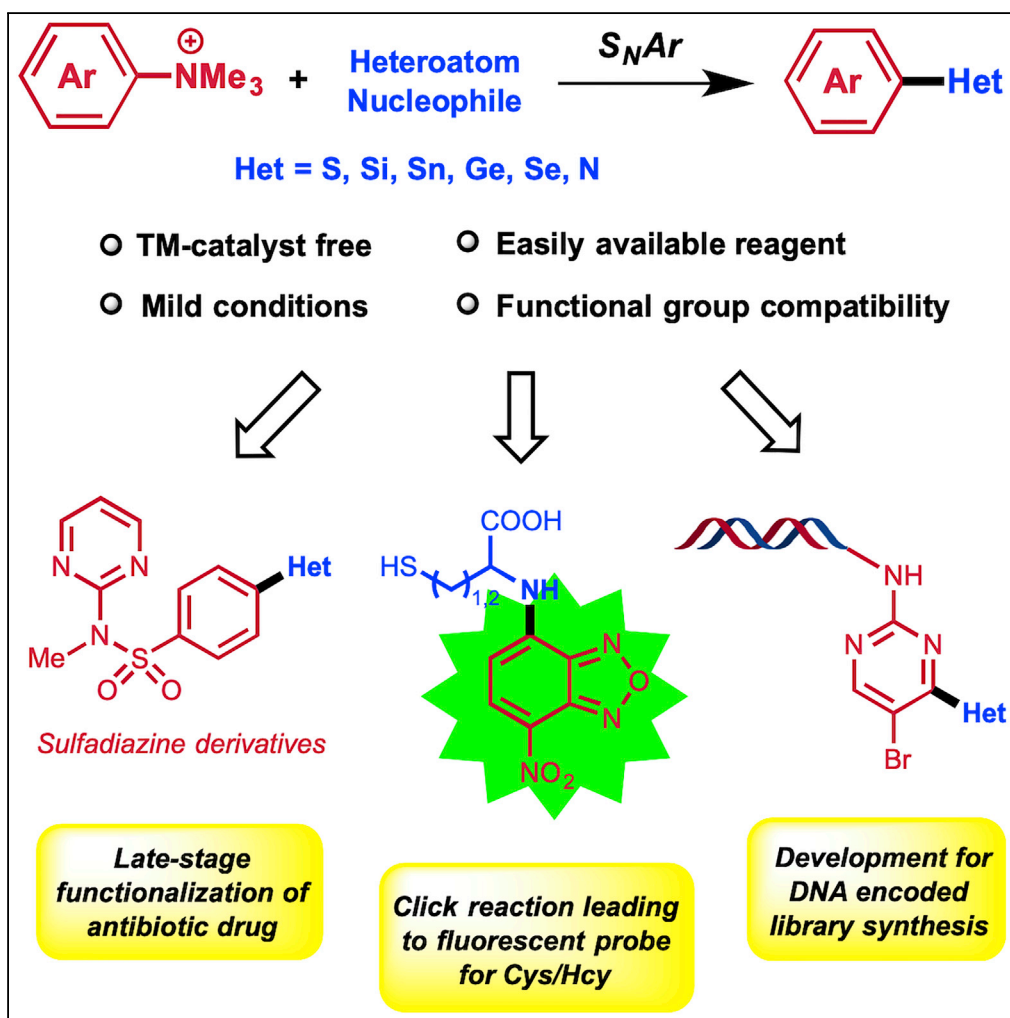


## Article

## Non-transition Metal-Mediated Diverse Aryl–Heteroatom Bond Formation of Arylammonium Salts



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**HIGHLIGHTS**

An efficient approach to construct various C–heteroatom bonds

Readily accessible ammonium salts as substrates

No request of transition metal catalyst and broad functional group compatibility

Great applicability in late-stage functionalization, fluorescent probe, and DEL

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## Article

## Non-transition Metal-Mediated Diverse Aryl–Heteroatom Bond Formation of Arylammonium Salts

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## SUMMARY

**Aryl–heteroatom (C–X) bonds ubiquitously exist in organic, medicinal, and material chemistry, but a universal method to construct diverse C–X bonds is lacking. Here we report our discovery of a convenient and efficient approach to construct various C–X bonds using arylammonium salts as the substrate via an  $S_NAr$  process. This strategy features mild reaction condition, no request of transition metal catalyst, and easy formation of various C–X bonds (C–S, C–Si, C–Sn, C–Ge, C–Se, C–N). The method was successfully applied to a late-stage functionalization of an existing antibiotic drug, to a Clickable reaction of NBD-based ammonium salt as turn-on fluorescent probe to recognize L-cysteine and homocysteine, and to the synthesis of a DNA encoded library (DEL) bearing different C–X bonds.**

## INTRODUCTION

Aryl carbon–heteroatom (C–X) bonds are prevalent in natural and unnatural organic molecules with ample capacities. Some common C–X bonds such as C–O, C–S (Feng et al., 2016), C–N (Ruiz-Castillo and Buchwald, 2016), and C–Si (Franz and Wilson, 2013) bonds are widely embedded in many organic intermediates and therapeutic drugs, whereas the relatively less common C–X bonds such as C–Se (Mugesh et al., 2001), C–Sn (Cordovilla et al., 2015), and C–Ge (Nakamura et al., 2002) bonds generally serve as synthetic precursors for many pharmaceuticals, organic materials, and polymers. In recent years, numerous synthetic methods for C–X bond formations have been developed (Jones et al., 2018; Shen et al., 2014; Liu et al., 2017; Wang et al., 2018a; Hartwig, 2008; Surry and Buchwald, 2008; Bariwal and Van der Eycken, 2013; Cheng and Hartwig, 2015; Zarate and Martin, 2014; Taniguchi and Onami, 2004; Shu et al., 2016; Yoshida, 2016; Gu and Martín, 2017; Komami et al., 2018). Normally, these aryl C–X bonds were formed starting from the same substrate aryl (pseudo)halides through cross-couplings with appropriate heteroatom nucleophiles under transition-metal (TM) catalysis (Scheme 1). However, these methods suffer from limited applications because of several drawbacks, including the additional steps necessary to presynthesize aryl halides, harsh reaction conditions, costive metal catalysts that are either toxic or difficult to remove, especially in the pharmaceutical industry (Wu et al., 2012; Chan et al., 2013). Therefore, it is highly desired to invent a universal method to construct diverse C–X bonds starting from a same substrate (Li et al., 2017; Xu et al., 2016). Ideally, this method should feature (1) using a ubiquitous readily available substrate; (2) wide scope to form various C–X bonds; (3) no TM catalyst needed.

Anilines are one of the most prevalent naturally abundant or readily synthetic accessible reagents in organic synthesis. Therefore, use of anilines, instead of aryl halides, as substrates to undergo the cross-coupling has long been a synthetic aspiration, but only with limited success (Ouyang et al., 2015; Li et al., 2014; Xu et al., 2017), owing to the high inertness of the C–N bond and the high reactivity of the  $NH_2$  group itself. Fortunately, conversion of anilines to the arylammonium species has been reported to enable the TM-catalyzed cross-couplings with appropriate partners (Wenkert et al., 1988; Blakey and MacMillan, 2003; Xie and Wang, 2011; Wang et al., 2016; Zhang et al., 2015; Zhang and Wang, 2014). However, transformations of arylammonium salts through an  $S_NAr$  mechanism in the absence of TM catalyst are rare. Limited examples include the fluorination of ammonium salts (Irie et al., 1982) to radiolabel bio-active molecules for positron-emission tomography imaging and the formation of aryl ethers via C–N bond cleavage in the absence of TM catalyst (Wang et al., 2018b). Inspired by these work, we herein describe a universal method to access diverse aryl–heteroatom, especially those uncommon C–Sn/C–Ge/C–Se bonds using aryl ammonium salts as the ubiquitous substrate under mild reaction conditions.

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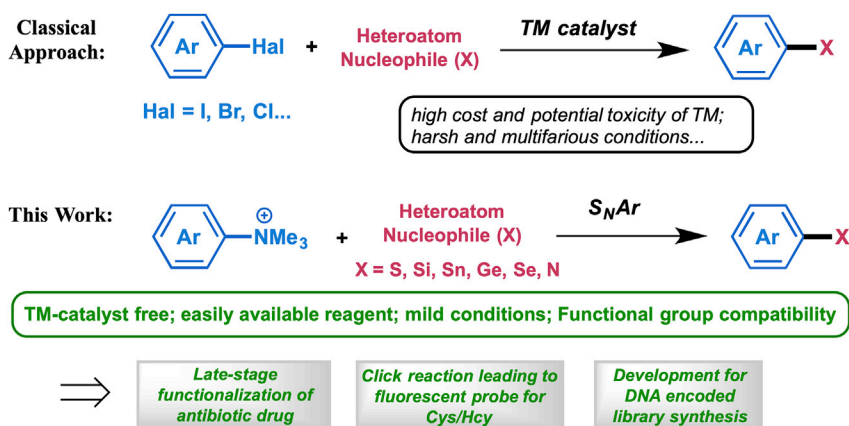
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Scheme 1. Strategies for Diverse Aryl-heteroatom Bond Formation

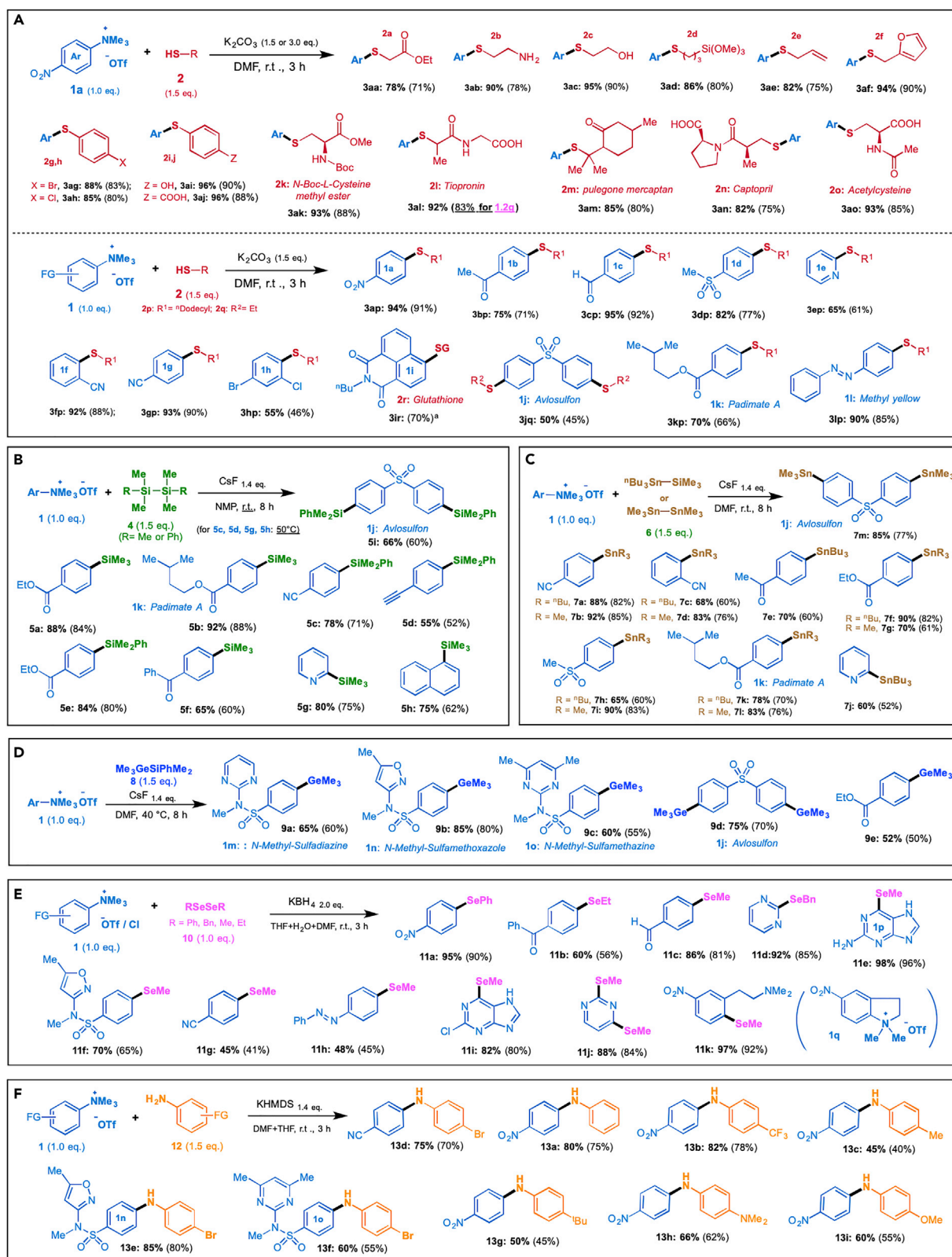
## RESULTS AND DISCUSSION

### C–X Bond Formation

TM-catalyzed thiolation of aryl halides typically requires the strong base to generate thiolates from thiols and a high temperature or specially designed ligands to avoid the deactivation of TM catalyst by the strong coordination of the thiolates (Feng et al., 2016; Hartwig, 2008). Herein, we report the first example of conversion of aryltrimethylammonium salts to aryl thioethers in the presence of a weak base under room temperature, without the need for any TM catalyst and ligand. In the beginning, we chose the reaction of 4-cyanophenyltrimethylammonium salt with 1-dodecanethiol as the model reaction and optimized the substitution conditions in the absence of TM catalyst (for details, see Table S1). It was found that the best result was obtained by using TfO<sup>−</sup> as the counter anion of **1** in DMF with K<sub>2</sub>CO<sub>3</sub> as base at room temperature in 3 h without the need of argon protection. We next focused on the synthetic scope and functional group compatibility of the reaction (Scheme 2A). Thiols bearing an ester (**2a**), free amino (**2b**), hydroxyl (**2c**, **i**), silyl (**2d**), allyl (**2e**), furyl (**2f**), halogen (**2g**, **h**), or carboxylic (**2j**) group, as well as the sterically congested tertiary thiol (**2m**), were found to proceed the reaction without difficulty, generating the desired thioetheric products in 71%–90% isolated yields. To further evaluate the synthetic applicability of this protocol, we examined reactions of **1a** with several biologically active molecules or their derivatives containing an -SH moiety (**2k**–**o**). All the reactions occurred smoothly affording corresponding C–S bond-containing products **3ak**–**3ao** in 75%–88% yields. To illustrate the scalable potential of this method, we conducted the reaction of *Tiopronin* (antidote) derivative **2l** with **1a** on a gram scale, and the product **3al** was obtained in 83% yield after a simple workup procedure.

Meanwhile, the functional group tolerance on the aryl trimethylammonium triflate was also investigated (Scheme 2A). It was found that aryl ammonium salts **1** bearing acyl (**1b**), formyl (**1c**), sulfonyl (**1d**), cyano (**1f**, **1g**), halogen (**1h**), ester (**1k**), and heterocycle (**1e**) group reacted without difficulty, providing corresponding C–S bond products in up to 92% yields. It is worth highlighting that ammonium salts **1j**–**l** derived from the antibiotic drug *Avlosulfon*, sunscreen lotion *Padimate A*, and *Methyl Yellow*, respectively, took part in the C–S bond formation as well to afford the thioetheric products, suggesting the potential use of this reaction in the late-stage functionalization of existing drugs. Interestingly, the tricyclic substrate **1i** prepared from naphthalimide, a well-known fluorophore, was found to readily react with glutathione, providing the corresponding C–S bond product **3ir** in 70% yield. In view of the strong internal charge transfer character of naphthalimides (Zhou et al., 2016) and involvement of glutathione in many biological processes, the current C–S bonding formation process might be used as a biomarker *in vivo*.

Since the C–Si/Sn/Ge bonds belong to the same group in the periodic table of elements, they are widely used in drug design as a bioisosteric replacement of C–C bond or as a precursor for further transformation. Traditional methods to generate Ar–Si/Ge/Sn involved the reaction of Si/Ge/Sn electrophiles with air-sensitive organometallic reagents, alternatively TM-catalyzed C–Si/Ge/Sn coupling reactions at high temperature (McNeill et al., 2007; Komami et al., 2018; Corcoran et al., 2012). We, herein, report an unprecedented silylation, germylation, and stannylation of various ammonium salts via the S<sub>N</sub>Ar process with stable substrates at low temperature without the need of TM-catalyst. First, we examined the feasibility of C–Si/Sn/Ge bond formation by simply



### Scheme 2. Substrate Scope Investigation

(A) Thioesterification reactions.  $K_2CO_3$ : 1.5 eq. (for **2i**, **2j**, **2l**, **2n**, **2o**: 3.0 eq.). <sup>a</sup>For **3ir**, a mixture of DMF and  $H_2O$  was used as the solvent. (B) Silylation reactions; (C) Stannylation reactions; (D) Germylation reactions; (E) Selenation reactions; (F) Amination reactions. For **11d**, **11e**, **11i** and **11j**,  $Cl^-$  was used as the counter anion of **1**. Yields were calculated based on NMR (bold) and isolation (in parentheses). See also Figures S1–S6.

treating arylammonium salts with appropriate heteroatom nucleophiles. A quick survey of the reaction conditions (for details, see Tables S2 and S3) suggested that the optimum conditions for C–Si/Sn/Ge bond formation are to use CsF as the base, NMP/DMF as the solvent, at room temperature (r.t.) within 8 h. With this result in hand, a small series of arylammonium salts were used to explore the substrate scope. As shown in Scheme 2B–2D, arylammonium salts bearing an ester (**5a**, **5e**, **7f**, **7g**, **9e**), acetylene (**5d**), acyl (**5f**, **7e**), pyridyl (**5g**, **7j**), sulfonyl (**7h**, **7i**), or cyano (**5c**, **7a–d**) substituent went through the reaction very well providing the corresponding C–Si/Sn/Ge bond products in moderate to high yields. Interestingly, 1-naphthyl ammonium salt lacking an electron-withdrawing substituent also participated in the reaction nicely yielding compound **5h** in 75% yield. *Padimate A* derivatives (**5b**, **7k**, **7l**), *Sulfonamides* derivatives (**9a–9c**), and the dual functionalized derivatives of the antibiotic drug *Avlo-sulfon* (**5i**, **7m**, **9d**) were also easily prepared in moderate to high yields.

Organoselenium compounds have gained more and more interests recently; however, methods to construct C–Se bond are rather limited. To explore the potential of our current method using arylammonium salts to build up C–Se bond, we used  $RSeSeR$  ( $R = Ph, Bn, Me, Et$ ) as the selenation source and  $KBH_4$  as the base (for optimization details, see Table S4). As shown in Scheme 2E, arylammonium salts containing a nitro, acyl, formyl, cyano, sulfonyl substituent and purine/pyrimidine derivatives were tolerant in the reaction conditions yielding corresponding C–Se products **11a–j** in up to 96% yields. Meanwhile, the cyclic ammonium salts **1q** prepared from indoline derivative was also suitable substrate, affording the ring-opened product **11k** in 92% yield.

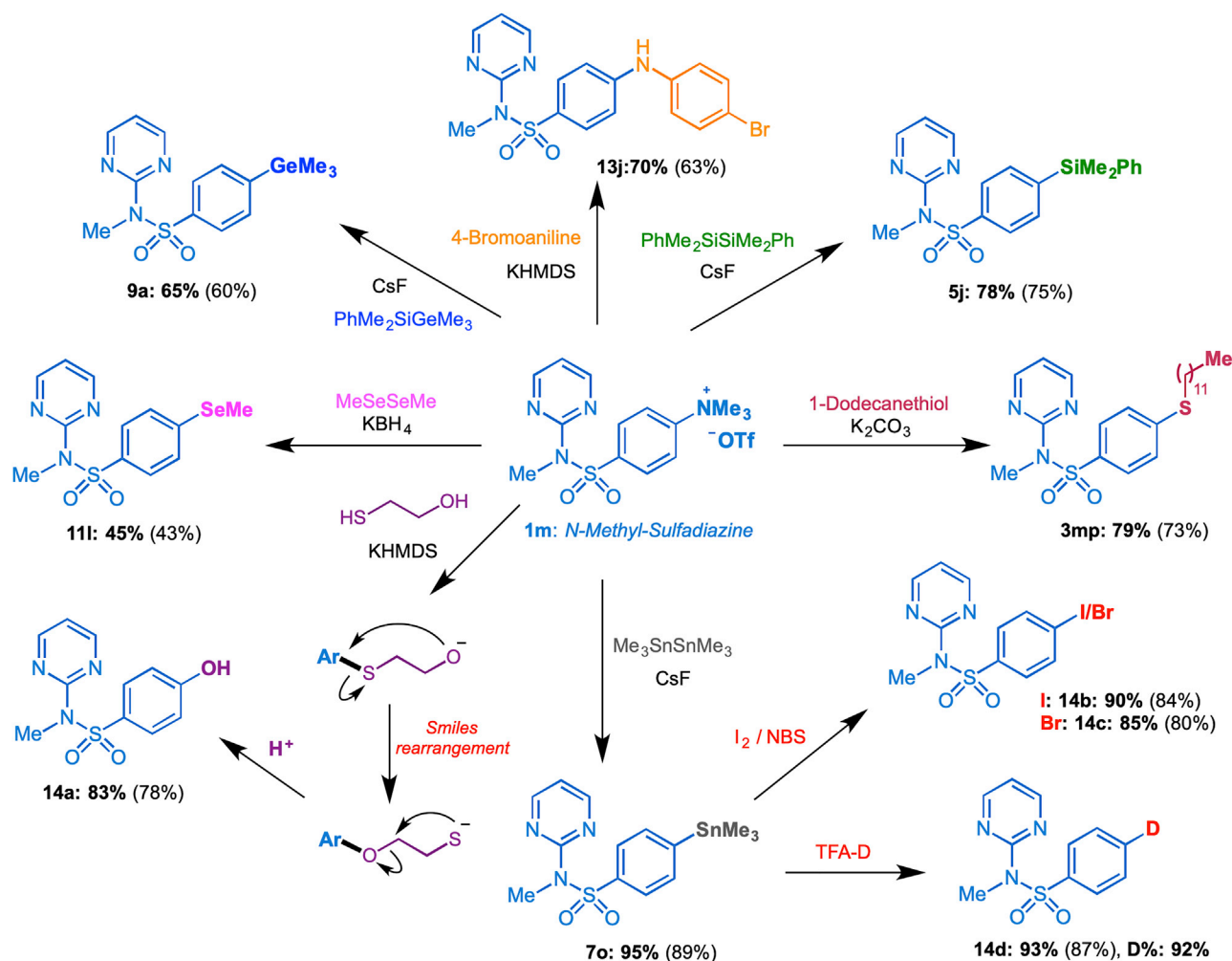
Finally, we decided to explore the feasibility of constructing C–N bond under our  $S_NAr$  substitution protocol without the TM-involved catalysis. With this optimized reaction condition in hand (for details, Table S5), we tested the substrate scope by using various arylammonium salts and differently substituted anilines. As shown in Scheme 2F, arylammonium salts with an aminosulfonyl, nitro, or cyano substituent were well tolerant, and the corresponding diaryl amines were obtained in moderate to high yields. Anilines bearing either electron-donating or electron-withdrawing substituents are suitable nucleophiles.

### Late-Stage Functionalization of Biologically Active Compounds

To evaluate the utility of our current protocol in the construction of diverse C–X bonds, we conducted a late-stage diversification of the antibiotic drug *Sulfadiazine*. As shown in Scheme 3, *Sulfadiazine* was first converted to the ammonium salt **1m**, which was then subjected to the corresponding C–X bond formation reactions. A small library of sulfadiazine analogues bearing a new C–S (**3mp**), C–Se (**11h**), C–Sn (**7o**), C–Si (**5j**), C–Ge (**9a**), and C–N (**13h**) was conveniently established in moderate to good yields. Interestingly, phenol **14a** bearing a new C–O(H) bond was obtained by treating **1m** with 2-mercaptoethan-1-ol in the presence of KHMDS as the base. Likely, a Smiles rearrangement of the initially formed aryl thioether to the aryl ether, followed by elimination of thiirane was involved in the transformation (Boschi et al., 2001). All these products can be used as key intermediates for further functional group transformation. For example, treatment of aryltrimethyltin derivative **7o** with iodine, NBS, or deuterated trifluoroacetic acid provided corresponding iodo-, bromo-, or deuterated derivatives **14b–d** in 80%–87% yields.

### Clickable Synthesis of Fluorescent Probes from NBD-Ammonium Salt with Biological Thiols

7-Nitrobenz-2-oxa-1,3-diazole (NBD) moiety has been widely used as a fluorophore in many fluorescent chemosensors because of its emission at longer wavelengths and good cell permeability (Uchiyama et al., 2001). To explore the application of our C–X bond formation protocol, we first prepared C4-ammonium NBD **1r** and tested its sensitivity to various biological thiols, including small-molecule L-cysteine (Cys, **2v**), homocysteine (Hcy, **2w**), glutathione (**2r**), coenzyme A (**2s**), cyclopeptide (**2t**), as well as biomacromolecule antibody  $\beta$ -Lactoglobulin (**2u**). As shown in Scheme 4A, all the reactions proceeded very well just by “Clicking” the ammonium salt **1r** with an appropriate thiol in water at r.t. for 20 min, providing corresponding products in moderate to high yields. Notably, the reactions with complex thiols **2r–2u** afforded the expected C–S bond products, whereas reactions with simple thiols **2v–w** gave products bearing a C–N bond. The production of **15e** and **15f** is likely formed through Smiles rearrangement that converted

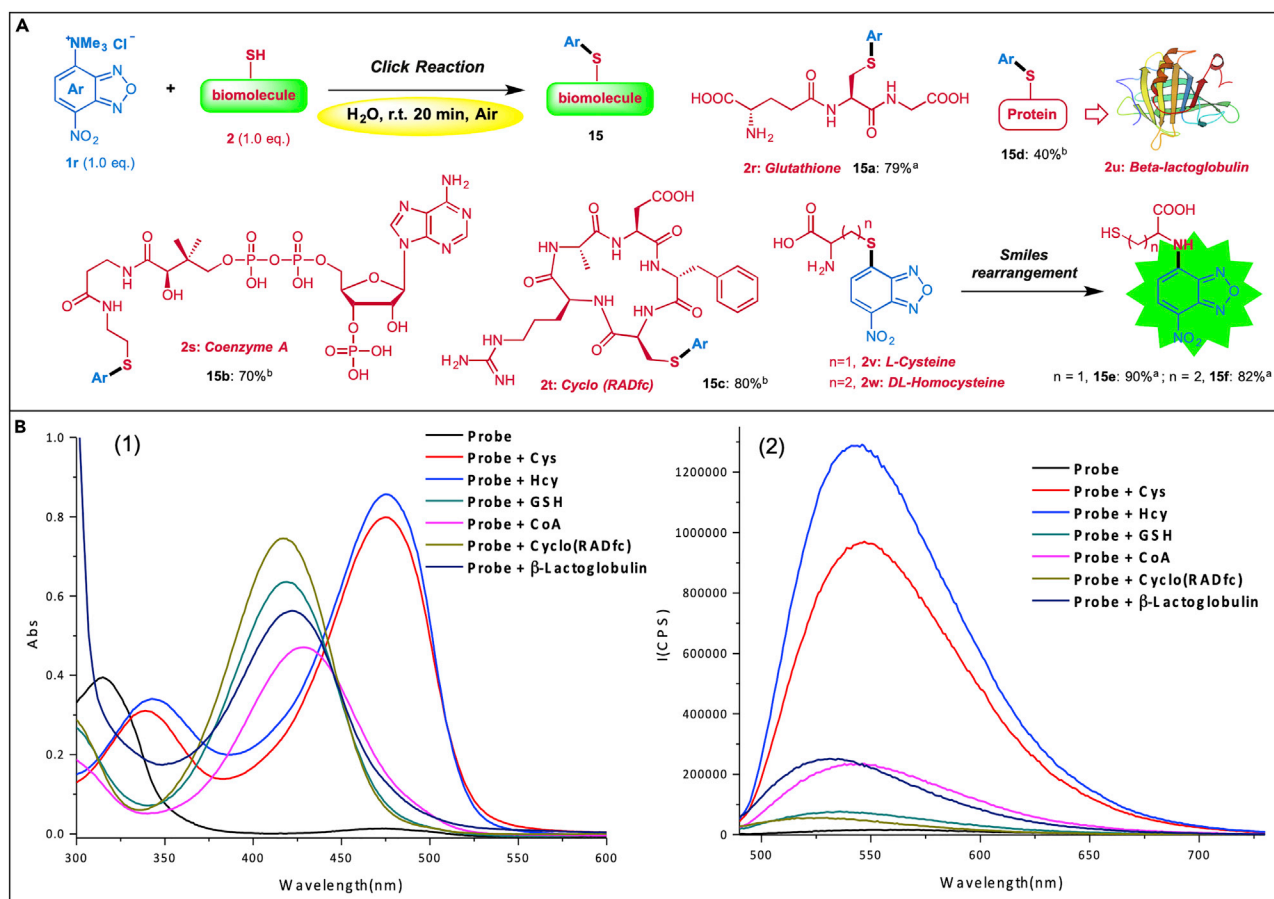


**Scheme 3. Late-stage Functionalization of the Antibiotic Drug Sulfadiazine**

the initial C–S bond products to the *N*-substituted NBDs. This rearrangement has been further verified by spectroscopic comparison (Wood et al., 2003) (see Figures S7 and S8). In general, the *N*-substituted NBDs have longer-wavelength absorption and stronger fluorescence than the corresponding *S*-substituted ones (Chen et al., 2016); we then tested the fluorescent properties of these NBD compounds. The absorption and fluorescence emission responses (Scheme 4B) showed that probe 1r was non-fluorescent, whereas treatment of 1r with simple thiols Cys/Hcy induced a dramatic increase of fluorescence intensity at 550 nm. Treatment of 1r with complex thiols 2r, 2s, or 2t showed an absorption maximum at 419, 427, and 417 nm, respectively, and no significant fluorescence response was observed. These results indicated that our NBD probe 1r could specifically recognize and discriminate Cys/Hcy over other more complex bioactive thiols. Since Cys/Hcy play critically important roles in maintaining redox homeostasis in physiological processes (Wood et al., 2003), our NBD-ammonium salt probe and the readily clickable reaction conditions may find use in monitoring biological process *in vivo*.

### On-DNA Reaction Development for DNA Encoded Library Synthesis

DNA-encoded library (DEL) is a powerful tool for hit identification in small molecule drug discovery (Goodnow et al., 2017; Mullard, 2016; Buller et al., 2010), and several compounds derived from their original DEL hits have progressed to clinical development (Belyanskaya et al., 2017). The chemical diversity of DEL library is the key to successful discovery of drug-like molecules but is often limited to DNA compatible synthetic reactions (Wang et al., 2014; Satz et al., 2015; Li et al., 2016). Since our C–X bond formation protocol proceeded in mild reaction conditions, it is ideal to be used for the DEL synthesis. 2,4-Dichloropyrimidine



#### Scheme 4. Clickable Synthesis of Turn-on Fluorescent Probe

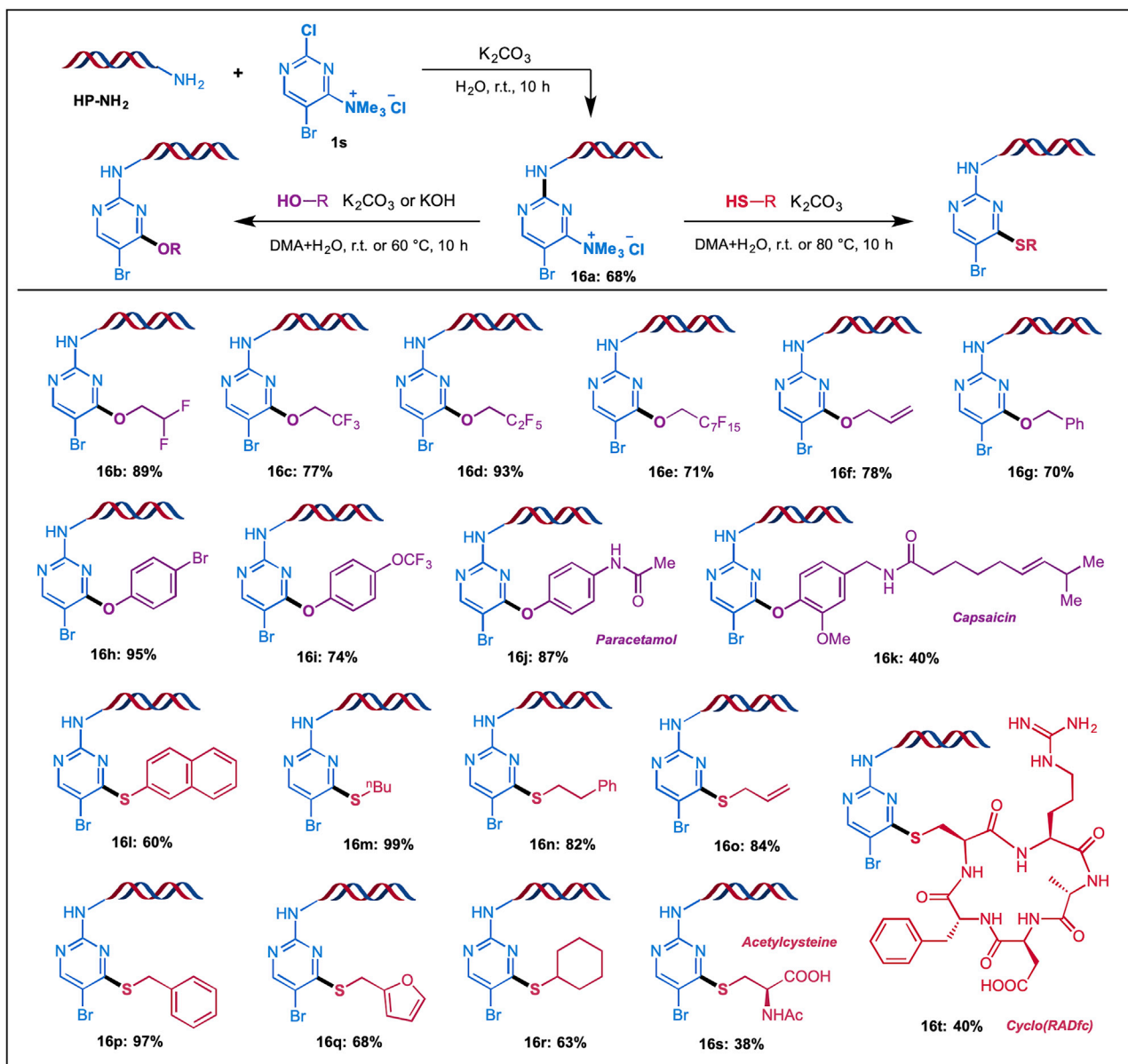
(A) Clickable thioetherification of NBD-ammonium salts with various biological thiols. <sup>a</sup>NMR yield; <sup>b</sup>liquid chromatography-mass spectrometry conversion. (B) Absorption (1) and fluorescence (2) spectra of probe **1r** (50  $\mu\text{M}$ ) before (black curve) and after addition of 250  $\mu\text{M}$  Cys (red), Hcy (blue), GSH (green), Coenzyme A (pink), cyclopeptide (brown), and  $\beta$ -Lactoglobulin (purple), respectively, incubated for 30 min in  $\text{H}_2\text{O}$  at 25°C. Excitation wavelength: 480nm. See also Figure S7.

derivatives, a widely used core structure of kinase inhibitors, could be used as valuable building blocks (BB) in the DNA encoded library synthesis (Ding et al., 2016).  $\text{S}_{\text{N}}\text{Ar}$  reaction of DNA headpiece (HP, Figure S9) with excessive 2,4-dichloropyrimidine derivatives routinely provides C-4 DNA-conjugated pyrimidine in high regioselectivity (Satz et al., 2015).

In contrast, we developed a novel ammonium building block (**1s**), which could be reacted with HP to give C-2 DNA-conjugated pyrimidine (**16a**) selectively (Scheme 5). By following our protocol, the corresponding C–O/S bond formations occurred smoothly in dilute conditions and provided DNA-conjugated pyrimidines **16b-t** bearing various functional groups (Scheme 5). Several biologically active molecules as well as fluorine-containing functional groups could also be introduced. Alcohol BBs are quite challenging for on-DNA reactions, but our new on-DNA reaction could tolerate a series of alcohol BBs, which significantly increases the diversity of DEL. It is noteworthy that the Br moiety in pyrimidine scaffold might be used for further functionalization through cross-coupling reactions (Ding and Clark, 2015) to provide a more complex compound library with ample chemical diversity. Such novel chemical selectivity brought by **1s** enables the design and synthesis of different types of DNA encoded pyrimidine library that is currently under development for library synthesis.

#### Conclusion

In summary, we have established a convenient and efficient approach to construct diverse aryl–heteroatom bonds using arylammonium salts as the common substrates via a  $\text{S}_{\text{N}}\text{Ar}$  process. This strategy features mild reaction condition, no request of transition metal catalyst, and wide scope for various C–X bonds, especially



### Scheme 5. On-DNA Reaction Development.

Reactions were carried out in dilute conditions (1 mM). Conversion determined by liquid chromatography-mass spectrometry. See also Figure S10.

those uncommon C–Sn/C–Ge/C–Se formation. The application of this method was exemplified by a late-stage functionalization of an existing antibiotic drug and by a Clickable reaction using NBD-based ammonium salt as a turn-on fluorescent probe for Cys and Hcy. Meanwhile, on-DNA reaction development for DEL was also successfully realized starting from a pyrimidinylammonium salt.

### Limitation of Study

Ammonium salts derived from electron-rich anilines (e.g., *p*-R-C<sub>6</sub>H<sub>4</sub>-NMe<sub>3</sub><sup>+</sup>, R = Me, MeO) showed poor or no reactivity toward heteroatom nucleophiles. Silylation product with acetyl group could not be obtained probably due to the strong basicity of silyl anions.

### METHODS

All methods can be found in the accompanying [Transparent Methods supplemental file](#).



## SUPPLEMENTAL INFORMATION

Supplemental Information can be found online at <https://doi.org/10.1016/j.isci.2019.04.038>.

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## AUTHOR CONTRIBUTIONS

D.-Y.W. planned, carried out most of experiments, analyzed, and summarized the experiments. X.W. performed the DEL experiment. J.-N.Z., C.-D.X., and C.-Y.D. participated in the experiments or discussions. Q.M. and H.Z. performed biological thiols analysis. C.W. and M.U. conceived and designed the project. X.-J.L. directed the study on DNA encoded library synthesis. A.Z. supervised the whole research and wrote the manuscript with feedback from all authors.

## DECLARATION OF INTERESTS

The authors declare no competing interests.

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**ISCI, Volume 15**

**Supplemental Information**

**Non-transition Metal-Mediated Diverse**

**Aryl–Heteroatom Bond Formation**

**of Arylammonium Salts**

**Dong-Yu Wang, Xin Wen, Chao-Dong Xiong, Jian-Nan Zhao, Chun-Yong Ding, Qian Meng, Hu Zhou, Chao Wang, Masanobu Uchiyama, Xiao-Jie Lu, and Ao Zhang**

## Supplementary Information

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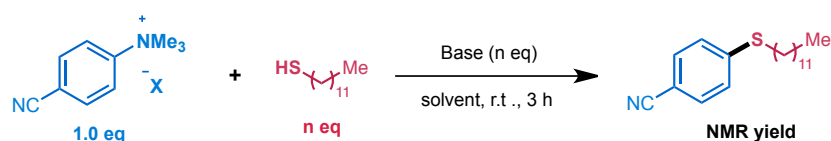
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## 1. General Methods for Experiments

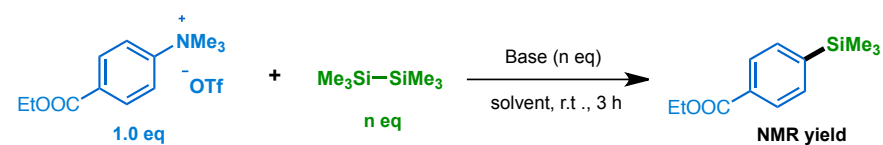
All solvents and chemical reagents were obtained from commercial sources such as *Strem Chemicals*, *Adamas-beta*, *Sigma-Aldrich*, *J&K*, *Accela* and *TCl*, which were used without further purification.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded with tetramethylsilane as an internal reference. Low and high-resolution mass spectra were recorded on EI-TOF (electrospray ionization-time of flight) or ESI-TOF. Normal-phase column chromatography was performed with silica gel 60 (230–400 mesh) from Merck and thin-layer chromatography was carried out on 0.25 mm Merck silica gel plates (60F-254). DNA headpiece HP-NH2 (5'-/5phos/GAGTCA/iSp9/iUniAmM/iSp9/TGACTCCC-3') was obtained from Biosearch Technologies, Novato, CA.

## 2. Optimization for Reaction Conditions

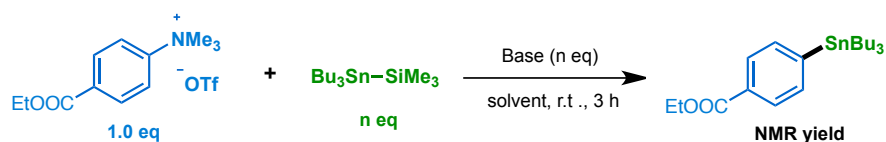
**Table S1.** Screening of Thioetherification Conditions, related to **Scheme 2a**.



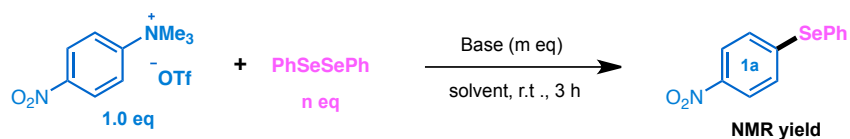
Entry	X	Base	n	solvent	NMR Yield
1	OTf	NaO <sup>t</sup> Bu	2.0	DMF	46%
2	OTf	KO <sup>t</sup> Bu	2.0	DMF	90%
3	OTf	KHMDS	2.0	DMF+THF	87%
4	OTf	K <sub>2</sub> CO <sub>3</sub>	2.0	DMF	98%
5	I	K <sub>2</sub> CO <sub>3</sub>	2.0	DMF	90%
6	BF <sub>4</sub>	K <sub>2</sub> CO <sub>3</sub>	2.0	DMF	85%
7	OTf	Li <sub>2</sub> CO <sub>3</sub>	2.0	DMF	trace
8	OTf	Na <sub>2</sub> CO <sub>3</sub>	2.0	DMF	35%
9	OTf	Cs <sub>2</sub> CO <sub>3</sub>	2.0	DMF	93%
10	OTf	K <sub>3</sub> PO <sub>4</sub>	2.0	DMF	82%
11	OTf	K <sub>2</sub> CO <sub>3</sub>	2.0	THF	88%
12	OTf	K <sub>2</sub> CO <sub>3</sub>	2.0	DMSO	45%
13	OTf	K <sub>2</sub> CO <sub>3</sub>	2.0	DMA	78%
14	OTf	K <sub>2</sub> CO <sub>3</sub>	2.0	NMP	53%
15	OTf	K <sub>2</sub> CO <sub>3</sub>	2.0	DCM	38%
16	OTf	K <sub>2</sub> CO <sub>3</sub>	1.5	DMF	96%
17	OTf	K <sub>2</sub> CO <sub>3</sub>	1.1	DMF	80%
18	OTf	KO <sup>t</sup> Bu (with 2.0eq. TEMPO)	1.5	DMF	92%

**Table S2.** Screening of Silylation Conditions, related to **Scheme 2b**.

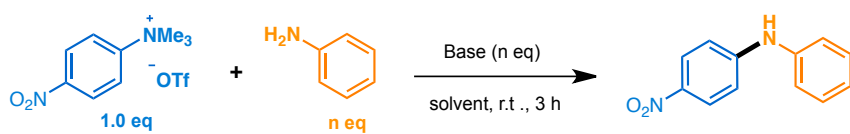
Entry	Base	n	solvent	NMR
1	KO <sup>t</sup> Bu	2.0	NMP	0%
2	KF	2.0	NMP	25%
3	KOAc	2.0	NMP	0%
4	NaOEt	2.0	NMP	0%
5	TBAF	2.0	NMP	32%
6	CsF	2.0	DMF	65%
7	CsF	2.0	DMSO	42%
8	CsF	2.0	CH <sub>3</sub> CN	trace
9	CsF	2.0	DCM	trace
10	CsF	1.5	NMP	88%
11	CsF	1.1	NMP	55%
12	CsF (with 2.0eq. TEMPO)	1.5	NMP	72%

**Table S3.** Screening of Stannylation Conditions, related to **Scheme 2c**.

Entry	Base	n	solvent	NMR Yield
1	KF	2.0	DMF	83%
2	CsF	2.0	DMF	92%
3	NaOMe	2.0	DMF	76%
4	TBAF	2.0	DMF	80%
5	CsF	2.0	THF	75%
6	CsF	2.0	DMSO	47%
7	CsF	2.0	CH <sub>3</sub> CN	62%
8	CsF	2.0	NMP	83%
9	CsF	1.5	DMF	90%
10	CsF	1.1	DMF	77%
11	CsF (with 2.0eq. TEMPO)	1.5	DMF	85%

**Table S4.** Screening of Selenation Conditions, related to **Scheme 2e**.

Entry	Base	n	m	solvent	NMR Yield
1	KO <sup>t</sup> Bu	1.5	1.5	DMF	0%
2	NaH	1.5	1.5	DMF	trace
3	KH	1.5	1.5	DMF	65%
4	KHMDS	1.5	1.5	DMF+THF	trace
5	NaBH <sub>4</sub>	1.5	3.0	THF+H <sub>2</sub> O+DMF	80%
6	KBH <sub>4</sub>	1.5	3.0	THF+H <sub>2</sub> O+DMF	98%
7	KBH <sub>4</sub>	1.0	2.0	THF+H <sub>2</sub> O+DMF	95%
8	KBH <sub>4</sub>	0.6	1.2	THF+H <sub>2</sub> O+DMF	55%

**Table S5.** Screening of Amination Conditions, related to **Scheme 2f**.

Entry	Base	n	solvent	NMR Yield
1	KO <sup>t</sup> Bu	2.0	DMF	15%
2	K <sub>2</sub> CO <sub>3</sub>	2.0	DMF	0%
3	Cs <sub>2</sub> CO <sub>3</sub>	2.0	DMF	0%
4	KH	2.0	DMF	35%
5	KOH	2.0	DMF	40%
6	KHMDS	2.0	DMF	83%
7	KHMDS	2.0	DMSO	42%
8	KHMDS	1.5	DMF	80%
9	KHMDS	1.1	DMF	56%

### 3. Transparent Methods

#### 3.1 General Procedure for Preparations of Aryltrimethylammonium Salts.

**3.1.1 Preparations of ArNMe<sub>3</sub>OTf:** To a stirred solution of *N,N*-dimethylaniline (10 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added dropwise methyl trifluoromethanesulfonate (1.24 mL, 11.0 mmol, 1.1 equiv.) at 25 °C. The resulting solution was stirred for 4 h or 12 h at room temperature (r.t.). For some anilines bearing strong electron-withdrawing groups, the reactions may need heating up to 70 °C in MeCN in stead of CH<sub>2</sub>Cl<sub>2</sub>. Solvent was then removed in

vacuum and the residue was washed with Et<sub>2</sub>O, dried under vacuum to give a white solid. (Wang et al., 2016)

**3.1.2 Preparations of ArNMe<sub>3</sub>Cl:** To a stirred solution of aryl chloride (10 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added dropwise NMe<sub>3</sub> (2M in THF, 6 mL, 12.0 mmol, 1.2 equiv.; For **1s**, 0.7 equiv.) at 25°C. The resulting solution was stirred for 2 h at room temperature (r.t.). Solvent was then removed in vacuum and the residue was washed with Et<sub>2</sub>O, dried under vacuum to give a white solid.

### 3.2 General Procedure for the Reactions of Aryltrimethylammonium Salts with Thiols (Fig. S1)

A flask was charged with aryltrimethylammonium triflates (0.2 mmol), thiols (0.3 mmol), K<sub>2</sub>CO<sub>3</sub> (0.3 or 0.6 mmol) and DMF (3 mL). The reaction mixture was stirred at r.t. for 3 h to give a colorless or (pale) yellow suspended solution. Then water (30 mL) was added to remove DMF. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated. The residue was purified on column chromatography or preparative TLC (silica gel) or preparative HPLC (for **3ir**) to give the product and NMR yields with mesitylene as an internal standard.

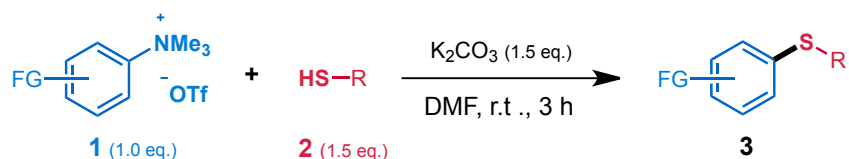
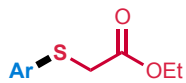


Fig.S1, related to Scheme 2a.



**3aa:** White solid, isolated yield 71%; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.15 (d, *J* = 8.9 Hz, 2H), 7.42 (d, *J* = 8.9 Hz, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.77 (s, 2H), 1.28 (d, *J* = 7.1 Hz, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 168.60, 145.73, 145.46, 126.89, 124.07, 62.14, 34.67, 14.10.; All spectral data match those previously reported. (Nagao et al., 2006)



**3ab:** Yellow solid, isolated yield 78%; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.13 (d, *J* = 9.0 Hz, 2H), 7.37 (d, *J* = 8.9 Hz, 2H), 3.14 (t, *J* = 6.0 Hz, 2H), 3.04 (t, *J* = 5.9 Hz, 2H), 1.52 (s, 2H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 146.94, 145.24, 126.63, 124.02, 40.68, 36.12. HRMS (EI) *m/z*: calcd for C<sub>8</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>S [M<sup>+</sup>] 198.0458, found 198.0462.



**3ac:** Yellow solid, isolated yield 90%; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.13 (d, *J* = 9.0 Hz, 2H), 7.40 (d, *J* = 9.0 Hz, 2H), 3.89 (t, *J* = 6.1 Hz, 2H), 3.25 (t, *J* = 6.1 Hz, 2H), 2.04 (s, 1H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 146.30, 145.41, 126.88, 124.04, 60.54, 35.12.; All spectral data match those previously reported. (Irie et al., 1980)



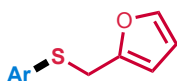
**3ad:** Colorless oil, isolated yield 80%; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.11 (d, *J* = 9.0 Hz, 2H), 7.32 (d, *J* = 9.0 Hz,



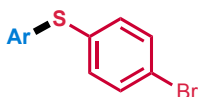
2H), 3.57 (s, 9H), 3.07 – 3.01 (m, 2H), 1.83 (dt,  $J = 15.2, 7.7$  Hz, 2H), 0.85 – 0.77 (m, 2H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  147.85, 144.92, 126.12, 123.94, 50.61, 34.47, 22.28, 8.69. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{12}\text{H}_{19}\text{NO}_5\text{SSi}$  [ $\text{M}^+$ ] 317.0748, found 317.0760.



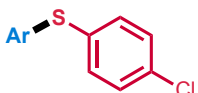
**3ae:** Yellow solid, isolated yield 75%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.11 (d,  $J = 9.1$  Hz, 2H), 7.34 (d,  $J = 9.1$  Hz, 2H), 5.89 (ddt,  $J = 16.7, 10.1, 6.5$  Hz, 1H), 5.26 (ddd,  $J = 13.5, 11.2, 1.1$  Hz, 2H), 3.68 (d,  $J = 6.5$  Hz, 2H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  146.83, 145.23, 131.96, 126.81, 123.86, 119.04, 35.21.; All spectral data match those previously reported. (Pace et al., 2012)



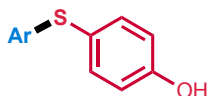
**3af:** Colorless oil, isolated yield 90%;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.12 (d,  $J = 9.0$  Hz, 2H), 7.39 (d,  $J = 9.1$  Hz, 2H), 7.36 (dd,  $J = 1.9, 0.8$  Hz, 1H), 6.31 (dd,  $J = 3.2, 1.9$  Hz, 1H), 6.24 (dd,  $J = 3.2, 0.8$  Hz, 1H), 4.24 (s, 2H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  149.04, 145.79, 145.11, 142.23, 126.83, 123.52, 110.29, 108.11, 29.18.



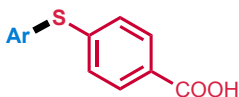
**3ag:** White solid, isolated yield 83%;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 (d,  $J = 9.0$  Hz, 2H), 7.57 (d,  $J = 8.5$  Hz, 2H), 7.39 (d,  $J = 8.5$  Hz, 2H), 7.19 (d,  $J = 9.0$  Hz, 2H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  146.86, 145.07, 135.43, 132.69, 129.31, 126.52, 123.63.; All spectral data match those previously reported. (Taniguchi et al., 2017)



**3ah:** White solid, isolated yield 80%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 (d,  $J = 9.1$  Hz, 2H), 7.45 (q,  $J = 8.6$  Hz, 4H), 7.21 – 7.15 (m, 2H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  147.59, 145.66, 136.08, 135.84, 130.29, 129.20, 127.00, 124.17.; All spectral data match those previously reported. (Taniguchi et al., 2017)

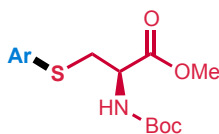


**3ai:** White solid, isolated yield 90%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.04 (d,  $J = 9.0$  Hz, 2H), 7.44 (d,  $J = 8.7$  Hz, 2H), 7.10 (d,  $J = 9.0$  Hz, 2H), 6.94 (d,  $J = 8.7$  Hz, 2H), 5.53 (s, 1H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  157.37, 150.07, 144.96, 137.38, 125.57, 123.96, 120.29, 117.19.; All spectral data match those previously reported. (Tian et al., 2014)

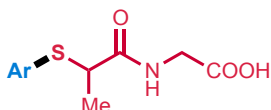


**3aj:** Yellow solid, isolated yield 88%;  $^1\text{H}$  NMR (300 MHz, DMSO)  $\delta$  8.19 (d,  $J = 9.0$  Hz, 2H), 8.00 (d,  $J = 8.2$  Hz, 2H), 7.61 (d,  $J = 8.3$  Hz, 2H), 7.47 (d,  $J = 9.0$  Hz, 2H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  166.58, 145.85, 144.77, 136.88, 132.45, 131.03, 130.71, 129.09, 124.48. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{13}\text{H}_8\text{NO}_4\text{S}$  [ $\text{M-H}$ ] $^-$  274.0180, found

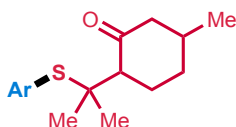
274.0182.



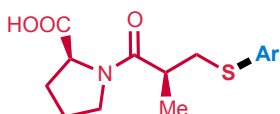
**3ak:** White solid, isolated yield 88%;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.12 (d,  $J = 8.8$  Hz, 2H), 7.43 (d,  $J = 8.8$  Hz, 2H), 5.34 (d,  $J = 6.7$  Hz, 1H), 4.65 (dd,  $J = 11.7, 4.9$  Hz, 1H), 3.70 (s, 3H), 3.57 (dd,  $J = 14.0, 4.8$  Hz, 1H), 3.44 (dd,  $J = 14.0, 4.8$  Hz, 1H), 1.41 (s, 9H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  170.52, 154.88, 145.61, 127.60, 123.97, 80.52, 53.16, 52.79, 35.01, 28.21. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_6\text{S}$  [ $\text{M}^+$ ] 356.1037, found 356.1043.



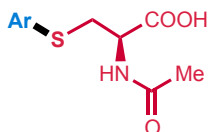
**3al:** White solid, isolated yield 83%;  $^1\text{H}$  NMR (300 MHz, DMSO)  $\delta$  12.61 (s, 1H), 8.61 (t,  $J = 5.8$  Hz, 1H), 8.13 (d,  $J = 9.1$  Hz, 2H), 7.55 (d,  $J = 9.1$  Hz, 2H), 4.29 (q,  $J = 7.0$  Hz, 1H), 3.79 (dd,  $J = 5.9, 2.2$  Hz, 2H), 1.46 (d,  $J = 7.0$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  171.44, 171.39, 146.23, 145.43, 128.20, 124.35, 44.28, 41.39, 18.53. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{11}\text{H}_{13}\text{N}_2\text{O}_5\text{S}$  [ $\text{M}+\text{H}]^+$  285.0540, found 285.0544.



**3am:** White solid, isolated yield 80%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.17 (d,  $J = 8.9$  Hz, 2H), 7.65 (d,  $J = 8.9$  Hz, 2H), 2.66 (d,  $J = 13.2$  Hz, 1H), 2.40 – 2.26 (m, 2H), 1.97 (d,  $J = 11.7$  Hz, 3H), 1.64 (dd,  $J = 13.1, 3.1$  Hz, 2H), 1.43 (d,  $J = 11.1$  Hz, 6H), 1.02 (d,  $J = 6.0$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  209.98, 148.02, 141.38, 137.50, 123.39, 57.98, 52.93, 52.26, 36.75, 34.54, 29.78, 28.20, 24.67, 22.19. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{16}\text{H}_{21}\text{NO}_3\text{S}$  [ $\text{M}^+$ ] 307.1237, found 307.1236.

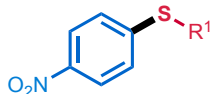


**3an:** Colorless oil, isolated yield 75%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.14 (d,  $J = 8.6$  Hz, 2H), 7.35 (d,  $J = 8.6$  Hz, 2H), 4.56 (d,  $J = 5.5$  Hz, 1H), 3.59 – 3.51 (m, 1H), 3.42 (dd,  $J = 12.6, 8.9$  Hz, 2H), 3.10 (dd,  $J = 13.0, 5.3$  Hz, 1H), 2.92 (dd,  $J = 14.5, 6.0$  Hz, 1H), 2.01 (s, 2H), 1.33 (d,  $J = 6.8$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  175.45, 172.92, 146.58, 145.38, 126.55, 124.10, 59.72, 47.66, 38.11, 35.16, 27.72, 24.80, 17.53. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{15}\text{H}_{19}\text{N}_2\text{O}_5\text{S}$  [ $\text{M}+\text{H}]^+$  339.1009, found 339.1007.

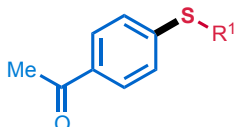


**3ao:** Colorless oil, isolated yield 85%;  $^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  12.99 (s, 1H), 8.42 (d,  $J = 8.0$  Hz, 1H), 8.14 (d,  $J = 9.1$  Hz, 2H), 7.54 (d,  $J = 9.1$  Hz, 2H), 4.47 (td,  $J = 8.4, 4.9$  Hz, 1H), 3.54 (dd,  $J = 13.6, 5.0$  Hz, 1H), 3.33 (d,  $J = 5.1$  Hz, 1H), 1.83 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  171.55, 169.52, 146.60, 144.68, 126.62, 123.95,

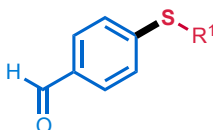
51.15, 32.73, 22.29. HRMS (ESI)  $m/z$ : calcd for  $C_{11}H_{11}N_2O_5S$   $[M-H]^-$  283.0394, found 283.0393.



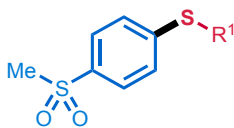
**3ap:** White solid, isolated yield 91%;  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  8.10 (d,  $J = 9.0$  Hz, 2H), 7.30 (d,  $J = 9.0$  Hz, 2H), 3.04 – 2.96 (m, 2H), 1.76 – 1.65 (m, 2H), 1.50 – 1.40 (m, 2H), 1.25 (s, 16H), 0.87 (t,  $J = 6.7$  Hz, 3H).  $^{13}C$  NMR (151 MHz,  $CDCl_3$ )  $\delta$  148.16, 144.72, 125.86, 123.84, 31.85, 29.57, 29.50, 29.41, 29.29, 29.06, 28.82, 28.41, 22.64, 14.07.; All spectral data match those previously reported. (Kondoh et al., 2006)



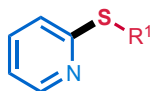
**3bp:** White solid, isolated yield 71%;  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  7.85 (d,  $J = 8.7$  Hz, 2H), 7.29 (d,  $J = 8.6$  Hz, 2H), 3.02 – 2.94 (m, 2H), 2.57 (s, 3H), 1.74 – 1.65 (m, 2H), 1.44 (s, 2H), 1.25 (s, 16H), 0.87 (t,  $J = 6.7$  Hz, 3H).  $^{13}C$  NMR (126 MHz,  $CDCl_3$ )  $\delta$  197.15, 145.03, 133.75, 128.74, 126.28, 32.01, 31.92, 29.63, 29.63, 29.57, 29.48, 29.34, 29.15, 28.90, 28.76, 26.41, 22.69, 14.11.; All spectral data match those previously reported. (Xu et al., 2013)



**3cp:** Colorless oil, isolated yield 92%;  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  9.91 (s, 1H), 7.75 (d,  $J = 8.6$  Hz, 2H), 7.34 (d,  $J = 8.3$  Hz, 2H), 3.03 – 2.96 (m, 2H), 1.70 (dd,  $J = 15.0, 7.6$  Hz, 2H), 1.52 – 1.41 (m, 2H), 1.25 (s, 16H), 0.87 (t,  $J = 6.6$  Hz, 3H).  $^{13}C$  NMR (126 MHz,  $CDCl_3$ )  $\delta$  191.18, 147.17, 133.13, 130.00, 126.31, 31.92, 31.84, 29.63, 29.63, 29.56, 29.48, 29.34, 29.14, 28.91, 28.66, 22.69, 14.12.; All spectral data match those previously reported. (Kondoh et al., 2006)

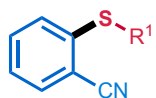


**3dp:** White solid, isolated yield 77%;  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  7.80 (d,  $J = 8.7$  Hz, 2H), 7.36 (d,  $J = 8.7$  Hz, 2H), 3.03 (s, 3H), 2.99 (t,  $J = 7.4$  Hz, 2H), 1.75 – 1.65 (m, 2H), 1.45 (s, 2H), 1.25 (s, 16H), 0.87 (t,  $J = 6.7$  Hz, 3H).  $^{13}C$  NMR (126 MHz,  $CDCl_3$ )  $\delta$  146.43, 136.45, 127.67, 126.66, 44.67, 31.96, 31.91, 29.62, 29.56, 29.47, 29.34, 29.13, 28.88, 28.58, 22.69, 14.11. HRMS (EI)  $m/z$ : calcd for  $C_{19}H_{23}O_2S_2$   $[M^+]$  356.1838, found 356.1834.

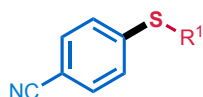


**3ep:** Colorless oil, isolated yield 61%;  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  8.42 (ddd,  $J = 5.0, 1.8, 0.9$  Hz, 1H), 7.46 (ddd,  $J = 8.1, 7.4, 1.9$  Hz, 1H), 7.16 (dt,  $J = 8.1, 1.0$  Hz, 1H), 6.95 (ddd,  $J = 7.3, 4.9, 1.1$  Hz, 1H), 3.21 – 3.09 (m, 2H), 1.69 (dd,  $J = 15.1, 7.5$  Hz, 2H), 1.48 – 1.40 (m, 2H), 1.25 (s, 16H), 0.88 (t,  $J = 6.6$  Hz, 3H).  $^{13}C$  NMR (151 MHz,  $CDCl_3$ )  $\delta$  159.65, 149.42, 135.75, 122.11, 119.12, 31.91, 30.14, 29.65, 29.62, 29.59, 29.51, 29.33, 29.31, 29.20,

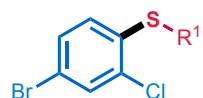
28.96, 22.68, 14.11.; All spectral data match those previously reported. (Kanemura et al., 2008)



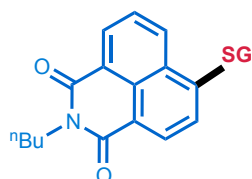
**3fp:** Colorless oil, isolated yield 88%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.60 (d,  $J = 7.7$  Hz, 1H), 7.49 (t,  $J = 7.7$  Hz, 1H), 7.39 (d,  $J = 8.0$  Hz, 1H), 7.24 (d,  $J = 9.3$  Hz, 1H), 3.00 (t,  $J = 7.4$  Hz, 2H), 1.74 – 1.59 (m, 2H), 1.44 (s, 2H), 1.25 (s, 16H), 0.87 (t,  $J = 6.5$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  142.31, 133.65, 132.73, 128.66, 125.69, 117.19, 113.38, 33.56, 31.92, 29.63, 29.62, 29.56, 29.46, 29.34, 29.12, 28.82, 28.77, 22.69, 14.12. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{19}\text{H}_{29}\text{NS}$  [ $\text{M}^+$ ] 303.2015, found 303.2022.



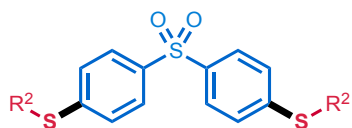
**3gp:** White solid, isolated yield 90%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.52 (d,  $J = 8.7$  Hz, 2H), 7.28 (d,  $J = 8.7$  Hz, 2H), 3.01 – 2.92 (m, 2H), 1.75 – 1.62 (m, 2H), 1.49 – 1.37 (m, 2H), 1.25 (s, 16H), 0.87 (t,  $J = 6.6$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  145.35, 132.19, 126.68, 118.97, 107.91, 31.92, 29.62, 29.55, 29.46, 29.34, 29.12, 28.87, 28.57, 22.69, 14.11.; All spectral data match those previously reported. (Kondoh et al., 2006)



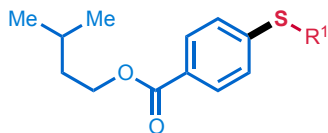
**3hp:** Colorless oil, isolated yield 46%;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.51 (d,  $J = 2.1$  Hz, 1H), 7.33 (dd,  $J = 8.5, 2.1$  Hz, 1H), 7.10 (d,  $J = 8.5$  Hz, 1H), 2.92 – 2.88 (m, 2H), 1.67 (dt,  $J = 15.0, 7.4$  Hz, 2H), 1.48 – 1.41 (m, 2H), 1.26 (s, 16H), 0.88 (t,  $J = 7.0$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  136.02, 133.94, 132.12, 130.14, 128.89, 118.54, 32.55, 31.92, 29.63, 29.56, 29.46, 29.34, 29.15, 28.91, 28.50, 22.69, 14.12.



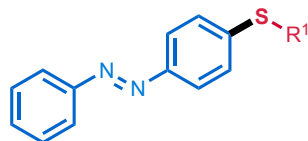
**3ir:** Yellow solid, isolated yield 70%;  $^1\text{H}$  NMR (500 MHz,  $\text{D}_2\text{O}$ )  $\delta$  7.88 – 7.78 (m, 2H), 7.67 (d,  $J = 7.7$  Hz, 1H), 7.29 (t,  $J = 7.3$  Hz, 1H), 7.19 (d,  $J = 7.6$  Hz, 1H), 4.74 – 4.69 (m, 1H), 3.83 – 3.74 (m, 3H), 3.71 – 3.64 (m, 2H), 3.59 (d,  $J = 9.5$  Hz, 1H), 3.35 (s, 1H), 2.54 – 2.43 (m, 2H), 2.10 – 2.01 (m, 2H), 1.57 (s, 2H), 1.43 (dd,  $J = 13.8, 6.7$  Hz, 2H), 1.02 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{D}_2\text{O}$ )  $\delta$  176.01, 175.56, 174.92, 170.97, 164.30, 164.17, 143.71, 131.29, 130.27, 129.95, 127.83, 126.50, 125.99, 123.38, 120.52, 117.24, 54.42, 52.36, 43.41, 40.44, 33.28, 31.63, 30.10, 29.47, 27.12, 19.91, 13.17. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{26}\text{H}_{31}\text{N}_4\text{O}_8\text{S}$  [ $\text{M}+\text{H}$ ] $^+$  559.1857, found 559.1848.



**3jq:** White solid, isolated yield 45%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.78 (d,  $J = 8.7$  Hz, 4H), 7.30 (d,  $J = 8.7$  Hz, 4H), 2.99 (q,  $J = 7.4$  Hz, 4H), 1.35 (t,  $J = 7.4$  Hz, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  145.33, 137.81, 127.84, 126.72, 26.05, 13.79. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{16}\text{H}_{18}\text{O}_2\text{S}_3$  [ $\text{M}^+$ ] 338.0463, found 338.0458.



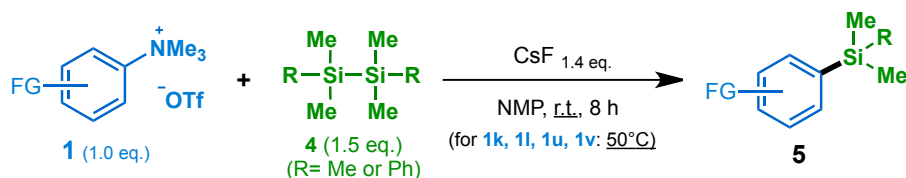
**3kp:** White solid, isolated yield 66%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.92 (d,  $J$  = 8.6 Hz, 2H), 7.27 (d,  $J$  = 8.4 Hz, 2H), 4.33 (t,  $J$  = 6.7 Hz, 2H), 3.01 – 2.92 (m, 2H), 1.79 (dt,  $J$  = 13.3, 6.7 Hz, 1H), 1.71 – 1.59 (m, 4H), 1.44 (s, 2H), 1.25 (s, 16H), 0.97 (d,  $J$  = 6.5 Hz, 6H), 0.88 (t,  $J$  = 6.7 Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.40, 144.29, 129.83, 126.90, 126.30, 63.52, 37.42, 32.10, 31.89, 29.61, 29.61, 29.55, 29.46, 29.32, 29.13, 28.88, 28.76, 25.21, 22.67, 22.51, 14.10. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{24}\text{H}_{40}\text{O}_2\text{S}$  [ $\text{M}^+$ ] 392.2744, found 392.2748.



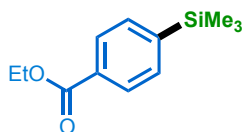
**3lp:** Yellow solid, isolated yield 85%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.94 – 7.81 (m, 4H), 7.56 – 7.44 (m, 3H), 7.39 (d,  $J$  = 8.6 Hz, 2H), 3.01 (t,  $J$  = 7.4 Hz, 2H), 1.70 (dd,  $J$  = 14.8, 7.5 Hz, 2H), 1.45 (d,  $J$  = 5.6 Hz, 2H), 1.27 (s, 16H), 0.89 (t,  $J$  = 6.5 Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  152.69, 150.18, 141.86, 130.76, 129.05, 127.56, 123.33, 122.73, 32.67, 31.90, 29.63, 29.62, 29.56, 29.48, 29.33, 29.15, 28.89, 22.68, 14.11. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{24}\text{H}_{34}\text{N}_2\text{S}$  [ $\text{M}^+$ ] 382.2437, found 382.2435.

### 3.3 General Procedure for the C-Si/Sn/Ge Bond-forming Reaction of Arylammonium Salts (Fig. S2, S3, S4)

A Schlenk tube was charged with aryltrimethylammonium triflate (0.2 mmol), Si/Sn/Ge reagents (0.3 mmol), CsF (0.28 mmol), and DMF (3 mL) under a argon atmosphere. The reaction mixture was stirred at r.t. or 50°C for 8 hours to give a colorless or (pale) yellow transparent solution (slightly suspended for some cases). Then water (30 mL) was added to remove DMF. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated. The residue was purified on column chromatography or preparative TLC (silica gel) to give the product and NMR yields with mesitylene as an internal standard.

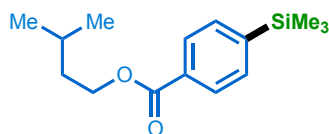


**Fig.S2**, related to **Scheme 2b**.

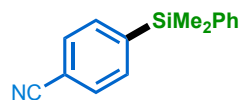


**5a:** Colorless oil, isolated yield 84%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.01 (d,  $J$  = 8.1 Hz, 2H), 7.60 (d,  $J$  = 8.1 Hz, 2H), 4.39 (q,  $J$  = 7.1 Hz, 2H), 1.40 (t,  $J$  = 7.1 Hz, 3H), 0.29 (s, 9H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  166.82, 146.70, 133.27, 130.67, 128.49, 60.91, 14.37, -1.29.; All spectral data match those previously reported. (Tobisu et al.,

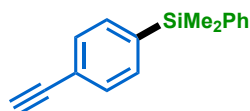
2008)



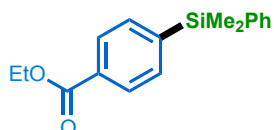
**5b:** Colorless oil, isolated yield 88%;  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.00 (d,  $J = 8.2$  Hz, 2H), 7.59 (d,  $J = 8.2$  Hz, 2H), 4.36 (t,  $J = 6.7$  Hz, 2H), 1.81 (dt,  $J = 13.6, 6.5$  Hz, 1H), 1.66 (q,  $J = 6.7$  Hz, 2H), 0.97 (d,  $J = 6.5$  Hz, 6H), 0.29 (s, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.87, 146.71, 133.27, 130.67, 128.47, 63.59, 37.44, 25.25, 22.54, -1.31.



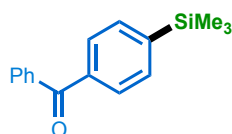
**5c:** Colorless oil, isolated yield 71%;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.61 (s, 4H), 7.50 (dd,  $J = 7.7, 1.7$  Hz, 2H), 7.43 – 7.35 (m, 3H), 0.58 (s, 6H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  145.41, 136.48, 134.62, 134.11, 131.04, 129.65, 128.09, 118.97, 112.71, -2.74. All spectral data match those previously reported. (Guo et al., 2015)



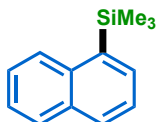
**5d:** Colorless oil, isolated yield 52%;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.50 (dd,  $J = 7.6, 1.8$  Hz, 2H), 7.47 (d,  $J = 1.5$  Hz, 4H), 7.39 – 7.34 (m, 3H), 3.09 (s, 1H), 0.55 (s, 6H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  139.55, 137.60, 134.12, 134.01, 131.25, 129.26, 127.88, 122.68, 83.70, 77.66, -2.56. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{16}\text{H}_{16}\text{Si}$  [ $\text{M}^+$ ] 236.1016, found 236.1009.



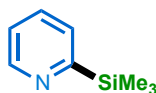
**5e:** Colorless oil, isolated yield 80%;  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.01 (d,  $J = 7.9$  Hz, 2H), 7.60 (d,  $J = 7.9$  Hz, 2H), 7.55 – 7.47 (m, 2H), 7.37 (d,  $J = 5.9$  Hz, 3H), 4.38 (d,  $J = 7.1$  Hz, 2H), 1.39 (t,  $J = 7.1$  Hz, 3H), 0.58 (s, 6H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.76, 144.51, 137.40, 134.15, 134.14, 130.96, 129.36, 128.53, 127.94, 60.95, 14.35, -2.55.; All spectral data match those previously reported. (Hamze et al., 2006)



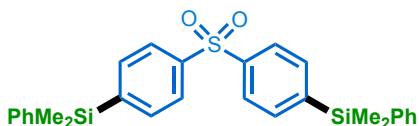
**5f:** Colorless oil, isolated yield 60%;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.81 (dd,  $J = 8.3, 1.3$  Hz, 2H), 7.76 (d,  $J = 8.2$  Hz, 2H), 7.64 (d,  $J = 8.2$  Hz, 2H), 7.59 (t,  $J = 7.4$  Hz, 1H), 7.48 (t,  $J = 7.6$  Hz, 2H), 0.32 (s, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  196.88, 146.29, 137.69, 137.63, 133.16, 132.38, 130.07, 129.00, 128.24, -1.30. All spectral data match those previously reported. (McNeill et al., 2007)



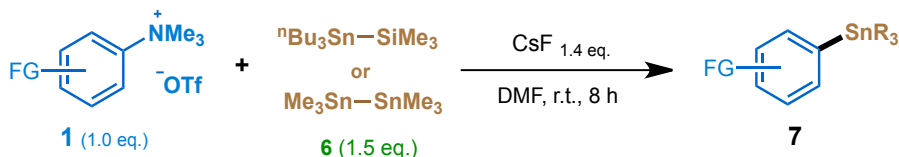
**5g:** Colorless oil, isolated yield 75%;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.16 (d,  $J = 8.0$  Hz, 1H), 7.90 (dd,  $J = 7.8, 5.9$  Hz, 2H), 7.75 (d,  $J = 6.8$  Hz, 1H), 7.52 (ddd,  $J = 21.9, 15.0, 6.7$  Hz, 3H), 0.53 (s, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  138.12, 136.89, 133.41, 133.15, 129.71, 129.11, 128.12, 125.56, 125.26, 125.08, 0.24.; All spectral data match those previously reported. (Tobisu et al., 2008)



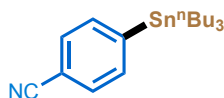
**5h:** Colorless oil, isolated yield 62%;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.77 (d,  $J = 4.5$  Hz, 1H), 7.58 (td,  $J = 7.6, 1.7$  Hz, 1H), 7.50 (d,  $J = 7.5$  Hz, 1H), 7.19 (ddd,  $J = 7.5, 4.9, 1.4$  Hz, 1H), 0.32 (s, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  167.89, 149.60, 133.63, 128.31, 122.28, -2.25. All spectral data match those previously reported. (Chau et al., 2008)



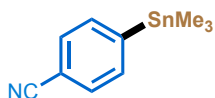
**5i:** Colorless oil, isolated yield 60%;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.88 (d,  $J = 8.3$  Hz, 4H), 7.62 (d,  $J = 8.3$  Hz, 4H), 7.48 (dd,  $J = 7.8, 1.6$  Hz, 4H), 7.41 – 7.33 (m, 6H), 0.55 (s, 12H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  145.70, 141.92, 136.51, 134.86, 134.06, 129.57, 128.02, 126.54, -2.73. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{28}\text{H}_{30}\text{O}_2\text{Si}_2\text{S}$  [ $\text{M}^+$ ] 486.1500, found 486.1503.



