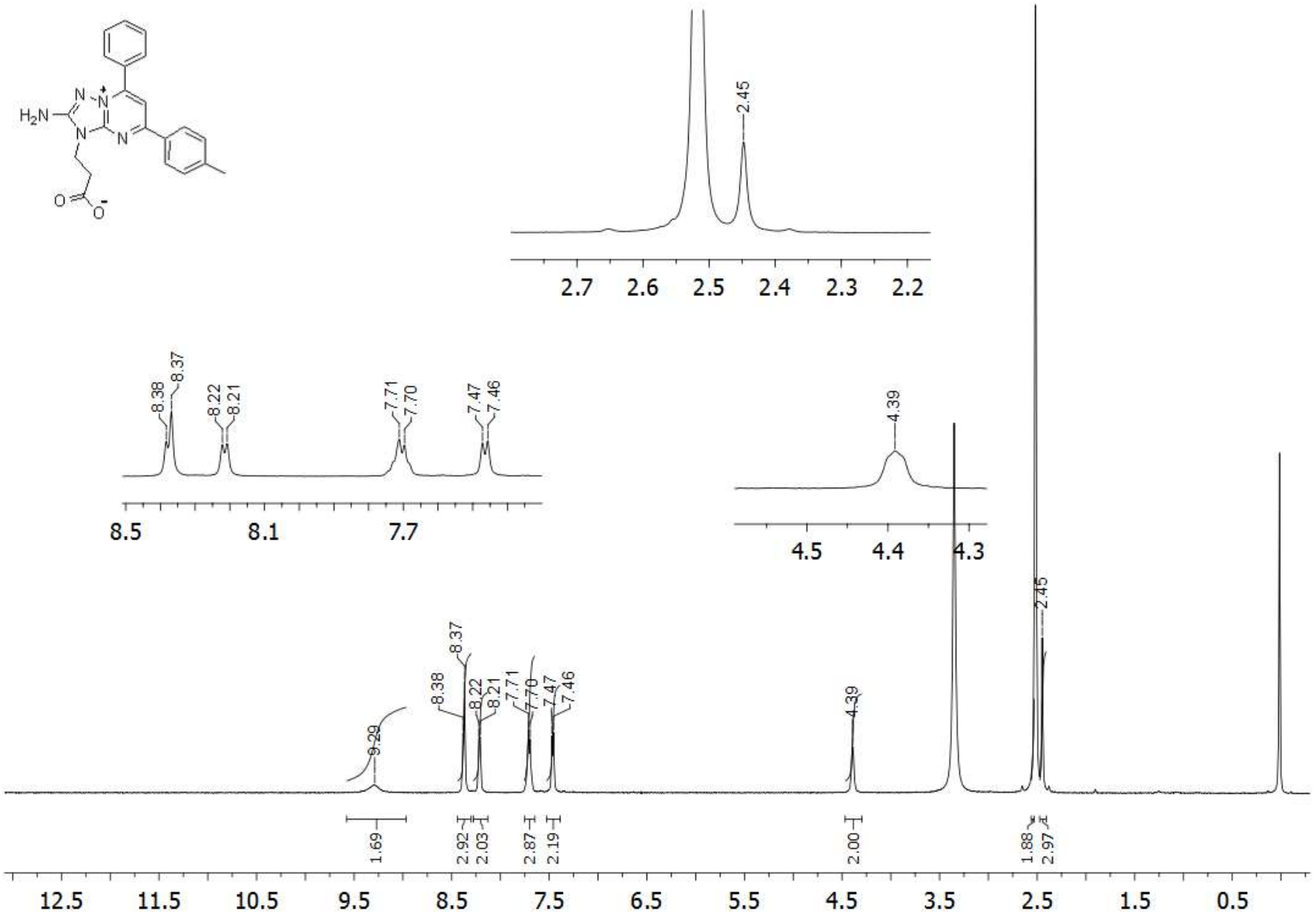
FTIR spectrum of compound **17** (ATR).



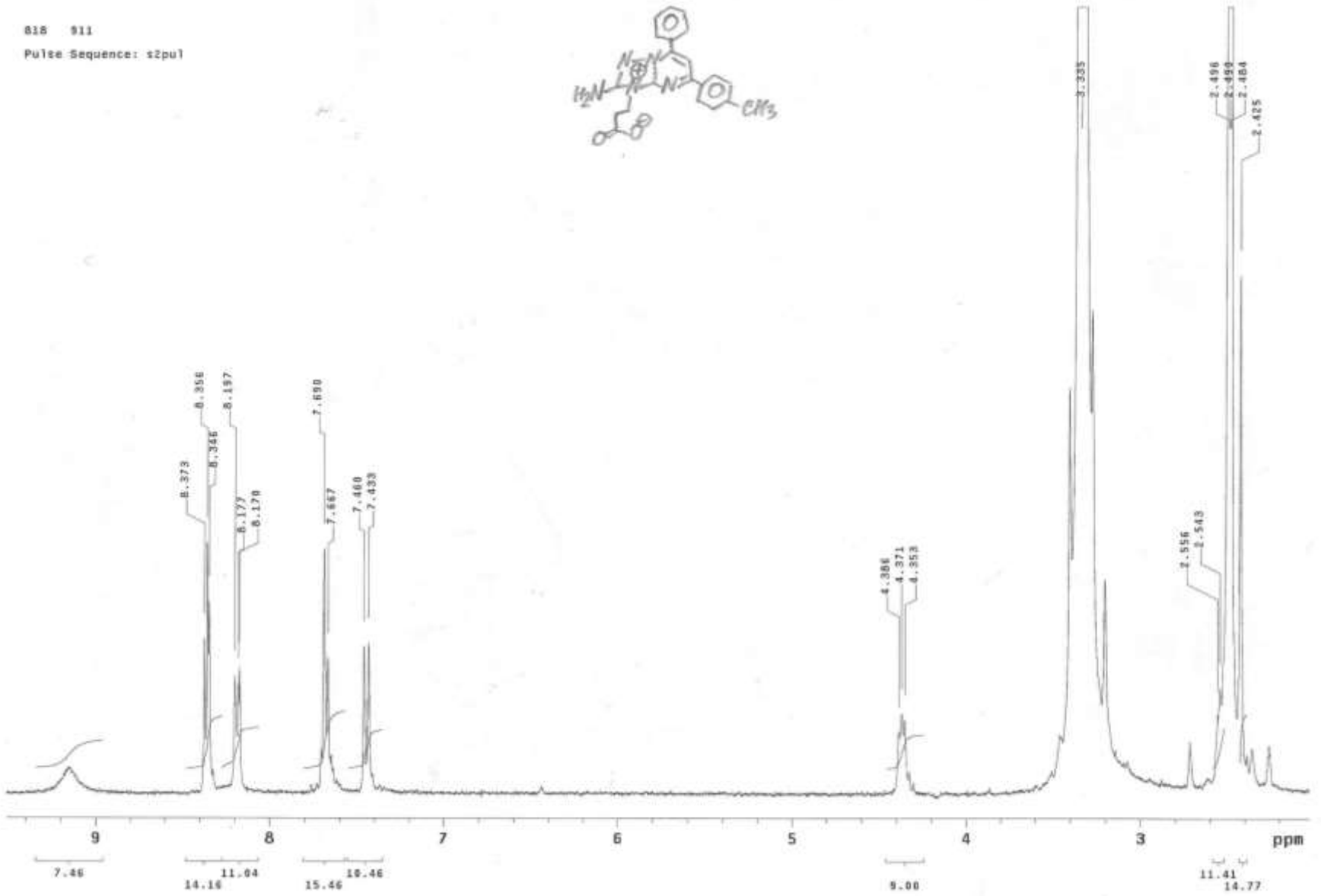
^{1}H NMR spectrum of compound **17** (DMSO-d_6, 300 MHz).



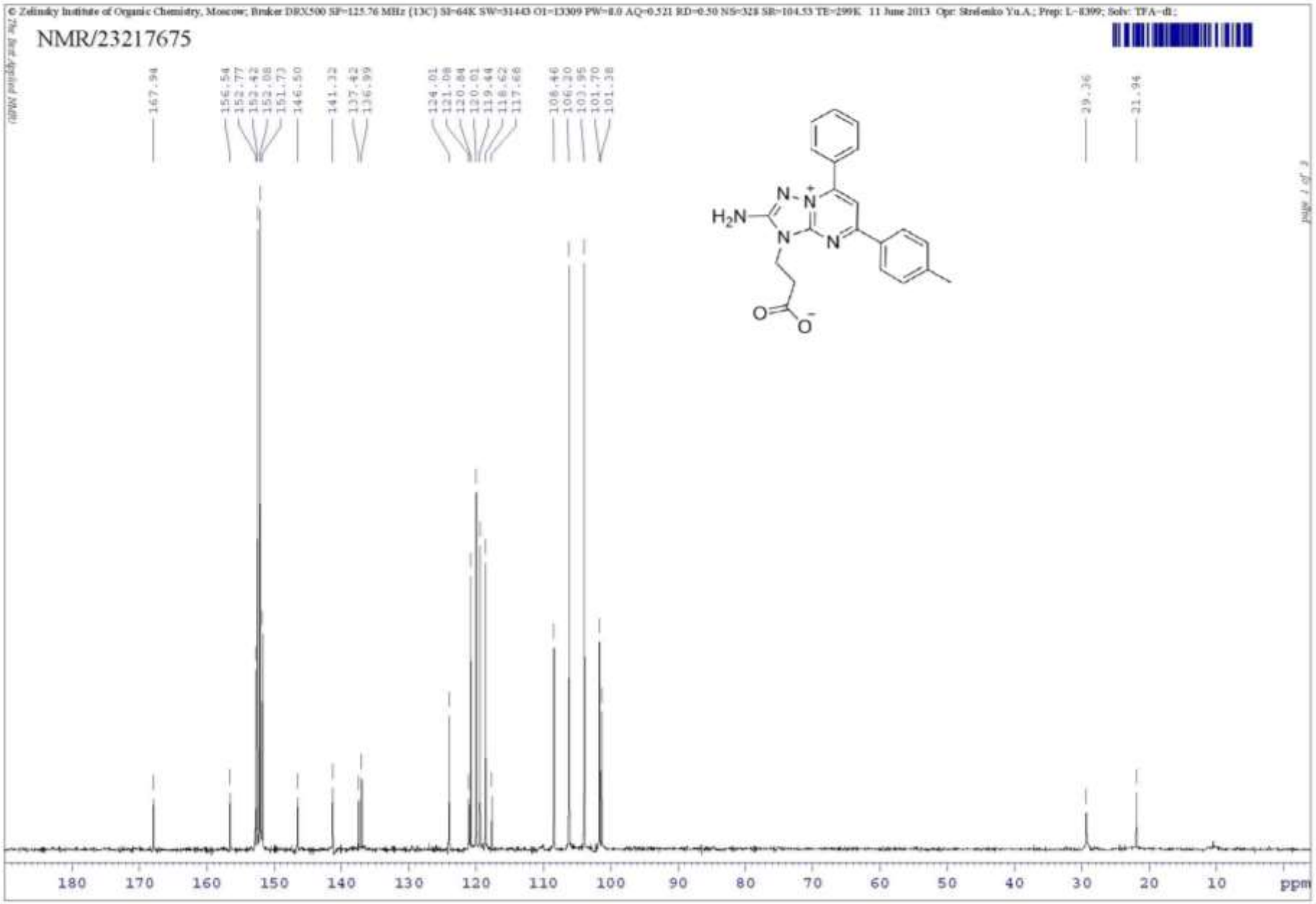
FTIR spectrum of compound **18** (ATR).



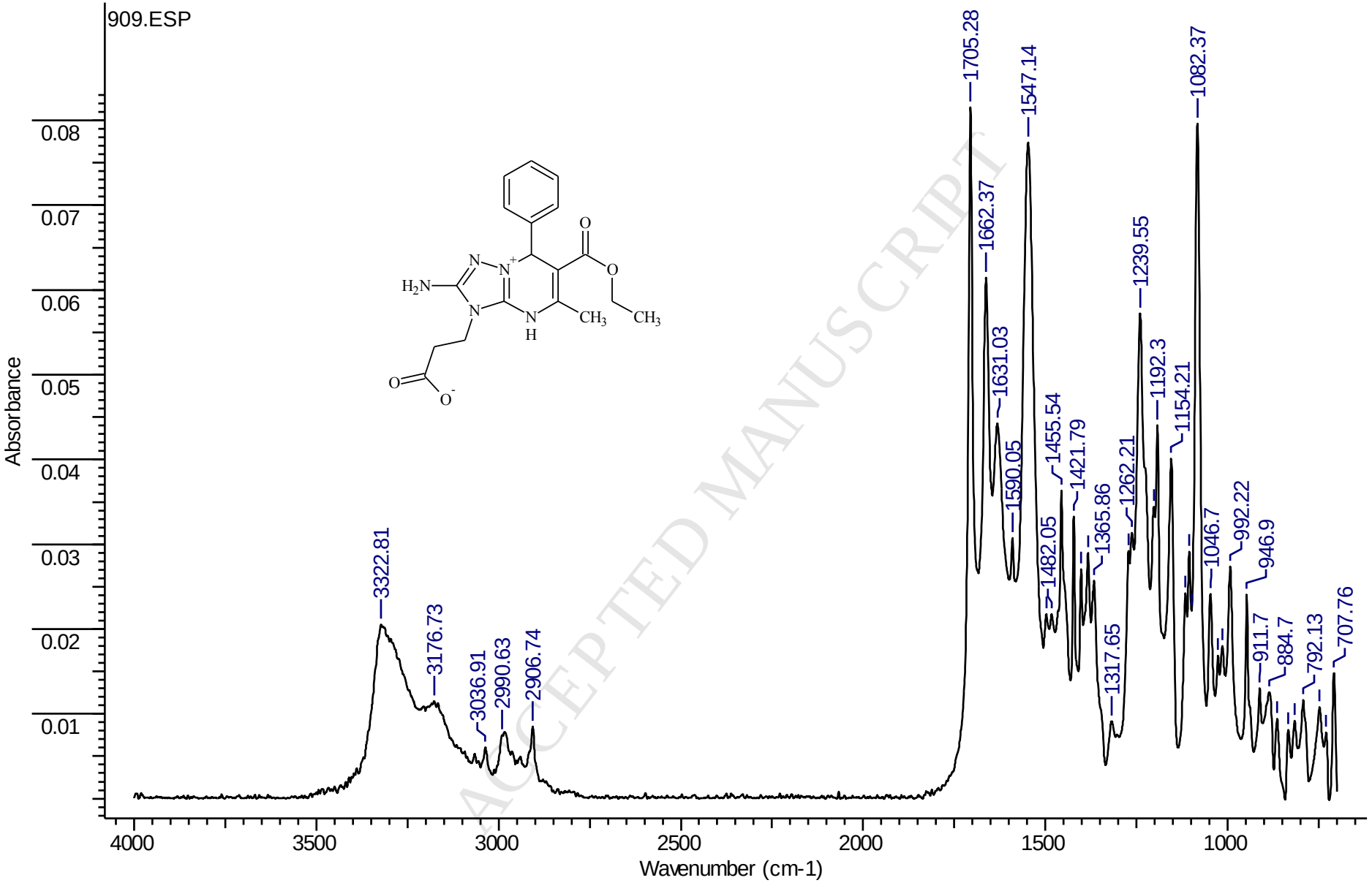
^{1}H NMR spectrum of compound **18** (DMSO-d_6, 500 MHz).



