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Graphical Abstract

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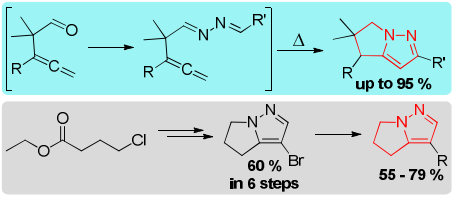

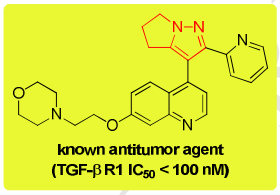

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ABSTRACT

In the paper we indicate the increasing importance of derivatives containing a dihydropyrrolo[1,2-*b*]pyrazole (DPP) core. We try to show our synthetic approach based on an improved Kulinkovich method as well as our new synthetic pathway. A complex methodology involving the preparation of substituted DPPs focuses on withasomnine and the synthesis of several structurally related compounds. The developed reaction protocols enable the preparation of the mentioned bicyclic system with broadly diverse substitution. Thus, we are able to prepare systems with aliphatic, aromatic, polyaromatic, heteroaromatic, TMS, and even adamantane substitution with known biologically active properties. The reaction protocol, consisting of two multi-step synthetic pathways, includes Sonogashira and Suzuki-Miyaura cross-coupling reactions, allenyl synthon formation, Kulinkovich cyclopropanation, ring transformations, and nonsymmetrical homoallenyl azines cycloadditions. Moreover, we prepared compounds with a resemblance to other bioactive species: fadrozole, nagstatine, an antitumor agent LY2109761 and a mixed lineage kinase 7 inhibitor DHP-2.

1. Introduction

Small biologically active molecules that mimic natural products are nowadays being produced and tested by many research groups. This has led to the concept of function-oriented synthesis introduced recently by Paul Wender, who simplified analogues of biologically active natural products by means of step-economy synthesis.[1] These products exhibited preserved or even superior activities to those of the natural products. In this regard we have investigated a comprehensive methodology for the synthesis of dihydropyrrolo[1,2-*b*]pyrazoles (DPP) consisting of two multi-step reaction pathways. One of them is based on the application of the allene synthon.

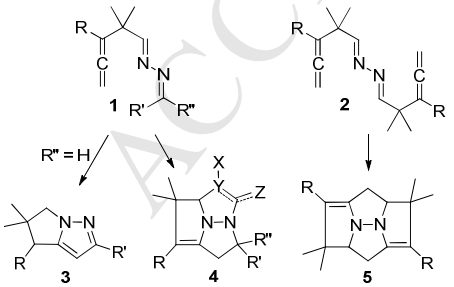

Fig. 1. Thermally initiated cycloadditions of homoallenyl azines **1** and **2** leading to bi-, tri- and tetracyclic heterocycles.

The preparation and investigation of the reactivity of nonsymmetrical and symmetrical allenyl azines **1** and **2** have a tradition in our laboratory (Fig. 1).[2] The presence of a dipole and dipolarophile within one molecule is a very potent combination for heterocyclic chemistry. Thus, during our research we have published papers dealing with the first example of the intramolecular criss-cross cycloaddition of symmetrical azines **2** leading to products **5** with four fused centrally connected five-membered rings[3a], as well as criss-cross cycloaddition reactions of nonsymmetrical azines **1** with various dipolarophiles, combining both an intra- and intermolecular approach.[3b] The latter resulted in heterocycles **4** with three fused five-membered rings. Moreover, in some cases we were even able to isolate stable bicyclic systems **3** with a DPP core,[3b-d] identical to that of naturally occurring plant alkaloid withasomnine **6** (Fig. 2).

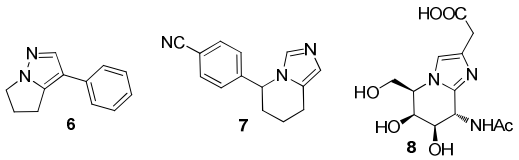

Fig. 2. Bioactive withasomnine **6**, fadrozole **7** and nagstatine **8**.

Compound **6** was originally isolated in 1966 from the root bark of *Withania Somnifera* (Solanaceae).[4] It exhibited a depression of the CNS and circulatory systems, a mild analgesic effect, narcosis in higher doses, and the inhibition of cyclooxygenase 1 and 2 (COX-1 and COX-2) and leukotriene B_4 (LTB_4) metabolism.[5] There are several reports[6] on the synthesis of **6** and, recently, Ichikawa[7a] with co-workers applied several synthetic steps including a regioselective Claisen rearrangement

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of their prepared 4-*O*-allyl-4-hydroxy-1*H*-pyrazoles in very good overall yields. Foster et al.[7b] reported the divergent synthesis of **6** via sydnone-alkynylboronate cycloaddition. More than 15 years ago, Kulinkovich[7c] published a synthetic protocol but without any experimental evidence or spectroscopic characterizations of synthesized compounds. Thus, we decided to re-examine and improve this synthesis with full identifications of intermediates and products. Fadrazole **7** appeared as another biologically active compound, which is a potent, selective, nonsteroidal aromatase inhibitor (type II). It suppresses estrogen production when administered orally and in this way works as a suitable candidate for testing as a potential aromatase inhibitor in estrogen-dependent diseases, including breast cancer.[8] Moreover, a further similarity was found with the imidazole-sugar nagstatine **8**[9] (a natural product and a very potent inhibitor of some glucosaminidases) and similar compounds.[10] An alicyclic side chain fused to the nitrogen-containing heterocycle is also known from the chemistry of cannabinoid antagonist analogues.[11] In view of the beneficial pharmacological properties of CB_1 receptor ligands (G-protein-coupled membrane receptors primarily present in the central nervous system) in the treatment of a number of diseases,[12] a major aim in medicinal chemistry is the development of novel CB_1 cannabinoid receptor ligands exhibiting more favorable pharmacological features. It is worth noting that the 2012 Nobel Prize in Chemistry was awarded for work on G-protein-coupled receptors.

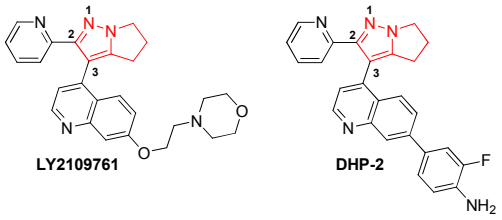
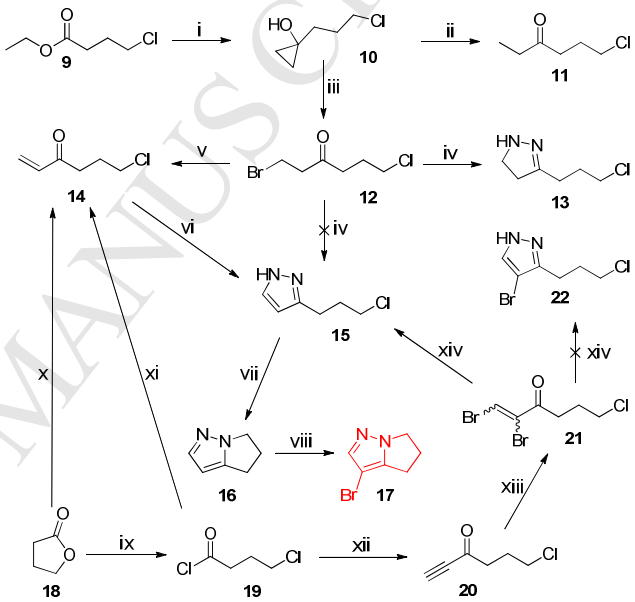


Fig. 3. Bioactive compounds LY2109761 and DHP-2 with DPP core.

One can find several other papers dealing with bioactive molecules containing a DPP core.[13] We chose two potent examples, **LY2109761**[13f,g] (an antitumor agent) and **DHP-2**[13c] (Fig. 3) as a selective inhibitor of MLK7 (mixed lineage kinase 7), which is a mitogen-activated protein kinase (MAPK).[14] MAPKs are a highly conserved family of signal transduction molecules that transmit extracellular signals from the membrane to the nucleus. Such small molecules deserve attention, especially with respect to recognizing and specifying their potential applications and benefits.[16]

2. Results and discussion

In this paper, we present two approaches to a series of variously substituted DPPs. The first pathway is represented by a modified Kulinkovich procedure consisting of a cyclopropanation / ring transformation / aromatization / bicyclic skeleton formation in the reaction cascade (Scheme 1).[7c] We investigated this convenient synthetic procedure more deeply and made several changes and improvements. The first and a key step in the method is the Kulinkovich reaction[17] (cyclopropanation) of ester **9** in the presence of EtMgBr with 10 mol% of Ti(*i*PrO)$_4$ in Et_2O. However, cyclopropanol **10** was unstable, even in refrigerated conditions, and within several hours the formation of stable ketone **11** was observed. This transformation took several days at room temperature to be completed. Therefore, compound **10** was immediately used in the following reaction step without purification. Here, the ring opening step proceeds with bromine in the presence of K_2CO_3 in DCM (retro-Barbier fragmentation[18]) affording a brownish liquid **12** – 1-bromo-6-chlorohexan-3-one. It is worth noting that the reaction protocol from the original paper,[7c] where bromine was used in 80 % aq. *i*PrOH, did not work. We observed just traces of the desired product only with the majority of **11**. Product **12** was not purified and treatment with TEA (2 eq.) afforded 6-chlorohex-1-en-3-one (**14**) in an almost quantitative yield (2 h). Using less than 2 eq. of TEA led to a significantly increased reaction time (>10 h). After vacuum distillation of **14** we isolated a colorless liquid in 78 % yield with respect to **9**. The following 3-substituted pyrazole ring formation (**15**) and its intramolecular cyclization afforded under basic conditions a key non-substituted intermediate **16** – 5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole. Although the bromination of such a structure in position 3 is described with Br_2 / NaOAc in 60 % AcOH,[7c] we successfuly utilized NBS (1 eq.) in $CHCl_3$ at room temperature and after 5 min we observed the formation of a pure light yellow solid **17** in 77 % yield with respect to **14**. The overall yield of this six-step synthesis is 60 % (see Experimental Section) with a significantly reduced reaction time compared to a published[7c] procedure.