**Fig.S3**, related to **Scheme 2c**.

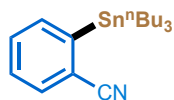


**7a:** Colorless oil, isolated yield 82%;  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.87 (d,  $J = 7.5$  Hz, 2H), 7.58 (d,  $J = 7.6$  Hz, 2H), 2.59 (s, 3H), 1.59 – 1.48 (m, 6H), 1.33 (dd,  $J = 14.6, 7.3$  Hz, 6H), 1.20 – 0.98 (m, 6H), 0.88 (t,  $J = 7.2$  Hz, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  198.66, 150.30, 136.64, 136.59, 127.10, 29.04, 27.33, 26.55, 13.66, 9.68.; All spectral data match those previously reported. (Komeyama et al., 2015)



**7b:** Colorless oil, isolated yield 85%;  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.66 – 7.50 (m, 4H), 0.33 (s, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  150.28, 136.31, 130.87, 119.13, 111.85, -9.49.; All spectral data match those previously

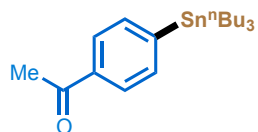
reported. (Chen et al., 2016)



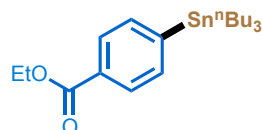
**7c:** Colorless oil, isolated yield 60%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.65 (d,  $J = 7.7$  Hz, 1H), 7.57 – 7.43 (m, 2H), 7.36 (td,  $J = 7.5, 1.5$  Hz, 1H), 1.63 – 1.48 (m, 6H), 1.41 – 1.26 (m, 6H), 1.26 – 1.17 (m, 6H), 0.89 (t,  $J = 7.3$  Hz, 9H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  148.37, 136.96, 132.89, 131.37, 128.27, 120.60, 120.28, 28.98, 27.23, 13.63, 10.05.; All spectral data match those previously reported. (Shirakawa et al., 2003)



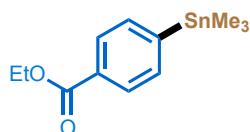
**7d:** Colorless oil, isolated yield 76%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.66 (ddd,  $J = 7.6, 1.3, 0.7$  Hz, 1H), 7.60 – 7.47 (m, 2H), 7.39 (td,  $J = 7.5, 1.6$  Hz, 1H), 0.44 (s, 9H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  148.03, 136.40, 132.79, 131.51, 128.59, 120.31, 120.03, -9.02.; All spectral data match those previously reported. (Chen et al., 2016)



**7e:** Colorless oil, isolated yield 60%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.56 (s, 4H), 1.51 (d,  $J = 7.7$  Hz, 6H), 1.32 (d,  $J = 7.2$  Hz, 6H), 1.19 – 0.99 (m, 6H), 0.88 (t,  $J = 7.2$  Hz, 9H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  150.37, 136.89, 130.73, 119.26, 111.57, 28.98, 27.30, 13.64, 9.75.; All spectral data match those previously reported. (Komeyama et al., 2015)

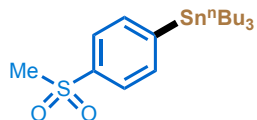


**7f:** Colorless oil, isolated yield 82%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 (d,  $J = 8.0$  Hz, 2H), 7.54 (d,  $J = 8.0$  Hz, 2H), 4.37 (q,  $J = 7.1$  Hz, 2H), 1.63 – 1.47 (m, 6H), 1.35 (dd,  $J = 16.0, 7.3$  Hz, 10H), 1.14 – 1.01 (m, 5H), 0.88 (s, 9H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  167.10, 149.49, 136.39, 129.93, 128.35, 60.83, 29.04, 27.33, 14.36, 13.66, 9.66.; All spectral data match those previously reported. (Reed et al., 2012)

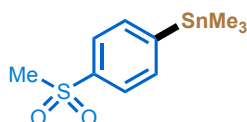


**7g:** Colorless oil, isolated yield 61%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.98 (d,  $J = 8.1$  Hz, 2H), 7.57 (d,  $J = 8.1$  Hz, 2H), 4.38 (q,  $J = 7.1$  Hz, 2H), 1.39 (t,  $J = 7.1$  Hz, 3H), 0.32 (s, 9H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.94, 149.44, 135.72, 130.16, 128.47, 60.85, 14.33, -9.55.; All spectral data match those previously reported. (Chen et al., 2016)

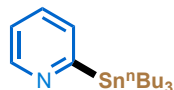




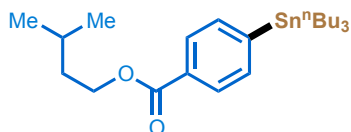
**7h:** Colorless oil, isolated yield 60%;  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.85 (d,  $J = 8.1$  Hz, 2H), 7.67 (d,  $J = 8.1$  Hz, 2H), 3.05 (s, 3H), 1.59 – 1.46 (m, 6H), 1.33 (dq,  $J = 14.2, 7.1$  Hz, 6H), 1.15 – 1.04 (m, 6H), 0.89 (t,  $J = 7.3$  Hz, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  151.36, 140.01, 137.16, 125.88, 44.50, 28.98, 27.30, 13.63, 9.79. All spectral data match those previously reported. (Tang et al., 2010)



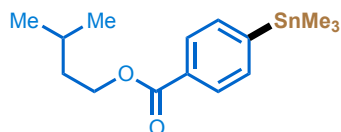
**7i:** Colorless oil, isolated yield 83%;  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.87 (d,  $J = 8.2$  Hz, 2H), 7.70 (d,  $J = 8.2$  Hz, 2H), 3.04 (s, 3H), 0.35 (s, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  151.29, 140.30, 136.60, 126.06, 44.53, -9.45. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{10}\text{H}_{16}\text{O}_2\text{SSn}$  [ $\text{M}^+$ ] 319.9888, found 319.9896.



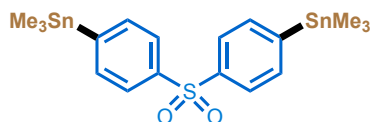
**7j:** Colorless oil, isolated yield 52%;  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.73 (ddd,  $J = 4.9, 1.6, 1.0$  Hz, 1H), 7.49 (td,  $J = 7.5, 1.8$  Hz, 1H), 7.40 (d,  $J = 7.4$  Hz, 1H), 7.11 (ddd,  $J = 7.6, 4.9, 1.4$  Hz, 1H), 1.59 – 1.52 (m, 6H), 1.33 (dq,  $J = 14.6, 7.3$  Hz, 6H), 1.14 – 1.10 (m, 6H), 0.88 (t,  $J = 7.3$  Hz, 9H).  $^{13}\text{C NMR}$  (151 MHz,  $\text{CDCl}_3$ )  $\delta$  174.09, 150.51, 133.24, 132.36, 121.97, 29.06, 27.33, 13.66, 9.76. All spectral data match those previously reported. (Fargeas et al., 2003)



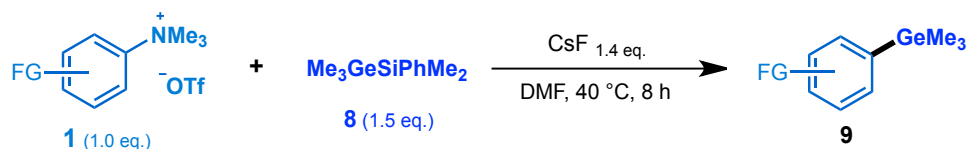
**7k:** Colorless oil, isolated yield 70%;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 (d,  $J = 8.1$  Hz, 2H), 7.55 (d,  $J = 8.1$  Hz, 2H), 4.34 (t,  $J = 6.7$  Hz, 2H), 1.85 – 1.75 (m, 1H), 1.66 (q,  $J = 6.8$  Hz, 2H), 1.52 (dd,  $J = 15.7, 8.1$  Hz, 5H), 1.37 – 1.28 (m, 7H), 1.14 – 1.02 (m, 6H), 0.97 (d,  $J = 6.6$  Hz, 6H), 0.88 (t,  $J = 7.3$  Hz, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  167.12, 149.47, 136.38, 129.93, 128.33, 63.49, 37.45, 29.04, 27.33, 25.22, 22.53, 13.66, 9.66. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{24}\text{H}_{42}\text{O}_2\text{Sn}$  [ $\text{M}^+$ ] 482.2201, found 482.2197.



**7l:** Colorless oil, isolated yield 76%;  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 (d,  $J = 8.1$  Hz, 2H), 7.57 (d,  $J = 8.1$  Hz, 2H), 4.35 (t,  $J = 6.7$  Hz, 2H), 1.79 (tt,  $J = 12.9, 6.4$  Hz, 1H), 1.66 (q,  $J = 6.7$  Hz, 2H), 0.97 (d,  $J = 6.5$  Hz, 6H), 0.31 (s, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  167.01, 149.46, 135.76, 130.22, 128.50, 63.57, 37.45, 25.26, 22.53, -9.55. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{15}\text{H}_{24}\text{O}_2\text{Sn}$  [ $\text{M}^+$ ] 356.0793, found 356.0793.



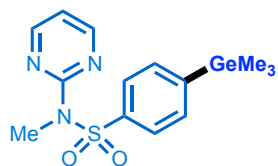
**7m**: Colorless oil, isolated yield 77%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.86 (d,  $J$  = 8.2 Hz, 4H), 7.62 (d,  $J$  = 8.2 Hz, 4H), 0.30 (s, 18H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  150.43, 141.45, 136.46, 126.33, -9.52. All spectral data match those previously reported. (Jeon et al., 2014)



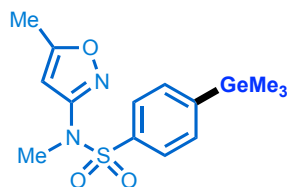
**Fig.S4**, related to **Scheme 2d**.

#### Procedure for the Preparation of $\text{Me}_3\text{GeSiPhMe}_2$ :

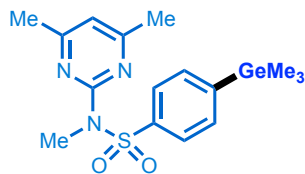
To a solution of naphthalene (0.4 mmol) in THF (16 mL), were added lithium clippings (24 mmol). The resulting mixture started turning dark green and was stirred at room temperature for 1 h under an argon atmosphere. Then chlorodimethylphenylsilane (4 mmol) was added dropwise and the mixture was stirred at room temperature for 3 h. The resulting solution was added into a stirred a solution of  $\text{Me}_3\text{GeCl}$  (4 mmol) in THF at  $0^\circ\text{C}$ . The reaction was stirred at room temperature for 8 h followed by extraction with hexane and  $\text{H}_2\text{O}$ . The organic phase was washed with brine and dried over  $\text{Na}_2\text{SO}_4$ . The residue was purified on column chromatography to give the product **8** as colorless oil: isolated yield 78%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.49 – 7.41 (m, 2H), 7.39 – 7.29 (m, 3H), 0.39 (s, 6H), 0.15 (s, 9H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  139.25, 133.64, 128.53, 127.78, -3.09, -3.39.



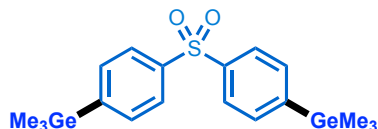
**9a**: Colorless oil, isolated yield 60%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.47 (d,  $J$  = 4.8 Hz, 2H), 8.02 (d,  $J$  = 8.3 Hz, 2H), 7.58 (d,  $J$  = 8.3 Hz, 2H), 6.88 (t,  $J$  = 4.8 Hz, 1H), 3.68 (s, 3H), 0.40 (s, 9H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  158.78, 157.46, 149.73, 140.12, 132.97, 127.28, 115.38, 34.23, -1.91. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{14}\text{H}_{19}\text{N}_3\text{O}_2\text{GeS}$  [ $\text{M}^+$ ] 367.0404, found 367.0404.



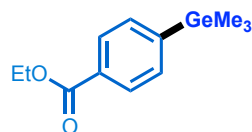
**9b**: Colorless oil, isolated yield 80%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.66 (d,  $J$  = 8.3 Hz, 2H), 7.58 (d,  $J$  = 8.3 Hz, 2H), 6.51 (s, 1H), 3.26 (s, 3H), 2.38 (s, 3H), 0.40 (s, 9H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  170.33, 160.86, 150.80, 136.55, 133.79, 126.05, 97.58, 35.12, 12.67, -1.96. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{13}\text{H}_{17}\text{O}_3\text{N}_2\text{GeS}$  [ $\text{M}-\text{CH}_3$ ] $^+$  355.0166, found 355.0136.



**9c:** Colorless oil, isolated yield 55%;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.04 (d,  $J = 8.3$  Hz, 2H), 7.56 (d,  $J = 8.3$  Hz, 2H), 6.57 (s, 1H), 3.66 (s, 3H), 2.31 (s, 6H), 0.39 (s, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  167.24, 158.20, 149.33, 140.59, 132.59, 127.74, 114.45, 33.85, 23.62, -1.89. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{16}\text{H}_{24}\text{N}_3\text{O}_2\text{SGe}$   $[\text{M}+\text{H}]^+$  396.0801, found 396.0811.



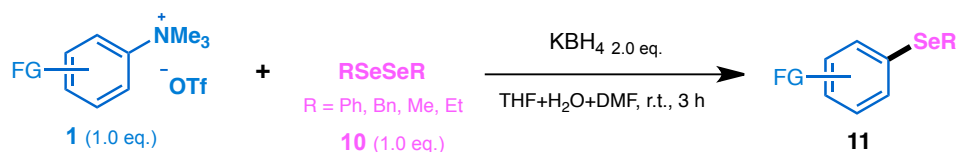
**9d:** Colorless oil, isolated yield 70%;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.88 (d,  $J = 8.2$  Hz, 4H), 7.59 (d,  $J = 8.2$  Hz, 4H), 0.38 (s, 18H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  150.14, 141.47, 133.76, 126.58, -1.95. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{17}\text{H}_{21}\text{O}_2\text{Ge}_2\text{S}$   $[\text{M}-\text{CH}_3]^+$  436.9680, found 436.9686.



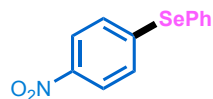
**9e:** Colorless oil, isolated yield 50%;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.99 (d,  $J = 8.0$  Hz, 2H), 7.55 (d,  $J = 8.0$  Hz, 2H), 4.37 (q,  $J = 7.1$  Hz, 2H), 1.39 (t,  $J = 7.1$  Hz, 3H), 0.40 (s, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.89, 149.20, 132.91, 130.25, 128.60, 60.87, 14.34, -1.90. All spectral data match those previously reported. (Komami et al., 2018)

### 3.4 General Procedure for the Selenation Reaction of Arylammonium Salts (Fig. S5)

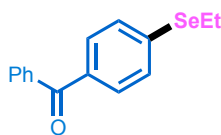
A flask was charged with  $\text{RSeSeR}$  (0.2 mmol) and 1 mL THF,  $\text{KBH}_4$  (0.4 mmol) in 1 mL  $\text{H}_2\text{O}$  was added. The reaction mixture was stirred at r.t. for 10 minutes and then aryltrimethylammonium triflates (0.2 mmol) in 1 mL DMF was added. After 3 h, the water (30 mL) was added to remove DMF. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated. The residue was purified on column chromatography or preparative TLC (silica gel) to give the product and NMR yields with mesitylene as an internal standard.



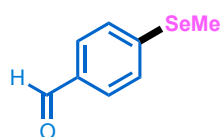
**Fig.S5**, related to **Scheme 2e**.



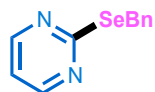
**11a:** Yellow oil, isolated yield 90%;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.03 (d,  $J = 9.0$  Hz, 2H), 7.64 (dd,  $J = 8.1, 1.4$  Hz, 2H), 7.42 (dt,  $J = 14.2, 7.0$  Hz, 3H), 7.36 (d,  $J = 9.0$  Hz, 2H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  146.22, 143.94, 135.89, 130.06, 129.74, 129.39, 127.24, 123.98.; All spectral data match those previously reported. (Maity et al., 2017)



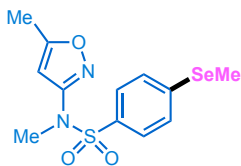
**11b:** Colorless oil, isolated yield 56%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.80 (d,  $J = 7.7$  Hz, 2H), 7.72 (d,  $J = 7.3$  Hz, 2H), 7.61 (t,  $J = 7.4$  Hz, 1H), 7.52 (dd,  $J = 15.6, 7.7$  Hz, 4H), 3.06 (q,  $J = 7.1$  Hz, 2H), 1.53 (t,  $J = 7.2$  Hz, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  196.08, 138.04, 137.64, 135.15, 132.32, 130.57, 130.16, 129.89, 128.28, 20.58, 15.19. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{15}\text{H}_{14}\text{OSe}$  [ $\text{M}^+$ ] 290.0204, found 290.0196.



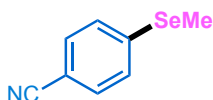
**11c:** Colorless oil, isolated yield 81%;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.93 (s, 1H), 7.73 (d,  $J = 8.3$  Hz, 2H), 7.49 (d,  $J = 8.3$  Hz, 2H), 2.42 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  191.45, 142.40, 133.95, 129.95, 128.85, 6.43.; All spectral data match those previously reported. (Sugiura et al., 1990)



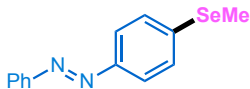
**11d:** Colorless oil, isolated yield 85%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.54 (d,  $J = 4.8$  Hz, 2H), 7.45 (d,  $J = 7.5$  Hz, 2H), 7.31 (dd,  $J = 12.6, 5.7$  Hz, 2H), 7.27 – 7.21 (m, 1H), 7.03 (t,  $J = 4.2$  Hz, 1H), 4.49 (s, 2H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  170.72, 157.24, 138.58, 129.06, 128.48, 126.93, 117.27, 30.32.; All spectral data match those previously reported. (Ma et al., 2017)



**11f:** Colorless oil, isolated yield 65%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.56 (d,  $J = 8.5$  Hz, 2H), 7.43 (d,  $J = 8.5$  Hz, 2H), 6.48 (s, 1H), 3.25 (s, 3H), 2.38 (d,  $J = 2.0$  Hz, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  170.39, 160.79, 141.28, 133.69, 129.11, 127.39, 97.60, 35.15, 12.68, 6.54. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{15}\text{H}_{19}\text{N}_2\text{O}_5\text{S}$  [ $\text{M}+\text{H}$ ] $^+$  339.1009, found 339.1007. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{12}\text{H}_{15}\text{N}_2\text{O}_3\text{SSe}$  [ $\text{M}+\text{H}$ ] $^+$  346.9969, found 346.9973.



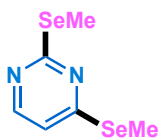
**11g:** Colorless oil, isolated yield 41%;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.49 (d,  $J = 8.5$  Hz, 2H), 7.43 (d,  $J = 8.5$  Hz, 2H), 2.40 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  140.28, 132.17, 129.19, 118.90, 108.98, 6.58. All spectral data match those previously reported. (Lewis et al., 1987)



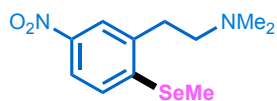
**11h:** Yellow solid, isolated yield 45%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.91 (d,  $J$  = 7.2 Hz, 2H), 7.83 (d,  $J$  = 8.4 Hz, 2H), 7.56 – 7.45 (m, 5H), 2.43 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  152.23, 150.35, 136.38, 130.44, 129.29, 128.65, 122.92, 122.34, 6.46. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{13}\text{H}_{13}\text{N}_2\text{Se}$   $[\text{M}+\text{H}]^+$  277.0244, found 277.0249.



**11i:** White solid, isolated yield 80%;  $^1\text{H}$  NMR (400 MHz, DMSO)  $\delta$  13.75 (s, 1H), 8.52 (s, 1H), 2.55 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  174.33, 152.18, 144.70, 129.62, 123.99. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{15}\text{H}_{19}\text{N}_2\text{O}_5\text{S}$   $[\text{M}+\text{H}]^+$  339.1009, found 339.1007. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_6\text{H}_6\text{ClN}_4\text{Se}$   $[\text{M}+\text{H}]^+$  248.9446, found 248.9451.



**11j:** Colorless oil, isolated yield 84%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.00 (d,  $J$  = 5.3 Hz, 1H), 6.97 (d,  $J$  = 5.3 Hz, 1H), 2.45 (d,  $J$  = 1.9 Hz, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  169.84, 168.20, 154.00, 117.84, 6.79, 5.27. All spectral data match those previously reported. (Dhau et al., 2014)



**11k:** Yellow oil, isolated yield 92%;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.03 – 7.94 (m, 2H), 7.35 (d,  $J$  = 8.6 Hz, 1H), 2.93 – 2.87 (m, 2H), 2.62 – 2.57 (m, 2H), 2.41 (s, 3H), 2.32 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  145.83, 143.75, 140.41, 127.48, 123.43, 121.60, 58.82, 45.37, 33.25, 6.74. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{11}\text{H}_{17}\text{N}_2\text{O}_2\text{Se}$   $[\text{M}+\text{H}]^+$  289.0455, found 289.0448.

### 3.5 General Procedure for the Amination Reaction of Arylammonium Salts (Fig. S6)

A Schlenk tube was charged with  $\text{ArNH}_2$  (0.3 mmol), KHMDS (0.28 mL, 1M in THF) and DMF (3mL). The reaction mixture was stirred at r.t. for 5 minutes and then aryltrimethylammonium triflates (0.2 mmol) was added. After 3 h, the water (30 mL) was added to remove DMF. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated. The residue was purified on column chromatography or preparative TLC (silica gel) to give the product and NMR yields with mesitylene as an internal standard.

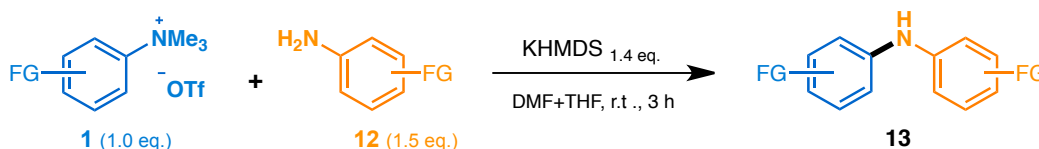
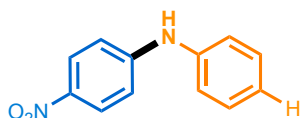
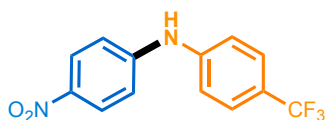


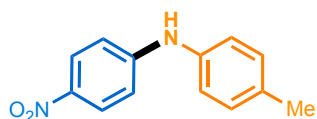
Fig.S6, related to Scheme 2f.



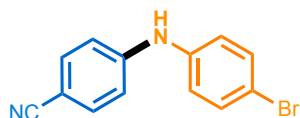
**13a:** Yellow oil, isolated yield 75%;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.12 (d,  $J = 9.2$  Hz, 2H), 7.39 (dd,  $J = 8.4, 7.5$  Hz, 2H), 7.23 – 7.19 (m, 2H), 7.17 (t,  $J = 7.4$  Hz, 1H), 6.94 (d,  $J = 9.2$  Hz, 2H), 6.31 (s, 1H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  150.16, 139.77, 139.48, 129.72, 126.22, 124.65, 121.91, 113.67.; All spectral data match those previously reported. (Ding et al., 2017)



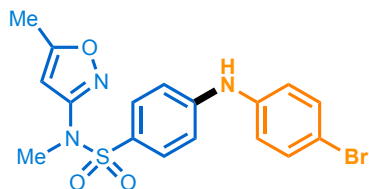
**13b:** Yellow oil, isolated yield 78%;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.17 (d,  $J = 9.1$  Hz, 2H), 7.62 (d,  $J = 8.4$  Hz, 2H), 7.27 (d,  $J = 8.4$  Hz, 2H), 7.09 (d,  $J = 9.2$  Hz, 2H), 6.47 (s, 1H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  148.29, 143.18, 141.02, 127.01 (q,  $^3J_{\text{C-F}} = 3.7$  Hz), 126.13, 125.40 (q,  $^2J_{\text{C-F}} = 33.0$  Hz), 124.05 (q,  $^1J_{\text{C-F}} = 271.4$  Hz), 119.59, 115.31. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{13}\text{H}_9\text{N}_2\text{O}_2\text{F}_3$  [ $\text{M}^+$ ] 282.0611, found 282.0606.



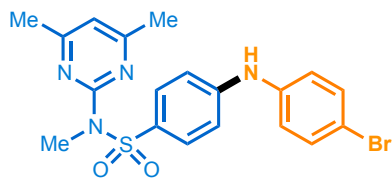
**13c:** White solid, isolated yield 40%;  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.10 (d,  $J = 9.1$  Hz, 2H), 7.20 (d,  $J = 8.1$  Hz, 2H), 7.11 (d,  $J = 8.3$  Hz, 2H), 6.86 (d,  $J = 9.2$  Hz, 2H), 6.22 (s, 1H), 2.36 (s, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  150.83, 139.48, 136.73, 134.86, 130.31, 126.28, 122.71, 113.22, 20.93.; All spectral data match those previously reported. (Fors et al., 2009)



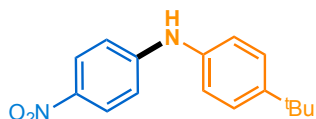
**13d:** Colorless oil, isolated yield 70%;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.49 (d,  $J = 8.8$  Hz, 2H), 7.45 (d,  $J = 8.8$  Hz, 2H), 7.05 (d,  $J = 8.8$  Hz, 2H), 6.96 (d,  $J = 8.8$  Hz, 2H), 6.07 (s, 1H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  147.42, 139.25, 133.85, 132.66, 122.56, 119.65, 116.29, 115.28, 102.28. All spectral data match those previously reported. (Miti et al., 2011)



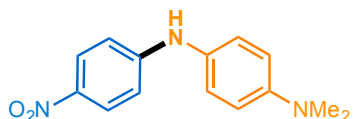
**13e:** Colorless oil, isolated yield 80%;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.55 (d,  $J = 8.8$  Hz, 2H), 7.44 (d,  $J = 8.7$  Hz, 2H), 7.03 (d,  $J = 8.7$  Hz, 2H), 6.93 (d,  $J = 8.9$  Hz, 2H), 6.49 (d,  $J = 0.7$  Hz, 1H), 6.11 (s, 1H), 3.24 (s, 3H), 2.37 (d,  $J = 0.5$  Hz, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  170.21, 161.05, 148.39, 139.14, 132.65, 129.33, 126.67, 122.81, 116.47, 114.78, 97.69, 35.02, 12.67. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{17}\text{H}_{17}\text{N}_3\text{O}_3\text{SBr}$  [ $\text{M}+\text{H}$ ] $^+$  422.0169, found 422.0177.



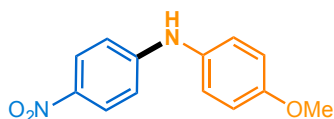
**13f:** Colorless oil, isolated yield 55%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 (d,  $J$  = 8.9 Hz, 2H), 7.42 (d,  $J$  = 8.8 Hz, 2H), 7.04 – 6.99 (m, 2H), 6.95 (d,  $J$  = 8.9 Hz, 2H), 6.57 (s, 1H), 6.07 (s, 1H), 3.64 (s, 3H), 2.32 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  167.17, 158.31, 147.32, 139.71, 132.55, 131.06, 130.92, 122.10, 115.71, 114.26, 114.10, 33.82, 23.69. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{19}\text{H}_{20}\text{N}_4\text{O}_2\text{BrS}$   $[\text{M}+\text{H}]^+$  447.0485, found 447.0482.



**13g:** Yellow oil, isolated yield 45%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.10 (d,  $J$  = 9.2 Hz, 2H), 7.41 (d,  $J$  = 8.5 Hz, 2H), 7.15 (d,  $J$  = 8.5 Hz, 2H), 6.90 (d,  $J$  = 9.2 Hz, 2H), 6.27 (s, 1H), 1.34 (s, 9H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  150.63, 148.00, 139.45, 136.67, 126.56, 126.24, 122.03, 113.30, 34.48, 31.34. All spectral data match those previously reported. (Kayama et al., 2016)



**13h:** Yellow solid, isolated yield 62%;  $^1\text{H}$  NMR (400 MHz, DMSO)  $\delta$  9.02 (s, 1H), 8.02 (d,  $J$  = 9.2 Hz, 2H), 7.08 (d,  $J$  = 8.6 Hz, 2H), 6.79 (dd,  $J$  = 15.7, 7.7 Hz, 4H), 2.89 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  152.74, 147.92, 136.62, 128.58, 126.35, 124.22, 113.30, 111.94, 40.41. All spectral data match those previously reported. (Novak et al., 1989)

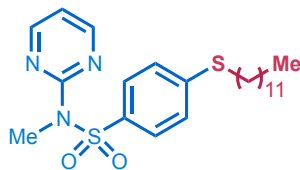


**13i:** Yellow solid, isolated yield 55%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 (d,  $J$  = 9.2 Hz, 2H), 7.16 (d,  $J$  = 8.8 Hz, 2H), 6.93 (d,  $J$  = 8.9 Hz, 2H), 6.76 (d,  $J$  = 9.2 Hz, 2H), 6.18 (s, 1H), 3.83 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  157.43, 151.69, 139.09, 131.97, 126.30, 125.49, 114.95, 112.60, 55.53. All spectral data match those previously reported. (McNulty et al., 2007)

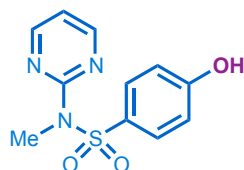
### 3.6 Procedure for the Late-stage Diversification of Pharmaceutical Ammonium Derivative (Fig. 4)

Various aryl-heteroatom bonds formation products **3mp**, **5j**, **7o**, **9a**, **11h**, **13h** were prepared following a similar procedure above. **14b**, **14c**, **14d** were prepared with previously reported methods. (Lang et al., 2009)

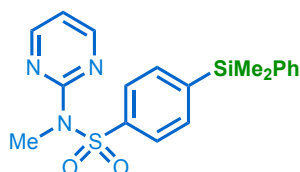
**Procedure for the Preparation of 14a:** A flask was charged with aryltrimethylammonium triflates (0.2 mmol), 2-mercaptoethanol (0.3 mmol), KHMDs (0.6 mmol, 2M in THF) and DMF (3 mL). The reaction mixture was stirred at r.t. for 3 h to give a yellow suspended solution. Then 1M HCl (30 mL) was added and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated. The residue was purified on column chromatography to give the product and NMR yields with mesitylene as an internal standard.



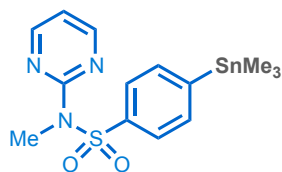
**3mp:** Colorless oil, isolated yield 73%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.46 (d,  $J$  = 4.8 Hz, 2H), 7.94 (d,  $J$  = 8.5 Hz, 2H), 7.28 (d,  $J$  = 8.8 Hz, 2H), 6.88 (t,  $J$  = 4.8 Hz, 1H), 3.67 (s, 3H), 2.96 (t,  $J$  = 7.4 Hz, 2H), 1.68 (dt,  $J$  = 14.8, 7.2 Hz, 2H), 1.48 – 1.36 (m, 2H), 1.25 (s, 16H), 0.87 (t,  $J$  = 6.5 Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  158.71, 157.44, 145.16, 136.23, 128.77, 125.87, 115.37, 34.15, 32.01, 31.91, 29.62, 29.56, 29.47, 29.33, 29.13, 28.89, 28.63, 22.69, 14.11. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{23}\text{H}_{36}\text{N}_3\text{O}_2\text{S}_2$  [ $\text{M}^+$ ] 450.2243, found 450.2268.



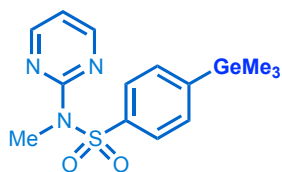
**14a:** Colorless oil, isolated yield 78%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.45 (d,  $J$  = 4.8 Hz, 2H), 7.97 – 7.90 (m, 2H), 6.90 – 6.83 (m, 3H), 3.65 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  160.23, 158.69, 157.48, 131.33, 130.86, 115.39, 115.25, 34.20. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{11}\text{H}_{12}\text{N}_3\text{O}_3\text{S}$  [ $\text{M}+\text{H}$ ] $^+$  266.0594, found 266.0594.



**5j:** Colorless oil, isolated yield 75%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.46 (d,  $J$  = 4.8 Hz, 2H), 8.02 (d,  $J$  = 8.3 Hz, 2H), 7.62 (d,  $J$  = 8.3 Hz, 2H), 7.52 – 7.44 (m, 2H), 7.40 – 7.32 (m, 3H), 6.88 (t,  $J$  = 4.8 Hz, 1H), 3.68 (s, 3H), 0.57 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  158.76, 157.47, 145.15, 140.86, 136.78, 134.14, 129.53, 128.01, 127.19, 115.44, 34.25, -2.63. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{19}\text{H}_{22}\text{N}_3\text{O}_2\text{SSi}$  [ $\text{M}^+$ ] 384.1197, found 384.1195.

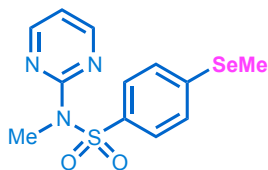


**7o:** Colorless oil, isolated yield 43%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.46 (d,  $J$  = 4.8 Hz, 2H), 7.99 (d,  $J$  = 7.4 Hz, 2H), 7.60 (d,  $J$  = 7.4 Hz, 2H), 6.87 (t,  $J$  = 4.8 Hz, 1H), 3.68 (s, 3H), 0.31 (s, 9H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  158.77, 157.46, 150.06, 140.10, 135.72, 127.10, 115.39, 34.23, -9.46. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{14}\text{H}_{20}\text{O}_2\text{N}_3\text{SnS}$  [ $\text{M}^+$ ] 414.0293, found 414.0300.

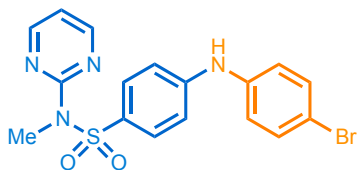




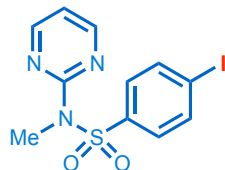
**9a:** Colorless oil, isolated yield 60%;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.47 (d,  $J = 4.8$  Hz, 2H), 8.02 (d,  $J = 8.3$  Hz, 2H), 7.58 (d,  $J = 8.3$  Hz, 2H), 6.88 (t,  $J = 4.8$  Hz, 1H), 3.68 (s, 3H), 0.40 (s, 9H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  158.78, 157.46, 149.73, 140.12, 132.97, 127.28, 115.38, 34.23, -1.91. HRMS (EI)  $m/z$ : calcd for  $\text{C}_{14}\text{H}_{19}\text{N}_3\text{O}_2\text{GeS}$   $[\text{M}^+]$  367.0404, found 367.0404.



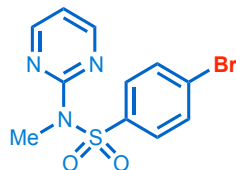
**11h:** Colorless oil, isolated yield 43%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.45 (d,  $J = 4.8$  Hz, 2H), 7.92 (d,  $J = 8.4$  Hz, 2H), 7.42 (d,  $J = 8.5$  Hz, 2H), 6.88 (t,  $J = 4.8$  Hz, 1H), 3.67 (s, 3H), 2.38 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  158.67, 157.46, 140.03, 137.37, 128.73, 128.39, 115.43, 34.16, 6.54. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{12}\text{H}_{14}\text{N}_3\text{O}_2\text{SSe}$   $[\text{M}+\text{H}]^+$  343.9972, found 343.9994.



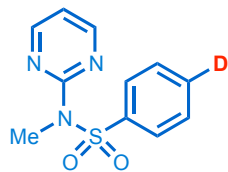
**13h:** Colorless oil, isolated yield 63%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.46 (d,  $J = 4.8$  Hz, 2H), 7.92 (d,  $J = 8.9$  Hz, 2H), 7.43 (d,  $J = 8.8$  Hz, 2H), 7.03 (d,  $J = 8.7$  Hz, 2H), 6.95 (d,  $J = 8.9$  Hz, 2H), 6.87 (t,  $J = 4.8$  Hz, 1H), 3.65 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  158.85, 157.42, 147.64, 139.53, 132.57, 130.66, 130.33, 122.34, 115.95, 115.19, 114.27, 34.16. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{17}\text{H}_{16}\text{N}_4\text{O}_2\text{SBr}$   $[\text{M}+\text{H}]^+$  419.0172, found 419.0169.



**14b:** Colorless oil, isolated yield 84%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.46 (d,  $J = 4.8$  Hz, 2H), 7.84 (d,  $J = 8.8$  Hz, 2H), 7.79 (d,  $J = 8.8$  Hz, 2H), 6.90 (s, 1H), 3.67 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  158.51, 157.48, 140.12, 137.68, 129.81, 115.62, 100.38, 34.15. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{11}\text{H}_{11}\text{N}_3\text{O}_2\text{SI}$   $[\text{M}+\text{H}]^+$  375.9611, found 375.9618.



**14c:** Colorless oil, isolated yield 80%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.46 (d,  $J = 4.8$  Hz, 2H), 7.94 (d,  $J = 8.7$  Hz, 2H), 7.62 (d,  $J = 8.8$  Hz, 2H), 6.90 (t,  $J = 4.8$  Hz, 1H), 3.67 (s, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  158.50, 157.53, 139.38, 131.74, 130.01, 127.94, 115.69, 34.20. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{11}\text{H}_{11}\text{N}_3\text{O}_2\text{SBr}$   $[\text{M}+\text{H}]^+$  327.9750, found 327.9751.



**14d**: Colorless oil, isolated yield 87%;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.45 (d,  $J = 4.8$  Hz, 2H), 8.07 (d,  $J = 8.5$  Hz, 2H), 7.48 (d,  $J = 8.3$  Hz, 2H), 6.87 (t,  $J = 4.8$  Hz, 1H), 3.69 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  158.71, 157.45, 140.43, 128.45, 128.34, 128.32, 115.44, 34.19. HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{11}\text{H}_{11}\text{N}_3\text{O}_2\text{SD}$   $[\text{M}+\text{H}]^+$  251.0708, found 251.0712.

### 3.7 Procedure for Click Reaction of NBD-ammonium Salt and Biological Thiols (Fig. 5)

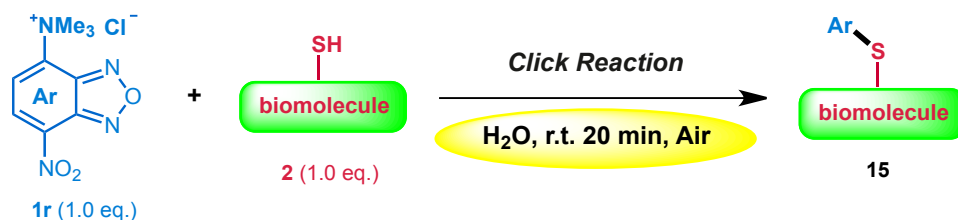
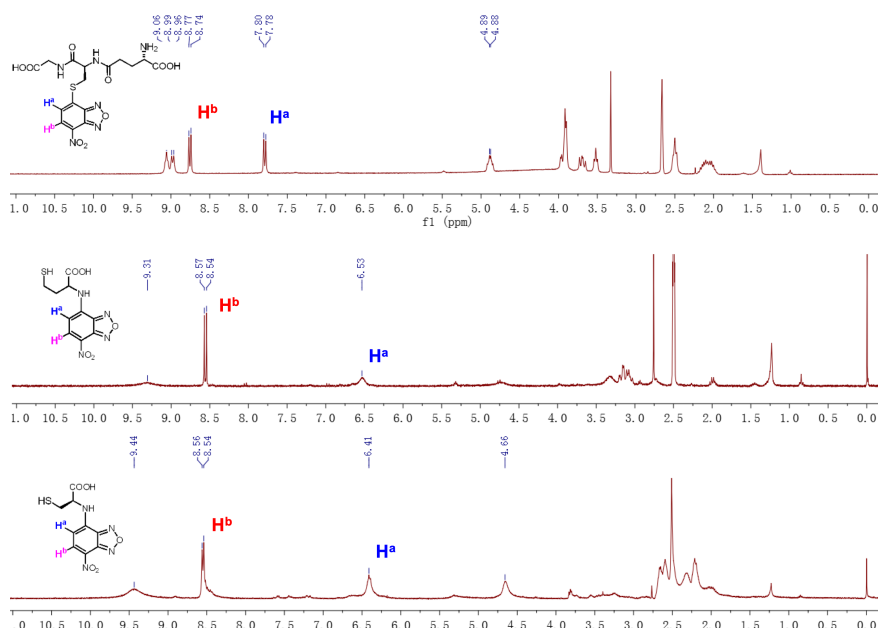


Fig.S7, related to Scheme 4a.

**3.7.1** An open-air vial was charged with NBD-ammonium salt **1r** (0.01 mmol; for **15d**: 0.005mmol), biological thiols (0.01 mmol; for **15d**: 0.005mmol) and  $\text{H}_2\text{O}$  (1 mL). The reaction mixture was stirred at r.t. for 20 minutes and then determined by LCMS.

**3.7.2** An open-air vial was charged with NBD-ammonium salt **1r** (0.05 mmol), biological thiols (**2r**, **2v**, **2w**) (0.05 mmol) and  $\text{D}_2\text{O}$  (0.5 mL). The reaction mixture was stirred at r.t. for 20 minutes and then was analyzed by  $^1\text{H}$ -NMR in  $\text{DMSO-d}_6$ - $\text{D}_2\text{O}$  (4:1, v/v). When Cys or Hcy was the reactant, the  $\text{H}^a$  and  $\text{H}^b$  protons of the product NBD moiety showed upfield shifts, especially for  $\text{H}^a$ , which were different from NBD-SR (GSH as reactant) was being formed. (Chen et al., 2016) (**Fig. S8**)



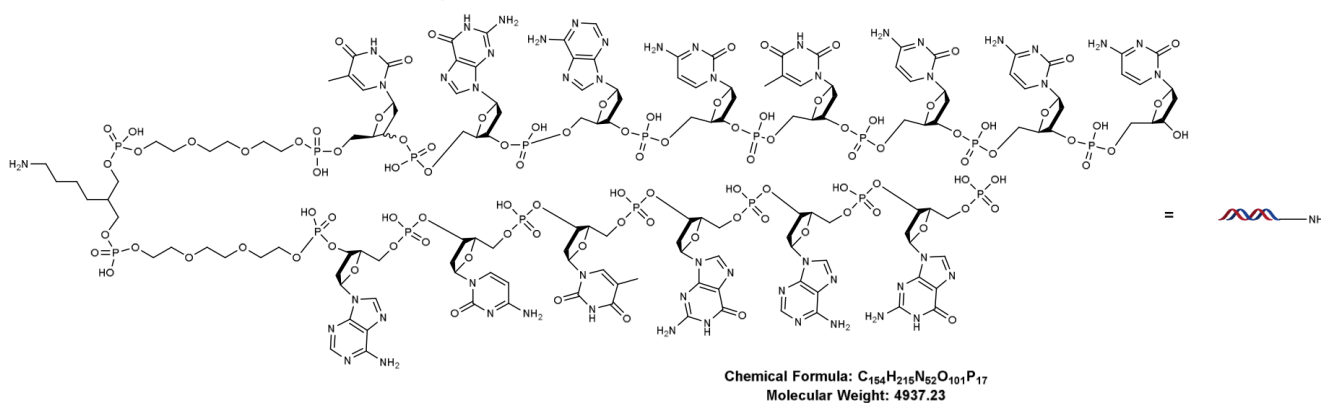
**Fig.S8**, related to **Scheme 4a**.

**3.7.3** For the procedure of fluorescence measurement: stock solutions of probe (**1r**) and biological thiols were freshly prepared in H<sub>2</sub>O prior to each experiment. 5eq. biological thiols (250μM) were added to separate portions of the probe (50μM) solution and mixed thoroughly. The reaction mixture was shaken uniformly before absorption and fluorescence spectra were measured.

### 3.8 Procedure for on-DNA Reactions

#### 3.8.1 Headpiece Structure (Fig. S9)

DNA headpiece HP-NH<sub>2</sub> (5'-/5phos/GAGTCA/iSp9/iUniAmM/iSp9/TGACTCCC-3', Figure 1) was obtained from Biosearch Technologies, Novato, CA.



**Fig.S9**, related to **Scheme 5**.

#### 3.8.2 Preparation of HP-Ar-N<sup>+</sup>Me<sub>3</sub>Cl<sup>-</sup>

##### Materials

Headpiece: 2 mM in water

B: 200 mM in water

K<sub>2</sub>CO<sub>3</sub>: 200 mM in water

##### Procedure

- 1) To the headpiece in H<sub>2</sub>O (100 nmol, 50 μL), was added 100 eq. of K<sub>2</sub>CO<sub>3</sub> (in 50 μL H<sub>2</sub>O) and 60 eq. of ammonium salt **1s** (in 30 μL H<sub>2</sub>O). The mixture was vortexed.
- 2) React at room temperature for 10 h.
- 3) Add 5 M NaCl solution (10 % by volume) and cold ethanol (2.5 times by volume, ethanol stored at -20°C). The mixture was stored at a -80°C freezer for more than 30 minutes.
- 4) Centrifuge the sample for around 30 minutes at 4°C in a microcentrifuge at 10000 rpm. The above supernatant was removed and the pellet (precipitate) was cooled in liquid nitrogen and then placed on a lyophilizer. After lyophilization, the dry pellet was recovered.
- 5) To gain a higher yield, the dry pellet was solute in water (50 μL), then repeat step1-4.

Molecular Weight: 5151.65

68% conversion determined by LCMS.

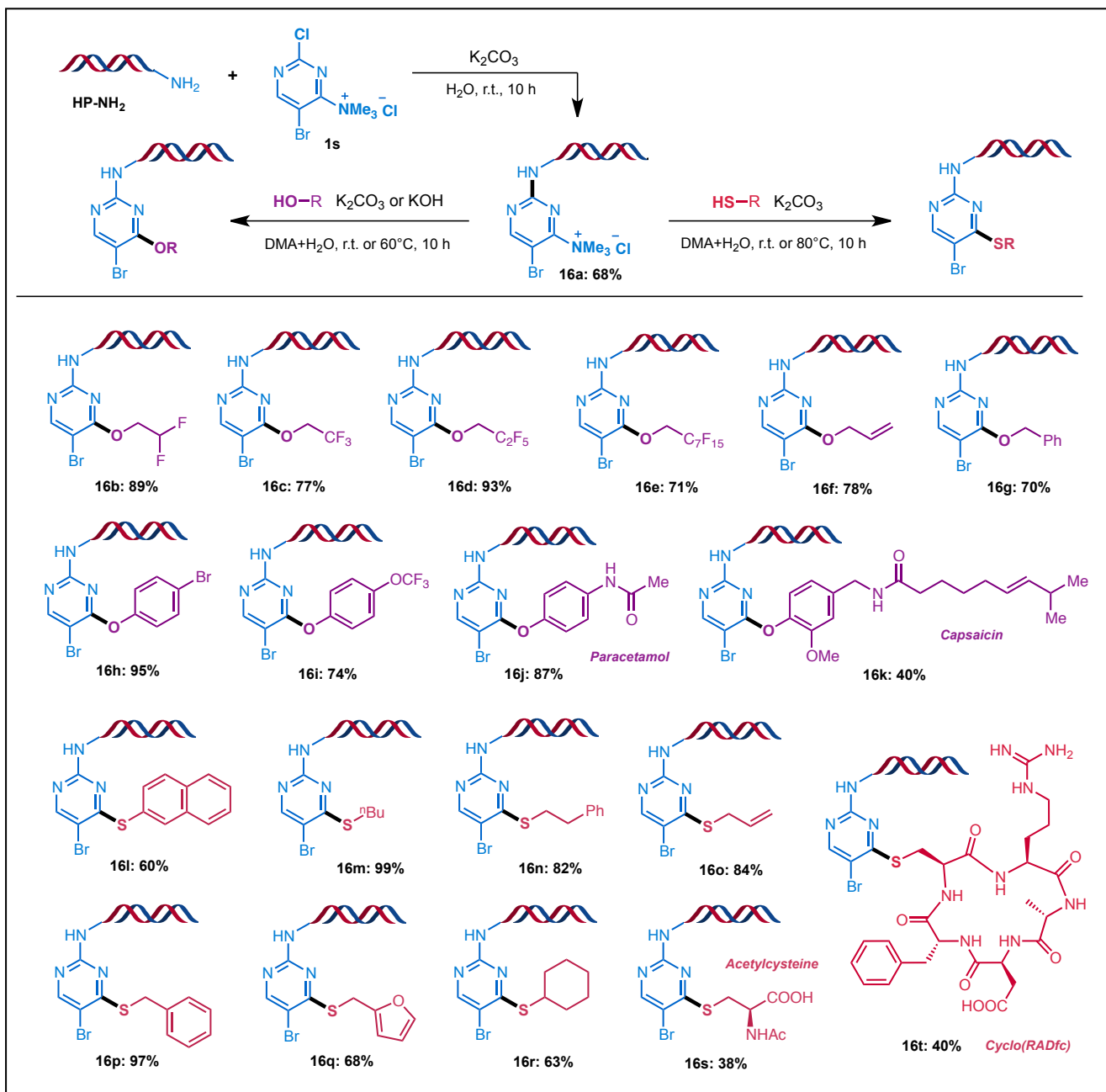


Fig.S10, related to Scheme 5.

### 3.8.3 C–O bond formations of arylammonium salts on DNA

#### Materials

**16a:** 1 mM in water

ROH: 200 mM in DMA

$\text{K}_2\text{CO}_3$  (or KOH): 1M in water

#### Procedure

1) To **16a** solution (5 nmol, 5  $\mu\text{L}$ ), was added 35 $\mu\text{L}$   $\text{H}_2\text{O}$ , 1000 eq. of ROH (25  $\mu\text{L}$ ) and 1000 eq. of  $\text{K}_2\text{CO}_3$  (for

**16c–f, 16i–k**) or KOH (for **16b, 16g–h**) (5  $\mu$ L). The mixture was vortexed.

2) React at room temperature (or 60°C for **16h–k**) for 10 h.

3) Add 5 M NaCl solution (10 % by volume) and cold ethanol (2.5 times by volume, ethanol stored at -20°C). The mixture was stored at a -80°C freezer for more than 30 minutes.

4) Centrifuge the sample for around 30 minutes at 4 °C in a microcentrifuge at 10000 rpm. The above supernatant was removed and the pellet (precipitate) was cooled in liquid nitrogen and then placed on a lyophilizer. After lyophilization, the dry pellet was recovered.

Conversion determined by LCMS.

### **3.8.4 C–S bond formations of arylammonium salts on DNA**

#### **Materials**

**16a**: 1 mM in water

RSH: 200 mM in DMA

K<sub>2</sub>CO<sub>3</sub>: 200 mM in water

#### **Procedure**

1) To **16a** solution (5 nmol, 5  $\mu$ L), was added 35  $\mu$ L H<sub>2</sub>O, 1000 eq. of RSH (25  $\mu$ L) and 200 eq. of K<sub>2</sub>CO<sub>3</sub> (5  $\mu$ L). The mixture was vortexed.

2) React at room temperature (or 80°C for **16s, 16t**) for 10 h.

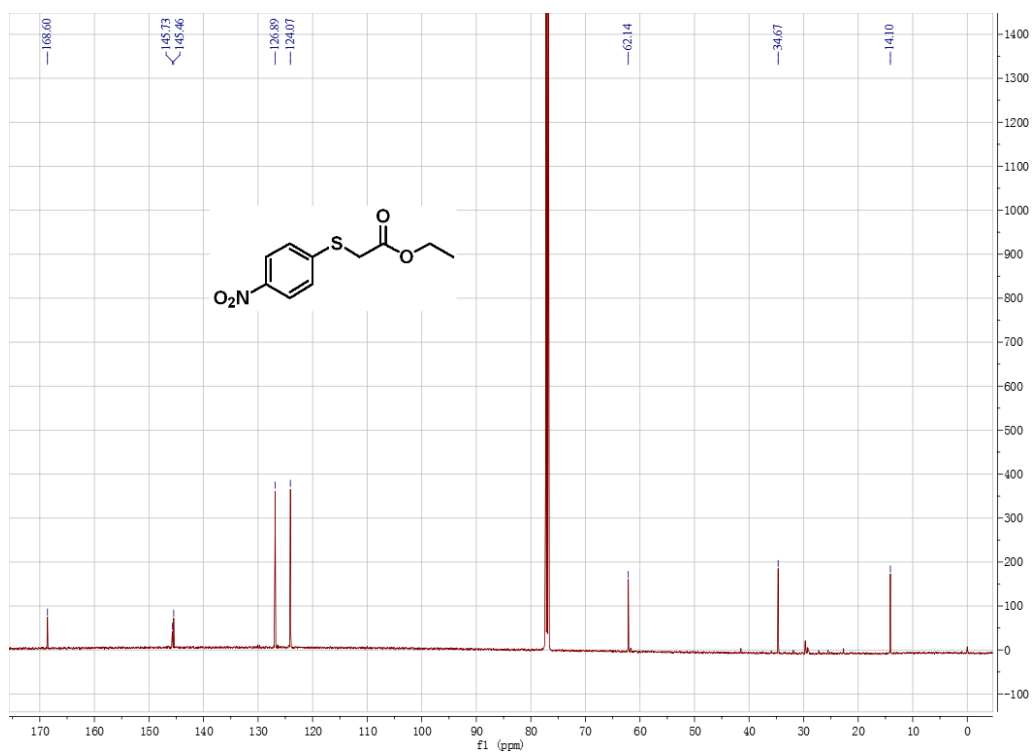
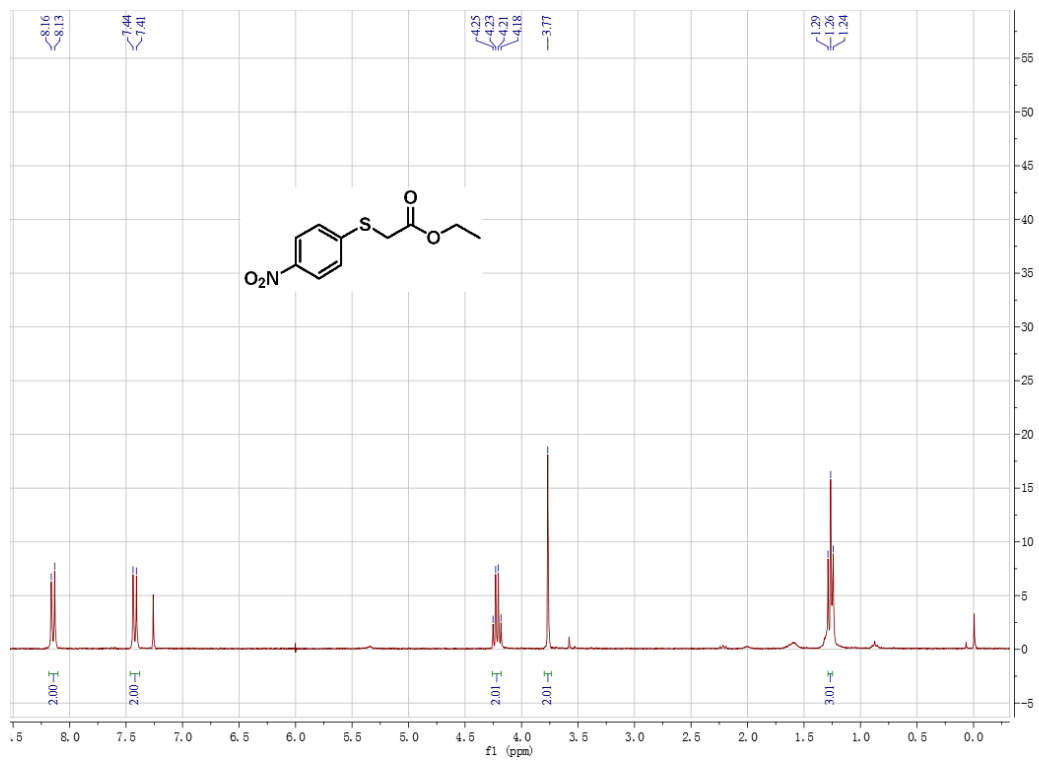
3) Add 5 M NaCl solution (10 % by volume) and cold ethanol (2.5 times by volume, ethanol stored at -20°C). The mixture was stored at a -80°C freezer for more than 30 minutes.

4) Centrifuge the sample for around 30 minutes at 4 °C in a microcentrifuge at 10000 rpm. The above supernatant was removed and the pellet (precipitate) was cooled in liquid nitrogen and then placed on a lyophilizer. After lyophilization, the dry pellet was recovered.

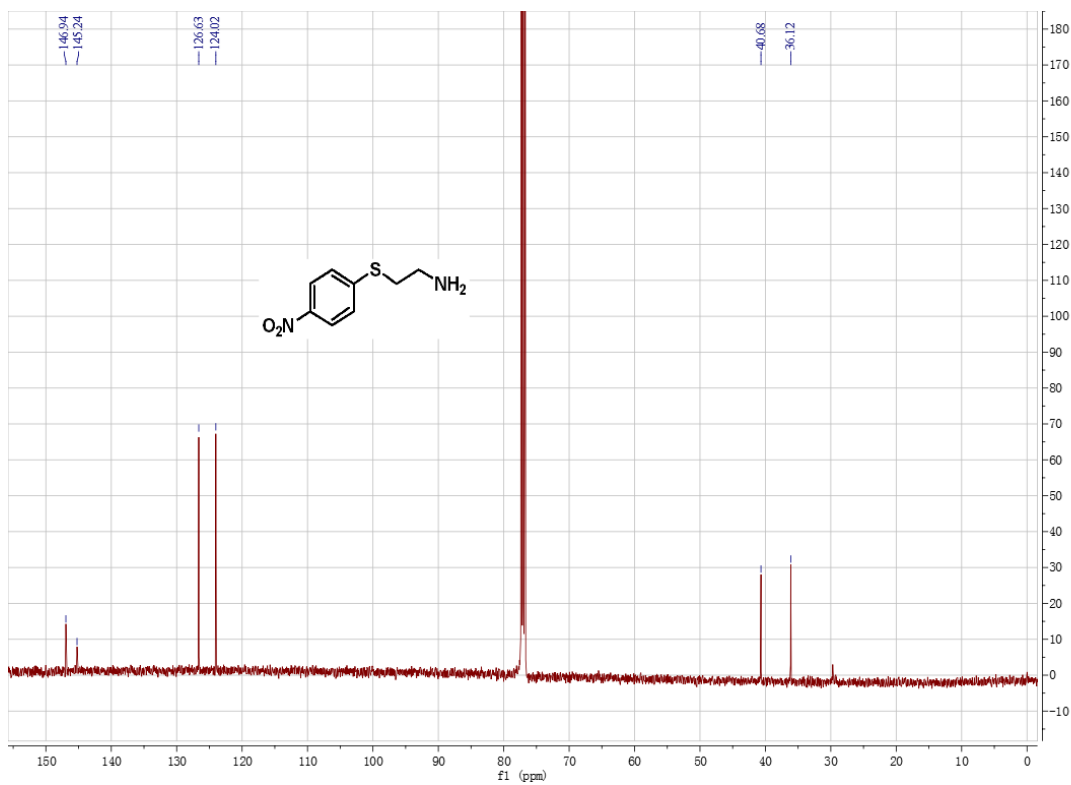
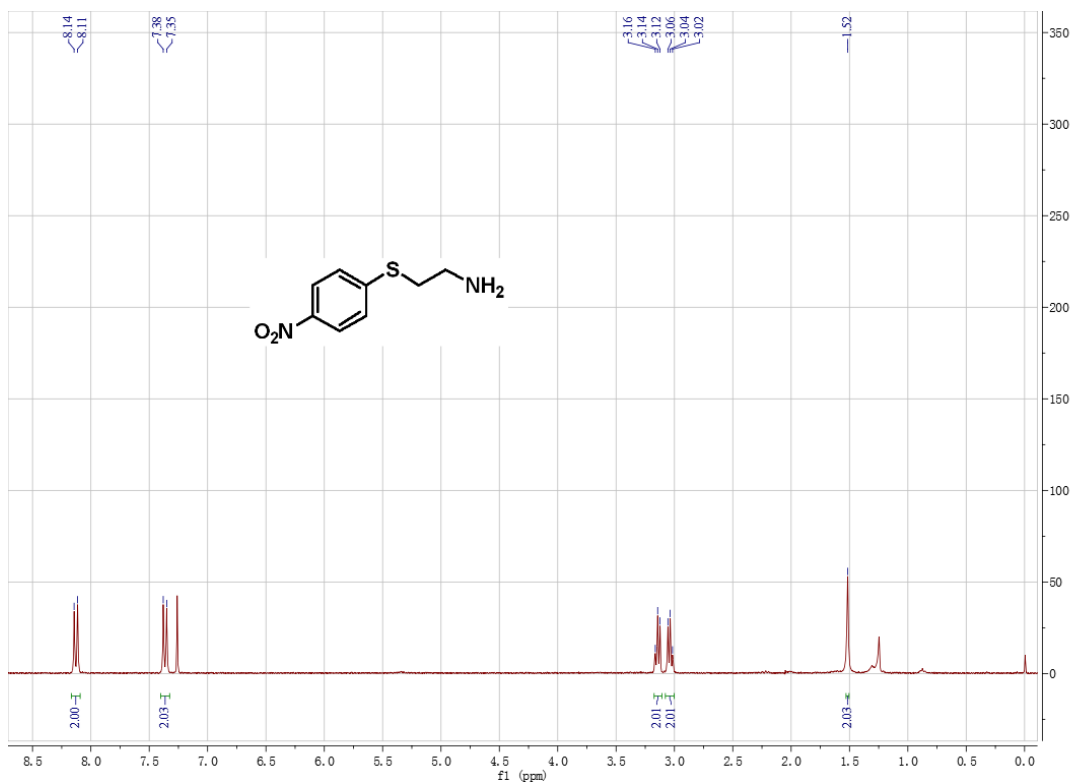
Conversion determined by LCMS.

## 4. Copies of NMR Spectrums for All Compounds

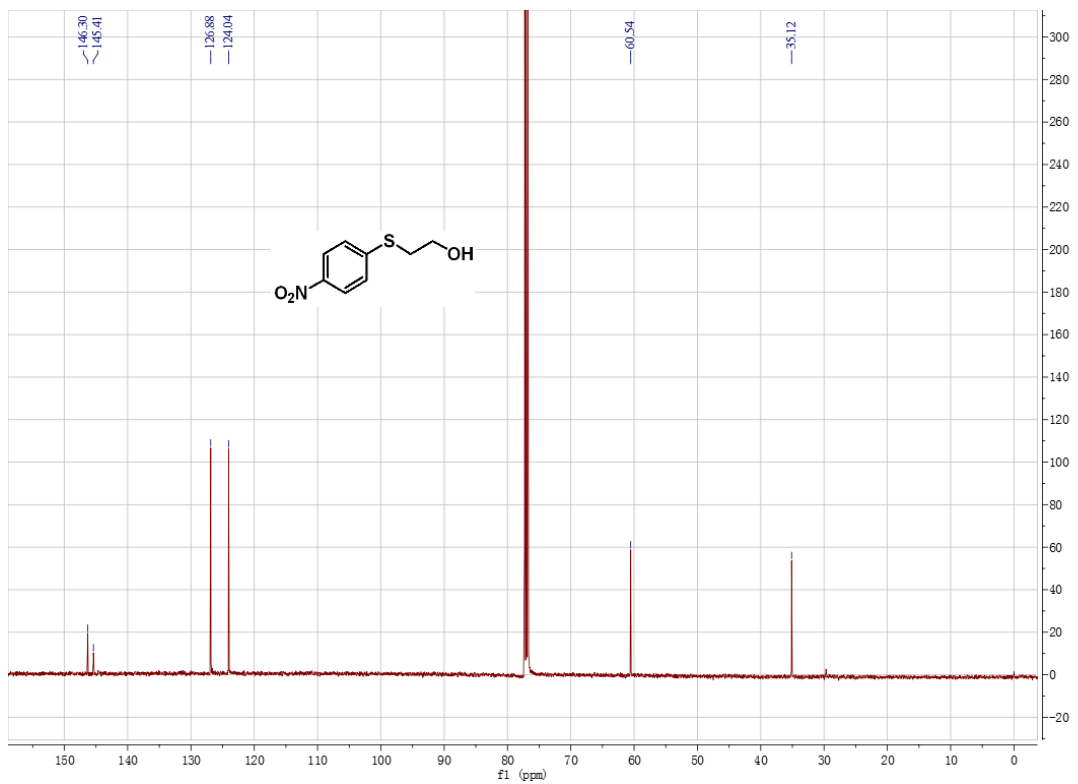
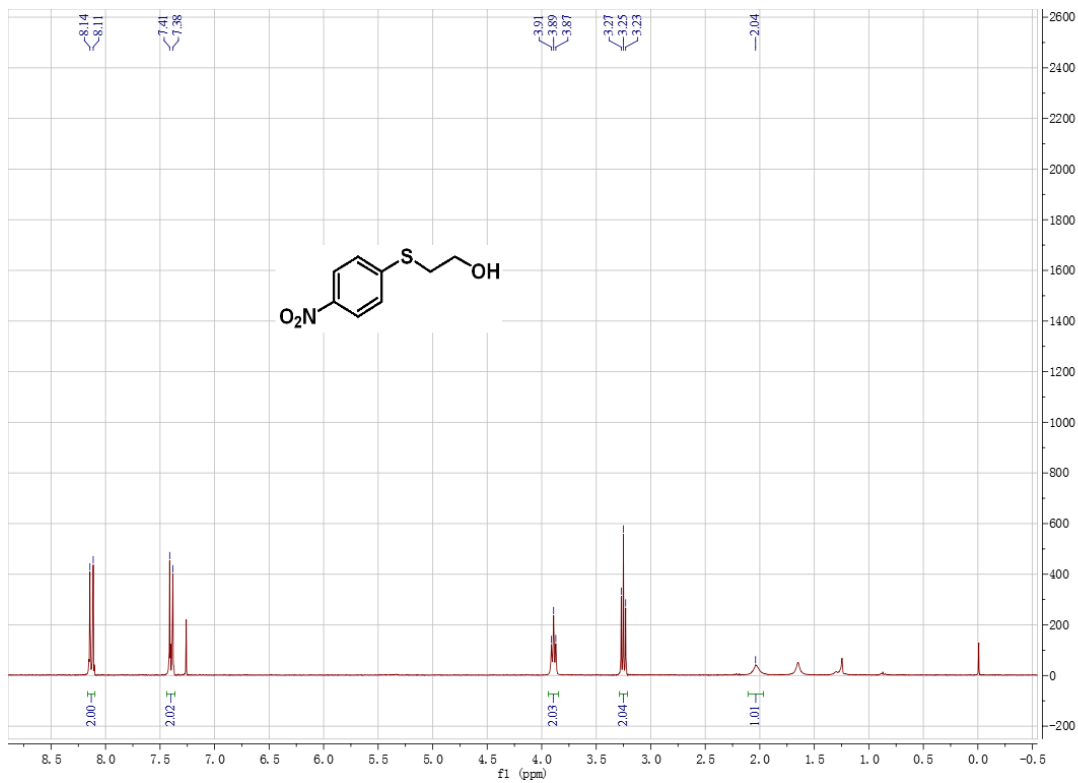
Compound 3aa



Compound 3ab

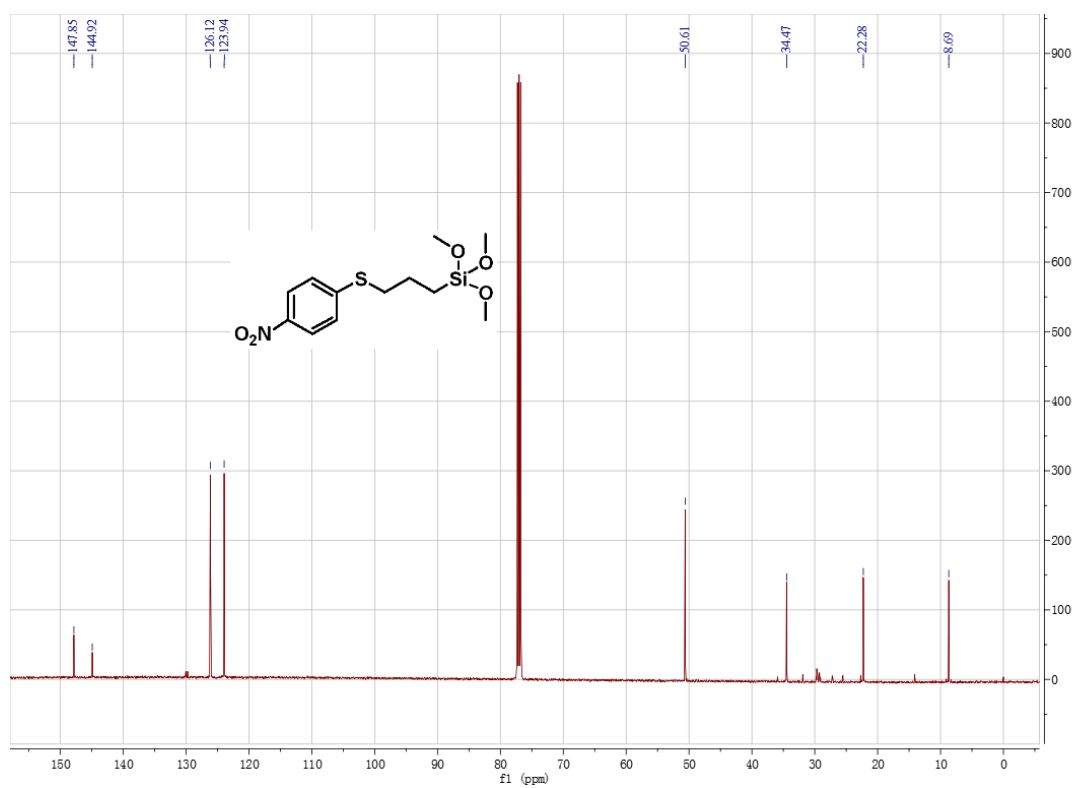
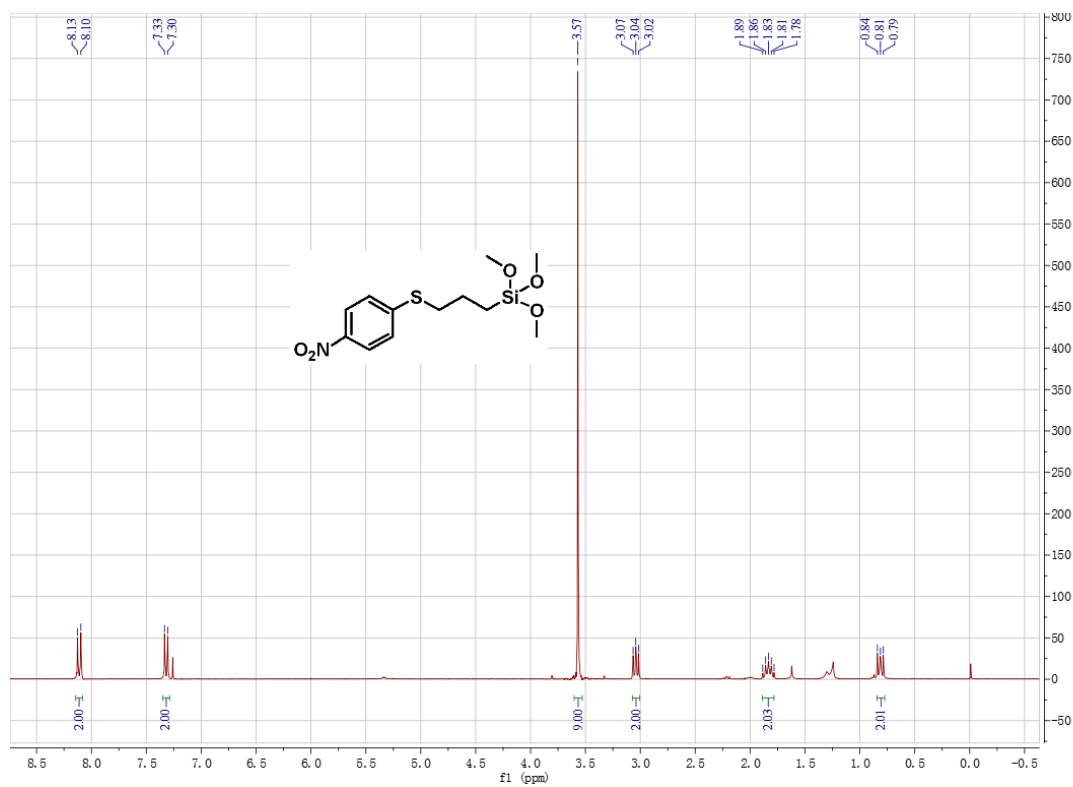


Compound **3ac**

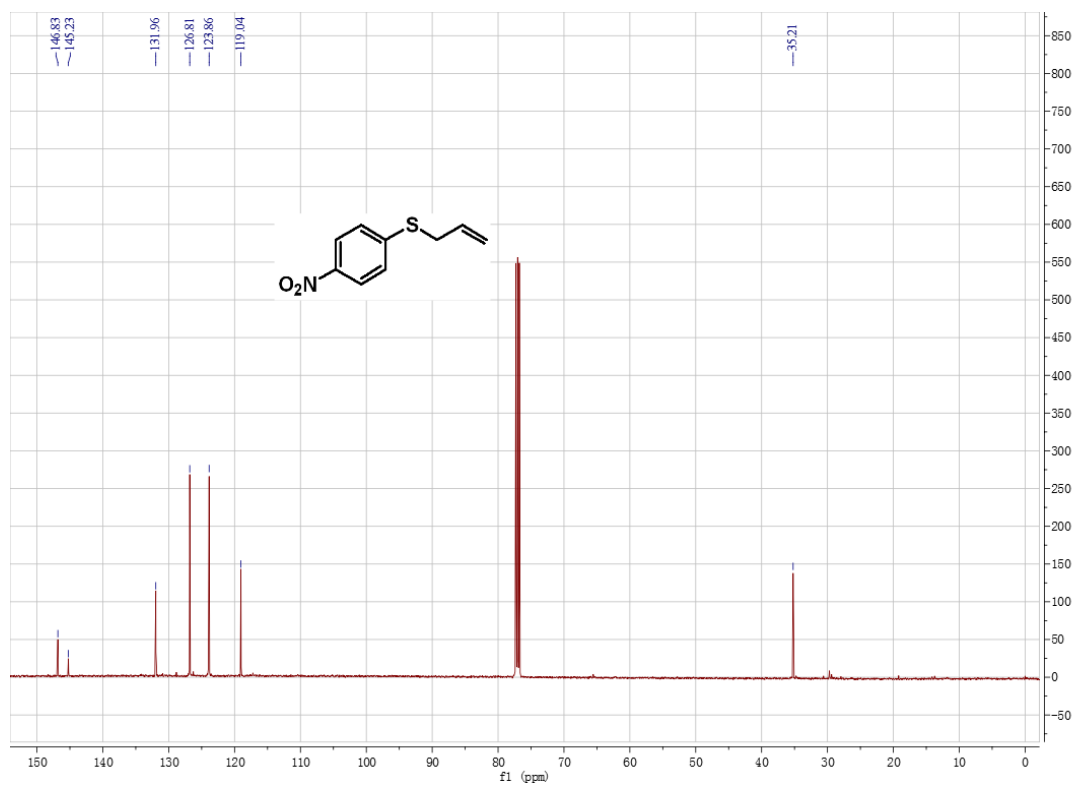
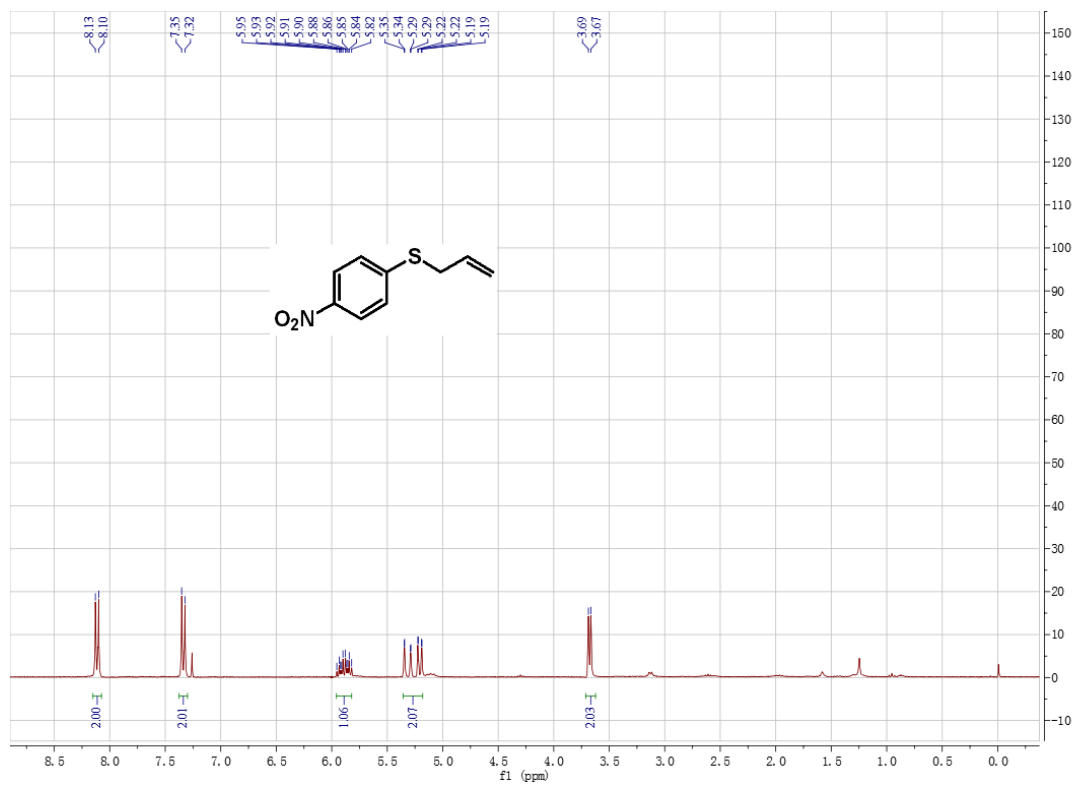




