Spring 5-18-2017

C(sp2)–H Functionalizations Employing 2-Aminophenyl-1H-pyrazole as a New Removable Directing Group

WAN-CHEN LEE
vbala0130@gmail.com

Recommended Citation

LEE, WAN-CHEN, "C(sp2)–H Functionalizations Employing 2-Aminophenyl-1H-pyrazole as a New Removable Directing Group" (2017). *Master's Theses*. 223.
https://repository.usfca.edu/thes/223

University of San Francisco

C(sp^2)–H Functionalizations Employing 2-Aminophenyl-1*H*-pyrazole as a New Removable Directing Group

by

Wan-Chen Cindy Lee

Submitted in fulfillment of the requirements
for the degree of

Master of Science

Li group
Department of Chemistry

Spring 2017

The University of San Francisco Graduate School

Statement of Dissertation Approval

Dr. Jie Jack Li Date
Research Advisor

Dr. Ryan West Date
Assistant Professor

Dr. Giovanni Meloni Date
Chair, Department of Chemistry

Dr. Marcelo Camperi Date
Dean, College of Arts and Sciences

Abstracts

2-Aminophenyl-1*H*-pyrazole (2-APP) was discovered as a novel removable bidentate directing group for copper-mediated aerobic oxidative C(sp^2)–H bond amidation and sulfonamidation bearing a wide range of sulfonamides, When $Cu(OAc)_2$ was employed as the copper source, 1,1,3,3-tetramethylguanidine (TMG) as an organic base, the reaction, optimally carried out overnight in DMSO at 80 °C in open air, produced a variety of products in moderate to excellent yields. In addition, C(sp^2)–H bond chlorination has been developed by using this auxiliary, employing trichloroacetamide as a new chlorine source. Furthermore, this unprecedented directing group also can assist copper-mediated regio-selective hydroxylation, and *ortho*-alkynylation/annulation by using $Cu(OAc)_2$ as an oxidant.

Acknowledgements

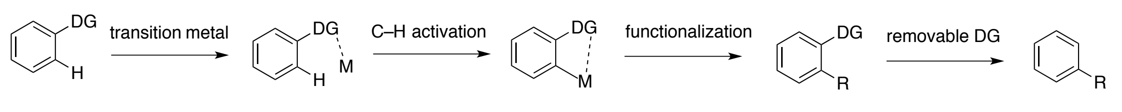
I would like to thank my advisor Dr. Jie Jack Li for teaching and mentoring me throughout my graduate life. I appreciate deeply my best mentor David A. Gutierrez and my lovely colleague Yuning Shen for helping me and always standing by my side when I was frustrated with chemistry during the past two years. Thanks also go to smart undergraduates especially Arya Tehrani for working hard with me even though I was a demanding boss. I am grateful to all faculty in the department of chemistry for instructing and encouraging me to pursue a Ph.D. program. Finally, I thank USF for giving me this opportunity to grow stronger and to have those amazing memories in here.

Table of Contents

Chapter 1: Introduction

Transition metal-catalyzed C–H functionalization has been widely explored since this has proven to be one of the more environmentally friendly routes to the formation of complex organic frameworks.[1,2] Previously, chemists obtained desired products by using reactive functional groups such as halides or unsaturated bonds with metals to form a new C–M bond for further reactions. Grignard reagents and organolithium compounds are good examples for this category. In recent years, chemists have developed C–H activation as an efficient strategy to achieve direct catalytic cleavage and transformation of C–H bond, which also conquers the challenging problems: regioselectivity of reactions and eliminates the multiple steps and limitations associated with the preparation of functionalized starting materials.[3] Furthermore, removable directing group is a preferred approach in synthetic strategies since the products can be further manipulated after the directing group is removed (Scheme 1).[4,5]

This thesis highlights an interesting alternative to bidentate directing group for the development of new strategies for the functionalization of C–H bonds.

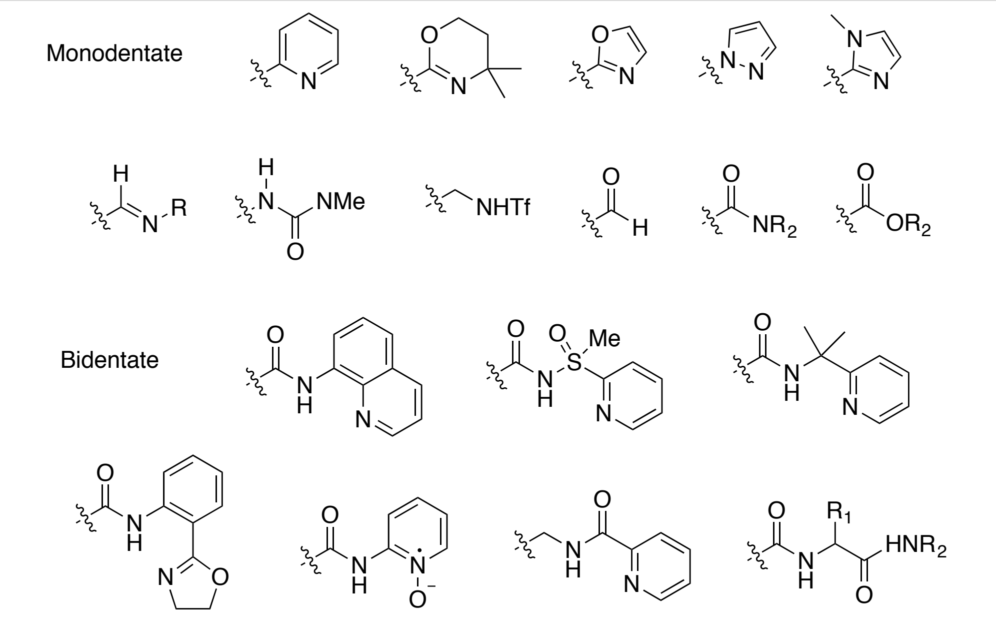


Scheme 1 Transitionmetal-catalyzed functionalization with removable directing group; DG = directing group

Chapter 2: Background

2.1 Removable bidentate directing groupS

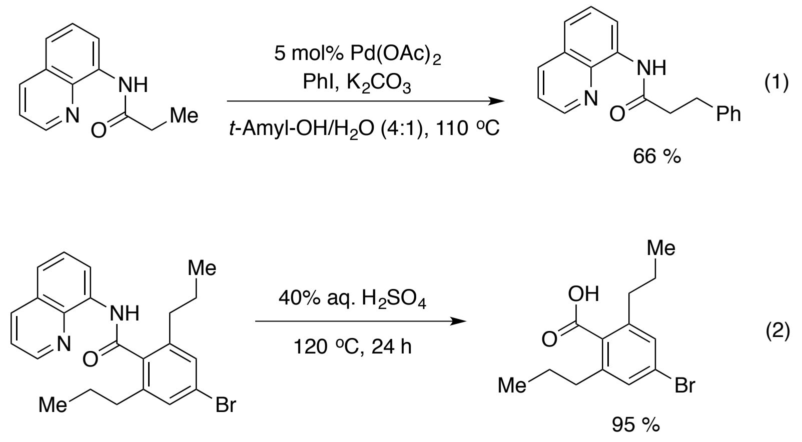
Directing group-assisted functionalization has been investigated in recent decades, and many research groups achieved significant breakthroughs in this area. Assorted directing groups such as pyradines, amides, esters, amidines, pyrazoles, aldehydes, ketones, etc. have been released by researchers. These directing groups can be classified as monodentate and bidentate as shown in Scheme 2.



Scheme 2 Examples of monodentate and bidentate directing groups

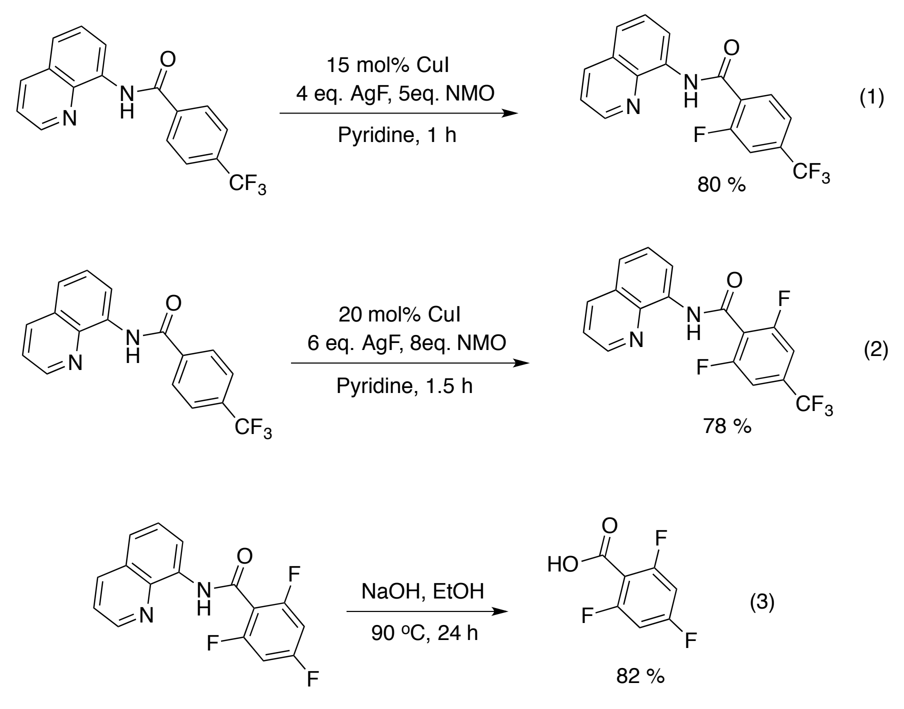
C–H functionalization through the aid of monodentate directing group was a breakthrough in the area of organic synthesis; however, some inherent limitations still remain. By the efforts of chemists, the results demonstrated this limitation can be improved by a new type of directing group—bidentate one. This type of auxiliaries can achieve catalytic transformations that cannot be completed with conventional one: to get a stable metallacycle.[6] Since it is a promising strategy to synthesize products through metal-consisted catalysts, nowadays, researchers prefer conducting catalytic C–H activation with assistance of bidentate directing groups.

On the other hand, for further applications of substrates, many research groups have focused on exploring removable directing groups, which can be removed by hydrolysis reactions. Daugulis was the first to employ 8-aminoquinoline as a novel directing group in 2005 for the purpose of C–H bond activation.[7] This report explored arylation of unactivated C(sp^3)–H bond (Scheme 3),[8,9] which encouraged others to use systems based on removable bidentate directing groups to develop methodologies for synthesizing desired C–H functionalization products.



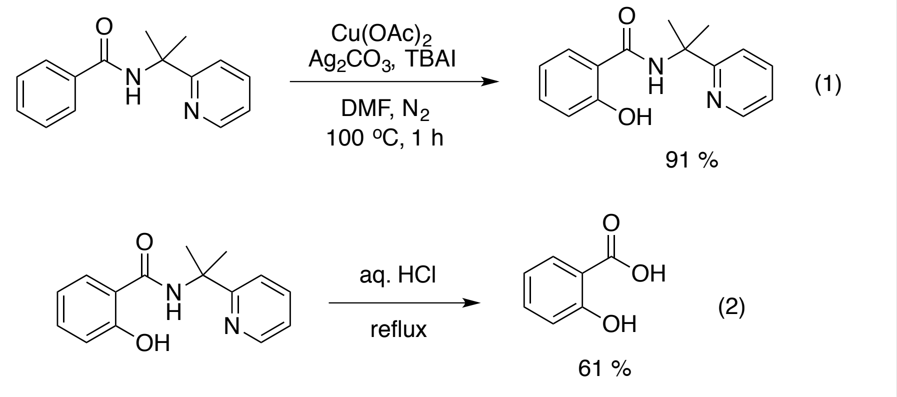
Scheme 3 (1) C(sp^3)–H arylation of aromatic rings with 8-aminoquinoline as a directing group; (2) Removal of a directing group by strong acid hydrolysis

Subsequently, Daugulis's group discovered the auxiliary-assisted C–H fluorination[10] employing CuI as the catalyst, AgF as the nucleophilic fluoride reagent and NMO as the oxidant. This reaction tolerates the wide scope of substrates and provides a straightforward way for the preparation of *ortho*-fluorinated benzoic acid derivatives. By adjusting the amount of CuI and AgF, selective mono- or di-fluorinated products can be obtained respectively in excellent yields. As a removable auxiliary, 8-aminoquinoline can be cleaved under basic hydrolysis conditions (Scheme 4).



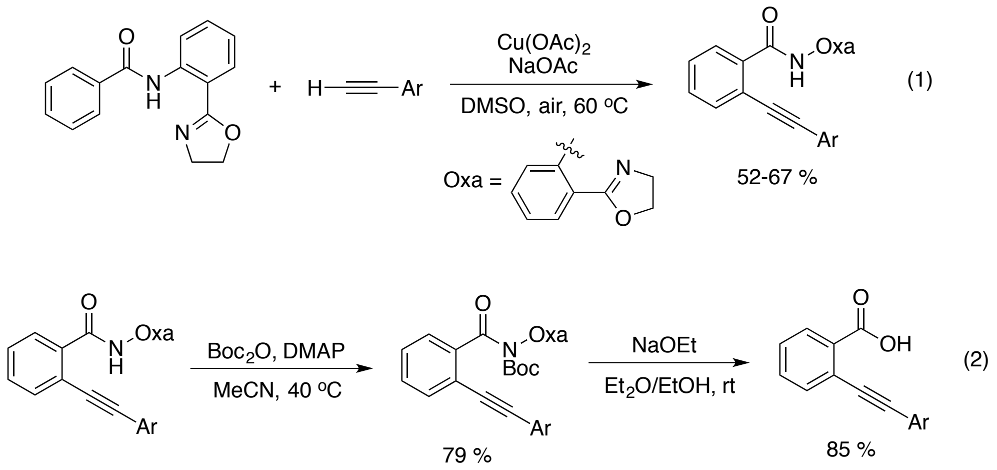
Scheme 4 (1) C(sp^2)–H monofluorination of arenes; (2) C(sp^2)–H difluorination of arenes; (3) Removal of the directing group under basic conditions.

2-(Pyridine-2-yl)isopropylamine (PIPamine) also can be utilized to promote various C–H functionalization. In 2014, Shi's group reported copper-mediated hydroxylation[11] of arenes and heteroarenes employing this removable bidentate auxiliary. Although this reaction required excessive $Cu(OAc)_2$ to gain high conversions, the broad scope of substrates made this synthesis useful. The plausible mechanism they proposed indicated the hydroxyl group was possibly produced from the –OAc group hydrolysis. Besides, this C–H hydroxylation reaction can be conducted smoothly in large-scale to obtain hydroxylation products in excellent yields, and a bidentate directing group (PIPamine) can be removed under acidic and high temperature conditions to obtain salicylic acid in 61% yield (Scheme 5). A year later, Shi's group accomplished methoxylation[12] of C–H bonds by using the same directing group with Cu(II) as the catalyst, tolerating various types of arenes and heteroarenes.

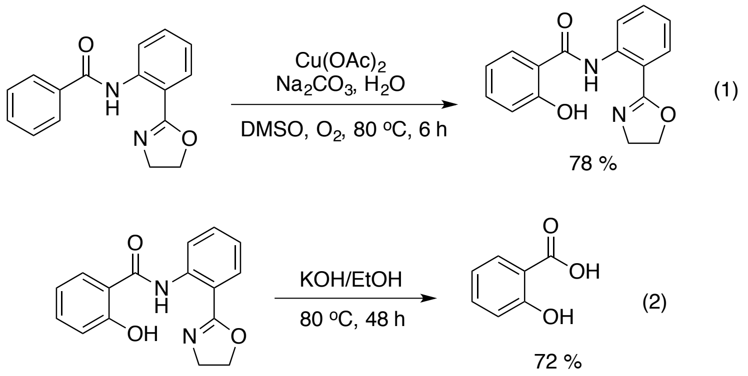


Scheme 5 (1) C(sp^2)–H hydroxylation by using PIPamine as the auxiliary; (2) Removal of the auxiliary under acidic conditions

Yu and co-workers have discovered the phenyl-oxazoline auxiliary to facilitate C–H bond activation, and the results indicated that this bidentate auxiliary can achieve amidation, amination,[13] hydroxylation,[14] trifluoromethylation,[15] alkynylation,[46] etc. Alkynylation is an important breakthrough since there are rare literatures relevant to alkynylation and terminal alkyne homocoupling is easy to occur under oxidative conditions. Yu's group has used the phenyl-oxazoline directing group to obtain alkynylated compounds in moderated yields, bearing a wide scope of benzoic acid derivatives and numerous compatible terminal alkynes. Albeit stoichiometry amount of Cu catalyst is required, it is a straightforward route to get selective, ortho C–H alkynylation arene products and an alternative disconnection to Sonogashira coupling.[16] Because of steric hindrance of aryl alkyne, the removal of the directing group became more challenging, the two steps of procedure are necessary for hydrolysis: install Boc on amide bond (N atom) then proceed to conduct readily hydrolysis (Scheme 6). During their effort to optimize the alkynylation synthesis, the side reaction is discovered, a surprising result, the hydroxylation[14] products can be gained by using the same Cu catalyst under O_2. Oxygen and water play a crucial role in this protocol, likewise, various substituted benzamides are tolerated and the directing group can be cleaved smoothly under basic conditions (Scheme 7).



Scheme 6 (1) C(sp^2)–H alkynylation with directing group; (2) Removing directing group with Boc_2O and NaOEt



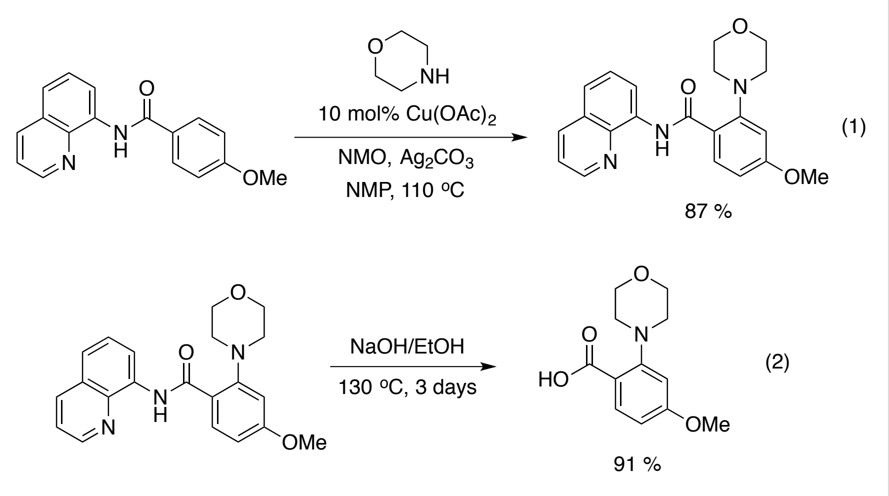
Scheme 7 (1) C(sp^2)–H hydroxylation by using auxiliary; (2) Removal of the auxiliary by hydrolysis

Until now, various bidentate directing groups have been developed in the area of metal-mediated C–H functionalizations, and more and more remarkable reactions are being discovered. Since some limitations still remain, chemists keep developing approaches to overcome problems and more significant results are expected to be reported in the near future.

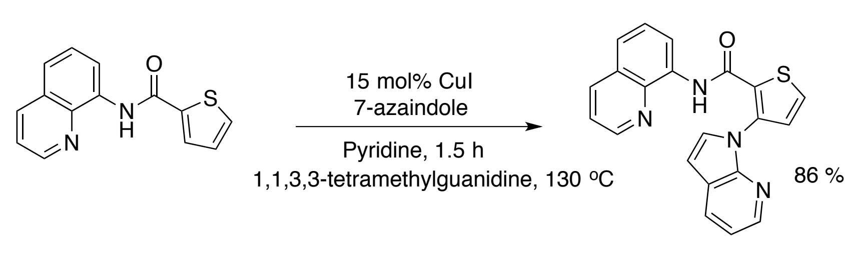
2.2 Copper-mediated C–H amidation and sulfonimidation

Since directly activating inert C–H bond can reduce wastes— chemists do not need to use traditional leaving groups and protecting groups,[17] recently many researchers are interested in developing direct C–H functionalization. In order to achieve greener approaches in organic synthesis, inexpensive and nontoxic copper is applied increasingly as the metal of choice for the C–H activation.[64]

In 2013, Daugulis described a directed amination of nonacidic arene C–H bonds using a Cu–Ag catalytic system.[18] In this case, they hypothesized that the 8-aminoquinoline can be employed as an auxiliary to promote effectively *ortho*-amination. This assumption has been proven in this condition: copper acetate as the catalyst, NMO as the oxidant and Ag_2CO_3 as the additive to achieve 74% conversion into the product (Scheme 8). This auxiliary can be removed under basic conditions at high temperature. Recently, Daugulis published an extension to amination[19] employing 1,1,3,3-tetramethylguanidine (TMG) as the organic base to reach higher yield of products (Scheme 9).

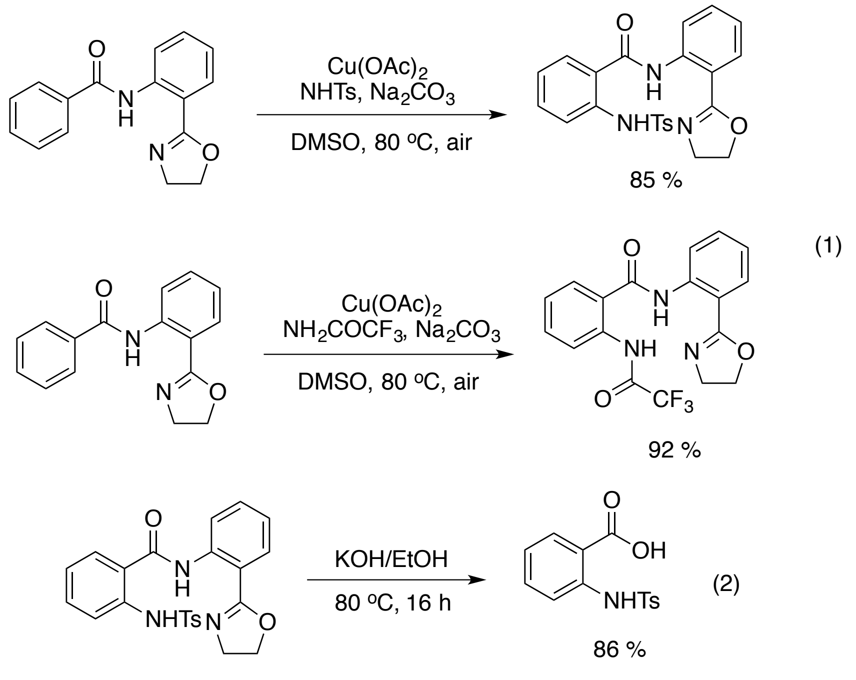


Scheme 8 (1) C(sp^2)–H amination by using an auxiliary; (2) Removal of an auxiliary



Scheme 9 (1) C(sp^2)–H amination by using an auxiliary and organic base

Yu's group reported a copper-mediated C–H amination and amidation in 2014.[13] This reaction is assisted by a removable directing group and numerous amides, sulfonamides and anilines as applicable in this protocol. In addition, this method is an alternative to synthesize a family of inhibitors including 2-benzamidibenzoic acids and *N*-phenylaminobenzoates, which make this approach valuable and promising. By using $Cu(OAc)_2$ as a metal catalyst and Na_2CO_3 as a base in DMSO under air, the method achieves moderate yields of products (Scheme 10). The directing group can be smoothly removed under basic conditions.

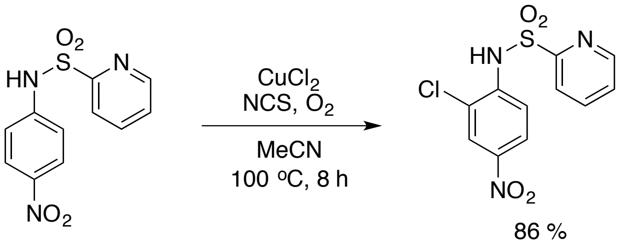


Scheme 10 (1) C(sp^2)–H amidation and sulfonamidation by using an auxiliary; (2) Removal of an auxiliary

2.3 Copper-mediated C–H chlorination

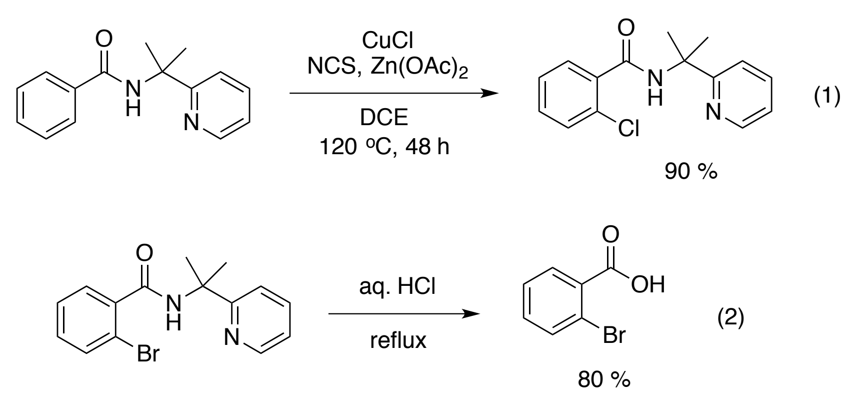
Organohalides are a class of the most useful chemicals due to their broad applications in the organic synthesis. The C–X bonds make contributions to construct natural products, medicinal, functional materials and agricultural chemicals.[20] Until now, more and more reactions relevant to copper-catalyzed or copper-mediated C–H halogenation are discovered by chemists since copper has distinct advantages such as low cost, high stability and flexible forms of presences.[64] Herein, some copper-catalyzed C–H chlorination is briefly described.

Carretero's group developed a method to achieve *o*-chlorination of anilines.[21] When they optimized the reaction, they found the use of different protecting groups can obtain different products: *o*-chlorination, *p*-chlorination or di-chlorination products. Eventually the *N*-(Me)(SO_2Py)-aniline is found to be especially efficient to gain *o*-chlorination products in excellent yield. Furthermore, this optimal condition achieved mono-substitution selectivity, high *ortho*-regiocontrol and large functional group tolerance (Scheme 11).



Scheme 11 C(sp^2)–H amidation and sulfonamidation by using an auxiliary

In 2015, Shi revealed a copper-catalyzed halogenation[22] by using PIPamine as the removable directing group, This reaction employed NCS, NBS and NIS as the halogen source and copper as the catalyst to produce the halides in moderate yields of products (Scheme 12). Although this method needs to be conducted at high temperature conditions in 24 h, it is still a valuable strategy since the broad scope of substrates including arenes and heteroarenes are tolerated. Furthermore, this reaction can accomplish C–H *ortho*-chlorination, bromination and iodination. The auxiliary can be smoothly cleaved under acidic conditions as shown in Scheme 12.

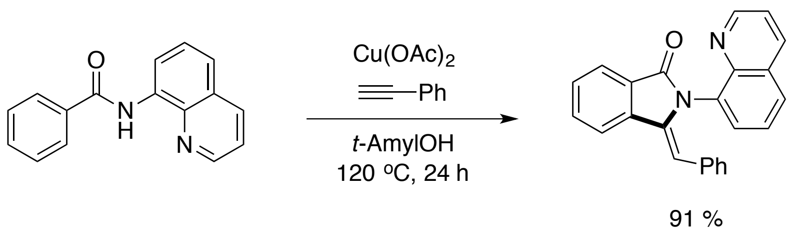


Scheme 12 (1) C(*sp*^{2})–H amidation and chlorination by using an auxiliary; (2) Removal of the auxiliary

2.4 Copper-mediated C–H alkynylation/annulation

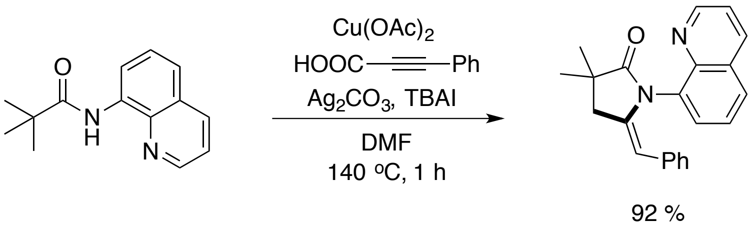
As mentioned previously, C–H functionalization is one of the most important topics in the area of organic chemistry; therefore, chemists developed many strategies to achieve C–H activation. Among of those methods, C–C bond formation is increasingly explored by researchers. For instance, alkynylation is revealed as a straightforward alternative to the Sonogashira reaction. Furthermore, many researchers have found the surprising result when they conducted metal-mediated C–H alkynylation, i.e., getting a cyclization product (annulation) instead of the alkynylation one.

You's group described a method, which employs 8-aminoquinoline as a directing group to assist C (sp^2)–H alkynylation and annulation of arenes with terminal alkynes.[61] In this case, they use excessive $Cu(OAc)_2$ since Cu(II) acts as both the promoter and terminal oxidant in the oxidative cross-coupling process. The excessive amount of terminal alkynes is also necessary because homocoupling would occur in the meantime. Despite the request for the huge amount of reagents, this reaction is sample, easily available and inexpensive, tolerating wide range of substituted substrates and exclusive chemo-, region-, and stereoselectivity (Scheme 13).



Scheme 13 C(sp^2)–H alkynylation/annulation by using an auxiliary

Zhang's group also reported the copper-catalyzed C–H alkynylation/annulation[23] in 2016. Although they only used 20 mol% of Cu(II) to conduct this C–H functionalization, the *4* equivalent expensive silver and additives were required in this condition to achieve products (Scheme 14). However, this strategy makes effort on developing C(sp^3)–H annulation novel, and the approach promising and warranting further investigation.

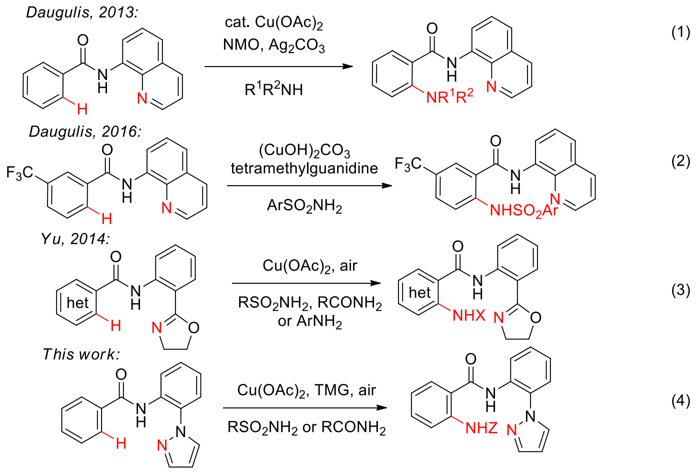


Scheme 14 C(sp^3)–H alkynylation/annulation by using an auxiliary

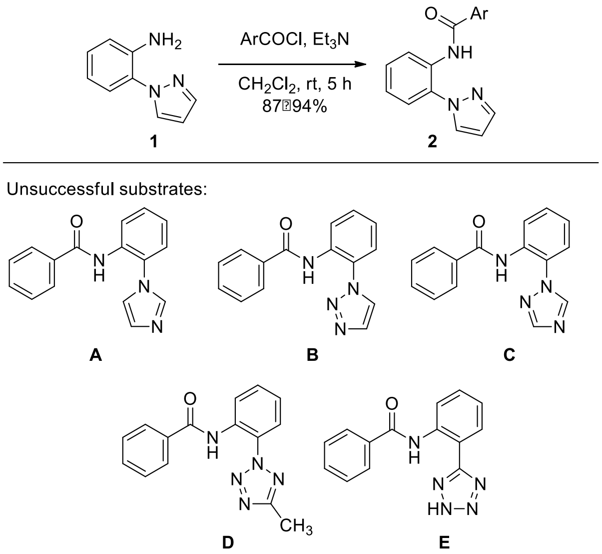
In summary, copper catalysis is popular in organic synthesis because it is inexpensive, nontoxic and ubiquitously available. Researchers have already done many investigations relevant to C(sp^2)–H functionalization, but C(sp^3)–H functionalization still remains challenging, which encourages chemists to explore newer strategies in the near future.

Chapter 3: Results and Discussions

3.1 Screening of Directing Groups



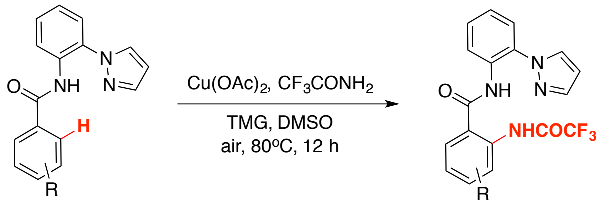
Akin to “rational drug design”, we proposed to rationally design removable DGs. It was speculated that 5-membered *N*-containing heteroaryls attached to an aniline in place of the 8-aminoquinoline and the 2-(4,5-dihydrooxazol-2-yl)aniline should serve as efficient removable DGs if a basic nitrogen atom occupies the strategic position to provide the requisite *N,N*-bidentate complex with copper to form a bicyclic complex [eq (4)]. To that end, we designed a series of 2-aminophenyl-5-membered heteroaryls as removable DGs and proceeded to test our hypothesis.



A total of six 5-membered 2-aminophenyl-5-membered heteroaryls were synthesized. In case of 2-aminophenyl-1*H*-pyrazole, it was assembled in 87% yield in a 2-step sequence involving an S_NAr reaction of 1-fluoro-2-nitrobenzene with pyrazole with the aid of NaH in DMF, followed by a palladium-catalyzed hydrogenation. In terms of cost, **1** is less expensive than commercially available 8-aminoquinoline, and is considerably less expensive than 2-(4,5-dihydrooxazol-2-yl) aniline.

Similar chemistry offered a series of substrates bearing 2-aminophenyl -1*H*-heterocycle **A**–**E**. Benzamide substrates **2** were easily assembled by coupling aniline **1** with a variety of benzoyl chlorides.

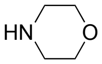
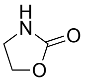
3.2 Copper-mediated C–H amidation and sulfonimidation



Optimization of copper-mediated amidation and sulfonamidation

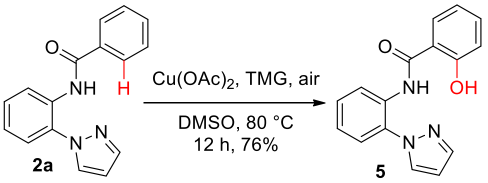
As shown in Table, initial screening of substrate did not show much promise at first. Experimentation with a variety of nitrogen sources (entries 1–7) including alkyl amines, anilines, carbamates, alkylsulfonamides, alkylamides, and arylamides with a combination of copper salts, oxidants, solvents and bases at 80 °C came to no avail. Only when trifluoroacetamide was employed as the nitrogen source did $Cu(OAc)_2$-mediated amidation take place smoothly with Cs_2CO_3 as the base and

DMF as the solvent to give anthranilamide in 76% yield (entry 8). Switching the solvent to DMSO boosted the yield an additional 5% (entry 9). Encouraged, $Cu(TFA)_2$ was chosen as the next "logical" choice of copper salt, which surprisingly failed to produce any amidation product (entry 10). An attempt using *N*-methylpiperidine (NMP, entry 11) as the solvent did not offer much advantage in terms of yields either. Later on, it was discovered that TMG provided the highest yield, presumably due to its higher solubility in DMSO than inorganic salts. As a testimony for how sensitive the reaction is for the nitrogen source, even 2,2-difluoroacetamide only produced a trace amount of the corresponding anthranilamide (entry 13). Gratifyingly, the methodology worked smoothly for all primary arylsulfonamides and alkylsulfonamides tested (entries 14 and 15, and *vide infra*).

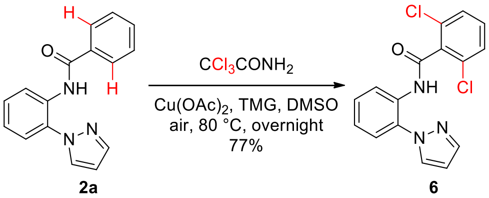
Entry	N source	Cu salt	Solvent	Base	Yield(%)[a]
1		CuBr	DMF	Li_2CO_3	0
2		CuI	DMF	K_2CO_3	0
3	CH_3CSNH_2	$Cu(NO_3)_2$	DMF	Na_2CO_3	0
4	*p*-O_2N-$PhNH_2$	$CuSO_4$	DMF	Cs_2CO_3	trace
5	$C_6F_5NH_2$	$CuSO_4$	DMF	Cs_2CO_3	trace
6	$PhCONH_2$	$Cu(OAc)_2$	DMF	TMG	trace
7	CH_3CONH_2	$CuSO_4$	DMF	Cs_2CO_3	trace
8	CF_3CONH_2	$Cu(OAc)_2$	DMF	Cs_2CO_3	76
9	CF_3CONH_2	$Cu(OAc)_2$	DMSO	Cs_2CO_3	81
10	CF_3CONH_2	$Cu(TFA)_2$	DMSO	Cs_2CO_3	0
11	CF_3CONH_2	$Cu(OAc)_2$	NMP	Cs_2CO_3	74
12	**CF_3CONH_2**	**$Cu(OAc)_2$**	**DMSO**	**TMG**	**94**
13	CHF_2CONH_2	$Cu(OAc)_2$	DMSO	TMG	trace
14	$CH_3SO_2NH_2$	$Cu(OAc)_2$	DMSO	TMG	84
15	$CF_3SO_2NH_2$	$Cu(OAc)_2$	DMSO	TMG	87

[a]The yield determined by ^1H NMR analysis of crude reaction using CH_2Br_2 as an internal standard.

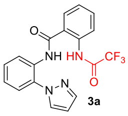
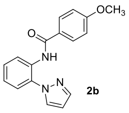
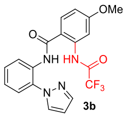
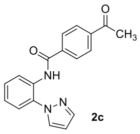
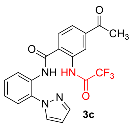
Results of Products

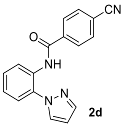
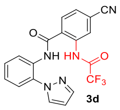
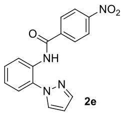
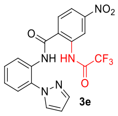
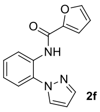
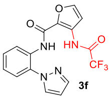
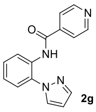
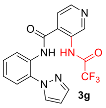
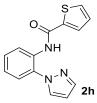
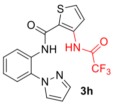
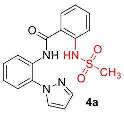
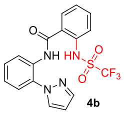
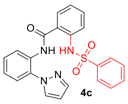
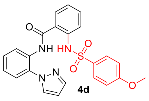
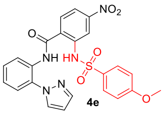
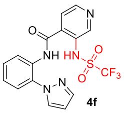
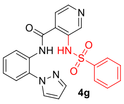
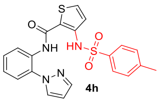


When the amidation failed to work well (entries 4–7, 13), a competing aerobic oxidation product, phenol **5**, was isolated. When the reaction was carried out without any nitrogen source, hydroxylation took place exclusively to offer phenol **5** in 76% yield (94% based on recovered starting material). While the reaction is catalytic for the copper source, stoichiometric amount of copper salts were employed due to their low cost.



It was intriguing to notice that when trichloroacetamide was employed as the nitrogen source, unexpectedly, no desired anthranilamide was isolated. Surprisingly, Cu(OAc)$_2$-mediated aerobic C(sp^2–H) dichlorination product **6** was isolated in good yield (Scheme 3). To the best of our knowledge, this is the first report of using trichloroacetamide as the chlorination agent for C–H halogenation.

substrate	product	yield[b]
2a		94
		53
		44

 **2d**	 **3d**	75
 **2e**	 **3e**	72
 **2f**	 **3f**	27
 **2g**	 **3g**	67
 **2h**	 **3h**	69
2a	 **4a**	84
2a	 **4b**	87
2a	 **4c**	99
2a	 **4d**	93
2e	 **4e**	77
2g	 **4f**	86
2g	 **4g**	98
2h	 **4h**	70

[b] The yield determined by flash column.

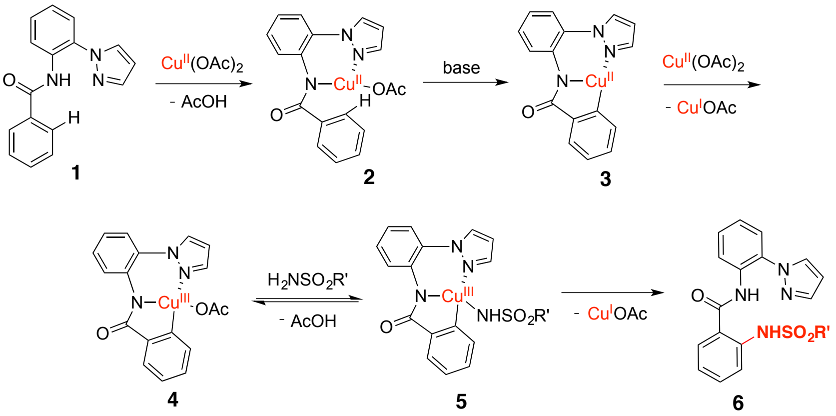
With reaction conditions optimized, the utility of $Cu(OAc)_2$-mediated C–H amidation using 2-aminophenyl-1*H*-pyrazole as the removable DG was explored. As shown in Table, the reaction worked for a variety of substituted benzamide substrates **2a**–**2e** when trifluoroacetamide was used as the nitrogen source. While the parent benzamide **2a** afforded anthranilamide **3a** in 94% yield. The amidation reaction worked on benzamide **2b** with an electron-donating substituent as well as benzamides **2c**–**2e** with electron-withdrawing substituents.

Attention was then turned to heterocyclic substrates. For the furan substrate **2f**, the desired anthranilamide **3f** was isolated in only 27% yield (82% based on recovered starting material) even elevated temperature (150 °C!) and additional $Cu(OAc)_2$ did not drive the reaction to completion. Meanwhile, pyridine substrate **2g** and thiophene substrate **2h** offered the desired anthranilamides **3g**, and **3h** in 67% and 69% yield, respectively.

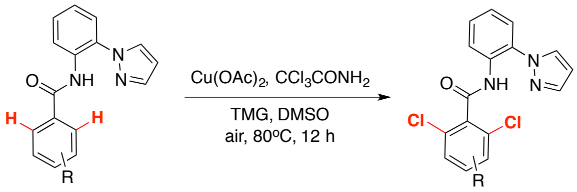
As a highlight, all substrates **2a**–**2h** were sulfonamidated in consistently high yields using this method. Methanesulfonamide, trifluoromethanesulfonamide, benzenesulfonamide, *p*-toluenesulfonamide, and *p*-methoxybenzenesulfonamide all worked smoothly as the nitrogen source to produce amide-sulfonamides **4a**–**4h** in 70–99%. Overall, 2-aminophenyl-1*H*-pyrazole appears to be superior to existing removable DGs in terms of sulfonamidation, providing good yields for all primary sulfonamides tested.

Mechanism

A plausible mechanism is postulated for the copper-mediated C–H amidation employing our bidentate removable DG. Therefore, *chelation* of $Cu(OAc)_2$ with *N,N*-bidentate substrate **1** affords Cu(II)-complex **2**. With the aid of the base, complex **2** undergoes *C–H cupration* to afford Cu(II)-complex **3**, which is *oxidized* by $Cu(OAc)_2$ to produce Cu(III)-complex **4**. *Ligand exchange* with methanesulfonamide then gives rise to intermediate **5**, which subsequently undergoes a *reductive elimination* to deliver amide-sulfonamide **6**.

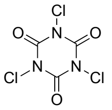
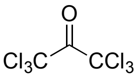


3.3 Copper-mediated C–H chlorination



Optimization of copper-mediated chlorination

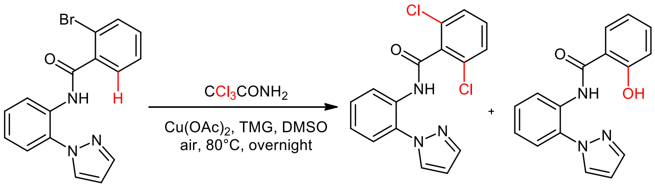
Employing benzamide as our substrate, we investigated the validity of trichloroacetamide as a new chloronium ion source in comparison to other chlorine sources in the context of C–H chlorination using removable DG, 2-aminophenyl-1*H*-pyrazole. As shown in Table 1, 2,2,2-trichloroacetonitrile failed to chlorinate the substrate when $Cu(OAc)_2$ was used as the copper salt and TMG as the organic base (Entry 1), so did tetrachloroethylene with CuI (Entry 2). Switching the copper salt to $Cu(OAc)_2$, tetrachloroethane provided the desired chlorinated product in 11% yield when the reaction was run at 55 °C (Entry 3). Since much left in the reaction was unreacted benzamide, it was logical to raise the temperature to 80 °C and the reaction was driven to completion to afford product in 77% yield (Entry 4). Trichloroisocyanuric acid, hexachloroacetone, and *N*-chlorosuccinimide (NCS) all proved to be viable chloronium ion sources with different degrees of success (Entry 5–9). We then turned our attention to trichloroacetamide as a new chloronium ion source fortuitously discovered in our labor- atory. Experimentation (Entry 10–14) revealed that the optimal conditions for the C–H chlorination of substrate are: $Cu(OAc)_2$ as the copper salt, TMG as the organic base, trichloroacetamide was superior to other chlorine sources when the reaction was run overnight in DMSO at 80 °C, open to air (Entry 12).

Entry	Cl source	Cu salt	Solvent	Base	Yield(%)[a]
1	CCl_3CN	$Cu(OAc)_2$	DMSO	TMG	0
2	$Cl_2CHCHCl_2$	CuI	DMSO	TMG	0
3	$Cl_2CHCHCl_2$	$Cu(OAc)_2$	DMSO	TMG	11
4	$Cl_2CHCHCl_2$	$Cu(OAc)_2$	DMSO	TMG	77
5		$Cu(OAc)_2$	DMSO	TMG	38
6	 $Cl_3CC(O)CCl_3$	$Cu(OAc)_2$	DMSO	TMG	54
7	NCS	CuI	DMSO	TMG	0
8	NCS	$Cu(OAc)_2$	DMSO	TMG	44
9	NCS	$Cu(OAc)_2$	DMSO	TMG	76
10	CCl_3CONH_2	$Cu(OAc)_2$	Dioxane	TMG	0
11	CCl_3CONH_2	$Cu(OAc)_2$	DMSO	TMG	48
12	**CCl_3CONH_2**	**$Cu(OAc)_2$**	**DMSO**	**TMG**	**80**

13	CCl_3CONH_2	$Cu(OAc)_2$	DMSO	Cs_2CO_3	53
14	CCl_3CONH_2	$Cu(OAc)_2$	DMSO	TMG	76

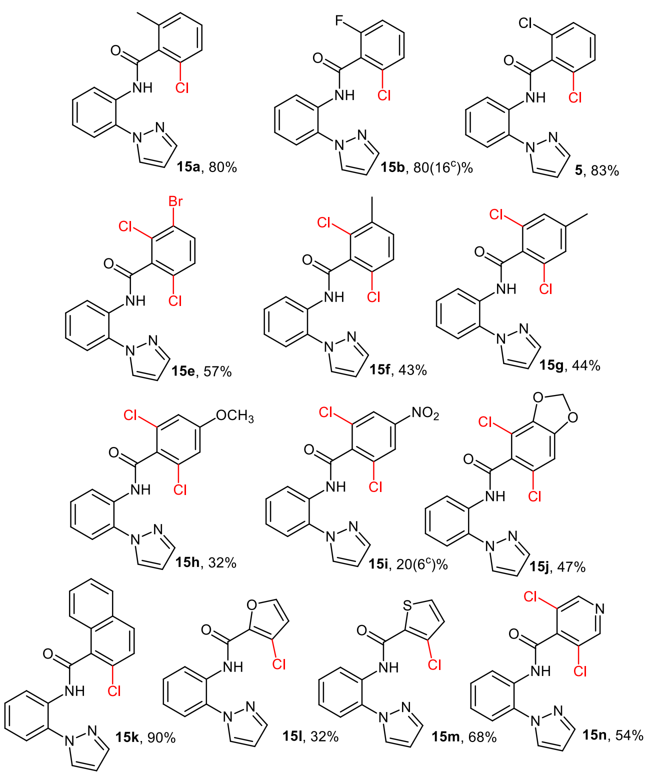
[a]The yield determined by ^{1}H NMR analysis of crude reaction using CH_2Br_2 as an internal standard.

Results of Products



14d **5** (60%) **17d** (10%)

More interestingly, when bromophenyl substrates **14d** was subjected to the C–H chlorination conditions, the Cl/Br halogen exchange reaction also took place to afford bis-chlorinated product **5** in 60% yield, along with debrominated and hydroxylated product **17d** in 10% yield (entry 4). This method adds one additional example to the small repertoire of copper-mediated Cl/Br halogen exchange reactions in the literature. In addition, instead of the Cl/Br halogen exchange, the copper-mediated C–H hydroxylation product **17d** lost its halogen atom. It is likely that a protonation reaction with the complex PhCuBr took place before the reductive elimination step. While the ramification on deciphering the detailed mechanism is not immediately clear, the Br/Cl and Br/H exchanges strongly suggest the participation of the DG in the processes of generating both **5** and **17d**. This is further evidenced by the fact that no Br/Cl and Br/H exchange products were observed from the *meta*-bromo-substrate **14e**, as the DG may affect the concerted metalation-deprotonation (CMD) with the aid of copper only on the *ortho* positions.



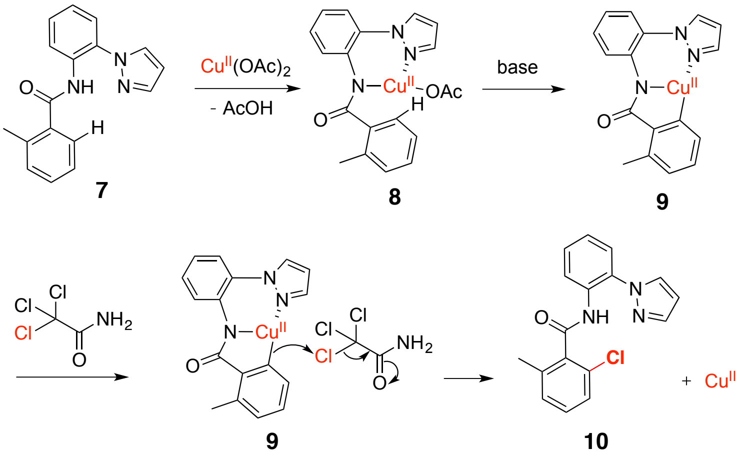
[b] The yield determined by flash column.

When there was no *ortho*-substituent to block one of the two *ortho* positions, bis-chlorination products were the major products as shown by *meta*-substituted substrates **14e** and **14f**, as well as *para*-substituted substrates **14g–14i**. As shown in entry 10, the methylenedioxy substrate **14j** afforded the bis-chlorination product **15j** in 47% isolated yield (62% based on recovered starting material). Naphthalenyl substrate **14k** gave an excellent isolated yield (90%) of the mono-chlorinated product **15k**, which has a very low solubility, presumably because of increased p-stacking effect.

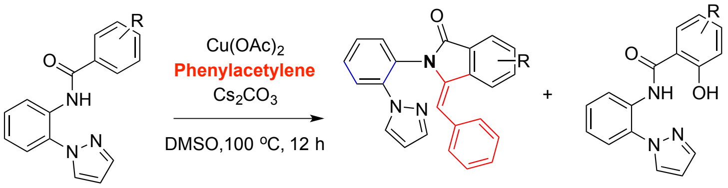
We then turned our attention to heteroaryl substrates. The chlorination reactions for both of the furan and thiophene substrates **14l** and **14m** could not be driven to completion even with elevated temperature and elongated reaction time. Mono-chlorinated furan product **15l** was isolated in 32% yield (72% based on recovered starting material). Similarly, mono-chlorinated thiophene product **15m** was isolated in 68% yield (91% based on recovered starting material). Finally, pyridyl substrate **14n** gave rise to bis-chloro-product **15n** in 54% yield.

Mechanism

A plausible mechanism is proposed as follows: *Chelation* of Cu(OAc)$_2$ with *N,N*-bidentate substrate **7** affords Cu(II)-complex **8**. With the aid of the base TMG, complex **8** undergoes *concerted metalation-deprotonation* (CMD) to afford the cyclocupration product as Cu(II)-complex **9**. In the presence of trichloroacetamide as the ion as an electrophile, Cu(II)- complex **9** may serve as an organocuprate and attack the pseudo- chloronium ion directly, giving rise to the chlorination product **10**.



3.4 Copper-mediated C–H alkynylation/annulation

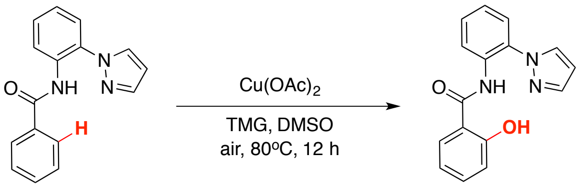


Optimization of copper-mediated alkynylation/annulation

Entry	Cu salt	Solvent	Base	Additive	Yield(%)[a]	Yield(%)[a]
1	$CuBr_2$	DMSO	Cs_2CO_3		20	0
2	$Cu(OAc)_2$	DMF	Cs_2CO_3		23	5
3	$Cu(OAc)_2$	DMSO	Cs_2CO_3	pyridine	25	6
4	$Cu(OAc)_2$	DMSO	Cs_2CO_3		54	18
5	$Cu(OAc)_2$	DMSO	Cs_2CO_3	NMO	65	24
6	$Cu(OAc)_2$	DMSO	TMG		48	18
7	**$Cu(OAc)_2$**	**DMSO**	**Cs_2CO_3**	**100 °C**	**75**	**18**
8	$Cu(OAc)_2$	DMSO	Cs_2CO_3	120 °C	45	0
9	$Cu(OAc)_2$	DMSO	Cs_2CO_3	O_2	25	70
10	$Cu(OAc)_2$	DMSO	CsOAc		23	74

[a] The yield determined by ^1H NMR analysis of crude reaction using CH_2Br_2 as an internal standard.

3.5 Copper-mediated C–H hydroxylation



Optimization of copper-mediated hydroxylation

Entry	Cu salt	Solvent	Base	Additive	Yield(%)[a]
1	$Cu(OAc)_2$	DMSO	Cs_2CO_3		7
2	$Cu(OAc)_2$	DMSO	TMG		31
3	**2 eq. $Cu(OAc)_2$**	**DMSO**	**TMG**		**97**
4	$Cu(OAc)_2$	DMSO	TMG	NMO	65
5	$Cu(OAc)_2$	DMSO	TMG	O_2	52
6	2 eq. $Cu(OAc)_2$	DMSO	CsOAc		90

[a] The yield determined by ^1H NMR analysis of crude reaction using CH_2Br_2 as an internal standard.

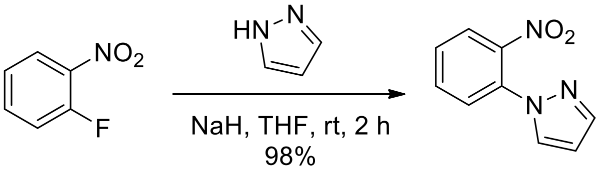
Chapter 4: Conclusion

In summary, an inexpensive removable bidentate directing group 2-aminophenyl-1*H*- pyrazole has been discovered for copper-mediated aerobic oxidative C(sp^2−H) bond amidation, sulfonamidation, chlorination and hydroxylation. They tolerate a wide range of substrates and especially can afford excellent yields for C−H sulfonamidation and hydroxylation products. In addition, this removable directing group can be applied to copper-mediated C–H alkynylation/annulation, employing $Cu(OAc)_2$ as a promoter and oxidant under high temperature conditions.

Chapter 5: Experimental Section

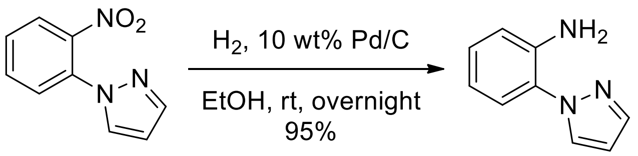
5.1 Preparation of substrates

All reactions were performed in anhydrous solvents under a N_2 atmosphere. Solvents were purchased from Alfa Aesar and utilized without further purifications. Analytical thin-layer chromatography (TLC) was carried out using Silica GTLC plates, 200 M with UV254 (SORBENT Technologies), with visualization by UV or iodine. Flash chromatography was performed using standard grade silica gel (60 Å, 230–400 mesh; SORBENT Technologies). Melting Points were taken using Vernier Melt Station LabQuest 2 and were not corrected. NMR spectra were acquired using an Agilent VNMRS spectrometer equipped with one NMR probe (500 MHz for ^1H, 125 MHz for ^{13}C, 470 MHz for ^{19}F). Spectra were processed using MNova software (Mestrelab). Chemical shifts are reported in parts per million (ppm), coupling constants (*J*) in Hz and are calibrated to residual protonated solvent. Infrared spectra of neat samples were acquired using a PerkinElmer Spectrum 100 FT-IR spectrometer, with solid samples analyzed using a Universal ATR (attenuated total reflectance) sampling accessory. GC–MS was performed on a Hewlett Packard HP6890 Series GC System and a 5973 Mass Selective Detector.



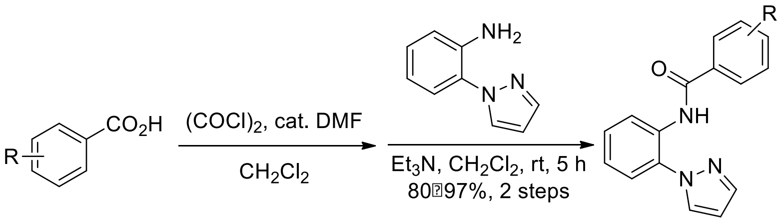
1-(2-Nitrophenyl)-1*H*-pyrazole

A 500 mL round-bottom flask was charged with 4.0 of NaH (60% in mineral oil, 99.3 mmol) followed by addition of 100 mL of THF. The suspension was cooled to 0 °C and a solution of pyrazole (5.79 g, 85.1 mmol) in 100 mL of THF was added dropwise via an additional funnel while H_2 bubbles were observed. After completion of addition, a solution of 1-fluoro-2-nitrobenzene (7.50 mL, 10.0 g, 70.9 mmol) in 100 mL of THF was added dropwise via an additional funnel. The ice-water bath was removed and the yellow solution was stirred at rt for 3 h, at which point an TLC analysis showed the disappearance of the starting material 1-fluoro-2-nitrobenzene. The reaction was then poured to a separatory funnel charged with 100 mL of saturated aqueous NH_4Cl solution and, after separation, the aqueous layer was extracted with EtOAc (2 × 200 mL). The combined organic layers were washed with brine (50 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue as a yellow solid was triturated with a mixture of acetone and hexanes (1:6) to give the desired product as a white crystalline solid that was pure enough to carry out the next step of palladium-catalyzed hydrogenation for the nitro group reduction (13.3 g, 98% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7. 80 (dt, $J = 8.1, 1.6$ Hz, 1H), 7.68 (s, 1H), 7.70 – 7.61 (m, 1H), 7.61 (ddd, $J = 7.6, 3.1, 1.4$ Hz, 1H), 7.52 (dt, $J = 8.0, 1.6$ Hz, 1H), 7.45 (td, $J = 7.8, 1.5$ Hz, 1H), 6.44 (t, $J = 2.2$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.5, 142.2, 133.3, 133.1, 129.7, 128.4, 126.0, 124.9, 108.2.



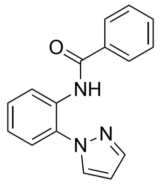
2-(1*H*-Pyrazol-1-yl)aniline

A 100 mL round-bottom flask was charged with 1-(2-nitrophenyl)-1*H*-pyrazole (5.00 g, 26.4 mmol) and 25 mL of EtOH. A catalytic amount of 10 wt% Pd/C (200 mg) was added and the flask was flushed with hydrogen. The reaction was then stirred overnight under a balloon of H_2 when the reaction was judged complete according to TLC. After flushing the flask with N_2, the catalyst was filtered and the solution concentrated *in vacuo*. The residue was purified via a flash chromatography eluting with Ethyl Acetate/ Hexane (1:2) to give the desired aniline as an oil (4.0 g, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ .75 – 7.68 (m, 2H), 7.24 (d, $J = 1.6$ Hz, 1H), 7.20 – 7.10 (m, 2H), 6.82 (dd, $J = 8.0, 1.4$ Hz, 1H), 6.81 – 6.73 (m, 1H), 6.45 – 6.40 (m, 1H), 4.66 (s, 2H, NH_2); ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.13, 140.48, 129.90, 128.49, 126.45, 124.15, 124.13, 117.95, 117.92, 117.26, 106.39, 77.43.



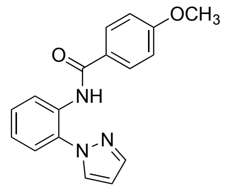
General procedure for amide formation

To a solution of the benzoic acid (3.66 mmol) and CH_2Cl_2 (5 mL) at 0°C was added 3–5 drops of DMF. After effervescing subsided, oxalyl chloride (5.12 mmol) was added drop wise. After stirring at rt for 1 h, the reaction was concentrated *in vacuo* to give the acid chloride as an oil. It was taken back with CH_2Cl_2 (5 mL), cooled back 0°C. A solution of 2-aminophenyl-1*H*-pyrazole (3.29 mmol) in CH_2Cl_2 (5 mL) was added, followed by triethylamine (3.66 mmol). The reaction was stirred at 0°C for 10 min, and rt for 2 h when the reaction was judged complete by TLC, the reaction mixture was filtered. The filtrate was washed with saturated ammonium chloride, and brine, the organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography eluting with Ethyl Acetate/ Hexane (1:6) to give the desired amide.



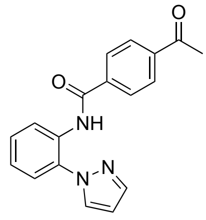
N-(2-(1*H*-pyrazol-1-yl)phenyl)benzamide

White solid (4.6 g, 87%), flash chromatography eluting with Ethyl Acetate/ Hexane (1:4) , $R_f = 0.51$ (CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$) δ 11.29 (bs, 1H, NH), 8.70 (dd, $J = 8.3, 1.4$ Hz, 1H), 7.94 (dd, $J = 8.04, 1.62$ Hz, 2H), 7.85 (dd, $J = 5.9, 2.2$ Hz, 2H), 7.56 – 7.33 (m, 5H), 7.19 (td, $J = 7.7, 1.4$ Hz, 1H), 6.51 (t, $J = 2.2$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.26, 141.08, 134.80, 131.82, 131.73, 130.25, 129.00, 128.68, 127.97, 127.26, 124.01, 122.81, 122.11, 107.29, 77.37. FTIR (neat, ATR, cm^{-1}) 3185, 1672, 1599, 1536, 1503, 1452, 1313, 949, 744, 680.



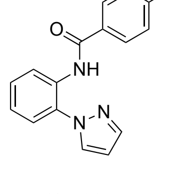
N-(2-(1H-pyrazol-1-yl)phenyl)-4-methoxybenzamide

White solid (0.52 g, 85%), flash chromatography eluting with Ethyl Acetate/ Hexane (1:4) , R_f = 0.40 (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.15 (s, 1H, NH), 8.65 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.84 (m, 2H), 7.35 (2H), 7.16 (t, *J* = 7.7 Hz, 1H), 6.94 (d, *J* = 8.3 Hz, 2H), 6.49 (t, *J* = 2.1 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.87, 162.43, 141.05, 132.00, 130.27, 129.13, 129.00, 128.06, 127.08, 123.73, 122.84, 122.19, 113.84, 107.21, 60.36, 55.41, 14.17. HRMS (ESI, m/z) calcd for $C_{17}H_{15}N_3O_2$ [M+1]: 293.1164, found: 294.1232.



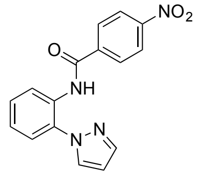
N-(2-(1H-pyrazol-1-yl)phenyl)-4-acetylbenzamide

White solid (0.87 g, 87%), flash chromatography eluting with Ethyl Acetate/ Hexane (1:4) , R_f = 0.30 (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.54 (s, 1H, NH), 8.70 (dd, *J* = 8.3, 1.4 Hz, 4H), 8.04 (qd, *J* = 8.5, 1.6 Hz, 4H), 8.70 (dd, *J* = 8.0, 2.5 Hz, 2H), 7.38 (m, 2H), 7.38 (td, *J* = 7.4, 1.4 Hz, 4H), 7.22 (q, *J* = 2.3 Hz, 1H), 2.65 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.42, 164.24, 141.70, 141.12, 139.33, 138.72, 131.36, 130.22, 129.83, 128.99, 128.59, 128.04, 127.96, 127.76, 127.55, 127.48, 125.12, 124.41, 124.37, 122.84, 122.47, 122.42, 121.96, 107.46, 107.39, 26.83. HRMS (ESI, m/z) calcd for $C_{18}H_{15}N_3O_2$ [M+1]: 306.1243, found: 306.1230.



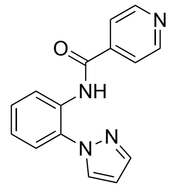
N-(2-(1H-pyrazol-1-yl)phenyl)-4-cyanobenzamide

White solid (0.51 g, 86%), flash chromatography eluting with Ethyl Acetate/ Hexane (1:4) , R_f = 0.61 (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.64 (s, 1H, NH), 8.67 (d, *J* = 8.22 Hz, 1H), 8.03 (dd, *J* = 8.30, 1.59 Hz, 2H), 7.89 (t, *J* = 1.73 Hz, 1H), 7.85 (t, *J* = 1.70 Hz, 1H), 7.78 (dd, *J* = 8.40, 1.69 Hz, 2H), 7.40 (td, *J* = 9.31, 1.68 Hz, 1H), 7.39 (td, *J* = 7.64, 1.41 Hz, 1H), 6.53 (q, *J* = 1.09 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.34, 141.13, 138.76, 132.74, 132.52, 131.01, 130.92, 130.22, 128.93, 128.03, 127.91, 124.64, 122.84, 121.83, 118.01, 115.28, 107.48. HRMS (ESI, m/z) calcd for $C_{17}H_{12}N_4O$ [M+1]: 289.1089, found: 289.1078.



N-(2-(1H-Pyrazol-1-yl)phenyl)-4-nitrobenzamide

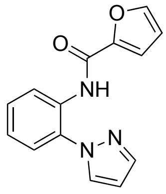
White solid (1.2 g, 97%), flash chromatography eluting with Ethyl Acetate/ Hexane (1:4) , R_f = 0.48 (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.74 (s, 1H, NH), 8.70 (d, *J* = 8.2 Hz, 1H), 8.34 (d, *J* = 8.3 Hz, 2H), 8.12 (d, *J* = 8.3 Hz, 2H), 7.94 – 7.86 (m, 2H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 7.7 Hz, 1H), 6.56 (d, *J* = 2.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.09, 149.73, 141.16, 140.44, 130.98, 130.22, 128.93, 128.42, 128.04, 124.73, 123.90, 122.83, 121.80, 107.52.



N-(2-(1H-Pyrazol-1-yl)phenyl)isonicotinamide

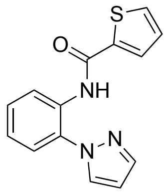
White solid (0.88 g, 80%), flash chromatography eluting with Ethyl Acetate/ Hexane (1:1) , R_f = 0.20 (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.71 (s, 1H, NH), 8.82 – 8.77 (m, 2H), 8.72 – 8.66 (m, 1H), 7.89 (dd, *J* = 9.1, 2.2 Hz, 2H), 7.81 – 7.76 (m, 2H), 7.40 (td, *J* = 7.8, 1.1 Hz, 2H), 7.26 – 7.19 (m, 1H), 6.54 (t, *J* = 2.2 Hz, 1H). ^{13}C NMR

(126 MHz, $CDCl_3$) δ 163.13, 150.54, 142.04, 141.16, 130.92, 130.19, 128.92, 127.99, 124.69, 122.85, 121.80, 121.03, 107.48.



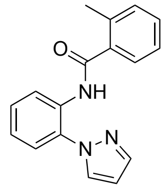
_N_-(2-(1_H_-Pyrazol-1-yl)phenyl)furan-2-carboxamide

White solid (0.75 g, 94%), flash chromatography eluting with Ethyl Acetate/ Hexane (1:4) , $R_f = 0.38$ (CH_2Cl_2). FTIR (neat, ATR, cm^{-1}) 3184, 1673, 1599, 1537, 1450, 1394, 1316, 786, 731; ^1H NMR (500 MHz, $CDCl_3$) δ 11.19 (s, 1H, NH), 8.64 – 8.58 (m, 1H), 7.85 (d, J = 1.9 Hz, 1H), 7.79 (d, J = 2.5 Hz, 1H), 7.49 (d, J = 1.6 Hz, 1H), 7.38 – 7.29 (m, 2H), 7.18 – 7.11 (m, 2H), 6.48 (t, J = 2.4 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.31, 148.10, 144.58, 141.12, 131.29, 130.11, 129.10, 128.03, 124.08, 122.77, 122.39, 114.89, 112.18, 107.24. HRMS (ESI, m/z) calcd for $C_{14}H_{11}N_3O_2$ [M+1]: 254.0931, found: 254.0919.



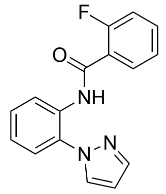
_N_-(2-(1_H_-Pyrazol-1-yl)phenyl)thiophene-2-carboxamide

White solid, (0.73 g, 89%), flash chromatography eluting with Ethyl Acetate/ Hexane (1:4) , $R_f = 0.40$ (CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$) δ 11.34 (s, 1H, NH), 8.64 (d, J = 8.3 Hz, 1H), 7.88 (dd, J = 12.4, 2.2 Hz, 2H), 7.63 (d, J = 3.7 Hz, 1H), 7.53 (d, J = 4.9 Hz, 1H), 7.38 (dd, J = 14.0, 7.7 Hz, 2H), 7.18 (t, J = 7.7 Hz, 1H), 7.12 (t, J = 4.3 Hz, 1H), 6.53 (d, J = 2.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.92, 141.06, 140.23, 131.46, 130.90, 130.24, 128.74, 128.31, 128.05, 127.76, 123.98, 122.72, 121.98, 107.32.



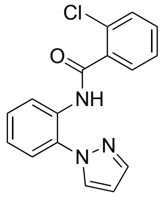
N-(2-(1H-Pyrazol-1-yl)phenyl)-2-methylbenzamide

White solid, 0.5 g, 91% yield. Flash chromatography solvent system: EtOAc/Hex (1: 3), R_f = 0.61 [EtOAc/Hex (1: 2)]. ^{1}H NMR (500 MHz, CDCl$_3$) δ 10.63 (s, 1H, NH), 8.69 (d, *J* = 8.3 Hz, 1H), 7.83 (d, *J* = 2.4 Hz, 1H), 7.72 (d, *J* = 1.8 Hz, 1H), 7.51 – 7.45 (m, 1H), 7.35 (td, *J* = 7.9, 1.4 Hz, 2H), 7.27 – 7.17 (m, 4H), 6.48 (t, *J* = 2.2 Hz, 1H), 2.49 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 167.89, 141.17, 137.03, 136.18, 131.88, 131.37, 130.30, 130.19, 129.22, 128.12, 127.02, 125.89, 124.13, 122.86, 122.51, 107.18, 20.08. GC-MS (ESI, m/z) calcd for $C_{17}H_{15}N_3O$: 277.1215, found: 277.



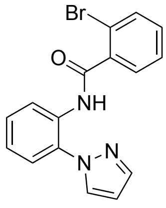
N-(2-(1H-Pyrazol-1-yl)phenyl)-2-fluorobenzamide

White solid, 0.42 g, 89% yield. Flash chromatography solvent system: EtOAc/Hex (1: 3), R_f = 0.57 [EtOAc/Hex (1: 2)]. ^{1}H NMR (500 MHz, CDCl$_3$) δ 10.85 – 10.80 (m, 1H, NH), 8.64 (d, *J* = 8.3 Hz, 1H), 8.06 (td, *J* = 7.8, 1.7 Hz, 1H), 7.80 (dd, *J* = 15.8, 2.1 Hz, 2H), 7.48 (d, *J* = 6.8 Hz, 1H), 7.46 – 7.39 (m, 1H), 7.38 – 7.32 (m, 1H), 7.29 – 7.18 (m, 2H), 7.13 (dd, *J* = 11.6, 8.3 Hz, 1H), 6.50 (t, *J* = 2.0 Hz, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 161.79–161.28 (dd, *J* = 63.88, 2.79 Hz), 159.29, 141.25–141.24 (d, *J* = 2.23 Hz), 133.52–133.43 (dd, *J* = 9.02, 2.25 Hz), 131.91, 131.83, 130.10, 129.97 (d, *J* = 2.47 Hz), 128.22, 128.20, 124.61 (m), 124.48–124.46 (d, *J* = 2.47 Hz), 123.70 123.25–123.23 (d, *J* = 2.47 Hz), 122.15–122.06 (d, *J* = 11.82 Hz), 116.34–116.13 (dd, *J* = 23.84, 2.86 Hz), 107.20–107.18 (d, *J* = 2.43 Hz). ^{19}F NMR (470 MHz, CDCl$_3$) δ –112.58. GC-MS (ESI, m/z) calcd for $C_{16}H_{12}FN_3O$: 281.0964, found: 281.



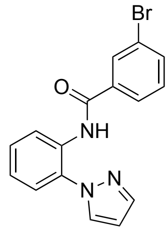
N-(2-(1H-Pyrazol-1-yl)phenyl)-2-chlorobenzamide

White solid, 0.47 g, 94% yield. Flash chromatography solvent system: EtOAc/Hex (1: 6), R_f = 0.38 [EtOAc/Hex (1: 2)]. ^{1}H NMR (500 MHz, CDCl$_3$) δ 10.69 (s, 1H, NH), 8.68 (d, J = 8.3 Hz, 1H), 7.82 (d, J = 2.4 Hz, 1H), 7.71 (d, J = 1.8 Hz, 1H), 7.61 (dd, J = 7.5, 1.8 Hz, 1H), 7.42 (s, 1H), 7.36 (ddd, J = 16.1, 8.7, 7.1 Hz, 3H), 7.28 – 7.20 (m, 1H), 6.47 (q, J = 1.8 Hz, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.88, 141.28, 135.78, 131.48, 131.39, 131.18, 130.46, 130.18, 129.60, 129.44, 128.16, 126.99, 124.52, 123.11, 122.64, 107.21. HRMS (ESI, m/z) for $C_{16}H_{13}ClN_3O$ [M+1]: 298.0747, found: 298.0737.



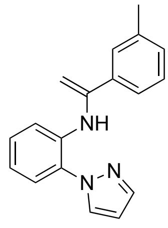
N-(2-(1H-Pyrazol-1-yl)phenyl)-2-bromobenzamide

Yellow solid, 0.45 g, 88% yield. Flash chromatography solvent system: EtOAc/Hex (1: 3), R_f = 0.46 [EtOAc/Hex (1: 2)]. ^{1}H NMR (500 MHz, CDCl$_3$) δ 10.65 (s, 1H, NH), 8.67 (d, J = 8.3 Hz, 1H), 7.83 (d, J = 2.4 Hz, 1H), 7.70 (d, J = 1.8 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.53 (dd, J = 7.6, 1.7 Hz, 1H), 7.46 – 7.28 (m, 4H), 7.31 – 7.18 (m, 2H), 6.48 (q, J = 2.2, 1.6 Hz, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 165.81, 141.29, 138.14, 133.67, 131.40, 131.37, 130.19, 129.40, 129.20, 128.13, 127.51, 124.55, 123.12, 122.52, 119.64, 107.22. GC-MS (ESI, m/z) calcd for $C_{16}H_{12}BrN_3O$: 341.0164, found: 341.



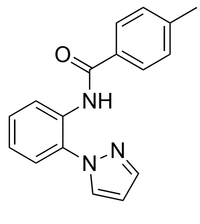
N-(2-(1H-Pyrazol-1-yl)phenyl)-3-bromobenzamide

White solid (0.14 g, 81%), flash chromatography eluting with ethyl acetate/hexane (1:6), *Rf* = 0.62 (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.50 (s, 1H), 8.70 (d, *J* = 8.2 Hz, 1H), 8.12 (s, 1H), 7.93 – 7.85 (m, 3H), 7.67 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.46 – 7.34 (m, 3H), 7.23 (t, *J* = 7.4 Hz, 1H), 6.55 (t, *J* = 2.3 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.71, 141.14, 136.82, 134.70, 131.40, 130.66, 130.21, 128.98, 128.05, 125.79, 124.29, 122.89, 122.84, 121.91, 107.42. GC-MS (ESI, m/z) calcd for $C_{16}H_{12}BrN_3O$: 341.0164, found: 341.



