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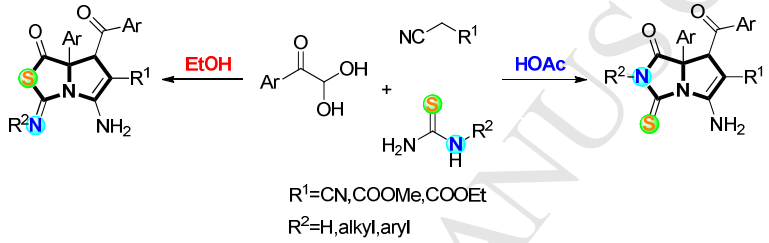

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ABSTRACT

A highly efficient chemoselective synthesis of multifunctionalized tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole and tetrahydropyrrolo[1,2-*c*]thiazole derivatives has been established from arylglyoxal monohydrates, nitriles, and thioureas. A series of control experiments suggested that this reaction proceeded through the convergent integration of two self-sorting domino sequences. This synthetic strategy is promising for diversity-oriented synthesis of alkaloid analogues.

1. Introduction

In recent years, multicomponent domino reactions (MDRs) have been broadly utilized for the construction of diverse and complex molecules through the sequential combination of three or more simple substrates in a single synthetic operation.[1] In most cases, the reported MDRs proceeded along a linear synthetic route (Scheme 1a).[2] Based on our interest in novel domino reactions, we have successfully developed a self-sorting domino reaction, which allowed a single substrate to be simultaneously involved in multiple different domino sequences and generated suitable intermediates to converge on the product in a one-pot process (Scheme 1b).[3] In this work, a novel synthetic strategy, the combination of MDRs and self-sorting domino reactions is discussed. In this multicomponent self-sorting domino reaction strategy, it was envisioned that the single substrate **A** could be divided into two parts to react with substrates **B** and **C**, respectively, in two independent branching synthetic routes; and the corresponding intermediates **A-B** and **A-C** could finally react with each other to converge on the target molecule (Scheme 1c).

Tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole derivatives have broad applications in medicinal[4] and agrochemical[5] chemistry. However, up to now, rare examples have been reported for their synthesis, which proceeded through the construction of pyrrolidine ring from limited substrates imidazolidine-2,4-dione or 2-thioxoimidazolidin-4-one (Scheme 2a).[6] Functionalized pyrrolothiazoles are the central skeletons for numerous alkaloids and endowed with a wide range of biological activities such as hepatoprotective,[7] antibiotic,[8] antidiabetic,[9] anticonvulsant,[10] and antileukemic[11] actions. The synthetic analogues of pyrrolo[1,2-*c*]thiazoles also have significance in drug discovery[12] and agrochemical applications[13]. However, reports on their synthesis are scarce.[12,14] The main and universal synthetic method focused on the construction of pyrrolidine ring via 1,3-dipolar cycloaddition of azomethine ylides generated in situ from the reaction of thiazolidine-4-carboxylic acid and dicarbonyl compounds to dipolarophiles[12c-12e,14] (Scheme 2b). In this work, based on the aforementioned multicomponent self-sorting domino reaction strategy, we reported a novel method for chemoselective synthesis of multifunctionalized tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole and tetrahydropyrrolo[1,2-*c*]thiazole derivatives from simple and readily available substrates, which went through the simultaneous construction of pyrrolidine and imidazolidine or thiazolidine rings (Scheme 2c).

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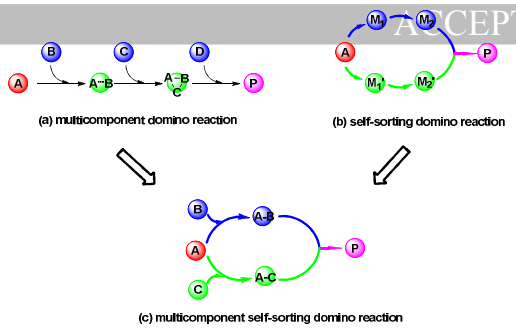
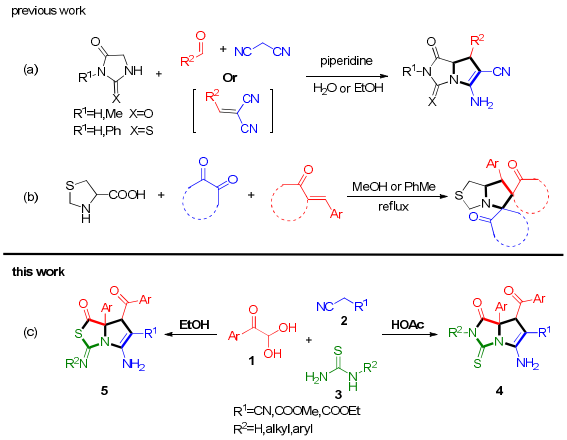


Scheme 1. Domino reaction strategies.



Scheme 2. Protocols for the synthesis of pyrrolo[1,2-*c*]imidazole and pyrrolo[1,2-*c*]thiazoles.

2. Results and Discussion

Our study commenced by optimizing the reaction conditions in order to achieve the chemoselectivity towards skeleton **4** or **5** respectively, using phenylglyoxal monohydrate **1a**, malononitrile **2a** and thiourea **3a** as model substrates. To our delight, product **4aa** was provided in 26% yield in refluxing methanol, with **5aa** obtained in 38% yield (Table 1, Entry 1). Subsequently, a series of other alcohols (ethanol, isopropanol, *t*-butanol, and glycol) were screened as the solvent (Table 1, Entries 2-5). Much to our satisfaction, EtOH was found most effective to produce **5aa** with trace amount of **4aa**. Other solvents, such as CH_3CN, 1,4-dioxane and THF nearly gave no reaction (Table 1, Entries 6-8), and DMF, DMSO and Ac_2O gave the poor conversion (Table 1, Entries 9-11). To our surprise, when the reaction proceeded in HOAc at 60 °C, **4aa** was obtained in 48% isolated yield without **5aa** produced (Table 1, Entry 12). Then, a range of different temperatures were examined to improve the yields, and 100 °C was found to give the best yield of compound **4aa** (Table 1, Entries 13-15). In addition, variations to the temperature gradient in EtOH were also tested, but better yields of **5aa** were not achieved (Table 1, Entries 16-18 vs Entry 2). Based on the experiments described above, the optimal reaction conditions were determined as follows: the reaction in HOAc at 100 °C yielded compound **4aa** as a sole product, while in EtOH at 80 °C gave compound **5aa** as the major product.

Table 1. Optimization of the reaction conditions for the selective synthesis of **4aa** and **5aa**.[a]

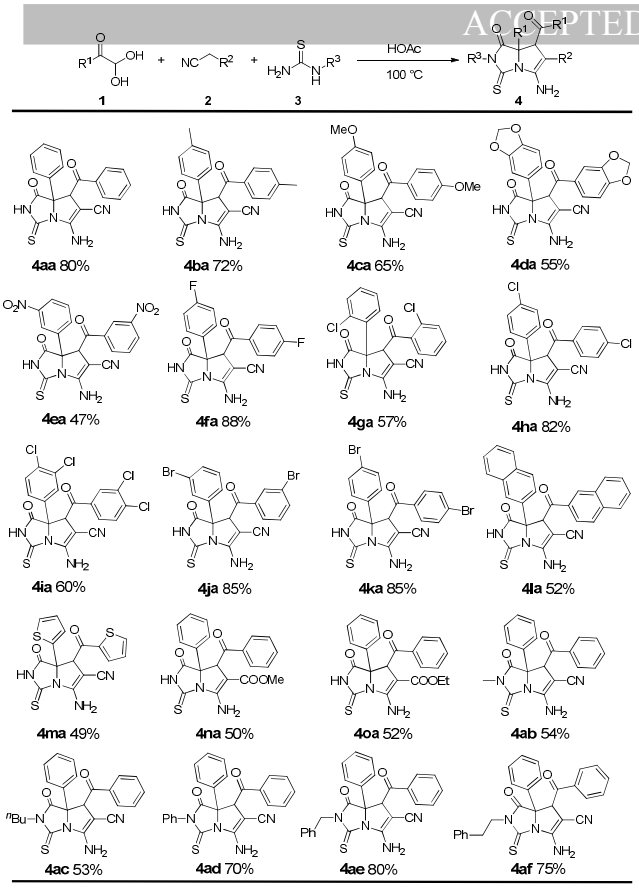
Entry	Solvent	Temp (°C)	Time (min)	yield[b] (%) **4aa**	**5aa**
1	MeOH	65	40	26	38
2	**EtOH**	**80**	**40**	**trace**	**85**
3	*i*-PrOH	80	40	trace	78
4	*t*-BuOH	80	20	12	15
5	glycol	80	30	trace	0
6	CH_3CN	80	30	trace	0
7	1,4-dioxane	100	60	trace	0
8	THF	66	60	0	0
9	DMF	130	40	10	12
10	DMSO	110	30	14	17
11	Ac_2O	110	60	11	0
12	HOAc	60	60	48	0
13	HOAc	80	40	66	0
14	**HOAc**	**100**	**20**	**80**	**0**
15	HOAc	120	30	68	0
16	EtOH	r.t.	30	trace	50
17	EtOH	40	30	trace	54
18	EtOH	60	30	trace	60

[a]Reaction was performed with **1a** (2.0 mmol), **2a** (1.2 mmol), **3a** (1.0 mmol), solvent (3 mL).
[b]Isolated yields.

With the optimized conditions in hand, the generality and scope of tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazoles **4** synthesis with HOAc as the solvent was investigated. To our delight, the reaction demonstrated wide tolerence for diverse substituents of arylglyoxals, nitriles, and thioureas, as shown in Table 2. Arylglyoxals bearing electron-neutral (e.g., 4-H, 4-Me), electron-rich (e.g., 4-OMe, 3,4-OCH_2O), electron-deficient (e.g., 3-NO_2), and halogenated (e.g., 4-F, 2-Cl, 4-Cl, 3,4-Cl_2, 3-Br, 4-Br) substituents were converted to the corresponding products in moderate to excellent yields (47−88%; **4aa**−**4ka**). In addition, 2-naphthyl and heteroaryl substituents (e.g., 2-thienyl) gave the moderate yields (49−52%; **4la**−**4ma**). Notably, methyl 2-cyanoacetate and ethyl 2-cyanoacetate could also afford the products **4na** and **4oa** in 50% and 52% yields, respectively. Furthermore, a variety of thioureas with different substituents, such as methyl, *n*-butyl, phenyl, benzyl, and phenethyl groups, were also explored. Gratifyingly, both *N*-alkyl and *N*-aryl thioureas were well tolerated under the reaction conditions and afforded the expected products in satisfactory yields (53−80%; **4ab**−**4af**). The structures of **4ab** and **4ad** were also unambiguously confirmed by X-ray diffraction analysis (See Supplementary Information (SI)).

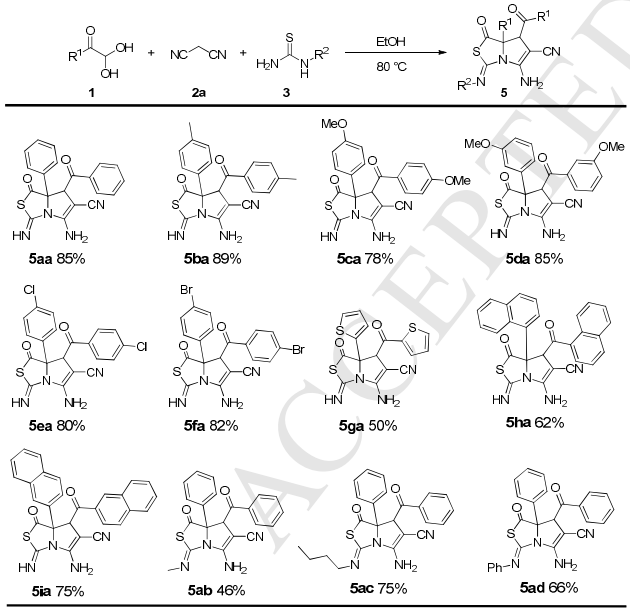
After the successful synthesis of tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazoles **4**, our attention turned to the reaction scope of tetrahydropyrrolo[1,2-*c*]thiazoles **5**, using EtOH to replace HOAc as the solvent (Table 3). Much to our satisfaction, a set of diverse substituted arylglyoxals with groups such as methyl, methoxy, chloro and bromo groups were found compatible under the optimal reaction conditions with good yields (78−89%; **5ba**−**5fa**). Meanwhile, heterocycle (e.g., 2-thiophenyl) and steric hindrance (e.g., 1-naphthyl and 2-naphthyl) arylglyoxals were also tolerated in this reaction to afford the desired products **5ga**-**5ia** in 50-75% yields. Additionally, *N*-alkyl and *N*-aryl thioureas were also examined, which reacted smoothly with **1a** and **2a** to obtain the desired products (46−75%; **5ab**−**5ad**). The structure of **5aa** was unambiguously confirmed by X-ray diffraction analysis (See SI).

Table 2. Scope of arylglyoxals, nitriles and thioureas for tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazoles **4** [a]

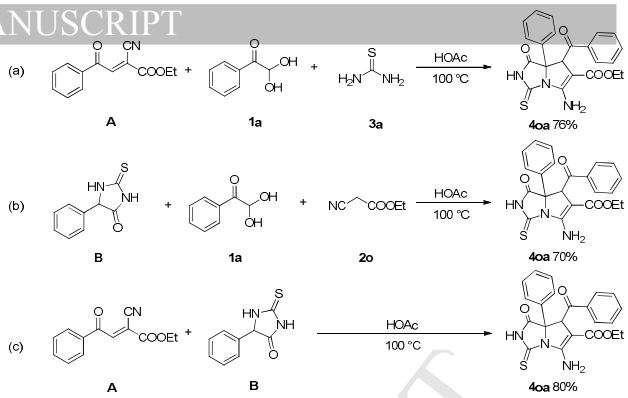


[a]Reaction was performed with **1** (2.0 mmol), **2** (1.2 mmol), **3** (1.0 mmol) in HOAc (3 mL) at 100 °C for 20-60 min.

Table 3. Scope of arylglyoxals and thioureas for tetrahydropyrrolo[1,2-*c*]thiazoles **5** [a]

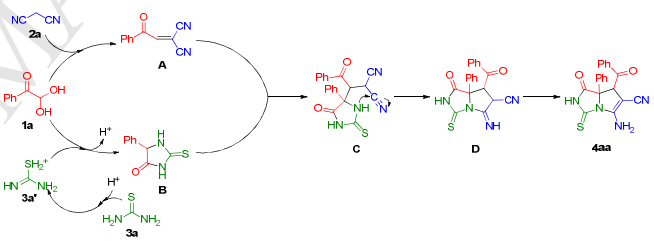


[a]Reaction was performed with **1** (2.0 mmol), **2a** (1.2 mmol), **3** (1.0 mmol) in EtOH (3 mL) at 80 °C for 20-60 min.

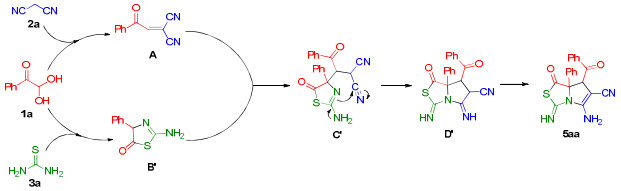


Scheme 3. Control experiments to prove the mechanism

To gain some insight into the mechanism of the tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazoles **4** synthesis, a series of control experiments were performed as shown in Scheme 3. (*E*)-Ethyl 2-cyano-4-oxo-4-phenylbut-2-enoate **A** was firstly synthesized according to a known method,[15] and subsequently reacted with phenylglyoxal monohydrate **1a** and thiourea **3a** under the standard conditions to afford the corresponding product **4oa** in 76% yield (Scheme 3a). The prefabricated 5-phenyl-2-thioxoimidazolidin-4-one **B** was subjected to the reaction with **1a** and ethyl 2-cyanoacetate **2o** under the standard conditions to furnish the product **4oa** in 70% yield (Scheme 3b). Moreover, treatment with **A** and **B** under the standard conditions directly generated the highest yield of the target product **4oa** (Scheme 3c). These results clearly confirmed that **A** and **B** were the key intermediates in this transformation.



Scheme 4. Possible mechanism for forming tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazoles **4**



Scheme 5. Possible mechanism for forming tetrahydropyrrolo [1,2-*c*]thiazoles **5**

Based on the above results and previous literature,[16] a feasible mechanism for the formation of tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazoles **4** was presented in Scheme 4. Initially, intermediate **A** was formed by means of a Knoevenagel condensation between phenylglyoxal monohydrate **1a** and malononitrile **2a**. Simultaneously, thiohydantoin intermediate **B** was formed via condensation of **1a** and thiourea **3a**.[16b-16c] Then, the Michael addition of intermediate **B** to intermediate **A** gave intermediate **C**,[16e] which subsequently underwent intramolecular cyclization to form intermediate **D**. Finally, **D** tautomerized to the product **4aa**.

A possible and similar mechanism was also proposed for the synthesis of tetrahydropyrrolo[1,2-*c*]thiazole derivatives **5** in accordance with the relative literature,[16,17] as shown in Scheme 5. The phenylglyoxal monohydrate **1a** reacted with malononitrile **2a** and thiourea **3a**, respectively, to afford intermediate **A** and 2-

aminothiazol-5(4*H*)-one **B'**, which further reacted with each other to form intermediate **C'**. Subsequently, **C'** underwent intramolecular cyclization and tautomerization to yield product **5aa**. These reaction mechanisms were consistent with the designed multicomponent self-sorting domino reactions strategy.

It can be postulated that the chemoselectivity towards skeletons **4** and **5** depends on the relative acidity of the solvents. We thought the S-lone pair electron on the sulfur atom of the thiourea **3a** would combine with the acid proton to form **3a'** and the affinity of sulfur atom would be reduced with HOAc as the solvent, so we proposed the condensation product of **1a** and **3a** would be **B** (Scheme 4). This orientation led to the product **4aa**. Acid solvent favored skeleton **4**, while neutral solvent led to skeleton **5** as the major product because the protonation ability of sulfur atom of the thiourea in neutral solvent (EtOH) was worse than that in acid solvent (HOAc).

3. Conclusion

In conclusion, a convenient and efficient multicomponent self-sorting domino reaction has been established for the chemoselective synthesis of tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole and tetrahydropyrrolo[1,2-*c*]thiazole derivatives through solvent-switching. Initial studies of the mechanism suggest that this reaction proceeded through the convergent integration of two self-sorting domino sequences. This practical synthetic strategy also demonstrated potential for the construction of complex heterocyclic compounds. Further studies of the application of this multicomponent self-sorting domino reaction are currently underway in our laboratory and will be reported in due course.

4. Experimental

4.1. General

All substrates and reagents were commercially available and used without further purification. TLC analysis was performed using pre-coated glass plates. Column chromatography was performed using silica gel (200–300 mesh). IR spectra were recorded on a Perkin-Elmer PE-983 infrared spectrometer as KBr pellets with absorption in cm^{-1}.^{1}H spectra were recorded in $CDCl_3$ or DMSO-d_6 on 400/600 MHz NMR spectrometers and resonances (δ) are given in parts per million relative to tetramethylsilane. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz) and integration. ^{13}C spectra were recorded in $CDCl_3$ or DMSO-d_6 on 100/150 MHz NMR spectrometers and resonances (δ) are given in ppm. HRMS were obtained on a Bruker Apex-Ultra 7.0T FTMS equipped with an electrospray source (ESI or APCI). The X-ray crystal structure determination of **4ab**, **4ad** and **5aa** were obtained on a Bruker SMART APEX CCD system. Melting points were determined using XT-4 apparatus and not corrected.

4.2. General procedure for synthesis of 4 and 5

4.2.1 General procedure for synthesis of 4 (4aa as an example)

A mixture of phenylglyoxal monohydrate **1a** (2.0 mmol), malononitrile **2a** (1.2 mmol), thiourea **3a** (1.0 mmol) in HOAc (3 mL) was stirred at 100 °C for 20 min till almost completed conversion of the substrates by TLC analysis, then extracted with EtOAc three times (3×50 mL). The extract was washed with 10% $NaHCO_3$ solution (w/w), dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc) to afford the product **4aa** as a yellow solid.

4.2.2 General procedure for synthesis of 5 (5aa as an example)

A mixture of phenylglyoxal monohydrate **1a** (2.0 mmol), malononitrile **2a** (1.2 mmol), thiourea **3a** (1.0 mmol) in EtOH (3 mL) was stirred at 80 °C for 40 min till almost completed conversion of the substrates by TLC analysis, then extracted with EtOAc three times (3×50 mL). The extract was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc) to afford the product **5aa** as a yellow solid.

4.3. Characterization data

4.3.1 *5-amino-7-benzoyl-1-oxo-7a-phenyl-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile (**4aa**)*

Yield 80%; yellow solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.87 (s, 1H), 8.15 (d, J = 8.0 Hz, 2H), 8.00 (s, 2H), 7.74 (t, J = 7.0 Hz, 1H), 7.66-7.56 (m, 4H), 7.55-7.42 (m, 3H), 5.08 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 196.0, 181.0, 172.9, 154.7, 136.1, 134.7, 133.9, 129.5, 129.3, 129.1, 128.9, 125.0, 117.1, 76.4, 59.7, 55.1. IR (KBr): 3438, 3300, 3141, 2923, 2361, 2195, 1770, 1669, 1634, 1583, 1465, 1448, 1239, 1163, 1105, 738, 694, 544 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{15}N_4O_2S$: 375.0910; found: 375.0908.

4.3.2 *5-amino-7-(4-methylbenzoyl)-1-oxo-3-thioxo-7a-(p-tolyl)-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile (**4ba**)*

Yield 72%; yellow solid. mp 103-104 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.81 (s, 1H), 8.02 (d, J = 7.6 Hz, 2H), 7.95 (s, 2H), 7.43 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 7.6 Hz, 2H), 4.97 (s, 1H), 2.40 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 195.6, 181.0, 173.0, 154.7, 145.4, 138.9, 133.2, 131.6, 129.6, 129.5, 129.1, 124.8, 117.1, 76.3, 59.9, 55.0, 21.3, 20.6. IR (KBr): 3403, 2957, 2924, 2853, 2189, 1765, 1670, 1644, 1460, 1361, 1251, 1021, 851, 816, 599 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{19}N_4O_2S$: 403.1223; found: 403.1231.

4.3.3 *5-amino-7-(4-methoxybenzoyl)-7a-(4-methoxyphenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile (**4ca**)*

Yield 65%; yellow solid. mp 128-129 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.77 (s, 1H), 8.11 (d, J = 8.8 Hz, 2H), 7.92 (s, 1H), 7.46 (d, J = 8.8 Hz, 2H), 7.08 (t, J = 8.8 Hz, 4H), 4.94 (s, 1H), 3.88 (s, 3H), 3.79 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 194.6, 181.6, 164.4, 160.0, 132.1, 127.9, 126.9, 126.4, 117.3, 114.5, 114.3, 76.2, 60.1, 55.8, 55.4, 55.0. IR (KBr): 3408, 2959, 2925, 2853, 2187, 1764, 1644, 1598, 1257, 1024, 803, 541 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{19}N_4O_4S$: 435.1122; found: 435.1124.

4.3.4 *5-amino-7a-(benzo[d][1,3]dioxol-5-yl)-7-(benzo[d][1,3]dioxole-5-carbonyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile (**4da**)*

Yield 55%; white solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.77 (s, 1H), 7.92 (s, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.59 (s, 1H), 7.14-7.07 (m, 2H), 7.03 (d, J = 8.4 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 6.19 (d, J = 4.0 Hz, 2H), 6.09 (d, J = 7.2 Hz, 2H), 4.95 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 194.2, 181.0, 173.1, 154.5, 152.9, 148.2, 148.2, 148.0, 129.6, 128.6, 126.9, 118.3, 117.3, 108.5, 108.3, 106.1, 102.5, 101.8,

76.3, 60.1, 54.9. IR (KBr): 3408, 3131, 2194, 1766, 1664, 1644, 1442, 1250, 1110, 1039, 820, 538 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{15}N_4O_6S$: 463.0707; found: 463.0703.

4.3.5 *5-amino-7-(3-nitrobenzoyl)-7a-(3-nitrophenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile (**4ea**)*
Yield 47%; yellow solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 13.12 (s, 1H), 8.85 (s, 1H), 8.57 (t, J = 8.4 Hz, 2H), 8.44 (s, 1H), 8.38 (d, J = 8.4 Hz, 1H), 8.20 (s, 2H), 8.05 (d, J = 8.0 Hz, 1H), 7.94-7.83 (m, 2H), 5.38 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 193.7, 181.2, 172.2, 154.7, 148.2, 148.1, 137.8, 135.8, 134.9, 131.9, 131.9, 130.8, 128.9, 124.4, 124.1, 120.4, 117.0, 75.5, 58.3, 55.5. IR (KBr): 3457, 3318, 3172, 2194, 1741, 1686, 1529, 1489, 1346, 1184, 728, 678 cm^{-1}. HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{20}H_{13}N_6O_6S$: 465.0612; found: 465.0614.

4.3.6 *5-amino-7-(4-fluorobenzoyl)-7a-(4-fluorophenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile (**4fa**)*
Yield 88%; yellow solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 12.89 (s, 1H), 8.28-8.18 (m, 2H), 8.00 (s, 2H), 7.65-7.56 (m, 2H), 7.43 (t, J = 9.0 Hz, 2H), 7.38 (t, J = 9.0 Hz, 2H), 5.08 (s, 1H).^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 194.5, 181.1, 172.9, 167.3, 164.8, 163.9, 161.4, 154.7, 132.9, 132.8, 132.1, 130.7, 127.5, 127.4, 117.1, 116.2, 116.0, 75.9, 59.4, 55.1. IR (KBr): 3382, 3305, 3254, 3195, 2195, 1765, 1647, 1592, 1458, 1361, 1237, 1157, 1091, 838, 699, 543cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{13}F_2N_4O_2S$: 411.0722; found: 411.0726.

4.3.7 *5-amino-7-(2-chlorobenzoyl)-7a-(2-chlorophenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile (**4ga**)*
Yield 57%; yellow solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 12.94 (s, 1H), 8.15 (d, J = 8.4 Hz, 2H), 8.02 (s, 2H), 7.66 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 9.0 Hz, 2H), 7.58 (d, J = 8.4 Hz, 2H), 5.09 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 194.7, 181.0, 172.5, 154.6, 139.8, 138.6, 135.3, 134.9, 134.2, 132.7, 132.6, 131.4, 129.4, 129.1, 127.1, 117.0, 75.8, 59.2, 55.0. IR (KBr): 3320, 3132, 2182, 1760, 1672, 1646, 1588, 1371, 1260, 1094, 1011, 859, 762, 538 cm^{-1}. HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{20}H_{13}Cl_2N_4O_2S$: 443.0131; found: 443.0128.

4.3.8 *5-amino-7-(4-chlorobenzoyl)-7a-(4-chlorophenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile (**4ha**)*
Yield 82%; yellow solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.92 (s, 1H), 8.15 (d, J = 8.8 Hz, 2H), 8.00 (s, 2H), 7.66 (d, J = 8.4 Hz, 2H), 7.64-7.57 (m, 4H), 5.09 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 194.7, 181.1, 172.6, 154.7, 139.9, 134.9, 134.3, 132.6, 131.5, 129.1, 127.1, 117.1, 75.8, 59.2, 55.1. IR (KBr): 3380, 3305, 3252, 3192, 2968, 2361, 2195, 1764, 1645, 1586, 1490, 1458, 1362, 1250, 1092, 1009, 853, 696, 547 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{13}Cl_2N_4O_2S$: 443.0131; found: 443.0138.

4.3.9 *5-amino-7-(3,4-dichlorobenzoyl)-7a-(3,4-dichlorophenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile (**4ia**)*
Yield 60%; yellow solid. mp 274-275 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 13.08 (s, 1H), 8.46 (s, 1H), 8.13 (d, J = 8.4 Hz, 3H), 7.94 (d, J = 8.4 Hz, 1H), 7.91-7.88 (m, 2H), 7.58 (d, J = 8.4 Hz, 1H), 5.28 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 193.5, 181.1, 172.2, 154.6, 137.8, 136.6, 134.0, 132.5, 132.2, 132.0, 131.8, 131.3, 131.2, 129.4, 127.7, 125.5, 117.0, 75.3, 58.7, 55.1. IR (KBr): 3385, 3325, 3191, 2188, 1766, 1652, 1581, 1463, 1359, 1243, 1031, 703, 574 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{11}Cl_4N_4O_2S$: 510.9351; found: 510.9350.

4.3.10 *5-amino-7-(3-bromobenzoyl)-7a-(3-bromophenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile (**4ja**)*
Yield 85%; white solid. mp 284-285 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 12.95 (s, 1H), 8.32 (s, 1H), 8.12 (d, J = 7.8 Hz, 1H), 8.07 (s, 2H), 7.95 (d, J = 7.8 Hz, 1H), 7.76 (s, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.62-7.53 (m, 2H), 7.50 (t, J = 7.8 Hz, 1H), 5.20 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 194.3, 180.9, 172.3, 154.6, 138.3, 137.3, 135.7, 132.3, 132.2, 131.1, 131.0, 128.5, 128.0, 124.2, 122.4, 122.3, 117.0, 75.6, 59.0, 55.0. IR (KBr): 3396, 3143, 2200, 1751, 1651, 1585, 1472, 1441, 1368, 1242, 1158, 680, 630 cm^{-1}. HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{20}H_{13}Br_2N_4O_2S$: 530.9121; found: 530.9118.

4.3.11 *5-amino-7-(4-bromobenzoyl)-7a-(4-bromophenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile (**4ka**)*
Yield 85%; yellow solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 13.00 (s, 1H), 8.13 (d, J = 7.8 Hz, 2H), 8.10 (s, 1H), 7.87 (d, J = 8.4 Hz, 2H), 7.80 (d, J = 8.4 Hz, 2H), 7.58 (d, J = 7.8 Hz, 2H), 5.14 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 195.0, 181.1, 172.5, 154.7, 135.4, 132.9, 132.1, 131.6, 129.3, 127.4, 123.0, 117.1, 75.9, 59.2, 55.0. IR (KBr): 3427, 2962, 2924, 2360, 2191, 1767, 1647, 1584, 1262, 1097, 1024, 802, 683 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{13}Br_2N_4O_2S$: 530.9121; found: 530.9117.

4.3.12 *7-(2-naphthoyl)-5-amino-7a-(naphthalen-2-yl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile (**4la**)*
Yield 52%; yellow solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 12.99 (s, 1H), 9.05 (s, 1H), 8.16-8.13 (m, 2H), 8.12 (s, 1H), 8.09 (s, 3H), 8.04 (d, J = 7.2 Hz, 2H), 8.02-7.95 (m, 2H), 7.79 (d, J = 9.0 Hz, 1H), 7.73 (t, J = 7.8 Hz, 1H), 7.65 (t, J = 7.8 Hz, 1H), 7.63-7.58 (m, 2H), 5.43 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 195.8, 181.3, 173.1, 154.9, 135.7, 133.6, 133.1, 132.5, 132.2, 131.2, 130.0, 129.6, 129.1, 128.8, 128.4, 127.9, 127.7, 127.3, 127.1, 124.2, 123.9, 123.5, 122.9 117.4, 76.6, 59.9, 56.1, 55.3. IR (KBr): 3405, 3189, 2197, 1744, 1647, 1468, 1363, 1245, 737, 701, 538 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{28}H_{19}N_4O_2S$: 475.1223; found: 475.1228.

4.3.13 *5-amino-1-oxo-7a-(thiophen-2-yl)-7-(thiophene-2-carbonyl)-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile (**4ma**)*
Yield 49%; yellow solid. mp 173-174 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.98 (s, 1H), 8.32 (d, J = 4.0 Hz, 1H), 8.22 (d, J = 4.8 Hz, 1H), 7.95 (s, 2H), 7.67 (d, J = 5.2 Hz, 1H), 7.39 (d, J = 3.6 Hz, 1H), 7.37-7.32 (m, 1H), 7.18-7.12 (m, 1H), 4.99 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 189.2, 181.2, 172.1, 154.7, 141.1, 138.9, 138.4, 137.1, 129.5, 127.9, 127.3, 126.1, 117.2, 75.1, 60.3, 55.6. IR (KBr): 3369, 2922, 2195, 1763, 1643, 1465, 1439, 1408, 1357, 1250, 1025, 734, 712, 531 cm^{-1}. HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{16}H_{11}N_4O_2S_3$: 387.0039; found: 387.0038.

4.3.14 *methyl 5-amino-7-benzoyl-1-oxo-7a-phenyl-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carboxylate (**4na**)*
Yield 50%; yellow solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.87 (s, 1H), 8.13 (d, J = 7.6 Hz, 2H), 7.73 (t, J

= 7.6 Hz, 1H), 7.68 (s, 1H), 7.63-7.54 (m, 5H), 7.53-7.46 (m, 3H), 4.94 (s, 1H), 3.33 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 200.7, 181.8, 173.3, 165.1, 153.6, 136.9, 135.8, 134.3, 129.3, 129.2, 128.8, 127.6, 124.7, 82.8, 77.3, 54.4, 50.1. IR (KBr): 3413, 3296, 3109, 1761, 1679, 1606, 1523, 1443, 1380, 1312, 1109, 962, 720, 695 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{21}H_{18}N_3O_4S$: 408.1013; found: 408.1014.

4.3.15 *ethyl 5-amino-7-benzoyl-1-oxo-7a-phenyl-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carboxylate* ***(4oa)***

Yield 52%; yellow solid. mp 135-136 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.86 (s, 1H), 8.12 (d, J = 7.6 Hz, 2H), 7.72 (t, J = 7.2 Hz, 1H), 7.63 (s, 2H), 7.60-7.55 (m, 4H), 7.51 (t, J = 7.6 Hz, 2H), 7.47-7.43 (m, 1H), 4.94 (s, 1H), 3.84-3.68 (m, 2H), 0.76 (t, J = 6.8 Hz, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 201.0, 181.9, 173.3, 164.9, 153.9, 136.9, 136.0, 134.1, 129.3, 129.1, 128.7, 124.6, 82.9, 77.3, 58.6, 54.2. IR (KBr): 3380, 3276, 2975, 1744, 1664, 1530, 1312, 1258, 1203, 1103, 773, 690, 530 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{22}H_{20}N_3O_4S$: 422.1169; found: 422.1171.

4.3.16 *5-amino-7-benzoyl-2-methyl-1-oxo-7a-phenyl-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile* ***(4ab)***

Yield 54%; yellow solid. mp 244-245 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 8.14 (d, J = 8.0 Hz, 2H), 8.10 (s, 1H), 7.75 (t, J = 7.2 Hz, 1H), 7.63-7.56 (m, 4H), 7.55-7.48 (m, 3H), 5.19 (s, 1H), 3.21 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 195.9, 181.0, 171.8, 154.8, 135.7, 134.8, 133.7, 129.7, 129.5, 129.1, 129.0, 125.3, 117.1, 75.2, 59.4, 55.9, 28.2. IR (KBr): 3361, 3188, 2194, 1753, 1648, 1579, 1392, 1305, 1041, 701, 574 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{21}H_{17}N_4O_2S$: 389.1067; found: 389.1070.

4.3.17 *5-amino-7-benzoyl-2-butyl-1-oxo-7a-phenyl-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile* ***(4ac)***

Yield 53%; white solid. mp 227-228 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.97 (d, J = 7.2 Hz, 2H), 7.65 (t, J = 7.6 Hz, 1H), 7.56-7.48 (m, 4H), 7.47-7.42 (m, 3H), 6.62 (s, 2H), 4.71 (s, 1H), 3.86-3.75 (m, 2H), 1.78-1.68 (m, 2H), 1.40-1.30 (m, 2H), 0.93 (t, J = 7.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 194.8, 181.1, 171.6, 155.7, 135.9, 134.7, 133.9, 129.5, 129.3, 129.2, 129.0, 124.7, 75.0, 61.7, 57.4, 41.9, 28.7, 19.9, 13.6. IR (KBr): 3376, 3306, 3244, 3188, 2956, 2196, 1757, 1675, 1652, 1589, 1389, 1055, 696, 572 cm^{-1}. HRMS (APCI): m/z [M+H]$^+$ calcd for $C_{24}H_{23}N_4O_2S$: 431.1536; found: 431.1540.

4.3.18 *5-amino-7-benzoyl-1-oxo-2,7a-diphenyl-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile* ***(4ad)***

Yield 70%; white solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 8.22 (d, J = 8.0 Hz, 2H), 8.17 (s, 2H), 7.77 (t, J = 7.2 Hz, 1H), 7.71 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 7.6 Hz, 2H), 7.60-7.55 (m, 4H), 7.54-7.50 (m, 2H), 7.36 (d, J = 7.6 Hz, 2H), 5.31 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 196.2, 180.6, 171.3, 154.8, 135.5, 134.8, 133.7, 132.7, 129.7, 129.6, 129.5, 129.4, 129.2, 128.92, 128.3, 125.3, 117.0, 75.6, 59.7, 56.1. IR (KBr): 3336, 3241, 3181, 2190, 1770, 1649, 1582, 1447, 1374, 1286, 703, 563cm^{-1}. HRMS (APCI): m/z [M+H]$^+$ calcd for $C_{26}H_{19}N_4O_2S$: 451.1223; found: 451.1224.