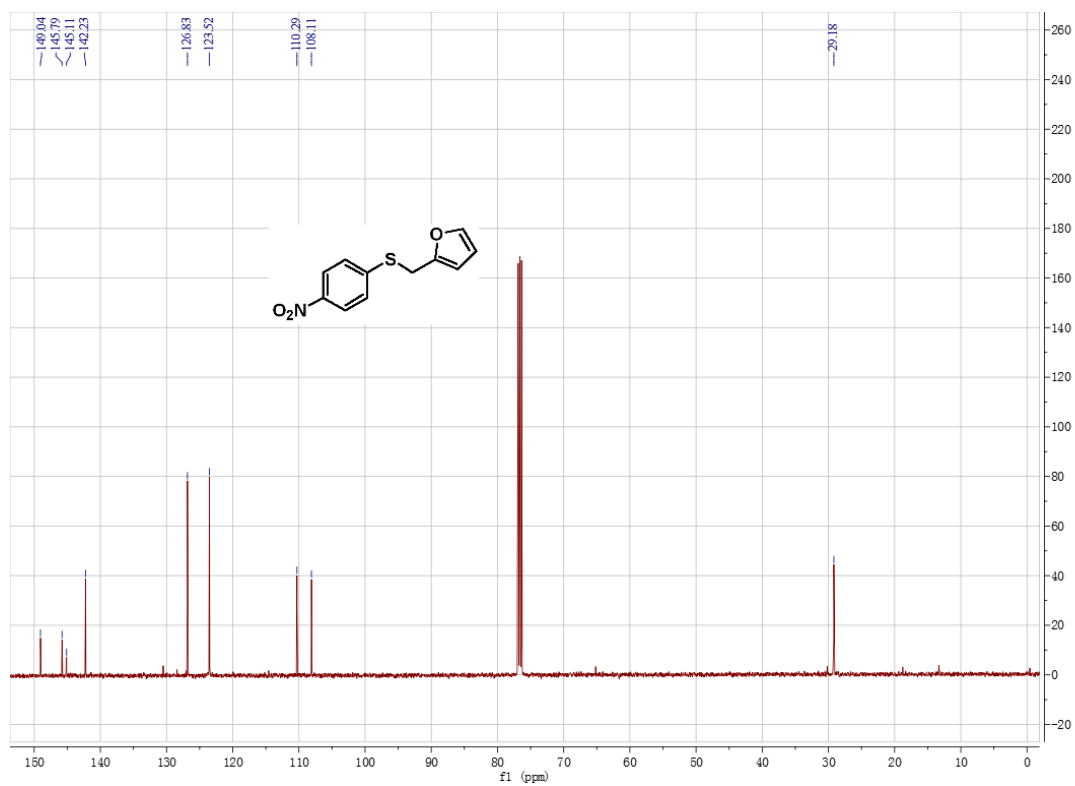
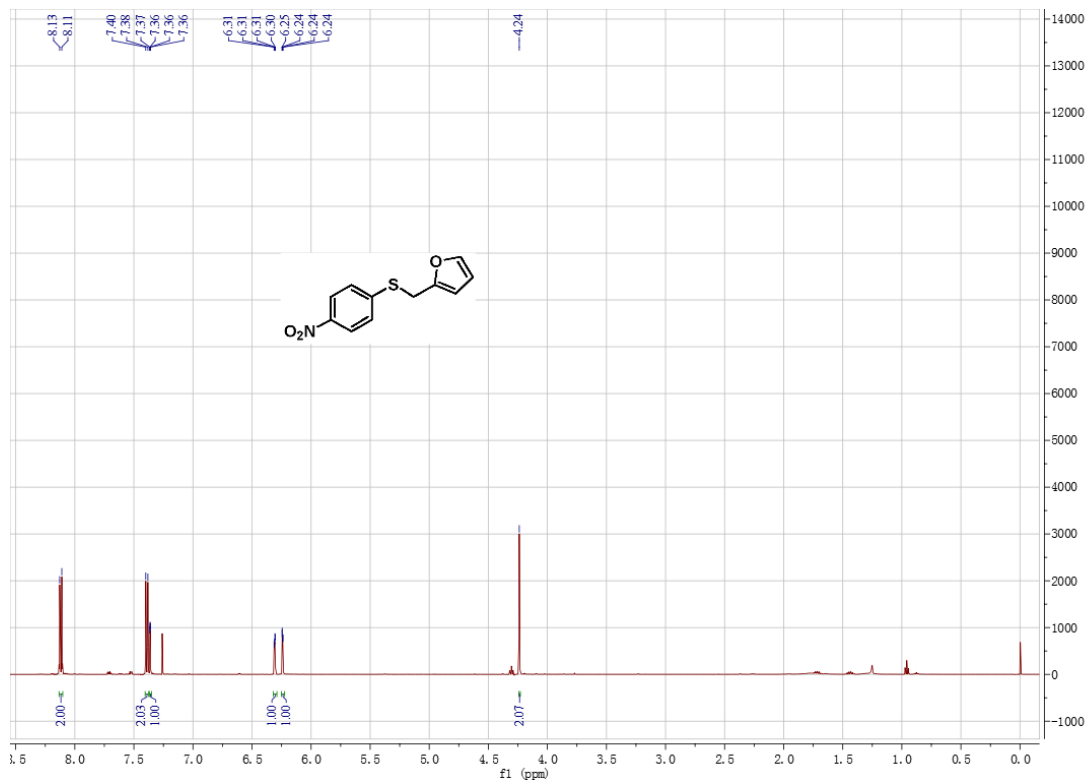
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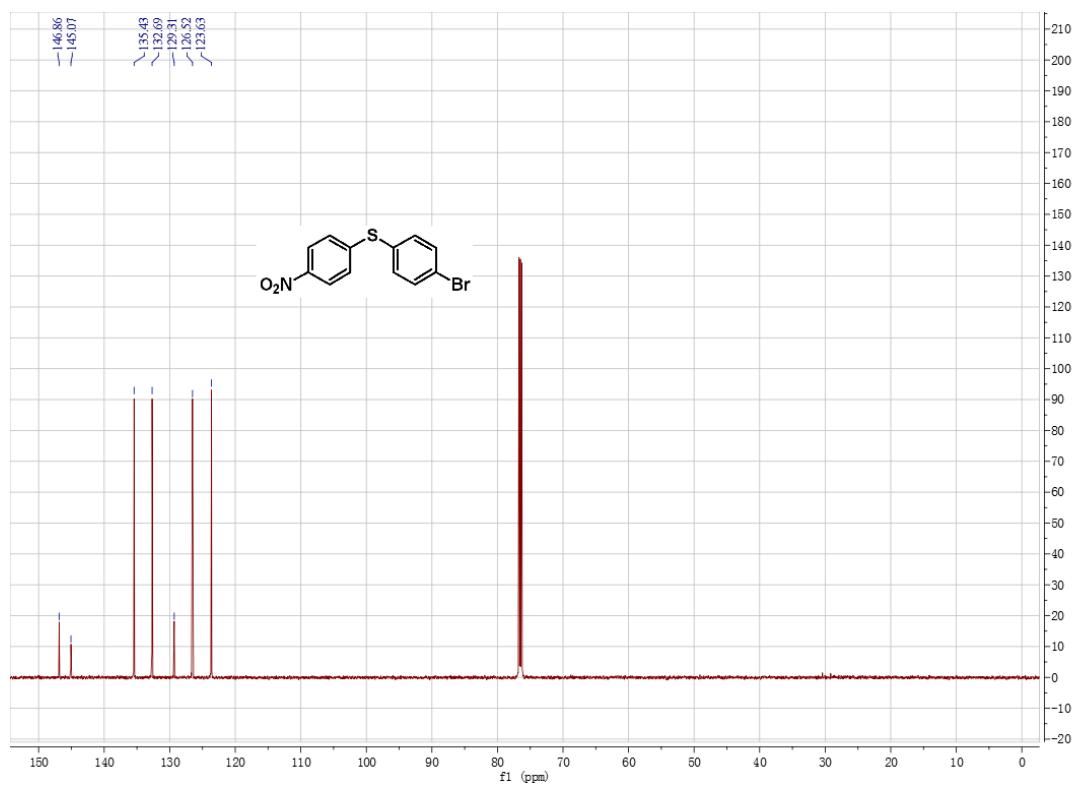
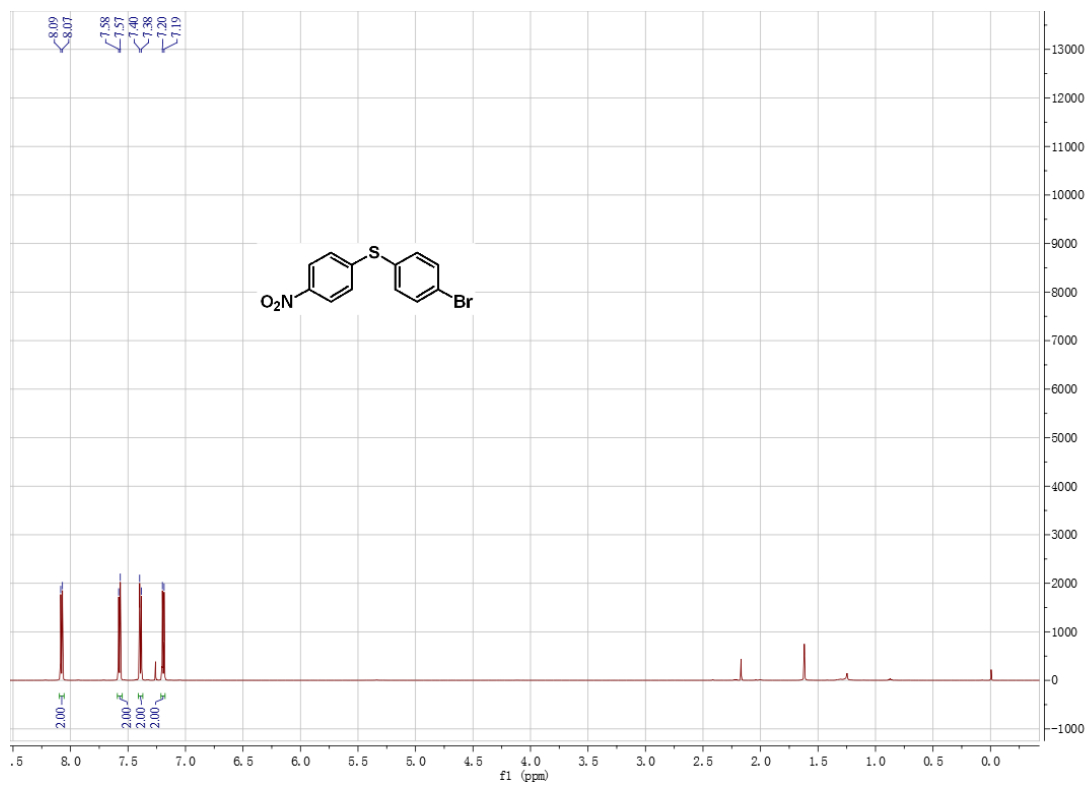
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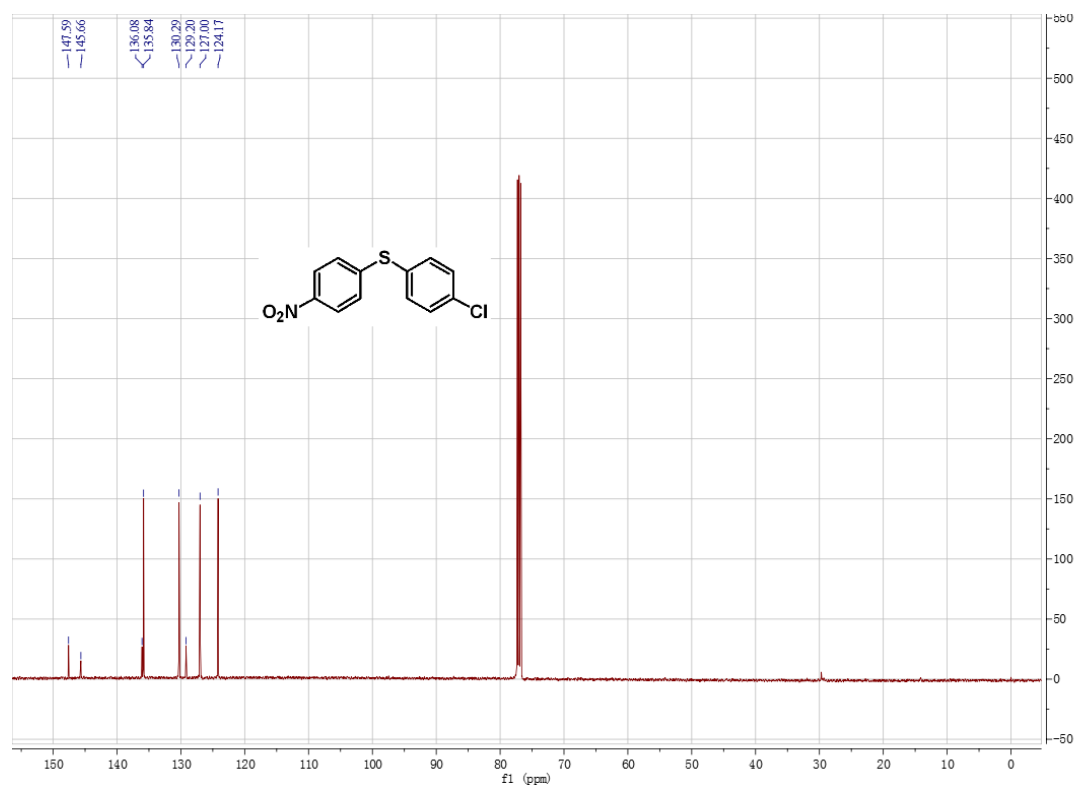
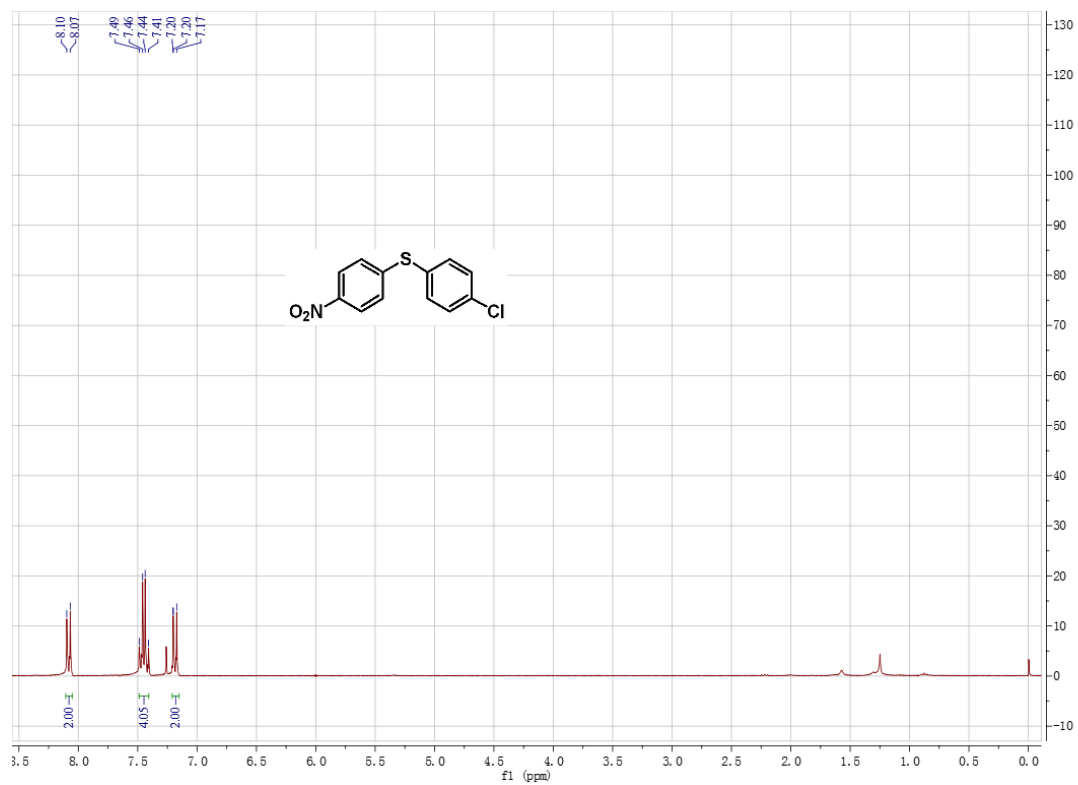
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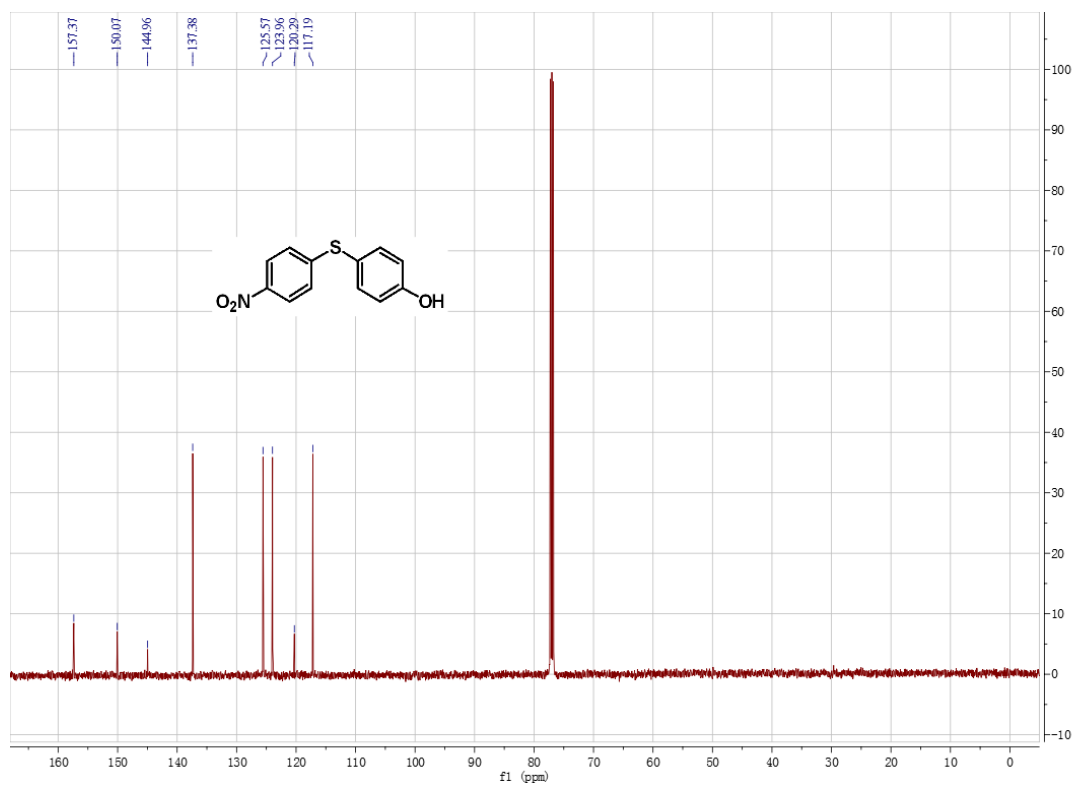
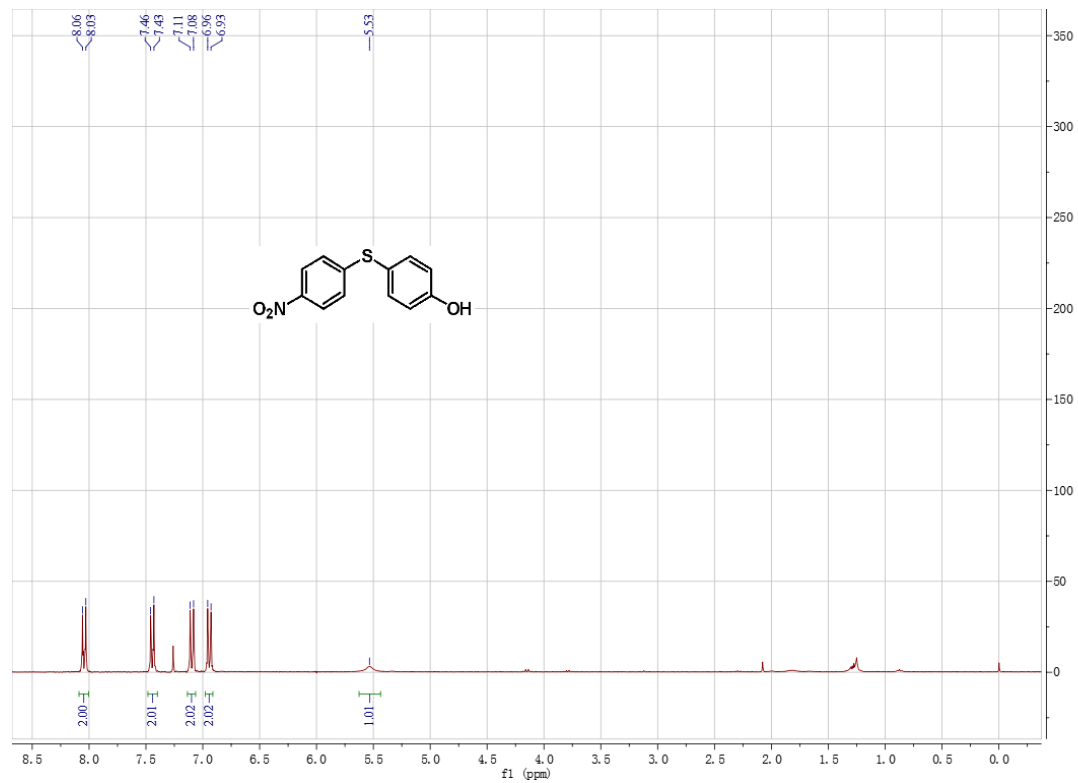
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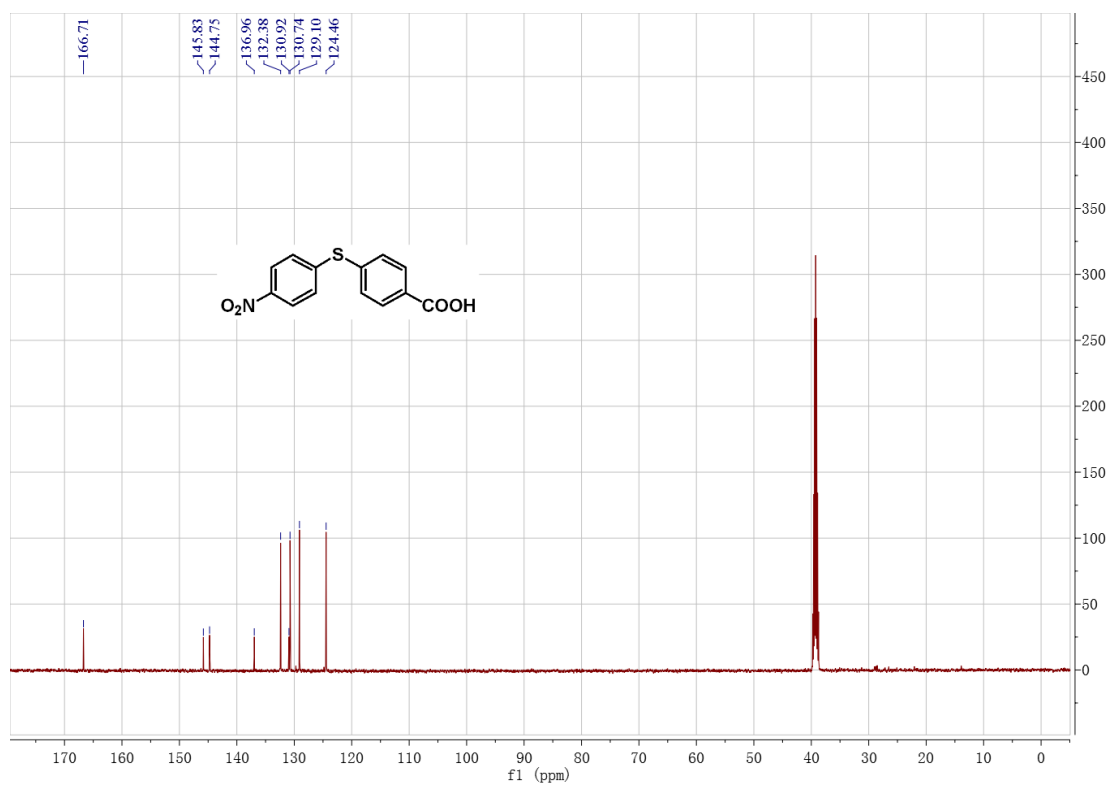
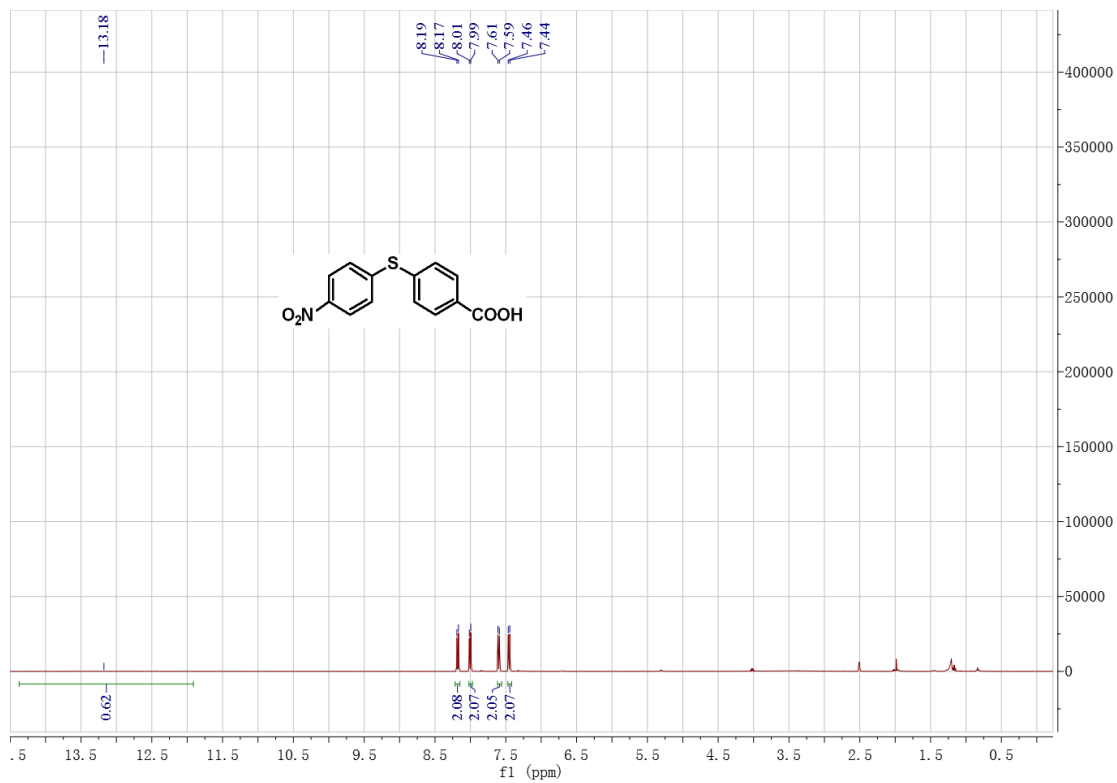
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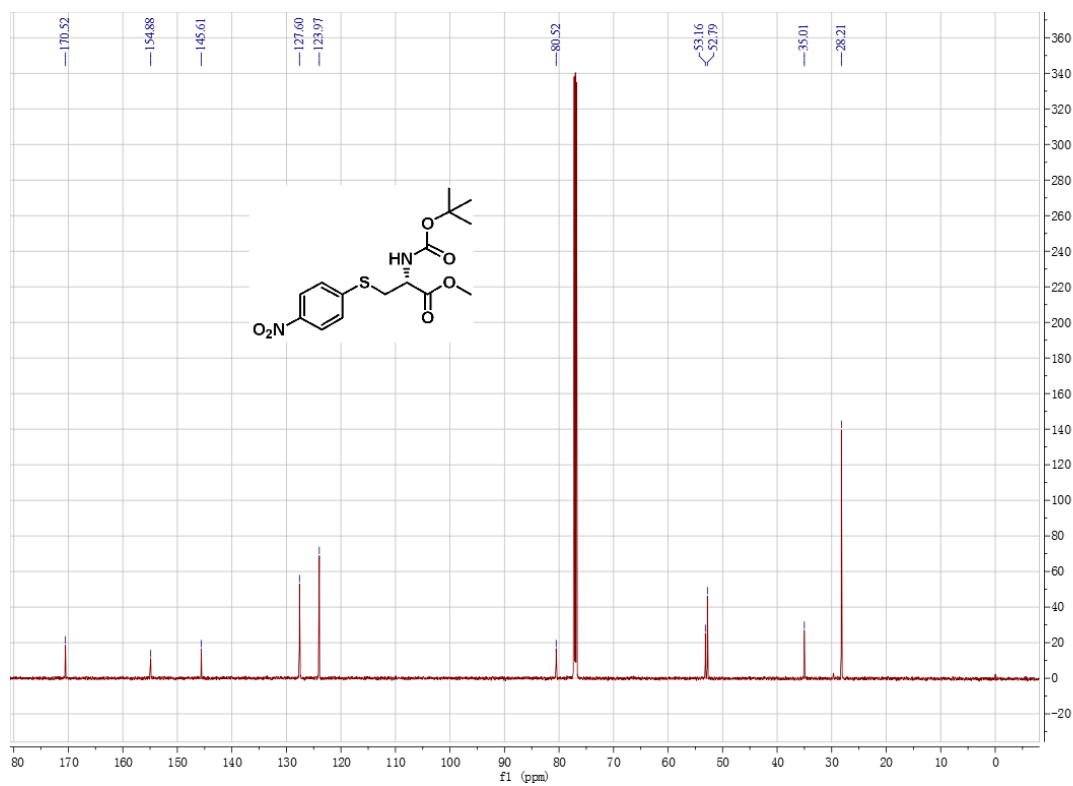
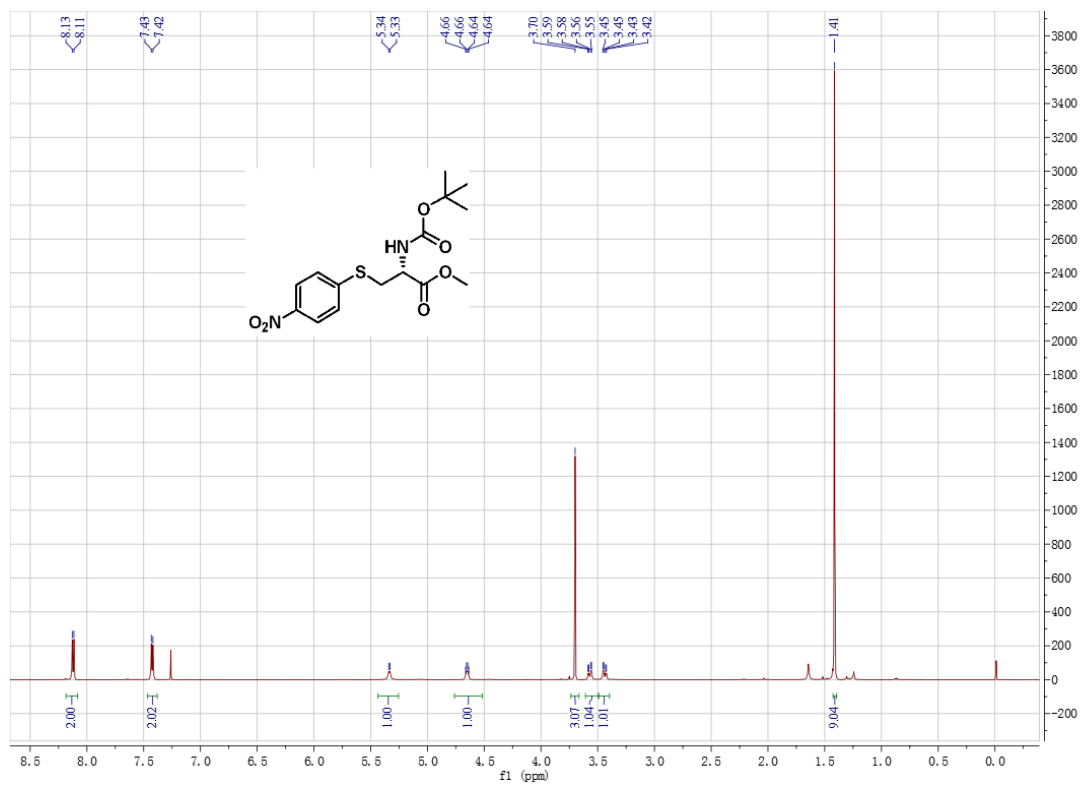
# Compound 3ai



# Compound 3aj

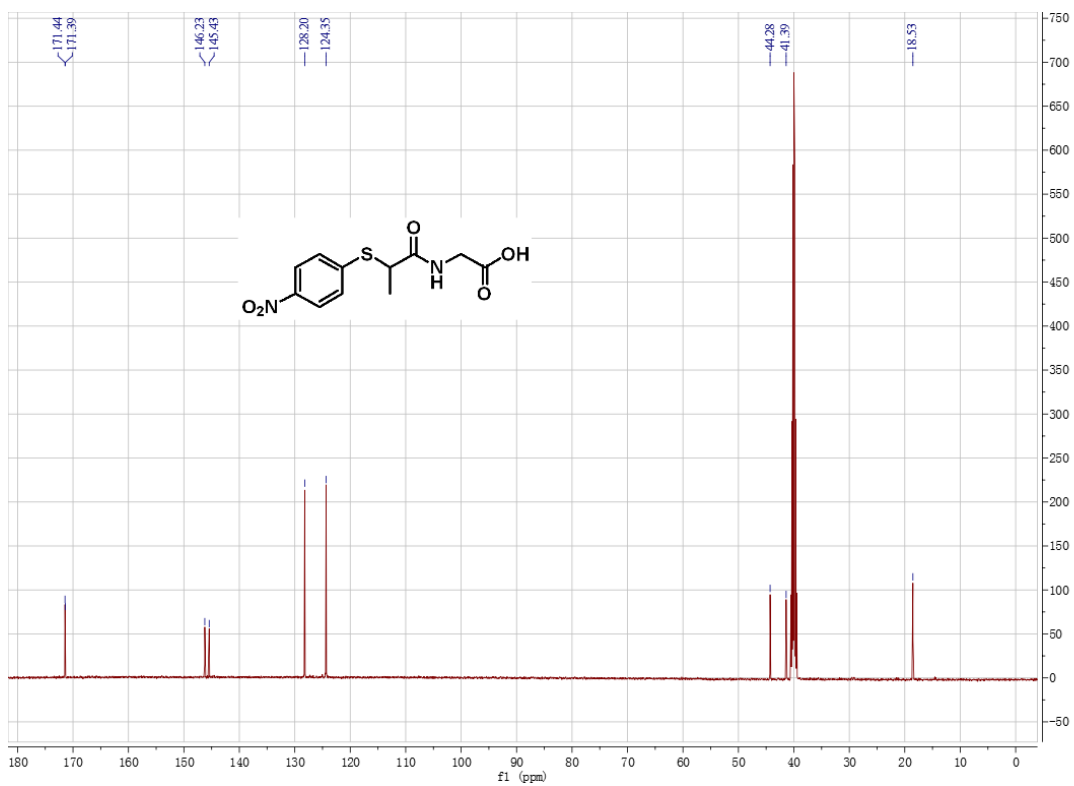
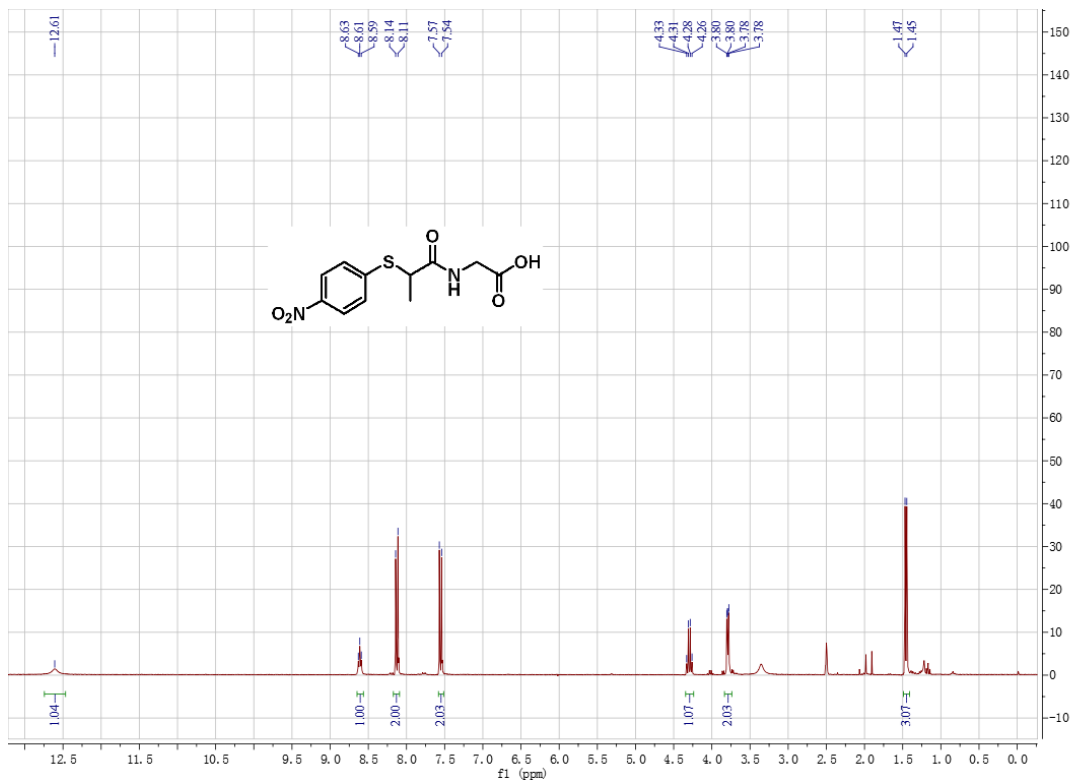


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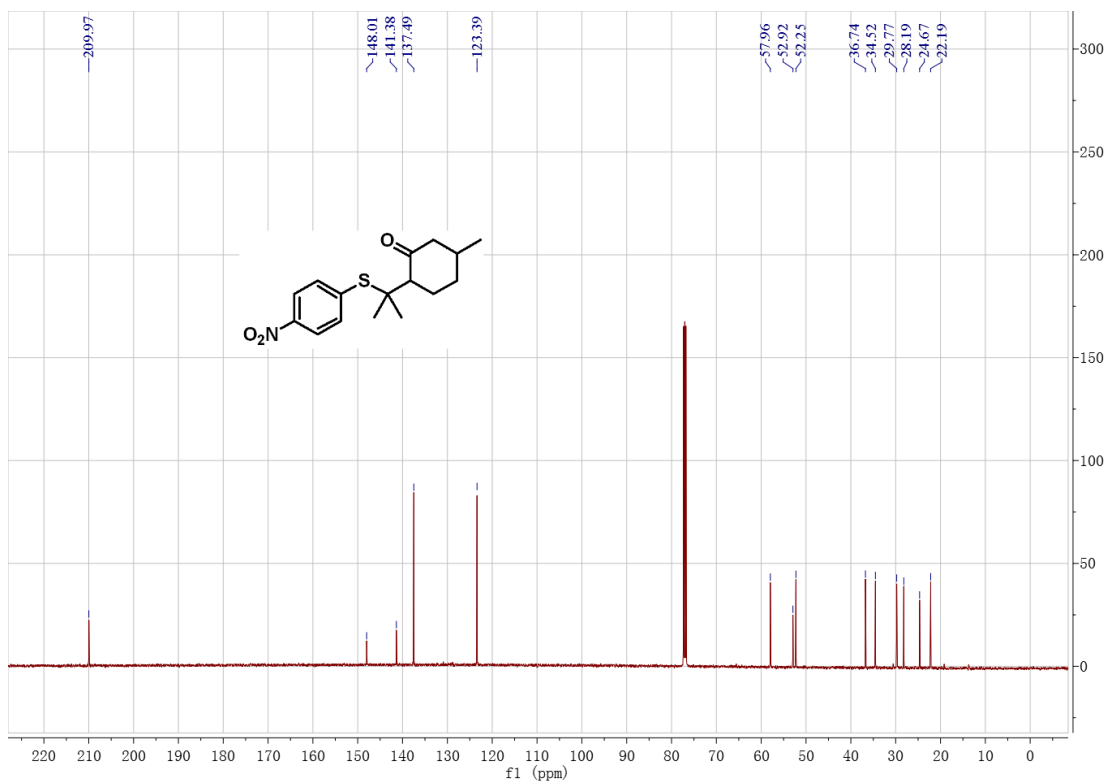
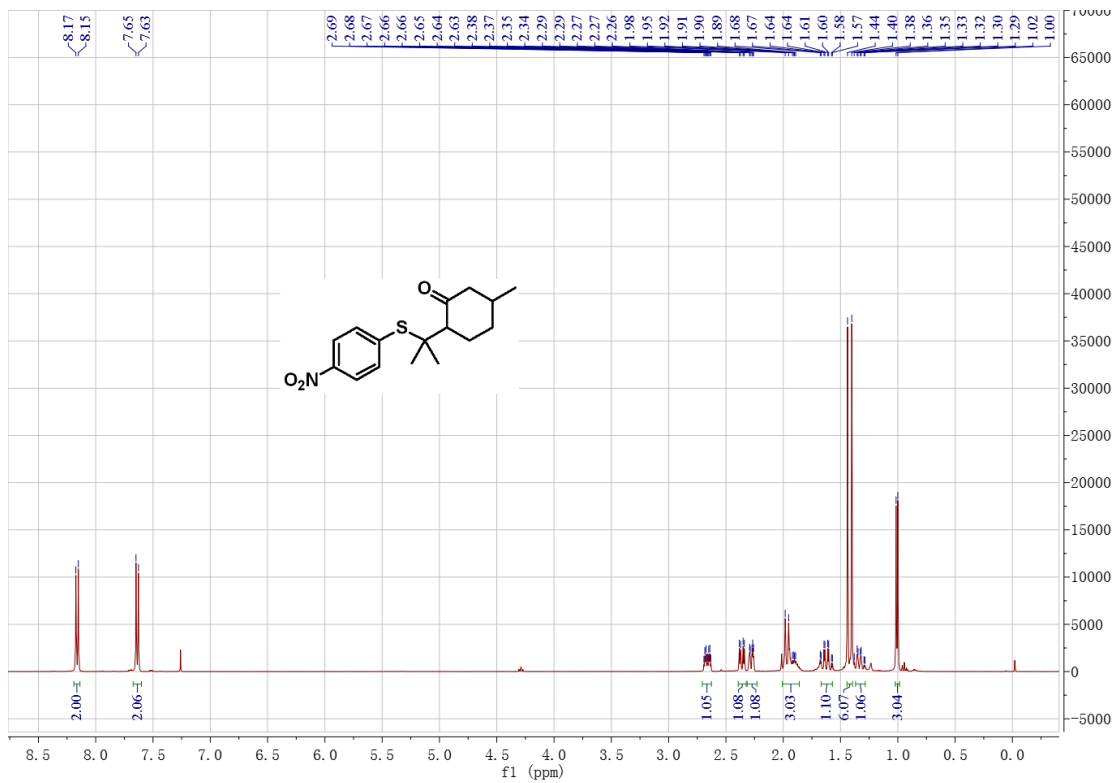




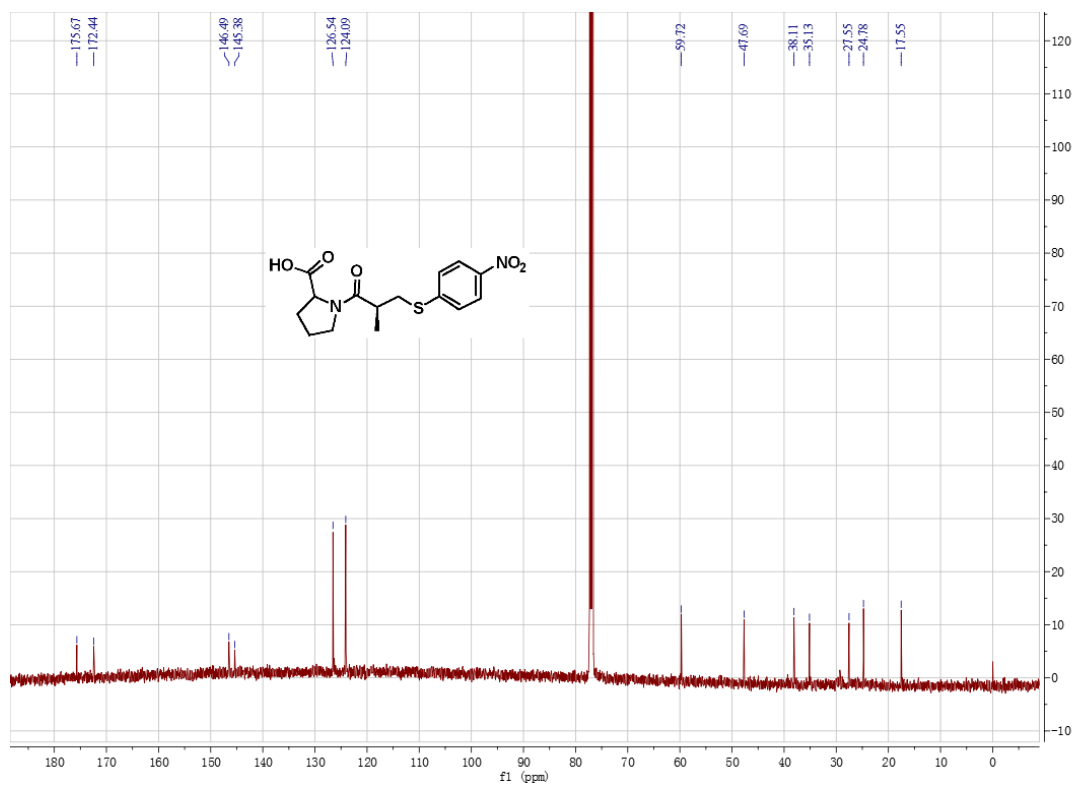
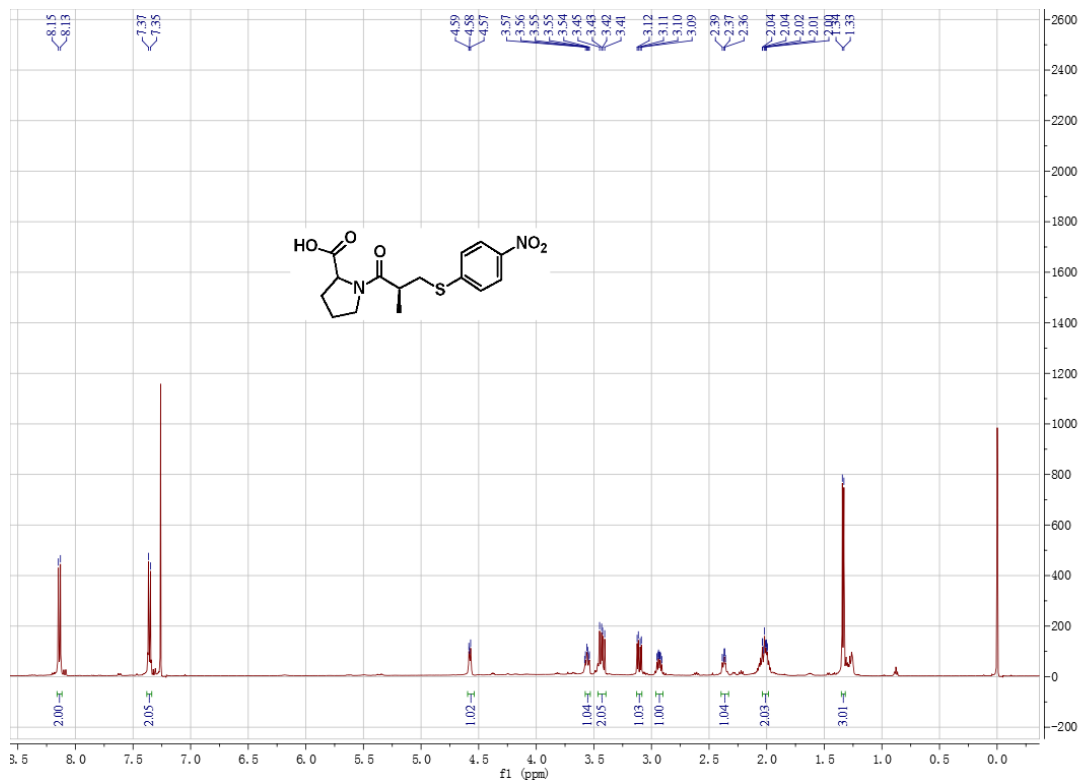
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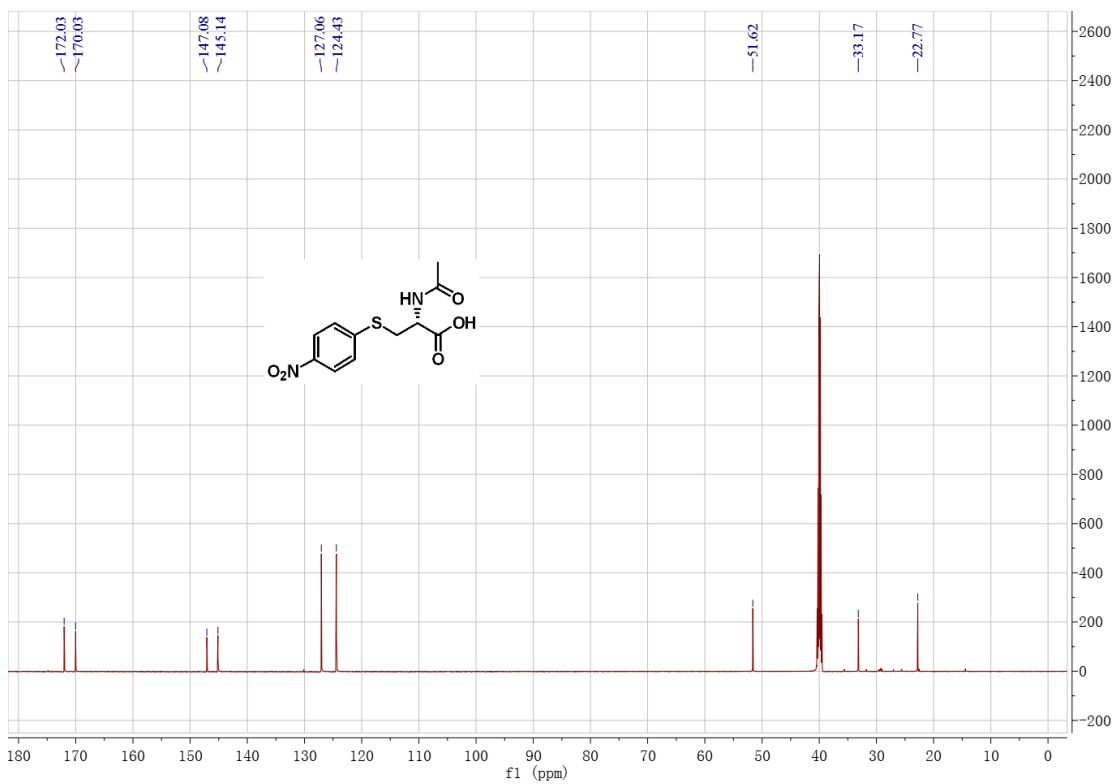
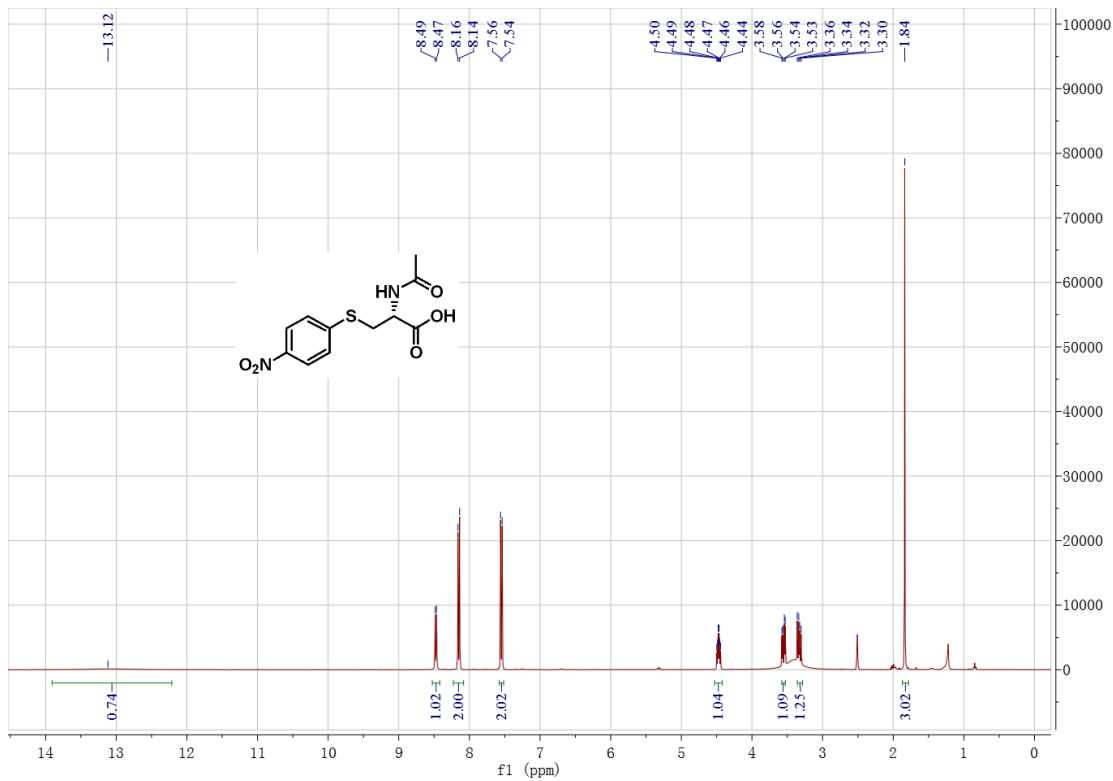
Compound **3am**



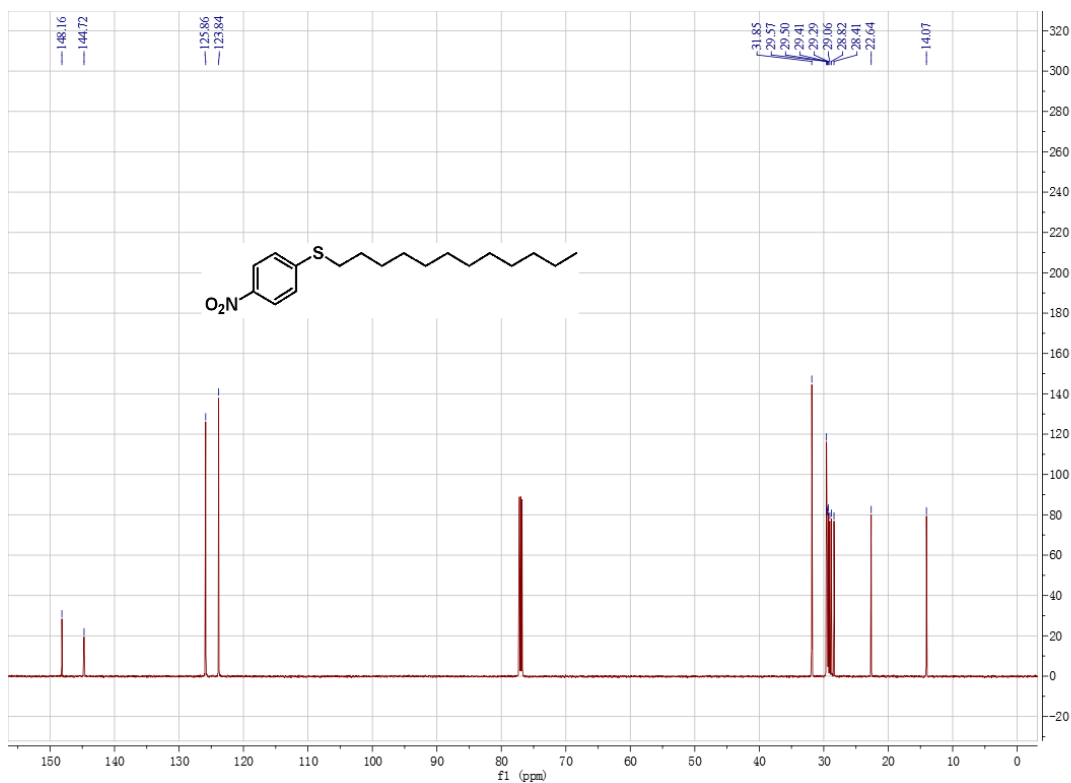
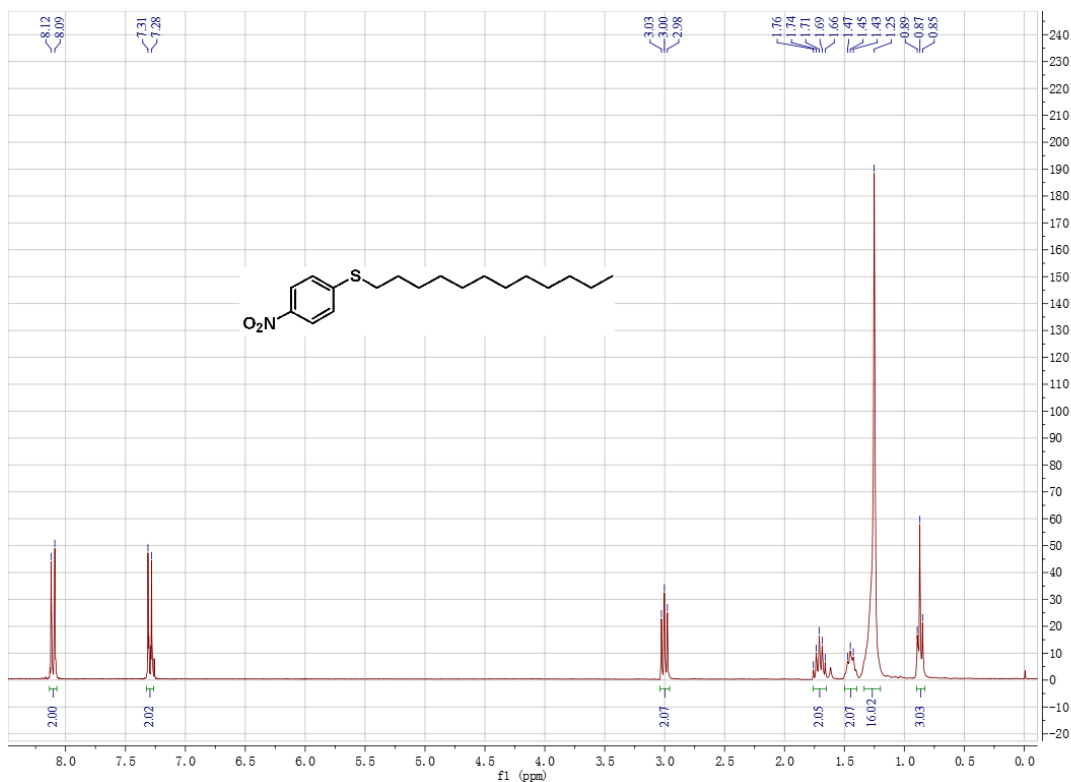
Compound **3an**



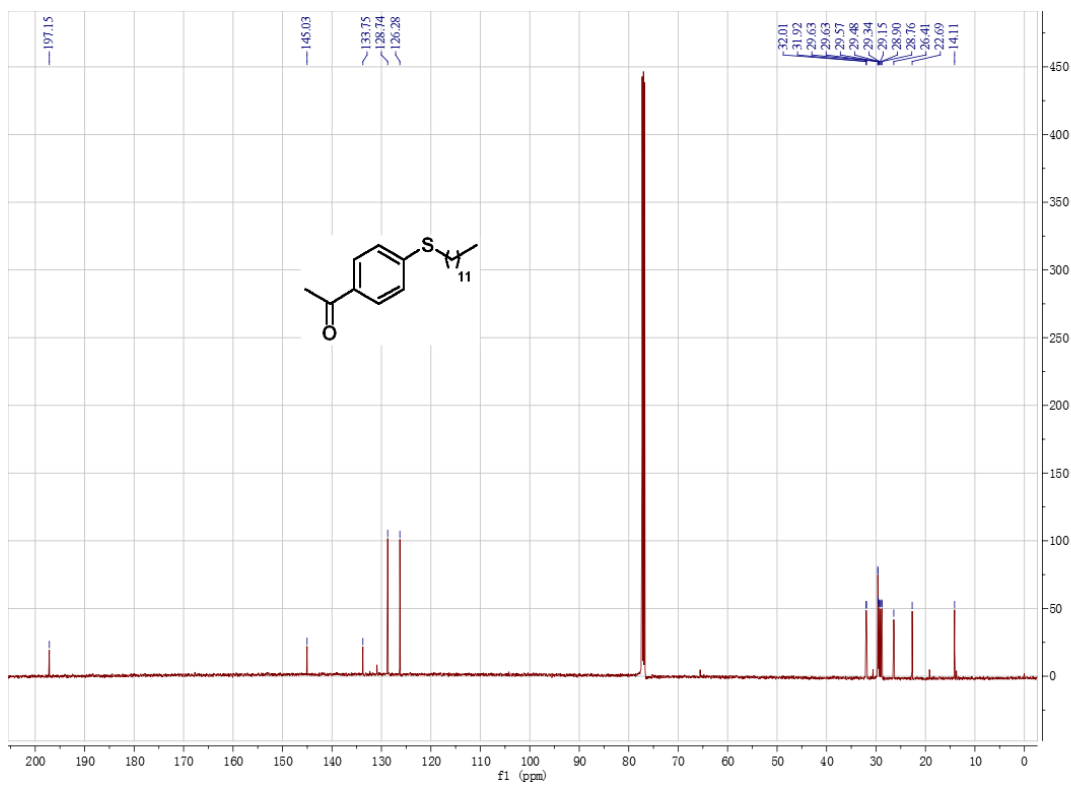
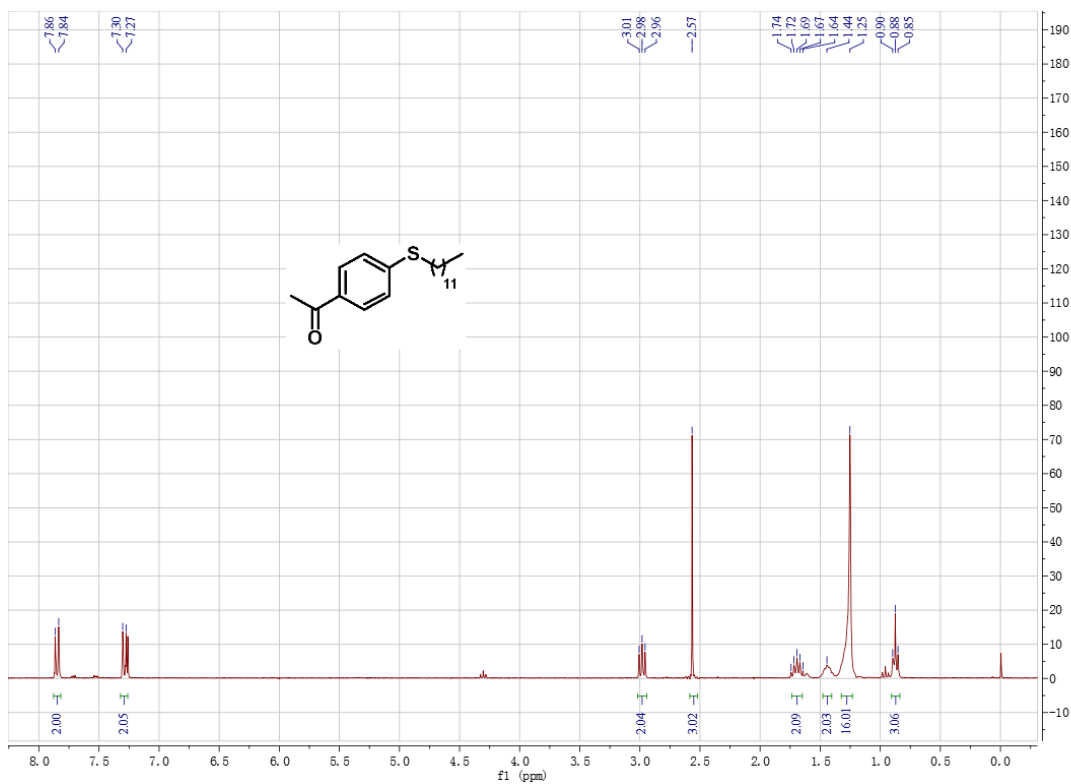
Compound 3ao



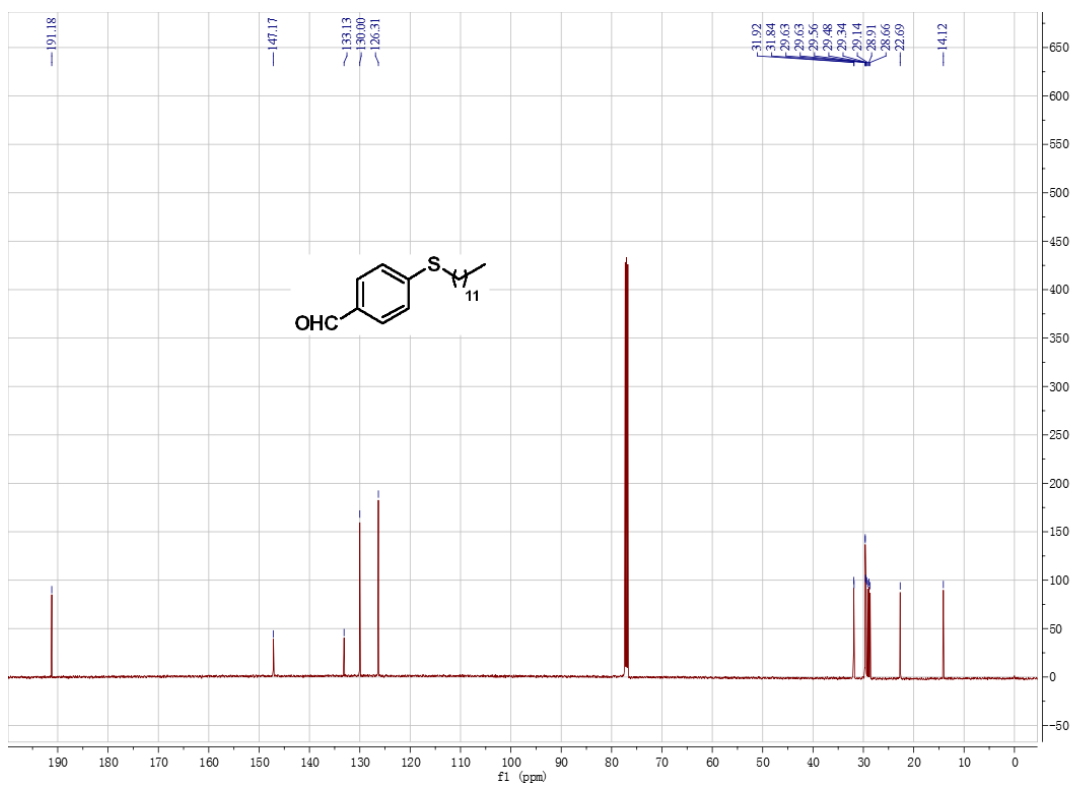
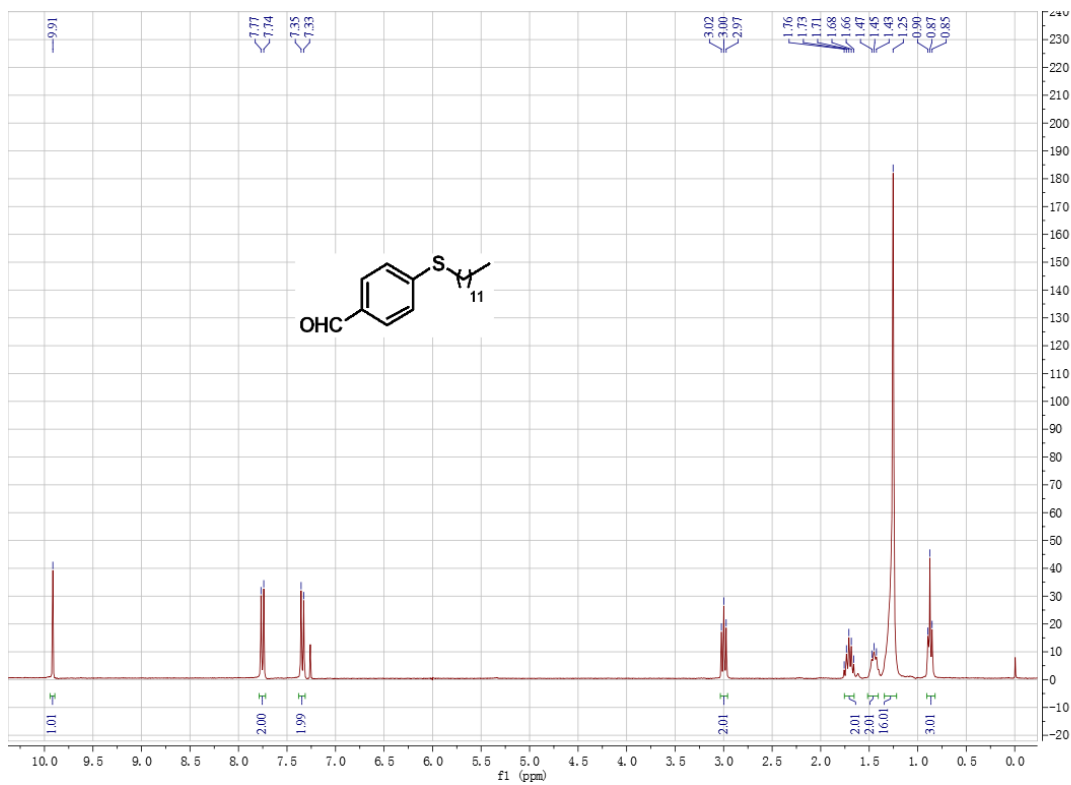
# Compound 3ap



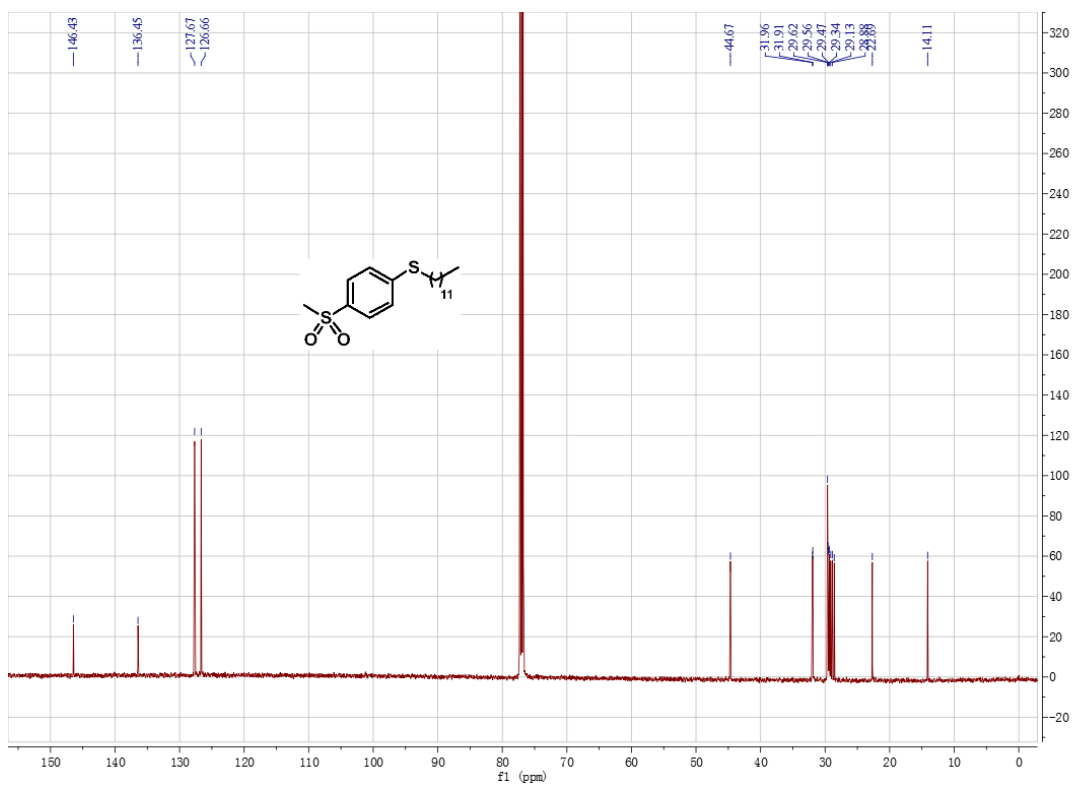
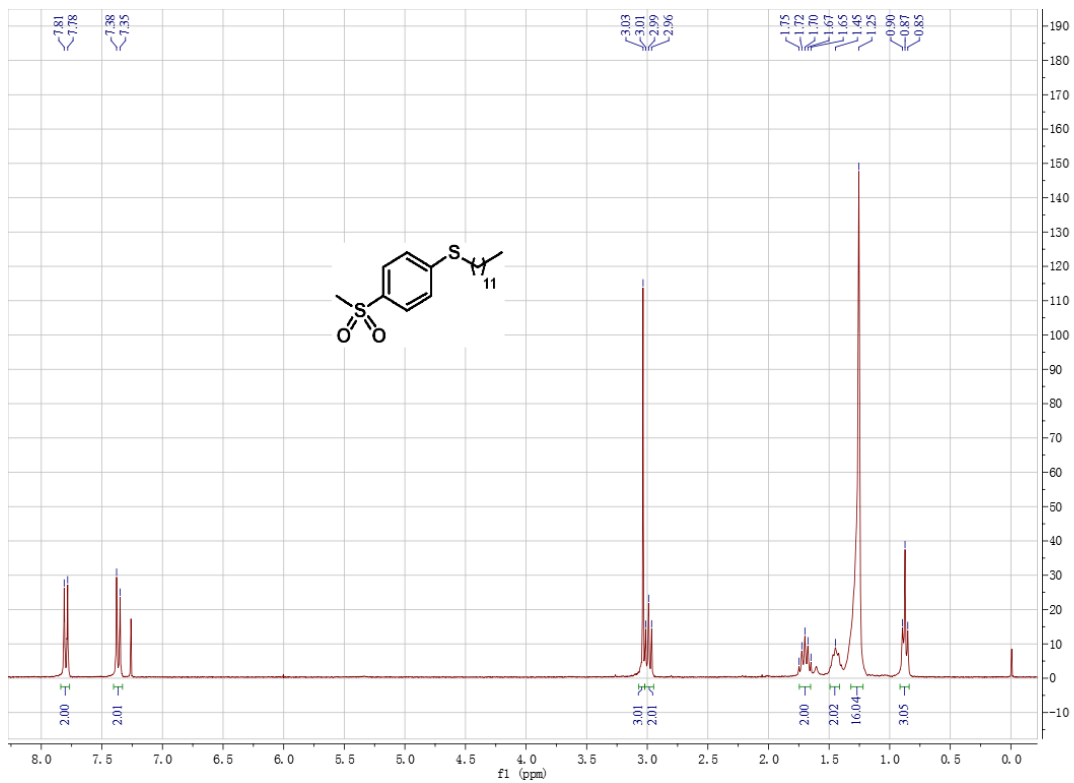
# Compound 3bp



# Compound 3cp

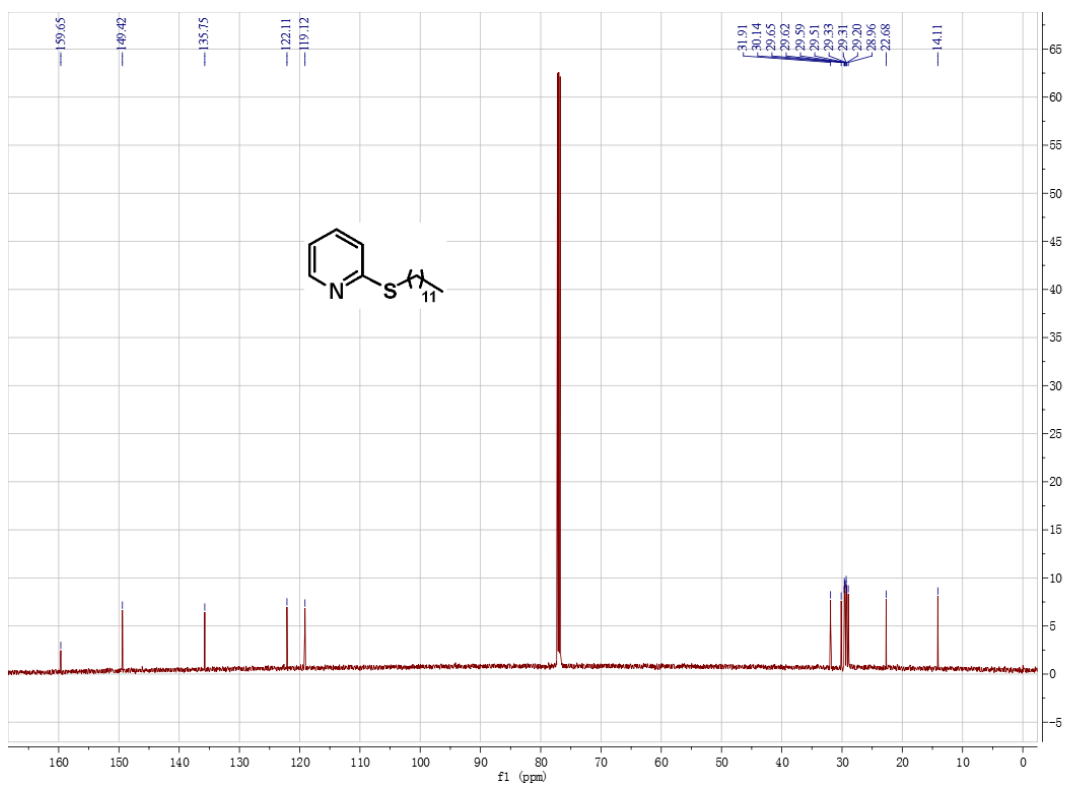
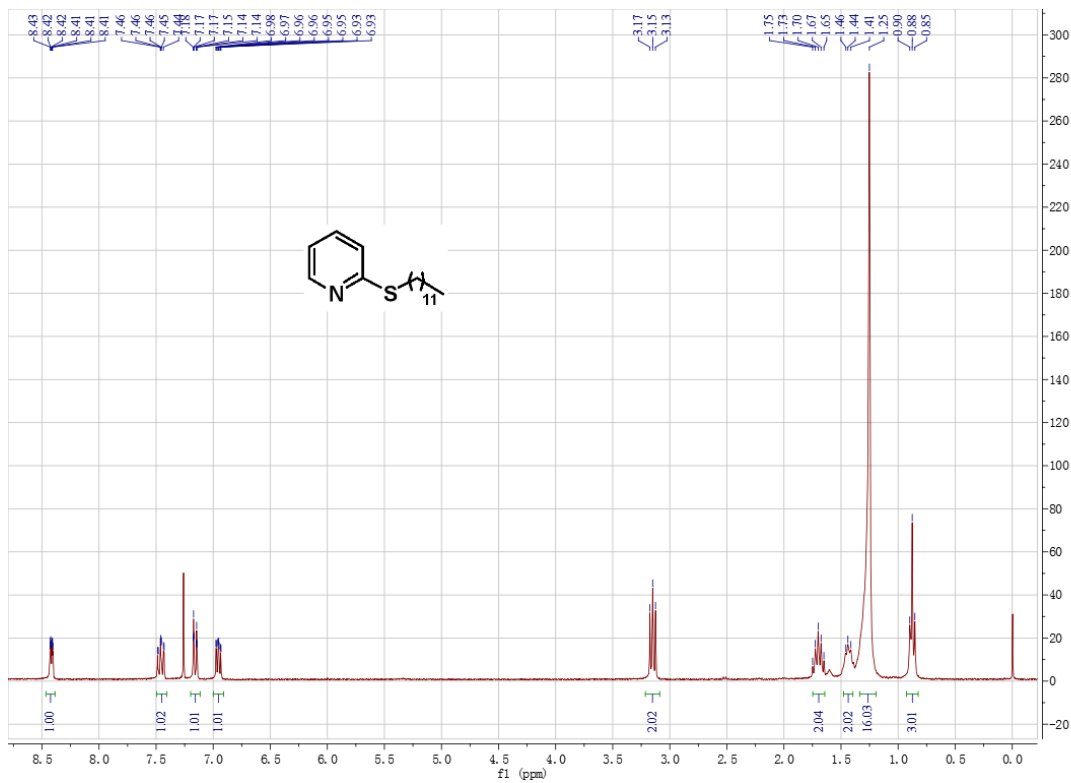