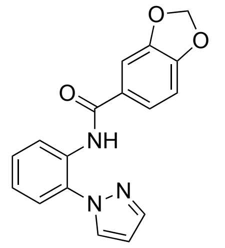
N-(2-(1H-Pyrazol-1-yl)phenyl)-3-methylbenzamide

White solid, 0.62 g, 95% yield. Flash chromatography solvent system: EtOAc/Hex (1: 3), R_f = 0.47 [EtOAc/Hex (1: 2)]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.26 (s, 1H, NH), 8.71 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.86 (dd, *J* = 5.0, 2.1 Hz, 2H), 7.77 (s, 1H), 7.75 – 7.69 (m, 1H), 7.43 – 7.32 (m, 4H), 6.52 (t, *J* = 2.2 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.49, 141.03, 138.44, 134.76, 132.53, 131.88, 130.28, 129.09, 128.52, 128.11, 128.09, 124.21, 123.95, 122.88, 122.20, 107.27, 21.42. GC-MS (ESI, m/z) calcd for $C_{17}H_{15}N_3O$: 277.1215, found: 277.



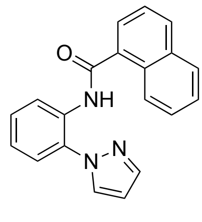
N-(2-(1H-Pyrazol-1-yl)phenyl)-4-methylbenzamide

White solid, 0.24 g, 83% yield, flash chromatography eluting with EtOAc/Hex (1:6), R_f = 0.52 [EtOAc/Hex (1: 2)]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.22 (s, 1H), 8.69 (d, J = 8.3 Hz, 1H), 7.84 (dd, J = 11.0, 7.8 Hz, 4H), 7.42 – 7.33 (m, 2H), 7.28 (d, J = 7.9 Hz, 2H), 6.51 (t, J = 2.2 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.30, 142.27, 141.07, 132.01, 131.96, 130.26, 129.33, 129.07, 128.08, 127.28, 123.85, 122.89, 122.21, 107.23, 21.47. GC-MS (ESI, m/z) calcd for 277.1215: $C_{17}H_{15}N_3O$, found: 277.



N-(2-(1H-Pyrazol-1-yl)phenyl)benzo[d][1,3]dioxole-5-carboxamide

White solid (0.16 g, 92%), flash chromatography eluting with ethyl acetate/hexane (1:4), Rf = 0.38 (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.21 (s, 1H), 8.68 (dd, J = 8.3, 1.4 Hz, 1H), 7.88 (dd, J = 8.0, 2.2 Hz, 2H), 7.50 (dd, J = 8.1, 1.8 Hz, 1H), 7.46 – 7.34 (m, 3H), 7.19 (d, J = 1.3 Hz, 1H), 6.89 (d, J = 8.1 Hz, 1H), 6.53 (t, J = 2.2 Hz, 1H), 6.05 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.54, 150.64, 148.06, 141.11, 131.86, 130.27, 129.07, 128.99, 128.05, 123.88, 122.84, 122.22, 122.13, 108.12, 107.80, 107.28, 101.74. HRMS (ESI, m/z) for $C_{17}H_{15}N_3O_3$ [M+1]: 308.1035; found: 308.1026.



N-(2-(1H-Pyrazol-1-yl)phenyl)-1-naphthamide

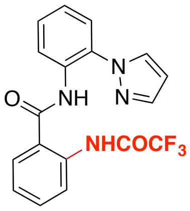
Yellow solid, 0.34 g, 85% yield. Flash chromatography solvent system: EtOAc/Hex

(1: 6), R_f = 0.38 [EtOAc/Hex (1: 2)].). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.94 (s, 1H, NH), 8.80 (d, *J* = 8.3 Hz, 1H), 8.49 – 8.43 (m, 1H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.91 – 7.82 (m, 2H), 7.75 (d, *J* = 7.0 Hz, 1H), 7.64 (d, *J* = 1.9 Hz, 1H), 7.56 – 7.43 (m, 4H), 7.38 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.27 – 7.21 (m, 1H), 6.46 (t, *J* = 2.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.43, 141.19, 134.30, 133.84, 131.91, 131.26, 130.32, 130.16, 129.32, 128.29, 128.13, 127.18, 126.41, 125.55, 125.49, 124.75, 124.30, 123.02, 122.47, 107.18. HRMS (ESI, m/z) for $C_{20}H_{16}N_3O$ [M+1]: 314.1293; found: 314.1284.

5.2 Copper-mediated C–H amidation and sulfonimidation

General procedure for amidation and sulfonamidation

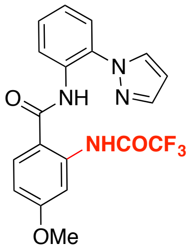
A 10 mL microwave vial was charged with the substrate (0.38 mmol), followed by the addition of the nitrogen source (0.76 mmol), copper acetate (0.38 mmol) and 1,1,3,3,-tetramethylguanidine (0.76 mmol). After adding the solvent DMSO (3 mL), the reaction was heated at 80 °C open to air. After stirring at 80 °C for 12 h, the reaction was judged complete by TLC, the reaction mixture was filtered. The filtrate was washed with saturated ammonium chloride, and brine, the organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography to give the desired product.



N-(2-(1H-Pyrazol-1-yl)phenyl)-2-(2,2,2-trifluoroacetamido)benzamide

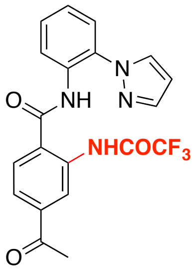
White solid, 0.18 g, 94% yield, flash chromatography eluting with Dichloromethane/ Hexane (4:1) , R_f = 0.69 (Ethyl Acetate/ Hexane (1: 2)). ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.74 (bs, 1H, NH), 11.74 (bs, 1H, NH), 8.64 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.55 (dd, *J* =

8.3, 1.4 Hz, 1H), 7.89 (d, *J* = 2.4 Hz, 1H),), 7.86 – 7.79 (m, 2H), 7.58 (ddd, *J* = 8.7, 7.4, 1.5 Hz, 1H), 7.42 (ddd, *J* = 16.8, 8.4, 1.5 Hz, 2H), 7.34 – 7.22 (m, 3H), 6.53 (t, *J* = 2.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 155.5 (q, *J* = 37.33 Hz), 141.2, 138.2, 133.3, 130.5, 130.2, 129.4, 128.0, 127.2, 125.0, 124.9, 123.4, 122.0, 121.7, 120.8, 115.6 (q, *J* = 288.84 Hz), 107.5. ^{19}F NMR (470 MHz $CDCl_3$) δ –76.15. HRMS (ESI, m/z) calcd for $C_{18}H_{13}F_3N_4O_2$ [M+1]: 375.1069, found: 375.1059.



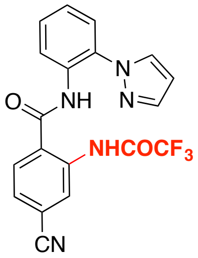
N-(2-(1H-Pyrazol-1-yl)phenyl)-4-methoxy-2-(2,2,2-trifluoroacetamido)benzamide

White solid, 0.07 g, 53% yield, flash chromatography eluting with Dichloromethane/ Hexane (4:1) , R_f = 0.62 (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 13.19 (s, 1H, NH), 11.58 (s, 1H, NH), 8.53 (dd, *J* = 8.3, 1.4 Hz, 1H), 8.31 (d, *J* = 2.6 Hz, 1H), 7.88 (ddd, *J* = 11.7, 2.2, 0.6 Hz, 2H), 7.76 (d, *J* = 8.9 Hz, 1H), 7.47 – 7.37 (m, 2H), 7.28 – 7.21 (m, 2H), 6.81 (dd, *J* = 8.9, 2.6 Hz, 1H), 6.54 (t, *J* = 2.2 Hz, 1H), 3.91 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.84, 163.33, 155.56 (q, *J* = 37.29 Hz), 141.17, 140.62, 130.74, 130.19, 129.38, 128.66, 128.00, 124.74, 123.41, 122.03, 114.58 (q, *J* = 288.53 Hz), 111.56, 107.46, 105.89, 77.25, 77.19, 76.99, 76.74, 55.68. ^{19}F NMR (470 MHz $CDCl_3$) δ –76.18. HRMS (ESI, m/z) calcd for $C_{19}H_{15}F_3N_4O_3$ [M+1]: 405.1176, found: 405.1162.



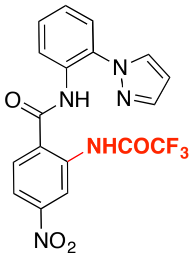
N-(2-(1H-Pyrazol-1-yl)phenyl)-4-acetyl-2-(2,2,2-trifluoroacetamido)benzamide

White solid, 0.12 g, 44% yield, flash chromatography eluting with Dichloromethane/ Hexane (4:1) , R_f = 0.51 (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.75 (s, 1H, NH), 12.01 (s, 1H, NH), 9.24 (d, *J* = 1.6 Hz, 1H), 8.59 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.97 – 7.87 (m, 3H), 7.86 (d, *J* = 2.0 Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 2H), 7.29 (td, *J* = 8.4, 8.0, 1.4 Hz, 1H), 7.26 (s, 1H), 6.55 (t, *J* = 2.2 Hz, 1H), 2.68 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.9, 166.0, 155.5 (q, *J* = 37.8 Hz), 141.3, 140.4, 130.2, 130.1, 129.3, 128.0, 127.5, 125.4, 124.0, 123.3, 121.8, 121.7, 112.0 (q, *J* = 289.8 Hz), 107.6, 26.8. ^{19}F NMR (470 MHz $CDCl_3$) δ –76.12. HRMS (ESI, m/z) calcd for $C_{20}H_{15}F_3N_4O_3$ [M+1]: 417.1175, found: 417.1165.



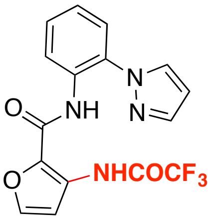
N-(2-(1H-Pyrazol-1-yl)phenyl)-4-cyano-2-(2,2,2-trifluoroacetamido)benzamide

White solid, 0.04 g, 75% yield, flash chromatography eluting with Dichloromethane/ Hexane (4:1) , R_f = 0.77 (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.75 (s, 1H, NH), 12.12 (s, 1H, NH), 9.02 (d, *J* = 1.5 Hz, 1H), 8.57 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.98 – 7.91 (m, 2H), 7.85 (dd, *J* = 2.0, 0.6 Hz, 1H), 7.60 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.49 – 7.42 (m, 2H), 7.35 – 7.27 (m, 1H), 6.57 (dd, *J* = 2.5, 1.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.25, 155.68 (q, *J* = 37.29 Hz), 141.27, 138.75, 130.16, 129.82, 129.22, 128.03, 127.99, 127.85, 125.66, 124.91, 124.33, 123.30, 121.67, 117.18, 116.80, 116.62, 114.32 (q, *J* = 288.45 Hz), 107.74. ^{19}F NMR (470 MHz $CDCl_3$) δ –76.16. HRMS (ESI, m/z) calcd for $C_{19}H_{12}F_3N_5O_2$ [M+1]: 400.1021, found: 400.1011.



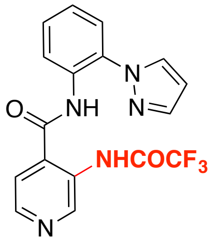
N-(2-(1H-Pyrazol-1-yl)phenyl)-4-nitro-2-(2,2,2-trifluoroacetamido)benzamide

Yellowish solid, 0.05 g, 72% yield, flash chromatography eluting with Dichloromethane/ Hexane (4:1) , R_f = 0.66 (CH_2Cl_2). ^1H NMR (500 MHz, DMSO-d_6) δ 12.12 (s, 1H, NH), 11.26 (s, 1H, NH), 8.77 (s, 1H), 8.25 (d, J = 12.6 Hz, 2H), 8.04 (d, J = 8.6 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.74 (s, 1H), 7.65 (d, J = 7.9 Hz, 1H), 7.47 – 7.37 (m, 2H), 6.57 (dd, J = 2.5, 1.9 Hz, 1H) . ^{19}F NMR (470 MHz DMSO-d_6) δ –74.86. The ^{13}C NMR was not taken because the presence of the nitro-group and two amides makes this compound extremely insoluble in all solvents tested.



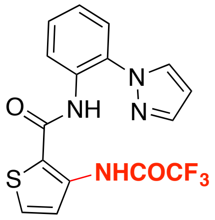
N-(2-(1H-Pyrazol-1-yl)phenyl)-3-(2,2,2-trifluoroacetamido)furan-2-carboxamide

White solid, 0.03 g, 27% isolated yield (82% based on recovered starting material), flash chromatography eluting with Dichloromethane/ Hexane (4:1) , R_f = 0.63 (CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$) δ 11.40 (s, 1H, NH), 10.60 (s, 1H, NH), 8.54 (d, J = 8.3 Hz, 1H), 7.88 (d, J = 13.3 Hz, 2H), 7.45 (s, 1H), 7.39 (d, J = 8.8 Hz, 3H), 7.25 (d, J = 15.6 Hz, 2H), 6.54 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.09, 154.50 (q, J = 38.56 Hz), 144.13, 141.23, 132.84, 130.51, 130.27, 129.94, 129.29, 127.93, 124.79, 122.93, 122.22, 114.32 (q, J = 287.92 Hz), 107.40. ^{19}F NMR (470 MHz $CDCl_3$) δ –76.03. HRMS (ESI, m/z) calcd for $C_{16}H_{11}F_3N_4O_3$ [M+1]: 365.0861, found: 365.0848.



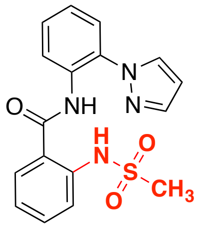
N-(2-(1H-Pyrazol-1-yl)phenyl)-3-(2,2,2-trifluoroacetamido)isonicotinamide

Yellow solid, 0.15 g, 67% yield, flash chromatography eluting with Dichloromethane/ Acetone (10:1) , $R_f = 0.32$ (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.39 (s, 1H, NH), 12.20 (s, 1H, NH), 9.94 (s, 1H), 8.63 (d, J = 5.1 Hz, 1H), 8.57 (d, J = 8.3 Hz, 1H), 7.93 (s, 1H), 7.87 (s, 1H), 7.65 (d, J = 5.1 Hz, 1H), 7.43 (d, J = 7.8 Hz, 2H), 7.30 (d, J = 7.8 Hz, 1H), 6.55 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.82, 155.24 (q, J = 38.1 Hz), 146.26, 144.14, 141.37, 133.58, 130.14, 129.70, 129.17, 127.95, 126.87, 125.71, 123.25, 121.62, 119.64, 113.00 (q, J = 288.5 Hz), 107.76. ^{19}F NMR (470 MHz $CDCl_3$) δ –75.92.



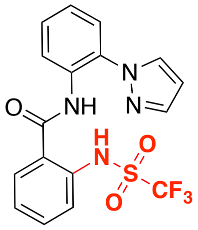
N-(2-(1H-Pyrazol-1-yl)phenyl)-3-(2,2,2-trifluoroacetamido)thiophene-2-carboxamide

Yellowish solid, 0.13 g, 69% yield (91% based on recovered starting material), flash chromatography eluting with Dichloromethane/ Hexane (4:1), $R_f = 0.66$ (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.15 (s, 1H, NH), 11.48 (s, 1H, NH), 8.53 – 8.47 (m, 1H), 8.12 (d, J = 5.4 Hz, 1H), 7.89 (dd, J = 6.7, 2.1 Hz, 2H), 7.49 (d, J = 5.4 Hz, 1H), 7.41 (dd, J = 8.1, 6.5 Hz, 2H), 7.23 (dd, J = 7.8, 1.4 Hz, 1H), 6.54 (t, J = 2.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.12, 154.36 (q, J = 38.0 Hz), 141.13, 141.08, 130.37, 129.90, 129.15, 128.64, 127.89, 124.85, 123.36, 122.86, 121.74, 116.78, 114.60 (q, J = 288.1 Hz), 107.47. ^{19}F NMR (470 MHz $CDCl_3$) δ –75.88.



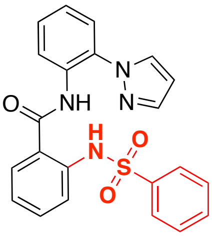
N-(2-(1H-pyrazol-1-yl)phenyl)-2-(methylsulfonamido)benzamide

White solid, 0.12 g, 84% yield, flash chromatography eluting with Dichloromethane/ Hexane (2:1) , $R_f = 0.45$ (CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$) δ 11.65 (s, 1H, NH), 10.86 (s, 1H, NH), 8.56 (d, $J = 8.2$ Hz, 1H), 7.90 (d, $J = 2.5$ Hz, 1H), 7.88 – 7.83 (m, 1H), 7.77 (dd, $J = 8.1, 5.1$ Hz, 2H), 7.53 (t, $J = 7.9$ Hz, 1H), 7.41 (d, $J = 7.7$ Hz, 2H), 7.29 – 7.17 (m, 3H), 6.54 (t, $J = 2.3$ Hz, 1H), 3.03 (s, 3H). ^{13}C NMR (126 MHz, $cdcl_3$) δ 166.79, 141.22, 140.10, 133.38, 130.64, 130.22, 129.34, 127.94, 127.57, 124.93, 123.35, 123.18, 122.02, 120.34, 119.68, 107.52, 39.90. HRMS (ESI, m/z) calcd for $C_{17}H_{13}F_3N_4O_3S$ [M+1]: 411.0739, found: 411.0730.



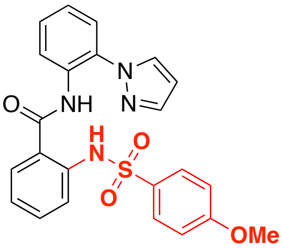
N-(2-(1H-Pyrazol-1-yl)phenyl)-2-(trifluoromethylsulfonamido)benzamide

White solid, 0.07 g, 87% yield, flash chromatography eluting with Dichloromethane/ Hexane (2:1) , $R_f = 0.73$ (CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$) δ 12.22 (s, 1H, NH), 11.86 (s, 1H, NH), 8.55 (dd, $J = 8.6, 1.4$ Hz, 1H), 7.90 (dd, $J = 21.8, 2.2$ Hz, 2H), 7.84 – 7.76 (m, 2H), 7.59 – 7.52 (m, 1H), 7.43 (ddt, $J = 5.6, 4.2, 2.0$ Hz, 2H), 7.34 – 7.25 (m, 2H), 6.56 (t, $J = 2.2$ Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.75, 141.25, 138.05, 133.47, 130.20, 129.44, 127.92, 127.29, 125.29, 124.88, 123.44, 121.89, 120.92, 120.58, 120.11 (q, $J = 323.79$ Hz), 118.52, 115.95, 107.60. ^{19}F NMR (470 MHz $CDCl_3$) δ –76.15. HRMS (ESI, m/z) calcd for $C_{17}H_{13}F_3N_4O_3S$ [M+1]: 411.0739, found: 411.0730.



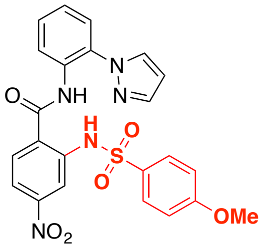
N-(2-(1H-Pyrazol-1-yl)phenyl)-2-(phenylsulfonamido)benzamide

White solid, 0.28 g, 99% yield, flash chromatography eluting with Dichloromethane/ Hexane (2:1) , $R_f = 0.59$ (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.34 (s, 1H, NH), 10.82 (s, 1H, NH), 8.50 (d, J = 8.2 Hz, 1H), 7.90 (d, J = 2.5 Hz, 1H), 7.82 – 7.70 (m, 3H), 7.57 (d, J = 7.9 Hz, 1H), 7.48 – 7.37 (m, 2H), 7.31 (t, J = 7.3 Hz, 1H), 7.29 – 7.21 (m, 2H), 7.14 (t, J = 7.6 Hz, 1H), 6.54 (t, J = 2.3 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.54, 141.08, 139.20, 132.86, 132.63, 130.52, 130.07, 129.10, 128.76, 127.81, 127.12, 127.06, 124.85, 124.04, 123.05, 122.40, 121.99, 121.86, 107.49. HRMS (ESI, m/z) calcd for $C_{22}H_{18}N_4O_3S$ [M+1]: 419.1178, found: 419.1167.



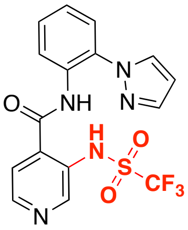
N-(2-(1H-Pyrazol-1-yl)phenyl)-2-(4-methoxyphenylsulfonamido)benzamide

White solid, 0.16 g, 93% yield, flash chromatography eluting with Dichloromethane/ Hexane (2:1) , $R_f = 0.45$ (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.33 (s, 1H, NH), 10.69 (s, 1H, NH), 8.52 (d, J = 8.3 Hz, 1H), 7.87 (d, J = 2.5 Hz, 1H), 7.81 – 7.77 (m, 1H), 7.69 (dd, J = 8.8, 3.2 Hz, 3H), 7.55 (d, J = 7.9 Hz, 1H), 7.41 (dt, J = 18.5, 8.5 Hz, 3H), 7.23 (d, J = 15.6 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 6.72 (d, J = 8.5 Hz, 2H), 3.65 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.58, 162.82, 141.07, 139.38, 132.78, 130.97, 130.74, 130.15, 129.33, 129.07, 127.88, 126.94, 124.69, 123.75, 122.98, 122.33, 121.93, 121.89, 113.99, 107.40, 55.35.



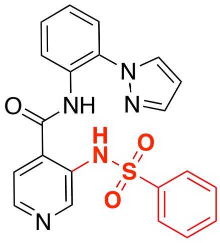
N-(2-(1H-Pyrazol-1-yl)phenyl)-2-(4-methoxyphenylsulfonamido)-4-nitrobenzamide

White solid, 0.08 g, 77% yield, flash chromatography eluting with Dichloromethane/ Hexane (2:1) , R_f = 0.52 (CH_2Cl_2). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.11 (s, 1H, NH), 10.63 (s, 1H, NH), 8.23 (d, J = 2.5 Hz, 1H), 8.12 (s, 1H), 8.04 (d, J = 8.6 Hz, 1H), 7.93 (dd, J = 23.6, 8.3 Hz, 1H), 7.76 (s, 1H), 7.65 (dd, J = 20.0, 8.2 Hz, 2H), 7.45 (t, J = 7.8 Hz, 1H), 7.39 (t, J = 7.7 Hz, 1H), 7.00 (d, J = 8.5 Hz, 1H), 6.50 (s, 1H), 3.72 (s, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.90, 163.43, 149.44, 141.39, 132.97, 131.36, 130.17, 129.88, 129.59, 128.02, 126.98, 126.22, 124.32, 119.22, 115.82, 115.12, 107.64, 56.13. FTIR (neat, ATR, cm^{-1}) 3129, 1652, 1593, 1547, 1523, 1499, 1332, 1132, 885, 762.



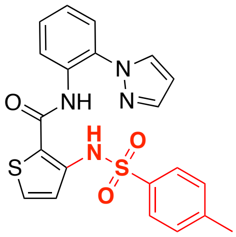
N-(2-(1H-Pyrazol-1-yl)phenyl)-3-(trifluoromethylsulfonamido)isonicotinamide

Yellow solid, 0.11 g, 86% yield, flash chromatography eluting with Dichloromethane/ Acetone (20:1) , R_f = 0.28 (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.21 (s, 1H, NH), 9.07 (s, 1H, NH), 8.55 (d, J = 5.2 Hz, 1H), 8.49 (d, J = 8.2 Hz, 1H), 7.93 (d, J = 2.4 Hz, 1H), 7.87 (d, J = 1.9 Hz, 1H), 7.66 (d, J = 5.2 Hz, 1H), 7.46 – 7.38 (m, 2H), 7.30 (td, J = 7.7, 1.3 Hz, 1H), 6.56 (t, J = 2.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.44, 142.99, 141.37, 130.28, 129.67, 129.59, 128.05, 125.95, 123.57, 122.03, 121.09, 120.25, 118.52, 107.76. ^{19}F NMR (470 MHz $CDCl_3$) δ –76.34. FTIR (neat, ATR, cm^{-1}) 3129 (b, NH), 1667, 1596, 1513, 1323, 1167, 1127, 1100, 979, 754.



***N*-(2-(1*H*-Pyrazol-1-yl)phenyl)-3-(phenylsulfonamido)isonicotinamide**

Yellow solid, 0.11 g, 98% yield, flash chromatography eluting with Dichloromethane/ Acetone (20:1) , R_f = 0.35 (CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$) δ 11.76 (s, 1H, NH), 10.37 (s, 1H, NH), 9.04 (s, 1H), 8.47 (t, *J* = 7.7 Hz, 2H), 7.93 (d, *J* = 2.5 Hz, 1H), 7.82 – 7.74 (m, 3H), 7.44 – 7.37 (m, 3H), 7.32 (q, *J* = 10.6, 9.0 Hz, 2H), 7.26 (t, *J* = 5.1 Hz, 3H), 6.55 (d, *J* = 2.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.42, 145.17, 144.34, 141.16, 138.83, 132.97, 130.00, 129.79, 128.99, 128.90, 128.64, 127.84, 127.22, 125.45, 122.98, 121.51, 119.50, 107.66.



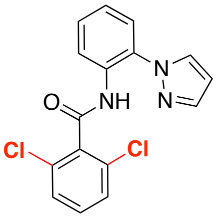
***N*-(2-(1*H*-Pyrazol-1-yl)phenyl)-3-(4-methylphenylsulfonamido)thiophene-2-carboxamide**

White solid, 0.06 g, 70% yield, flash chromatography eluting with Dichloromethane/ Hexane (2:1) , R_f = 0.37 (CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$) δ 11.12 (s, 1H, NH), 10.58 (s, 1H, NH), 8.45 (d, *J* = 8.2 Hz, 1H), 7.84 (s, 2H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 5.4 Hz, 1H), 7.39 – 7.23 (m, 3H), 7.20 (d, *J* = 7.7 Hz, 3H), 6.50 (d, *J* = 2.3 Hz, 1H), 2.33 (s, 3H).. ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.05, 143.86, 143.28, 141.00, 136.67, 130.66, 129.89, 129.69, 128.98, 128.44, 127.81, 126.99, 124.48, 123.10, 121.81, 121.51, 113.68, 107.36, 21.50.

5.3 Copper-mediated C–H chlorination

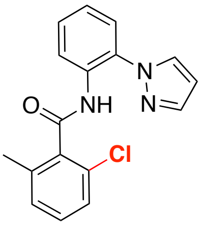
General procedure for chlorination

A 10 mL microwave vial was charged with the substrate (0.38 mmol), then was added the trichloroacetamide (0.76 mmol), copper acetate (0.38 mmol) and 1,1,3,3,-tetramethylguanidine (0.76 mmol). After adding the solvent DMSO (3 mL), the reaction was heated at 80 °C open to air. After stirring at 80 °C for 12 h, the reaction was judged complete by TLC, the reaction mixture was filtered. The filtrate was washed with saturated ammonium chloride, and brine, the organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography to give the desired product as a white solid



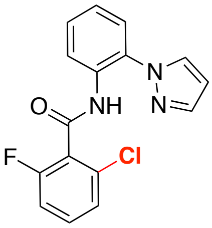
N-(2-(1H-Pyrazol-1-yl)phenyl)-2,6-dichlorobenzamide

White solid, 0.19 g, 77% yield, flash chromatography eluting with dichloromethane/ hexane (3:1) , $R_f = 0.56$ (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.56 (s, 1H, NH), 8.54 (dd, $J = 8.3$, 1.4 Hz, 1H), 7.82 (d, $J = 2.4$ Hz, 1H), 7.66 (d, $J = 1.8$ Hz, 1H), 7.43 (td, $J = 7.8$, 1.5 Hz, 1H), 7.40 – 7.31 (m, 2H), 7.31 – 7.21 (m, 3H), 6.46 (t, $J = 2.2$ Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.63, 141.20, 136.07, 132.25, 130.73, 130.70, 130.10, 129.90, 128.11, 128.02, 125.12, 124.04, 122.39, 107.16. FTIR (neat, ATR, cm^{-1}) 3258 (NH), 1670 (amide carbonyl), 1454, 1429, 1393, 1308, 938, 776. GC-MS (ESI, m/z) calcd for $C_{16}H_{11}Cl_2N_3O$: 331.0279, found: 331.



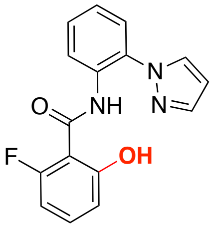
N-(2-(1H-Pyrazol-1-yl)phenyl)-2-chloro-6-methylbenzamide

White solid, 0.10 g, 80% yield (88% based on recovered starting material), flash chromatography eluting with dichloromethane/hexane (4:1), $R_f = 0.48$ [EtOAc/Hex (1: 2)]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.34 – 10.30 (m, 1H, NH), 8.56 (dd, $J = 8.3$, 1.4 Hz, 1H), 7.81 (d, $J = 2.3$ Hz, 1H), 7.66 (d, $J = 1.8$ Hz, 1H), 7.49 – 7.40 (m, 1H), 7.36 (dd, $J = 8.1$, 1.4 Hz, 1H), 7.28 – 7.17 (m, 3H), 7.12 (q, $J = 4.4$ Hz, 1H), 6.47 (s, 1H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.53, 141.21, 137.02, 136.70, 131.05, 130.60, 130.16, 129.94, 129.89, 128.63, 128.09, 126.89, 124.88, 123.93, 122.57, 107.15. HRMS (ESI, m/z) for $C_{17}H_{15}ClN_3O$ [M+1]: 312.0904, found: 312.0895.



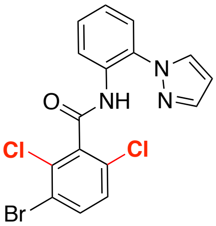
N-(2-(1H-Pyrazol-1-yl)phenyl)-2-chloro-6-fluorobenzamide

White solid, 0.09 g, 76% yield. Flash chromatography solvent system: EtOAc/Hex (1: 6), R_f = 0.46 (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.72 (s, 1H, NH), 8.62 (d, $J = 8.3$ Hz, 1H), 7.82 (d, $J = 2.5$ Hz, 1H), 7.67 (d, $J = 1.9$ Hz, 1H), 7.45 – 7.38 (m, 1H), 7.34 (ddd, $J = 20.0$, 8.2, 1.9 Hz, 2H), 7.27 – 7.19 (m, 2H), 7.05 (t, $J = 8.5$ Hz, 1H), 6.46 (t, $J = 2.2$ Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.56, 158.55, 141.18, 132.34, 131.28, 131.13, 130.84, 129.48, 127.95, 125.68, 124.93, 124.87, 123.46, 122.32, 122.28, 114.65, 107.12. ^{19}F NMR (470 MHz, $CDCl_3$) δ –112.8. HRMS (ESI, m/z) for $C_{16}H_{12}FN_3O$ [M+1]: 281.0964, found: 316.0643.



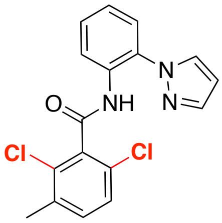
N-(2-(1H-Pyrazol-1-yl)phenyl)-2-fluoro-6-hydroxybenzamide

White solid, 0.03 g, 16% yield. Flash chromatography solvent system: EtOAc/Hex (1: 6), R_f = 0.50 (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.91 (s, 1H, OH), 11.04 (d, J = 16.5 Hz, 1H, NH), 8.40 (d, J = 8.3 Hz, 1H), 7.83 (s, 1H), 7.77 (d, J = 2.3 Hz, 1H), 7.43 (t, J = 7.9 Hz, 1H), 7.37 (d, J = 7.9 Hz, 1H), 7.36 – 7.25 (m, 2H), 6.79 (d, J = 8.4 Hz, 1H), 6.60 (dd, J = 12.4, 8.2 Hz, 1H), 6.50 (s, 1H). 166.52-163.88 (dd, J = 327.13, 3.94 Hz), 162.05, 160.07, 141.35, 134.14 (m), 130.64, 129.90, 127.94, 125.41, 124.93, 123.47, 114.52, 107.35, 105.90–105.63 (dd, J = 25.28, 4.39 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 104.34, 104.24. ^{19}F NMR (470 MHz, $CDCl_3$) δ –110.05. HRMS (ESI, m/z) for $C_{16}H_{13}FN_3O_2$ [M+1]: 298.0992, found: 298.0981.



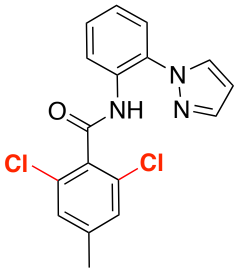
N-(2-(1H-Pyrazol-1-yl)phenyl)-2,3,6-trichlorobenzamide

White solid, 0.03 g, 57% yield, flash chromatography eluting with Dichloromethane/ Hexane (4:1), Rf = 0.70 (CH_2Cl_2) ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.66 (s, 1H), 8.53 (d, J = 8.2 Hz, 1H), 7.85 (t, J = 1.9 Hz, 1H), 7.69 (d, J = 2.1 Hz, 1H), 7.62 (dd, J = 8.6, 1.5 Hz, 1H), 7.47 – 7.37 (m, 3H), 7.32 – 7.19 (m, 4H), 6.49 (q, J = 2.0 Hz, 1H), 1.27 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.02, 141.28, 137.57, 134.55, 132.75, 131.13, 130.44, 130.04, 129.90, 129.02, 128.01, 125.31, 124.10, 122.25, 121.94, 107.25. HRMS (ESI, m/z) for $C_{16}H_{11}BrCl_2N_3O$ [M+1]: 409.9463, found: 409.9457.



N-(2-(1H-Pyrazol-1-yl)phenyl)-2,6-dichloro-3-methylbenzamide

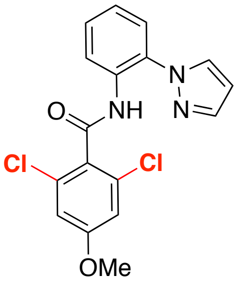
Yellow solid, 0.06 g, 43% yield (46% based on recovered starting material), flash chromatography eluting with EtOAc/Hex (1:6), R_f = 0.43 [EtOAc/Hex (1: 2)]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.47 (s, 1H, NH), 8.54 (d, J = 8.2 Hz, 1H), 7.81 (d, J = 2.5 Hz, 1H), 7.65 (d, J = 1.9 Hz, 1H), 7.42 (d, J = 7.3 Hz, 1H), 7.39 – 7.33 (m, 1H), 7.28 – 7.23 (m, 1H), 6.46 (t, J = 2.2 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.17, 141.18, 136.09, 135.74, 132.08, 131.87, 130.79, 130.09, 129.94, 129.15, 128.03, 127.62, 125.05, 124.10, 122.43, 107.12, 19.94. GC-MS (ESI, m/z) calcd for $C_{17}H_{13}Cl_2N_3O$: 345.0436, found: 345. HRMS (ESI, m/z) for $C_{17}H_{14}Cl_2N_3O$ [M+1]: 346.0514, found: 346.0505.



N-(2-(1H-Pyrazol-1-yl)phenyl)-2,6-dichloro-4-methylbenzamide

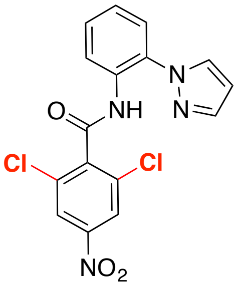
White solid, 0.04 g, 44% yield (79% based on recovered starting material), flash chromatography eluting with CH_2Cl_2/Hex (4:1), Rf = 0.58 (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.47 (s, 1H), 8.54 (dd, J = 8.2, 1.3 Hz, 1H), 7.81 (d, J = 2.5 Hz, 1H), 7.67 (d, J = 1.8 Hz, 1H), 7.43 (t, J = 7.9 Hz, 1H), 7.36 (dd, J = 8.1, 1.4 Hz, 1H), 7.32 – 7.21 (m, 1H), 7.14 (s, 2H), 6.46 (s, 1H), 6.46 (d, J = 4.5 Hz, 0H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.83, 141.56, 141.20, 141.18, 133.25, 131.84, 131.83, 130.86, 130.10, 130.08, 129.86, 128.66, 128.64, 128.05, 128.03, 124.98, 124.97, 123.98, 123.96, 122.42, 122.40, 107.12, 107.10, 20.94, 20.92. GC-MS (ESI, m/z) calcd for $C_{17}H_{13}Cl_2N_3O$: 345.0436, found: 345. HRMS (ESI, m/z) for $C_{17}H_{14}Cl_2N_3O$

[M+1]: 346.0514, found: 346.0506.



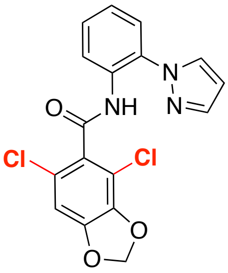
N-(2-(1H-Pyrazol-1-yl)phenyl)-2,6-dichloro-4-methoxybenzamide

White solid, 0.03 g, 32% yield (68% based on recovered starting material), flash chromatography eluting with CH2Cl2/ Hex (4:1), Rf = 0.43 (CH2Cl2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.45 (s, 1H, NH), 8.54 (d, J = 8.2 Hz, 1H), 7.81 (d, J = 2.4 Hz, 1H), 7.68 (d, J = 1.8 Hz, 1H), 7.42 (s, 1H), 7.36 (d, J = 7.8 Hz, 1H), 7.25 (d, J = 8.1 Hz, 1H), 6.85 (s, 2H), 6.46 (t, J = 2.0 Hz, 1H), 3.81 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.73, 160.38, 141.20, 132.96, 130.94, 130.92, 130.13, 129.83, 128.79, 128.06, 124.94, 123.90, 122.45, 114.05, 107.12, 55.86, 29.68. HRMS (ESI, m/z) for $C_{17}H_{14}Cl_2N_3O_2$ [M+1]: 362.0463, found: 362.0454.



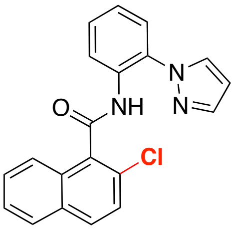
N-(2-(1H-Pyrazol-1-yl)phenyl)-2,6-dichloro-4-nitrobenzamide

Yellow solid, 0.02 g, 20% yield. Flash chromatography solvent system: CH_2Cl_2/Hex (4: 1), R_f = 0.56 (CH_2Cl_2). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.14 (s, 1H, NH), 8.40 (d, J = 8.3 Hz, 1H), 8.19 (d, J = 2.3 Hz, 1H), 8.11 (d, J = 9.2 Hz, 1H), 7.80 (d, J = 1.7 Hz, 1H), 7.75 – 7.69 (m, 2H), 7.53 – 7.44 (m, 2H), 7.30 (d, J = 7.6 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.64, 156.99, 150.36, 141.59, 132.82, 132.11, 131.75, 131.34, 128.65, 125.45, 125.43, 125.11, 124.06, 114.21, 111.80, 107.74. GC-MS (ESI, m/z) calcd for $C_{16}H_{10}Cl_2N_4O_3$: 376.0130, found: 376.



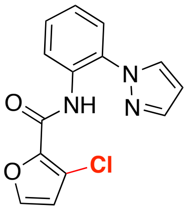
N-(2-(1H-Pyrazol-1-yl)phenyl)-4,6-dichlorobenzo[d][1,3]dioxole-5-carboxamide

White solid, 0.04 g, 47% yield (62% based on recovered starting material), flash chromatography eluting with Dichloromethane/ Hexane (4:1), $Rf = 0.53$ (CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$) δ 10.54 (s, 1H), 8.55 (dd, $J = 8.3, 1.4$ Hz, 1H), 7.83 (d, $J = 2.4$ Hz, 1H), 7.70 (d, $J = 1.8$ Hz, 1H), 7.43 (td, $J = 7.9, 1.5$ Hz, 2H), 7.37 (dd, $J = 8.0, 1.5$ Hz, 2H), 7.29 – 7.22 (m, 1H), 6.79 (s, 1H), 6.48 (t, $J = 2.2$ Hz, 1H), 6.10 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.13, 148.91, 144.06, 141.27, 130.81, 130.12, 129.81, 129.71, 128.04, 125.05, 124.58, 123.87, 122.42, 112.35, 108.79, 107.19, 102.78, 77.30, 77.04, 76.79. HRMS (ESI, m/z) for $C_{17}H_{12}Cl_2N_3O_3$ [M+1]: 376.0256, found: 376.0248.



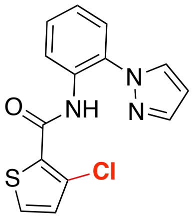
N-(2-(1H-Pyrazol-1-yl)phenyl)-2-chloro-1-naphthamide

White solid, 0.14 g, 90% yield, flash chromatography eluting with CH2Cl2/ Hex (4:1), $Rf = 0.46$ (CH2Cl2). ^1H NMR (500 MHz, $CDCl_3$) δ 10.66 (s, 1H), 8.74 (d, $J = 8.2$ Hz, 1H, NH), 7.89 – 7.79 (m, 4H), 7.53 – 7.41 (m, 5H), 7.38 (d, $J = 7.9$ Hz, 1H), 7.27 (s, 1H), 6.42 (d, $J = 2.2$ Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.03, 141.03, 140.11, 139.26, 136.67, 135.42, 131.25, 129.91, 129.44, 129.32, 129.04, 128.33, 128.15, 127.96, 127.38, 127.00, 124.32, 123.30, 122.71, 107.02. HRMS (ESI, m/z) for $C_{20}H_{15}ClN_3O$ [M+1]: 348.0904, found: 348.0896.



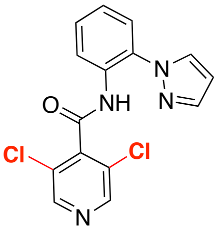
N-(2-(1H-Pyrazol-1-yl)phenyl)-3-chlorofuran-2-carboxamide

White solid, 0.03 g, 32% yield (78% based on recovered starting material). Flash chromatography solvent system: CH_2Cl_2/hex (3:1), $R_f = 0.50$ (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.05 (s, 1H, NH), 8.62 (d, $J = 8.3$ Hz, 1H), 7.82 (d, $J = 14.4$ Hz, 2H), 7.45 (s, 1H), 7.41 – 7.31 (m, 2H), 7.19 (t, $J = 7.7$ Hz, 1H), 6.51 (d, $J = 8.0$ Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ. 155.38, 143.48, 141.59, 141.16, 131.13, 130.10, 129.34, 128.10, 124.35, 123.09, 122.60, 121.32, 114.83, 107.28. HRMS (ESI, m/z) for $C_{14}H_{11}ClN_3O_2$ [M+1]: 288.0540, found: 288.0532.



N-(2-(1H-Pyrazol-1-yl)phenyl)-3-chlorothiophene-2-carboxamide

White solid, 0.08 g, 68% yield. Flash chromatography solvent system: CH_2Cl_2/hex (4:1), $R_f = 0.34$ (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.64 (s, 1H, NH), 8.51 (d, $J = 8.4$ Hz, 1H), 7.78 (d, $J = 6.0$ Hz, 2H), 7.45 (dd, $J = 5.4, 1.4$ Hz, 1H), 7.33 (d, $J = 7.9$ Hz, 1H), 7.22 (d, $J = 7.7$ Hz, 1H), 6.96 (dd, $J = 5.3, 1.4$ Hz, 1H), 6.49 (d, $J = 2.1$ Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.69, 141.38, 133.08, 131.59, 130.15, 129.71, 129.69, 128.32, 124.72, 124.66, 123.83, 123.62, 107.35. HRMS (ESI, m/z) for $C_{14}H_{11}ClN_3OS$ [M+1]: 304.0311, found: 304.0303.



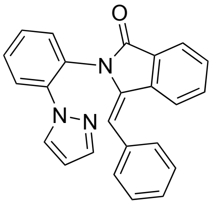
N-(2-(1H-Pyrazol-1-yl)phenyl)-3,5-dichloroisonicotinamide

White solid, 0.08 g, 55% yield, flash chromatography eluting with CH_2Cl_2/Acetone (10: 1), *Rf* = 0.37 [EtOAc/ Hex (1: 2)]. ^1H NMR (500 MHz, $CDCl_3$) δ 10.92 (s, 1H), 8.54 (d, *J* = 15.4 Hz, 3H), 7.85 (d, *J* = 2.4 Hz, 1H), 7.67 (d, *J* = 1.8 Hz, 1H), 7.47 – 7.37 (m, 2H), 7.28 (t, *J* = 7.7 Hz, 1H), 6.48 (t, *J* = 2.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.11, 147.87, 142.10, 141.28, 130.03, 129.99, 129.67, 128.94, 127.98, 125.53, 123.88, 122.05, 107.33. GC-MS (ESI, m/z) calcd for: 332.0232, found: 332. HRMS (ESI, m/z) for $C_{15}H_{11}Cl_2N_4O$ [M+1]: 333.0310, found: 333.0303.

5.4 Copper-mediated C–H alkynylation/annulation

General procedure for alkynylation/annulation

A 10 mL microwave vial was charged with the substrate (0.32 mmol), then was added the phenylacetylene (0.96 mmol), copper acetate (0.64 mmol) and Cs_2CO_3 (0.64 mmol). After adding the solvent DMSO (3 mL), the reaction was heated at 100 °C open to air. After stirring at 100 °C for 12 h, the reaction was judged complete by TLC, the reaction mixture was filtered. The filtrate was washed with saturated ammonium chloride, and brine, the organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo.* The residue was purified by flash chromatography to give the desired product as a white solid



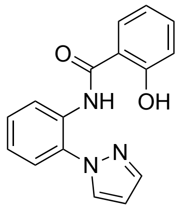
2-(1H-pyrazol-1-yl)phenyl-3-benzylideneisoindolin-1-one

White solid, 0.08 g, 72% yield, flash chromatography eluting with Ethyl Acetate/ Hexane (1:2) , R_f = 0.25 (Ethyl Acetate/ Hexane (1:2)). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 7.8 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.59 – 7.47 (m, 2H), 7.45 (d, *J* = 2.4 Hz, 1H), 7.31 – 7.22 (m, 3H), 7.22 – 7.17 (m, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.03 – 6.93 (m, 4H), 6.65 (s, 1H), 6.27 (s, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.09, 140.91, 138.82, 137.46, 134.13, 132.93, 132.37, 130.66, 129.94, 129.61, 129.08, 129.02, 128.81, 128.73, 127.52, 127.42, 127.11, 126.64, 125.03, 123.95, 119.44, 107.60, 106.60. GC-MS (ESI, m/z) calcd for: $C_{24}H_{17}N_3O$ [M+1]: 363.1372, found: 363.

5.5 Copper-mediated C–H hydroxylation

General procedure for hydroxylation

A 10 mL microwave vial was charged with the substrate (0.38 mmol), then was added the copper acetate (0.76 mmol) and 1,1,3,3,-tetramethylguanidine (0.76 mmol). After adding the solvent DMSO (3 mL), the reaction was heated at 80 °C open to air. After stirring at 80 °C for 12 h, the reaction was judged complete by TLC, the reaction mixture was filtered. The filtrate was washed with saturated ammonium chloride, and brine, the organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo.* The residue was purified by flash chromatography to give the desired product as a white solid

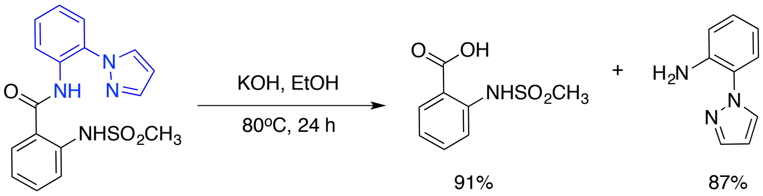


N-(2-(1*H*-pyrazol-1-yl)phenyl)-2-hydroxybenzamide

White solid, 0.09 g, 93% yield, flash chromatography eluting with Dichloromethane/ Hexane (5:1) , R_f = 0.73 (Ethyl Acetate/ Hexane (1: 2)). ^{1}H NMR (500 MHz, $CDCl_3$)

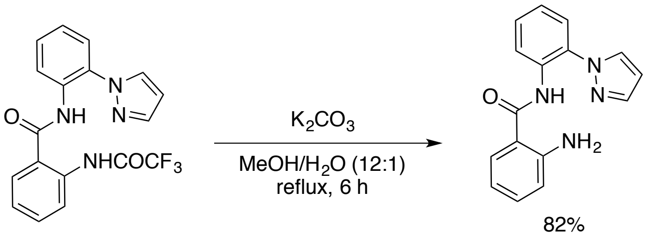
δ 12.23 (s, 1H, NH), 11.63 (s, 1H, OH), 8.53 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.89 (dd, *J* = 11.8, 2.2 Hz, 2H), 7.65 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.45 – 7.37 (m, 2H), 7.24 (td, *J* = 7.7, 1.3 Hz, 1H), 6.99 (dd, *J* = 8.4, 1.1 Hz, 1H), 6.92 (ddd, *J* = 8.2, 7.2, 1.2 Hz, 1H), 6.53 (t, *J* = 2.2 Hz, 1H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 168.68, 162.15, 141.21, 134.47, 130.55, 130.18, 129.48, 127.90, 126.04, 124.73, 123.52, 122.07, 118.94, 118.66, 114.88, 107.46. FTIR (neat, ATR, cm^{-1}) 3236, 3127 (b, OH), 1652, 1610, 1593, 1548, 1499, 1454, 1239, 1164, 1053, 940, 720; HRMS (ESI, m/z) calcd for $C_{16}H_{13}N_3O_2$ [M+1]: 280.1086, found: 280.1077.

5.6 Removal of directing groups



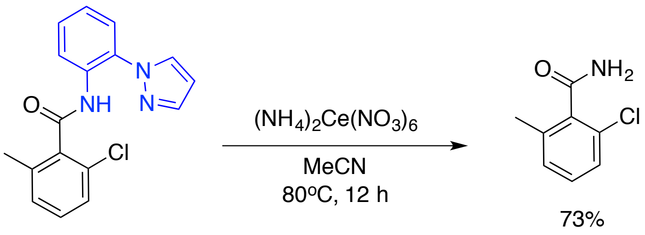
2-(Methylsulfonamido)benzoic acid

Greyish-brown solid, 0.20 g, 91% yield, flash chromatography eluting with Ethyl Acetate/ Hexane (1:3) , R_f = 0.25 (Ethyl Acetate/ Hexane (1:1)). ^{1}H NMR (500 MHz, CDCl$_3$) δ 10.26 (s, 1H, NH), 8.15 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.3 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.18 (t, *J* = 7.8 Hz, 1H), 3.11 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 171.53, 141.50, 136.11, 132.72, 123.21, 118.13, 114.17, 40.28. FTIR (neat, ATR, cm^{-1}) 3300–2000 (broad), 1659, 1582, 1490, 1334, 1326, 1253, 1144, 1087, 966.



N-(2-(1H-Pyrazol-1-yl)phenyl)-2-aminobenzamide

White solid, 0.13 g, 82% yield , flash chromatography eluting with Ethyl Acetate/ Hexane (1:2) , R_f = 0.36 (Ethyl Acetate/ Hexane (1:2)). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.06 (s, 1H), 8.55 (d, J = 8.3 Hz, 1H), 7.83 (d, J = 2.9 Hz, 2H), 7.56 (d, J = 7.9 Hz, 1H), 7.43 – 7.33 (m, 2H), 7.21 (dt, J = 29.0, 7.9 Hz, 2H), 6.73 (t, J = 8.0 Hz, 2H), 6.50 (d, J = 2.2 Hz, 1H), 5.88 (s, 2H, NH_2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.57, 149.16, 141.15, 132.73, 131.79, 130.19, 129.43, 127.92, 127.53, 123.92, 123.91, 123.13, 122.40, 117.69, 117.00, 107.23. FTIR (neat, ATR, cm^{-1}) 3467, 3362, 3249, 1654, 1584, 1501, 1453, 1310, 1244, 1159, 947, 687.



2-Chloro-6-methylbenzamide

To a solution of the N-(2-(1H-pyrazol-1-yl)phenyl)-2-chloro-6-methylbenzamide (120 mg, 0.38 mmol) and CAN (2.08 g, 3.80 mmol) was added MeCN (5 mL). After stirring at 80 °C for 12 h, the reaction was judged complete by TLC. The filtrate was washed with saturated brine, the organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography eluting with Ethyl Acetate/Hexane (1:6) to give the desired amide as a white solid, 0.046 g, 73% yield. Flash chromatography solvent system: EtOAc/Hex (1: 6), R_f = 0.40 [EtOAc/Hex (1: 1)] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 6.96 (m, 3H), 6.53 – 6.28 (m, 1H), 5.89 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.53, 136.86, 135.91, 130.10, 129.89, 128.60, 126.79, 19.36. GC-MS (ESI, m/z) calcd for $C_{17}H_{15}N_3O_2$: 169.0294, found: 169.

Reference

(1) Tsuji, J. *Transition Metal Reagents and Catalysts: Innovations in Organic Synthesis*; John Wiley & Sons, 2002.
(2) Rouquet, G.; Chatani, N. *Angew. Chem. Int. Ed.* **2013**, *52* (45), 11726.
(3) Shang, M.; Sun, S.-Z.; Wang, H.-L.; Wang, M.-M.; Dai, H.-X. *Synthesis* **2016**, *48* (24), 4381.
(4) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2009**, *48* (28), 5094.
(5) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45* (6), 788.
(6) Alsters, P. L.; Engel, P. F.; Hogerheide, M. P.; Copijn, M.; Spek, A. L.; van Koten, G. *Organometallics* **1993**, *12* (5), 1831.
(7) Zaitsev, V. G.; Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2005**, *127* (38), 13154.
(8) Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2010**, *132* (11), 3965.
(9) Nadres, E. T.; Santos, G. I. F.; Shabashov, D.; Daugulis, O. *J. Org. Chem.* **2013**, *78* (19), 9689.
(10) Truong, T.; Klimovica, K.; Daugulis, O. *J. Am. Chem. Soc.* **2013**, *135* (25), 9342.
(11) Li, X.; Liu, Y.-H.; Gu, W.-J.; Li, B.; Chen, F.-J.; Shi, B.-F. *Org. Lett.* **2014**, *16* (15), 3904.
(12) Yin, X.-S.; Li, Y.-C.; Yuan, J.; Gu, W.-J.; Shi, B.-F. *Org. Chem. Front.* **2015**, *2* (2), 119.
(13) Shang, M.; Sun, S.-Z.; Dai, H.-X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2014**, *136* (9), 3354.
(14) Sun, S.-Z.; Shang, M.; Wang, H.-L.; Lin, H.-X.; Dai, H.-X.; Yu, J.-Q. *J. Org. Chem.* **2015**, *80* (17), 8843.
(15) Shang, M.; Sun, S.-Z.; Wang, H.-L.; Laforteza, B. N.; Dai, H.-X.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2014**, *53* (39), 10439.
(16) Sonogashira, K. *J. Organomet. Chem.* **2002**, *653* (1–2), 46.
(17) Cai, X.; Xie, B. *Synthesis* **2015**, *47* (6), 737.
(18) Tran, L. D.; Roane, J.; Daugulis, O. *Angew. Chem. Int. Ed.* **2013**, *52* (23), 6043.
(19) Roane, J.; Daugulis, O. *J. Am. Chem. Soc.* **2016**, *138* (13), 4601.
(20) Hao, W.; Liu, Y. *Beilstein J. Org. Chem.* **2015**, *11* (1), 2132.
(21) Urones, B.; Martínez, Á. M.; Rodríguez, N.; Arrayás, R. G.; Carretero, J. C. *Chem. Commun.* **2013**, *49* (94), 11044.
(22) Li, B.; Liu, B.; Shi, B.-F. *Chem. Commun.* **2015**, *51* (24), 5093.
(23) Zhang, J.; Li, D.; Chen, H.; Wang, B.; Liu, Z.; Zhang, Y. *Adv. Synth. Catal.* **2016**, *358* (5), 792.
(24) Chen, C.; Wang, C.; Zhang, J.; Zhao, Y. *J. Org. Chem.* **2015**, *80* (2), 942.
(25) Rao, W.-H.; Shi, B.-F. *Org. Lett.* **2015**, *17* (11), 2784.
(26) Romero-Revilla, J. A.; García-Rubia, A.; Goméz Arrayás, R.;

Fernández-Ibáñez, M. Á.; Carretero, J. C. *J. Org. Chem.* **2011**, *76* (22), 9525.

(27) Hao, X.-Q.; Chen, L.-J.; Ren, B.; Li, L.-Y.; Yang, X.-Y.; Gong, J.-F.; Niu, J.-L.; Song, M.-P. *Org. Lett.* **2014**, *16* (4), 1104.

(28) Iwasaki, M.; Kaneshika, W.; Tsuchiya, Y.; Nakajima, K.; Nishihara, Y. *J. Org. Chem.* **2014**, *79* (23), 11330.

(29) Liu, Z.; Zeng, T.; Yang, K. S.; Engle, K. M. *J. Am. Chem. Soc.* **2016**, *138* (46), 15122.

(30) Yu, M.; Liang, Z.; Wang, Y.; Zhang, Y. *J. Org. Chem.* **2011**, *76* (12), 4987.

(31) Parella, R.; Babu, S. A. *J. Org. Chem.* **2015**, *80* (24), 12379.

(32) Hernando, E.; Villalva, J.; Martínez, Á. M.; Alonso, I.; Rodríguez, N.; Gómez Arrayás, R.; Carretero, J. C. *ACS Catal.* **2016**, *6* (10), 6868.

(33) Testa, C.; Roger, J.; Scheib, S.; Fleurat-Lessard, P.; Hierso, J.-C. *Adv. Synth. Catal.* **2015**, *357* (13), 2913.

(34) Ye, X.; Shi, X. *Org. Lett.* **2014**, *16* (17), 4448.

(35) Zhu, Q.; Ji, D.; Liang, T.; Wang, X.; Xu, Y. *Org. Lett.* **2015**, *17* (15), 3798.

(36) Chan, K. S. L.; Wasa, M.; Wang, X.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2011**, *50* (39), 9081.

(37) Lou, S.-J.; Chen, Q.; Wang, Y.-F.; Xu, D.-Q.; Du, X.-H.; He, J.-Q.; Mao, Y.-J.; Xu, Z.-Y. *ACS Catal.* **2015**, *5* (5), 2846.

(38) Kinuta, H.; Tobisu, M.; Chatani, N. *J. Am. Chem. Soc.* **2015**, *137* (4), 1593.

(39) Van Steijvoort, B. F.; Kaval, N.; Kulago, A. A.; Maes, B. U. W. *ACS Catal.* **2016**, *6* (7), 4486.

(40) Zhang, L.-B.; Hao, X.-Q.; Zhang, S.-K.; Liu, K.; Ren, B.; Gong, J.-F.; Niu, J.-L.; Song, M.-P. *J. Org. Chem.* **2014**, *79* (21), 10399.

(41) Li, Q.; Zhang, S.-Y.; He, G.; Ai, Z.; Nack, W. A.; Chen, G. *Org. Lett.* **2014**, *16* (6), 1764.

(42) Li, X.; Liu, Y.-H.; Gu, W.-J.; Li, B.; Chen, F.-J.; Shi, B.-F. *Org. Lett.* **2014**, *16* (15), 3904.

(43) Pan, C.; Jin, H.; Xu, P.; Liu, X.; Cheng, Y.; Zhu, C. *J. Org. Chem.* **2013**, *78* (18), 9494.

(44) Urones, B.; Arrayás, R. G.; Carretero, J. C. *Org. Lett.* **2013**, *15* (5), 1120.

(45) Liu, B.; Huang, X.; Wang, X.; Ge, Z.; Li, R. *Org. Chem. Front.* **2015**, *2* (7), 797.

(46) Shang, M.; Wang, H.-L.; Sun, S.-Z.; Dai, H.-X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2014**, *136* (33), 11590.

(47) Zhao, S.; Liu, B.; Zhan, B.-B.; Zhang, W.-D.; Shi, B.-F. *Org. Lett.* **2016**, *18* (18), 4586.

(48) Landge, V. G.; Midya, S. P.; Rana, J.; Shinde, D. R.; Balaraman, E. *Org. Lett.* **2016**, *18* (20), 5252.

(49) Zhang, Q.; Yin, X.-S.; Chen, K.; Zhang, S.-Q.; Shi, B.-F. *J. Am. Chem. Soc.* **2015**, *137* (25), 8219.

(50) Liang, S.; Liu, N.-W.; Manolikakes, G. *Adv. Synth. Catal.* **2016**, *358* (1), 159.

(51) Gurak, J. A.; Yang, K. S.; Liu, Z.; Engle, K. M. *J. Am. Chem. Soc.* **2016**, *138* (18), 5805.

(52) Pastine, S. J.; Gribkov, D. V.; Sames, D. *J. Am. Chem. Soc.* **2006**, *128* (44), 14220.

(53) Chu, J.-H.; Wu, C.-C.; Chang, D.-H.; Lee, Y.-M.; Wu, M.-J. *Organometallics* **2013**, *32* (1), 272.

(54) Chen, F.-J.; Liao, G.; Li, X.; Wu, J.; Shi, B.-F. *Org. Lett.* **2014**, *16* (21), 5644.

(55) Zheng, X.-X.; Du, C.; Zhao, X.-M.; Zhu, X.; Suo, J.-F.; Hao, X.-Q.; Niu, J.-L.; Song, M.-P. *J. Org. Chem.* **2016**, *81* (10), 4002.

(56) Schinkel, M.; Wang, L.; Bielefeld, K.; Ackermann, L. *Org. Lett.* **2014**, *16* (7), 1876.

(57) Ackermann, L.; Diers, E.; Manvar, A. *Org. Lett.* **2012**, *14* (4), 1154.

(58) Lee, W.-C. C.; Shen, Y.; Gutierrez, D. A.; Li, J. J. *Org. Lett.* **2016**, *18* (11), 2660.

(59) Chen, X.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128* (39), 12634.

(60) Jia, X.; Yin, K.; Li, C.; Li, J.; Bian, H. *Green Chem.* **2011**, *13* (8), 2175.

(61) Dong, J.; Wang, F.; You, J. *Org. Lett.* **2014**, *16* (11), 2884.

(62) Zhang, Y.; Wang, Q.; Yu, H.; Huang, Y. *Org. Biomol. Chem.* **2014**, *12* (44), 8844.

(63) Zhang, L.-B.; Hao, X.-Q.; Liu, Z.-J.; Zheng, X.-X.; Zhang, S.-K.; Niu, J.-L.; Song, M.-P. *Angew. Chem. Int. Ed.* **2015**, *54* (34), 10012.

(64) Wendlandt, A. E.; Suess, A. M.; Stahl, S. S. *Angew. Chem. Int. Ed.* **2011**, *50* (47), 11062.

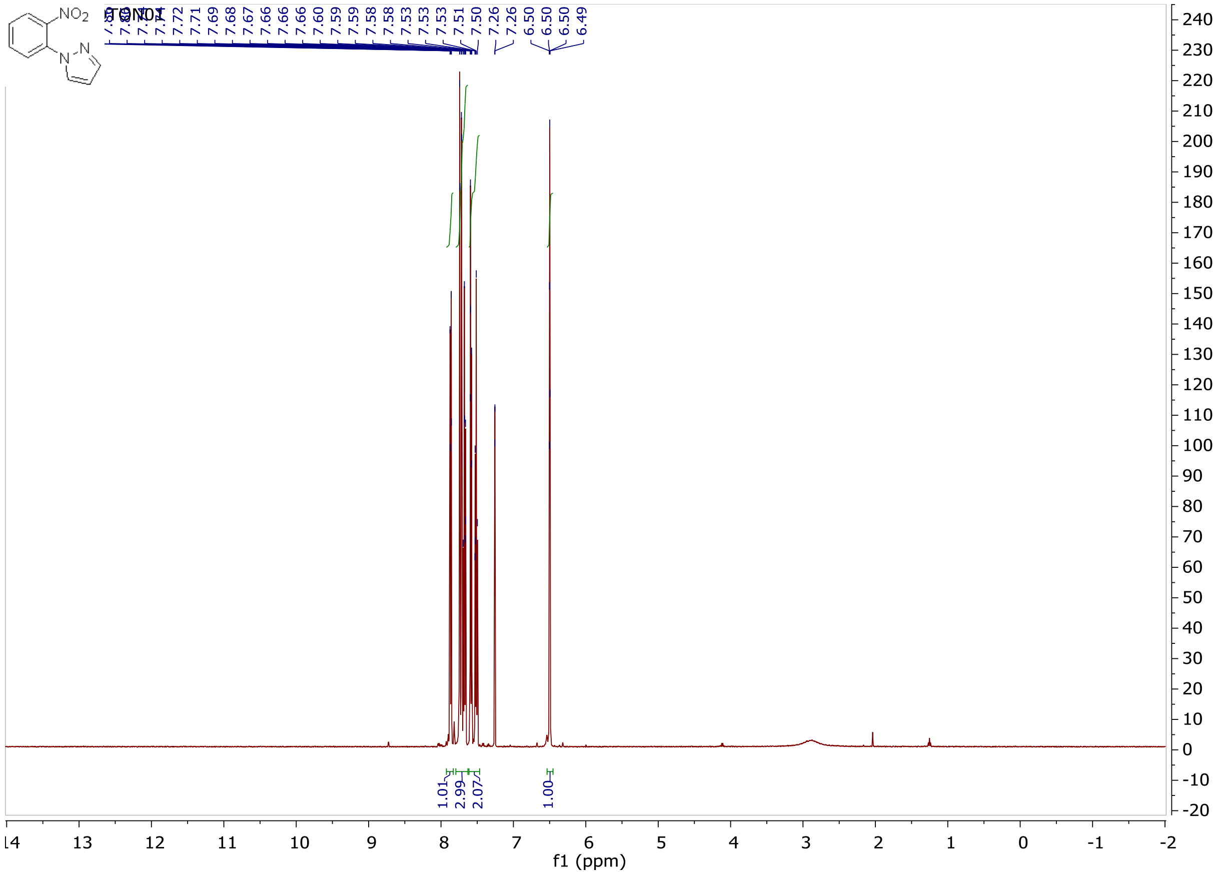
(65) Daugulis, O.; Roane, J.; Tran, L. D. *Acc. Chem. Res.* **2015**, *48* (4), 1053.

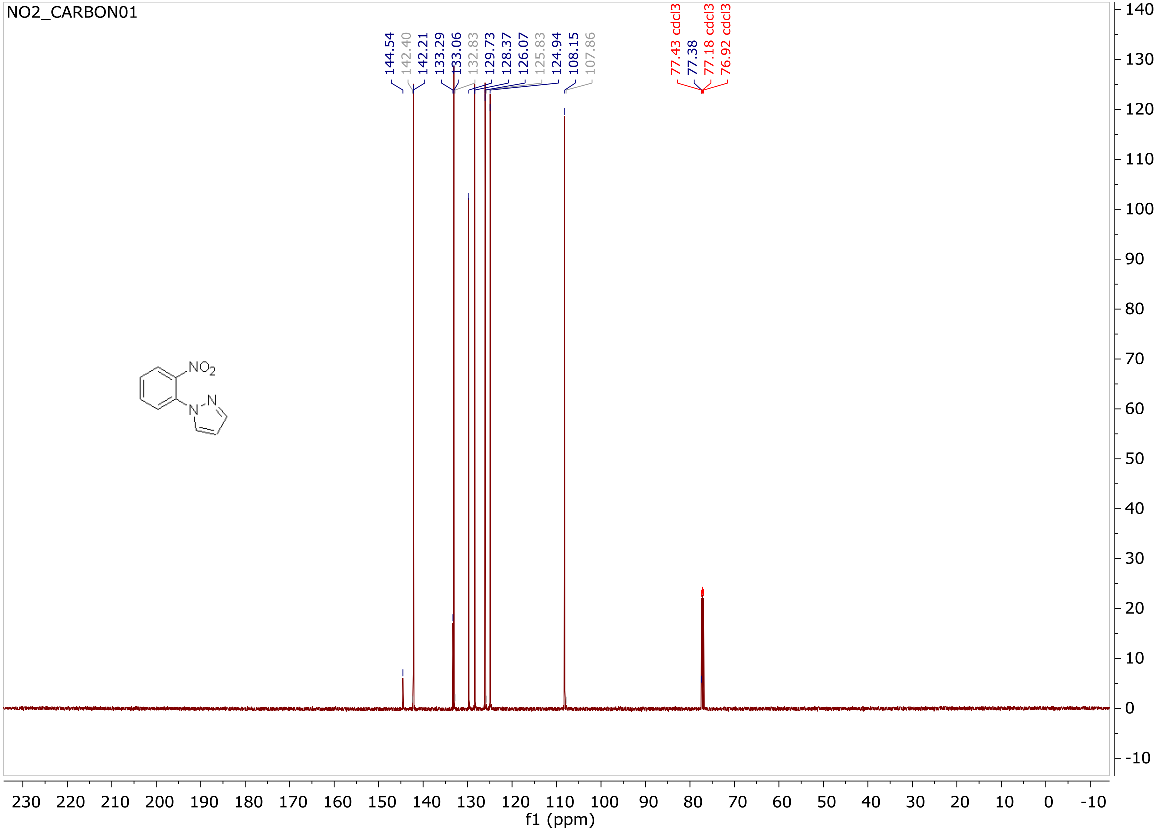
(66) Li, X.; Liu, Y.-H.; Gu, W.-J.; Li, B.; Chen, F.-J.; Shi, B.-F. *Org. Lett.* **2014**, *16* (15), 3904.

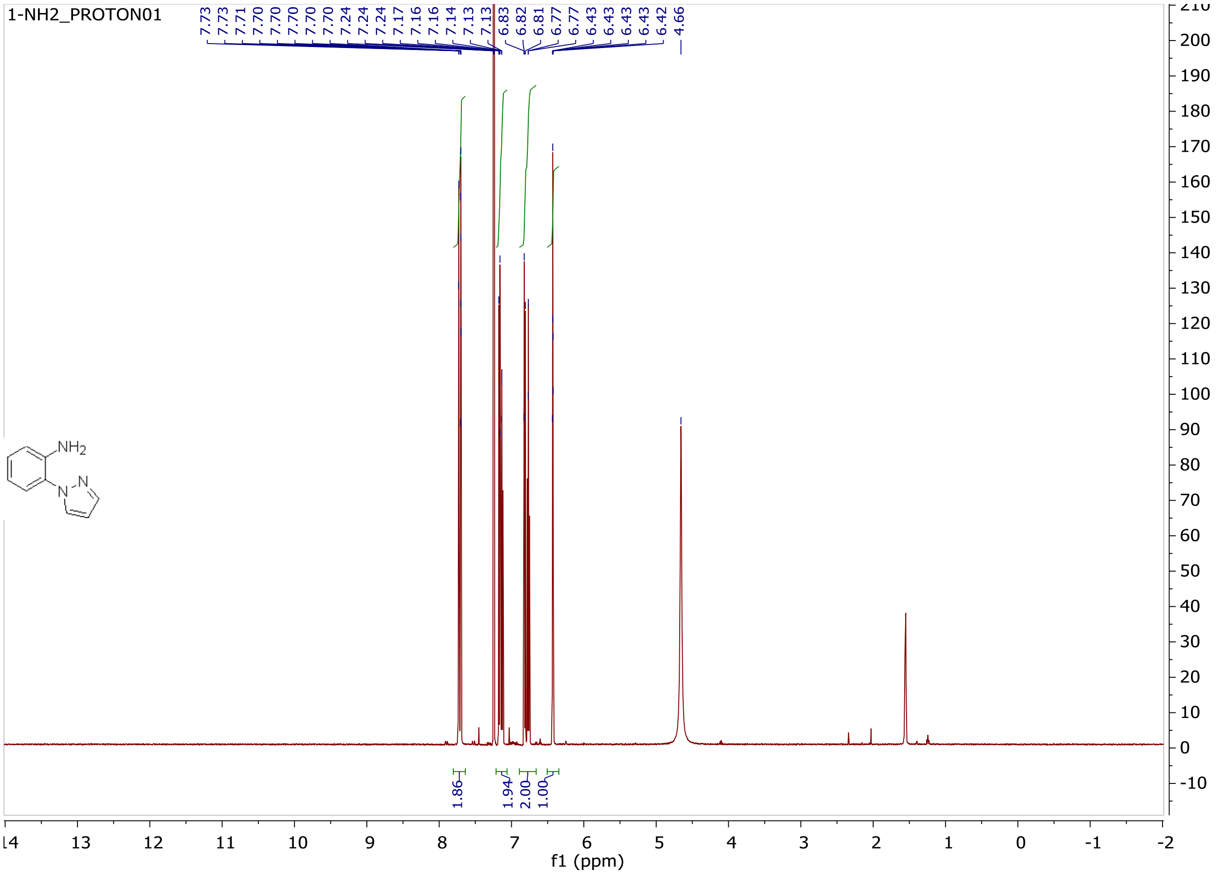
(67) Allen, S. E.; Walvoord, R. R.; Padilla-Salinas, R.; Kozlowski, M. C. *Chem. Rev.* **2013**, *113* (8), 6234.

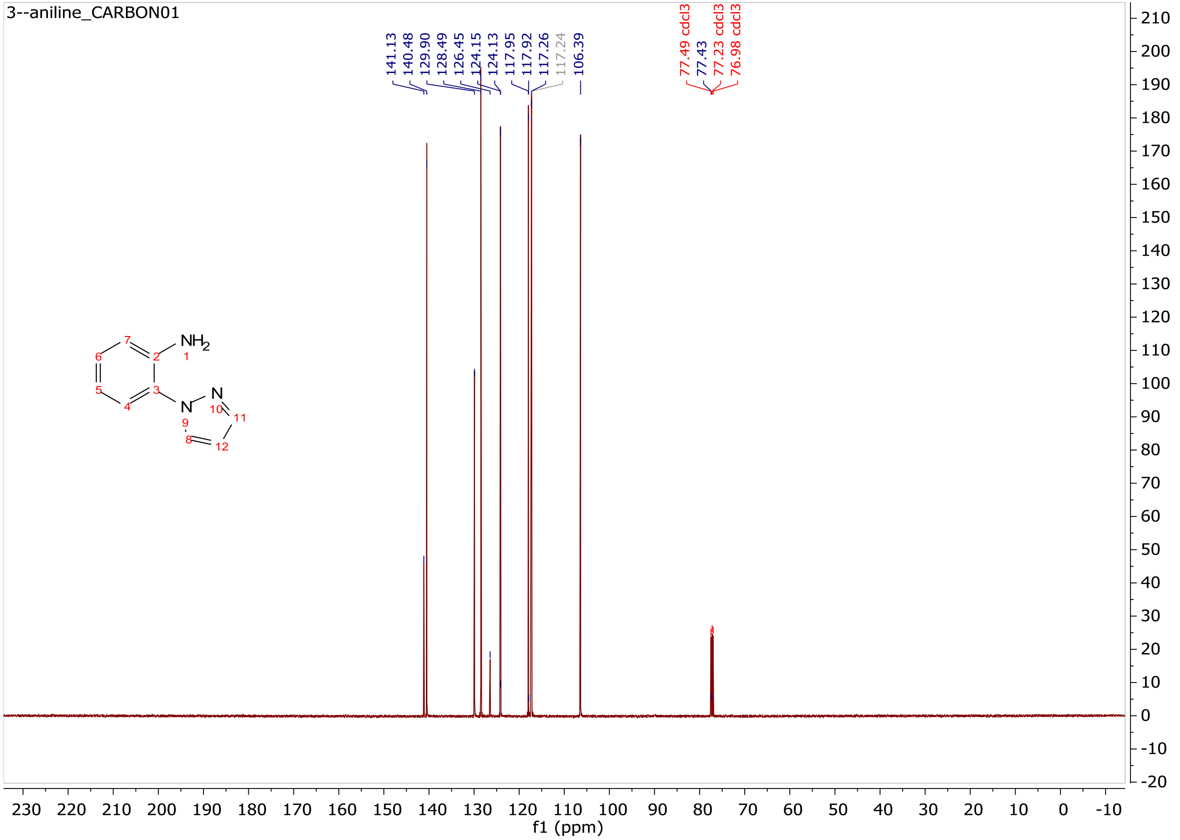
(68) Selvakumar, J.; Sankar Grandhi, G.; Sahoo, H.; Baidya, M. *RSC Adv.* **2016**, *6* (83), 79361.