4.3.19 *5-amino-7-benzoyl-2-benzyl-1-oxo-7a-phenyl-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile* ***(4ae)***

Yield 80%; yellow solid. mp 240-241 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) 7.96 (d, J = 7.8 Hz, 2H), 7.66 (t, J = 7.8 Hz, 1H), 7.57-7.48 (m, 4H), 7.48-7.42 (m, 3H), 7.33 (d, J = 7.2 Hz, 2H), 7.28 (t, J = 7.2 Hz, 2H), 7.26-7.23 (m, 1H), 6.46 (s, 2H), 5.15-4.95 (m, 2H), 4.76 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 194.6, 180.4, 171.6, 155.5, 135.8, 134.8, 134.4, 133.8, 129.6, 129.3, 129.2, 128.9, 128.4, 128.1, 127.7, 124.8, 116.7, 75.2, 61.6, 57.3, 45.1. IR (KBr): 3356, 3241, 3181, 2194, 1754, 1675, 1650, 1588, 1396, 1251, 940, 697, 527 cm^{-1}. HRMS (APCI): m/z [M+H]$^+$ calcd for $C_{27}H_{21}N_4O_2S$: 465.1380; found: 465.1381

4.3.20 *5-amino-7-benzoyl-1-oxo-2-phenethyl-7a-phenyl-3-thioxo-2,3,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole-6-carbonitrile* ***(4af)***

Yield 75%; yellow solid. mp 246-247 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) 7.97 (d, J = 7.8 Hz, 2H), 7.66 (t, J = 7.2 Hz, 1H), 7.57-7.48 (m, 4H), 7.47-7.38 (m, 3H), 7.24-7.05 (m, 5H), 6.52 (s, 2H), 4.70 (s, 1H), 4.05 (t, J = 7.8 Hz, 2H), 3.11-2.98 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 194.9, 180.9, 171.4, 155.7, 137.4, 135.8, 134.8, 133.9, 129.5, 129.3, 129.2, 129.0, 128.8, 128.4, 126.5, 124.8, 75.1, 61.8, 57.6, 43.0, 32.6. IR (KBr): 3392, 3279, 3061, 2190, 1729, 1671, 1638, 1586, 1446, 1372, 1249, 705, 574 cm^{-1}. HRMS (APCI): m/z [M+H]$^+$ calcd for $C_{28}H_{23}N_4O_2S$: 479.1536; found: 479.1536.

4.3.21 *5-amino-7-benzoyl-3-imino-1-oxo-7a-phenyl-1,3,7,7a-tetrahydropyrrolo[1,2-c]thiazole-6-carbonitrile (**5aa**)*

Yield 85%; yellow solid. mp 190-192 °C. 1H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.10 (s, 1H), 8.15 (d, J = 7.8 Hz, 2H), 8.01 (s, 1H), 7.74 (t, J = 7.2 Hz, 1H), 7.65 (d, J = 7.2 Hz, 2H), 7.59 (t, J = 7.8 Hz, 2H), 7.55 (t, J = 7.8 Hz, 2H), 7.53-7.49 (m, 1H), 5.08 (s, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 196.2, 195.4, 155.8, 155.7, 151.6, 136.8, 134.7, 134.1, 129.7, 129.6, 129.3, 129.0, 125.3, 118.0, 82.6, 56.1. IR (KBr): 3325, 3168, 2188, 1748, 1667, 1645, 1447, 1347, 1104, 915, 704 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{20}H_{15}N_4O_2S$: 375.09102; found: 375.09054.

4.3.22 *5-amino-3-imino-7-(4-methylbenzoyl)-1-oxo-7a-(p-tolyl)-1,3,7,7a-tetrahydropyrrolo[1,2-c]thiazole-6-carbonitrile (**5ba**)*

Yield 89%; white solid. mp 188-190 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.05 (s, 1H), 8.02 (d, J = 7.8 Hz, 2H), 7.97 (s, 1H), 7.51 (d, J = 7.8 Hz, 2H), 7.39 (d, J = 7.8 Hz, 2H), 7.34 (d, J = 7.8 Hz, 2H), 4.98 (s, 1H), 2.41 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 195.8, 195.5, 155.8, 155.7, 151.8, 145.4, 139.3, 134.0, 131.7, 129.8, 129.6, 129.6, 125.1, 118.0, 82.5, 56.1, 21.4, 20.7. IR (KBr): 3318, 3176, 2186, 1747, 1644, 1570, 1447, 1350, 1109, 915, 753 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{22}H_{19}N_4O_2S$: 403.12232; found: 403.12155.

4.3.23 *5-amino-3-imino-7-(4-methoxybenzoyl)-7a-(4-methoxyphenyl)-1-oxo-1,3,7,7a-tetrahydropyrrolo[1,2-c]thiazole-6-carbonitrile (**5ca**)*

Yield 78%; yellow solid. mp 176-178 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.01 (s, 1H), 8.10 (d, J = 8.4 Hz, 2H), 7.92 (s, 2H), 7.52 (d, J = 8.4 Hz, 2H), 7.12-7.06 (m, 4H), 4.94 (s, 1H), 3.88 (s, 3H), 3.80 (s, 3H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 195.5, 194.9, 164.2, 160.2, 155.8, 151.7, 132.0, 128.5, 127.0, 126.5, 118.1, 114.6, 114.2, 82.3, 56.5, 55.9, 55.7, 55.4. IR (KBr): 3415, 3308, 2187, 1748, 1641, 1599, 1510, 1443, 1343, 1255, 1105, 915, 836 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{22}H_{19}N_4O_4S$: 435.11215; found: 435.11139.

4.3.24 *5-amino-3-imino-7-(3-methoxybenzoyl)-7a-(3-methoxyphenyl)-1-oxo-1,3,7,7a-tetrahydropyrrolo[1,2-c]thiazole-6-carbonitrile (**5da**)*

Yield 85%; yellow solid. mp 131-133 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.06 (s, 1H), 8.00 (s, 2H), 7.75 (d, J = 5.4 Hz, 1H), 7.62 (s, 1H), 7.53-7.42 (m, 2H), 7.33-7.27 (m, 1H), 7.22-7.12 (m, 2H), 7.09 (d, J = 8.4 Hz, 1H), 5.10 (s, 1H), 3.85 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 195.5, 195.1, 159.7, 159.5, 155.7, 151.4, 138.3, 135.3, 130.3, 130.0, 122.2, 121.2, 118.1, 117.1, 114.7, 113.5, 111.6, 82.5, 56.1, 56.1, 55.5, 55.3. IR (KBr): 3391, 3274, 3077, 2833, 2186, 1752, 1644, 1487, 1447, 1346, 1264, 1116, 928, 741, 549 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{22}H_{19}N_4O_4S$: 435.11215; found: 435.11161.

4.3.25 *5-amino-7-(4-chlorobenzoyl)-7a-(4-chlorophenyl)-3-imino-1-oxo-1,3,7,7a-tetrahydropyrrolo[1,2-c]thiazole-6-carbonitrile (**5ea**)*

Yield 80%; yellow solid. mp 179-180 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.14 (s, 1H), 8.15 (d, J = 8.4 Hz, 2H), 8.01 (s, 2H), 7.76-7.53 (m, 6H), 5.09 (s, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 195.1, 194.8, 155.7, 151.2, 139.8, 135.6, 134.5, 132.7, 131.5, 129.2, 129.1, 127.2, 117.8, 82.0, 55.9, 55.6. IR (KBr): 3335, 3174, 2189, 1739, 1648, 1445, 1347, 1095, 978, 917 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{20}H_{13}C_{l2}N_4O_2S$: 443.01308; found: 443.01286.

4.3.26 *5-amino-7-(4-bromobenzoyl)-7a-(4-bromophenyl)-3-imino-1-oxo-1,3,7,7a-tetrahydropyrrolo[1,2-c]thiazole-6-carbonitrile (**5fa**)*

Yield 82%; yellow solid. mp 188-189 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.14 (s, 1H), 8.07 (d, J = 8.4 Hz, 2H), 8.01 (s, 2H), 7.81 (d, J = 8.4 Hz, 2H), 7.76 (d, J = 9.0 Hz, 2H), 7.57 (d, J = 8.4 Hz, 2H), 5.08 (s, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 195.0, 155.7, 151.1, 136.0, 133.0, 132.1, 132.0, 131.5, 129.1, 127.5, 123.1, 117.8, 82.0, 55.8, 55.6. IR (KBr): 3382, 2975, 2896, 1923, 1757, 1654, 1452, 1382, 1088, 1049, 881, 667 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{20}H_{13}Br_2N_4O_2S$: 530.91205; found: 530.91138.

4.3.27 *5-amino-3-imino-1-oxo-7a-(thiophen-2-yl)-7-(thiophene-2-carbonyl)-1,3,7,7a-tetrahydropyrrolo[1,2-c]thiazole-6-carbonitrile (**5ga**)*

Yield 50%; gray solid. mp 179-181 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.15 (s, 1H), 8.31 (d, J = 2.4 Hz, 1H), 8.22 (d, J = 4.8 Hz, 1H), 7.93 (s, 1H), 7.68 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 3.0 Hz, 1H), 7.35 (t, J = 4.2 Hz, 1H), 7.18 (t, J = 4.2 Hz, 1H), 4.99 (s, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 194.7, 189.8, 155.8, 151.1, 141.2, 141.1, 138.1, 136.8, 129.4, 128.4, 127.5, 126.3, 117.9, 81.1, 57.0, 56.8. IR (KBr): 3328, 3166, 2187, 1746, 1645, 1452, 1413, 1351, 1099, 851, 719 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{16}H_{11}N_4O_2S_3$: 387.00386; found: 387.00335.

4.3.28 *7-(1-naphthoyl)-5-amino-3-imino-7a-(naphthalen-1-yl)-1-oxo-1,3,7,7a-tetrahydropyrrolo[1,2-c]thiazole-6-carbonitrile (**5ha**)*

Yield 62%; yellow solid. mp 196-197 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.25 (s, 1H), 8.71 (d, J = 8.4 Hz, 1H), 8.44-8.40 (m, 1H), 8.33 (s, H_{CHCl3}), 8.31 (d, J = 8.4 Hz, 1H), 8.26 (d, J = 7.2 Hz, 1H), 8.19 (s, 2H), 8.15-8.08 (m, 3H), 7.88-7.83 (m, 1H), 7.78-7.73 (m, 1H), 7.72-7.65 (m, 3H), 7.65-7.59 (m, 2H), 5.45 (s, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 198.0, 193.8, 155.4, 151.7, 134.9, 134.9, 134.8, 134.8, 133.7, 132.0, 131.8, 131.4, 130.6, 130.2, 129.6, 128.9, 128.8, 128.5, 126.9, 126.8, 126.3, 125.6, 125.0, 123.6, 117.6, 83.8, 79.2(C_{CHCl3}), 56.8, 56.8. IR (KBr): 3452, 3258, 2188, 1739, 1637, 1568, 1440, 1350, 1270, 1120, 911, 876, 737 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{28}H_{19}N_4O_2S$: 475.12232; found: 475.12191.

4.3.29 *7-(2-naphthoyl)-5-amino-3-imino-7a-(naphthalen-2-yl)-1-oxo-1,3,7,7a-tetrahydropyrrolo[1,2-c]thiazole-6-carbonitrile (**5ia**)*

Yield 75%; yellow solid. mp 210-212 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.19 (s, 1H), 9.03 (s, 1H), 8.22 (s, 1H), 8.17-8.05 (m, 7H), 8.05-8.00 (m, 2H), 7.82 (d, J = 9.0 Hz, 1H), 7.72 (t, J = 7.8 Hz, 1H), 7.68-7.59 (m, 3H), 5.43 (s, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 196.0, 195.4, 156.0, 151.6, 135.6, 134.2, 133.2, 132.5, 132.1, 131.3, 130.0, 129.5, 129.2, 128.7, 128.5, 127.8, 127.6, 127.4, 127.2, 127.1, 124.5, 123.9, 122.8, 118.0, 82.8, 56.4, 56.2. IR (KBr): 3380, 3279, 2176, 1741, 1637, 1449, 1353, 1105, 917, 751 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{28}H_{19}N_4O_2S$: 475.12232; found: 475.12188.

4.3.30 *5-amino-7-benzoyl-3-(methylimino)-1-oxo-7a-phenyl-1,3,7,7a-tetrahydropyrrolo[1,2-c]thiazole-6-carbonitrile (**5ab**)*

Yield 46%; yellow solid. mp 192-194 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) 7.99 (d, J = 7.8 Hz, 2H), 7.65 (t, J = 7.8 Hz, 1H), 7.58 (d, J = 6.0 Hz, 2H), 7.52 (t, J = 7.8 Hz, 2H), 7.48-7.42 (m, 3H), 6.59 (s, 2H), 4.70 (s, 1H), 3.22 (s, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ (ppm) 195.8, 193.4, 156.7, 148.7, 136.8, 134.6, 134.2, 129.6, 129.3, 129.2, 129.0, 125.0, 117.8, 81.9, 58.3, 57.6, 41.0. IR (KBr): 3359, 2975, 2895, 1925, 1661, 1446, 1381, 1089, 1049, 881, 665 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{21}H_{17}N_4O_2S$: 389.1067; found: 389.1073.

4.3.31 *5-amino-7-benzoyl-3-(butylimino)-1-oxo-7a-phenyl-1,3,7,7a-tetrahydropyrrolo[1,2-c]thiazole-6-carbonitrile (**5ac**)*

Yield 75%; red solid. mp 170-172 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.98 (d, J = 8.0 Hz, 2H), 7.63 (t, J = 7.6 Hz, 1H), 7.58-7.55 (m, 2H), 7.51 (t, J = 8.0 Hz, 2H), 7.46-7.34 (m, 3H), 6.78 (s, 2H), 4.68 (s, 1H), 3.42-3.20 (m, 2H), 1.72-1.57 (m, 2H), 1.47-1.32 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 195.7, 193.7, 156.8, 146.8, 136.9, 134.5, 134.3, 129.5, 129.2, 129.1, 128.9, 124.9, 118.0, 81.5, 58.2, 57.0, 54.7, 32.7, 20.4, 13.8. IR (KBr): 3324, 3223, 2959, 2188, 1742, 1655, 1448, 1215, 1035, 916, 811, 702 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{24}H_{23}N_4O_2S$: 431.15362; found: 431.15439.

4.3.32 *5-amino-7-benzoyl-1-oxo-7a-phenyl-3-(phenylimino)-1,3,7,7a-tetrahydropyrrolo[1,2-c]thiazole-6-carbonitrile (**5ad**)*

Yield 66%; yellow solid. mp 228-230 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) 8.01 (d, J = 7.2 Hz, 2H), 7.69-7.63 (m, 3H), 7.57-7.46 (m, 5H), 7.37 (t, J = 7.8 Hz, 2H), 7.20 (t, J = 7.2 Hz, 1H), 7.06 (d, J = 7.8 Hz, 2H), 6.62 (s, 2H), 4.74 (s, 1H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ (ppm) 195.7, 193.3, 156.1, 149.4, 147.4, 136.5, 134.7, 134.2, 129.8, 129.5, 129.2, 129.1, 125.7, 124.9, 121.3, 82.1, 59.2, 58.1. IR (KBr): 3394, 3238, 2924, 2189, 1770, 1664, 1443, 1344, 1138, 1025, 927, 759, 701 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{26}H_{19}N_4O_2S$: 451.12232; found: 451.12252.

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Supplementary data

Supplementary data related to this article can be found online at doi:

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Supporting Information Available

Chemoselective synthesis of biheterocyclic skeletons tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole and tetrahydropyrrolo[1,2-*c*]thiazole derivatives via multicomponent self-sorting domino strategy

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Table of Contents **page**

1. General

All substrates and reagents were commercially available and used without further purification. TLC analysis was performed using pre-coated glass plates. Column chromatography was performed using silica gel (200-300 mesh). IR spectra were recorded on a Perkin-Elmer PE-983 infrared spectrometer as KBr pellets with absorption in cm^{-1}. ^1H spectra were recorded in $CDCl_3$ or DMSO-d_6 on 400/600 MHz NMR spectrometers and resonances (δ) are given in parts per million relative to tetramethylsilane. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz) and integration. ^{13}C spectra were recorded in $CDCl_3$ or DMSO-d_6 on 100/150 MHz NMR spectrometers and resonances (δ) are given in ppm. HRMS were obtained on a Bruker Apex-Ultra 7.0T FTMS equipped with an electrospray source (ESI or APCI). The X-ray crystal structure determination of **4ab**, **4ad** and **5aa** were obtained on a Bruker SMART APEX CCD system. Melting points were determined using XT-4 apparatus and not corrected.

2. General procedure for synthesis of 4, 5, A and B

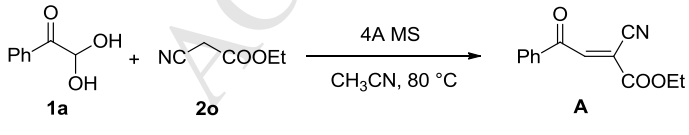
2.1 General procedure for synthesis of 4 (4aa as an example)

A mixture of phenylglyoxal monohydrate **1a** (2.0 mmol), malononitrile **2a** (1.2 mmol), thiourea **3a** (1.0 mmol) in HOAc (3 mL) was stirred at 100 °C for 20 min till almost completed conversion of the substrates by TLC analysis, then extracted with EtOAc three times (3 × 50 mL). The extract was washed with 10% $NaHCO_3$ solution (w/w), dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc) to afford the product **4aa** as a yellow solid.

2.2 General procedure for synthesis of 5 (5aa as an example)

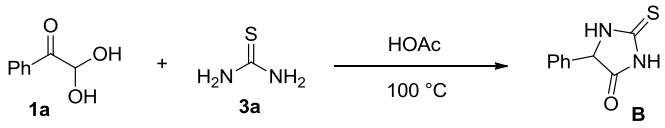
A mixture of phenylglyoxal monohydrate **1a** (2.0 mmol), malononitrile **2a** (1.2 mmol), thiourea **3a** (1.0 mmol) in EtOH (3 mL) was stirred at 80 °C for 40 min till almost completed conversion of the substrates by TLC analysis, then extracted with EtOAc three times (3 × 50 mL). The extract was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc) to afford the product **5aa** as a yellow solid.

2.3 General procedure for synthesis of A[1]



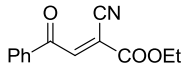
A solution of phenylglyoxal monohydrate **1a** (1.38 g, 10 mmol) and MS4A (2.0 g) in MeCN (20 mL) was added ethyl cyanoacetate **2o** (10 mmol), and the mixture was stirred overnight at 80 °C. The resulting mixture was filtered through short silica gel pad, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel to afford corresponding compound Ethyl 2-cyano-4-oxo-4-phenylbut-2-enoate **A** as yellow solids.

2.4 General procedure for synthesis of B



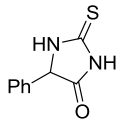
A mixture of phenylglyoxal monohydrate **1a** (1.0 mmol) and thiourea **3a** (1.0 mmol) in HOAc (3 mL) was stirred at 100 °C for 20 min till almost completed conversion of the substrates by TLC analysis, then extracted with EtOAc three times (3 × 20 mL). The extract was washed with 10% $NaHCO_3$ solution (w/w), dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc) to afford the product **B** as a white solid.

3. Spectral data of compounds 4, 5, A and B.



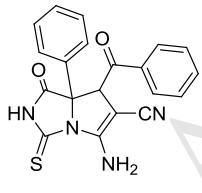
(*E*)-ethyl 2-cyano-4-oxo-4-phenylbut-2-enoate (A)

Yield 87%; yellow solid. mp 64-65 °C (ref.[1] 64 °C). ^{1}H NMR ($CDCl_3$, 400 MHz): 8.44 (s, 1H), 8.04-7.94 (m, 2H), 7.72-7.67 (m, 1H), 7.56 (t, J = 7.6 Hz, 2H), 4.44 (q, J = 7.2 Hz, 2H), 1.43 (t, J = 7.2 Hz, 3H). HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_{13}H_{11}NNaO_3$: 252.0631; found: 252.0634.



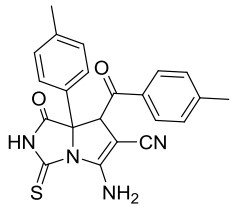
5-phenyl-2-thioxoimidazolidin-4-one (B)

Yield 83%; white solid. mp 188-189 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 11.87 (s, 1H), 10.50 (s, 1H), 7.45-7.41 (m, 2H), 7.40-7.36 (m, 1H), 7.27 (d, J = 7.2 Hz, 2H), 5.40 (s, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 183.0, 174.9, 134.6, 129.0, 128.6, 126.8, 64.0. IR (KBr): 3459, 3333, 3159, 2898, 1741, 1536, 1496, 1406, 1263, 1163, 723, 697 cm^{-1}. HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_9H_8N_2NaOS$: 215.02495; found: 215.02486.



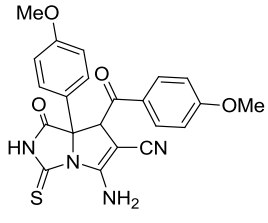
5-amino-7-benzoyl-1-oxo-7a-phenyl-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*] imidazole-6-carbonitrile (4aa)

Yield 80%; yellow solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.87 (s, 1H), 8.15 (d, J = 8.0 Hz, 2H), 8.00 (s, 2H), 7.74 (t, J = 7.0 Hz, 1H), 7.66-7.56 (m, 4H), 7.55-7.42 (m, 3H), 5.08 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 196.0, 181.0, 172.9, 154.7, 136.1, 134.7, 133.9, 129.5, 129.3, 129.1, 128.9, 125.0, 117.1, 76.4, 59.7, 55.1. IR (KBr): 3438, 3300, 3141, 2923, 2361, 2195, 1770, 1669, 1634, 1583, 1465, 1448, 1239, 1163, 1105, 738, 694, 544 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{15}N_4O_2S$: 375.0910; found: 375.0908.



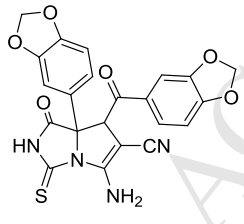
5-amino-7-(4-methylbenzoyl)-1-oxo-3-thioxo-7a-(p-tolyl)-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4ba)

Yield 72%; yellow solid. mp 103-104 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.81 (s, 1H), 8.02 (d, J = 7.6 Hz, 2H), 7.95 (s, 2H), 7.43 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 7.6 Hz, 2H), 4.97 (s, 1H), 2.40 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 195.6, 181.0, 173.0, 154.7, 145.4, 138.9, 133.2, 131.6, 129.6, 129.5, 129.1, 124.8, 117.1, 76.3, 59.9, 55.0, 21.3, 20.6. IR (KBr): 3403, 2957, 2924, 2853, 2189, 1765, 1670, 1644, 1460, 1361, 1251, 1021, 851, 816, 599 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{22}H_{19}N_4O_2S$: 403.1223; found: 403.1231.



5-amino-7-(4-methoxybenzoyl)-7a-(4-methoxyphenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4ca)

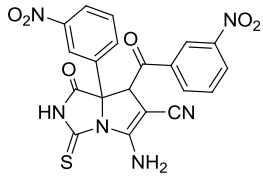
Yield 65%; yellow solid. mp 128-129 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.77 (s, 1H), 8.11 (d, J = 8.8 Hz, 2H), 7.92 (s, 1H), 7.46 (d, J = 8.8 Hz, 2H), 7.08 (t, J = 8.8 Hz, 4H), 4.94 (s, 1H), 3.88 (s, 3H), 3.79 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 194.6, 181.6, 164.4, 160.0, 132.1, 127.9, 126.9, 126.4, 117.3, 114.5, 114.3, 76.2, 60.1, 55.8, 55.4, 55.0. IR (KBr): 3408, 2959, 2925, 2853, 2187, 1764, 1644, 1598, 1257, 1024, 803, 541 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{22}H_{19}N_4O_4S$: 435.1122; found: 435.1124.



5-amino-7a-(benzo[d][1,3]dioxol-5-yl)-7-(benzo[d][1,3]dioxole-5-carbonyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4da)

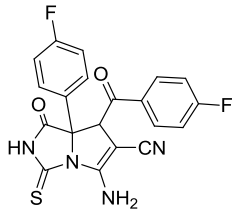
Yield 55%; white solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.77 (s, 1H), 7.92 (s, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.59 (s, 1H), 7.14-7.07 (m, 2H), 7.03 (d, J = 8.4 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 6.19 (d, J = 4.0 Hz, 2H), 6.09 (d, J = 7.2 Hz, 2H), 4.95 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 194.2, 181.0, 173.1, 154.5, 152.9, 148.2, 148.2, 148.0, 129.6, 128.6, 126.9, 118.3, 117.3, 108.5, 108.3, 106.1, 102.5, 101.8, 76.3, 60.1, 54.9. IR

(KBr): 3408, 3131, 2194, 1766, 1664, 1644, 1442, 1250, 1110, 1039, 820, 538 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{15}N_4O_6S$: 463.0707; found: 463.0703.



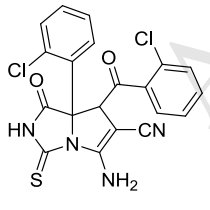
5-amino-7-(3-nitrobenzoyl)-7a-(3-nitrophenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4ea)

Yield 47%; yellow solid. mp >300 ℃. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 13.12 (s, 1H), 8.85 (s, 1H), 8.57 (t, J = 8.4 Hz, 2H), 8.44 (s, 1H), 8.38 (d, J = 8.4 Hz, 1H), 8.20 (s, 2H), 8.05 (d, J = 8.0 Hz, 1H), 7.94-7.83 (m, 2H), 5.38 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 193.7, 181.2, 172.2, 154.7, 148.2, 148.1, 137.8, 135.8, 134.9, 131.9, 131.9, 130.8, 128.9, 124.4, 124.1, 120.4, 117.0, 75.5, 58.3, 55.5. IR (KBr): 3457, 3318, 3172, 2194, 1741, 1686, 1529, 1489, 1346, 1184, 728, 678 cm^{-1}. HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{20}H_{13}N_6O_6S$: 465.0612; found: 465.0614.



5-amino-7-(4-fluorobenzoyl)-7a-(4-fluorophenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4fa)

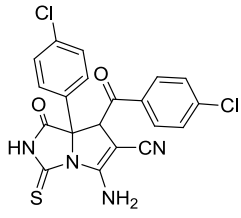
Yield 88%; yellow solid. mp >300 ℃. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 12.89 (s, 1H), 8.28-8.18 (m, 2H), 8.00 (s, 2H), 7.65-7.56 (m, 2H), 7.43 (t, J = 9.0 Hz, 2H), 7.38 (t, J = 9.0 Hz, 2H), 5.08 (s, 1H).^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 194.5, 181.1, 172.9, 167.3, 164.8, 163.9, 161.4, 154.7, 132.9, 132.8, 132.1, 130.7, 127.5, 127.4, 117.1, 116.2, 116.0, 75.9, 59.4, 55.1. IR (KBr): 3382, 3305, 3254, 3195, 2195, 1765, 1647, 1592, 1458, 1361, 1237, 1157, 1091, 838, 699, 543cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{13}F_2N_4O_2S$: 411.0722; found: 411.0726.



5-amino-7-(2-chlorobenzoyl)-7a-(2-chlorophenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4ga)

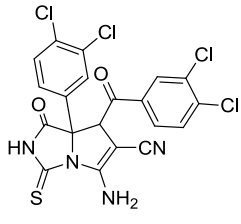
Yield 57%; yellow solid. mp >300 ℃. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 12.94 (s, 1H), 8.15 (d, J = 8.4 Hz, 2H), 8.02 (s, 2H), 7.66 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 9.0 Hz, 2H), 7.58 (d, J = 8.4 Hz, 2H), 5.09 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 194.7, 181.0, 172.5, 154.6, 139.8, 138.6, 135.3, 134.9, 134.2, 132.7, 132.6, 131.4, 129.4, 129.1, 127.1,

117.0, 75.8, 59.2, 55.0. IR (KBr): 3320, 3132, 2182, 1760, 1672, 1646, 1588, 1371, 1260, 1094, 1011, 859, 762, 538 cm^{-1}. HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{20}H_{13}Cl_2N_4O_2S$: 443.0131; found: 443.0128.



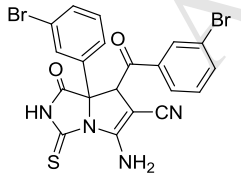
5-amino-7-(4-chlorobenzoyl)-7a-(4-chlorophenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4ha)

Yield 82%; yellow solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.92 (s, 1H), 8.15 (d, J = 8.8 Hz, 2H), 8.00 (s, 2H), 7.66 (d, J = 8.4 Hz, 2H), 7.64-7.57 (m, 4H), 5.09 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 194.7, 181.1, 172.6, 154.7, 139.9, 134.9, 134.3, 132.6, 131.5, 129.1, 127.1, 117.1, 75.8, 59.2, 55.1. IR (KBr): 3380, 3305, 3252, 3192, 2968, 2361, 2195, 1764, 1645, 1586, 1490, 1458, 1362, 1250, 1092, 1009, 853, 696, 547 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{13}Cl_2N_4O_2S$: 443.0131; found: 443.0138.



5-amino-7-(3,4-dichlorobenzoyl)-7a-(3,4-dichlorophenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4ia)

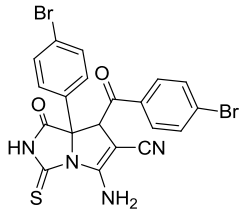
Yield 60%; yellow solid. mp 274-275 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 13.08 (s, 1H), 8.46 (s, 1H), 8.13 (d, J = 8.4 Hz, 3H), 7.94 (d, J = 8.4 Hz, 1H), 7.91-7.88 (m, 2H), 7.58 (d, J = 8.4 Hz, 1H), 5.28 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 193.5, 181.1, 172.2, 154.6, 137.8, 136.6, 134.0, 132.5, 132.2, 132.0, 131.8, 131.3, 131.2, 129.4, 127.7, 125.5, 117.0, 75.3, 58.7, 55.1. IR (KBr): 3385, 3325, 3191, 2188, 1766, 1652, 1581, 1463, 1359, 1243, 1031, 703, 574 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{11}Cl_4N_4O_2S$: 510.9351; found: 510.9350.



5-amino-7-(3-bromobenzoyl)-7a-(3-bromophenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4ja)

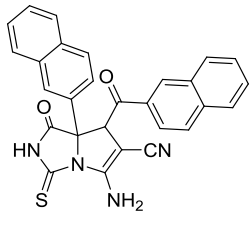
Yield 85%; white solid. mp 284-285 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 12.95 (s, 1H), 8.32 (s, 1H), 8.12 (d, J = 7.8 Hz, 1H), 8.07 (s, 2H), 7.95 (d, J = 7.8 Hz, 1H), 7.76 (s, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.62-7.53 (m, 2H), 7.50 (t, J = 7.8 Hz, 1H), 5.20 (s, 1H). ^{13}C NMR

(DMSO-d_6, 100 MHz): δ (ppm) 194.3, 180.9, 172.3, 154.6, 138.3, 137.3, 135.7, 132.3, 132.2, 131.1, 131.0, 128.5, 128.0, 124.2, 122.4, 122.3, 117.0, 75.6, 59.0, 55.0. IR (KBr): 3396, 3143, 2200, 1751, 1651, 1585, 1472, 1441, 1368, 1242, 1158, 680, 630 cm^{-1}. HRMS (APCI): m/z [M+H]$^+$ calcd for $C_{20}H_{13}Br_2N_4O_2S$: 530.9121; found: 530.9118.



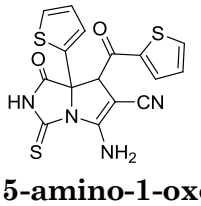
5-amino-7-(4-bromobenzoyl)-7a-(4-bromophenyl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4ka)

Yield 85%; yellow solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 13.00 (s, 1H), 8.13 (d, J = 7.8 Hz, 2H), 8.10 (s, 1H), 7.87 (d, J = 8.4 Hz, 2H), 7.80 (d, J = 8.4 Hz, 2H), 7.58 (d, J = 7.8 Hz, 2H), 5.14 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 195.0, 181.1, 172.5, 154.7, 135.4, 132.9, 132.1, 131.6, 129.3, 127.4, 123.0, 117.1, 75.9, 59.2, 55.0. IR (KBr): 3427, 2962, 2924, 2360, 2191, 1767, 1647, 1584, 1262, 1097, 1024, 802, 683 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{20}H_{13}Br_2N_4O_2S$: 530.9121; found: 530.9117.



7-(2-naphthoyl)-5-amino-7a-(naphthalen-2-yl)-1-oxo-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4la)

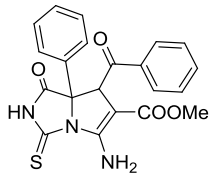
Yield 52%; yellow solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 12.99 (s, 1H), 9.05 (s, 1H), 8.16-8.13 (m, 2H), 8.12 (s, 1H), 8.09 (s, 3H), 8.04 (d, J = 7.2 Hz, 2H), 8.02-7.95 (m, 2H), 7.79 (d, J = 9.0 Hz, 1H), 7.73 (t, J = 7.8 Hz, 1H), 7.65 (t, J = 7.8 Hz, 1H), 7.63-7.58 (m, 2H), 5.43 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 195.8, 181.3, 173.1, 154.9, 135.7, 133.6, 133.1, 132.5, 132.2, 131.2, 130.0, 129.6, 129.1, 128.8, 128.4, 127.9, 127.7, 127.3, 127.1, 124.2, 123.9, 123.5, 122.9 117.4, 76.6, 59.9, 56.1, 55.3. IR (KBr): 3405, 3189, 2197, 1744, 1647, 1468, 1363, 1245, 737, 701, 538 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{28}H_{19}N_4O_2S$: 475.1223; found: 475.1228.



5-amino-1-oxo-7a-(thiophen-2-yl)-7-(thiophene-2-carbonyl)-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4ma)

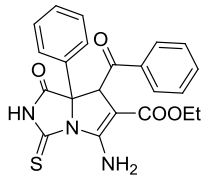
Yield 49%; yellow solid. mp 173-174 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.98 (s, 1H), 8.32 (d, J = 4.0 Hz, 1H), 8.22 (d, J = 4.8 Hz, 1H), 7.95 (s, 2H), 7.67 (d, J = 5.2 Hz, 1H),

7.39 (d, J = 3.6 Hz, 1H), 7.37-7.32 (m, 1H), 7.18-7.12 (m, 1H), 4.99 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 189.2, 181.2, 172.1, 154.7, 141.1, 138.9, 138.4, 137.1, 129.5, 127.9, 127.3, 126.1, 117.2, 75.1, 60.3, 55.6. IR (KBr): 3369, 2922, 2195, 1763, 1643, 1465, 1439, 1408, 1357, 1250, 1025, 734, 712, 531 cm^{-1}. HRMS (APCI): m/z [M+H]$^+$ calcd for $C_{16}H_{11}N_4O_2S_3$: 387.0039; found: 387.0038.



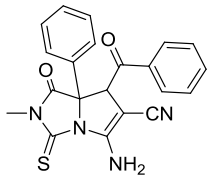
methyl
5-amino-7-benzoyl-1-oxo-7a-phenyl-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carboxylate (4na)

Yield 50%; yellow solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.87 (s, 1H), 8.13 (d, J = 7.6 Hz, 2H), 7.73 (t, J = 7.6 Hz, 1H), 7.68 (s, 1H), 7.63-7.54 (m, 5H), 7.53-7.46 (m, 3H), 4.94 (s, 1H), 3.33 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 200.7, 181.8, 173.3, 165.1, 153.6, 136.9, 135.8, 134.3, 129.3, 129.2, 128.8, 127.6, 124.7, 82.8, 77.3, 54.4, 50.1. IR (KBr): 3413, 3296, 3109, 1761, 1679, 1606, 1523, 1443, 1380, 1312, 1109, 962, 720, 695 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{21}H_{18}N_3O_4S$: 408.1013; found: 408.1014.



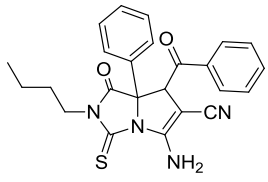
ethyl
5-amino-7-benzoyl-1-oxo-7a-phenyl-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carboxylate (4oa)

Yield 52%; yellow solid. mp 135-136 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 12.86 (s, 1H), 8.12 (d, J = 7.6 Hz, 2H), 7.72 (t, J = 7.2 Hz, 1H), 7.63 (s, 2H), 7.60-7.55 (m, 4H), 7.51 (t, J = 7.6 Hz, 2H), 7.47-7.43 (m, 1H), 4.94 (s, 1H), 3.84-3.68 (m, 2H), 0.76 (t, J = 6.8 Hz, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 201.0, 181.9, 173.3, 164.9, 153.9, 136.9, 136.0, 134.1, 129.3, 129.1, 128.7, 124.6, 82.9, 77.3, 58.6, 54.2. IR (KBr): 3380, 3276, 2975, 1744, 1664, 1530, 1312, 1258, 1203, 1103, 773, 690, 530 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{22}H_{20}N_3O_4S$: 422.1169; found: 422.1171.



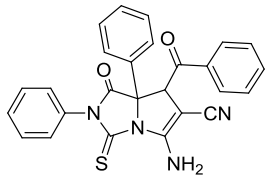
5-amino-7-benzoyl-2-methyl-1-oxo-7a-phenyl-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4ab)

Yield 54%; yellow solid. mp 244-245 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 8.14 (d, J = 8.0 Hz, 2H), 8.10 (s, 1H), 7.75 (t, J = 7.2 Hz, 1H), 7.63-7.56 (m, 4H), 7.55-7.48 (m, 3H), 5.19 (s, 1H), 3.21 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 195.9, 181.0, 171.8, 154.8, 135.7, 134.8, 133.7, 129.7, 129.5, 129.1, 129.0, 125.3, 117.1, 75.2, 59.4, 55.9, 28.2. IR (KBr): 3361, 3188, 2194, 1753, 1648, 1579, 1392, 1305, 1041, 701, 574 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{21}H_{17}N_4O_2S$: 389.1067; found: 389.1070.