Compound **3dp**

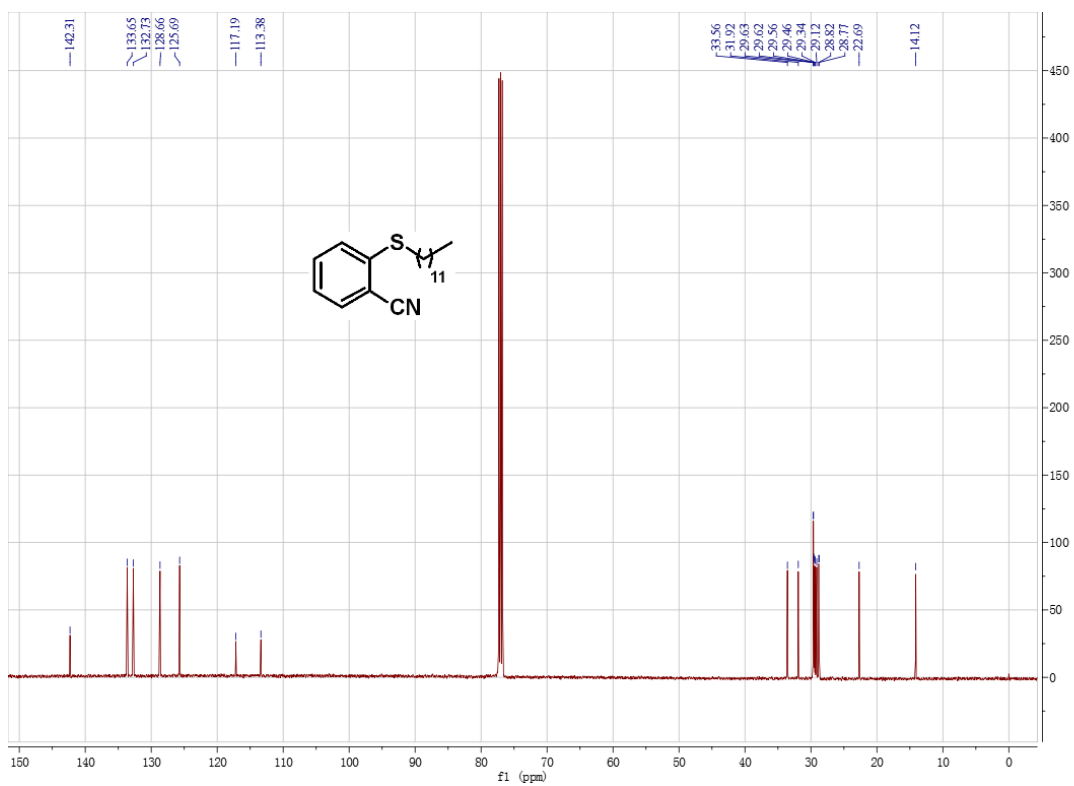
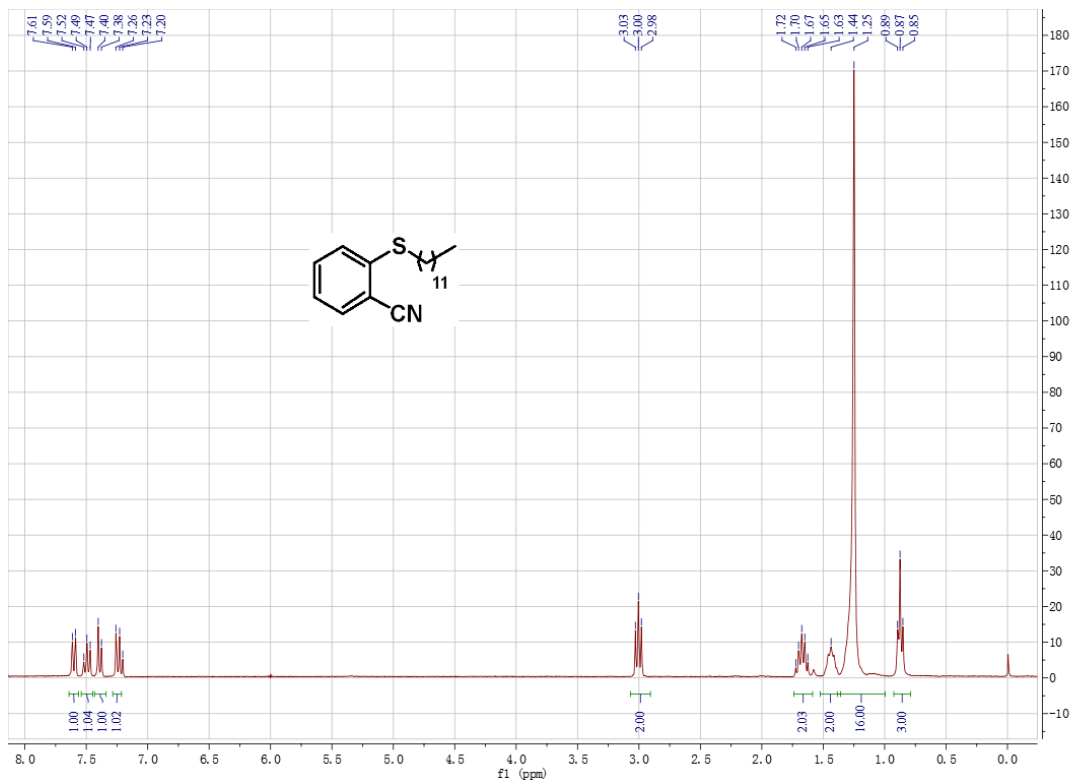




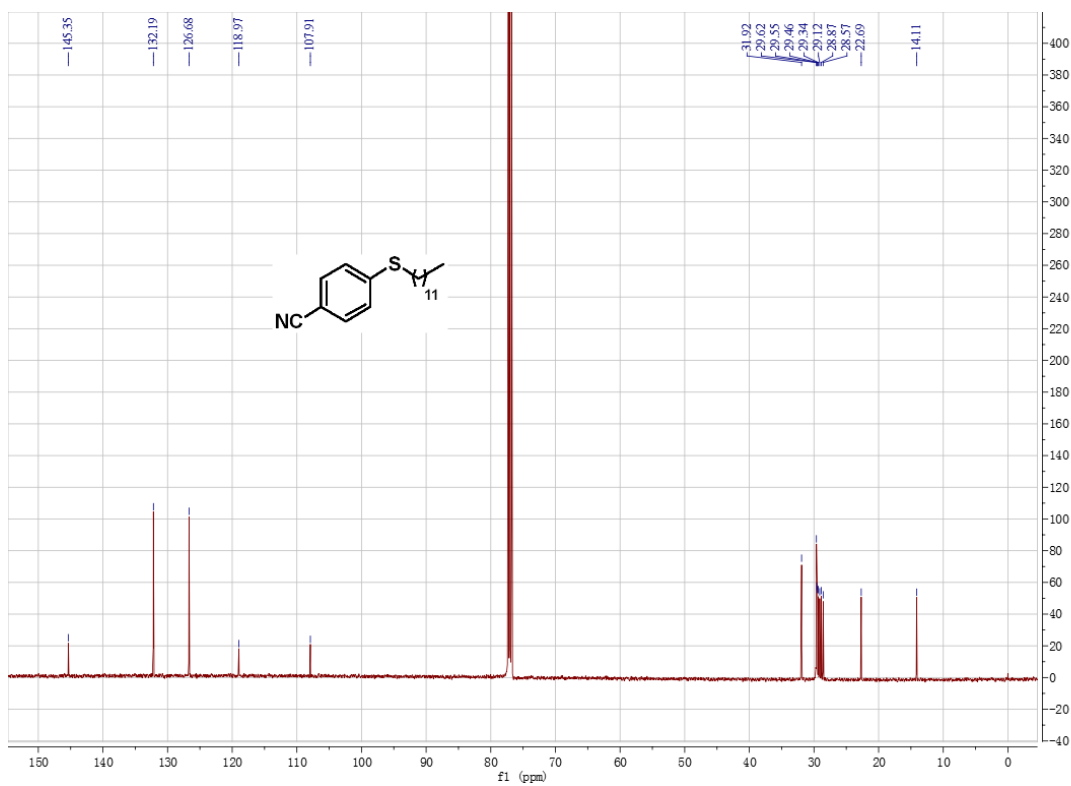
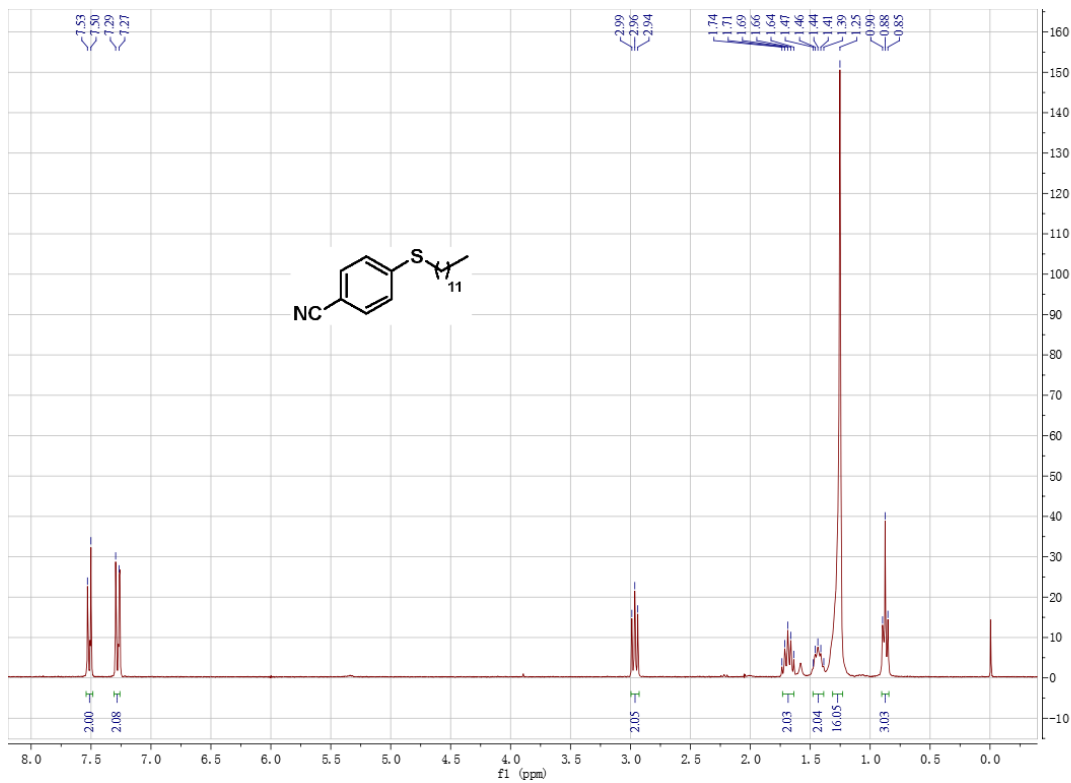
Compound 3ep



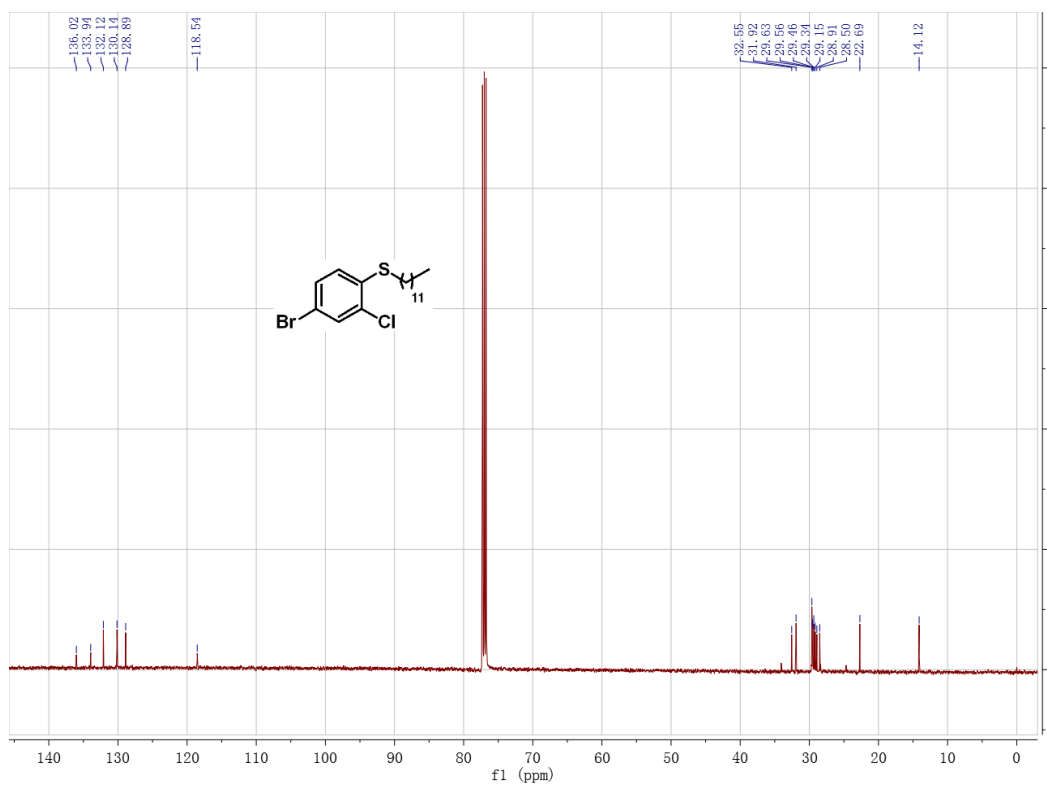
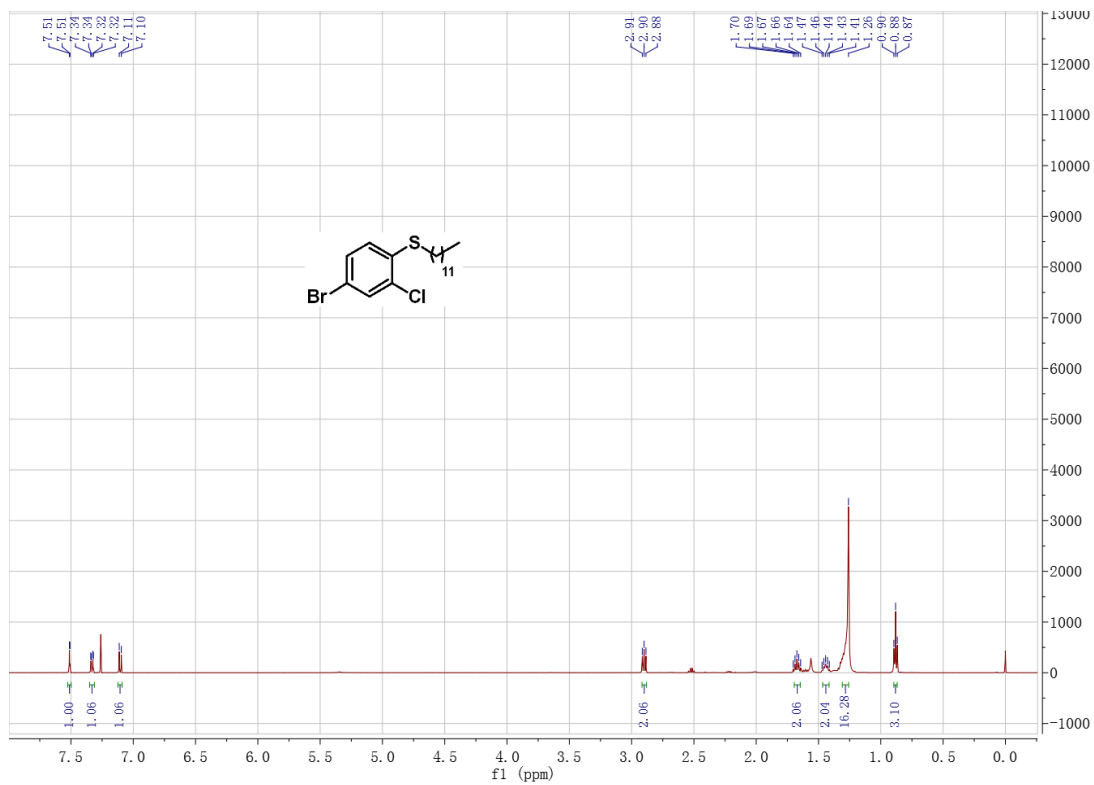
Compound **3fp**



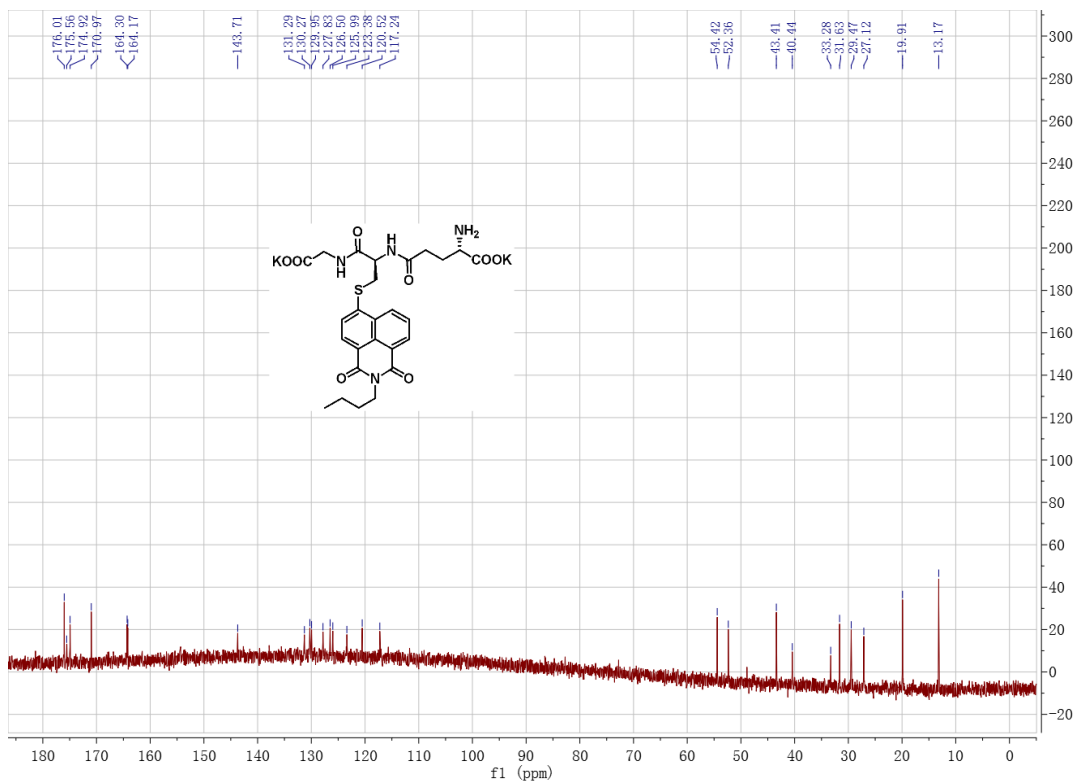
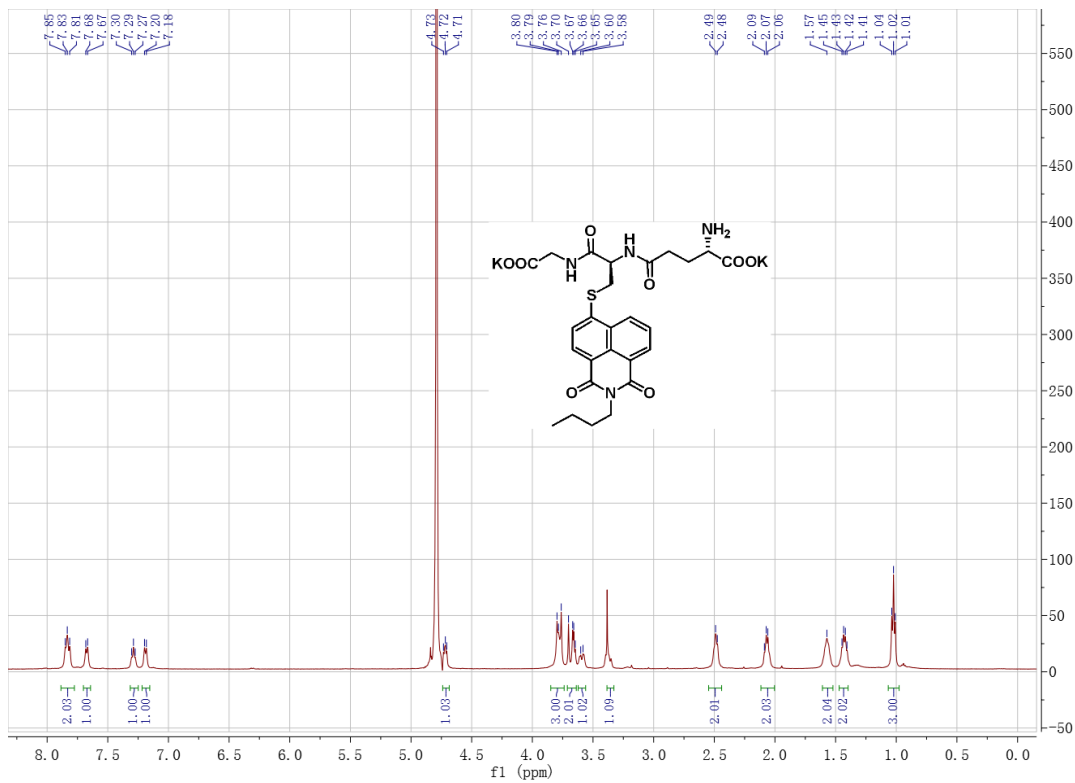
Compound 3gp



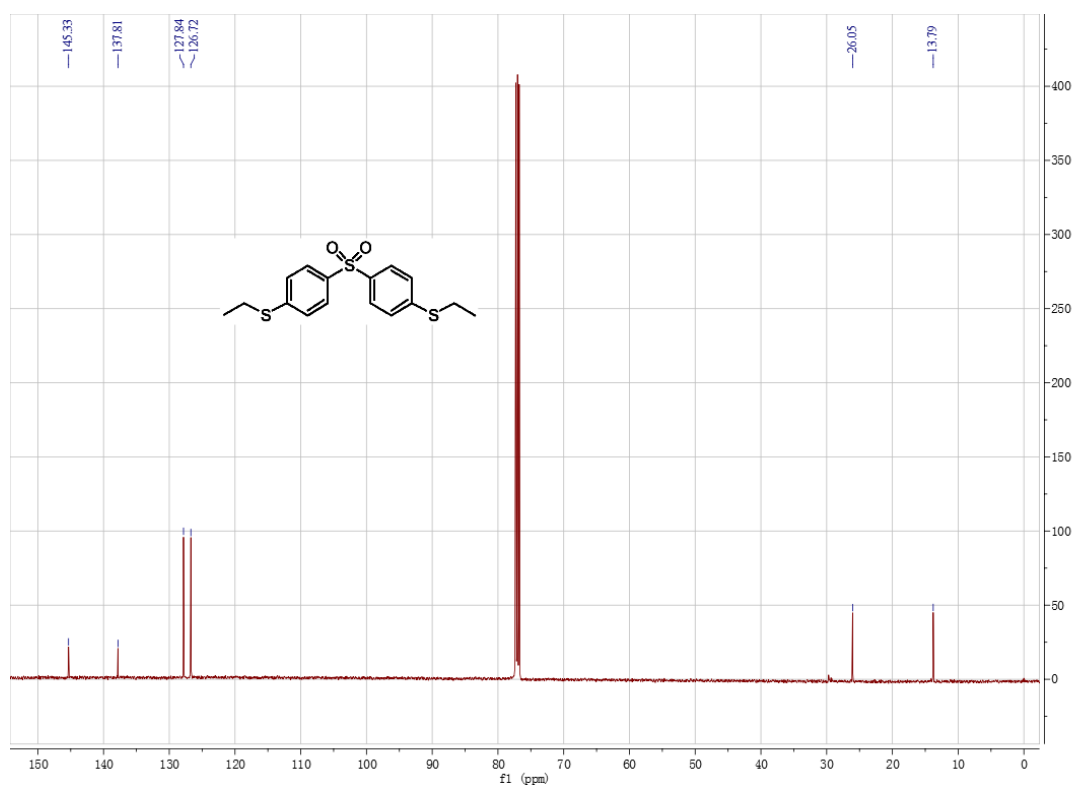
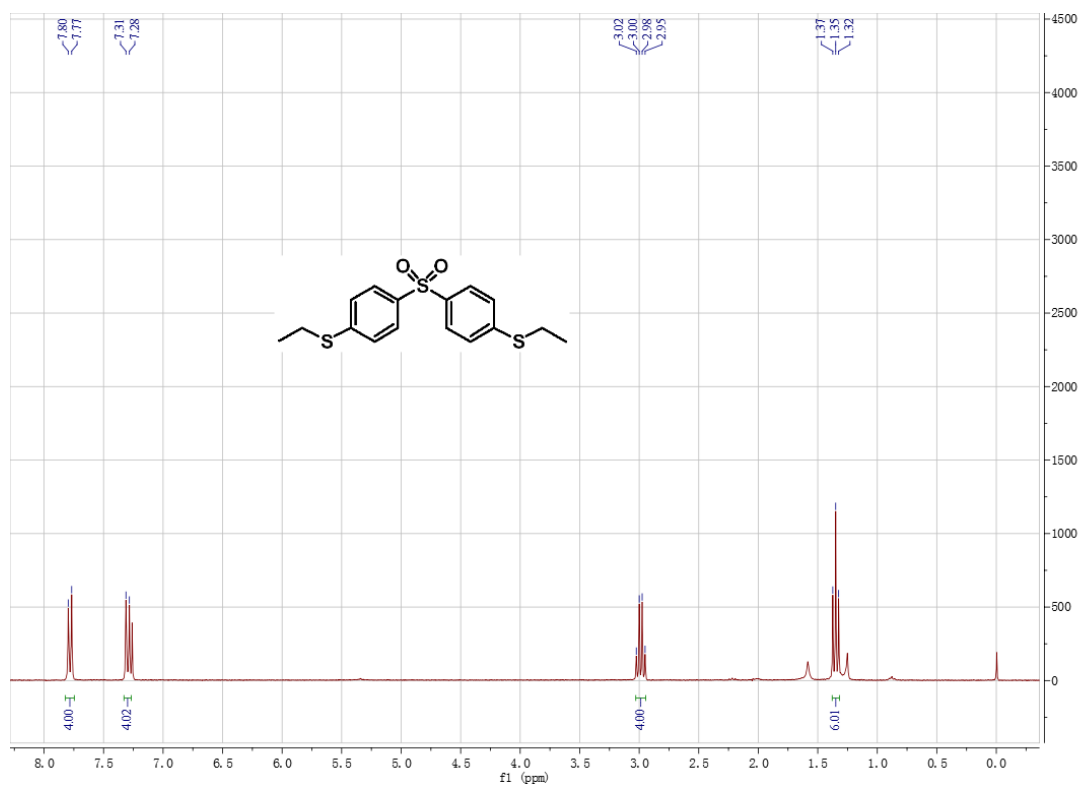
# Compound 3hp



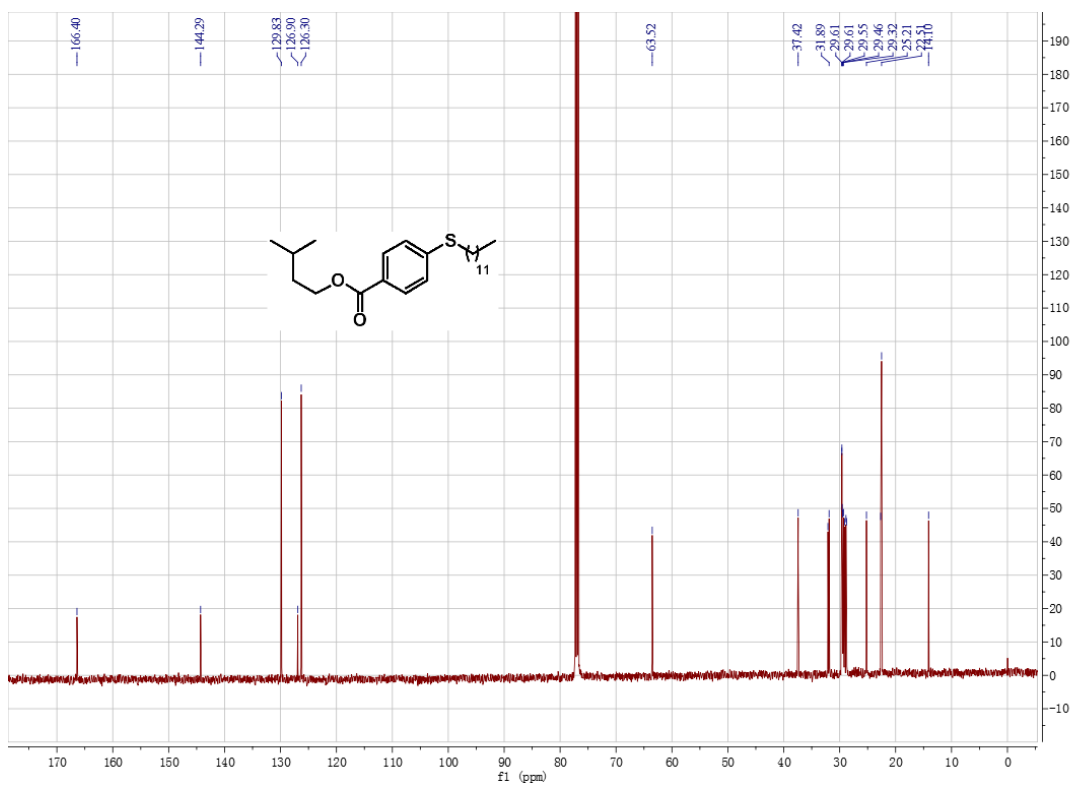
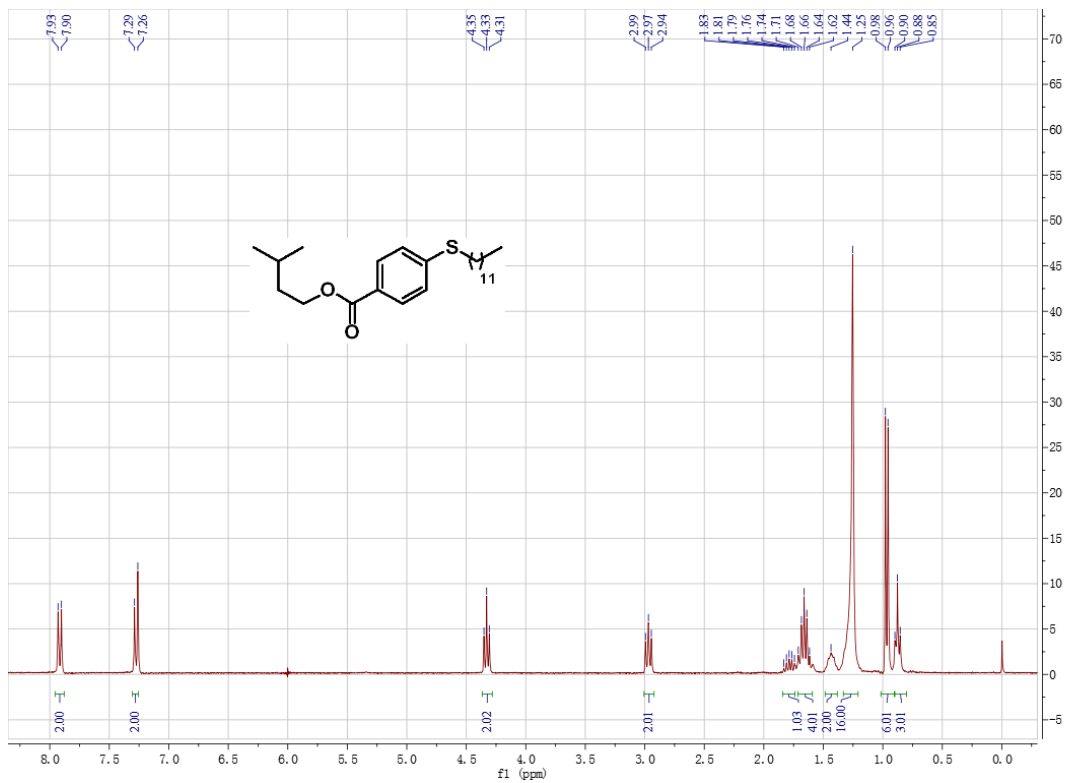
Compound **3ir**



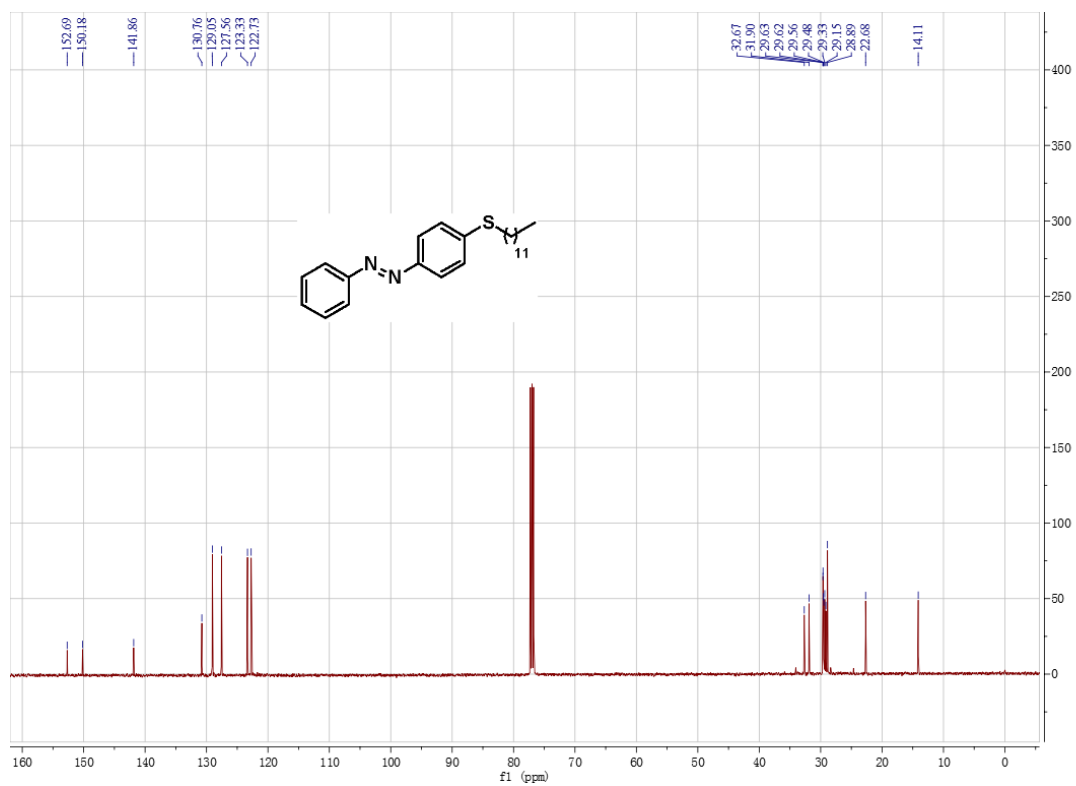
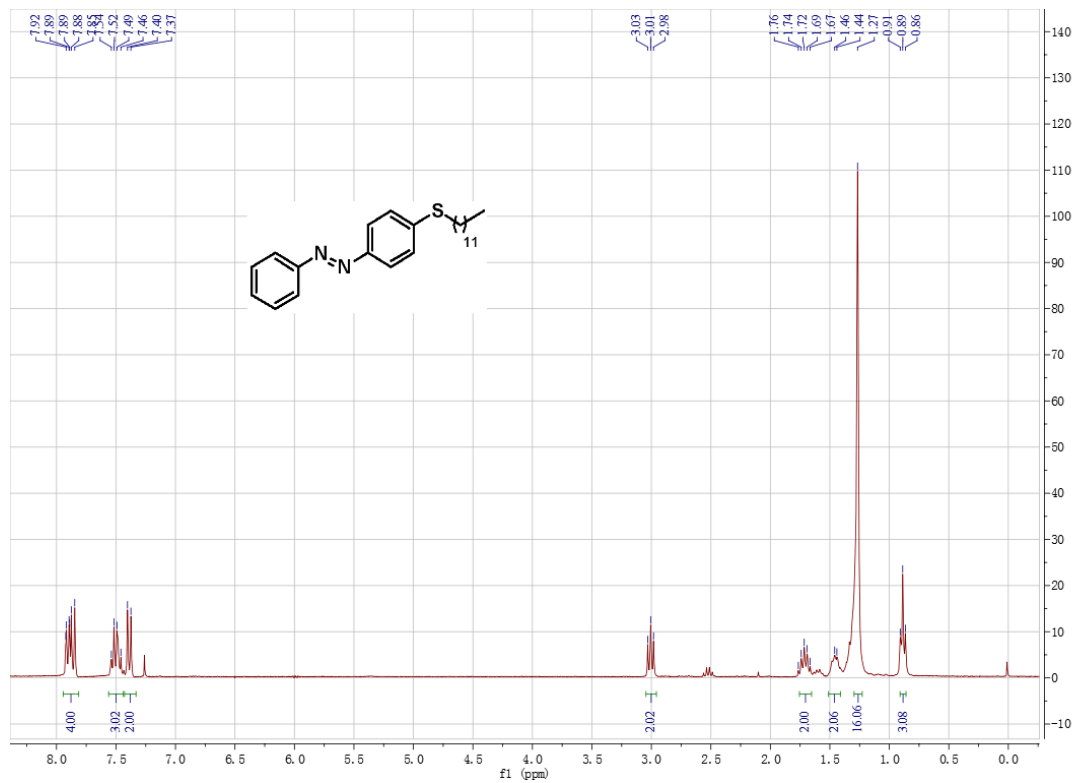
# Compound 3jq



Compound **3kp**

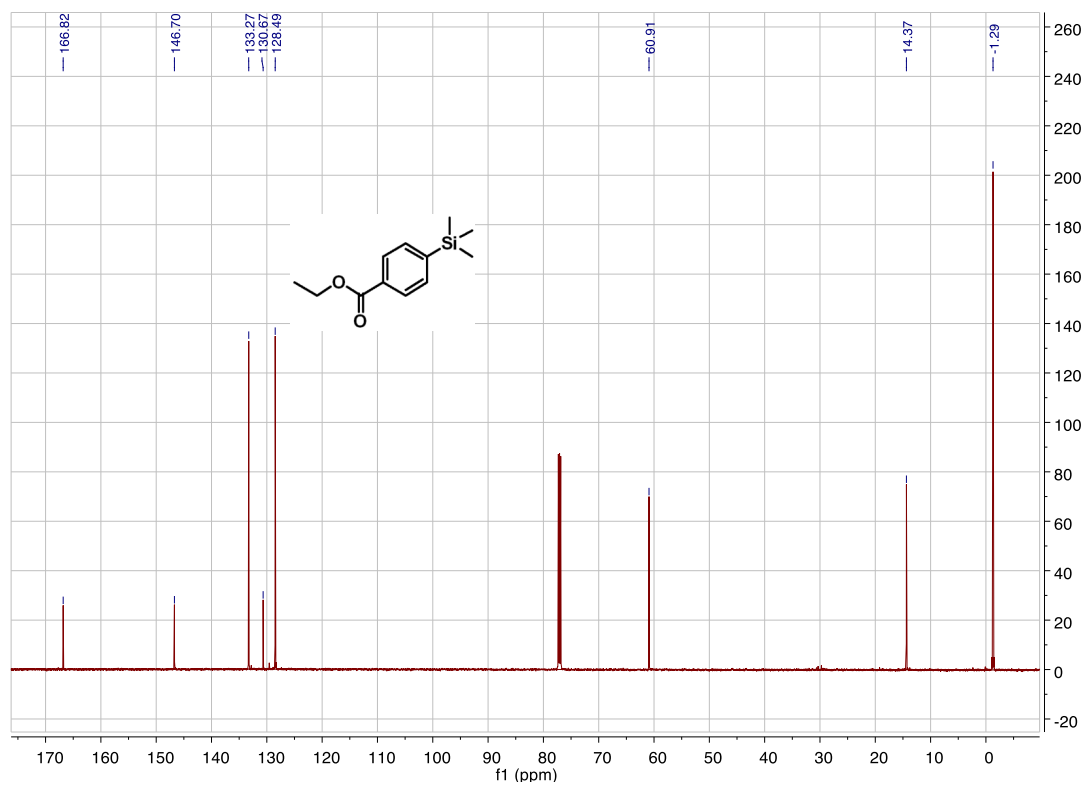
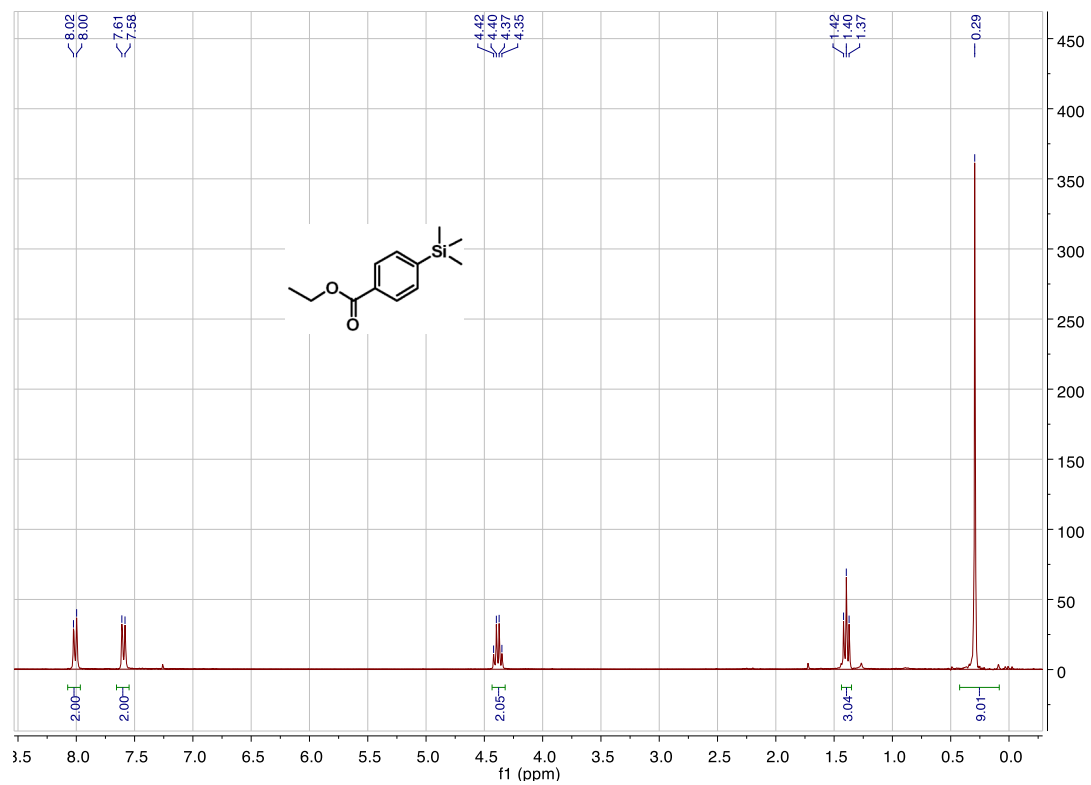


# Compound 3Ip

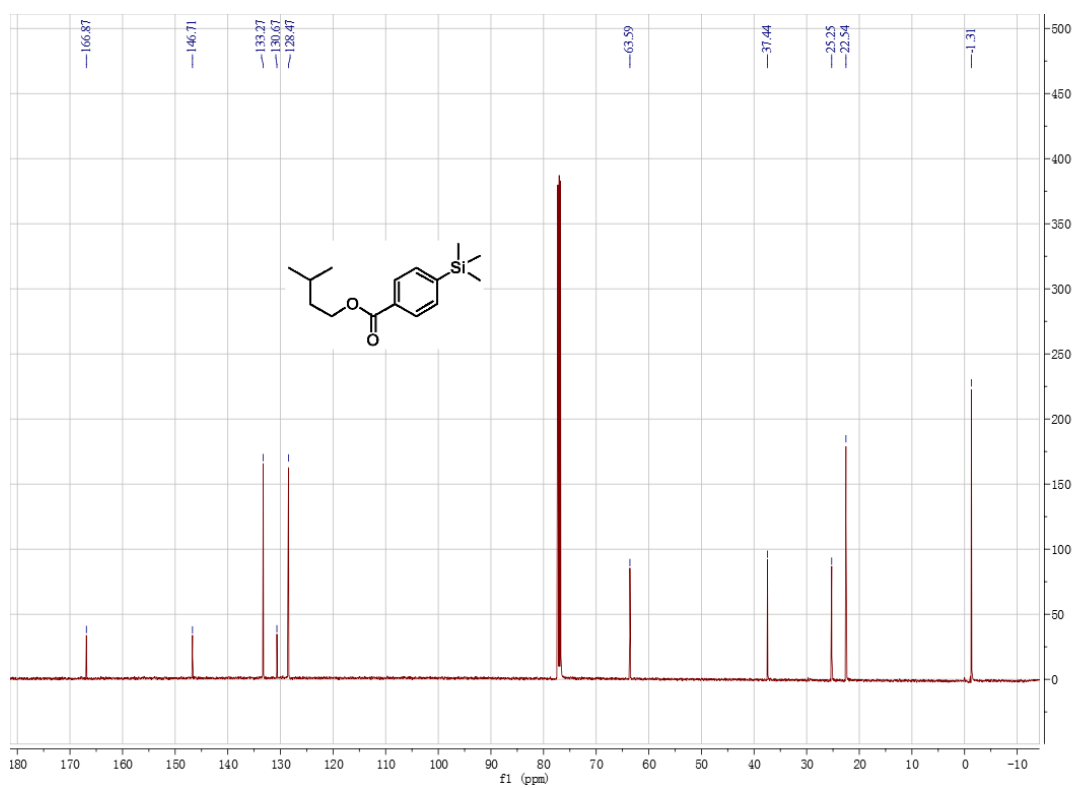
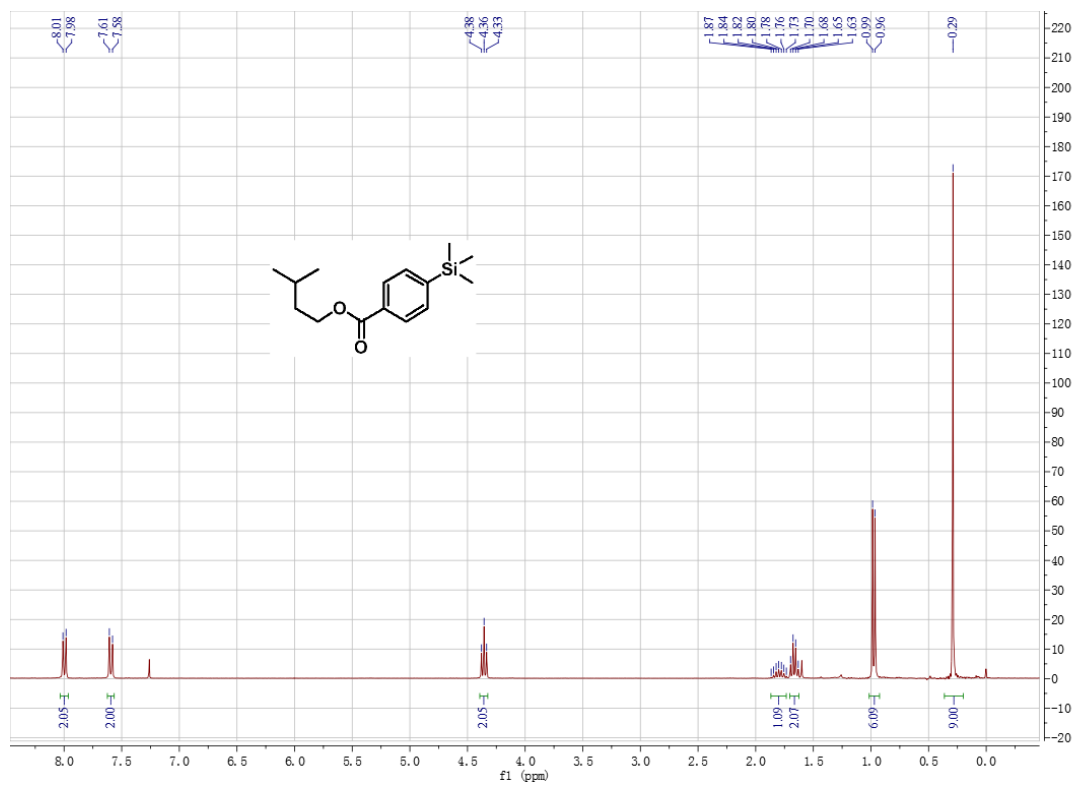




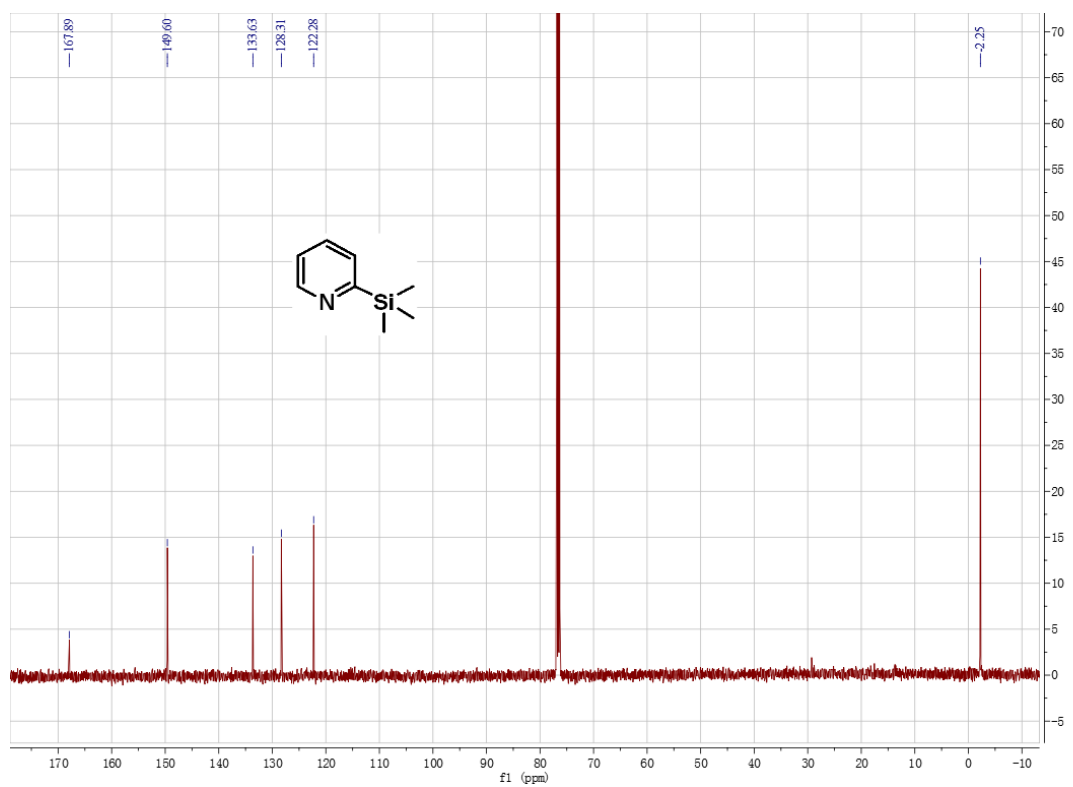
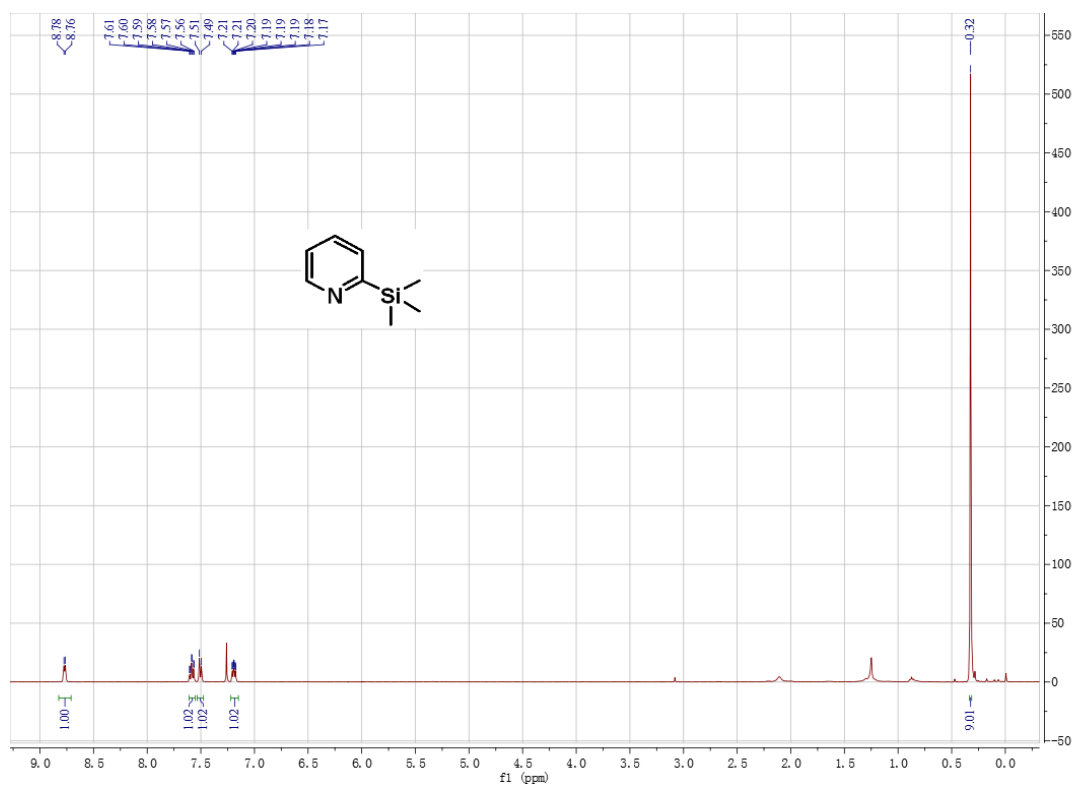
Compound 5a



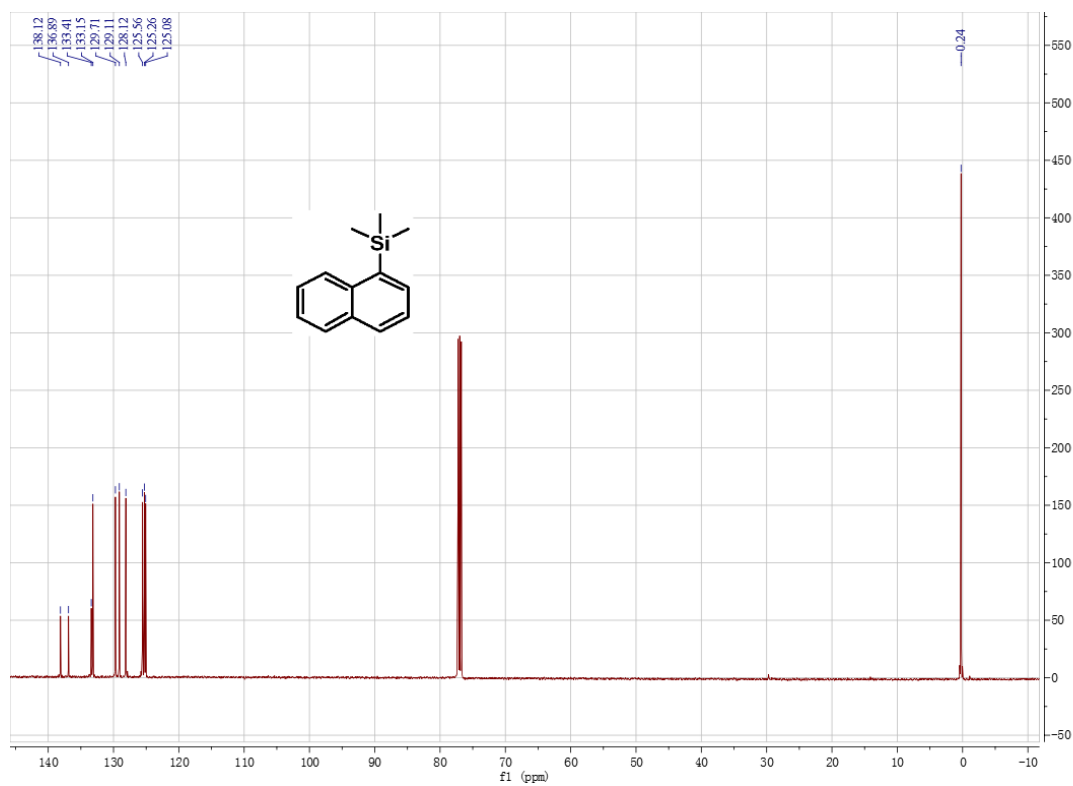
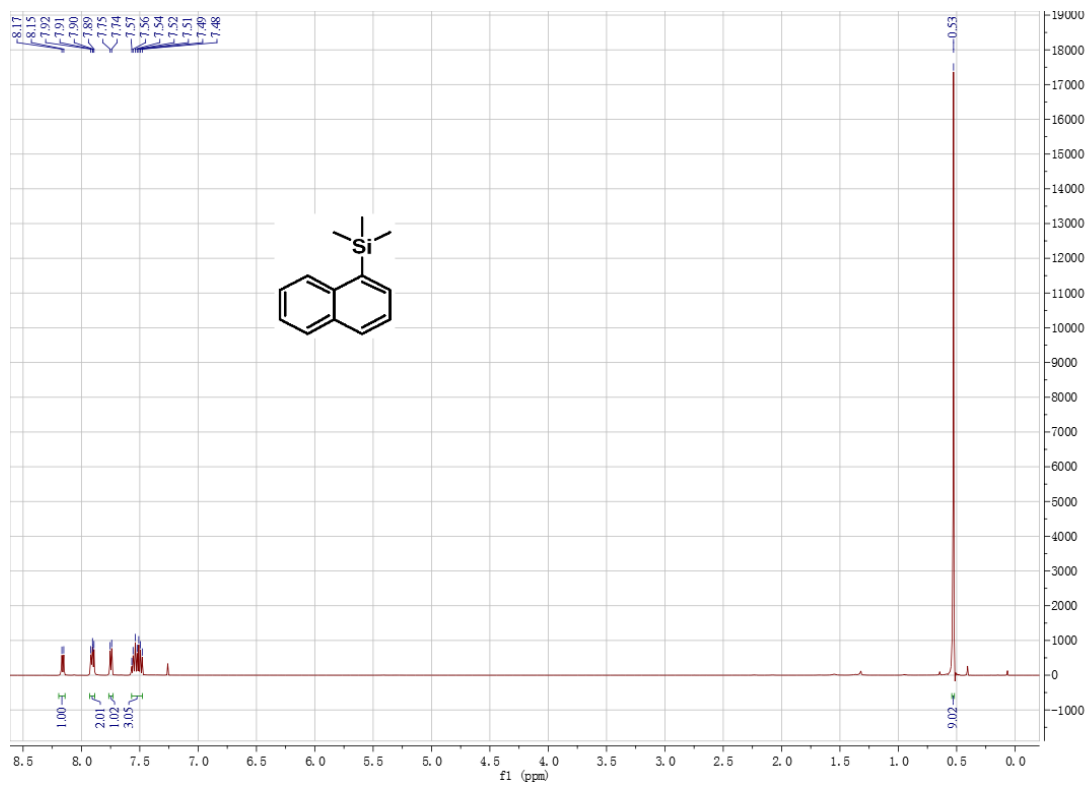
# Compound 5b



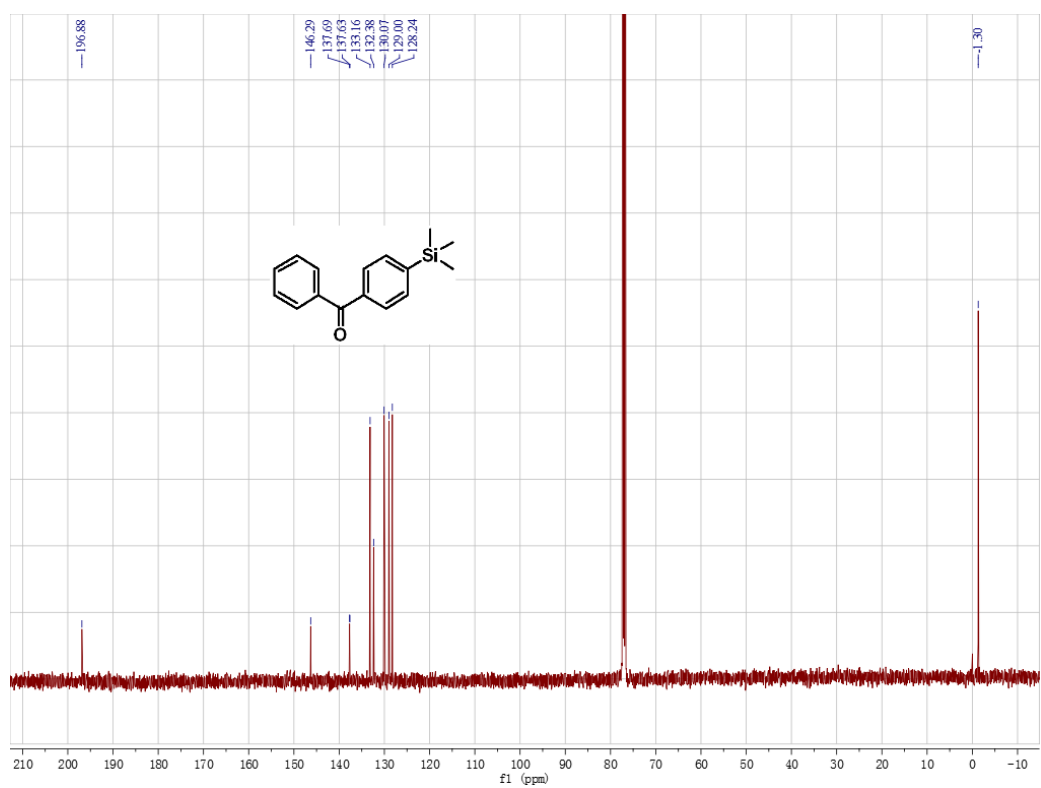
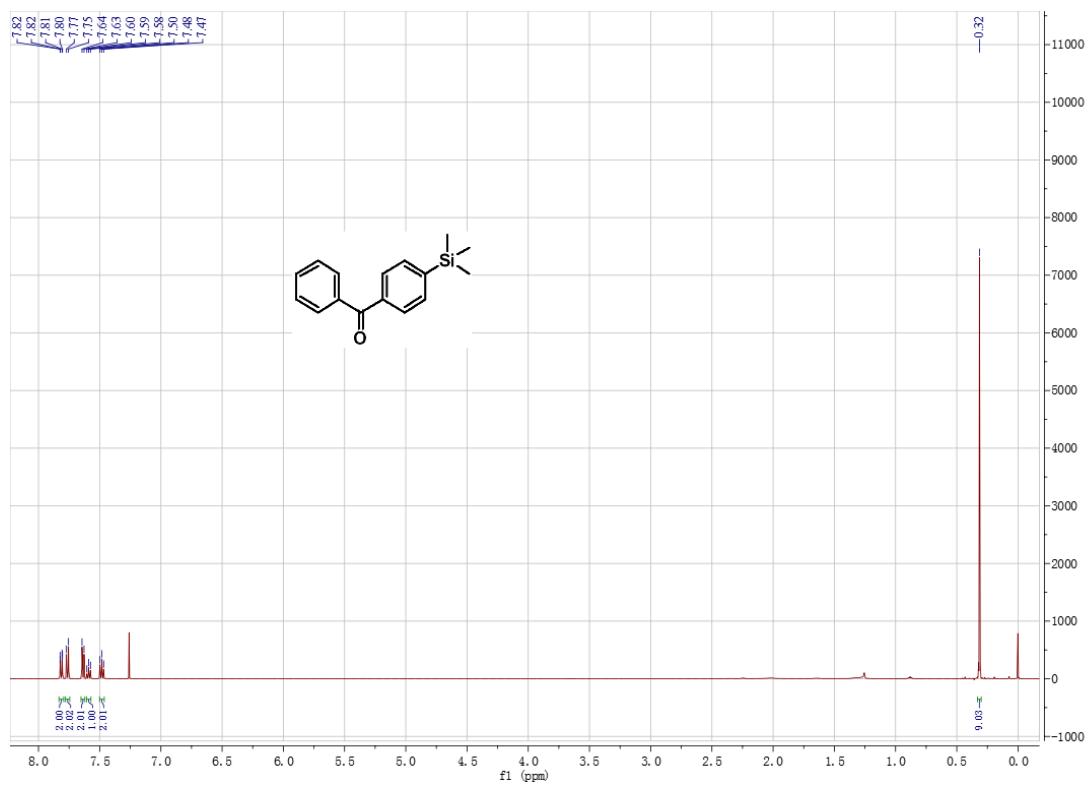
# Compound 5h



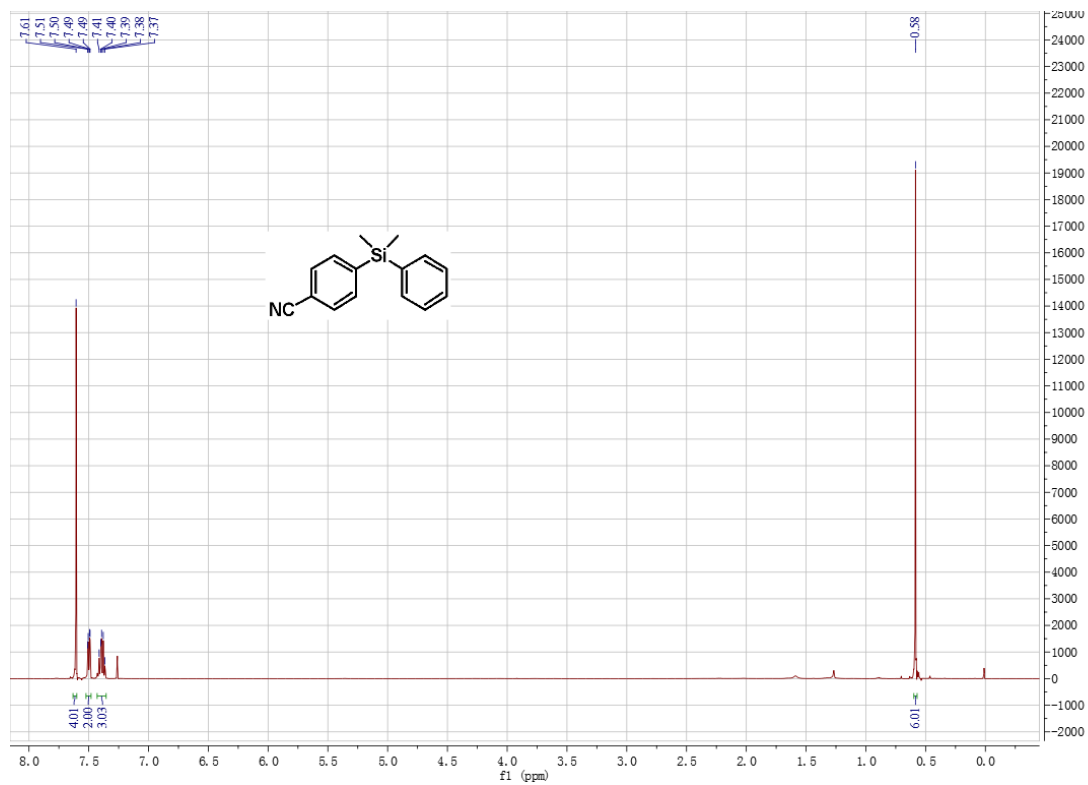
Compound 5g



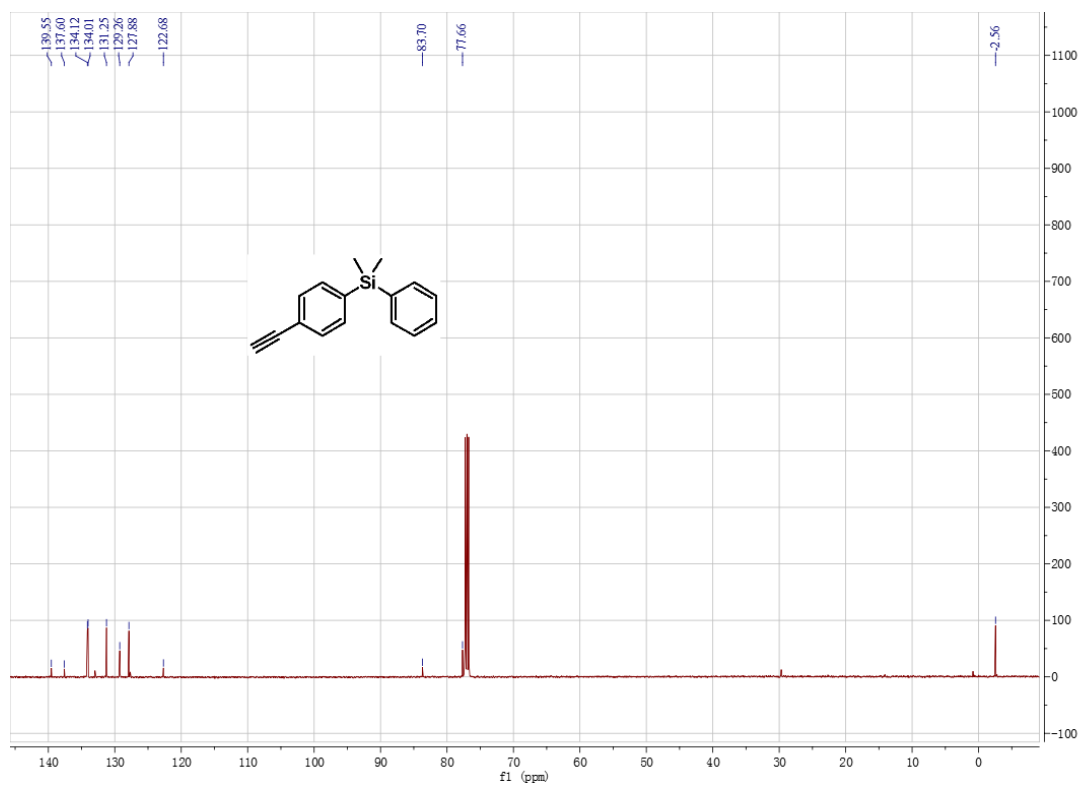
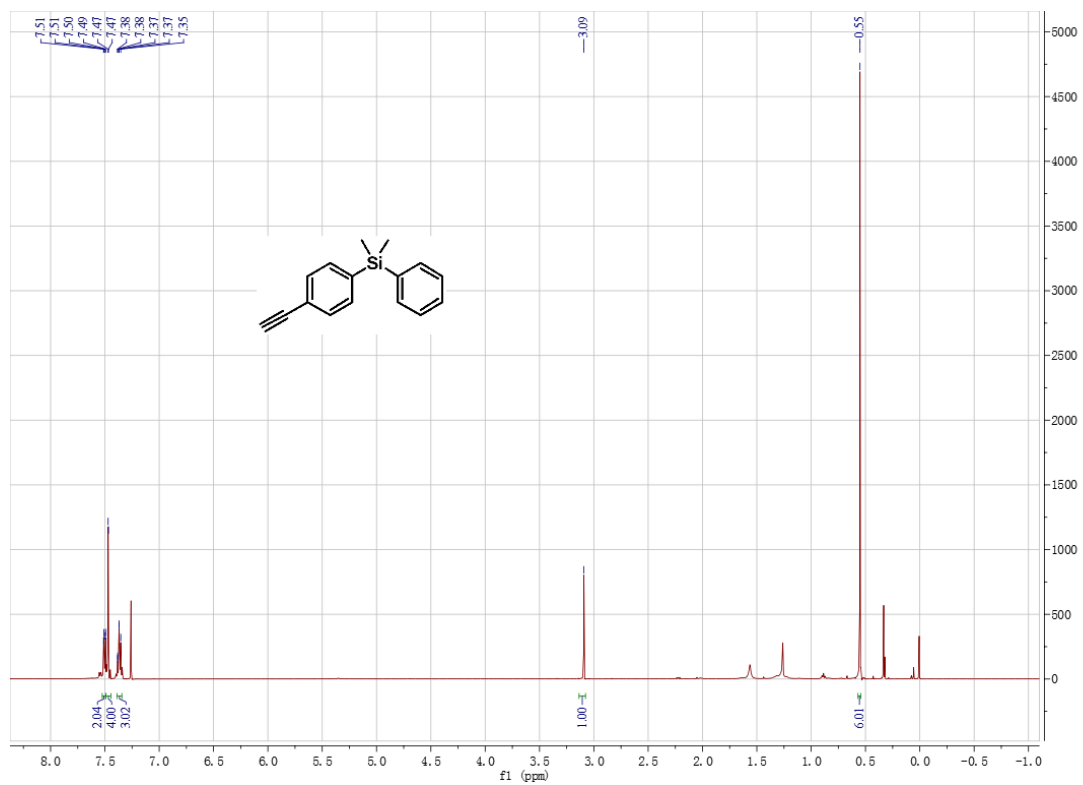
# Compound 5f



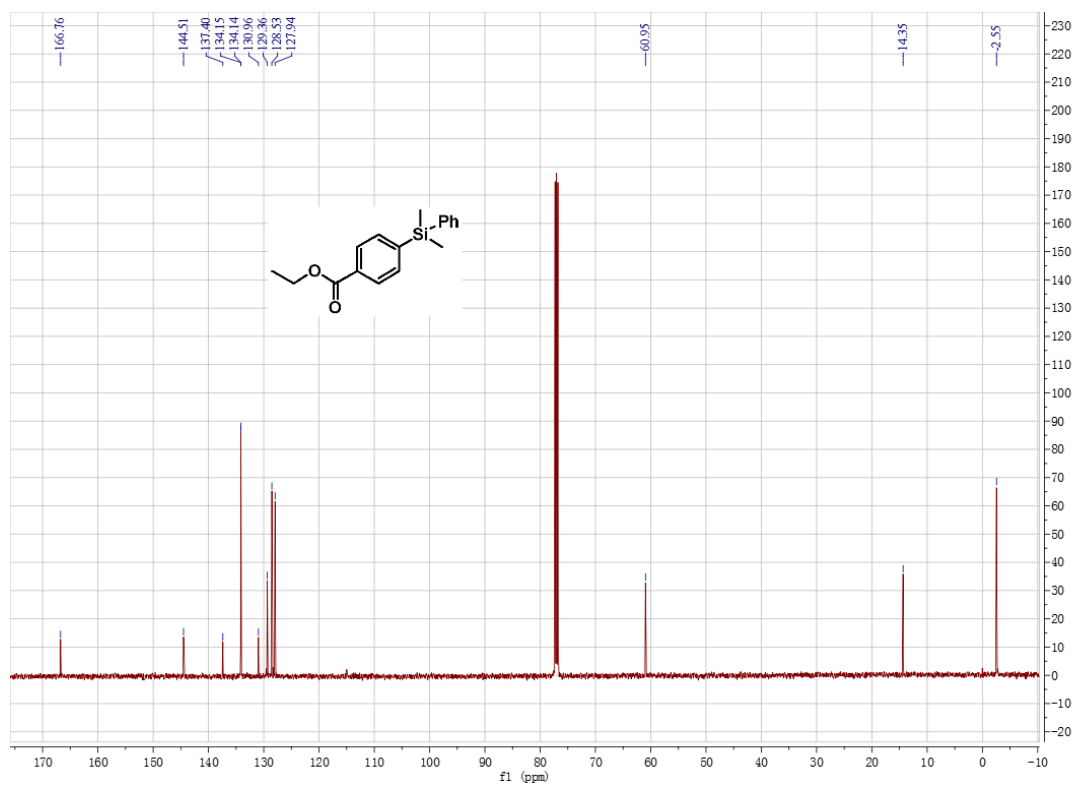
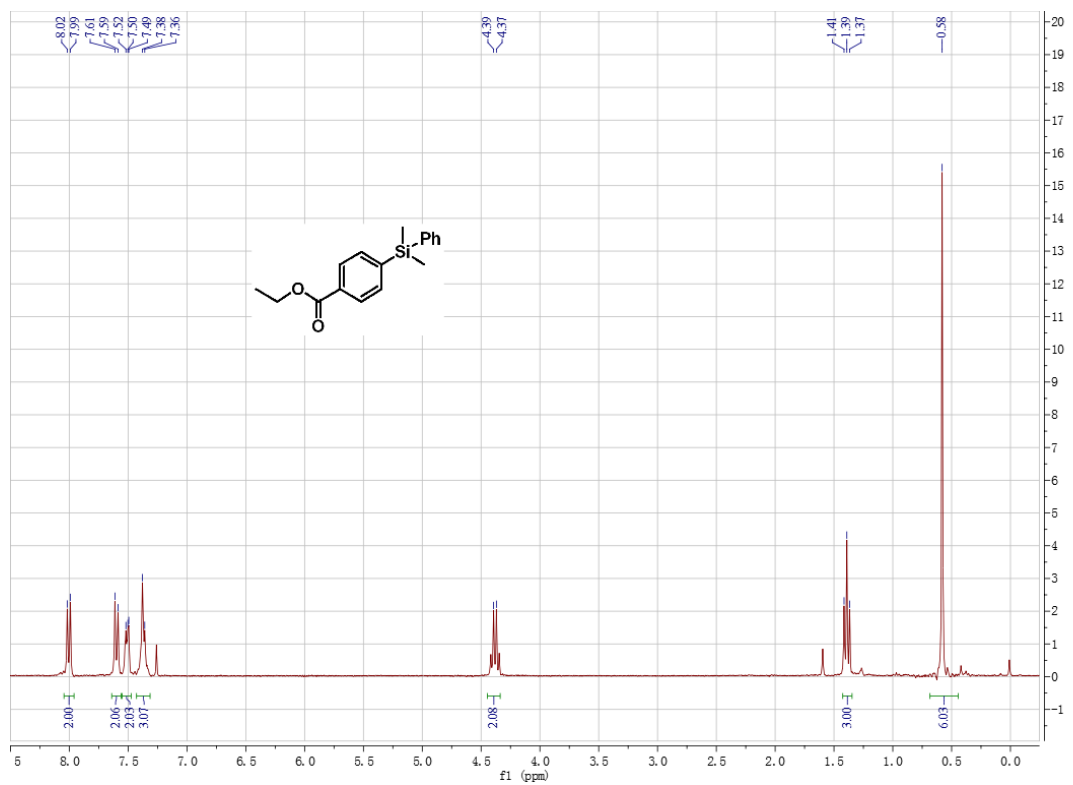
# Compound 5c