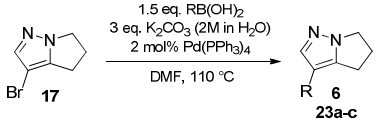


Scheme 1. Six synthetic steps to brominated heterocycle **17** from ester **9** in 60 % overall yield. Scheme also includes trasformations of γ-butyrolactone **18** into pyrazole intermediate **15**. Reagents and conditions: (i) Ti(*i*PrO)$_4$ (0.1 eq.), EtMgBr (2 eq.), Et_2O, r.t., overnight; (ii) few days standing at the room temperature; (iii) Br_2 (1.1 eq.), K_2CO_3 (1.2 eq.), DCM, 0 °C, 1.5 h; (iv) $N_2H_4.H_2O$ (2 eq.), DCM, reflux, 4 h, 70 % from **9**; (v) Et_3N (2 eq.), Et_2O, r.t., 2 h, 78 % from **9**; (vi) 1. KBr_3 (1.1 eq.), 80 % *i*PrOH, 0 °C, 1 h; 2. $N_2H_4.H_2O$ (5 eq.), 80 % *i*PrOH, r.t., overnight; (vii) KOH (1.1 eq.), 80 % *i*PrOH, reflux, 4 h; (viii) NBS (1.1 eq.), $CHCl_3$, r.t., 5 min, 77 % from **14**; (ix) $SOCl_2$ (2.5 eq.), $ZnCl_2$ (0.08 eq.), 55 °C, 20 h, 75 %; (x) vinylMgBr (1 eq.), THF, -78 °C, 3 h and then $SOCl_2$; (xi) **19** (1.1 eq.), DMF (1.2 eq.), vinylMgBr (1 eq.), $PhCH_3$, -5 °C, 4 h; (xii) ethynylMgBr (1 eq.), CuI (0.08 eq.), THF, 0 °C, 2 h, 52 %; (xiii) Br_2 (1 eq.), CCl_4, r.t., 30 min, 93 %; (xiv) $N_2H_4.H_2O$ (5 eq.), 80 % *i*PrOH, r.t., 14 h, 70 %.

Another source for the synthesis of the required compound **14** is the inexpensive compound γ-butyrolactone (**18**) via 4-chlorobutanoyl chloride (**19**) by means of ring opening by $SOCl_2$[19] and a subsequent reaction with vinyl magnesium bromide. Because the same ring opening leading to **14** by a Grignard reagent is described in the literature,[20] we utilized

vinylmagnesium bromide with the idea of simplifying the whole procedure. However, several attempts to perform this reaction failed. A different situation occured with ethynylmagnesium bromide, where, surprisingly, the reaction worked and 6-chlorohex-1-yn-3-one (**20**) was isolated in 52 % yield. Following this, an almost quantitative addition of bromine to the triple bond was performed affording dibromo derivative **21** in 30 min. Both, *cis* and *trans* isomers in the ratio ~ 3 : 7 were isolated. Our intention to synthesize substituted pyrazole **22** bearing bromine at the desired position by the reaction with hydrazine hydrate failed and, surprisingly, we obtained only non-brominated pyrazole **15** (70 %). Nevertheless, we have already described its cyclization to compound **16** and transformation to 3-brominated DPP **17**. The final step to obtaining withasomnine **6** was a Suzuki – Miyaura coupling reaction of brominated pyrazole **17** with substituted boronic acids (Table 1).

Table 1. Overview of optimization conditions used in Suzuki–Miyaura coupling reactions of brominated heterocycle **17***

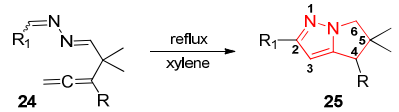


Entry	R	Solvent	T [°C]	Catalyst	Mol%	Reaction time [h]	Conversion [%]	Yield [mg (%)]	Biphenyl [mg]
1.	Ph	MeOH	reflux	$PdCl_2(PPh_3)_2$	5	4	NR	-	-
2.	Ph	THF	reflux	$PdCl_2(PPh_3)_2$	5	24	NR	-	-
3.	Ph	$PhCH_3$	110	$PdCl_2(PPh_3)_2$	5	5	50	-	-
4.	Ph	Xylene	reflux	$PdCl_2(PPh_3)_2$	5	2.5	100	53 (57)	28
5.	Ph	DMF	110	$Pd(PPh_3)_4$	5	0.25	100	59 (64)	11
6.	**Ph**	**DMF**	**110**	**$Pd(PPh_3)_4$**	**2**	**1**	**100**	**58 (63)**	**11**
7.	Ph	DMF	110	$Pd(PPh_3)_4$	1	6	<80	-	-
8.	Ph	DMF	110	$Pd(dppf)Cl_2$	5	2.5	100	41 (45)	6
9.	Ph	DMF	110	$Pd(OAc)_2$	5	6	<50	-	-
10.	Ph	DMF	110	$Pd(dba)_2$	5	6	<50	-	-
11.	Ph	DMF	110	$NiCl_2(PPh_3)_2$	5	7	NR	-	-
12.	**4-Cl-Ph**	**DMF**	**110**	**$Pd(PPh_3)_4$**	**2**	**1.5**	**100**	**60 (55)**	**10**
13.	**4-Pyridine**	**DMF**	**110**	**$Pd(PPh_3)_4$**	**2**	**1**	**100**	**72 (79)**	**8**
14.	**1-Pyrenyl**	**DMF**	**110**	**$Pd(PPh_3)_4$**	**2**	**1**	**100**	**107 (70)**	**20**
15.	Cyclohexyl	DMF	110	$Pd(PPh_3)_4$	5	3	NR	-	-
16.	Cyclohexyl	Dioxane	90	$Pd(dppf)Cl_2$	20	24	NR	-	-

*reactant **17** (0.5 mmol), $RB(OH)_2$ (0.75 mmol), 5 ml of solvent, preheated oil bath; NR = no reaction.

Initially, we utilized conditions from literature[21], in which we tested several palladium catalysts in different loadings (2–5 mol%). Later, we made some corrections to make this reaction applicable for all the used boronic acids. Reaction with phenylboronic acid (entries 1–11; Table 1) served as a model reaction. During testing, our attention was devoted to the solvent (DMF, xylene, dioxane, THF, methanol), the temperature, and the reaction time (0.25–24 h). Full conversion was observed with three Pd-catalysts – $PdCl_2(PPh_3)_2$, $Pd(dppf)Cl_2$ and $Pd(PPh_3)_4$ in 45–64 % yield within 0.25–2.5 h. The remaining catalysts ($Pd(OAc)_2$, $Pd(dba)_2$) showed lower conversions and $NiCl_2(PPh_3)_2$ did not react at all. Thus, based on the performed reactions, we chose as optimal conditions 2 mol% $Pd(PPh_3)_2$ in DMF at 110 °C. These conditions were succesfully applied with other boronic acids – 4-chlorophenyl (entry 12, 55 %), 4-pyridine (entry 13, 79 %) and 1-pyrene (entry 14, 70 %). The reaction time did not exceed 90 min (Table 1). When the concentration of catalyst was increased to 5 mol%, the reaction worked four times faster but with the same result (compare entry 5 vs 6). Moreover, several attempts at using microwave irradiation yielded much lower conversions than the reactions with conventional heating. After 90 min with 5 mol% of $Pd(PPh_3)_4$ we isolated just 37 % of desired product **6**, and a prolongation of the reaction time led to unspecified slow decomposition. Any attempt to introduce the cyclohexyl substitution to our skeleton failed (entries 15, 16). Moreover, along with the Suzuki product we observed the characteristic formation of side biphenyl compounds arising from boronic acid and a phenyl group from the catalyst (biphenyl, 4-chlorobiphenyl, etc). These structures were confirmed by NMR and GC–MS after separation.

We have already mentioned two examples of potent bioactive compounds (Fig. 3) with a DPP core. The aim is to broaden this area and to continue in successfully utilizing small molecules, such as dorsomorphin.[22] Thus, beside withasomnine **6** and its analogues (**23a-c**), we examined the preparation of similar bicyclic compounds bearing two methyl groups at C5 and various substitutions at C2 and C4 (aliphatic, aromatic, polyaromatic, heteroaromatic, TMS, 1-adamantyl). These derivatives **25** were prepared by the thermally initiated intramolecular cycloaddition of nonsymmetrical homoallenyl azines **24** (Scheme 2).[23]



Scheme 2. Intramolecular cycloaddition of nonsymmetrical homoallenyl azines **24** to 2,4-disubstituted-3,3-dimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazoles **25**.