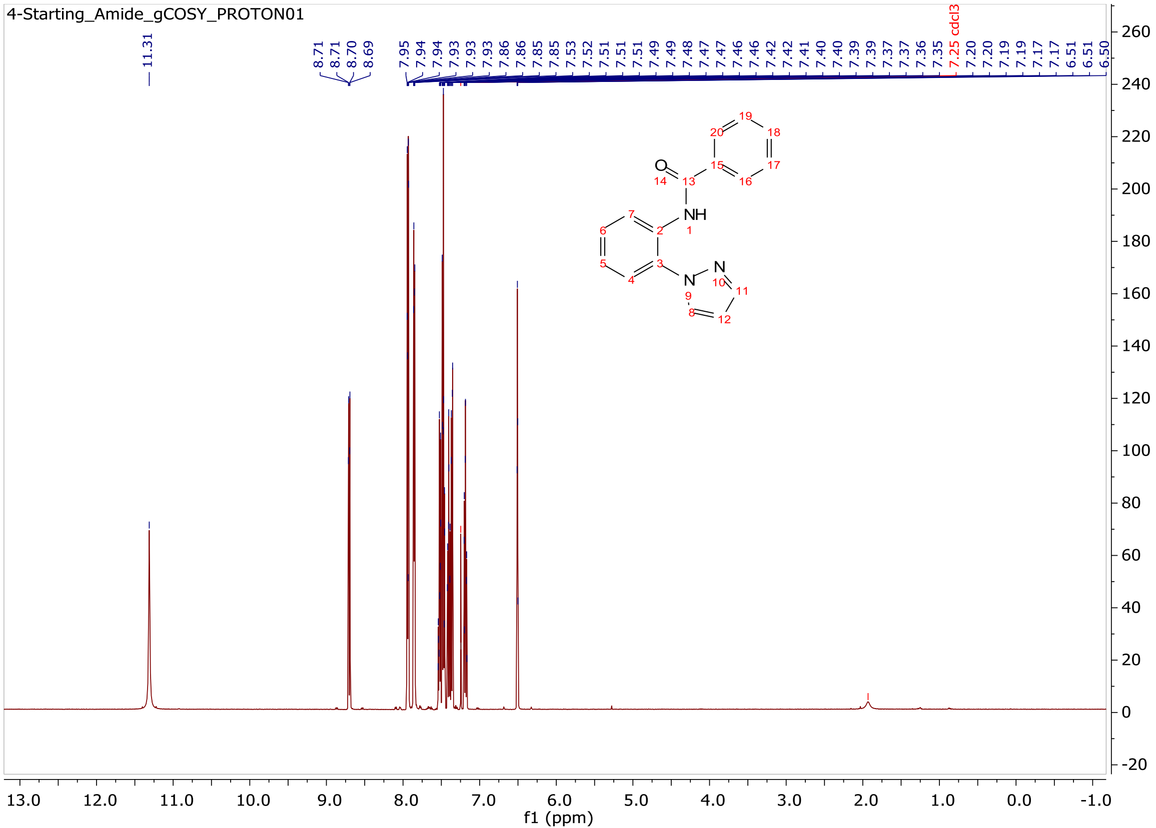
Appendix A

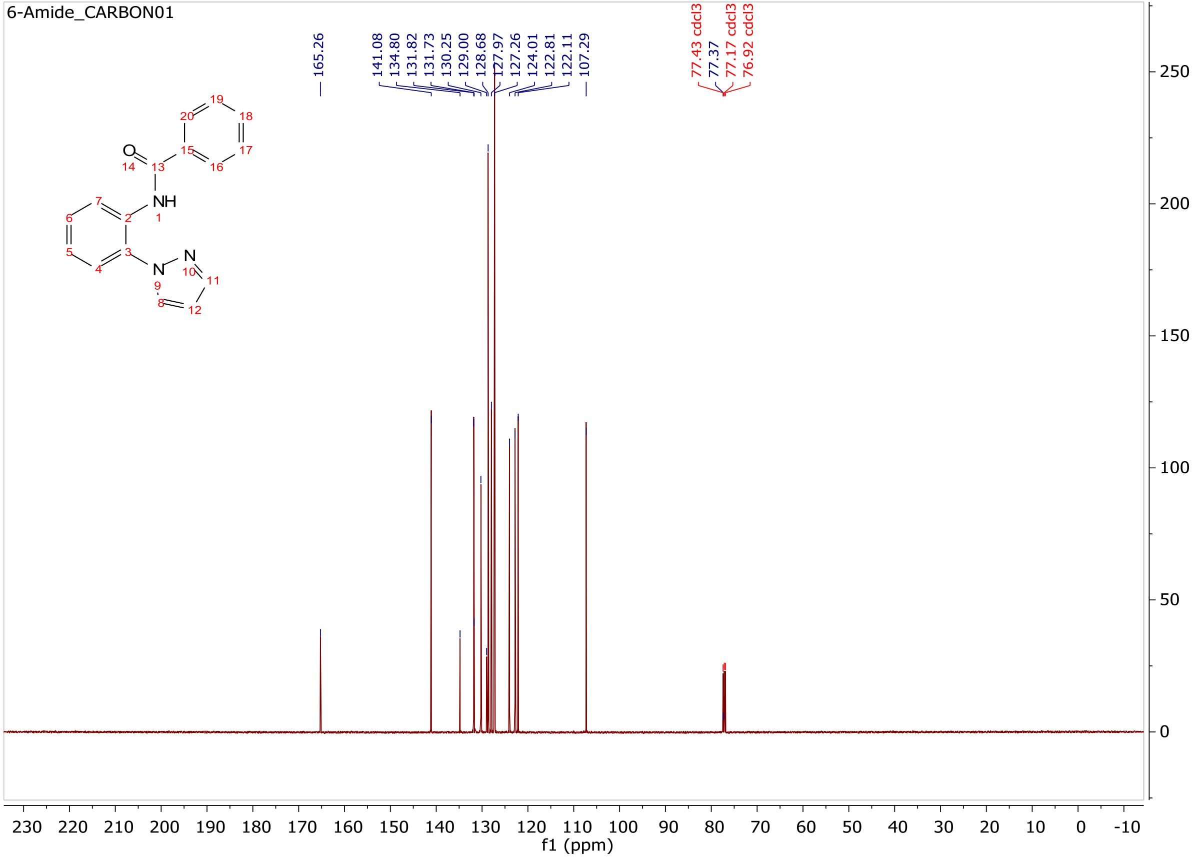

NO2
N
N
7.72
7.71
7.69
7.68
7.67
7.66
7.66
7.66
7.60
7.59
7.59
7.58
7.58
7.53
7.53
7.53
7.51
7.50
7.26
7.26
6.50
6.50
6.50
6.49
1.01
2.99
2.07
1.00
f1 (ppm)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20

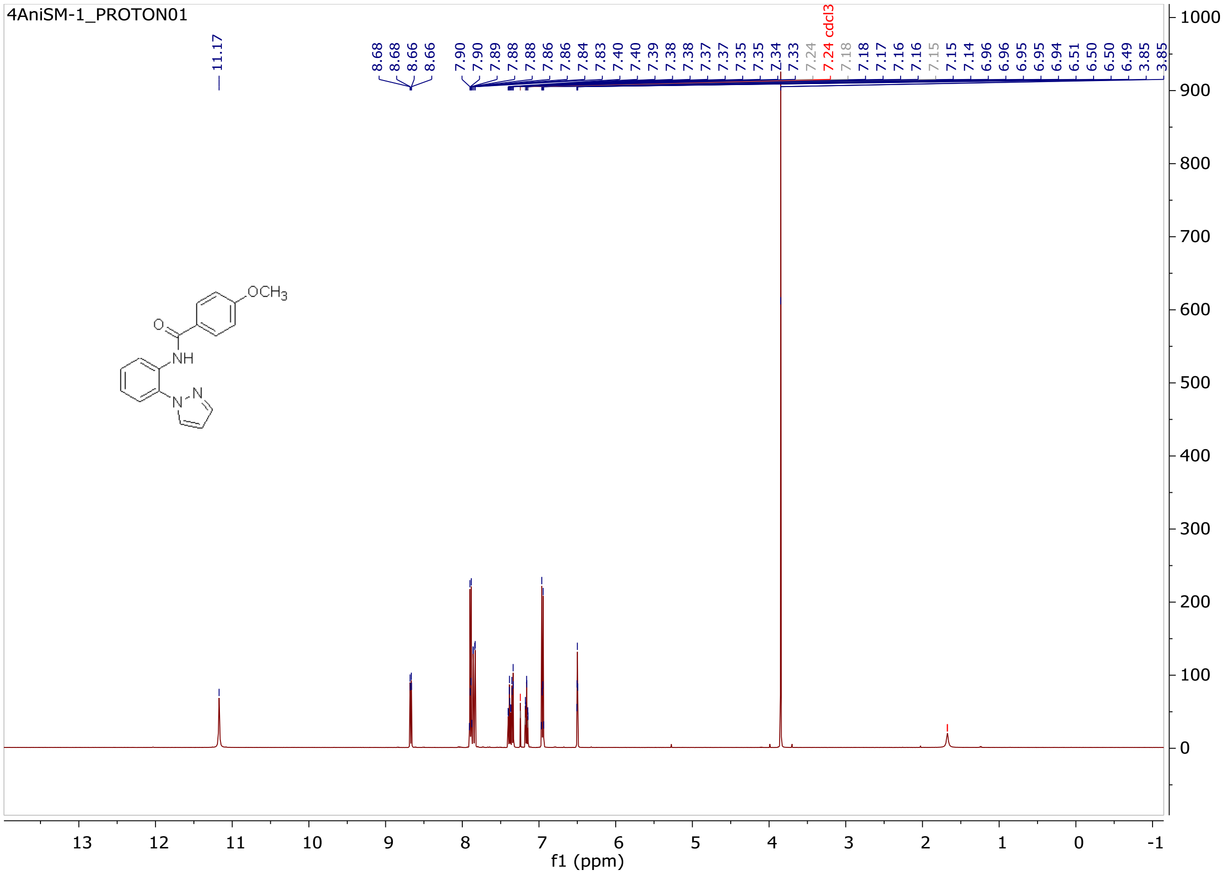

NO2_CARBON01
144.54
142.40
142.21
133.29
133.06
132.83
129.73
128.37
126.07
125.83
124.94
108.15
107.86
77.43 cdcl3
77.38
77.18 cdcl3
76.92 cdcl3
NO2
N
N
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

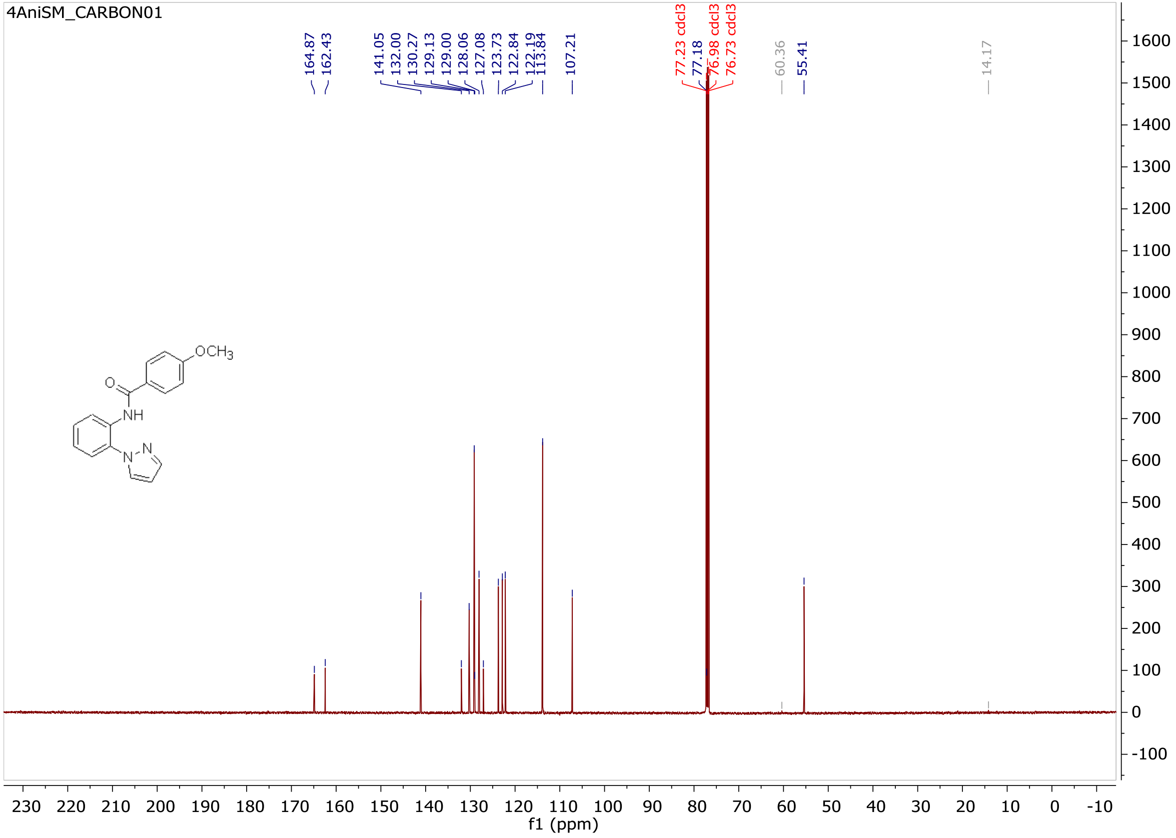

1-NH2_PROTON01
7.73
7.73
7.71
7.70
7.70
7.70
7.70
7.70
7.24
7.24
7.24
7.17
7.16
7.14
7.13
7.13
6.83
6.82
6.81
6.77
6.77
6.43
6.43
6.43
6.43
6.42
4.66
NH2
N
N
1.86
1.94
2.00
1.00
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

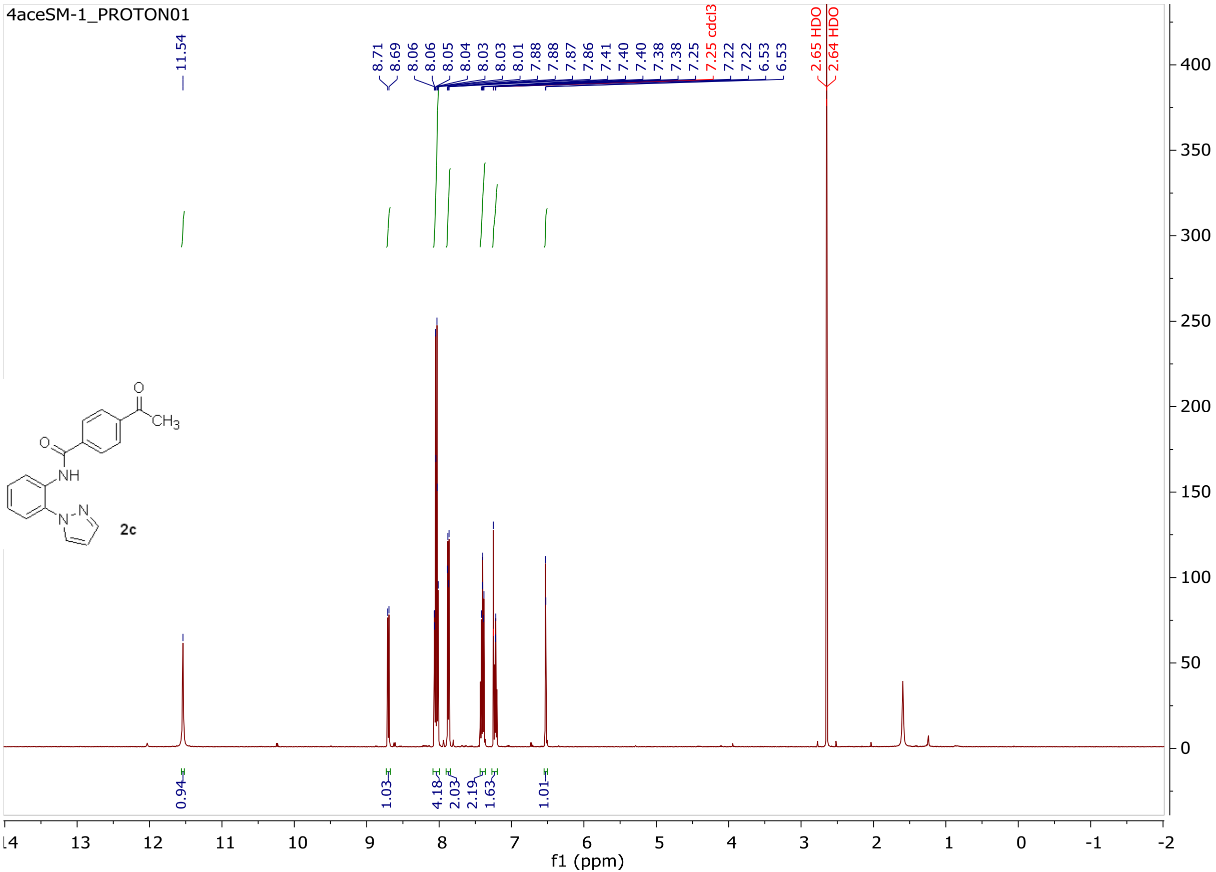

3--aniline_CARBON01
141.13
140.48
129.90
128.49
126.45
124.15
124.13
117.95
117.92
117.26
117.24
106.39
77.49 cdcl3
77.43
77.23 cdcl3
76.98 cdcl3
NH2
1
2
3
4
5
6
7
N
9
N
10
11
12
8
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20

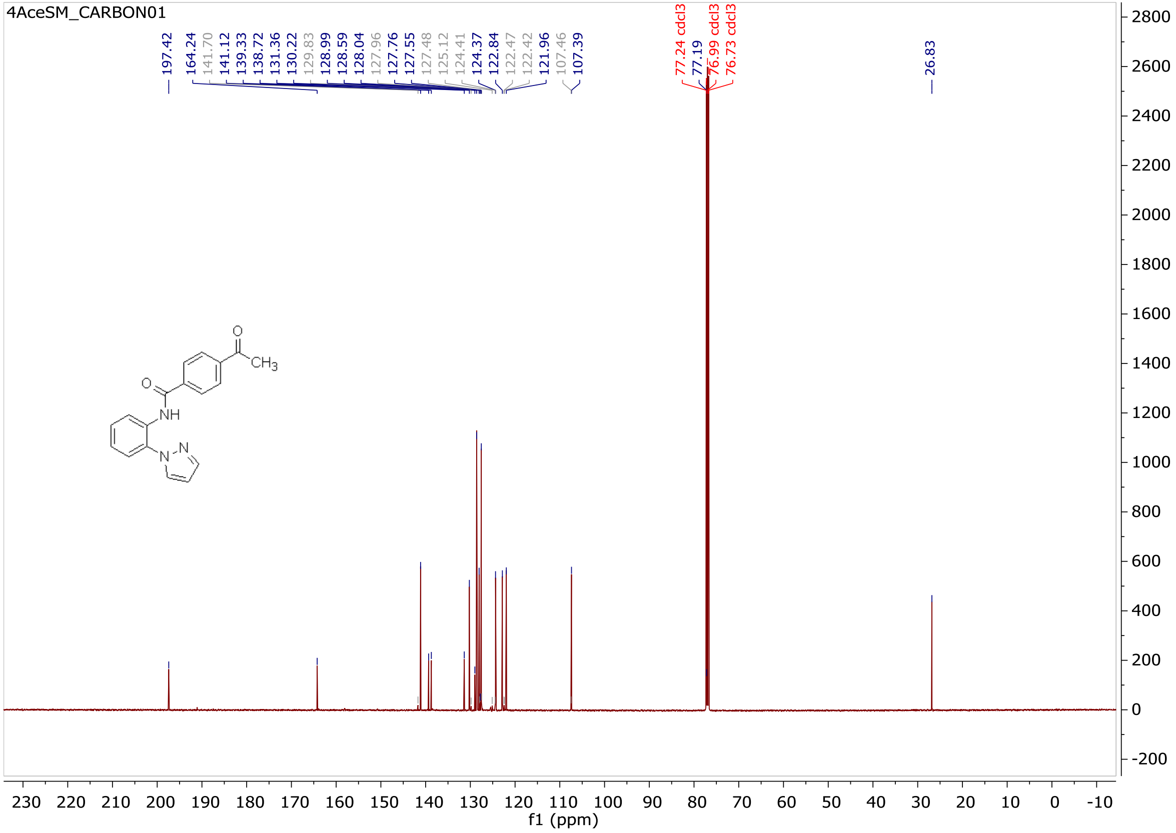

4-Starting_Amide_gCOSY_PROTON01
11.31
8.71
8.71
8.70
8.69
7.95
7.94
7.94
7.93
7.93
7.93
7.86
7.85
7.85
7.53
7.52
7.51
7.51
7.51
7.49
7.49
7.48
7.47
7.47
7.46
7.46
7.42
7.42
7.41
7.40
7.40
7.39
7.39
7.37
7.37
7.36
7.35
7.25 cdcl3
7.20
7.20
7.19
7.19
7.17
7.17
6.51
6.51
6.50
O
14
13
15
16
17
18
19
20
NH
1
2
3
4
5
6
7
N
9
8
12
11
10
N
f1 (ppm)
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20

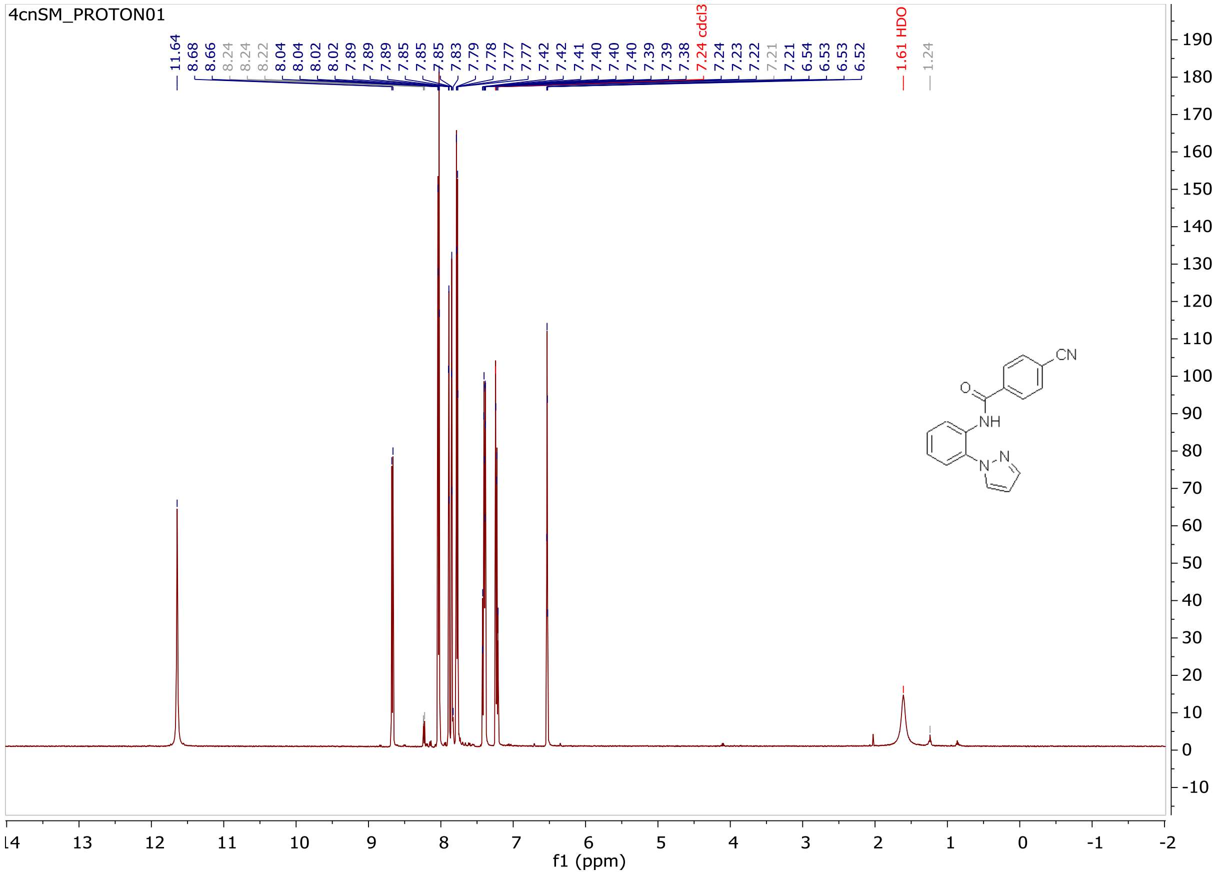

6-Amide_CARBON01
165.26
141.08
134.80
131.82
131.73
130.25
129.00
128.68
127.97
127.26
124.01
122.81
122.11
107.29
77.43 cdcl3
77.37
77.17 cdcl3
76.92 cdcl3
O
14
13
15
16
17
18
19
20
NH
1
2
3
4
5
6
7
N
9
8
12
11
10
N
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
250
200
150
100
50
0

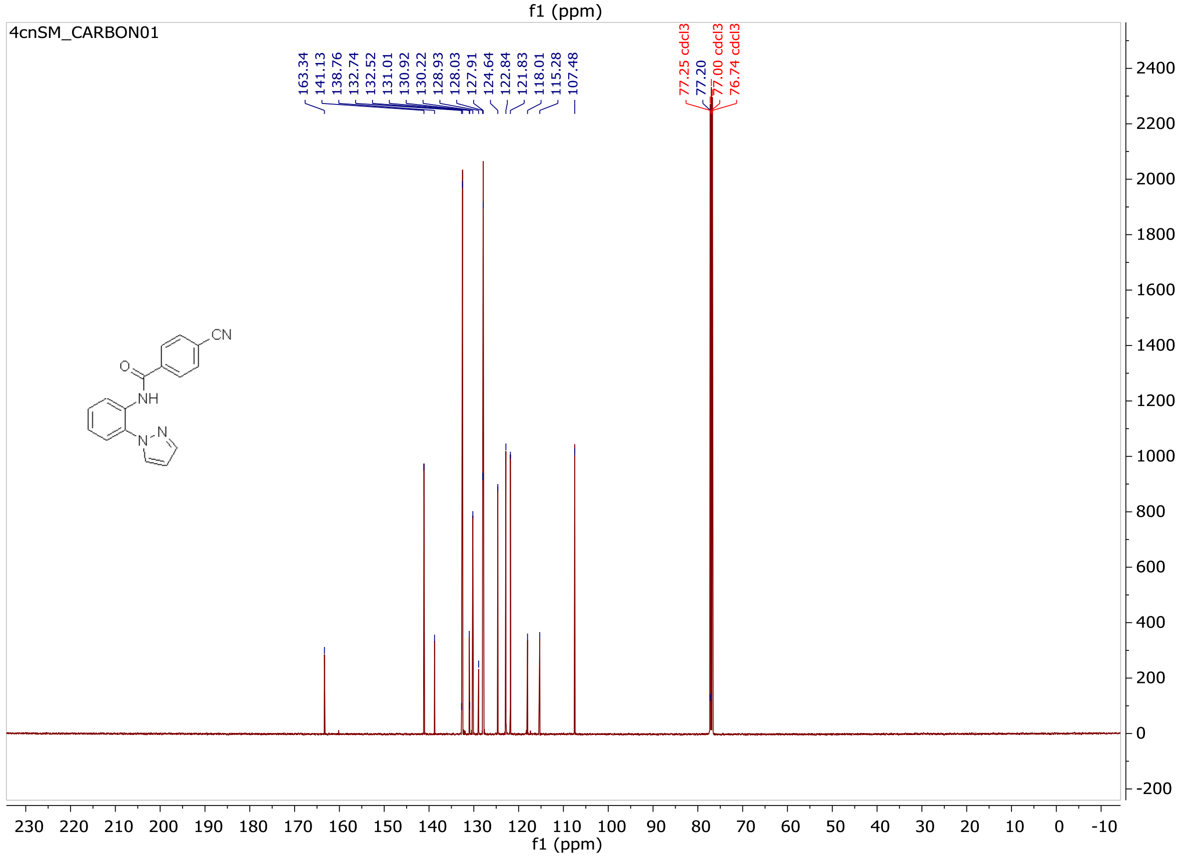

4AniSM-1_PROTON01
11.17
8.68
8.68
8.66
8.66
7.90
7.90
7.89
7.88
7.88
7.86
7.86
7.84
7.83
7.40
7.40
7.39
7.38
7.38
7.37
7.37
7.35
7.35
7.34
7.33
7.24
7.24 cdcl3
7.18
7.18
7.17
7.16
7.16
7.15
7.15
7.14
6.96
6.96
6.95
6.95
6.94
6.51
6.50
6.50
6.49
3.85
3.85
OCH3
O
NH
N
N
1000
900
800
700
600
500
400
300
200
100
0
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

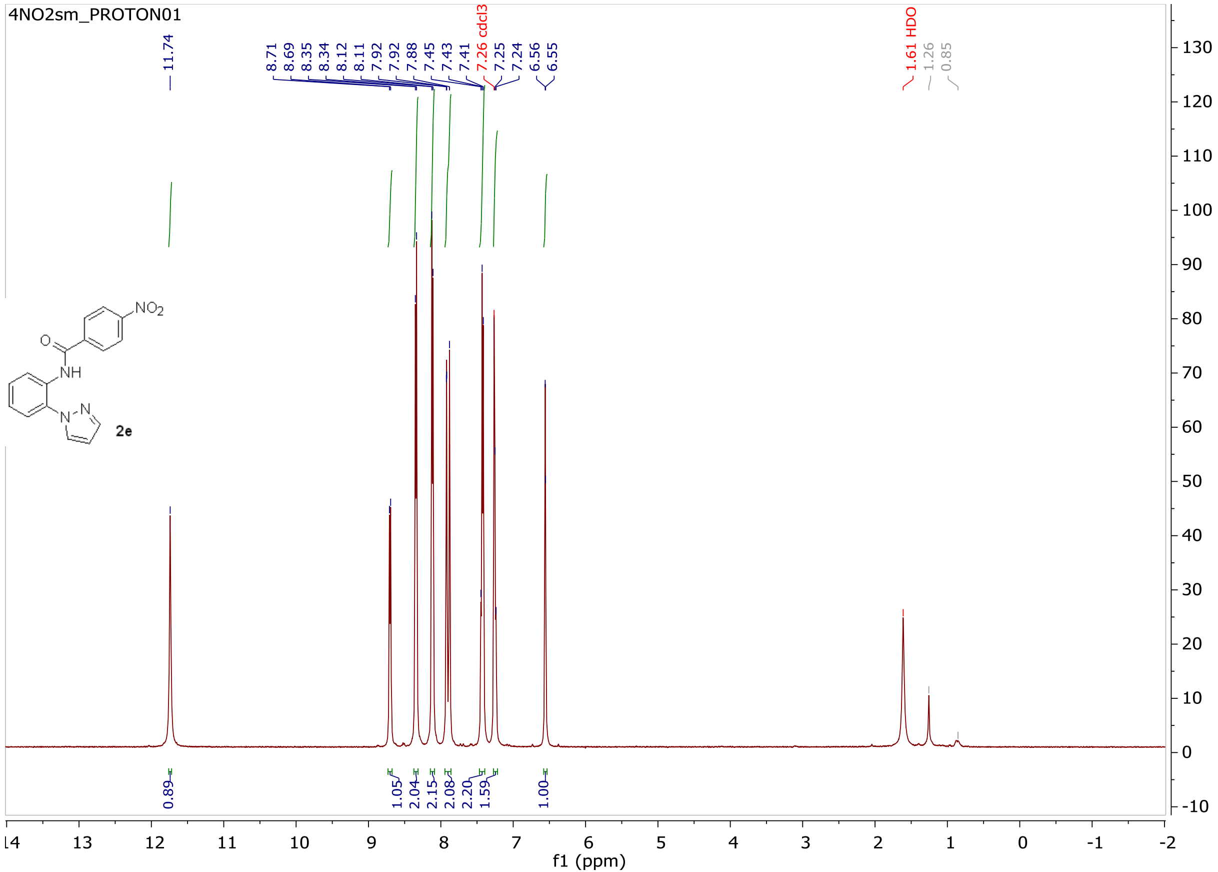

4AniSM_CARBON01
164.87
162.43
141.05
132.00
130.27
129.13
129.00
128.06
127.08
123.73
122.84
122.19
113.84
107.21
77.23 cdcl3
77.18
76.98 cdcl3
76.73 cdcl3
60.36
55.41
14.17
OCH3
O
NH
N
N
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


4aceSM-1_PROTON01
11.54
8.71
8.69
8.06
8.05
8.04
8.03
8.03
8.01
7.88
7.87
7.86
7.41
7.40
7.40
7.38
7.38
7.25
7.25 cdcl3
7.22
7.22
7.22
6.53
6.53
2.65 HDO
2.64 HDO
O
CH3
O
NH
N
N
2c
0.94
1.03
4.18
2.03
2.19
1.63
1.01
400
350
300
250
200
150
100
50
0
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)

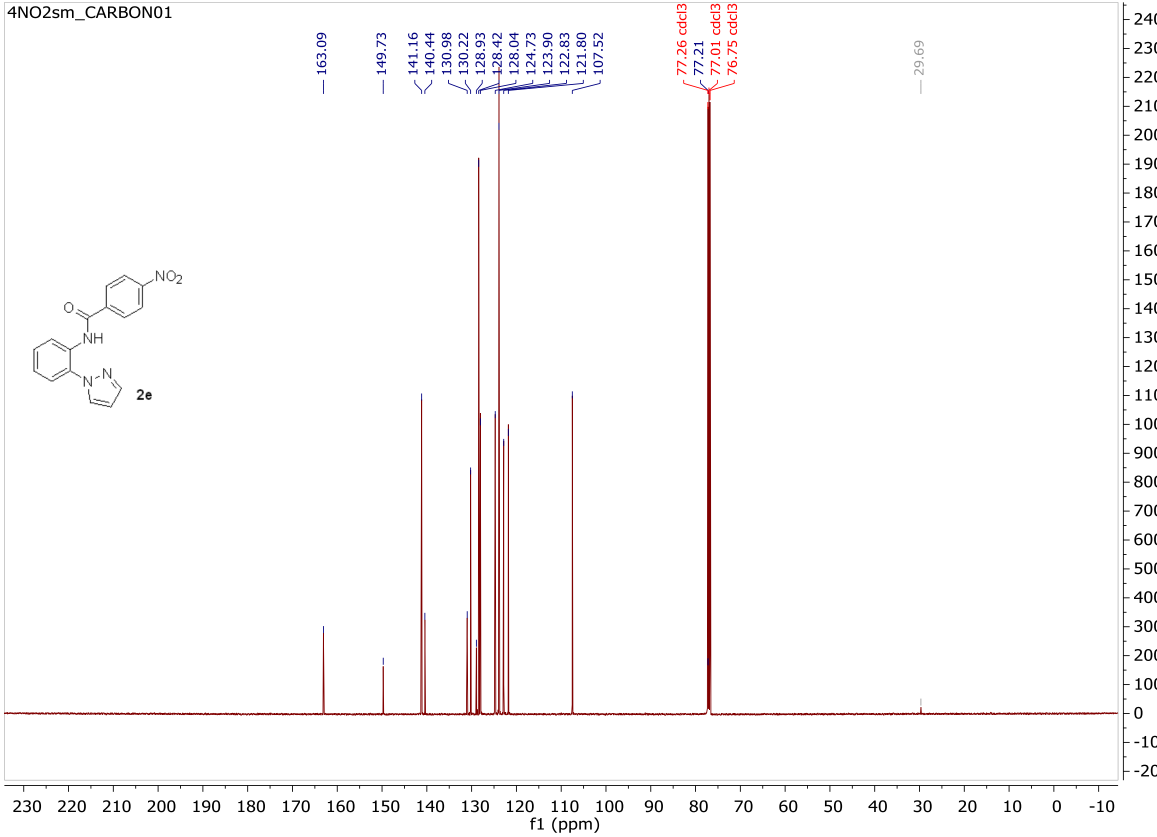

4AceSM_CARBON01
197.42
164.24
141.70
141.12
139.33
138.72
131.36
130.22
129.83
128.99
128.59
128.04
127.96
127.76
127.55
127.48
125.12
124.41
124.37
122.84
122.47
122.42
121.96
107.46
107.39
77.24 cdcl3
77.19
76.99 cdcl3
76.73 cdcl3
26.83
O
CH3
O
NH
N
N
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


4cnSM_PROTON01
11.64
8.68
8.66
8.24
8.24
8.22
8.04
8.04
8.02
8.02
7.89
7.89
7.89
7.85
7.85
7.85
7.83
7.79
7.78
7.77
7.77
7.42
7.42
7.41
7.40
7.40
7.39
7.39
7.38
7.24 cdcl3
7.24
7.23
7.22
7.21
7.21
6.54
6.53
6.53
6.52
1.61 HDO
1.24
CN
O
NH
N
N
f1 (ppm)

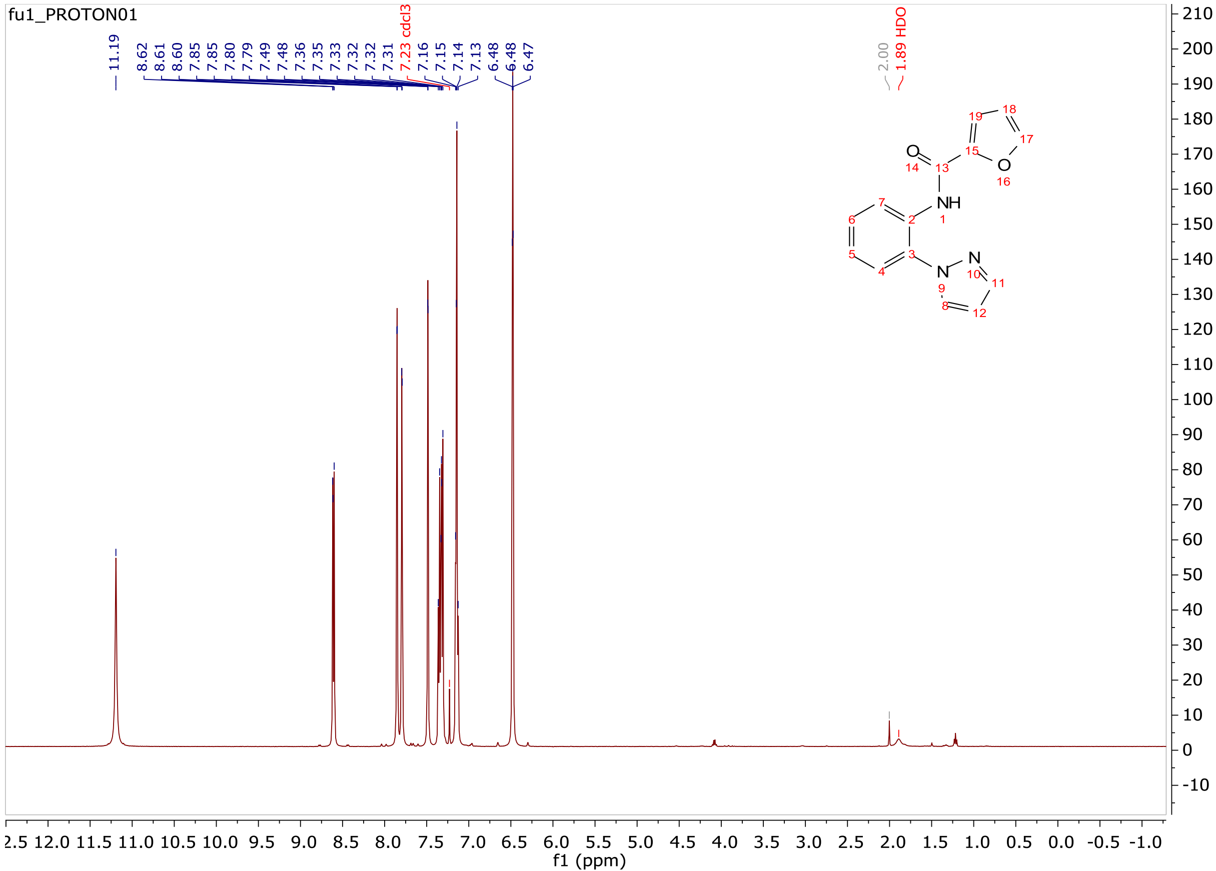

4cnSM_CARBON01
163.34
141.13
138.76
132.74
132.52
131.01
130.92
130.22
128.93
128.03
127.91
124.64
122.84
121.83
118.01
115.28
107.48
77.25 cdcl3
77.20
77.00 cdcl3
76.74 cdcl3
CN
O
NH
N
N
f1 (ppm)

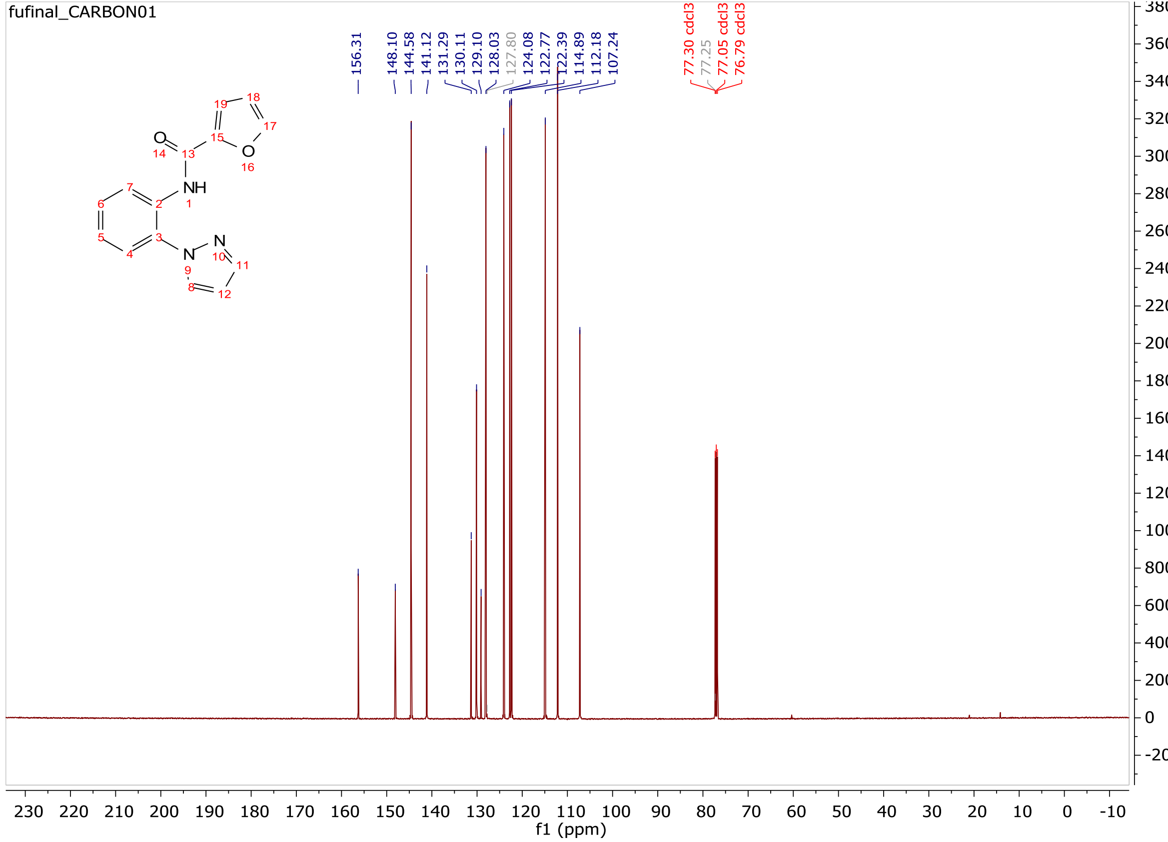


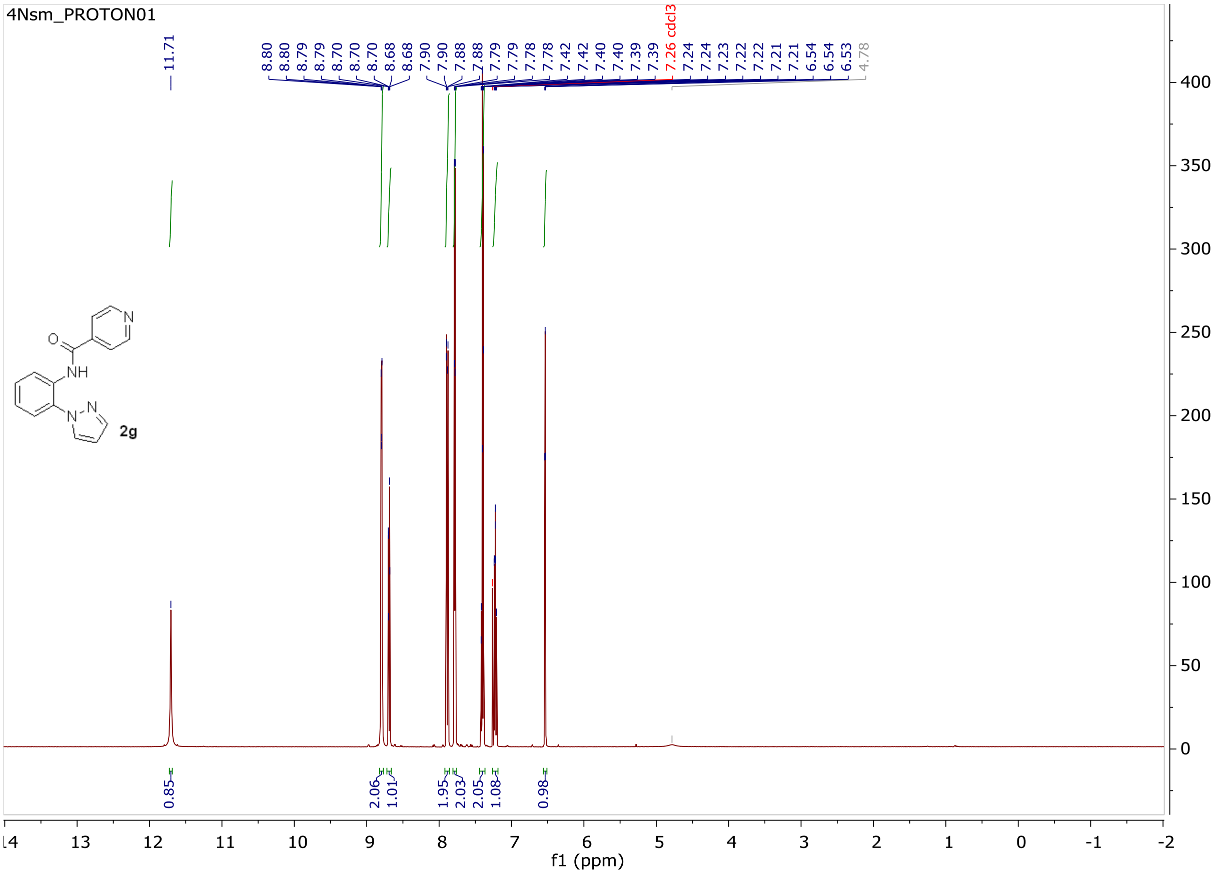
4NO2sm_PROTON01
11.74
8.71
8.69
8.35
8.34
8.12
8.11
7.92
7.92
7.88
7.45
7.43
7.41
7.26 cdcl3
7.25
7.24
6.56
6.55
1.61 HDO
1.26
0.85
0.89
1.05
2.04
2.15
2.08
2.20
1.59
1.00
NO2
O
NH
N
N
2e
f1 (ppm)

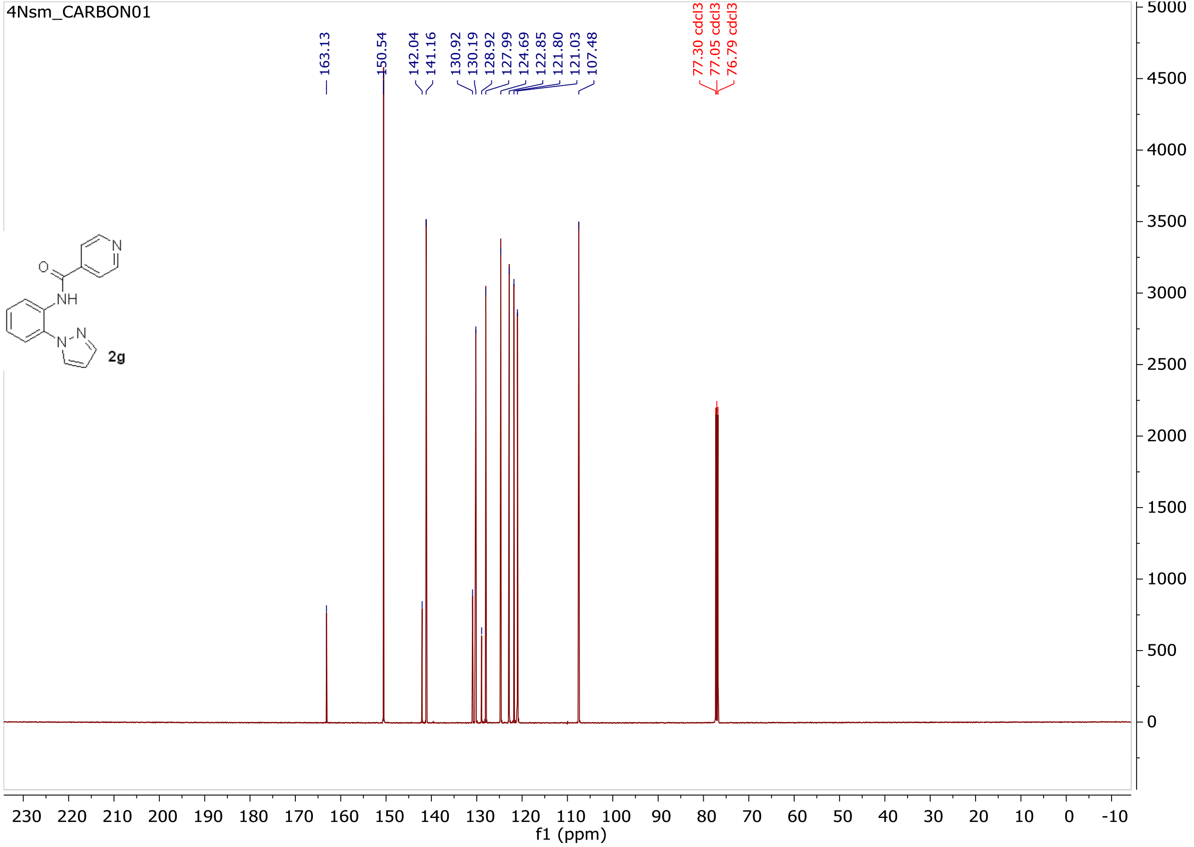


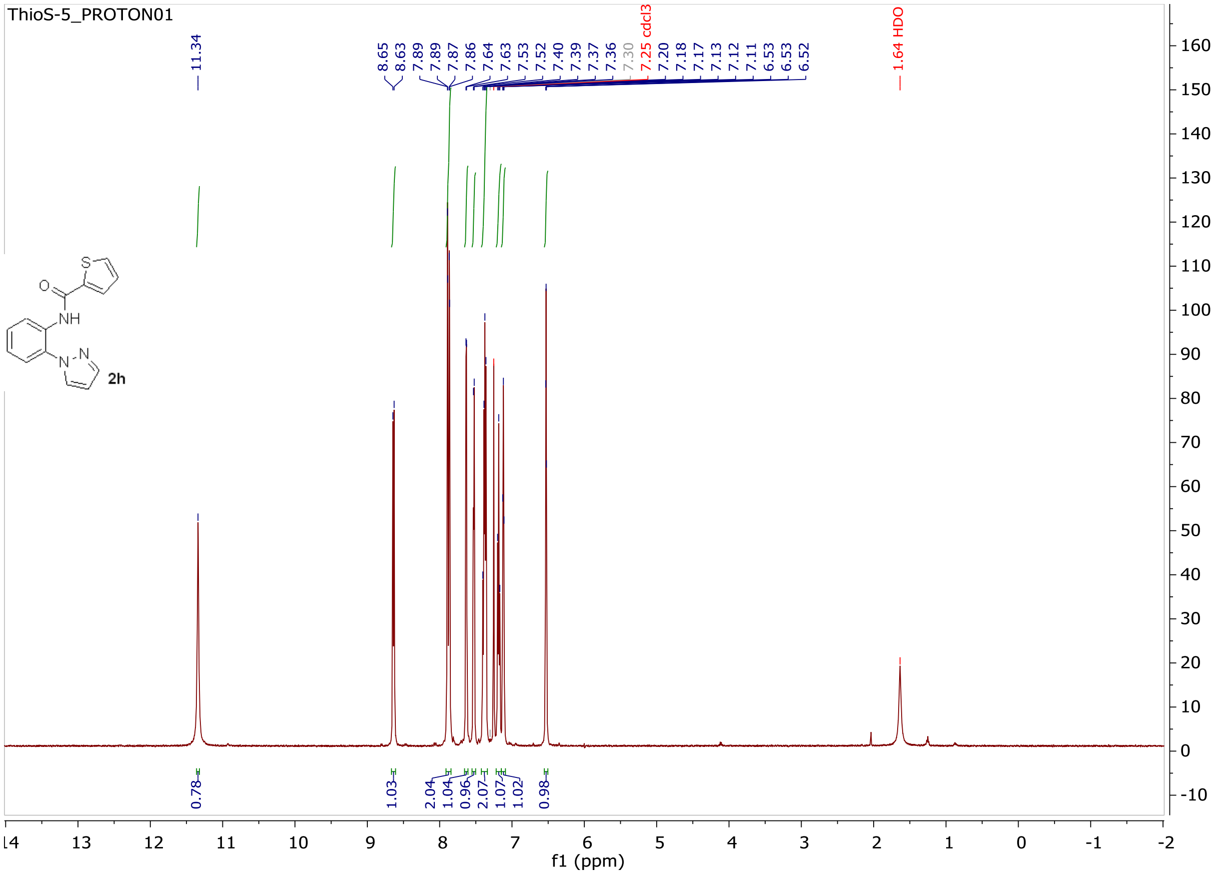
4NO2sm_CARBON01
163.09
149.73
141.16
140.44
130.98
130.22
128.93
128.42
128.04
124.73
123.90
122.83
121.80
107.52
77.26 cdcl3
77.21
77.01 cdcl3
76.75 cdcl3
29.69
NO2
O
NH
N
N
2e
f1 (ppm)

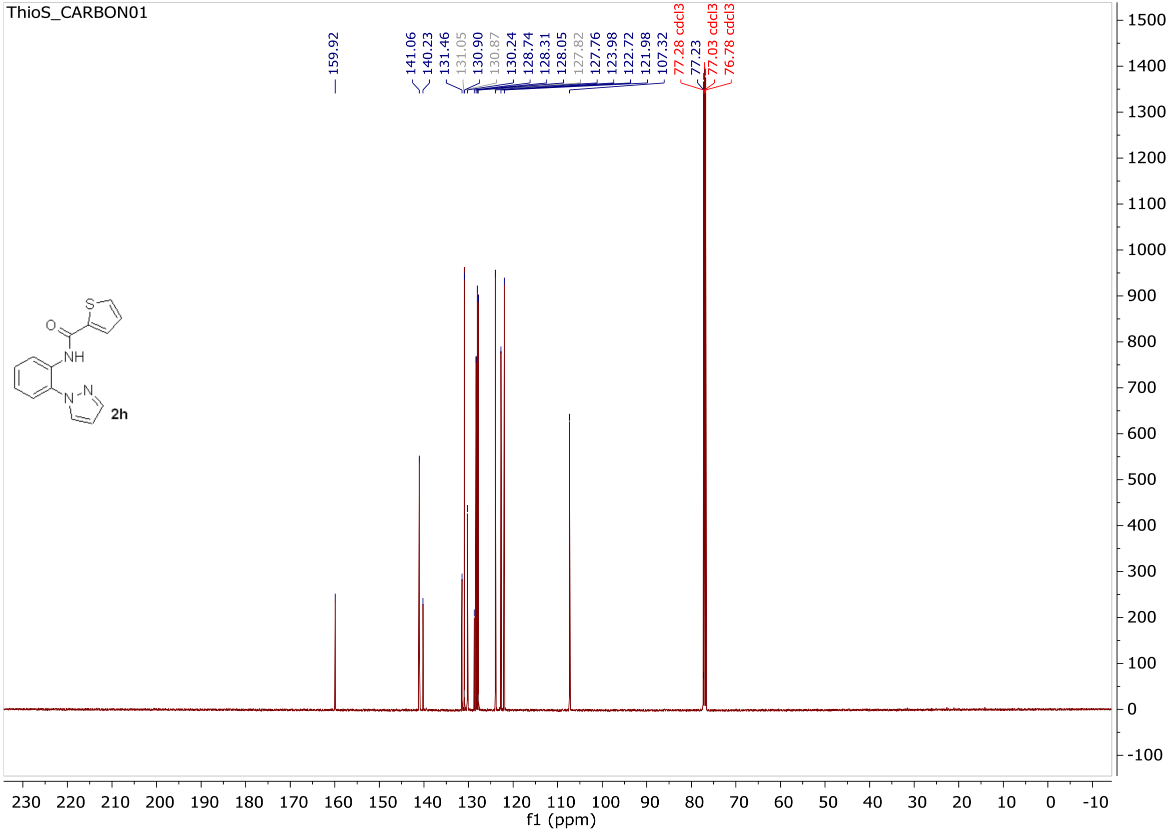

fu1_PROTON01
11.19
8.62
8.61
8.60
7.85
7.85
7.80
7.79
7.49
7.48
7.36
7.35
7.33
7.32
7.32
7.31
7.23 cdcl3
7.16
7.15
7.14
7.13
6.48
6.48
6.47
2.00
1.89 HDO
O
14
13
15
19
18
17
16
O
NH
1
7
2
6
5
4
3
N
N
10
11
9
8
12
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
2.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

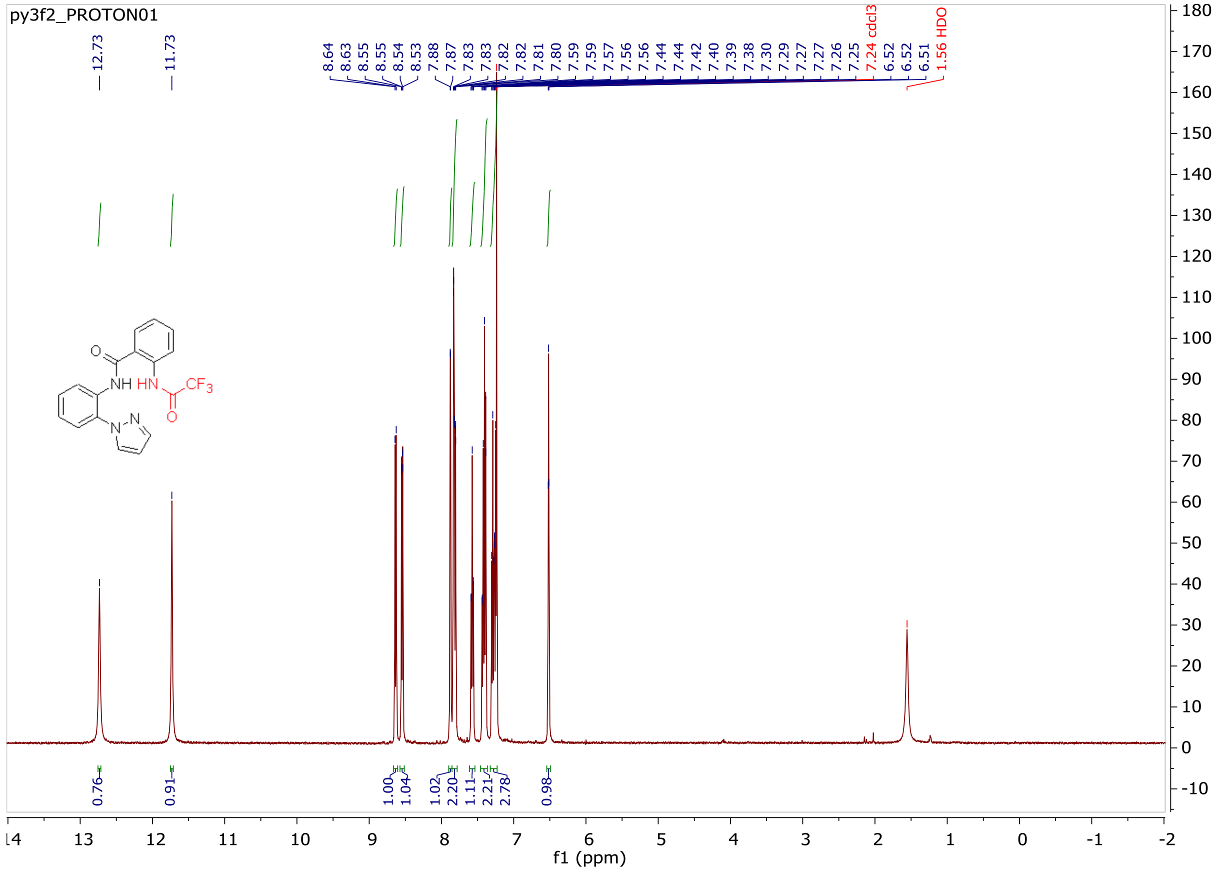

fufinal_CARBON01
156.31
148.10
144.58
141.12
131.29
130.11
129.10
128.03
127.80
124.08
122.77
122.39
114.89
112.18
107.24
77.30 cdcl3
77.25
77.05 cdcl3
76.79 cdcl3
O
14
13
15
19
18
17
16
O
NH
1
7
2
6
5
4
3
N
N
10
11
9
8
12
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

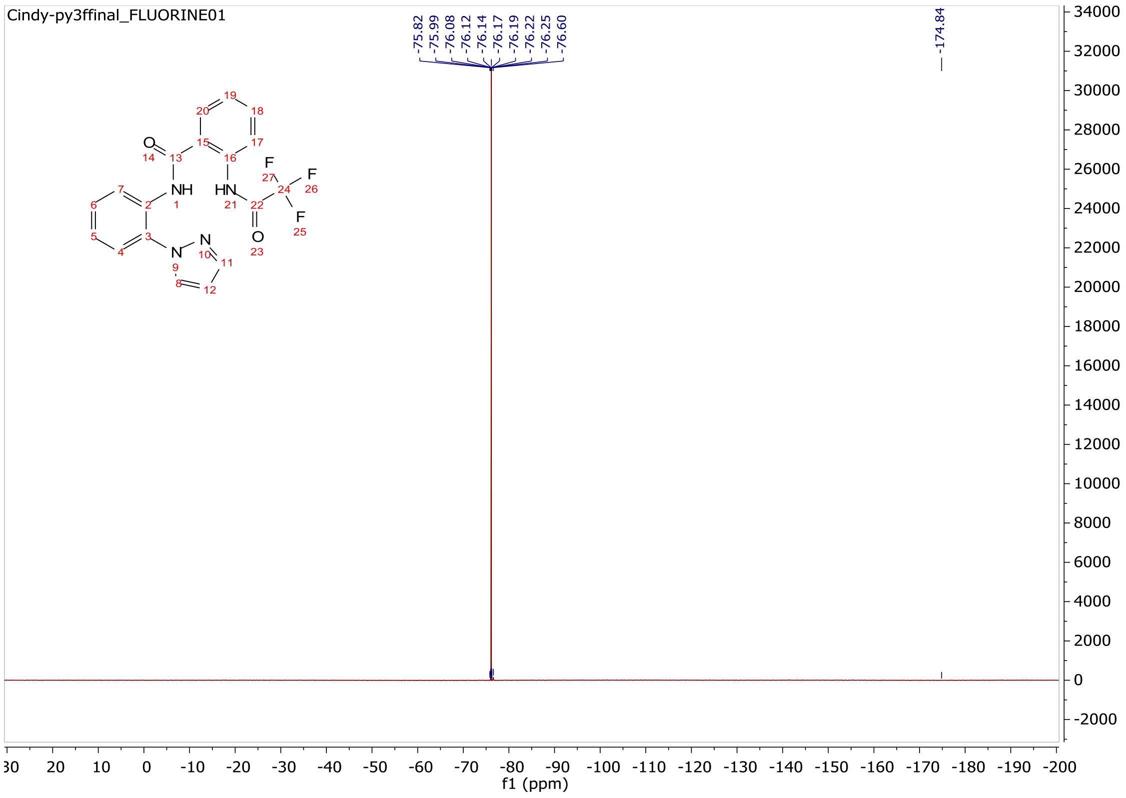

4Nsm_PROTON01
11.71
8.80 8.80 8.79 8.79 8.70 8.70 8.70 8.68 8.68 7.90 7.90 7.88 7.88 7.79 7.79 7.78 7.78 7.42 7.42 7.40 7.40 7.39 7.39
7.26 cdcl3
7.24 7.24 7.23 7.22 7.22 7.21 7.21 6.54 6.54 6.53 4.78
0.85 2.06 1.01 1.95 2.03 2.05 1.08 0.98
O
NH
N
N
N
2g
f1 (ppm)
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
400 350 300 250 200 150 100 50 0

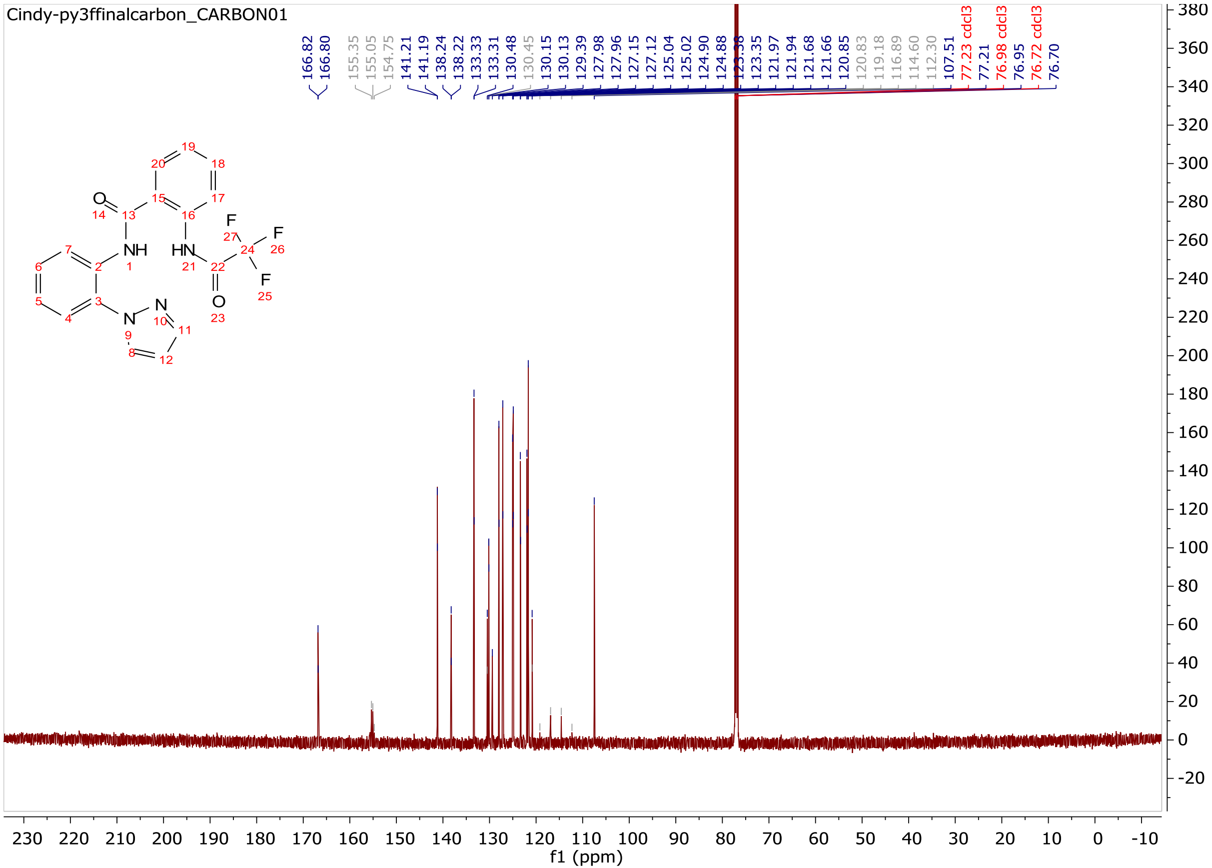

4Nsm_CARBON01
163.13
150.54
142.04 141.16
130.92 130.19 128.92 127.99 124.69 122.85 121.80 121.03 107.48
77.30 cdcl3 77.05 cdcl3 76.79 cdcl3
O
NH
N
N
N
2g
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
5000 4500 4000 3500 3000 2500 2000 1500 1000 500 0

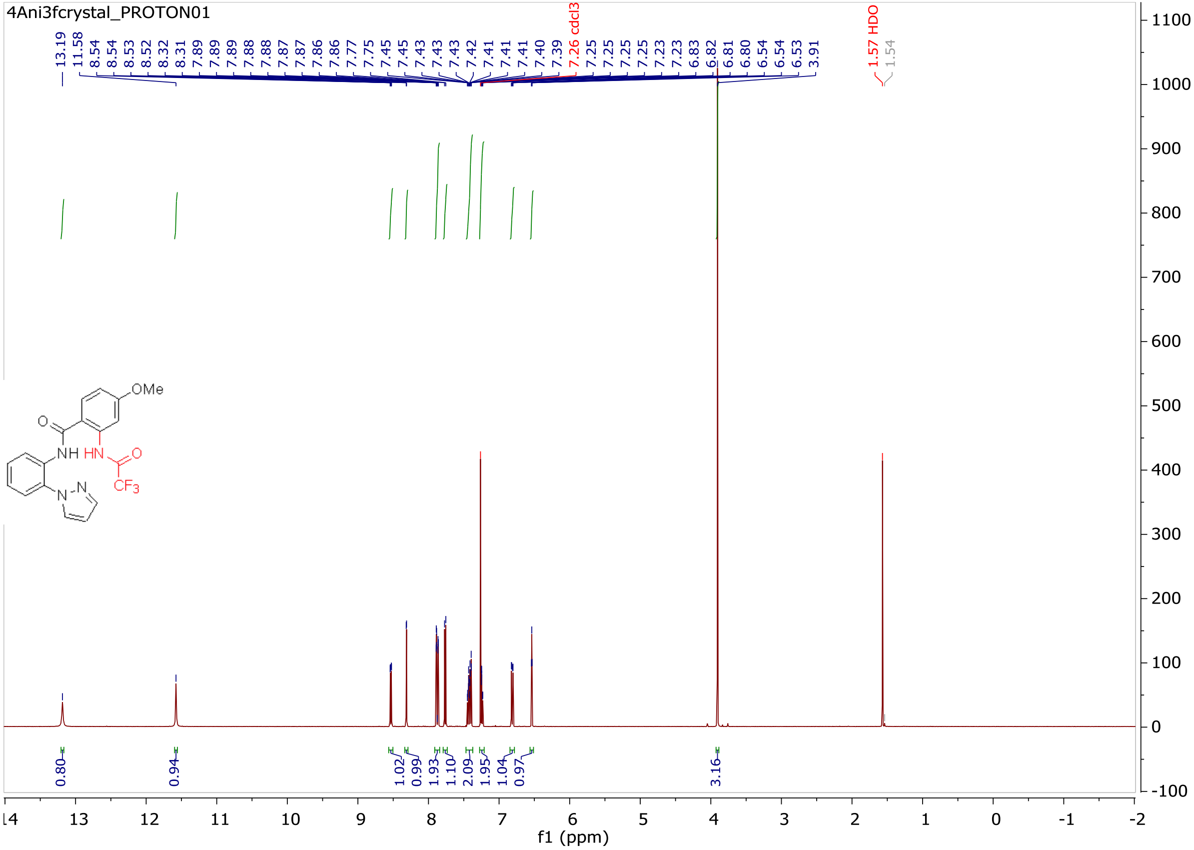

ThioS-5_PROTON01
11.34
8.65
8.63
7.89
7.89
7.87
7.86
7.64
7.63
7.53
7.52
7.40
7.39
7.37
7.36
7.30
7.25 cdcl3
7.20
7.18
7.17
7.13
7.12
7.11
6.53
6.53
6.52
1.64 HDO
0.78
1.03
2.04
1.04
0.96
2.07
1.07
1.02
0.98
S
O
NH
N
N
2h
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)

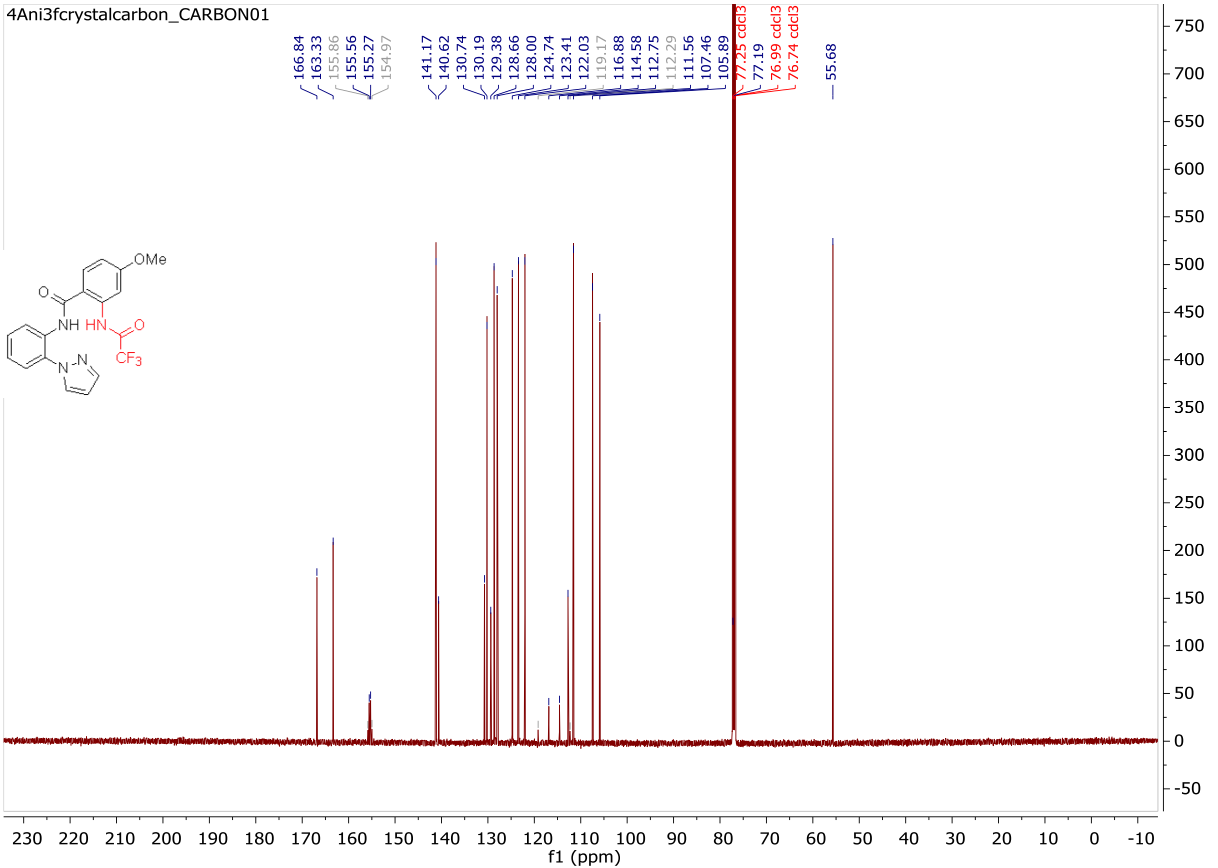

ThioS_CARBON01
159.92
141.06
140.23
131.46
131.05
130.90
130.87
130.24
128.74
128.31
128.05
127.82
127.76
123.98
122.72
121.98
107.32
77.28 cdcl3
77.23
77.03 cdcl3
76.78 cdcl3
S
O
NH
N
N
2h
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

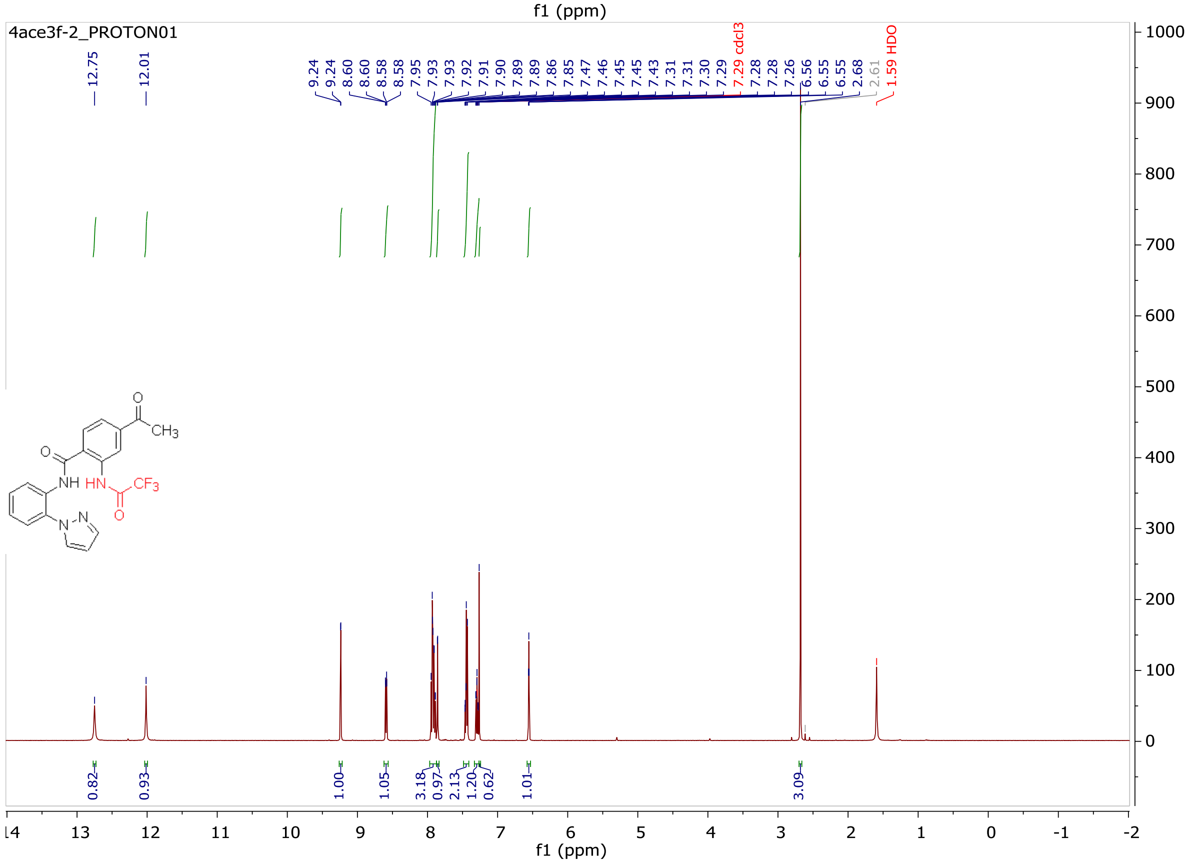

py3f2_PROTON01
12.73
11.73
8.64
8.63
8.55
8.55
8.54
8.53
7.88
7.87
7.83
7.83
7.82
7.82
7.81
7.80
7.59
7.59
7.57
7.56
7.56
7.44
7.44
7.42
7.40
7.39
7.38
7.30
7.29
7.27
7.27
7.26
7.25
7.24 cdcl3
6.52
6.52
6.51
1.56 HDO
0.76
0.91
1.00
1.04
1.02
2.20
1.11
2.21
2.78
0.98
O
NH
HN
CF3
O
N
N
f1 (ppm)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