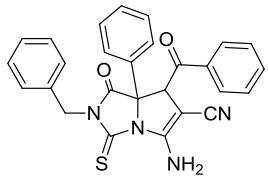
5-amino-7-benzoyl-2-butyl-1-oxo-7a-phenyl-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4ac)

Yield 53%; white solid. mp 227-228 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.97 (d, J = 7.2 Hz, 2H), 7.65 (t, J = 7.6 Hz, 1H), 7.56-7.48 (m, 4H), 7.47-7.42 (m, 3H), 6.62 (s, 2H), 4.71 (s, 1H), 3.86-3.75 (m, 2H), 1.78-1.68 (m, 2H), 1.40-1.30 (m, 2H), 0.93 (t, J = 7.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 194.8, 181.1, 171.6, 155.7, 135.9, 134.7, 133.9, 129.5, 129.3, 129.2, 129.0, 124.7, 75.0, 61.7, 57.4, 41.9, 28.7, 19.9, 13.6. IR (KBr): 3376, 3306, 3244, 3188, 2956, 2196, 1757, 1675, 1652, 1589, 1389, 1055, 696, 572 cm^{-1}. HRMS (APCI): m/z [M+H]$^+$ calcd for $C_{24}H_{23}N_4O_2S$: 431.1536; found: 431.1540.



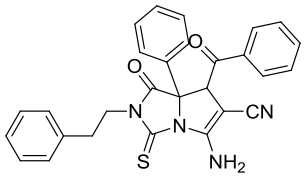
5-amino-7-benzoyl-1-oxo-2,7a-diphenyl-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4ad)

Yield 70%; white solid. mp >300 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 8.22 (d, J = 8.0 Hz, 2H), 8.17 (s, 2H), 7.77 (t, J = 7.2 Hz, 1H), 7.71 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 7.6 Hz, 2H), 7.60-7.55 (m, 4H), 7.54-7.50 (m, 2H), 7.36 (d, J = 7.6 Hz, 2H), 5.31 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 196.2, 180.6, 171.3, 154.8, 135.5, 134.8, 133.7, 132.7, 129.7, 129.6, 129.5, 129.4, 129.2, 128.92, 128.3, 125.3, 117.0, 75.6, 59.7, 56.1. IR (KBr): 3336, 3241, 3181, 2190, 1770, 1649, 1582, 1447, 1374, 1286, 703, 563cm^{-1}. HRMS (APCI): m/z [M+H]$^+$ calcd for $C_{26}H_{19}N_4O_2S$: 451.1223; found: 451.1224.



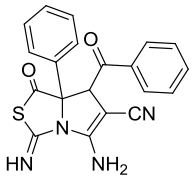
5-amino-7-benzoyl-2-benzyl-1-oxo-7a-phenyl-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4ae)

Yield 80%; yellow solid. mp 240-241 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) 7.96 (d, J = 7.8 Hz, 2H), 7.66 (t, J = 7.8 Hz, 1H), 7.57-7.48 (m, 4H), 7.48-7.42 (m, 3H), 7.33 (d, J = 7.2 Hz, 2H), 7.28 (t, J = 7.2 Hz, 2H), 7.26-7.23 (m, 1H), 6.46 (s, 2H), 5.15-4.95 (m, 2H), 4.76 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 194.6, 180.4, 171.6, 155.5, 135.8, 134.8, 134.4, 133.8, 129.6, 129.3, 129.2, 128.9, 128.4, 128.1, 127.7, 124.8, 116.7, 75.2, 61.6, 57.3, 45.1. IR (KBr): 3356, 3241, 3181, 2194, 1754, 1675, 1650, 1588, 1396, 1251, 940, 697, 527 cm^{-1}. HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{27}H_{21}N_4O_2S$: 465.1380; found: 465.1381.



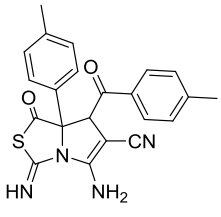
5-amino-7-benzoyl-1-oxo-2-phenethyl-7a-phenyl-3-thioxo-2,3,7,7a-tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole-6-carbonitrile (4af)

Yield 75%; yellow solid. mp 246-247 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) 7.97 (d, J = 7.8 Hz, 2H), 7.66 (t, J = 7.2 Hz, 1H), 7.57-7.48 (m, 4H), 7.47-7.38 (m, 3H), 7.24-7.05 (m, 5H), 6.52 (s, 2H), 4.70 (s, 1H), 4.05 (t, J = 7.8 Hz, 2H), 3.11-2.98 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 194.9, 180.9, 171.4, 155.7, 137.4, 135.8, 134.8, 133.9, 129.5, 129.3, 129.2, 129.0, 128.8, 128.4, 126.5, 124.8, 75.1, 61.8, 57.6, 43.0, 32.6. IR (KBr): 3392, 3279, 3061, 2190, 1729, 1671, 1638, 1586, 1446, 1372, 1249, 705, 574 cm^{-1}. HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{28}H_{23}N_4O_2S$: 479.1536; found: 479.1536.



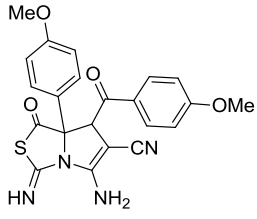
5-amino-7-benzoyl-3-imino-1-oxo-7a-phenyl-1,3,7,7a-tetrahydropyrrolo[1,2-*c*]thiazole-6-carbonitrile (5aa)

Yield 85%; yellow solid. mp 190-192 °C. 1H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.10 (s, 1H), 8.15 (d, J = 7.8 Hz, 2H), 8.01 (s, 1H), 7.74 (t, J = 7.2 Hz, 1H), 7.65 (d, J = 7.2 Hz, 2H), 7.59 (t, J = 7.8 Hz, 2H), 7.55 (t, J = 7.8 Hz, 2H), 7.53-7.49 (m, 1H), 5.08 (s, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 196.2, 195.4, 155.8, 155.7, 151.6, 136.8, 134.7, 134.1, 129.7, 129.6, 129.3, 129.0, 125.3, 118.0, 82.6, 56.1. IR (KBr): 3325, 3168, 2188, 1748, 1667, 1645, 1447, 1347, 1104, 915, 704 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{15}N_4O_2S$: 375.09102; found: 375.09054.



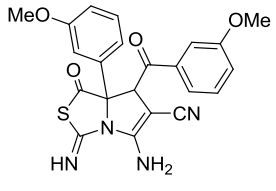
5-amino-3-imino-7-(4-methylbenzoyl)-1-oxo-7a-(p-tolyl)-1,3,7,7a-tetrahydropyrrolo[1,2-*c*]thiazole-6-carbonitrile (5ba)

Yield 89%; white solid. mp 188-190 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.05 (s, 1H), 8.02 (d, J = 7.8 Hz, 2H), 7.97 (s, 1H), 7.51 (d, J = 7.8 Hz, 2H), 7.39 (d, J = 7.8 Hz, 2H), 7.34 (d, J = 7.8 Hz, 2H), 4.98 (s, 1H), 2.41 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 195.8, 195.5, 155.8, 155.7, 151.8, 145.4, 139.3, 134.0, 131.7, 129.8, 129.6, 129.6, 125.1, 118.0, 82.5, 56.1, 21.4, 20.7. IR (KBr): 3318, 3176, 2186, 1747, 1644, 1570, 1447, 1350, 1109, 915, 753 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{22}H_{19}N_4O_2S$: 403.12232; found: 403.12155.



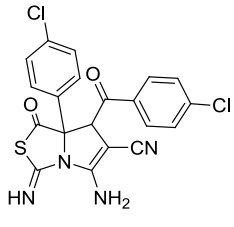
5-amino-3-imino-7-(4-methoxybenzoyl)-7a-(4-methoxyphenyl)-1-oxo-1,3,7,7a-tetra hydropyrrolo[1,2-*c*]thiazole-6-carbonitrile (5ca)

Yield 78%; yellow solid. mp 176-178 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.01 (s, 1H), 8.10 (d, J = 8.4 Hz, 2H), 7.92 (s, 2H), 7.52 (d, J = 8.4 Hz, 2H), 7.12-7.06 (m, 4H), 4.94 (s, 1H), 3.88 (s, 3H), 3.80 (s, 3H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 195.5, 194.9, 164.2, 160.2, 155.8, 151.7, 132.0, 128.5, 127.0, 126.5, 118.1, 114.6, 114.2, 82.3, 56.5, 55.9, 55.7, 55.4. IR (KBr): 3415, 3308, 2187, 1748, 1641, 1599, 1510, 1443, 1343, 1255, 1105, 915, 836 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{22}H_{19}N_4O_4S$: 435.11215; found: 435.11139.



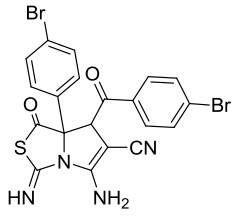
5-amino-3-imino-7-(3-methoxybenzoyl)-7a-(3-methoxyphenyl)-1-oxo-1,3,7,7a-tetra hydropyrrolo[1,2-*c*]thiazole-6-carbonitrile (5da)

Yield 85%; yellow solid. mp 131-133 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.06 (s, 1H), 8.00 (s, 2H), 7.75 (d, J = 5.4 Hz, 1H), 7.62 (s, 1H), 7.53-7.42 (m, 2H), 7.33-7.27 (m, 1H), 7.22-7.12 (m, 2H), 7.09 (d, J = 8.4 Hz, 1H), 5.10 (s, 1H), 3.85 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 195.5, 195.1, 159.7, 159.5, 155.7, 151.4, 138.3, 135.3, 130.3, 130.0, 122.2, 121.2, 118.1, 117.1, 114.7, 113.5, 111.6, 82.5, 56.1, 56.1, 55.5, 55.3. IR (KBr): 3391, 3274, 3077, 2833, 2186, 1752, 1644, 1487, 1447, 1346, 1264, 1116, 928, 741, 549 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{22}H_{19}N_4O_4S$: 435.11215; found: 435.11161.



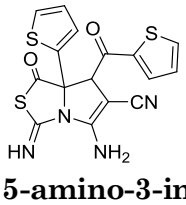
5-amino-7-(4-chlorobenzoyl)-7a-(4-chlorophenyl)-3-imino-1-oxo-1,3,7,7a-tetrahydropyrrolo[1,2-*c*]thiazole-6-carbonitrile (5ea)

Yield 80%; yellow solid. mp 179-180 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.14 (s, 1H), 8.15 (d, J = 8.4 Hz, 2H), 8.01 (s, 2H), 7.76-7.53 (m, 6H), 5.09 (s, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 195.1, 194.8, 155.7, 151.2, 139.8, 135.6, 134.5, 132.7, 131.5, 129.2, 129.1, 127.2, 117.8, 82.0, 55.9, 55.6. IR (KBr): 3335, 3174, 2189, 1739, 1648, 1445, 1347, 1095, 978, 917 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{20}H_{13}C_{l2}N_4O_2S$: 443.01308; found: 443.01286.



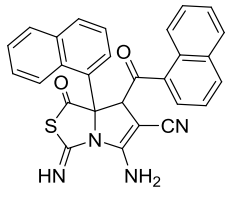
5-amino-7-(4-bromobenzoyl)-7a-(4-bromophenyl)-3-imino-1-oxo-1,3,7,7a-tetrahydropyrrolo[1,2-*c*]thiazole-6-carbonitrile (5fa)

Yield 82%; yellow solid. mp 188-189 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.14 (s, 1H), 8.07 (d, J = 8.4 Hz, 2H), 8.01 (s, 2H), 7.81 (d, J = 8.4 Hz, 2H), 7.76 (d, J = 9.0 Hz, 2H), 7.57 (d, J = 8.4 Hz, 2H), 5.08 (s, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 195.0, 155.7, 151.1, 136.0, 133.0, 132.1, 132.0, 131.5, 129.1, 127.5, 123.1, 117.8, 82.0, 55.8, 55.6. IR (KBr): 3382, 2975, 2896, 1923, 1757, 1654, 1452, 1382, 1088, 1049, 881, 667 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{20}H_{13}Br_2N_4O_2S$: 530.91205; found: 530.91138.



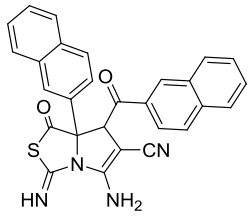
5-amino-3-imino-1-oxo-7a-(thiophen-2-yl)-7-(thiophene-2-carbonyl)-1,3,7,7a-tetrahydropyrrolo[1,2-*c*]thiazole-6-carbonitrile (5ga)

Yield 50%; gray solid. mp 179-181 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.15 (s, 1H), 8.31 (d, J = 2.4 Hz, 1H), 8.22 (d, J = 4.8 Hz, 1H), 7.93 (s, 1H), 7.68 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 3.0 Hz, 1H), 7.35 (t, J = 4.2 Hz, 1H), 7.18 (t, J = 4.2 Hz, 1H), 4.99 (s, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 194.7, 189.8, 155.8, 151.1, 141.2, 141.1, 138.1, 136.8, 129.4, 128.4, 127.5, 126.3, 117.9, 81.1, 57.0, 56.8. IR (KBr): 3328, 3166, 2187, 1746, 1645, 1452, 1413, 1351, 1099, 851, 719 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{16}H_{11}N_4O_2S_3$: 387.00386; found: 387.00335.



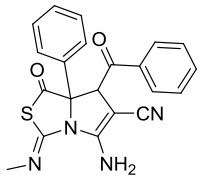
7-(1-naphthoyl)-5-amino-3-imino-7a-(naphthalen-1-yl)-1-oxo-1,3,7,7a-tetrahydropyrrolo[1,2-*c*]thiazole-6-carbonitrile (5ha)

Yield 62%; yellow solid. mp 196-197 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.25 (s, 1H), 8.71 (d, J = 8.4 Hz, 1H), 8.44-8.40 (m, 1H), 8.33 (s, H_{CHCl_3}), 8.31 (d, J = 8.4 Hz, 1H), 8.26 (d, J = 7.2 Hz, 1H), 8.19 (s, 2H), 8.15-8.08 (m, 3H), 7.88-7.83 (m, 1H), 7.78-7.73 (m, 1H), 7.72-7.65 (m, 3H), 7.65-7.59 (m, 2H), 5.45 (s, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 198.0, 193.8, 155.4, 151.7, 134.9, 134.9, 134.8, 134.8, 133.7, 132.0, 131.8, 131.4, 130.6, 130.2, 129.6, 128.9, 128.8, 128.5, 126.9, 126.8, 126.3, 125.6, 125.0, 123.6, 117.6, 83.8, 79.2(C_{CHCl_3}), 56.8, 56.8. IR (KBr): 3452, 3258, 2188, 1739, 1637, 1568, 1440, 1350, 1270, 1120, 911, 876, 737 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{28}H_{19}N_4O_2S$: 475.12232; found: 475.12191.



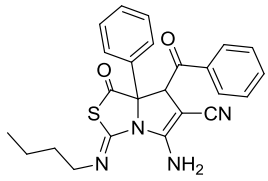
7-(2-naphthoyl)-5-amino-3-imino-7a-(naphthalen-2-yl)-1-oxo-1,3,7,7a-tetrahydropyrrolo[1,2-*c*]thiazole-6-carbonitrile (5ia)

Yield 75%; yellow solid. mp 210-212 °C. ^{1}H NMR (DMSO-d_6, 600 MHz): δ (ppm) 10.19 (s, 1H), 9.03 (s, 1H), 8.22 (s, 1H), 8.17-8.05 (m, 7H), 8.05-8.00 (m, 2H), 7.82 (d, J = 9.0 Hz, 1H), 7.72 (t, J = 7.8 Hz, 1H), 7.68-7.59 (m, 3H), 5.43 (s, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ (ppm) 196.0, 195.4, 156.0, 151.6, 135.6, 134.2, 133.2, 132.5, 132.1, 131.3, 130.0, 129.5, 129.2, 128.7, 128.5, 127.8, 127.6, 127.4, 127.2, 127.1, 124.5, 123.9, 122.8, 118.0, 82.8, 56.4, 56.2. IR (KBr): 3380, 3279, 2176, 1741, 1637, 1449, 1353, 1105, 917, 751 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{28}H_{19}N_4O_2S$: 475.12232; found: 475.12188.



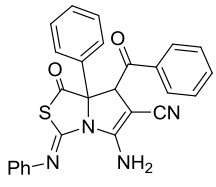
5-amino-7-benzoyl-3-(methylimino)-1-oxo-7a-phenyl-1,3,7,7a-tetrahydropyrrolo[1,2-*c*]thiazole-6-carbonitrile (5ab)

Yield 46%; yellow solid. mp 192-194 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) 7.99 (d, J = 7.8 Hz, 2H), 7.65 (t, J = 7.8 Hz, 1H), 7.58 (d, J = 6.0 Hz, 2H), 7.52 (t, J = 7.8 Hz, 2H), 7.48-7.42 (m, 3H), 6.59 (s, 2H), 4.70 (s, 1H), 3.22 (s, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ (ppm) 195.8, 193.4, 156.7, 148.7, 136.8, 134.6, 134.2, 129.6, 129.3, 129.2, 129.0, 125.0, 117.8, 81.9, 58.3, 57.6, 41.0. IR (KBr): 3359, 2975, 2895, 1925, 1661, 1446, 1381, 1089, 1049, 881, 665 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{21}H_{17}N_4O_2S$: 389.1067; found: 389.1073.



5-amino-7-benzoyl-3-(butylimino)-1-oxo-7a-phenyl-1,3,7,7a-tetrahydropyrrolo[1,2-*c*]thiazole-6-carbonitrile (5ac)

Yield 75%; red solid. mp 170-172 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.98 (d, J = 8.0 Hz, 2H), 7.63 (t, J = 7.6 Hz, 1H), 7.58-7.55 (m, 2H), 7.51 (t, J = 8.0 Hz, 2H), 7.46-7.34 (m, 3H), 6.78 (s, 2H), 4.68 (s, 1H), 3.42-3.20 (m, 2H), 1.72-1.57 (m, 2H), 1.47-1.32 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 195.7, 193.7, 156.8, 146.8, 136.9, 134.5, 134.3, 129.5, 129.2, 129.1, 128.9, 124.9, 118.0, 81.5, 58.2, 57.0, 54.7, 32.7, 20.4, 13.8. IR (KBr): 3324, 3223, 2959, 2188, 1742, 1655, 1448, 1215, 1035, 916, 811, 702 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{24}H_{23}N_4O_2S$: 431.15362; found: 431.15439.



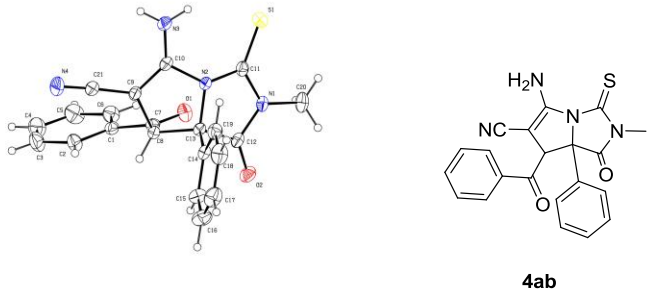
5-amino-7-benzoyl-1-oxo-7a-phenyl-3-(phenylimino)-1,3,7,7a-tetrahydropyrrolo[1,2-*c*]thiazole-6-carbonitrile (5ad)

Yield 66%; yellow solid. mp 228-230 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) 8.01 (d, J = 7.2 Hz, 2H), 7.69-7.63 (m, 3H), 7.57-7.46 (m, 5H), 7.37 (t, J = 7.8 Hz, 2H), 7.20 (t, J = 7.2 Hz, 1H), 7.06 (d, J = 7.8 Hz, 2H), 6.62 (s, 2H), 4.74 (s, 1H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ (ppm) 195.7, 193.3, 156.1, 149.4, 147.4, 136.5, 134.7, 134.2, 129.8, 129.5, 129.2, 129.1, 125.7, 124.9, 121.3, 82.1, 59.2, 58.1. IR (KBr): 3394, 3238, 2924, 2189, 1770, 1664, 1443, 1344, 1138, 1025, 927, 759, 701 cm^{-1}. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{26}H_{19}N_4O_2S$: 451.12232; found: 451.12252.

Reference:

(1) Murai, M.; Yoshida, S.; Miki, K.; Ohe, K. *Chem. Commun.*, **2010**, *46*, 3366.

4. Molecular structure and crystallographic data of compounds 4ab, 4ac and 5aa

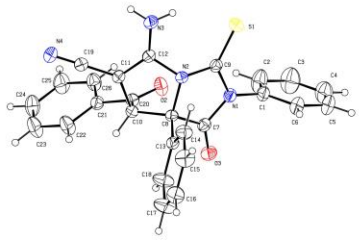


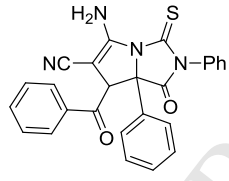
4ab

Figure S1 X-ray crystal structure of compounds **4ab**

Crystal Data for Compound **4ab**: $C_{21}H_{16}N_4O_2S$, MW = 388.44, triclinic, a = 8.2937(17) Å, b = 10.301(2) Å, c = 11.634(2) Å, α = 104.611(3)°, β = 90.670(3)°, γ = 99.561(3)°, V = 947.0(3)

Å^3, T = 298(2) K , space group P-1, Z = 2, m(Mo–Ka) = 0.196 mm^{-1}, 6761 reflections collected, 3862 unique [R(int) = 0.0234] which were used in all calculations. The final wR2 (F2) was 0.1360. CCDC 1010799 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

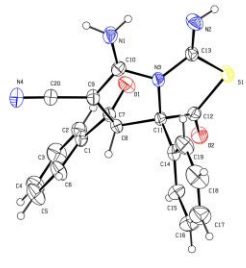


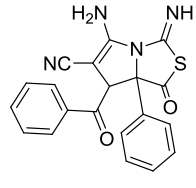


4ad

Figure S2 X-ray crystal structure of compounds **4ad**

Crystal Data for Compound **4ad**: $C_{26}H_{18}N_4O_2S$, MW = 450.50, monoclinic, a = 8.703(5) Å, b = 17.389(11) Å, c = 15.391(9) Å, α = 90° , β = 104.495(9)° , γ = 90° , V = 2255(2) Å^3, T = 298(2) K , space group P2(1)/n, Z = 4, m(Mo–Ka) = 0.175 mm^{-1}, 15624 reflections collected, 4652 unique [R(int) = 0.0253] which were used in all calculations. The final wR2 (F2) was 0.1241. CCDC 1010798 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.



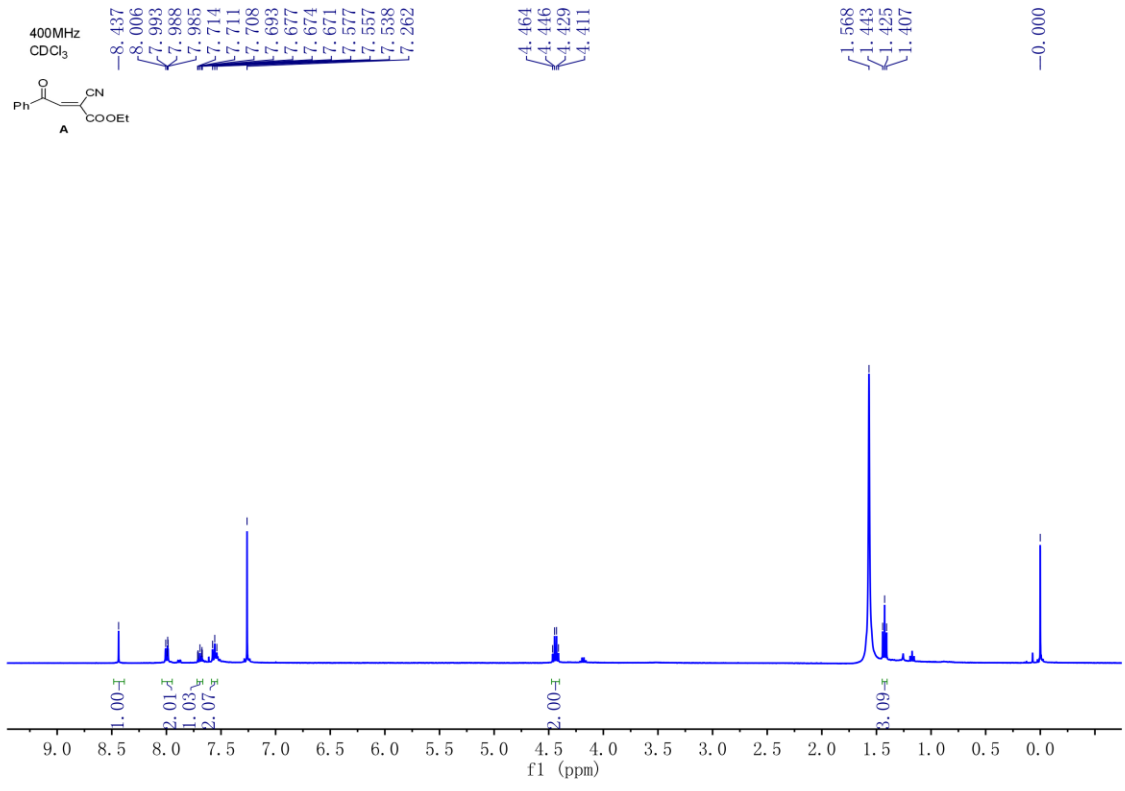


5aa

Figure S3 X-ray crystal structure of compounds **5aa**

Crystal Data for Compound **5aa**: $C_{20}H_{14}N_4O_2S$, MW = 374.41, triclinic, a = 9.2655(15) Å, b = 9.9525(16) Å, c = 12.714(2) Å, α = 111.089(2)° , β = 95.131(3)° , γ = 106.325(3)° , V = 1025.7(3) Å^3, T = 298(2) K , space group P-1, Z = 2, m(Mo–Ka) = 0.178 mm^{-1}, 3992 reflections collected, 3992 unique [R(int) = 0.0000] which were used in all calculations. The final wR2 (F2) was 0.1441. CCDC 1010796 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