Their formation was observed for the first time by Man et al.[3b] during his work on combined intra-intermolecular criss-cross cycloadditions of azines **24** with PhNCO. In summary, we prepared in this way a library of 49 such structures (Table 2) with full identification and characterization (see Supplementary Information). The products **25aa-ae** with aliphatic substitution afforded the lowest yields because of their difficult purification connected with their liquid character and non-absorbing (254 nm) properties. Products **25ao-bc** are illustrative examples suggesting a general trend in the reactivities of homoallenyl azines **24**. In other words, the substitution at the allene moiety (R) plays a crucial role, and methyl (or ethyl)-substituted compounds, compared to non-substituted ones, react much faster and almost always in higher yields (**25ao** in 59 %; **25ap** in 82 %). The purity of the starting material also has a significant influence upon the results. Differential scanning calorimetry identified the most effective temperature for each of the derivatives with different *p*-substitution. The ideal temperature for this kind of cycloaddition was around 180 °C; however, for nitro-derivatives, it was less than 150 °C. This fact is reflected in much shorter reaction times (**25ao** in 9 h; **25bb** in 30 min). An analogous conclusion can be found for 2-thiophenyl (**25bd**,**be**), 2-furyl (**25bg**,**bh**), 1-naphthyl (**25bj**,**bk**) and 9-anthryl (**25bm**,**bn**) substitutions. In addition, anthryl analogues possess a very intensive fluorescence (Fig. 4), which can be utilized in fluorescent labeling as a fluorescence probe.[24] After the incorporation of hydroxymethyl or a similar substitution on the alicyclic side chain, we plan to test its ability as a DNA-intercalator.[25]

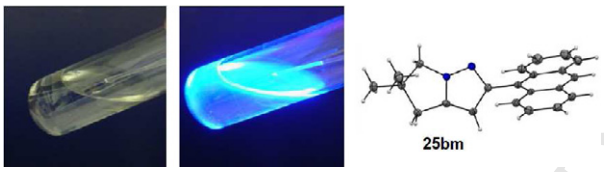
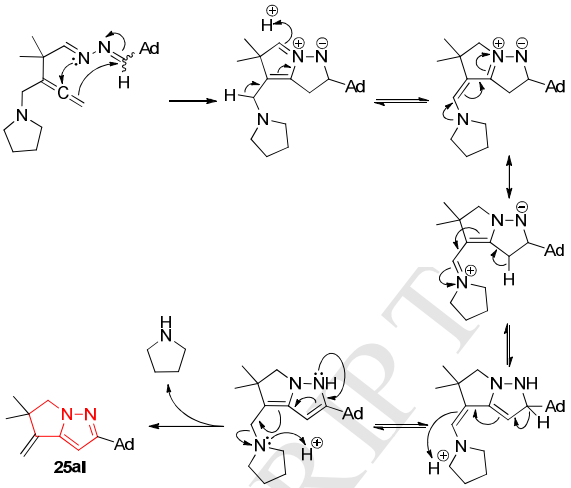


Fig. 4. ORTEP representation and fluorescence of **25bm** at 366 nm.

Since we are also interested in the chemistry of adamantane, we decided to combine its characteristic features with heterocyclic compounds in an attempt to achieve biologically potent systems. Adamantane has interested chemists for almost 80 years[26] and its derivatives have found numerous applications in medicinal[27] and material sciences.[28] Since the discovery of the potent inhibitory properties of amantadin[29]against several types of viruses in the early 1960s, a large number of investigations have been initiated. In the light of these, we prepared new adamantane-containing heterocycles **25af-am**, which appeared as colorless solids. Moreover, the reaction leading to products **25aj** and **25ak** afforded an unexpected bicyclic compound **25al** with an exocyclic double bond at C4 (Scheme 3). To explain its formation, we propose a mechanism in which we assume that the dipolar intermediate can be transformed *via* two pathways. Here, the formation of **25al** may be explained by an intramolecular attack of a nitrogen atom from the azine skeleton on the allenyl group producing a bicyclic 1,3-dipole. However, the electronegative nitrogen atom of pyrrolidine promotes a 1,5-proton shift followed by aromatization after amine elimination. This assumption is strongly supported by the experiment with D_2O, and similar products have also been isolated during our previous work.[2c] The second pathway leads to the expected products and is shown elsewhere.[3d]



Scheme 3. Proposed mechanism for the formation of unexpected product **25al** *via* proton migration and aromatization after amine elimination. The same transformation was observed with the morpholinomethyl substitution.

A considerable decomposition was observed along the formation of derivatives containing TMS group (**25bf**,**bi**,**bl**,**bo**). Thus, these reactions were carried out at a lower temperature (110 °C), which was reflected in the time prolongation (7.5 – 10 h); however, still low yields were produced (up to 29 % for **25bf**). Bromination with NBS carried out on selected dimethylated **25ap** and **25ba** afforded brominated products **25bx** and **25by** in high yields. Subsequent application of optimized conditions for Suzuki coupling (Table 1) was examined on **25by** and again we obtained the desired product **25bz** in very good yield. The structure of such systems was demonstrated by several crystallographic analyses (Fig. 4 and 5 and Supplementary Information).

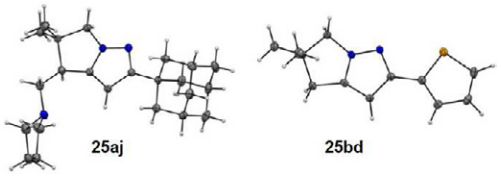


Fig. 5. ORTEP illustrations of **25aj** and **25bd** crystal structures.

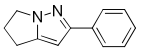
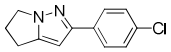
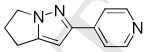
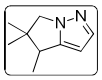
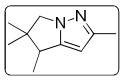
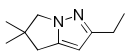
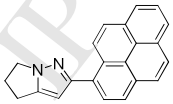
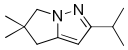
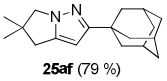
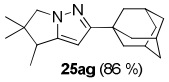
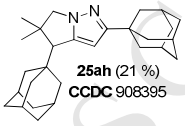
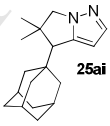
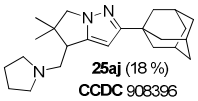
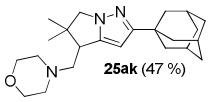
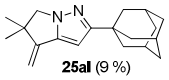
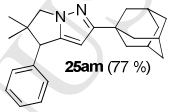
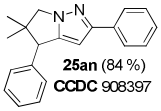
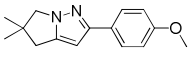
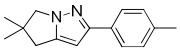
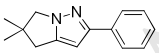
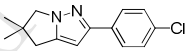
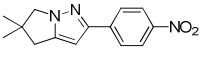
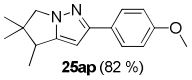
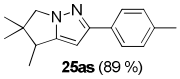
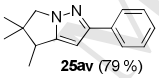
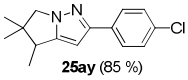
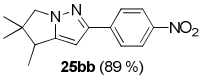
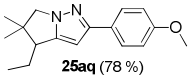
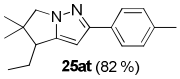
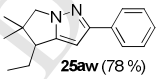
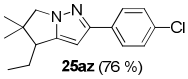
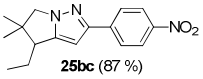
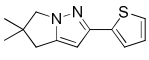
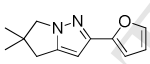
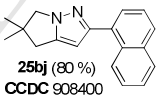
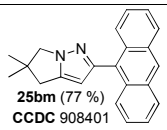
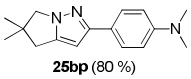
3. Conclusions

We investigated two reaction pathways leading to a library of 58 dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole target compounds. With the utilization of the improved Kulinkovich protocol, the first path yielded the withasomnine alkaloid (**6**) and three related structures (**23a-c**). We optimized this synthesis and fully characterized both the isolated intermediates and final compounds. We are able to synthesize 3-bromo-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (**17**) from cheap and accessible ethyl 4-chlorobutyrate (**9**) in less than 48 hours in 60 % overall yield. This means an almost 92 % average yield for all six steps. Optimized conditions for Suzuki-Miyaura coupling reactions now enable us to prepare the desired substituted withasomnines in up to 90 minutes. Another reaction pathway allowed us to produce analogous dimethylated compounds by the intramolecular cycloaddition of nonsymmetrical homoallenyl azines **24**. The broad usefulness of such a reaction is supported by the diverse substitution of the formed products. We demonstrated possible applications of molecules bearing polycyclic aromatic system in fluorescent labeling and even as

DNA-intercalators. We showed even biologically active molecules with DPP core, which is another promising area of continuing research. Nowadays, small molecules are being intensively developed in many research groups and our method is undoubtedly one of the most simple and accessible. We hope that small molecules will one day bring answers to many prominent questions.

Table 2. A comprehensive view of all prepared heterocyclic derivatives containing a DPP core with isolated yields and corresponding CCDC numbers.