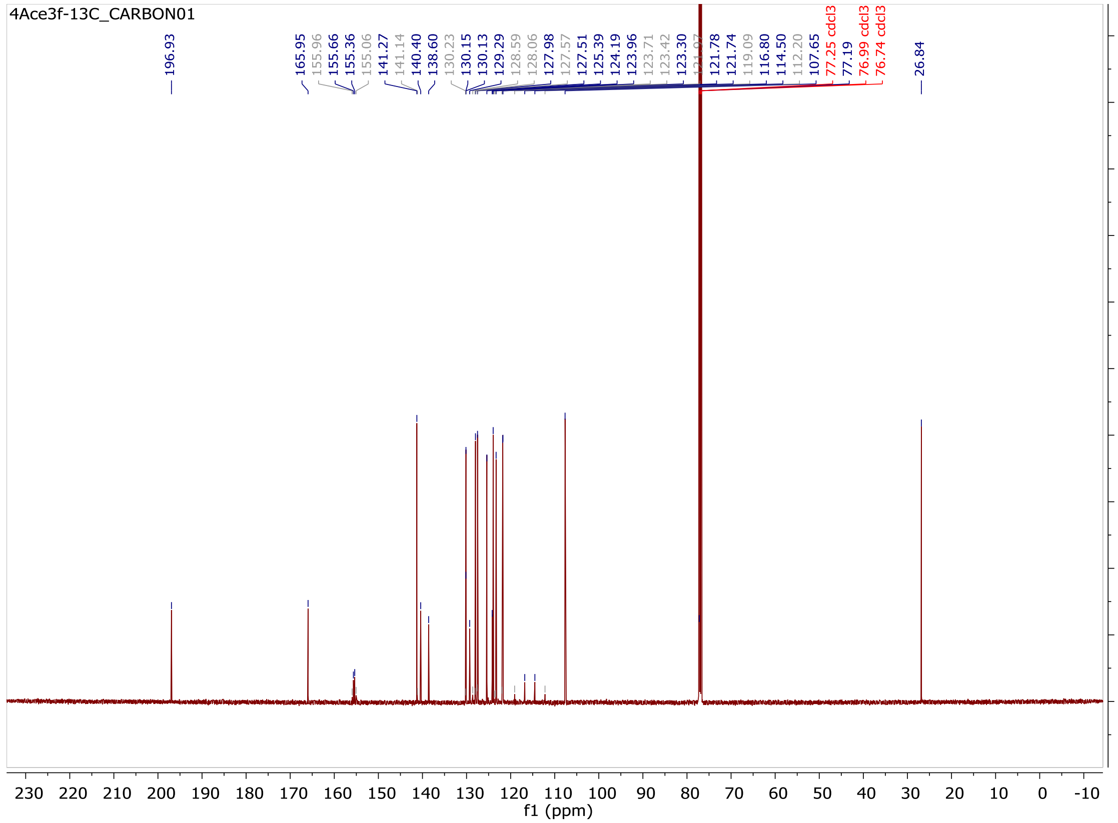

Cindy-py3ffinal_FLUORINE01
-75.82
-75.99
-76.08
-76.12
-76.14
-76.17
-76.19
-76.22
-76.25
-76.60
-174.84
O
14
13
NH
1
HN
21
22
O
23
F
27
24
F
26
F
25
19
18
20
17
15
16
7
6
5
4
2
3
N
9
N
10
11
8
12
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000

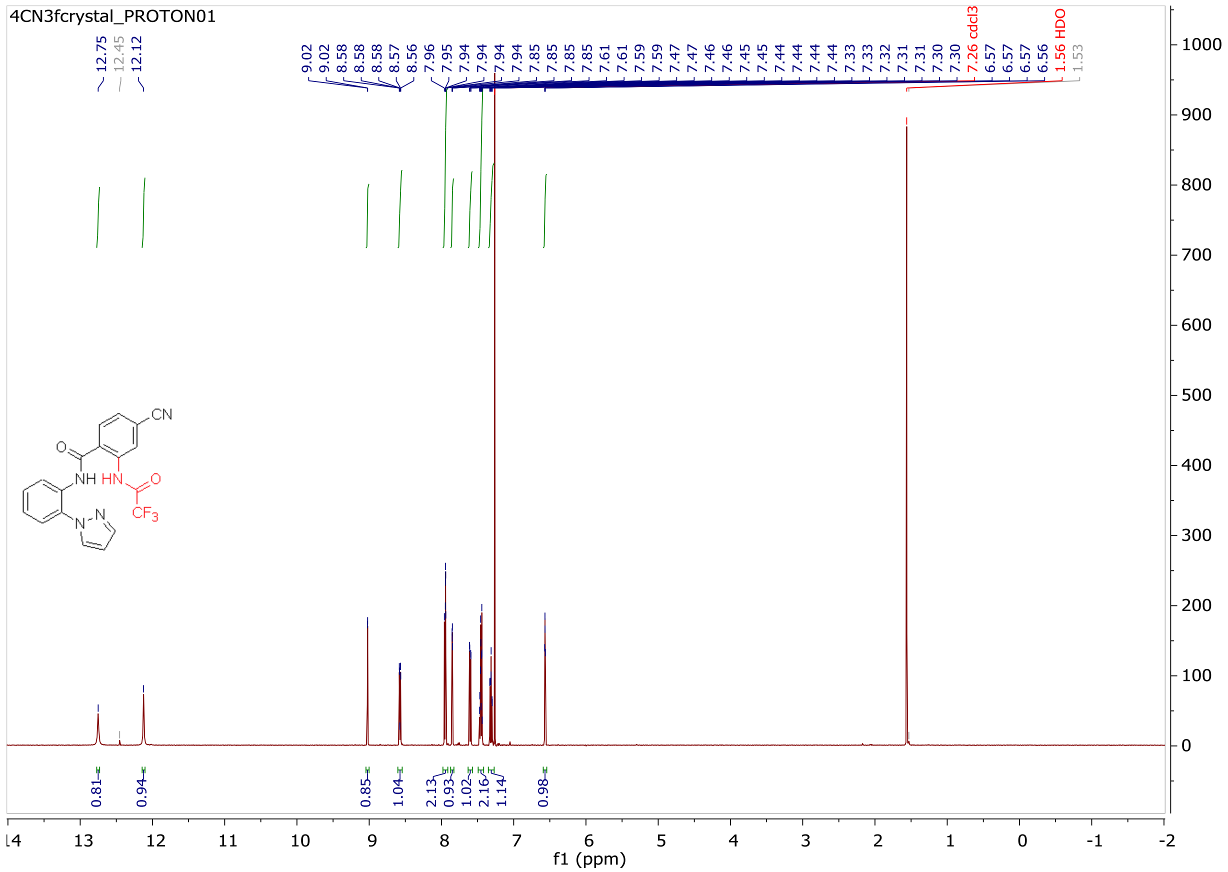

Cindy-py3ffinalcarbon_CARBON01
166.82
166.80
155.35
155.05
154.75
141.21
141.19
138.24
138.22
133.33
133.31
130.48
130.45
130.15
130.13
129.39
127.98
127.96
127.15
127.12
125.04
125.02
124.90
124.88
123.38
123.35
121.97
121.94
121.68
121.66
120.85
120.83
119.18
116.89
114.60
112.30
107.51
77.23 cdcl3
77.21
76.98 cdcl3
76.95
76.72 cdcl3
76.70
O
14
13
15
16
17
18
19
20
NH
1
HN
21
F
27
F
26
24
22
F
25
O
23
2
3
4
5
6
7
N
9
N
10
11
12
8
380
360
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

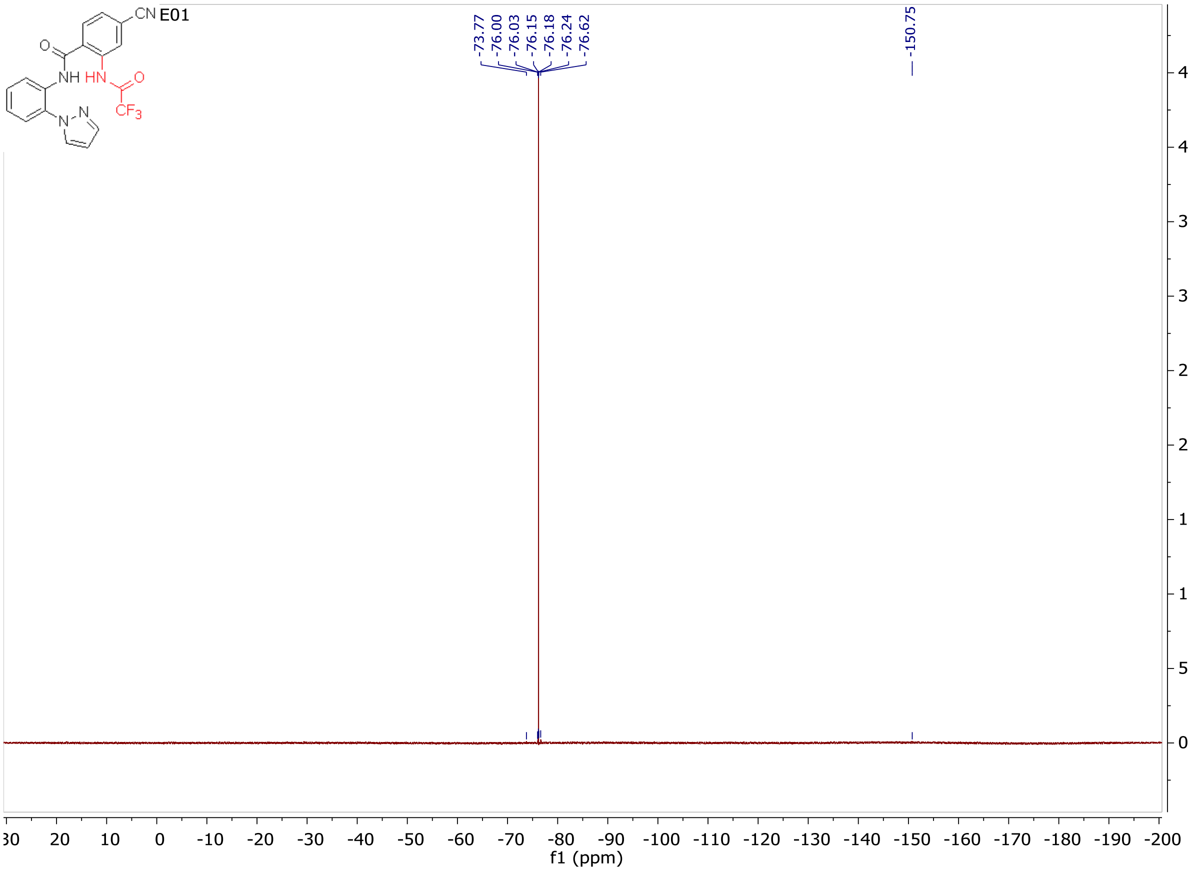

4Ani3fcrystal_PROTON01
13.19
11.58
8.54
8.54
8.53
8.52
8.32
8.31
7.89
7.89
7.89
7.88
7.87
7.87
7.86
7.77
7.75
7.45
7.45
7.43
7.43
7.42
7.41
7.41
7.41
7.40
7.39
7.26 cdcl3
7.25
7.25
7.25
7.25
7.23
7.23
6.83
6.82
6.81
6.80
6.54
6.54
6.53
3.91
1.57 HDO
1.54
OMe
O
NH
HN
O
CF3
N
N
0.80
0.94
1.02
0.99
1.93
1.10
2.09
1.95
1.04
0.97
3.16
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)

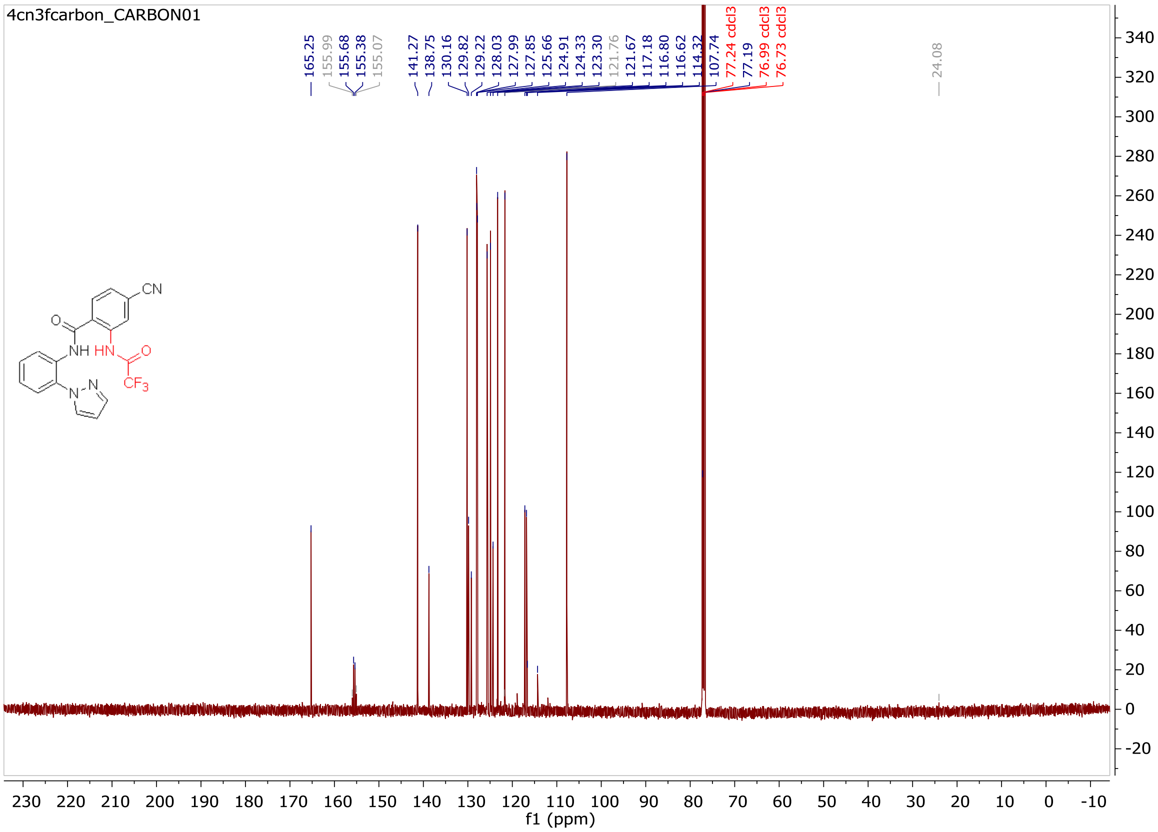

4Ani3fcrystalcarbon_CARBON01
166.84
163.33
155.86
155.56
155.27
154.97
141.17
140.62
130.74
130.19
129.38
128.66
128.00
124.74
123.41
122.03
119.17
116.88
114.58
112.75
112.29
111.56
107.46
105.89
77.25 cdcl3
77.19
76.99 cdcl3
76.74 cdcl3
55.68
OMe
O
NH
HN
O
CF3
N
N
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
750 700 650 600 550 500 450 400 350 300 250 200 150 100 50 0 -50

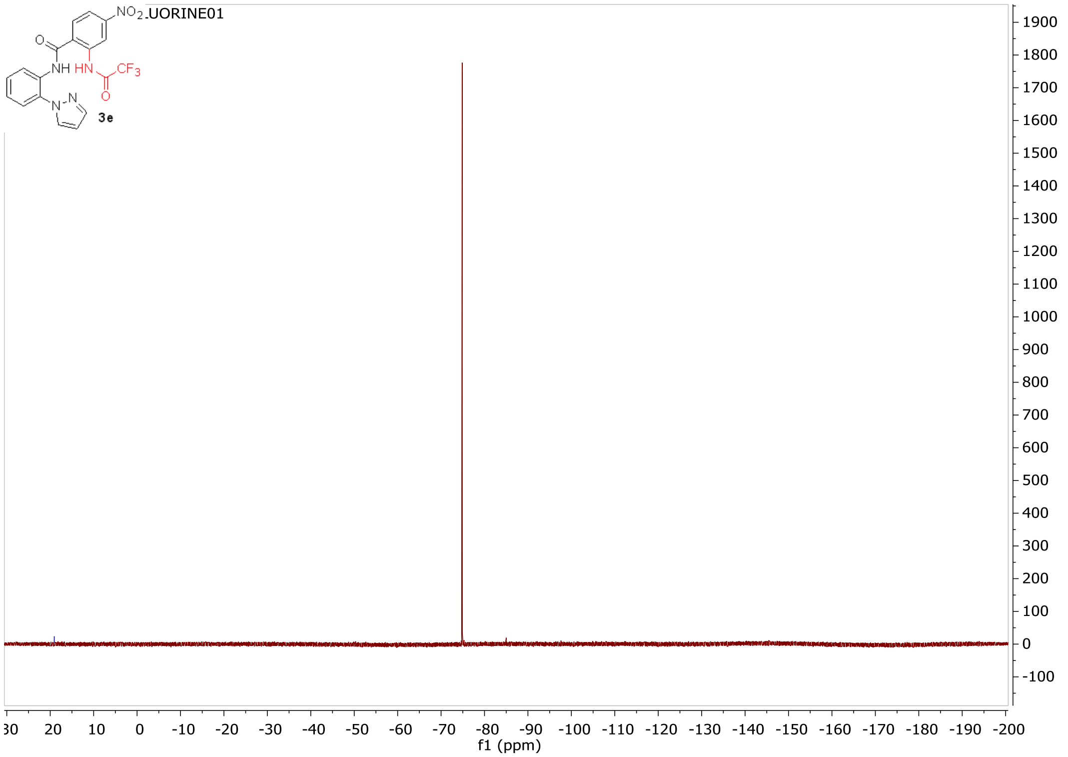

4ace3f-2_PROTON01
12.75
12.01
9.24
9.24
8.60
8.60
8.58
8.58
7.95
7.93
7.93
7.92
7.91
7.90
7.89
7.89
7.86
7.85
7.47
7.46
7.45
7.45
7.43
7.31
7.31
7.30
7.29
7.29 cdcl3
7.28
7.28
7.26
6.56
6.55
6.55
2.68
2.61
1.59 HDO
O
CH3
O
NH
HN
CF3
O
N
N
0.82
0.93
1.00
1.05
3.18
0.97
2.13
1.20
0.62
1.01
3.09
f1 (ppm)
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
1000 900 800 700 600 500 400 300 200 100 0

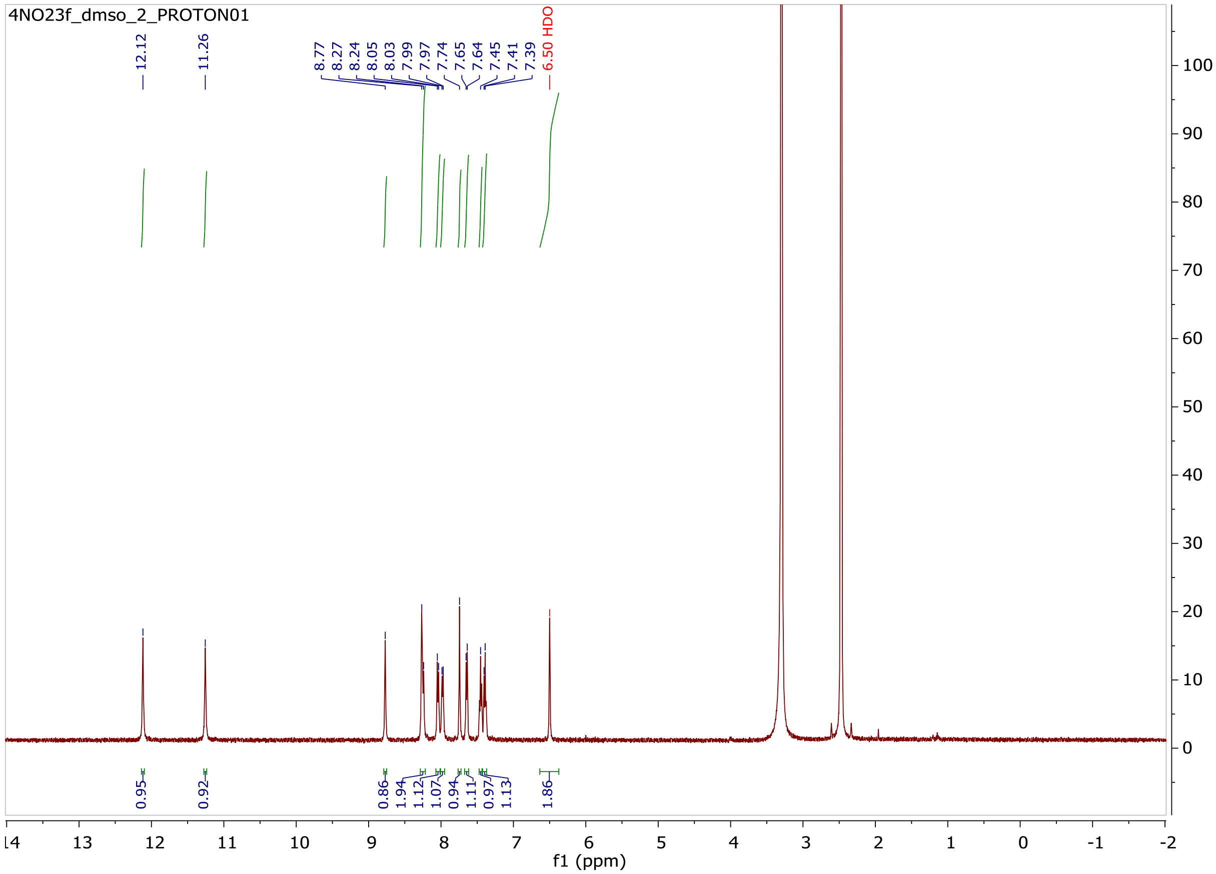

4Ace3f-13C_CARBON01
196.93
165.95
155.96
155.66
155.36
155.06
141.27
141.14
140.40
138.60
130.23
130.15
130.13
129.29
128.59
128.06
127.98
127.57
127.51
125.39
124.19
123.96
123.71
123.42
123.30
121.97
121.78
121.74
119.09
116.80
114.50
112.20
107.65
77.25 cdcl3
77.19
76.99 cdcl3
76.74 cdcl3
26.84
1000
900
800
700
600
500
400
300
200
100
0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

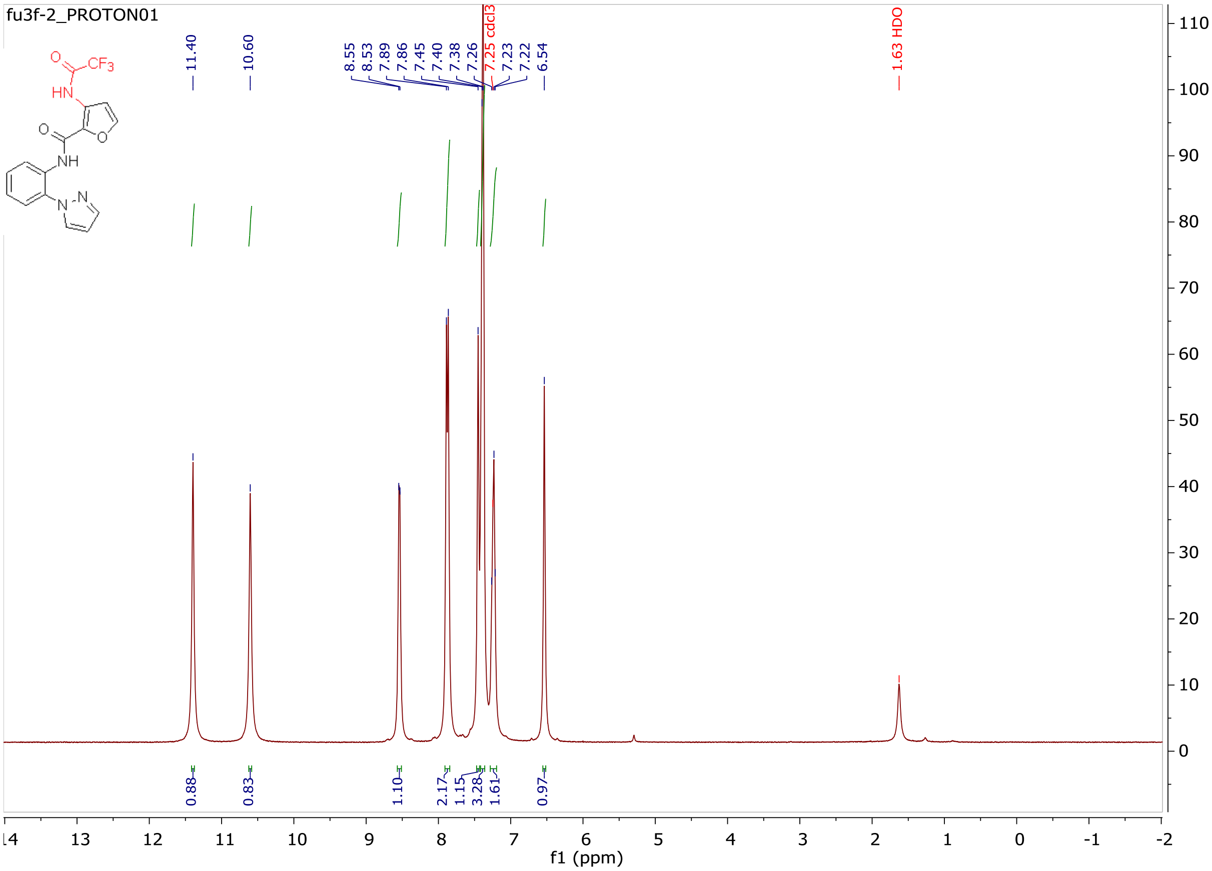

4CN3fcrystal_PROTON01
12.75
12.45
12.12
9.02
9.02
8.58
8.58
8.57
8.56
7.96
7.95
7.94
7.94
7.94
7.94
7.85
7.85
7.85
7.61
7.61
7.59
7.59
7.47
7.46
7.45
7.45
7.44
7.44
7.44
7.33
7.33
7.32
7.31
7.31
7.30
7.26 cdcl3
6.57
6.57
6.57
6.56
1.56 HDO
1.53
CN
O
NH
HN
O
CF3
N
N
0.81
0.94
0.85
1.04
2.13
0.93
1.02
2.16
1.14
0.98
1000
900
800
700
600
500
400
300
200
100
0
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)

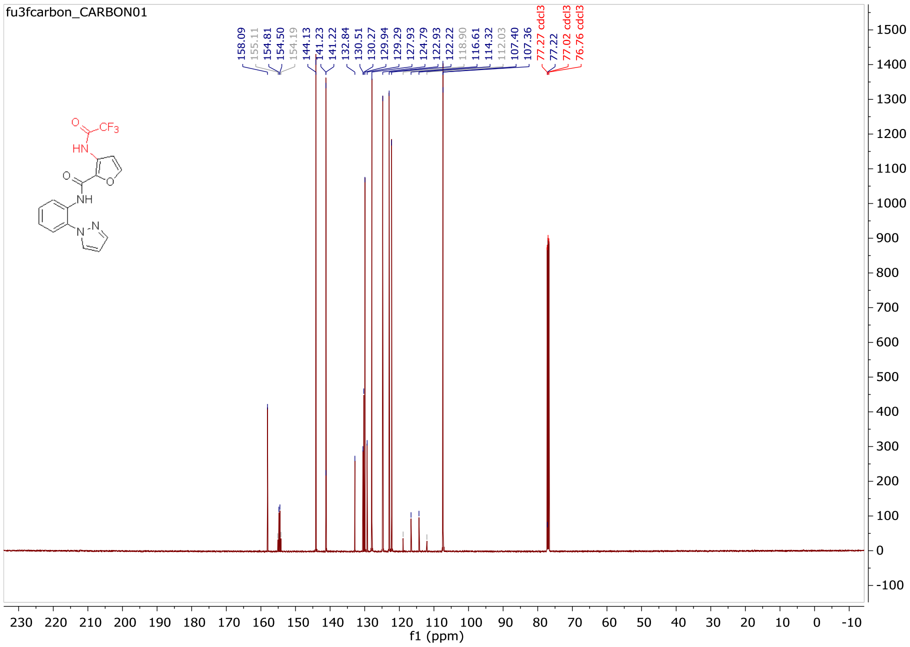

E01
CN
O
NH
HN
O
CF3
N
N
-73.77
-76.00
-76.03
-76.15
-76.18
-76.24
-76.62
-150.75
4500
4000
3500
3000
2500
2000
1500
1000
500
0
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

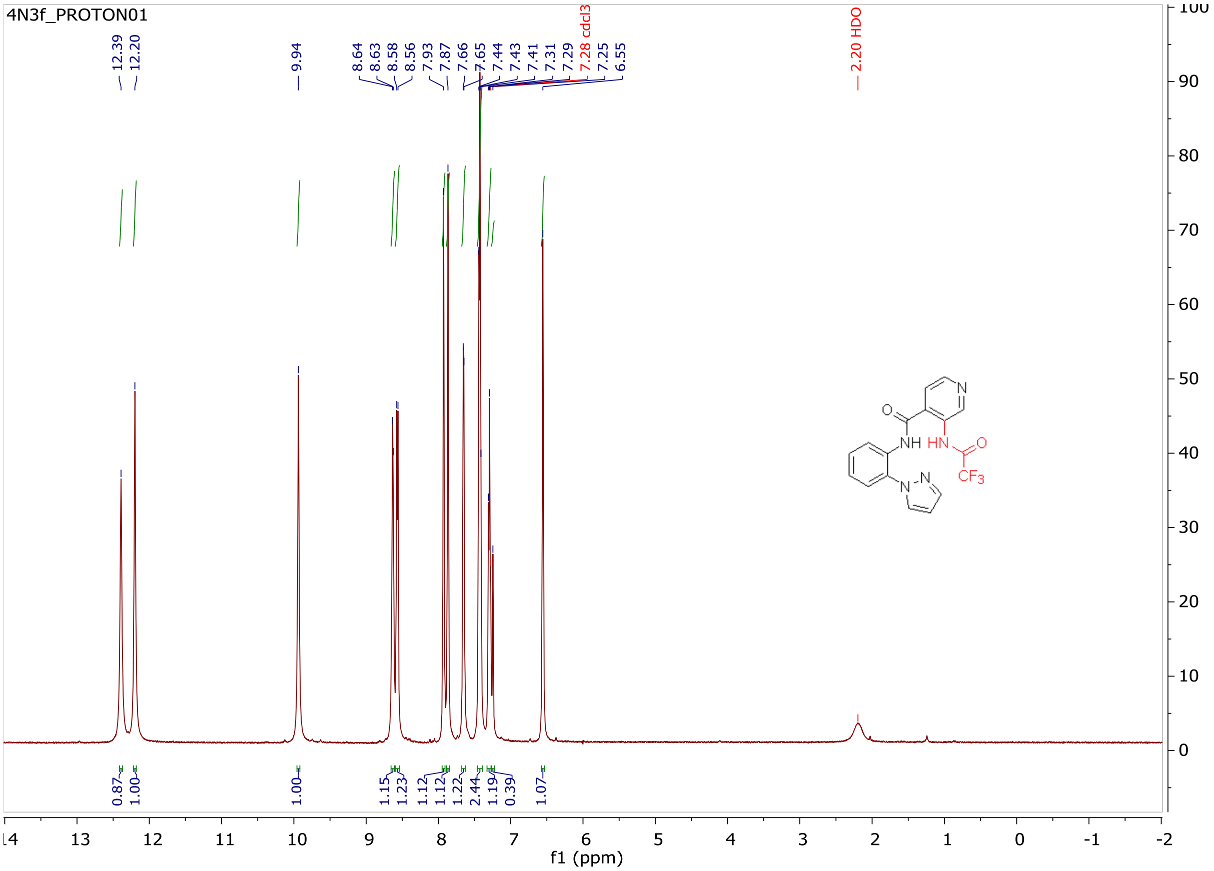

4cn3fcarbon_CARBON01
CN
O
NH
HN
O
CF3
N
N
165.25
155.99
155.68
155.38
155.07
141.27
138.75
130.16
129.82
129.22
128.03
127.99
127.85
125.66
124.91
124.33
123.30
121.76
121.67
117.18
116.80
116.62
114.32
107.74
77.24 cdcl3
77.19
76.99 cdcl3
76.73 cdcl3
24.08
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

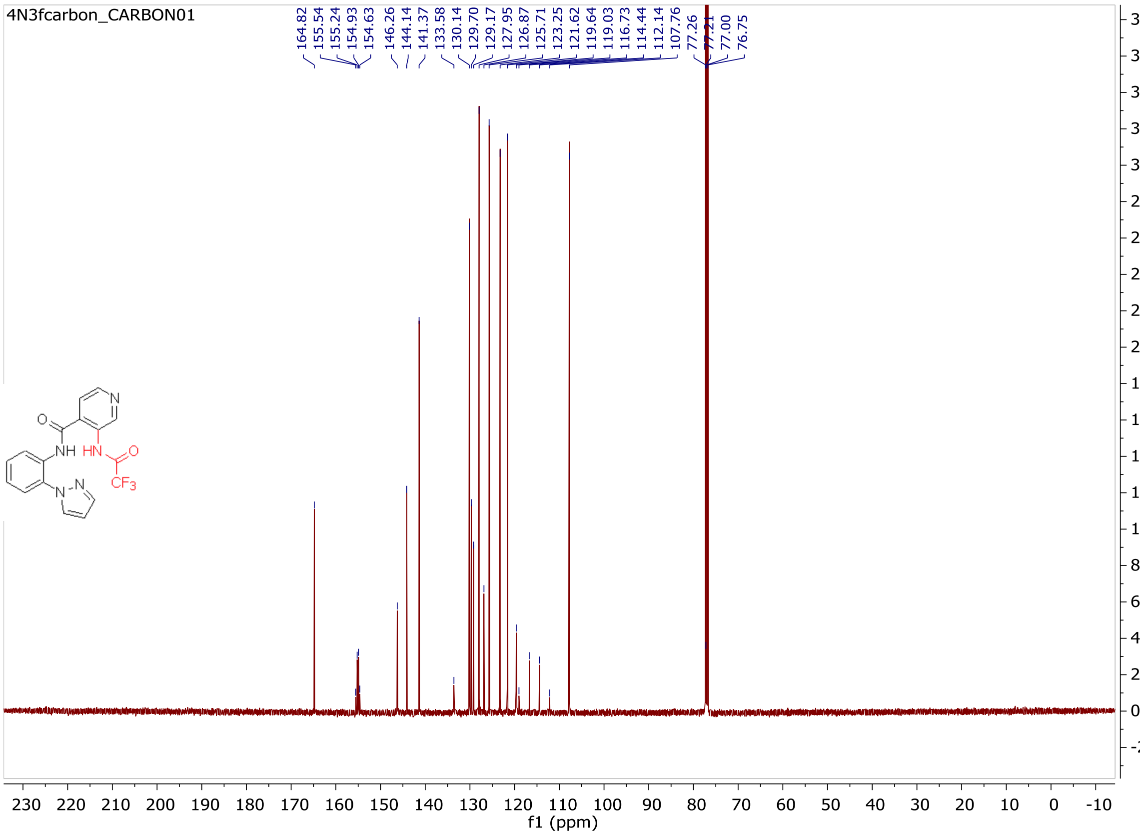

NO2
.UORINE01
O
NH
HN
CF3
O
N
N
3e
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

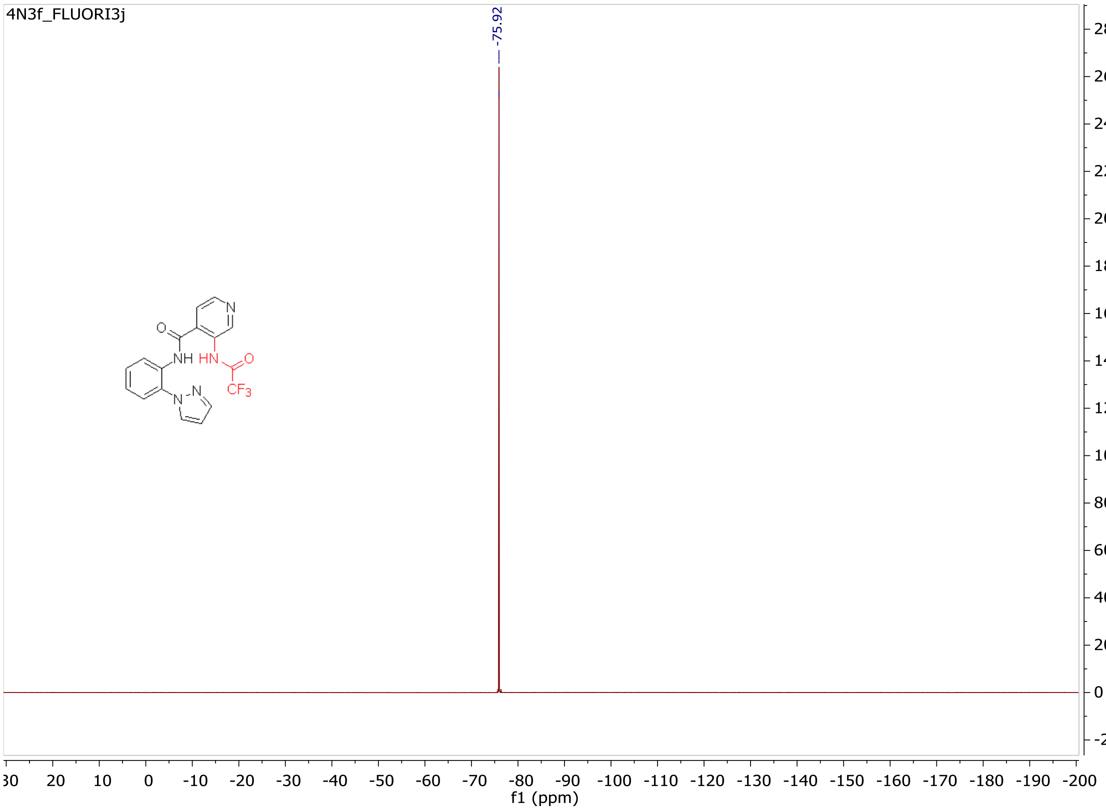

4NO23f_dmso_2_PROTON01
12.12
11.26
8.77
8.27
8.24
8.05
8.03
7.99
7.97
7.74
7.65
7.64
7.45
7.41
7.39
6.50 HDO
0.95
0.92
0.86
1.94
1.12
1.07
0.94
1.11
0.97
1.13
1.86
100
90
80
70
60
50
40
30
20
10
0
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)

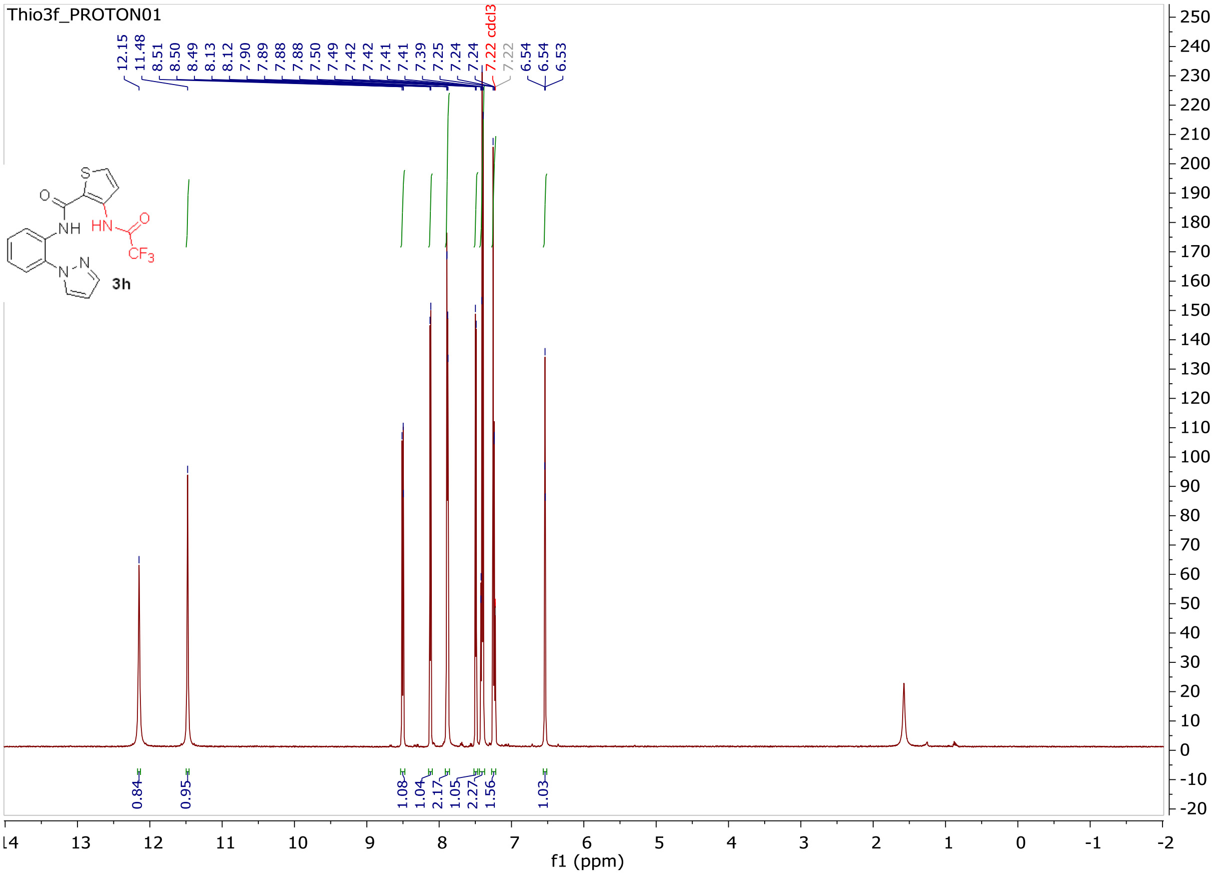

fu3f-2_PROTON01
O
CF3
HN
O
O
NH
N
N
11.40
10.60
8.55
8.53
7.89
7.86
7.45
7.40
7.38
7.26
7.25 cdcl3
7.23
7.22
6.54
1.63 HDO
0.88
0.83
1.10
2.17
1.15
3.28
1.61
0.97
110
100
90
80
70
60
50
40
30
20
10
0
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)

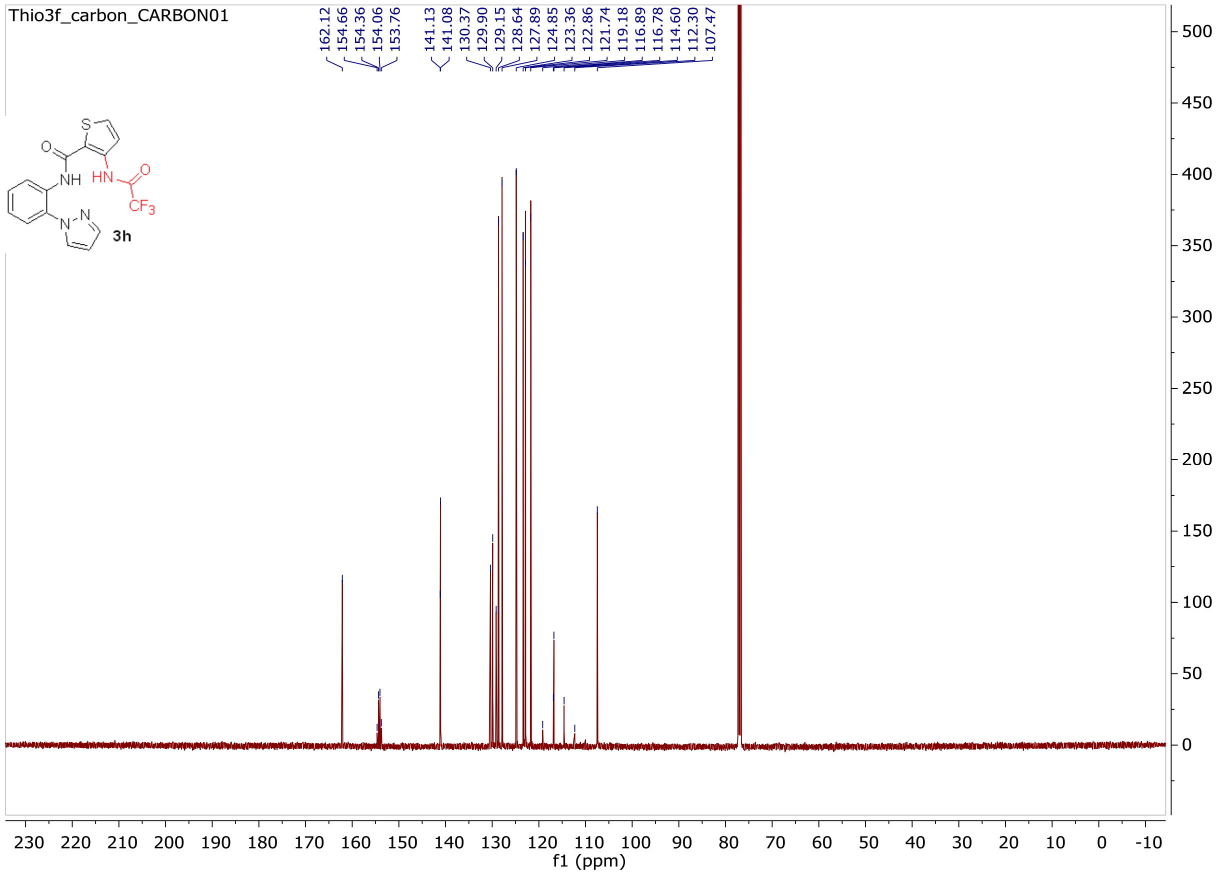

fu3fcarbon_CARBON01
O
CF3
HN
O
O
NH
N
N
158.09
155.11
154.81
154.50
154.19
144.13
141.23
141.22
132.84
130.51
130.27
129.94
129.29
127.93
124.79
122.93
122.22
118.90
116.61
114.32
112.03
107.40
107.36
77.27 cdcl3
77.22
77.02 cdcl3
76.76 cdcl3
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

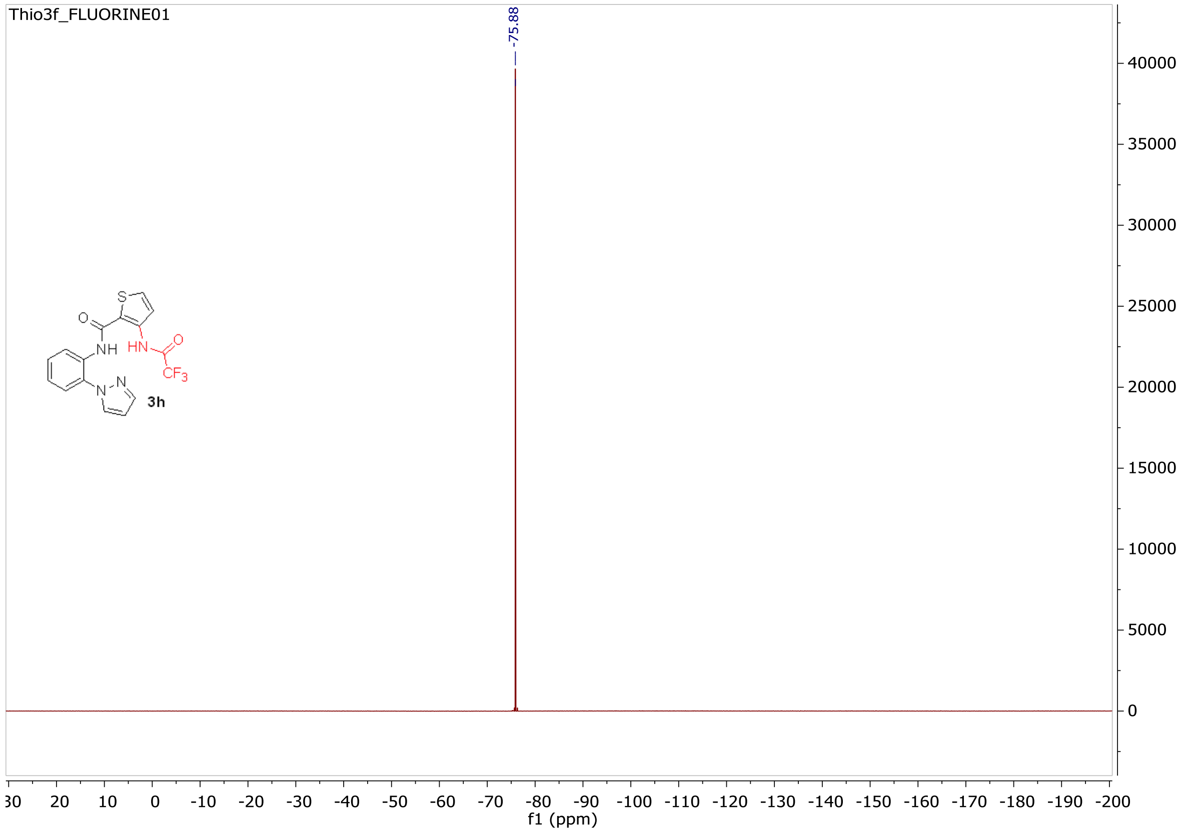

4N3f_PROTON01
12.39
12.20
9.94
8.64
8.63
8.58
8.56
7.93
7.87
7.66
7.65
7.44
7.43
7.41
7.31
7.29
7.28 cdcl3
7.25
6.55
2.20 HDO
0.87
1.00
1.00
1.15
1.23
1.12
1.12
1.22
2.44
1.19
0.39
1.07
O
NH
HN
O
N
N
N
CF3
f1 (ppm)

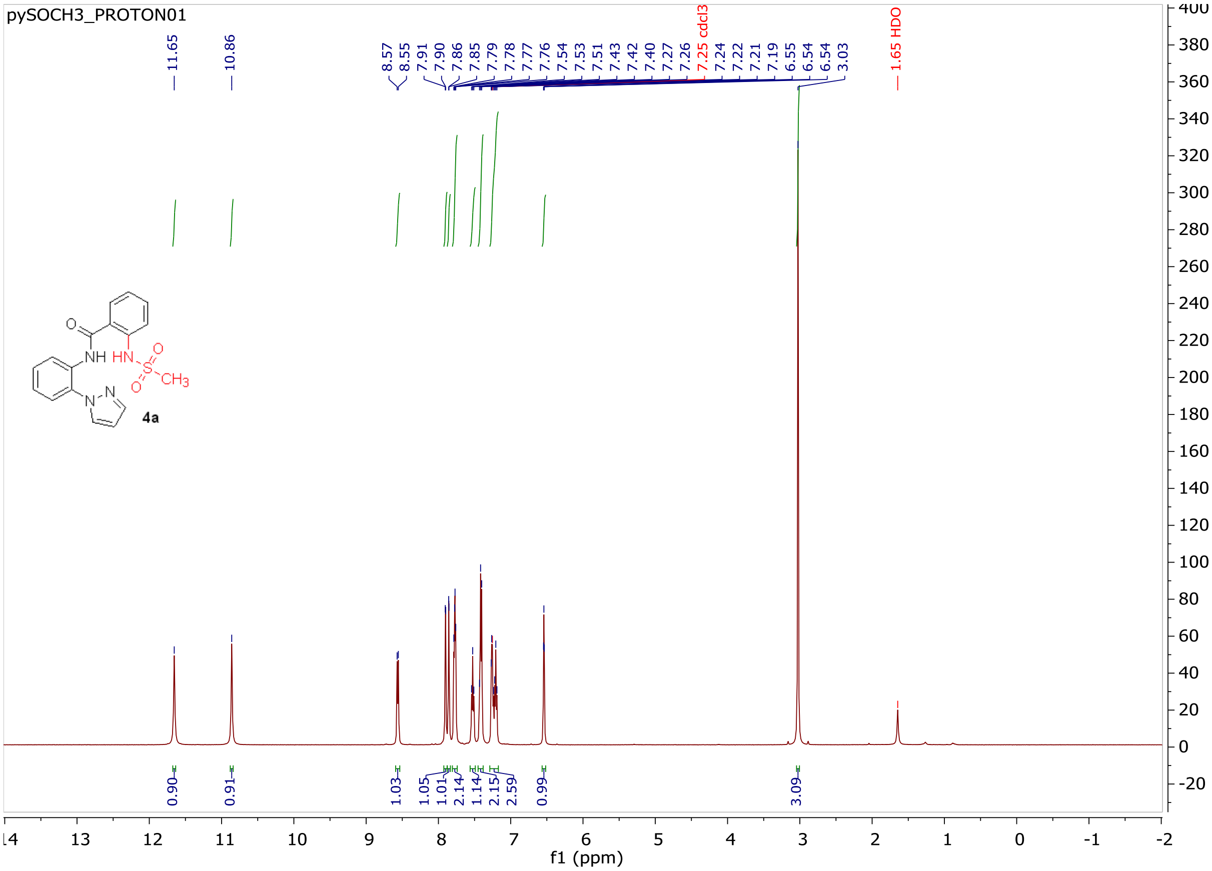

4N3fcarbon_CARBON01
164.82
155.54
155.24
154.93
154.63
146.26
144.14
141.37
133.58
130.14
129.70
129.17
127.95
126.87
125.71
123.25
121.62
119.64
119.03
116.73
114.44
112.14
107.76
77.26
77.21
77.00
76.75
O
NH
HN
O
N
N
N
CF3
f1 (ppm)

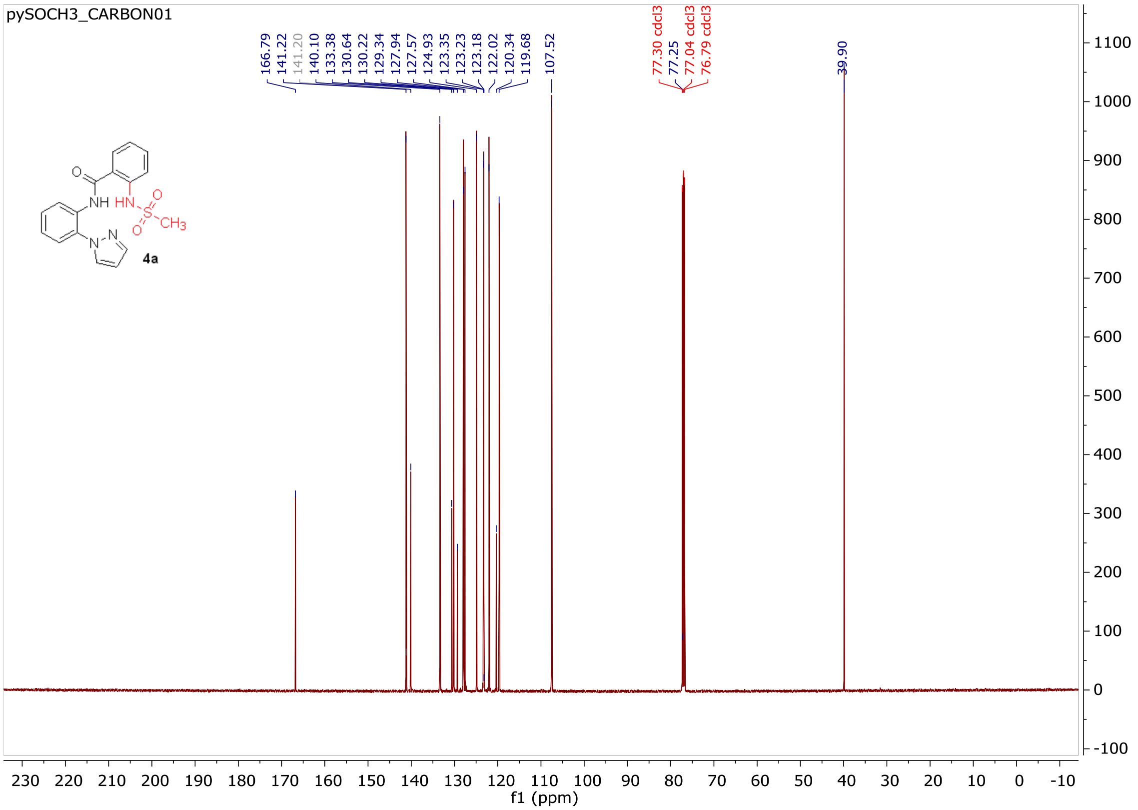

4N3f_FLUORI3j
-75.92
O
NH
N
HN
O
CF3
N
N
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

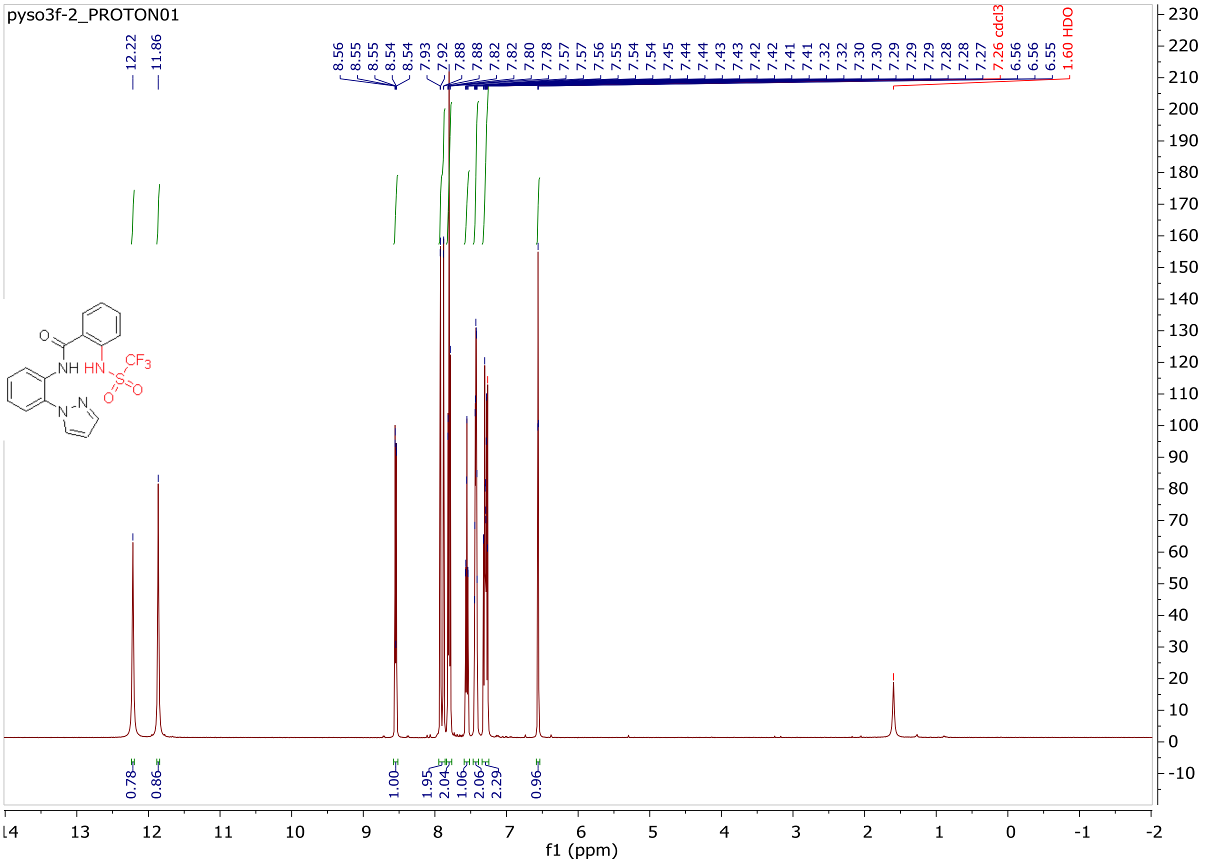

Thio3f_PROTON01
12.15
11.48
8.51
8.50
8.49
8.13
8.12
7.90
7.89
7.88
7.88
7.50
7.49
7.42
7.42
7.41
7.41
7.39
7.25
7.24
7.24
7.22 cdcl3
7.22
6.54
6.54
6.53
S
O
NH
HN
O
CF3
N
N
3h
0.84
0.95
1.08
1.04
2.17
1.05
2.27
1.56
1.03
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)

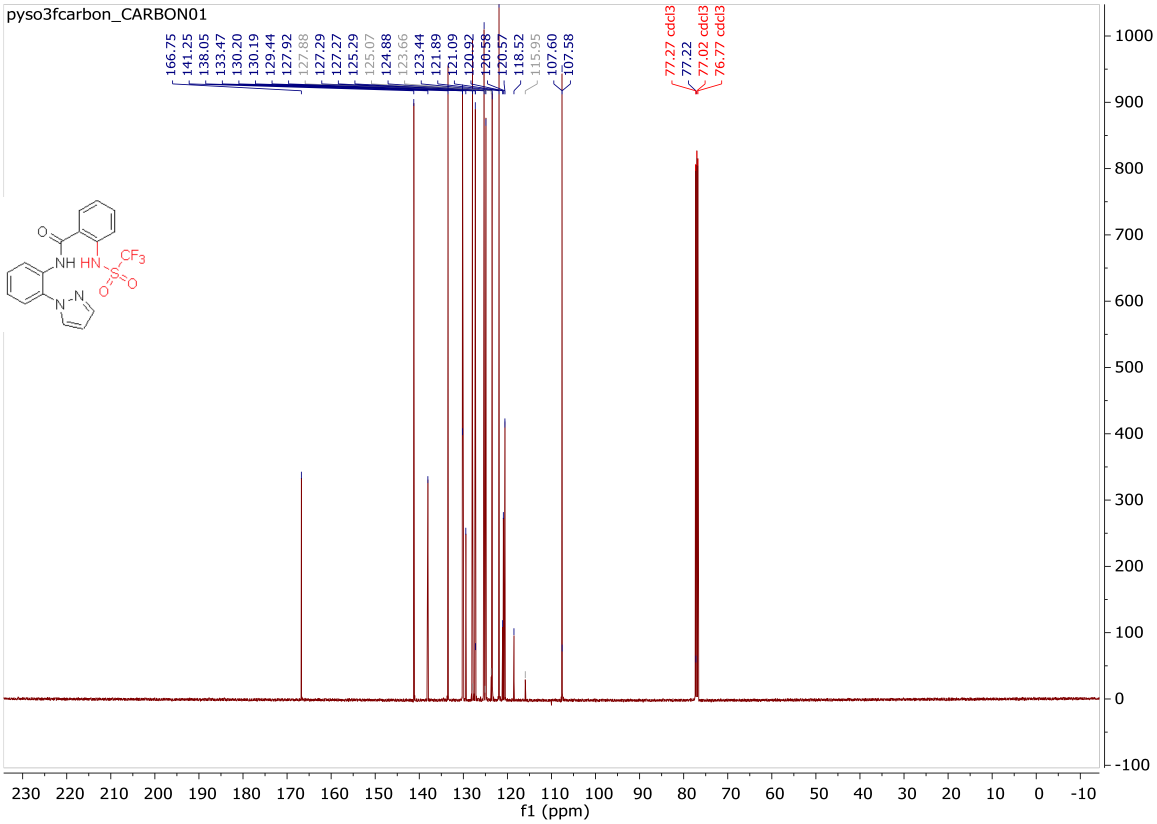

Thio3f_carbon_CARBON01
162.12
154.66
154.36
154.06
153.76
141.13
141.08
130.37
129.90
129.15
128.64
127.89
124.85
123.36
122.86
121.74
119.18
116.89
116.78
114.60
112.30
107.47
S
O
NH
HN
O
CF3
N
N
3h
500
450
400
350
300
250
200
150
100
50
0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

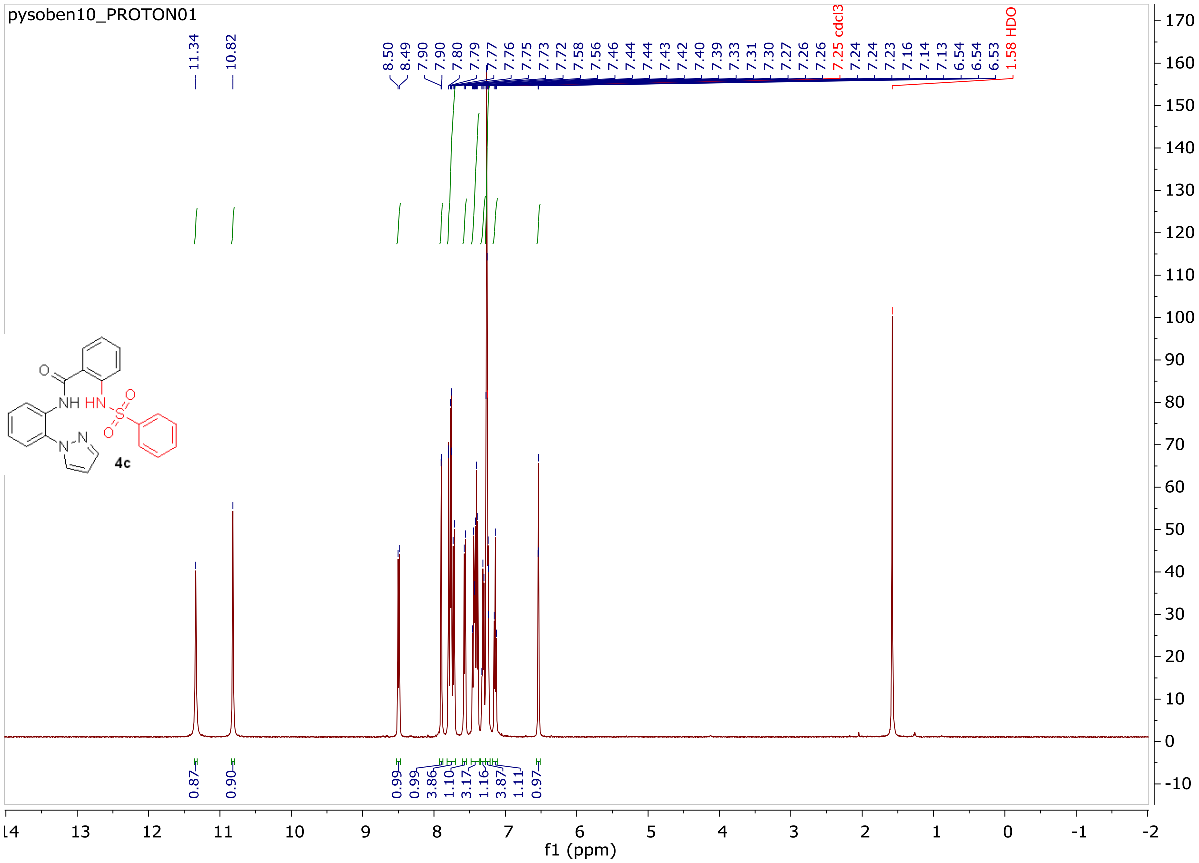

Thio3f_FLUORINE01
-75.88
S
O
NH
HN
O
CF3
N
N
3h
40000
35000
30000
25000
20000
15000
10000
5000
0
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

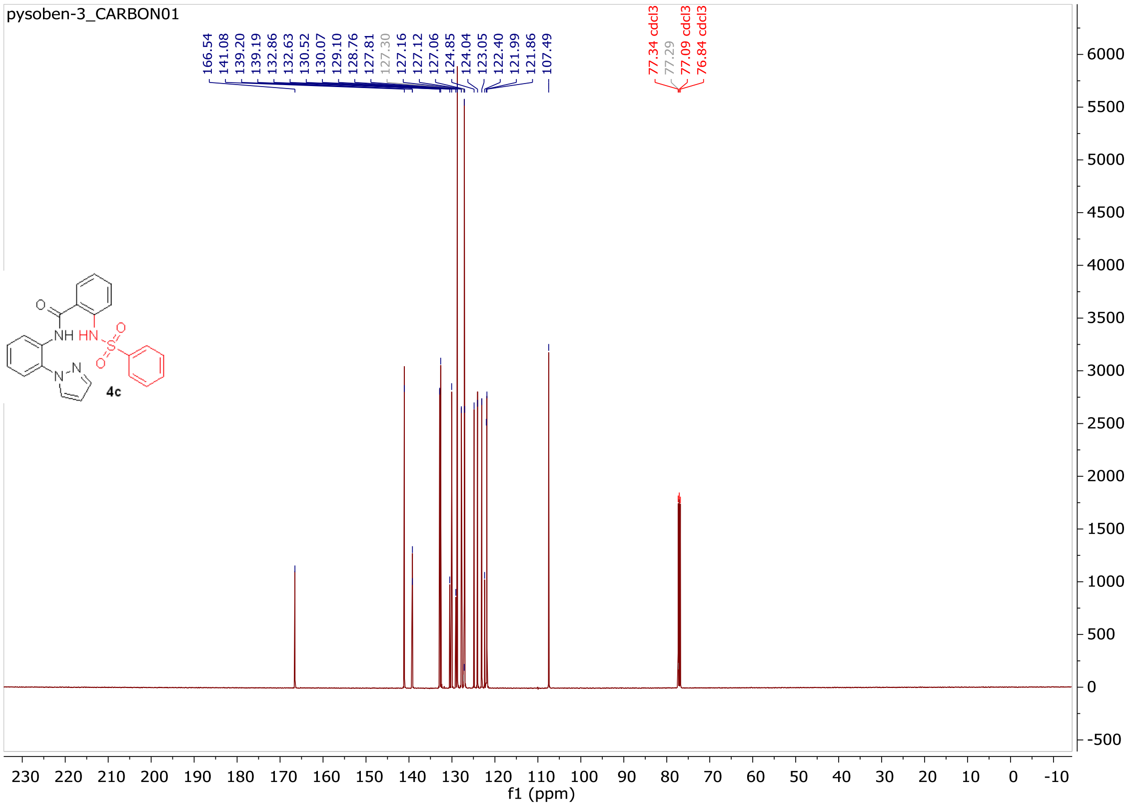

pySOCH3_PROTON01
11.65
10.86
8.57
8.55
7.91
7.90
7.86
7.85
7.79
7.78
7.77
7.76
7.54
7.53
7.51
7.43
7.42
7.40
7.27
7.26
7.25 cdcl3
7.24
7.22
7.21
7.19
6.55
6.54
6.54
3.03
1.65 HDO
O
NH
HN
S
O
O
CH3
N
N
4a
0.90
0.91
1.03
1.05
1.01
2.14
1.14
2.15
2.59
0.99
3.09
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)
400
380
360
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20

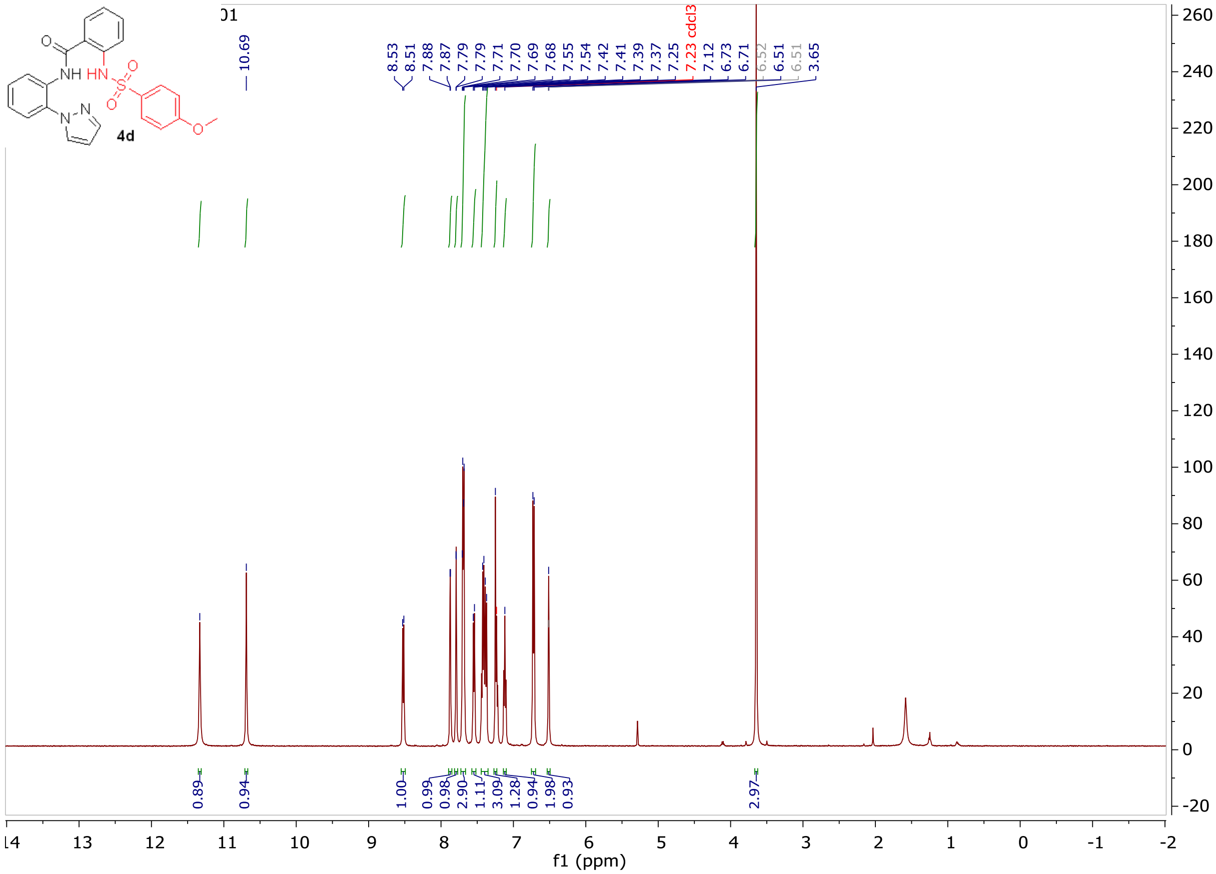

pySOCH3_CARBON01
166.79
141.22
141.20
140.10
133.38
130.64
130.22
129.34
127.94
127.57
124.93
123.35
123.23
123.18
122.02
120.34
119.68
107.52
77.30 cdcl3
77.25
77.04 cdcl3
76.79 cdcl3
39.90
O
NH
HN
S
O
O
CH3
N
N
4a
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

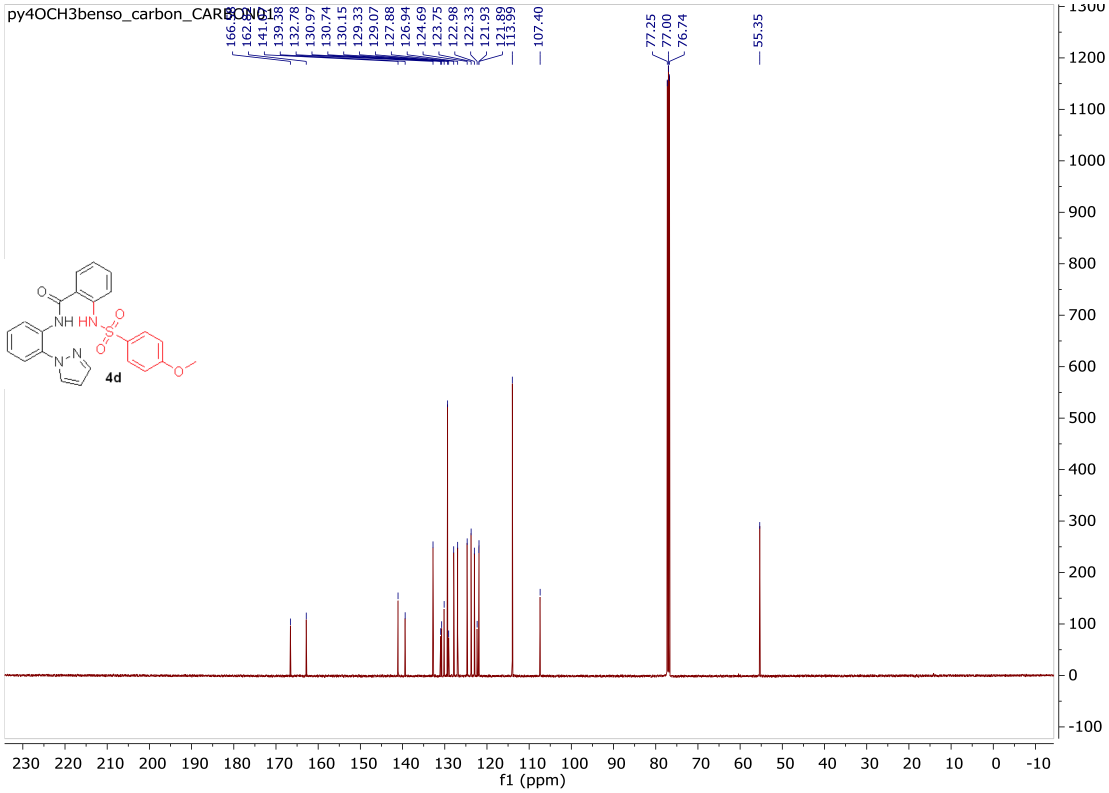

pyso3f-2_PROTON01
12.22
11.86
8.56
8.55
8.55
8.54
8.54
7.93
7.92
7.88
7.88
7.82
7.82
7.80
7.78
7.57
7.57
7.56
7.55
7.54
7.54
7.45
7.44
7.43
7.43
7.42
7.42
7.41
7.41
7.32
7.32
7.30
7.30
7.29
7.29
7.29
7.28
7.28
7.27
7.26 cdcl3
6.56
6.56
6.55
1.60 HDO
0.78
0.86
1.00
1.95
2.04
1.06
2.06
2.29
0.96
O
NH
HN
CF3
S
O
O
N
N
f1 (ppm)