5. ^{1}H NMR and ^{13}C NMR spectra of compounds 4, 5, A and B.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7.693
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7.674
7.671
7.577
7.557
7.538
7.262
4.464
4.446
4.429
4.411
1.568
1.443
1.425
1.407
0.000
Ph
CN
COOEt
A
1.00
2.01
1.03
2.07
2.00
3.09
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
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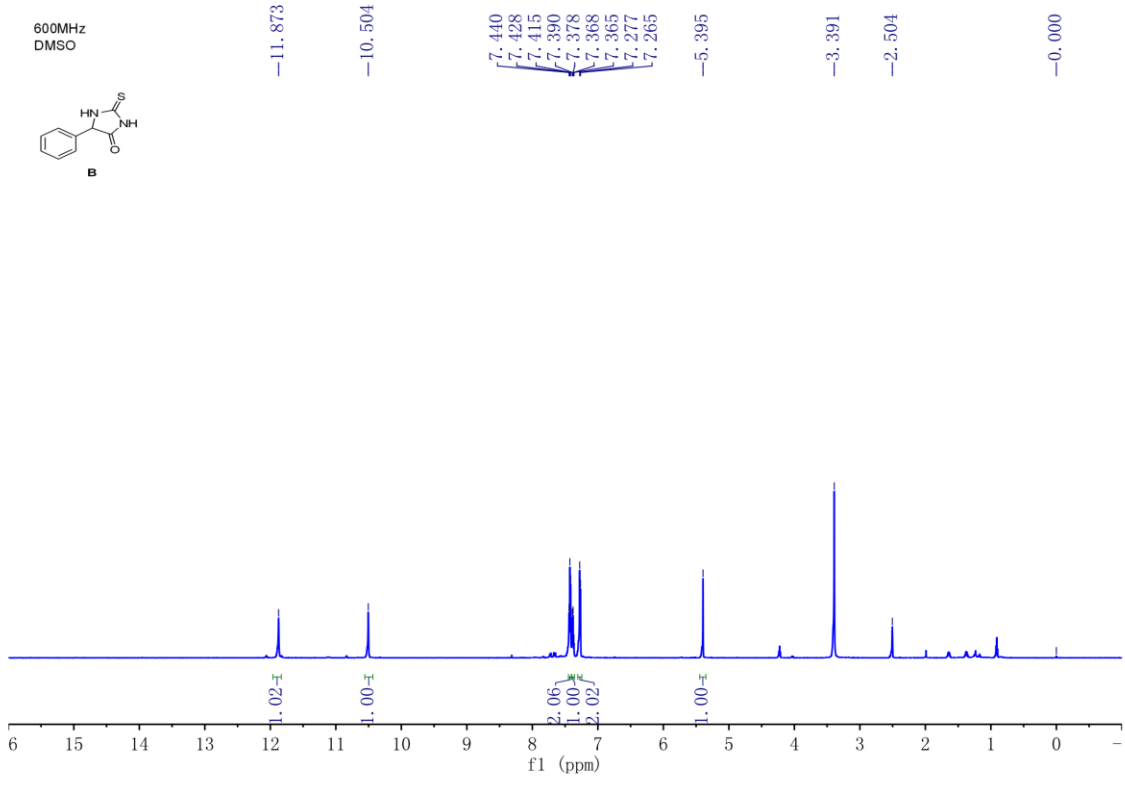
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0.000
HN
S
NH
O
B
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1.00
2.06
1.00
2.02
1.00
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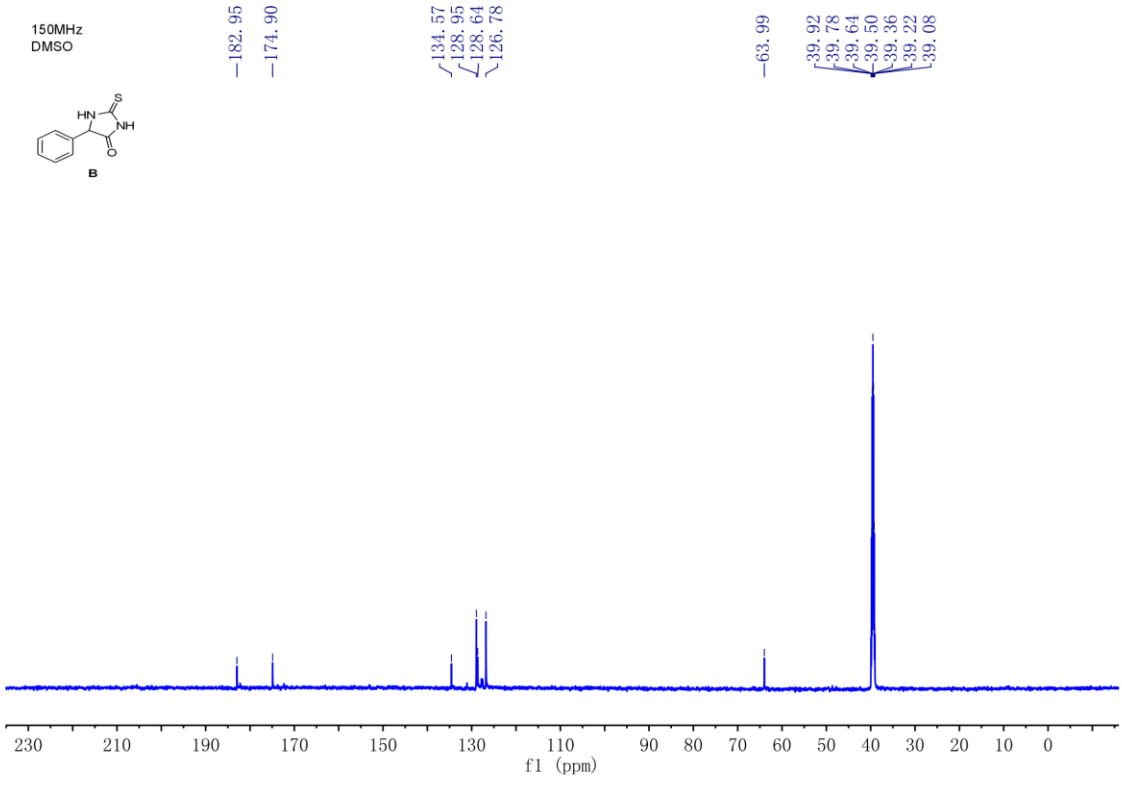
f1 (ppm)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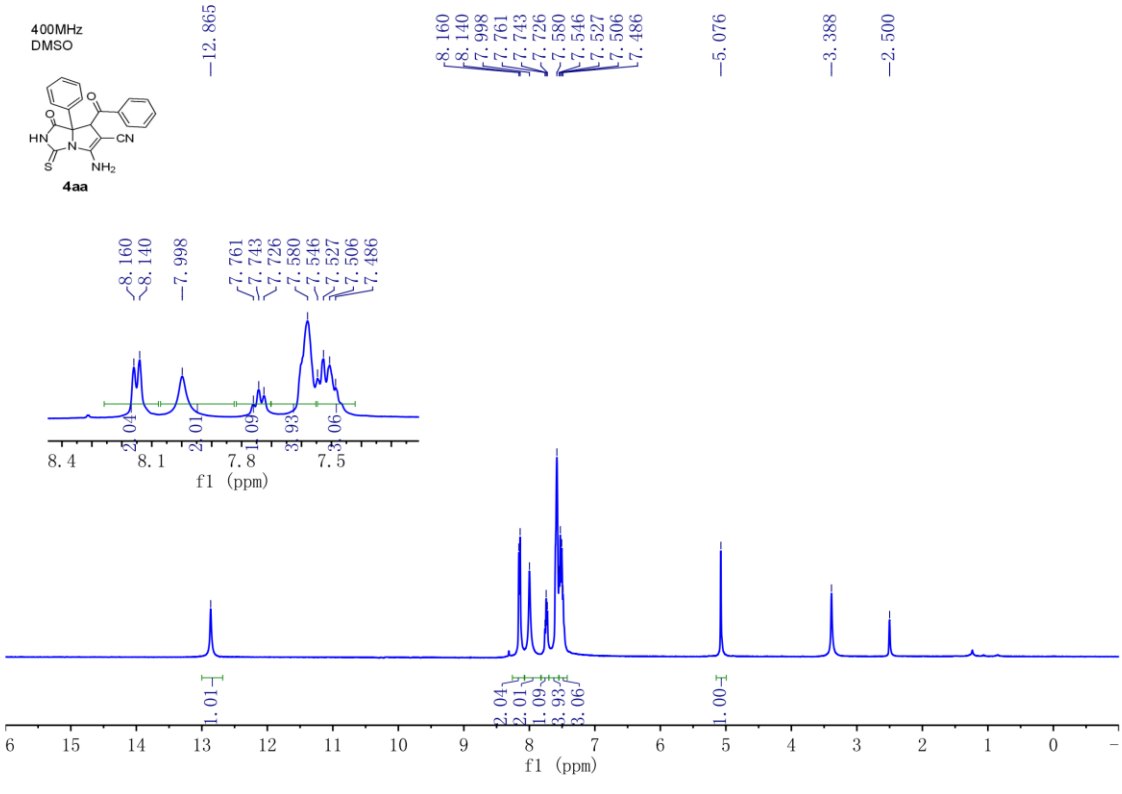
B
f1 (ppm)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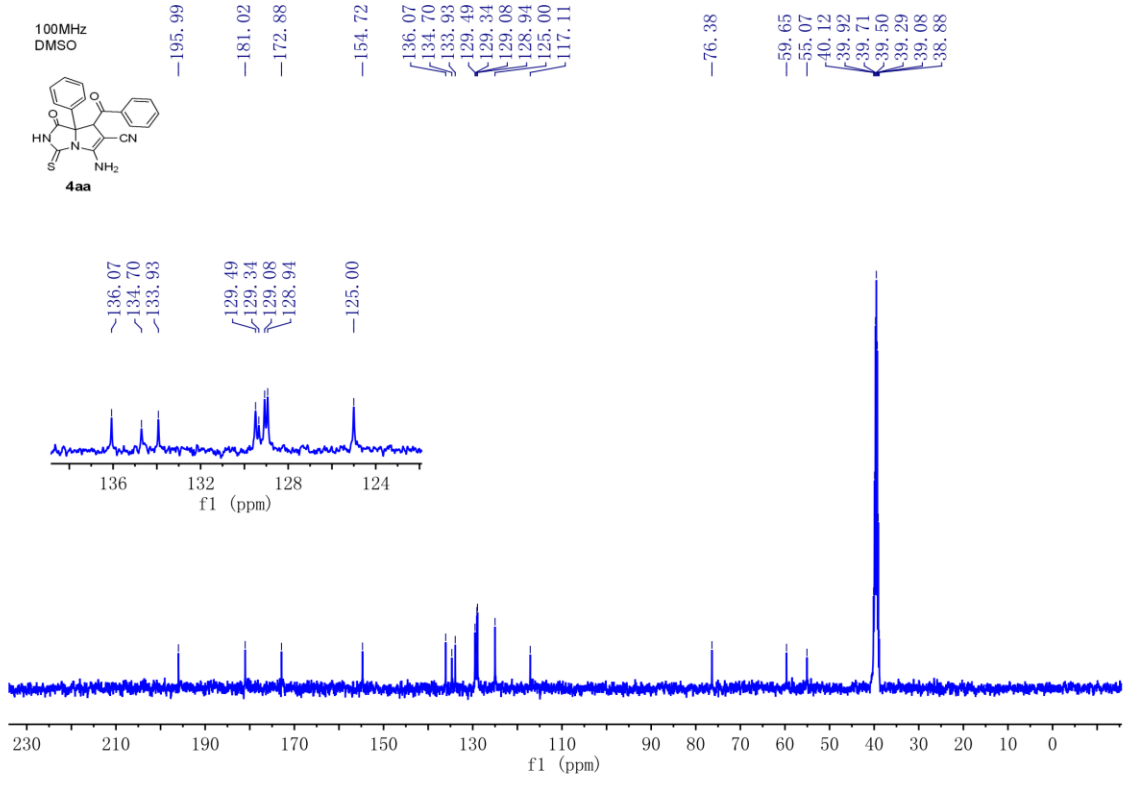
f1 (ppm)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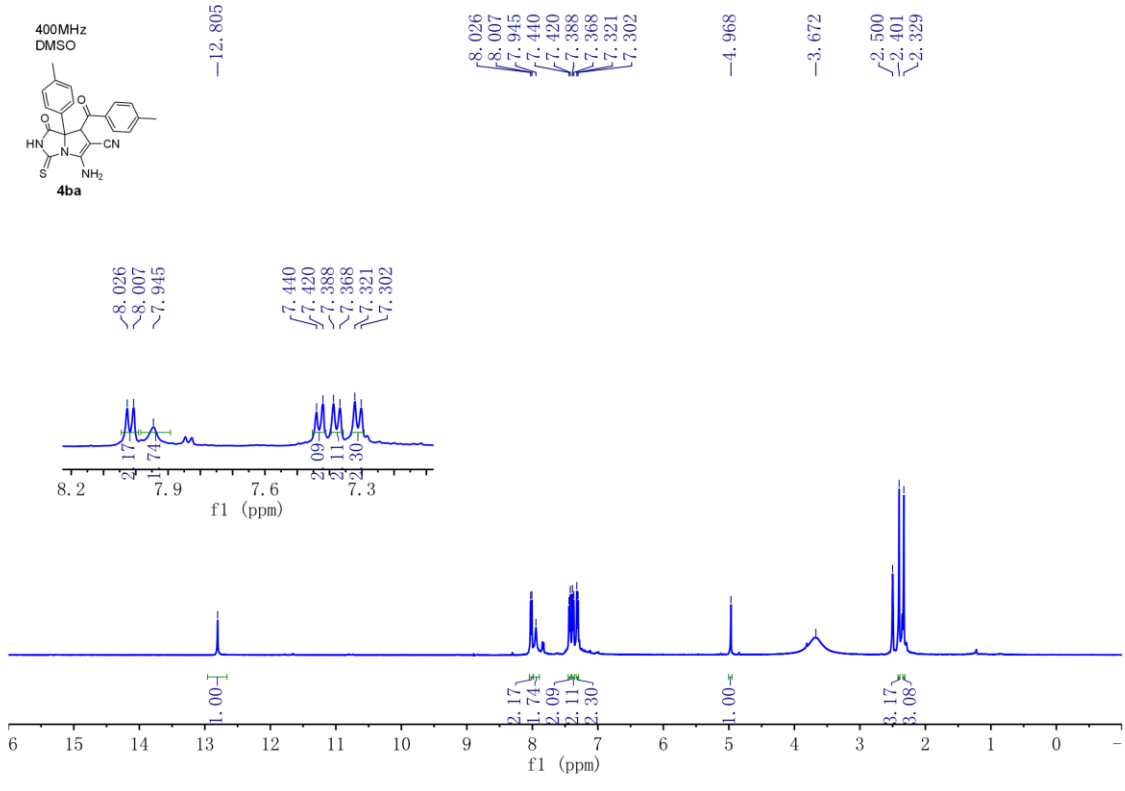
f1 (ppm)
f1 (ppm)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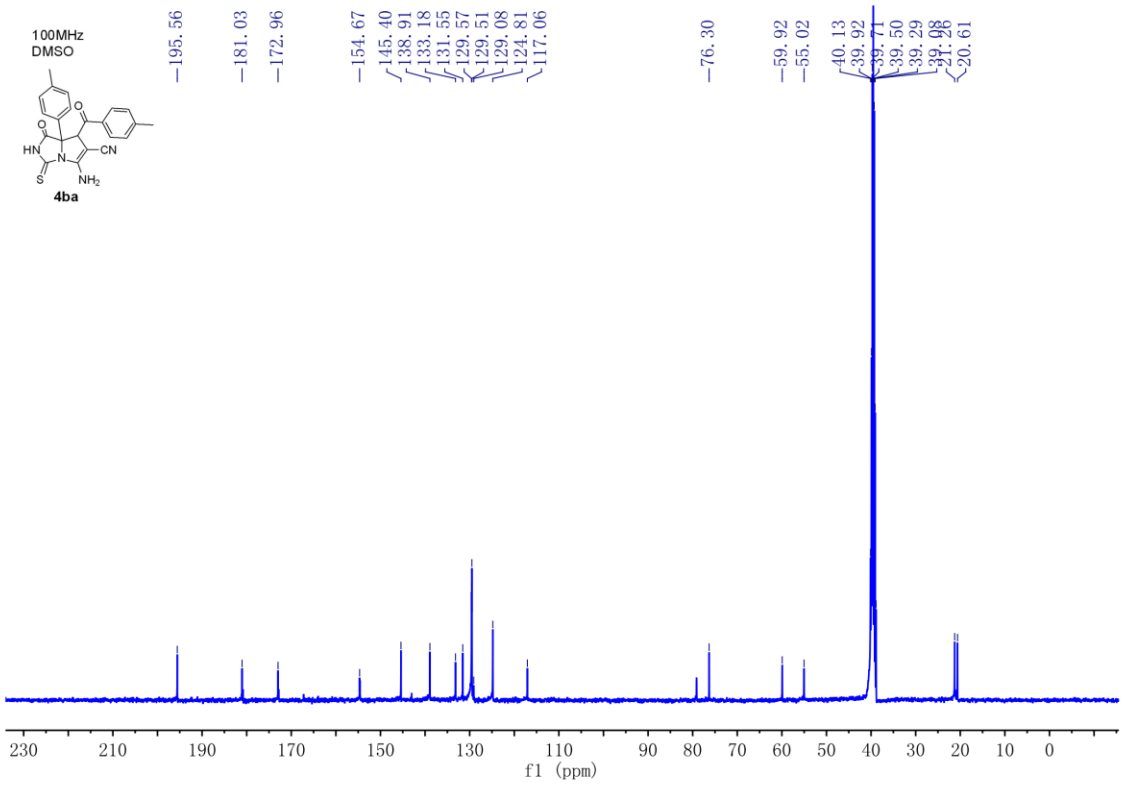
f1 (ppm)
f1 (ppm)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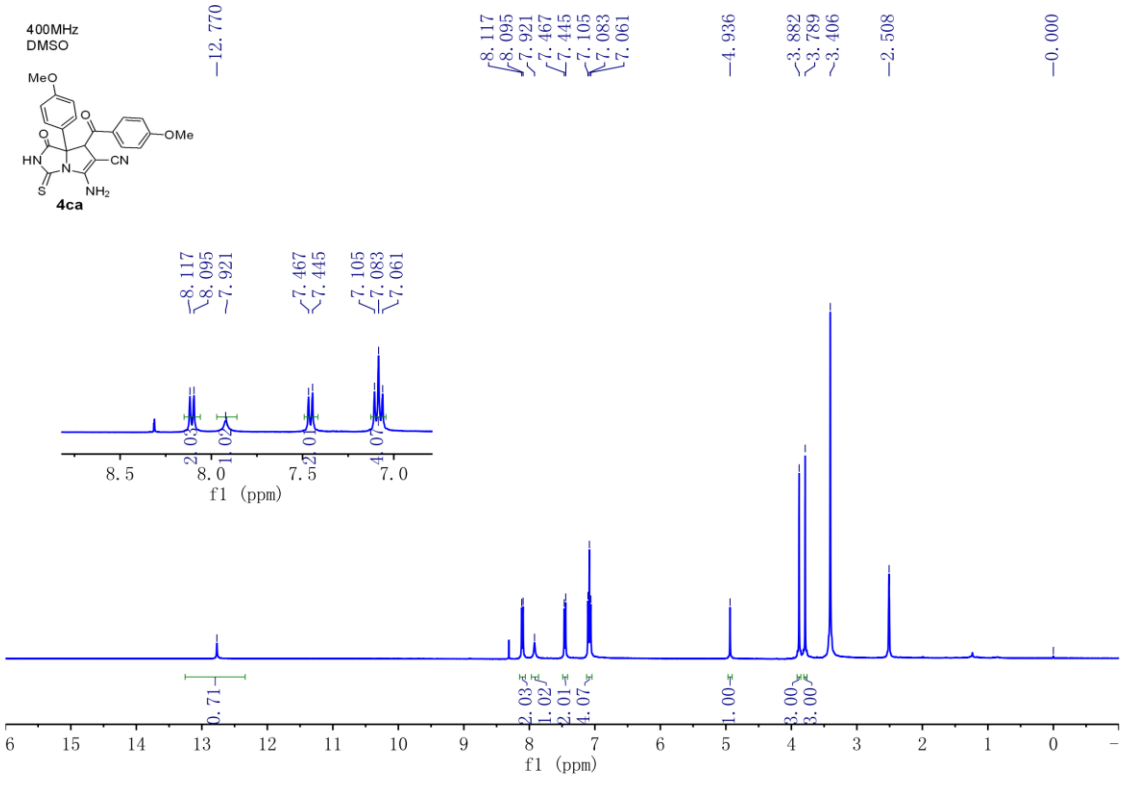
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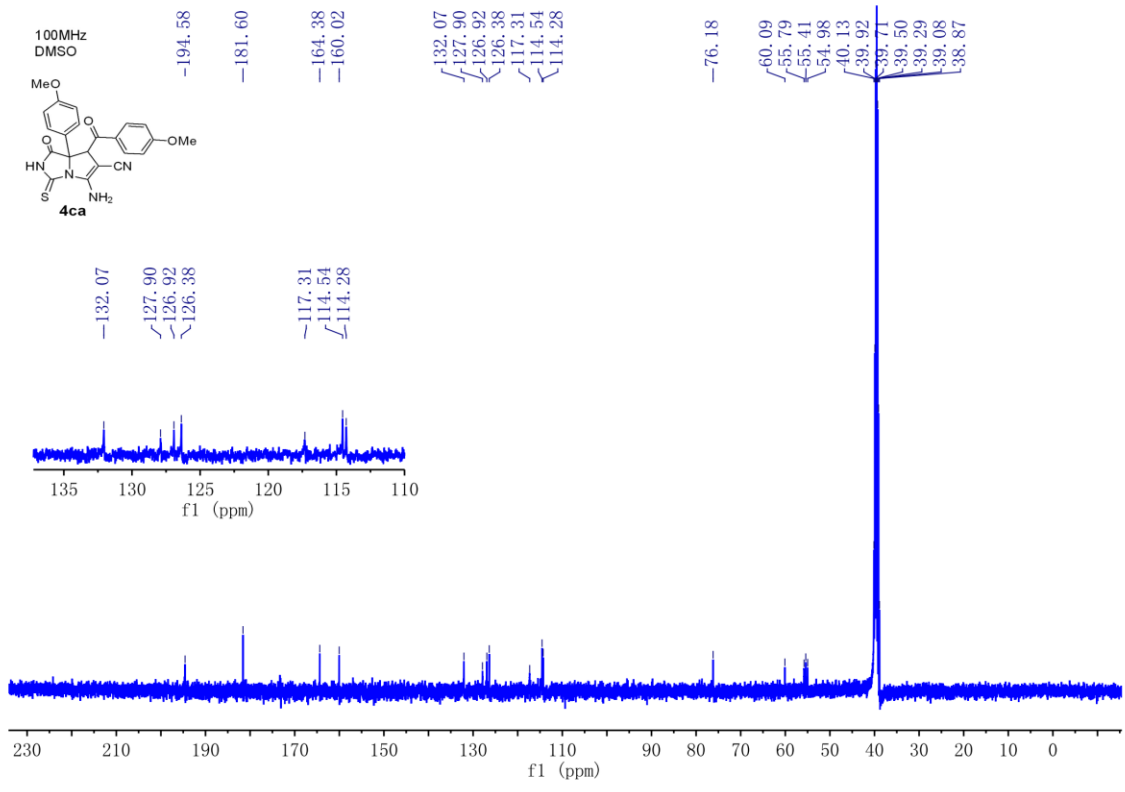
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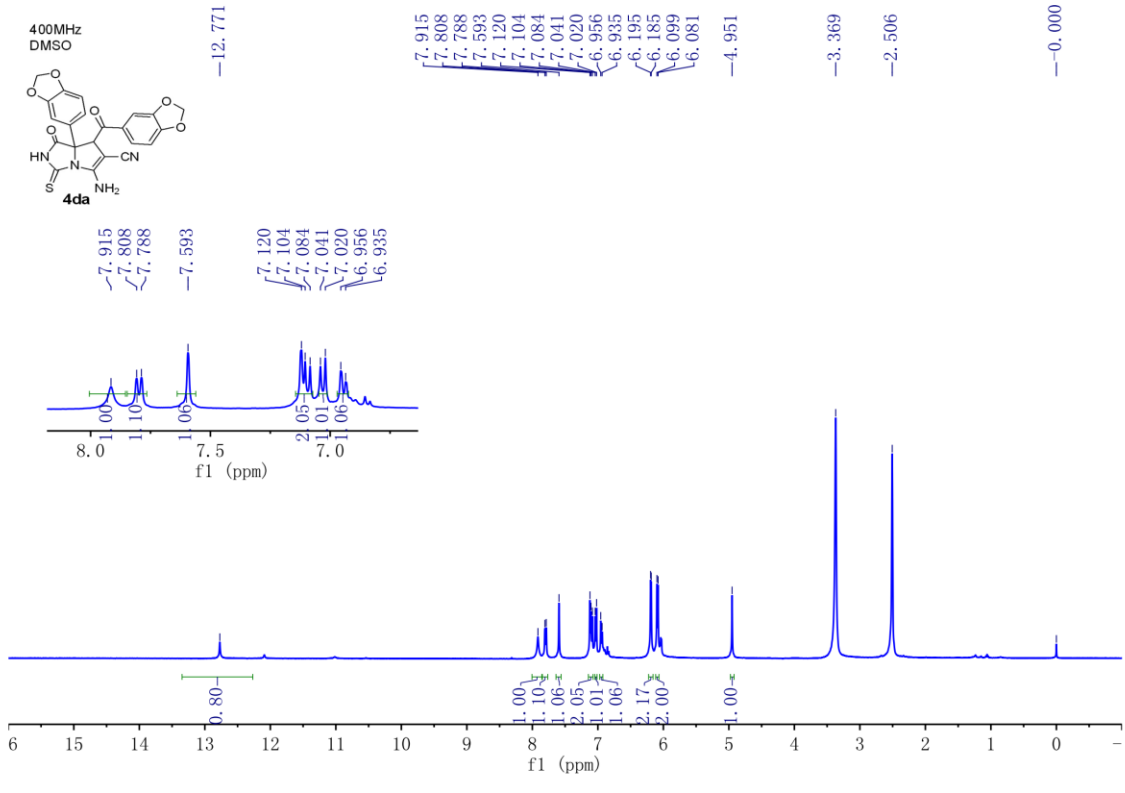
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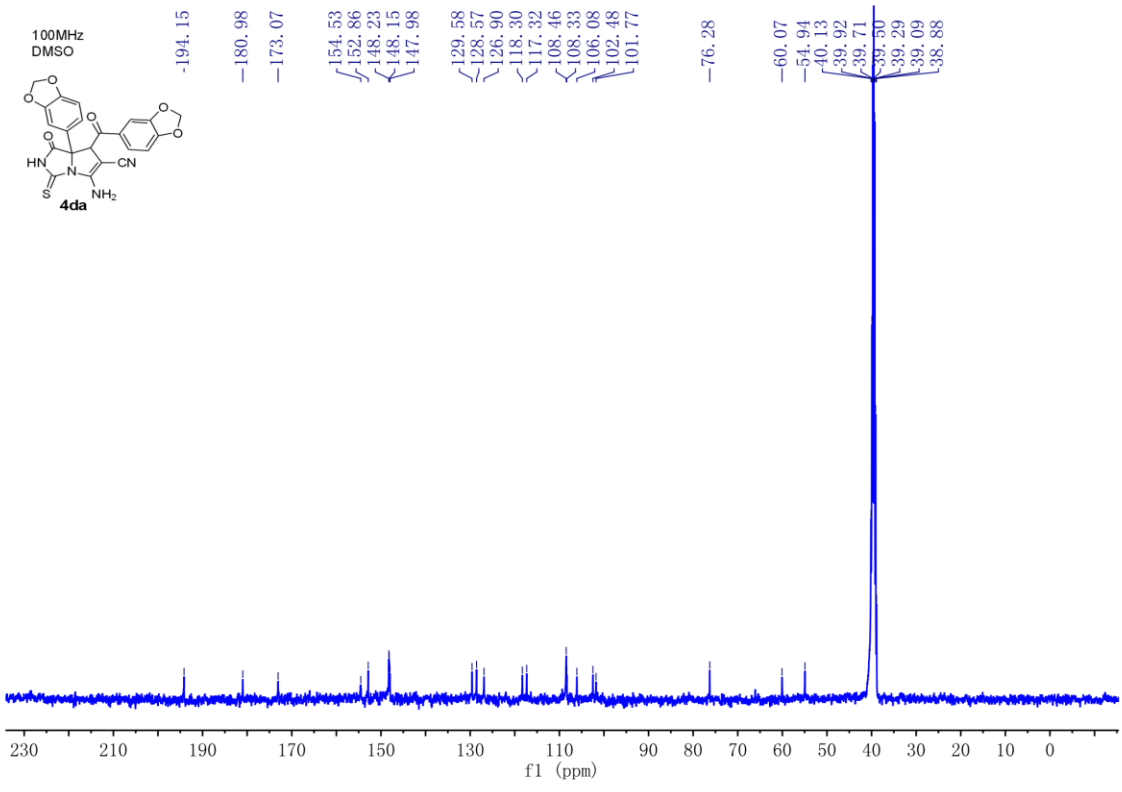
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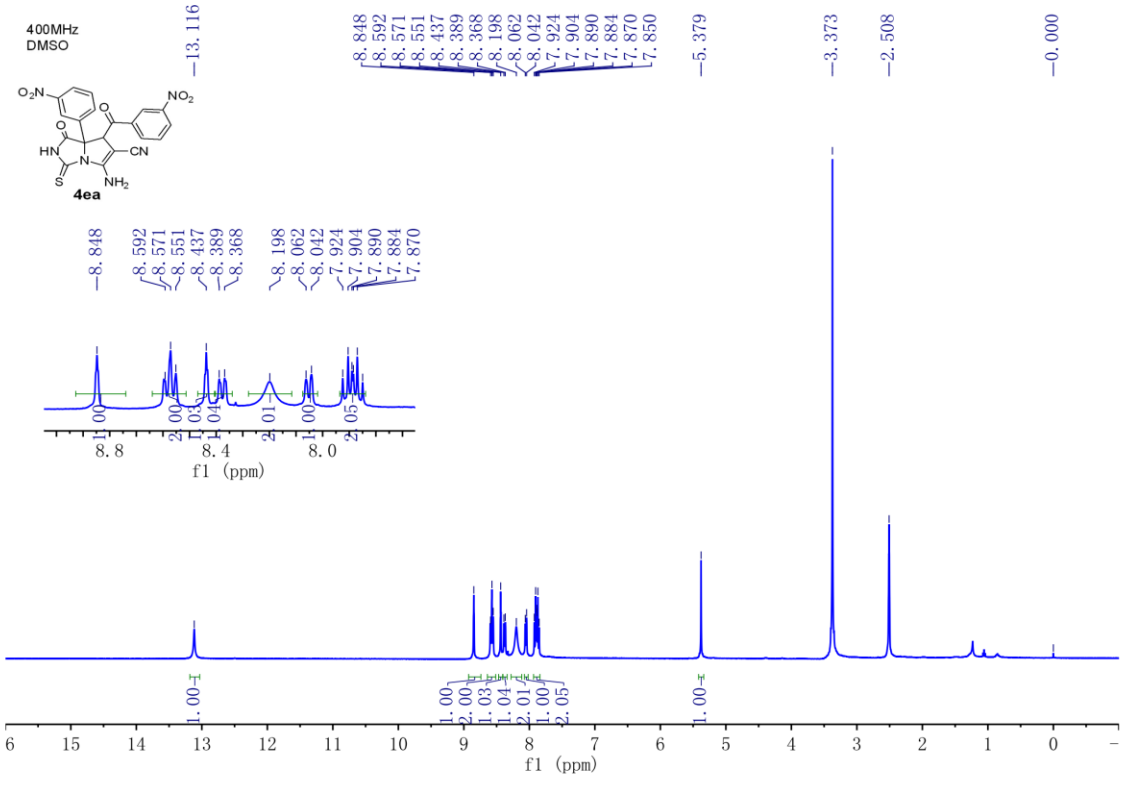
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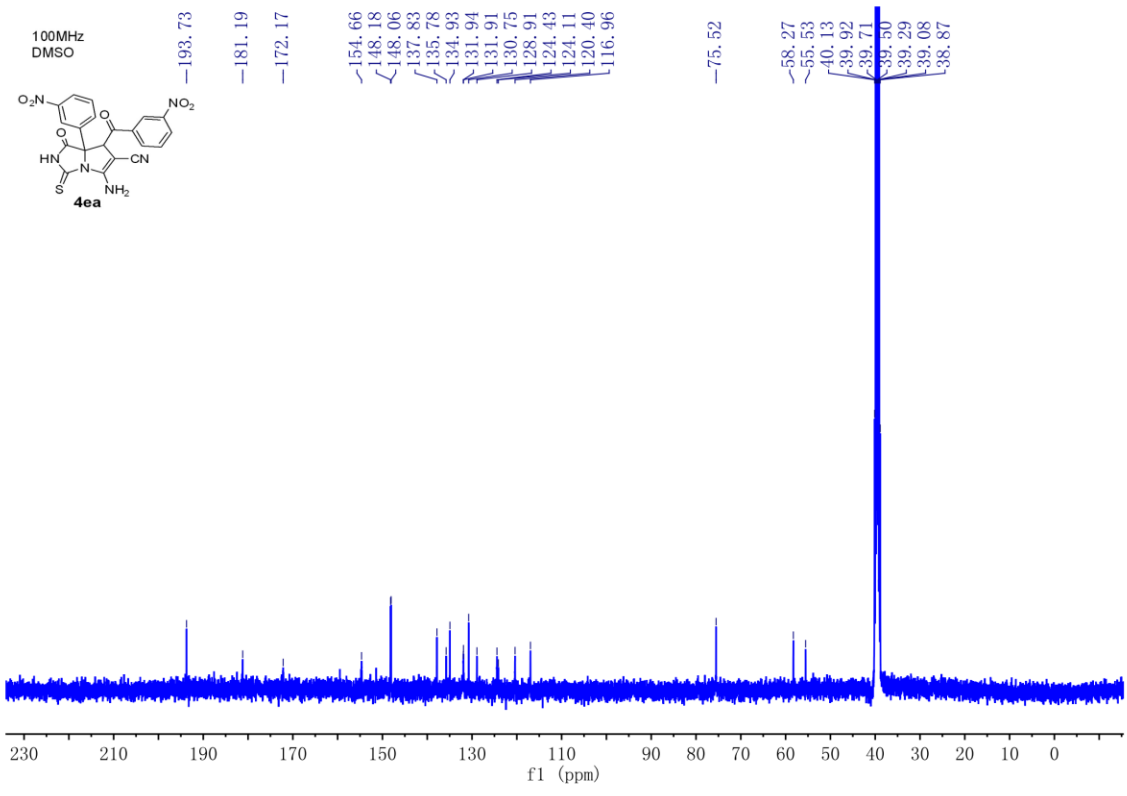
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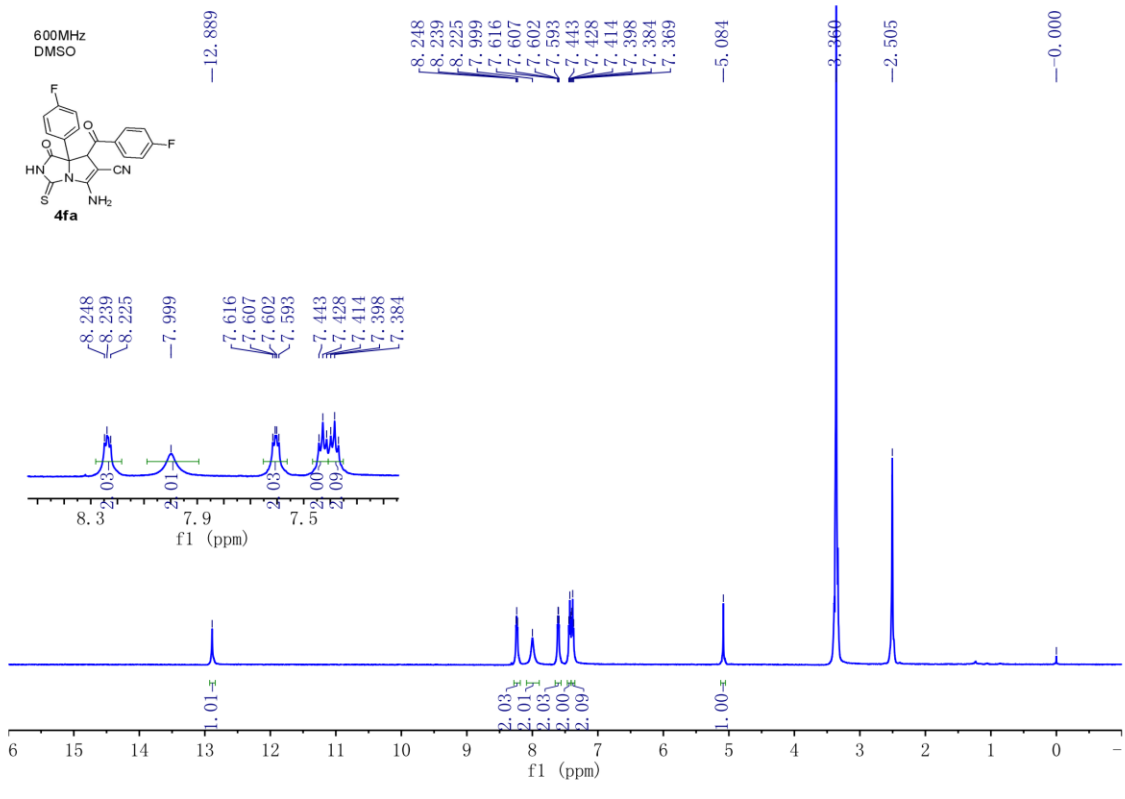
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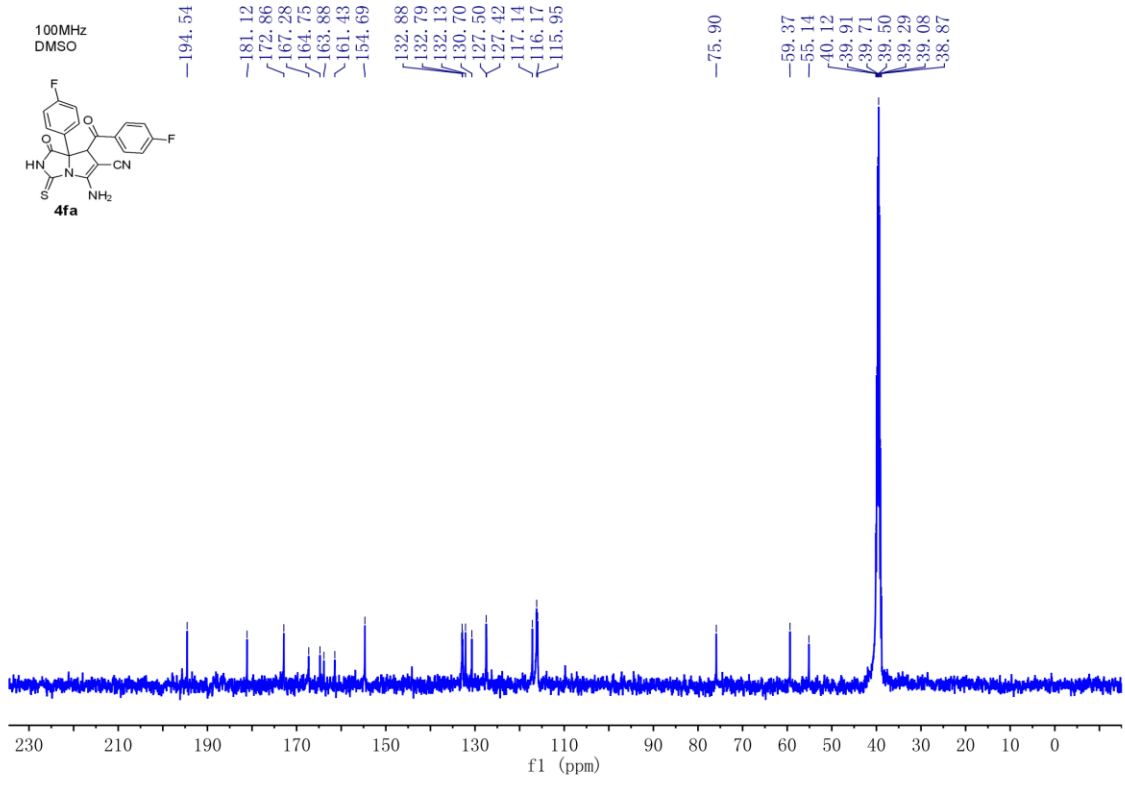
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181.12
172.86
167.28
164.75
163.88
161.43
154.69
132.88
132.79
132.13
130.70
127.50
127.42
117.14
116.17
115.95
75.90
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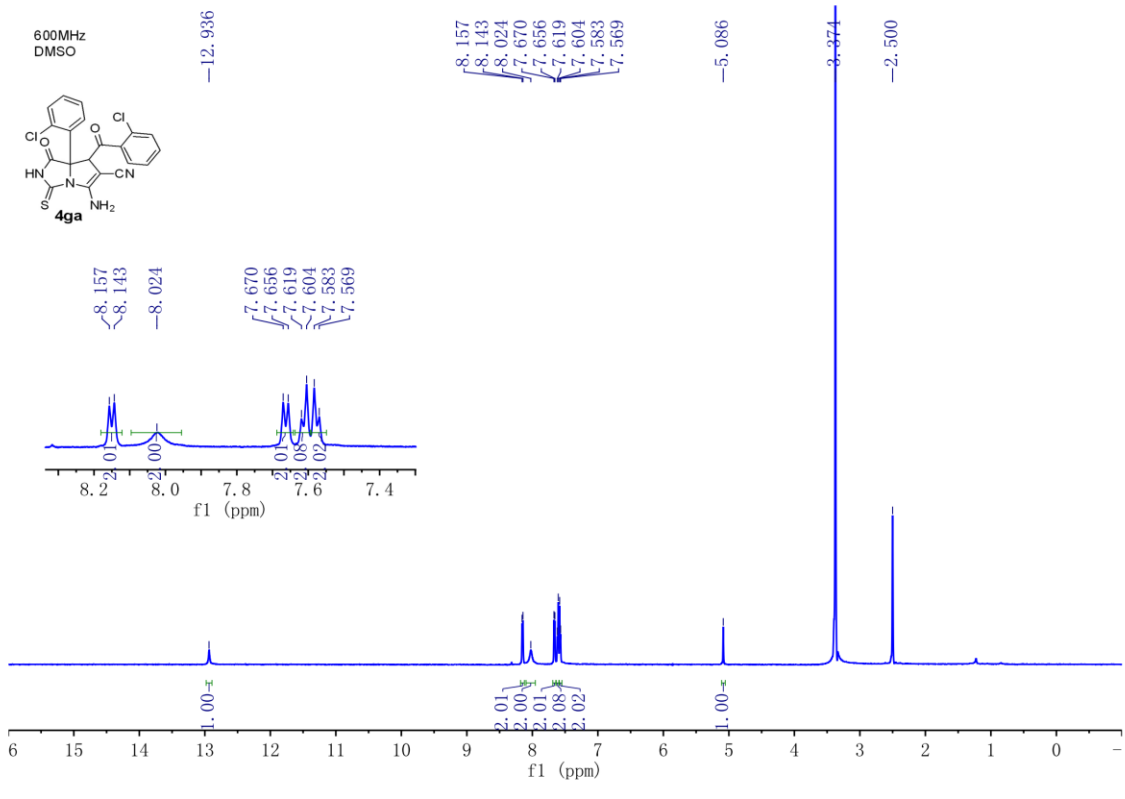
55.14
40.12
39.91
39.71
39.50
39.29
39.08
38.87
f1 (ppm)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DMSO
4ga
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8.143
8.024
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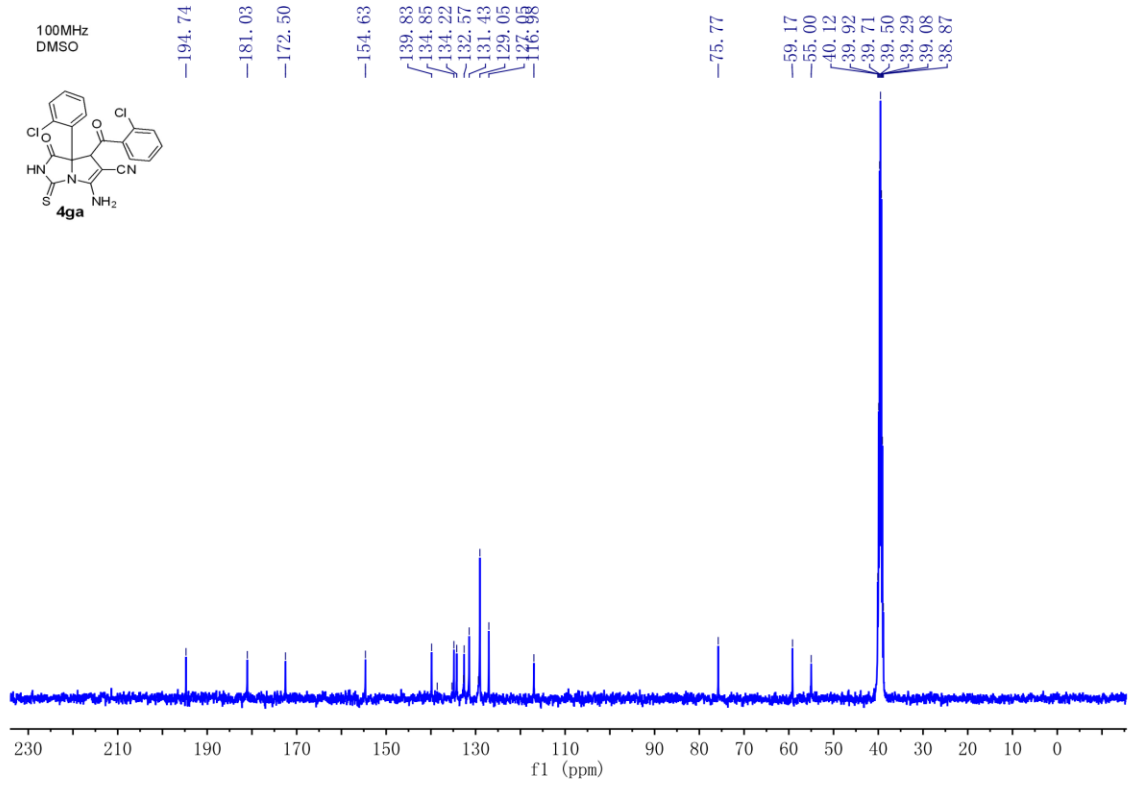
7.656
7.619
7.604
7.583
7.569
5.086
3.374
2.500
1.00
2.01
2.00
2.01
2.08
2.02
1.00
f1 (ppm)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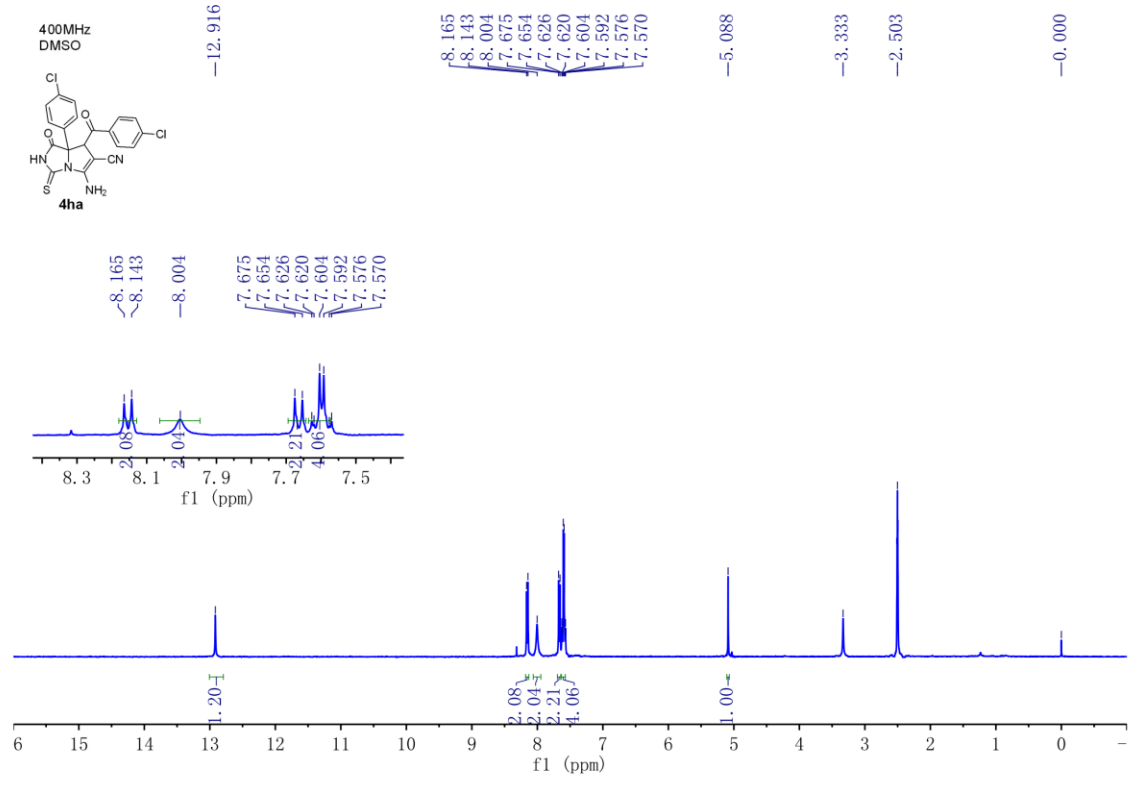