Compound **5d**

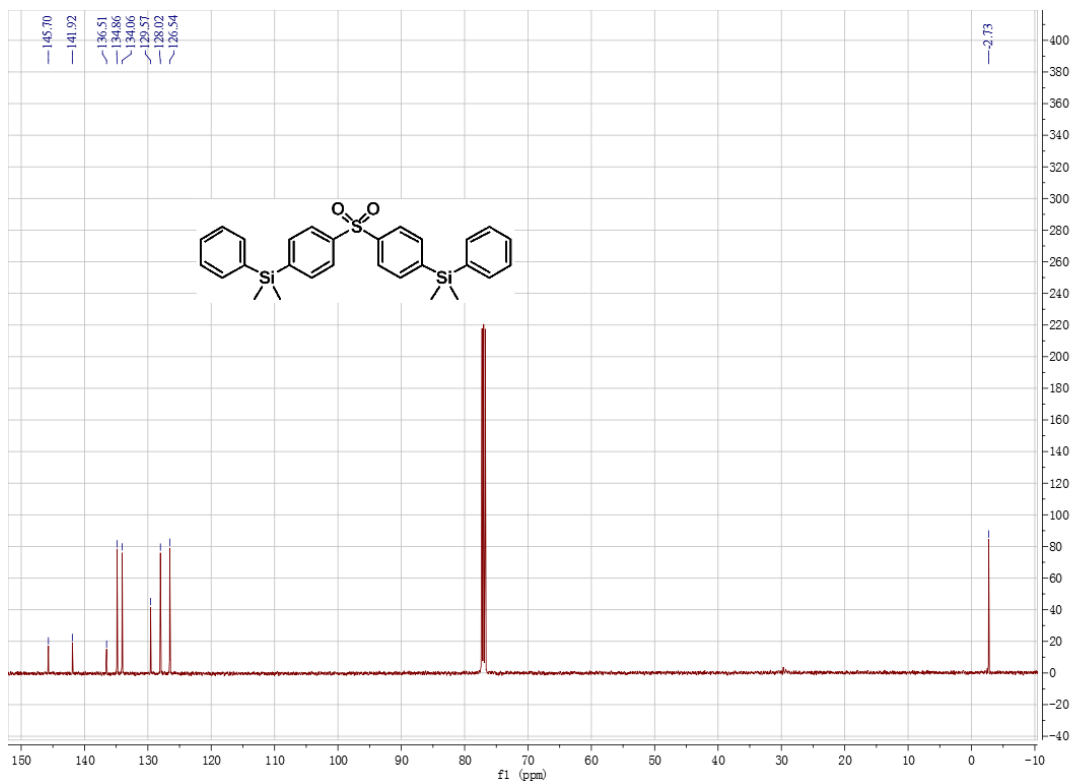
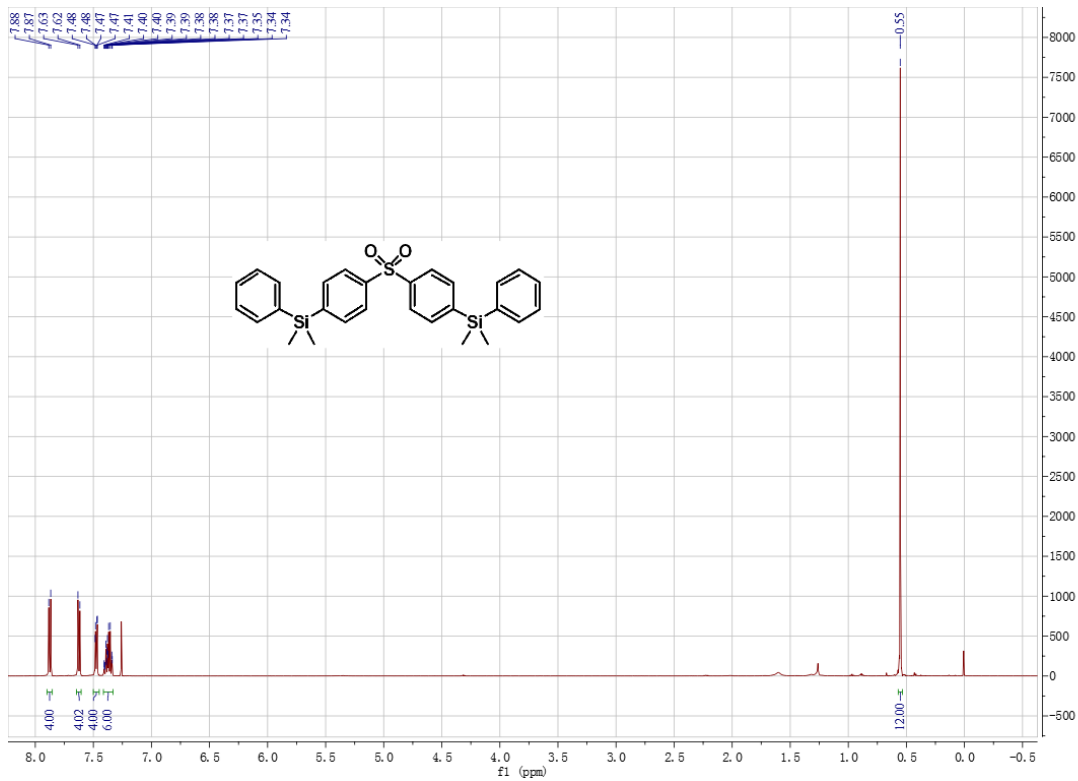


# Compound 5e

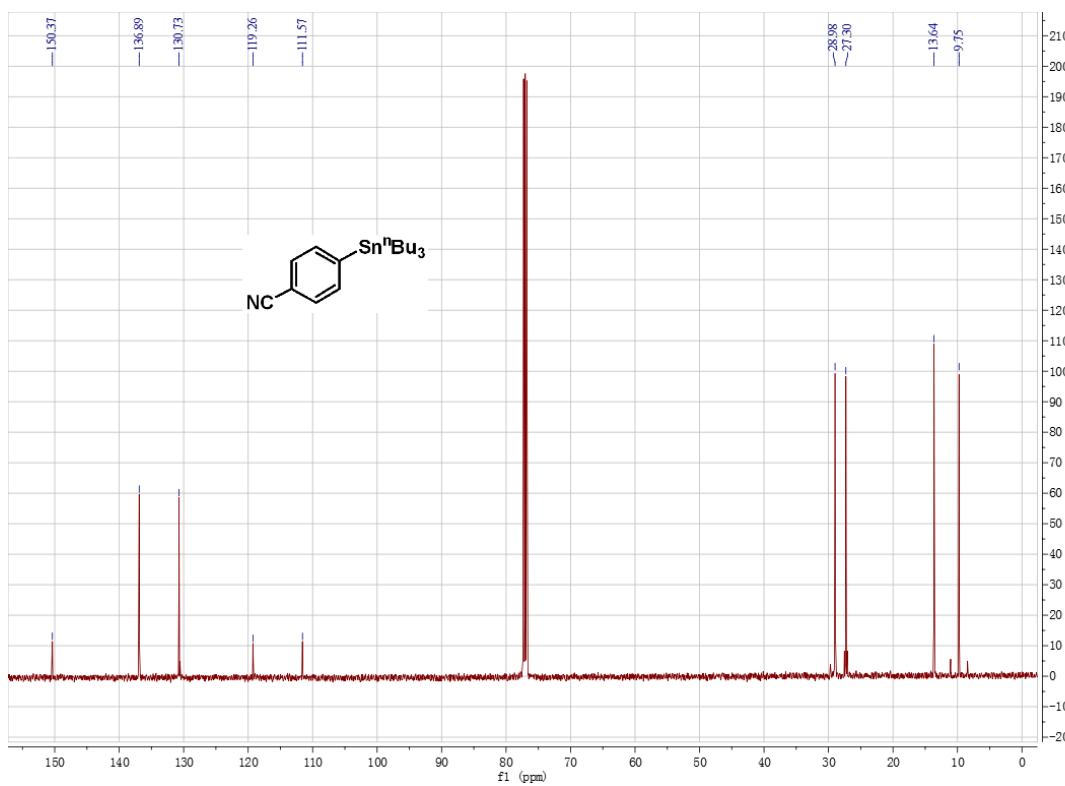
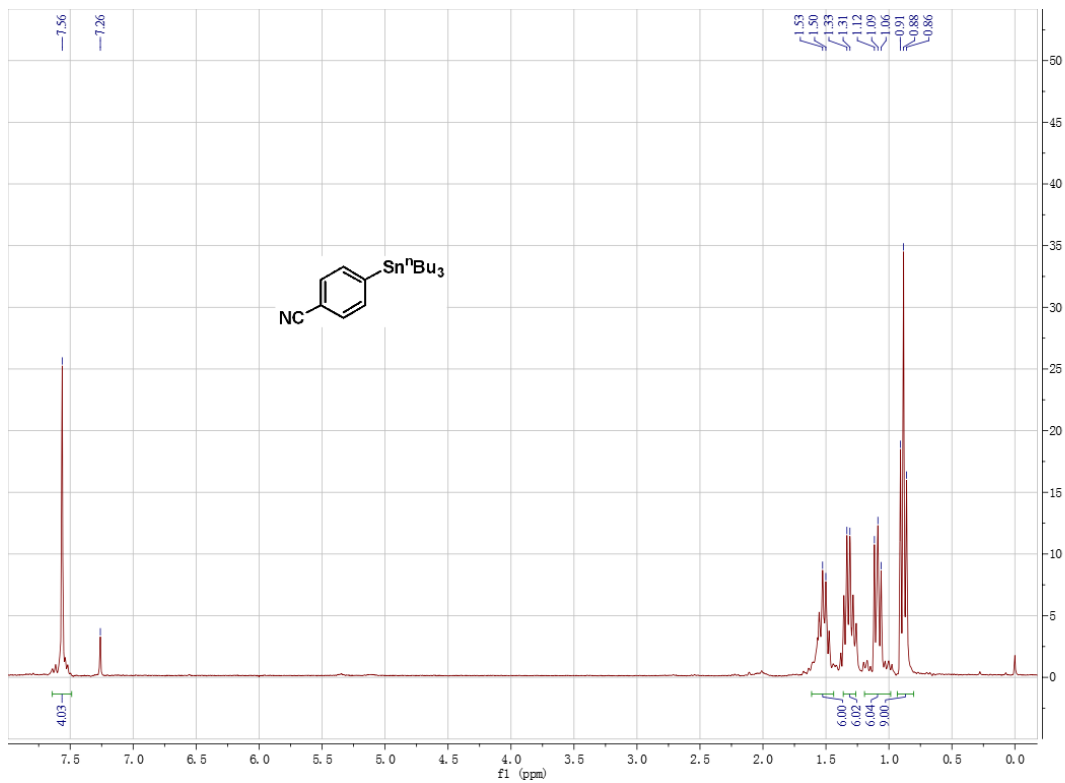




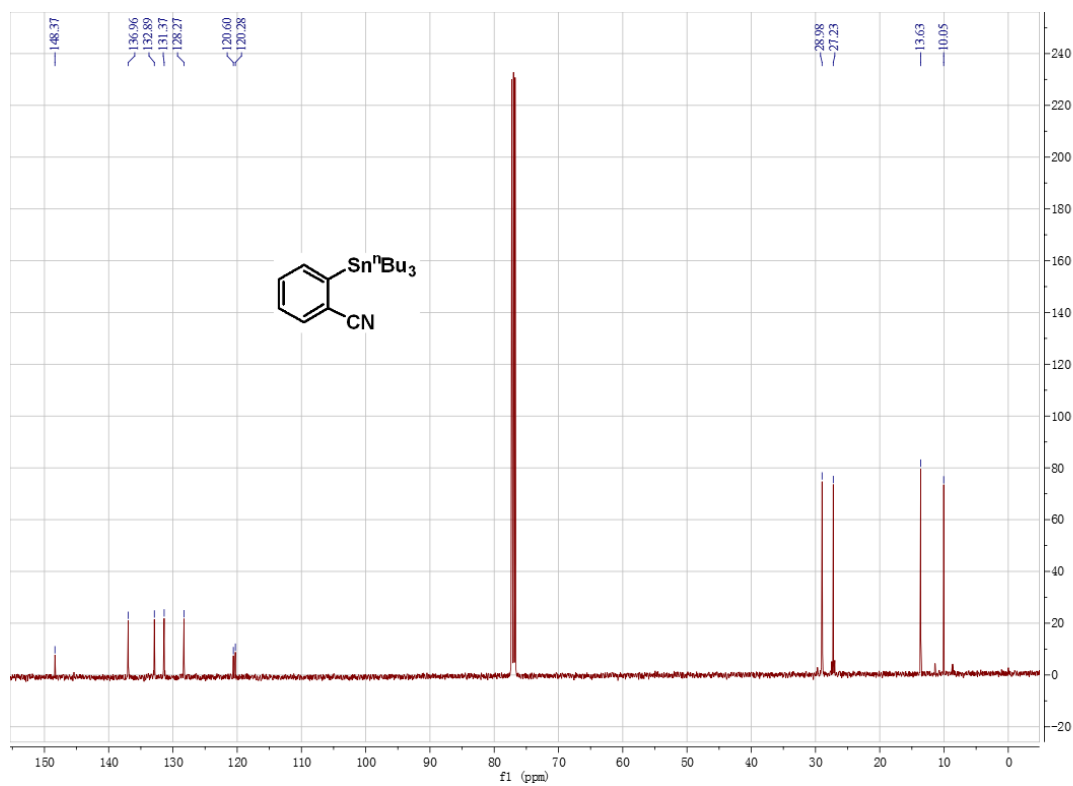
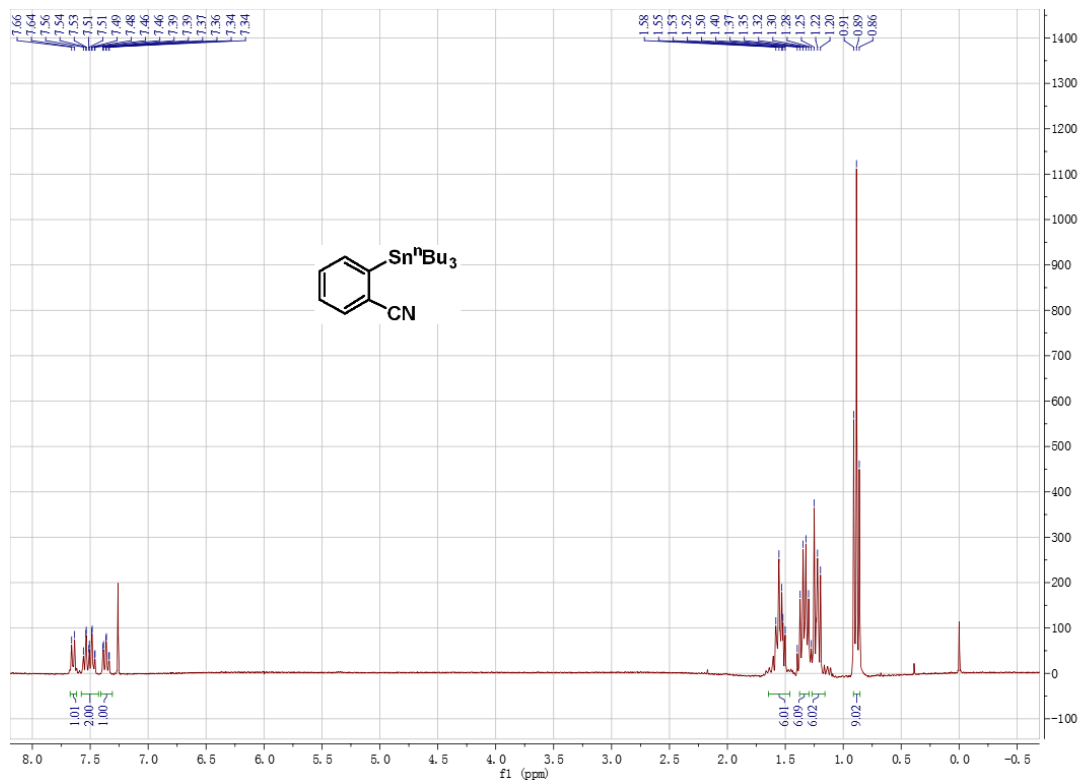
Compound 5i



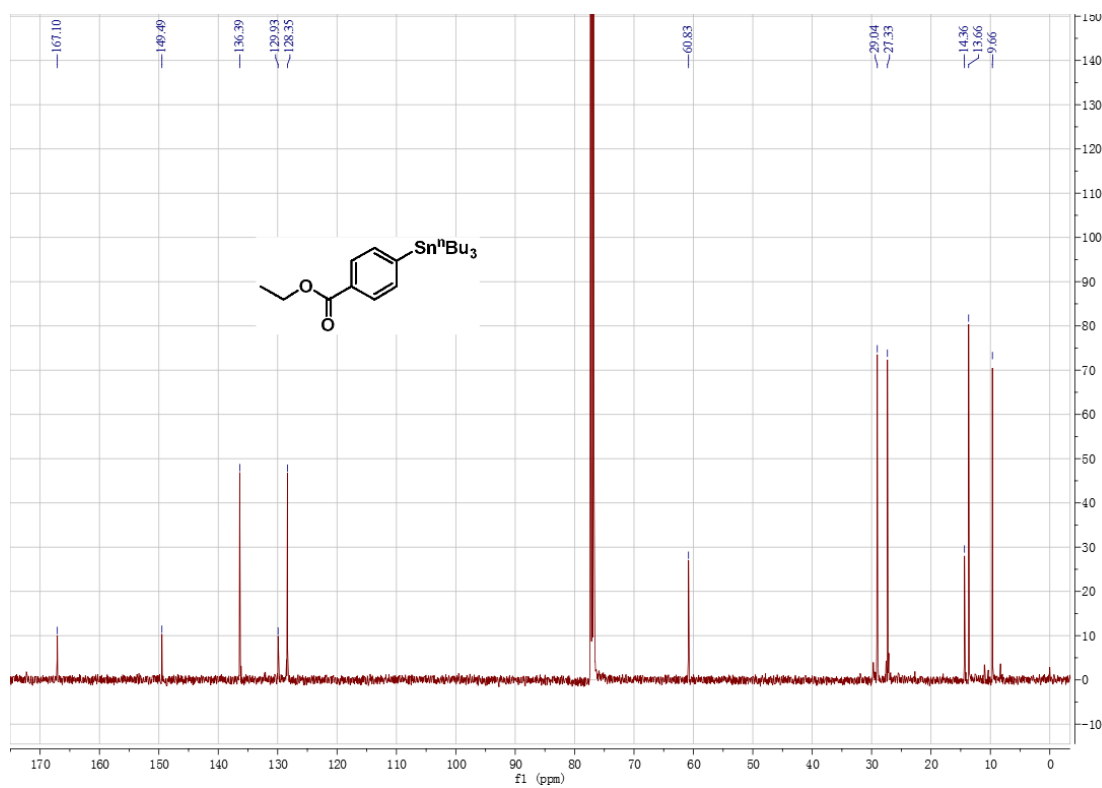
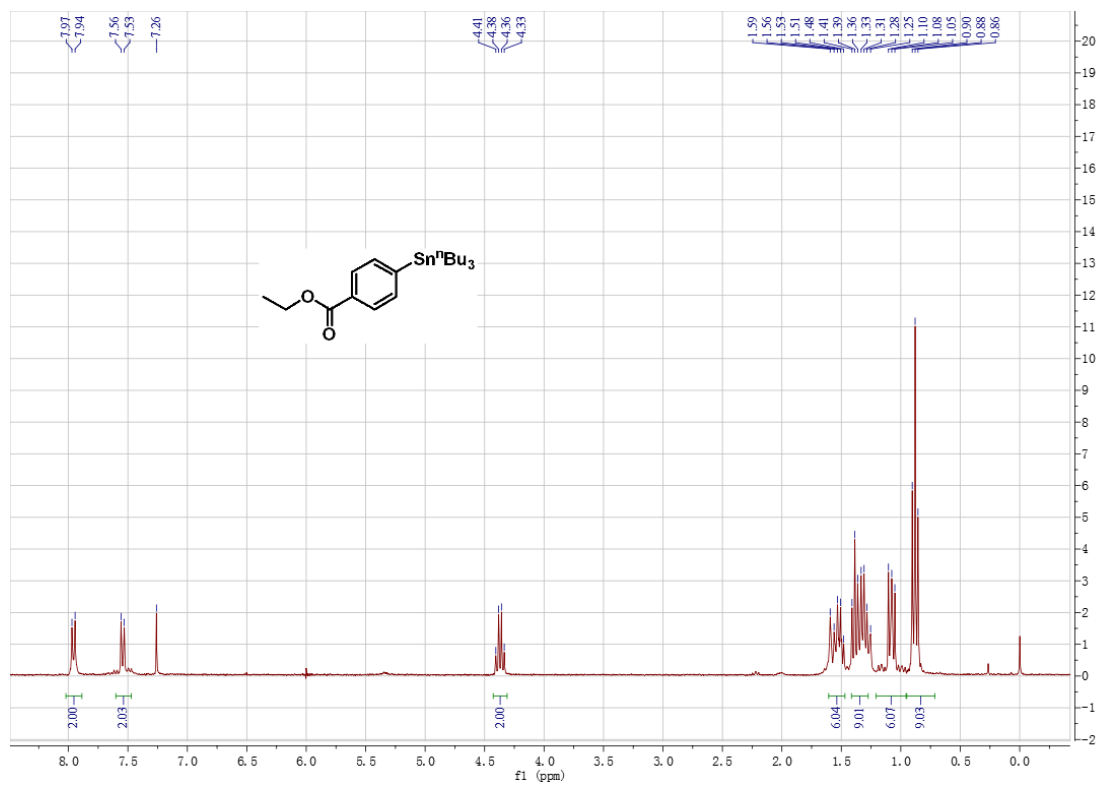
# Compound 7a



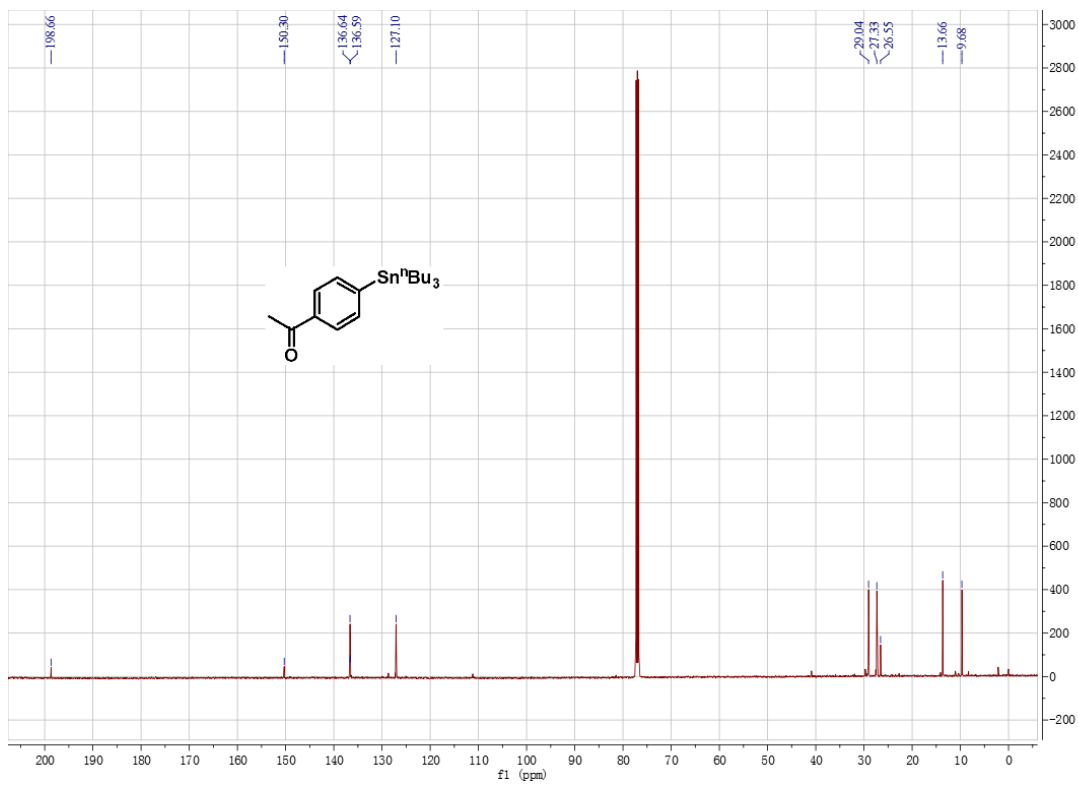
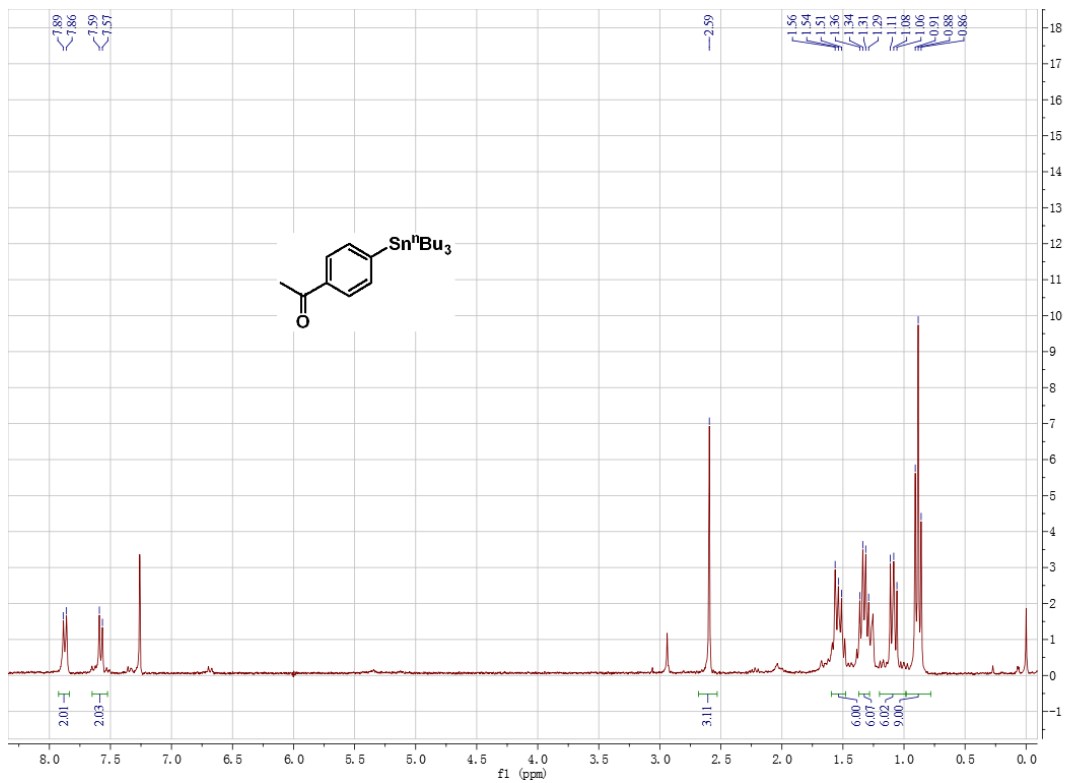
Compound 7c



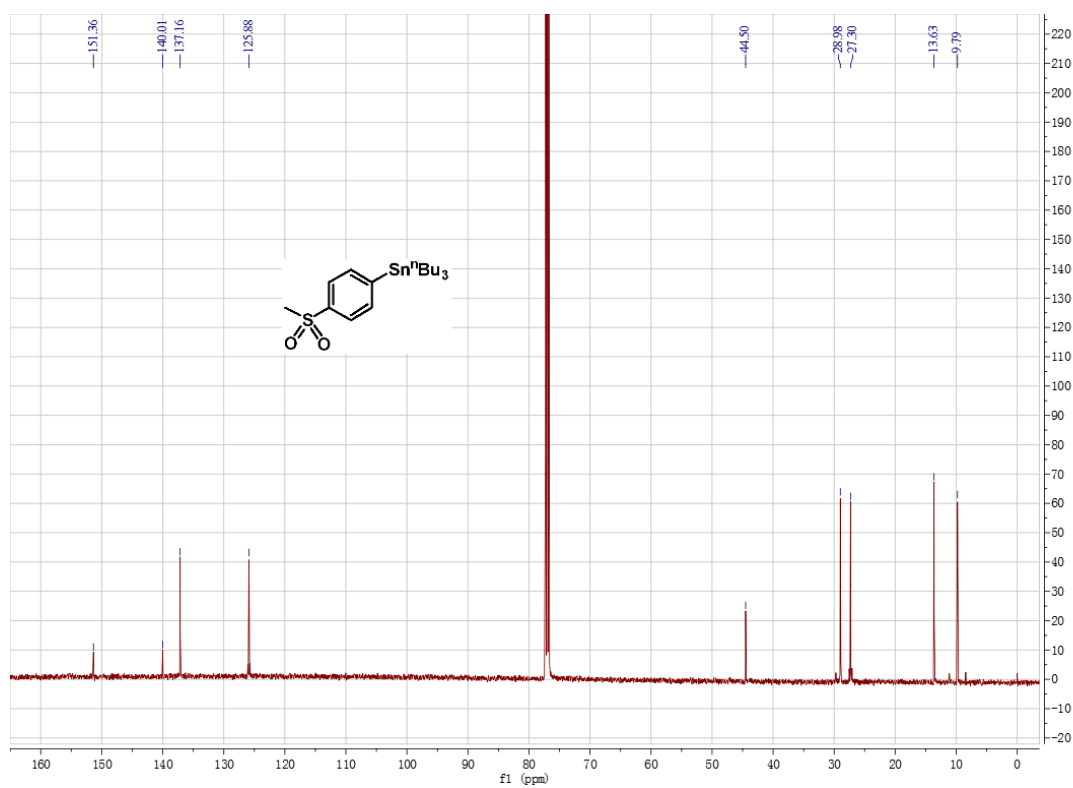
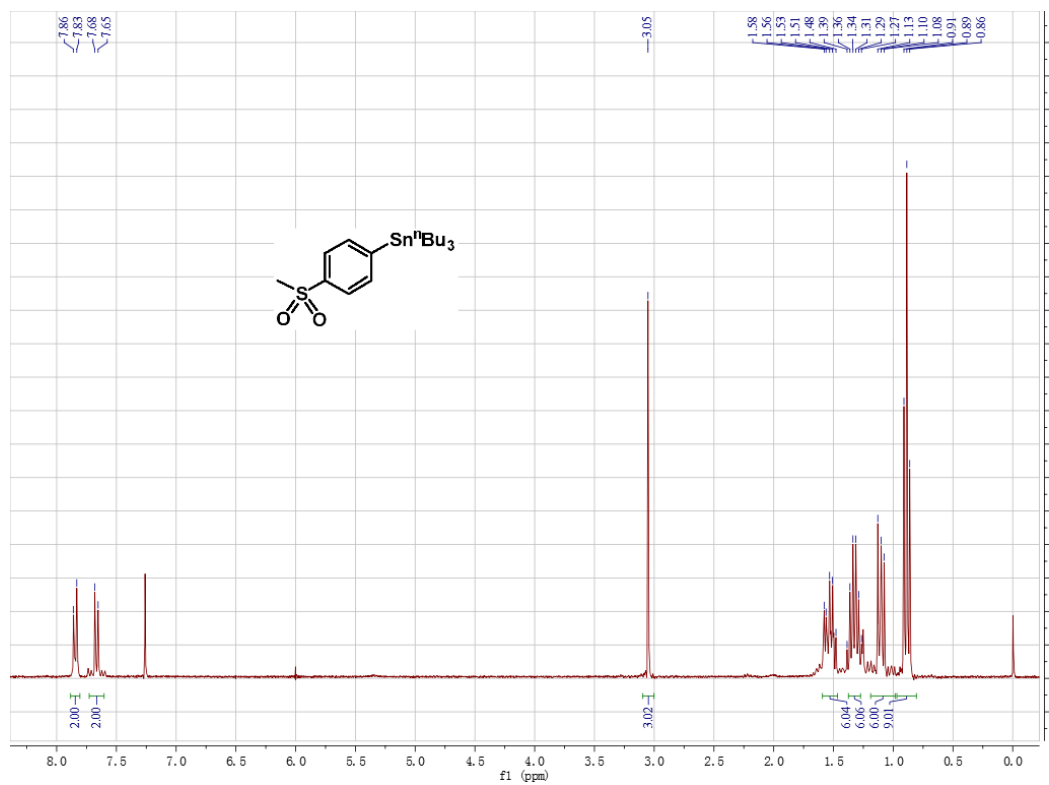
# Compound 7f



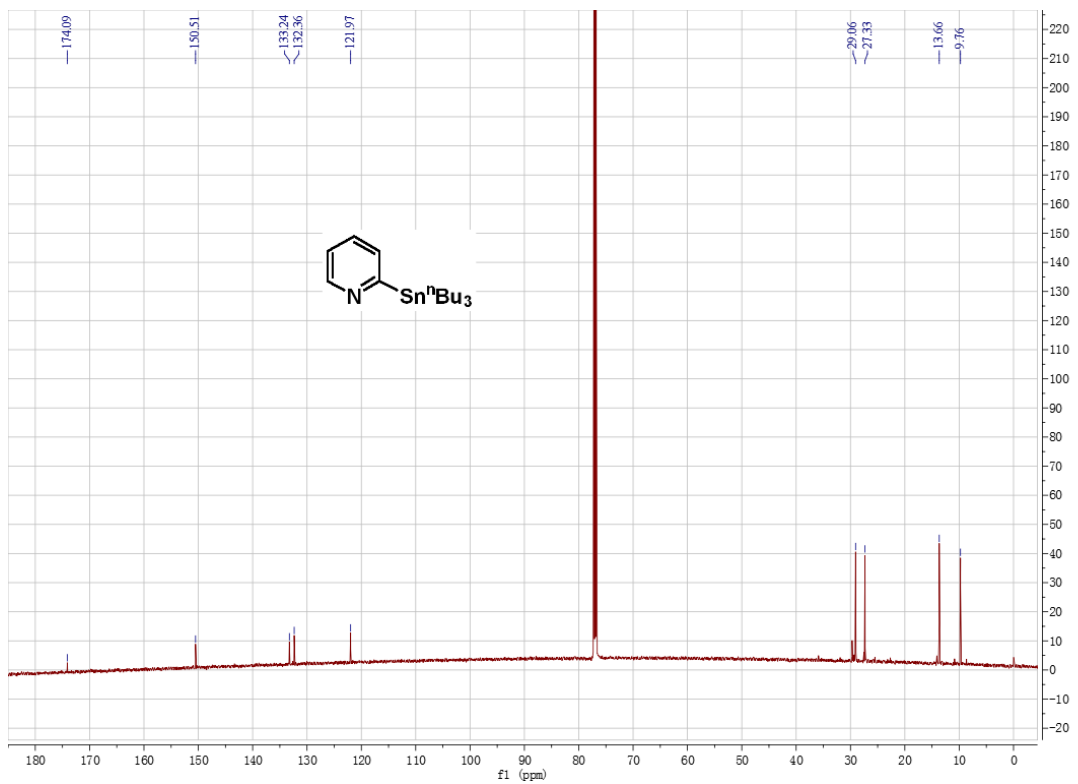
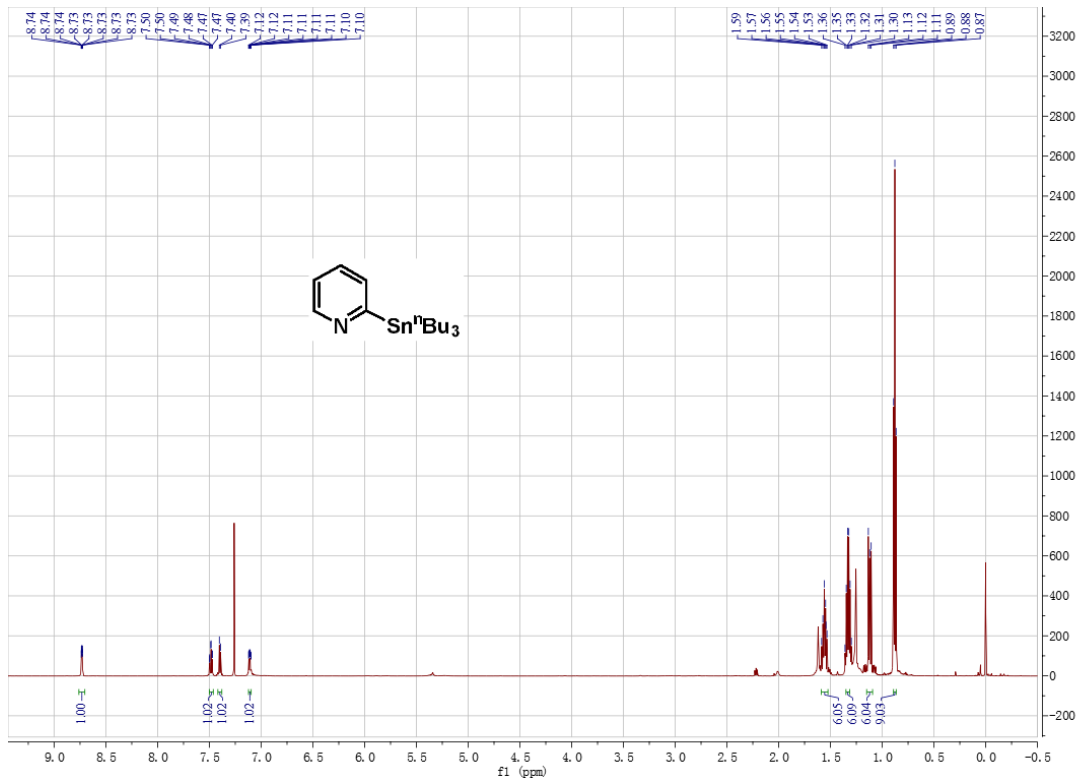
Compound 7e



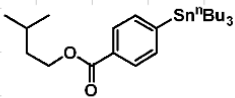
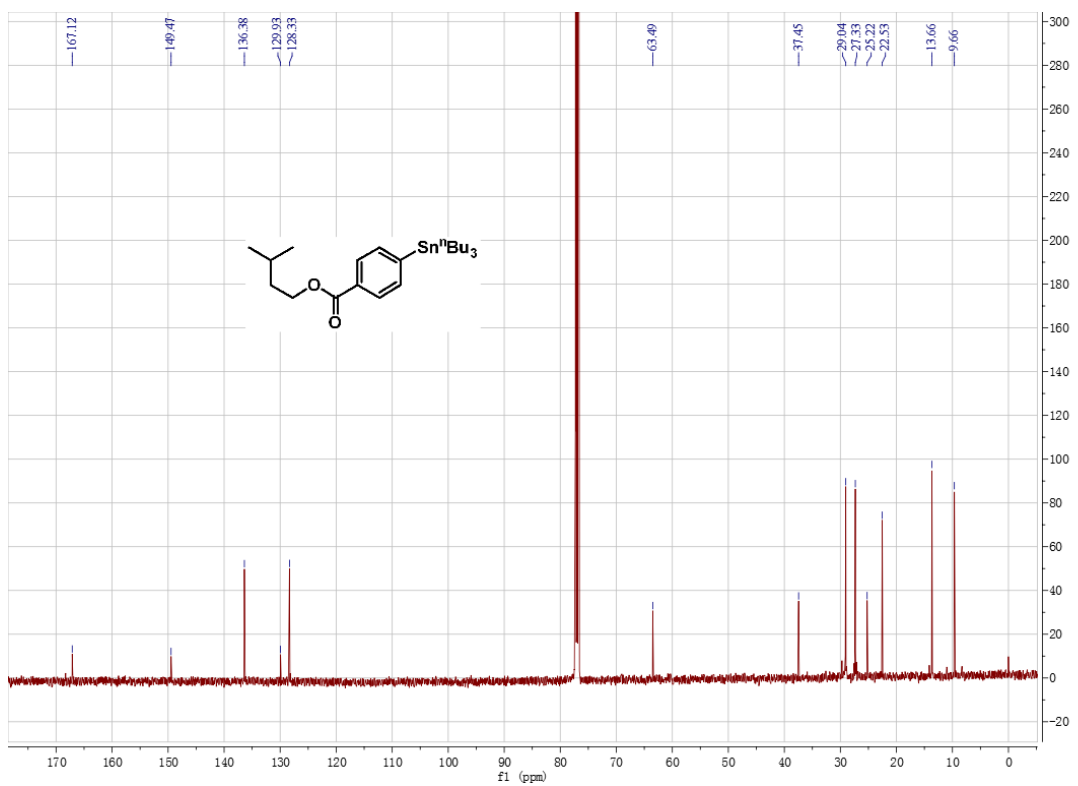
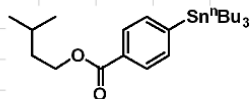
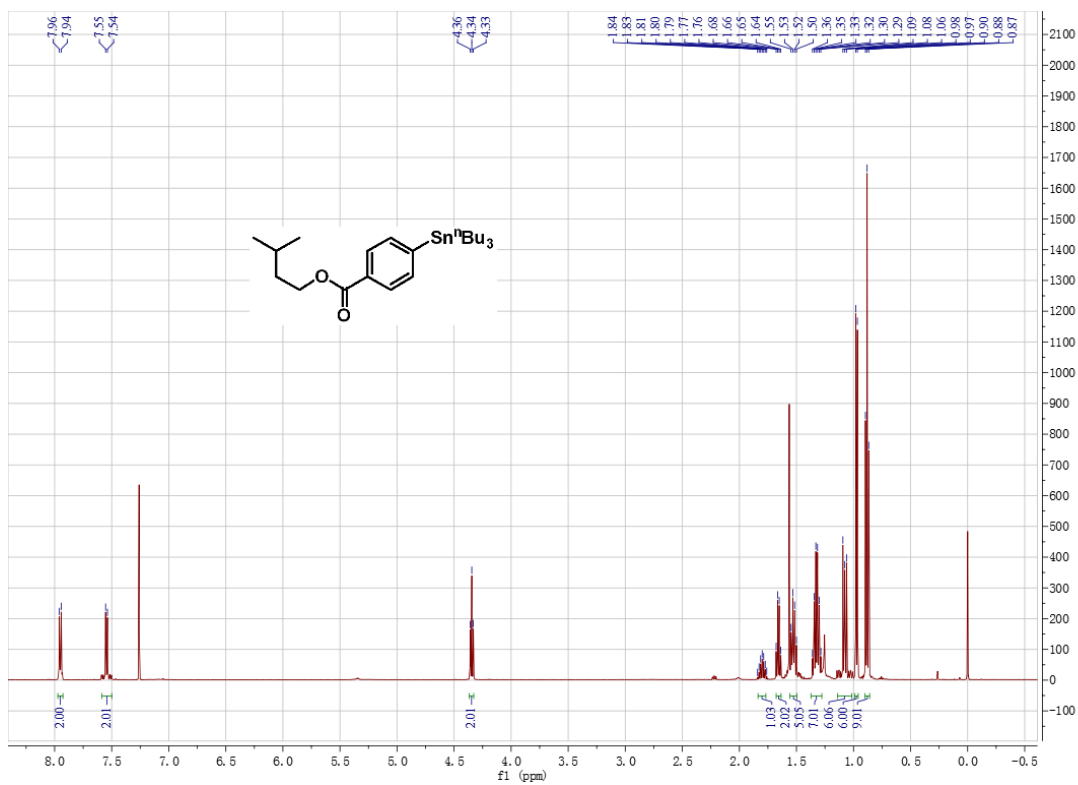
# Compound 7h



Compound 7j

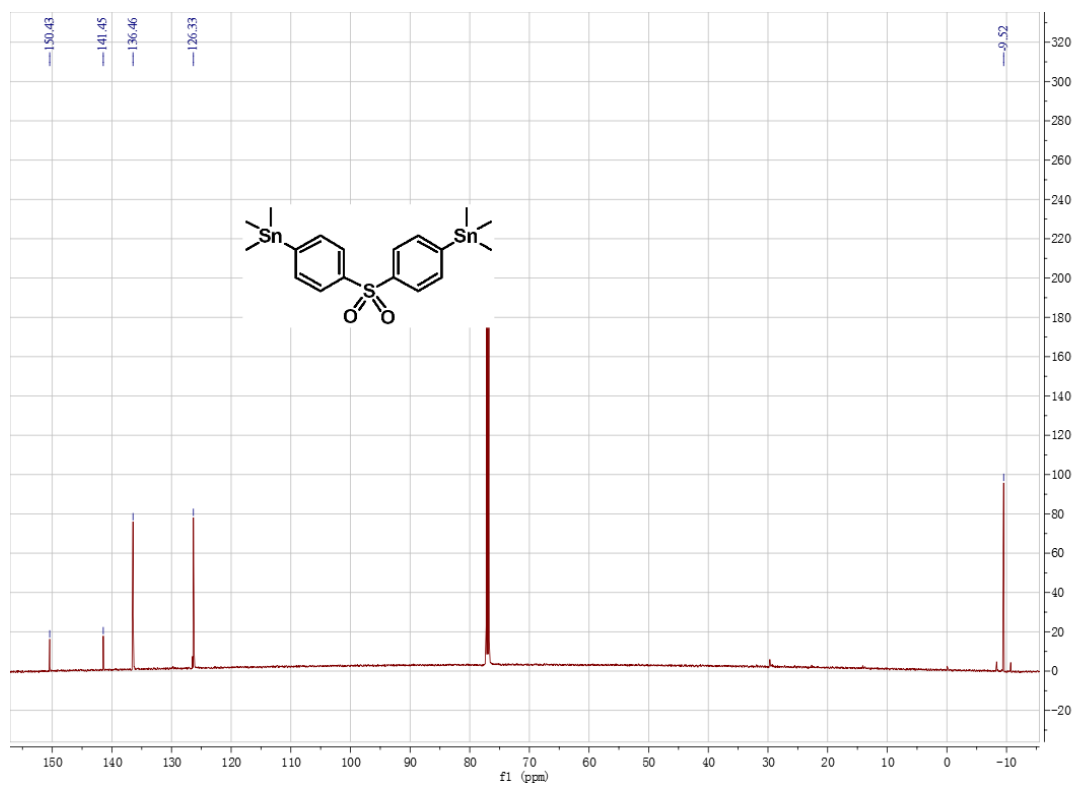
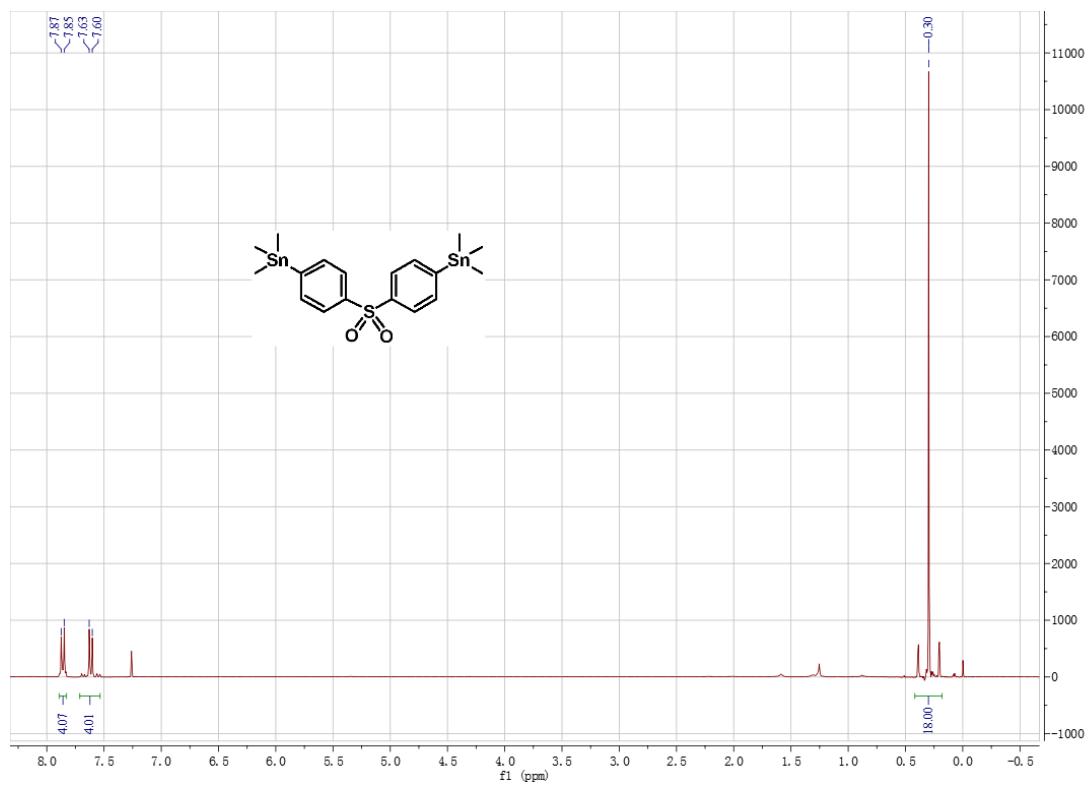


Compound 7k

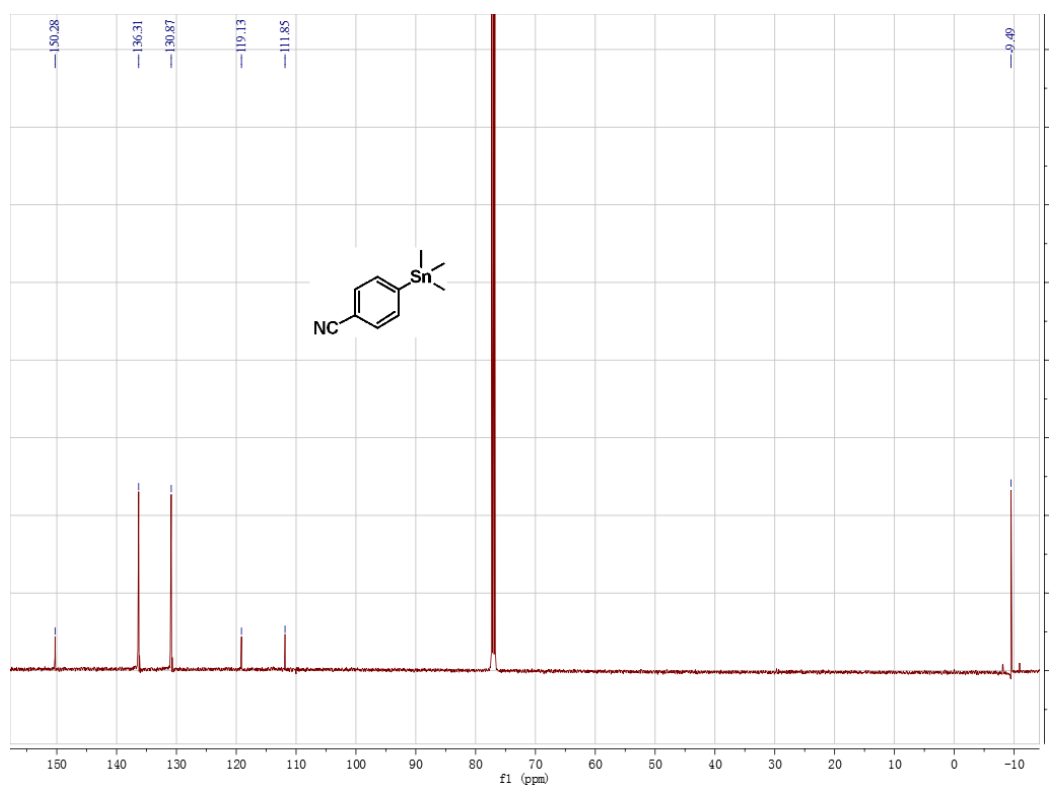
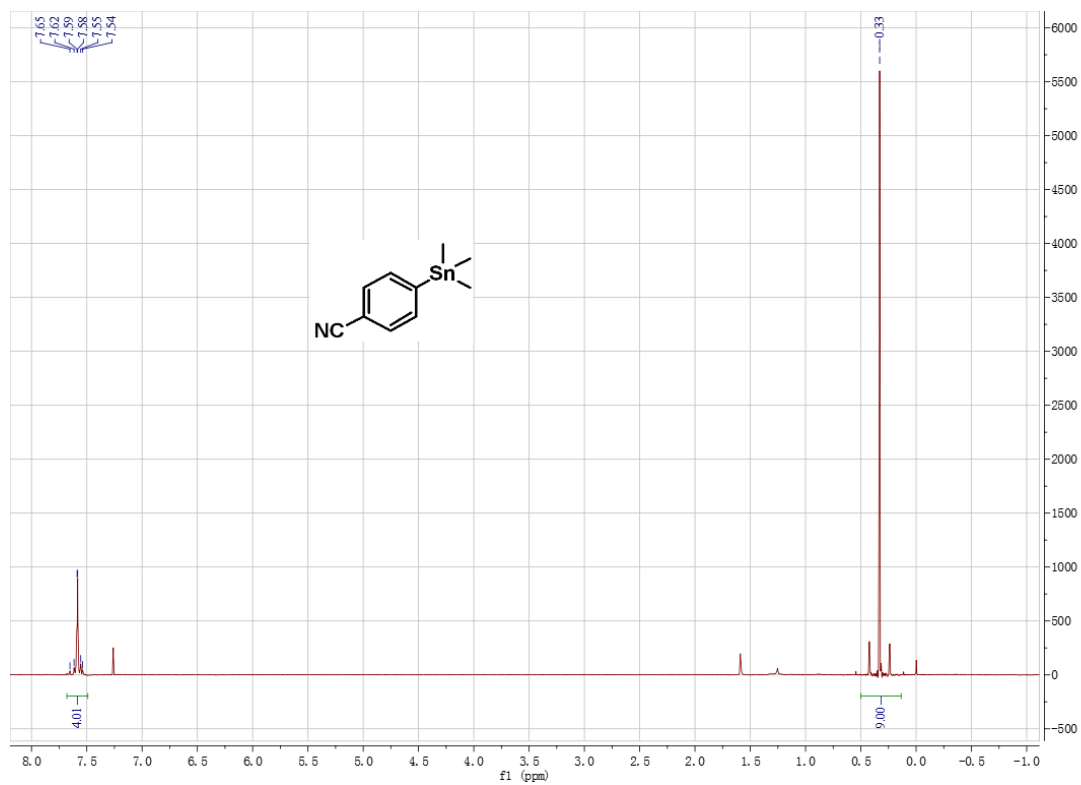




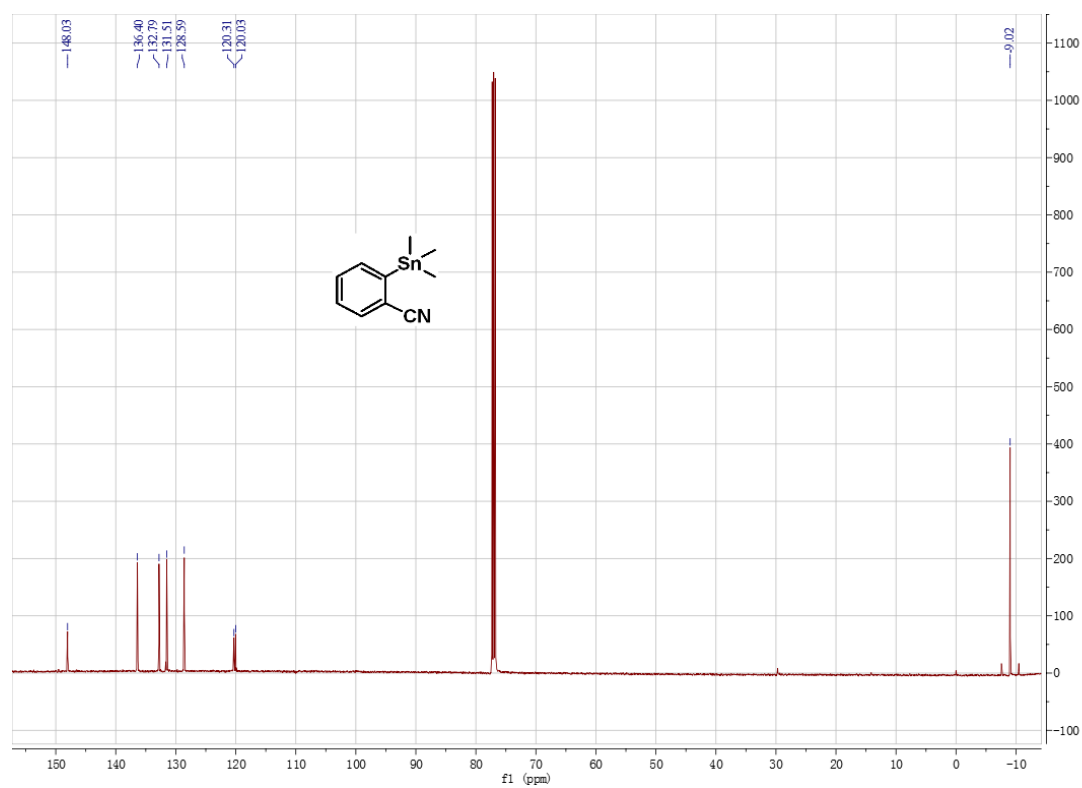
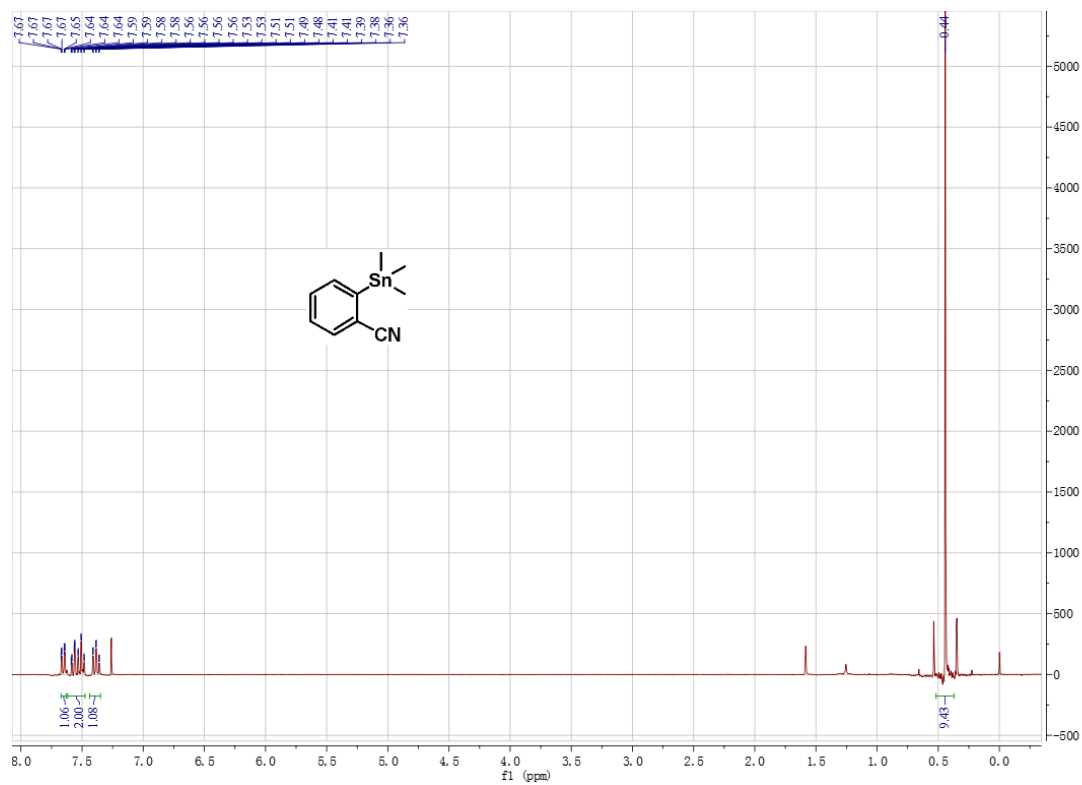
# Compound 7m



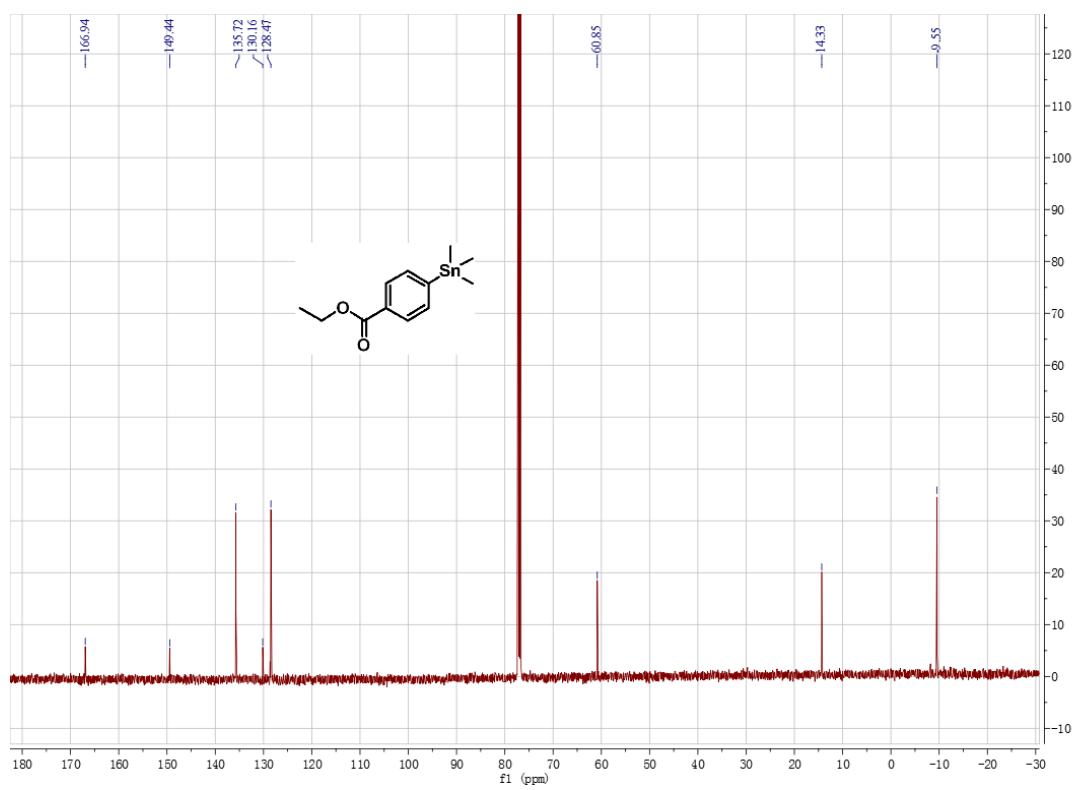
# Compound 7b



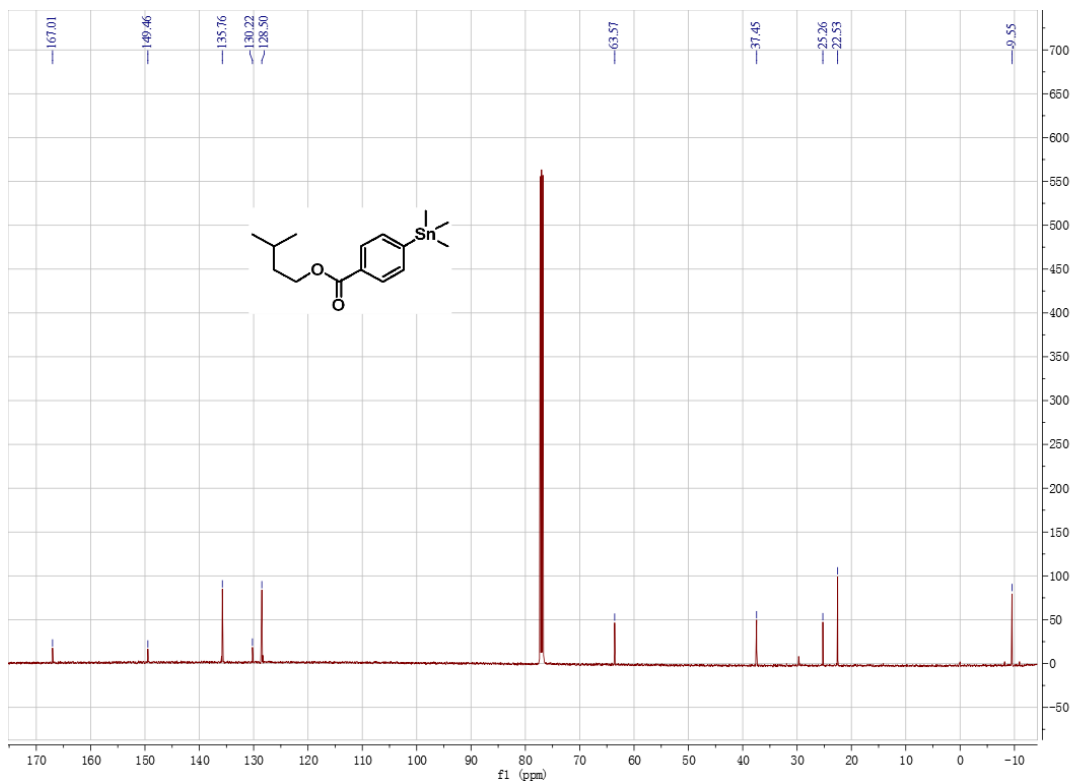
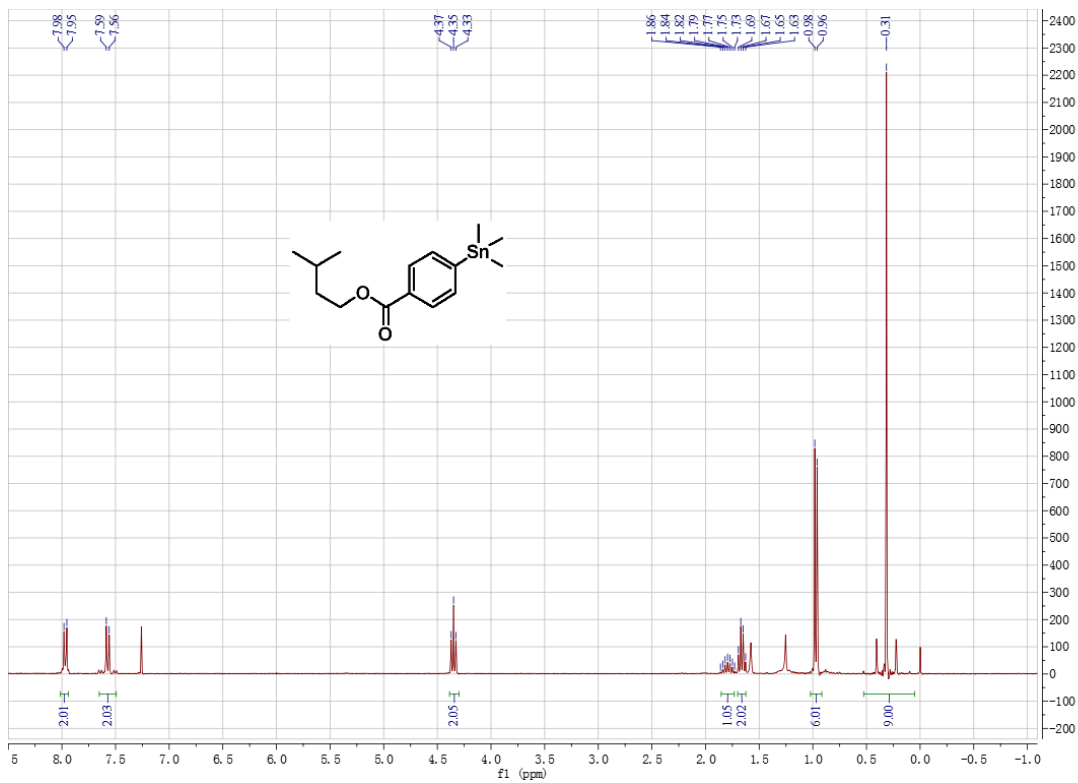
# Compound 7d



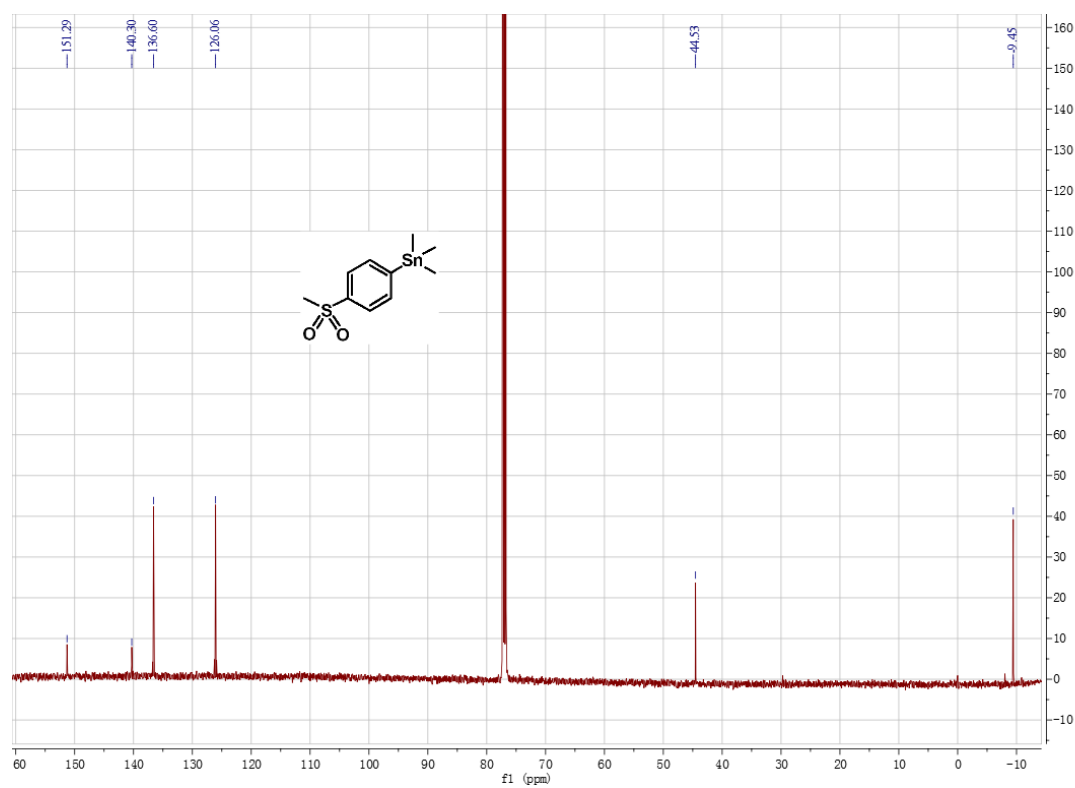
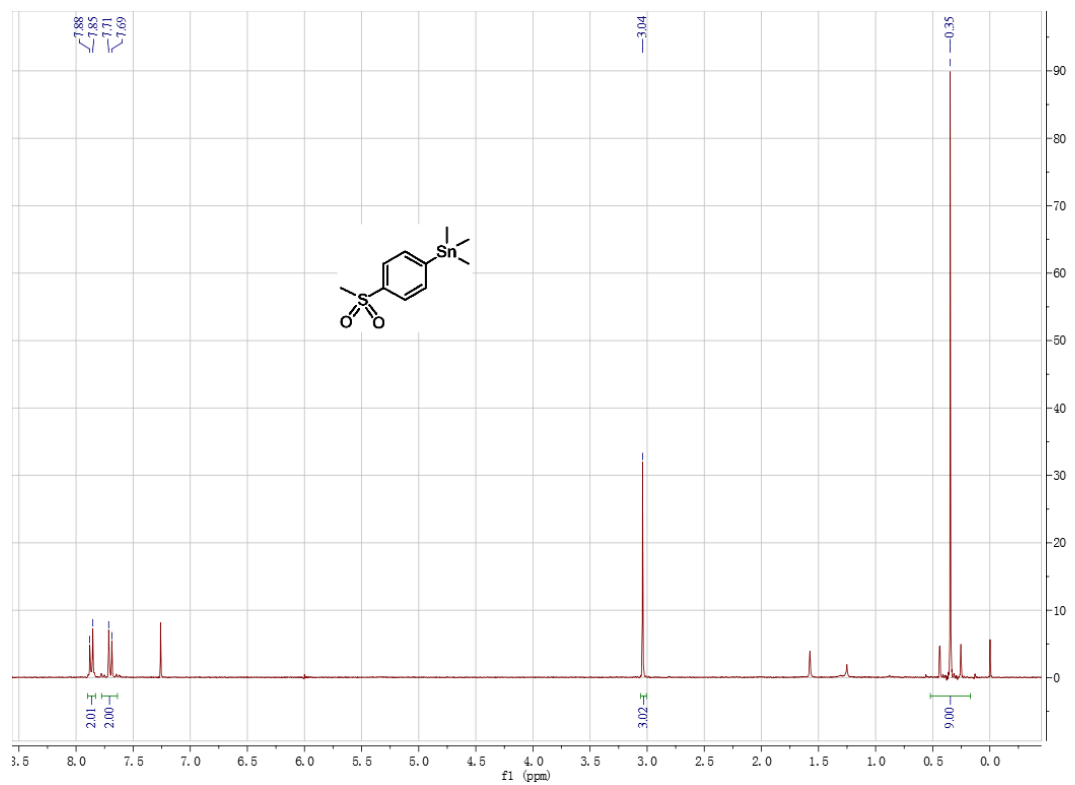
# Compound 7g



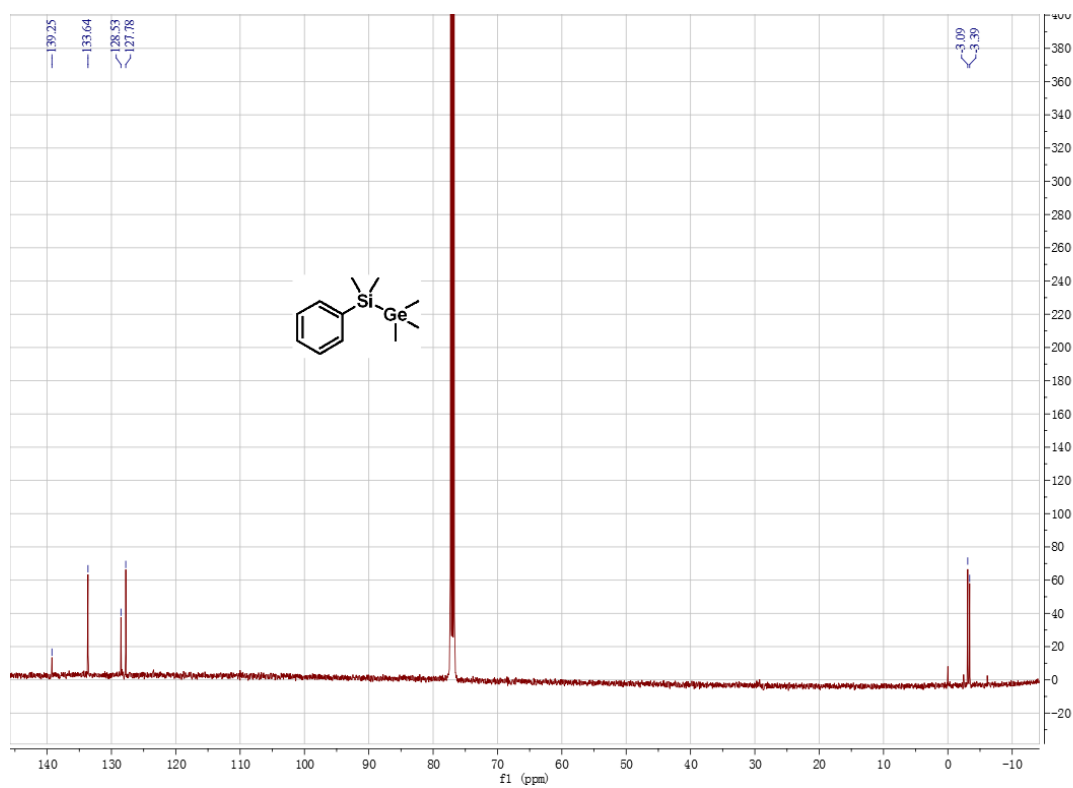
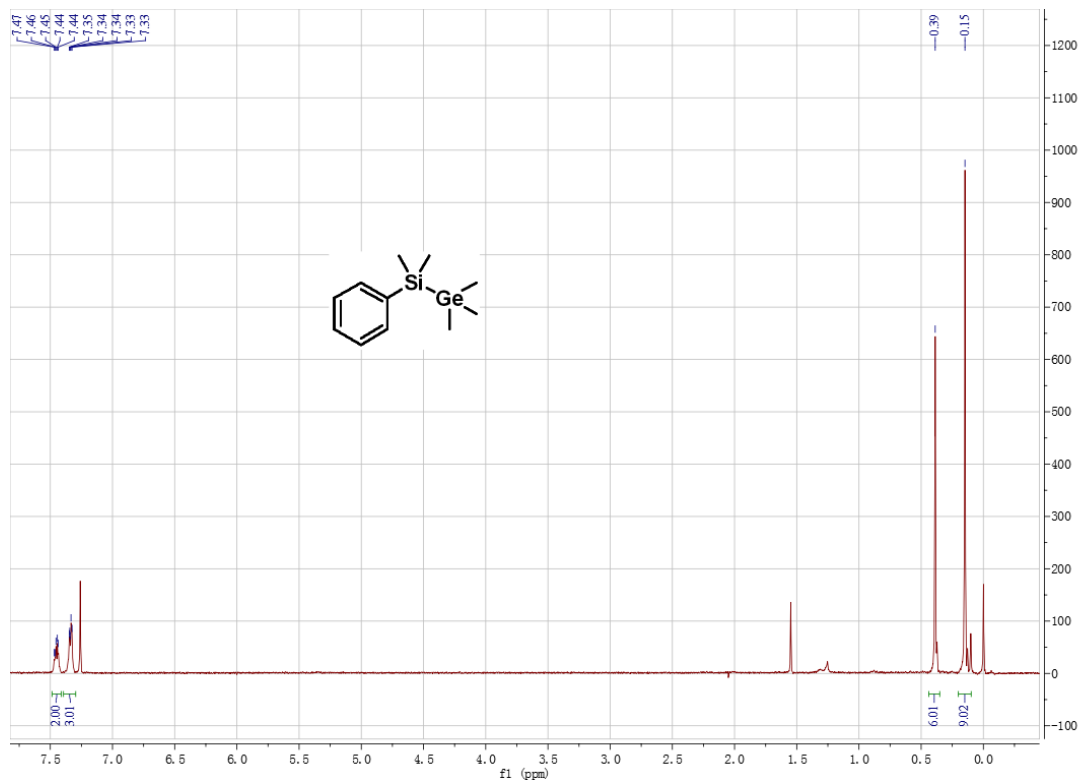
Compound 7I