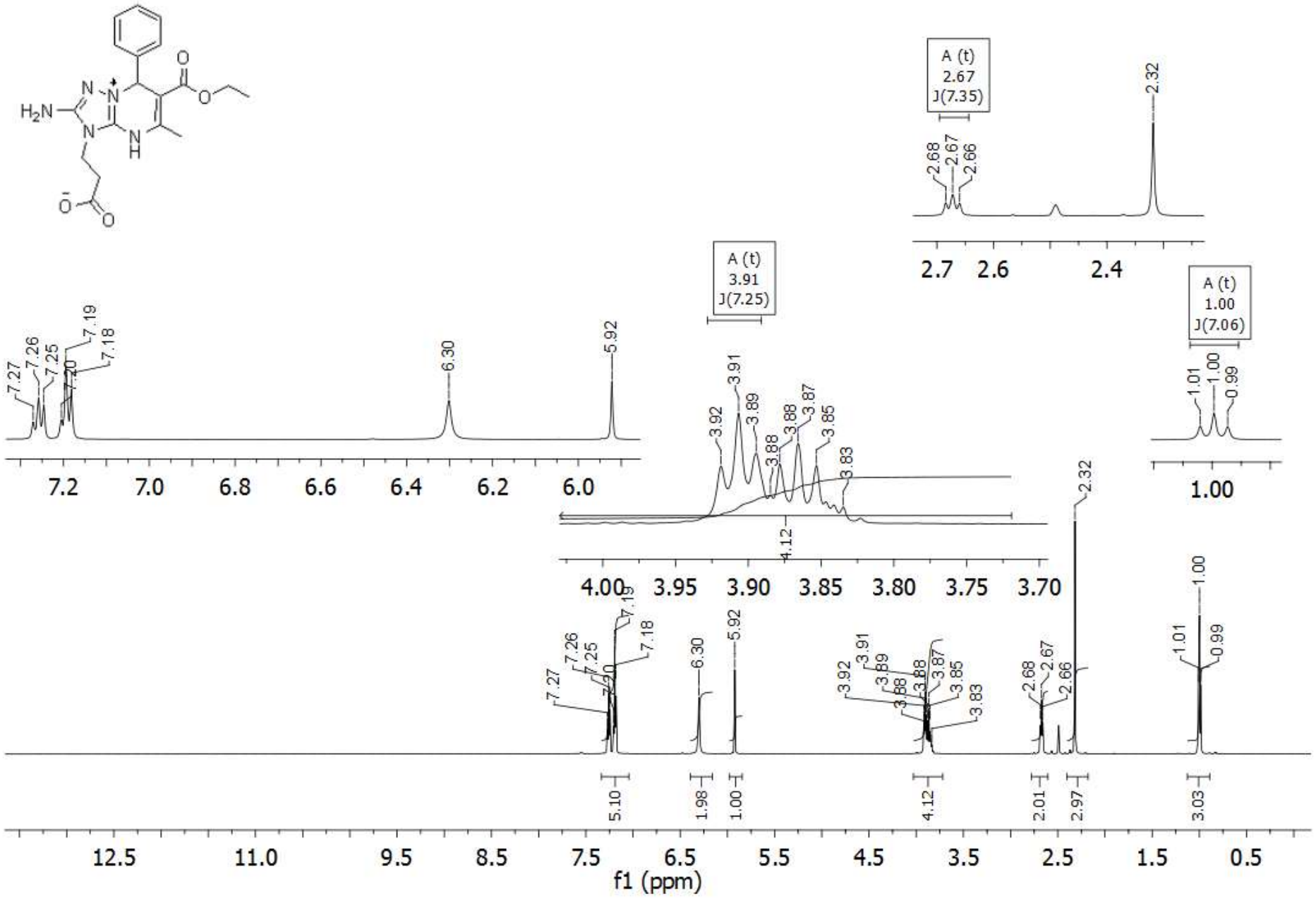
^{1}H NMR spectrum of compound **18** (DMSO-d_6, 300 MHz).



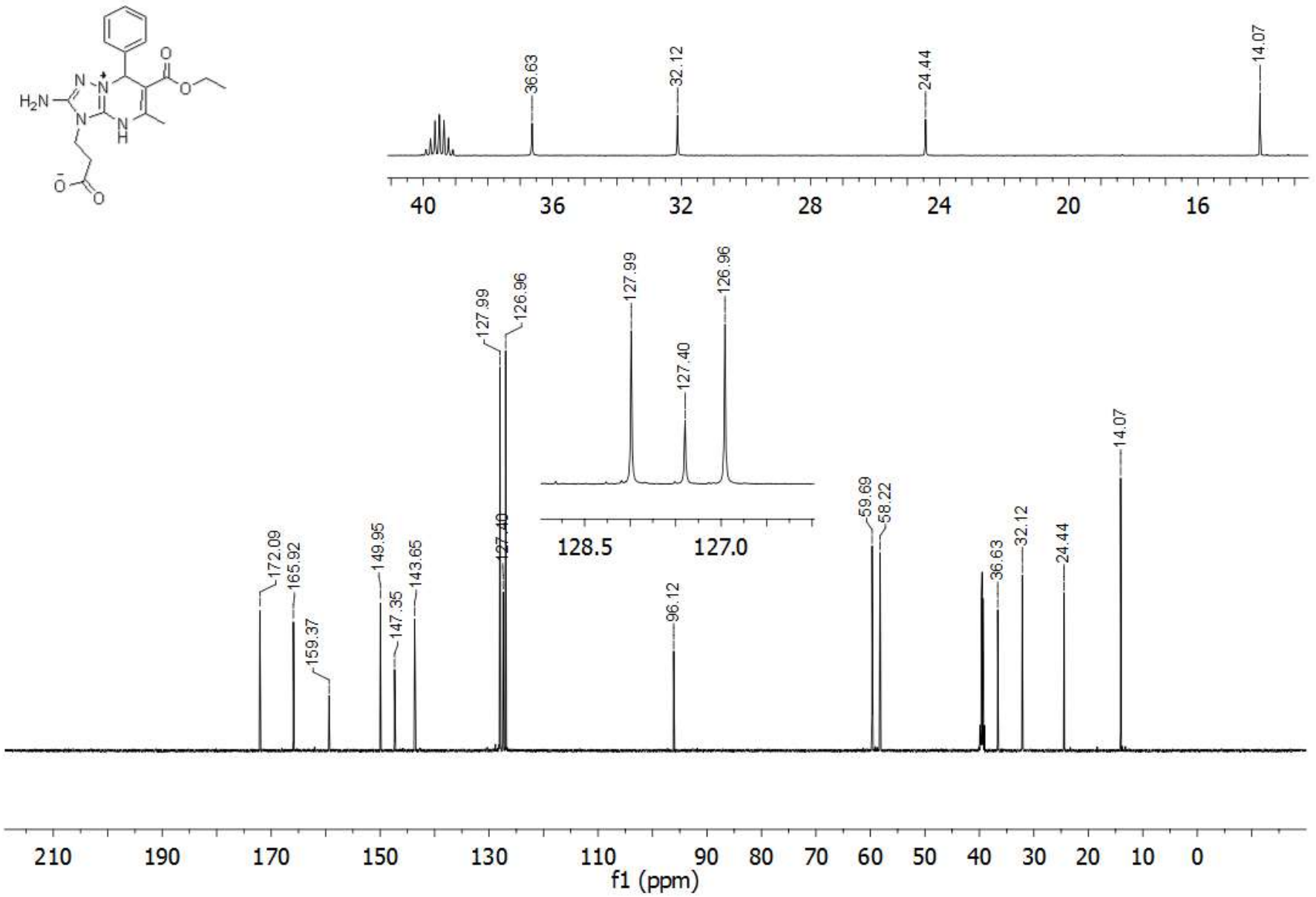
^{13}C NMR spectrum of compound **18** (TFA + 5%DMSO-d_6, 125 MHz).



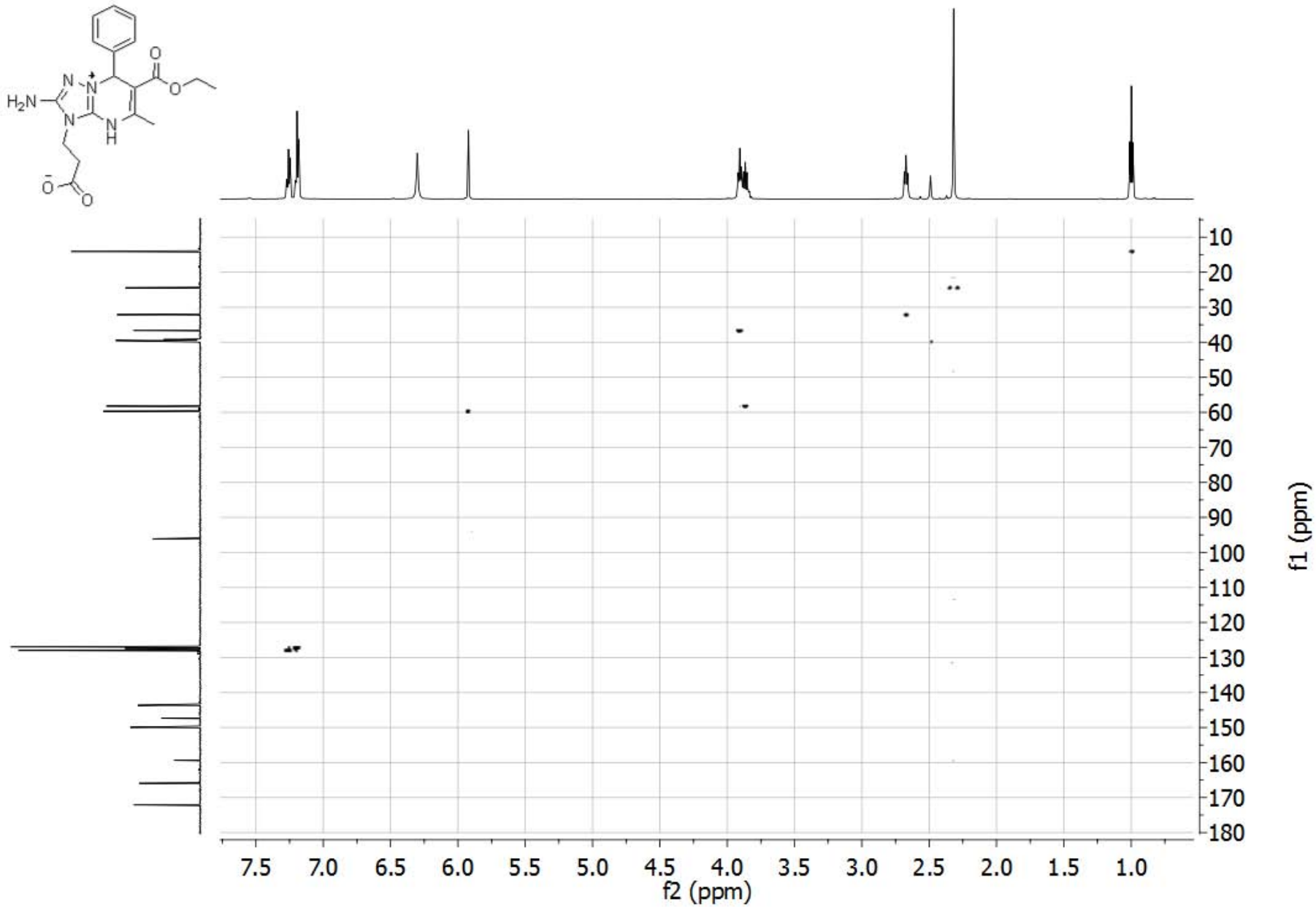
FTIR spectrum of compound **19** (ATR).



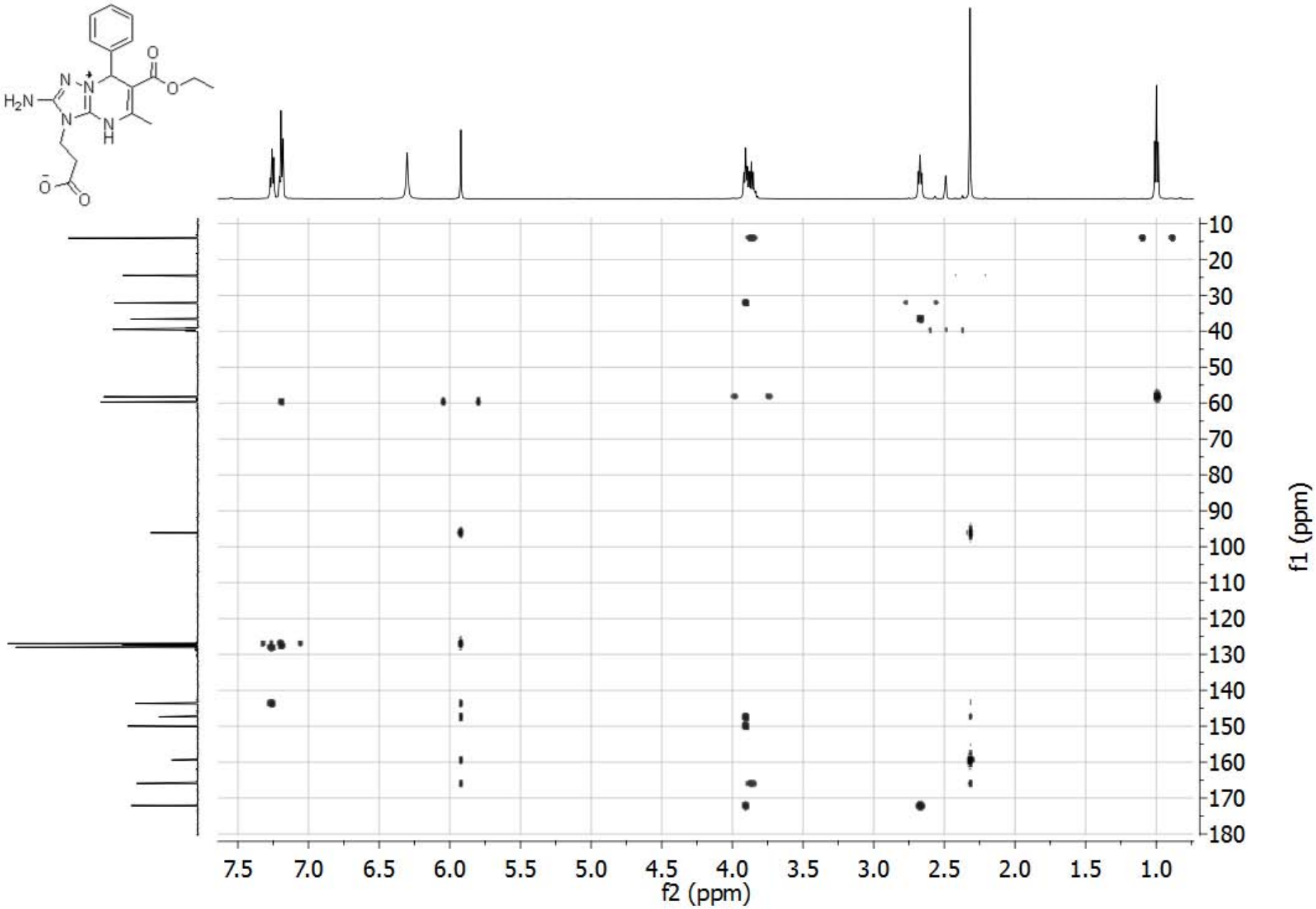
^{1}H NMR spectrum of compound **19** (DMSO-d_6, 600 MHz).