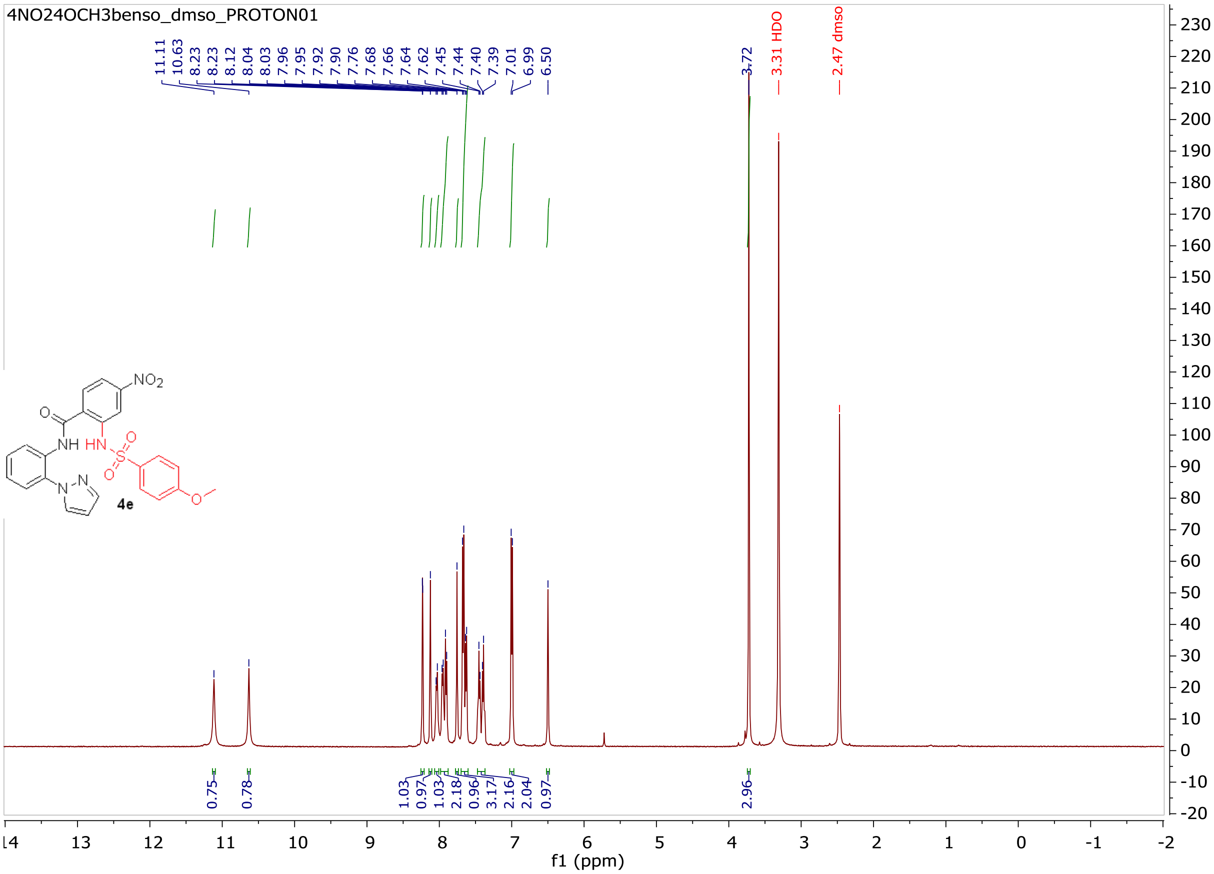

pyso3fcarbon_CARBON01
166.75
141.25
138.05
133.47
130.20
130.19
129.44
127.92
127.88
127.29
127.27
125.29
125.07
124.88
123.66
123.44
121.89
121.09
120.92
120.58
120.57
118.52
115.95
107.60
107.58
77.27 cdcl3
77.22
77.02 cdcl3
76.77 cdcl3
O
NH
HN
CF3
S
O
O
N
N
f1 (ppm)

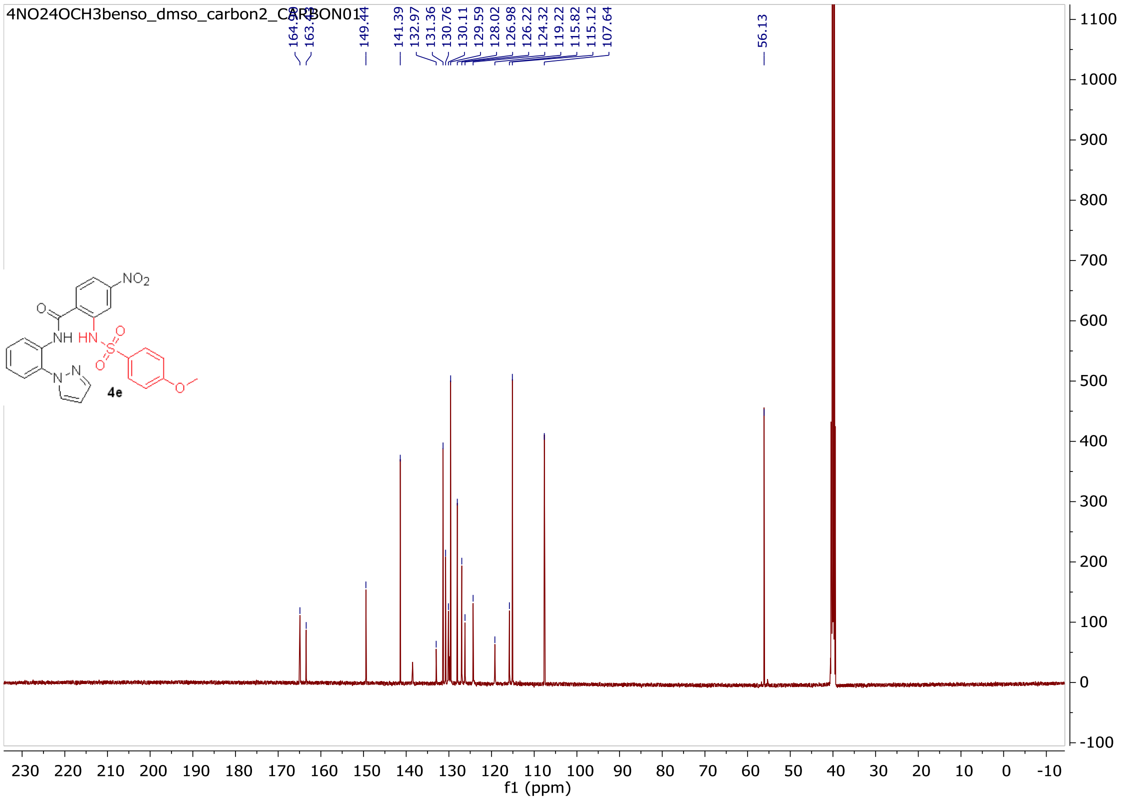

pysoben10_PROTON01
11.34
10.82
8.50
8.49
7.90
7.80
7.79
7.77
7.76
7.75
7.73
7.72
7.58
7.56
7.46
7.44
7.44
7.43
7.42
7.40
7.39
7.33
7.31
7.30
7.27
7.26
7.26
7.25 cdcl3
7.24
7.24
7.23
7.16
7.14
7.13
6.54
6.54
6.53
1.58 HDO
O
NH
HN
S
O
O
N
N
4c
0.87
0.90
0.99
0.99
3.86
1.10
3.17
1.16
3.87
1.11
0.97
f1 (ppm)

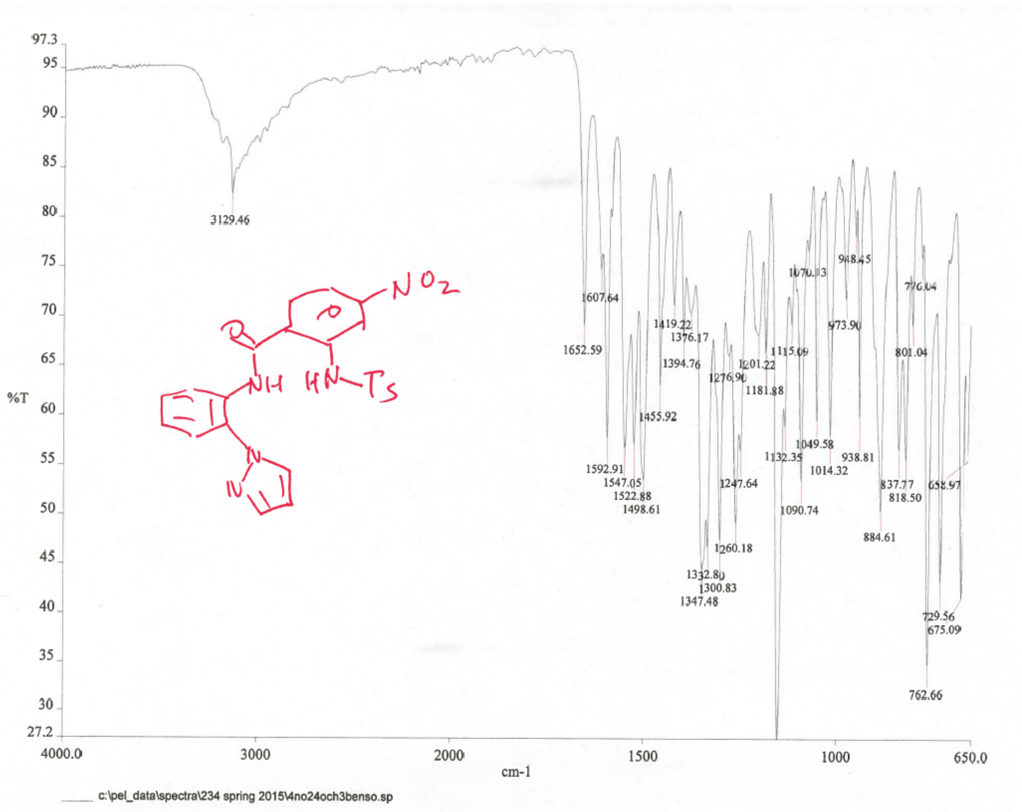

pysoben-3_CARBON01
166.54
141.08
139.20
139.19
132.86
132.63
130.52
130.07
129.10
128.76
127.81
127.30
127.16
127.12
127.06
124.85
124.04
123.05
122.40
121.99
121.86
107.49
77.34 cdcl3
77.29
77.09 cdcl3
76.84 cdcl3
O
NH
HN
S
O
O
N
N
4c
f1 (ppm)

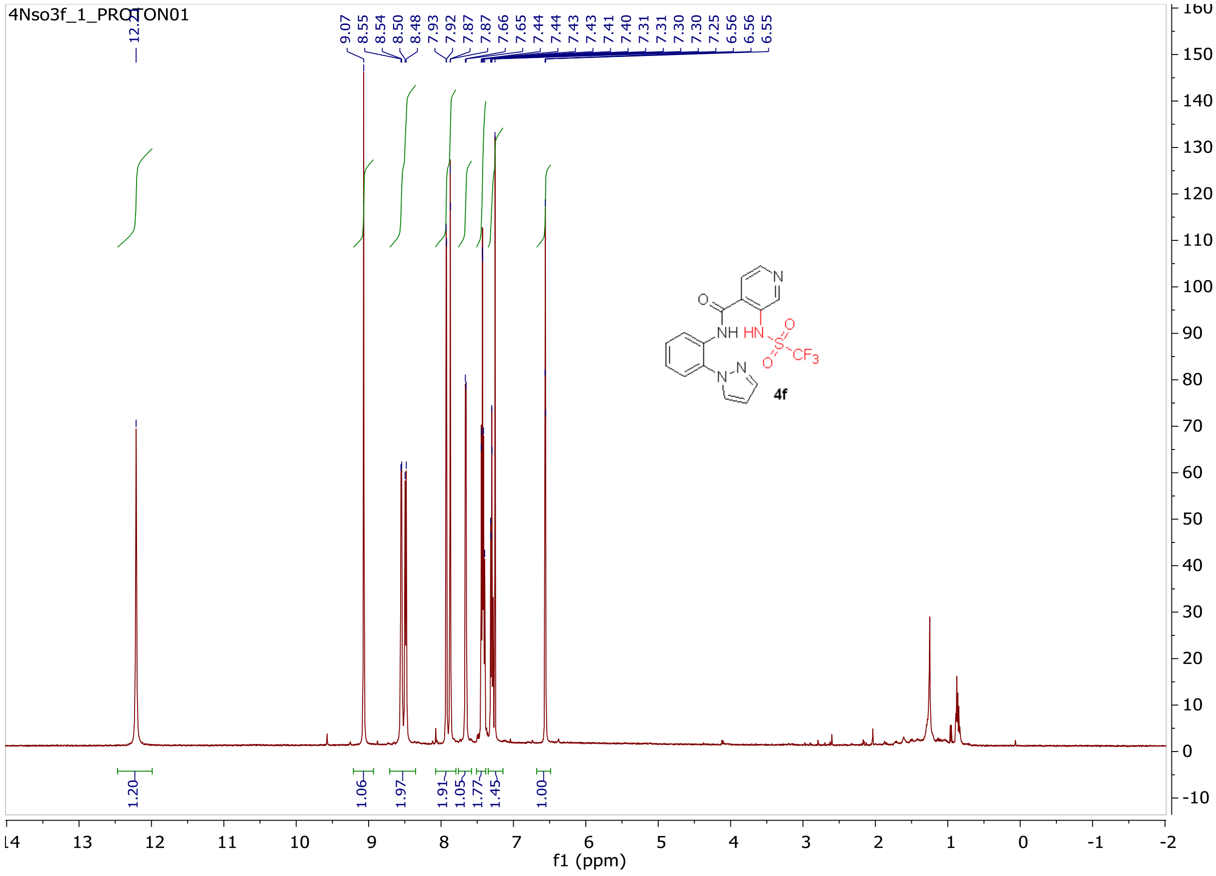

4d
O
NH
HN
S
O
O
N
N
O
01
10.69
8.53
8.51
7.88
7.87
7.79
7.79
7.71
7.70
7.69
7.68
7.55
7.54
7.42
7.41
7.39
7.37
7.25
7.23 cdcl3
7.12
6.73
6.71
6.52
6.51
6.51
3.65
0.89
0.94
1.00
0.99
0.98
2.90
1.11
3.09
1.28
0.94
1.98
0.93
2.97
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20

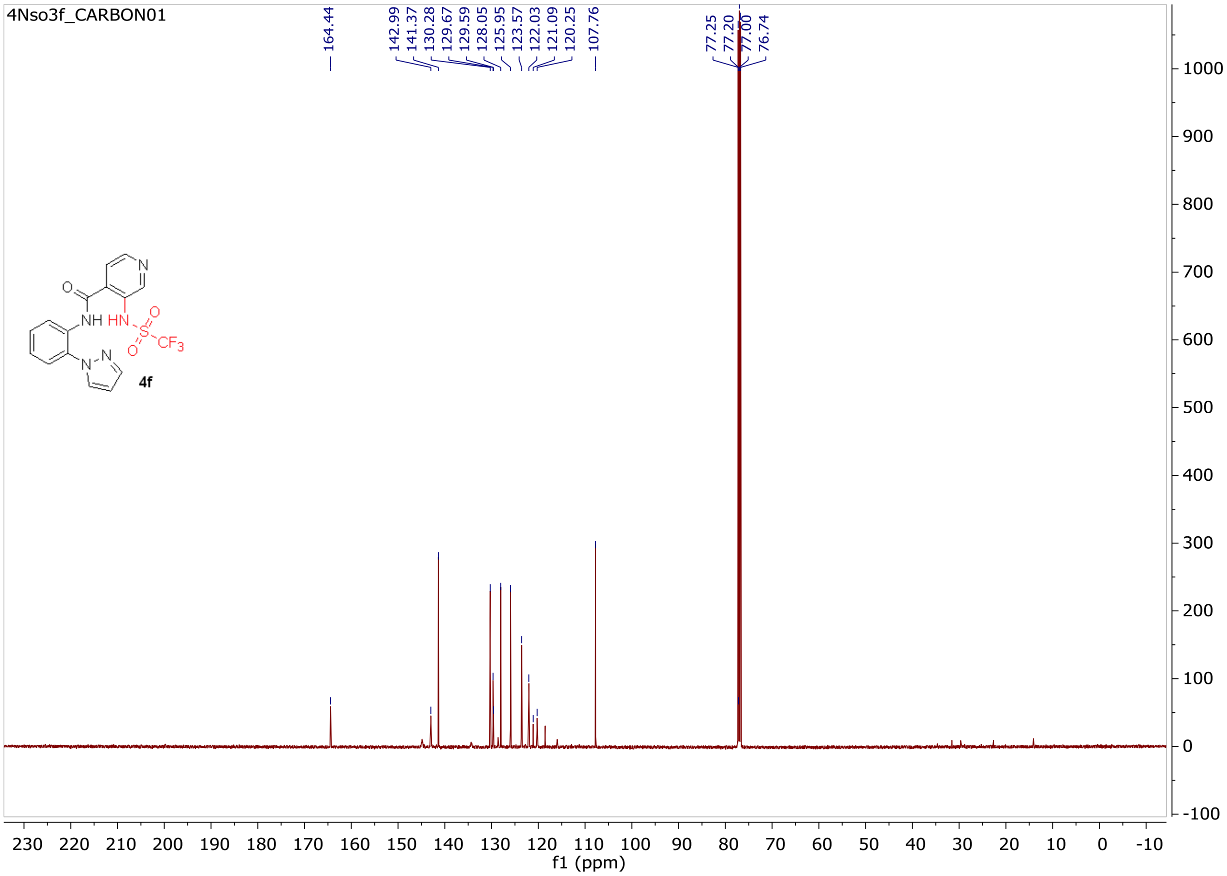

py4OCH3benso_carbon_CARBON01
166.58
162.82
141.07
139.38
132.78
130.97
130.74
130.15
129.33
129.07
127.88
126.94
124.69
123.75
122.98
122.33
121.93
121.89
113.99
107.40
77.25
77.00
76.74
55.35
4d
O
NH
HN
S
O
O
N
N
O
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

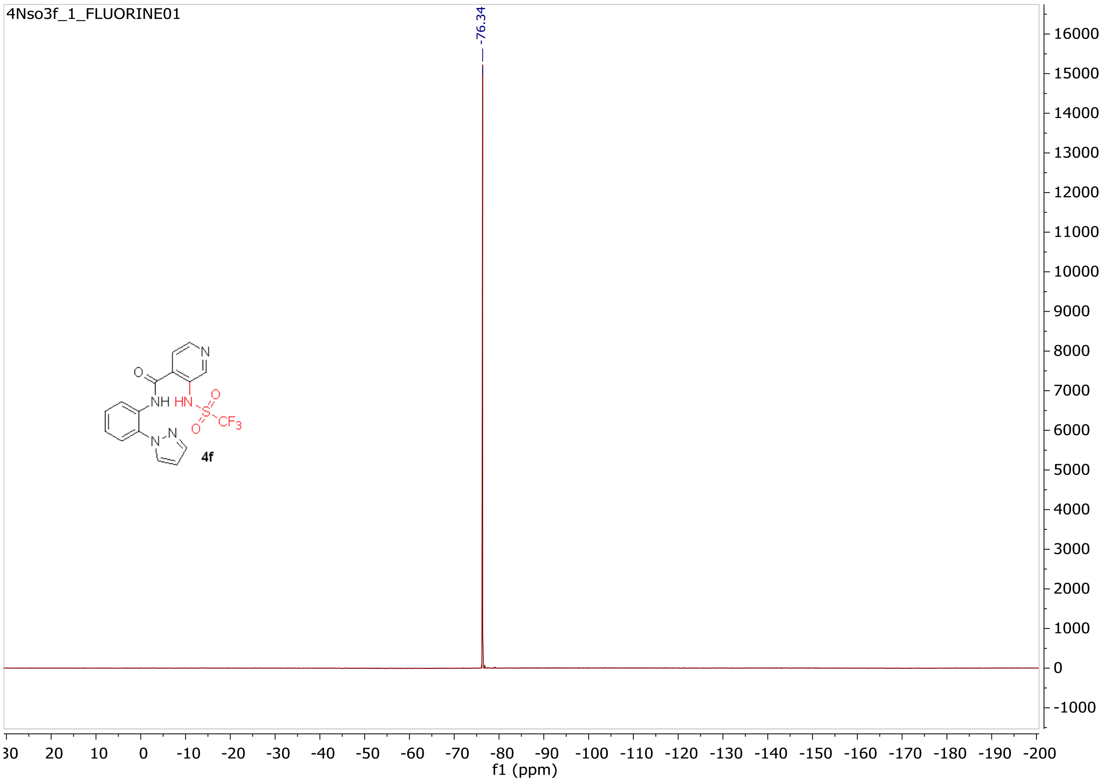

4NO24OCH3benso_dmso_PROTON01
11.11
10.63
8.23
8.23
8.12
8.04
8.03
7.96
7.95
7.92
7.90
7.76
7.68
7.66
7.64
7.62
7.45
7.44
7.40
7.39
7.01
6.99
6.50
3.72
3.31 HDO
2.47 dmso
NO2
O
NH
HN
S
O
O
N
N
O
4e
0.75
0.78
1.03
0.97
1.03
2.18
0.96
3.17
2.16
2.04
0.97
2.96
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20

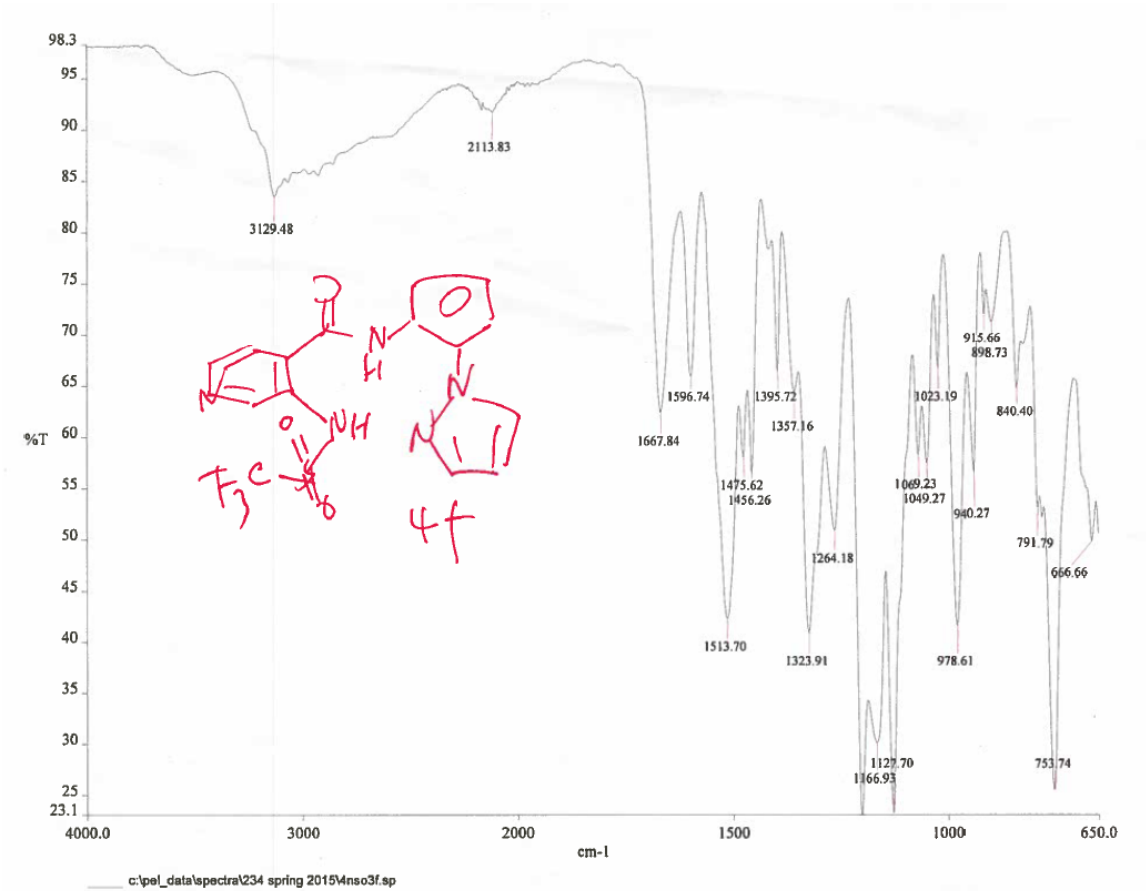

4NO24OCH3benso_dmso_carbon2_CARBON01
164.98
163.43
149.44
141.39
132.97
131.36
130.76
130.11
129.59
128.02
126.98
126.22
124.32
119.22
115.82
115.12
107.64
56.13
NO2
O
NH
HN
S
O
O
N
N
O
4e
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
1100 1000 900 800 700 600 500 400 300 200 100 0 -100

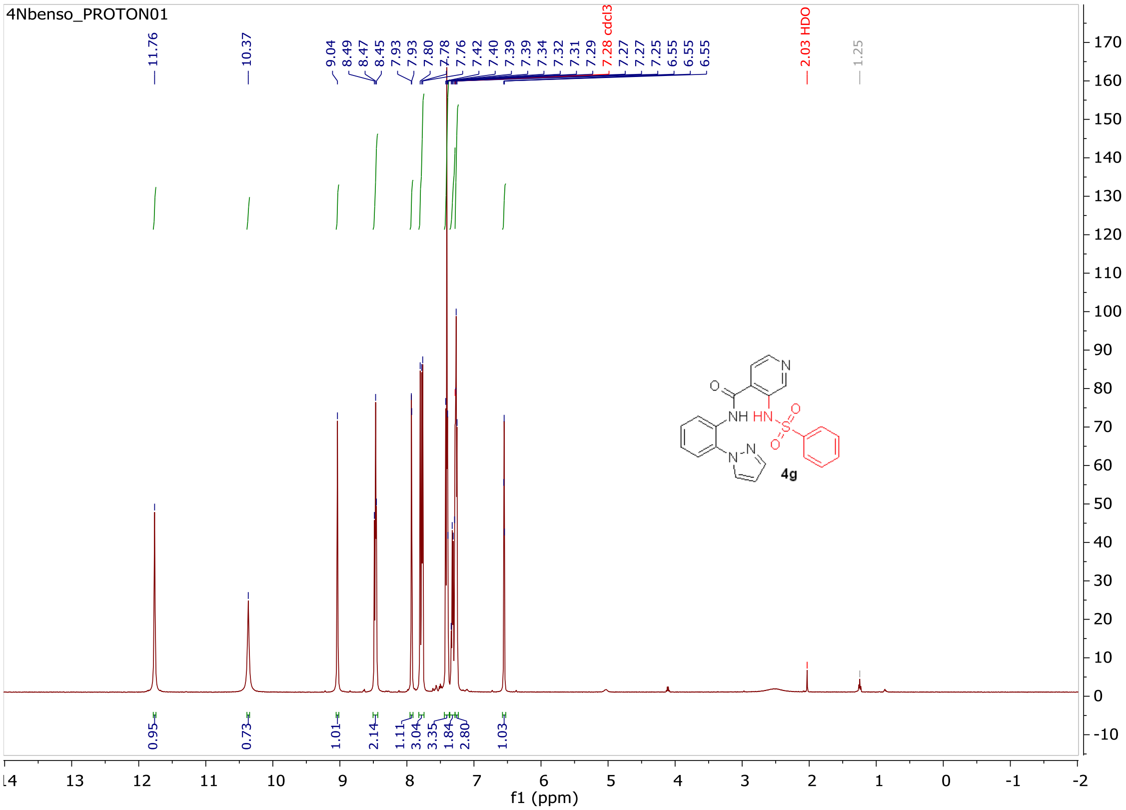

97.3
95
90
85
80
75
70
65
%T
60
55
50
45
40
35
30
27.2
4000.0
3000
2000
1500
1000
650.0
cm-1
3129.46
1607.64
1652.59
1419.22
1376.17
1394.76
1455.92
1592.91
1547.05
1522.88
1498.61
1276.90
1201.22
1181.88
1115.09
1070.13
948.45
973.90
776.04
801.04
1247.64
1132.35
1049.58
1014.32
938.81
837.77
818.50
658.97
1090.74
884.61
1260.18
1332.80
1300.83
1347.48
729.56
675.09
762.66
NO2
NH
HN-Ts
N
c:\pel_data\spectra\234 spring 2015\4no24och3benso.sp

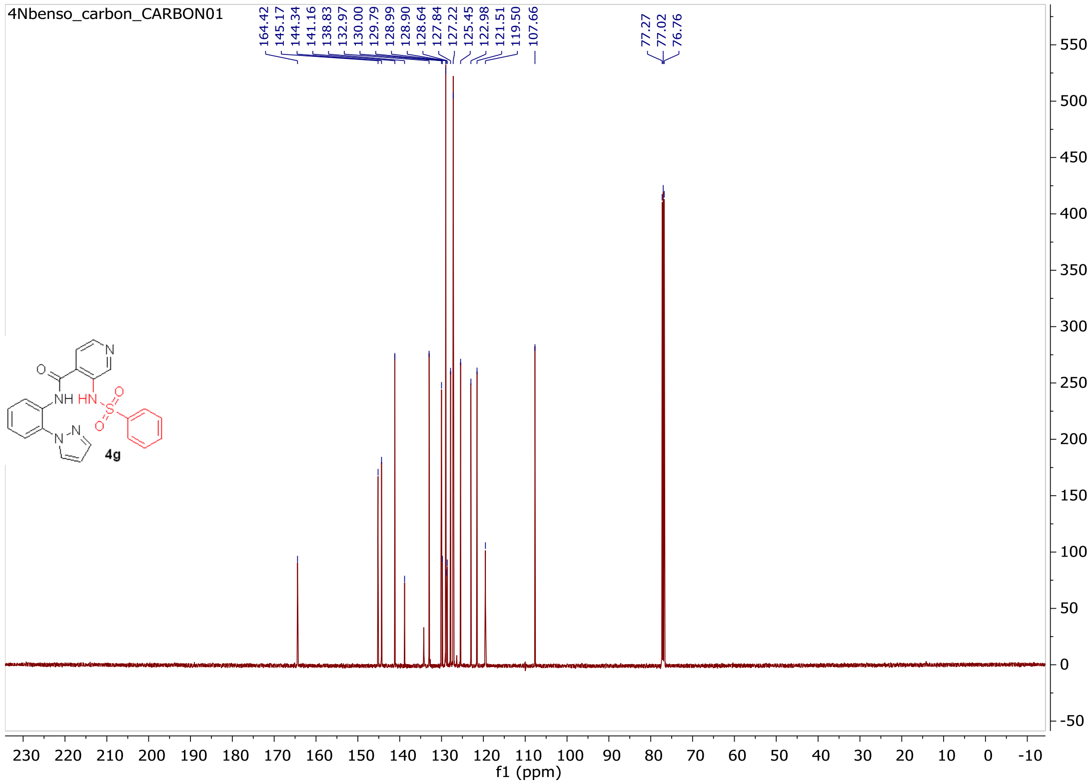

4Nso3f_1_PROTON01
12.21
9.07
8.55
8.54
8.50
8.48
7.93
7.92
7.87
7.87
7.66
7.65
7.44
7.44
7.43
7.43
7.41
7.40
7.31
7.30
7.30
7.25
6.56
6.56
6.55
O
NH
HN
S
O
O
CF3
N
N
N
4f
1.20
1.06
1.97
1.91
1.05
1.77
1.45
1.00
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

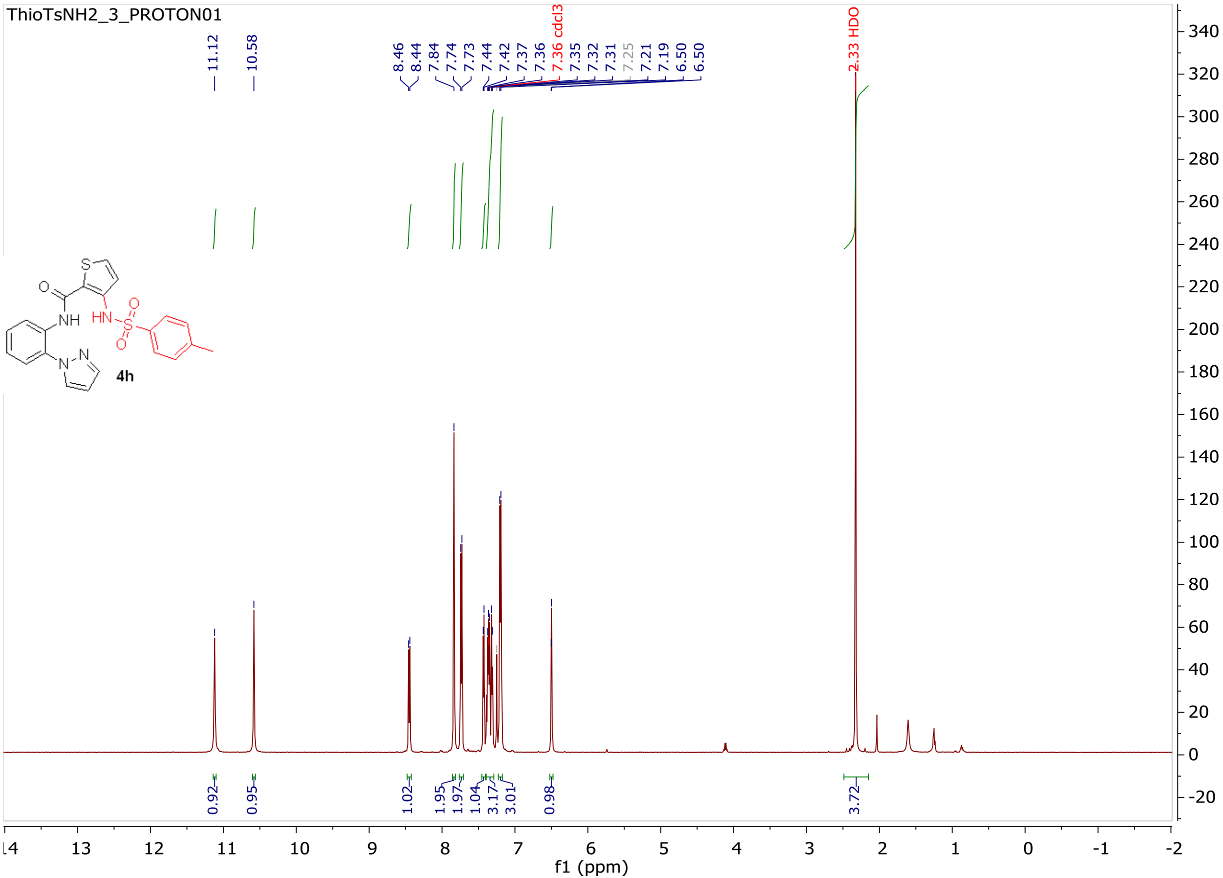

4Nso3f_CARBON01
164.44
142.99
141.37
130.28
129.67
129.59
128.05
125.95
123.57
122.03
121.09
120.25
107.76
77.25
77.20
77.00
76.74
O
N
NH
HN
S
O
O
CF3
N
N
4f
1000
900
800
700
600
500
400
300
200
100
0
-100
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

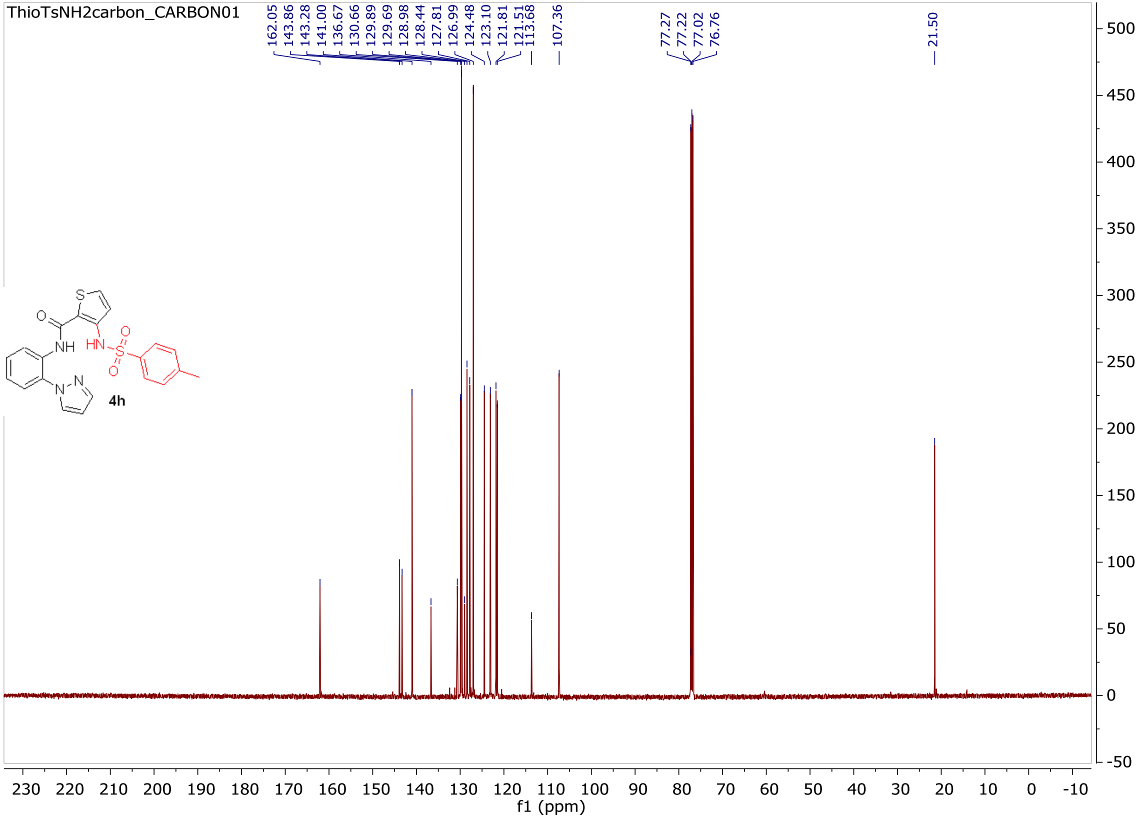

4Nso3f_1_FLUORINE01
-76.34
O
N
NH
HN
S
O
O
CF3
N
N
4f
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

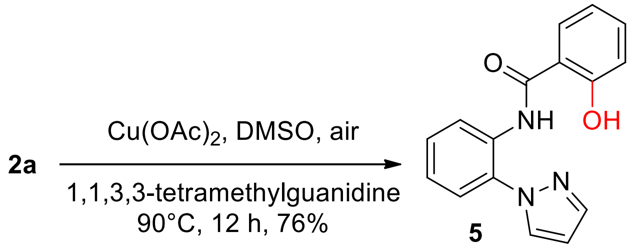

98.3
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
23.1
%T
4000.0
3000
2000
1500
1000
650.0
cm-1
3129.48
2113.83
1667.84
1596.74
1513.70
1475.62
1456.26
1395.72
1357.16
1323.91
1264.18
1166.93
1127.70
1069.23
1049.27
1023.19
978.61
940.27
915.66
898.73
840.40
791.79
753.74
666.66
c:\pel_data\spectra\234 spring 2015\4nso3f.sp
4f

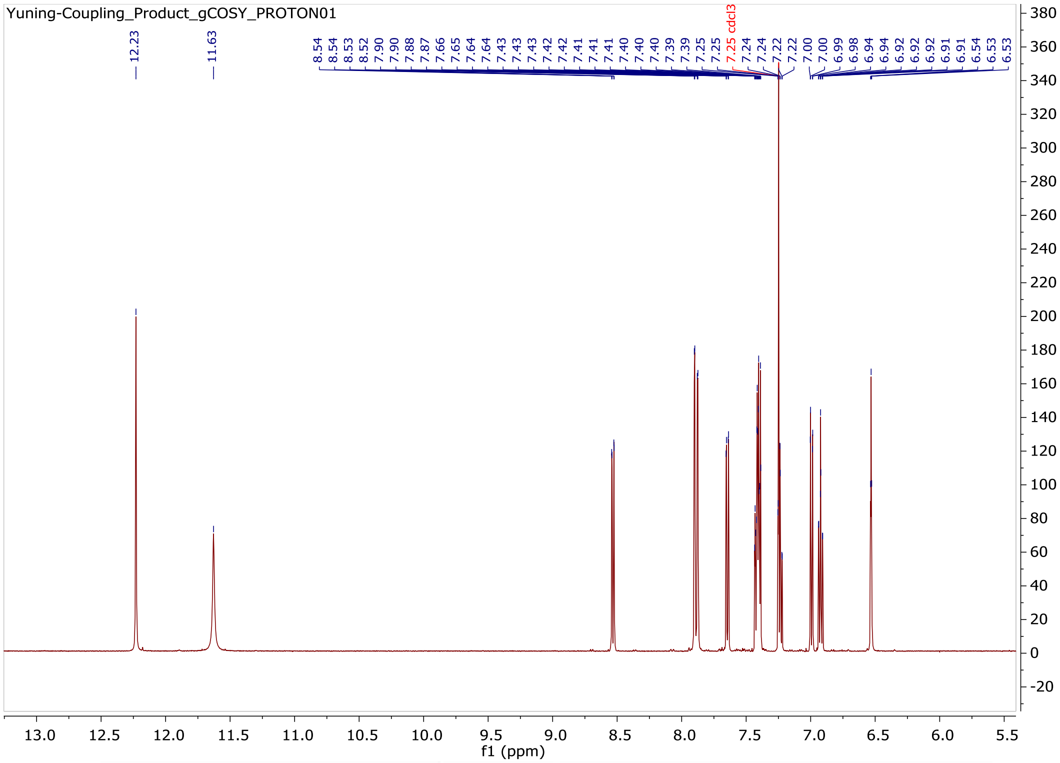

4Nbenso_PROTON01
11.76
10.37
9.04
8.49
8.47
8.45
7.93
7.93
7.80
7.78
7.76
7.42
7.40
7.39
7.39
7.34
7.32
7.31
7.29
7.28 cdcl3
7.27
7.27
7.25
6.55
6.55
6.55
2.03 HDO
1.25
0.95
0.73
1.01
2.14
1.11
3.04
3.35
1.84
2.80
1.03
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
4g

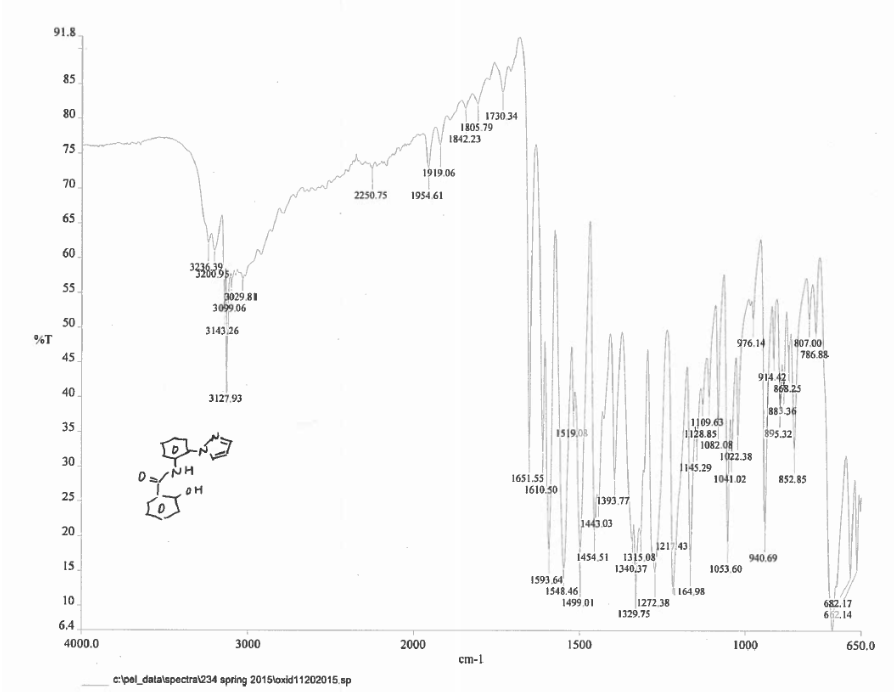

4Nbenso_carbon_CARBON01
164.42
145.17
144.34
141.16
138.83
132.97
130.00
129.79
128.99
128.90
128.64
127.84
127.22
125.45
122.98
121.51
119.50
107.66
77.27
77.02
76.76
O
NH
HN
S
O
O
N
N
N
4g
550
500
450
400
350
300
250
200
150
100
50
0
-50
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

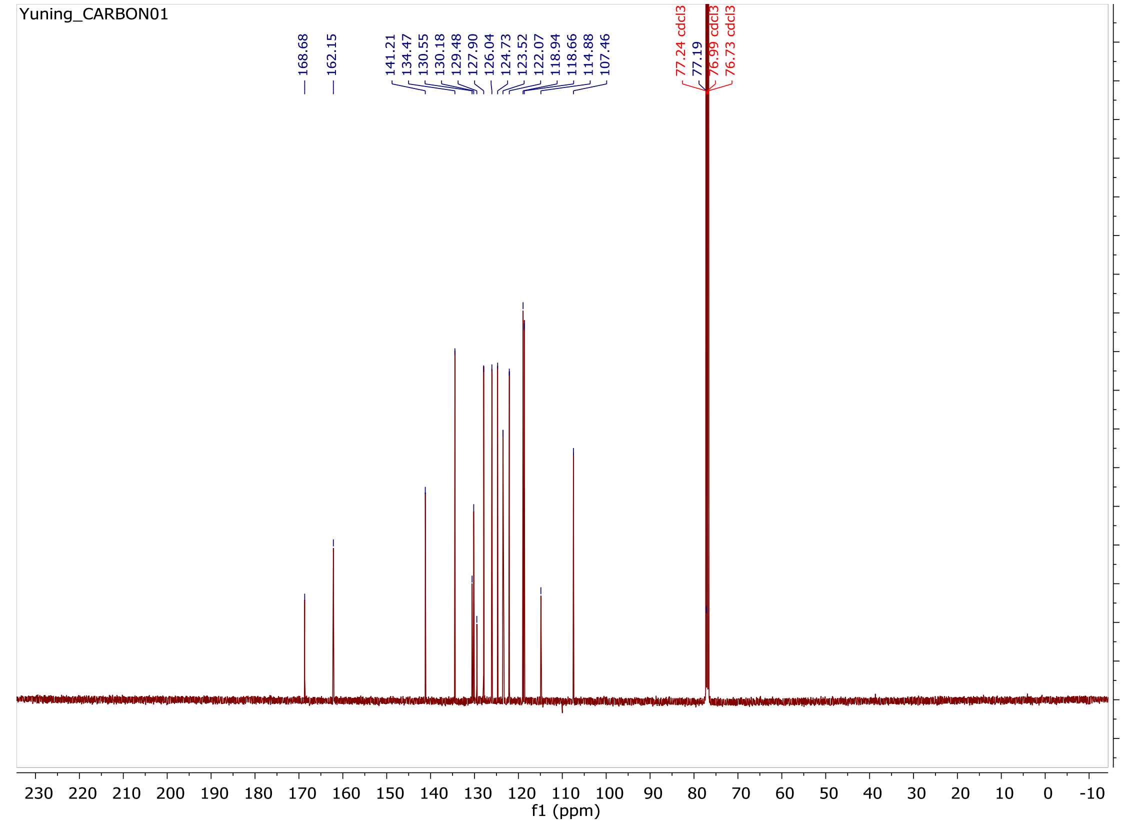

ThioTsNH2_3_PROTON01
11.12
10.58
8.46
8.44
7.84
7.74
7.73
7.44
7.42
7.37
7.36
7.36 cdcl3
7.35
7.32
7.31
7.25
7.21
7.19
6.50
6.50
2.33 HDO
O
NH
S
HN
S
O
O
N
N
4h
0.92
0.95
1.02
1.95
1.97
1.04
3.17
3.01
0.98
3.72
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)


ThioTsNH2carbon_CARBON01
162.05
143.86
143.28
141.00
136.67
130.66
129.89
129.69
128.98
128.44
127.81
126.99
124.48
123.10
121.81
121.51
113.68
107.36
77.27
77.22
77.02
76.76
21.50
O
NH
S
HN
S
O
O
N
N
4h
500
450
400
350
300
250
200
150
100
50
0
-50
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

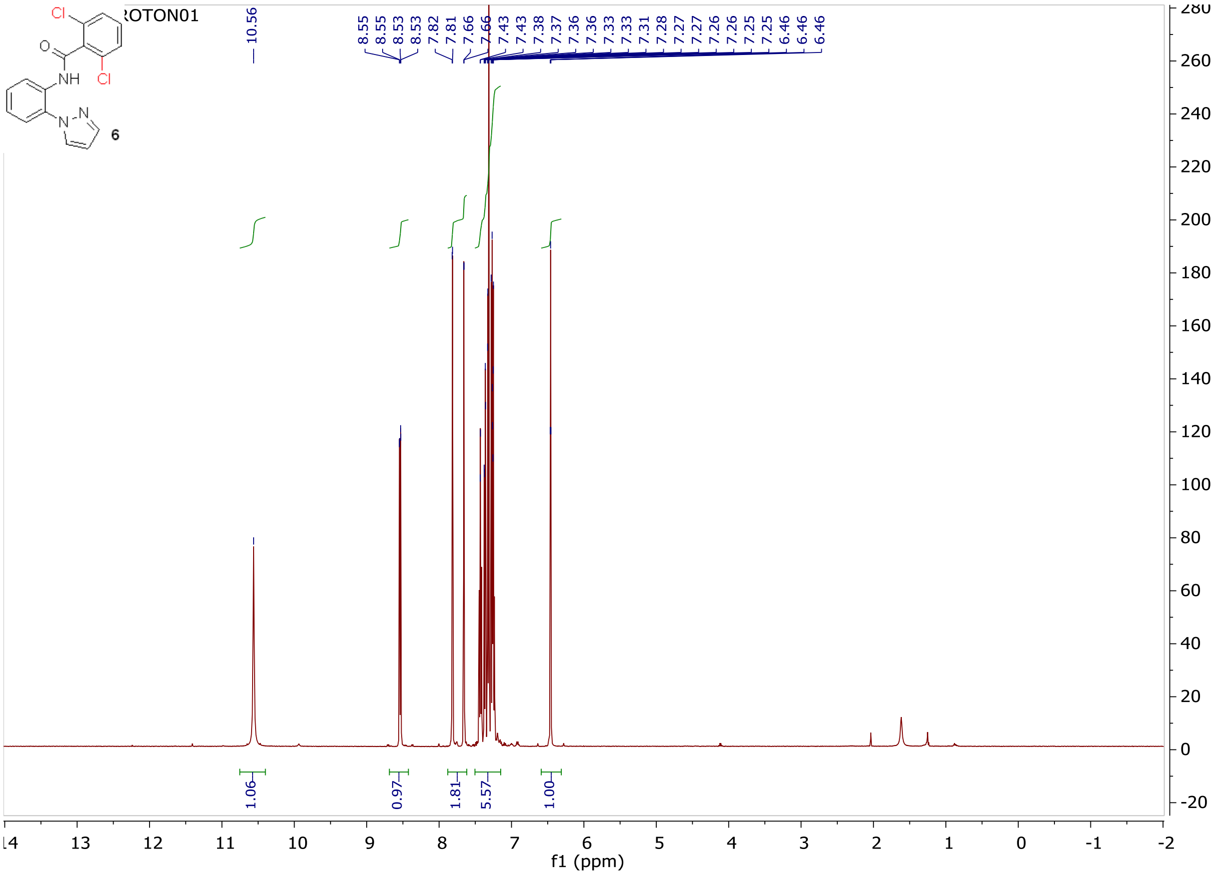

2a
Cu(OAc)2, DMSO, air
1,1,3,3-tetramethylguanidine
90°C, 12 h, 76%
O
NH
OH
N
N
5


Yuning-Coupling_Product_gCOSY_PROTON01
12.23
11.63
8.54
8.54
8.53
8.52
7.90
7.90
7.88
7.87
7.66
7.65
7.64
7.64
7.43
7.43
7.43
7.42
7.42
7.41
7.41
7.41
7.40
7.40
7.40
7.39
7.39
7.25
7.25
7.25 cdcl3
7.24
7.24
7.22
7.22
7.00
7.00
6.99
6.98
6.94
6.94
6.94
6.92
6.92
6.92
6.91
6.91
6.54
6.53
6.53
f1 (ppm)

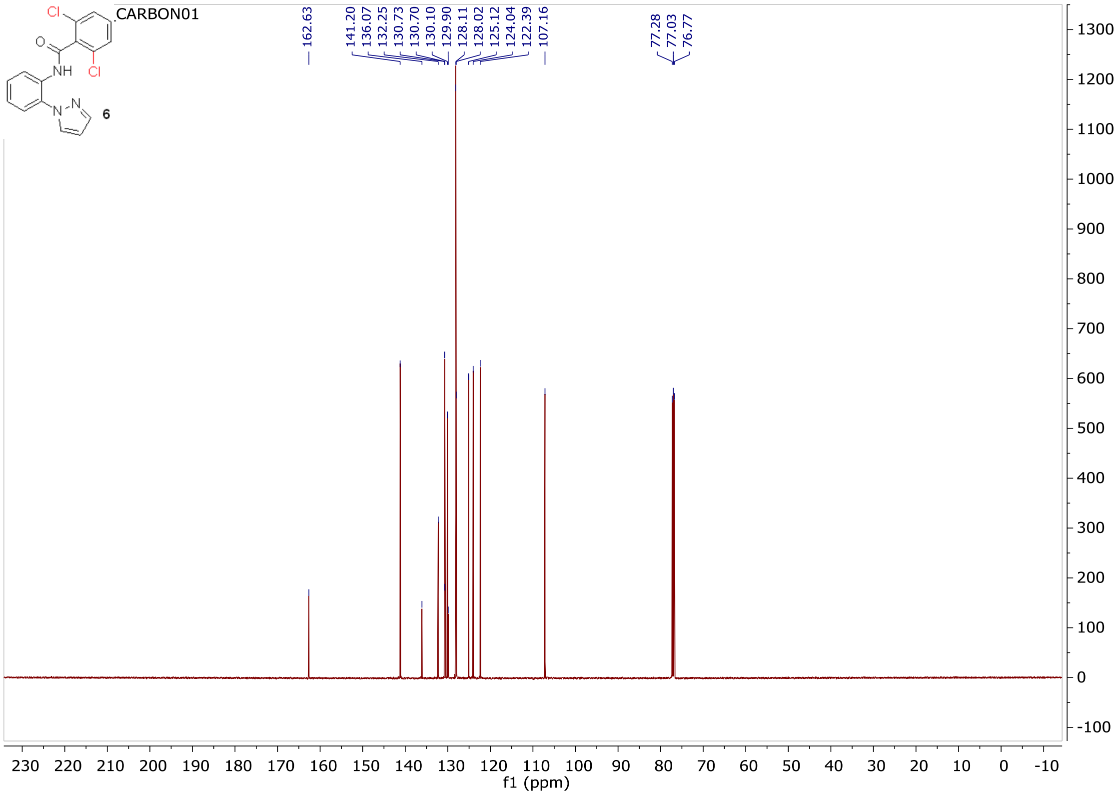

91.8
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
6.4
%T
4000.0
3000
2000
1500
1000
650.0
cm-1
3236.39
3200.95
3029.81
3099.06
3143.26
3127.93
2250.75
1954.61
1919.06
1842.23
1805.79
1730.34
1651.55
1610.50
1593.64
1548.46
1519.08
1499.01
1454.51
1443.03
1393.77
1340.37
1329.75
1315.08
1272.38
1217.43
1164.98
1145.29
1128.85
1109.63
1082.08
1053.60
1041.02
1022.38
976.14
940.69
914.42
895.32
883.36
868.25
852.85
807.00
786.88
682.17
662.14
O
NH
OH
c:\pel_data\spectra\234 spring 2015\oxid11202015.sp

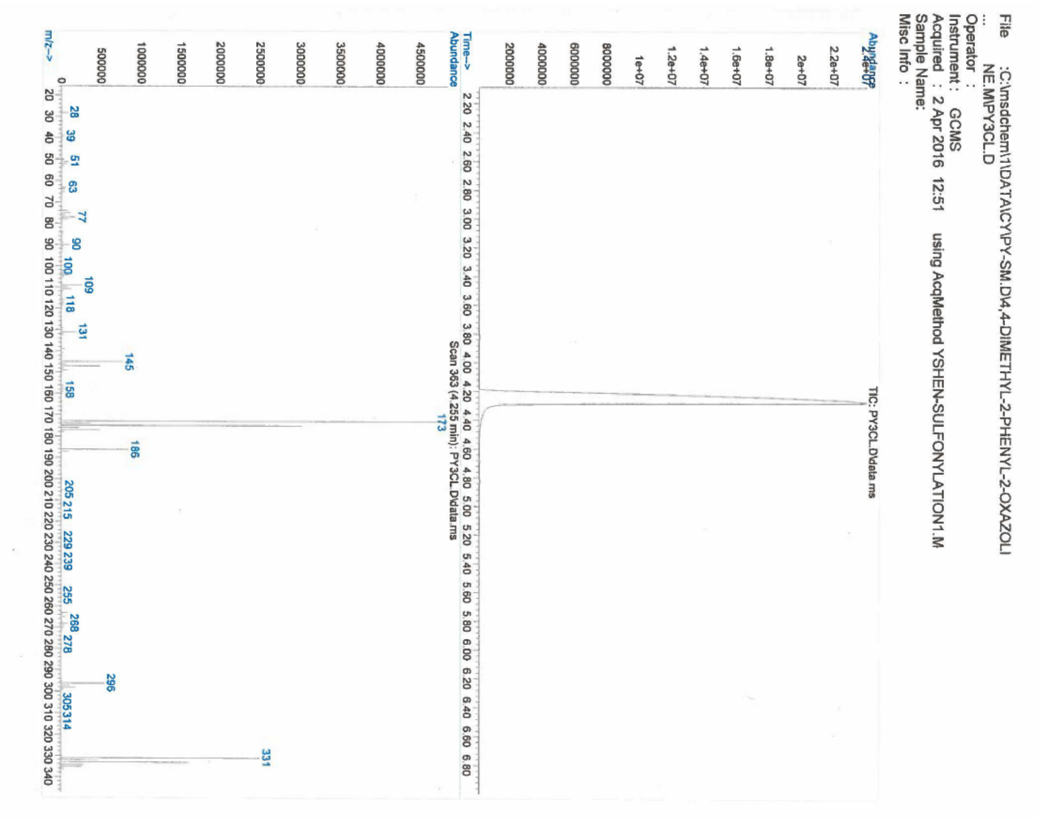


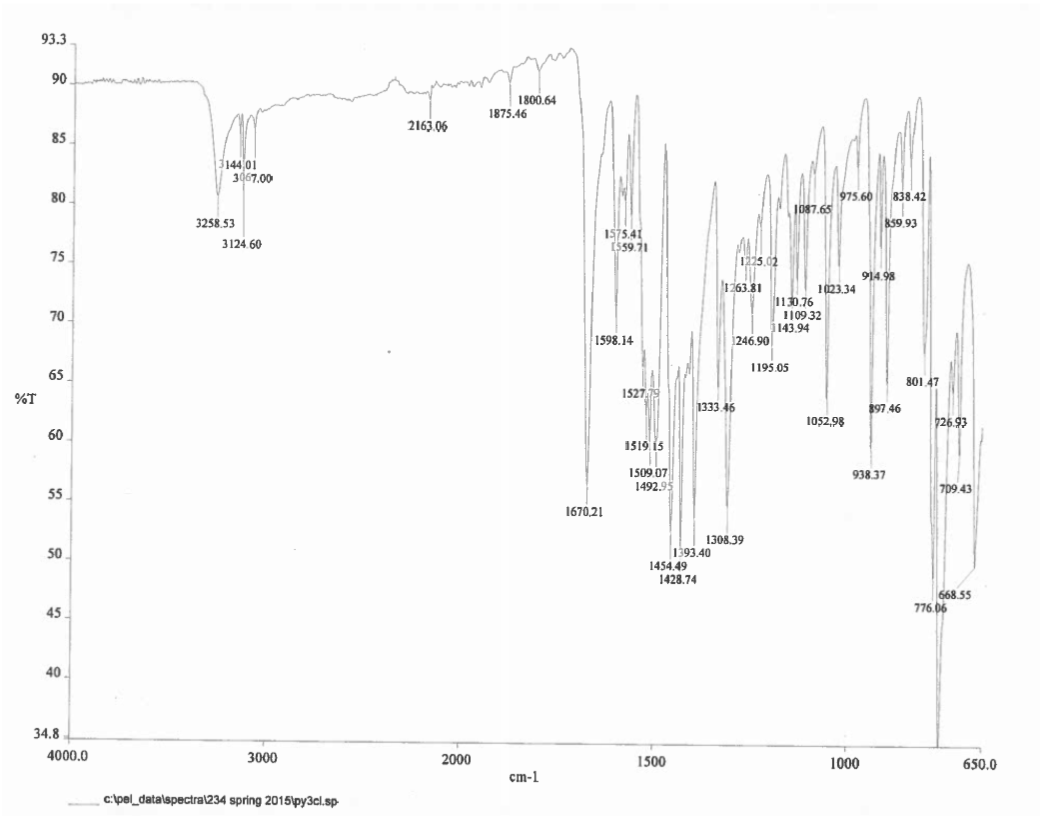
Yuning_CARBON01
168.68
162.15
141.21
134.47
130.55
130.18
129.48
127.90
126.04
124.73
123.52
122.07
118.94
118.66
114.88
107.46
77.24 cdcl3
77.19
76.99 cdcl3
76.73 cdcl3
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

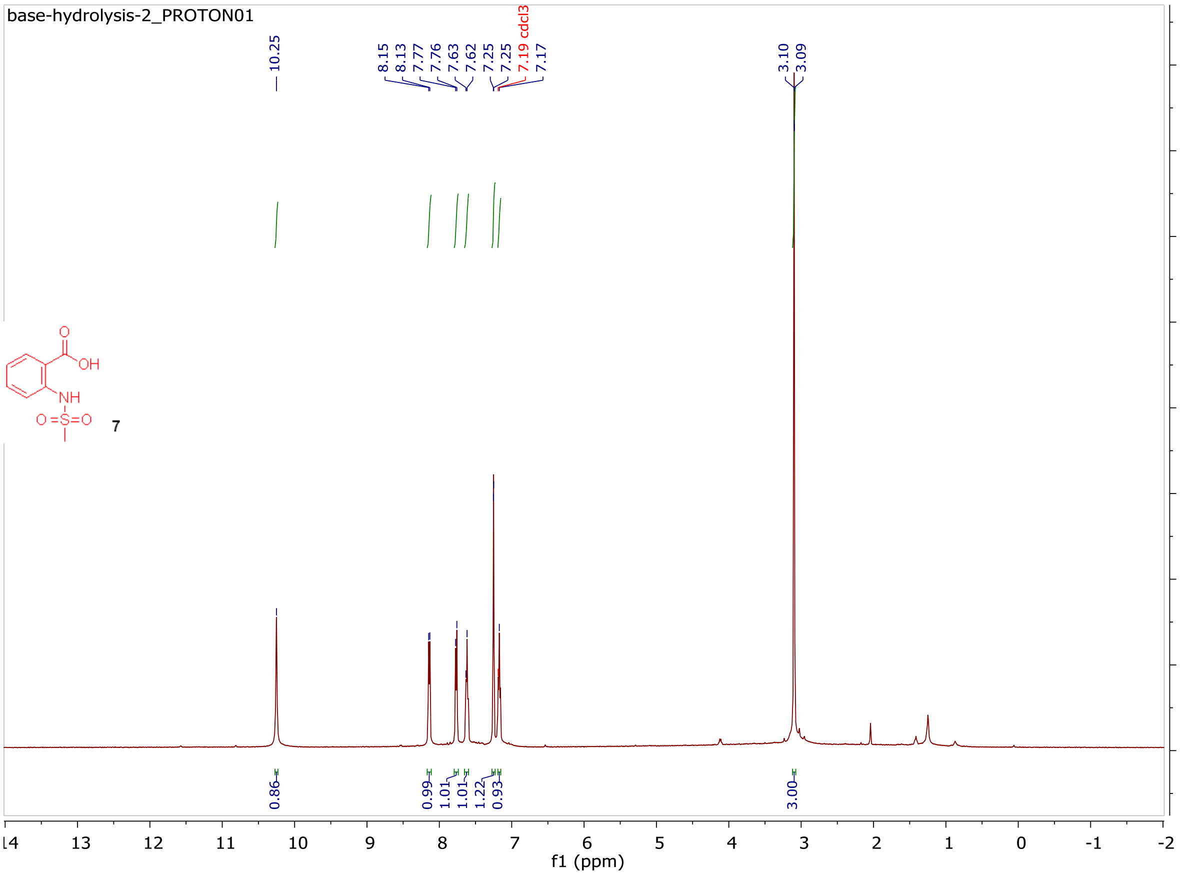


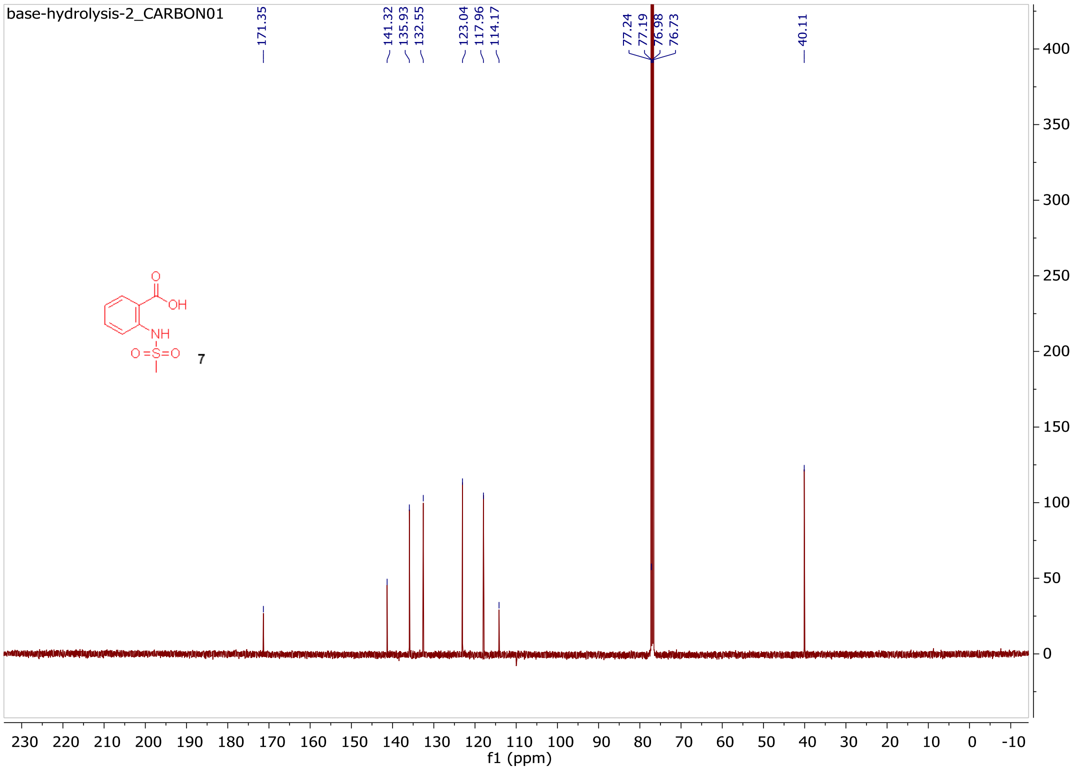
Cl
O
NH
Cl
N
N
6
ROTON01
10.56
8.55
8.55
8.53
8.53
7.82
7.81
7.66
7.66
7.43
7.43
7.38
7.37
7.36
7.33
7.33
7.31
7.28
7.27
7.27
7.26
7.26
7.25
6.46
6.46
6.46
1.06
0.97
1.81
5.57
1.00
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)

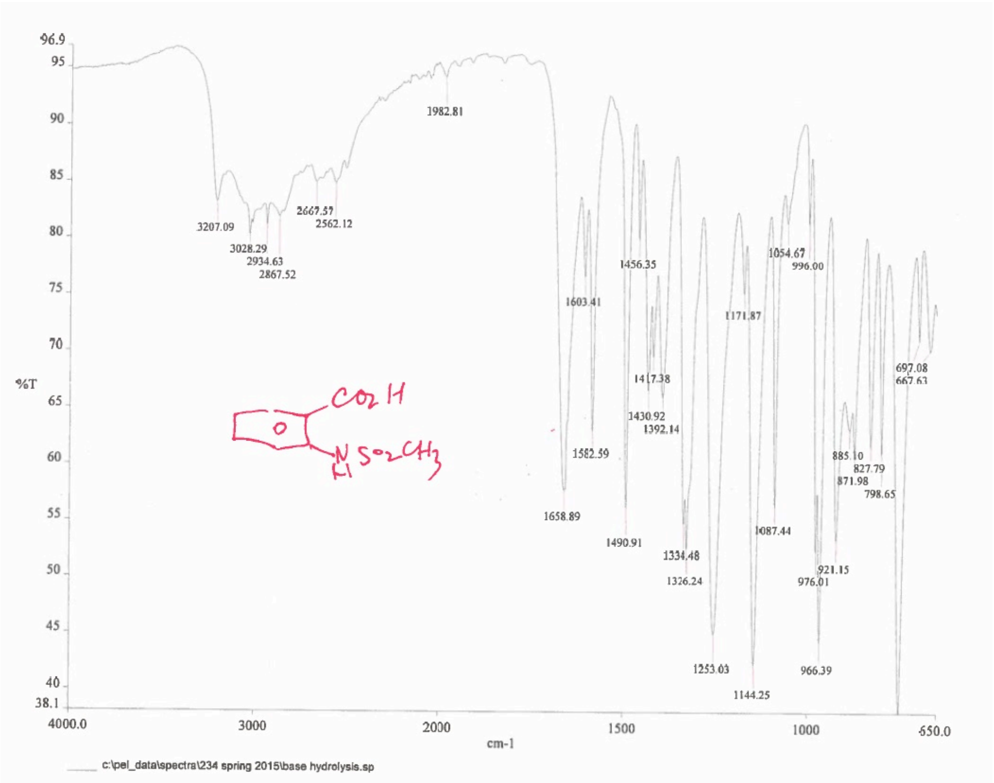


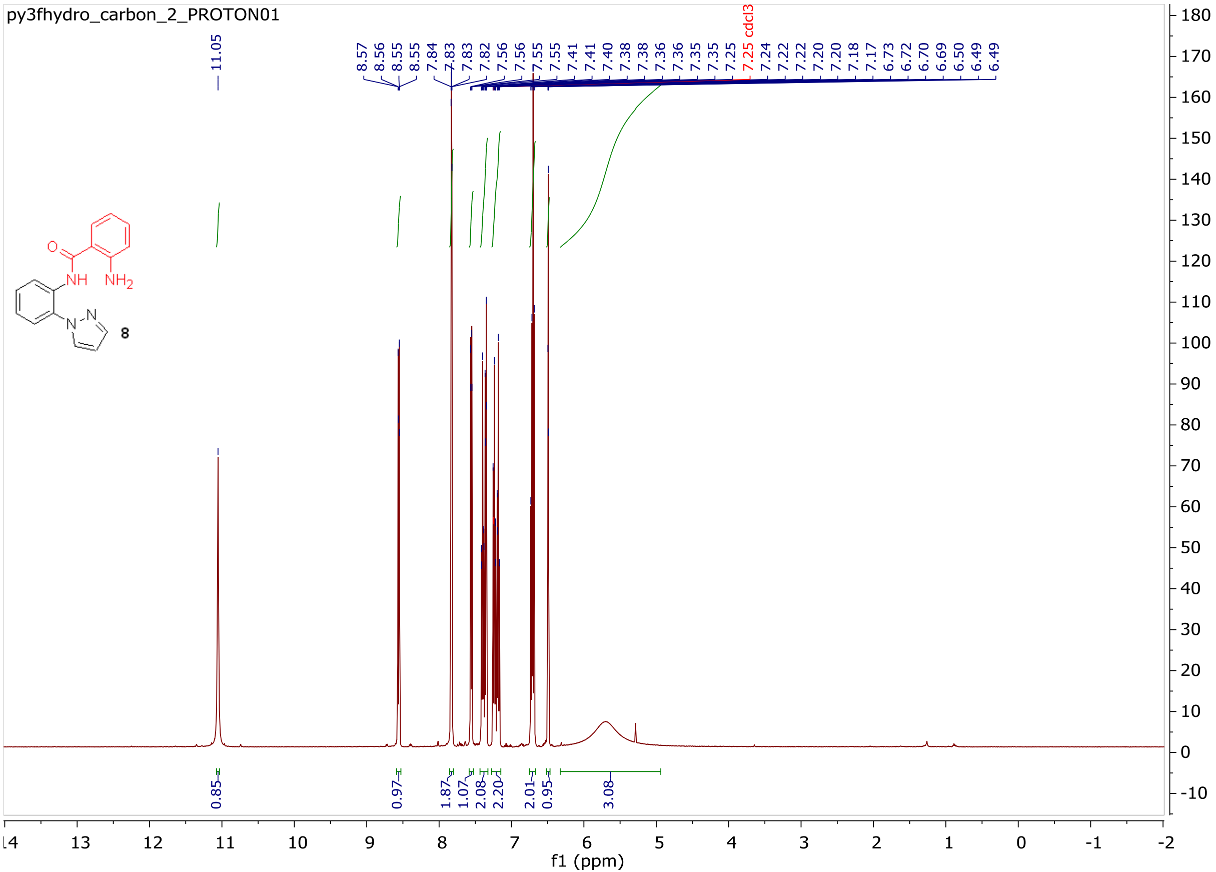

File :C:\msdchem\1\DATA\CY\PY-SM.D\4,4-DIMETHYL-2-PHENYL-2-OXAZOLI
.. NE.MPY3CL.D
Operator :
Instrument : GCMS
Acquired : 2 Apr 2016 12:51 using AcqMethod YSHEN-SULFONYLATION1.M
Sample Name:
Misc Info :

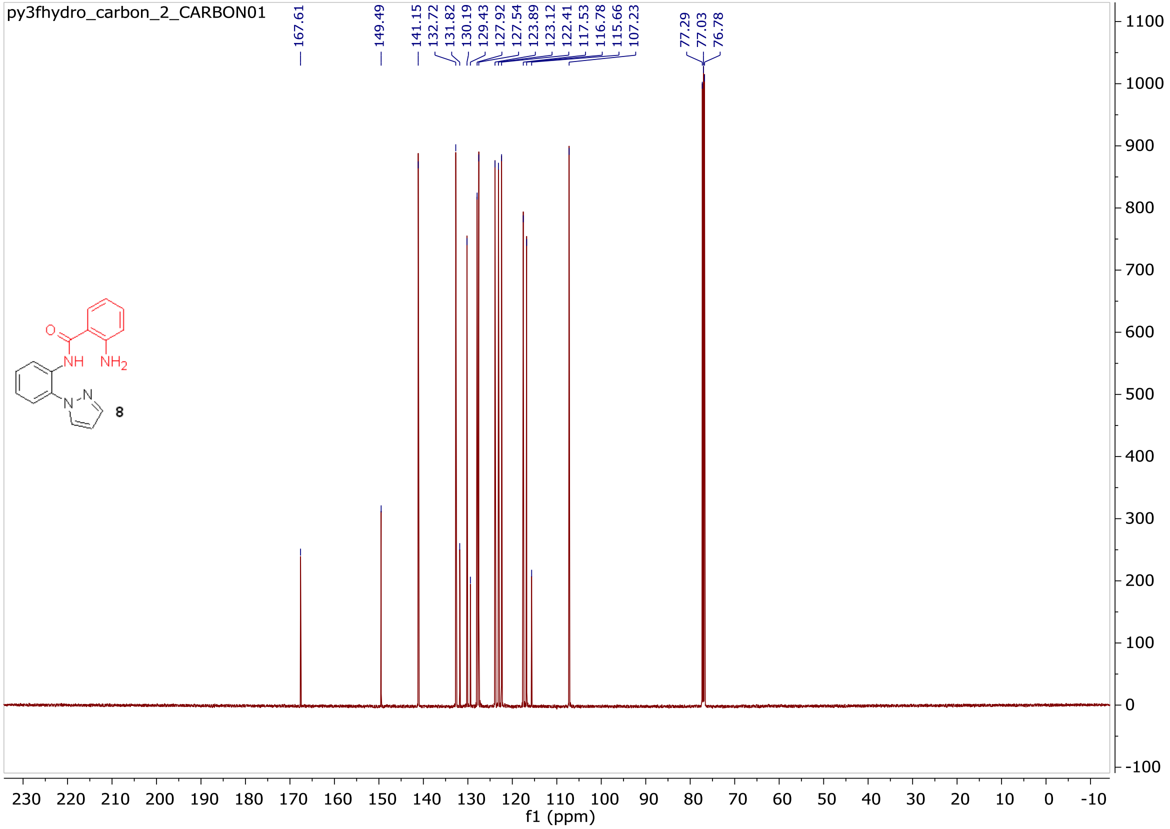

93.3
90
85
80
75
70
65
60
55
50
45
40
34.8
%T
4000.0
3000
2000
1500
1000
650.0
cm-1
3258.53
3144.01
3067.00
3124.60
2163.06
1875.46
1800.64
1670.21
1598.14
1575.41
1559.71
1527.79
1519.15
1509.07
1492.95
1454.49
1428.74
1393.40
1333.46
1308.39
1263.81
1246.90
1225.02
1195.05
1143.94
1130.76
1109.32
1087.65
1052.98
1023.34
975.60
938.37
914.98
897.46
859.93
838.42
801.47
776.06
726.93
709.43
668.55
c:\pel_data\spectra\234 spring 2015\py3cl.sp