Isolated dihydropyrrolo[1,2-*b*]pyrazoles

 **16** (~90 % over 2 steps)	 **17** (77 % over 3 steps)	 **6** (63 %)	 **23a** (55 %)	 **23b** (79 %)
 **25aa** (30 %)	 **25ab** (35 %)	 **25ac** (50 %)	 **25ad** (45 %)	 **23c** (70 %)
 **25ae** (17 %)	 **25af** (79 %) **CCDC** 908394	 **25ag** (86 %)	 **25ah** (21 %) **CCDC** 908395	 **25ai** (85 %)
 **25aj** (18 %) **CCDC** 908396	 **25ak** (47 %)	 **25al** (9 %)	 **25am** (77 %)	 **25an** (84 %) **CCDC** 908397
 **25ao** (59 %)	 **25ar** (77 %)	 **25au** (78 %)	 **25ax** (77 %)	 **25ba** (71 %) **CCDC** 908398
 **25ap** (82 %)	 **25as** (89 %)	 **25av** (79 %)	 **25ay** (85 %)	 **25bb** (89 %)
 **25aq** (78 %)	 **25at** (82 %)	 **25aw** (78 %)	 **25az** (76 %)	 **25bc** (87 %)
 **25bd** (44 %) **CCDC** 908399	 **25bg** (61 %)	 **25bj** (80 %) **CCDC** 908400	 **25bm** (77 %) **CCDC** 908401	 **25bp** (80 %) **CCDC** 908402
25be (81 %)	**25bh** (95 %)	**25bk** (92 %)	**25bn** (92 %)	**25bq** (83 %)
TMS **25bf** (29 %)	TMS **25bi** (25 %)	TMS **25bl** (21 %)	TMS **25bo** (23 %)	**25br** (83 %)
25bs (91 %)	**25bu** (88 %)	**25bw** (84 %)		
25bt (82 %)	**25bv** (82 %)	**25bx** (83 %)	**25by** (85 %)	**25bz** (78 %)

[a] Those two structures in rectangles have been published[3d]

4. Experimental section

4.1. General

All reagents were purchased from commercial suppliers and used as received. Diethylether and THF were distilled from sodium/benzophenone before use. Chloroform was dried and distilled from $CaCl_2$ and P_2O_5 and stored over 4Å molecular sieves. Xylene (mixture of isomers) was dried and distilled from sodium/benzophenone and stored over dry 4Å molecular sieves. All reactions were carried out under a dry argon atmosphere and were monitored by TLC (Merck F254 silica gel). Products were separated by preparative TLC or by liquid chromatography on a Horizon HPFC System (Biotage, Inc.) with Biotage Si 12+M and Si 25+M columns. Melting points were determined on a MPV-HV2 melting point meter in open capillaries. FT-IR spectra were recorded with a MIDAC Corporation Spectrafile IR apparatus or with a GENESIS ATI (Unicam) spectrometer. ^{1}H and ^{13}C spectra were recorded using a Bruker Avance 300 spectrometer operating at 300.13 MHz (^{1}H) and 75.47 MHz (^{13}C) with $CDCl_3$ as solvent. Tetramethylsilane (δ 0.00 ppm) or residual protons (δ 7.27 ppm) served as internal standards for ^{1}H NMR and $CDCl_3$ (δ 77.23 ppm) for ^{13}C NMR spectra. GC-MS data were obtained on a Shimadzu GCMS-QP2010 at 70 eV in the electron impact mode. MS data were obtained on a Fisons Instruments TRIO 1000 spectrometer at 70 eV in the electron impact mode and by thermal desorption. Elemental analyses were performed with a Perkin-Elmer CHN 2400 apparatus. High-resolution mass spectra (HRMS) were recorded on a Q-TOF Micro micromass instrument in the positive ESI (CV = 30 V) mode. X-ray diffraction data were collected on a Kuma KM-4 four-circle CCD diffractometer and corrected for Lorentz and polarization effects. The structures were resolved by direct methods and refined by full-matrix least-squares methods using the SHELXTL program package.[30,31] Hydrogen atoms were placed in calculated idealized positions.

1-(3-Chloropropyl)cyclopropanol 10: Ethyl 4-chlorobutyrate **9** (0.166 mol, 25.0 g, 23.3 mL) was dissolved in dry Et_2O (100 mL) and Ti(O*i*-Pr)$_4$ (0.02 mol, 5.80 g, 6.04 mL) was added by syringe over a period of 1 min. EtMgBr (0.349 mol, 46.5 g) in Et_2O (120 mL) was added dropwise over the course of 70 min. The reaction mixture was stirred at room temperature overnight (17 h). The reaction was quenched by the slow addition of saturated NH_4Cl (100 mL). The organic layer was decanted and the solid residue was dissolved in a mixture of water (200 mL) and 1M HCl (100 mL). Then it was extracted by Et_2O (2 × 100 mL). Combined organic phases were washed by 300 mL of saturated NaCl, dried over $MgSO_4$ and concentrated in vacuo. The crude product - bright yellow liquid (21.3 g) was used without further purification. ^{1}H NMR: δ = 3.63 (t, ^3J = 6.6, 2H, CH_2Cl), 3.39 (bs, 1H, OH), 1.95–2.09 (m, 2H, C$\underline{H}_2$CH$_2$Cl), 1.68 (t, ^3J = 7.0, 2H, C$\underline{H}_2$CH$_2$CH$_2$Cl), 0.72 (t, ^3J = 6.7, 2H, CH_2-cp), 0.46 (t, ^3J = 6.7, 2H, CH_2-cp); ^{13}C NMR: δ = 54.6 (C), 45.1 (CH_2), 35.4 (CH_2), 29.3 (CH_2), 13.3 (2×CH_2); GC-MS *m/z* (%): 134 (M^+, < 1), 105 (87), 88 (100), 77 (26), 60 (33), 41 (68); FTIR (film): 3404, 3333, 3000, 2953, 2850, 1451, 1381, 1295, 1246, 1142, 1106, 1011, 948, 931.

1-Bromo-6-chlorohexan-3-one 12: Compound **10** (0.149 mol, 20.0 g) was dissolved in DCM (300 mL) and powdered K_2CO_3 (0.178 mol, 24.6 g) was added. The reaction mixture was cooled down to 0 °C in a water-ice-NaCl bath. The solution of bromine (0.163 mol, 26.1 g, 8.37 mL) in DCM (75 mL) was added dropwise over the course of 80 min and the solution was stirred at 0 °C for another 90 min. The reaction process was monitored by TLC (DCM). The reaction was finished by the addition of saturated aq $Na_2S_2O_3$ (50 mL, gently exothermic) and water (200 mL). The organic layer was separated and washed with saturated aq $Na_2S_2O_3$ (100 mL) and water (100 mL), dried over $MgSO_4$ and concentrated in vacuo. The dark red product (28.4 g) was used without further purification. ^{1}H NMR: δ = 3.51–3.63 (m, 4H, 2×CH_2), 2.97–3.08 (m, 2H, CH_2), 2.59–2.70 (m, 2H, CH_2), 2.01–2.14 (m, 2H, CH_2); ^{13}C NMR: δ = 206.4 (C=O), 45.2 (CH_2), 44.4 (CH_2), 39.8 (CH_2), 26.1 (CH_2), 25.4 (CH_2); GC-MS *m/z* (%): 213 (M^+, < 1), 123 (16), 105 (63), 72 (46), 57 (47), 43 (100), 41 (63); FTIR (film): 2966, 2924, 1719 (C=O), 1609, 1443, 1414, 1376, 1308, 1265, 1212, 1095, 1012. HRMS *m/z* calcd. for $C_6H_{10}OClBr$: 212.9676. Found: 212.9670.

6-Chlorohex-1-en-3-one 14: Dry Et_3N (0.254 mol, 25.4 g, 35.0 mL) was added to compound **12** (0.127 mol, 27.0 g) dissolved in dry Et_2O (250 mL) over the course of 30 min at room temperature. The reaction mixture was stirred for 150 min and monitored by TLC (DCM). The precipitate was filtered and washed with Et_2O (100 mL). Combined organic phases were washed with water (300 mL), brine (100 mL) and again water (200 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude product was distilled with Kugelrohr apparatus (55–60 °C, ~0.5 mbar) yielding a colorless liquid (15.4 g, 78 % over 3 steps). ^{1}H NMR: 6.22–6.33 (m, 1H, =CH), 6.34 (d, ^2J = 10.1, 1H, =CH_2), 5.86 (d, ^2J = 10.1, 1H, =CH_2), 3.61 (t, ^3J = 6.3, 2H, CH_2), 2.80 (t, ^3J = 7.0, 2H, CH_2), 2.05–2.16 (m, 2H, CH_2); ^{13}C NMR: δ = 199.4 (C=O), 136.5 (=CH), 128.4 (=CH_2), 44.4 (CH_2), 36.2 (CH_2), 26.5 (CH_2); GC-MS *m/z* (%): 133 (M^+, 5), 97 (15), 70 (34), 55 (100), 41 (20); FTIR (film): 2961, 2922, 1679 (C=O), 1617, 1443, 1406, 1267, 1210, 1098, 964. HRMS *m/z* calcd. for C_6H_9OCl: 133.0415. Found: 133.0419.

3-(3-Chloropropyl)-1*H*-pyrazole 15: Compound **14** (0.115 mol, 15.3 g) was dissolved in a mixture of 2-propanol (400 mL) and water (20 mL). The reaction mixture was cooled down to 0 °C by a water-ice-NaCl bath and a freshly prepared solution of KBr_3 (0.127 mol, 35.4 g) in water (80 mL) – 1.15 eq. of KBr and 1.1 eq. of bromine in water (~60 mL for 0.1 mol KBr) mixed for 30 minutes – was added over a period of 45 minutes. The reaction was left stirring at 0 °C for 1 h and then allowed to warm up to ambient temperature over a period of 1 h. Hydrazine monohydrate (0.577 mol, 28.9 g, 28.1 mL) was slowly added (~15 min) and the reaction mixture was stirred overnight (12 h). The solvent was removed under reduced pressure and the residue was diluted with DCM (300 mL). The organic phase was washed with saturated $Na_2S_2O_3$ (60 mL), brine (60 mL) and water (60 mL), dried over $MgSO_4$ and concentrated in vacuo. The bright yellow liquid (16.5 g) was used without further purification. ^{1}H NMR: δ = 11.68 (bs, 1H, NH), 7.52 (d, ^3J = 1.8, 1H, CH), 6.12 (d, ^3J = 1.8, 1H, CH), 3.56 (t, ^3J = 6.4, 2H, CH_2), 2.88 (t, ^3J = 7.4, 2H, CH_2), 2.05–2.20 (m, 2H, CH_2); ^{13}C NMR: δ = 147.4 (C), 133.8 (CH), 103.9 (CH), 44.3 (CH_2), 32.4 (CH_2), 24.3 (CH_2); GC-MS *m/z* (%): 145 (M^+, 5), 82 (100), 41 (12); FTIR (film): 2960, 2936, 2855, 2221, 1644, 1536, 1469, 1443, 1383, 1297, 1266, 1100, 1050, 911. HRMS *m/z* calcd. for $C_6H_9N_2Cl$: 145.0527. Found: 145.0528.