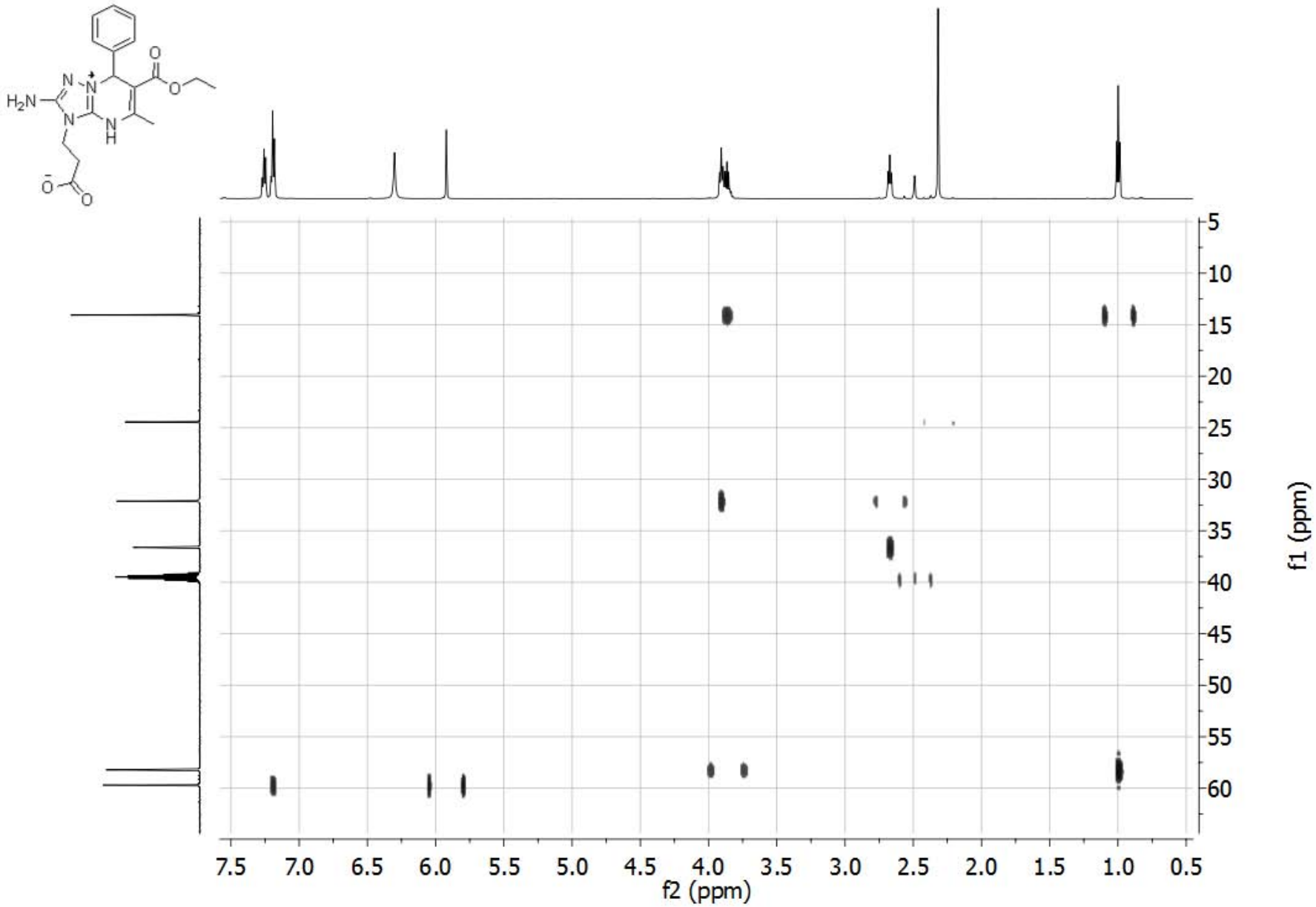
^{13}C NMR spectrum of compound **19** (DMSO-d_6, 150 MHz).



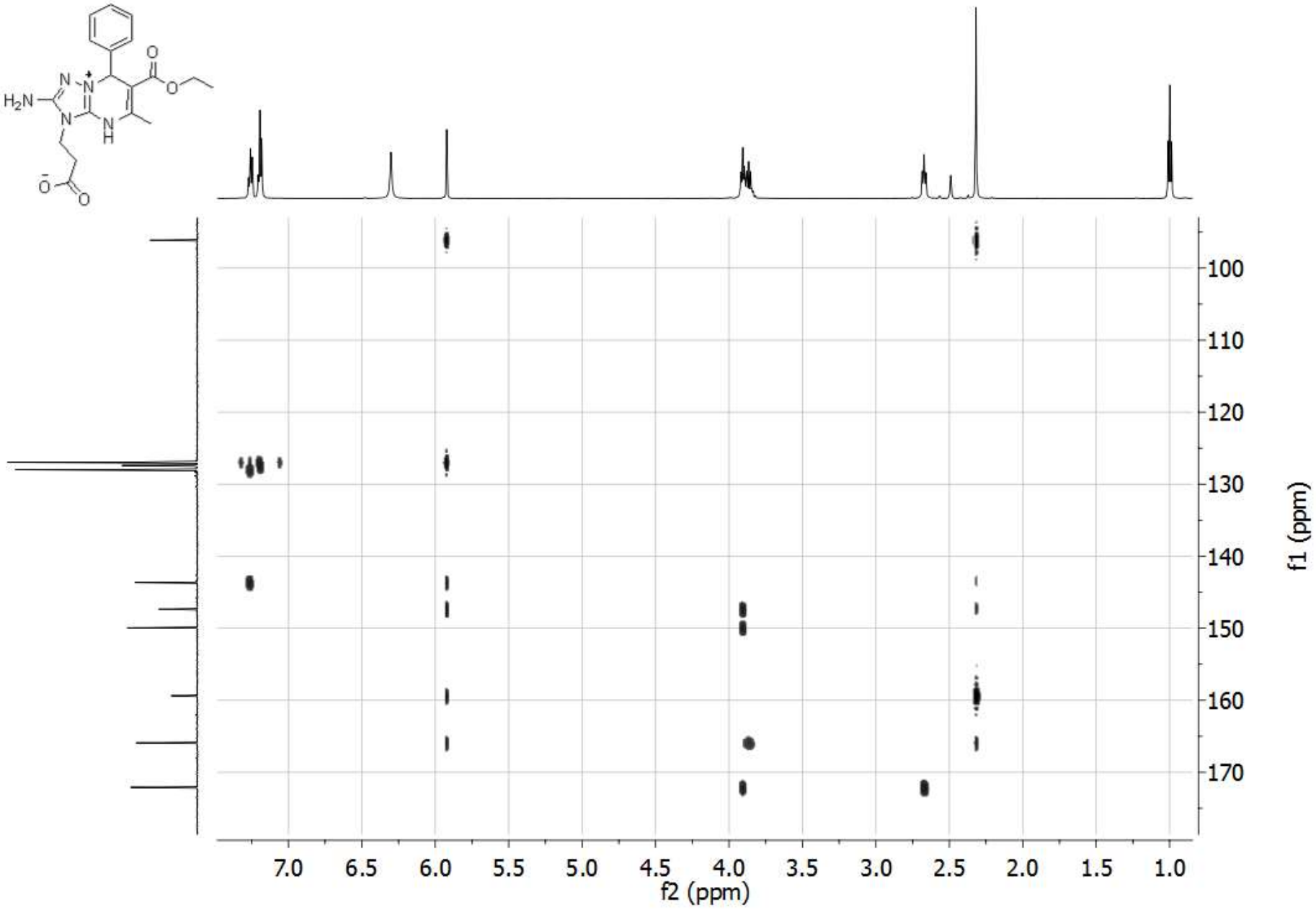
^{1}H-^{13}C HSQC spectrum of compound **19** (DMSO-d_6).



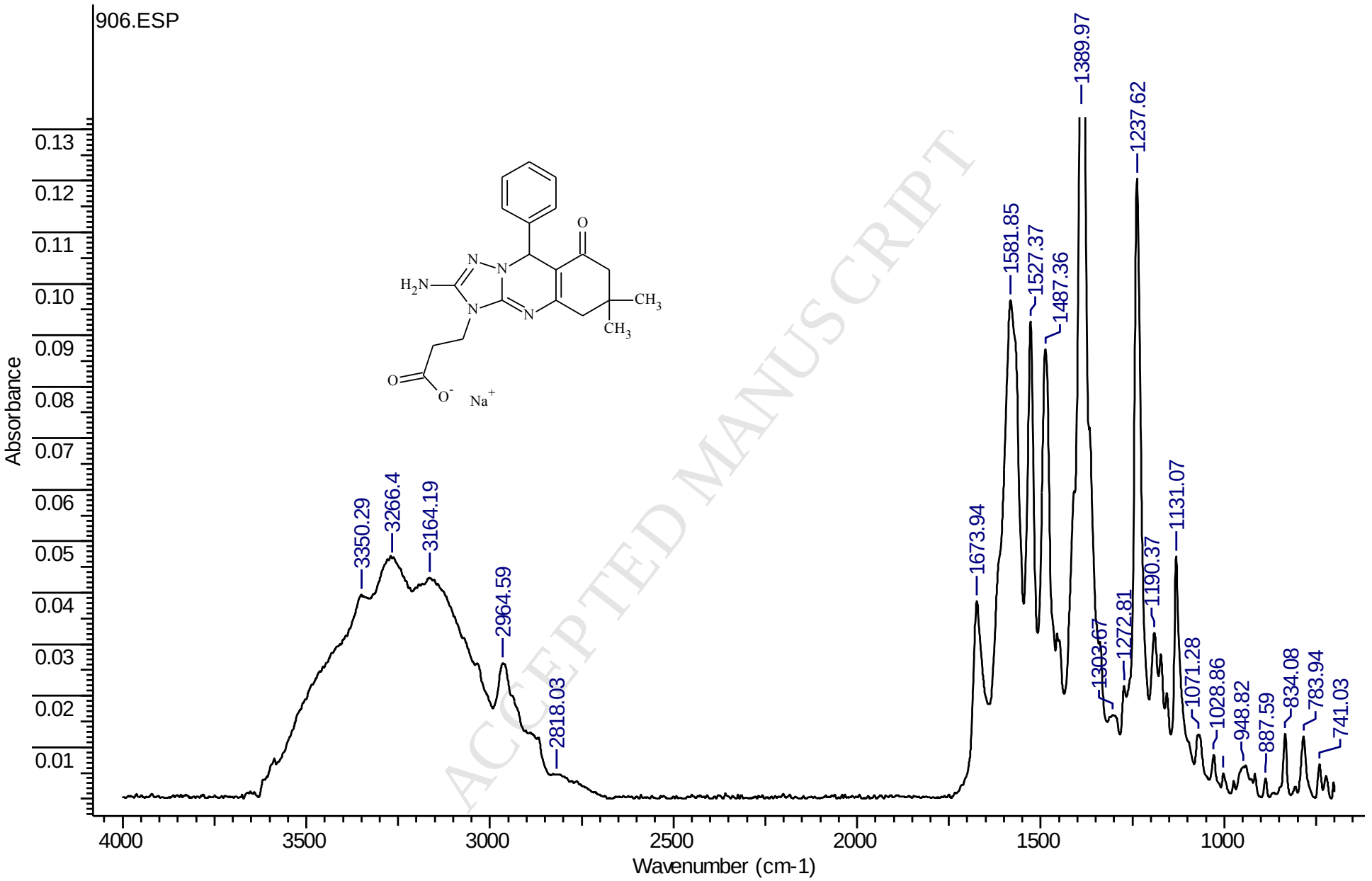
^{1}H-^{13}C HMBC spectrum of compound **19** (DMSO-d_6).



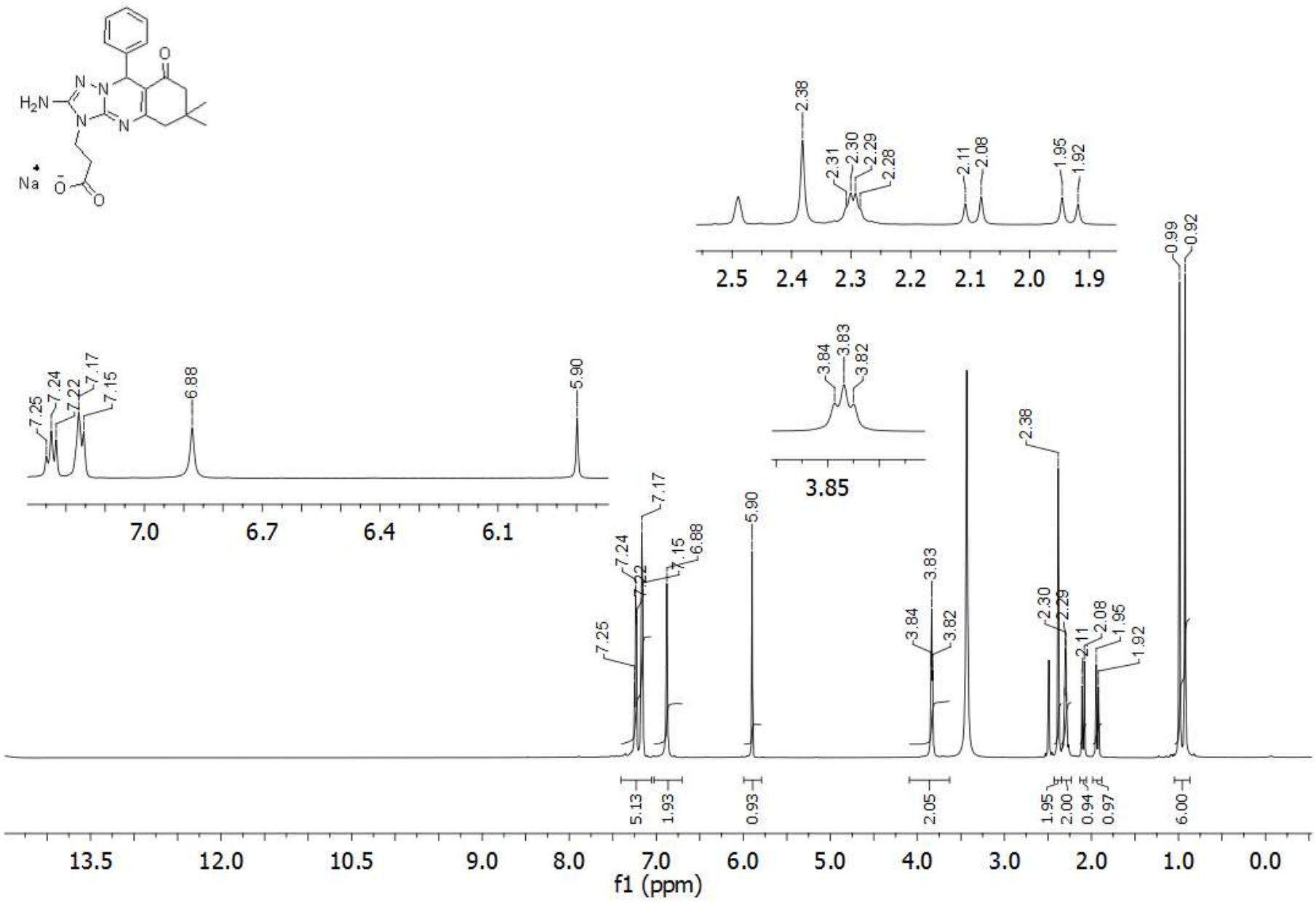
High-field fragment of ^{1}H-^{13}C HMBC spectrum of compound **19.**