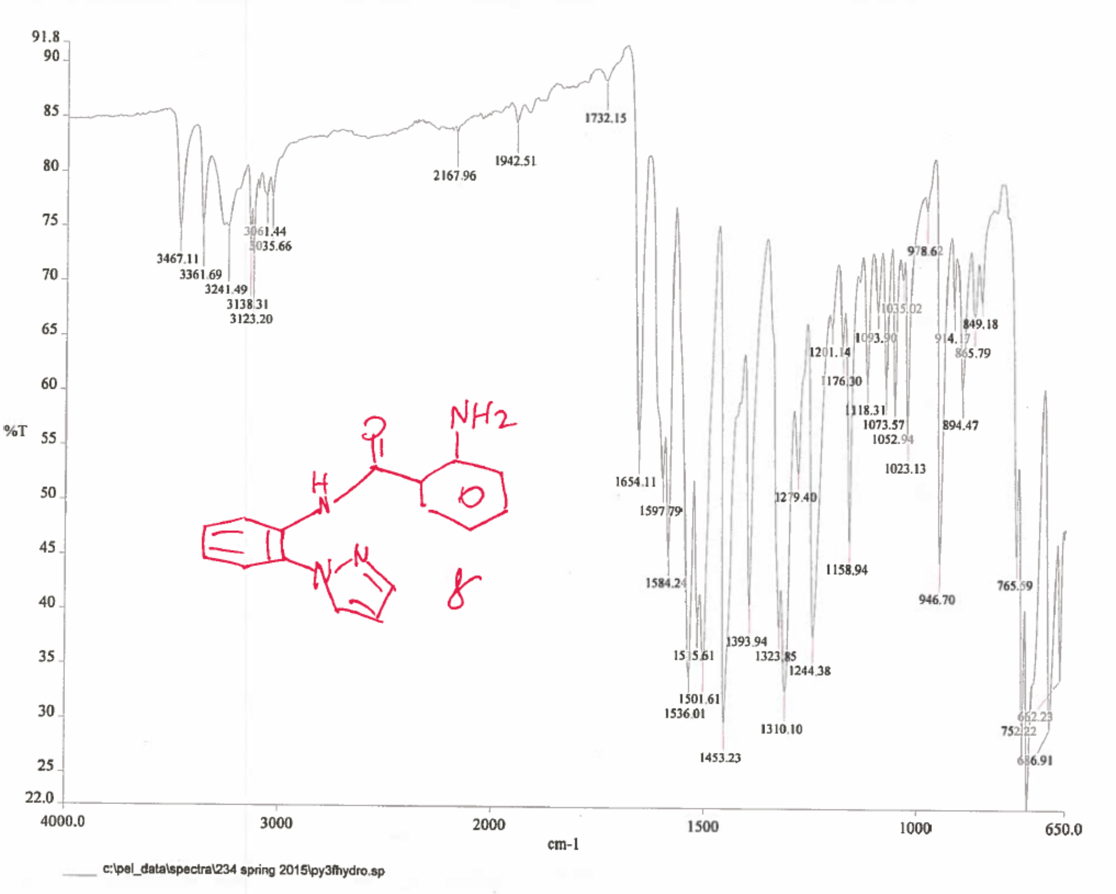

base-hydrolysis-2_PROTON01
10.25
8.15
8.13
7.77
7.76
7.63
7.62
7.25
7.25
7.19 cdcl3
7.17
3.10
3.09
O
OH
NH
O=S=O
7
0.86
0.99
1.01
1.01
1.22
0.93
3.00
4000
3500
3000
2500
2000
1500
1000
500
0
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)


base-hydrolysis-2_CARBON01
171.35
141.32
135.93
132.55
123.04
117.96
114.17
77.24
77.19
76.98
76.73
40.11
O
OH
NH
O=S=O
7
400
350
300
250
200
150
100
50
0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


96.9
95
90
85
80
75
70
65
60
55
50
45
40
38.1
%T
3207.09
3028.29
2934.63
2867.52
2667.57
2562.12
1982.81
1658.89
1603.41
1582.59
1490.91
1456.35
1417.38
1430.92
1392.14
1334.48
1326.24
1253.03
1171.87
1144.25
1087.44
1054.67
996.00
976.01
966.39
921.15
885.10
871.98
827.79
798.65
697.08
667.63
CO2H
N SO2CH3
H
4000.0
3000
2000
1500
1000
650.0
cm-1
c:\pel_data\spectra\234 spring 2015\base hydrolysis.sp

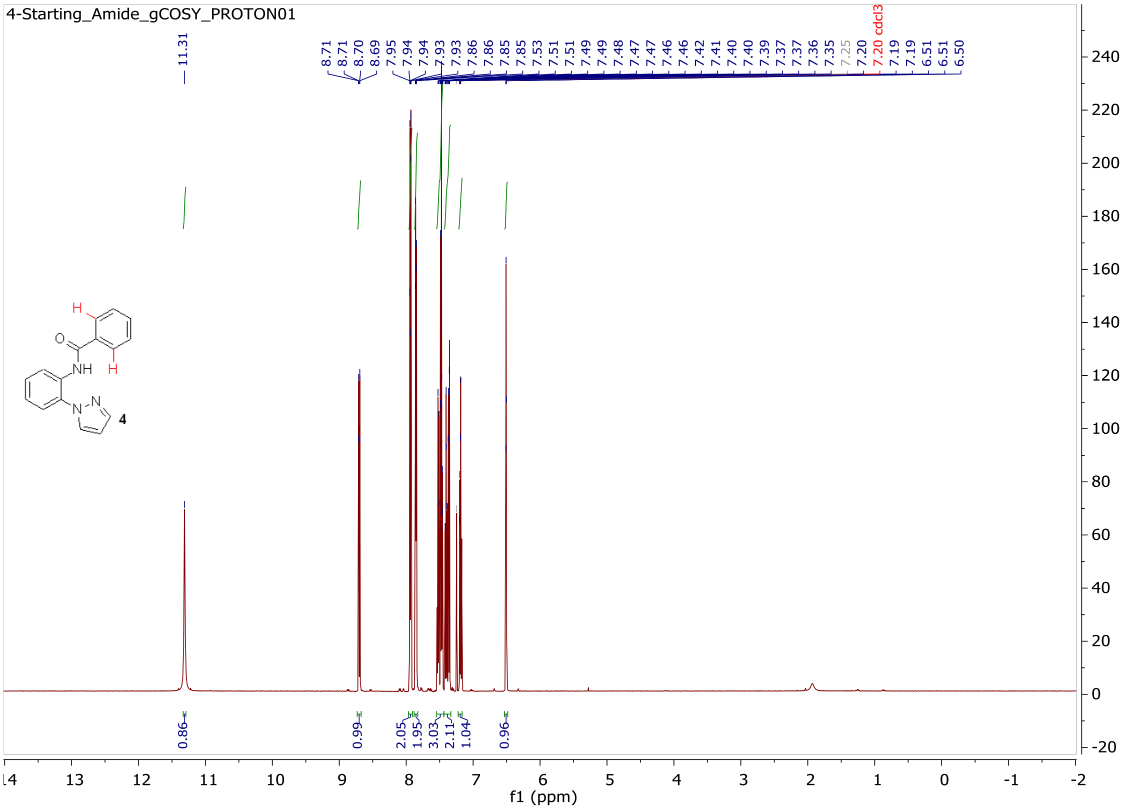

py3fhydro_carbon_2_PROTON01
11.05
8.57
8.56
8.55
8.55
7.84
7.83
7.83
7.82
7.56
7.56
7.55
7.55
7.41
7.40
7.38
7.38
7.36
7.36
7.35
7.35
7.25
7.25 cdcl3
7.24
7.22
7.22
7.20
7.20
7.18
7.17
6.73
6.72
6.70
6.69
6.50
6.49
6.49
O
NH
NH2
N
N
8
0.85
0.97
1.87
1.07
2.08
2.20
2.01
0.95
3.08
f1 (ppm)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

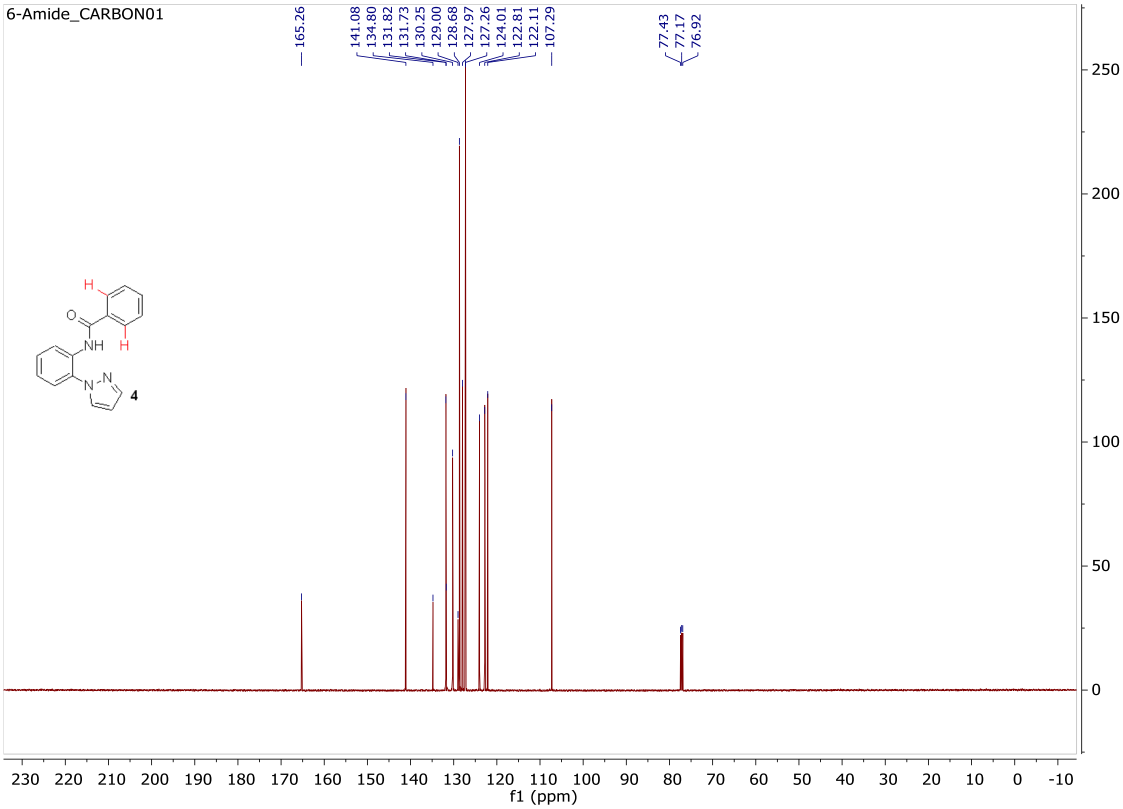

py3fhydro_carbon_2_CARBON01
167.61
149.49
141.15
132.72
131.82
130.19
129.43
127.92
127.54
123.89
123.12
122.41
117.53
116.78
115.66
107.23
77.29
77.03
76.78
O
NH
NH2
N
N
8
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
1100
1000
900
800
700
600
500
400
300
200
100
0
-100


91.8
90
85
80
75
70
65
60
%T
55
50
45
40
35
30
25
22.0
4000.0
3000
2000
1500
1000
650.0
cm-1
3467.11
3361.69
3241.49
3138.31
3123.20
3061.44
3035.66
2167.96
1942.51
1732.15
1654.11
1597.79
1584.24
1515.61
1501.61
1536.01
1453.23
1393.94
1323.85
1310.10
1279.40
1244.38
1201.14
1176.30
1158.94
1118.31
1093.90
1073.57
1052.94
1035.02
1023.13
978.62
946.70
914.17
894.47
865.79
849.18
765.59
752.22
662.23
686.91
NH2
H
N
O
N
N
8
c:\pel_data\spectra\234 spring 2015\py3fhydro.sp

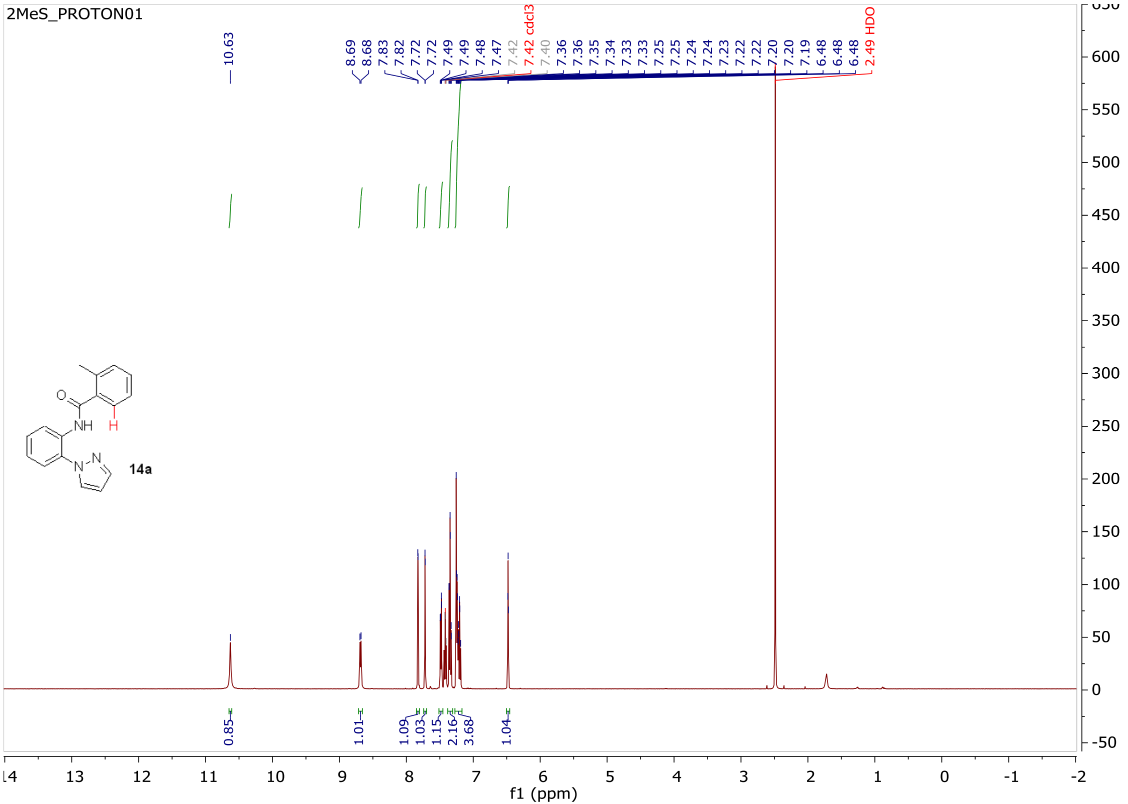
S

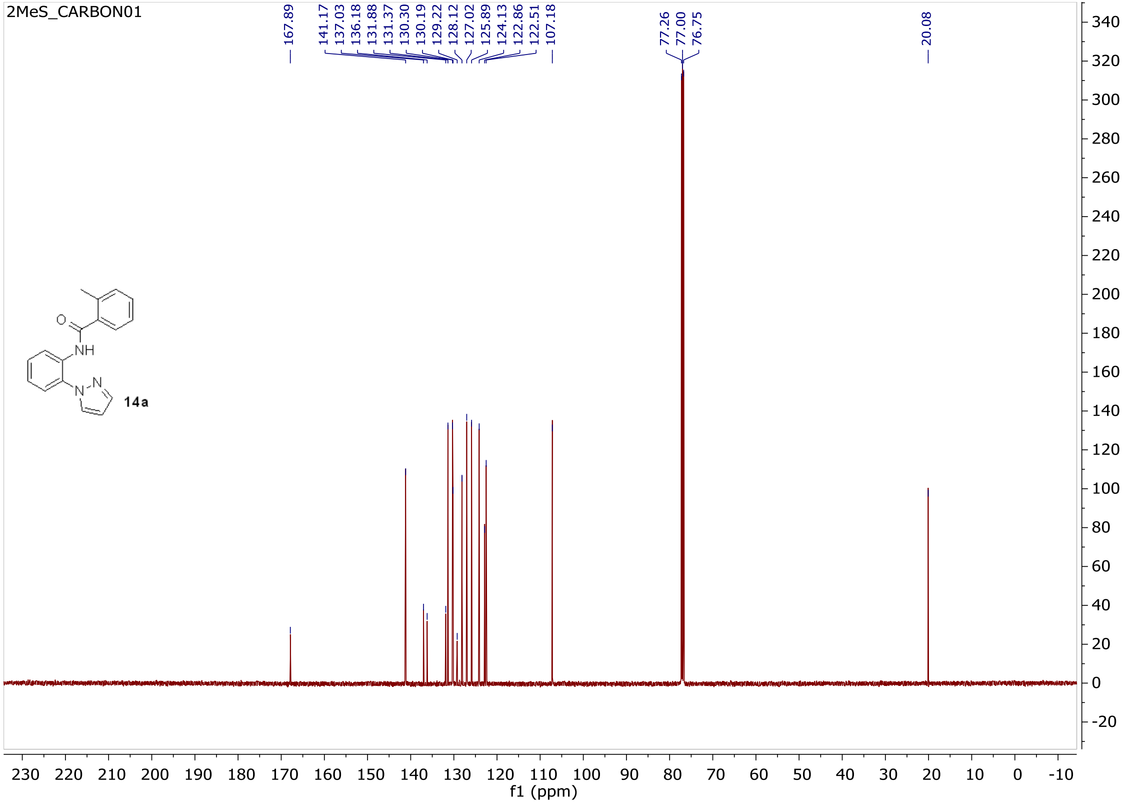
5. NMR Spectra of Substrates



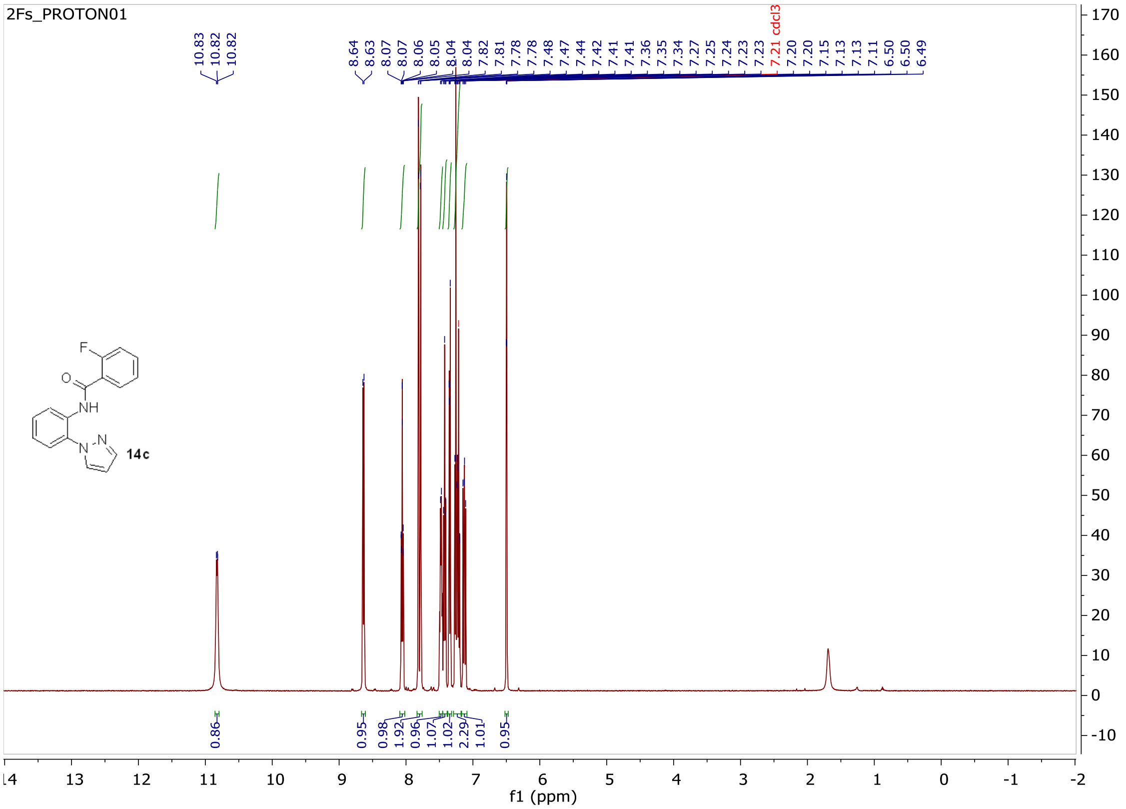


SI: C-H Chlorination

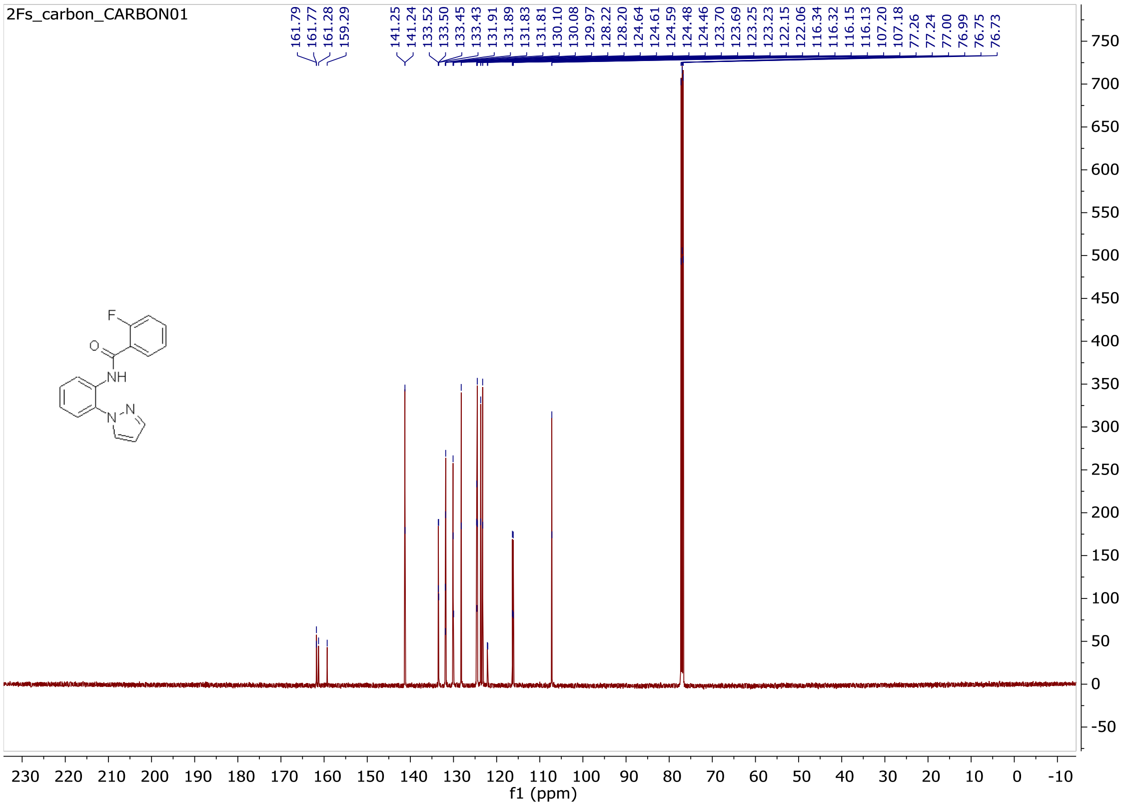




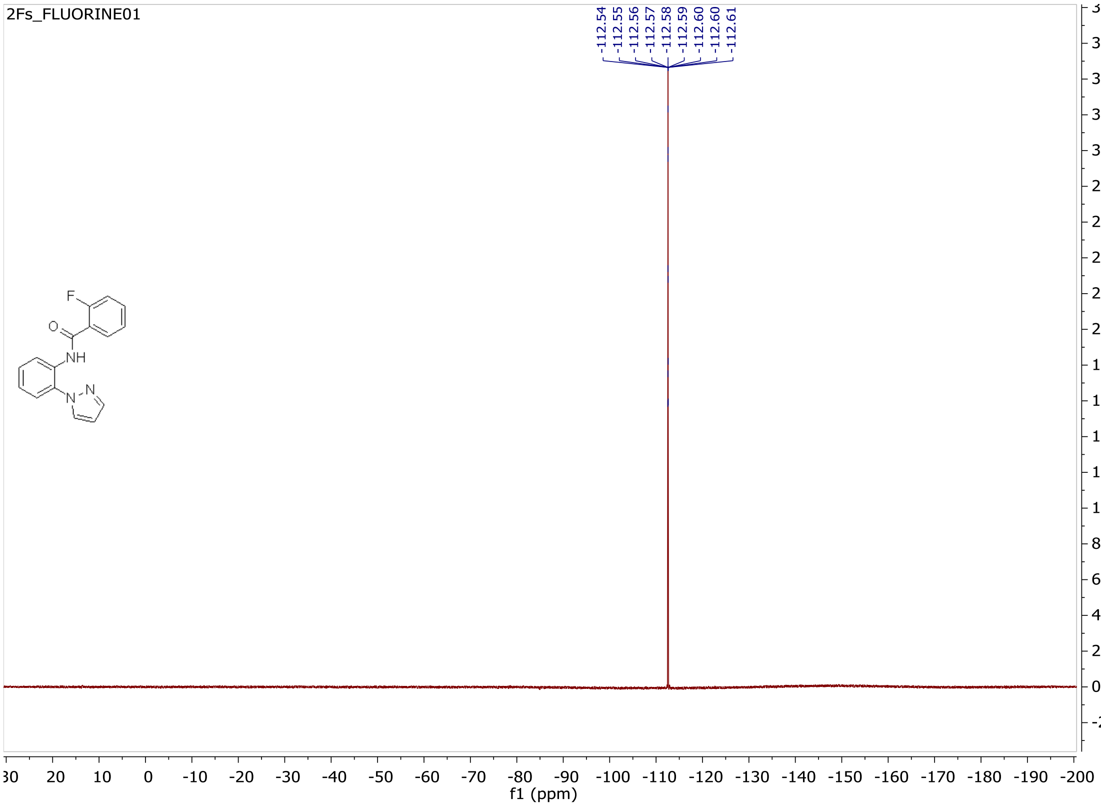
14b


2Fs_PROTON01
10.83
10.82
10.82
8.64
8.63
8.07
8.07
8.06
8.05
8.04
8.04
7.82
7.81
7.78
7.78
7.48
7.47
7.44
7.42
7.41
7.41
7.36
7.35
7.34
7.27
7.25
7.24
7.23
7.23
7.21 cdcl3
7.20
7.20
7.15
7.13
7.13
7.11
6.50
6.50
6.49
0.86
0.95
0.98
1.92
0.96
1.07
1.02
2.29
1.01
0.95
F
O
NH
N
N
14c
f1 (ppm)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

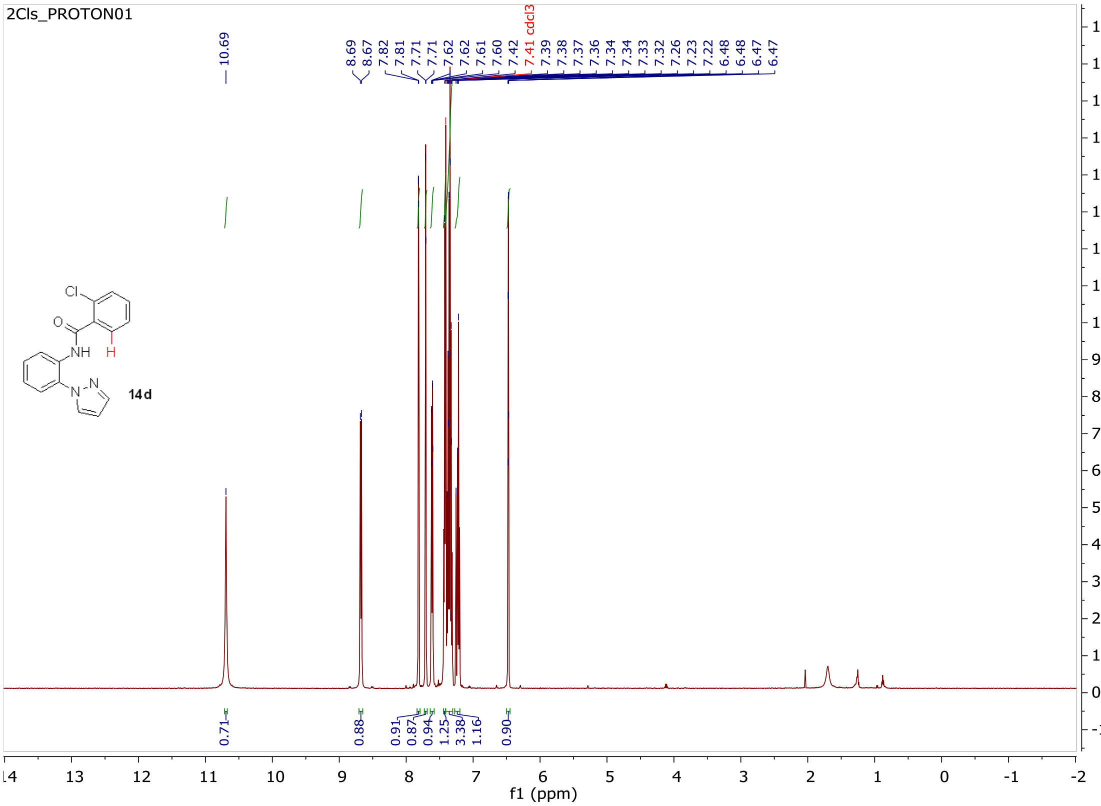
14b


2Fs_carbon_CARBON01
161.79
161.77
161.28
159.29
141.25
141.24
133.52
133.50
133.45
133.43
131.91
131.89
131.83
131.81
130.10
130.08
129.97
128.22
128.20
124.64
124.61
124.59
124.48
124.46
123.70
123.69
123.25
123.23
122.15
122.06
116.34
116.32
116.15
116.13
107.20
107.18
77.26
77.24
77.00
76.99
76.75
76.73
F
O
NH
N
N
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50

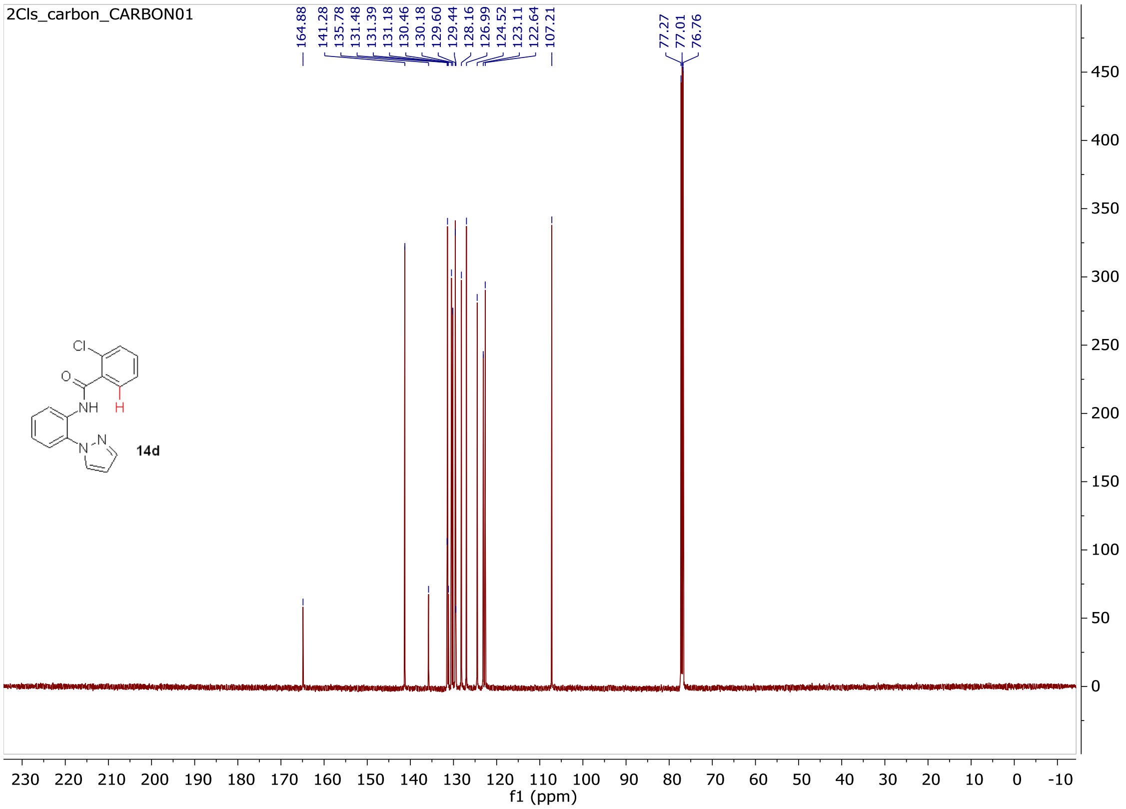
14b


2Fs_FLUORINE01
-112.54
-112.55
-112.56
-112.57
-112.58
-112.59
-112.60
-112.60
-112.61
F
O
NH
N
N
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

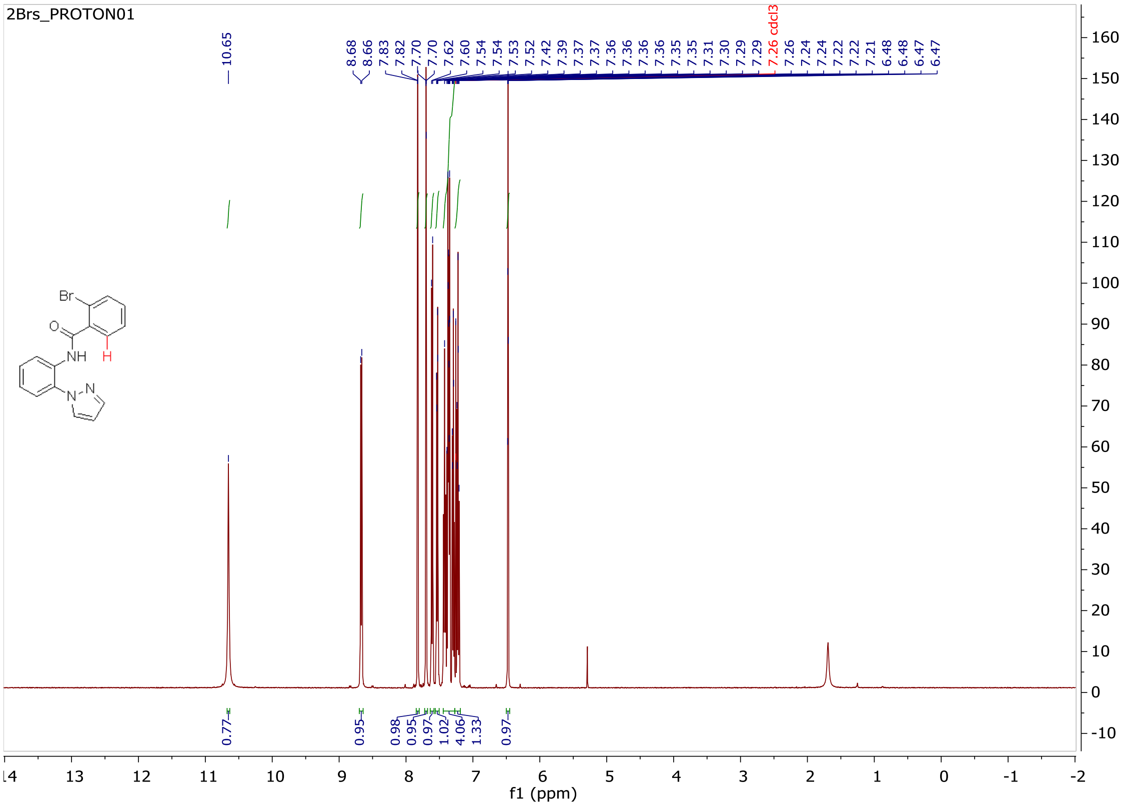
14c


2Cls_PROTON01
10.69
8.69
8.67
7.82
7.81
7.71
7.71
7.62
7.62
7.61
7.60
7.42
7.41 cdcl3
7.39
7.38
7.37
7.36
7.34
7.34
7.33
7.32
7.26
7.23
7.22
6.48
6.48
6.47
6.47
Cl
O
NH
H
N
N
14d
0.71
0.88
0.91
0.87
0.94
1.25
3.38
1.16
0.90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)

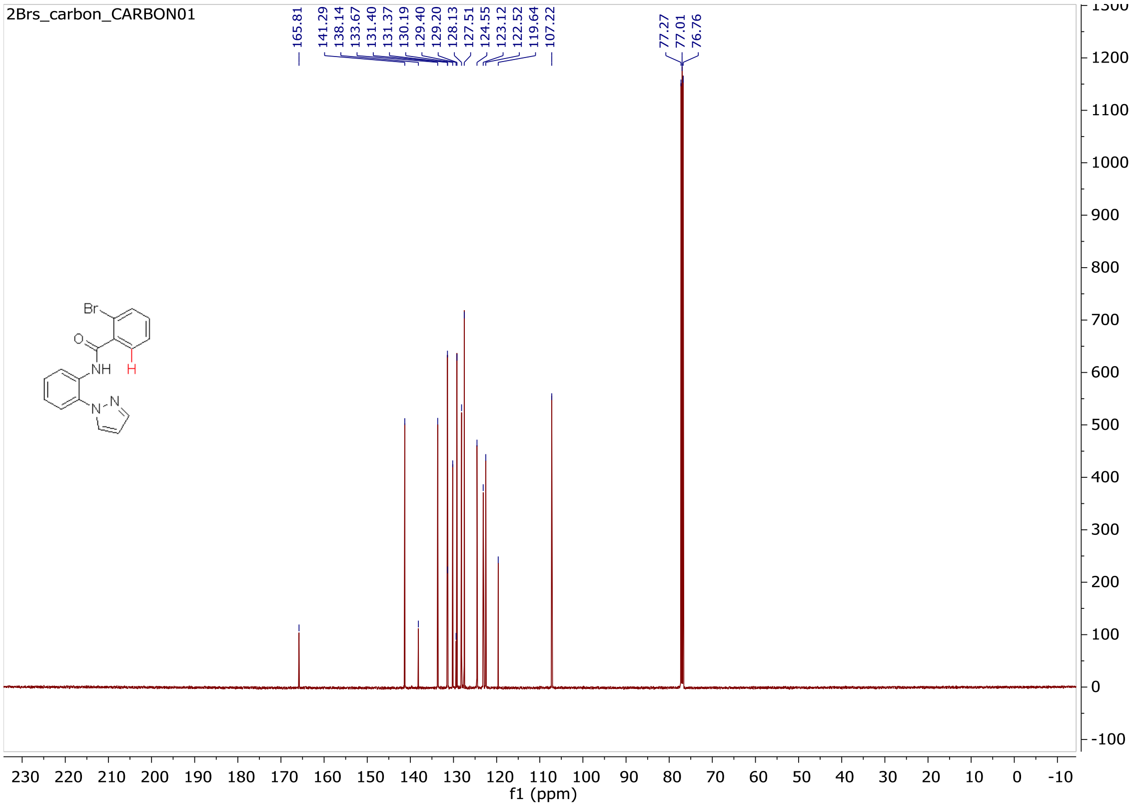
14c


2Cls_carbon_CARBON01
164.88
141.28
135.78
131.48
131.39
131.18
130.46
130.18
129.60
129.44
128.16
126.99
124.52
123.11
122.64
107.21
77.27
77.01
76.76
Cl
O
NH
H
N
N
14d
450
400
350
300
250
200
150
100
50
0
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

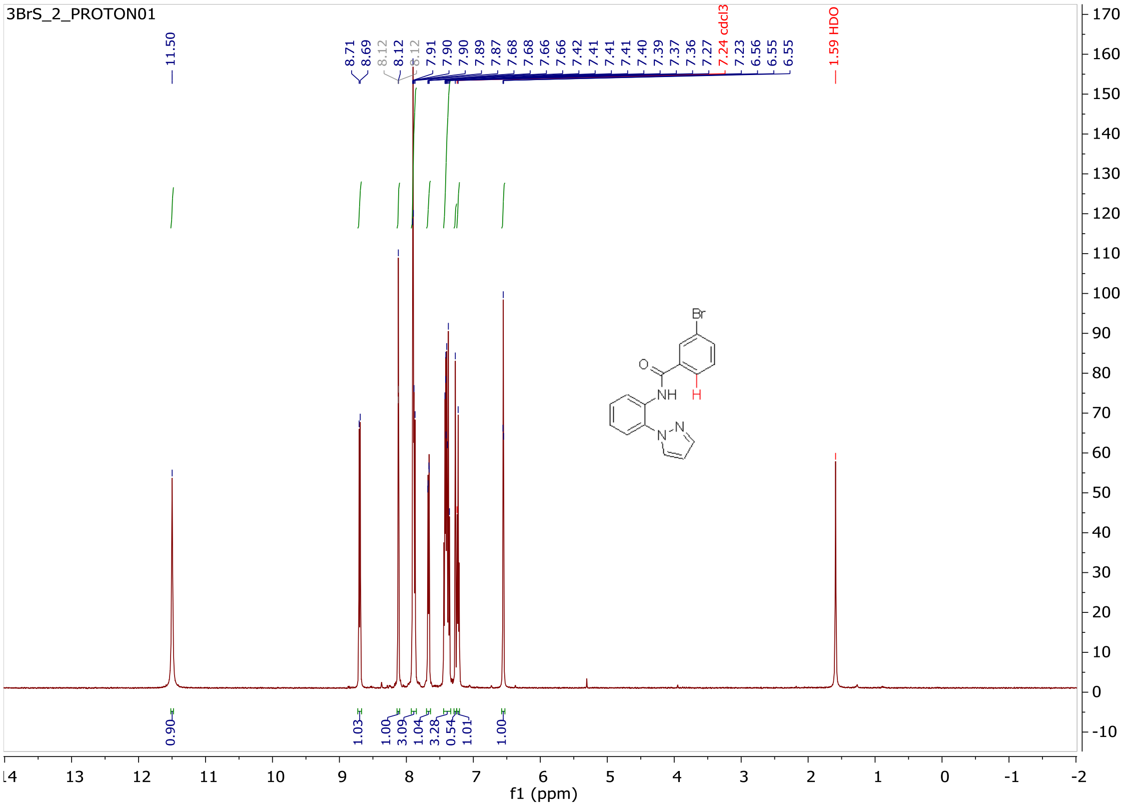
14d


2Brs_PROTON01
10.65
8.68
8.66
7.83
7.82
7.70
7.70
7.62
7.60
7.54
7.54
7.53
7.52
7.42
7.39
7.37
7.37
7.36
7.36
7.36
7.36
7.35
7.35
7.31
7.30
7.29
7.29
7.26 cdcl3
7.26
7.24
7.24
7.22
7.22
7.21
6.48
6.48
6.47
6.47
Br
O
NH
H
N
N
0.77
0.95
0.98
0.95
0.97
1.02
4.06
1.33
0.97
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)

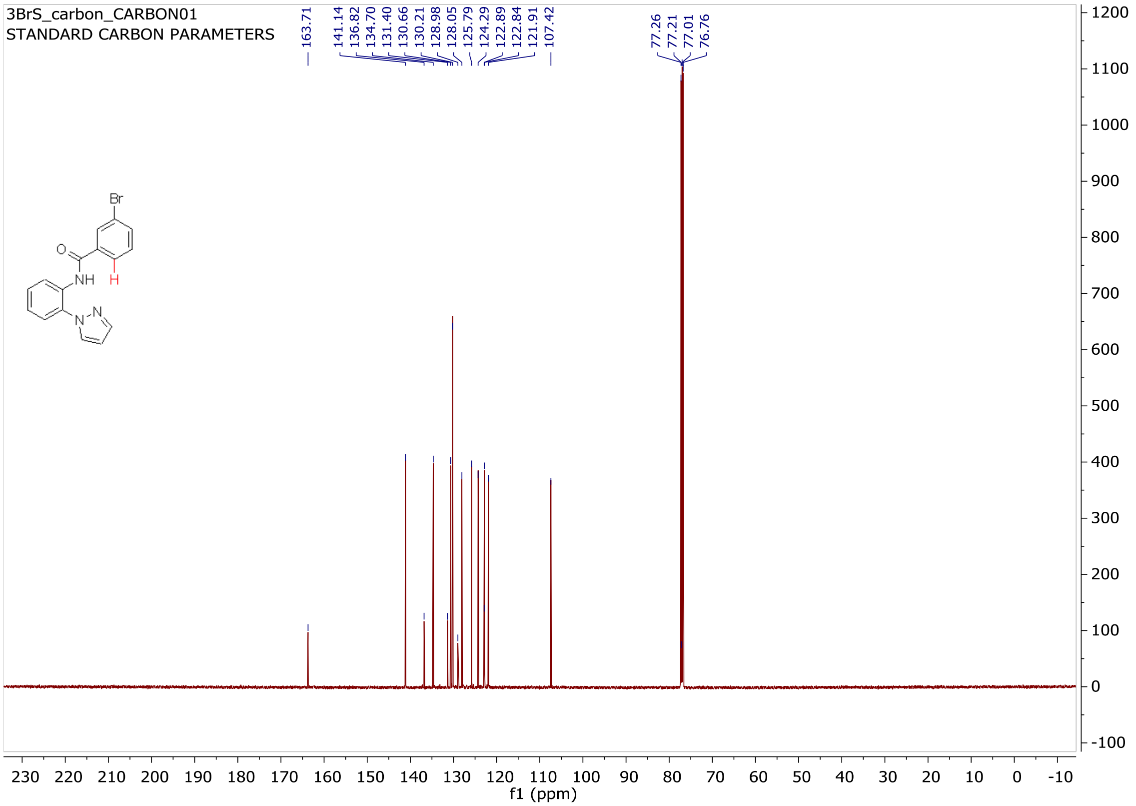
14d


2Brs_carbon_CARBON01
165.81
141.29
138.14
133.67
131.40
131.37
130.19
129.40
129.20
128.13
127.51
124.55
123.12
122.52
119.64
107.22
77.27
77.01
76.76
Br
O
NH
H
N
N
f1 (ppm)

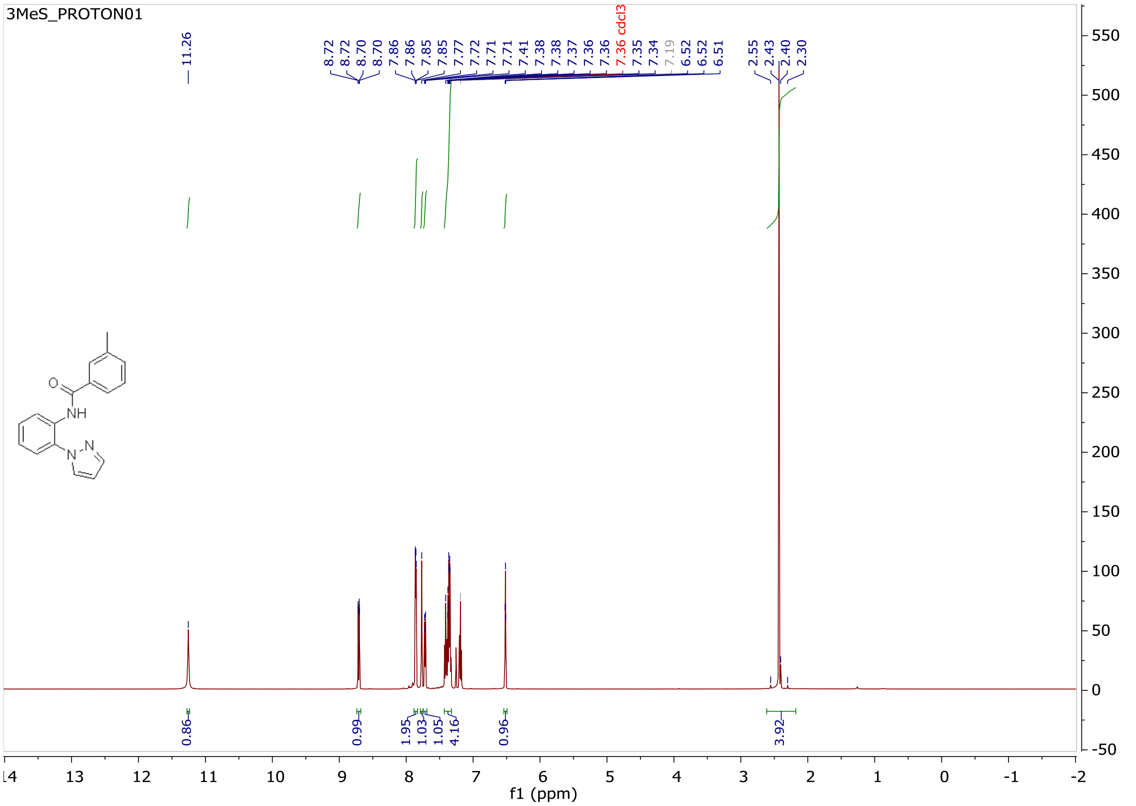
14e


3BrS_2_PROTON01
11.50
8.71
8.69
8.12
8.12
8.12
7.91
7.90
7.90
7.89
7.87
7.68
7.68
7.66
7.66
7.42
7.41
7.41
7.41
7.40
7.39
7.37
7.36
7.27
7.24 cdcl3
7.23
6.56
6.55
6.55
1.59 HDO
Br
O
NH
H
N
N
0.90
1.03
1.00
3.09
1.04
3.28
0.54
1.01
1.00
f1 (ppm)

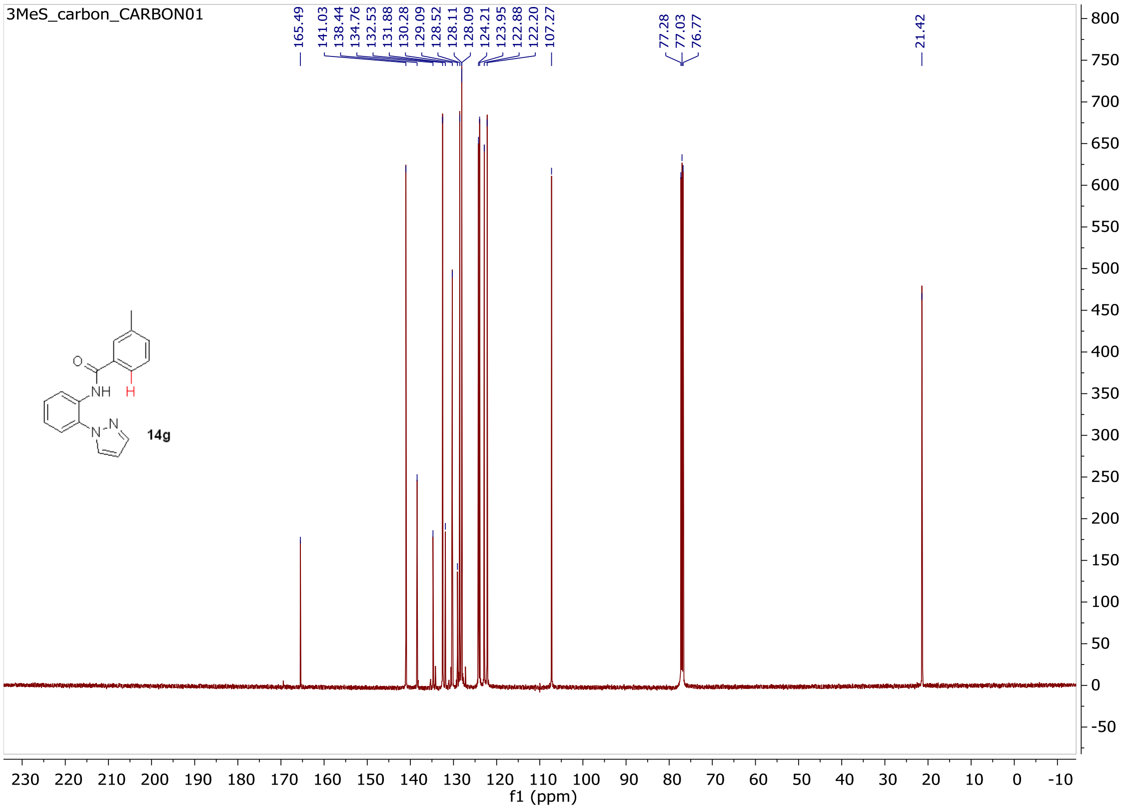
14e


3BrS_carbon_CARBON01
STANDARD CARBON PARAMETERS
163.71
141.14
136.82
134.70
131.40
130.66
130.21
128.98
128.05
125.79
124.29
122.89
122.84
121.91
107.42
77.26
77.21
77.01
76.76
Br
O
NH
H
N
N
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

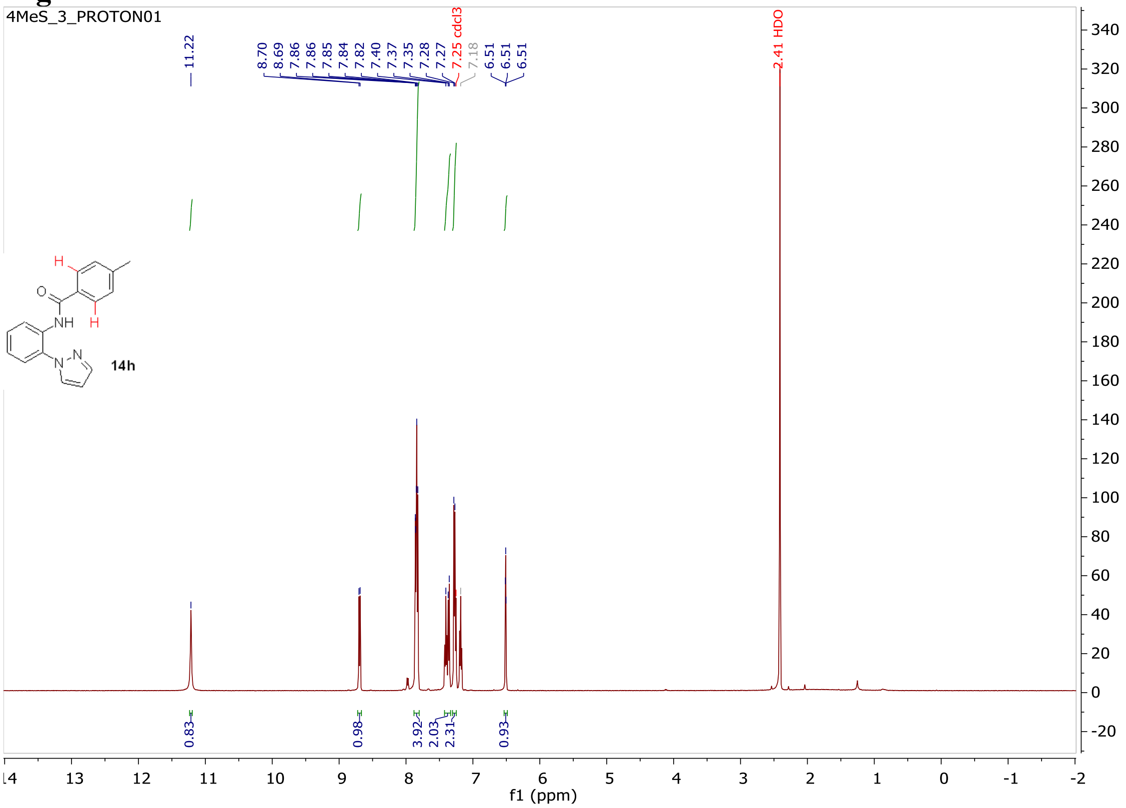
14f


3MeS_PROTON01
11.26
8.72
8.72
8.70
8.70
7.86
7.86
7.85
7.85
7.77
7.72
7.71
7.71
7.41
7.38
7.38
7.37
7.36
7.36
7.36 cdcl3
7.35
7.34
7.19
6.52
6.52
6.51
2.55
2.43
2.40
2.30
O
NH
N
N
0.86
0.99
1.95
1.03
1.05
4.16
0.96
3.92
550
500
450
400
350
300
250
200
150
100
50
0
-50
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)

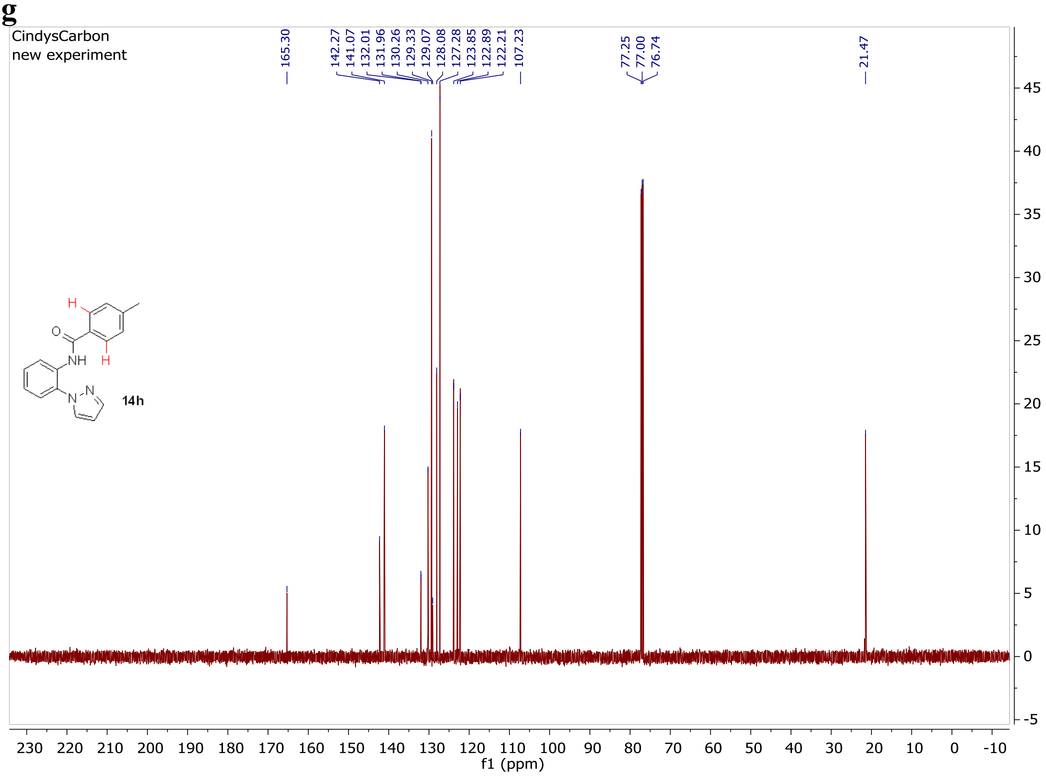
14f


3MeS_carbon_CARBON01
165.49
141.03
138.44
134.76
132.53
131.88
130.28
129.09
128.52
128.11
128.09
124.21
123.95
122.88
122.20
107.27
77.28
77.03
76.77
21.42
O
NH
H
N
N
14g
f1 (ppm)

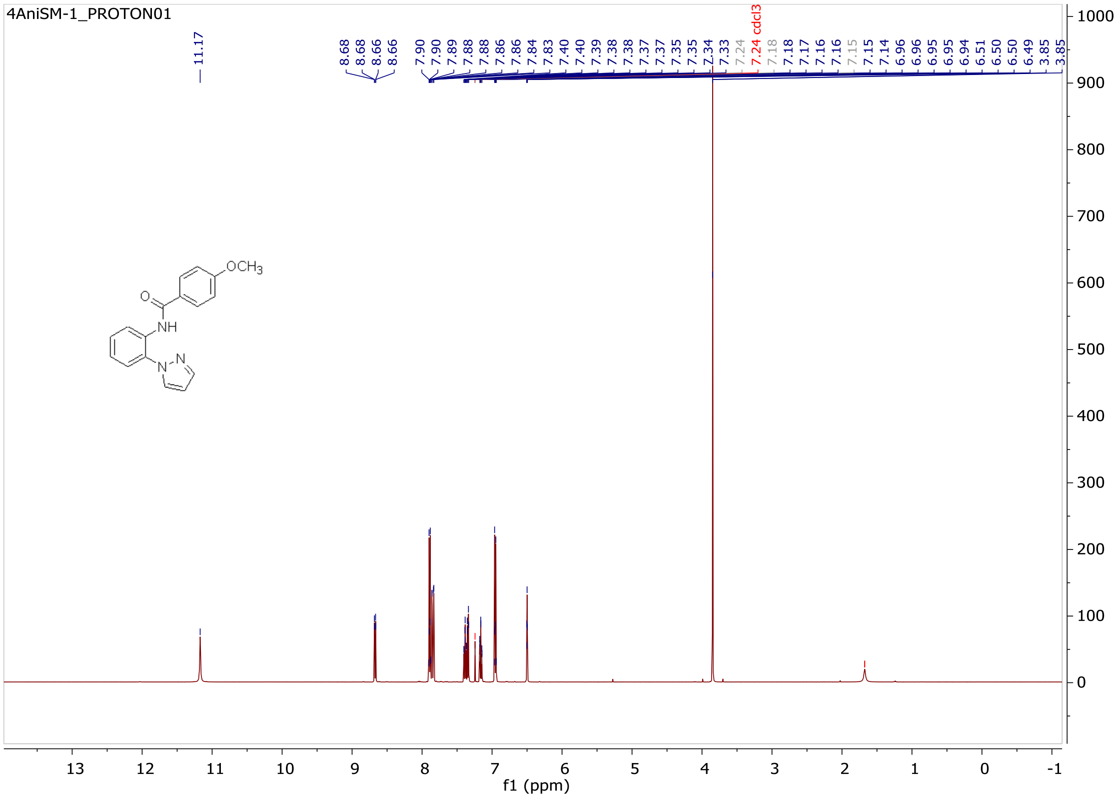
14g


4MeS_3_PROTON01
11.22
8.70
8.69
7.86
7.85
7.84
7.82
7.40
7.37
7.35
7.28
7.27
7.25 cdcl3
7.18
6.51
6.51
6.51
2.41 HDO
H
O
NH
H
N
N
14h
0.83
0.98
3.92
2.03
2.31
0.93
f1 (ppm)

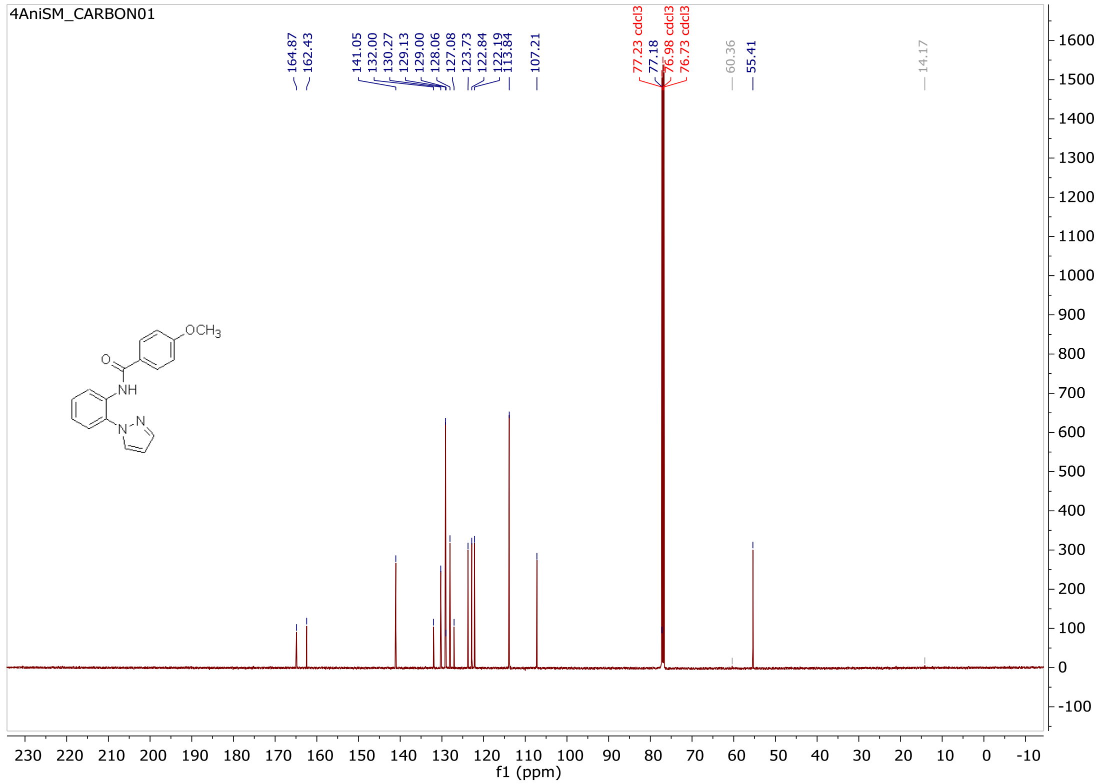
14g


CindysCarbon
new experiment
165.30
142.27
141.07
132.01
131.96
130.26
129.33
129.07
128.08
127.28
123.85
122.89
122.21
107.23
77.25
77.00
76.74
21.47
H
O
NH
H
N
N
14h
45
40
35
30
25
20
15
10
5
0
-5
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

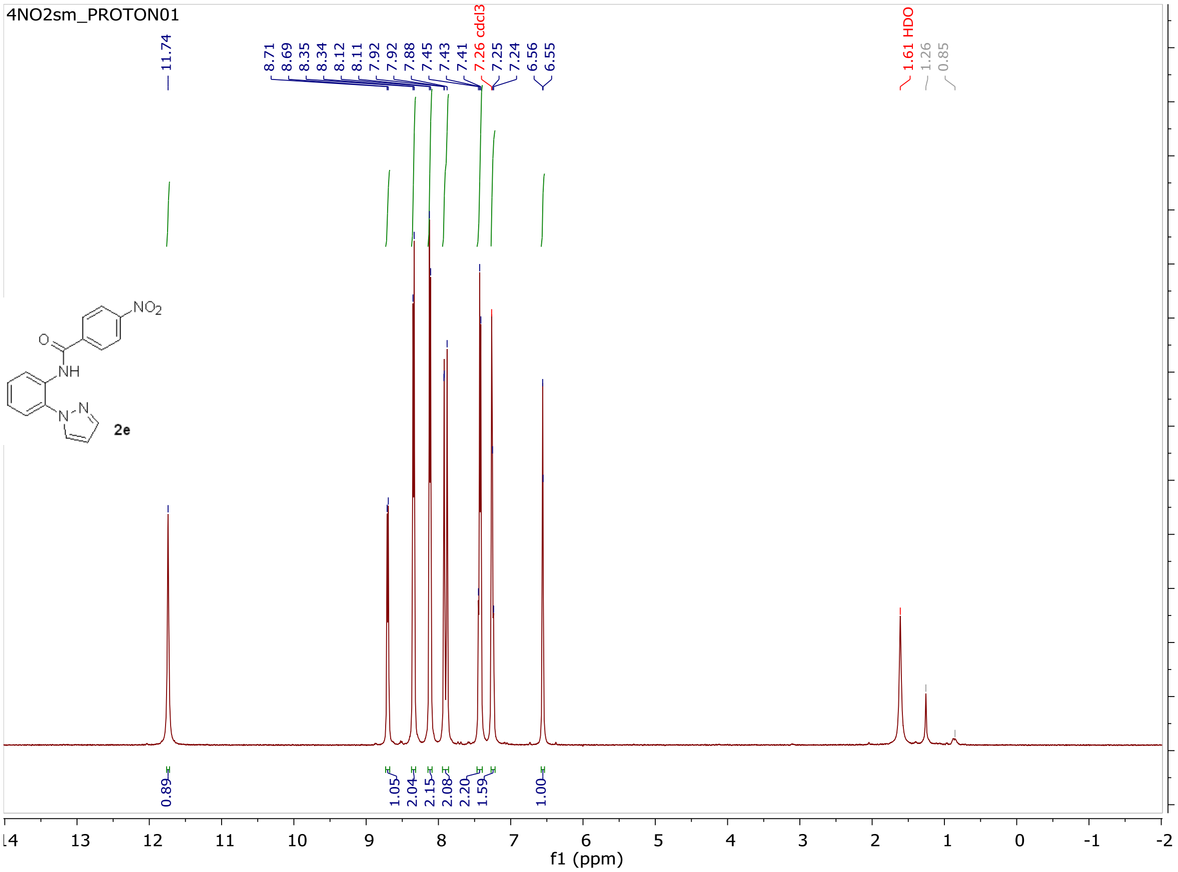
14h


4AniSM-1_PROTON01
11.17
8.68
8.68
8.66
8.66
7.90
7.90
7.89
7.88
7.88
7.86
7.86
7.84
7.83
7.40
7.40
7.39
7.38
7.38
7.37
7.37
7.35
7.35
7.34
7.33
7.24
7.24 cdcl3
7.18
7.17
7.16
7.16
7.15
7.15
7.14
6.96
6.96
6.95
6.95
6.94
6.51
6.50
6.50
6.49
3.85
OCH3
O
NH
N
N
1000
900
800
700
600
500
400
300
200
100
0
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

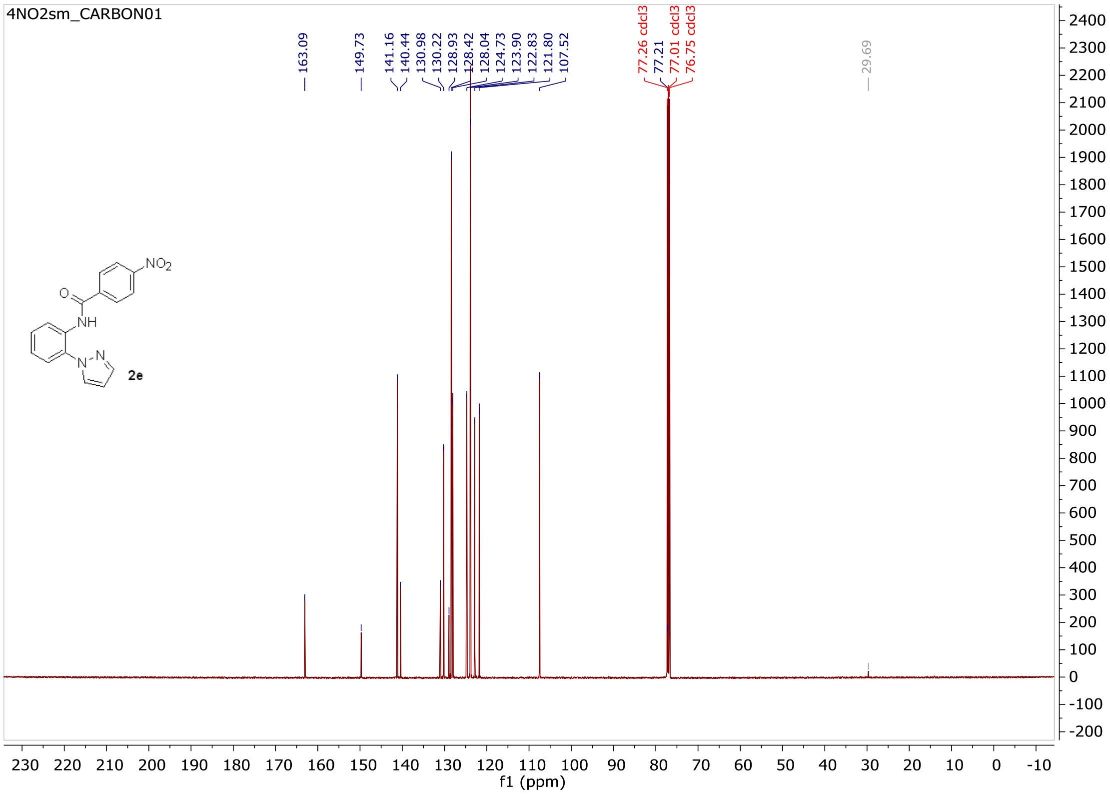
14h


4AniSM_CARBON01
164.87
162.43
141.05
132.00
130.27
129.13
129.00
128.06
127.08
123.73
122.84
122.19
113.84
107.21
77.23 cdcl3
77.18
76.98 cdcl3
76.73 cdcl3
60.36
55.41
14.17
OCH3
O
NH
N
N
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

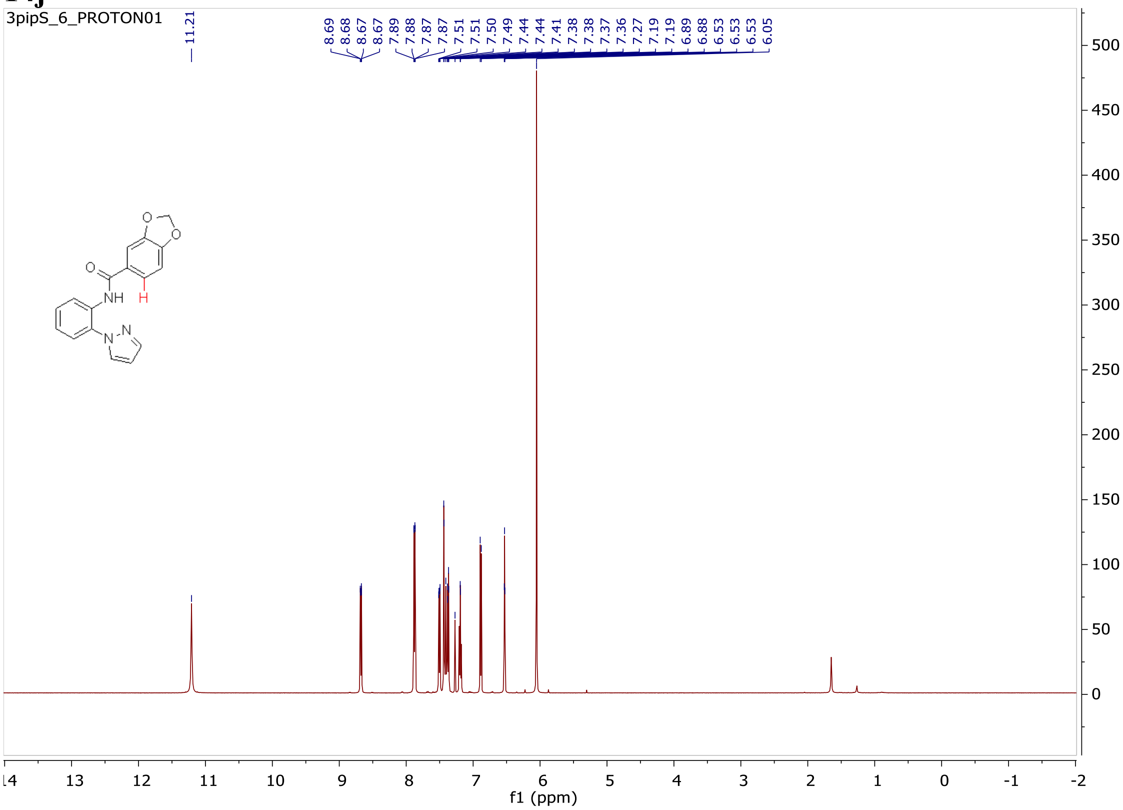
14i


4NO2sm_PROTON01
11.74
8.71
8.69
8.35
8.34
8.12
8.11
7.92
7.92
7.88
7.45
7.43
7.41
7.26 cdcl3
7.25
7.24
6.56
6.55
1.61 HDO
1.26
0.85
0.89
1.05
2.04
2.15
2.08
2.20
1.59
1.00
NO2
O
NH
N
N
2e
f1 (ppm)