5,6-Dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole 16: Compound **15** (0.111 mol, 16.0 g) was dissolved in a mixture of 2-propanol (240 mL) and water (30 mL) and KOH (0.122 mol, 6.80 g) in water (30 mL) was added. The reaction mixture was heated to reflux for 4 h, then the solution was concentrated and the residue was diluted by 50 ml of water. This suspension was

extracted with DCM (4 × 75 mL); the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product (10.9 g of a light yellow liquid) was used without further purification. ^{1}H NMR: δ = 7.49 (s, 1H, CH), 5.94 (s, 1H, CH), 4.12 (t, ^3J = 7.2, 2H, NCH_2), 2.84–2.92 (m, 2H, =C-CH_2), 2.53–2.65 (m, 2H, $NCH_2C\underline{H}_2$); ^{13}C NMR: δ = 145.7 (C), 143.8 (CH), 98.7 (CH), 47.6 (CH_2), 26.6 (CH_2), 23.0 (CH_2); GC-MS *m/z* (%): 108 (M^+, 100), 80 (35), 52 (32); FTIR (film): 2954, 2920, 1614, 1453, 1410, 1323, 1174, 1033, 943. HRMS *m/z* calcd. for $C_6H_9N_2$: 109.0760. Found: 109.0765.

3-Bromo-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole 17: The bicyclic compound **16** (9 mmol, 973 mg) was dissolved in dry $CHCl_3$ (40 mL) and NBS (10 mmol, 1.73 g) was added. The bright red reaction mixture was stirred for 30 minutes at room temperature. The mixture was diluted in $CHCl_3$ (20 mL), washed with water (3 × 50 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude brown solid was dissolved in Et_2O and filtered through a thin layer of silica gel. Evaporation of the solvent afforded a light yellow crystalline product (1.43 g) in 77 % yield (MP 82.6–84.0 °C) from **14**. It became dark after standing at room temperature and at a lower temperature. M.p. : 82.6–84.0 °C; ^{1}H NMR: δ = 7.43 (s, 1H, CH), 4.16 (t, ^3J = 7.3, 2H, NCH_2), 2.82–2.87 (m, 2H, =C-CH_2), 2.58–2.66 (m, 2H, $NCH_2C\underline{H}_2$); ^{13}C NMR: δ = 144.8 (C), 143.9 (CH), 86.7 (C-Br), 49.0 (CH_2), 26.2 (CH_2), 22.6 (CH_2); GC-MS *m/z* (%): 188 (M^++1, 64), 186 (63), 107 (93), 80 (49), 51 (100); FTIR (KCl): 2962, 2922, 2854, 1706, 1641, 1452, 1318, 1226, 1156, 1013, 986. HRMS *m/z* calcd. for $C_6H_8N_2Br$: 186.9871. Found: 186.9873.

4.2. General procedure for the Suzuki-Miyaura coupling reactions

Compound **17** (0.50 mmol, 94 mg), the corresponding boronic acid (0.75 mmol), and 2 mol% of $Pd(PPh_3)_4$ (0.010 mmol, 11 mg) were dissolved in DMF (5 mL) and K_2CO_3 (1.50 mmol, 207 mg) in water (0.8 mL) was added. The reaction mixture was heated at 110 °C and monitored by TLC (AcOEt). The mixture was filtered, diluted with 20 mL of DCM and extracted with 10 mL of water. The organic phase was separated, dried over $MgSO_4$ and concentrated in vacuo. The crude products were purified by column chromatography (AcOEt and AcOEt/MeOH = 3 : 1 for **23b**).

3-Phenyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole 6: 58 mg (63 %) of a off-white crystalline solid in 1 h; MP 116.3–116.4 °C; ^{1}H NMR: δ = 7.81 (s, 1H, N=CH), 7.41–7.48 (m, 2H, Ph), 7.31–7.40 (m, 2H, Ph), 7.15–7.22 (m, 1H, Ph), 4.17 (t, ^3J = 7.3, 2H, NCH_2), 3.06–3.13 (m, 2H, =C-CH_2), 2.62–2.74 (m, 2H, $NCH_2C\underline{H}_2$); ^{13}C NMR: δ = 142.8 (N-C), 141.2 (N=CH), 133.7 (C), 129.0 (2×CH), 125.9 (CH), 125.3 (2×CH), 115.6 (C-Ph), 47.8 (CH_2), 26.7 (CH_2), 24.1 (CH_2); GC-MS *m/z* (%): 184 (M^+, 100), 156 (21), 148 (28), 115 (17), 102 (21), 77 (17); FTIR (KCl): 3054, 2986, 1608, 1422, 1266; HRMS *m/z* calcd. for $C_{12}H_{13}N_2$: 185.1079. Found: 185.1080.

3-(4-Chlorophenyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole 23a: 60 mg (55 %) of a bright yellow crystalline solid in 1 h; MP 111.3–113.2 °C; ^{1}H NMR: δ = 7.77 (s, 1H, N=CH), 7.35 (d, ^3J = 8.5, 2H, Ar), 7.31 (d, ^3J = 8.5, 2H, Ar), 4.17 (t, ^3J = 7.3, 2H, NCH_2), 3.03–3.09 (m, 2H, =C-CH_2), 2.64–2.72 (m, 2H, $NCH_2C\underline{H}_2$); ^{13}C NMR: δ = 142.8 (N-C), 141.0 (N=CH), 132.2 (C), 131.4 (C), 129.1 (2×CH), 126.4 (2×CH), 114.5 (C-Ar), 47.8 (CH_2), 26.6 (CH_2), 24.0 (CH_2); GC-MS *m/z* (%): 218 (M^+, 100), 127 (17), 77 (10); FTIR (KCl): 3051, 2976, 2962, 2930, 2897, 2874, 2858, 1603, 1560, 1491, 1456, 1421, 1396, 1357, 1265, 1161, 1093, 1013; HRMS *m/z* calcd. for $C_{12}H_{12}{}^{35}ClN_2$: 219.0689. Found: 219.0687.

3-(Pyridin-4-yl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole 23b: 72 mg (79 %) of a white crystalline solid in 1 h; MP 102.9–104.5 °C; ^{1}H NMR: δ = 8.53 (d, ^3J = 6.2, 2H, Py), 7.90 (s, 1H, N=CH), 7.31 (d, ^3J = 6.2, 2H, Py), 4.20 (t, ^3J = 7.3, 2H, NCH_2), 3.11–3.16 (m, 2H, =C-CH_2), 2.69–2.77 (m, 2H, $NCH_2C\underline{H}_2$); ^{13}C NMR: δ = 150.4 (2×CH), 144.3 (N-C), 141.6 (N=CH), 141.1 (C), 119.5 (2×CH), 113.1 (C-Py), 47.9 (CH_2), 26.5 (CH_2), 24.3 (CH_2); GC-MS *m/z* (%): 185 (M^+, 100), 76 (10); FTIR (KCl): 3051, 2981, 2927, 2902, 1545, 1494, 1469, 1439, 1408, 1364, 1315, 1221, 1158; HRMS *m/z* calcd. for $C_{11}H_{12}N_3$: 186.1031. Found: 186.1027.

3-(Pyren-1-yl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole 23c: 107 mg (70 %) of a yellow crystalline solid in 1 h; MP 181.9–182.6 °C; ^{1}H NMR: δ = 8.29 (d, ^3J = 9.2, 1H, Ar), 8.13–8.18 (m, 3H, Ar), 8.04–8.08 (m, 3H, Ar), 7.99 (t, ^3J = 7.6, 1H, Ar), 7.94 (d, ^3J = 7.8, 1H, Ar), 7.88 (s, 1H, N=CH), 4.30 (t, ^3J = 7.3, 2H, NCH_2), 2.94–2.99 (m, 2H, =C-CH_2), 2.66–2.74 (m, 2H, $NCH_2C\underline{H}_2$); ^{13}C NMR: δ = 144.8 (N-C), 144.2 (N=CH), 131.7 (C), 131.3 (C), 130.3 (2×C), 129.2 (C), 128.7 (C), 127.6 (3×CH), 127.3 (CH), 126.2 (CH), 125.4 (CH), 125.4 (C), 125.2 (CH), 125.0 (CH), 124.9 (CH), 114.9 (C-Ar), 48.3 (CH_2), 26.7 (CH_2), 23.8 (CH_2); GC-MS *m/z* (%): 312 (M^+, 100), 252 (11); FTIR (KCl): 3042, 2953, 2922, 2892, 1601, 1560, 1489, 1454, 1407, 1349, 1319, 1294, 1243, 1185, 1043; HRMS *m/z* calcd. for $C_{22}H_{17}N_2$: 309.1392. Found: 309.1381.

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Supplementary data

The rest of experimental procedures and crystal structures, full spectral characterizations, copies of ^{1}H NMR and ^{13}C NMR spectra. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.xxx

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31. The crystal structures of compounds **25af**,**ah**,**aj**,**an**,**ba**,**bd**,**bj**,**bm** and **25bp** have been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition numbers CCDC 908394–908402.