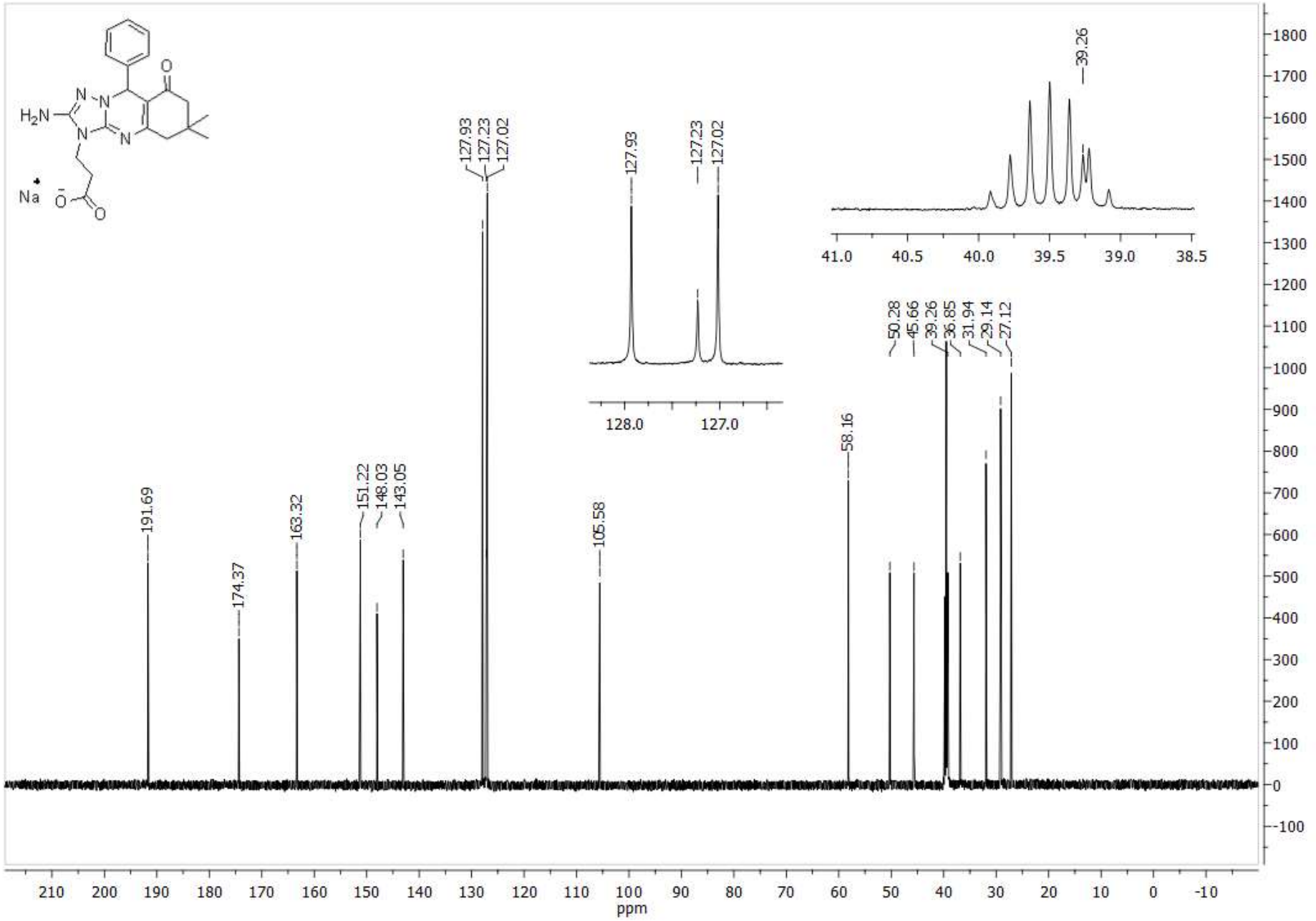
Low-field fragment of ^{1}H-^{13}C HMBC spectrum of compound **19.**



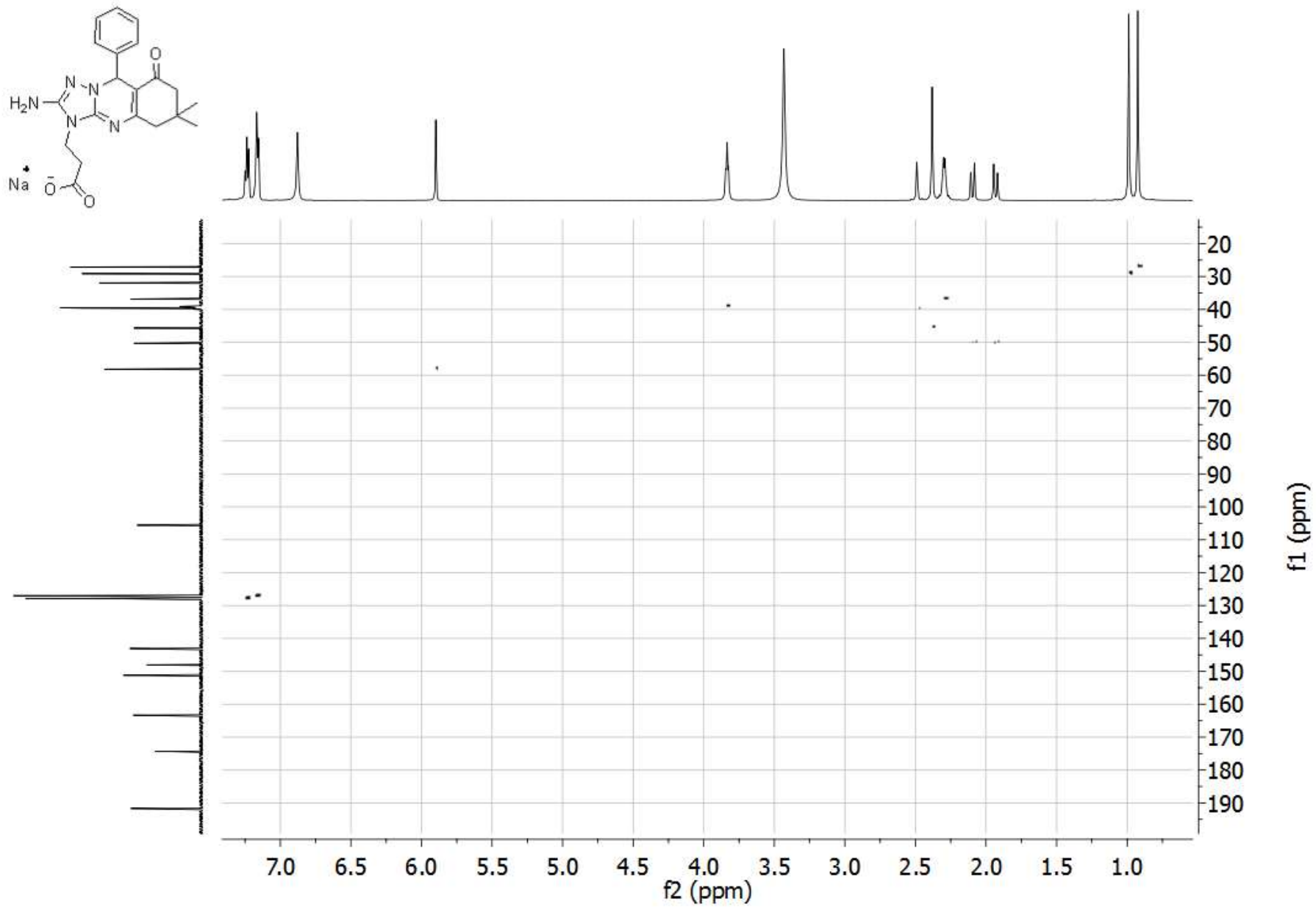
FTIR spectrum of compound **20**.



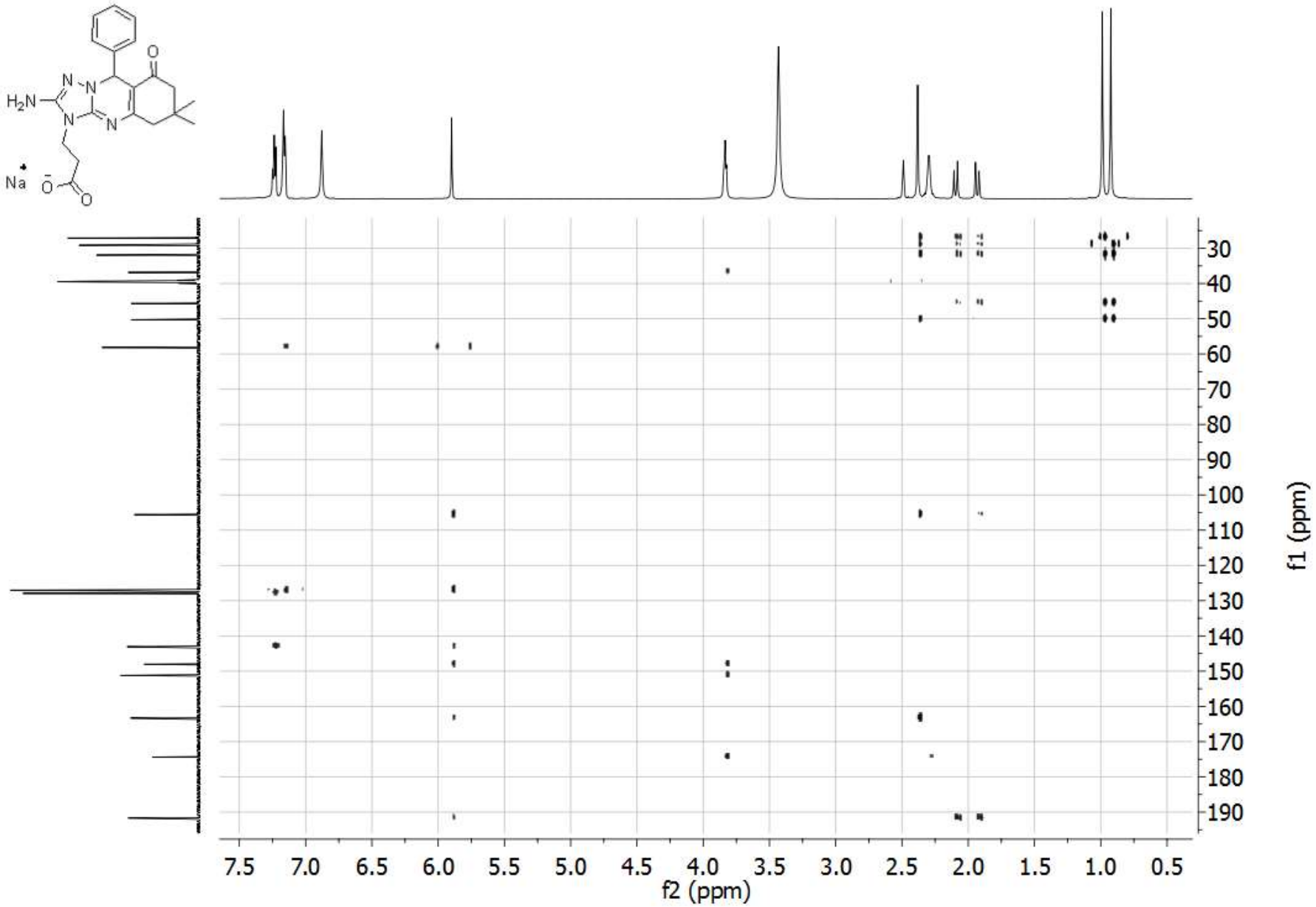
^{1}H NMR spectrum of compound **20** (DMSO-d_6, 600 MHz).



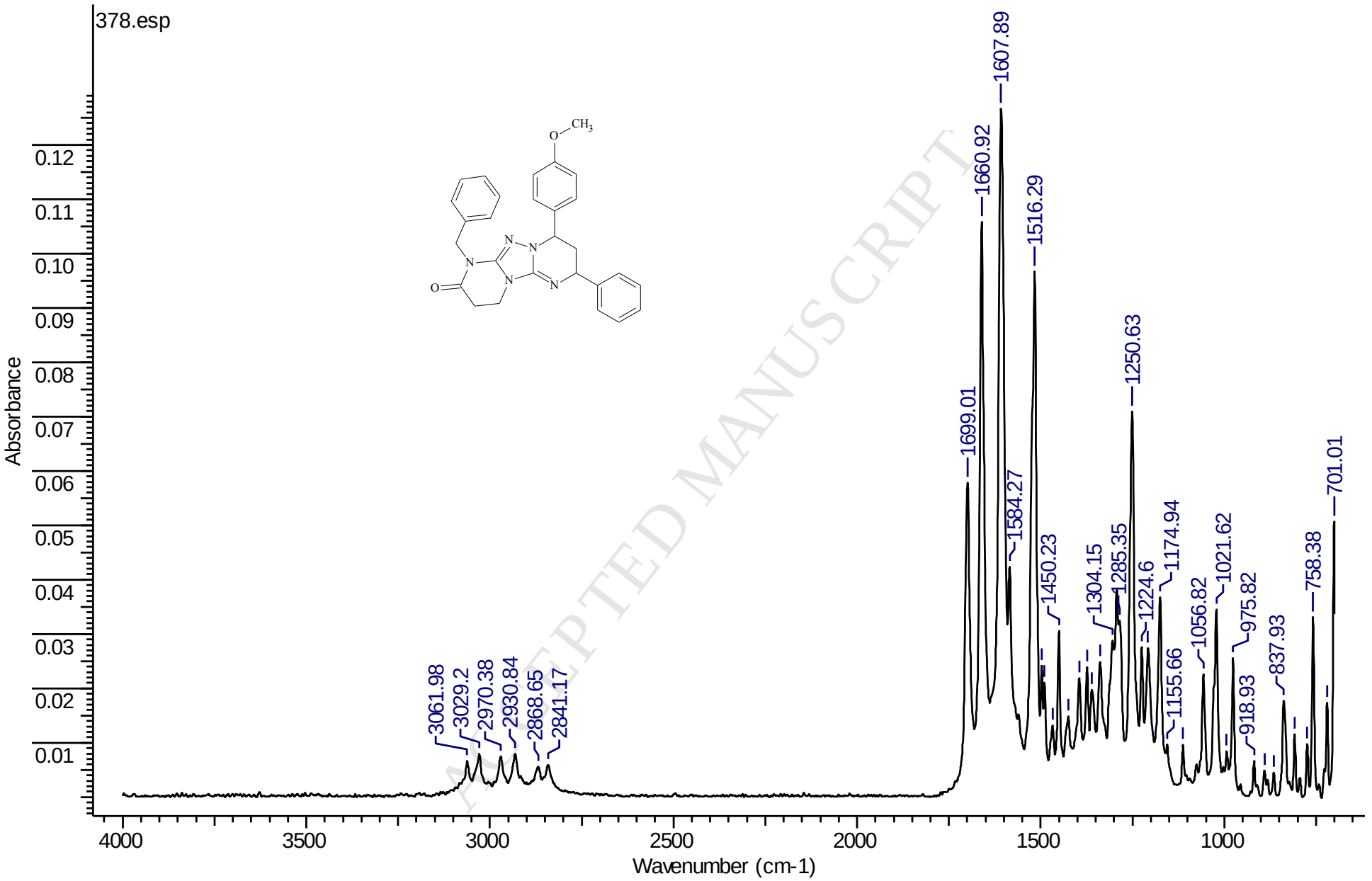
^{13}C NMR spectrum of compound **20** (DMSO-d_6, 150 MHz).