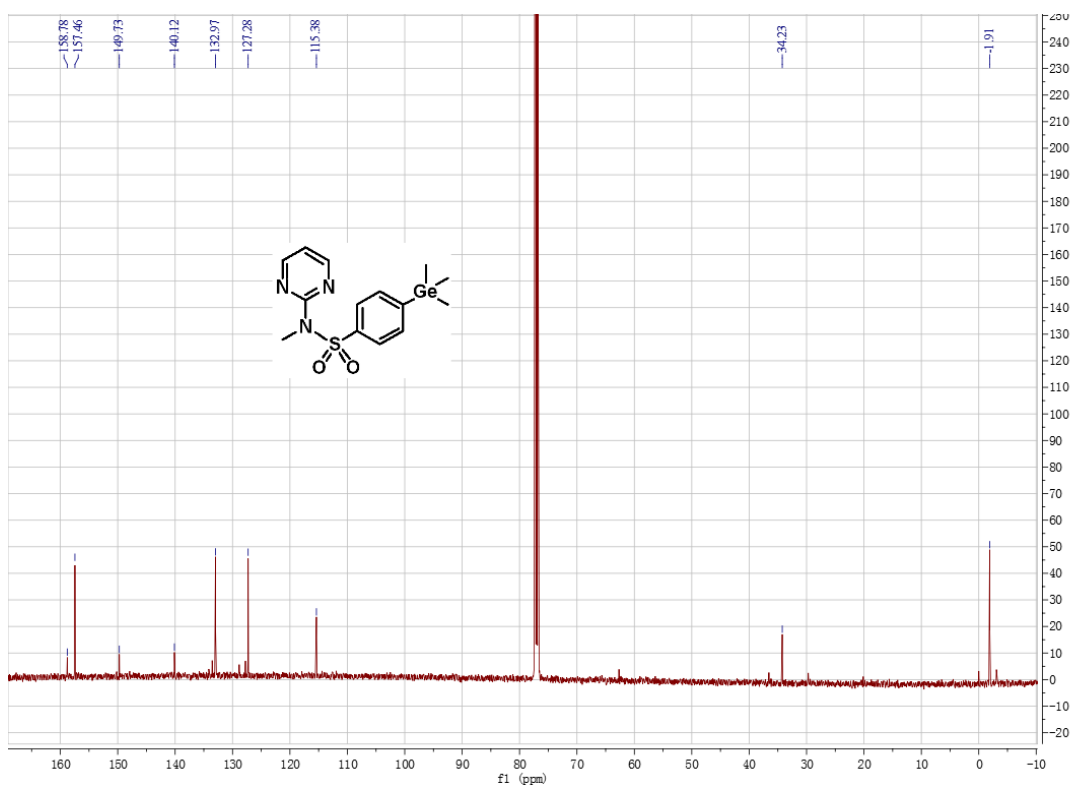
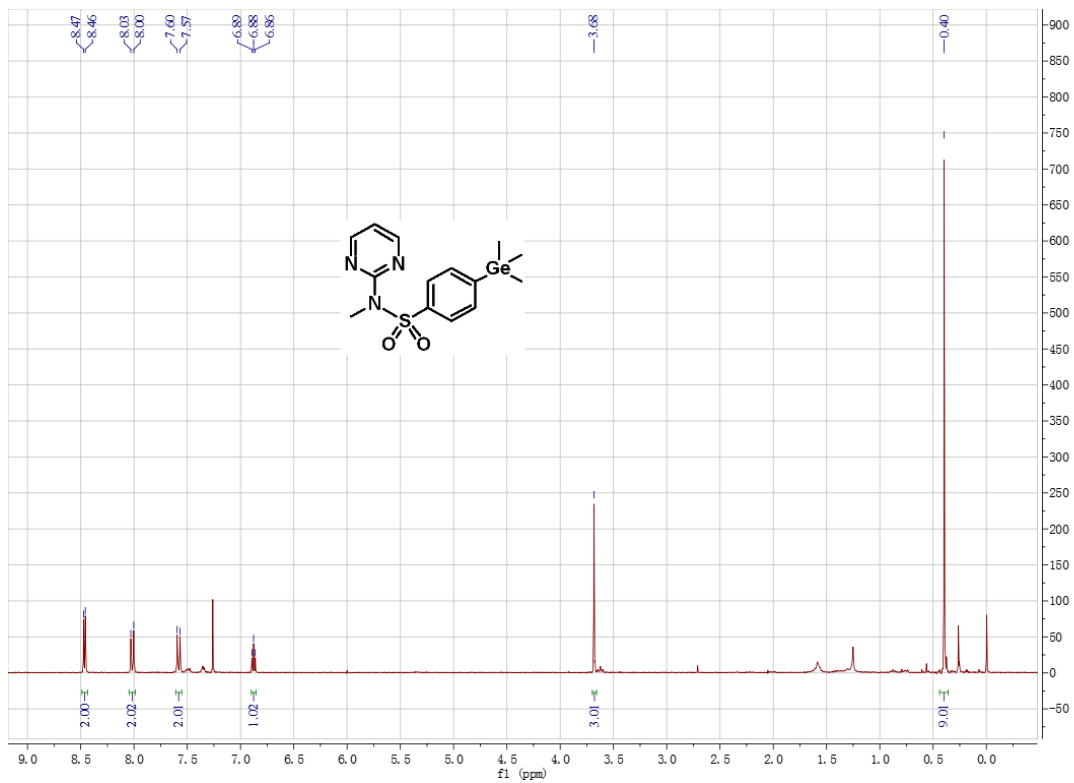
# Compound 7i



# Compound 8

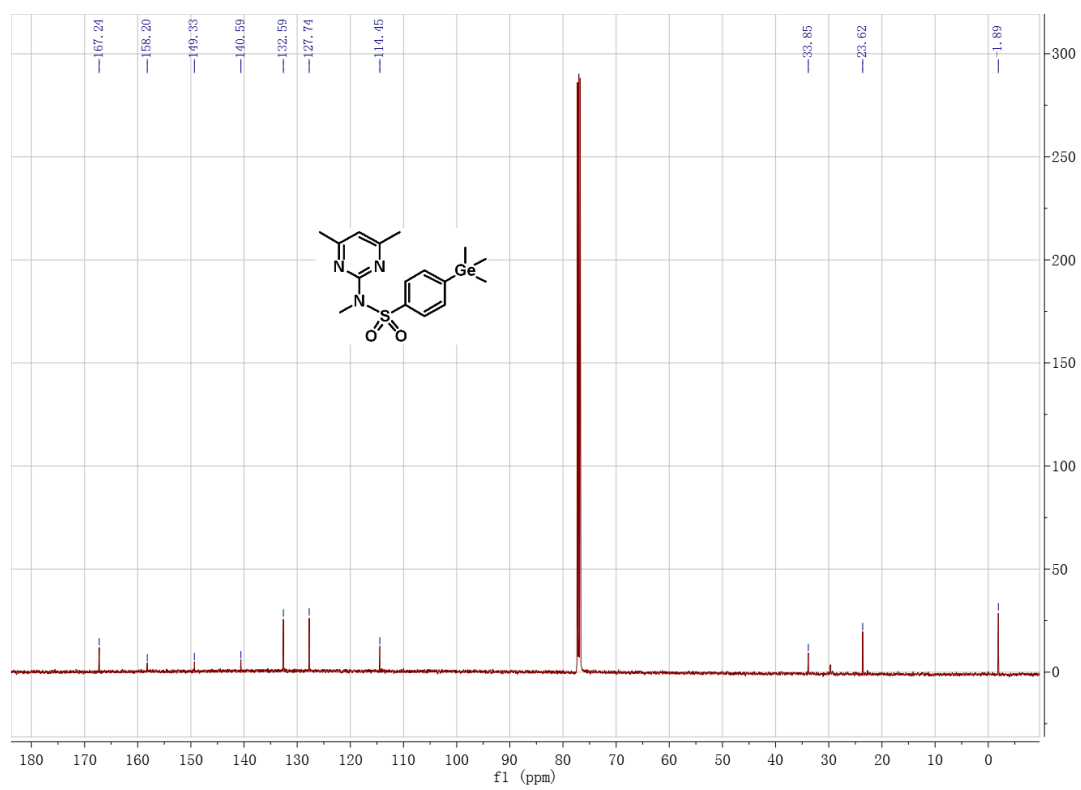
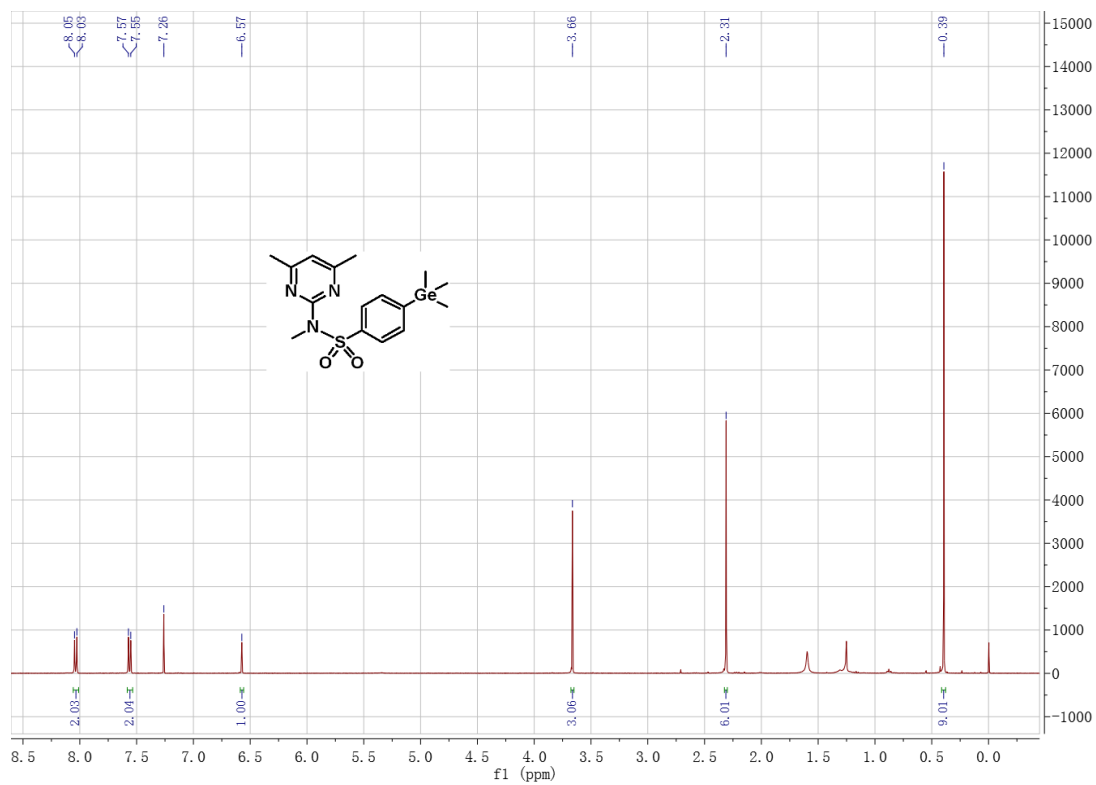


Compound 9a

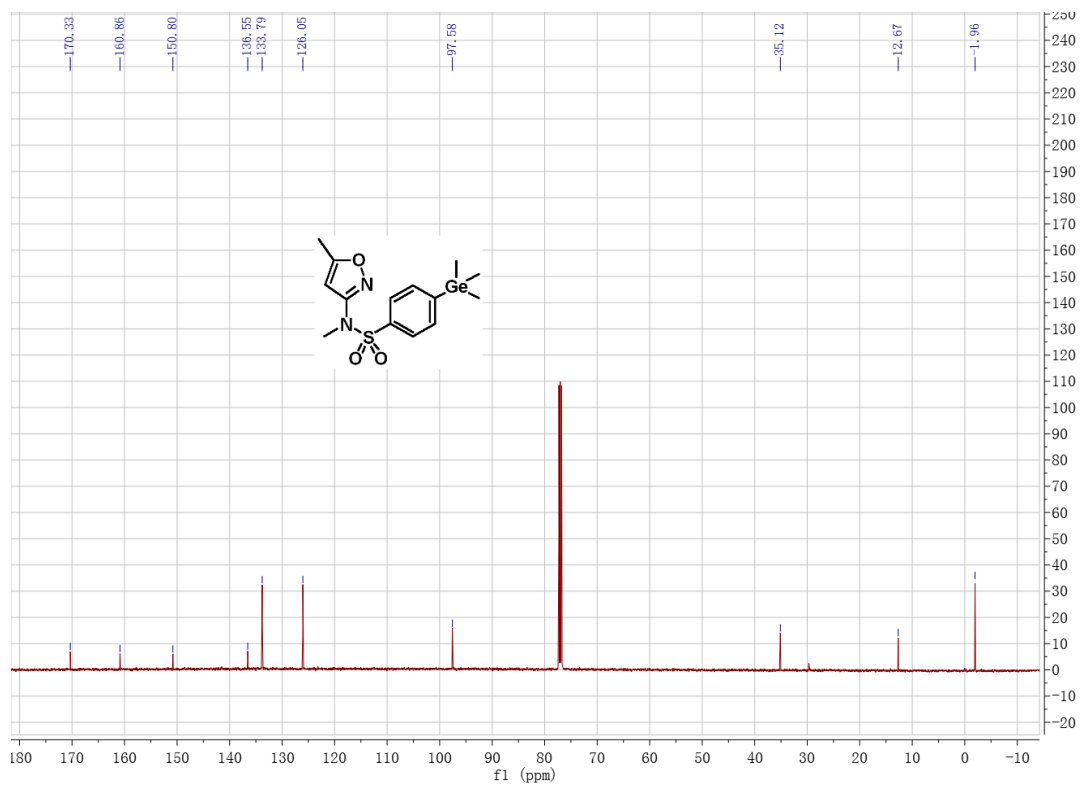
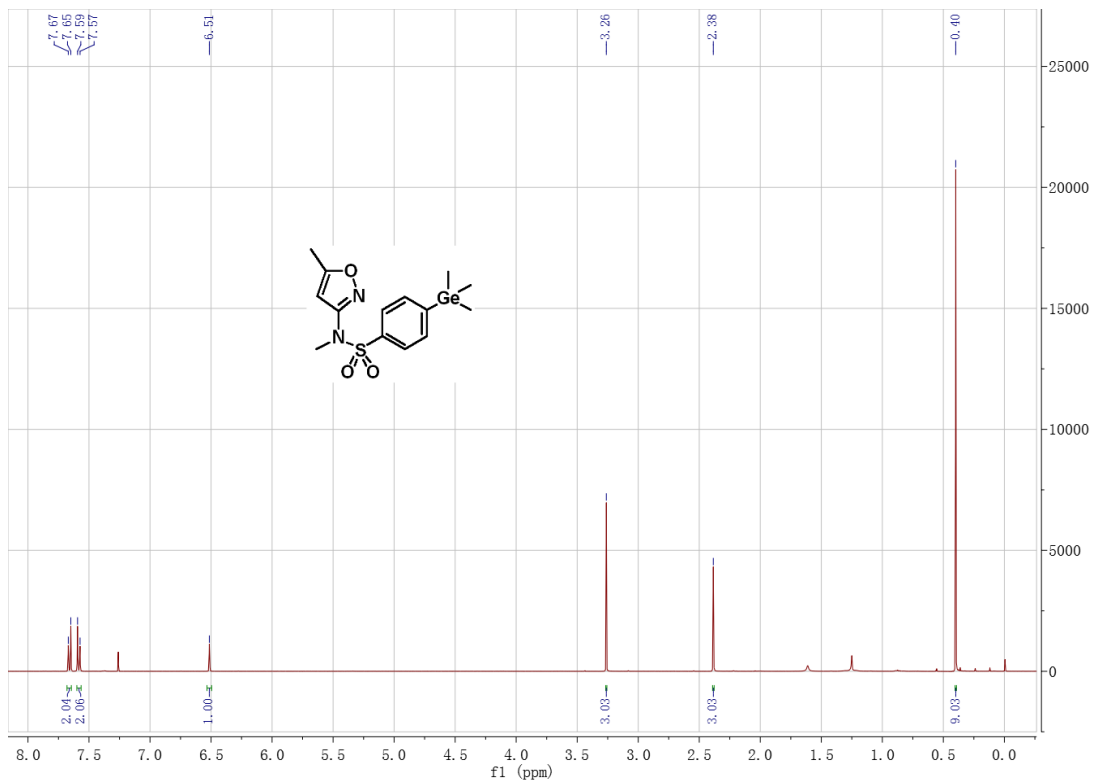




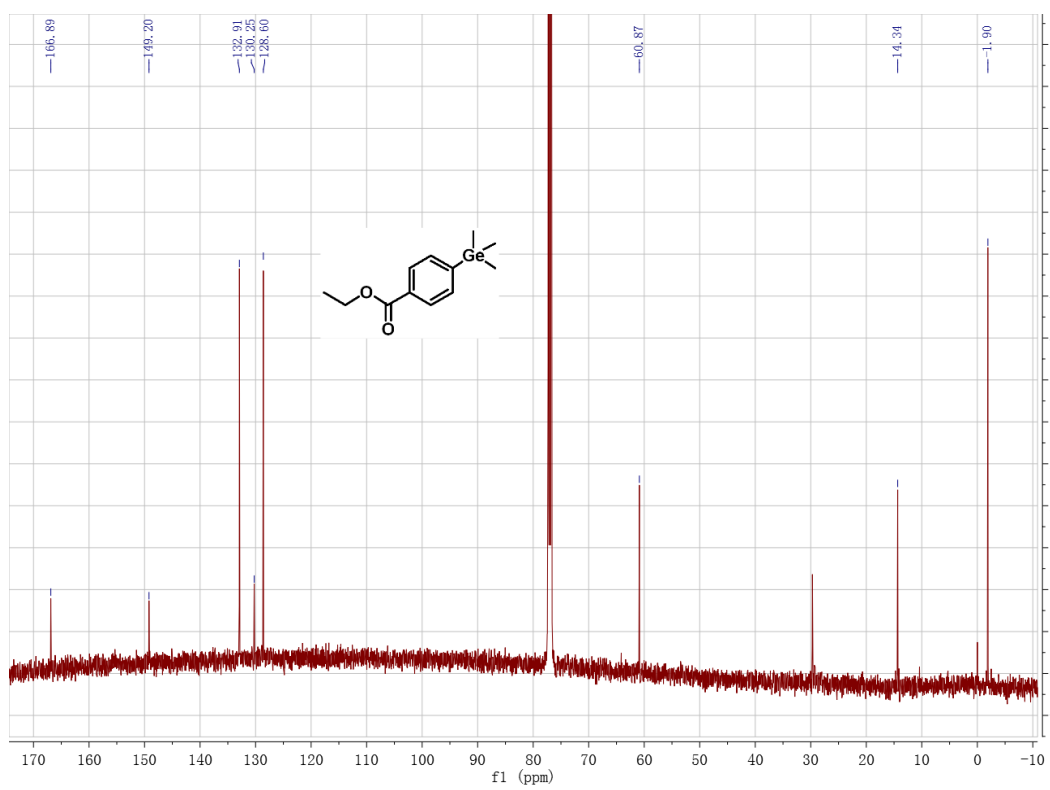
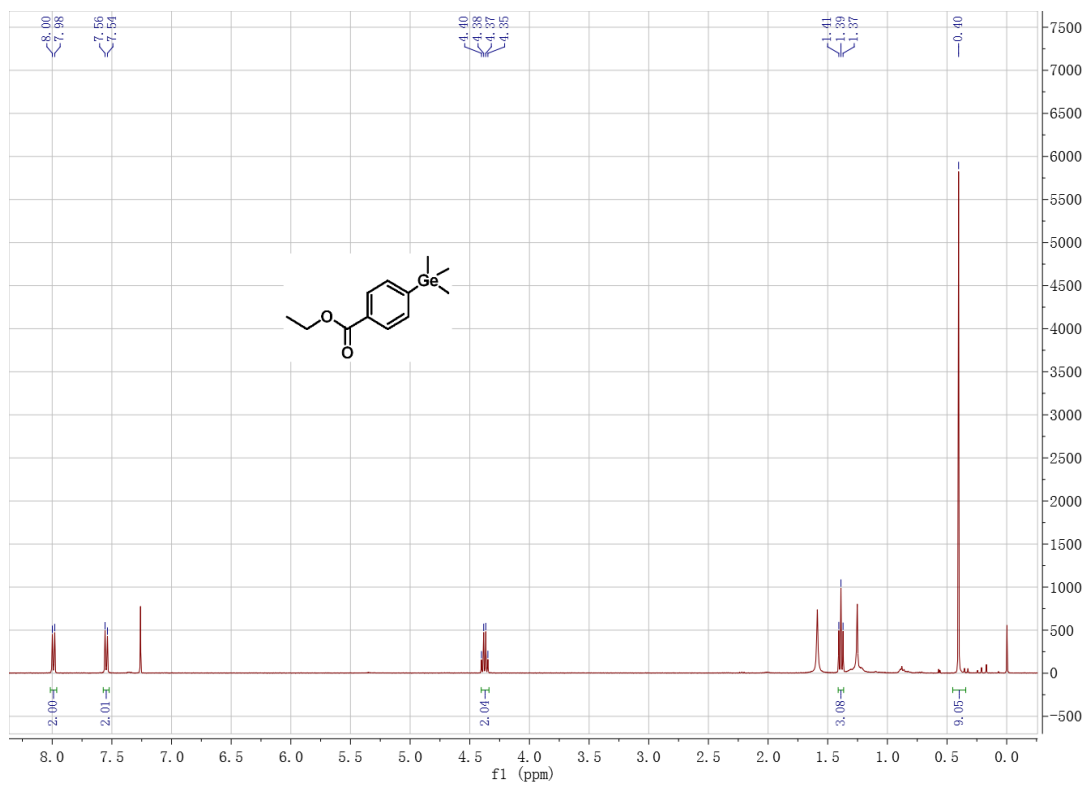
# Compound 9c



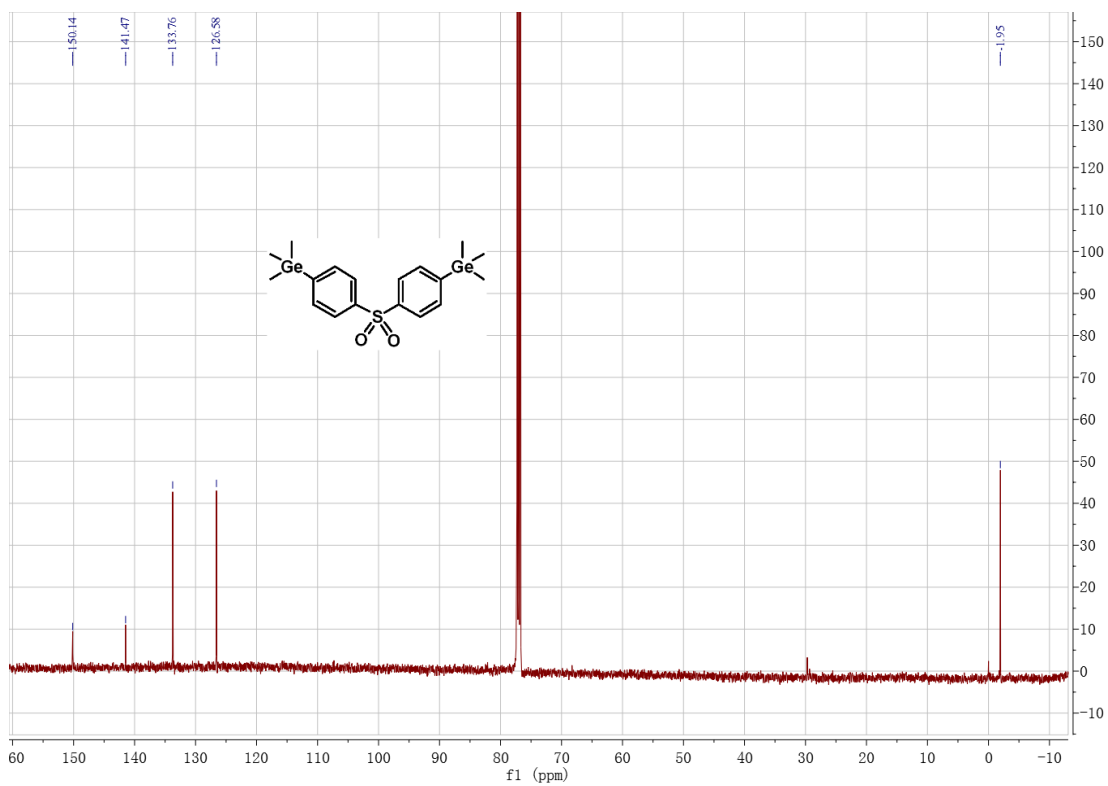
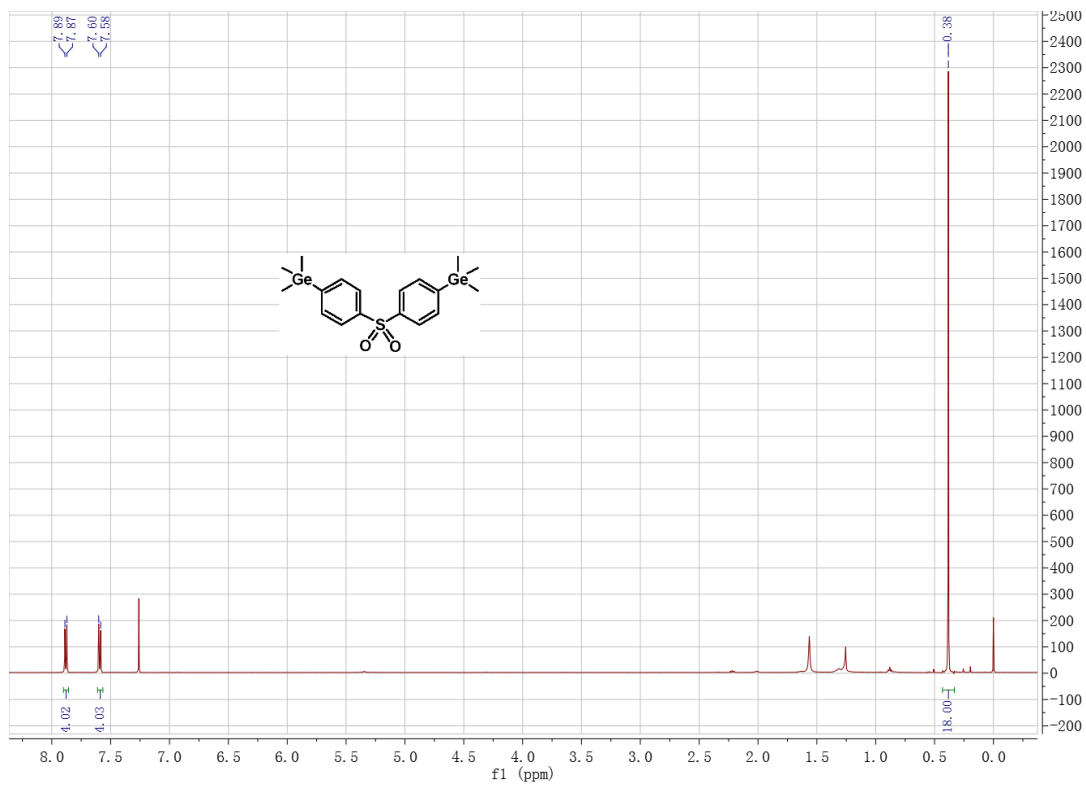
Compound 9b



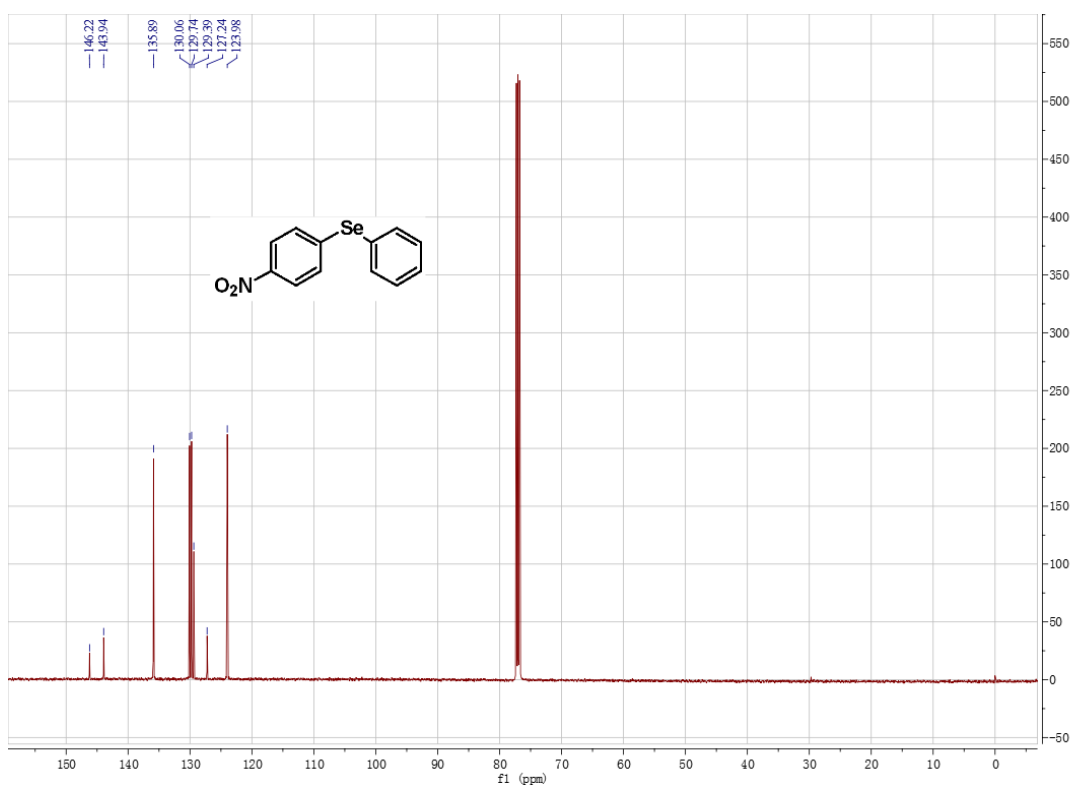
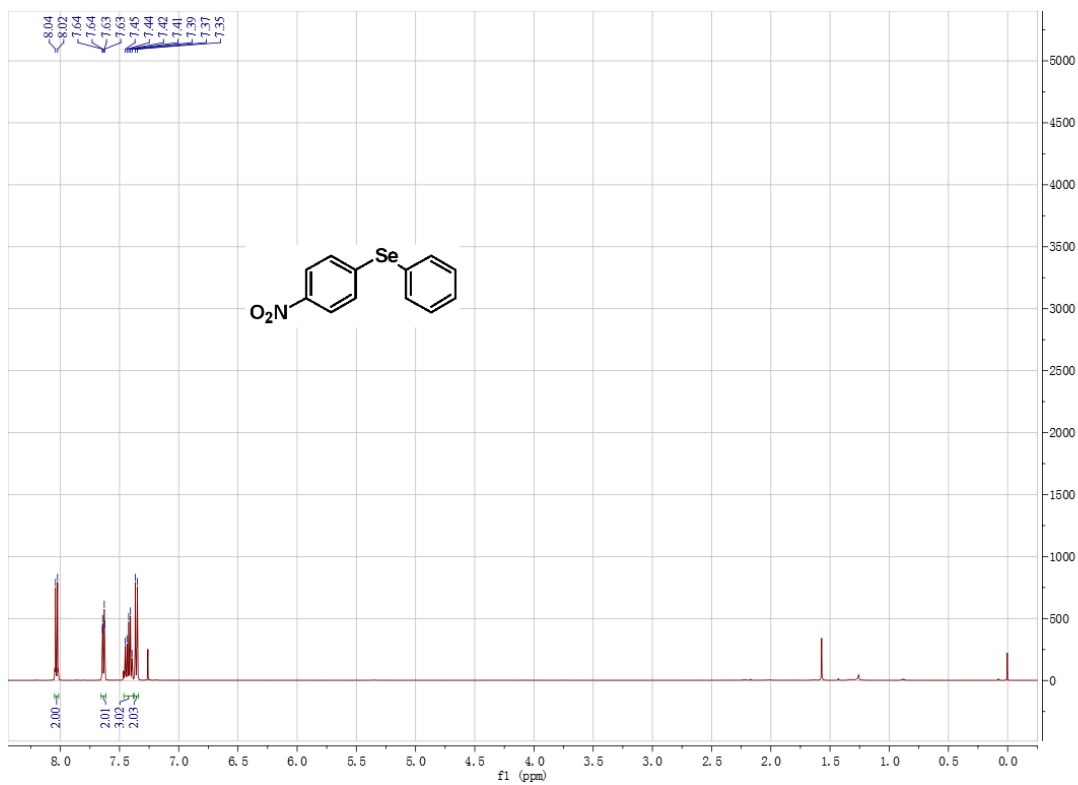
# Compound 9e



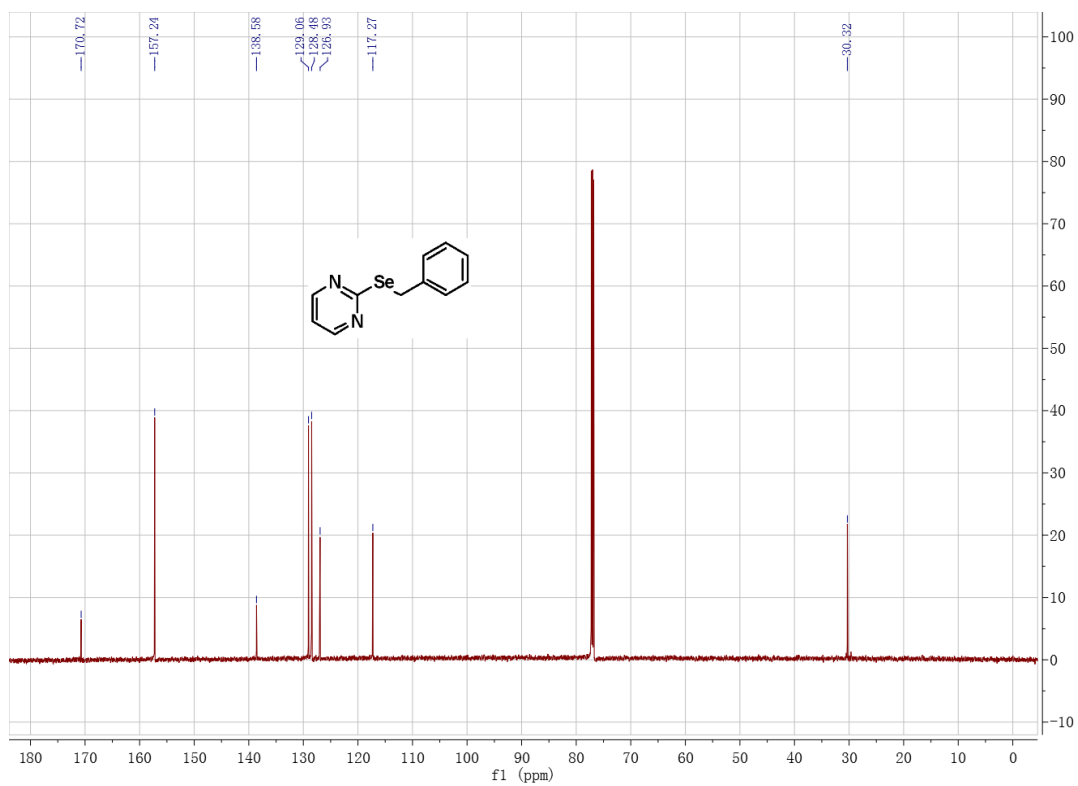
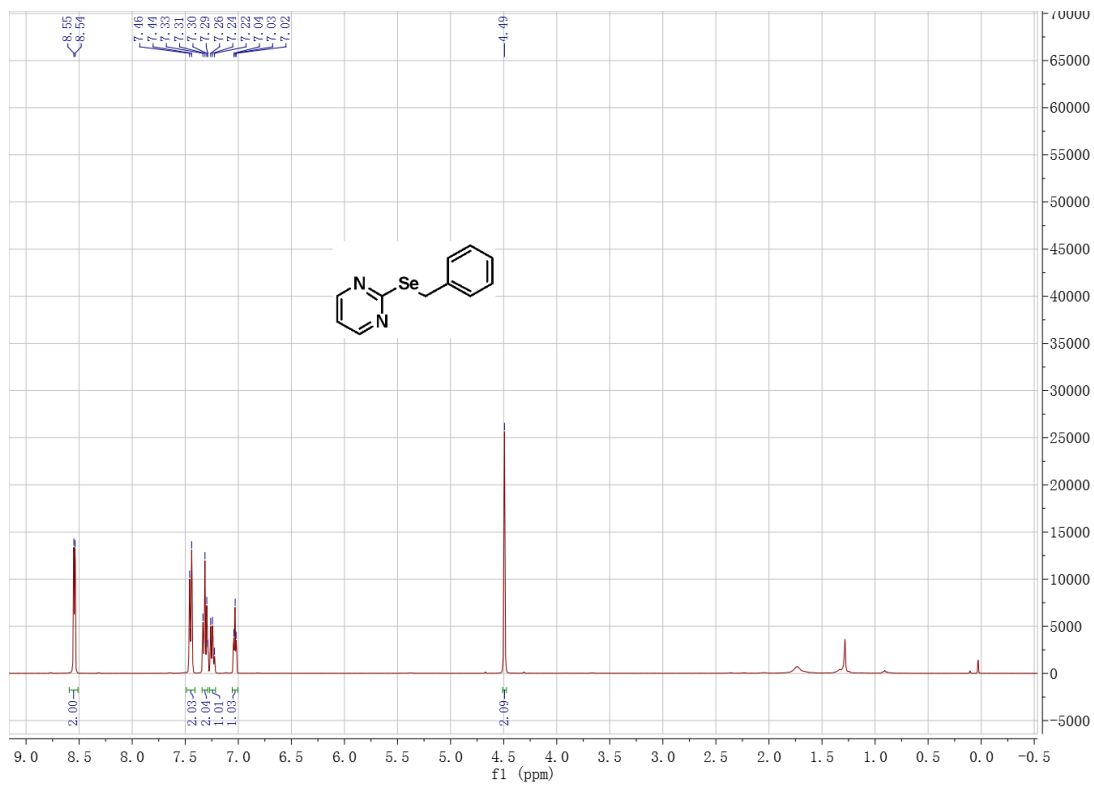
# Compound 9d



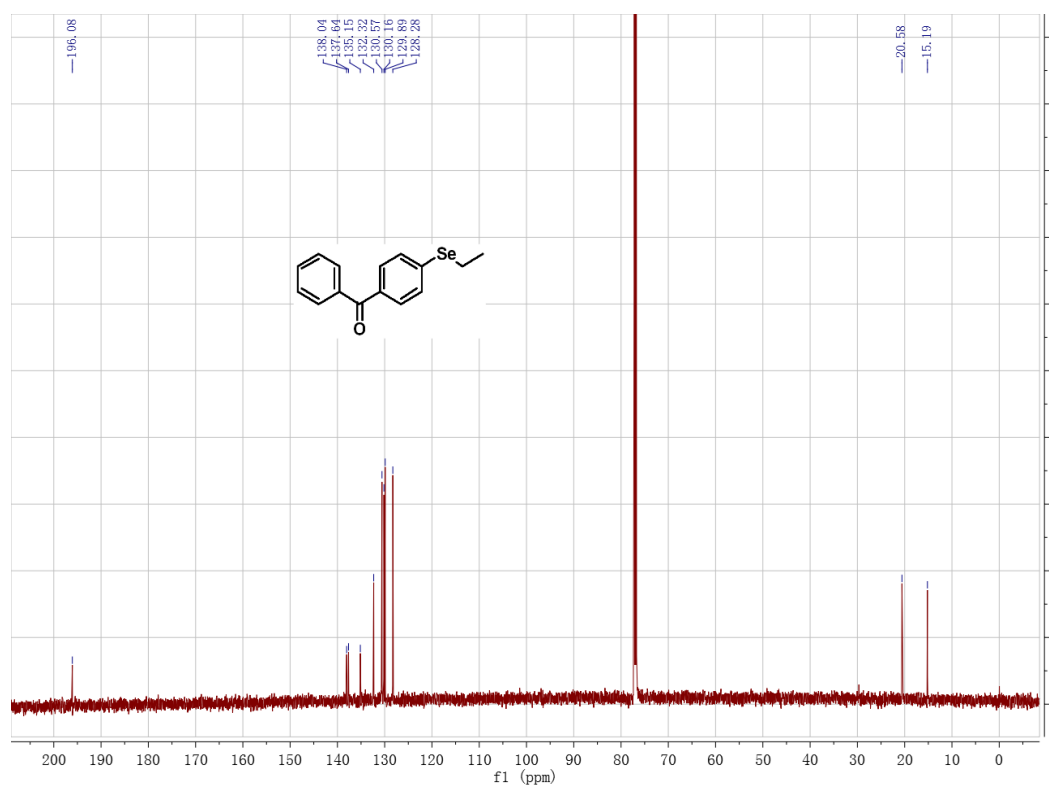
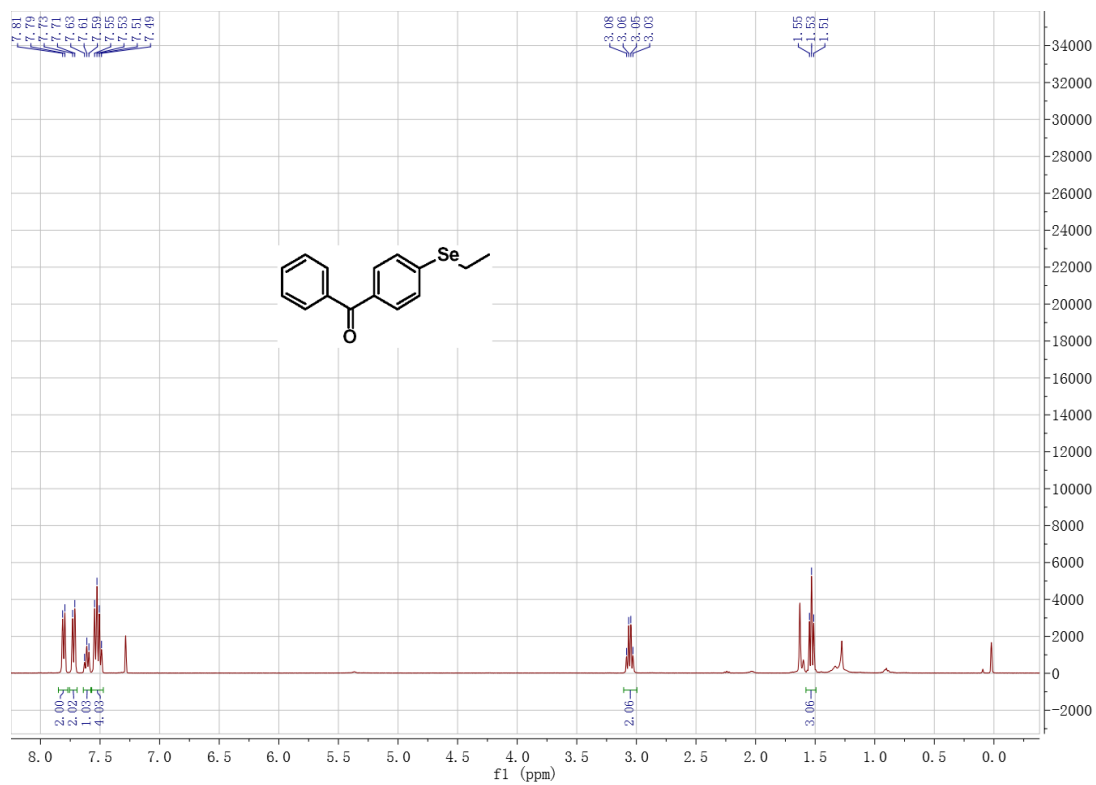
# Compound 11a



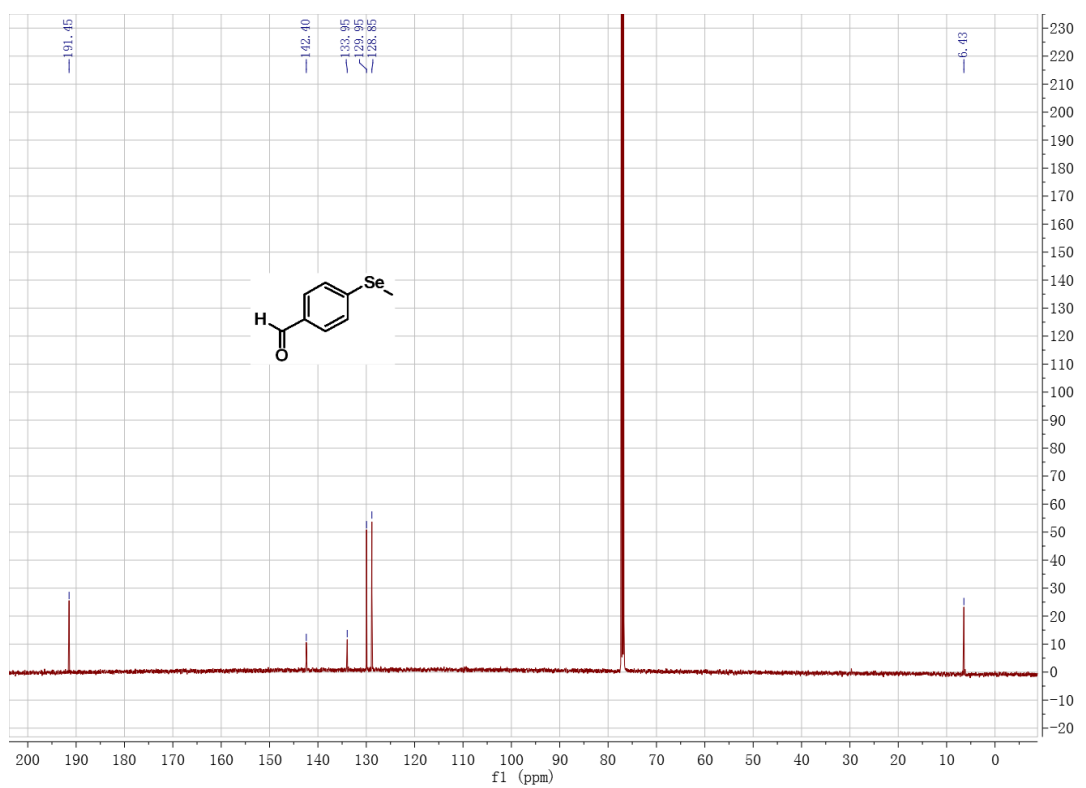
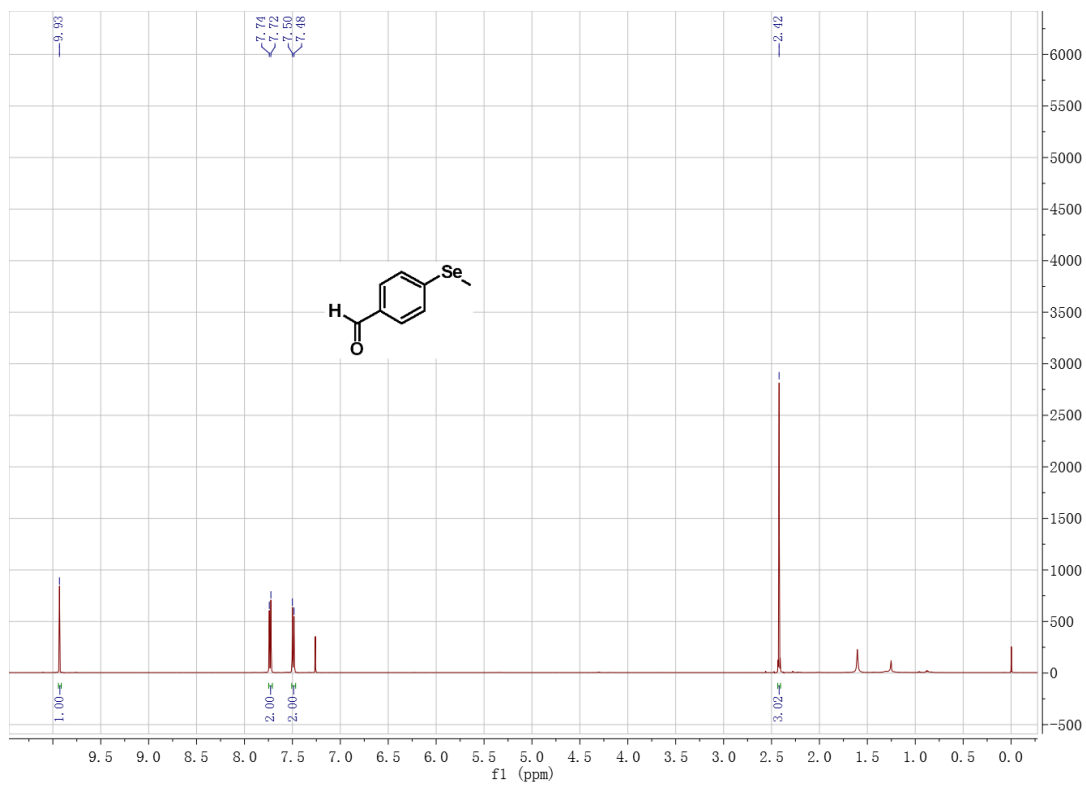
# Compound 11d



# Compound 11b

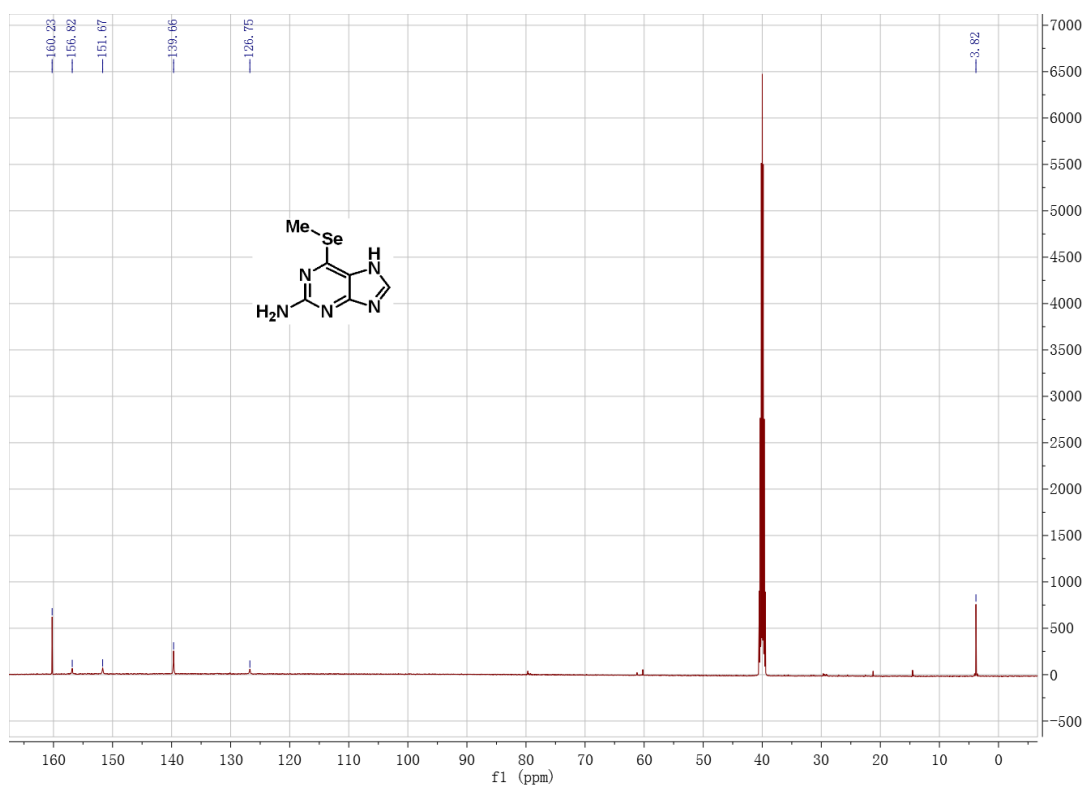
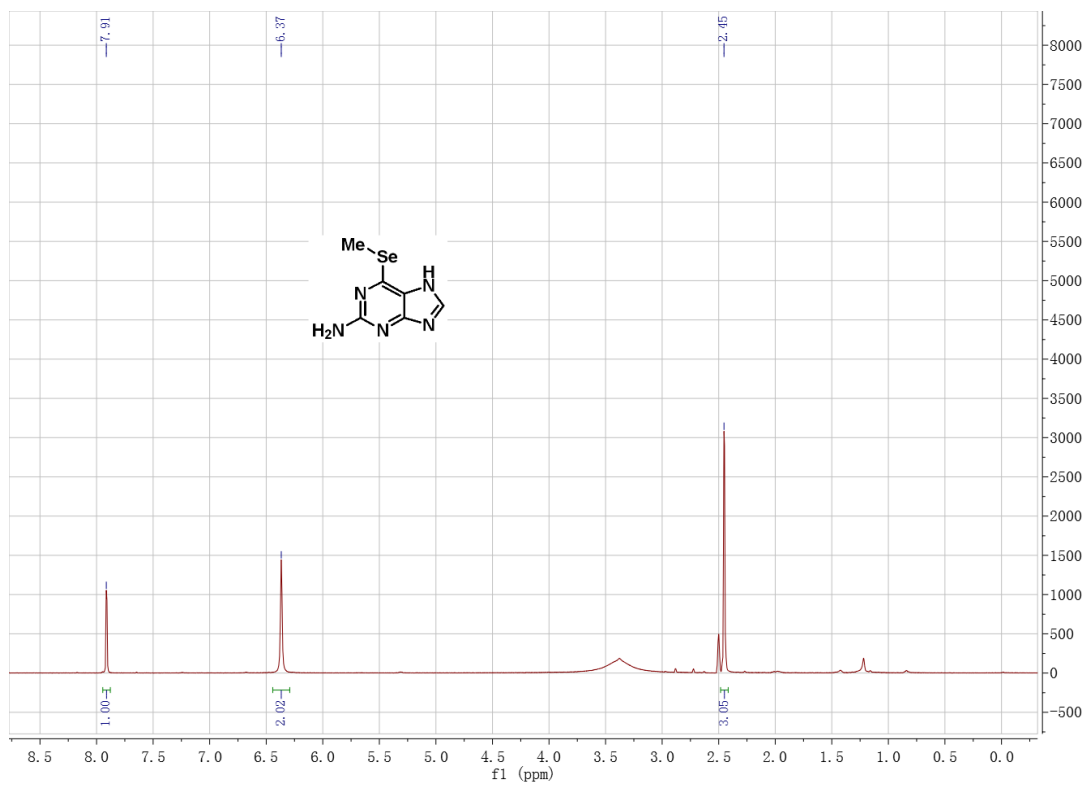


# Compound 11c

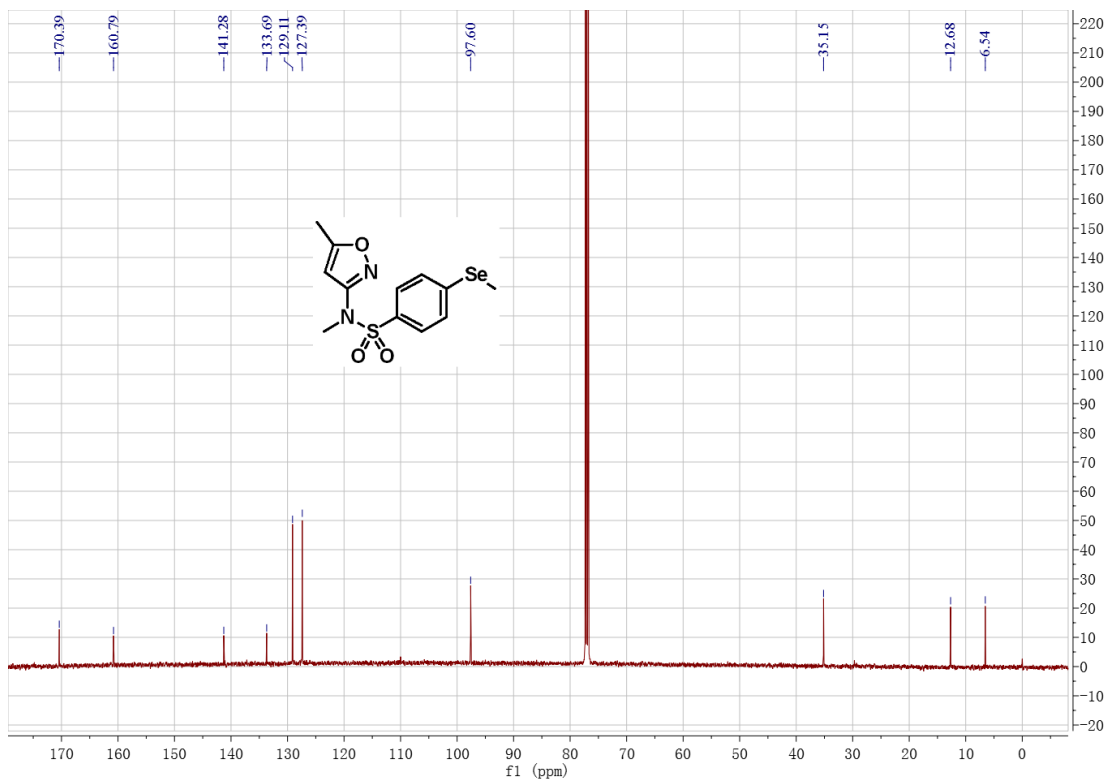
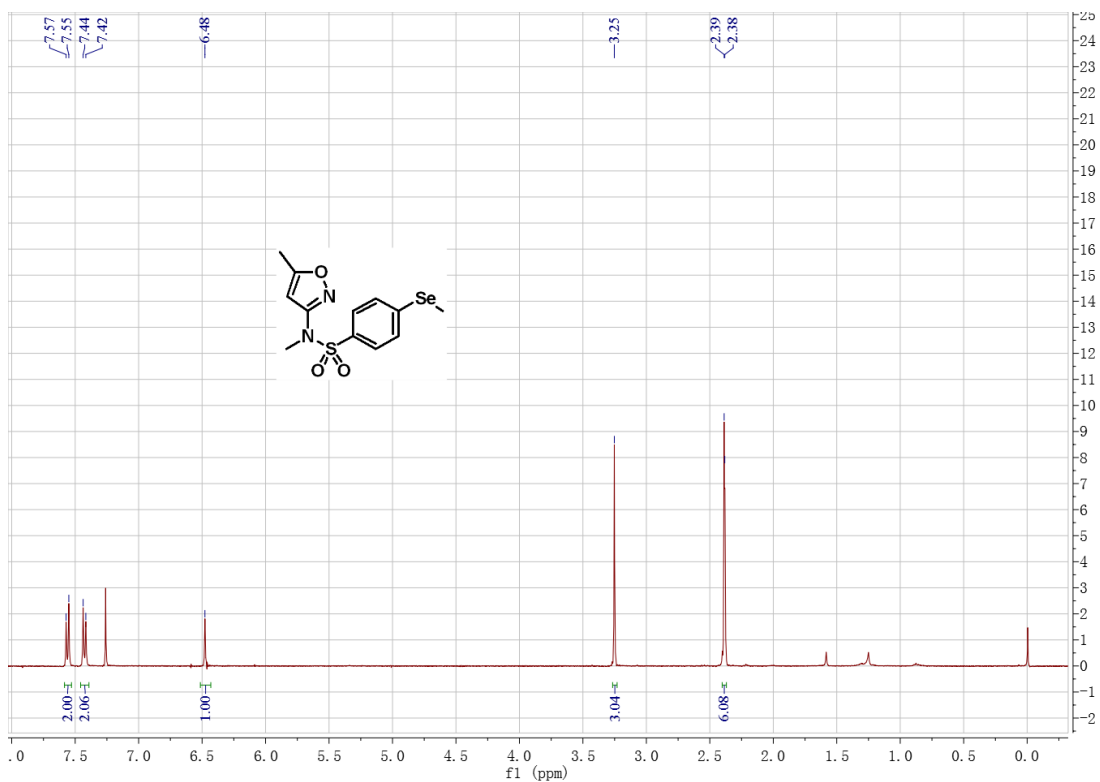




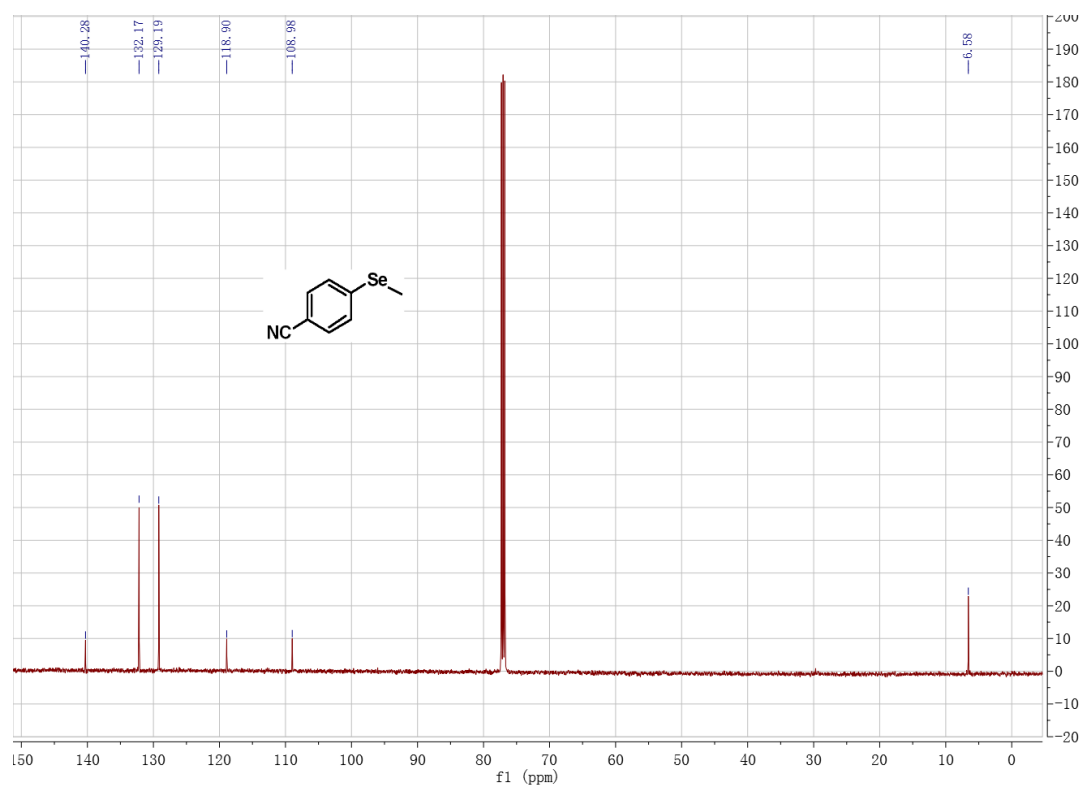
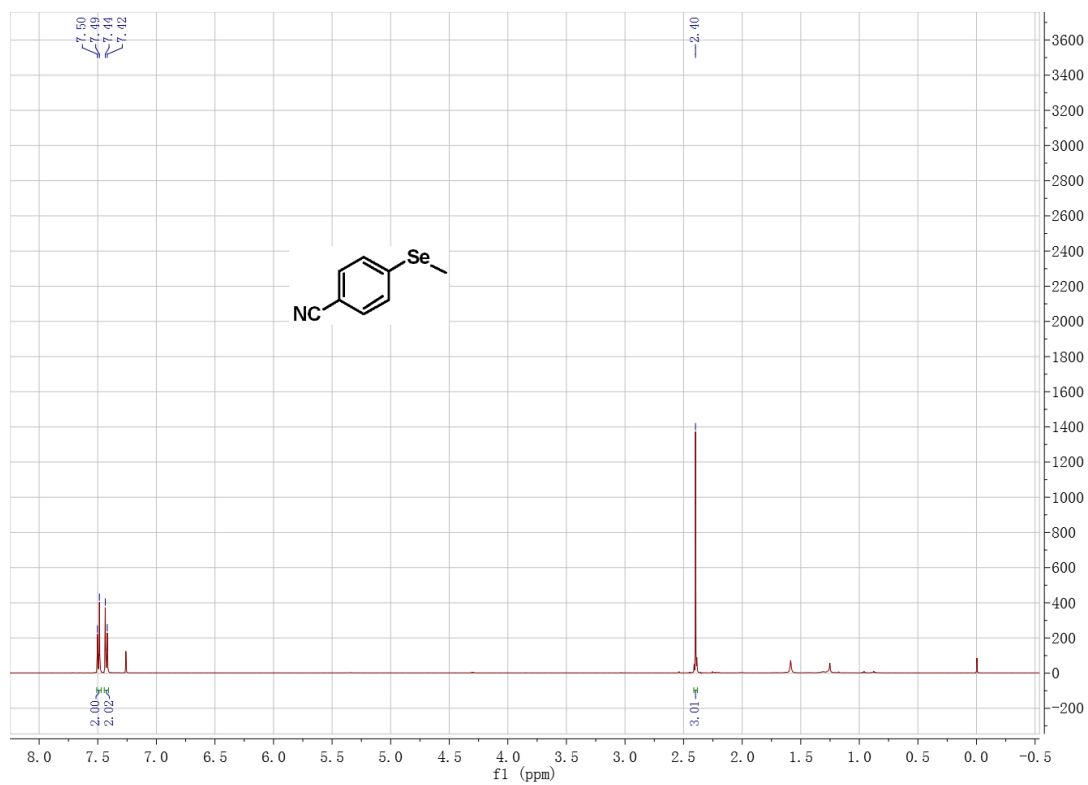
Compound 11e



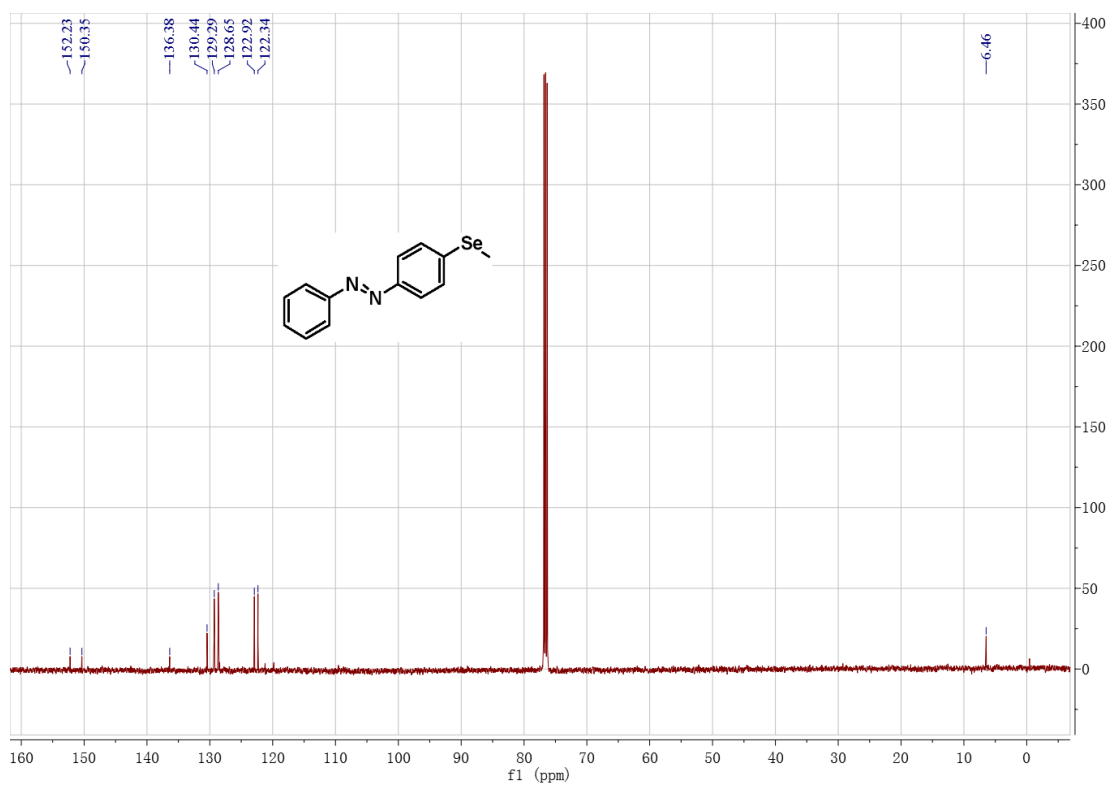
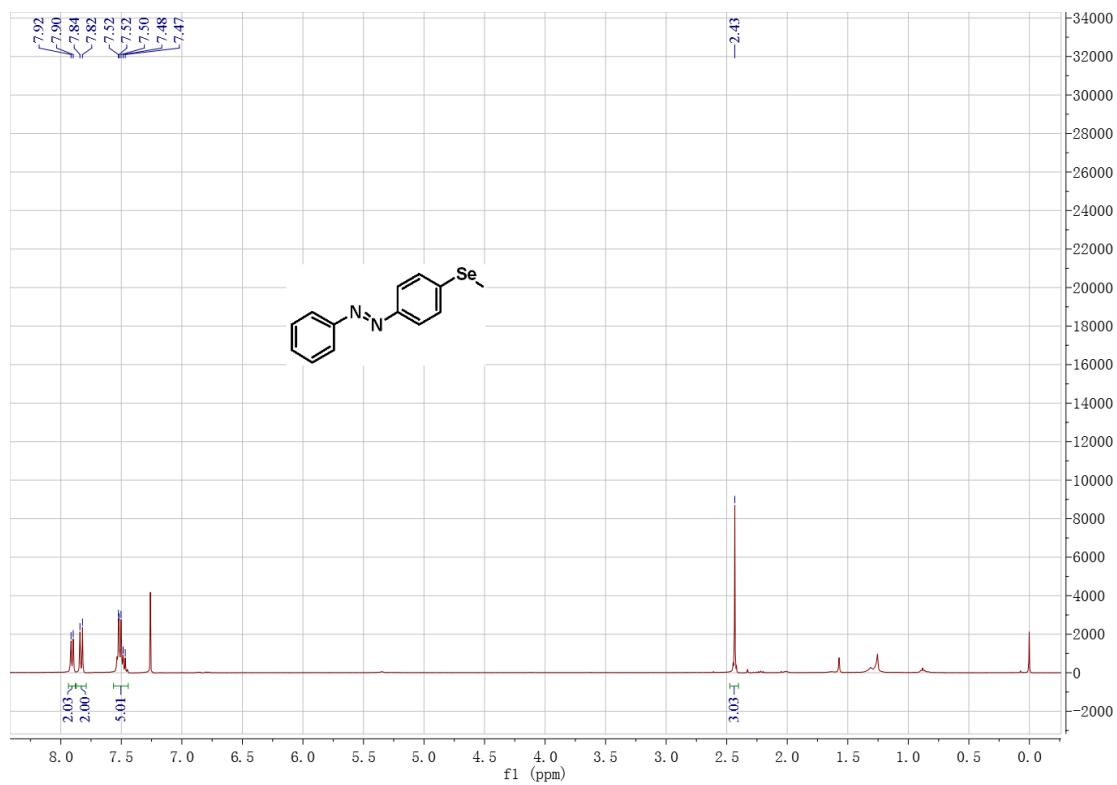
Compound 11f



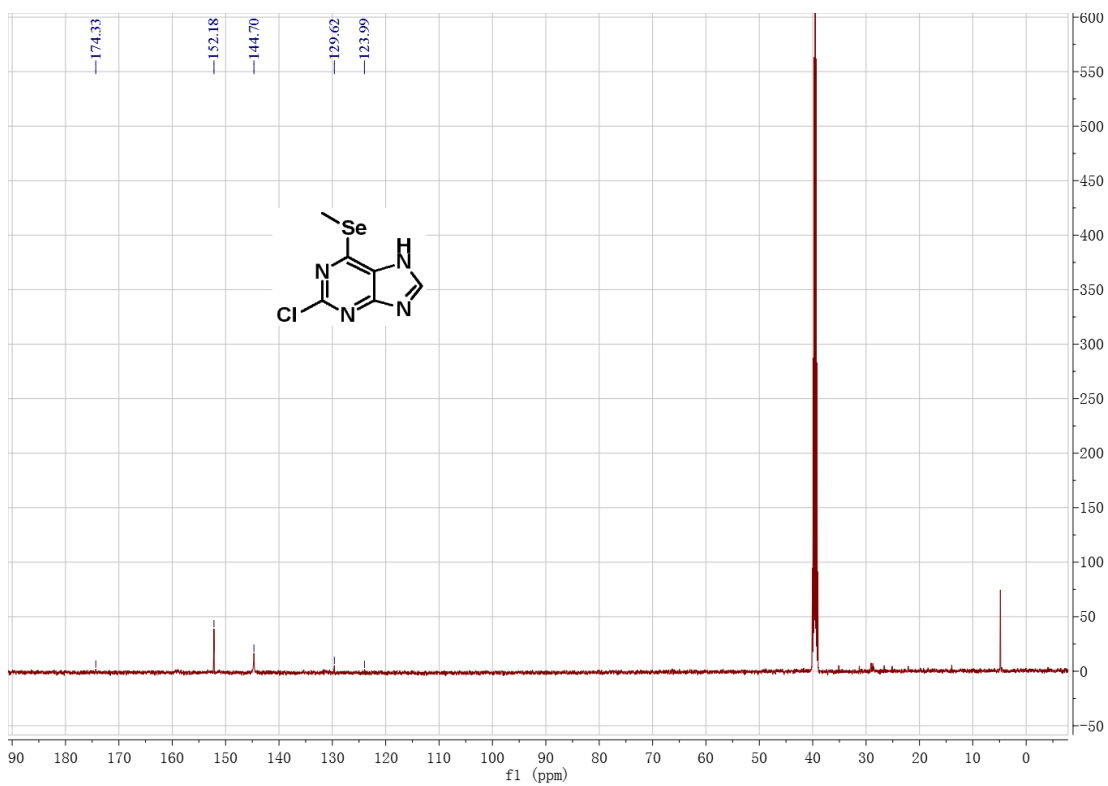
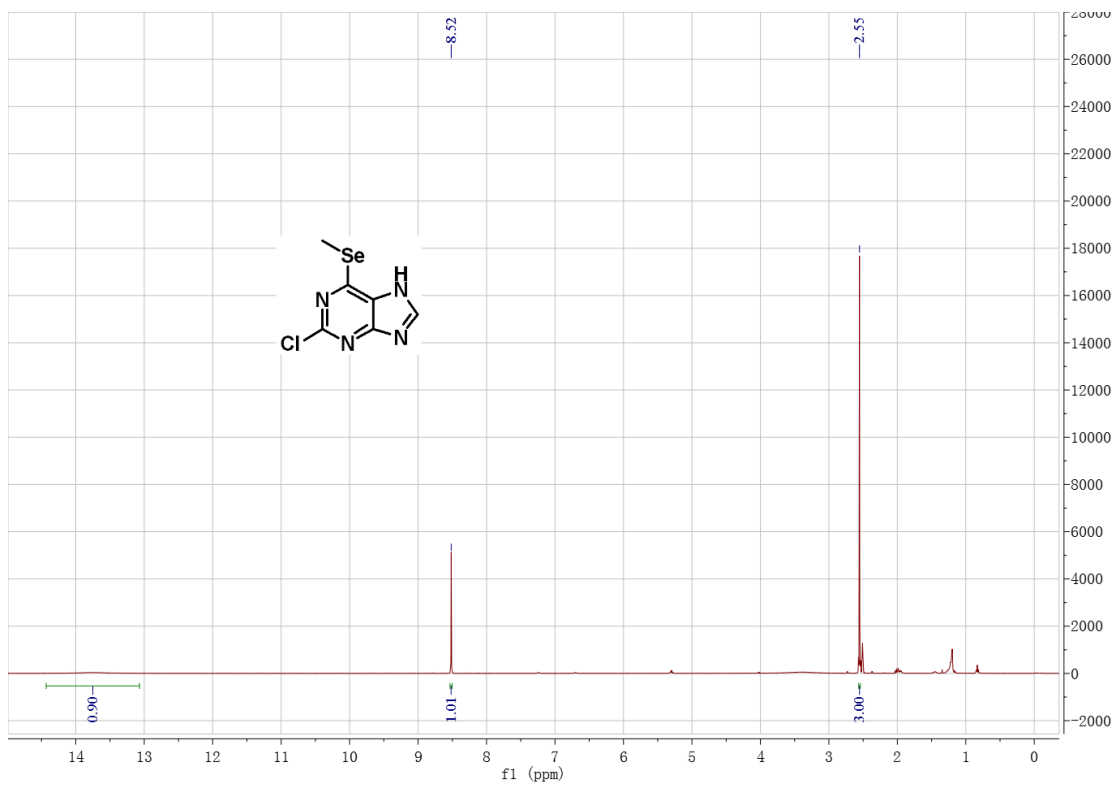
Compound **11g**



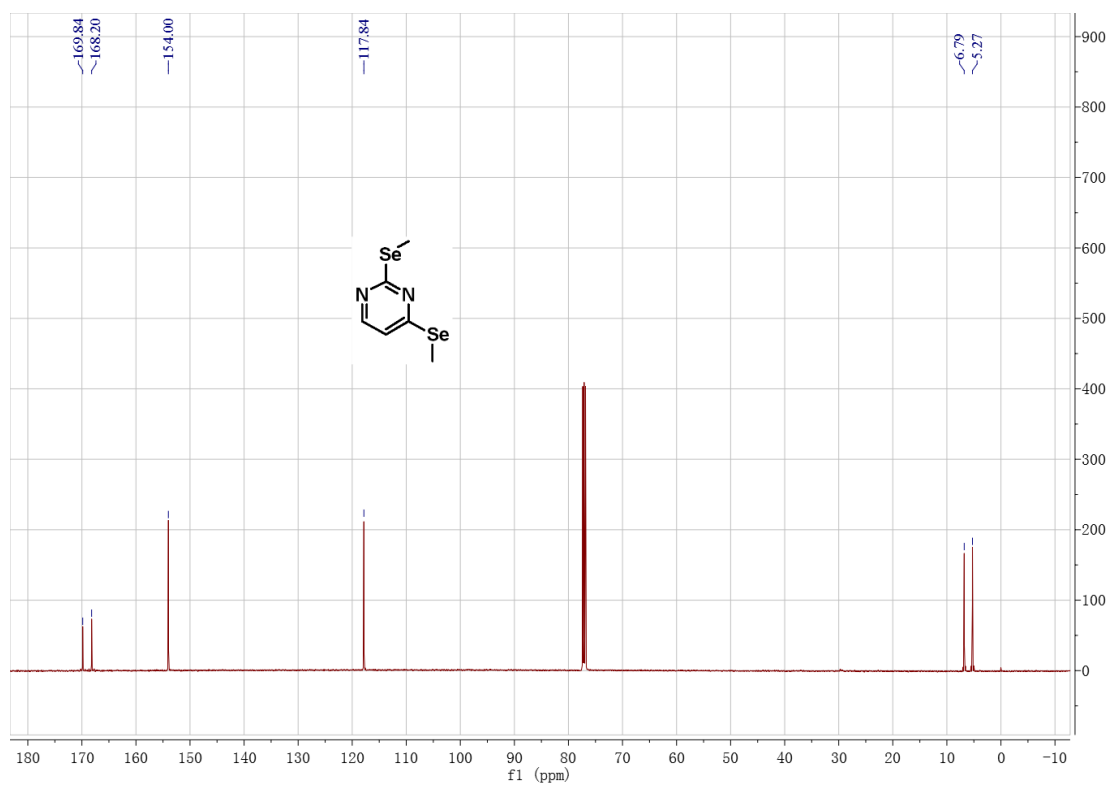
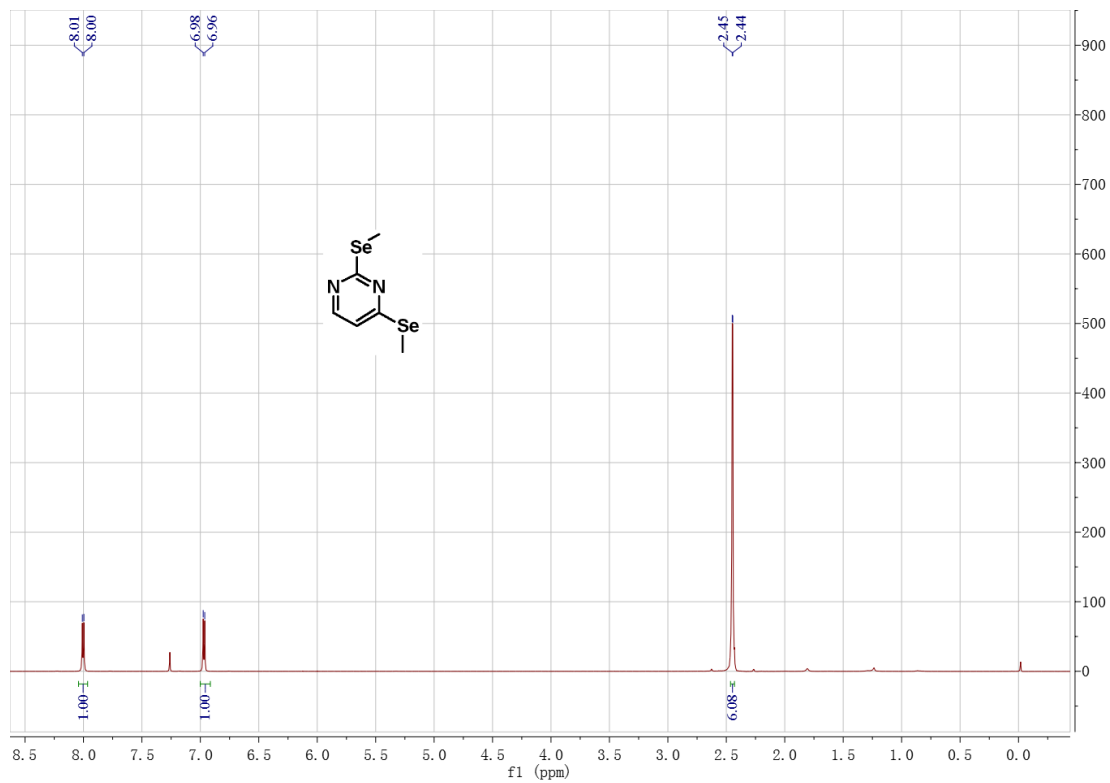
Compound 11h