139.83
134.85
134.22
132.57
131.43
129.05
75.77
59.17
55.00
40.12
39.92
39.71
39.50
39.29
39.08
38.87
4ga
f1 (ppm)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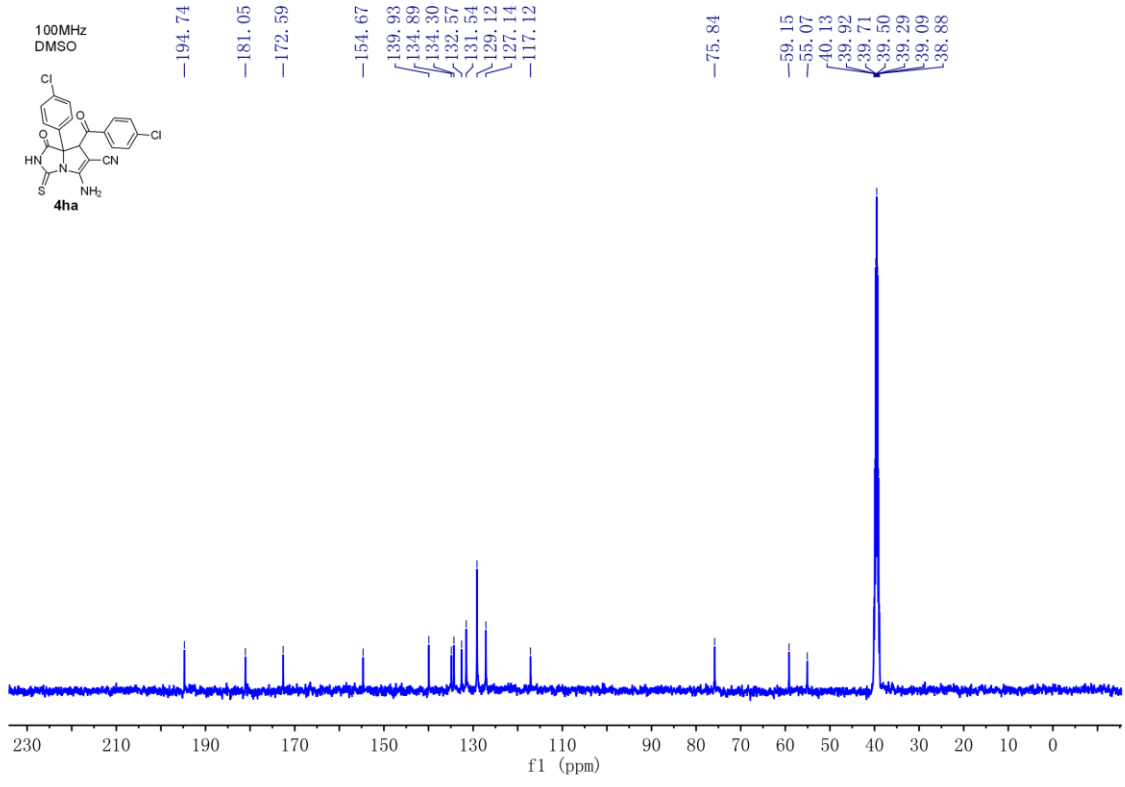
8.004
7.675
7.654
7.626
7.620
7.604
7.592
7.576
7.570
5.088
3.333
2.503
0.000
4ha
1.20
2.08
2.04
2.21
4.06
1.00
f1 (ppm)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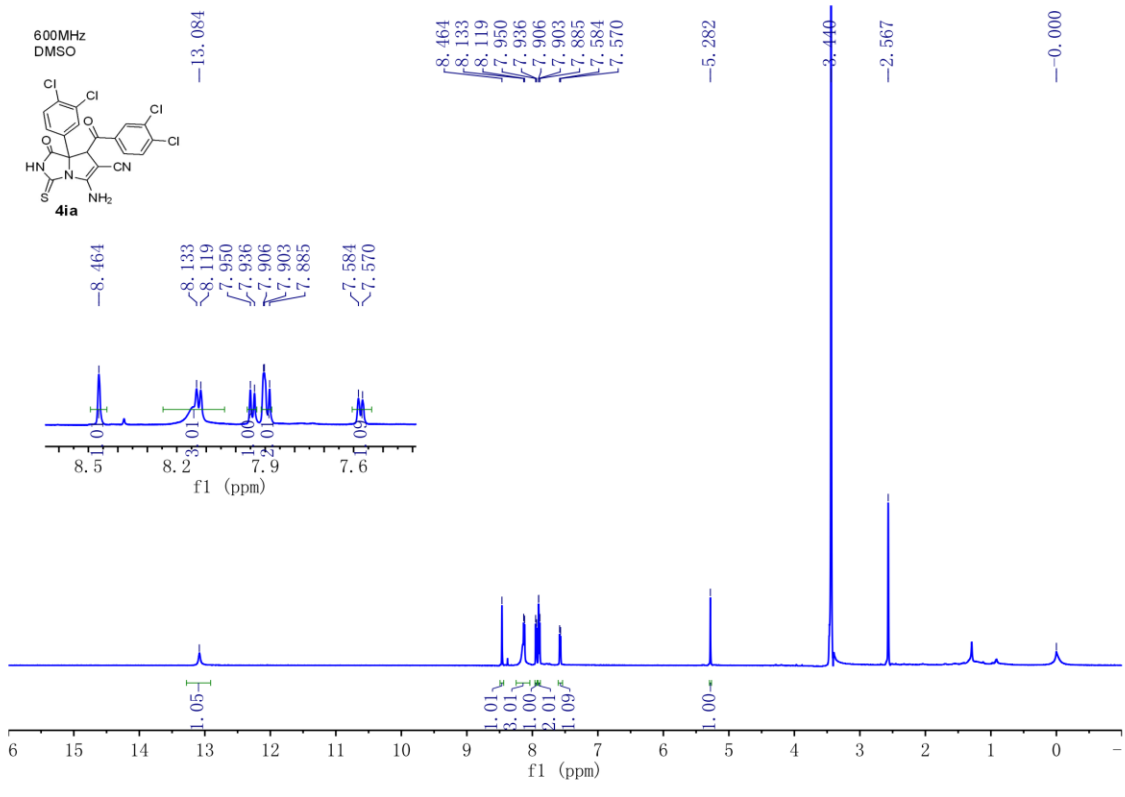
139.93
134.89
134.30
132.57
131.54
129.12
127.14
117.12
75.84
59.15
55.07
40.13
39.92
39.71
39.50
39.29
39.09
38.88
4ha
f1 (ppm)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8.119
7.950
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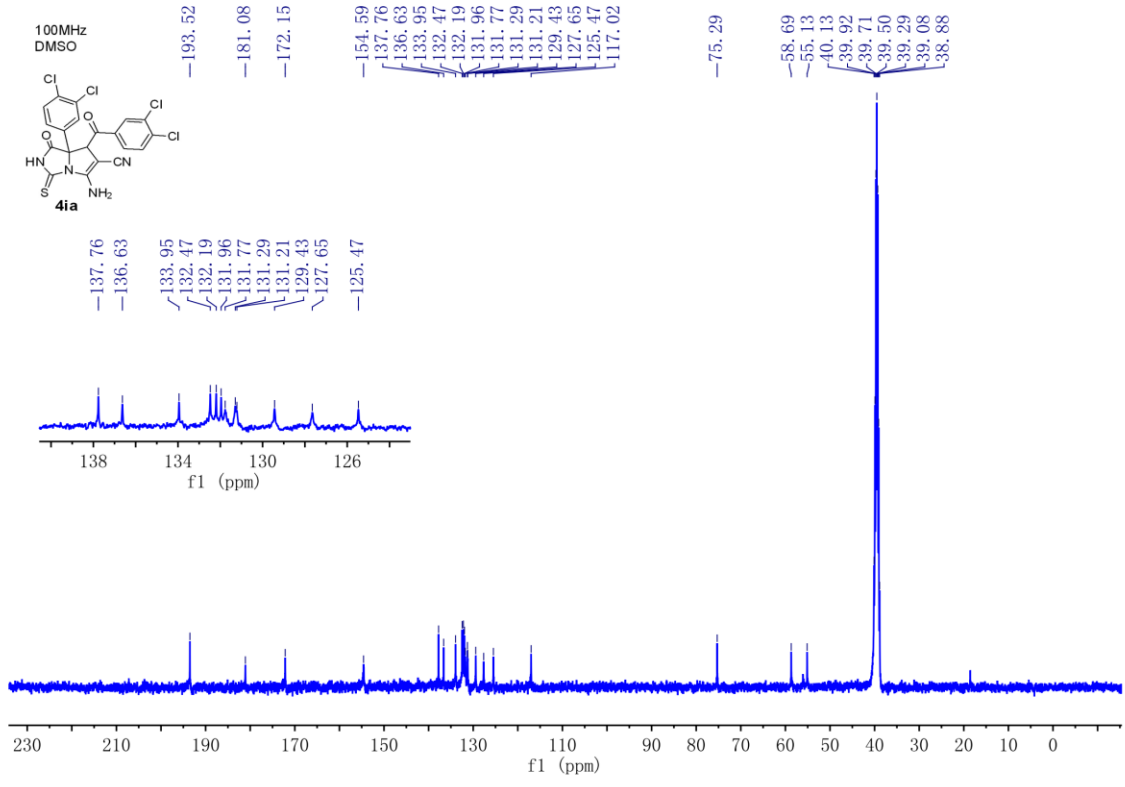
7.903
7.885
7.584
7.570
5.282
3.440
2.567
0.000
4ia
f1 (ppm)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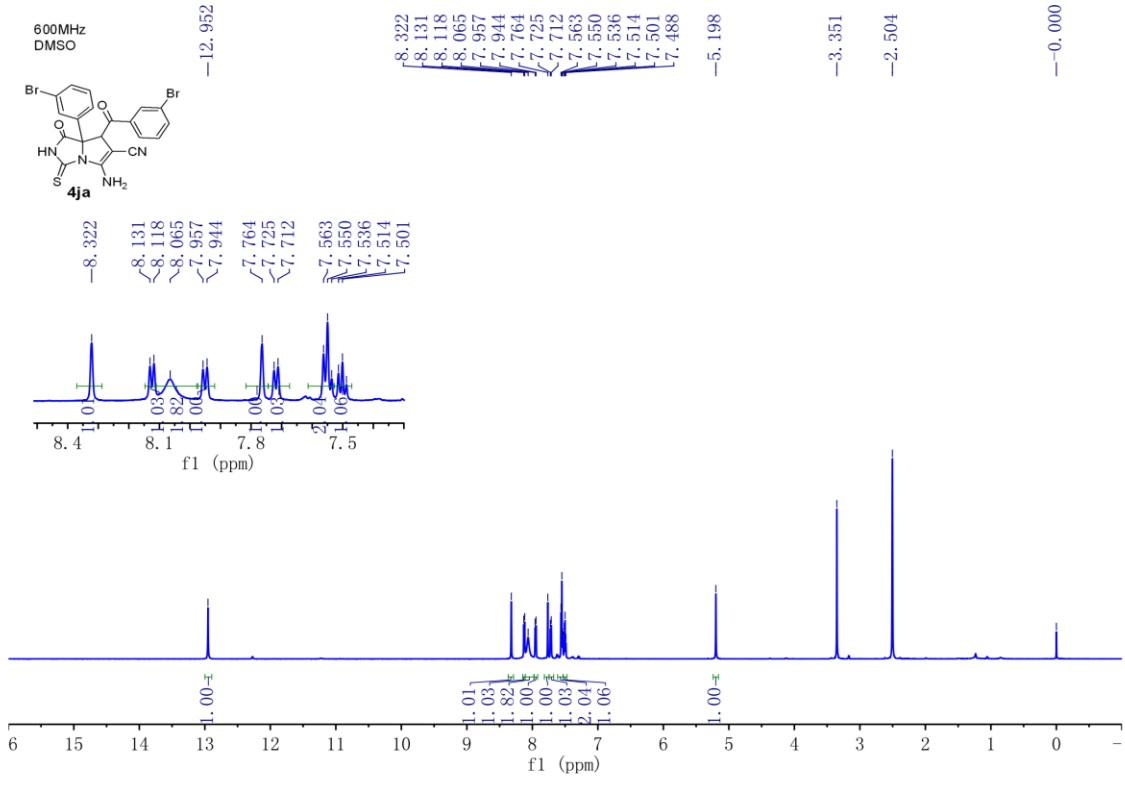
172.15
154.59
137.76
136.63
133.95
132.47
132.19
131.96
131.77
131.29
131.21
129.43
127.65
125.47
117.02
75.29
58.69
55.13
40.13
39.92
39.71
39.50
39.29
39.08
38.88
4ia
f1 (ppm)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8.118
8.065
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7.944
7.764
7.725
7.712
7.563
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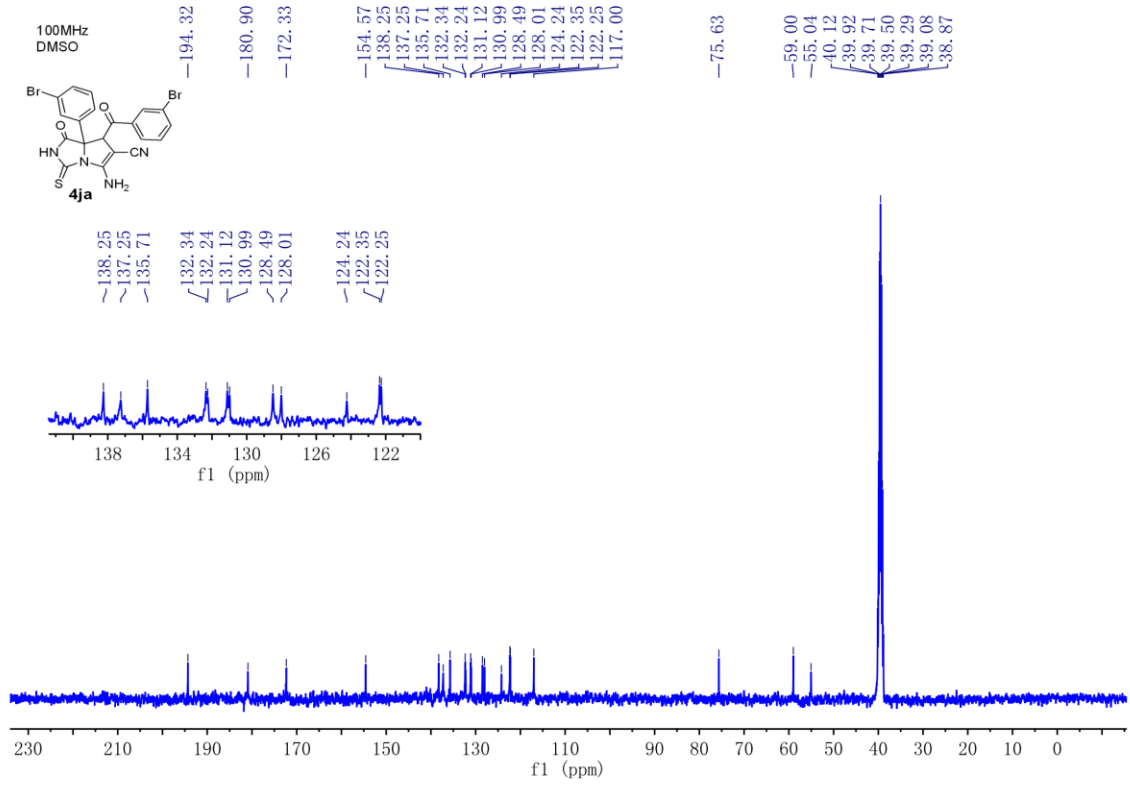
7.536
7.514
7.501
7.488
5.198
3.351
2.504
0.000
4ja
f1 (ppm)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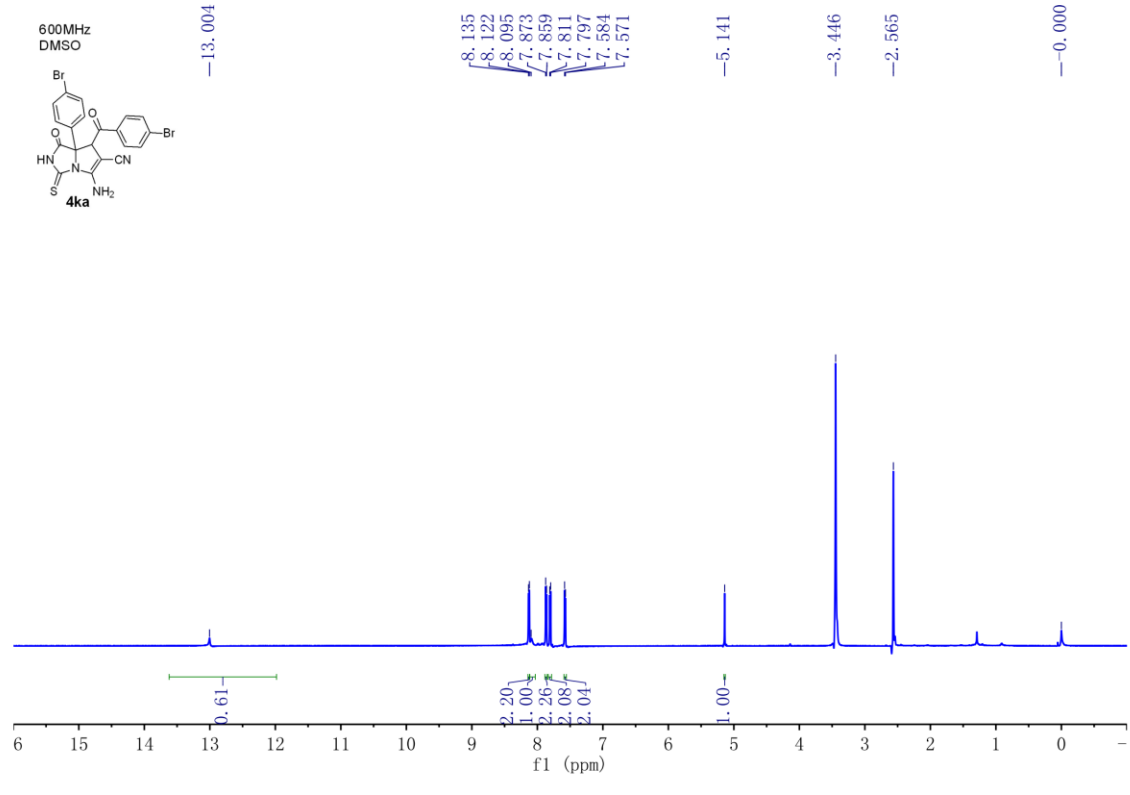
154.57
138.25
137.25
135.71
132.34
132.24
131.12
130.99
128.49
128.01
124.24
122.35
122.25
117.00
75.63
59.00
55.04
40.12
39.92
39.71
39.50
39.29
39.08
38.87
4ja
f1 (ppm)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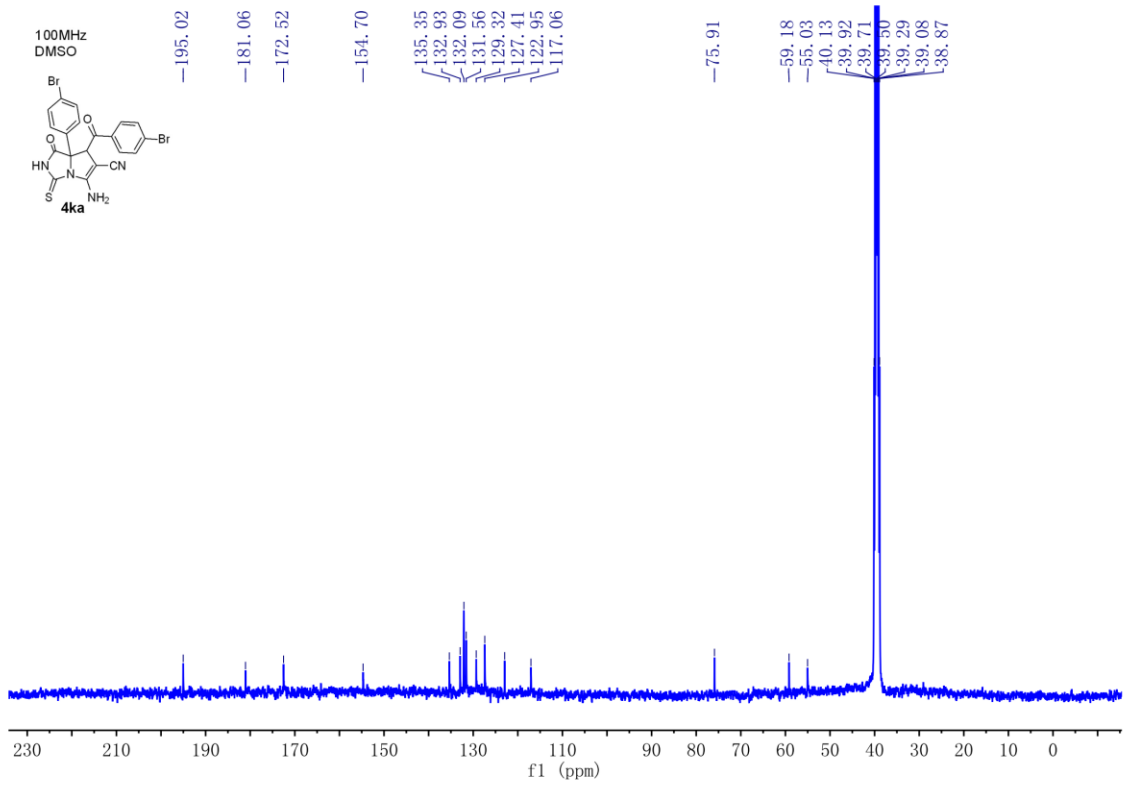
DMSO
13.004
8.135
8.122
8.095
7.873
7.859
7.811
7.797
7.584
7.571
5.141
3.446
2.565
0.000
4ka
0.61
2.20
1.00
2.26
2.08
2.04
1.00
f1 (ppm)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DMSO
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181.06
172.52
154.70
135.35
132.93
132.09
131.56
129.32
127.41
122.95
117.06
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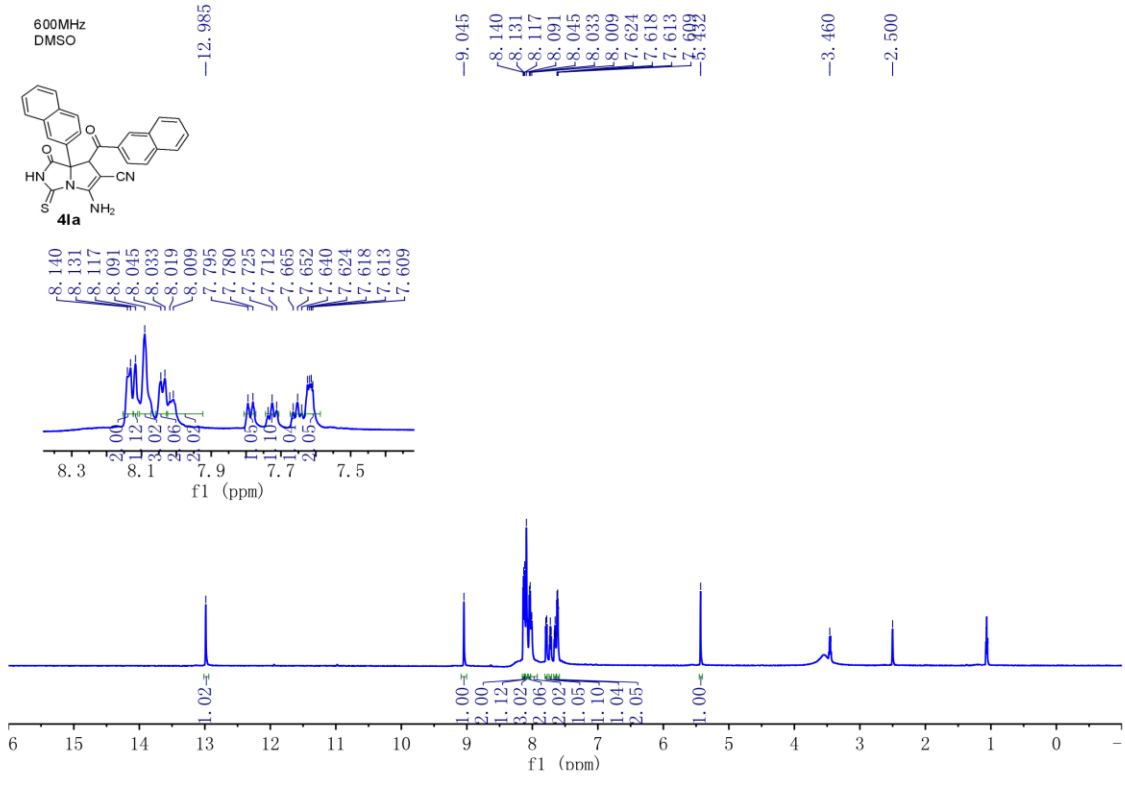
39.29
39.08
38.87
4ka
f1 (ppm)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DMSO
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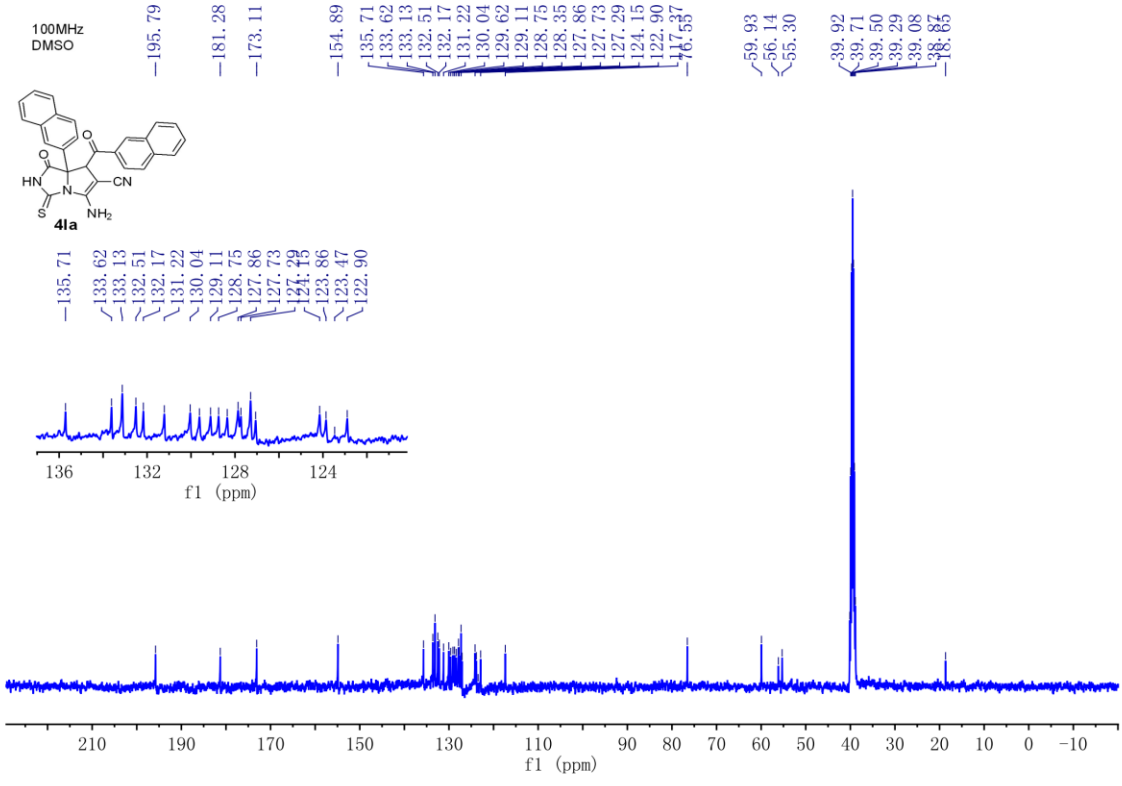
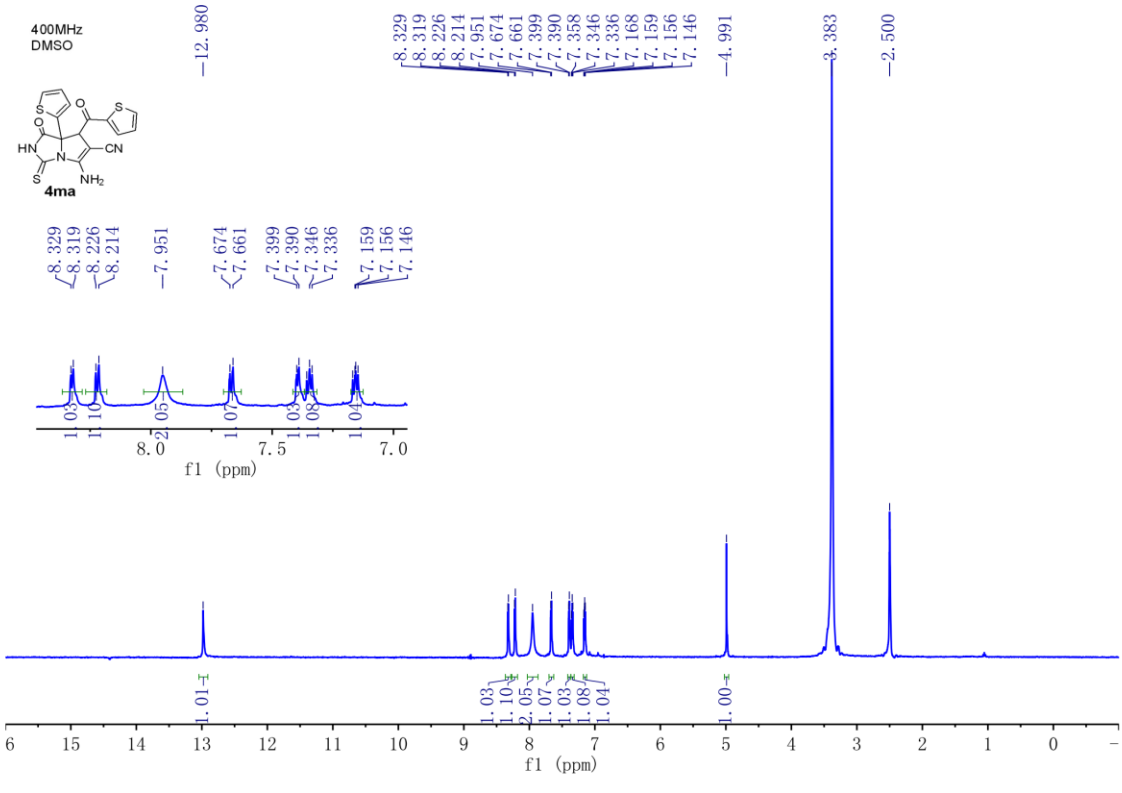
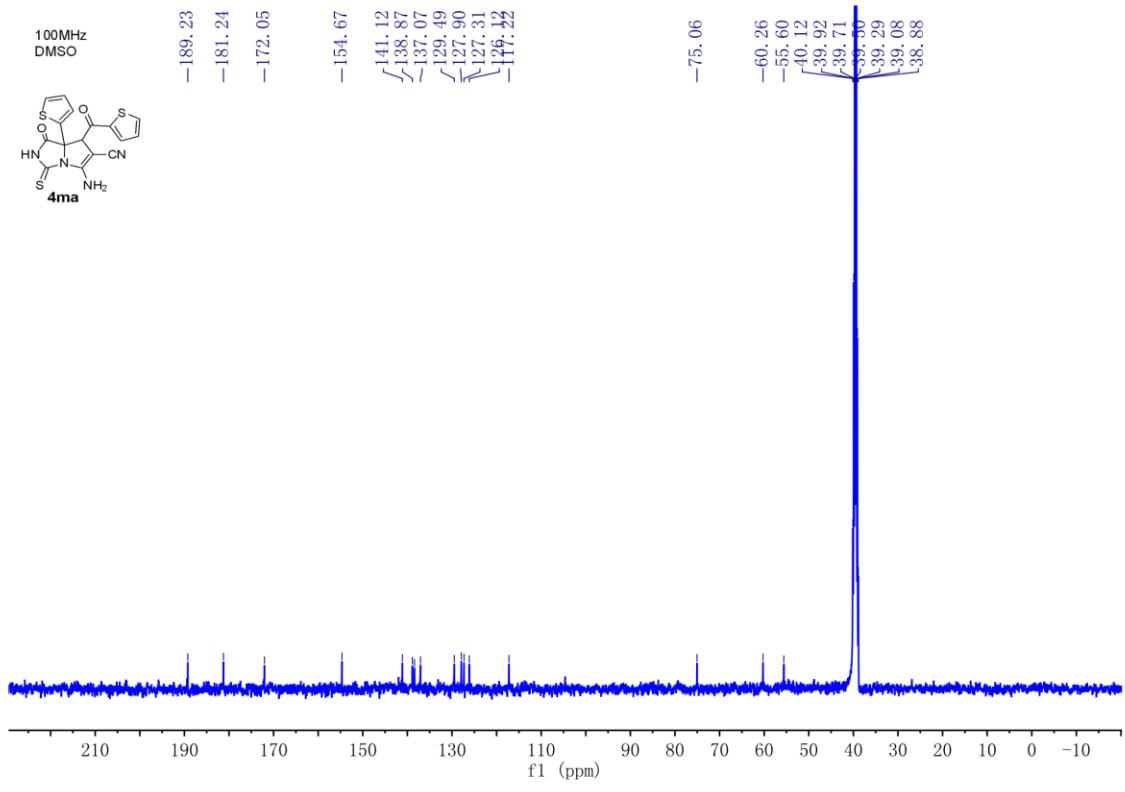
9.045
8.140
8.131
8.117
8.091
8.045
8.033
8.019
8.009
7.795
7.780
7.725
7.712
7.665
7.652
7.640
7.624
7.618
7.613
7.609
5.432
3.460
2.500
4la
f1 (ppm)