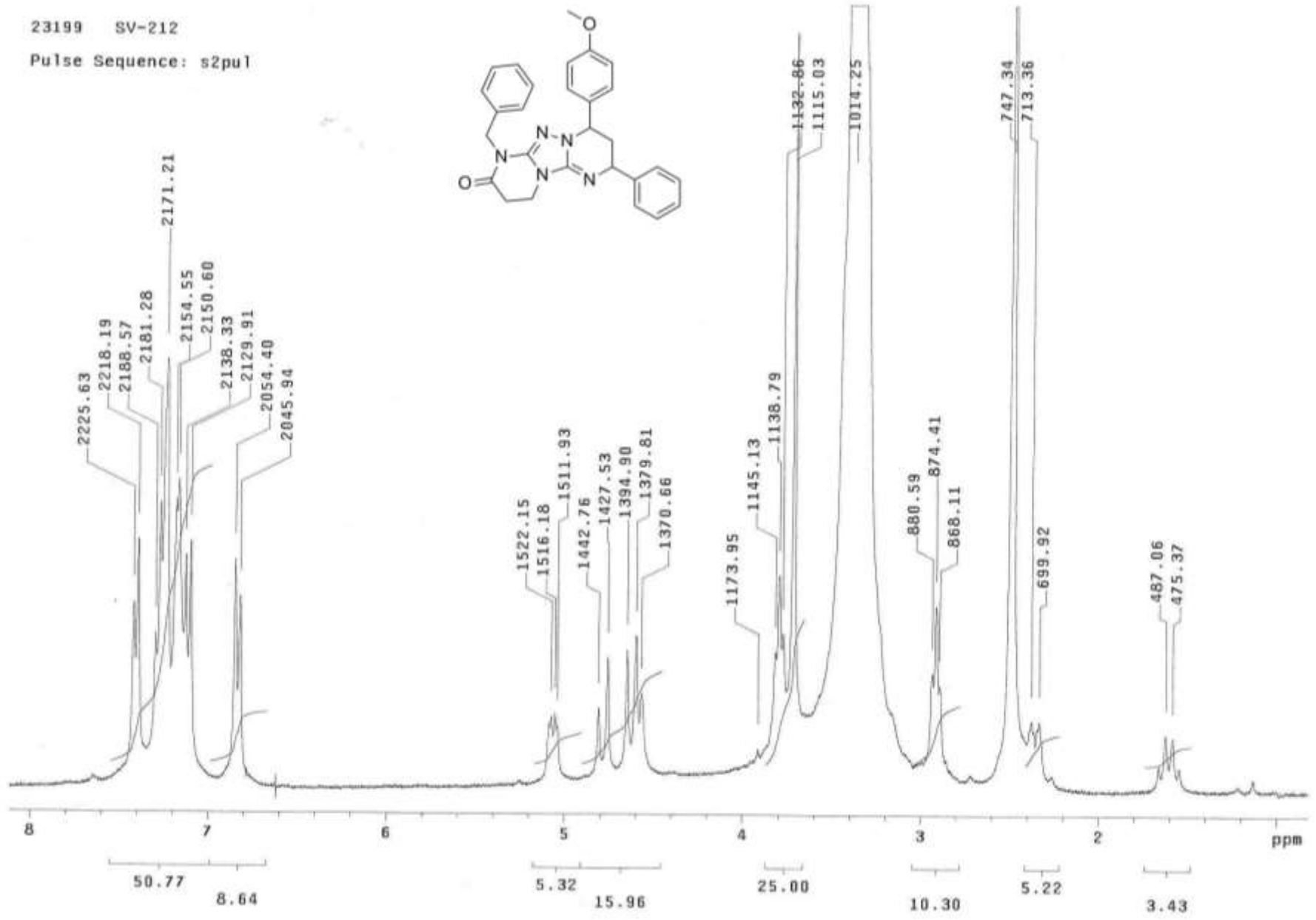
^{1}H-^{13}C HSQC spectrum of compound **20** (DMSO-d_6).



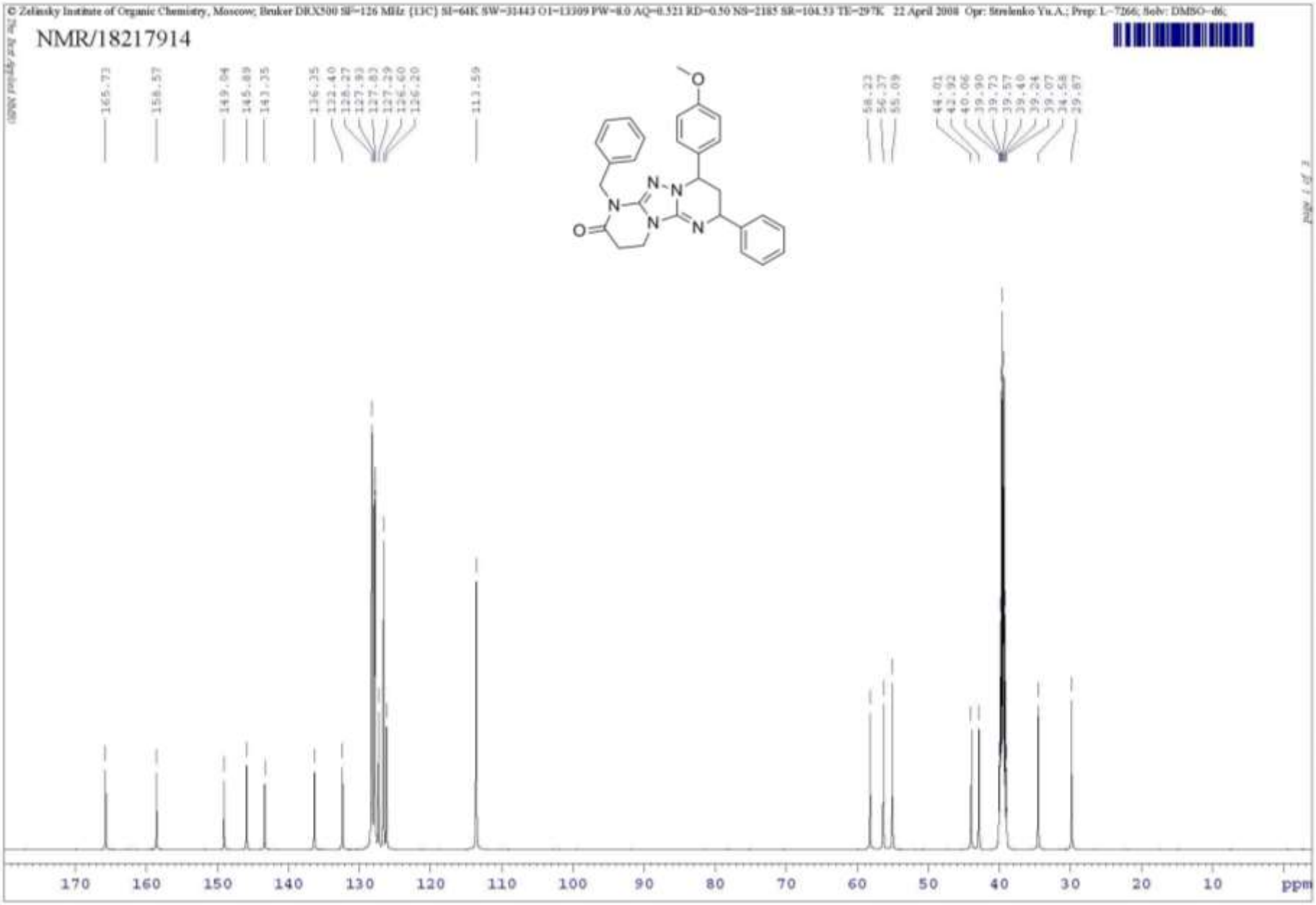
^{1}H-^{13}C HMBC spectrum of compound **20** (DMSO-d_6).



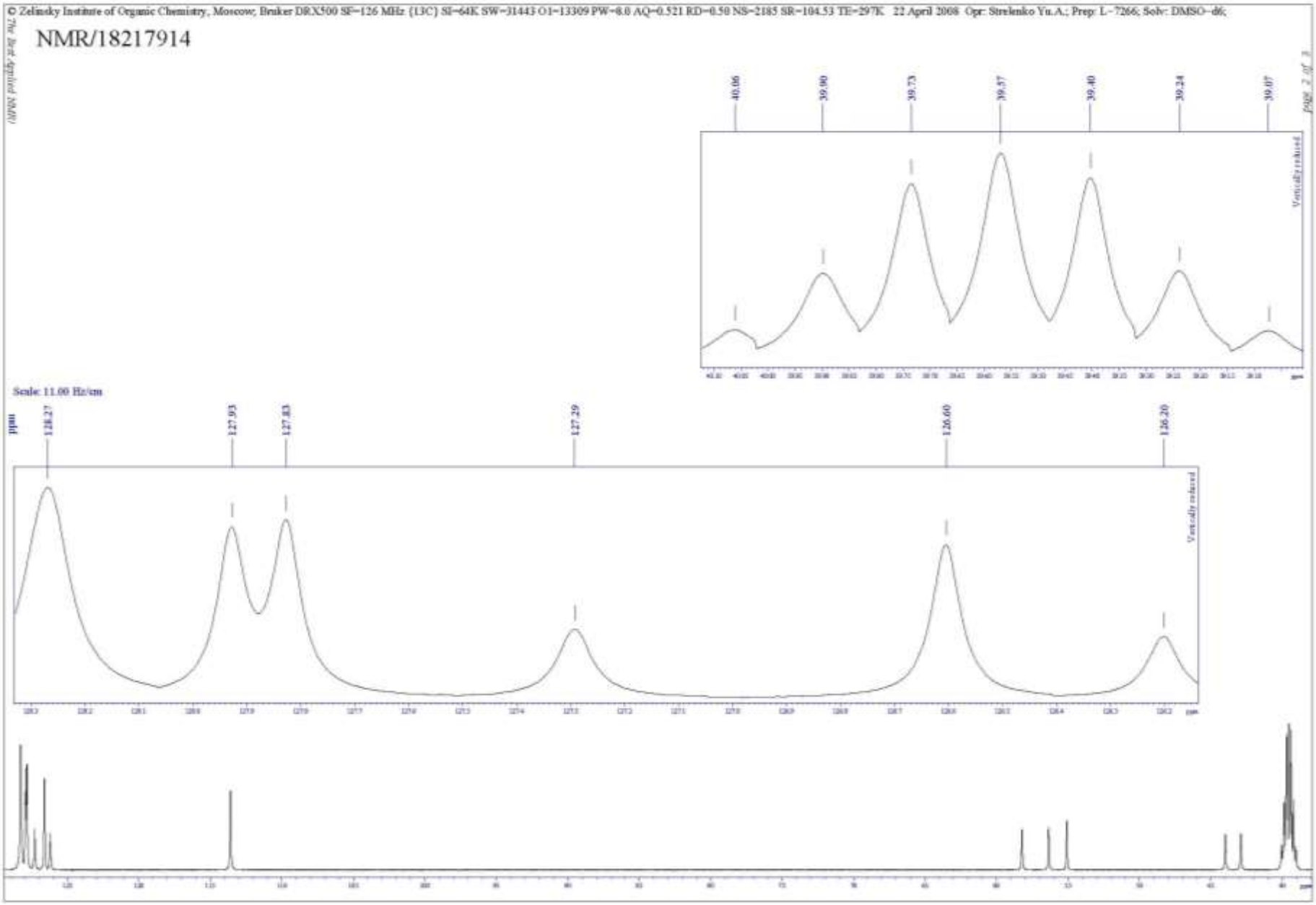
FTIR spectrum of compound **23** (ATR).



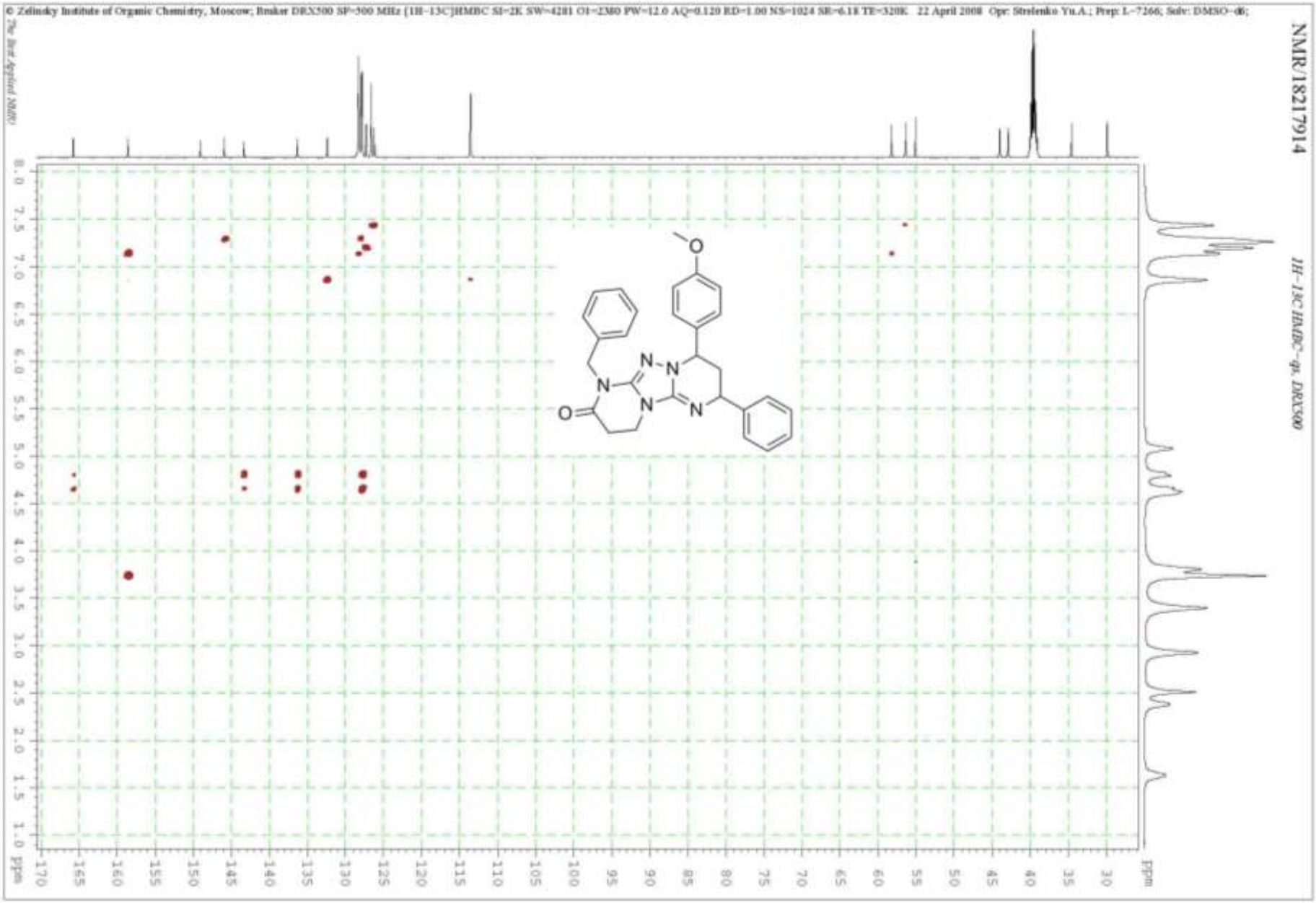
^{1}H NMR spectrum of compound **23** (300 MHz, DMSO-d_6).