Supporting Information

Dihydropyrrolo[1,2-*b*]pyrazoles: withasomnine and related compounds

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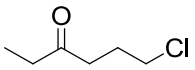
Note: NMR measurements were recorded at 300.13 MHz (^{1}H) and 75.47 MHz (^{13}C) in $CDCl_3$

1. Side products NMR characterizations

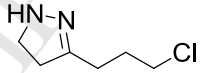
6-Chlorohexan-3-one (11)



^{1}H NMR 3.58 (t, ^3J = 6.3, 2H, CH_2Cl), 2.61 (t, ^3J = 7.0, 2H, $C\underline{H}_2CH_2CH_2Cl$), 2.46 (q, ^3J = 7.3, 2H, $C\underline{H}_2CH_3$), 1.98-2.10 (m, 2H, $C\underline{H}_2CH_2Cl$), 1.06 (t, ^3J = 7.3, 3H, $CH_2C\underline{H}_3$).

^{13}C NMR 210.3 (C=O), 44.6 (CH_2), 38.9 (CH_2), 36.1 (CH_2), 26.4 (CH_2), 7.8 (CH_3).

3-(3-Chloropropyl)-4,5-dihydro-1*H*-pyrazole (13)

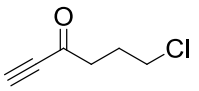


^{1}H NMR 6.62 (s, 1H, NH), 3.57–3.64 (m, 2H, CH_2), 3.39 (t, ^3J = 9.3, 2H, CH_2), 2.65 (t, ^3J = 9.3, 2H, CH_2), 2.40–2.54 (m, 2H, CH_2), 2.00–2.15 (m, 2H, CH_2).

^{13}C NMR 158.0 (C), 46.6 (CH_2), 44.4 (CH_2), 35.4 (CH_2), 29.0 (CH_2), 27.2 (CH_2).

2. Preparation of ynone **20** and dibromo derivative **21**

6-Chlorohex-1-yn-3-one (20)



4-chlorobutanoic chloride (**19**) (0.025 mol, 3.52 g) and CuI (0.002 mol, 0.38 g) were dissolved in freshly distilled Et_2O (30 mL) under argon atmosphere. The reaction mixture was cooled down to 0 °C and the solution (0.5 M) of ethynylmagnesium bromide (0.025 mol, 3.23 g) in THF (50 mL) was added dropwise over the course of 40 min. After 30 min it was warmed up to the room temperature. The reaction was quenched with saturated aq NH_4Cl (30 mL), the organic phase was decanted and the inorganic one was washed with Et_2O (30 mL). The combined organic fractions were washed with water (60 mL), brine (60 mL) and water (60 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude product was distilled at Kugelrohr apparatus (1 mbar, 90 °C) giving 1.63 g of a colorless liquid (52 %).

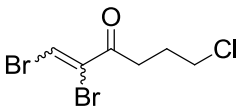
^{1}H NMR 3.59 (t, ^3J = 6.3, 2H, CH_2Cl), 3.27 (s, 1H, ≡CH), 2.82 (t, ^3J = 7.1, 2H, $C\underline{H}_2CH_2CH_2Cl$), 2.06–2.19 (m, 2H, $C\underline{H}_2CH_2Cl$).

^{13}C NMR 186.0 (C=O), 81.4 (≡C-), 79.1 (≡CH), 43.9 (CH_2), 42.5 (CH_2), 26.4 (CH_2).

GC-MS *m/z* (%): 130 (M^+, 5), 68 (100), 53 (88), 41 (22).

FTIR (film): 2963, 2926, 2855, 2095 (C≡C), 1684 (C=O), 1447, 1267, 1107, 1031.

1,2-Dibromo-6-chlorohex-1-en-3-one (21)



The compound **20** (2.6 mmol, 338 mg) was dissolved in CCl_4 (5 mL) and the solution of bromine (2.6 mmol, 414 mg) in CCl_4 (3 mL) was added during 10 min at the room temperature. The mixture was stirred for 20 min and then the

solvent was removed under reduced pressure. The crude product was purified by a column chromatography (AcOEt/PE = 1:4) giving 698 mg (93 %) of a bright yellow liquid - *cis* and *trans* isomers in ratio 3:7.

^{1}H NMR 8.18 (s, 1H, HC=C), 3.61 (t, ^3J = 5.8, 2H, CH_2Cl), 3.03 (t, ^3J = 6.8, 2H, $C\underline{H}_2CH_2CH_2Cl$), 2.13 (dt, ^3J = 12.7, ^3J = 6.3, 2H, $C\underline{H}_2CH_2Cl$).

^{13}C NMR 191.7 (C=O), 131.5 (C), 126.2 (CH), 44.2 (CH_2), 36.6 (CH_2), 27.0 (CH_2).

GC-MS *m/z* (%): 290 (M^+, 5), 228 (51), 213 (45), 185 (14), 105 (100), 77 (40), 53 (42), 41 (95).

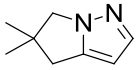
FTIR (film): 2961, 2922, 2853, 1694 (C=O), 1553, 1450, 1312, 1237, 1126, 1030.

3. Dihydropyrrolo[1,2-*b*]pyrazoles synthesis by cycloaddition reaction

General procedure. An appropriate allenyl azine (250 mg) was dissolved in dry xylene (10 mL) and the resulting mixture was heated to reflux under an argon atmosphere. Reactions were monitored by TLC and purified by a column chromatography or by a preparative TLC.

5,5-Dimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25aa)

Yield: 75 mg (30 %), yellowish oil.



Reaction time and purification: 6 h, HPFC (AcOEt/PE = 1:1).

^{1}H NMR 7.48 (bs, 1H, N=CH), 5.93 (bs, 1H, C=CH), 3.87 (s, 2H, N-CH_2), 2.67 (s, 2H, =C-CH_2), 1.28 (s, 6H, 2×CH_3).

^{13}C NMR 144.9 (N-C), 143.1 (N=CH), 99.3 (C=$\underline{C}$H), 61.0 (N-CH_2), 43.5 (CH_3-$\underline{C}$-CH_3), 38.8 (=C-$\underline{C}H_2$), 28.4 (2×CH_3).

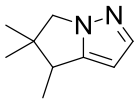
GC-MS *m/z* (%): 136 (M^+, 100), 121 (86), 109 (17), 95 (49), 81 (94), 67 (14), 52 (16), 41 (27).

FTIR (film): 2963, 2929, 2889, 2871 1539, 1462, 1405, 1386, 1325, 1260, 1169, 1116, 1033.

HRMS Calcd. for $C_8H_{13}N_2$: 137.1079. Found: 137.1054.

4,5,5-Trimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25ab)

Yield: 88 mg (35 %), yellowish oil.



Reaction time and purification: 5 h, HPFC (AcOEt/PE = 1:3).

^{1}H NMR 7.46 (bs, 1H, N=CH), 5.92 (bs, 1H, C=CH), 3.80–3.90 (m, 2H, N-CH_2), 2.86 (q, ^3J = 7.3, 1H, $\underline{H}$C-CH_3), 1.23 (s, 3H, CH_3), 1.16 (d, ^3J = 7.3, 3H, HC-$C\underline{H}_3$), 1.05 (s, 3H, CH_3).

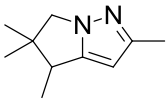
^{13}C NMR 150.0 (N-C), 142.7 (N=CH), 98.4 (C=$\underline{C}$H), 60.9 (N-CH_2), 46.4 (CH_3-$\underline{C}$-CH_3), 41.9 (H$\underline{C}$-CH_3), 26.9 (CH_3), 22.7 (CH_3), 13.1 (HC-$\underline{C}H_3$).

GC-MS *m/z* (%): 150 (M^+, 14), 135 (14), 95 (100), 83 (19), 41 (18).

FTIR (film): 2965, 2936, 2873, 1536, 1485, 1464, 1389, 1372, 1341, 1171, 940.

HRMS Calcd. for $C_9H_{15}N_2$: 151.1235. Found: 151.1221.

2,4,5,5-Tetramethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25ac)



Yield: 125 mg (50 %), yellowish oil.

Reaction time and purification: 5 h, HPFC (AcOEt/PE = 1:4).

^{1}H NMR 5.60 (bs, 1H, =CH), 3.62–3.73 (m, 2H, N-CH_2), 2.70 (q, ^{3}J = 7.3, 1H, H$\underline{C}$-CH_3), 2.16 (s, 3H, =C-CH_3), 1.11 (s, 3H, CH_3), 1.03 (d, ^{3}J = 7.3, 3H, HC-C$\underline{H}_3$), 0.94 (s, 3H, CH_3).

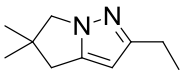
^{13}C NMR 151.8 (N=C), 150.6 (N-C), 97.6 (=CH), 60.4 (N-CH_2), 45.5 (CH_3-$\underline{C}$-CH_3), 41.8 (H$\underline{C}$-CH_3), 26.6 (CH_3), 22.4 (CH_3), 14.0 (=C-$\underline{C}H_3$), 12.8 (HC-$\underline{C}H_3$).

GC-MS *m/z* (%): 164 (M^+, 27), 149 (27), 123 (25), 109 (100) 79 (15).

FTIR (film): 2960, 2927, 2872, 1543, 1444, 1369, 1313, 1163, 1009.

HRMS Calcd. for $C_{10}H_{17}N_2$: 165.1392. Found: 165.1375.

2-Ethyl-5,5-dimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25ad)



Yield: 113 mg (45 %), yellowish oil.

Reaction time and purification: 22 h, HPFC (1. AcOEt/PE = 3:1; 2. AcOEt/DCM = 1:2).