100MHz
DMSO
4la
f1 (ppm)


400MHz
DMSO
4ma
f1 (ppm)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DMSO
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154.67
141.12
138.87
137.07
129.49
127.90
127.31
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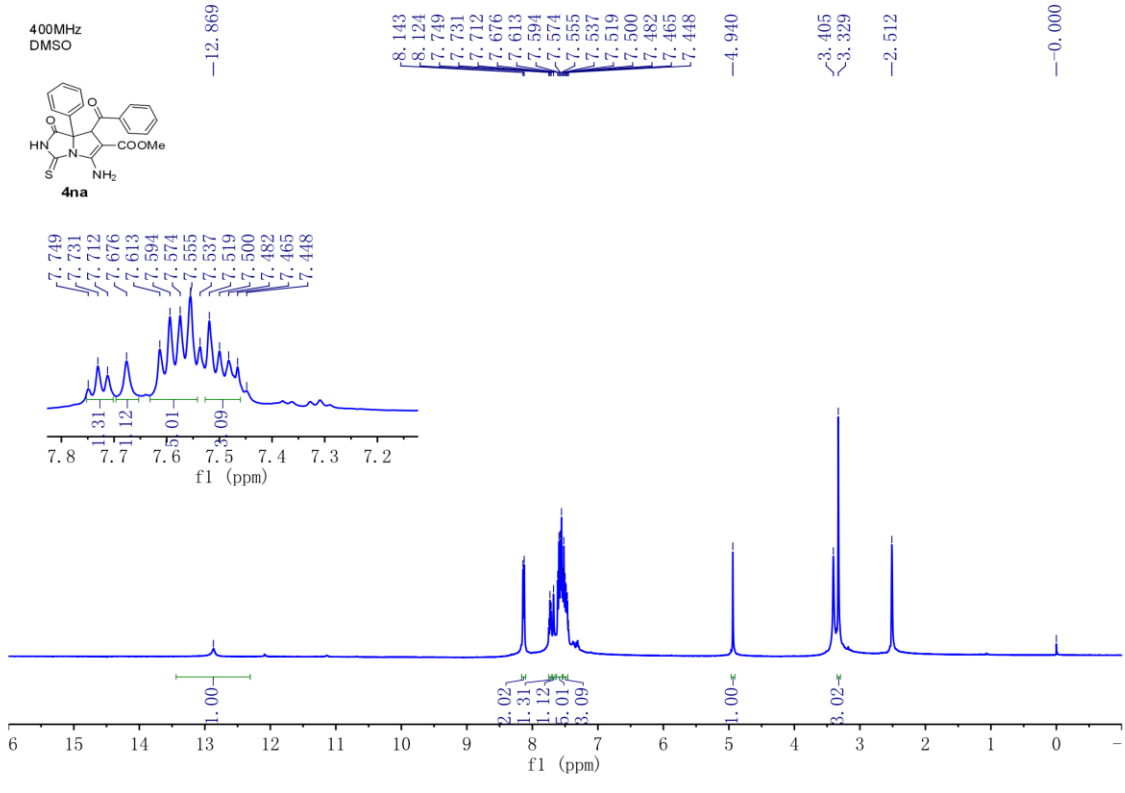
39.50
39.29
39.08
38.88
4ma
f1 (ppm)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DMSO
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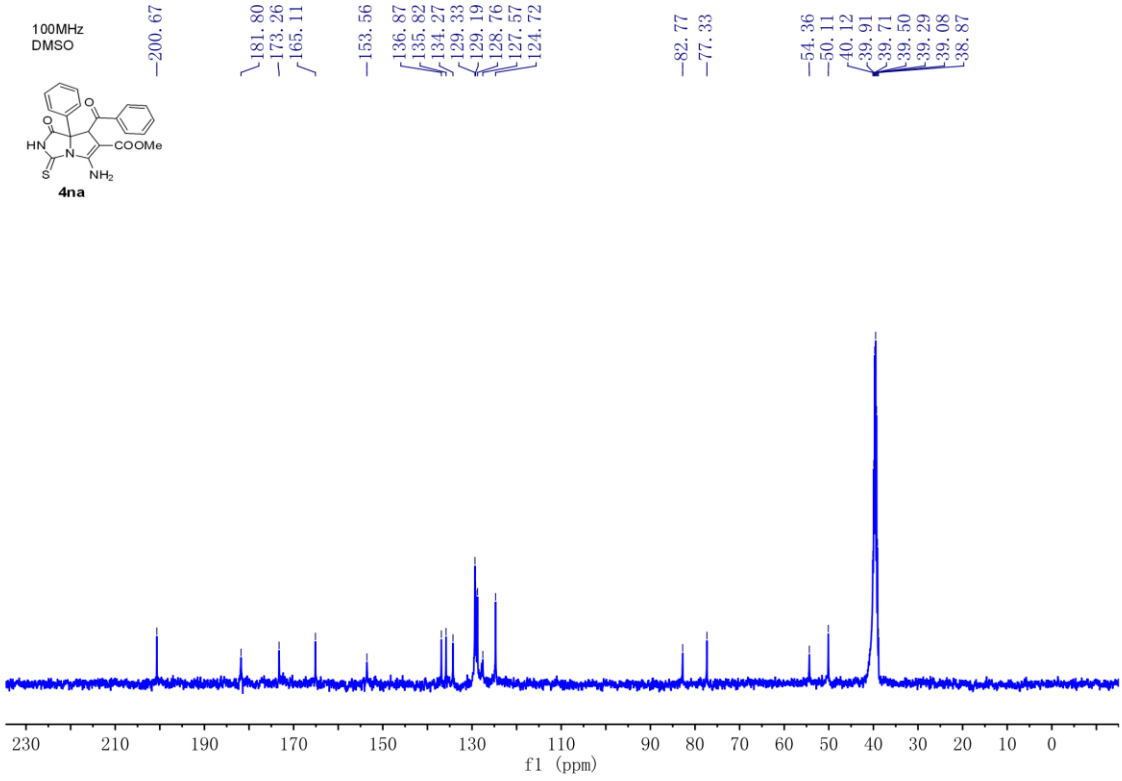
8.124
7.749
7.731
7.712
7.676
7.613
7.594
7.574
7.555
7.537
7.519
7.500
7.482
7.465
7.448
4.940
3.405
3.329
2.512
0.000
4na
1.00
2.02
1.31
1.12
5.01
3.09
1.00
3.02
f1 (ppm)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DMSO
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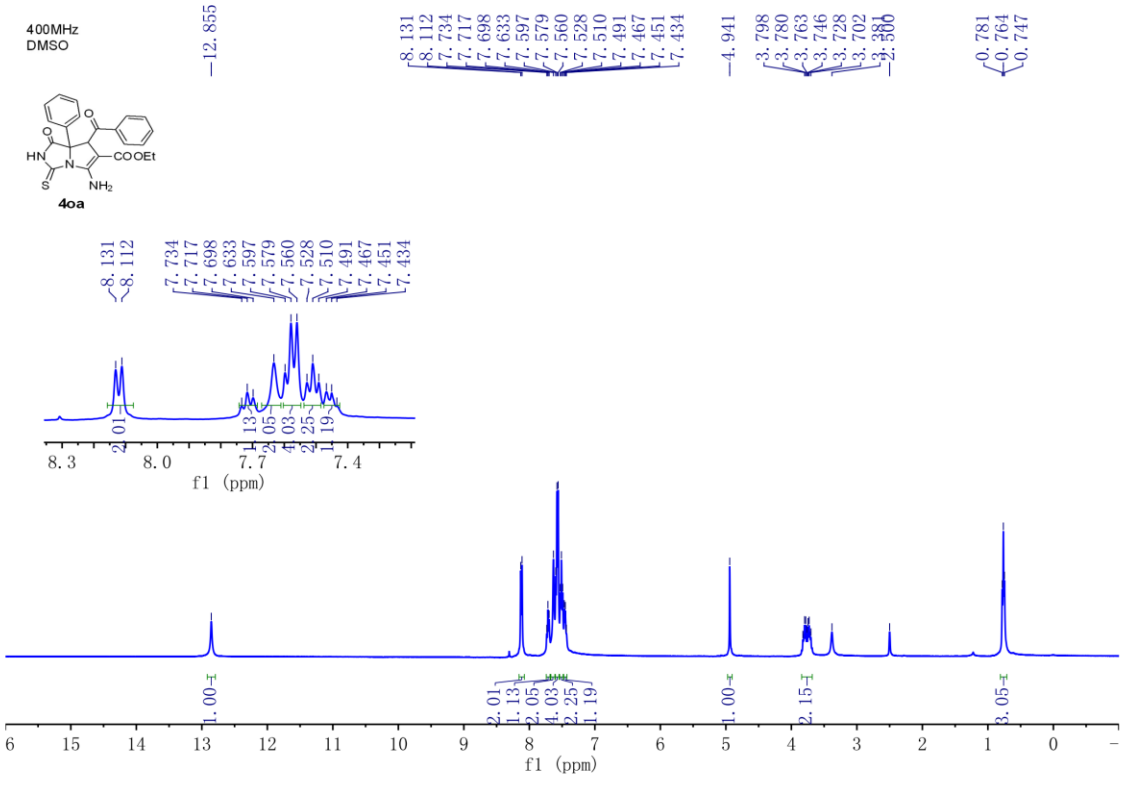
181.80
173.26
165.11
153.56
136.87
135.82
134.27
129.33
129.19
128.76
127.57
124.72
82.77
77.33
54.36
50.11
40.12
39.91
39.71
39.50
39.29
39.08
38.87
COOMe
NH2
4na
f1 (ppm)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DMSO
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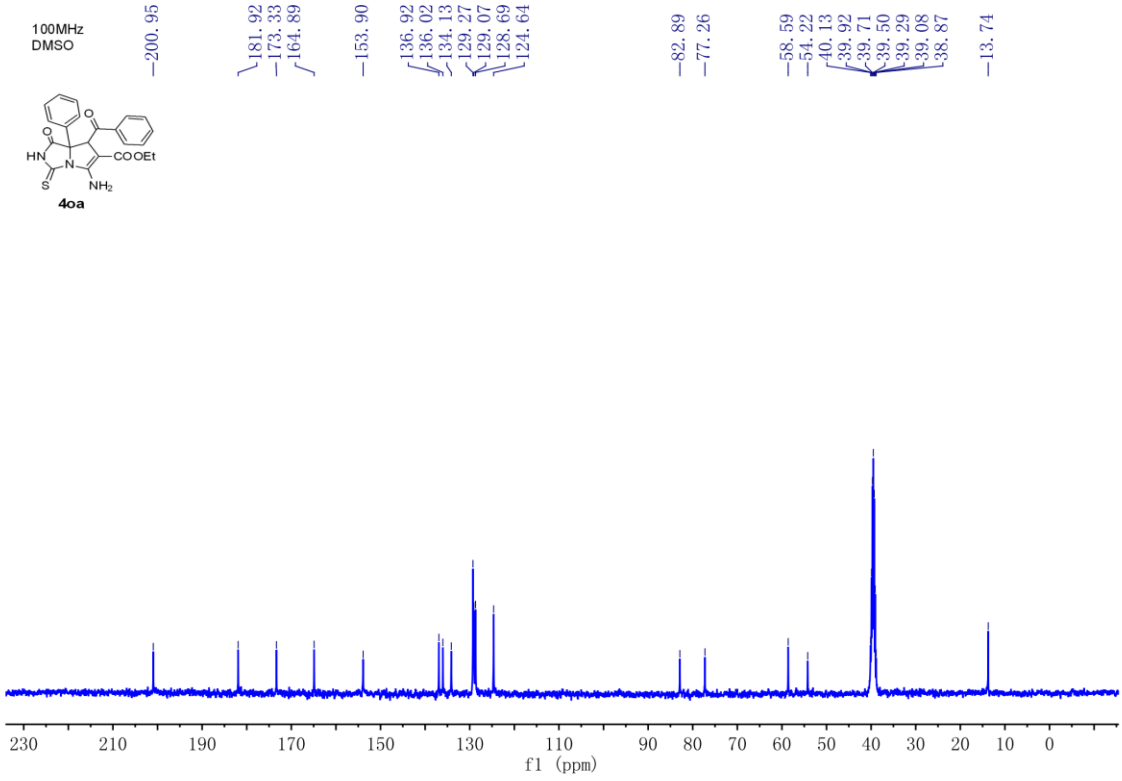
8.131
8.112
7.734
7.717
7.698
7.633
7.597
7.579
7.560
7.528
7.510
7.491
7.467
7.451
7.434
4.941
3.798
3.780
3.763
3.746
3.728
3.702
2.500
0.781
0.764
0.747
COOEt
NH2
4oa
f1 (ppm)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DMSO
200.95
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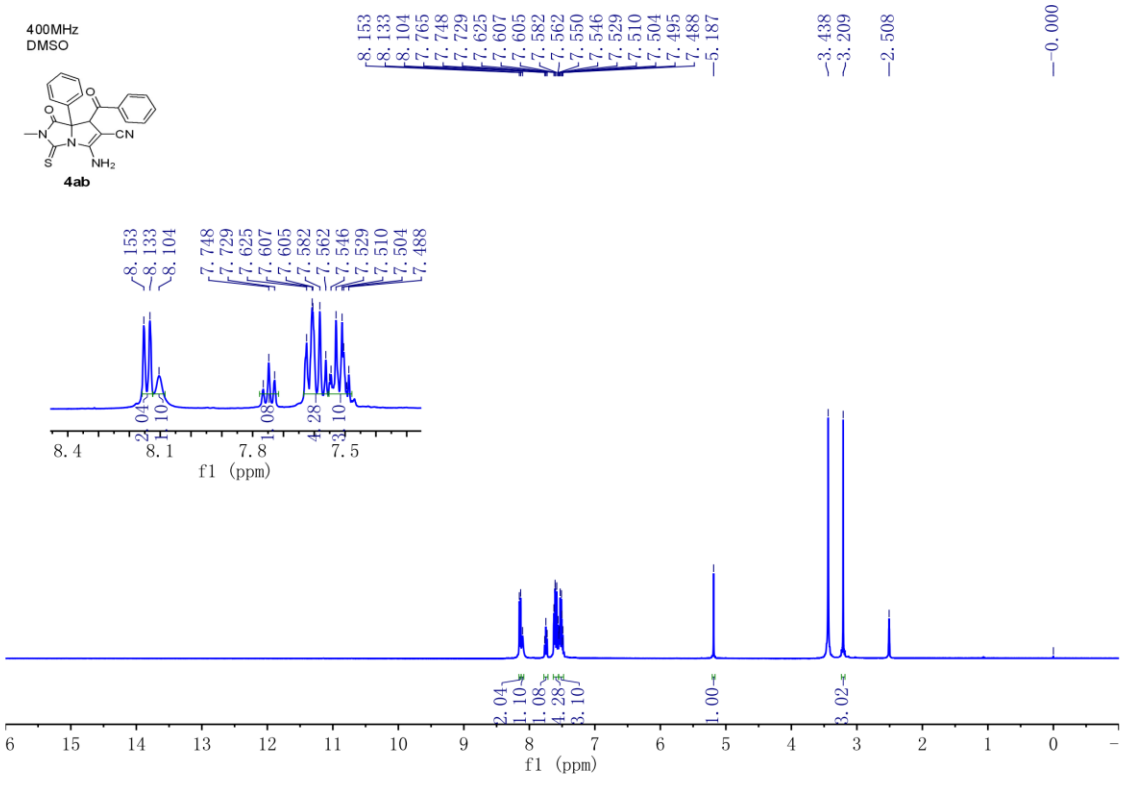
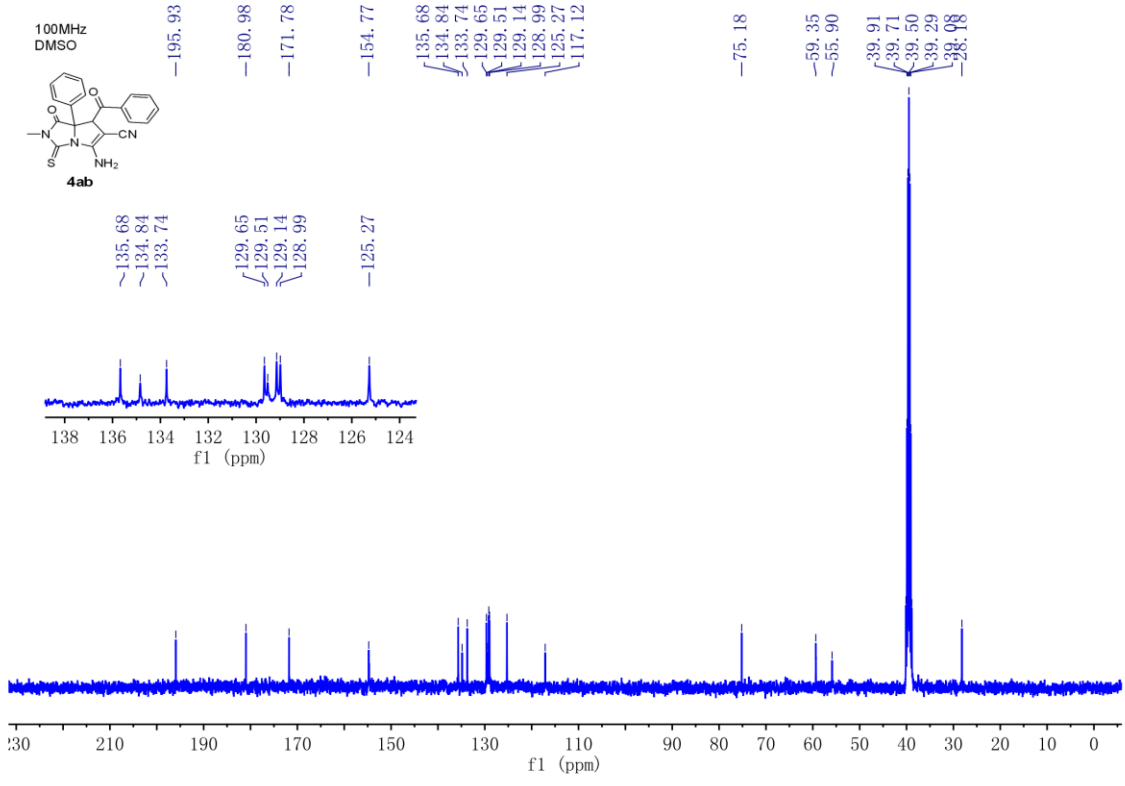
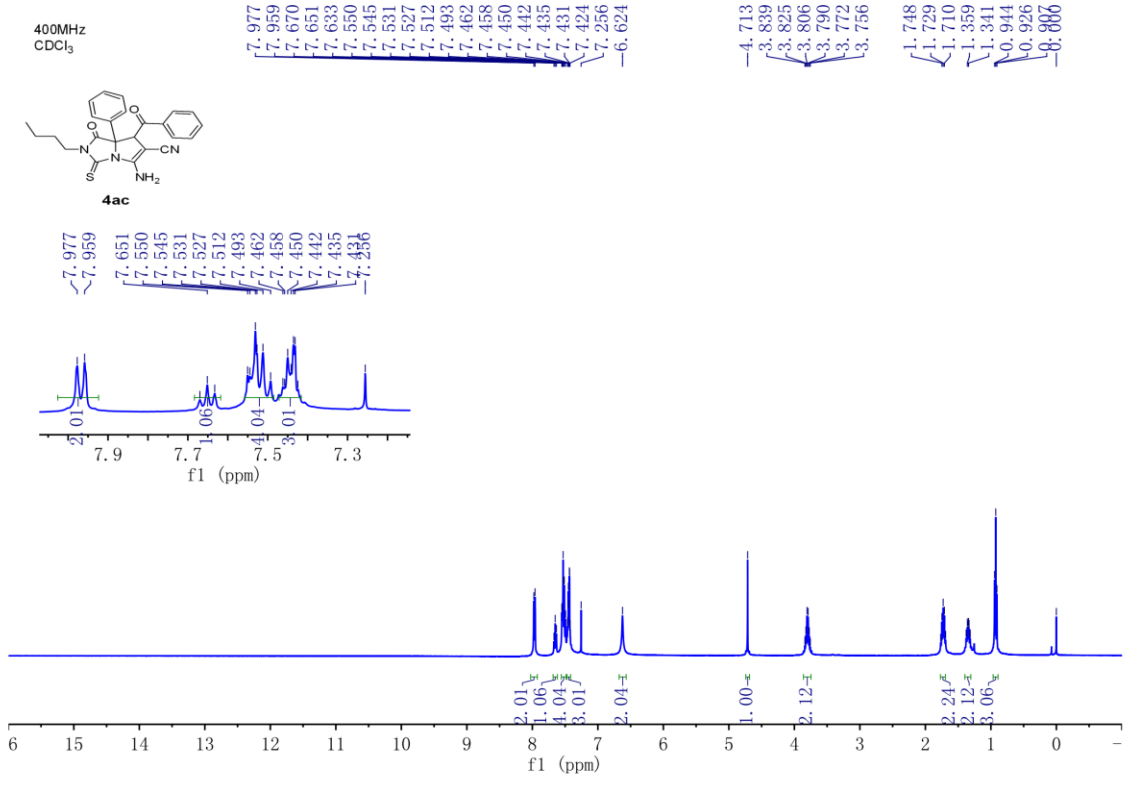
173.33
164.89
153.90
136.92
136.02
134.13
129.27
129.07
128.69
124.64
82.89
77.26
58.59
54.22
40.13
39.92
39.71
39.50
39.29
39.08
38.87
13.74
HN
O
O
N
S
NH2
COOEt
4oa
f1 (ppm)


400MHz
DMSO
8.153
8.133
8.104
7.765
7.748
7.729
7.625
7.607
7.605
7.582
7.562
7.550
7.546
7.529
7.510
7.504
7.495
7.488
5.187
3.438
3.209
2.508
0.000
N
O
O
N
S
NH2
CN
4ab
2.04
1.10
1.08
4.28
3.10
1.00
3.02
f1 (ppm)


100MHz
DMSO
4ab
f1 (ppm)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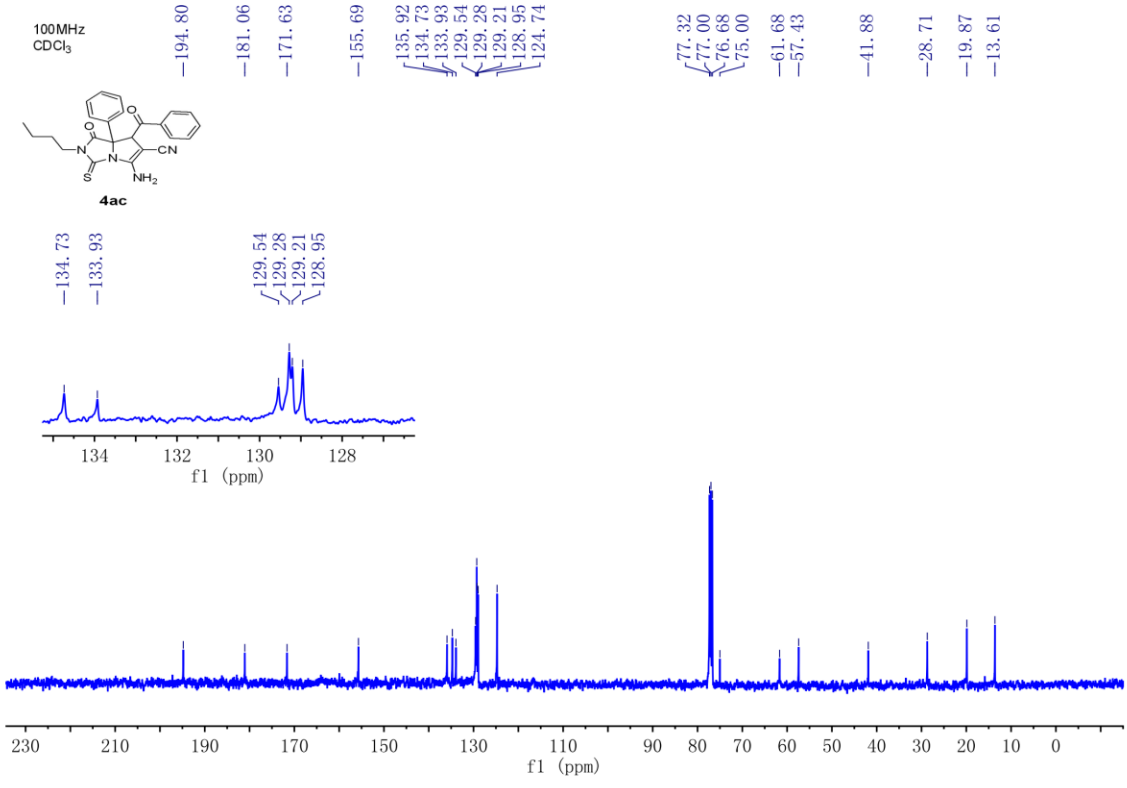
CDCl3
4ac
f1 (ppm)


100MHz
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155.69
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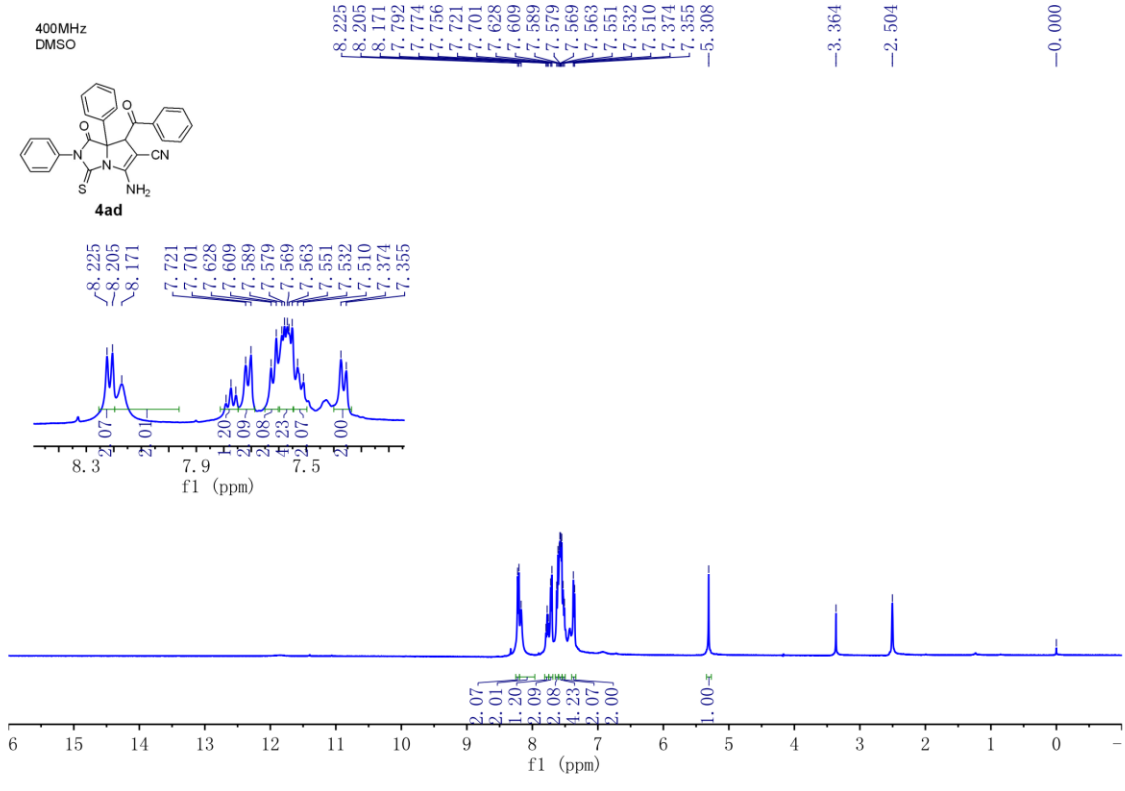
134.73
133.93
129.54
129.28
129.21
128.95
124.74
77.32
77.00
76.68
75.00
61.68
57.43
41.88
28.71
19.87
13.61
4ac
134.73
133.93
129.54
129.28
129.21
128.95
f1 (ppm)


400MHz
DMSO
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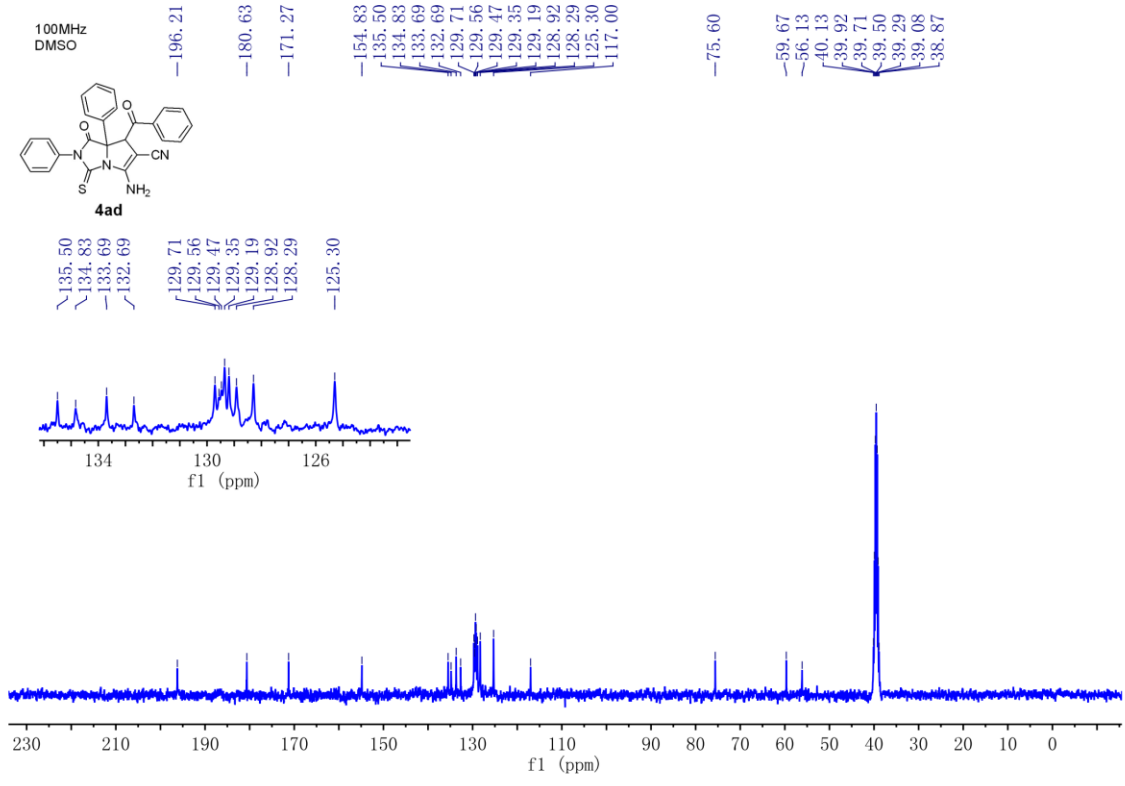
7.721
7.701
7.628
7.609
7.589
7.579
7.569
7.563
7.551
7.532
7.510
7.374
7.355
5.308
3.364
2.504
0.000
4ad
f1 (ppm)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DMSO
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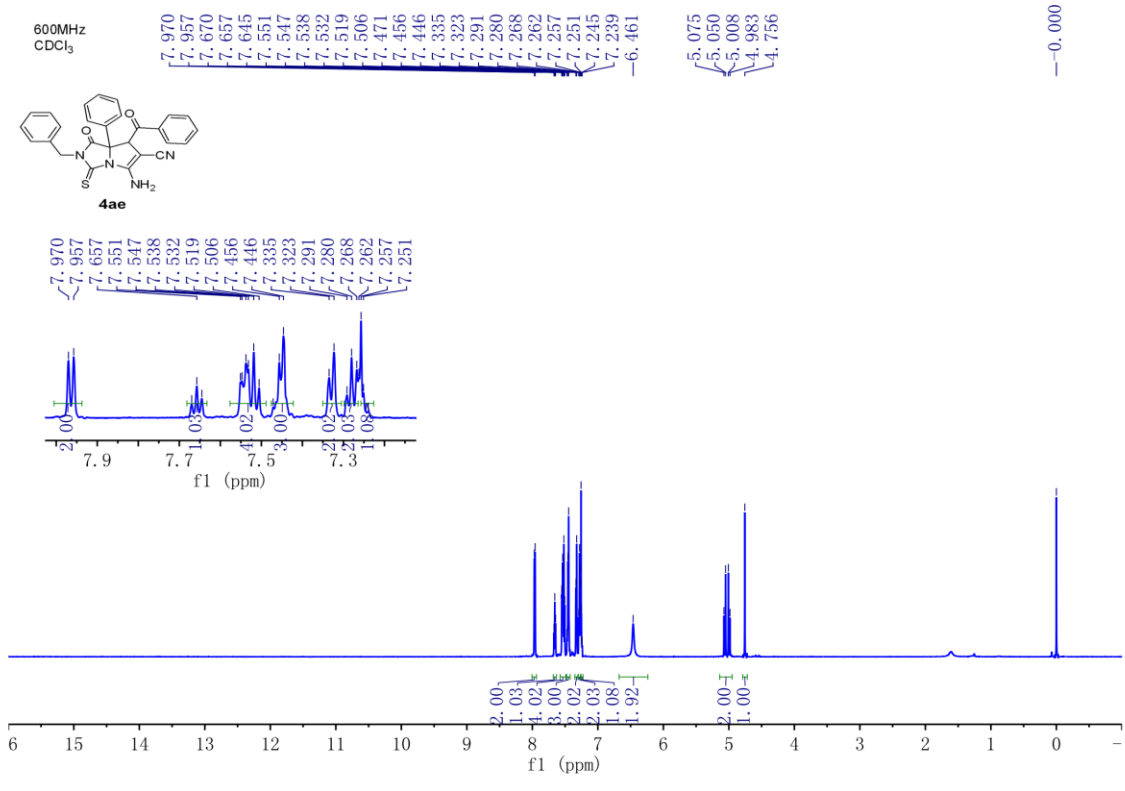
180.63
171.27
154.83
135.50
134.83
133.69
132.69
129.71
129.56
129.47
129.35
129.19
128.92
128.29
125.30
117.00
75.60
59.67
56.13
40.13
39.92
39.71
39.50
39.29
39.08
38.87
4ad
f1 (ppm)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7.657
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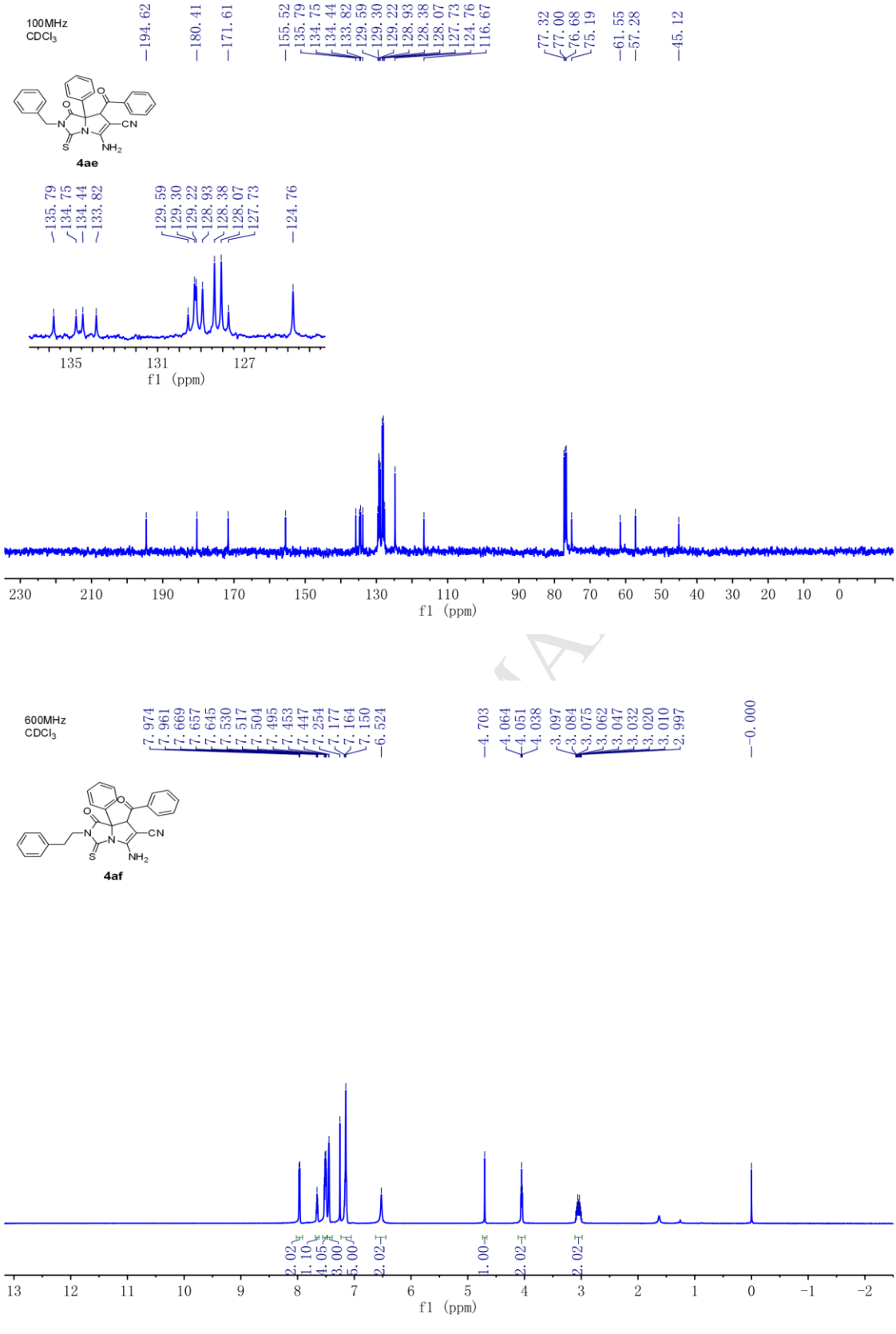
7.551
7.547
7.538
7.532
7.519
7.506
7.471
7.456
7.446
7.335
7.323
7.291
7.280
7.268
7.262
7.257
7.251
7.245
7.239
6.461
5.075
5.050
5.008
4.983
4.756
0.000
4ae
f1 (ppm)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CDCl3
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180.41
171.61
155.52
135.79
134.75
134.44
133.82
129.59
129.30
129.22
128.93
128.38
128.07
127.73
124.76
116.67
77.32
77.00
76.68
75.19
61.55
57.28
45.12
4ae
f1 (ppm)
600MHz
CDCl3
7.974
7.961
7.669
7.657
7.645
7.530
7.517
7.504
7.495
7.453
7.447
7.254
7.177
7.164
7.150
6.524
4.703
4.064
4.051
4.038
3.097
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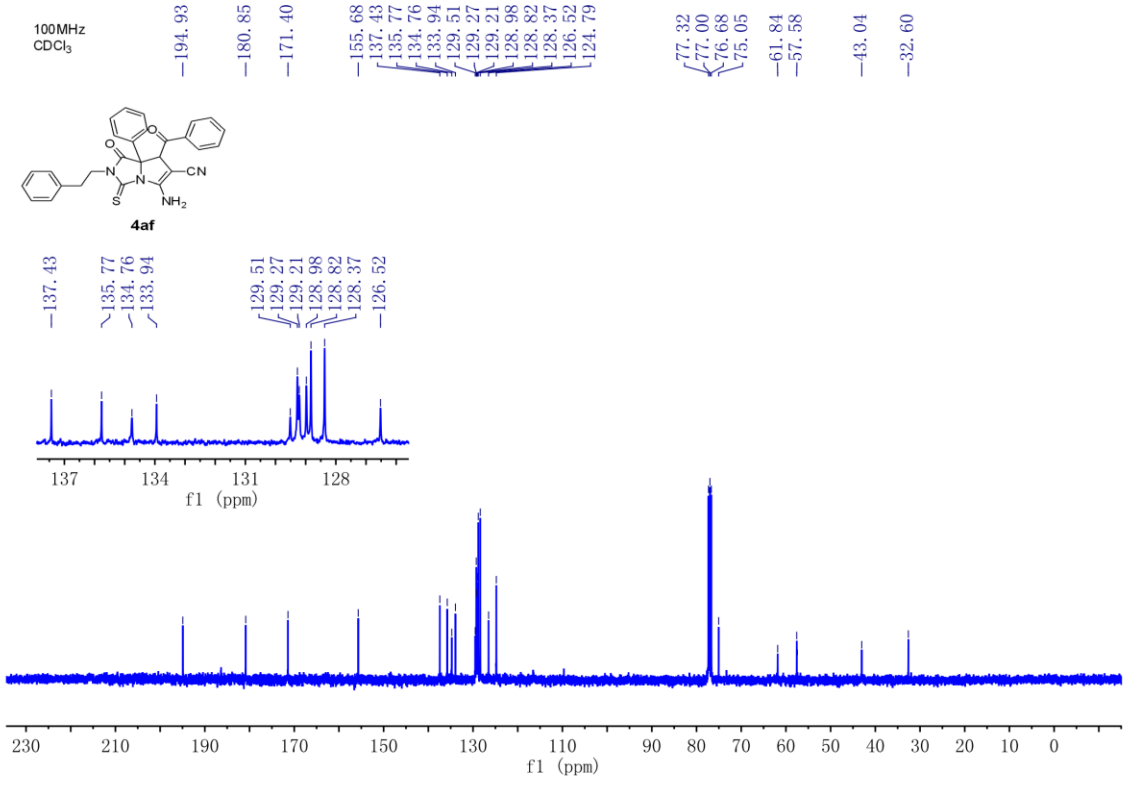
3.062
3.047
3.032
3.020
3.010
2.997
0.000
4af
f1 (ppm)