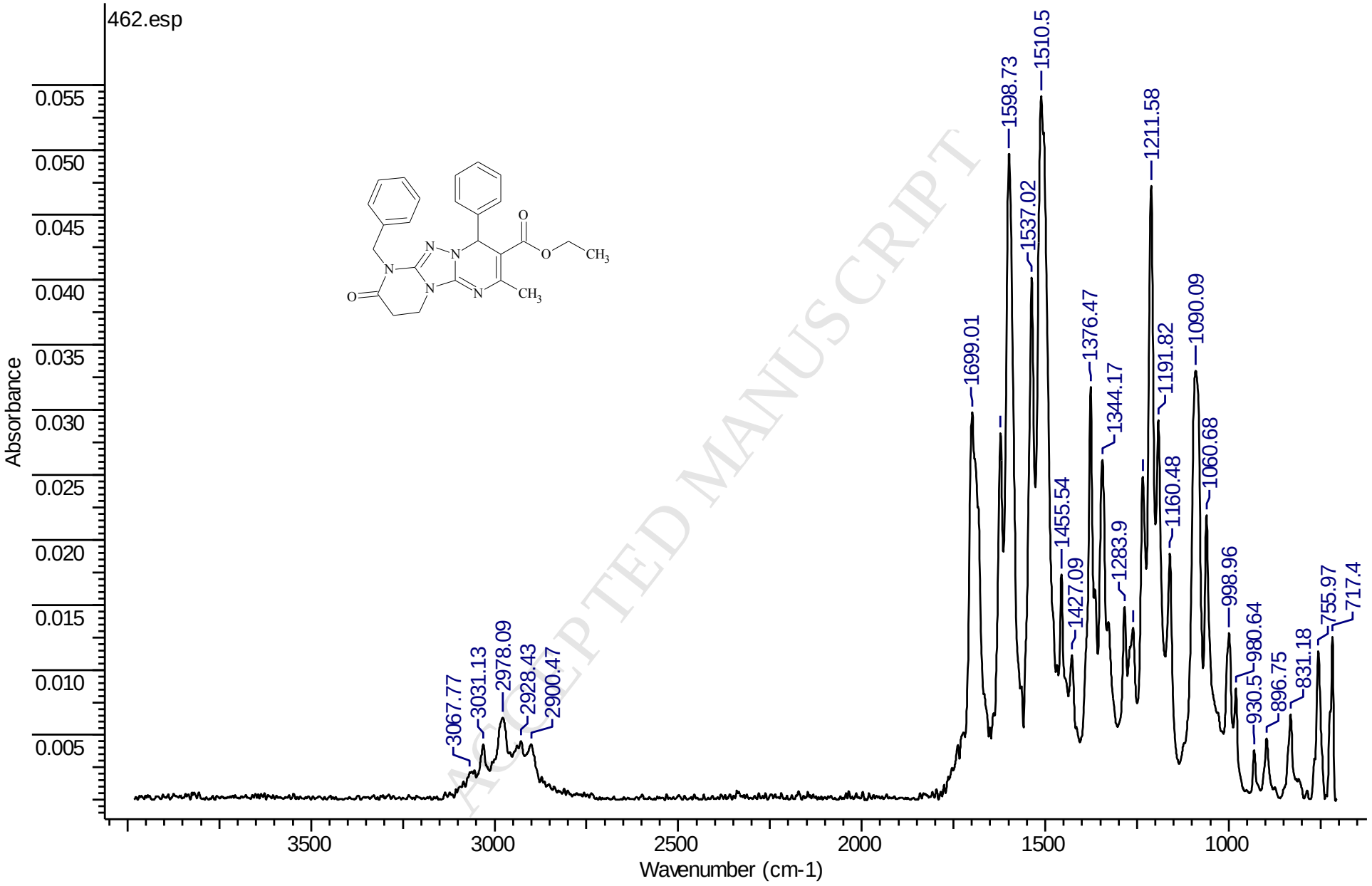
^{13}C NMR spectrum of compound **23** (125 MHz, DMSO-d_6).



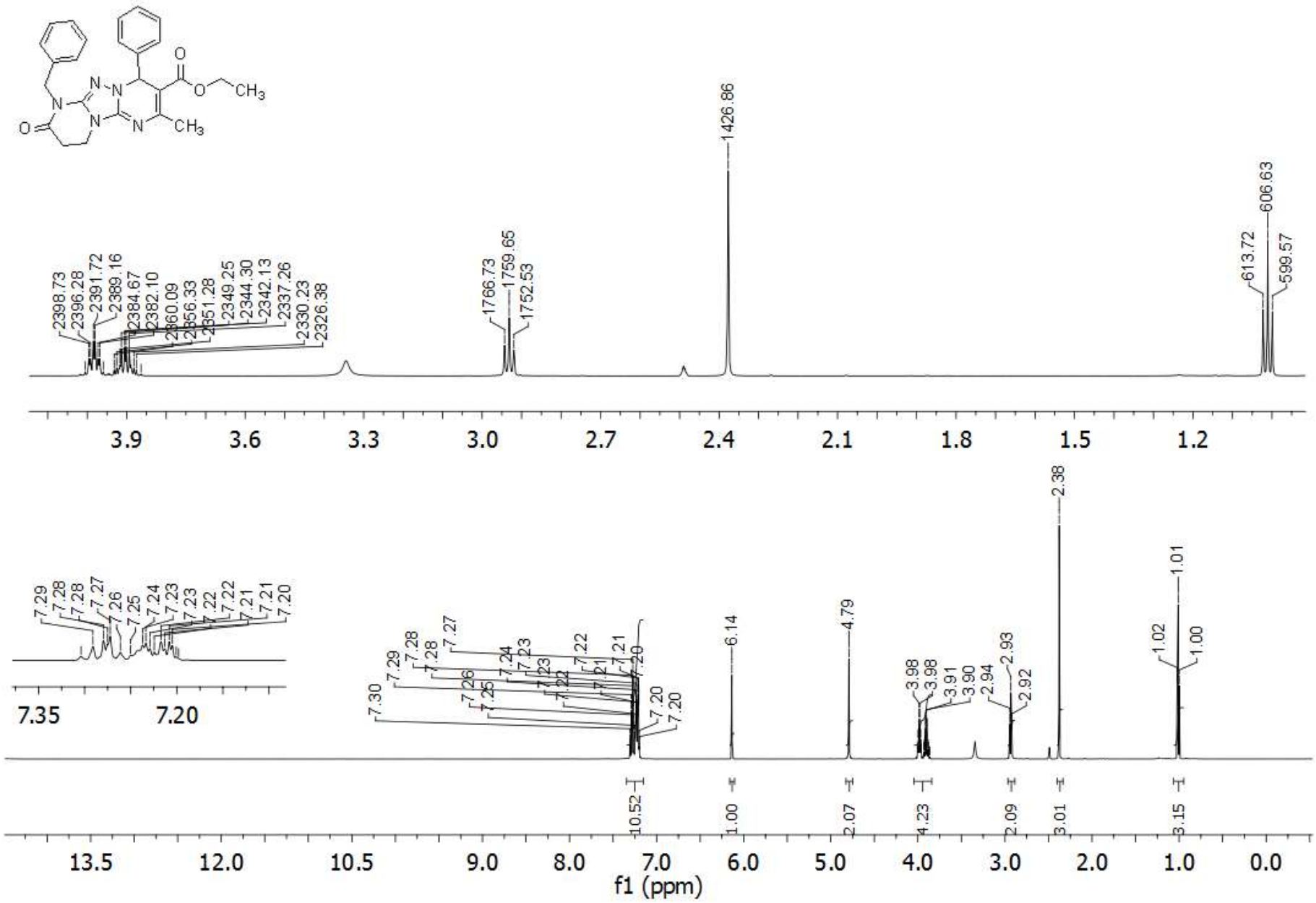
Enlarged fragments of ^{13}C NMR spectrum of compound **23** (125 MHz, DMSO-d_6).



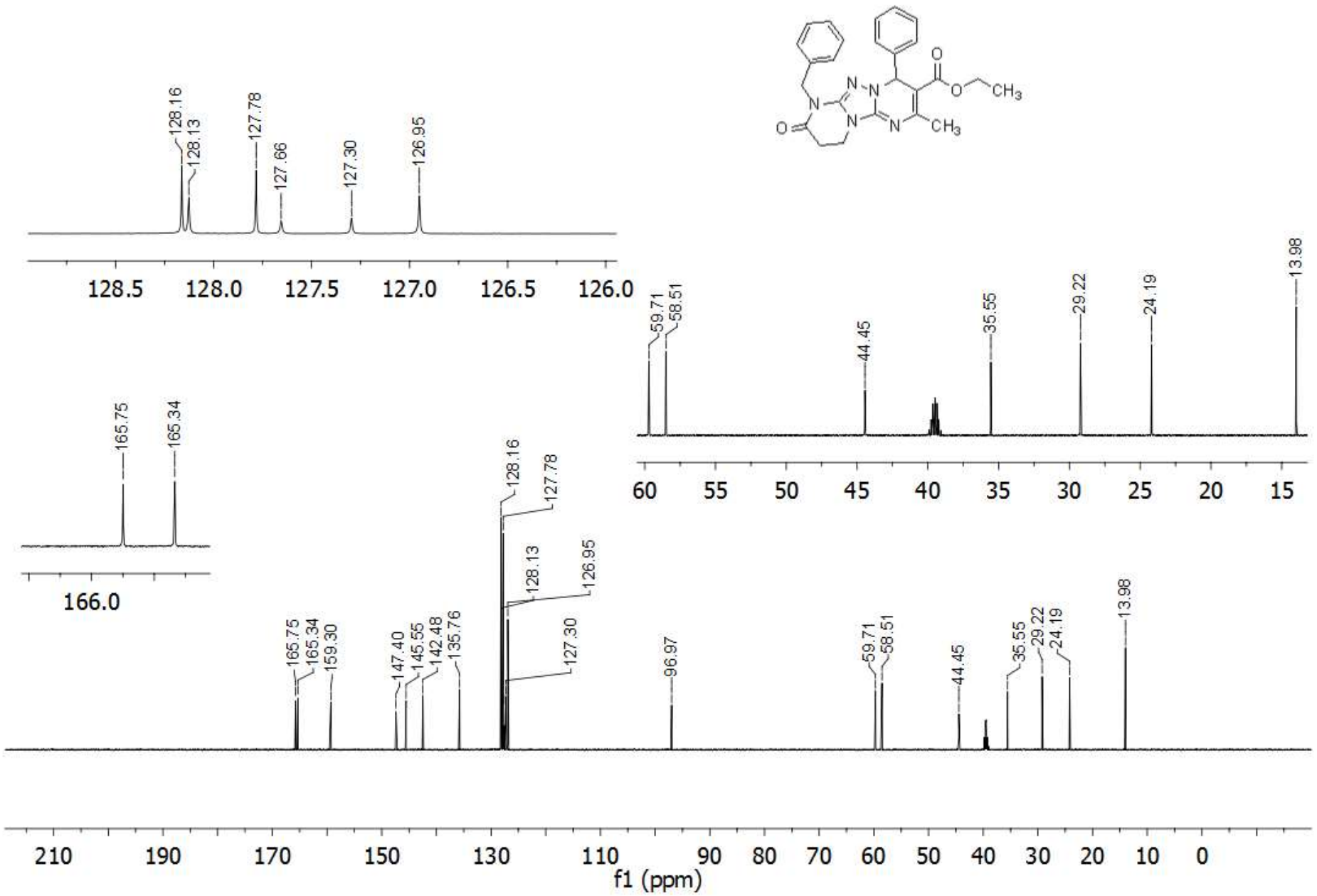
^{1}H-^{13}C HMBC spectrum of compound **23.**



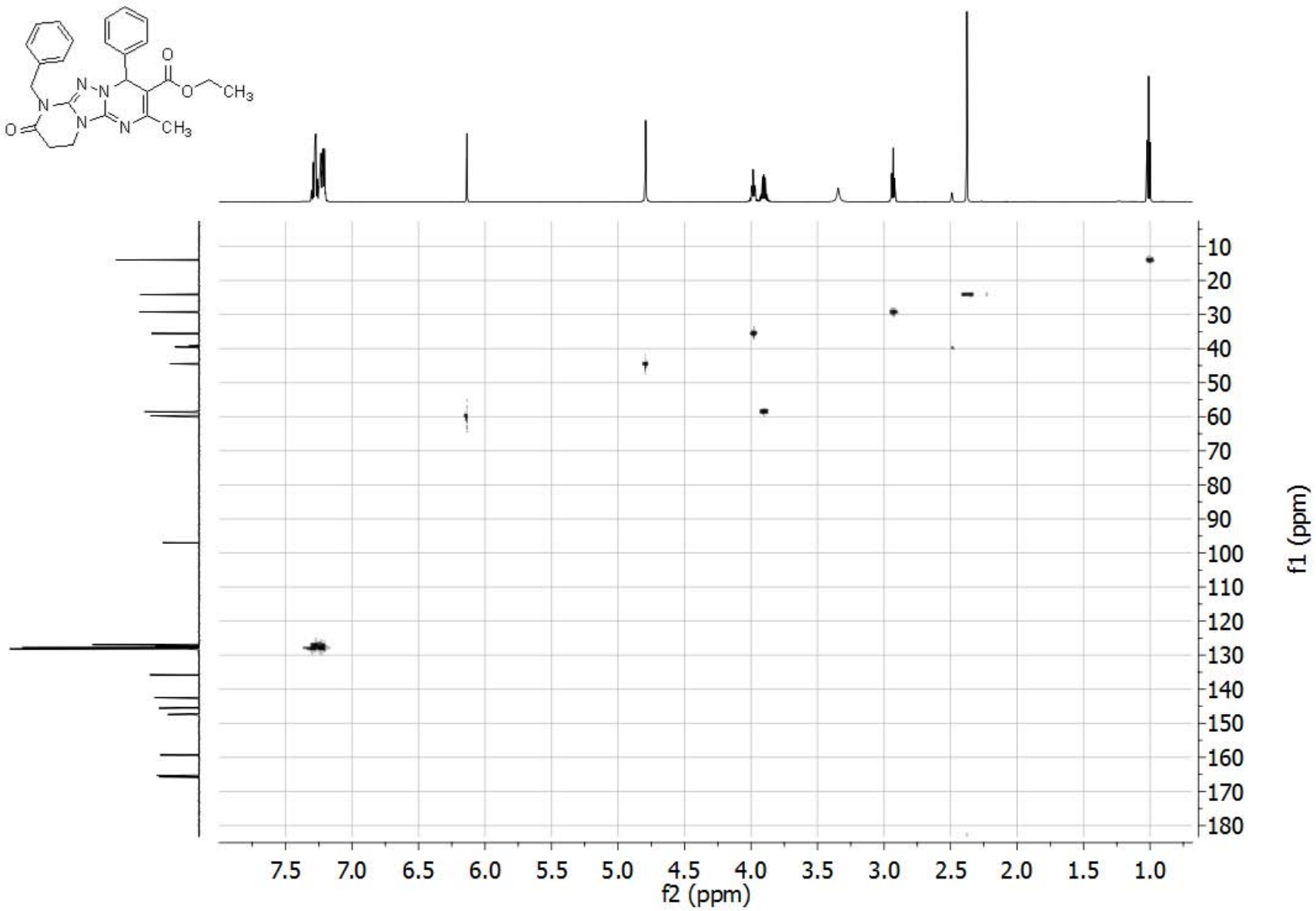
FTIR spectrum of compound **25** (ATR).