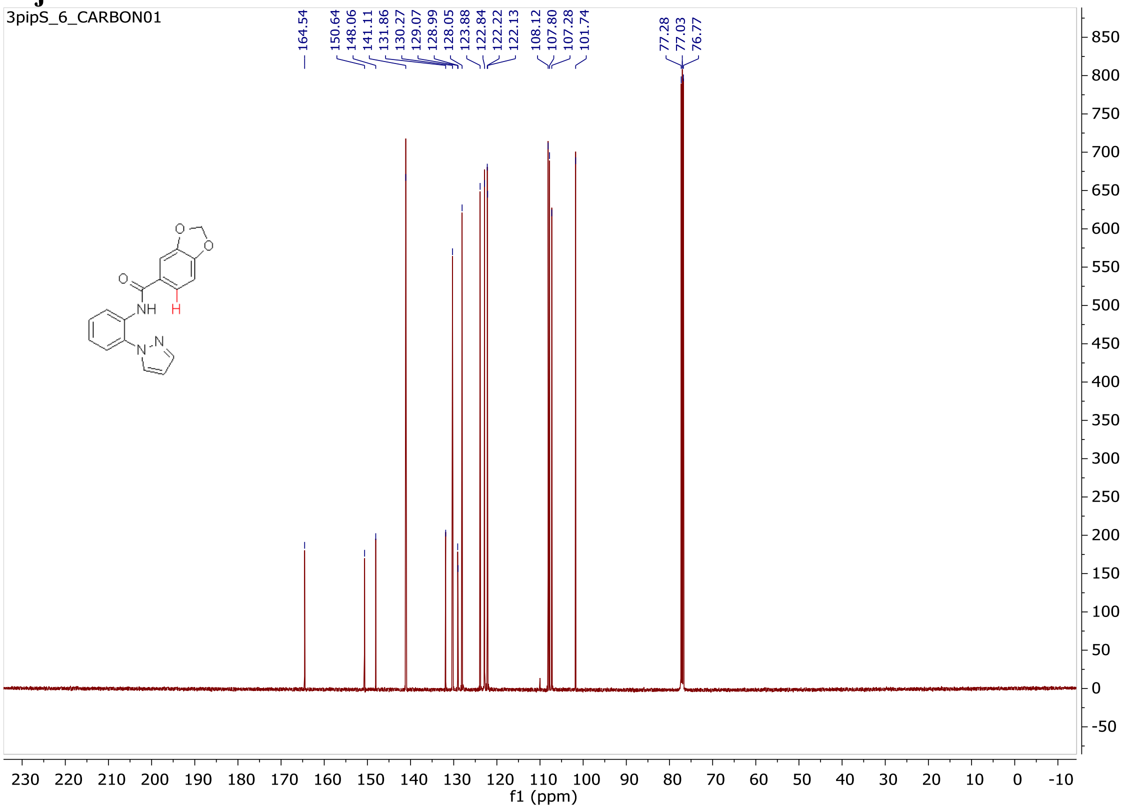
14i


4NO2sm_CARBON01
163.09
149.73
141.16
140.44
130.98
130.22
128.93
128.42
128.04
124.73
123.90
122.83
121.80
107.52
77.26 cdcl3
77.21
77.01 cdcl3
76.75 cdcl3
29.69
NO2
O
NH
N
N
2e
f1 (ppm)

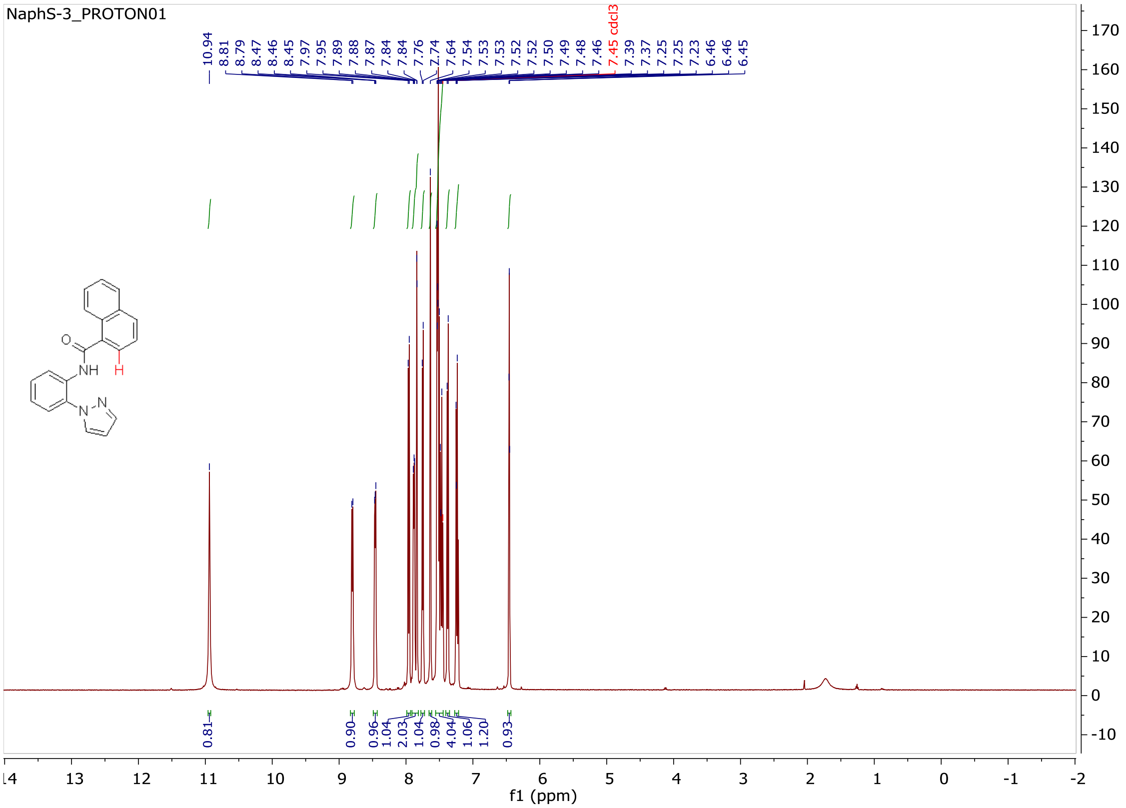
14j


3pipS_6_PROTON01
11.21
8.69
8.68
8.67
8.67
7.89
7.88
7.87
7.87
7.51
7.51
7.50
7.49
7.44
7.44
7.41
7.38
7.38
7.37
7.36
7.27
7.19
7.19
6.89
6.88
6.53
6.53
6.53
6.05
O
O
O
NH
H
N
N
f1 (ppm)

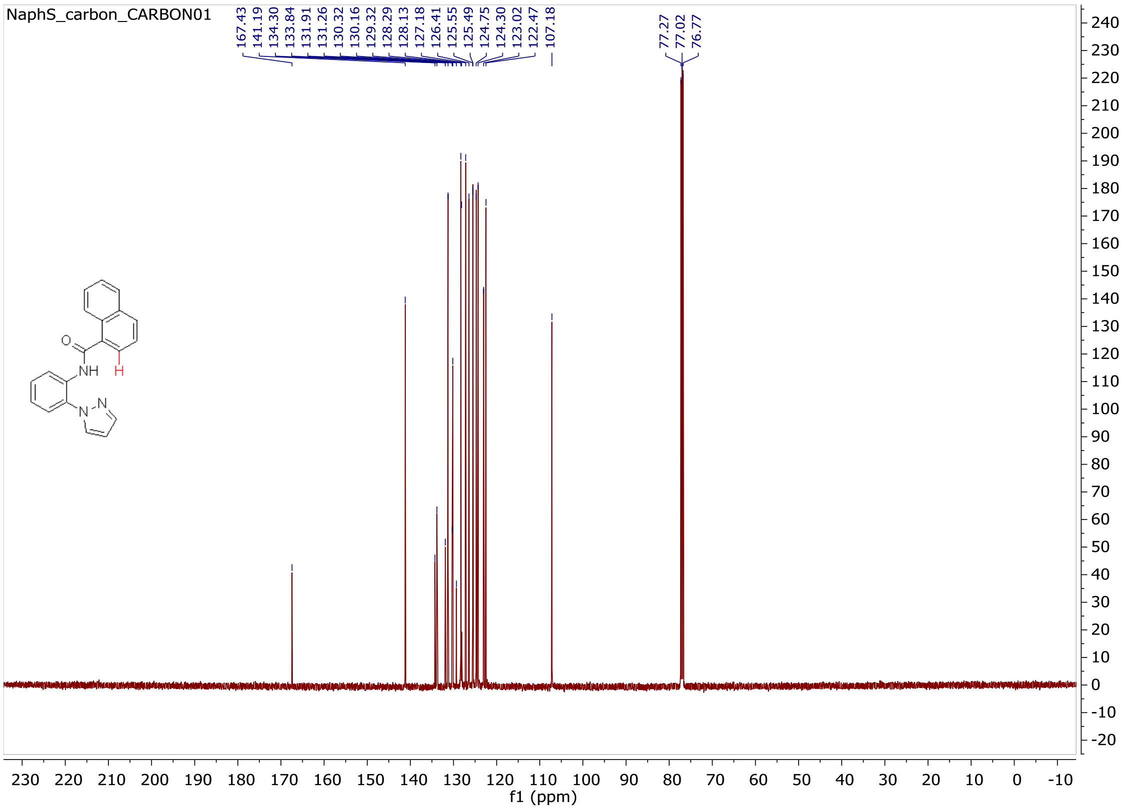
14j


3pipS_6_CARBON01
164.54
150.64
148.06
141.11
131.86
130.27
129.07
128.99
128.05
123.88
122.84
122.22
122.13
108.12
107.80
107.28
101.74
77.28
77.03
76.77
O
O
O
NH
H
N
N
f1 (ppm)

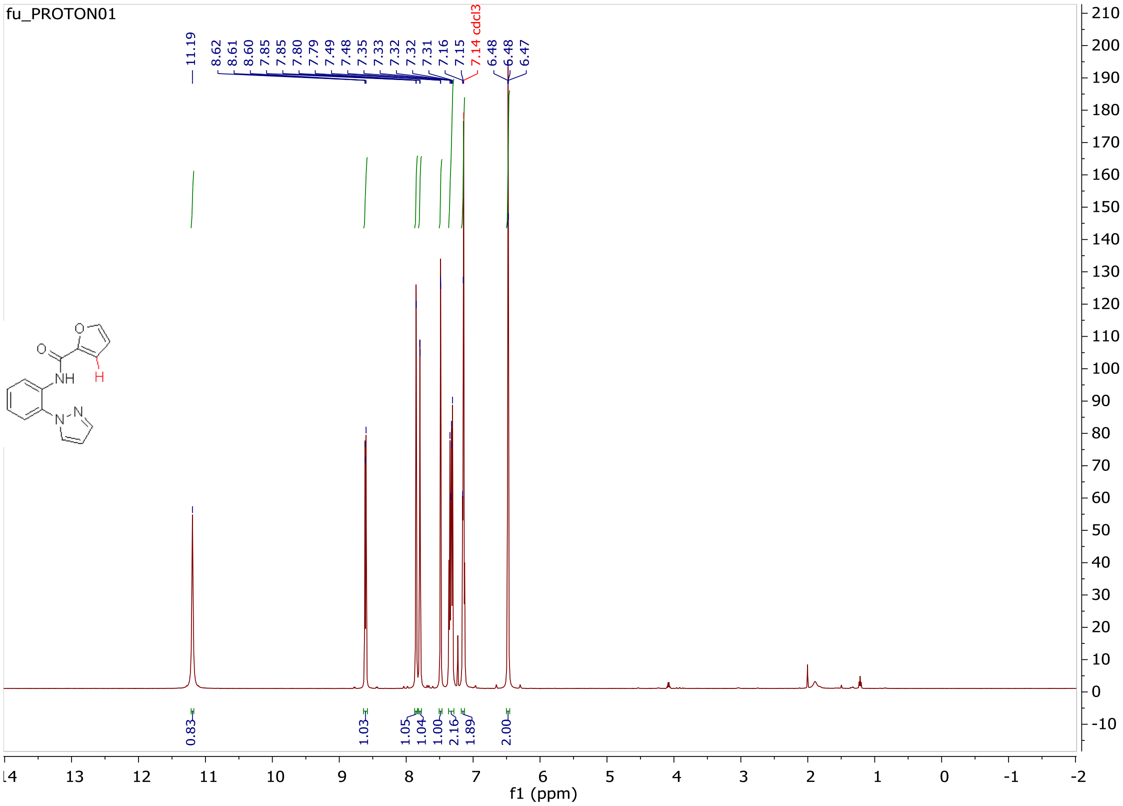
14k


NaphS-3_PROTON01
10.94
8.81
8.79
8.47
8.46
8.45
7.97
7.95
7.89
7.88
7.87
7.84
7.84
7.76
7.74
7.64
7.54
7.53
7.53
7.52
7.52
7.50
7.49
7.48
7.46
7.45 cdcl3
7.39
7.37
7.25
7.25
7.23
6.46
6.46
6.45
0.81
0.90
0.96
1.04
2.03
1.04
0.98
4.04
1.06
1.20
0.93
O
NH
H
N
N
f1 (ppm)

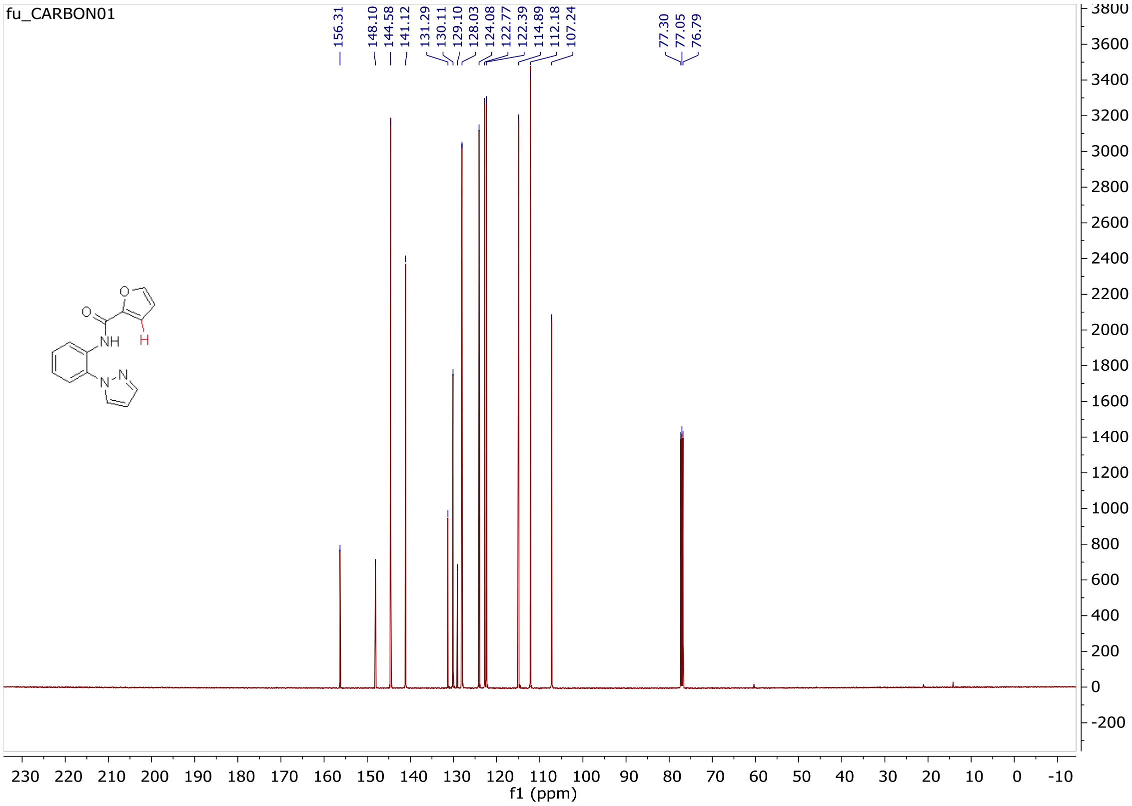
14k


NaphS_carbon_CARBON01
167.43
141.19
134.30
133.84
131.91
131.26
130.32
130.16
129.32
128.29
128.13
127.18
126.41
125.55
125.49
124.75
124.30
123.02
122.47
107.18
77.27
77.02
76.77
O
NH
H
N
N
f1 (ppm)

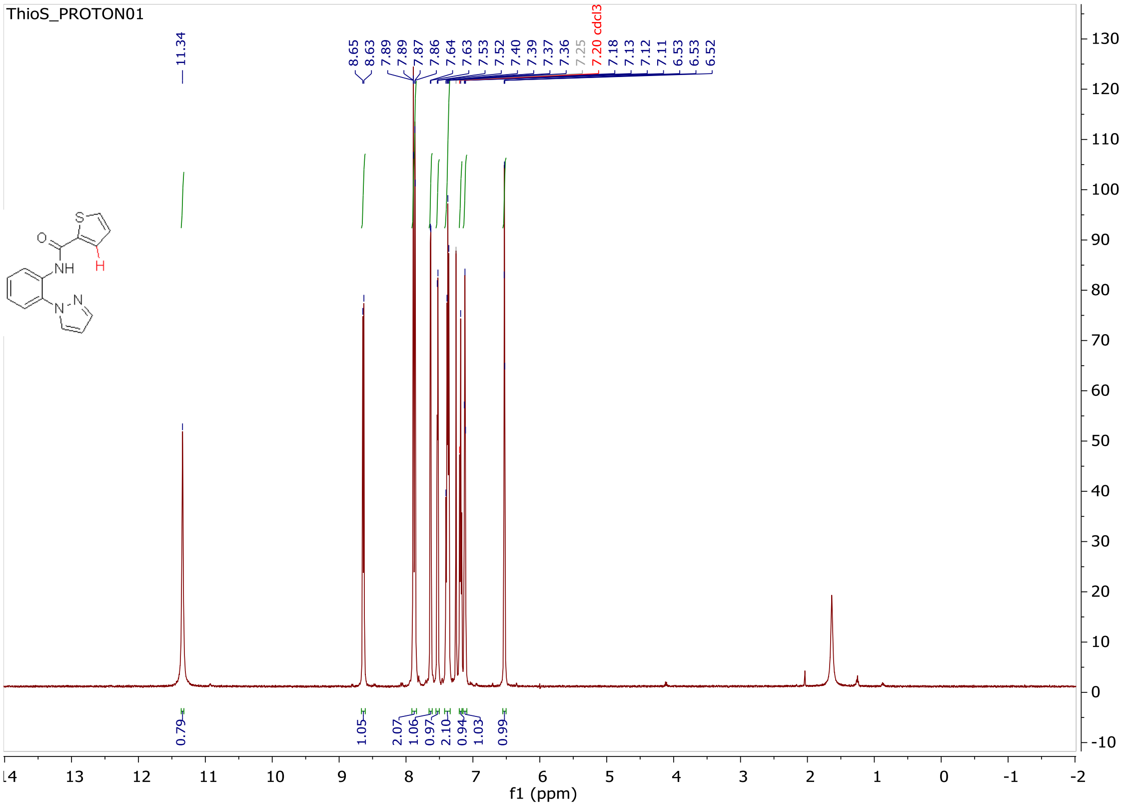
14l


fu_PROTON01
11.19
8.62
8.61
8.60
7.85
7.85
7.80
7.79
7.49
7.48
7.35
7.33
7.32
7.32
7.31
7.16
7.15
7.14 cdcl3
6.48
6.48
6.47
0.83
1.03
1.05
1.04
1.00
2.16
1.89
2.00
O
NH
H
N
N
f1 (ppm)

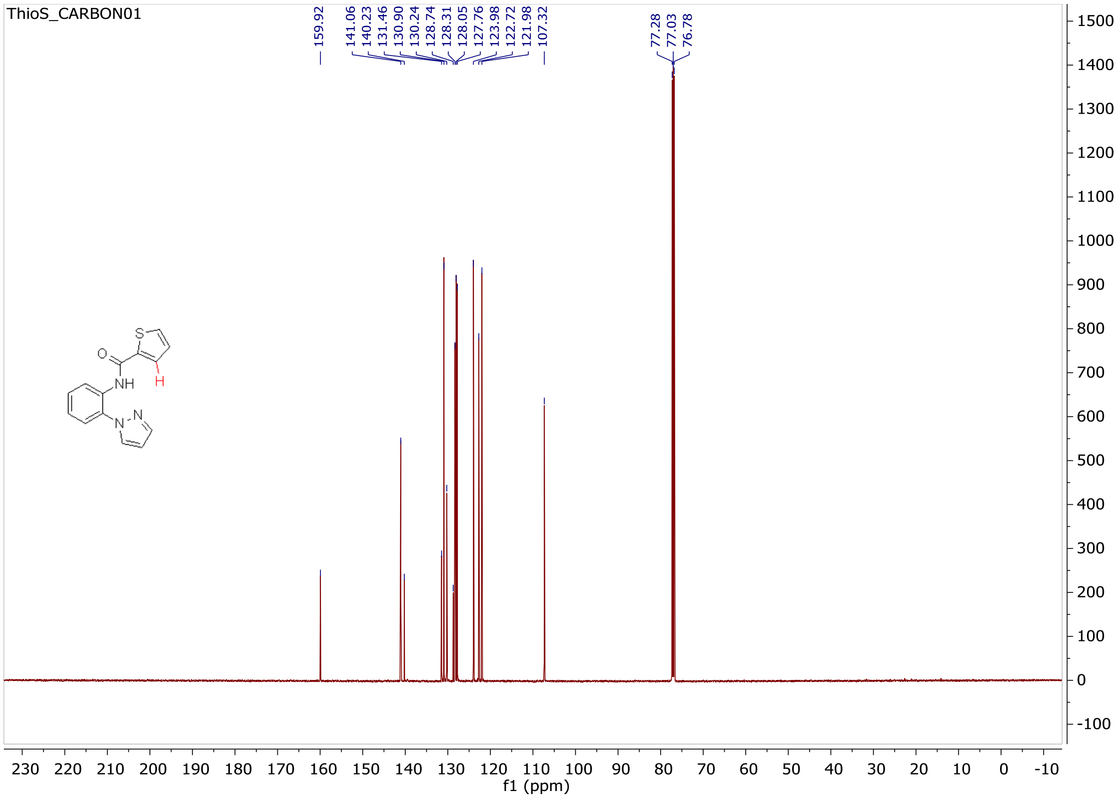
14l


fu_CARBON01
156.31
148.10
144.58
141.12
131.29
130.11
129.10
128.03
124.08
122.77
122.39
114.89
112.18
107.24
77.30
77.05
76.79
O
NH
H
N
N
f1 (ppm)

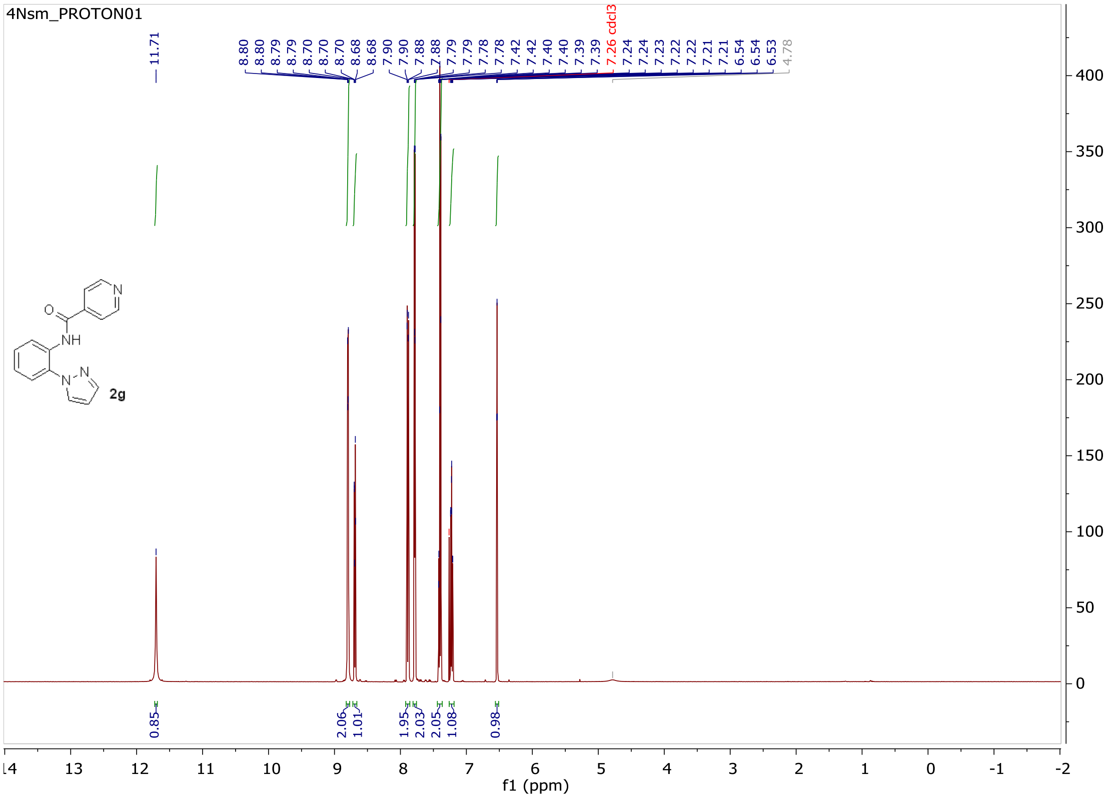
14m


ThioS_PROTON01
11.34
8.65
8.63
7.89
7.89
7.87
7.86
7.64
7.63
7.53
7.52
7.40
7.39
7.37
7.36
7.25
7.20 cdcl3
7.18
7.13
7.12
7.11
6.53
6.53
6.52
S
O
NH
H
N
N
0.79
1.05
2.07
1.06
0.97
2.10
0.94
1.03
0.99
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

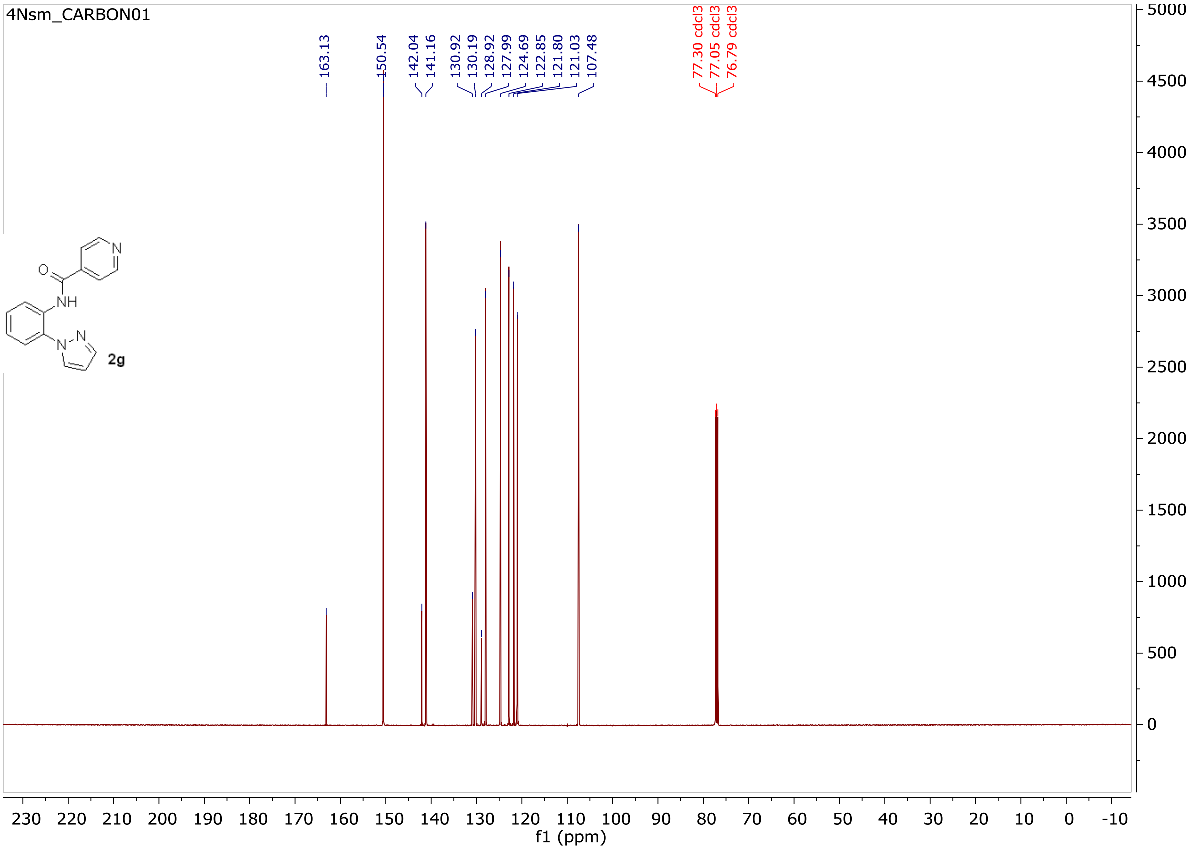
14m


ThioS_CARBON01
159.92
141.06
140.23
131.46
130.90
130.24
128.74
128.31
128.05
127.76
123.98
122.72
121.98
107.32
77.28
77.03
76.78
S
O
NH
H
N
N
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

14n

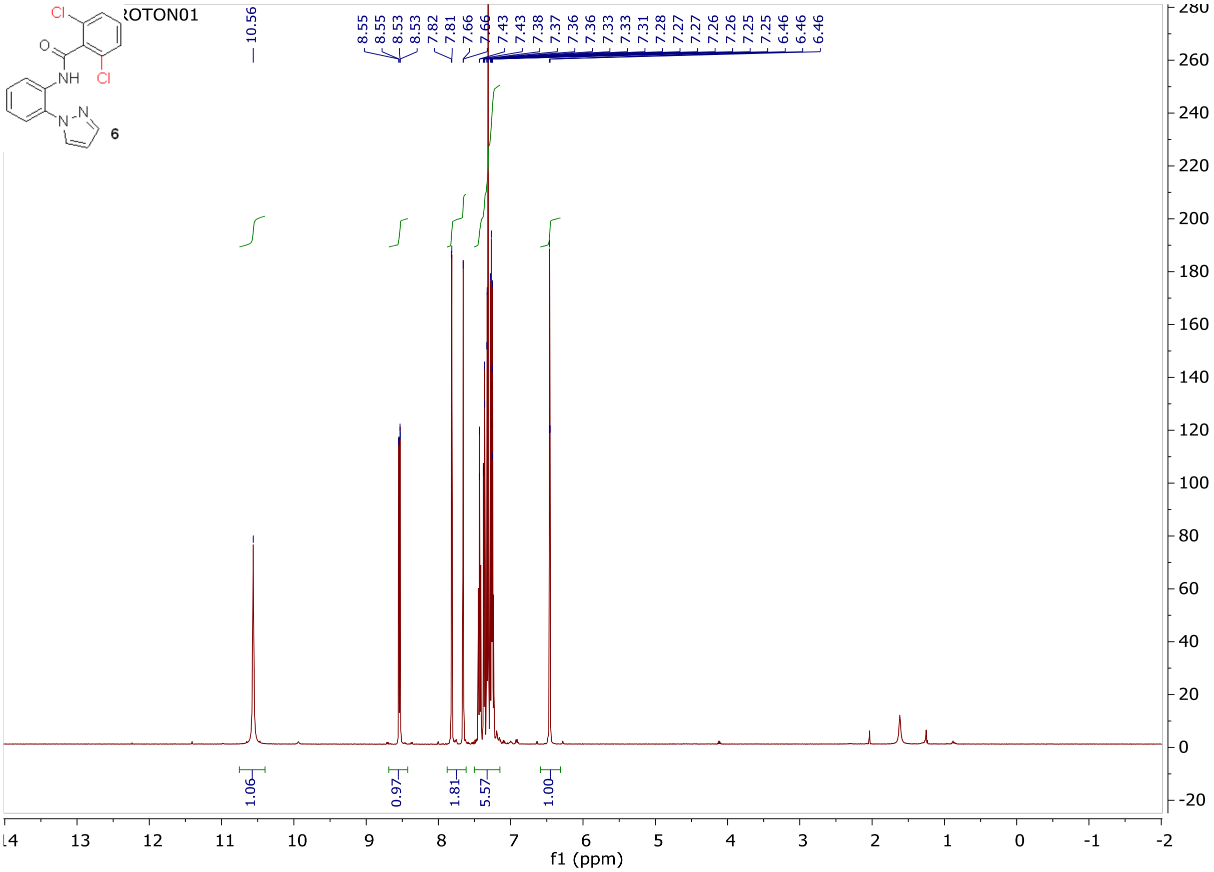

4Nsm_PROTON01
11.71
8.80
8.80
8.79
8.79
8.70
8.70
8.70
8.68
8.68
7.90
7.90
7.88
7.88
7.79
7.79
7.78
7.78
7.42
7.42
7.40
7.40
7.39
7.39
7.26 cdcl3
7.24
7.24
7.23
7.22
7.22
7.21
7.21
6.54
6.54
6.53
4.78
O
NH
N
N
N
2g
0.85
2.06
1.01
1.95
2.03
2.05
1.08
0.98
400
350
300
250
200
150
100
50
0
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)

14n

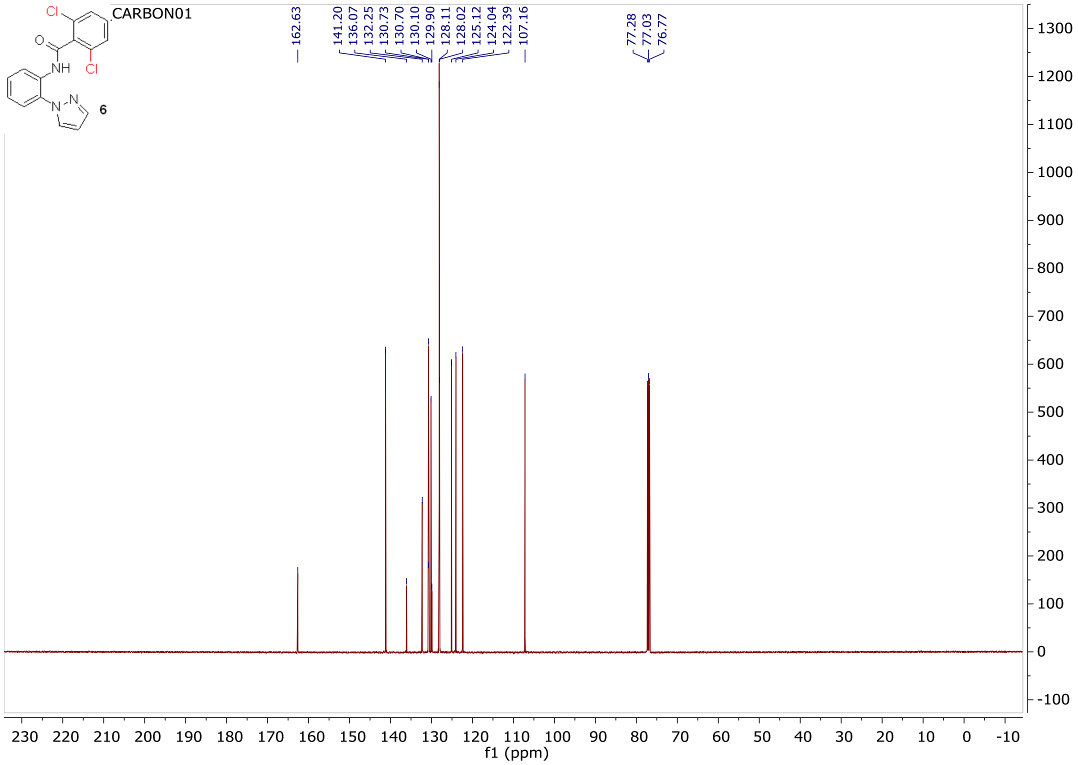

4Nsm_CARBON01
163.13
150.54
142.04
141.16
130.92
130.19
128.92
127.99
124.69
122.85
121.80
121.03
107.48
77.30 cdcl3
77.05 cdcl3
76.79 cdcl3
O
NH
N
N
N
2g
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

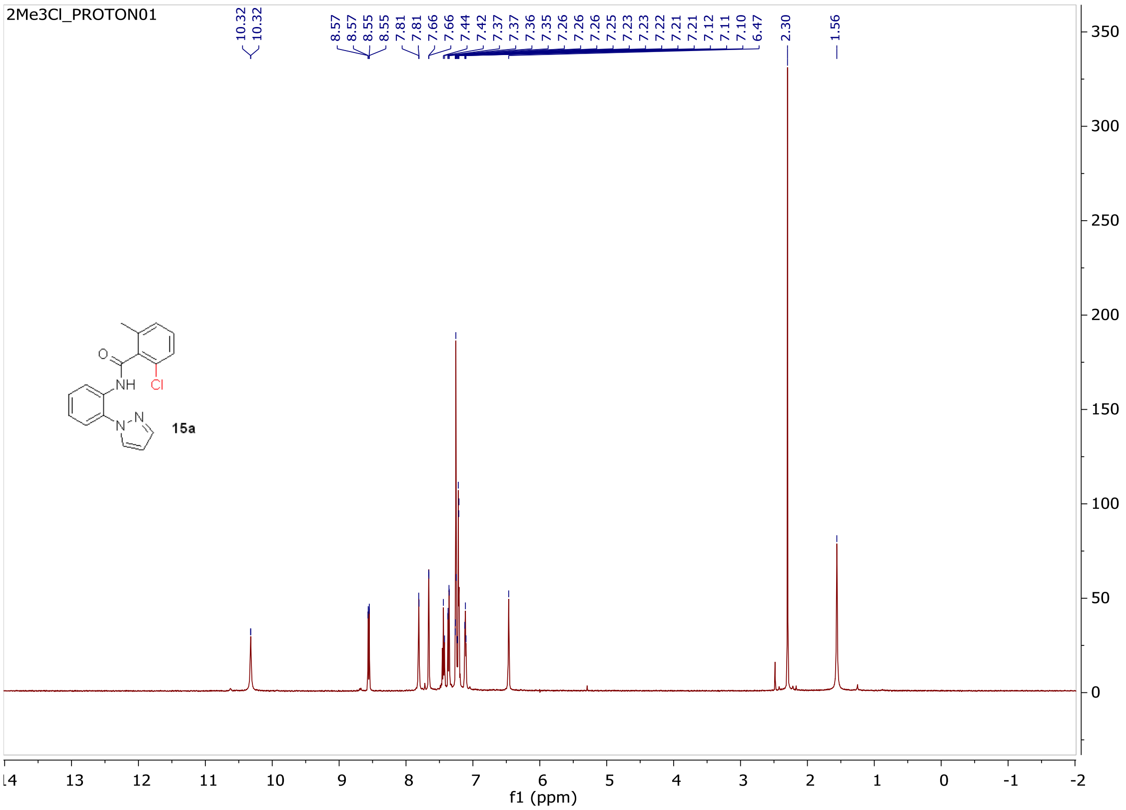
6. NMR Spectra of Products

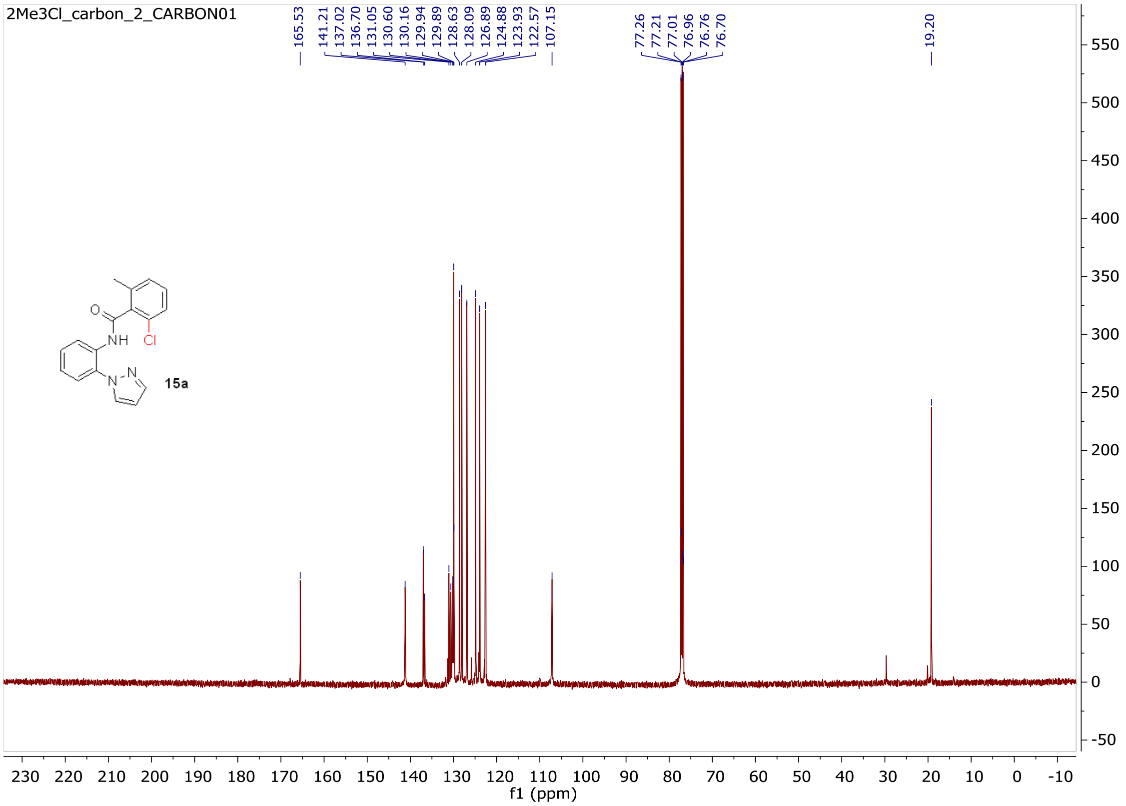
5



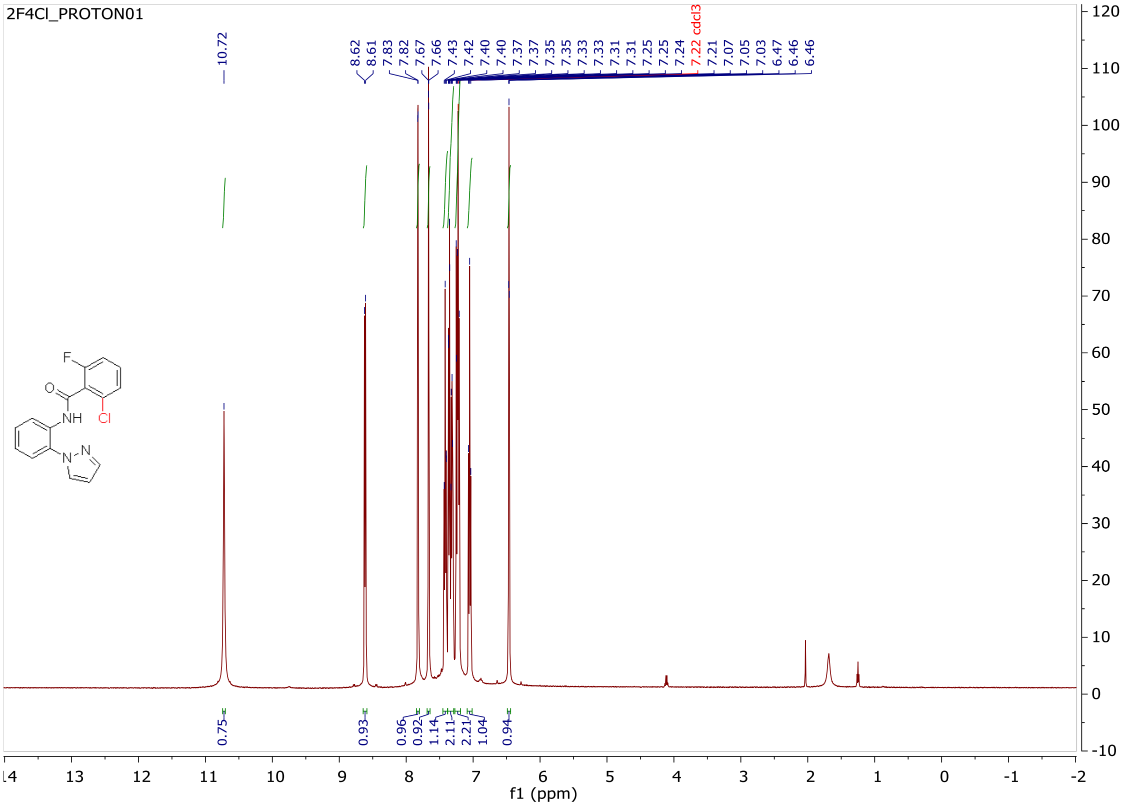
5



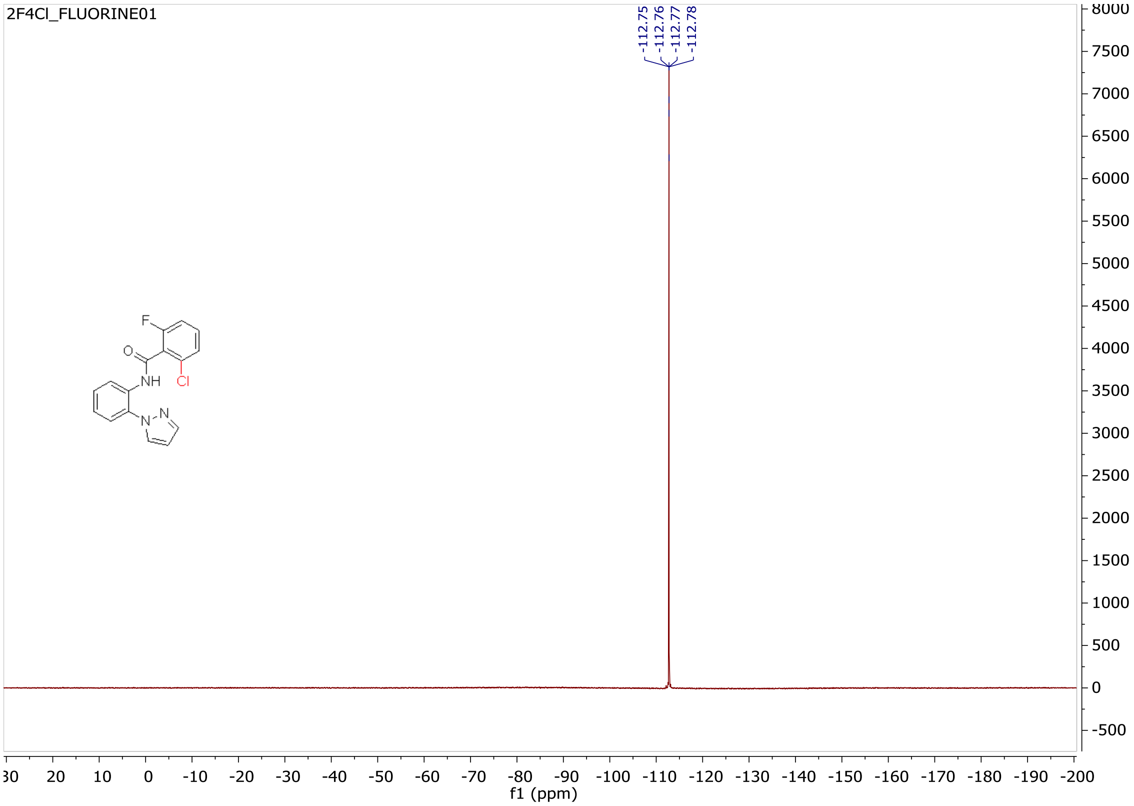

2Me3Cl_PROTON01
10.32
10.32
8.57
8.57
8.55
8.55
7.81
7.81
7.66
7.66
7.44
7.42
7.37
7.37
7.36
7.35
7.26
7.26
7.26
7.25
7.23
7.23
7.22
7.21
7.21
7.12
7.11
7.10
6.47
2.30
1.56
O
NH
Cl
N
N
15a
350
300
250
200
150
100
50
0
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)


2Me3Cl_carbon_2_CARBON01
165.53
141.21
137.02
136.70
131.05
130.60
130.16
129.94
129.89
128.63
128.09
126.89
124.88
123.93
122.57
107.15
77.26
77.21
77.01
76.96
76.76
76.70
19.20
O
NH
Cl
N
N
15a
550
500
450
400
350
300
250
200
150
100
50
0
-50
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

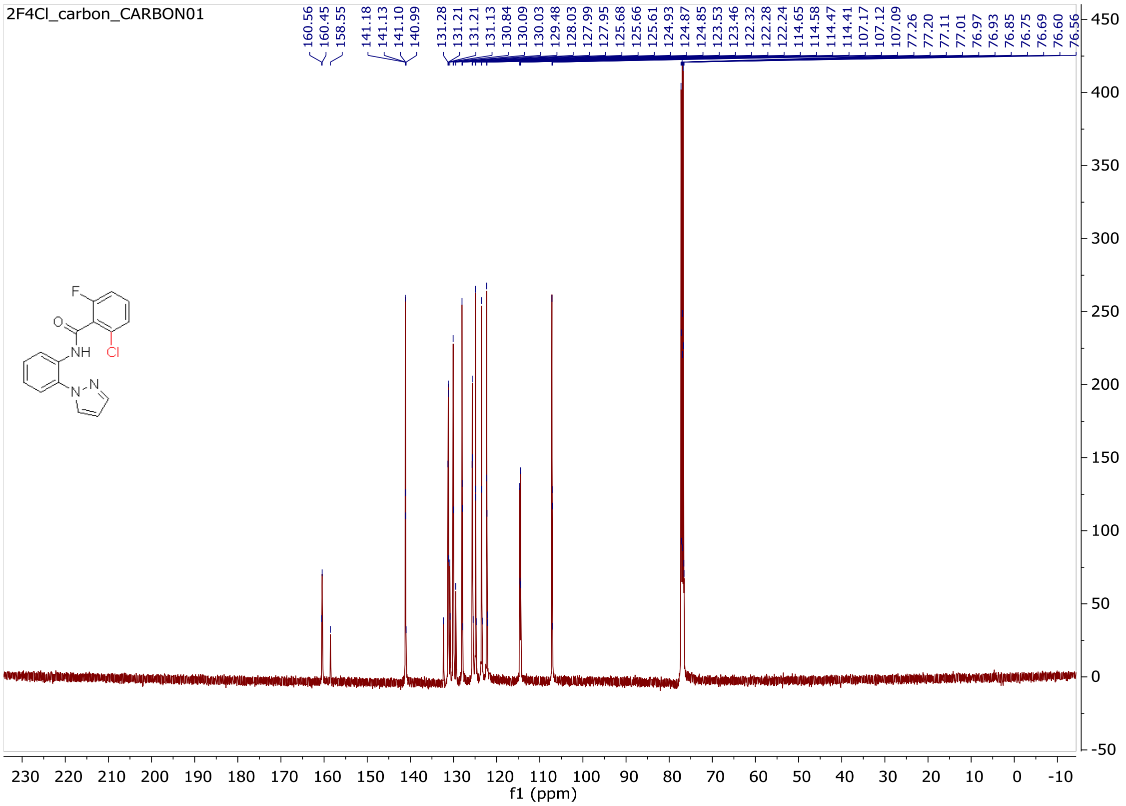
15c


2F4Cl_PROTON01
10.72
8.62
8.61
7.83
7.82
7.67
7.66
7.43
7.42
7.40
7.40
7.37
7.37
7.35
7.35
7.33
7.33
7.31
7.31
7.25
7.25
7.24
7.22 cdcl3
7.21
7.07
7.05
7.03
6.47
6.46
6.46
F
O
NH
Cl
N
N
0.75
0.93
0.96
0.92
1.14
2.11
2.21
1.04
0.94
f1 (ppm)

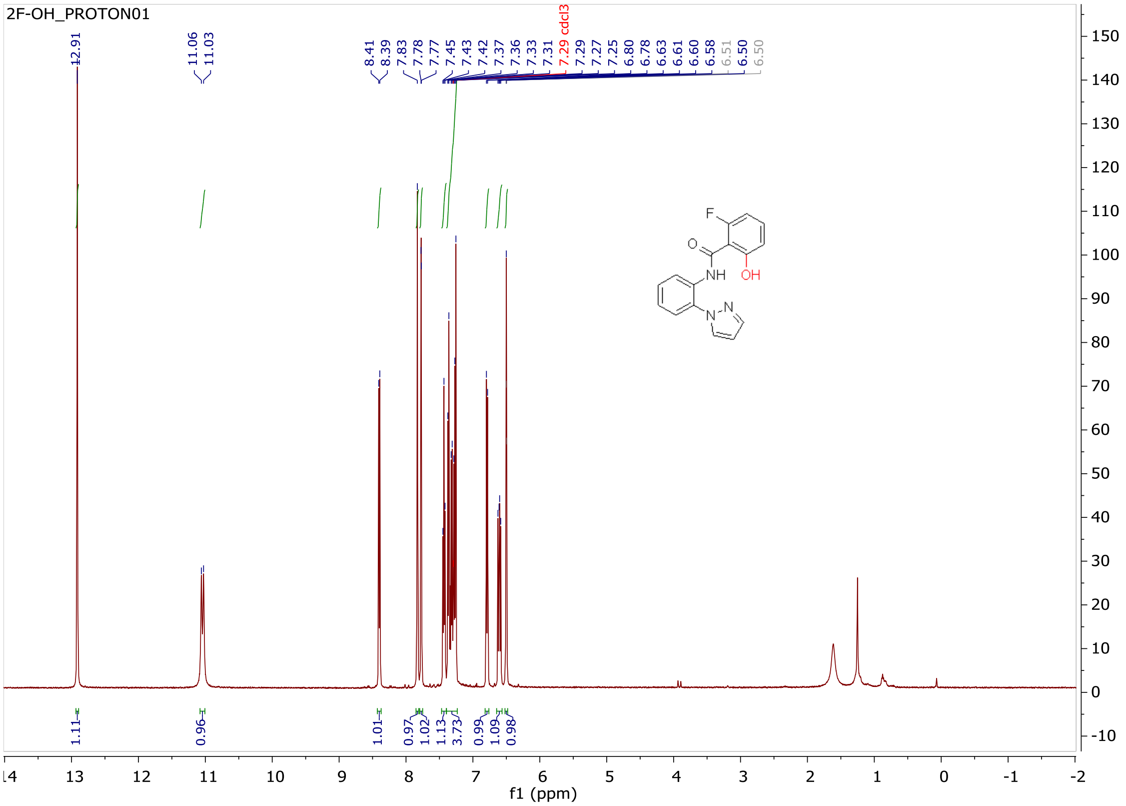
15c


2F4Cl_FLUORINE01
-112.75
-112.76
-112.77
-112.78
F
O
NH
Cl
N
N
f1 (ppm)

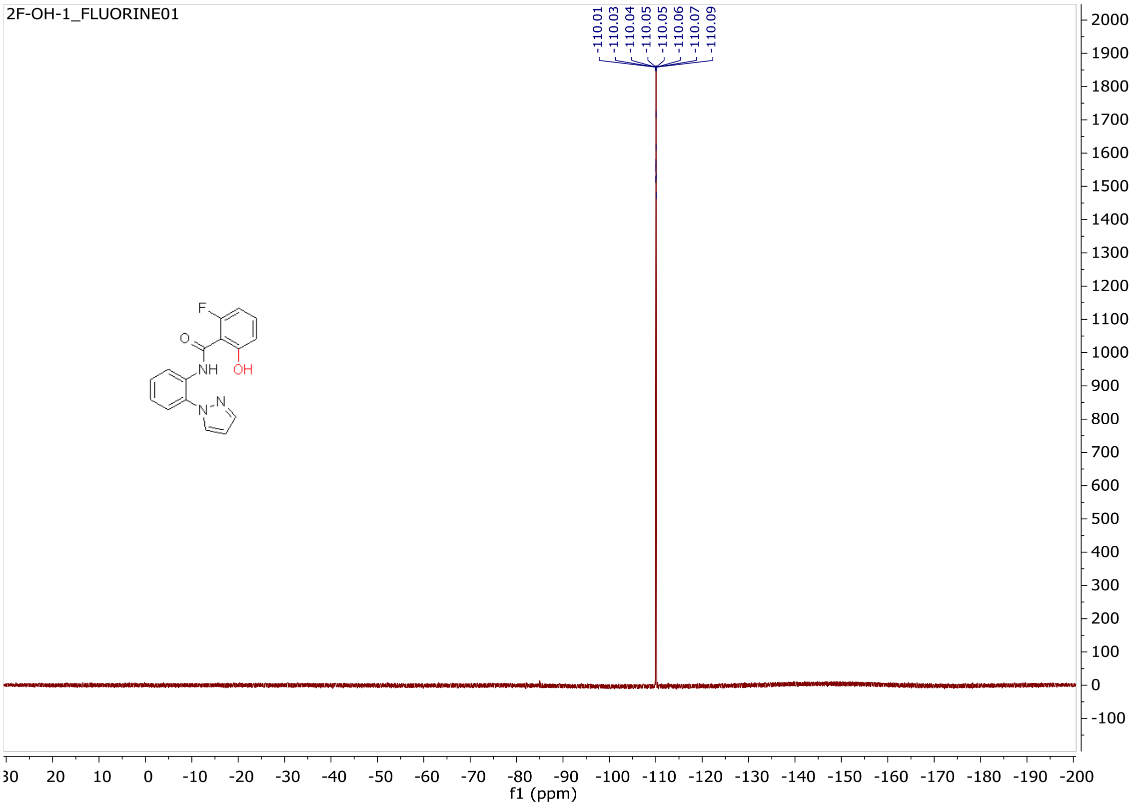
15c


2F4Cl_carbon_CARBON01
160.56
160.45
158.55
141.18
141.13
141.10
140.99
131.28
131.21
131.21
131.13
130.84
130.09
130.03
129.48
128.03
127.99
127.95
125.68
125.66
125.61
124.93
124.87
124.85
123.53
123.46
122.32
122.28
122.24
114.65
114.58
114.47
114.41
107.17
107.12
107.09
77.26
77.20
77.11
77.01
76.97
76.93
76.85
76.75
76.69
76.60
76.56
F
O
NH
Cl
N
N
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
450 400 350 300 250 200 150 100 50 0 -50

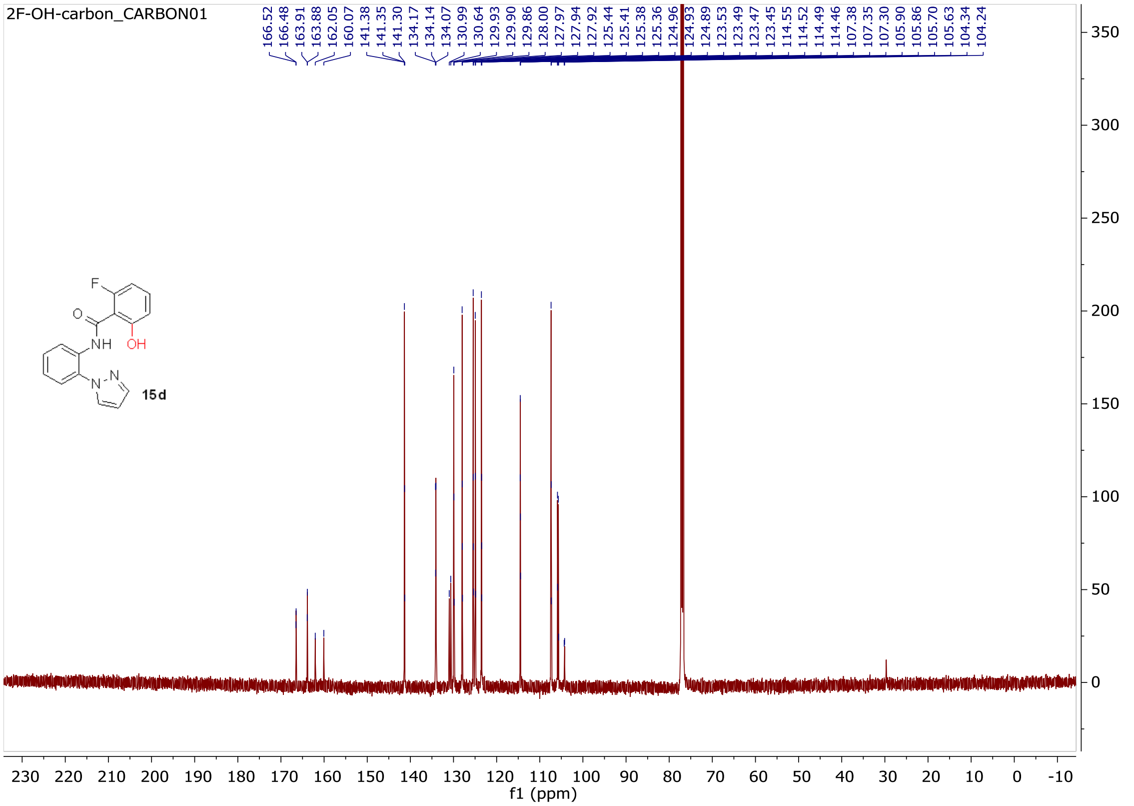
16c


2F-OH_PROTON01
12.91
11.06
11.03
8.41
8.39
7.83
7.78
7.77
7.45
7.43
7.42
7.37
7.36
7.33
7.31
7.29 cdcl3
7.29
7.27
7.25
6.80
6.78
6.63
6.61
6.60
6.58
6.51
6.50
6.50
F
O
NH
OH
N
N
1.11
0.96
1.01
0.97
1.02
1.13
3.73
0.99
1.09
0.98
f1 (ppm)
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

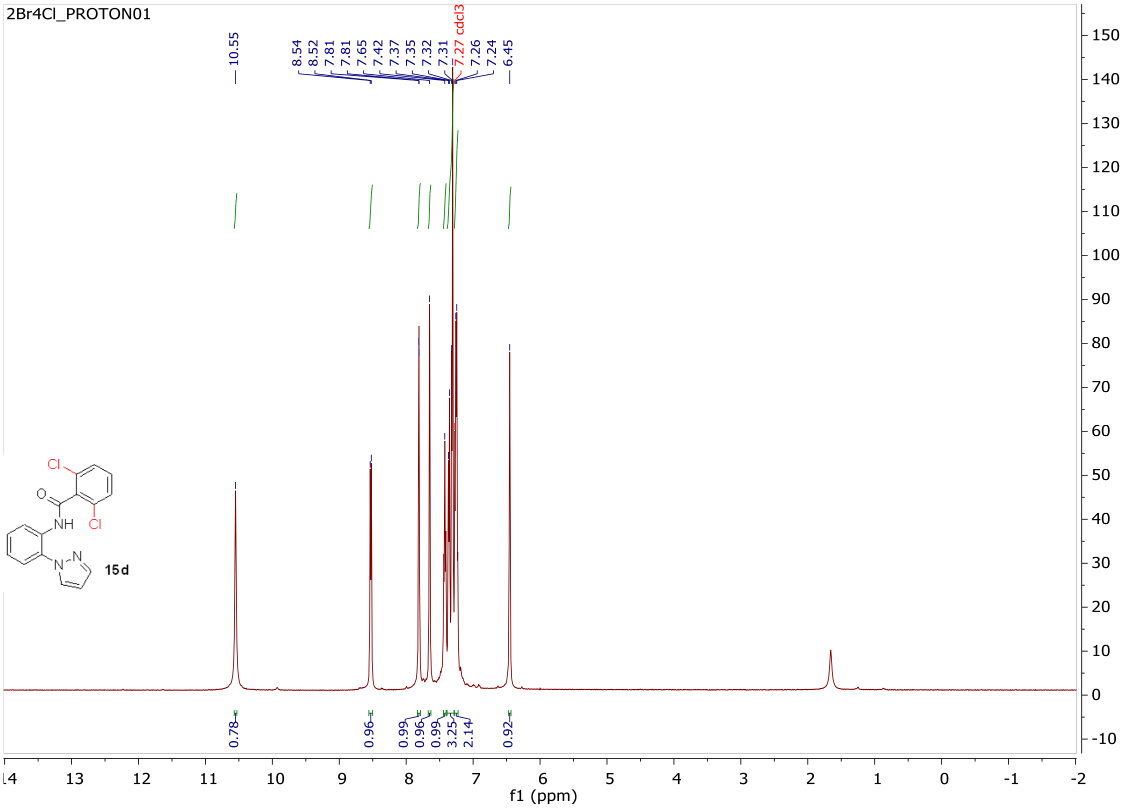
16c


2F-OH-1_FLUORINE01
-110.01
-110.03
-110.04
-110.05
-110.05
-110.06
-110.07
-110.09
F
O
NH
OH
N
N
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

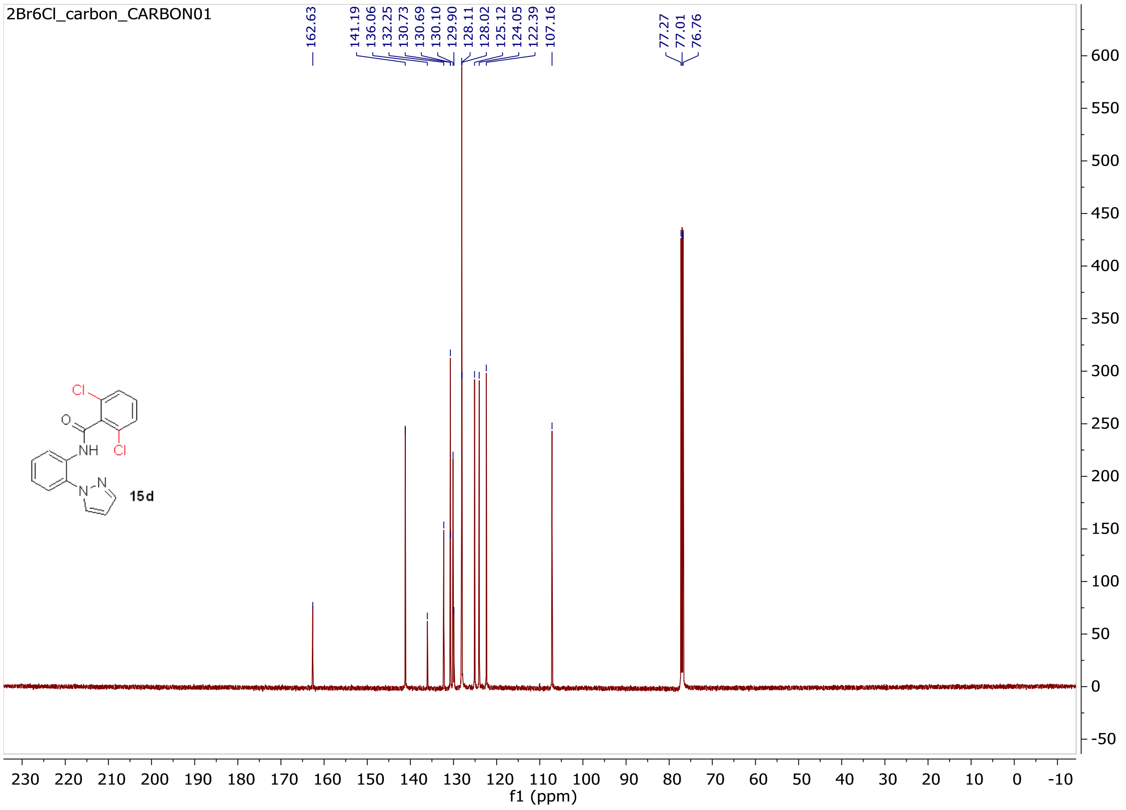
16c


2F-OH-carbon_CARBON01
166.52
166.48
163.91
163.88
162.05
160.07
141.38
141.35
141.30
134.17
134.14
134.07
130.99
130.64
129.93
129.90
129.86
128.00
127.97
127.94
127.92
125.44
125.41
125.38
125.36
124.96
124.93
124.89
123.53
123.49
123.47
123.45
114.55
114.52
114.49
114.46
107.38
107.35
107.30
105.90
105.86
105.70
105.63
104.34
104.24
F
O
NH
OH
N
N
15d
350
300
250
200
150
100
50
0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

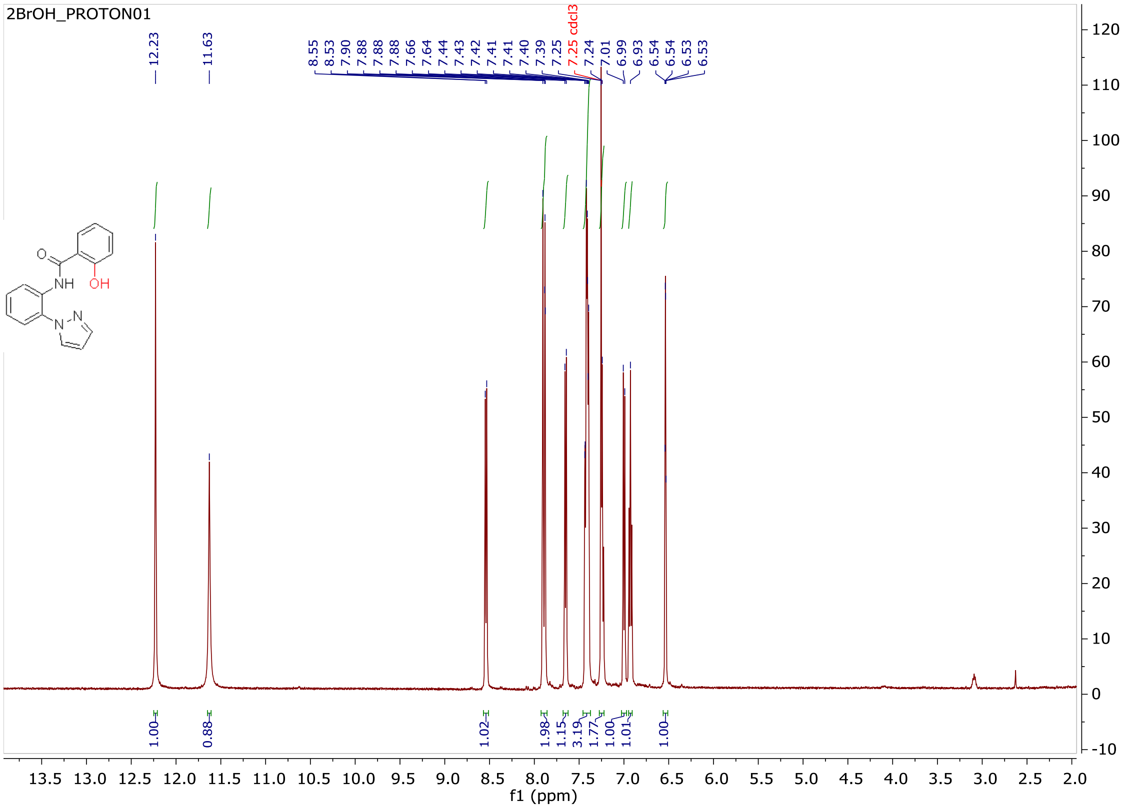
5


2Br4Cl_PROTON01
10.55
8.54
8.52
7.81
7.81
7.65
7.42
7.37
7.35
7.32
7.31
7.27 cdcl3
7.26
7.24
6.45
0.78
0.96
0.99
0.96
0.99
3.25
2.14
0.92
Cl
O
NH
Cl
N
N
15d
f1 (ppm)

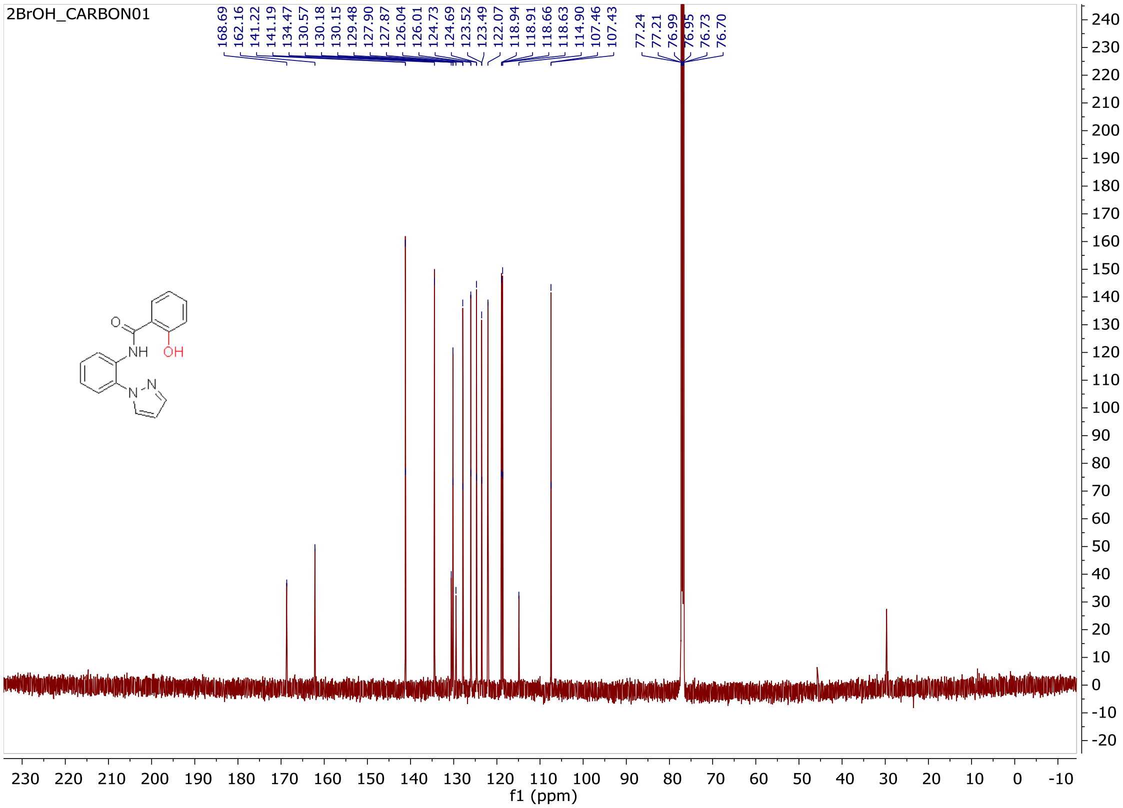
5


2Br6Cl_carbon_CARBON01
162.63
141.19
136.06
132.25
130.73
130.69
130.10
129.90
128.11
128.02
125.12
124.05
122.39
107.16
77.27
77.01
76.76
Cl
O
NH
Cl
N
N
15d
f1 (ppm)

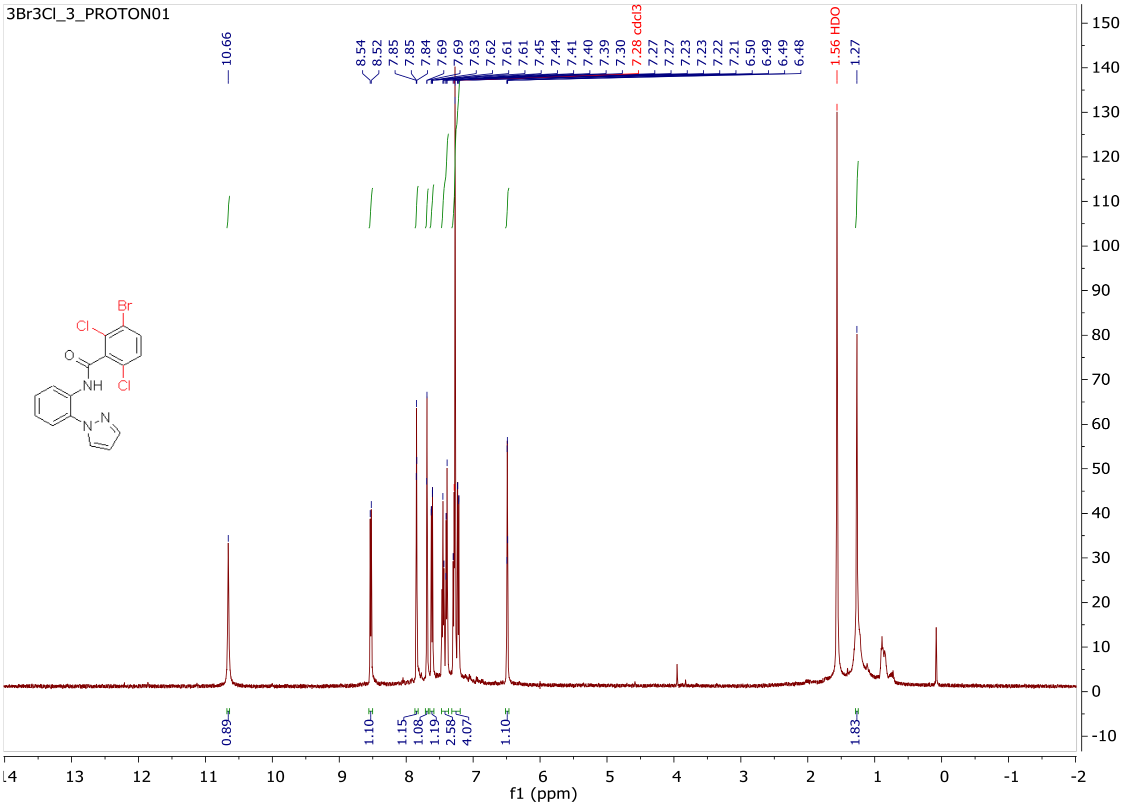
17d


2BrOH_PROTON01
12.23
11.63
8.55
8.53
7.90
7.88
7.88
7.88
7.66
7.64
7.44
7.43
7.42
7.41
7.41
7.40
7.39
7.25
7.25 cdcl3
7.24
7.01
6.99
6.93
6.54
6.54
6.53
6.53
O
NH
OH
N
N
1.00
0.88
1.02
1.98
1.15
3.19
1.77
1.00
1.01
1.00
f1 (ppm)