100MHz
CDCl3
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180.85
171.40
155.68
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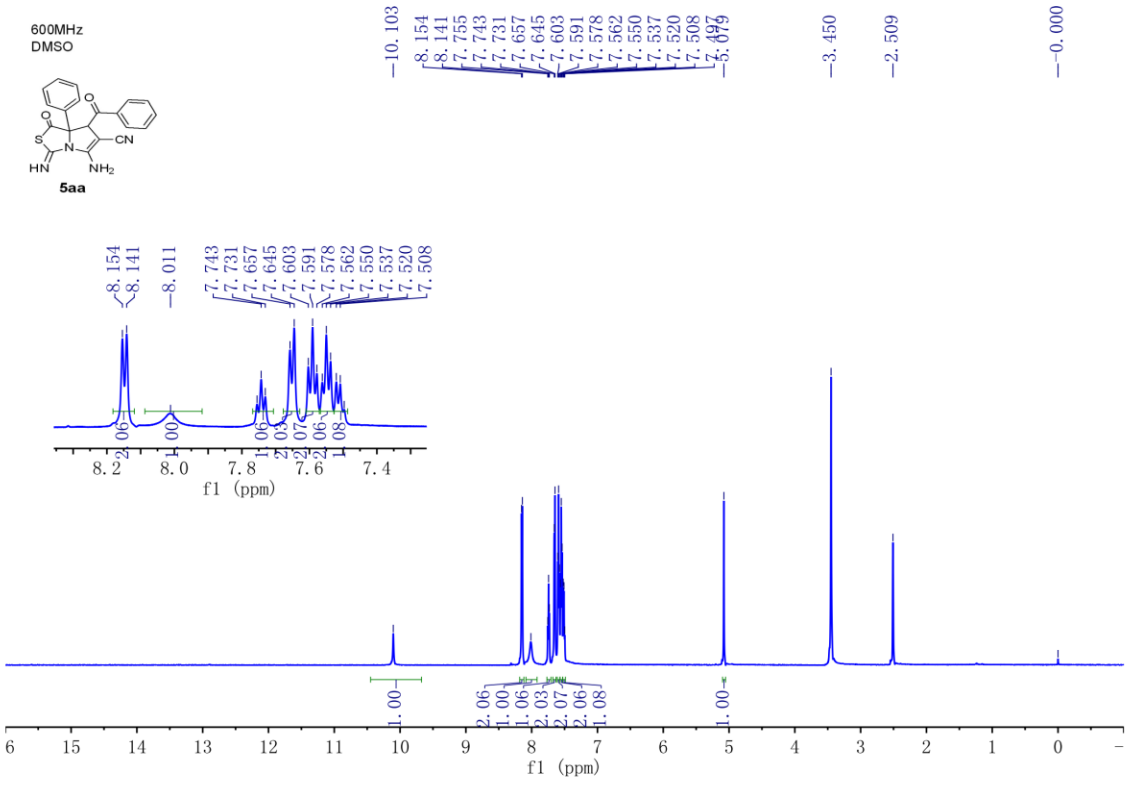
135.77
134.76
133.94
129.51
129.27
129.21
128.98
128.82
128.37
126.52
124.79
77.32
77.00
76.68
75.05
61.84
57.58
43.04
32.60
4af
f1 (ppm)


600MHz
DMSO
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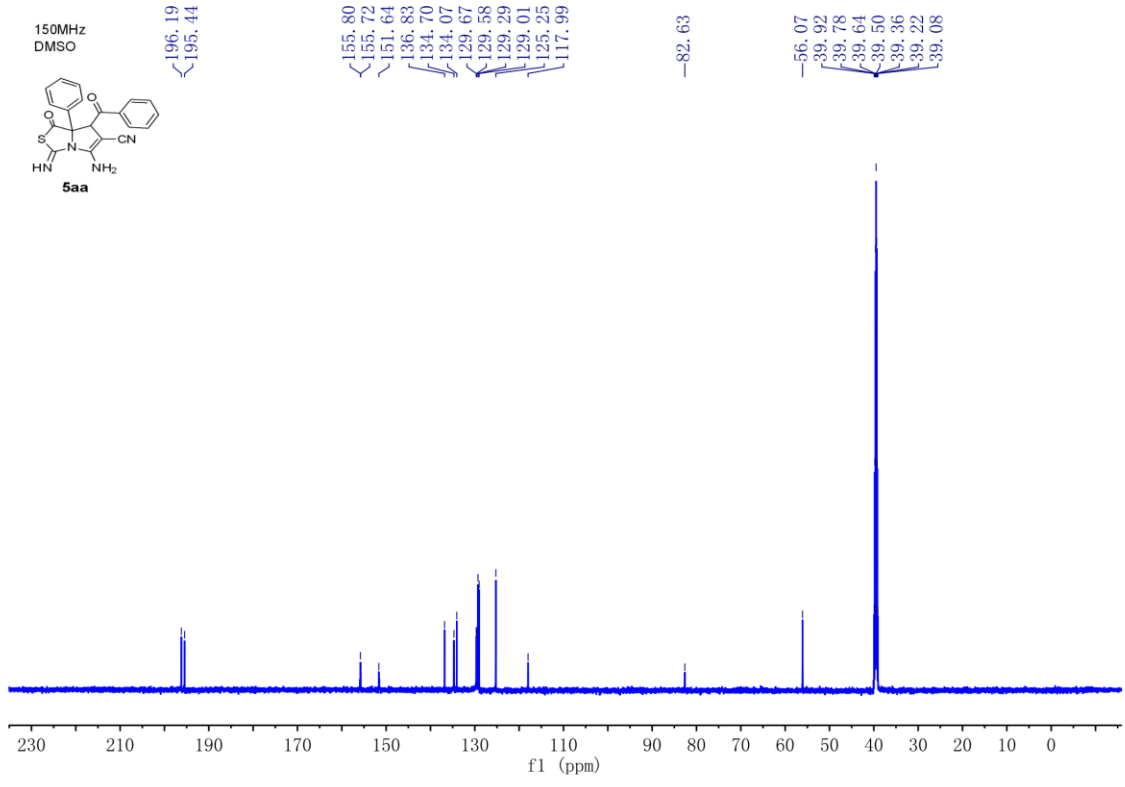
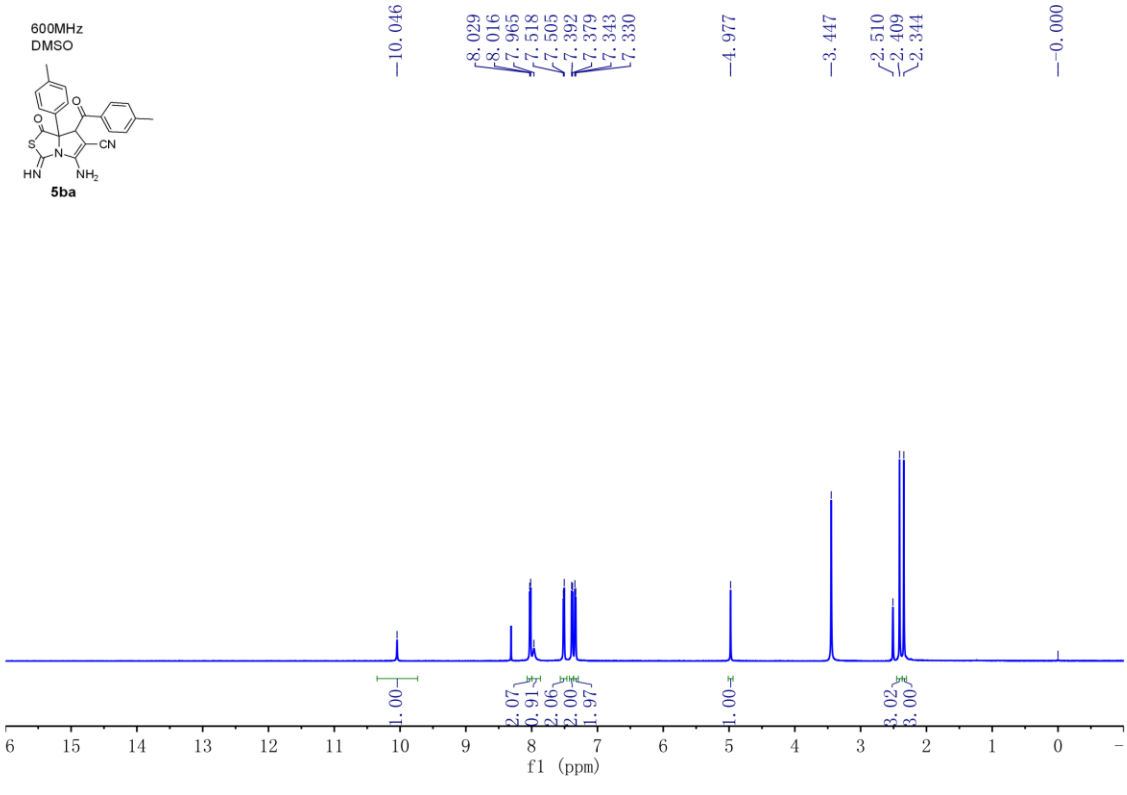
8.154
8.141
7.755
7.743
7.731
7.657
7.645
7.603
7.591
7.578
7.562
7.550
7.537
7.520
7.508
3.450
2.509
0.000
5aa
f1 (ppm)


150MHz
DMSO
196.19
195.44
155.80
155.72
151.64
136.83
134.70
134.07
129.67
129.58
129.29
129.01
125.25
117.99
82.63
56.07
39.92
39.78
39.64
39.50
39.36
39.22
39.08
5aa
f1 (ppm)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DMSO
10.046
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8.016
7.965
7.518
7.505
7.392
7.379
7.343
7.330
4.977
3.447
2.510
2.409
2.344
0.000
1.00
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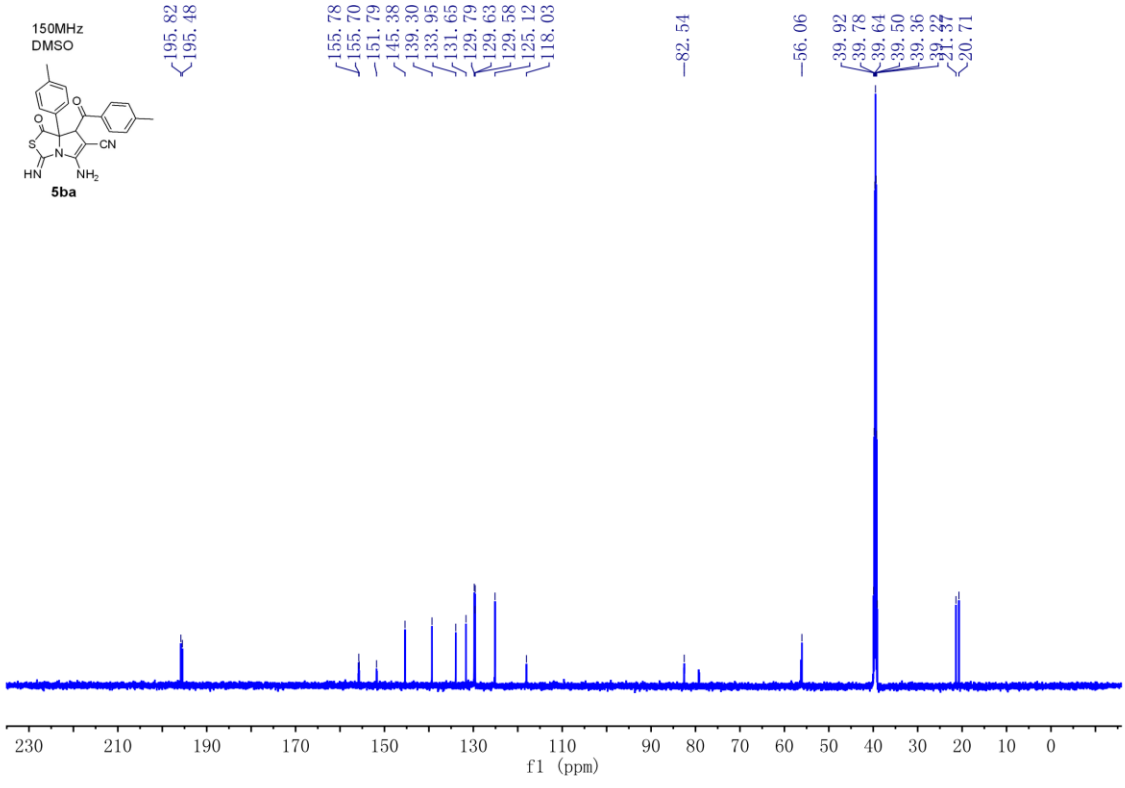
0.91
2.06
2.00
1.97
1.00
3.02
3.00
5ba
f1 (ppm)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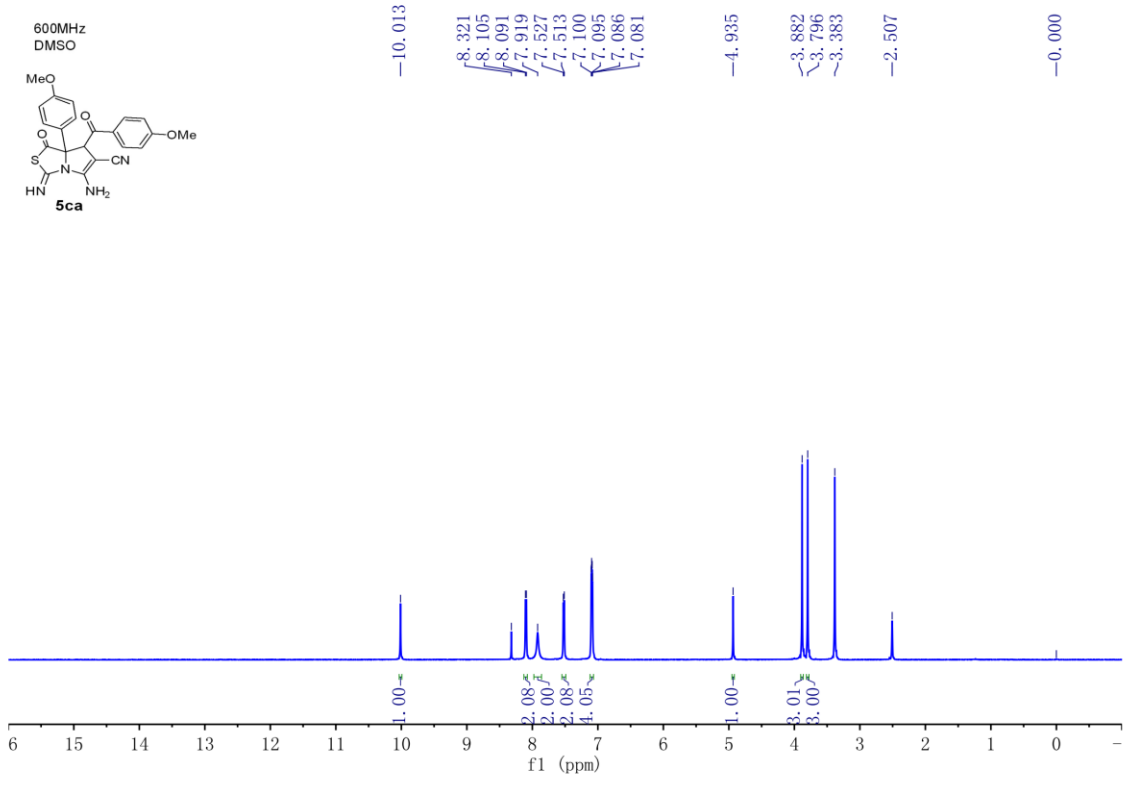
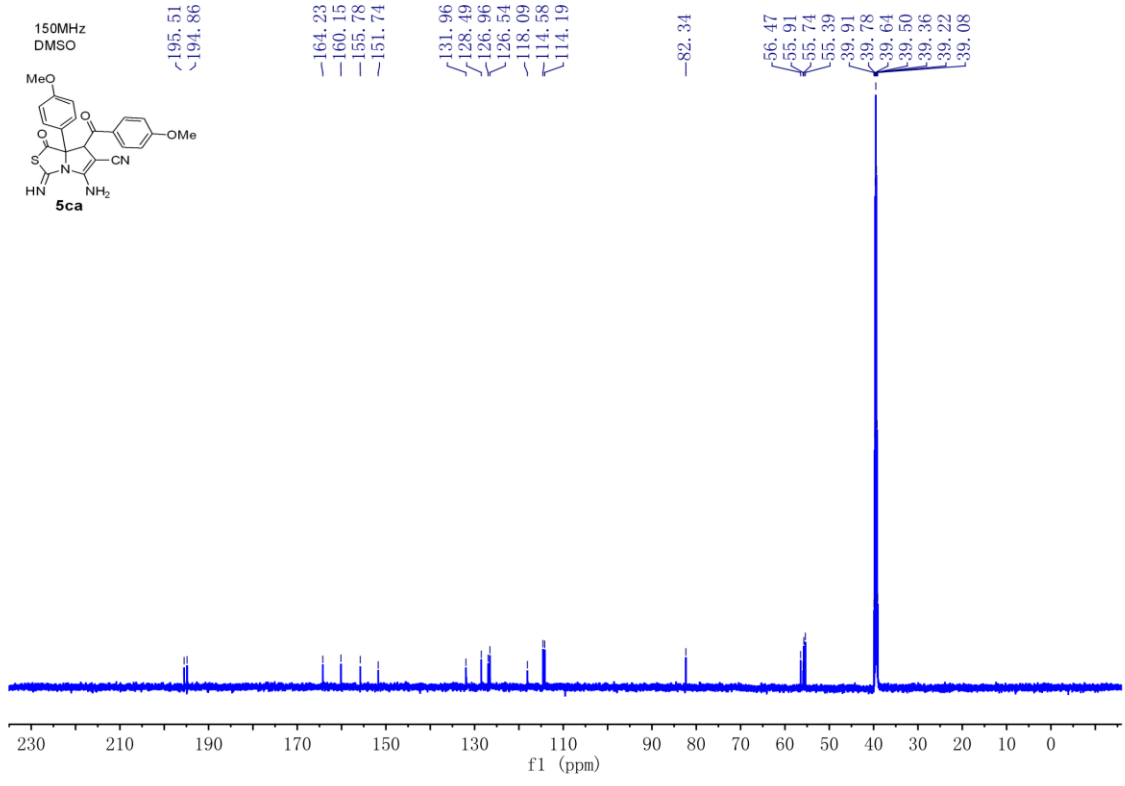
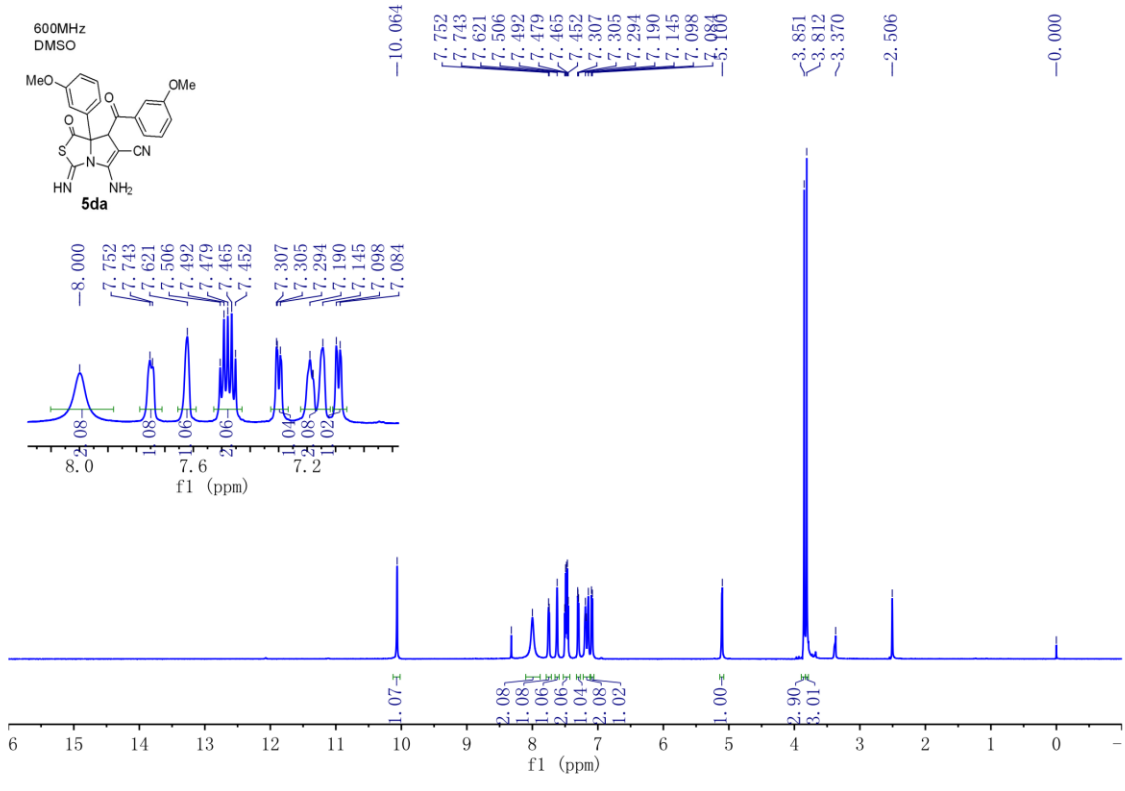
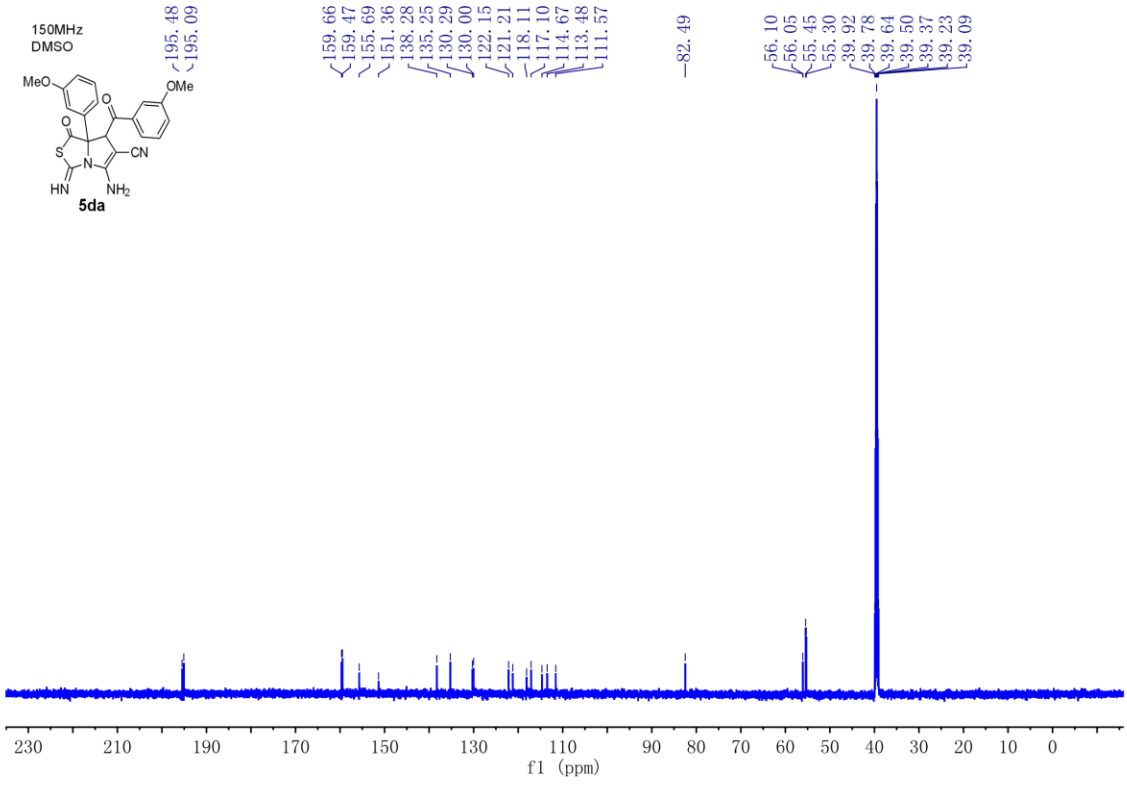
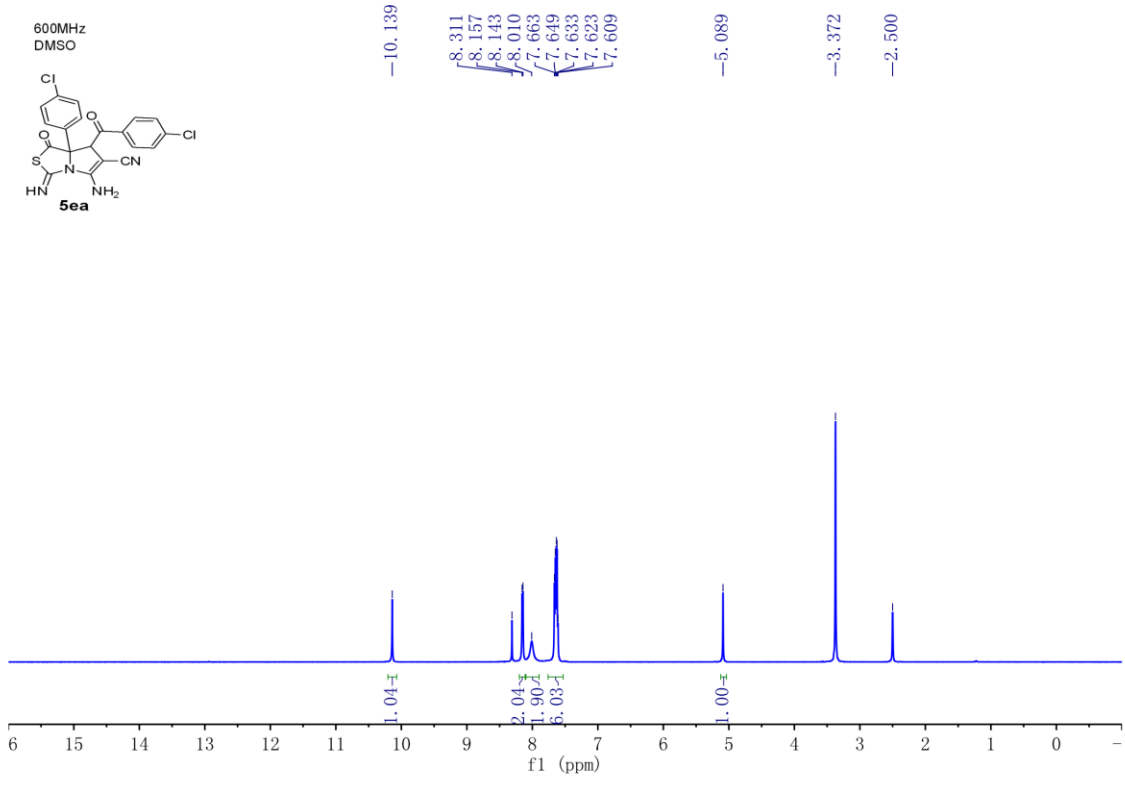
DMSO
195.82
195.48
155.78
155.70
151.79
145.38
139.30
133.95
131.65
129.79
129.63
129.58
125.12
118.03
82.54
56.06
39.92
39.78
39.64
39.50
39.36
21.37
20.71
5ba
f1 (ppm)

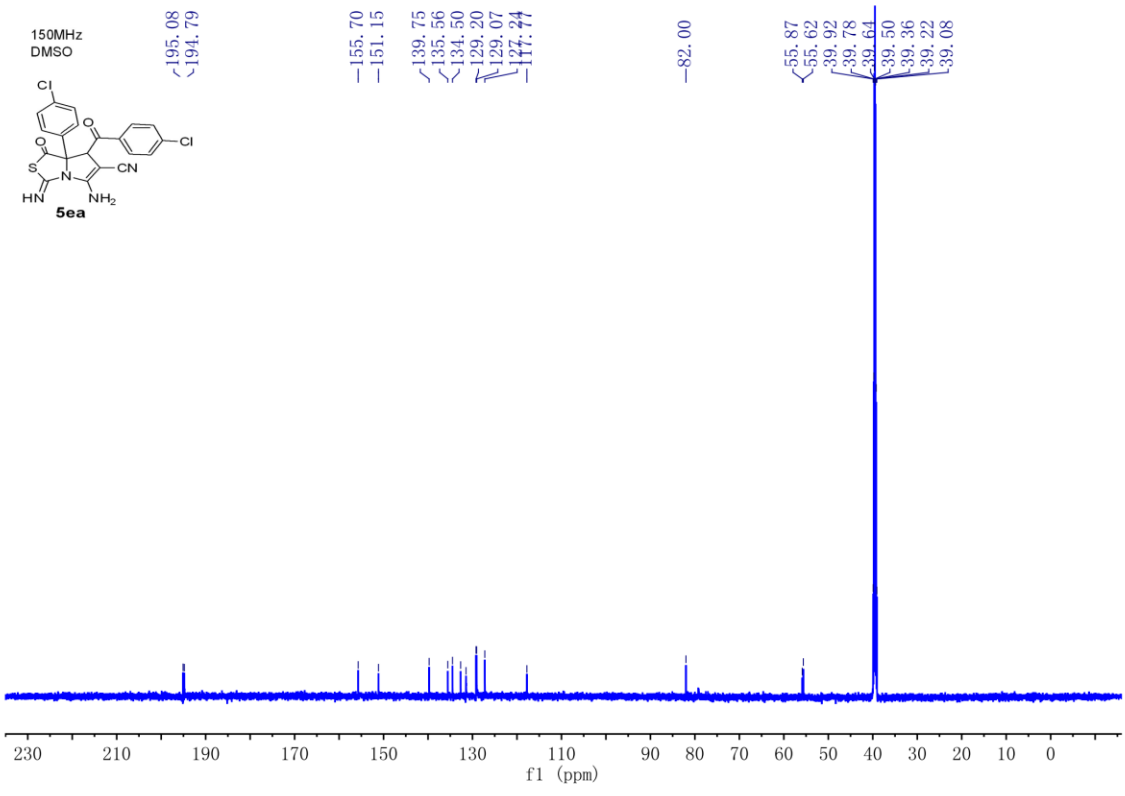

600MHz
DMSO
10.013
8.321
8.105
8.091
7.919
7.527
7.513
7.100
7.095
7.086
7.081
4.935
3.882
3.796
3.383
2.507
0.000
1.00
2.08
2.00
2.08
4.05
1.00
3.01
3.00
5ca
f1 (ppm)

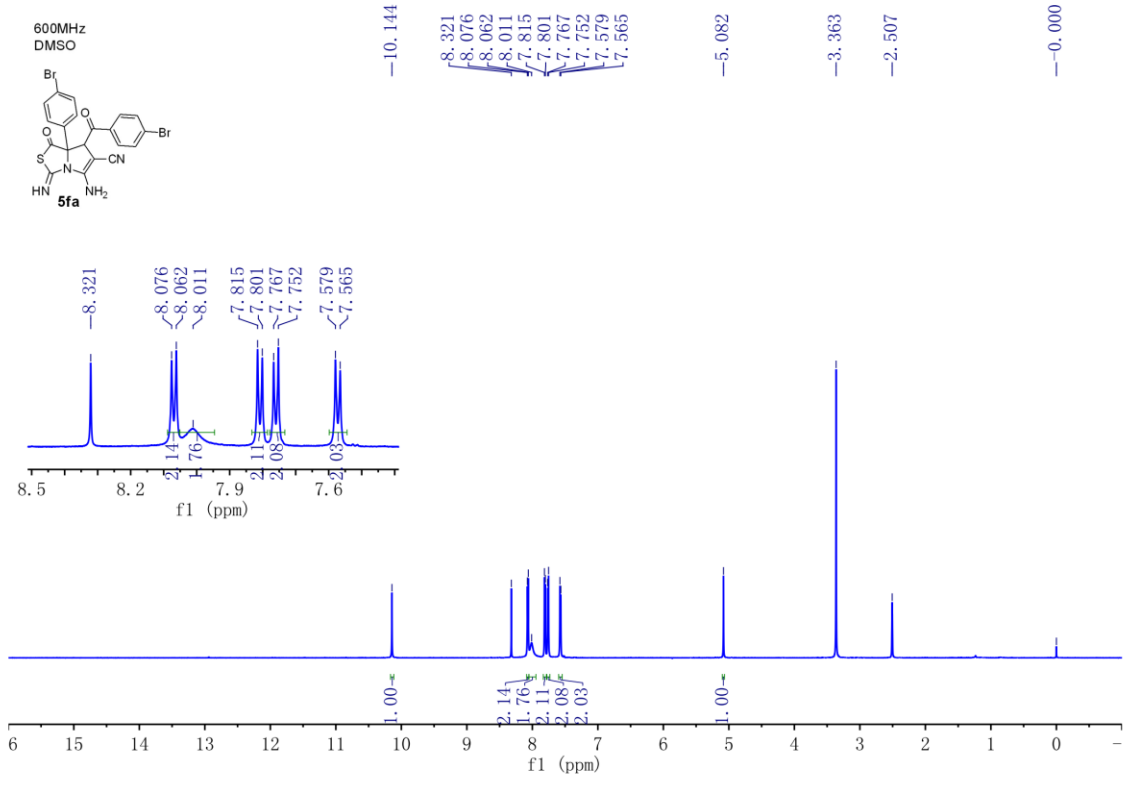

150MHz
DMSO
MeO
OMe
CN
HN
NH2
5ca
195.51
194.86
164.23
160.15
155.78
151.74
131.96
128.49
126.96
126.54
118.09
114.58
114.19
82.34
56.47
55.91
55.74
55.39
39.91
39.78
39.64
39.50
39.36
39.22
39.08
f1 (ppm)

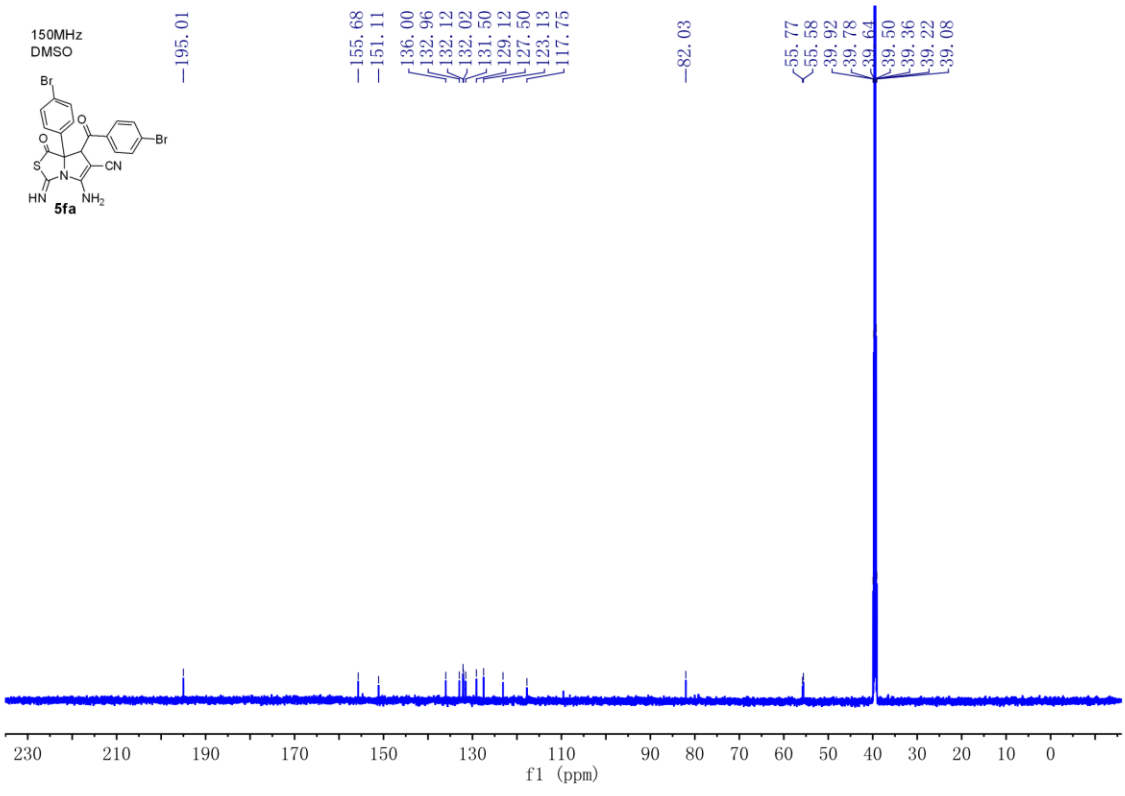

600MHz
DMSO
MeO
OMe
CN
HN
NH2
5da
10.064
7.752
7.743
7.621
7.506
7.492
7.479
7.465
7.452
7.307
7.305
7.294
7.190
7.145
7.098
7.084
3.851
3.812
3.370
2.506
0.000
f1 (ppm)

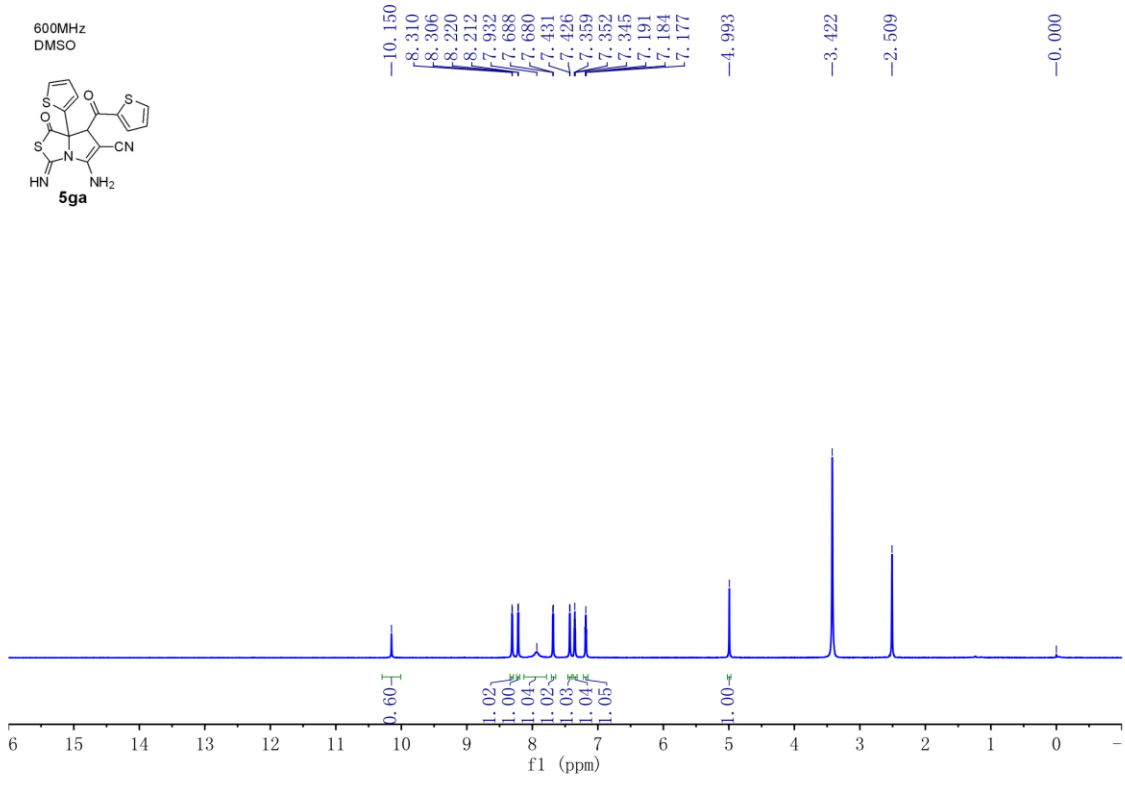

150MHz
DMSO
195.48
195.09
159.66
159.47
155.69
151.36
138.28
135.25
130.29
130.00
122.15
121.21
118.11
117.10
114.67
113.48
111.57
82.49
56.10
56.05
55.45
55.30
39.92
39.78
39.64
39.50
39.37
39.23
39.09
MeO
OMe
O
O
S
N
CN
HN
NH2
5da
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