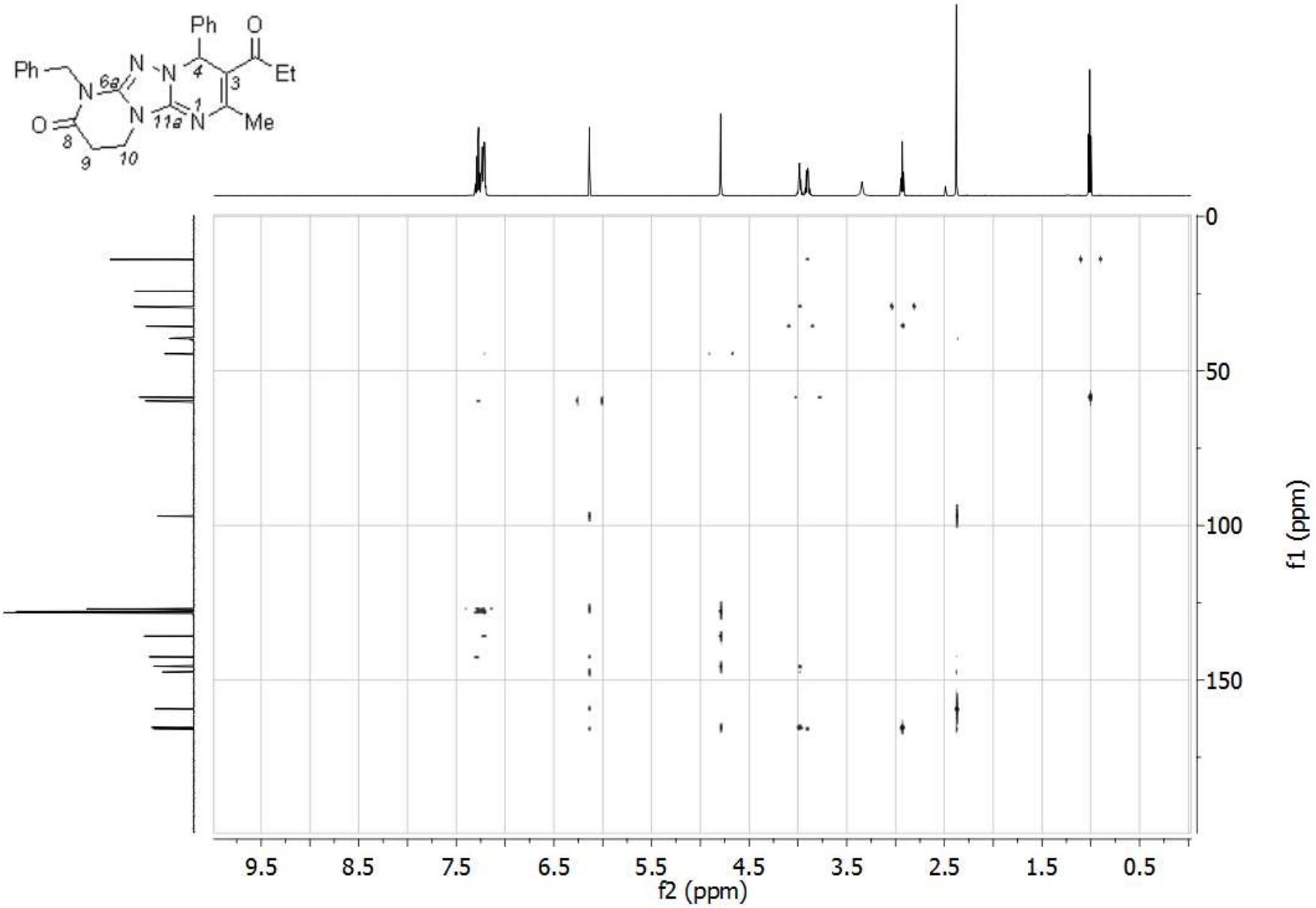
^{1}H NMR spectrum of compound **25** (600 MHz, DMSO-d_6).



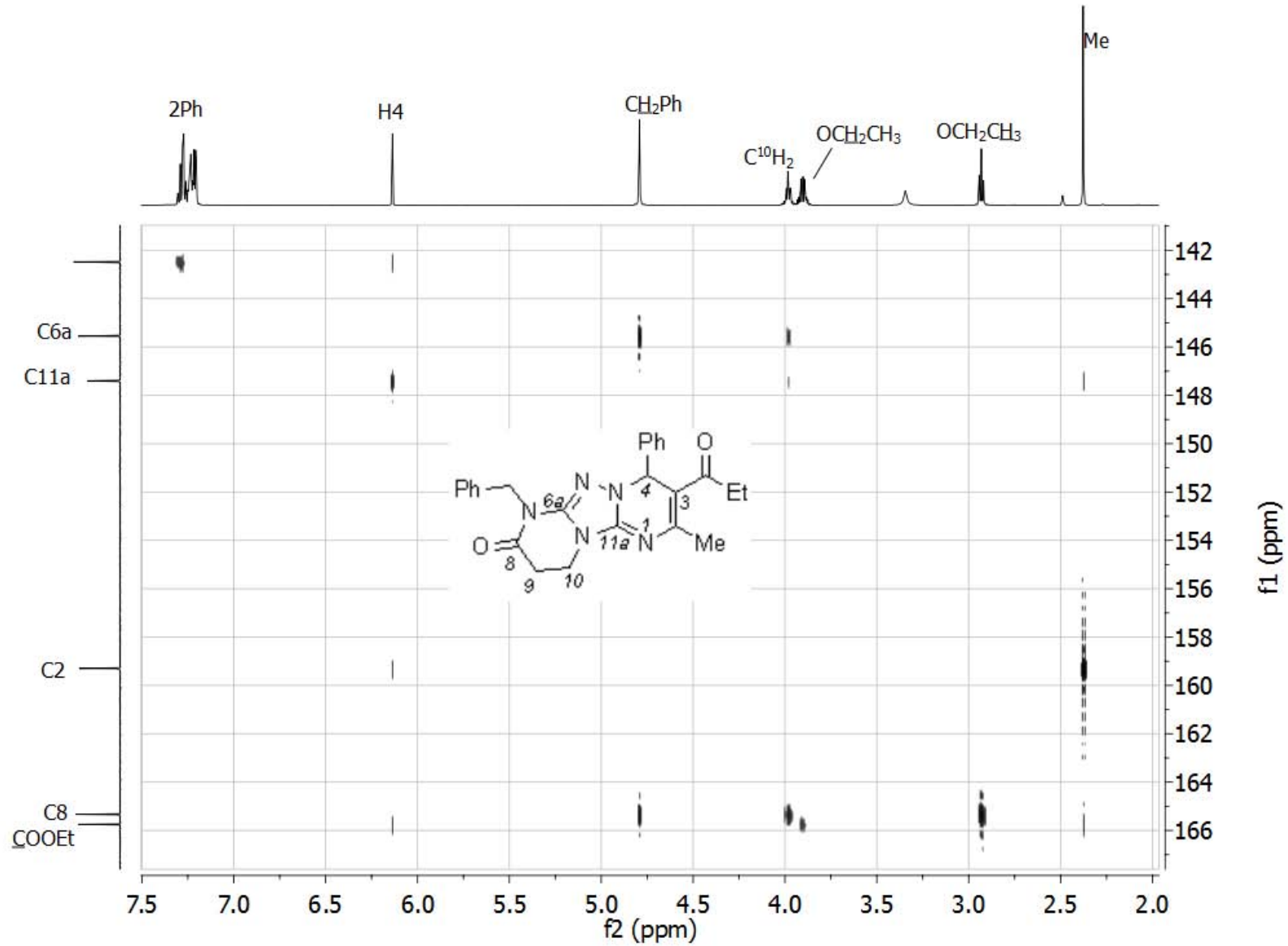
^{13}C NMR spectrum of compound **25** (150 MHz, DMSO-d_6).



^{1}H-^{13}C HSQC spectrum of compound **25** (DMSO-d_6).



^{1}H-^{13}C HMBC spectrum of compound **25** (DMSO-d_6).



Enlarged fragment of ^{1}H-^{13}C HMBC spectrum of compound **25.**

Detailed results of quantum chemical calculations

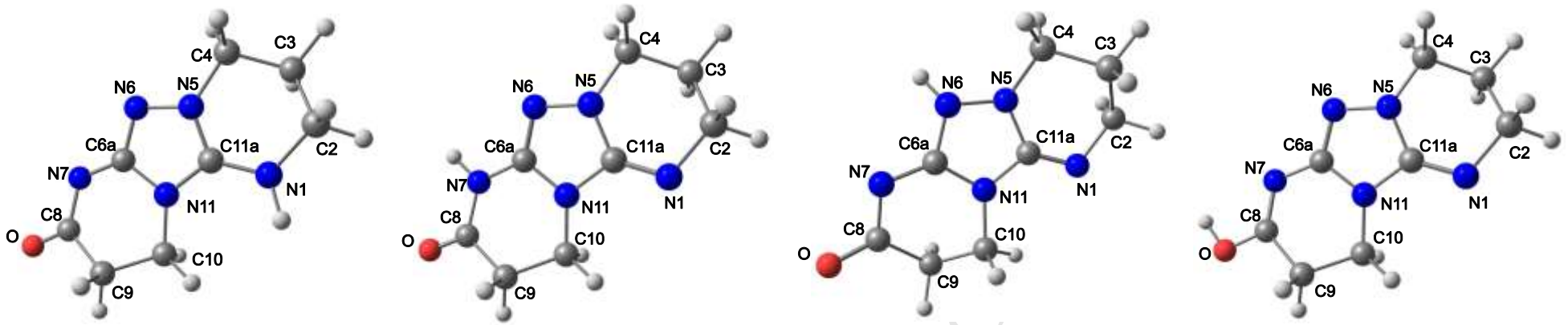
Table S1. Total Energies (*E*), Zero Point Energies (*ZPE*), Thermal corrections to Gibbs Free Energies (G_T^{298}) and Relative Energies[a], dipole moments (μ) and relative populations (*x*) of the stable conformers of tautomers **A-D** of compound **13** at 0 and 298 K calculated at the B3LYP 6-311++G(2d,2p)

Conformer	*E*, a.u	*ZPE*, kcal/mol	G_T^{298}, kcal/mol	Δ*E*, kcal/mol	ΔG^0, kcal/mol	ΔG^{298}, kcal/mol	ΔG^0, kJ/mol	ΔG^{298}, kJ/mol	*x*, %	μ, D
Vacuum (ε = 1)										
A-01	-660.628280	127.70	104.35	0.000	0.000	0.00	0.000	0.000	31.76	14.49
A-03	-660.628150	127.63	104.30	0.081	0.016	0.03	0.067	0.120	30.26	14.53
A-02	-660.627439	127.53	104.10	0.528	0.366	0.28	1.531	1.171	19.80	14.54
A-04	-660.626907	127.37	103.82	0.861	0.539	0.33	2.254	1.385	18.17	14.70
B-03	-660.652876	127.69	104.15	0.000	0.000	0.000	0.000	0.000	25.55	1.98
B-02	-660.652876	127.69	104.15	0.000	0.000	0.000	0.000	0.000	25.55	1.99
B-01	-660.652648	127.65	104.03	0.143	0.110	0.026	0.462	0.107	25.55	1.97
B-04	-660.652648	127.65	104.03	0.143	0.110	0.027	0.462	0.113	25.55	1.97
C-01	-660.633887	127.74	104.46	0.000	0.000	0.00	0.000	0.000	32.39	6.95
C-03	-660.633713	127.78	104.49	0.109	0.148	0.15	0.618	0.610	25.32	6.85
C-04	-660.633368	127.77	104.37	0.326	0.355	0.24	1.487	0.986	21.76	6.67
C-02	-660.633297	127.75	104.36	0.371	0.381	0.27	1.596	1.131	20.52	6.74
D-01	-660.637342	127.62	104.14	0.000	0.000	0.00	0.000	0.000	26.02	1.53
D-04	-660.637342	127.62	104.14	0.000	0.001	0.00	0.003	0.000	26.02	1.53
D-03	-660.637597	127.68	104.35	-0.160	-0.106	0.05	-0.442	0.199	24.02	1.52
D-02	-660.637597	127.68	104.35	-0.160	-0.105	0.05	-0.439	0.207	23.94	1.52
D-05	-660.627207	127.36	103.81	6.359	6.098	6.03	25.515	25.216	0.00	3.90
D-08	-660.627207	127.36	103.81	6.359	6.098	6.03	25.513	25.219	0.00	3.90
D-07	-660.627471	127.41	104.02	6.194	5.987	6.07	25.049	25.414	0.00	3.87
D-06	-660.627471	127.41	104.02	6.194	5.988	6.08	25.052	25.422	0.00	3.87
DMSO (ε = 46.7)										
A-04	-660.681008	127.10	103.61	0.000	0.000	0.00	0.000	0.000	39.03	20.45
A-02	-660.681095	127.19	103.93	-0.054	0.036	0.27	0.150	1.116	24.88	21.21
A-01	-660.681032	126.87	103.95	-0.015	-0.244	0.33	-1.020	1.379	22.38	21.18
A-03	-660.681067	127.38	104.26	-0.037	0.237	0.62	0.992	2.594	13.71	21.21
B-02	-660.677112	126.79	103.36	0.000	0.000	0.000	0.000	0.000	26.37	2.45
B-03	-660.677102	126.80	103.37	0.006	0.008	0.012	0.032	0.050	25.84	2.45
B-01	-660.676989	126.79	103.34	0.077	0.075	0.058	0.313	0.242	23.92	2.45
B-04	-660.676985	126.79	103.34	0.079	0.076	0.059	0.316	0.248	23.86	2.45
C-02	-660.664623	126.80	103.54	0.000	0.000	0.00	0.000	0.000	32.51	10.16
C-01	-660.664651	126.79	103.61	-0.018	-0.025	0.05	-0.106	0.227	29.66	10.35