^{1}H NMR 5.73 (bs, 1H, =CH), 3.80 (s, 2H, N-CH_2), 2.63 (q, ^{3}J = 7.6, 2H, C$\underline{H}_2$$CH_3$), 2.62 (s, 2H, =C-$CH_2$), 1.26 (s, 6H, 2×$CH_3$), 1.24 (t, ^{3}J = 7.6, 3H, CH_2C$\underline{H}_3$).

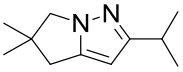
^{13}C NMR 158.7 (N=C), 145.2 (N-C), 97.0 (=CH), 60.7 (N-CH_2), 42.7 (CH_3-$\underline{C}$-CH_3), 38.8 (=C-$\underline{C}H_2$), 28.2 (2×CH_3), 22.1 ($\underline{C}H_2CH_3$), 13.9 ($CH_2\underline{C}H_3$).

GC-MS *m/z* (%): 164 (M^+, 100), 149 (98), 135 (20), 123 (28), 109 (45), 77 (14), 41 (22).

FTIR (film): 2962, 2936, 2875, 1542, 1464, 1443, 1377, 1318, 1265, 1179, 1056.

HRMS Calcd. for $C_{10}H_{17}N_2$: 165.1392. Found: 165.1379.

5,5-Dimethyl-2-(prop-2-yl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25ae)



Yield: 43 mg (17 %), yellowish oil.

Reaction time and purification: 22 h, HPFC (1. AcOEt/PE = 3:1; 2. AcOEt/DCM = 1:4).

^{1}H NMR 5.74 (bs, 1H, =CH), 3.81 (s, 2H, N-CH_2), 2.94 (sep, ^{3}J = 6.9, 1H, -CH), 2.63 (s, 2H, =C-CH_2), 1.25 (s, 6H, 2×CH_3), 1.24 (d, ^{3}J = 6.9, 6H, HC(C$\underline{H}_3$)$_2$).

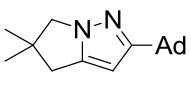
^{13}C NMR 163.6 (N=C), 145.3 (N-C), 95.8 (=CH), 60.9 (N-CH_2), 42.9 (CH_3-$\underline{C}$-CH_3), 39.1 (=C-$\underline{C}H_2$), 28.6 (-CH), 28.4 (2×CH_3), 23.1 (2×CH_3).

GC-MS *m/z* (%): 178 (M^+, 29), 163 (100), 121 (24), 107 (35), 41 (15).

FTIR (film): 2960, 2928, 2872, 1540, 1462, 1380, 1371, 1321, 1295, 1184.

HRMS Calcd. for $C_{11}H_{19}N_2$: 179.1548. Found: 179.1537.

2-(1-Adamantyl)-5,5-dimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25af)



Yield: 198 mg (79 %), white solid. MP 106.5–107.5 °C.

Reaction time and purification: 15 h, HPFC (AcOEt/PE = 1:4).

^{1}H NMR 5.76 (s, 1H, =CH), 3.83 (s, 2H, N-CH_2), 2.64 (s, 2H, =C-CH_2), 2.02–2.06 (m, 3H, CH, Ad), 1.93–1.96 (m, 6H, CH_2, Ad), 1.75–1.78 (m, 6H, CH_2, Ad), 1.27 (s, 6H, 2×CH_3).

^{13}C NMR 167.2 (N=C), 145.0 (N-C), 94.8 (=CH), 61.1 (N-CH_2), 43.2 (CH_2, Ad), 42.9 (CH_3-C-CH_3), 39.2 (=C-CH_2), 37.2 (CH_2, Ad), 34.6 (C, Ad), 29.0 (CH, Ad), 28.6 (2×CH_3).

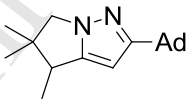
GC-MS *m/z* (%): 270 (M^+, 100), 213 (31), 85 (36), 83 (52), 45 (19).

FTIR (KBr): 2955, 2905, 2847, 1545, 1472, 1451, 1358, 1310, 1179, 1101, 1056.

HRMS Calcd. for $C_{18}H_{27}N_2$: 271.2174. Found: 271.2162.

Anal. Calcd. for $C_{18}H_{26}N_2$: C, 79.95; H, 9.69; N, 10.36. Found: C, 79.39; H, 9.89; N, 10.24.

2-(1-Adamantyl)-4,5,5-trimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25ag)



Yield: 215 mg (86 %), white solid. MP 124.0–126.0 °C.

Reaction time and purification: 5 h, HPFC (AcOEt/PE = 1:4).

^{1}H NMR 5.76 (s, 1H, =CH), 3.83 (d, ^3J = 10.3, 1H, N-CH_2), 3.80 (d, ^3J = 10.3, 1H, N-CH_2), 2.83 (q, ^3J = 7.2, 1H, H-C-CH_3), 2.02–2.06 (m, 3H, CH, Ad), 1.93–1.96 (m, 6H, CH_2, Ad), 1.74–1.78 (m, 6H, CH_2, Ad), 1.22 (s, 3H, CH_3), 1.15 (d, ^3J = 7.2, 3H, HC-CH_3), 1.05 (s, 3H, CH_3).

^{13}C NMR 166.7 (N=C), 150.1 (N-C), 93.8 (=CH), 61.0 (N-CH_2), 45.9 (CH_3-C-CH_3), 43.2 (CH_2, Ad), 42.2 (H-C-CH_3), 37.2 (CH_2, Ad), 34.7 (C, Ad), 29.0 (CH, Ad), 27.0 (CH_3), 22.9 (CH_3), 13.1 (HC-CH_3).

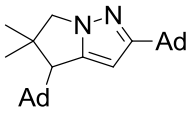
GC-MS *m/z* (%): 284 (M^+, 100), 227 (23).

FTIR (KBr): 2959, 2904, 2847, 1542, 1451, 1357, 1308, 1236, 1165, 1050.

HRMS Calcd. for $C_{19}H_{29}N_2$: 285.2331. Found: 285.2329.

Anal. Calcd. for $C_{19}H_{28}N_2$: C, 80.23; H, 9.92; N, 9.85. Found: C, 80.00; H, 9.90; N, 9.83.

2,4-Di-(1-adamantyl)-5,5-dimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25ah)



Yield: 53 mg (21 %), white solid. MP 179.0–179.5 °C.

Reaction time and purification: 6.5 h, recrystallization (PE).

^{1}H NMR 5.83 (s, 1H, =CH), 3.76 (d, ^2J = 10.2, 1H, N-CH_2), 3.65 (d, ^2J = 10.2, 1H, N-CH_2), 2.43 (s, 1H, HC-Ad),1.90–2.07 (m, 12H, CH_2, Ad), 1.84 (bs, 3H, CH, Ad), 1.65–1.82 (m, 12H, CH_2, Ad), 1.33 (s, 3H, CH_3), 1.26 (s, 3H, CH_3).

^{13}C NMR 166.0 (N=C), 146.7 (N-C), 97.4 (=CH), 62.5 (N-CH_2), 59.5 (HC-Ad), 48.1 (CH_3-C-CH_3), 43.2 (CH_2, Ad), 41.1 (CH_2, Ad), 37.3 (CH_2, Ad), 37.2 (CH_2, Ad), 36.6 (C, Ad), 34.6 (C, Ad), 30.0 (CH_3), 29.0 (CH, Ad), 28.9 (CH, Ad), 25.1 (CH_3).

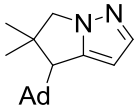
GC-MS *m/z* (%): 404 (M^+, 14), 135 (100), 49 (14).

FTIR (KBr): 2983, 2908, 2849, 1713, 1606, 1451, 1234, 1090, 1031.

HRMS Calcd. for $C_{28}H_{41}N_2$: 405.3270. Found: 405.3257.

Anal. Calcd. for $C_{28}H_{40}N_2$: C, 83.11; H, 9.96; N, 6.92. Found: C, 82.95; H, 10.21; N, 6.70.

4-(1-Adamantyl)-5,5-dimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25ai)



Yield: 213 g (85 %), white solid. MP 121.0–121.9 °C.

Reaction time and purification: 4 h, HPFC (DCM).

^{1}H NMR 7.46 (s, 1H, N=CH), 6.01 (s, 1H, N-C=CH), 3.83 (d, ^2J = 10.4, 1H, N-CH_2), 3.68 (d, ^2J = 10.4, 1H, N-CH_2), 2.44 (s, 1H, HC-Ad), 1.97 (bs, 3H, CH_2, Ad), 1.60–1.92 (m, 12H, CH_2, Ad), 1.36 (s, 3H, CH_3), 1.25 (s, 3H, CH_3).

^{13}C NMR 146.5 (N-C), 141.9 (N=CH), 102.0 (N-C=CH), 62.1 (N-CH_2), 59.0 (HC-Ad), 48.5 (CH_3-C-CH_3), 40.8 (CH_2, Ad), 37.1 (CH_2, Ad), 36.7 (C, Ad), 30.3 (CH_3), 28.7 (CH, Ad), 24.9 (CH_3).

GC-MS *m/z* (%): 270 (M^+, 24), 255 (41), 135 (100), 107 (15), 93 (19), 79 (17), 49 (14).

FTIR (KBr): 2883, 2845, 2677, 1515, 1449, 1395, 1364, 1344, 1319, 1176, 1141, 1099, 1049.

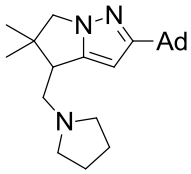
HRMS Calcd. for $C_{18}H_{27}N_2$: 271.2174. Found: 271.2166.