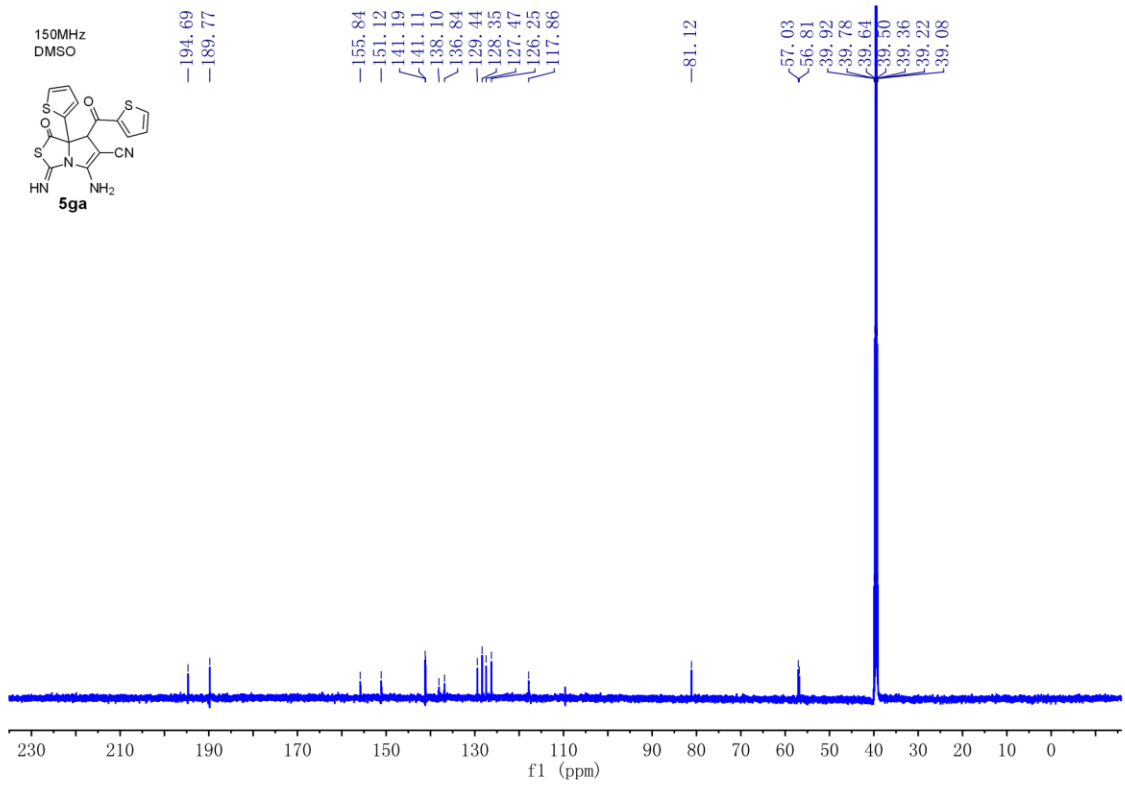

600MHz
DMSO
10.139
8.311
8.157
8.143
8.010
7.663
7.649
7.633
7.623
7.609
5.089
3.372
2.500
Cl
O
O
S
N
CN
HN
NH2
Cl
5ea
1.04
2.04
1.90
6.03
1.00
6
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

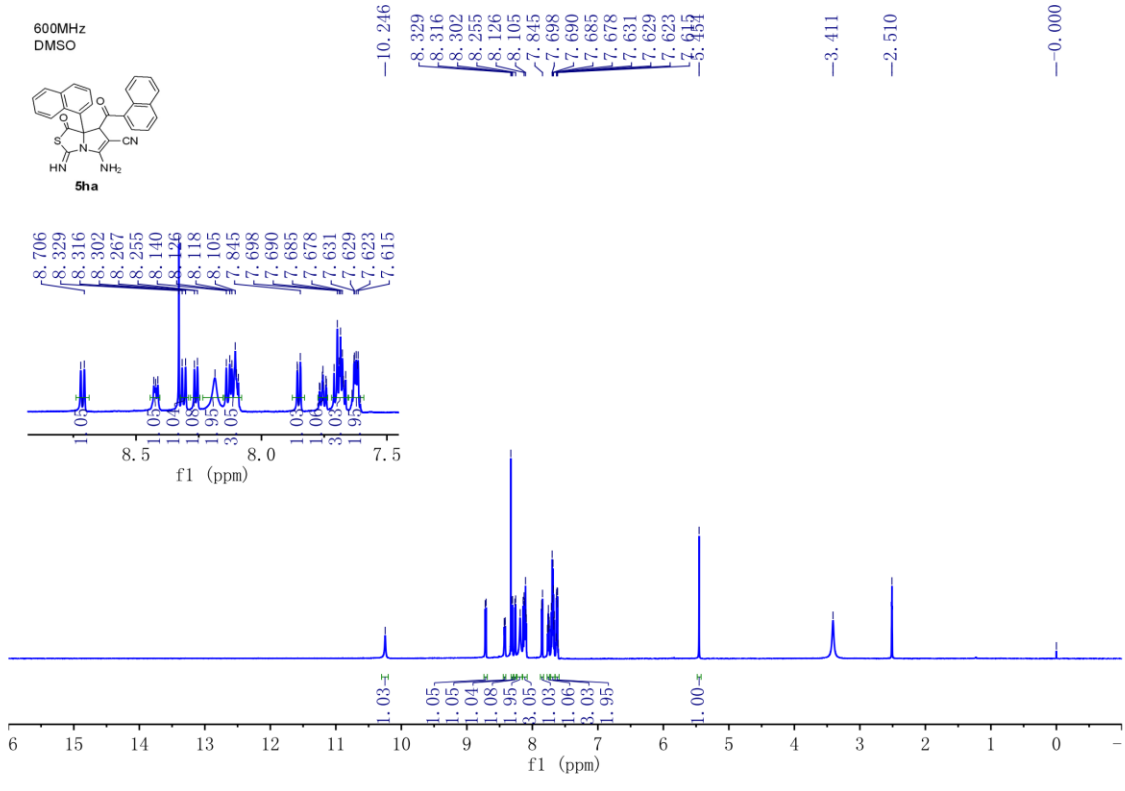

150MHz
DMSO
195.08
194.79
155.70
151.15
139.75
135.56
134.50
129.20
129.07
82.00
55.87
55.62
39.92
39.78
39.64
39.50
39.36
39.22
39.08
Cl
O
O
S
N
HN
NH2
CN
Cl
5ea
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

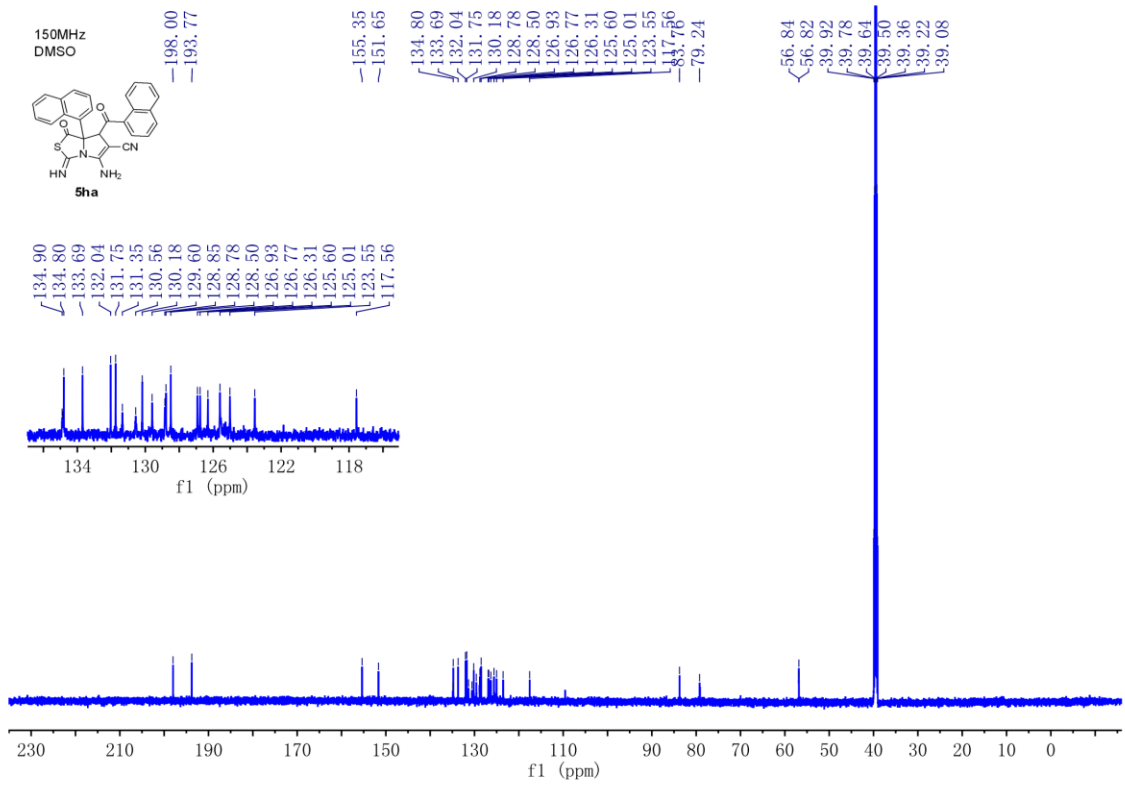

600MHz
DMSO
10.144
8.321
8.076
8.062
8.011
7.815
7.801
7.767
7.752
7.579
7.565
5.082
3.363
2.507
0.000
Br
O
O
S
N
HN
NH2
CN
Br
5fa
2.14
1.76
2.11
2.08
2.03
1.00
1.00
8.5
8.2
7.9
7.6
f1 (ppm)
6
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

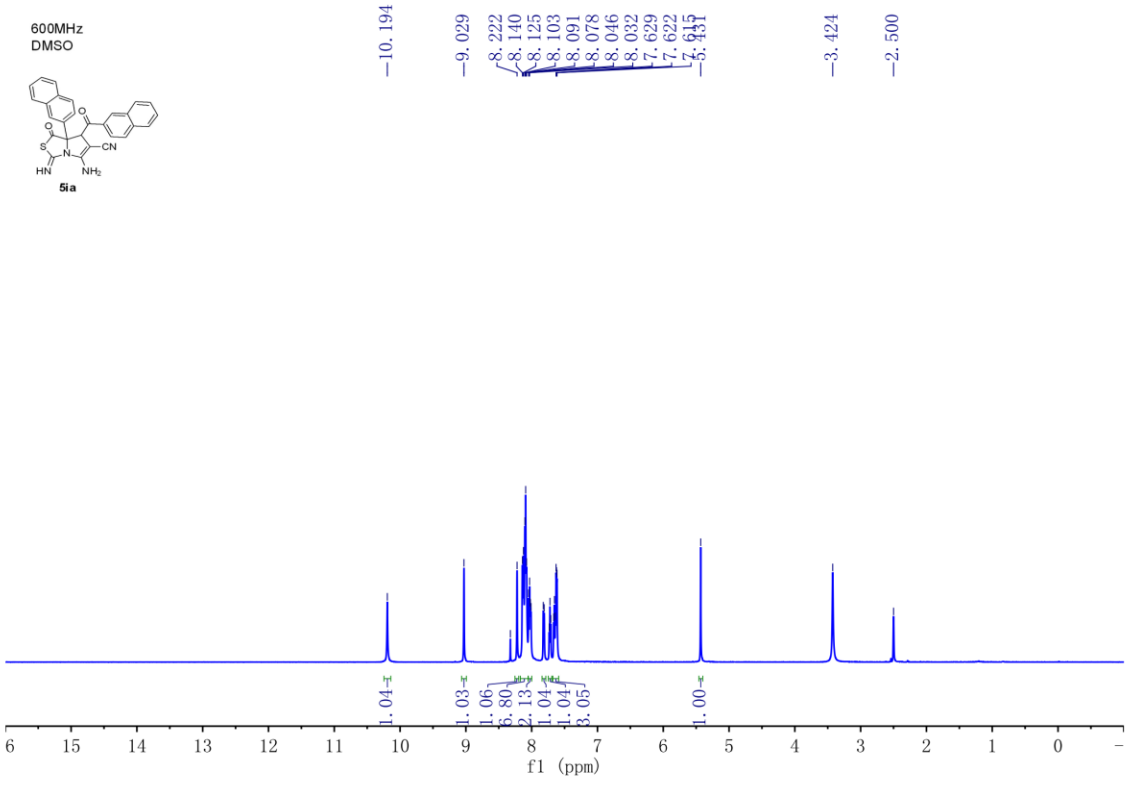

150MHz
DMSO
5fa
195.01
155.68
151.11
136.00
132.96
132.12
132.02
131.50
129.12
127.50
123.13
117.75
82.03
55.77
55.58
39.92
39.78
39.64
39.50
39.36
39.22
39.08
f1 (ppm)

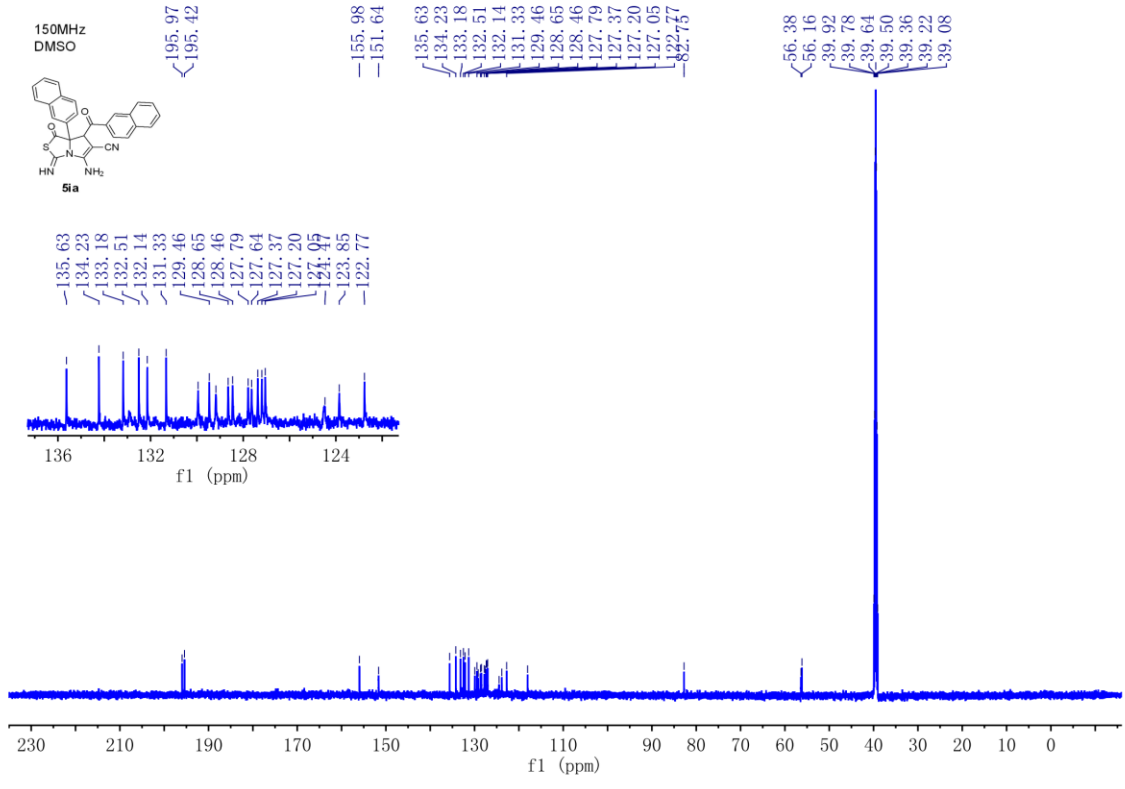

600MHz
DMSO
5ga
10.150
8.310
8.306
8.220
8.212
7.932
7.688
7.680
7.431
7.426
7.359
7.352
7.345
7.191
7.184
7.177
4.993
3.422
2.509
0.000
0.60
1.02
1.00
1.04
1.02
1.03
1.04
1.05
1.00
f1 (ppm)

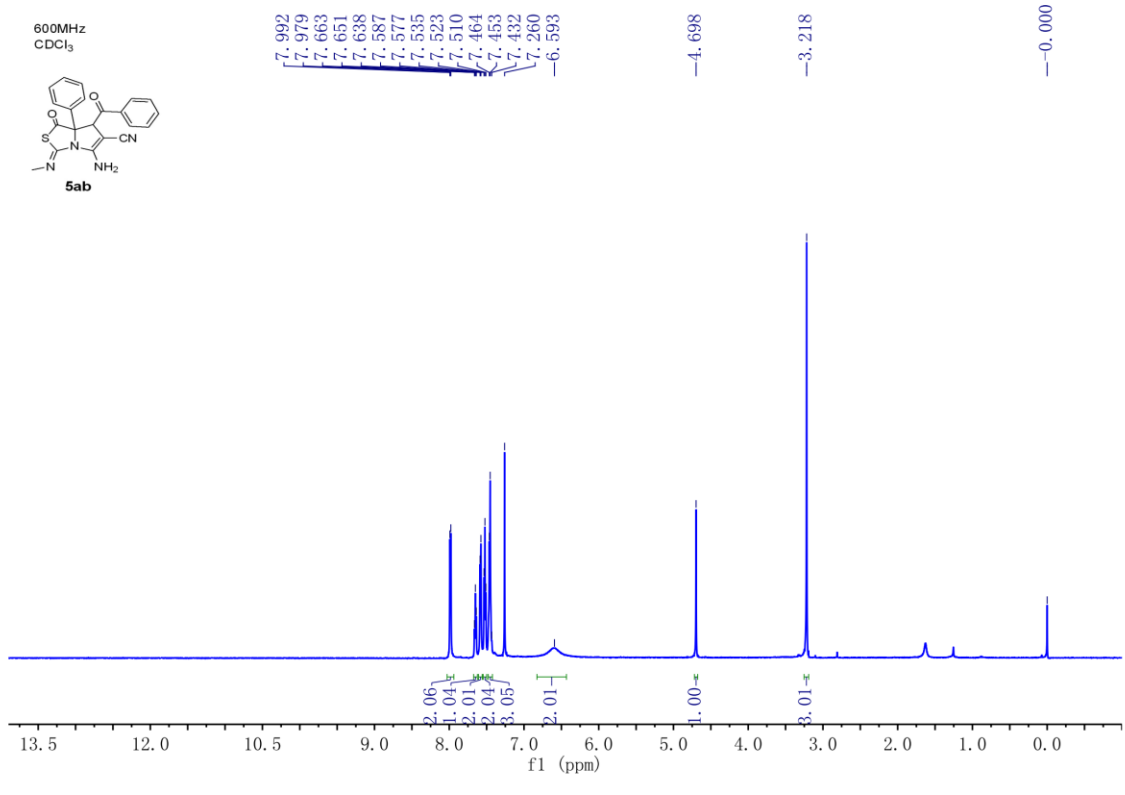

150MHz
DMSO
194.69
189.77
155.84
151.12
141.19
141.11
138.10
136.84
129.44
128.35
127.47
126.25
117.86
81.12
57.03
56.81
39.92
39.78
39.64
39.50
39.36
39.22
39.08
5ga
f1 (ppm)

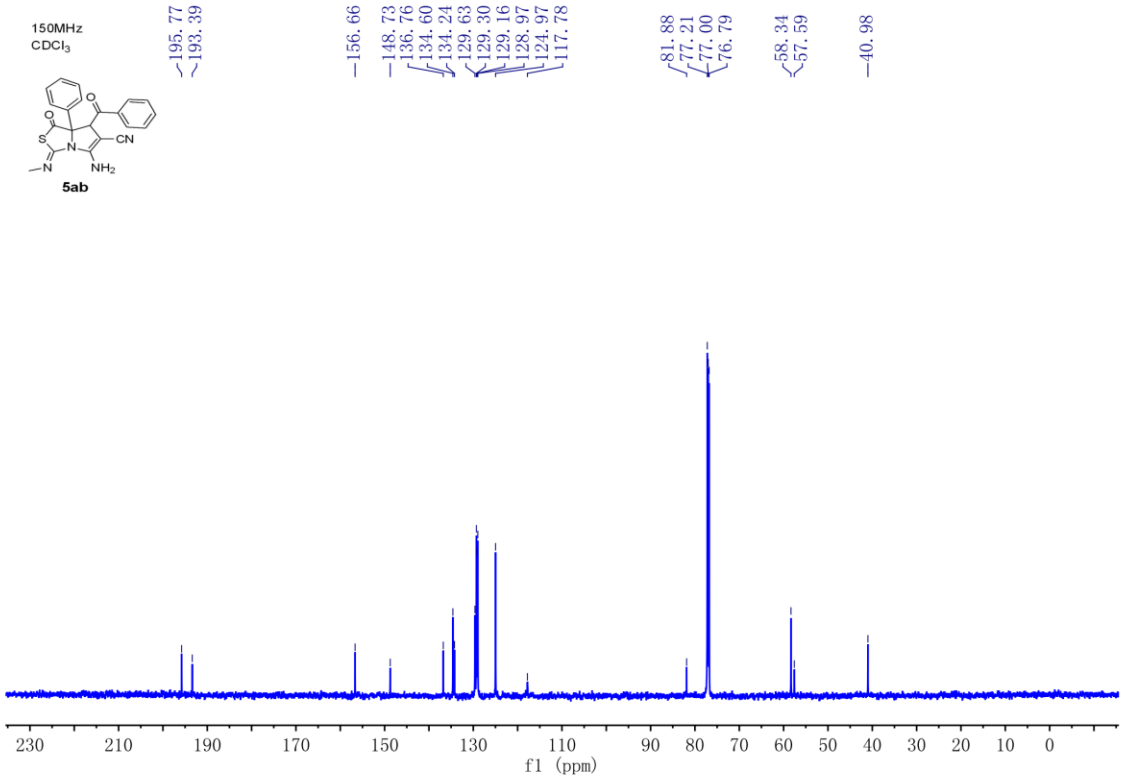

600MHz
DMSO
10.246
8.329
8.316
8.302
8.255
8.126
8.105
7.845
7.698
7.690
7.685
7.678
7.631
7.629
7.623
7.615
5.454
3.411
2.510
0.000
5ha
f1 (ppm)

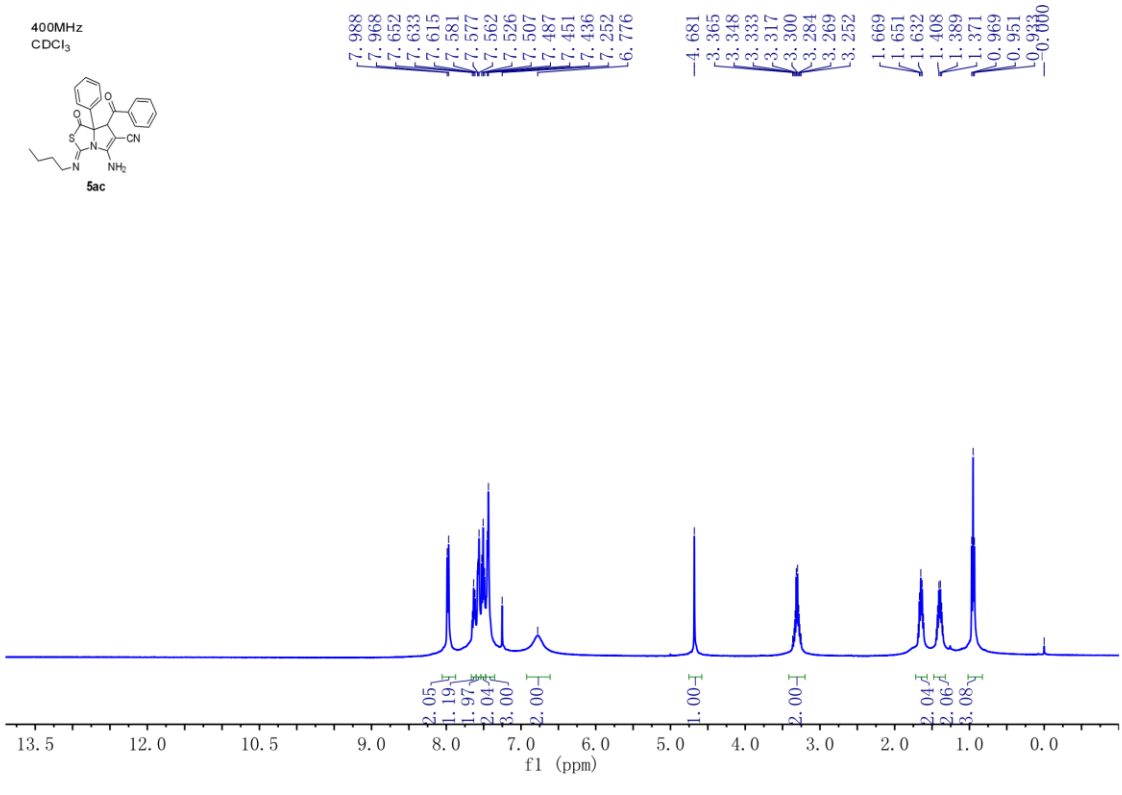

150MHz
DMSO
198.00
193.77
155.35
151.65
134.80
133.69
132.04
131.75
130.18
128.78
128.50
126.93
126.77
126.31
125.60
125.01
123.55
117.56
86.76
79.24
56.84
56.82
39.92
39.78
39.64
39.50
39.36
39.22
39.08
5ha
f1 (ppm)

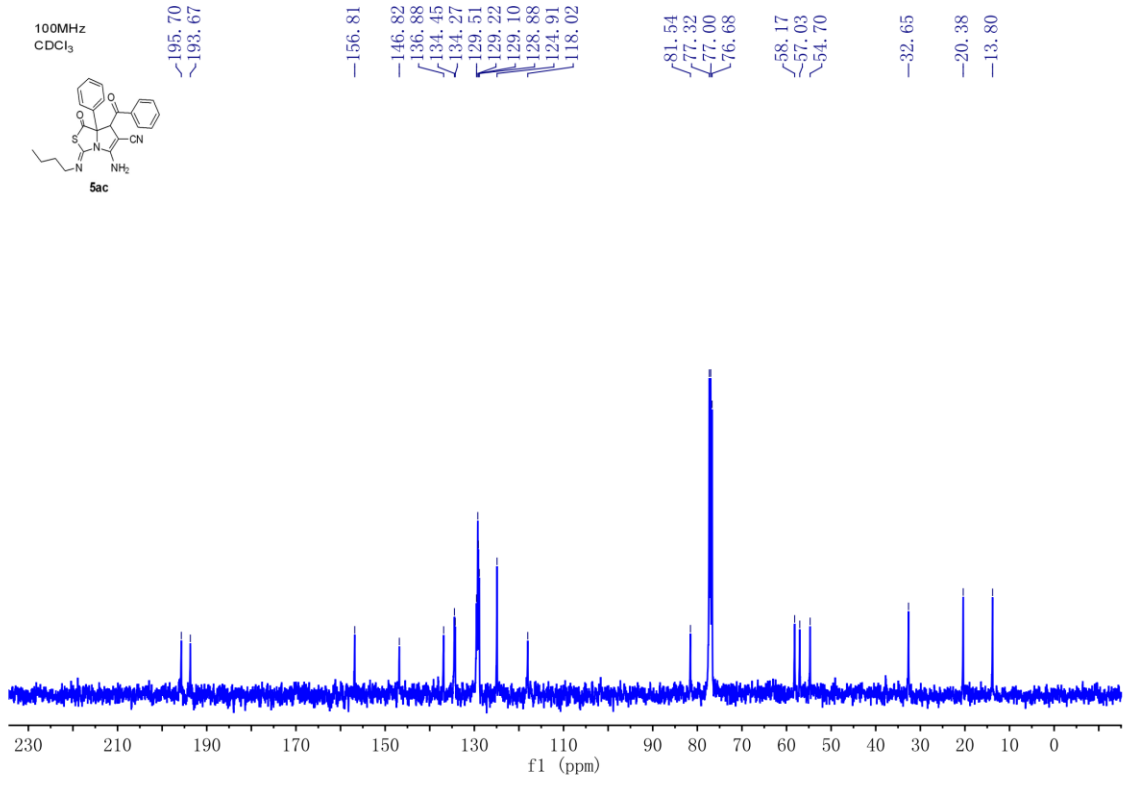

600MHz
DMSO
10.194
9.029
8.222
8.140
8.125
8.103
8.091
8.078
8.046
8.032
7.629
7.622
7.615
7.431
3.424
2.500
1.04
1.03
1.06
6.80
2.13
1.04
1.04
3.05
1.00
5ia
f1 (ppm)

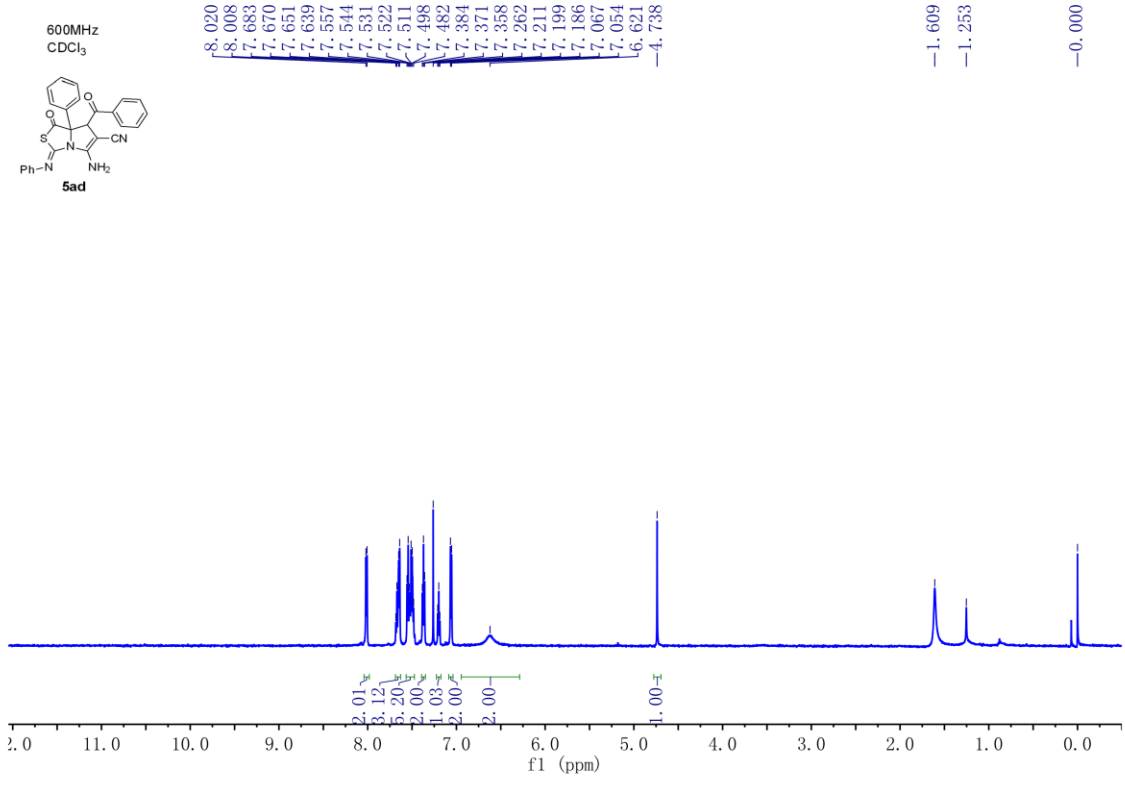

150MHz
DMSO
5ia
195.97
195.42
155.98
151.64
135.63
134.23
133.18
132.51
132.14
131.33
129.46
128.65
128.46
127.79
127.37
127.20
127.05
122.77
82.75
56.38
56.16
39.92
39.78
39.64
39.50
39.36
39.22
39.08
123.85
f1 (ppm)

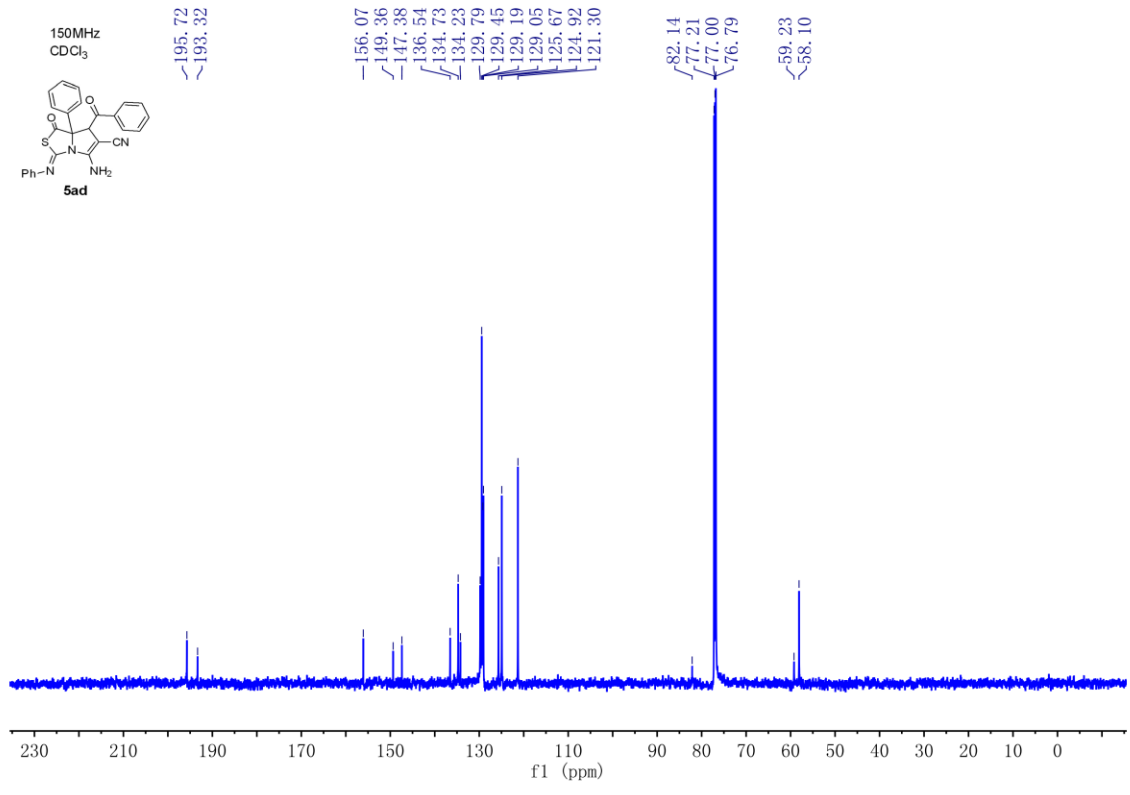

600MHz
CDCl3
5ab
7.992
7.979
7.663
7.651
7.638
7.587
7.577
7.535
7.523
7.510
7.464
7.453
7.432
7.260
6.593
4.698
3.218
0.000
2.06
1.04
2.01
2.04
3.05
2.01
1.00
3.01
f1 (ppm)


150MHz
CDCl3
195.77
193.39
156.66
148.73
136.76
134.60
134.24
129.63
129.30
129.16
128.97
124.97
117.78
81.88
77.21
77.00
76.79
58.34
57.59
40.98
5ab
f1 (ppm)


400MHz
CDCl3
7.988
7.968
7.652
7.633
7.615
7.581
7.577
7.562
7.526
7.507
7.487
7.451
7.436
7.252
6.776
4.681
3.365
3.348
3.333
3.317
3.300
3.284
3.269
3.252
1.669
1.651
1.632
1.408
1.389
1.371
0.969
0.951
0.933
0.000
5ac
2.05
1.19
1.97
2.04
3.00
2.00
1.00
2.00
2.04
2.06
3.08
f1 (ppm)


100MHz
CDCl3
195.70
193.67
156.81
146.82
136.88
134.45
134.27
129.51
129.22
129.10
128.88
124.91
118.02
81.54
77.32
77.00
76.68
58.17
57.03
54.70
32.65
20.38
13.80
5ac
f1 (ppm)


600MHz
CDCl3
8.020
8.008
7.683
7.670
7.651
7.639
7.557
7.544
7.531
7.522
7.511
7.498
7.482
7.384
7.371
7.358
7.262
7.211
7.199
7.186
7.067
7.054
6.621
4.738
1.609
1.253
0.000
5ad
2.01
3.12
5.20
2.00
1.03
2.00
2.00
1.00
f1 (ppm)


150MHz
CDCl3
195.72
193.32
156.07
149.36
147.38
136.54
134.73
134.23
129.79
129.45
129.19
129.05
125.67
124.92
121.30
82.14
77.21
77.00
76.79
59.23
58.10
5ad
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)