Table S1 (continued)

C-04	-660.664318	126.81	103.55	0.191	0.198	0.21	0.828	0.862	22.95	10.11
C-03	-660.664056	126.83	103.64	0.356	0.386	0.46	1.614	1.937	14.88	10.27
D-03	-660.663209	126.58	103.26	0.000	0.000	0.00	0.000	0.000	26.04	2.86
D-02	-660.663209	126.58	103.26	-0.001	0.002	0.01	0.008	0.024	26.04	2.86
D-01	-660.663026	126.57	103.18	0.114	0.103	0.04	0.431	0.148	24.77	2.86
D-04	-660.663027	126.58	103.22	0.114	0.117	0.08	0.489	0.342	22.90	2.91
D-06	-660.658813	126.61	103.27	2.759	2.793	2.77	11.686	11.597	0.24	6.05
D-07	-660.658805	126.61	103.27	2.763	2.798	2.77	11.705	11.608	0.24	6.04
D-08	-660.658634	126.59	103.18	2.871	2.886	2.79	12.076	11.677	0.24	6.08
D-05	-660.658641	126.60	103.20	2.866	2.884	2.81	12.067	11.760	0.23	6.11
Water (ε = 78.4)										
A-03	-660.682578	127.14	103.85	0.000	0.000	0.00	0.000	0.000	34.33	21.37
A-02	-660.682583	127.15	103.86	-0.003	0.006	0.01	0.025	0.062	33.48	21.37
A-01	-660.682525	127.15	103.83	0.034	0.042	0.02	0.177	0.088	33.13	21.33
A-04	-660.682513	127.15	103.84	0.041	0.057	0.03	0.237	0.132	32.55	21.34
B-03	-660.677922	126.75	103.30	0.000	0.000	0.000	0.000	0.000	37.17	2.45
B-02	-660.677917	126.75	103.31	0.003	0.007	0.016	0.030	0.067	36.18	2.45
B-04	-660.677787	126.75	103.30	0.085	0.088	0.088	0.367	0.370	32.02	2.46
B-01	-660.677776	126.75	103.32	0.091	0.096	0.111	0.403	0.466	30.80	2.46
C-02	-660.665520	126.74	103.44	0.000	0.000	0.00	0.000	0.000	33.73	10.24
C-01	-660.665556	126.74	103.55	-0.022	-0.016	0.08	-0.067	0.348	29.31	10.42
C-04	-660.665243	126.77	103.51	0.174	0.203	0.24	0.848	1.011	22.44	10.18
C-03	-660.664893	126.76	103.55	0.393	0.420	0.50	1.759	2.090	14.52	10.34
D-03	-660.664091	126.53	103.21	0.000	0.000	0.00	0.000	0.000	26.12	2.89
D-02	-660.664096	126.53	103.22	-0.003	-0.003	0.00	-0.013	0.018	25.93	2.88
D-01	-660.663899	126.52	103.16	0.120	0.113	0.07	0.475	0.275	23.38	2.93
D-04	-660.663888	126.52	103.15	0.127	0.120	0.07	0.502	0.302	23.12	2.93
D-07	-660.660083	126.56	103.20	2.515	2.543	2.51	10.638	10.496	0.38	6.12
D-06	-660.660084	126.56	103.21	2.515	2.545	2.52	10.647	10.526	0.37	6.12
D-05	-660.659929	126.55	103.15	2.612	2.635	2.56	11.026	10.690	0.35	6.17
D-08	-660.659917	126.55	103.15	2.619	2.643	2.56	11.059	10.723	0.35	6.17

[a] Relative Gibbs Free Energies ΔG^0 and ΔG^{298} were computed from the relationships $\Delta G^0 = \Delta E + ZPE$ and $\Delta G^{298} = \Delta E + G_T{}^{298}$



13A **13B** **13C** **13D**

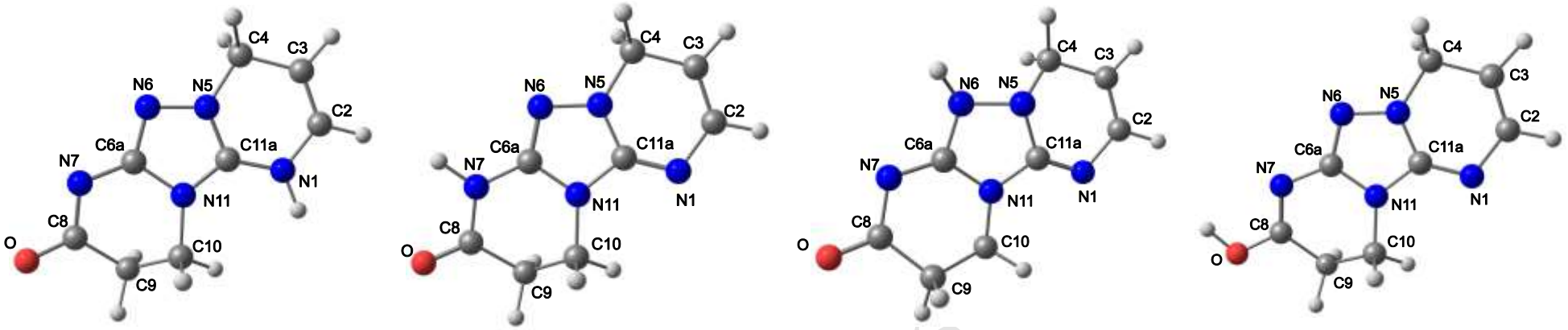
Figure S1. Optimized structures of tautomers **13A-D**

Table S2. Total Energies (*E*), Zero Point Energies (*ZPE*), Thermal corrections to Gibbs Free Energies (G_T^{298}) and Relative Energies[a], dipole moments (μ) and relative populations (*x*) of the most stable tautomers **A-D** of compound **13** at 0 and 298 K calculated at the B3LYP 6-311++G(2d,2p)

Tautomer	*E*, a.u	*ZPE*, kcal/mol	G_T^{298}, kcal/mol	Δ*E*, kcal/mol	ΔG^0, kcal/mol	ΔG^{298}, kcal/mol	ΔG^0, kJ/mol	ΔG^{298}, kJ/mol	*x*, %	μ, D
Vacuum (ε = 1)										
B-03	-660.652876	127.69	104.15	0.00	0.00	0.00	0.00	0.00	**100.00**	1.98
D-01	-660.637342	127.62	104.14	9.75	9.68	9.74	40.52	40.74	**0.00**	1.53
C-01	-660.633887	127.74	104.46	11.92	11.97	12.22	50.07	51.15	**0.00**	6.95
A-01	-660.628280	127.70	104.35	15.43	15.45	15.63	64.62	65.41	**0.00**	14.49
DMSO (ε = 46.7)										
A-04	-660.681008	127.10	103.61	0.00	0.00	0.00	0.00	0.00	**97.62**	21.21
B-02	-660.677112	126.79	103.36	2.44	2.14	2.20	8.94	9.21	**2.38**	2.45
C-02	-660.664623	126.80	103.54	10.28	9.98	10.21	41.75	42.73	**0.00**	10.16
D-03	-660.663209	126.58	103.26	11.17	10.64	10.82	44.53	45.27	**0.00**	2.86
Water (ε = 78.4)										
A-03	-660.682578	127.14	103.85	0.00	0.00	0.00	0.00	0.00	**98.21**	21.37
B-03	-660.677922	126.75	103.30	2.92	2.53	2.37	10.60	9.93	**1.79**	2.45
C-02	-660.665520	126.74	103.44	10.70	10.31	10.30	43.12	43.11	**0.00**	10.24
D-03	-660.664091	126.53	103.21	11.60	10.99	10.96	46.00	45.88	**0.00**	2.89

Table S3. Total Energies (*E*), Zero Point Energies (*ZPE*), Thermal corrections to Gibbs Free Energies (G_T^{298}) and Relative Energies[a], dipole moments (μ) and relative populations (*x*) of the stable conformers of tautomers **A-D** of compound **15** at 0 and 298 K calculated at the B3LYP 6-311++G(2d,2p)

Conformer	*E*, a.u	*ZPE*, kcal/mol	G_T^{298}, kcal/mol	Δ*E*, kcal/mol	ΔG^0, kcal/mol	ΔG^{298}, kcal/mol	ΔG^0, kJ/mol	ΔG^{298}, kJ/mol	*x*, %	μ, D
Vacuum (ε = 1)										
A-04	-659.399324	112.32	89.06	0.00	0.00	0.00	0.00	0.00	25.43	13.47
A-01	-659.399324	112.32	89.07	0.00	0.00	0.01	0.01	0.02	25.22	13.47
A-02	-659.399564	112.43	89.23	-0.15	-0.04	0.02	-0.16	0.08	24.67	13.41
A-03	-659.399564	112.43	89.23	-0.15	-0.04	0.02	-0.16	0.08	24.67	13.41
B-01	-659.429680	112.80	89.37	—	—	—	—	—	100.00	0.26
C-03	-659.407919	112.76	89.78	0.00	0.00	0.00	0.00	0.00	25.69	5.31
C-02	-659.407919	112.76	89.78	0.00	0.00	0.00	0.00	0.00	25.66	5.31
C-04	-659.407924	112.79	89.82	0.00	0.02	0.03	0.10	0.14	24.32	5.23
C-01	-659.407924	112.79	89.82	0.00	0.02	0.03	0.10	0.14	24.32	5.23
D-01	-659.414956	112.85	89.69	0.00	0.00	0.00	0.00	0.00	100.00	3.31
D-02	-659.404749	112.60	89.40	6.41	6.16	6.11	25.78	25.56	0.00	5.13
DMSO (ε = 46.7)										
A-01	-659.452134	111.64	88.21	—	—	—	—	—	100.00	19.99
B-01	-659.455165	111.81	88.53	—	—	—	—	—	100.00	0.31
C-02	-659.439565	111.65	88.72	0.00	0.00	0.00	0.00	0.00	28.64	8.34
C-03	-659.439561	111.66	88.73	0.00	0.01	0.01	0.02	0.05	28.08	8.34
C-01	-659.439320	111.67	88.73	0.15	0.17	0.16	0.70	0.66	21.91	8.29
C-04	-659.439304	111.67	88.73	0.16	0.18	0.17	0.74	0.73	21.36	8.31
D-01	-659.441717	111.63	88.50	0.00	0.00	0.00	0.00	0.00	99.13	5.21
D-02	-659.437287	111.67	88.52	2.78	2.82	2.81	11.80	11.74	0.87	7.80
Water (ε = 78.4)										
A-01	-659.453709	111.51	87.81	—	—	—	—	—	100.00	20.18
B-01	-659.455964	111.77	88.49	—	—	—	—	—	100.00	0.35
C-03	-659.440526	111.61	88.68	0.00	0.00	0.00	0.00	0.00	30.05	8.42
C-02	-659.440536	111.62	88.71	-0.01	0.01	0.02	0.02	0.10	28.86	8.40
C-01	-659.440229	111.63	88.71	0.19	0.21	0.22	0.88	0.92	20.76	8.36
C-04	-659.440220	111.64	88.72	0.19	0.22	0.23	0.91	0.97	20.32	8.36
D-01	-659.442607	111.57	88.42	0.00	0.00	0.00	0.00	0.00	98.77	5.24
D-02	-659.438552	111.62	88.48	2.54	2.60	2.60	10.88	10.88	1.23	7.87



15A **15B** **15C** **15D**

Figure S2. Optimized structures of tautomers **15A-D**

Table S4. Total Energies (*E*), Zero Point Energies (*ZPE*), Thermal corrections to Gibbs Free Energies (G_T^{298}) and Relative Energies[a], dipole moments (μ) and relative populations (*x*) of the most stable tautomers **A-D** of compound **15** at 0 and 298 K calculated at the B3LYP 6-311++G(2d,2p)

Tautomer	E, a.u	*ZPE*, kcal/mol	G_T^{298}, kcal/mol	ΔE, kcal/mol	ΔG^0, kcal/mol	ΔG^{298}, kcal/mol	ΔG^0, kJ/mol	ΔG^{298}, kJ/mol	*x*, %	μ, D
Vacuum (ε = 1)										
B-01	-659.429680	112.80	89.37	0.00	0.00	0.00	0.00	0.00	100.00	0.26
D-01	-659.414956	112.85	89.69	9.24	9.28	9.56	38.84	40.00	0.00	3.31
C-02	-659.407919	112.76	89.78	13.66	13.61	14.06	56.96	58.84	0.00	5.31
A-04	-659.399324	112.32	89.06	19.05	18.57	18.74	77.68	78.39	0.00	13.41
DMSO (ε = 46.7)										
B-01	-659.455165	111.81	88.53	0.00	0.00	0.00	0.00	0.00	93.54	0.31
A-01	-659.452134	111.64	88.21	1.90	1.73	1.58	7.23	6.63	6.46	19.99
D-01	-659.441717	111.63	88.50	8.44	8.26	8.41	34.56	35.17	0.00	5.21
C-02	-659.439565	111.65	88.72	9.79	9.63	9.98	40.31	41.76	0.00	8.34
Water (ε = 78.4)										
B-01	-659.455964	111.77	88.49	0.00	0.00	0.00	0.00	0.00	77.58	0.35
A-01	-659.453709	111.51	87.81	1.41	1.15	0.74	4.82	3.08	22.42	20.18
D-01	-659.442607	111.57	88.42	8.38	8.18	8.31	34.22	34.79	0.00	5.24
C-03	-659.440526	111.61	88.68	9.69	9.53	9.87	39.86	41.30	0.00	8.42

Crystallographic data and X-ray experimental parameters

Table S5. The crystallographic data and X-ray experimental parameters for compounds **5d, 14c** and **15a**.

Parameter	**5d**	**14c**	**15a**
Unit cell dimensions			
a, Å	9.371(1)	9.3966(5)	11.9256(6)
b, Å	12.718(2)	22.3229(7)	14.6014(6)
c, Å	13.094(2)	8.1870(4)	39.538(2)
α, deg.	93.590(3)	90.0	90.0
β, deg.	90.874(3)	103.447(5)	93.855(5)
γ, deg.	93.431(2)	90.0	90.0
V, Å^3	1554.3(4)	1670.2(1)	6869.2(5)
F(000)	672	776	2976
Crystal system	Triclinic	Monoclinic	Monoclinic
Space group	P-1	$P2_1/c$	C2/c
Z	4	4	16
T, K	100	293	293
μ, mm^{-1}	0.255	0.099	0.097
D_{calc}, g/cm^3	1.367	1.477	1.367
$2\Theta_{max}$, grad	52	50	50
Measured reflections	14030	9507	17997
Independent reflections	5998	2889	5843
R_{int}	0.034	0.025	0.045
Reflections with $F>4\sigma(F)$	5332	2017	3938
Parameters	400	255	482
R_1	0.079	0.040	0.062
wR_2	0.213	0.118	0.161
S	1.110	1.015	1.054
CCDC number	811047	957615	957616