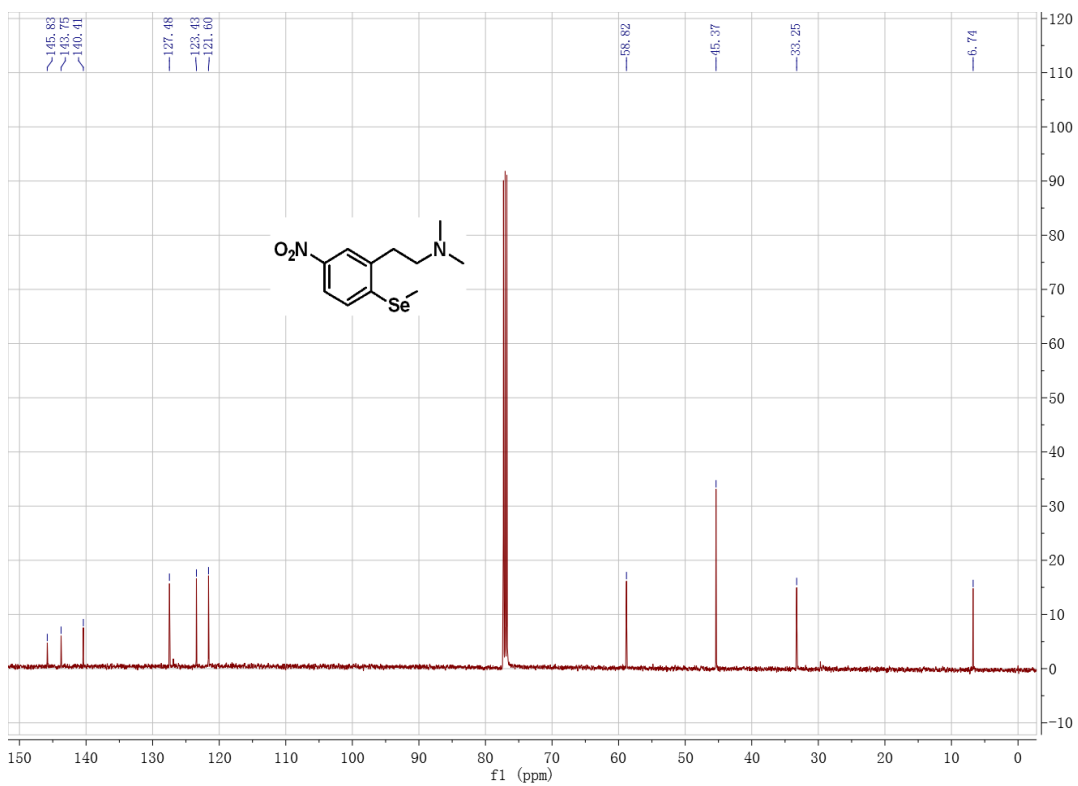
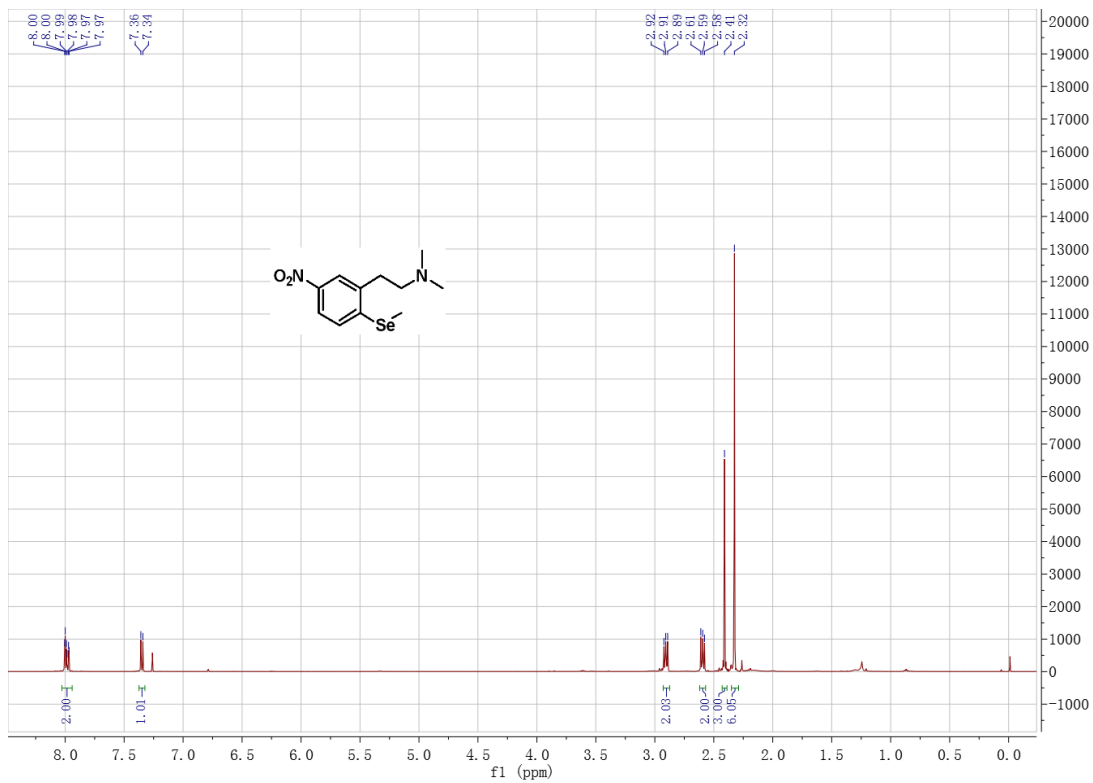
Compound 11i



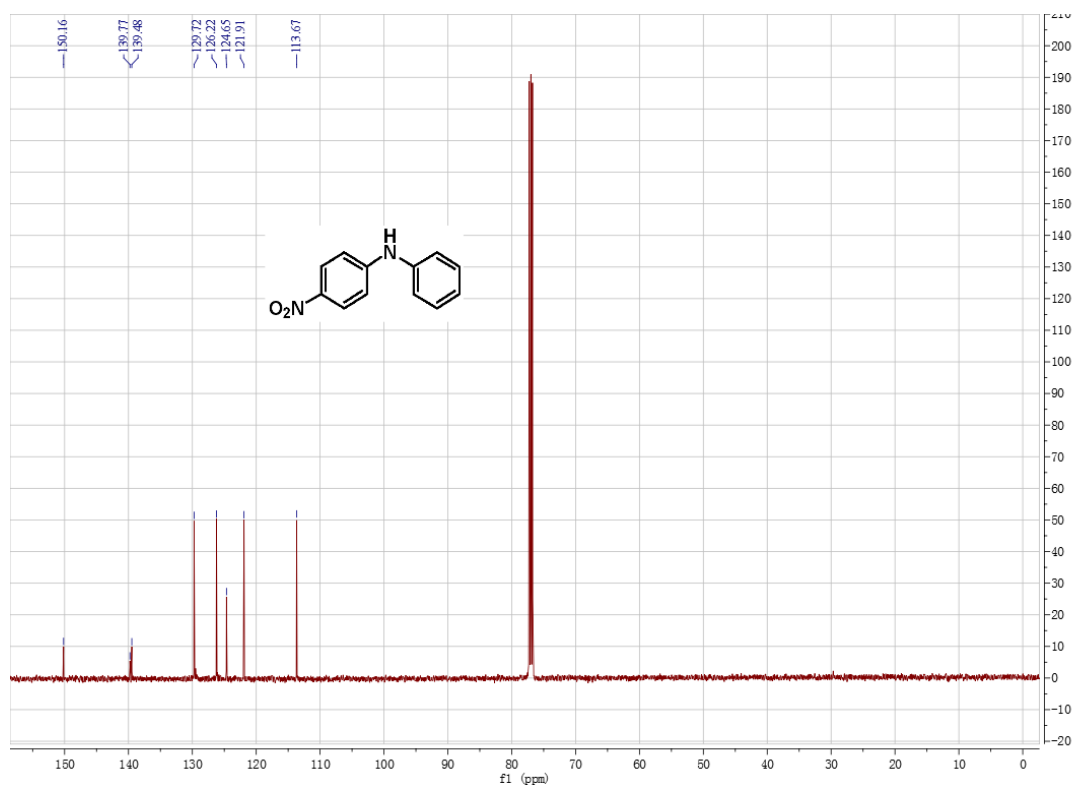
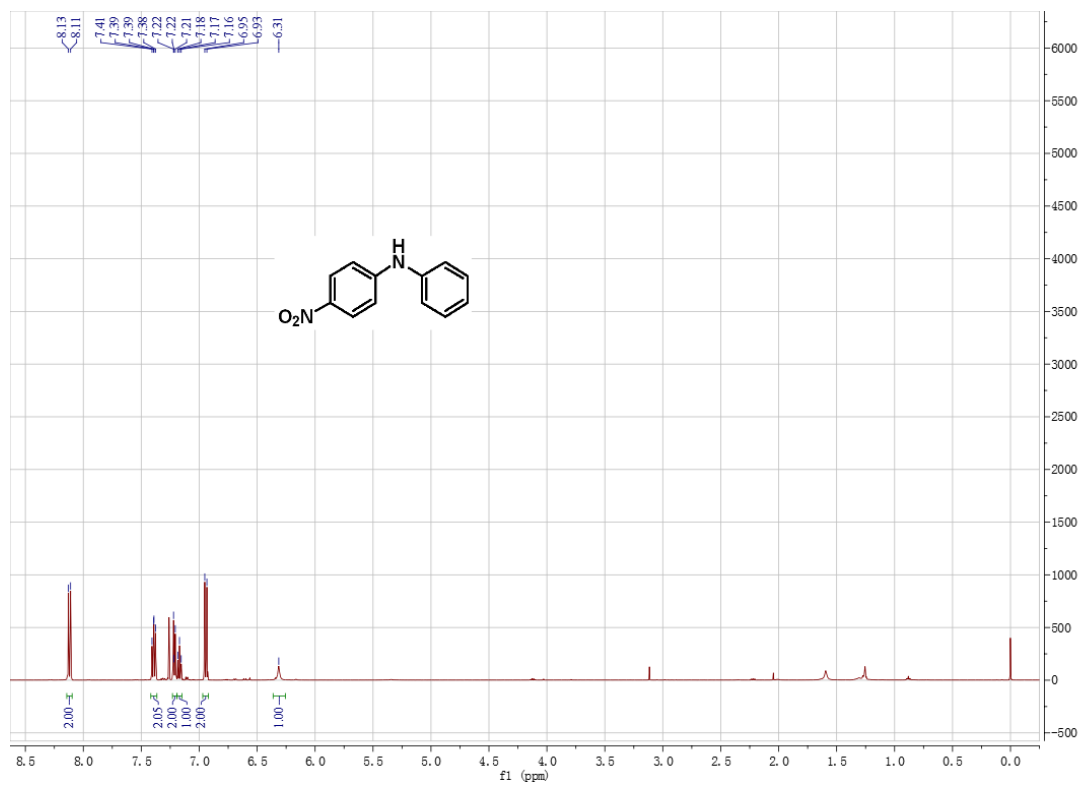
Compound 11j



Compound 11k

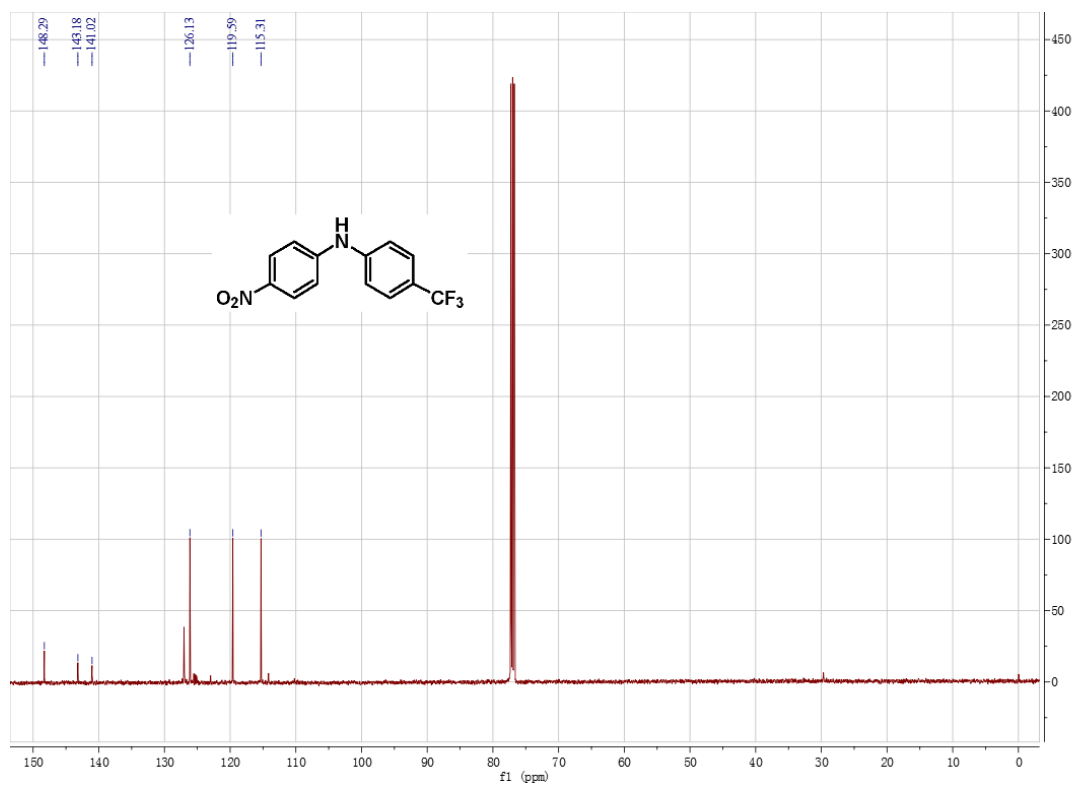
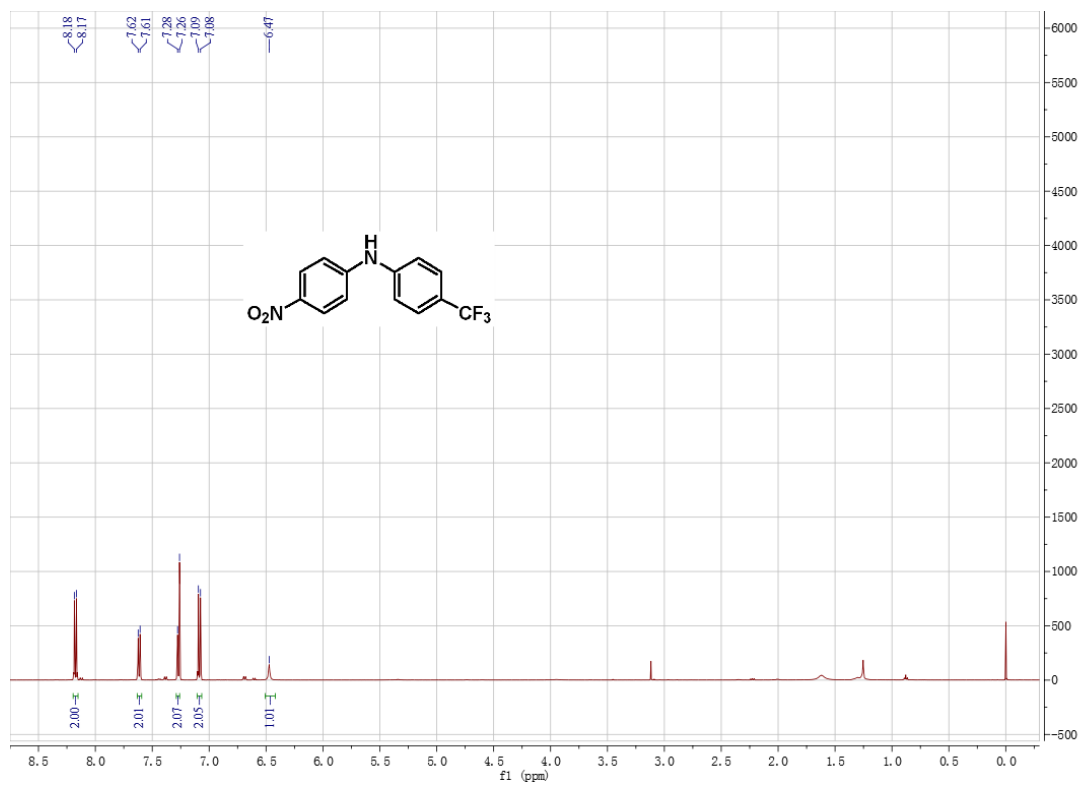


# Compound 13a

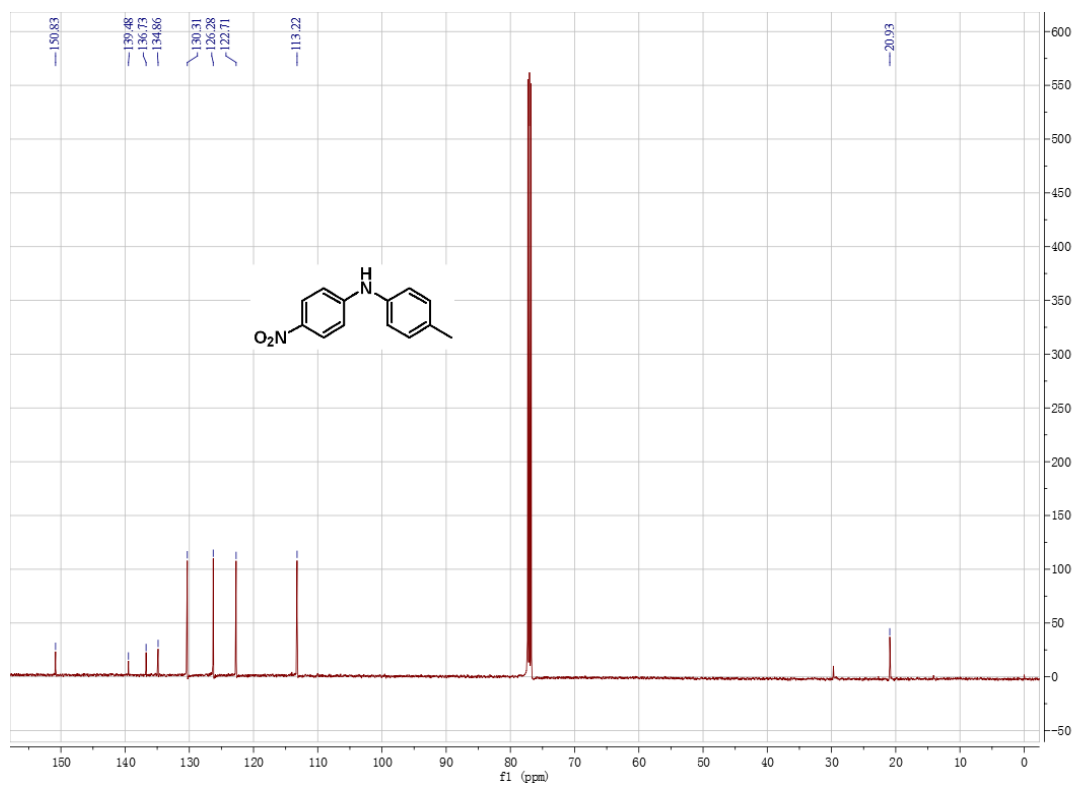
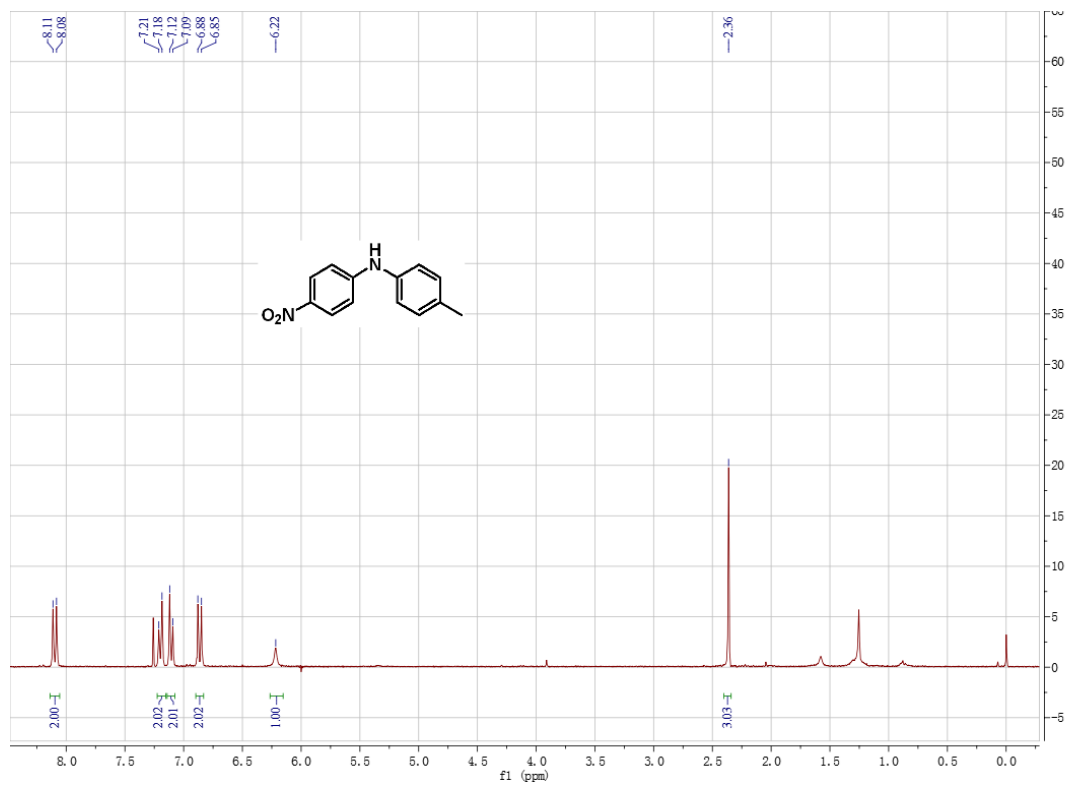




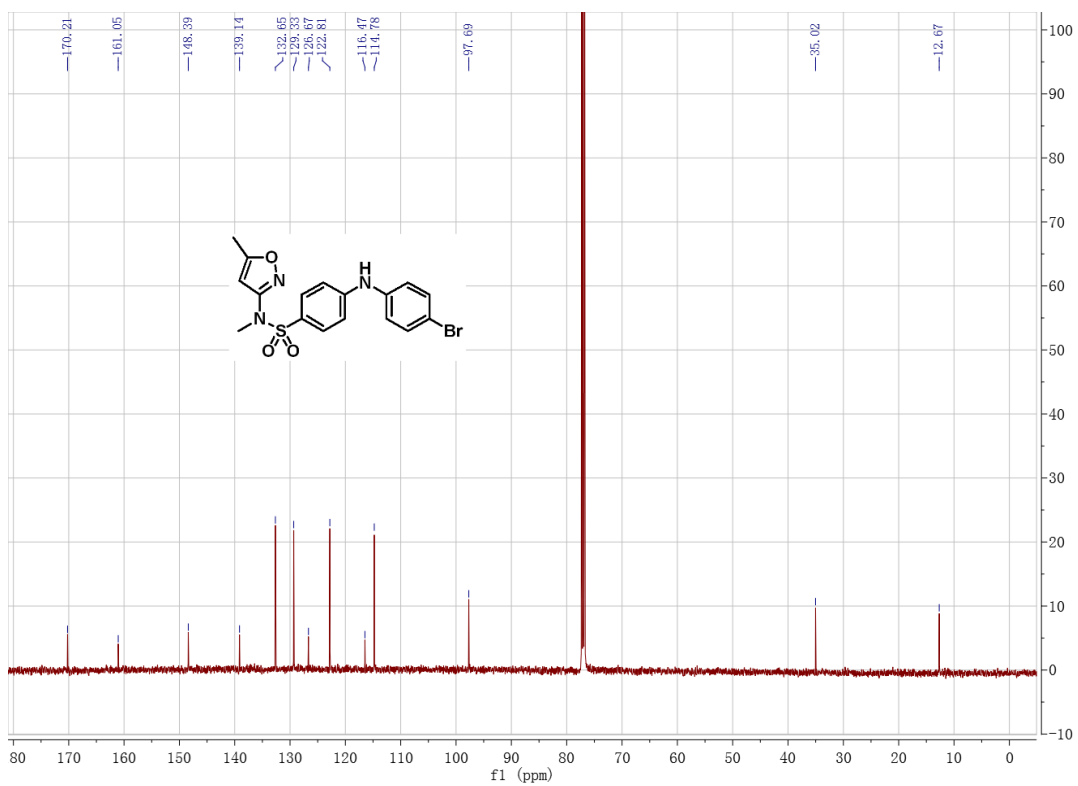
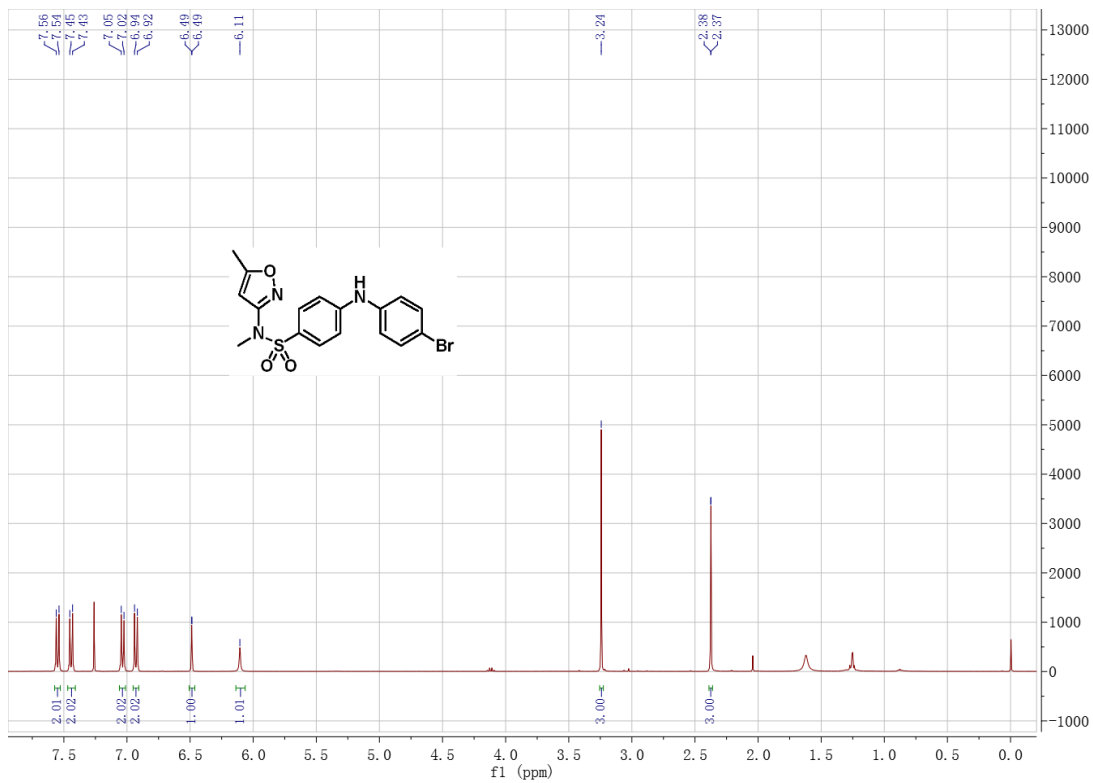
Compound **13b**



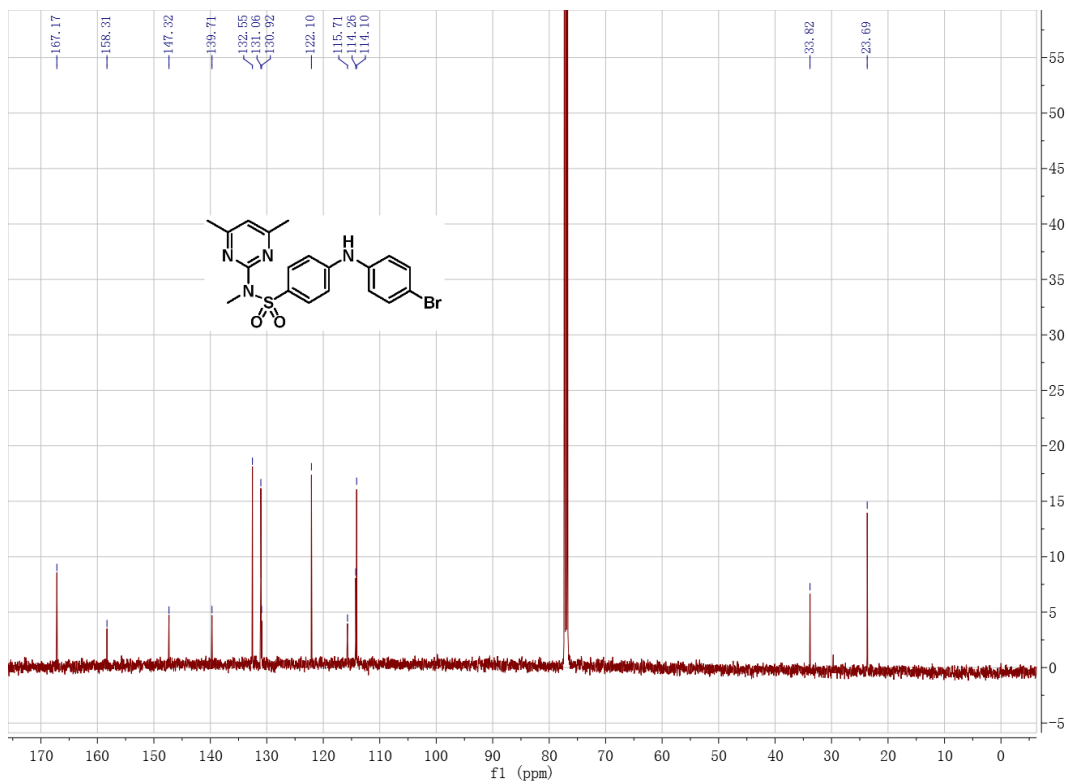
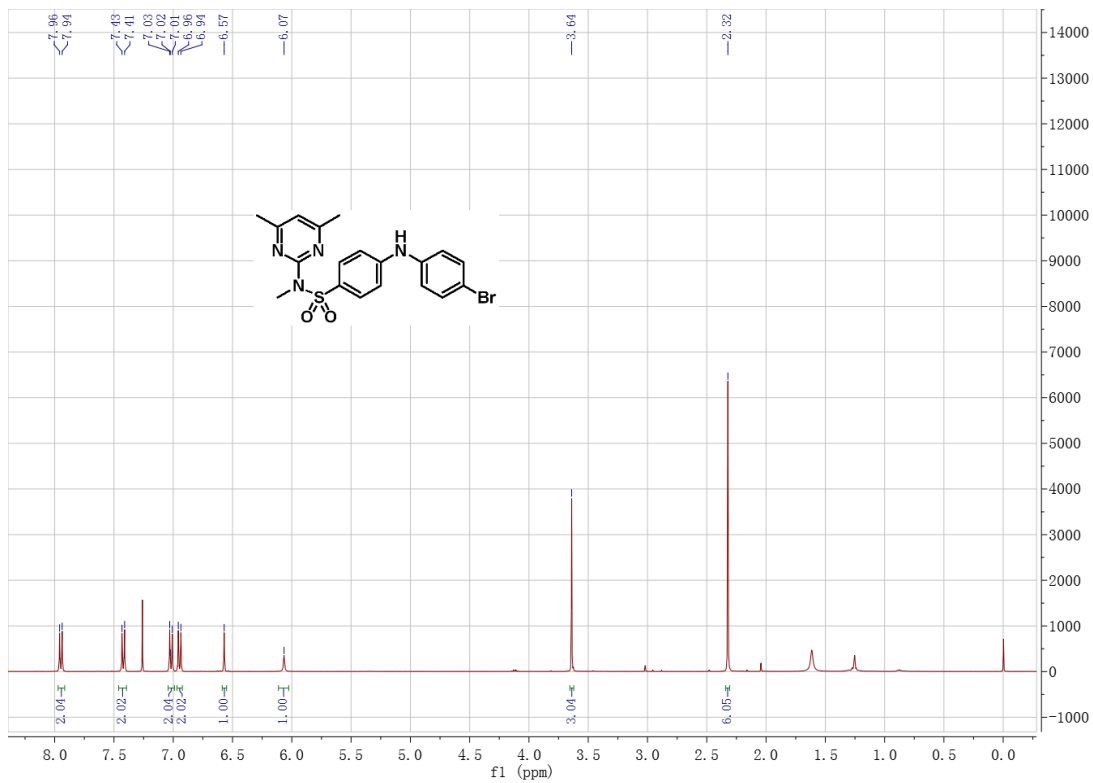
Compound **13c**



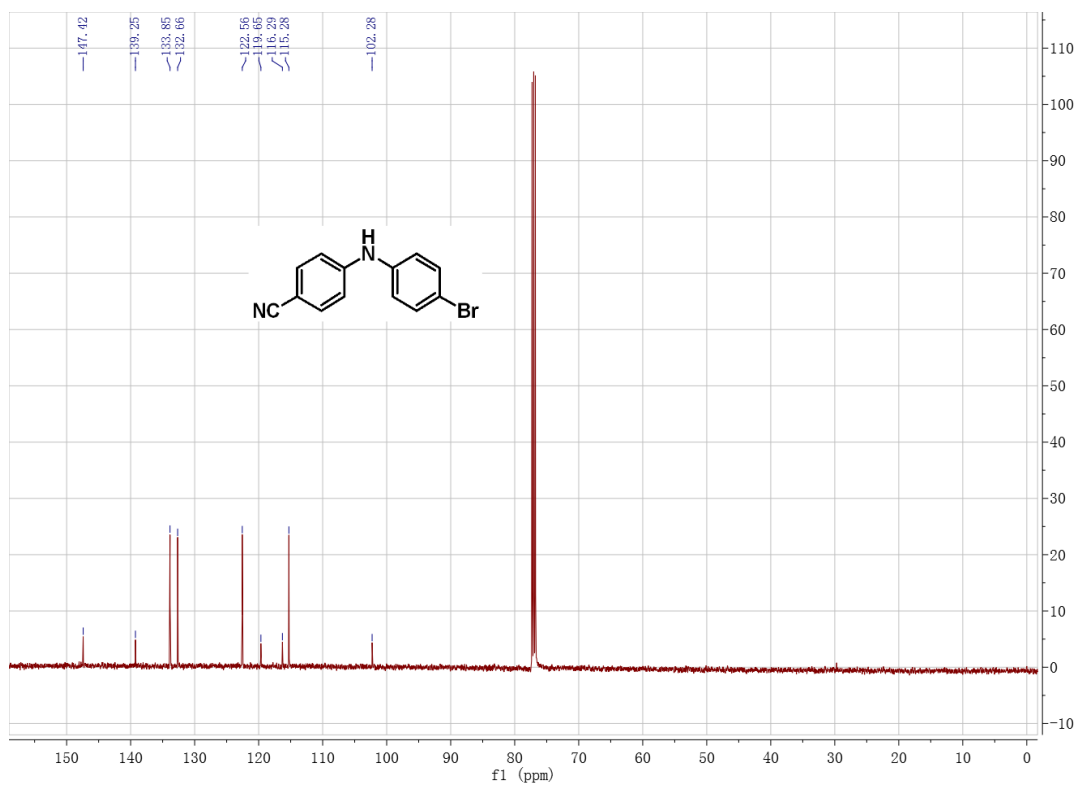
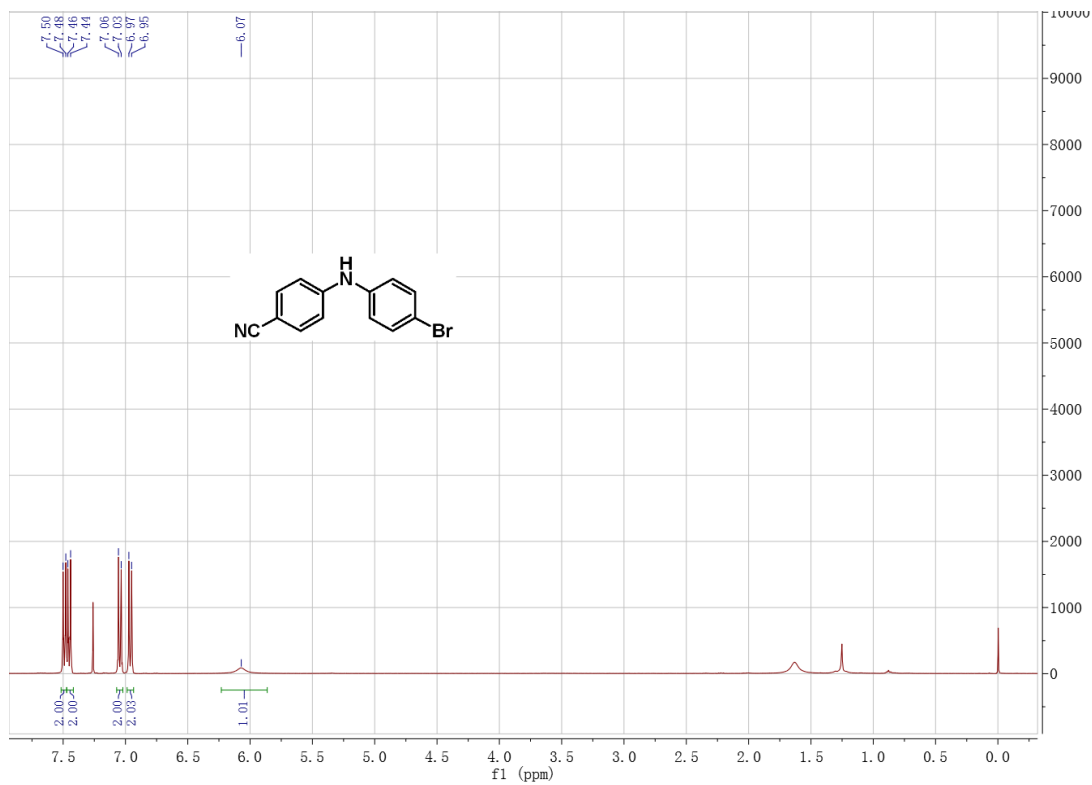
Compound 13e



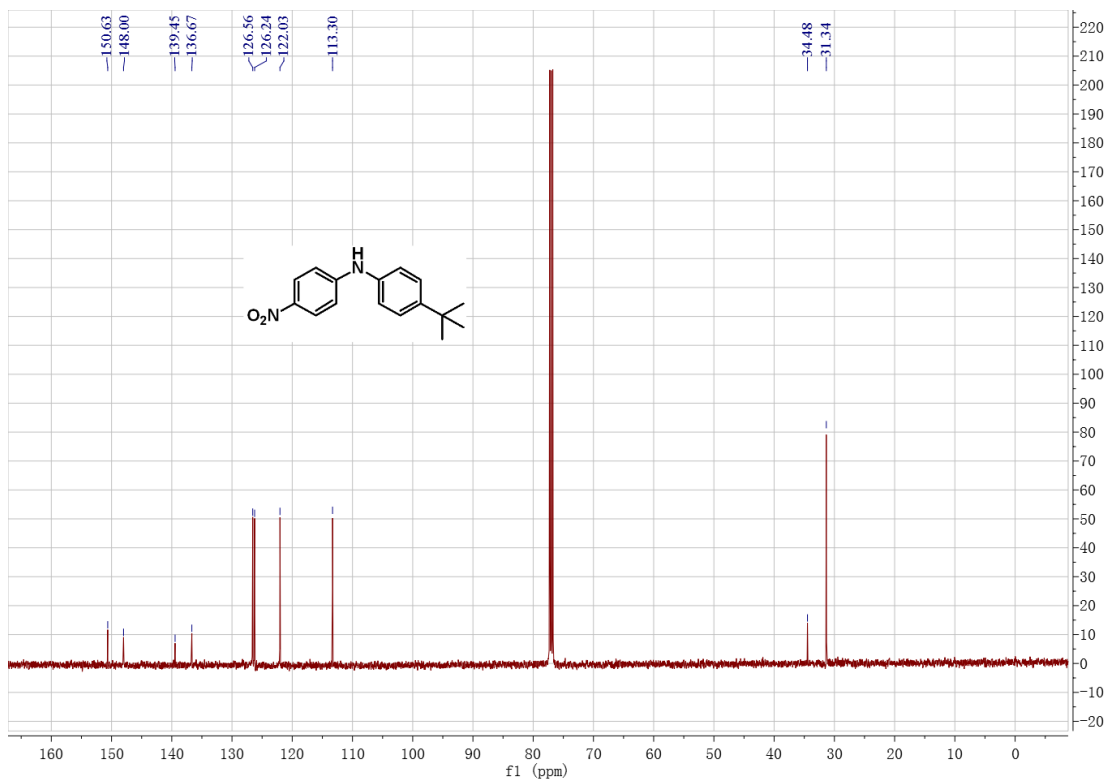
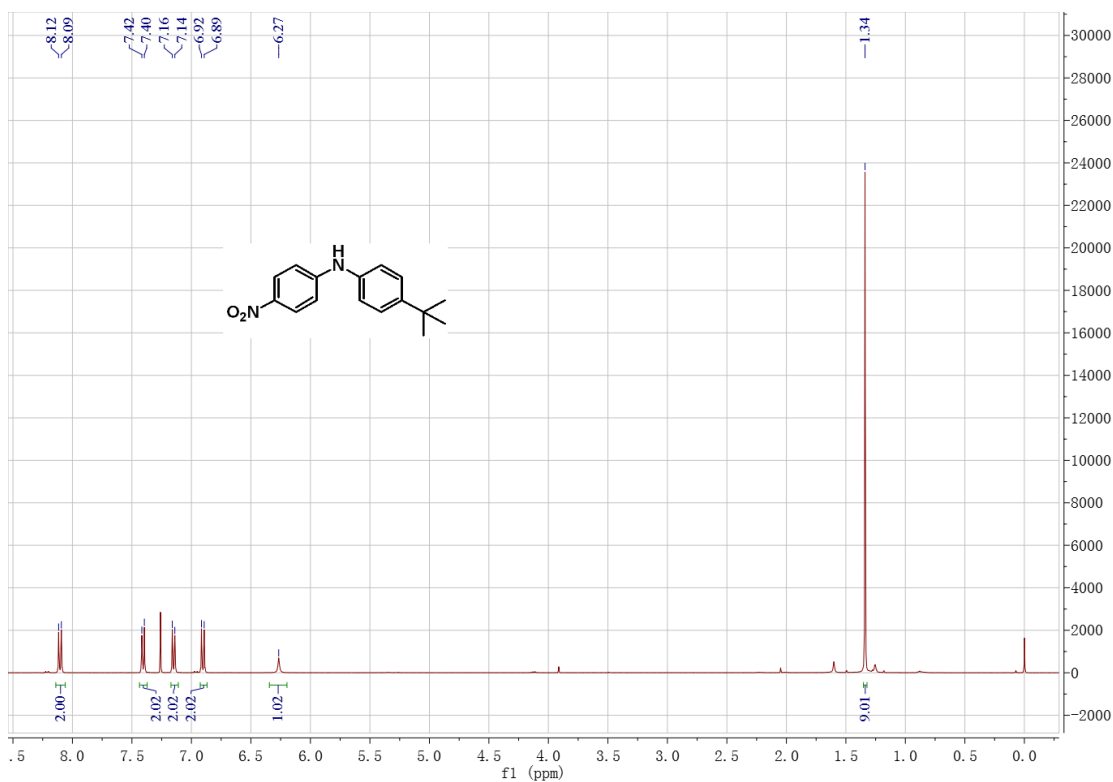
Compound 13f



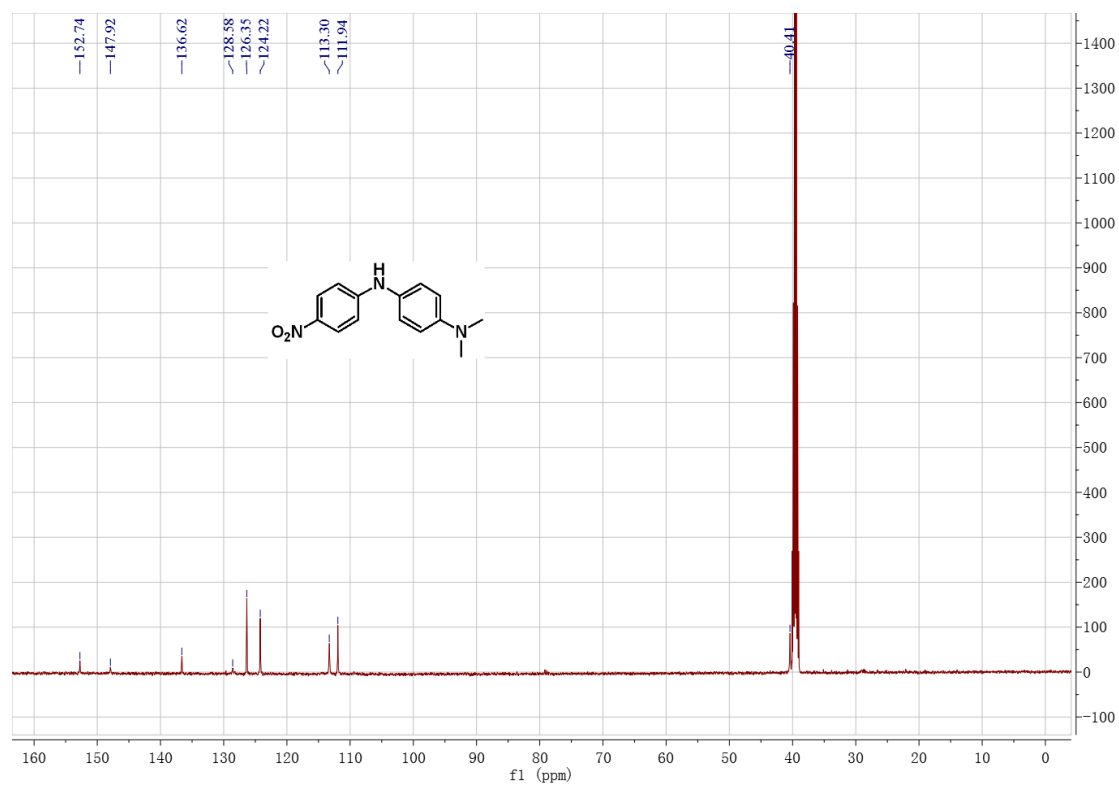
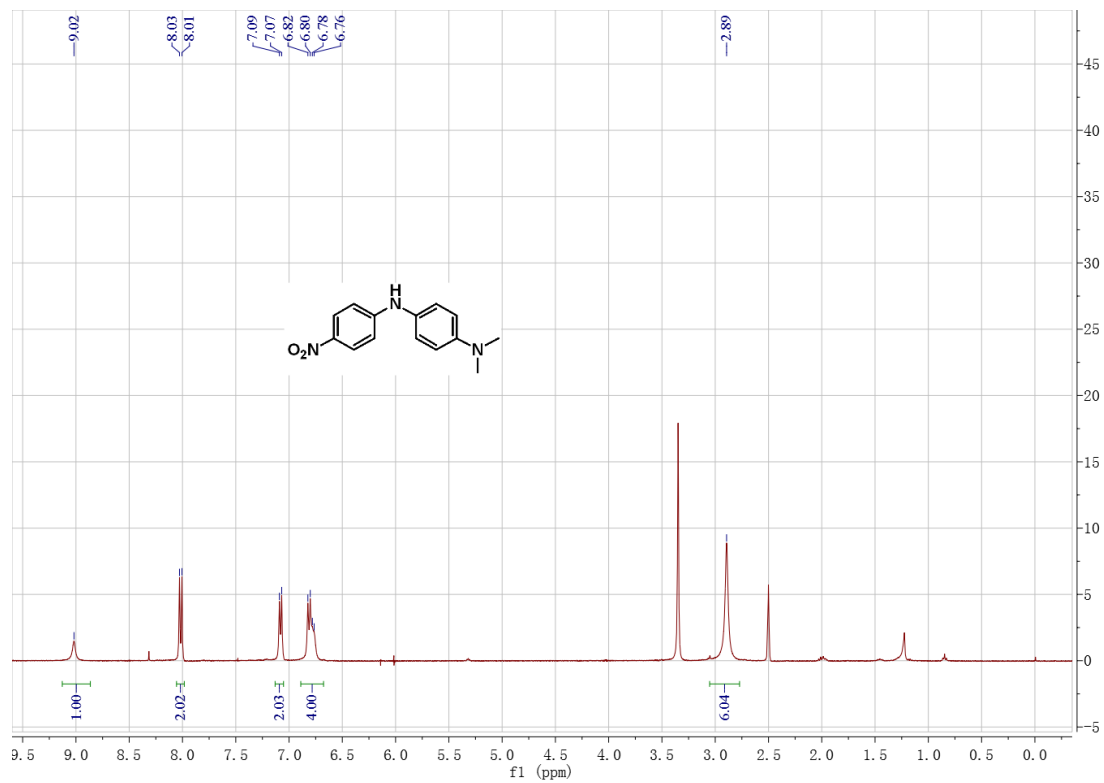
Compound **13d**



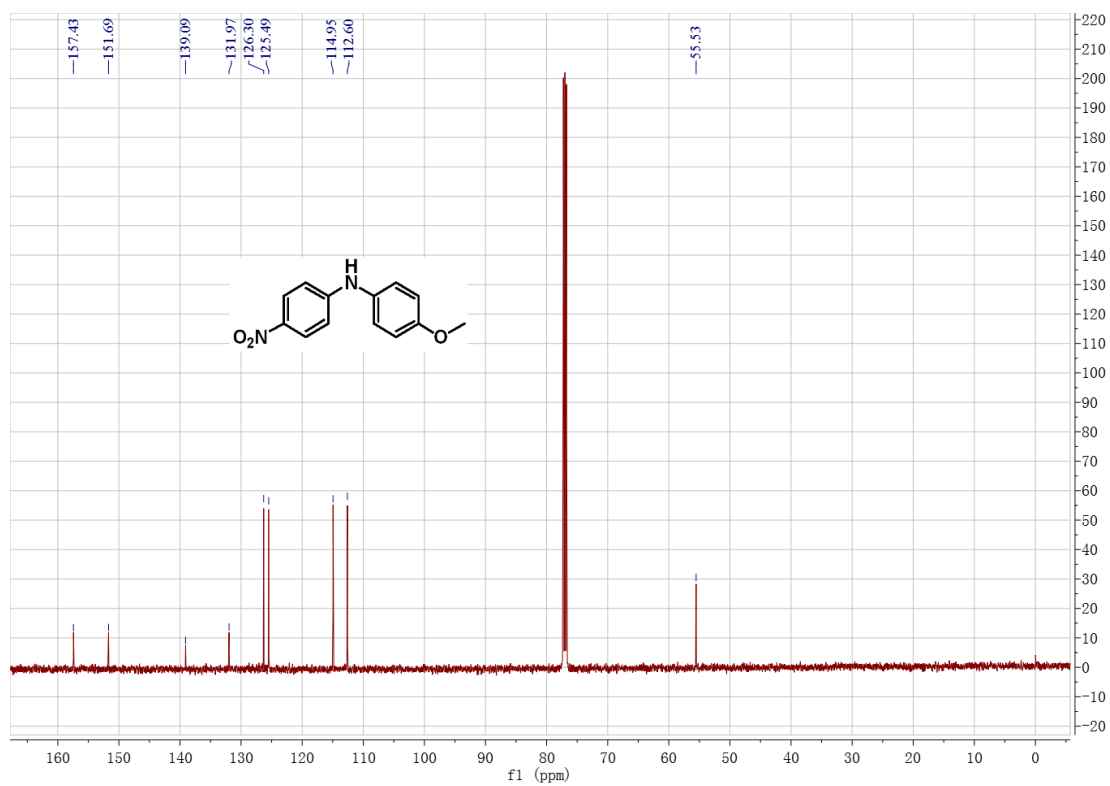
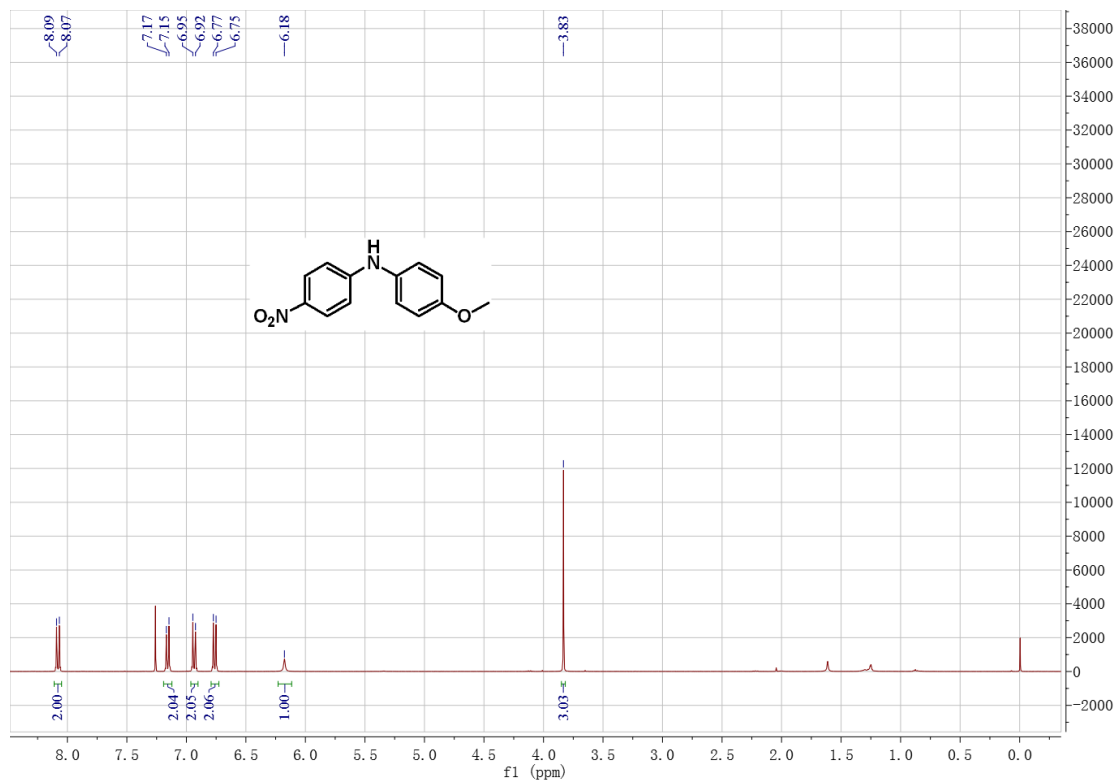
Compound 13g



Compound 13h

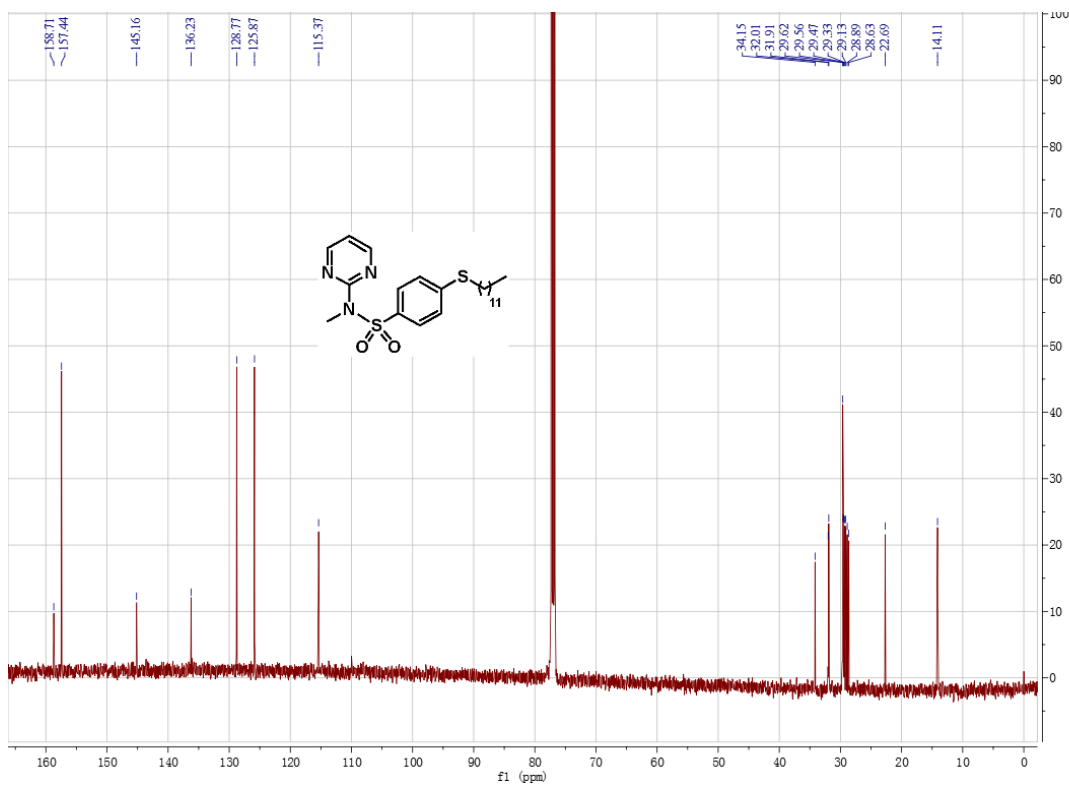
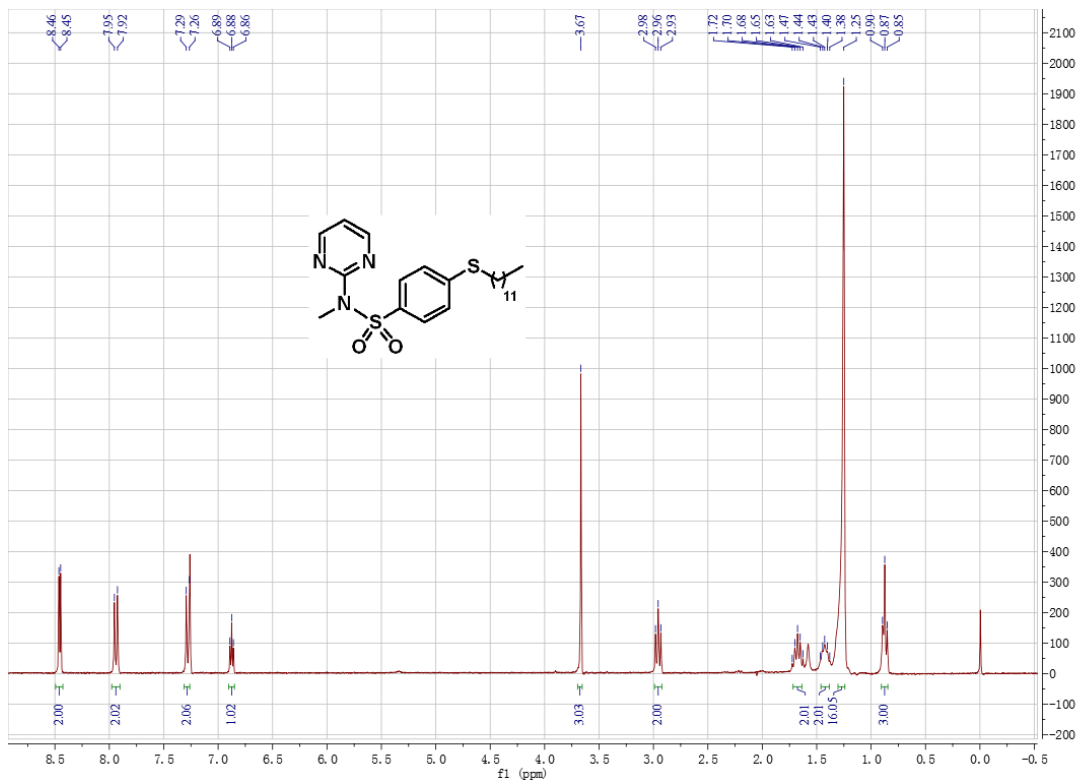


Compound 13i

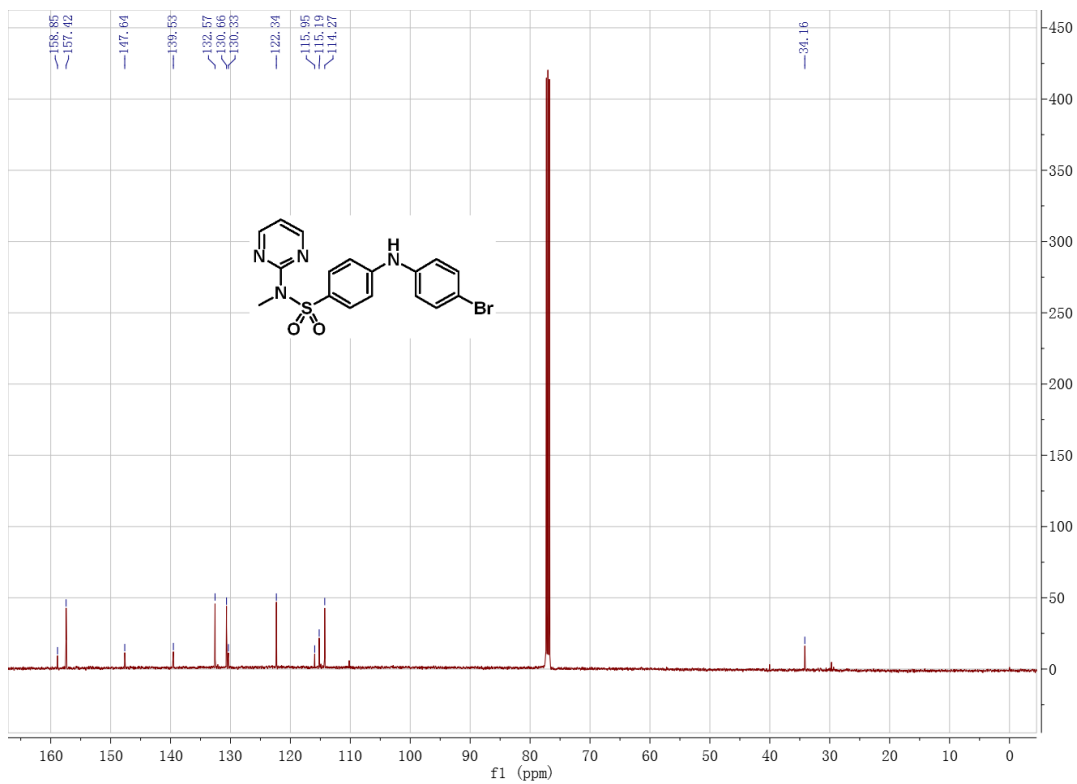
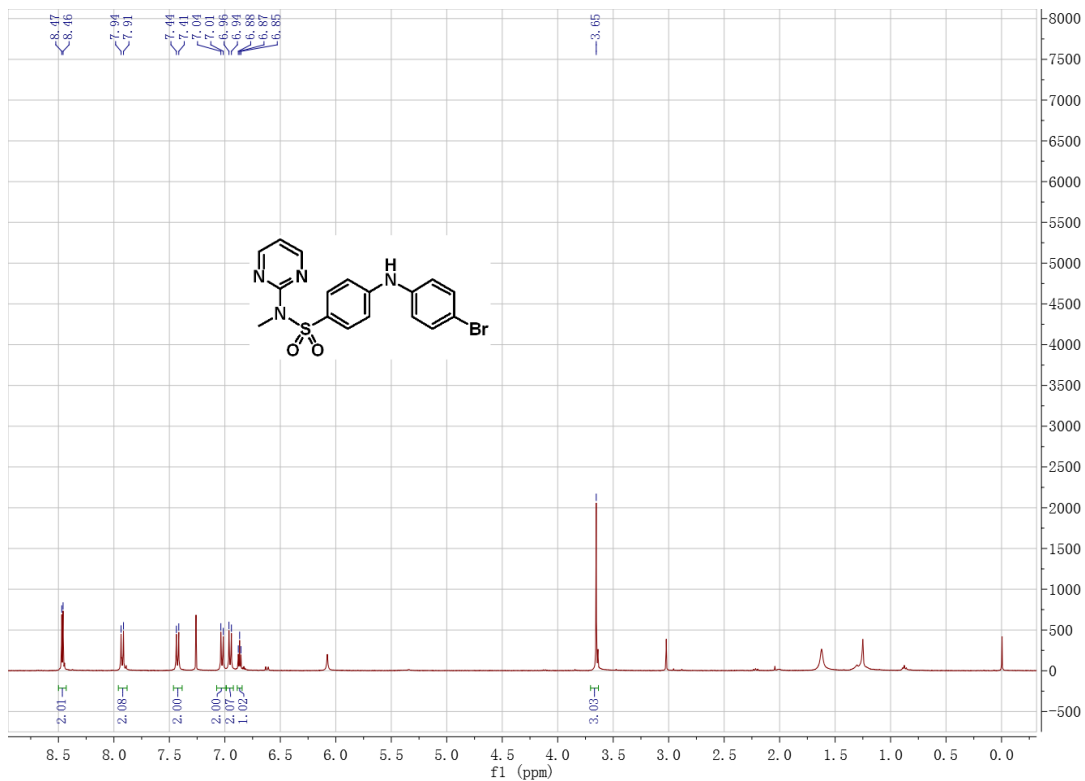




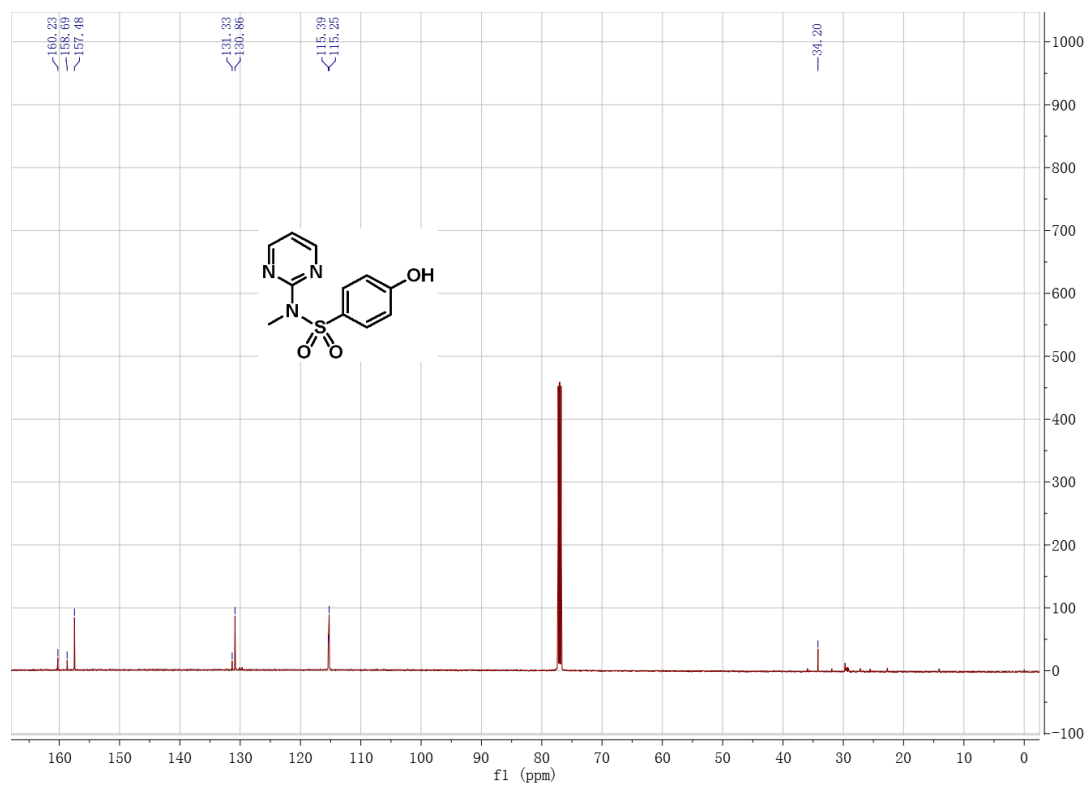
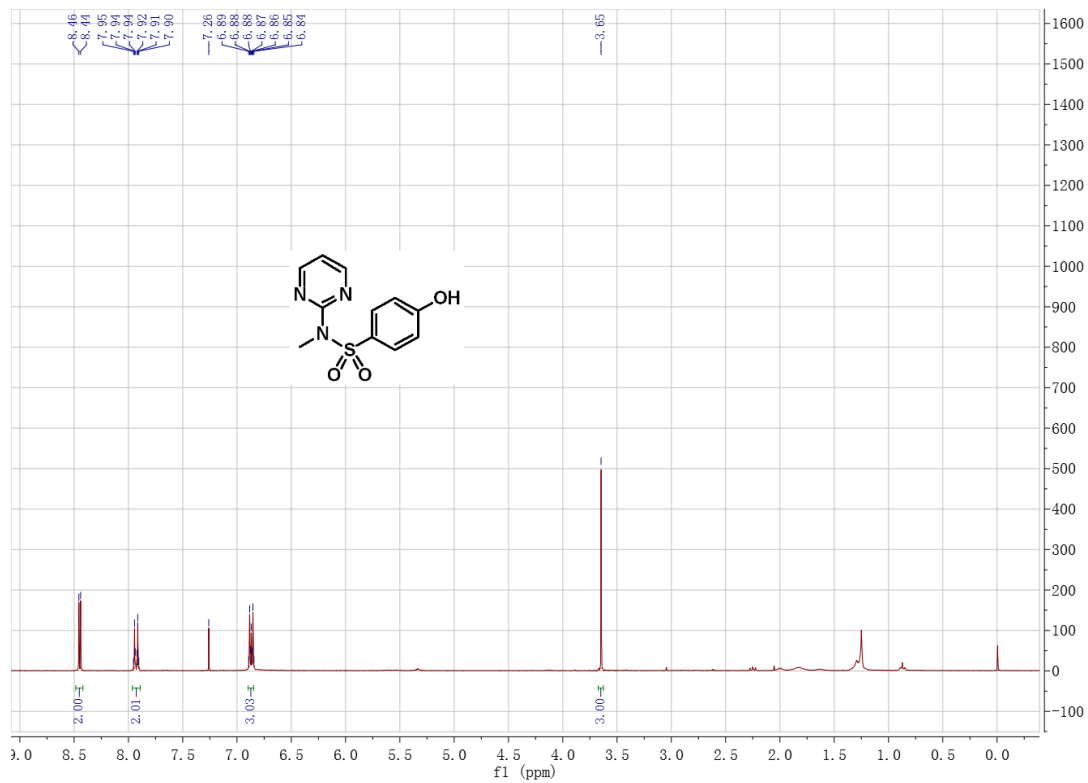
Compound **3mp**



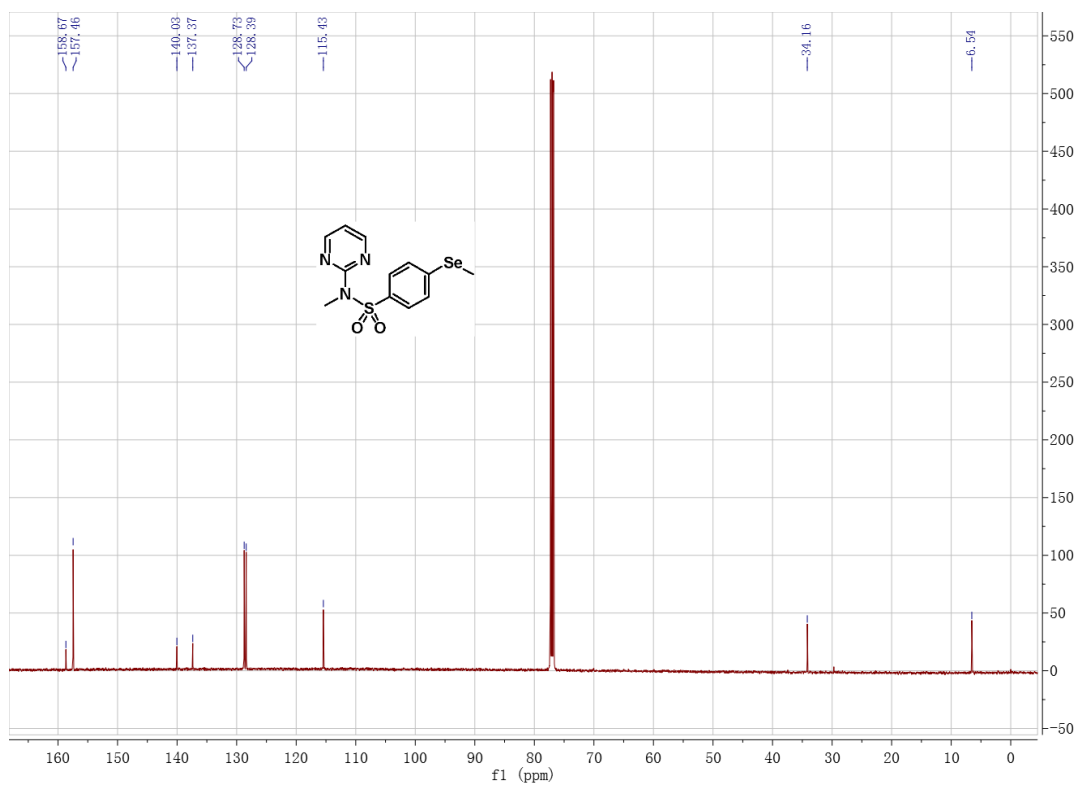
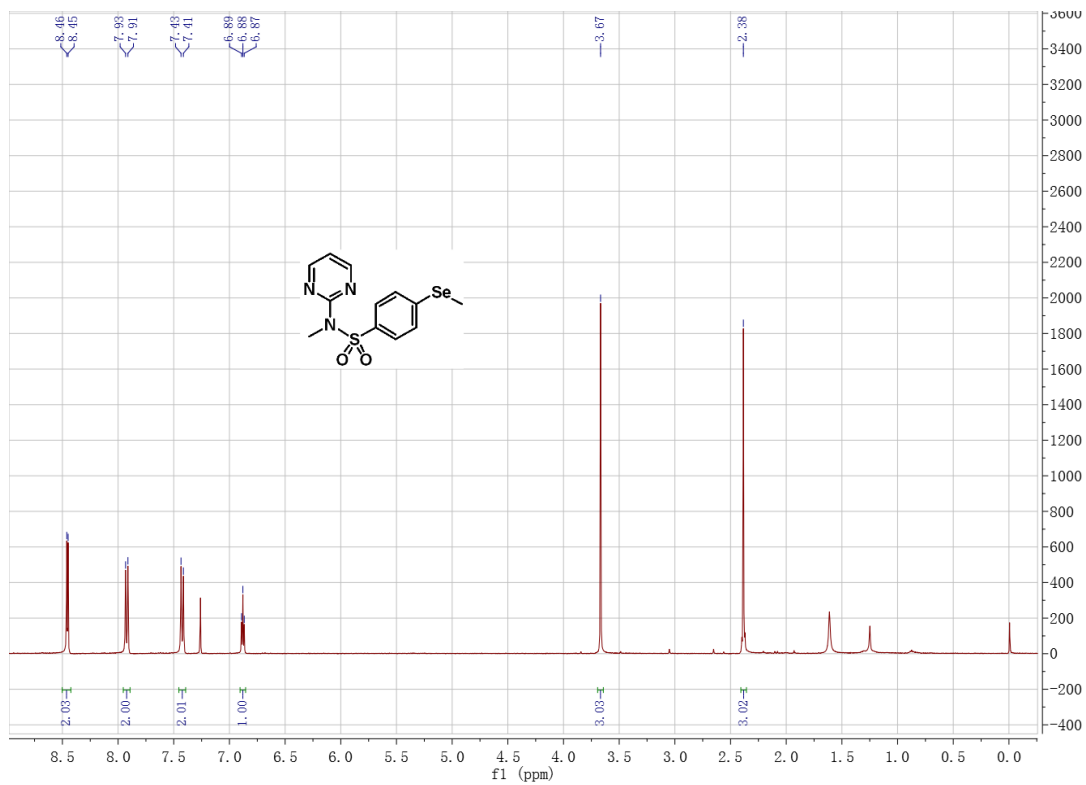
Compound 13h