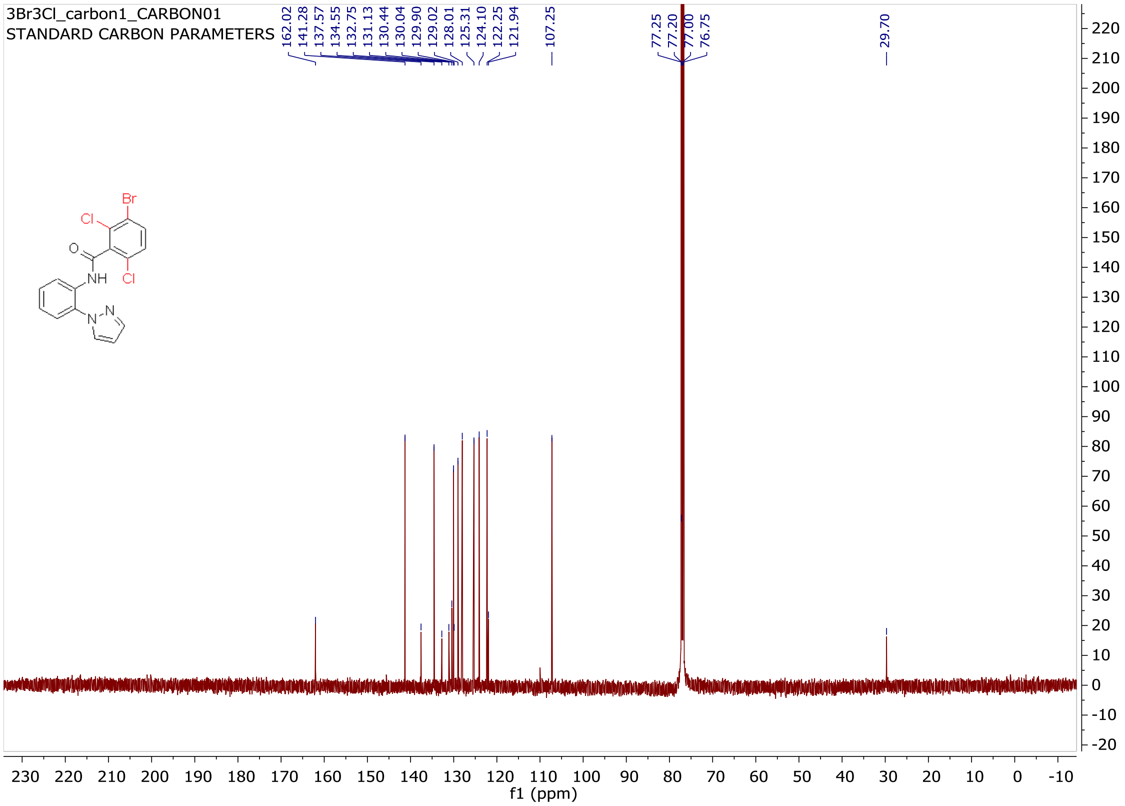
17d


2BrOH_CARBON01
168.69
162.16
141.22
141.19
134.47
130.57
130.18
130.15
129.48
127.90
127.87
126.04
126.01
124.73
124.69
123.52
123.49
122.07
118.94
118.91
118.66
118.63
114.90
107.46
107.43
77.24
77.21
76.99
76.95
76.73
76.70
O
NH
OH
N
N
f1 (ppm)

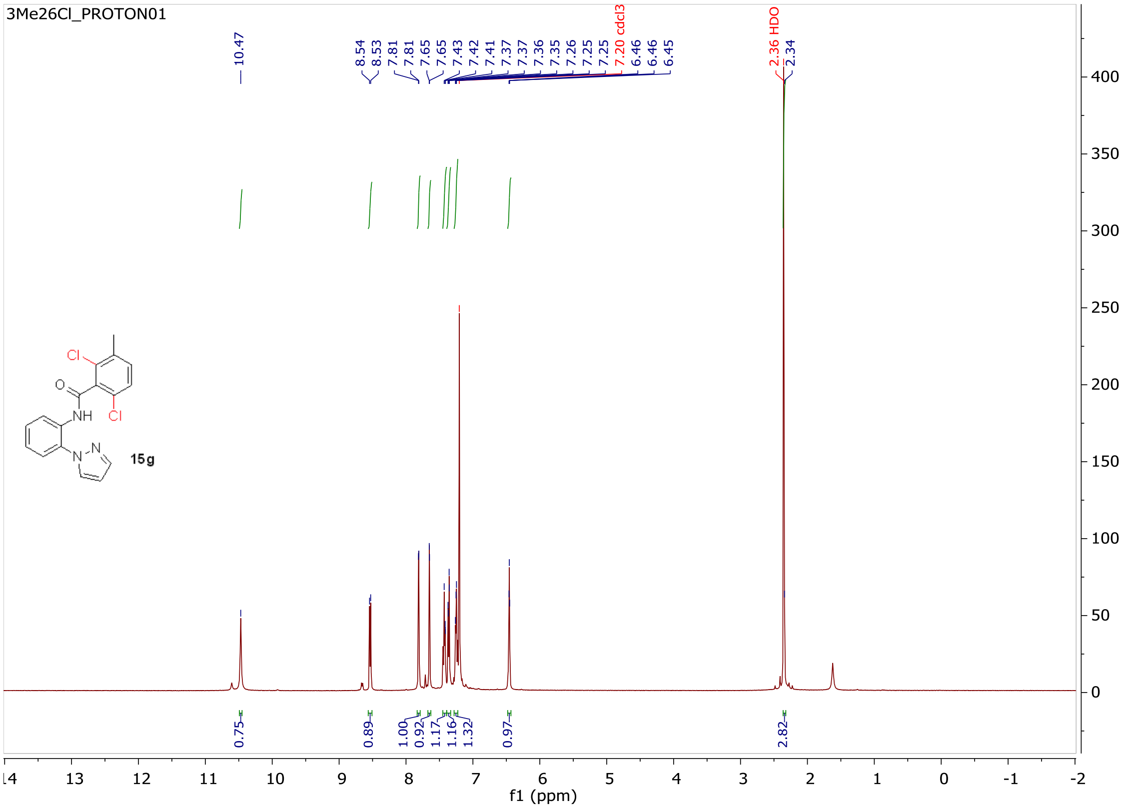
15e


3Br3Cl_3_PROTON01
10.66
8.54
8.52
7.85
7.85
7.84
7.69
7.69
7.63
7.62
7.61
7.61
7.45
7.44
7.41
7.40
7.39
7.30
7.28 cdcl3
7.27
7.27
7.23
7.23
7.22
7.21
6.50
6.49
6.49
6.48
1.56 HDO
1.27
0.89
1.10
1.15
1.08
1.19
2.58
4.07
1.10
1.83
Br
Cl
Cl
O
NH
N
N
f1 (ppm)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

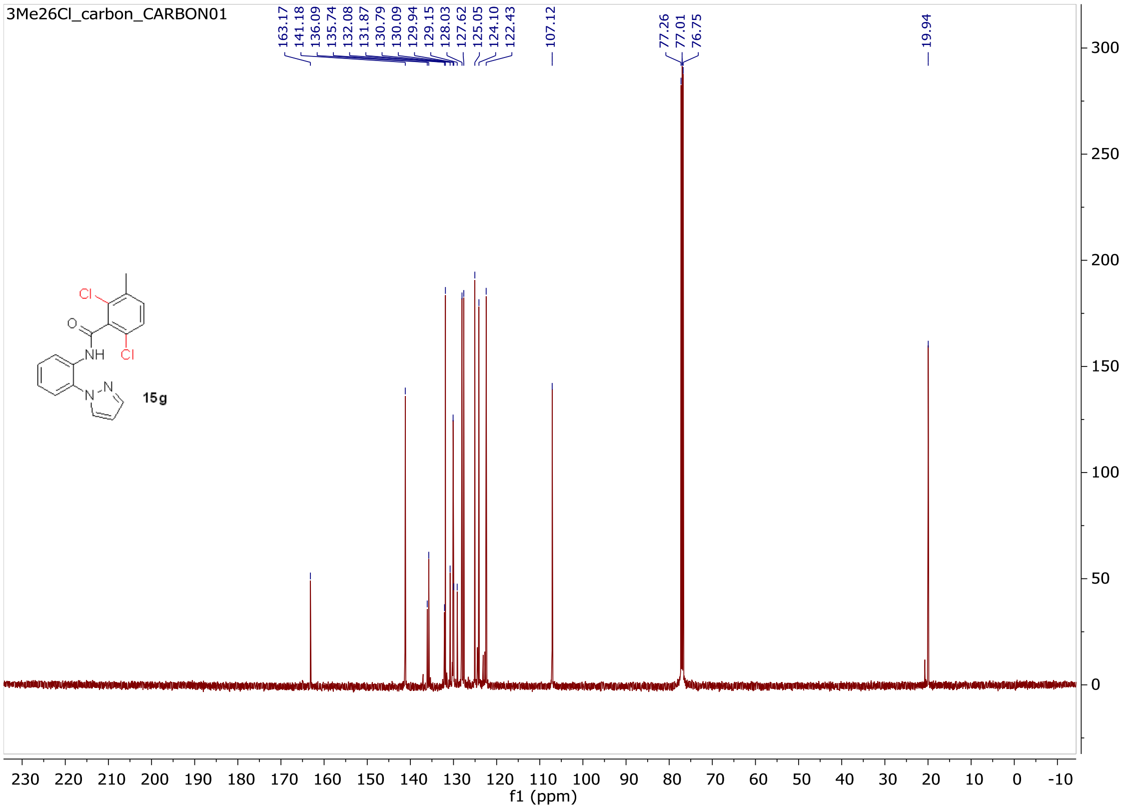
15e


3Br3Cl_carbon1_CARBON01
STANDARD CARBON PARAMETERS
162.02
141.28
137.57
134.55
132.75
131.13
130.44
130.04
129.90
129.02
128.01
125.31
124.10
122.25
121.94
107.25
77.25
77.20
77.00
76.75
29.70
Br
Cl
Cl
O
NH
N
N
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20

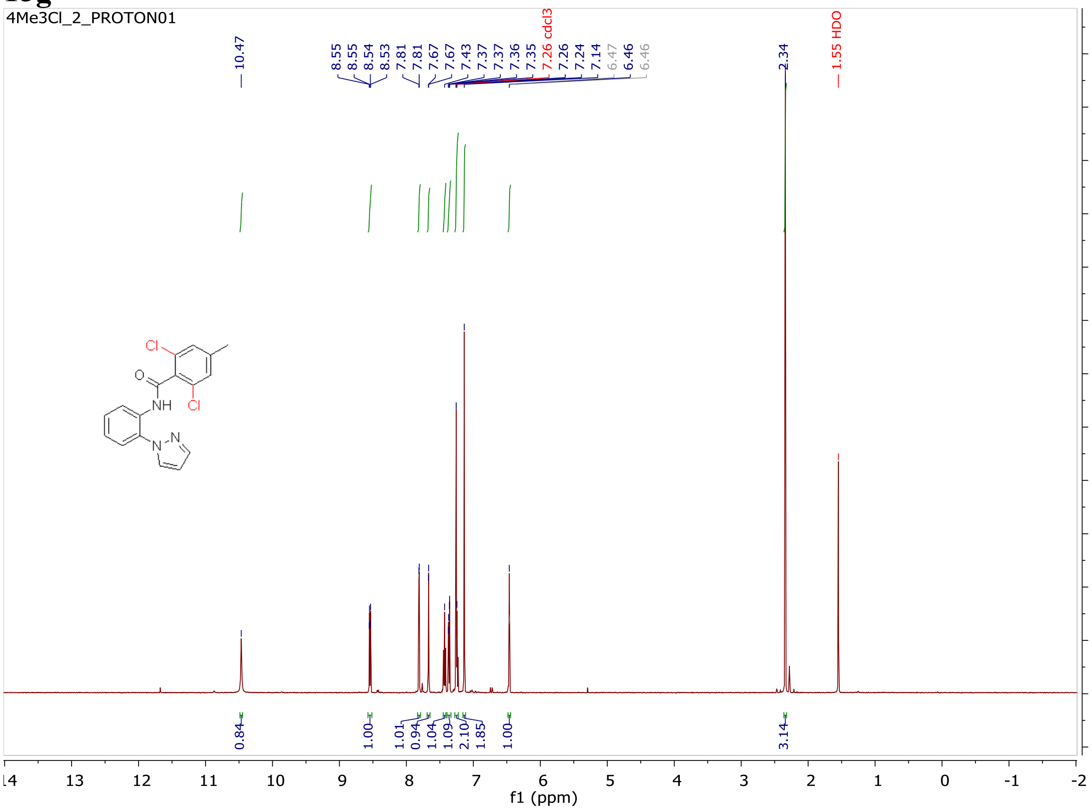
15f


3Me26Cl_PROTON01
10.47
8.54
8.53
7.81
7.81
7.65
7.65
7.43
7.42
7.41
7.37
7.37
7.36
7.35
7.26
7.25
7.25
7.20 cdcl3
6.46
6.46
6.45
2.36 HDO
2.34
0.75
0.89
1.00
0.92
1.17
1.16
1.32
0.97
2.82
Cl
O
NH
Cl
N
N
15g
f1 (ppm)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
400
350
300
250
200
150
100
50
0

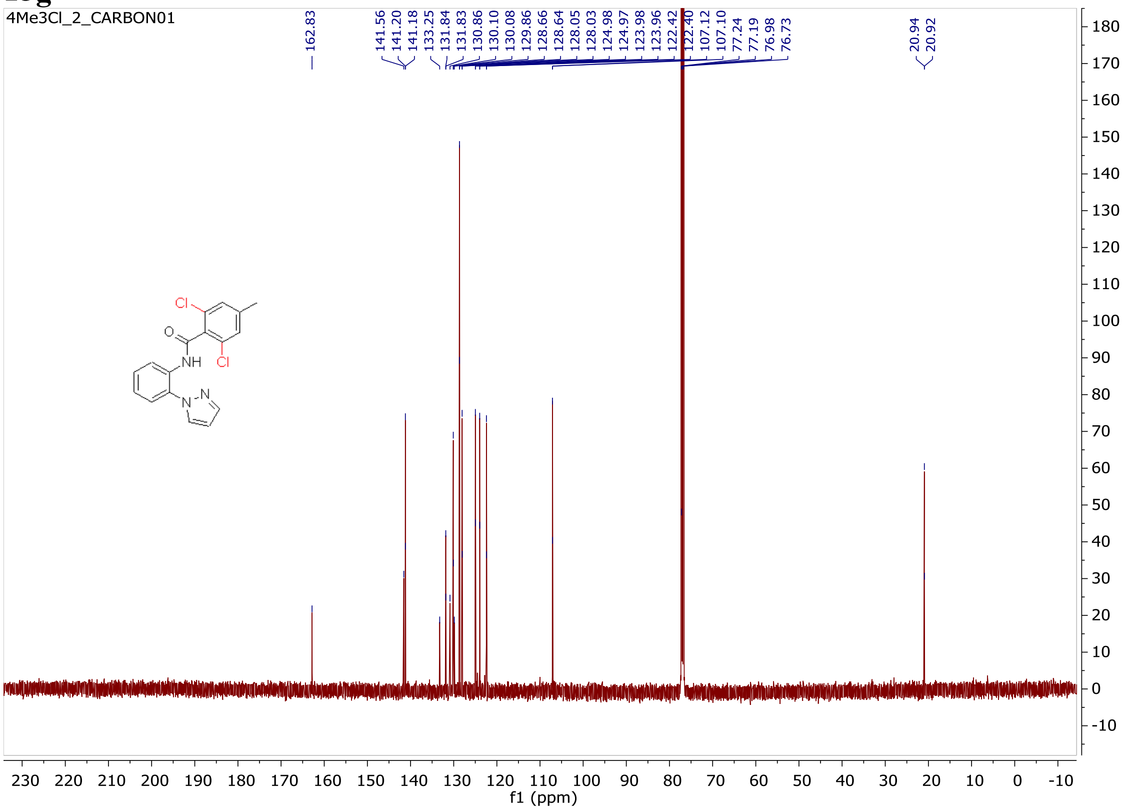
15f


3Me26Cl_carbon_CARBON01
163.17
141.18
136.09
135.74
132.08
131.87
130.79
130.09
129.94
129.15
128.03
127.62
125.05
124.10
122.43
107.12
77.26
77.01
76.75
19.94
Cl
O
NH
Cl
N
N
15g
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
300
250
200
150
100
50
0

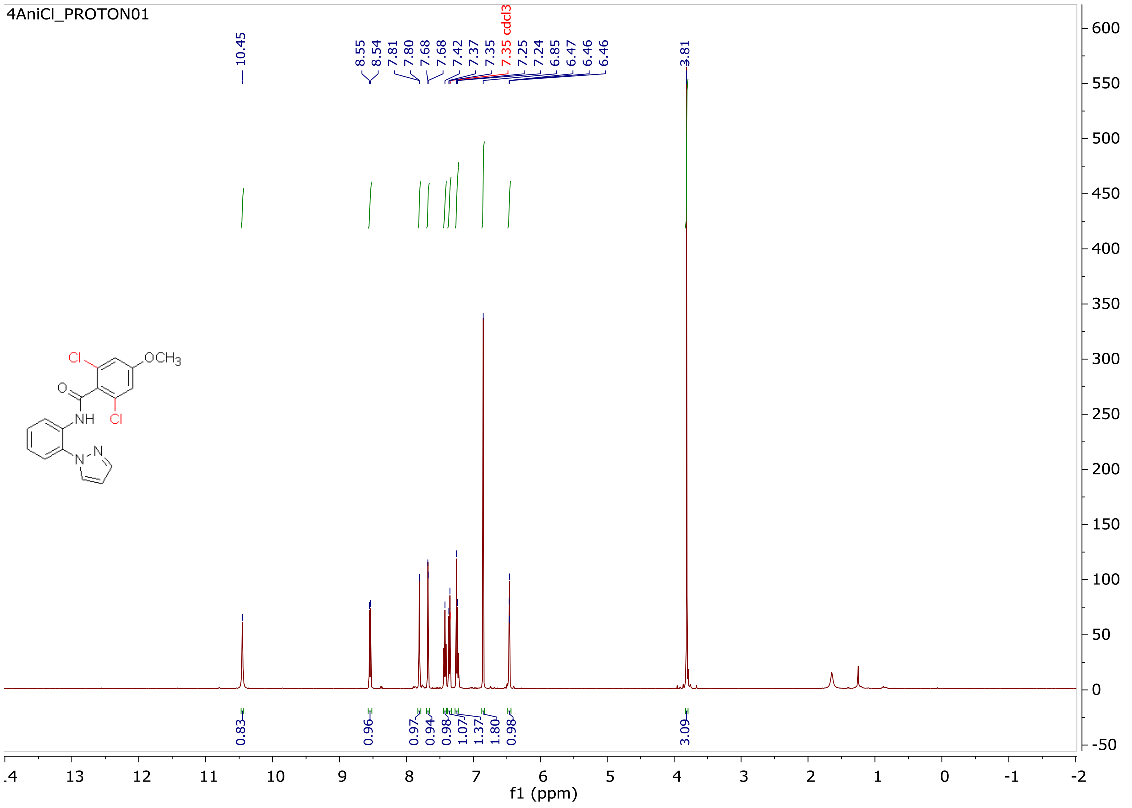
15g


4Me3Cl_2_PROTON01
10.47
8.55
8.55
8.54
8.53
7.81
7.81
7.67
7.67
7.43
7.37
7.37
7.36
7.35
7.26 cdcl3
7.26
7.24
7.14
6.47
6.46
6.46
2.34
1.55 HDO
0.84
1.00
1.01
0.94
1.04
1.09
2.10
1.85
1.00
3.14
Cl
O
NH
Cl
N
N
f1 (ppm)

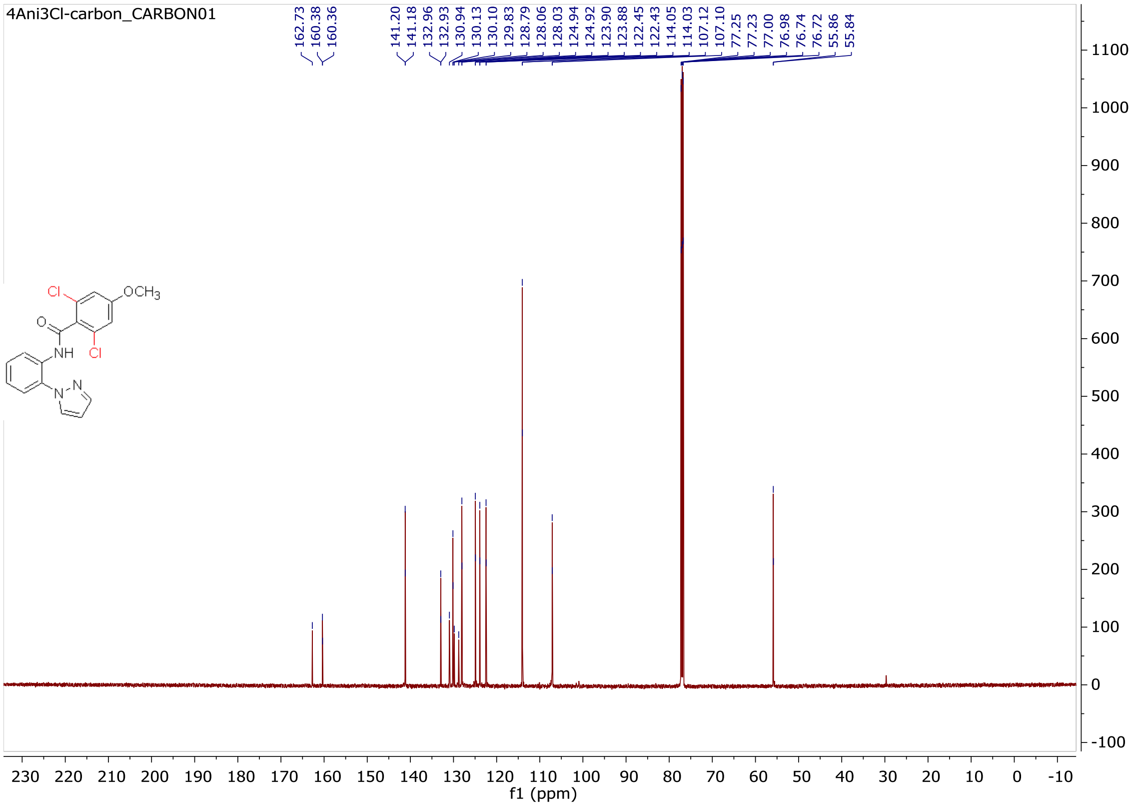
15g


4Me3Cl_2_CARBON01
162.83
141.56
141.20
141.18
133.25
131.84
131.83
130.86
130.10
130.08
129.86
128.66
128.64
128.05
128.03
124.98
124.97
123.98
123.96
122.42
122.40
107.12
107.10
77.24
77.19
76.98
76.73
20.94
20.92
Cl
O
NH
Cl
N
N
f1 (ppm)

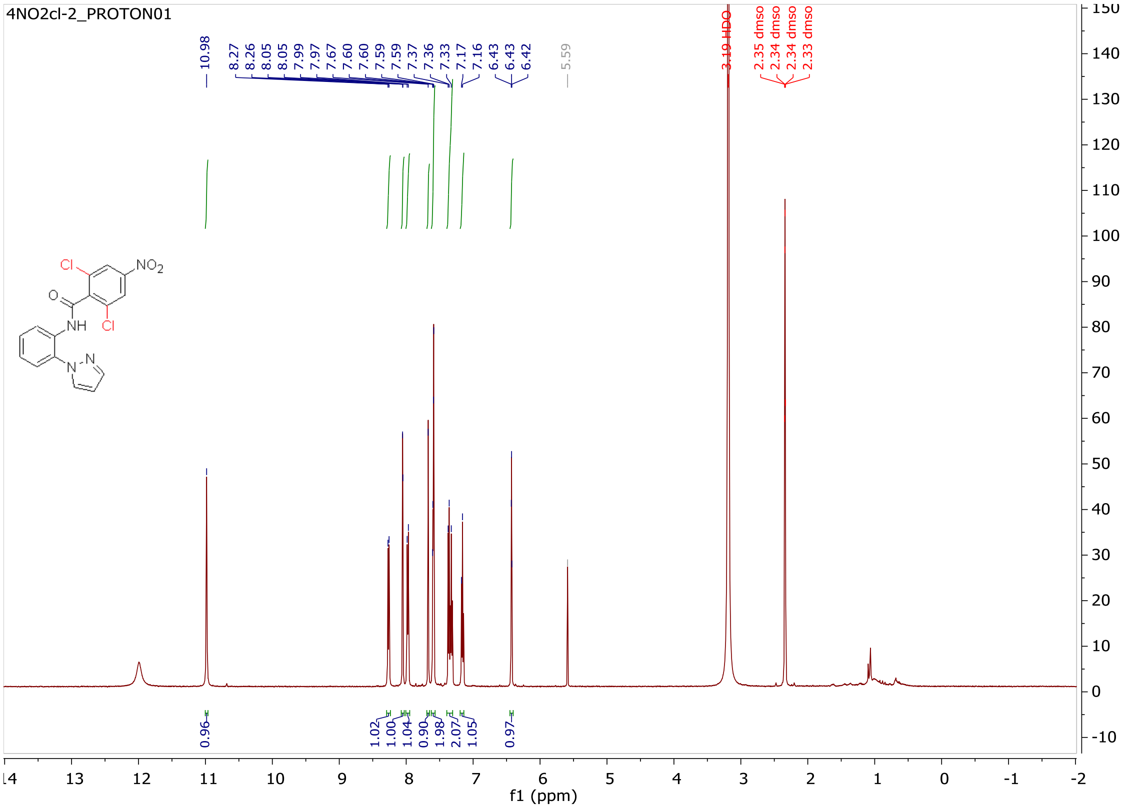
15h


4AniCl_PROTON01
10.45
8.55
8.54
7.81
7.80
7.68
7.68
7.42
7.37
7.35
7.35 cdcl3
7.25
7.24
6.85
6.47
6.46
6.46
3.81
0.83
0.96
0.97
0.94
0.98
1.07
1.37
1.80
0.98
3.09
Cl
OCH3
O
NH
Cl
N
N
f1 (ppm)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
600
550
500
450
400
350
300
250
200
150
100
50
0
-50

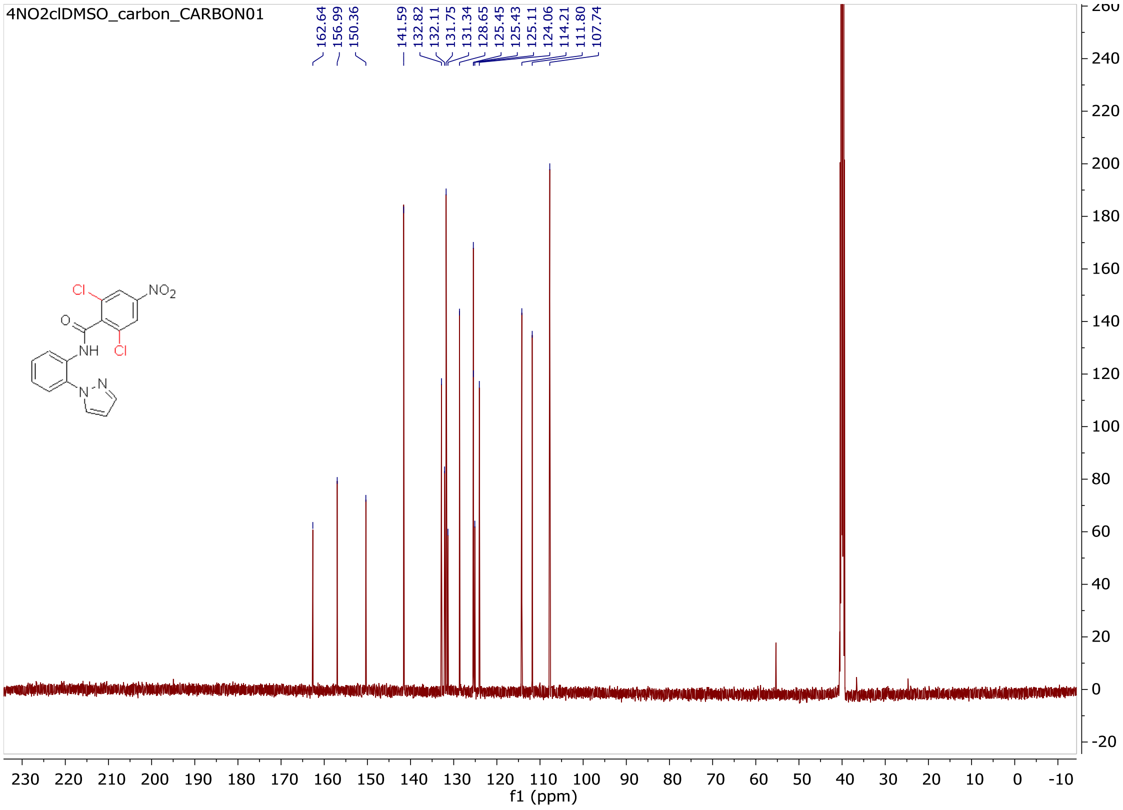
15h


4Ani3Cl-carbon_CARBON01
162.73
160.38
160.36
141.20
141.18
132.96
132.93
130.94
130.13
130.10
129.83
128.79
128.06
128.03
124.94
124.92
123.90
123.88
122.45
122.43
114.05
114.03
107.12
107.10
77.25
77.23
77.00
76.98
76.74
76.72
55.86
55.84
Cl
OCH3
O
NH
Cl
N
N
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

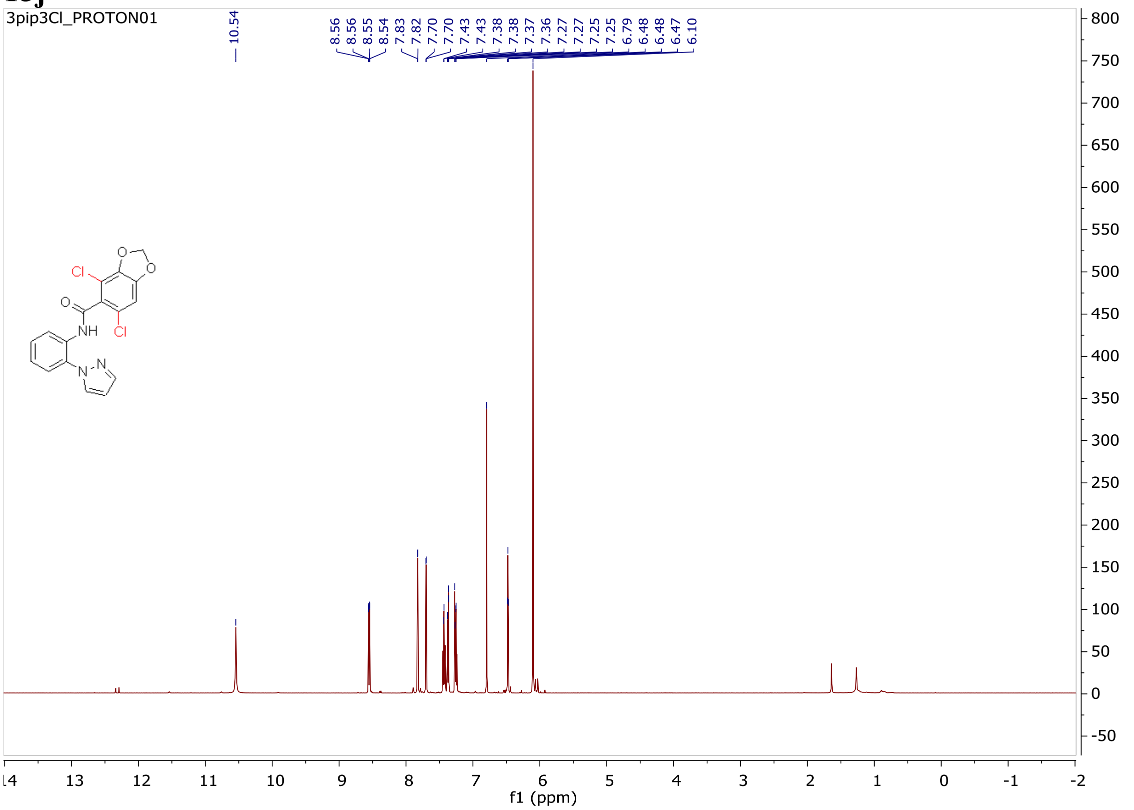
15i


4NO2cl-2_PROTON01
10.98
8.27
8.26
8.05
8.05
7.99
7.97
7.67
7.60
7.60
7.59
7.59
7.37
7.36
7.33
7.17
7.16
6.43
6.43
6.42
5.59
3.19 HDO
2.35 dmso
2.34 dmso
2.34 dmso
2.33 dmso
0.96
1.02
1.00
1.04
0.90
1.98
2.07
1.05
0.97
Cl
NO2
O
NH
Cl
N
N
f1 (ppm)

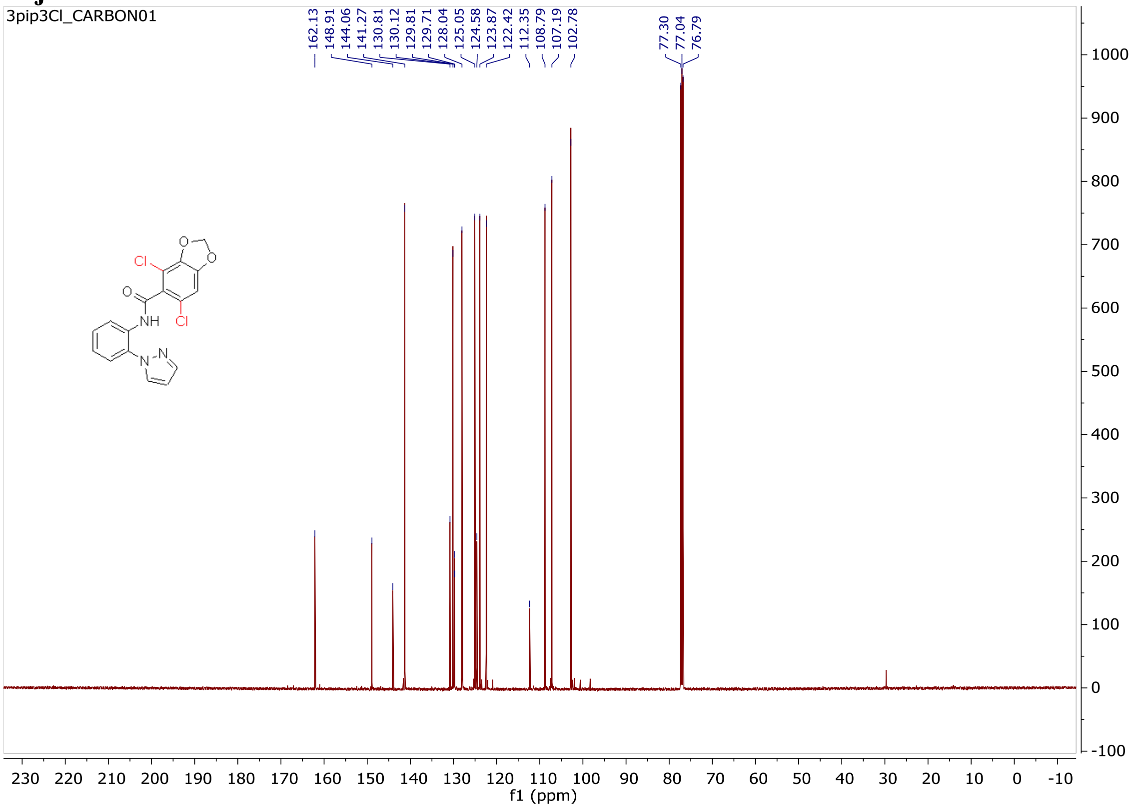
15i


4NO2clDMSO_carbon_CARBON01
162.64
156.99
150.36
141.59
132.82
132.11
131.75
131.34
128.65
125.45
125.43
125.11
124.06
114.21
111.80
107.74
Cl
NO2
O
NH
Cl
N
N
f1 (ppm)

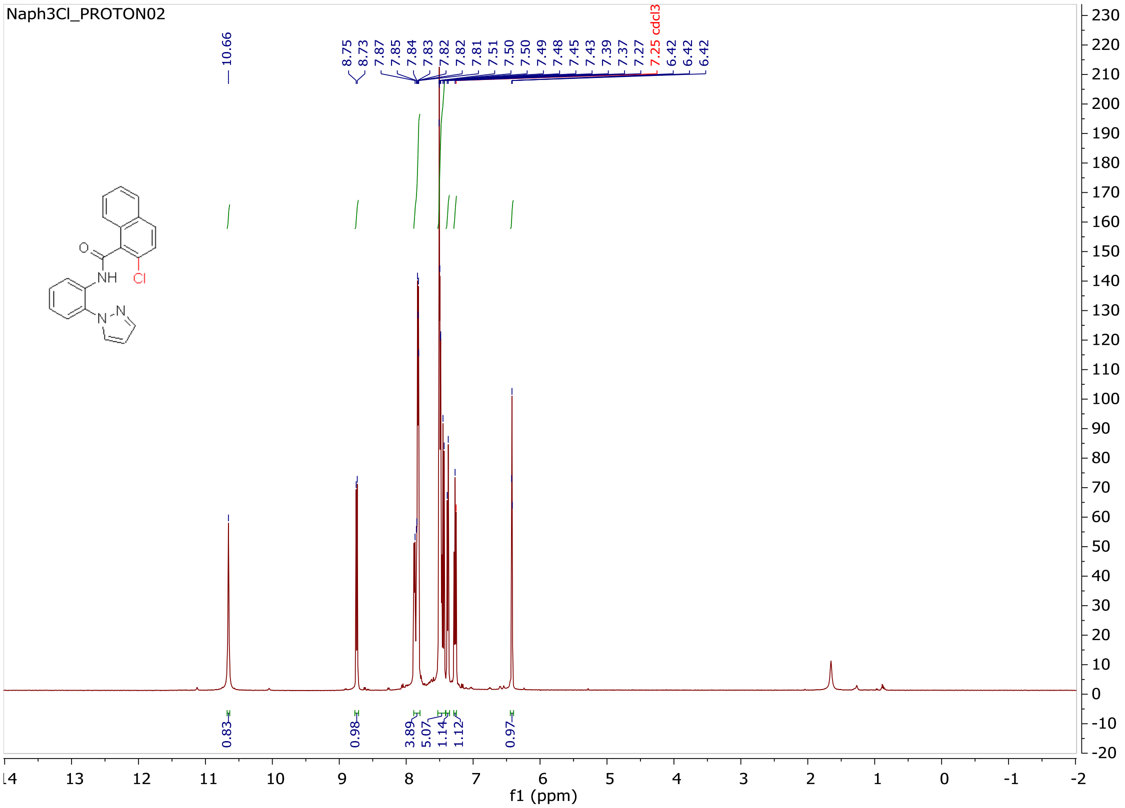
15j


3pip3Cl_PROTON01
10.54
8.56
8.56
8.55
8.54
7.83
7.82
7.70
7.70
7.43
7.43
7.38
7.38
7.37
7.36
7.27
7.27
7.25
7.25
6.79
6.48
6.48
6.47
6.10
Cl
O
O
O
NH
Cl
N
N
f1 (ppm)

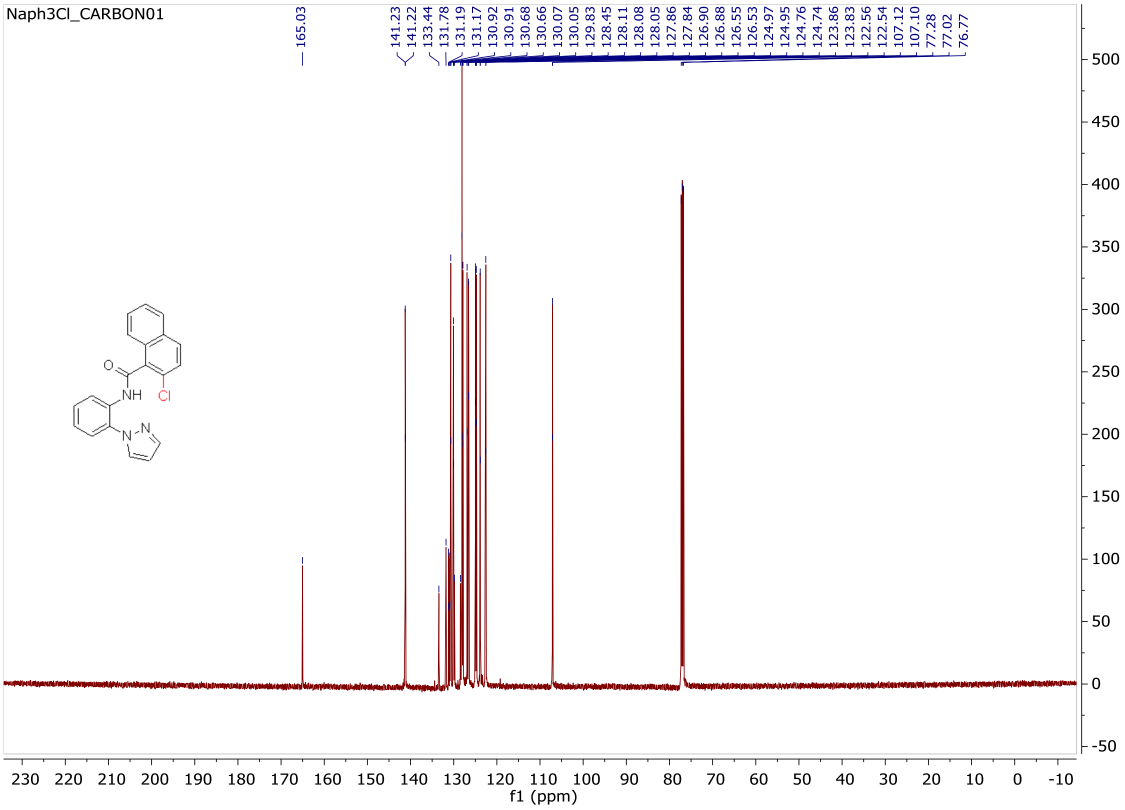
15j


3pip3Cl_CARBON01
162.13
148.91
144.06
141.27
130.81
130.12
129.81
129.71
128.04
125.05
124.58
123.87
122.42
112.35
108.79
107.19
102.78
77.30
77.04
76.79
Cl
O
O
O
NH
Cl
N
N
f1 (ppm)

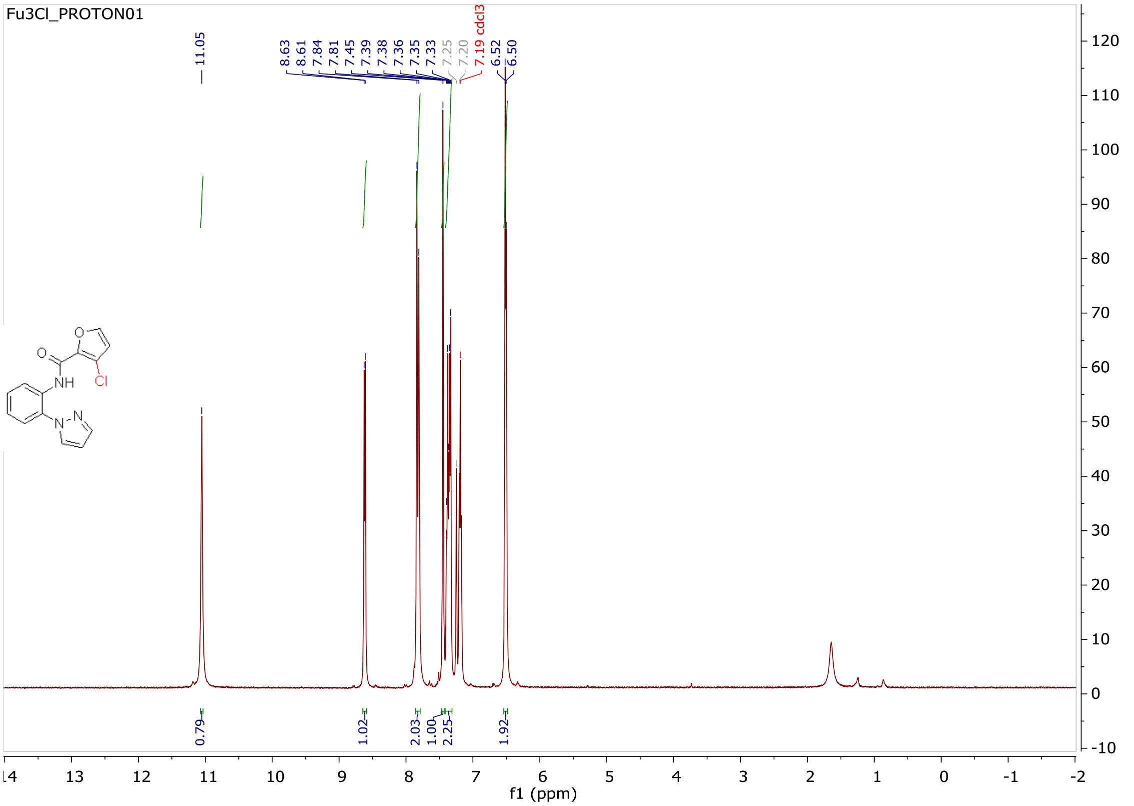
15k


Naph3Cl_PROTON02
10.66
8.75
8.73
7.87
7.85
7.84
7.83
7.82
7.82
7.81
7.51
7.50
7.50
7.49
7.48
7.45
7.43
7.39
7.37
7.27
7.25 cdcl3
6.42
6.42
6.42
0.83
0.98
3.89
5.07
1.14
1.12
0.97
O
NH
Cl
N
N
f1 (ppm)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20

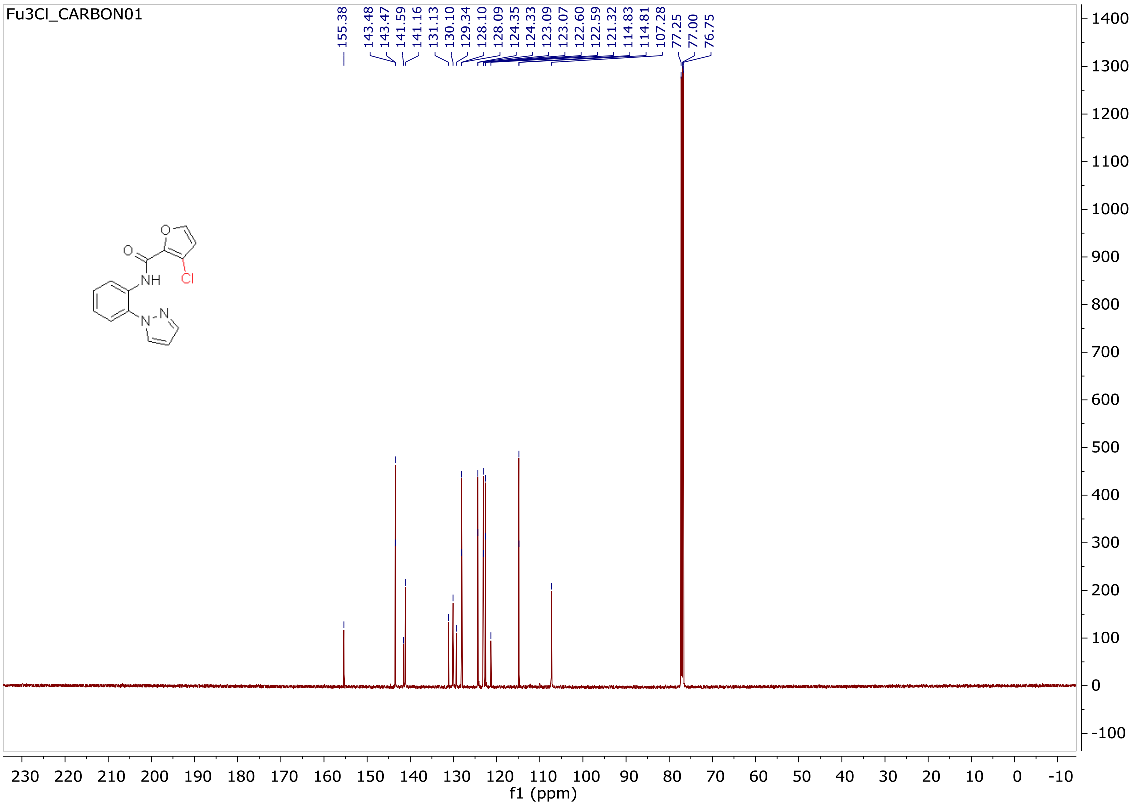
15k


Naph3Cl_CARBON01
165.03
141.23
141.22
133.44
131.78
131.19
131.17
130.92
130.91
130.68
130.66
130.07
130.05
129.83
128.45
128.11
128.08
128.05
127.86
127.84
126.90
126.88
126.55
126.53
124.97
124.95
124.76
124.74
123.86
123.83
122.56
122.54
107.12
107.10
77.28
77.02
76.77
O
NH
Cl
N
N
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
500
450
400
350
300
250
200
150
100
50
0
-50

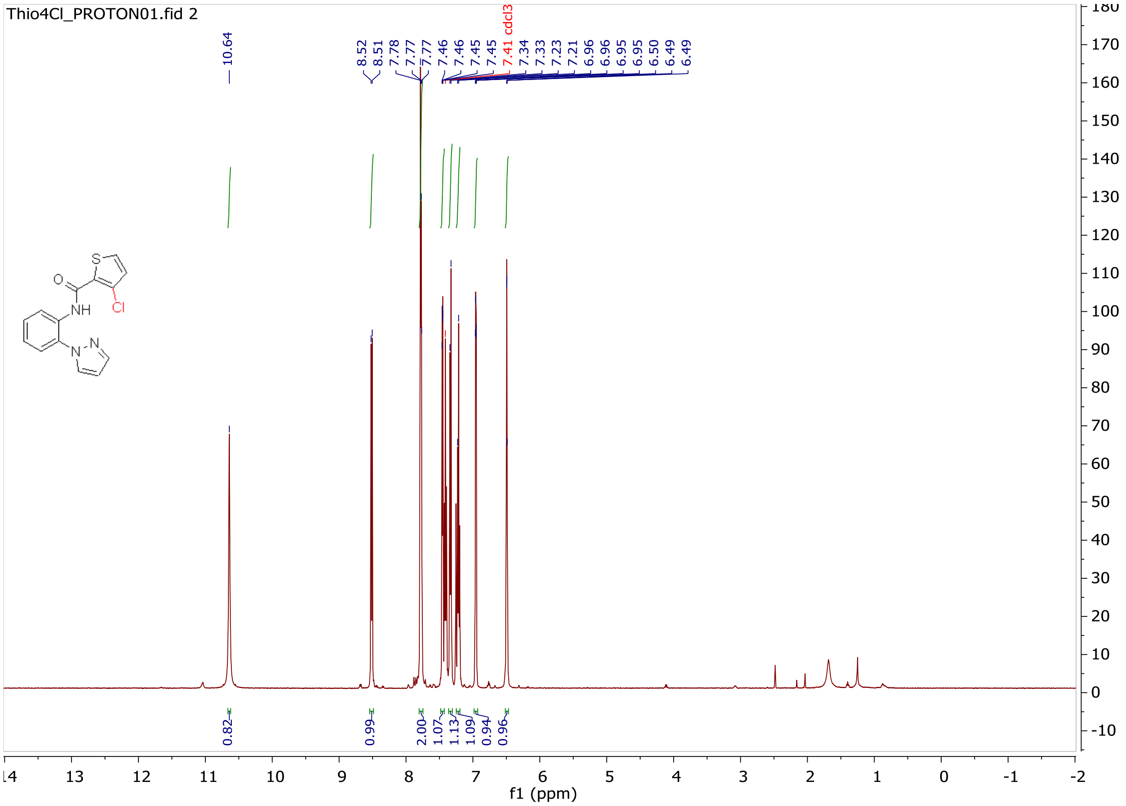
15l


Fu3Cl_PROTON01
11.05
8.63
8.61
7.84
7.81
7.45
7.39
7.38
7.36
7.35
7.33
7.25
7.20
7.19 cdcl3
6.52
6.50
0.79
1.02
2.03
1.00
2.25
1.92
O
NH
Cl
N
N
f1 (ppm)

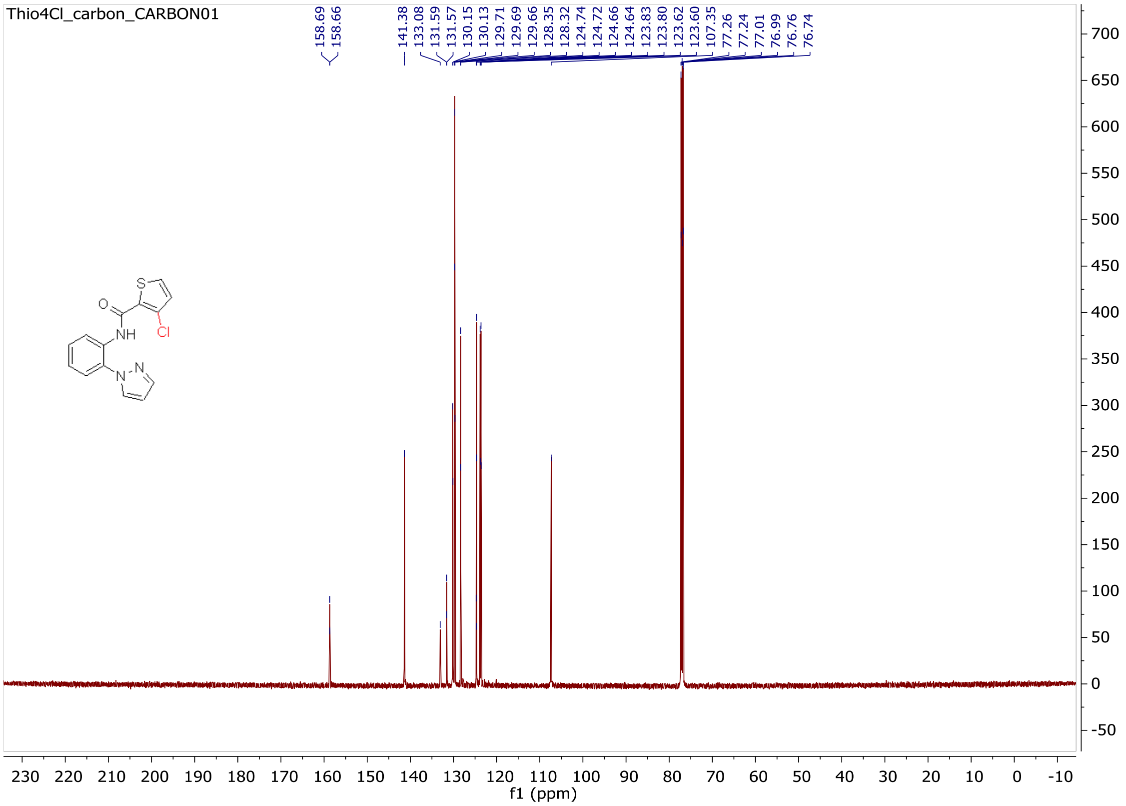
15l


Fu3Cl_CARBON01
155.38
143.48
143.47
141.59
141.16
131.13
130.10
129.34
128.10
128.09
124.35
124.33
123.09
123.07
122.60
122.59
121.32
114.83
114.81
107.28
77.25
77.00
76.75
O
NH
Cl
N
N
f1 (ppm)

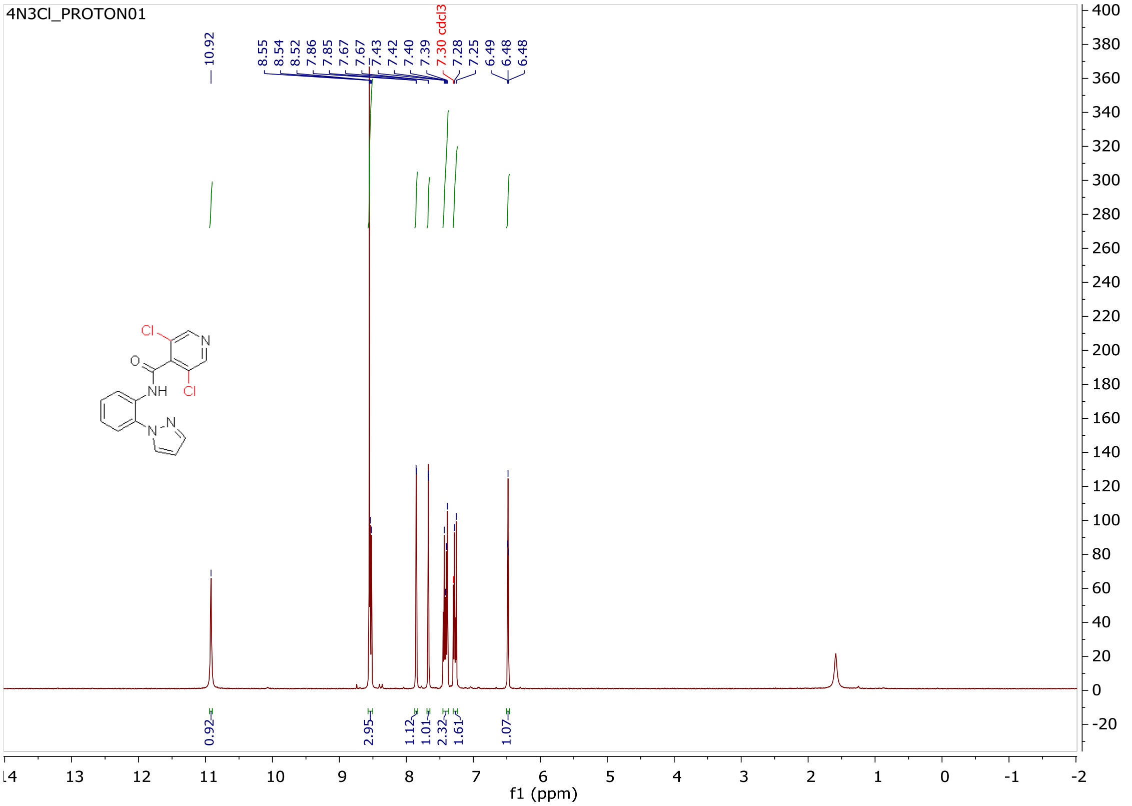
15m


Thio4Cl_PROTON01.fid 2
10.64
8.52
8.51
7.78
7.77
7.77
7.46
7.46
7.45
7.45
7.41 cdcl3
7.34
7.33
7.23
7.21
6.96
6.96
6.95
6.95
6.50
6.49
6.49
0.82
0.99
2.00
1.07
1.13
1.09
0.94
0.96
O
NH
S
Cl
N
N
f1 (ppm)

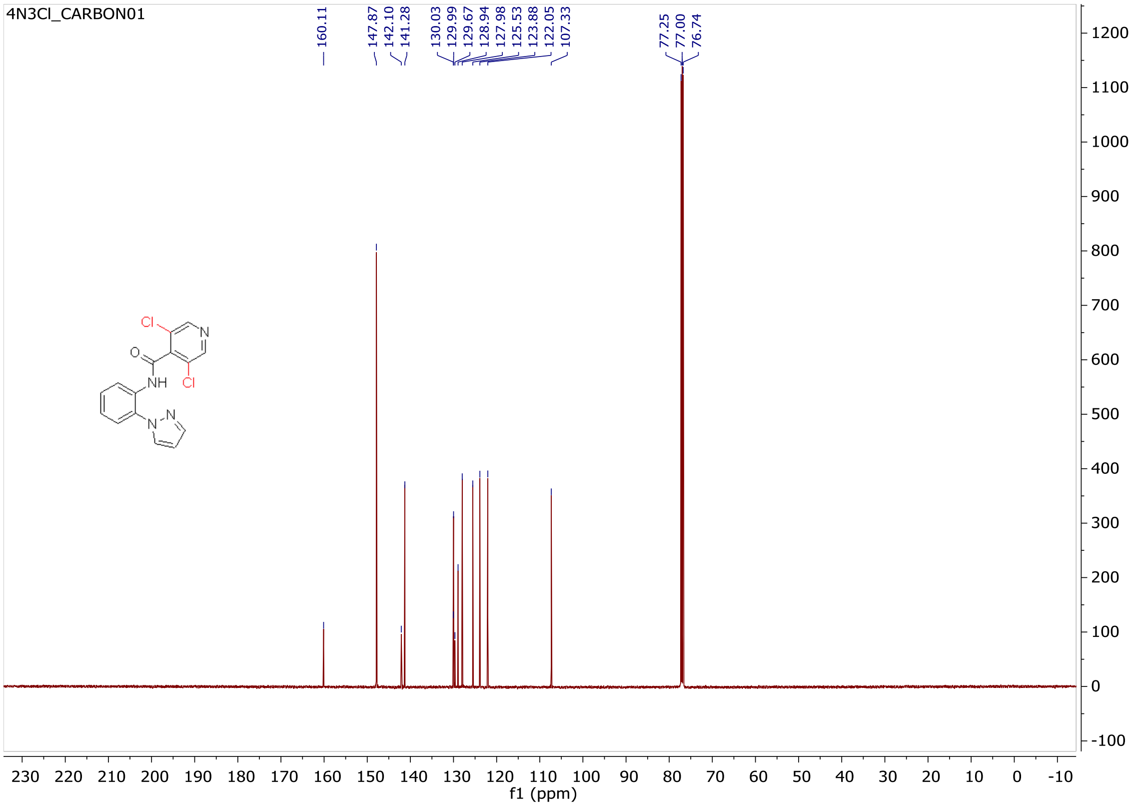
15m


Thio4Cl_carbon_CARBON01
158.69
158.66
141.38
133.08
131.59
131.57
130.15
130.13
129.71
129.69
129.66
128.35
128.32
124.74
124.72
124.66
124.64
123.83
123.80
123.62
123.60
107.35
77.26
77.24
77.01
76.99
76.76
76.74
O
NH
S
Cl
N
N
f1 (ppm)

15n

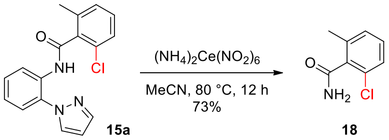

4N3Cl_PROTON01
10.92
8.55
8.54
8.52
7.86
7.85
7.67
7.67
7.43
7.42
7.40
7.39
7.30 cdcl3
7.28
7.25
6.49
6.48
6.48
0.92
2.95
1.12
1.01
2.32
1.61
1.07
Cl
N
O
NH
Cl
N
N
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)
400
380
360
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20

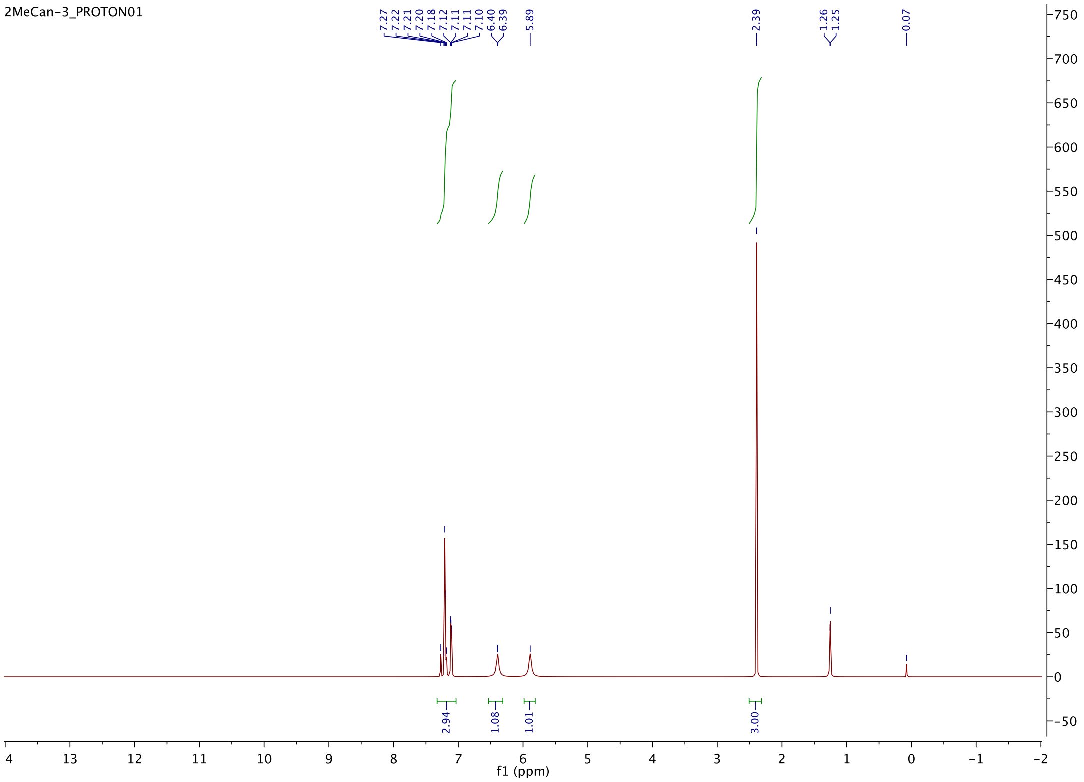
15n


4N3Cl_CARBON01
160.11
147.87
142.10
141.28
130.03
129.99
129.67
128.94
127.98
125.53
123.88
122.05
107.33
77.25
77.00
76.74
Cl
N
O
NH
Cl
N
N
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

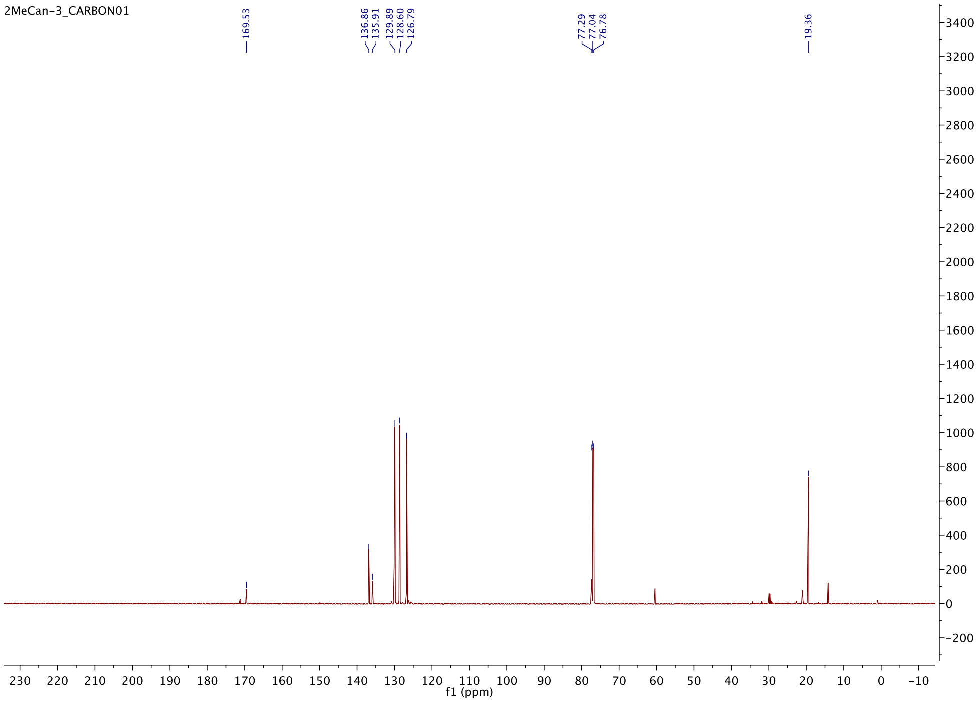
SI: C-H Chlorination

18

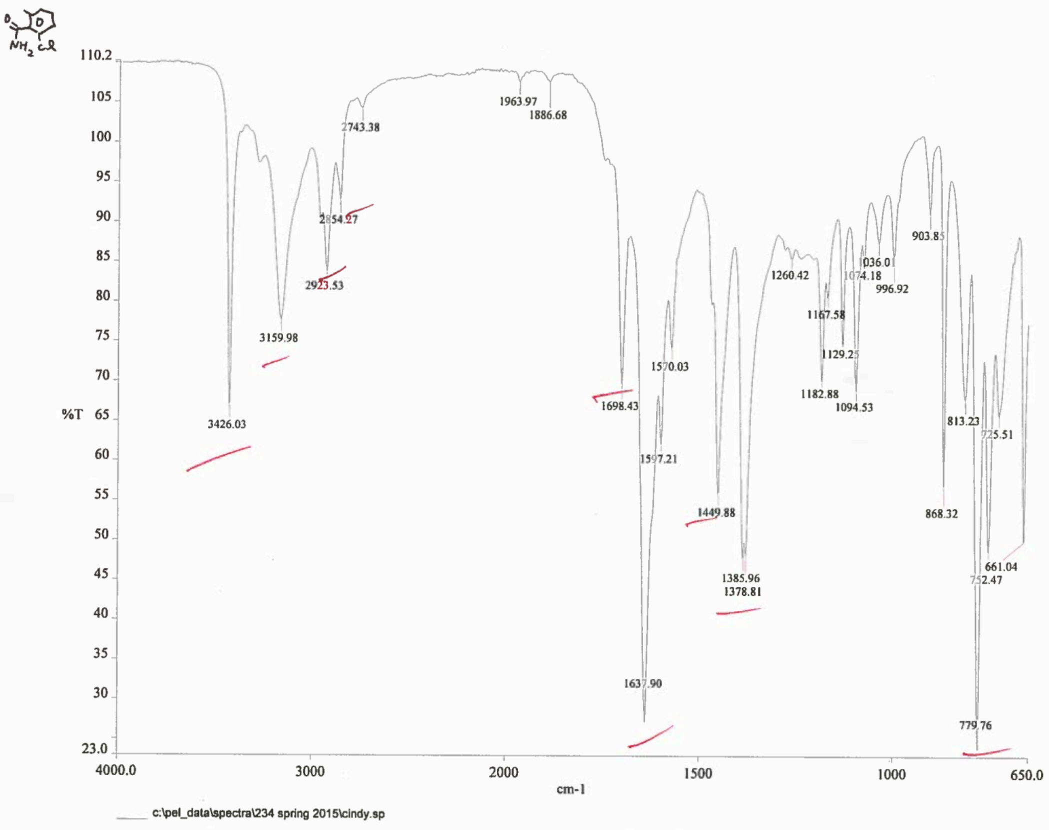


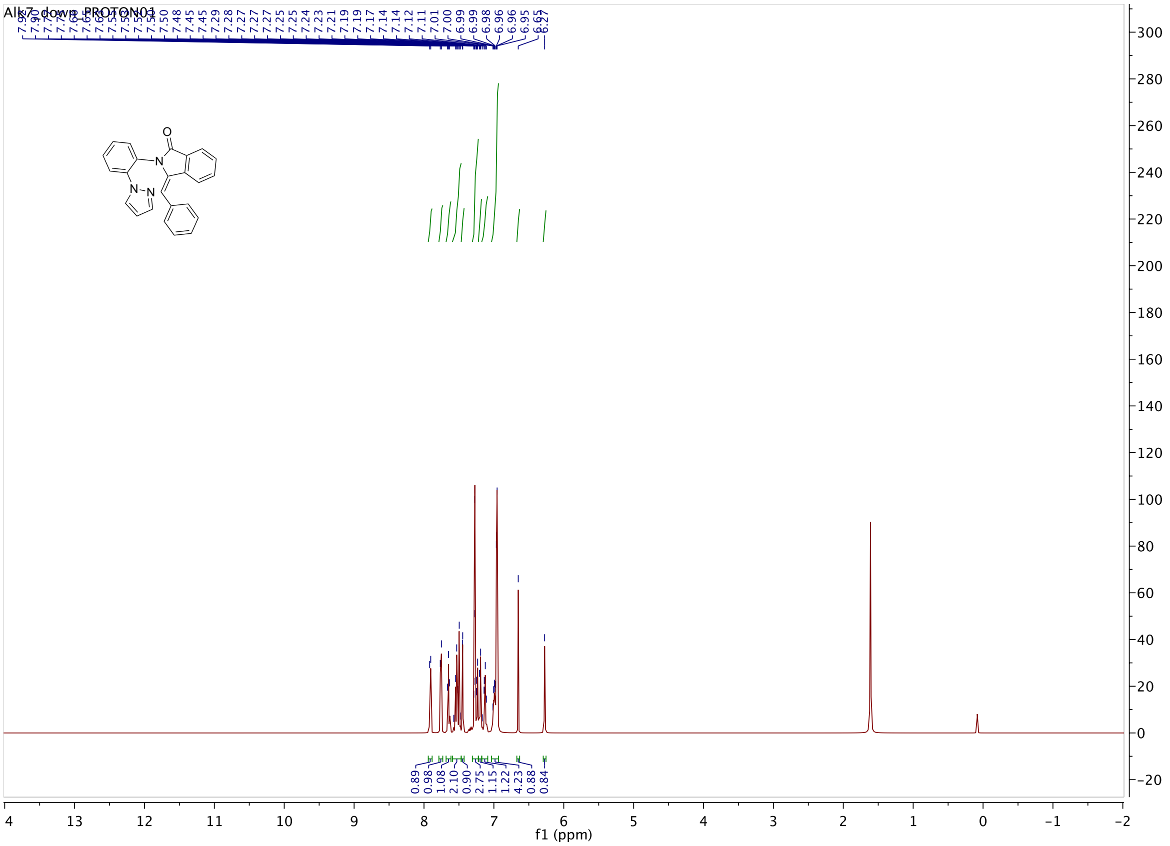


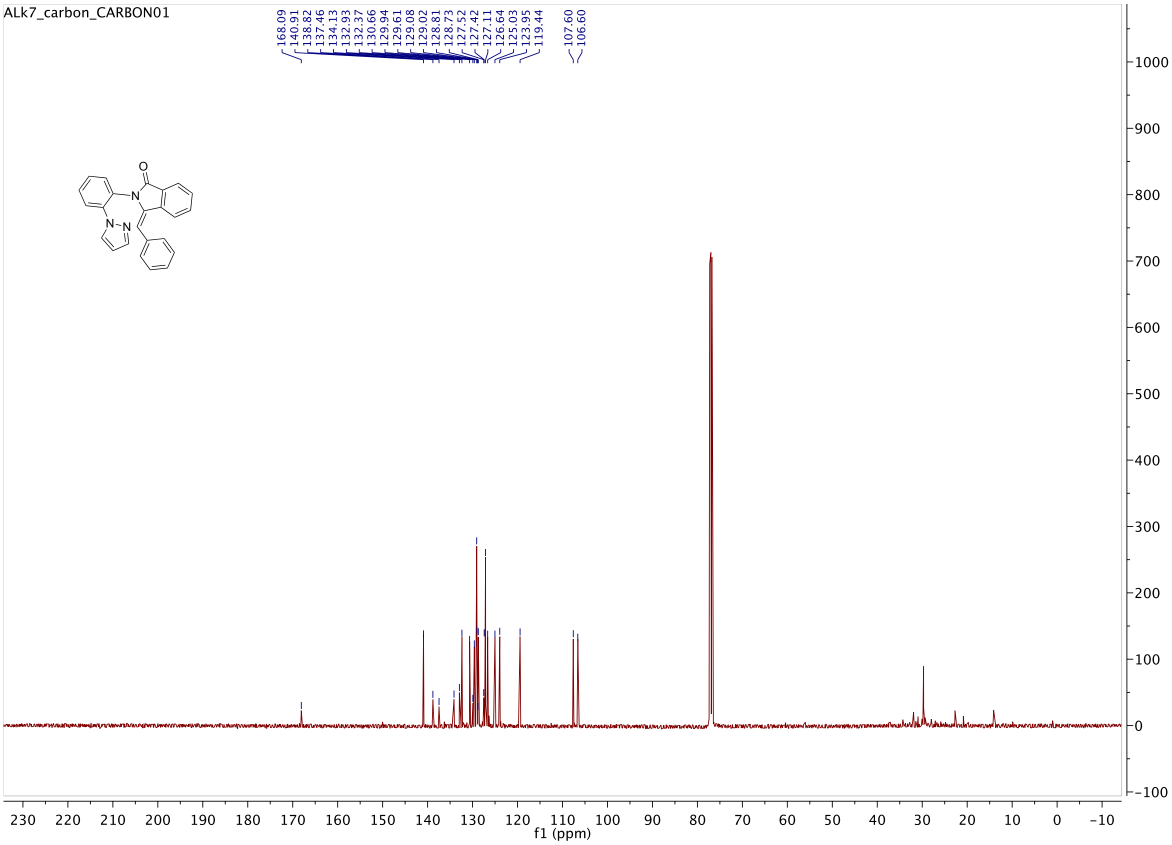
18



18


O
NH2
Cl
110.2
105
100
95
90
85
80
75
70
%T
65
60
55
50
45
40
35
30
23.0
4000.0
3000
2000
1500
1000
650.0
cm-1
3426.03
3159.98
2923.53
2854.27
2743.38
1963.97
1886.68
1698.43
1637.90
1597.21
1570.03
1449.88
1385.96
1378.81
1260.42
1182.88
1167.58
1129.25
1094.53
1074.18
1036.01
996.92
903.85
868.32
813.23
779.76
752.47
725.51
661.04
c:\pel_data\spectra\234 spring 2015\cindy.sp


Alk7_down_PROTON01
7.92
7.90
7.77
7.77
7.65
7.65
7.63
7.55
7.53
7.52
7.50
7.50
7.48
7.45
7.45
7.29
7.28
7.27
7.27
7.27
7.25
7.25
7.24
7.23
7.21
7.19
7.19
7.17
7.14
7.14
7.12
7.11
7.01
7.00
6.99
6.99
6.98
6.96
6.96
6.95
6.65
6.27
O
N
N
N
0.89
0.98
1.08
2.10
0.90
2.75
1.15
1.22
4.23
0.88
0.84
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)


ALk7_carbon_CARBON01
168.09
140.91
138.82
137.46
134.13
132.93
132.37
130.66
129.94
129.61
129.08
129.02
128.81
128.73
127.52
127.42
127.11
126.64
125.03
123.95
119.44
107.60
106.60
O
N
N
N
1000
900
800
700
600
500
400
300
200
100
0
-100
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)