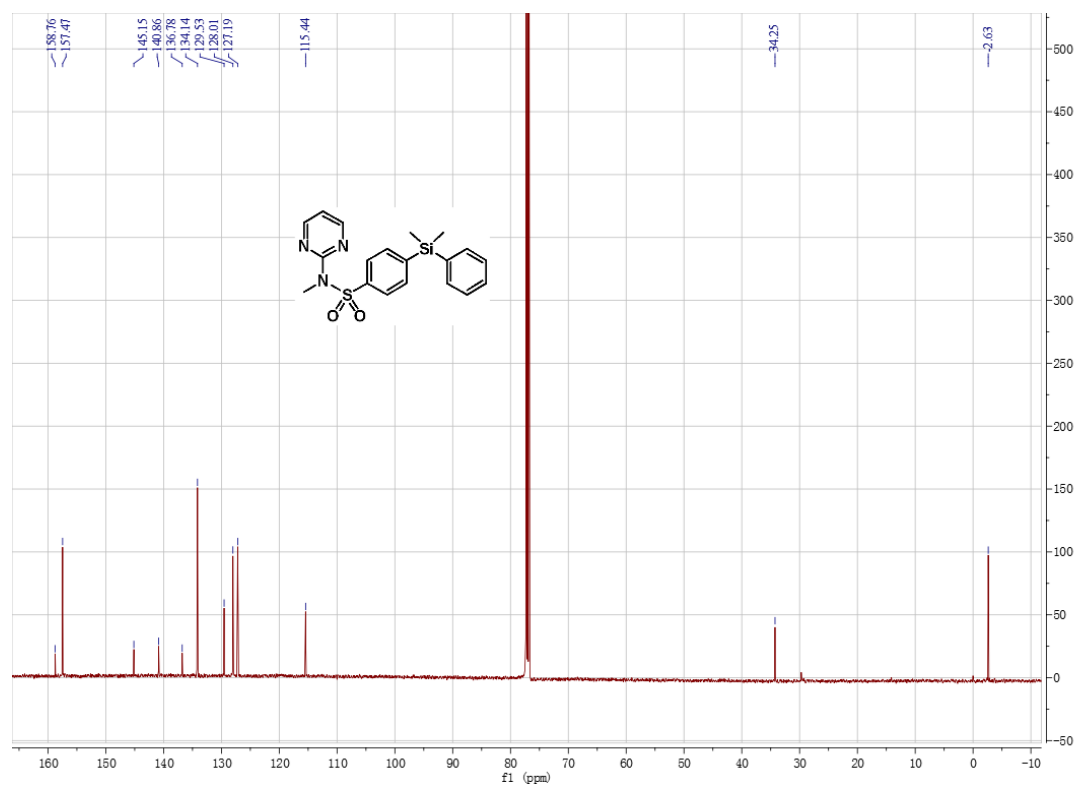
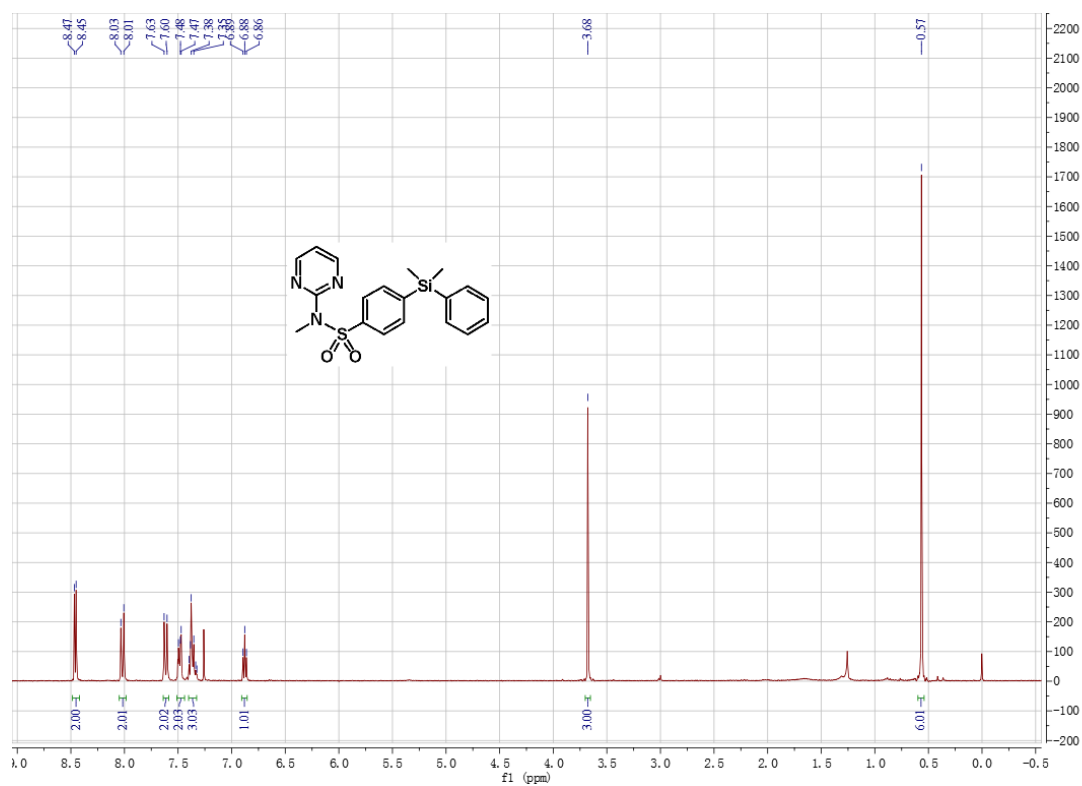
Compound 14a



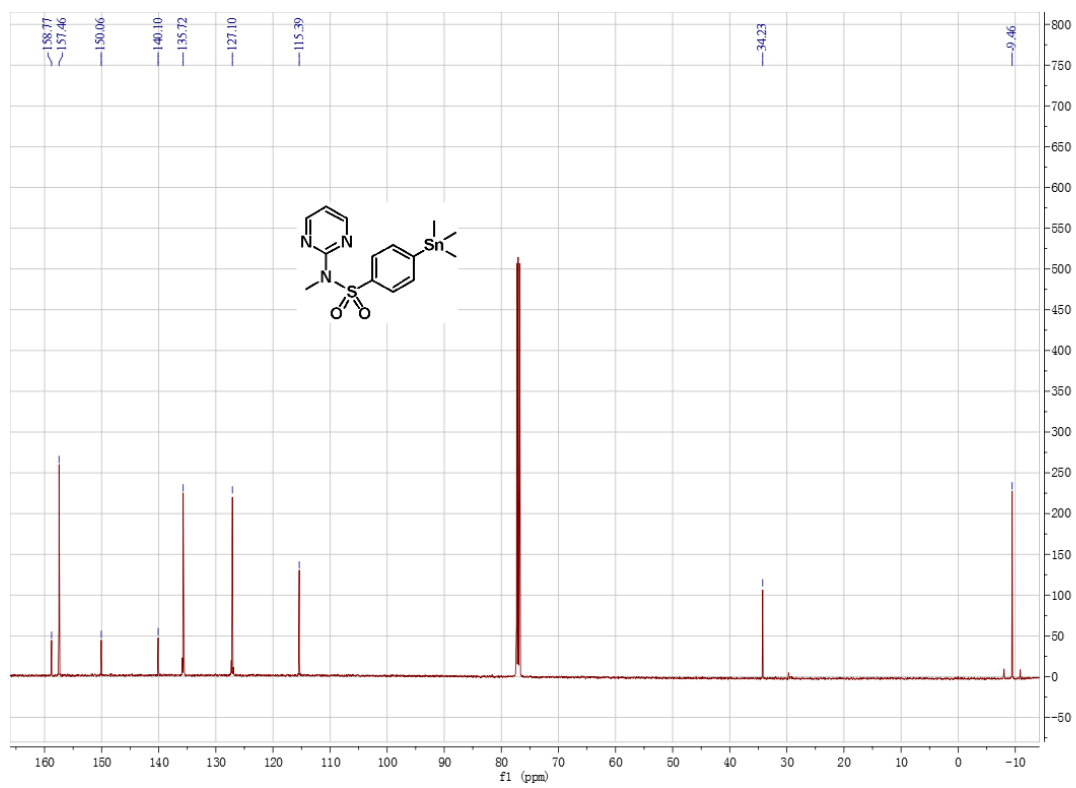
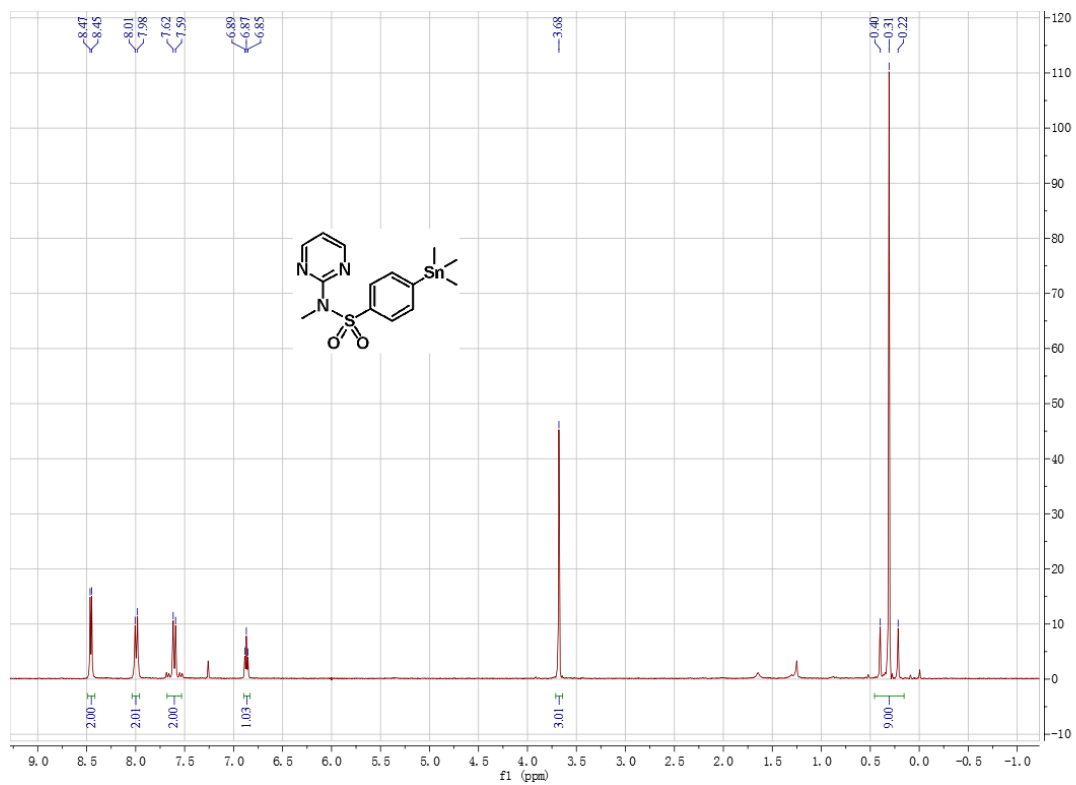
# Compound 11h



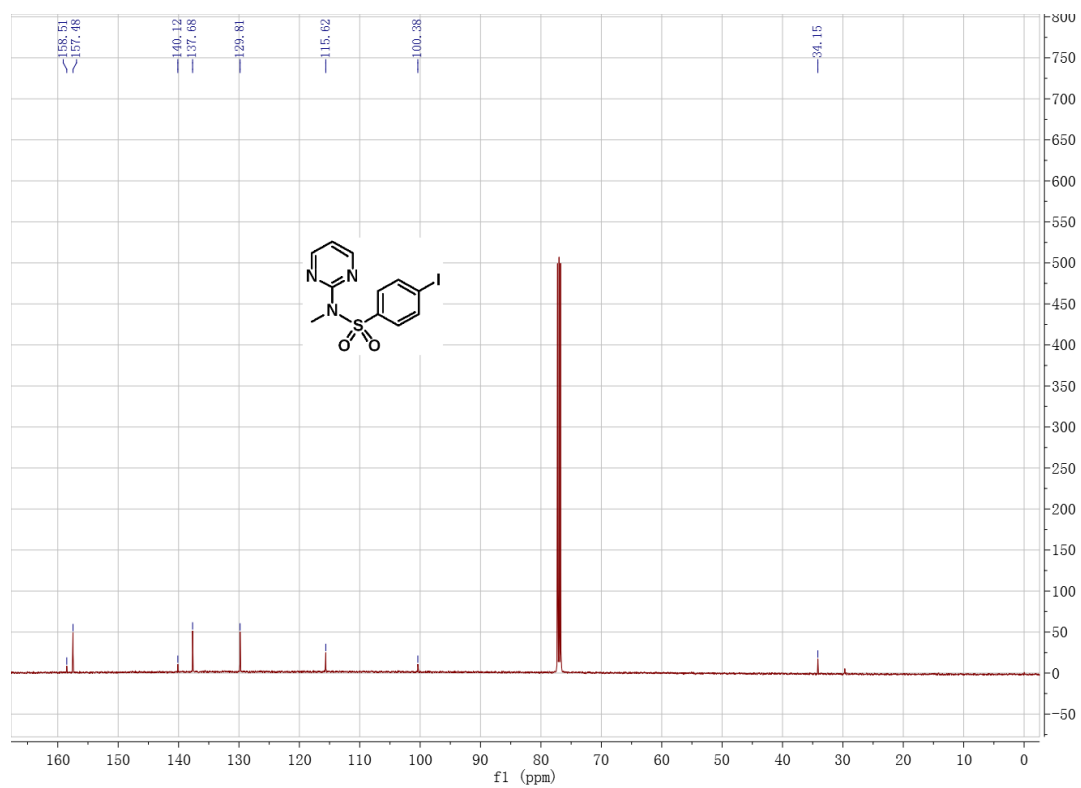
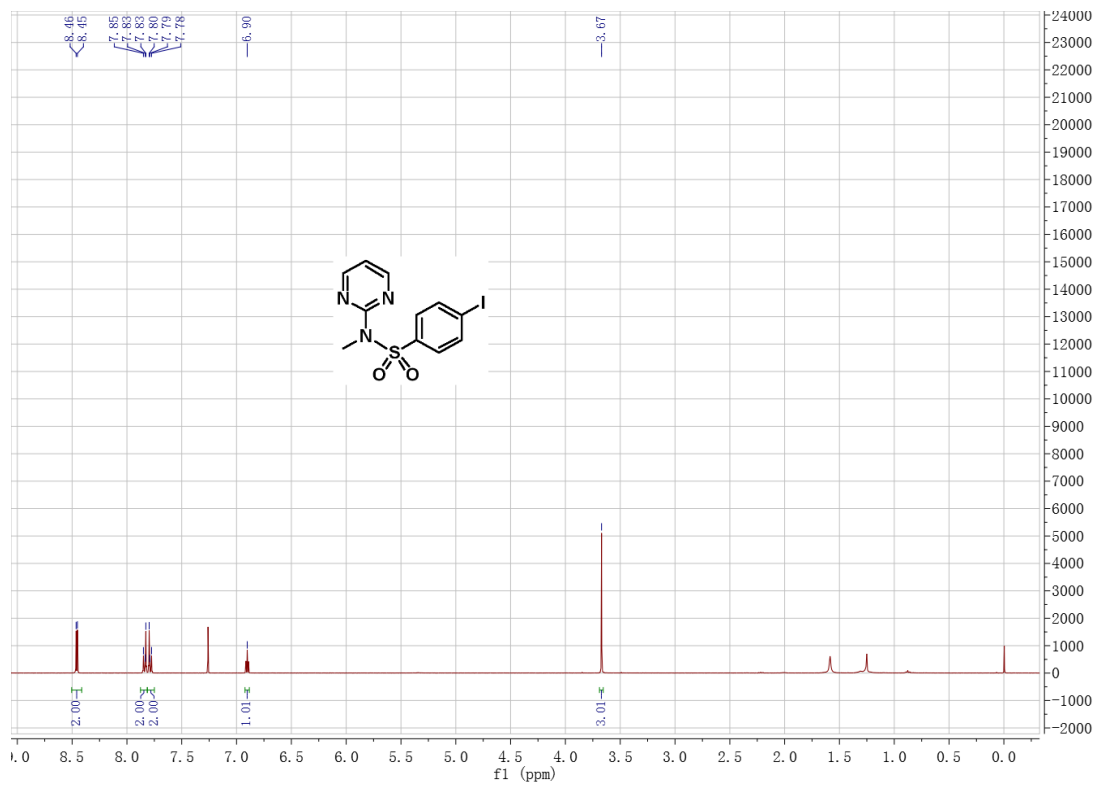
# Compound 5j



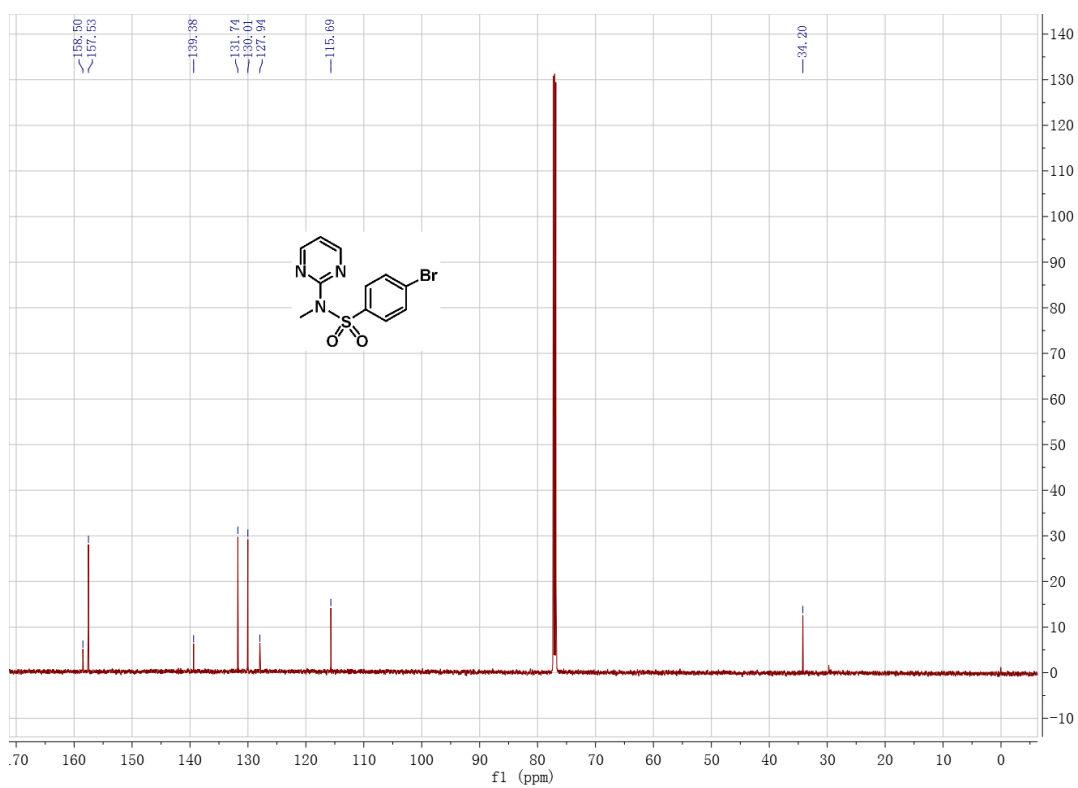
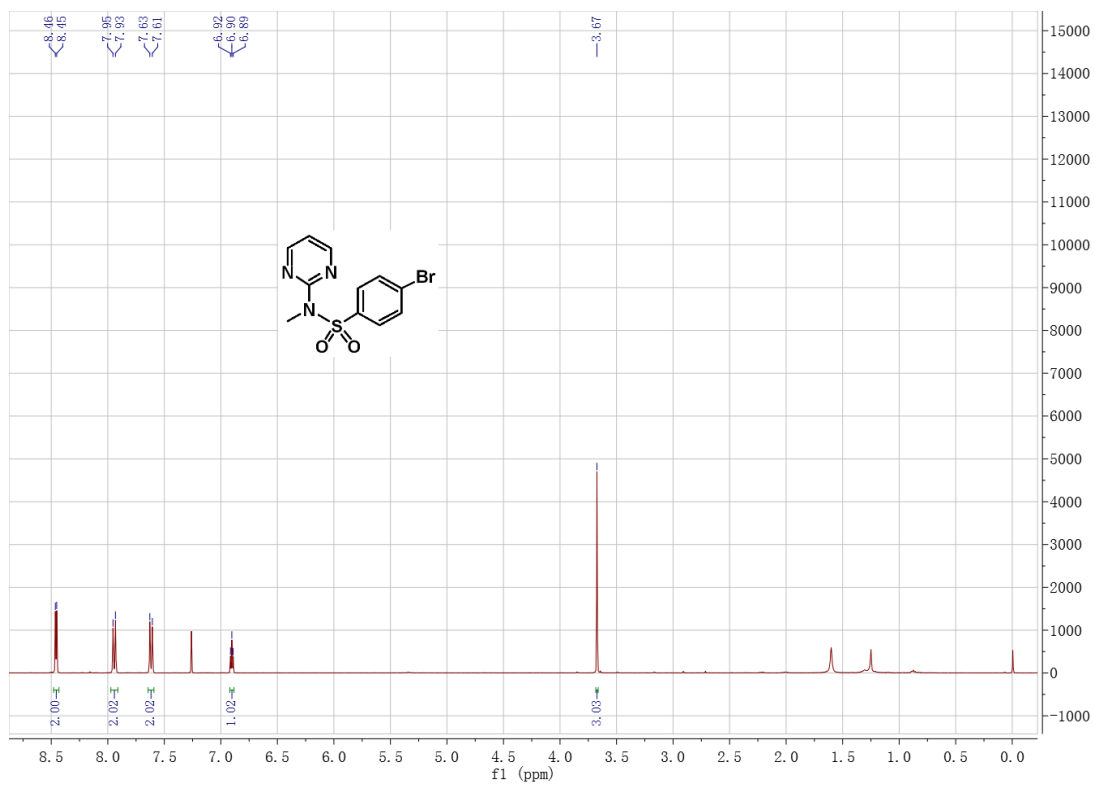
# Compound 7o



Compound **14b**

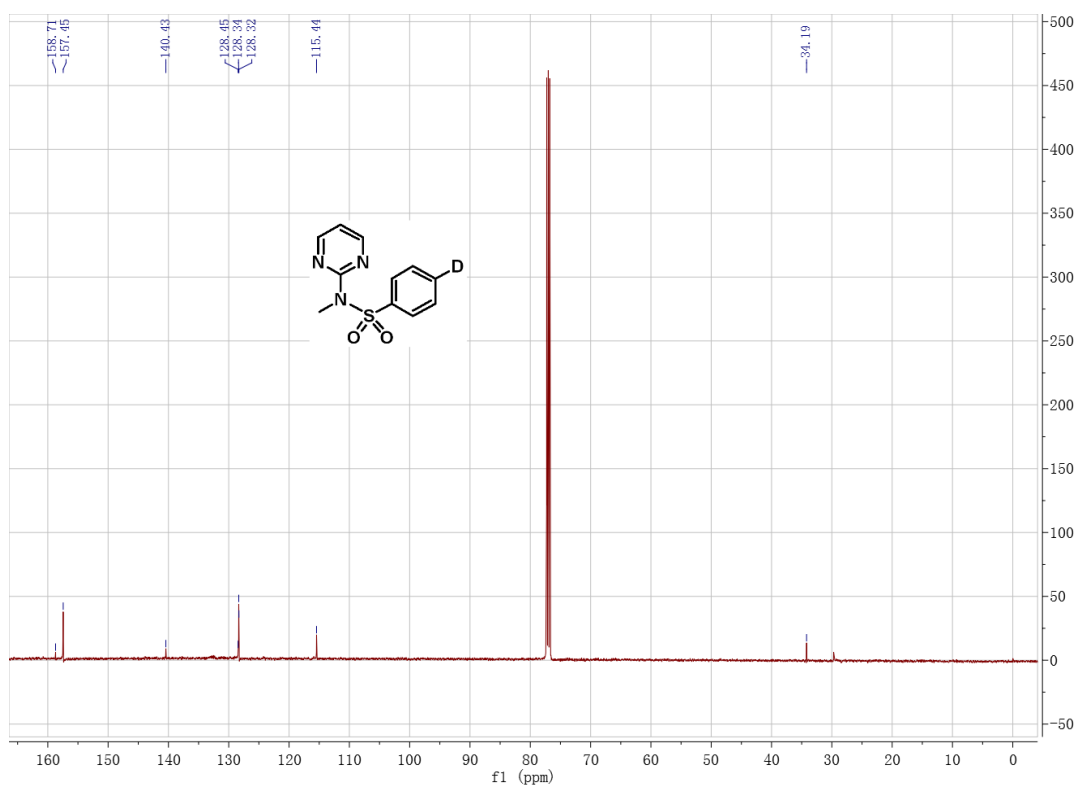
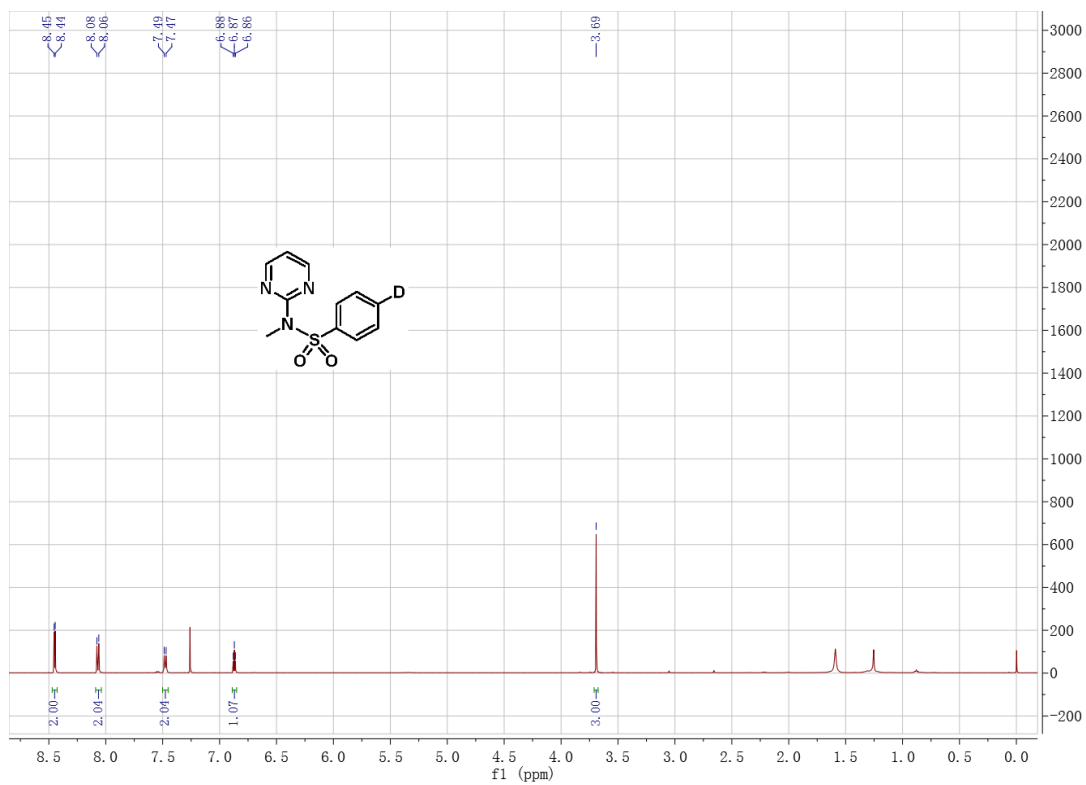


# Compound 14c



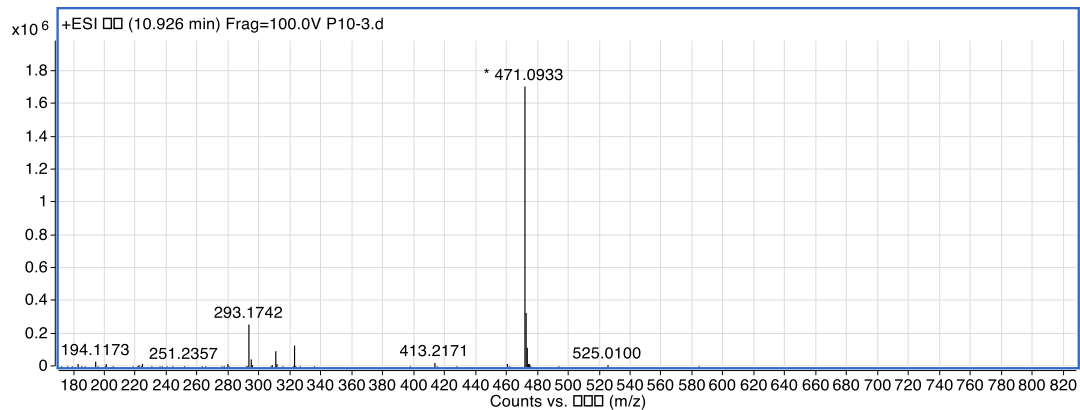


# Compound 14d

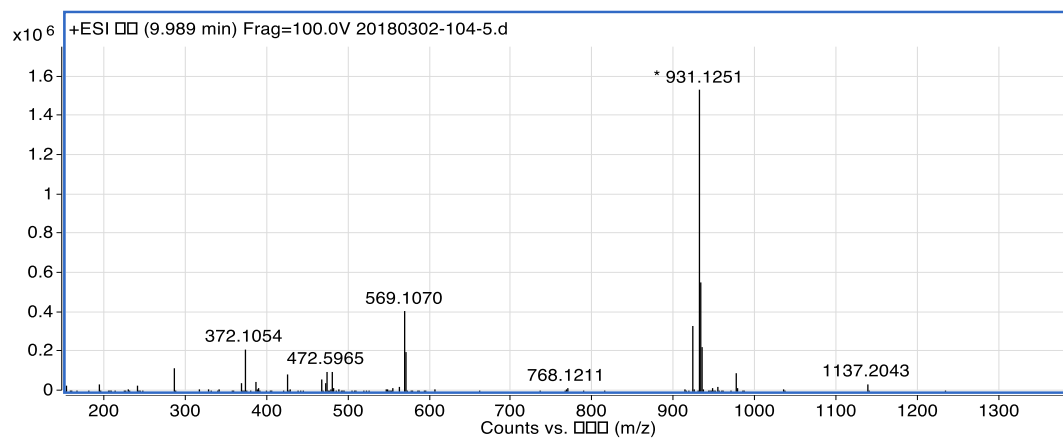


## 5. Copies of MS Spectrums for Compounds in Fig 5 and Fig 6.

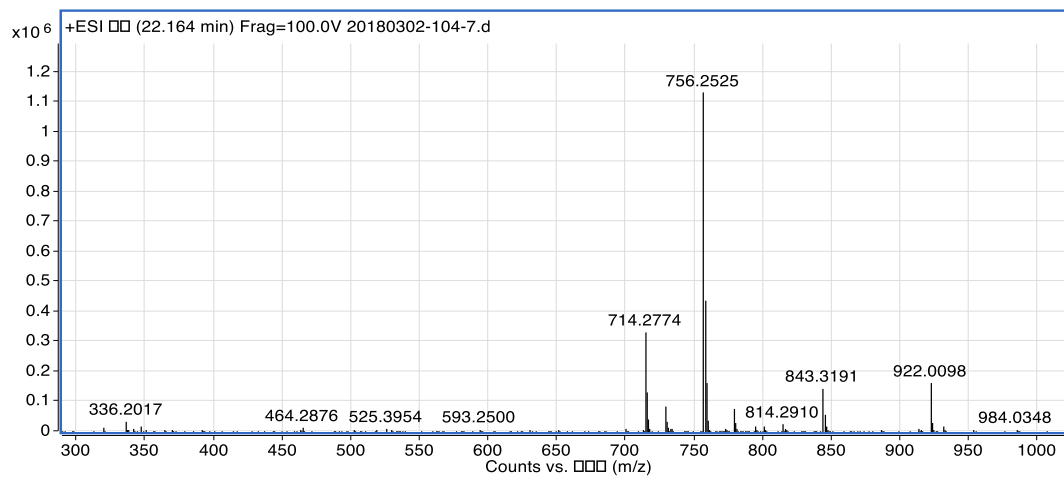
### Compound 15a



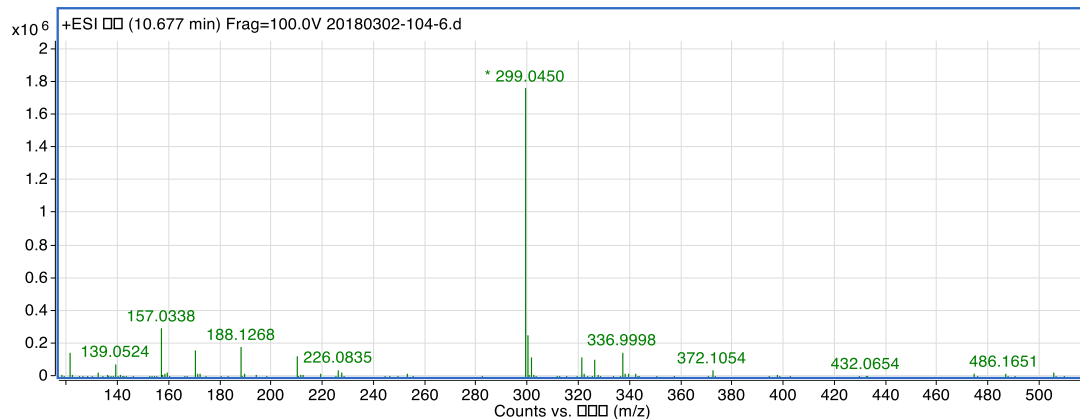
### Compound 15b



### Compound 15c

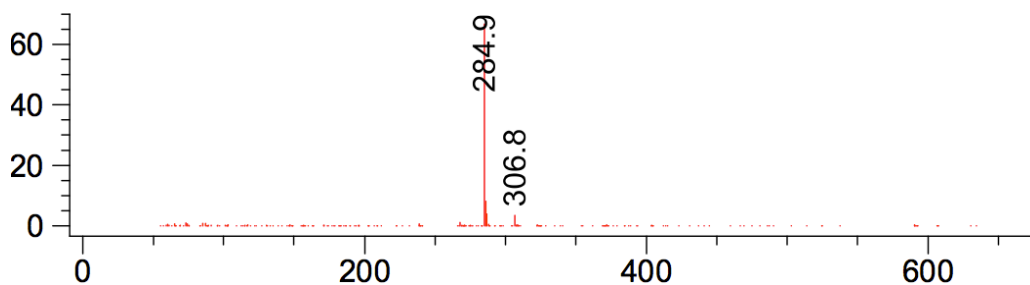


Compound 15f

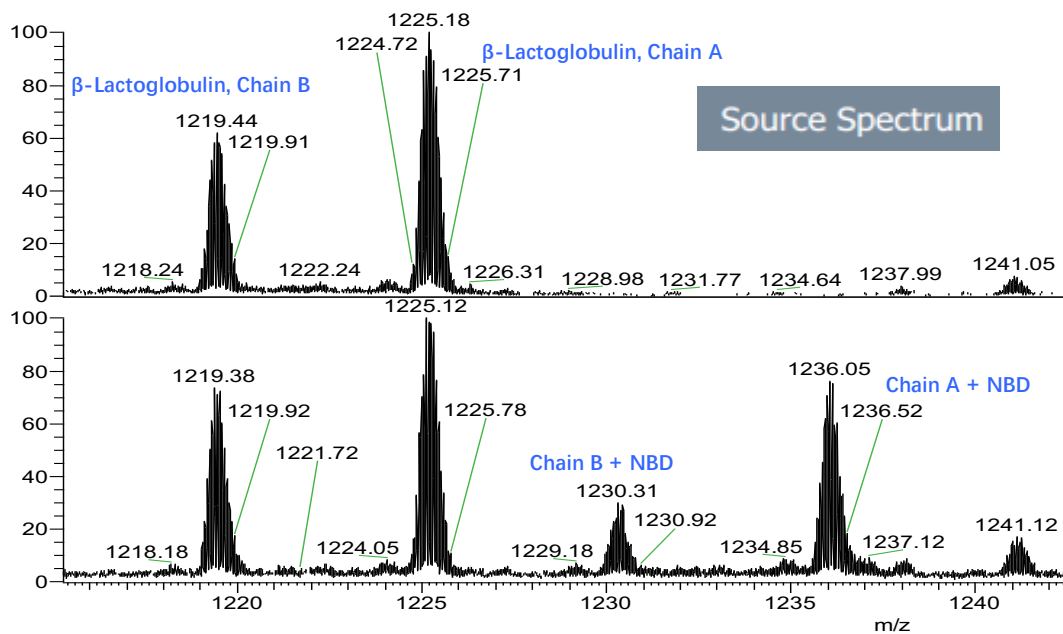


Compound 15e

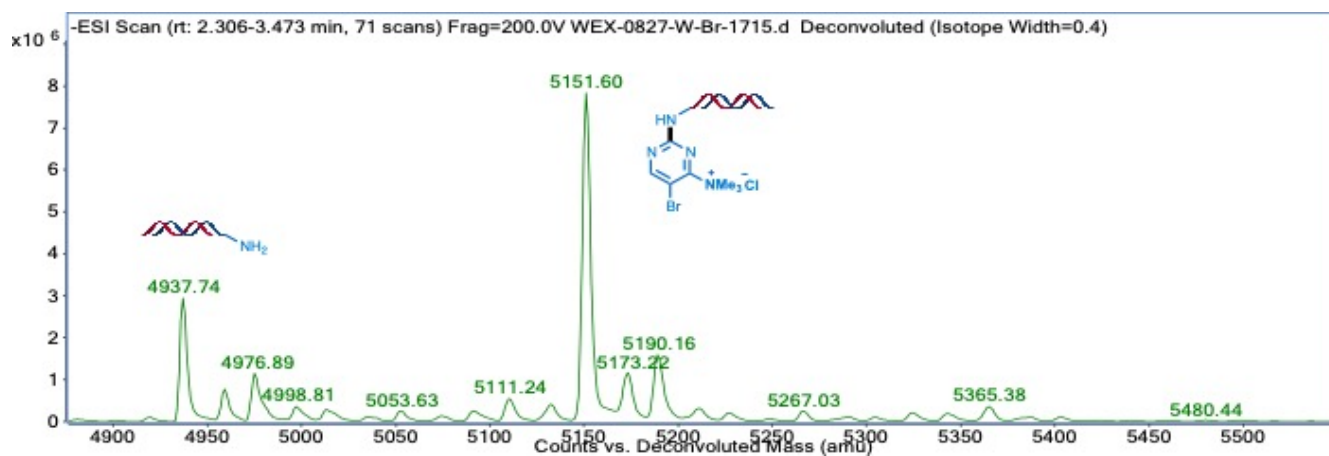
\*MSD1 SPC, time=5.317:5.773 of D:\DATA\20180313\DEF\_LC



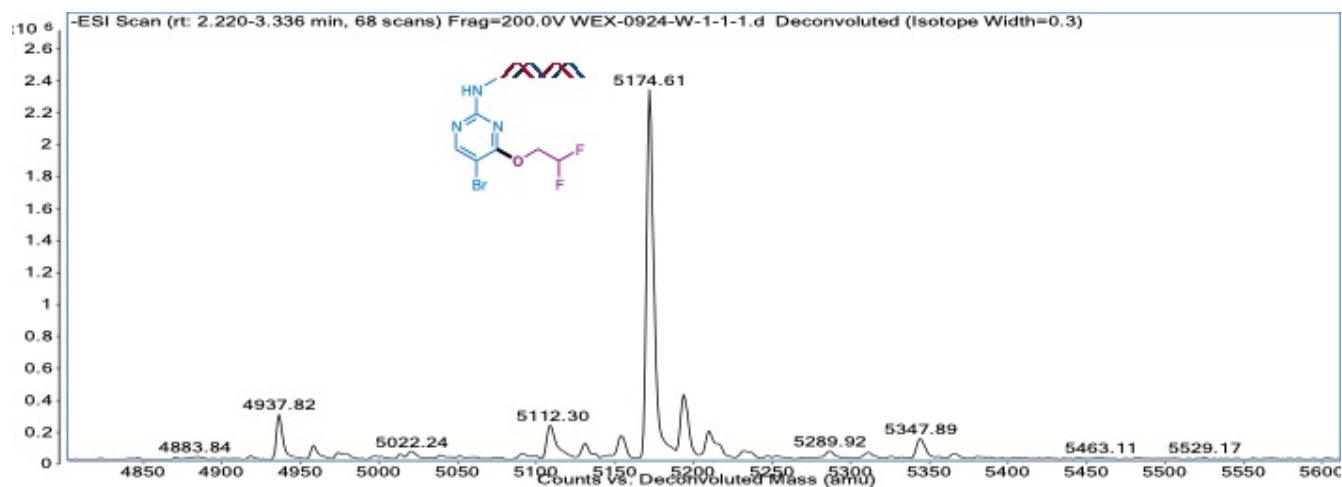
Compound 15d



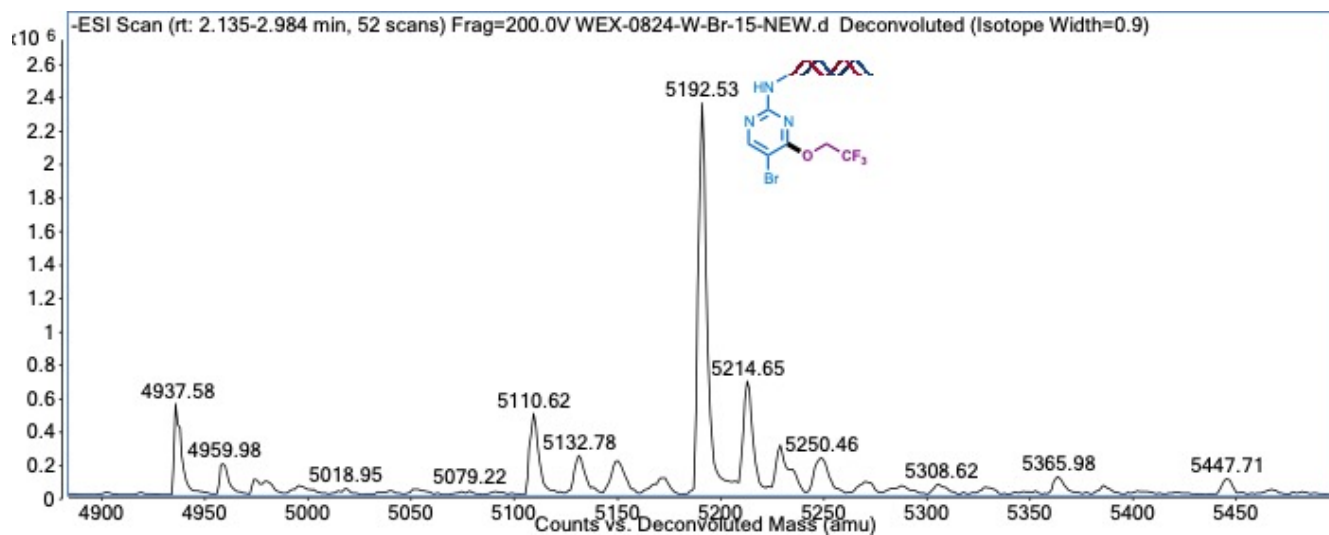
### Compound 16a



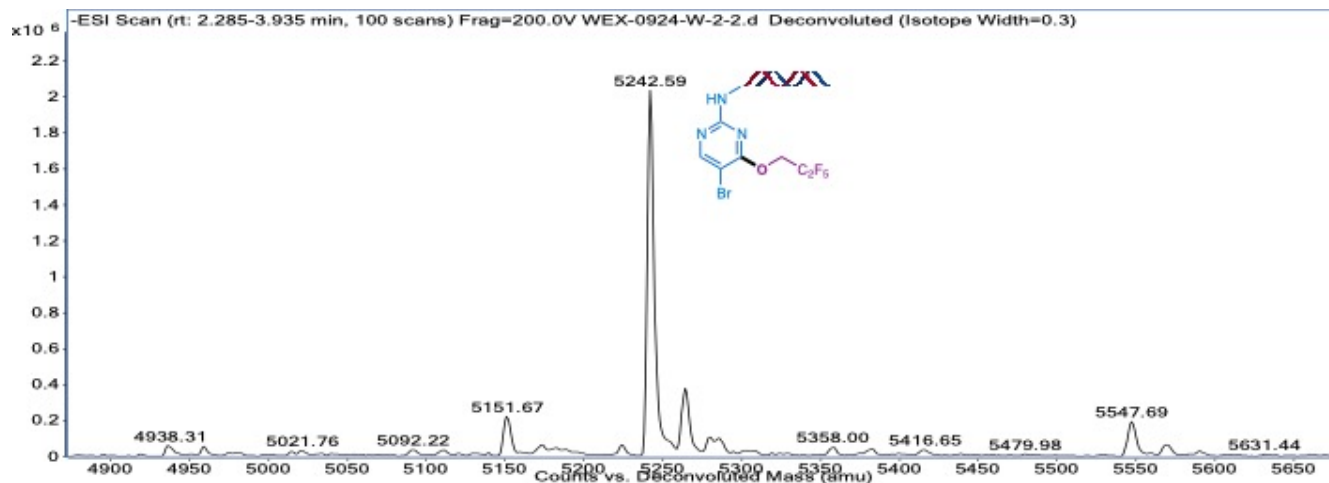
### Compound 16b



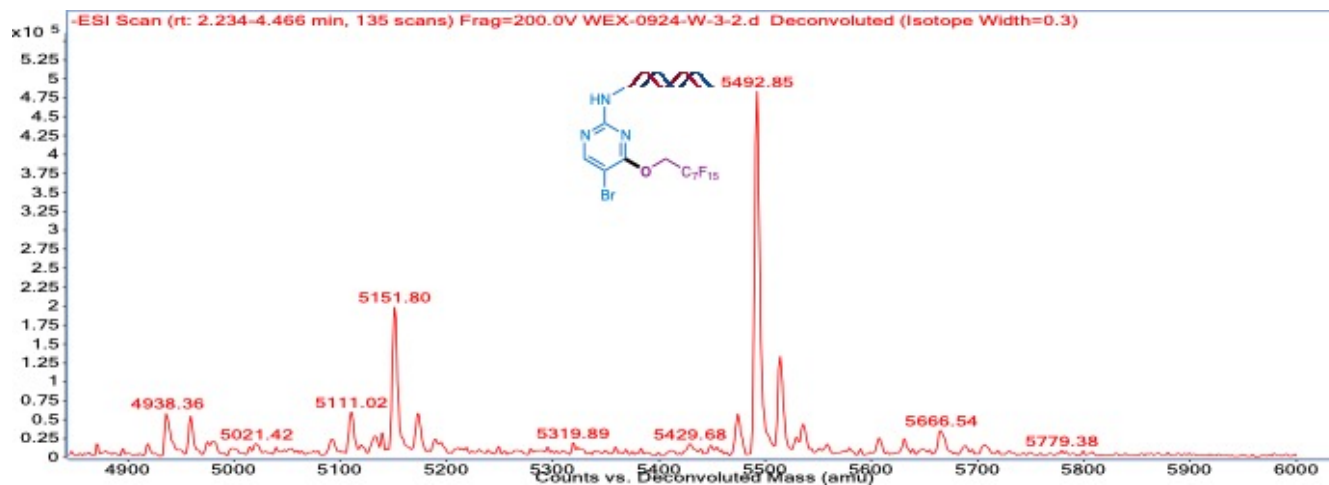
### Compound 16c



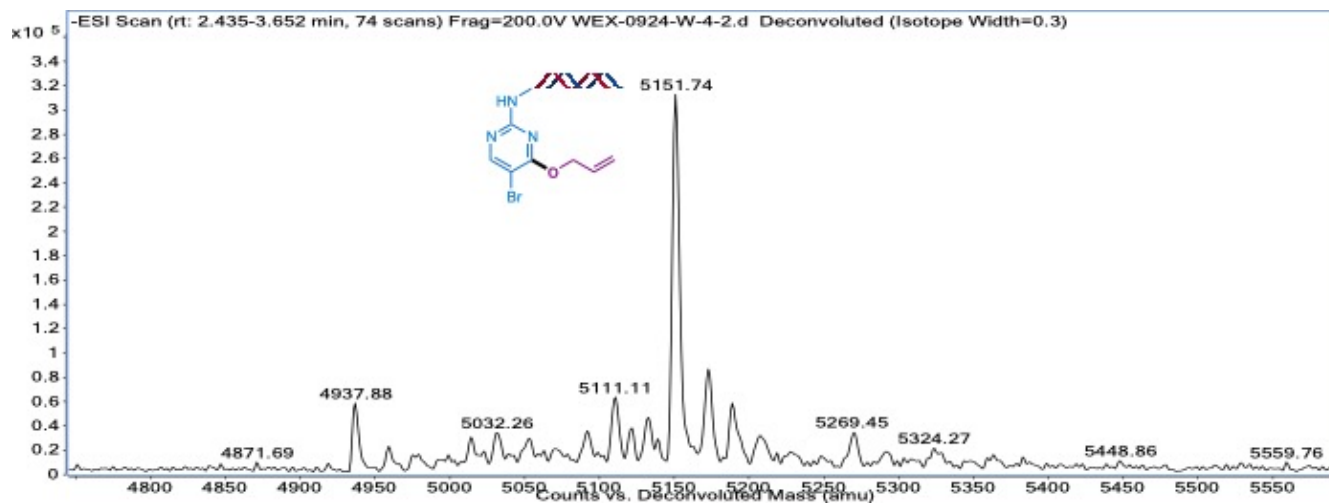
### Compound 16d



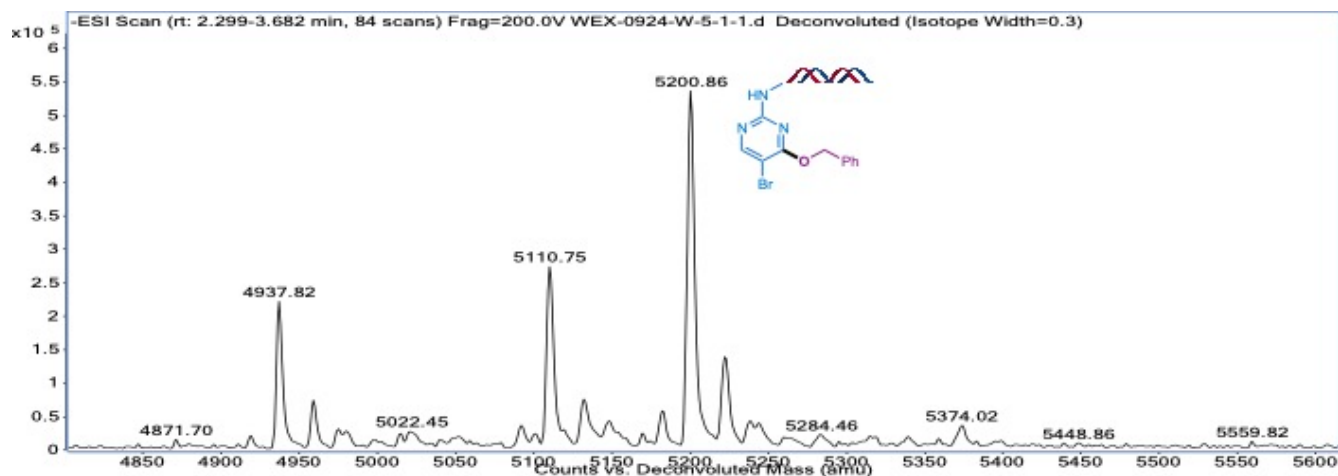
### Compound 16e



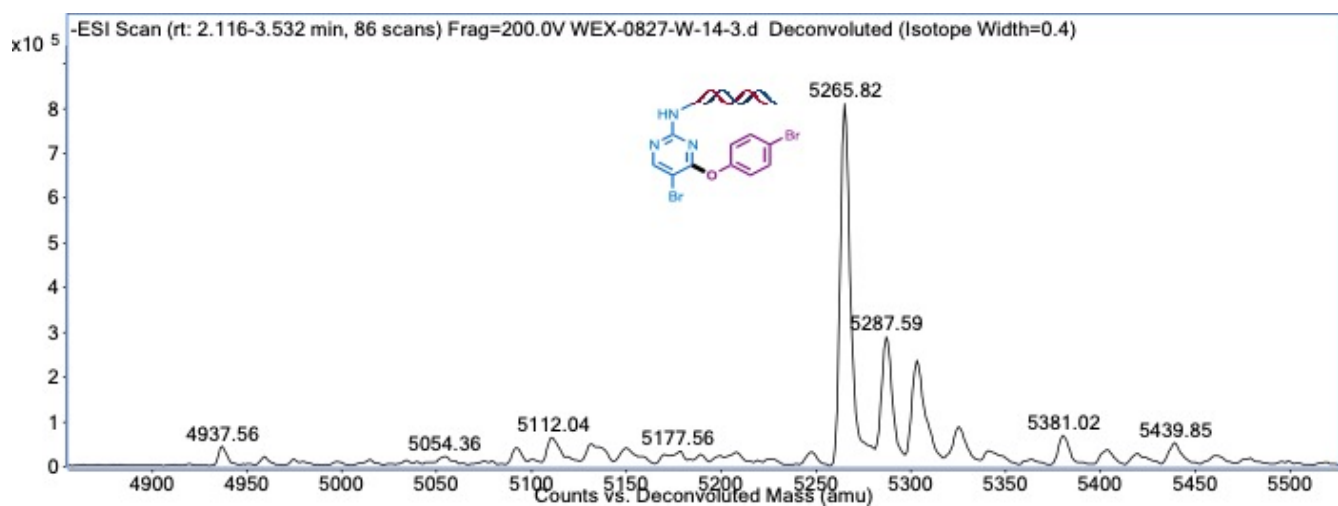
### Compound 16f



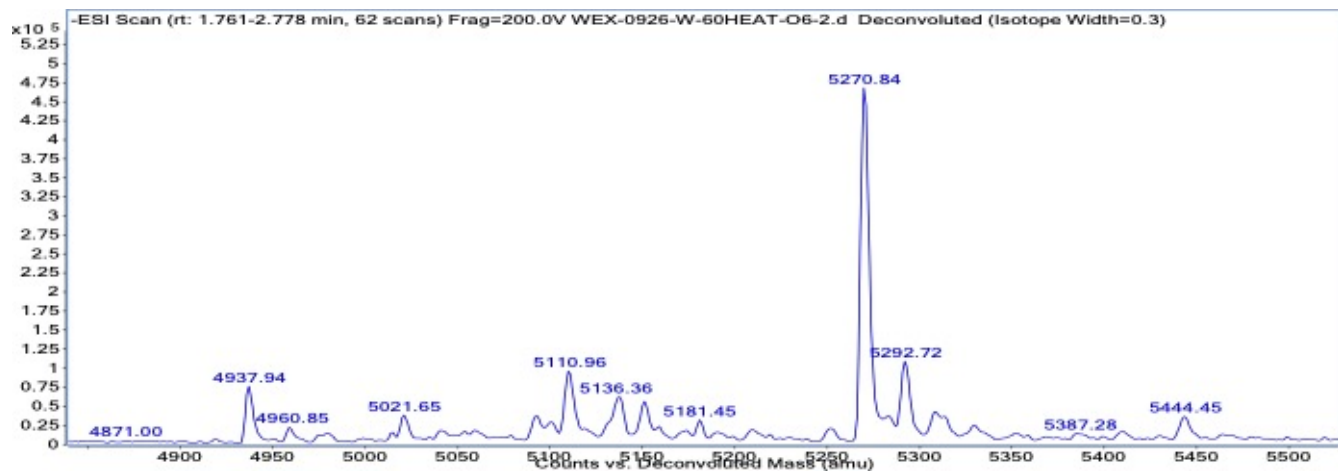
### Compound 16g



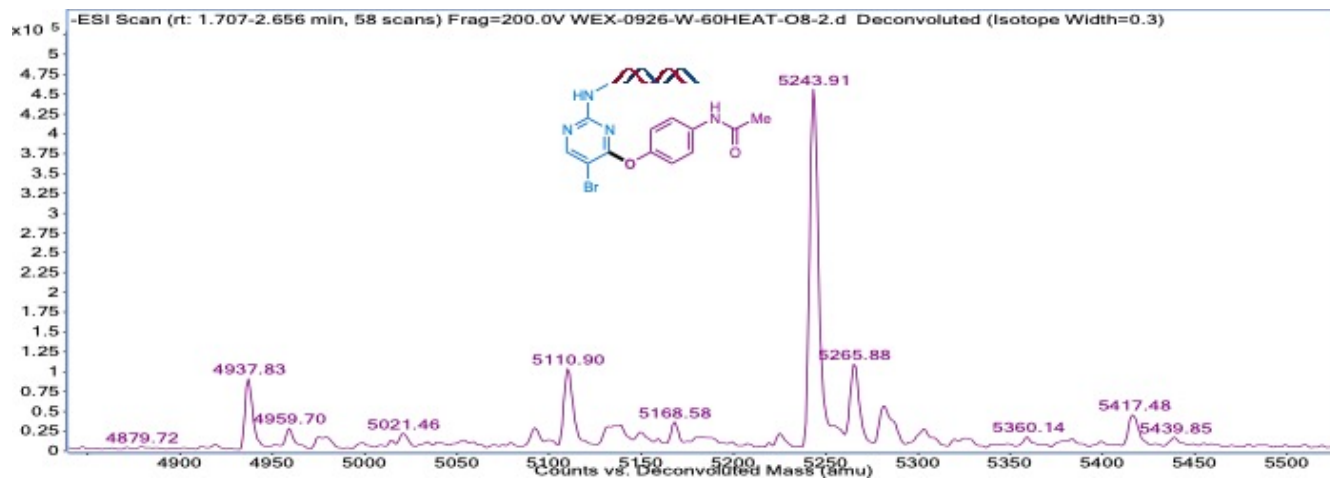
### Compound 16h



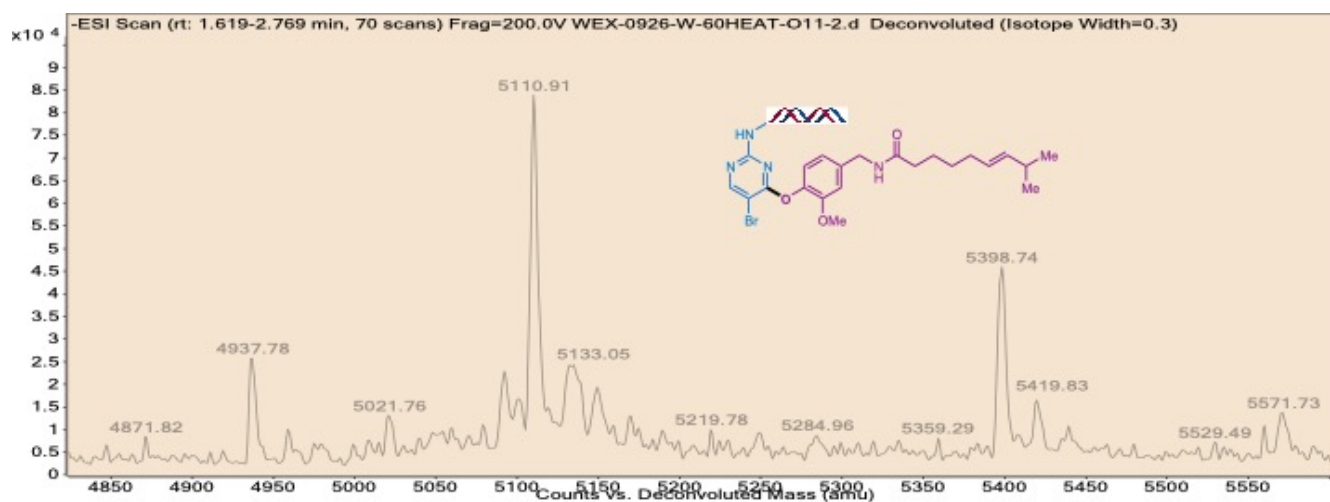
### Compound 16i



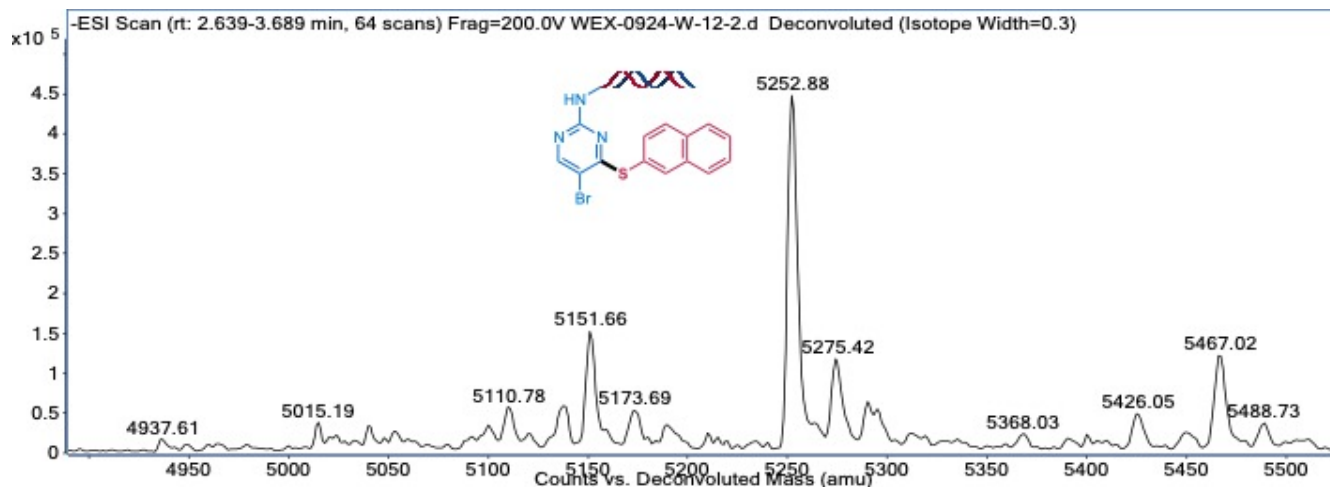
### Compound 16j



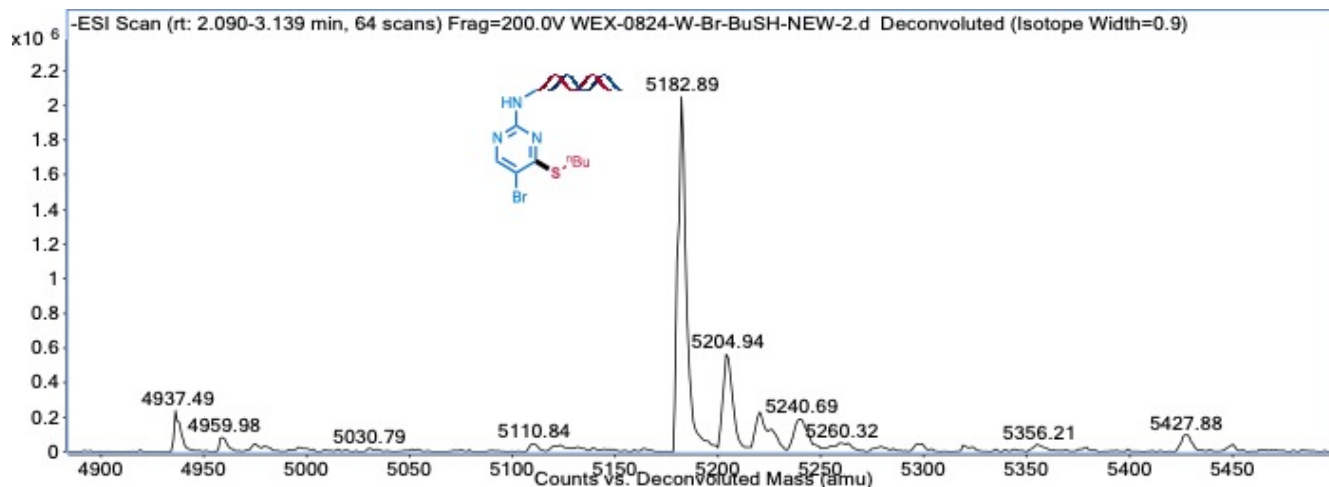
### Compound 16k



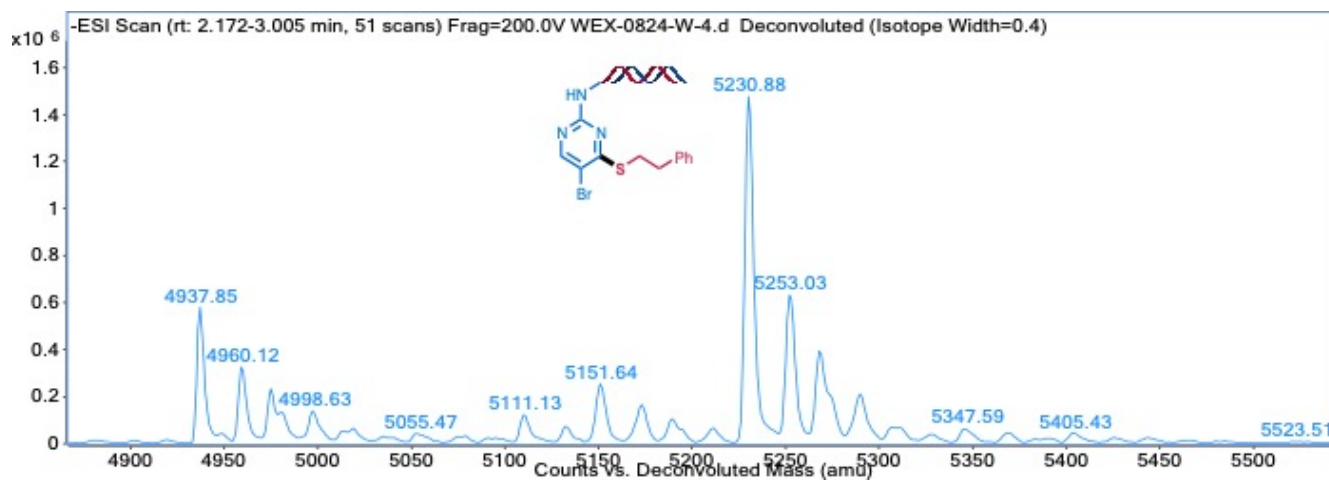
### Compound 16l



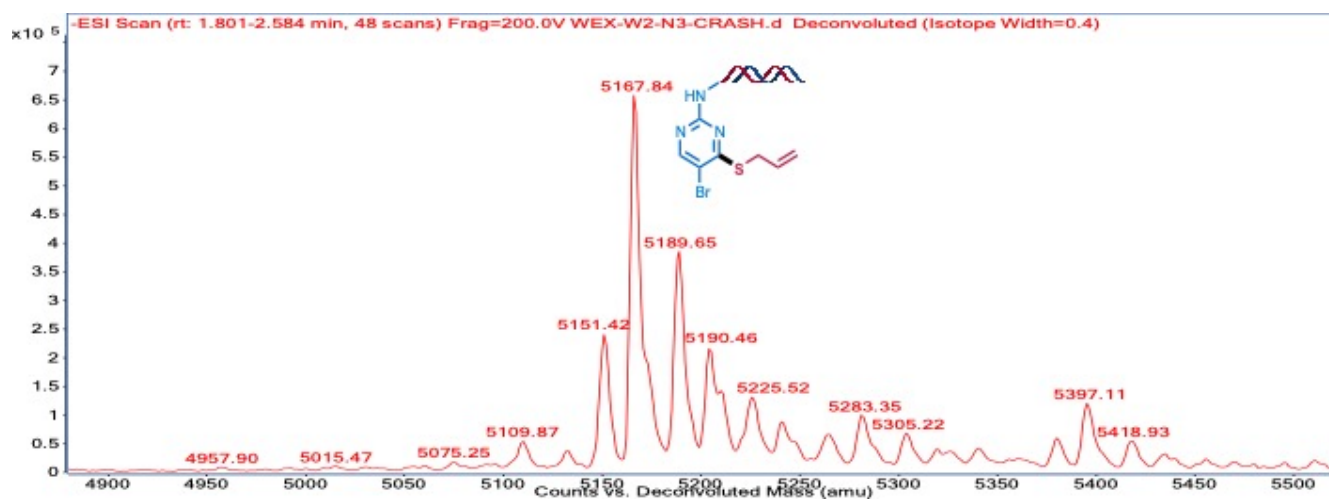
### Compound 16m



### Compound 16n

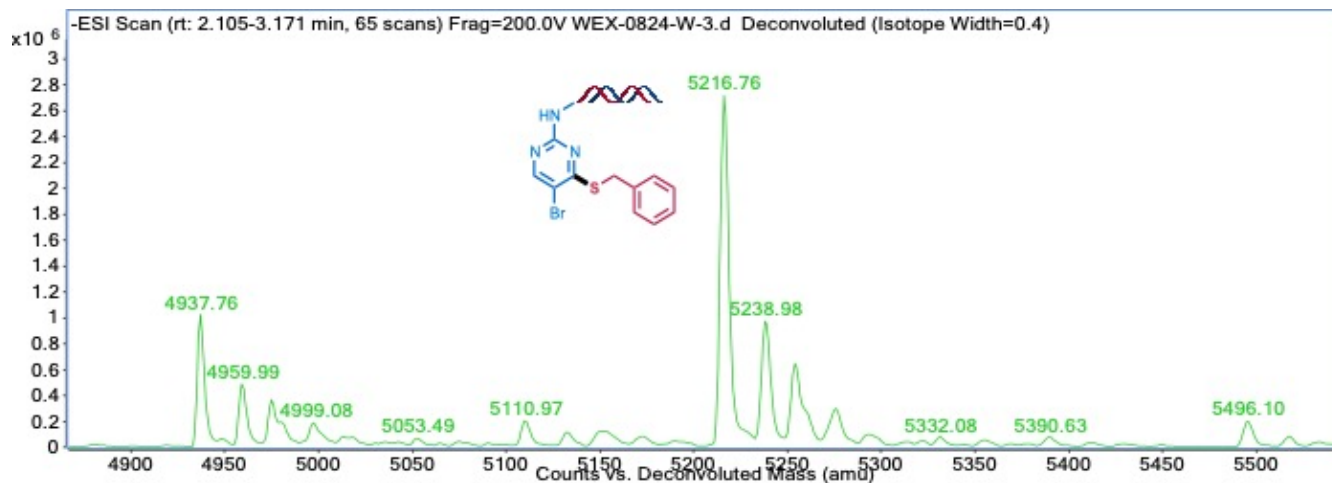


### Compound 16o

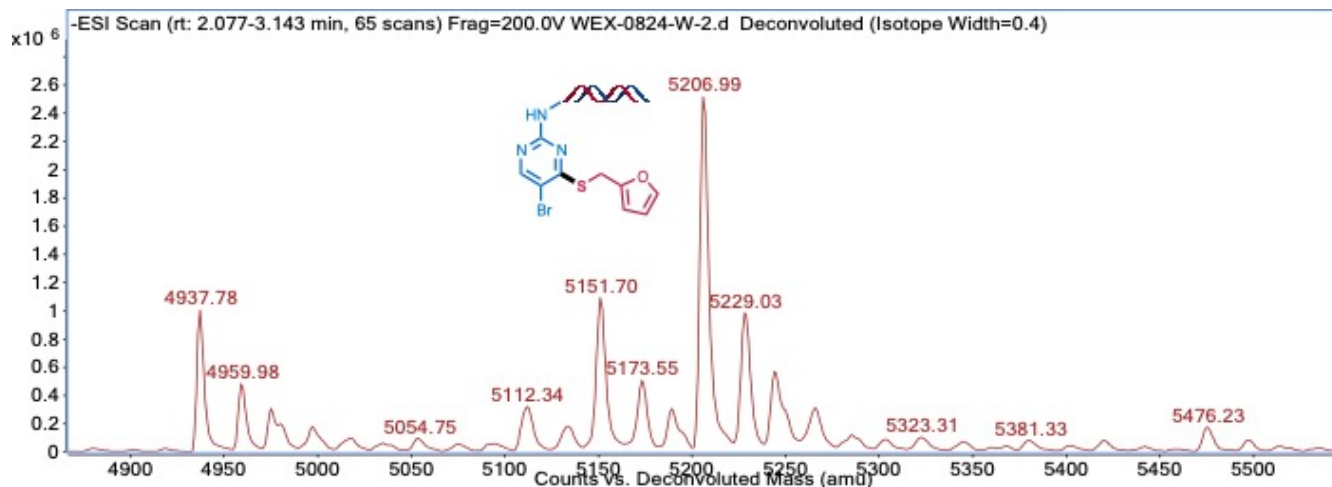




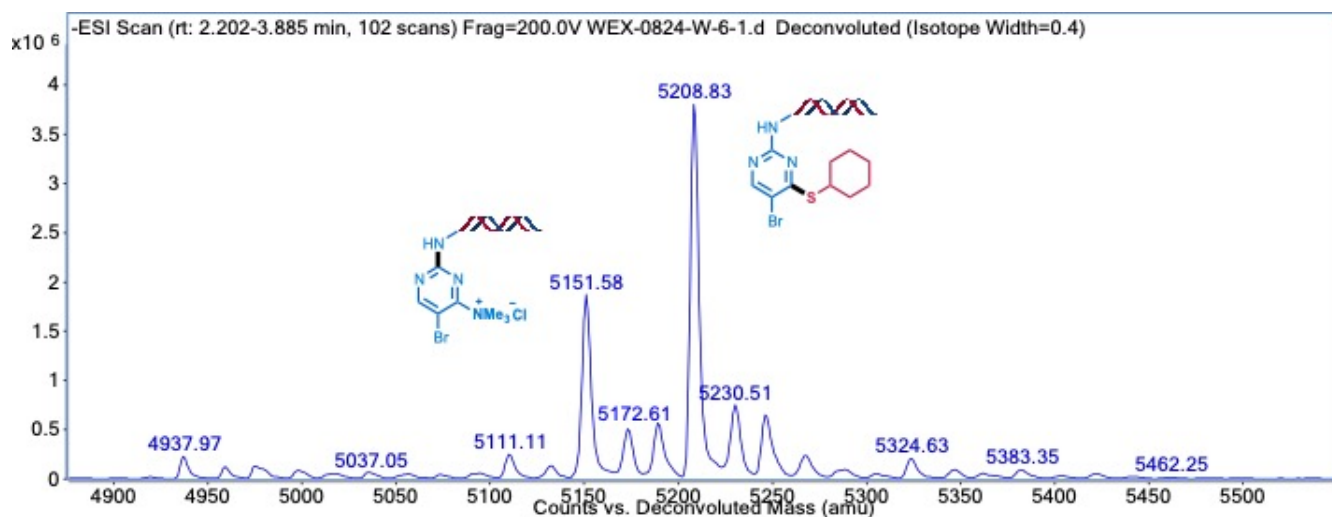
### Compound 16p



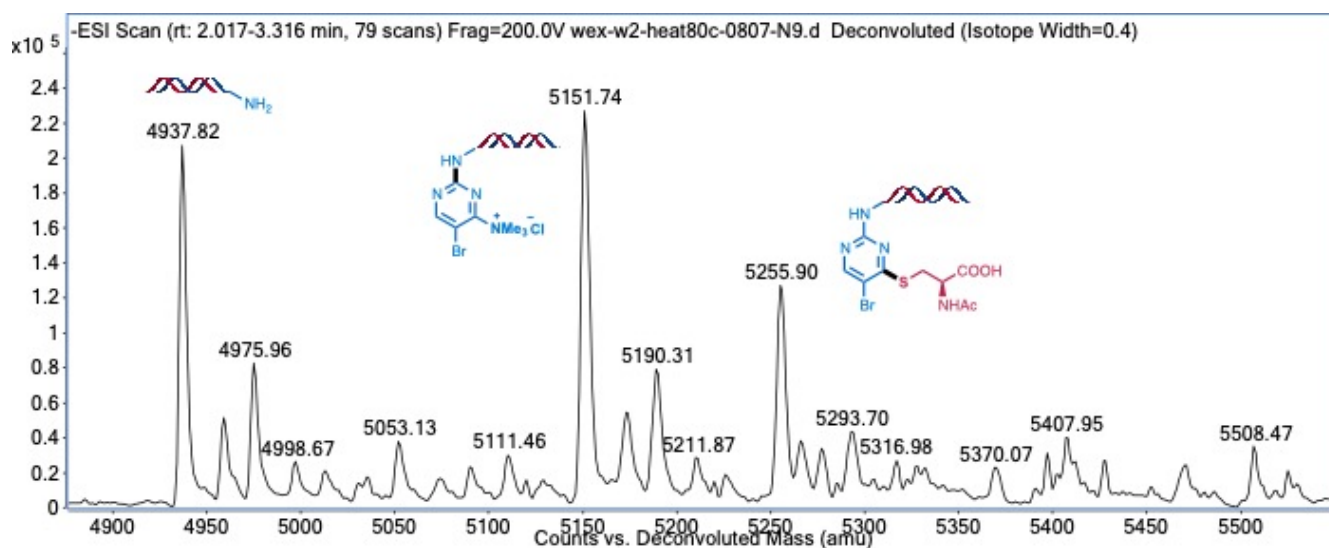
### Compound 16q



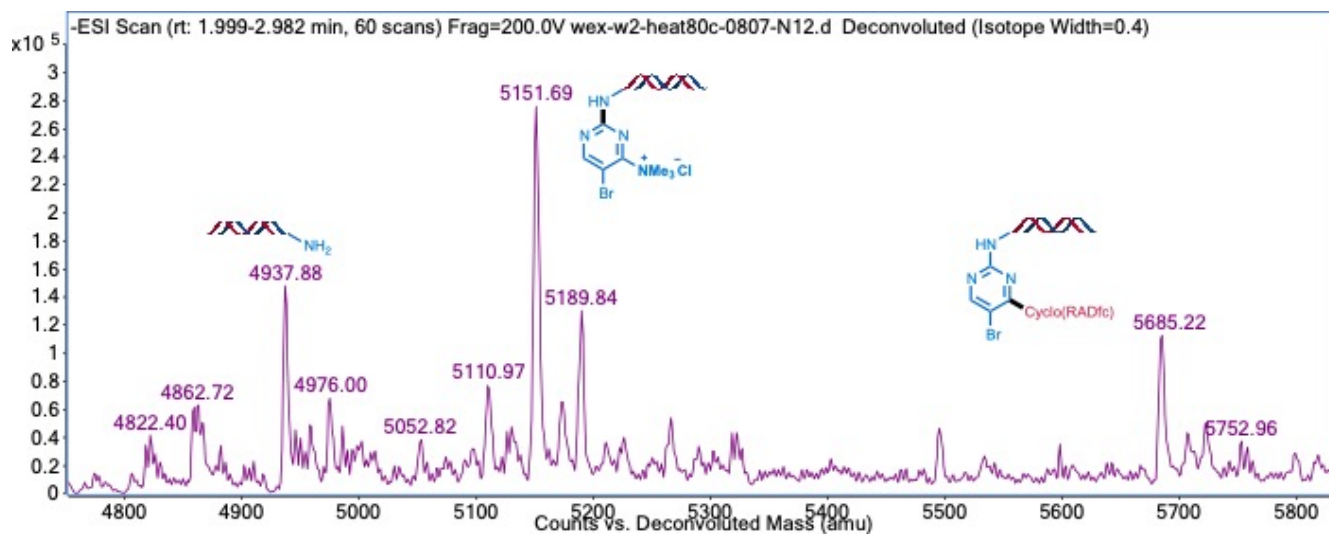
### Compound 16r



### Compound 16s



### Compound 16t



## 5. Reference

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