Anal. Calcd. for $C_{18}H_{26}N_2$: C, 79.95; H, 9.69; N, 10.36. Found: C, 79.87; H, 9.77; N, 10.11.

2-(1-Adamantyl)-5,5-dimethyl-4-pyrrolidinomethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25aj)

Yield: 45 mg (18 %), white solid. MP 142.0–143.5 °C.

Reaction time and purification: 4 h, HPFC (AcOEt).



^{1}H NMR 5.82 (s, 1H, =CH), 3.81 (bs, 2H, N-CH_2), 2.94–3.00 (m, 1H, HC-CH_2), 2.65–2.69 (m, 2H, HC-CH_2), 2.46–2.58 (m, 4H, N-CH_2CH_2), 2.04 (bs, 3H, CH, Ad), 1.93–1.98 (bs, 6H, CH_2, Ad), 1.70–1.83 (bs, 6H, CH_2, Ad), 1.76 (bs, 4H, N-CH_2CH_2), 1.31 (s, 3H, CH_3), 1.11 (s, 3H, CH_3).

^{13}C NMR 166.5 (N=C), 148.0 (N-C), 95.0 (=CH), 61.7 (N-CH_2), 55.0 (HC-CH_2), 54.4 (2×N-CH_2CH_2), 46.3 (HC-CH_2), 45.9 (CH_3-C-CH_3), 43.1 (CH_2, Ad), 37.1 (CH_2, Ad), 34.6 (C, Ad), 28.9 (CH, Ad), 27.2 (CH_3), 23.8 (2×N-CH_2CH_2), 22.8 (CH_3).

GC-MS *m/z* (%): 355 (M^++1, 13), 166 (20), 137 (37), 123 (31), 109 (33), 96 (100), 79 (26), 67 (53), 53 (25), 41 (50).

FTIR (KBr): 2959, 2905, 2846, 2781, 1715, 1537, 1486, 1451, 1364, 1323, 1151, 1064.

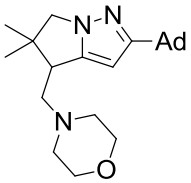
HRMS Calcd. for $C_{23}H_{36}N_3$: 354.2909. Found: 354.2904.

Anal. Calcd. for $C_{23}H_{35}N_3$: C, 78.14; H, 9.98; N, 11.89. Found: C, 78.16; H, 10.08; N, 11.90.

2-(1-Adamantyl)-5,5-dimethyl-4-morpholinomethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25ak)

Yield: 118 mg (47 %), white solid. MP 130.0–131.0 °C.

Reaction time and purification: 6 h, HPFC (AcOEt/PE = 1:4).



^{1}H NMR 5.81 (s, 1H, =CH), 3.84 (d, ^3J = 10.3, 1H, N-CH_2), 3.81 (d, ^3J = 10.3, 1H, N-CH_2), 3.71–3.75 (m, 4H, O-CH_2), 3.02 (t, ^3J = 7.7, 1H, HC-CH_2), 2.44–2.58 (m, 6H, CH_2), 2.04 (bs, 3H, CH, Ad), 1.92–1.96 (m, 6H, CH_2, Ad), 1.74–1.78 (m, 6H, CH_2, Ad), 1.32 (s, 3H, CH_3), 1.11 (s, 3H, CH_3).

^{13}C NMR 166.7 (N=C), 147.6 (N-C), 95.0 (=CH), 67.3 (2×O-CH_2), 61.8 (N-CH_2), 57.7 (HC-CH_2), 54.1 (2×N-CH_2), 45.8 (CH_3-C-CH_3), 44.0 (HC-CH_2), 43.2 (CH_2, Ad), 37.2 (CH_2, Ad), 34.6 (C, Ad), 29.0 (CH, Ad), 27.3 (CH_3), 23.0 (CH_3).

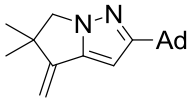
GC-MS *m/z* (%): 369 (M^+, < 1), 100 (100).

FTIR (KBr): 2961, 2850, 2814, 1793, 1752, 1663, 1537, 1453, 1374, 1312, 1141, 1117, 1035, 1010.

HRMS Calcd. for $C_{23}H_{36}N_3O$: 370.2858. Found: 370.2855.

Anal. Calcd. for $C_{23}H_{35}N_3O$: C, 74.75; H, 9.55; N, 11.37. Found: C, 74.85; H, 9.74; N, 11.39.

2-(1-Adamantyl)-5,5-dimethyl-4-methylene-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25al)



Yield: 23 mg (9 %), colorless oil.

Reaction time and purification: 4 h, HPFC (Et_2O/PE = 2:1).

^{1}H NMR 6.06 (s, 1H, =CH), 5.29 (s, 1H, =CH_2), 4.96 (s, 1H, =CH_2), 3.97 (s, 2H, N-CH_2), 2.06 (bs, 3H, CH, Ad), 1.93–1.99 (m, 6H, CH_2, Ad), 1.73–1.80 (m, 6H, CH_2, Ad), 1.34 (s, 6H, 2×CH_3).

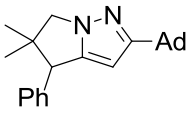
^{13}C NMR 168.2 (N=C), 147.5 (N-C), 145.4 (C=CH_2), 103.6 (=CH_2), 92.9 (=CH), 61.3 (N-CH_2), 46.3 (CH_3-C-CH_3), 43.1 (CH_2, Ad), 37.1 (CH_2, Ad), 34.7 (C, Ad), 28.9 (CH, Ad), 28.7 (2×CH_3).

GC-MS *m/z* (%): 284 (M^++1, 100), 227 (19), 171 (28), 79 (14), 41 (13).

FTIR (film): 2962, 2900, 2848, 1658, 1453, 1384, 1366, 1355, 1312, 1163, 1102, 1056.

HRMS Calcd. for $C_{19}H_{27}N_2$: 283.2174. Found: 283.2161.

2-(1-Adamantyl)-5,5-dimethyl-4-phenyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25am)



Yield: 193 mg (77 %), white solid. MP 138.0–139.0 °C.

Reaction time and purification: 1.5 h, HPFC (AcOEt/PE = 1:5).

^{1}H NMR 7.06–7.36 (m, 5H, Ph), 5.80 (s, 1H, =CH), 4.00 (s, 1H, HC-Ph), 3.98 (d, ^2J = 10.3, 1H, N-CH_2), 3.91 (d, ^2J = 10.3, 1H, N-CH_2), 2.05 (bs, 3H, CH, Ad), 1.99 (bs, 6H, CH_2, Ad), 1.77 (bs, 6H, CH_2, Ad), 1.33 (s, 3H, CH_3), 0.73 (s, 3H, CH_3).

^{13}C NMR 166.8 (N=C), 147.2 (N-C), 138.1 (C), 128.7 (2×CH), 128.2 (2×CH), 127.2 (CH), 95.4 (=CH), 60.7 (N-CH_2), 54.2 (HC-Ph), 47.5 (CH_3-C-CH_3), 43.0 (CH_2, Ad), 37.0 (CH_2, Ad), 34.5 (C, Ad), 28.8 (CH, Ad), 27.4 (CH_3), 24.2 (CH_3).

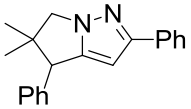
GC-MS *m/z* (%): 346 (M^+, 100), 305 (13), 291 (88), 135 (13).

FTIR (KBr): 2957, 2907, 2849, 1602, 1537, 1495, 1454, 1370, 1312, 1217, 1156, 1102.

HRMS Calcd. for $C_{24}H_{31}N_2$: 347.2487. Found: 347.2489.

Anal. Calcd. for $C_{24}H_{30}N_2$: C, 83.19; H, 8.73; N, 8.08. Found: C, 83.10; H, 8.93; N, 7.87.

5,5-Dimethyl-2,4-diphenyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25an)



Yield: 210 mg (84 %), white solid. MP 97.5–98.5 °C.

Reaction time and purification: 6 h, HPFC (AcOEt/PE = 1:4).

^{1}H NMR 7.81 (d, ^3J = 8.3, 2H, Ph), 7.15–7.40 (m, 8H, Ph), 6.31 (s, 1H, =CH), 4.07 (s, 1H, HC-Ph), 4.05 (d, ^2J = 10.3, 1H, N-CH_2), 4.00 (d, ^2J = 10.3, 1H, N-CH_2), 1.38 (s, 3H, CH_3), 0.78 (s, 3H, CH_3).

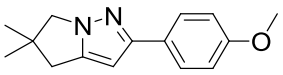
^{13}C NMR 155.6 (N=C), 148.9 (N-C), 137.9 (C), 134.4 (C), 128.8 (2×CH), 128.7 (2×CH), 128.5 (2×CH), 127.6 (CH), 127.5 (CH), 125.5 (2×CH), 97.4 (=CH), 61.0 (N-CH_2), 54.4 (HC-Ph), 47.9 (CH_3-C-CH_3), 27.6 (CH_3), 24.3 (CH_3).

GC-MS *m/z* (%): 288 (M^+, 5), 247 (20), 233 (100), 202 (20), 130 (20) 102 (50), 77 (20).

FTIR (KBr): 2960, 2925, 2871, 1650, 1602, 1538, 1450, 1430, 1389, 1076, 1029.

Anal. Calcd. for $C_{20}H_{20}N_2$: C, 83.30; H, 6.99; N, 9.71. Found: C, 83.40; H, 7.02; N, 9.66.

2-(4-Methoxyphenyl)-5,5-dimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25ao)



Yield: 148 mg (59 %), white solid. MP 106.5–108.0 °C.

Reaction time and purification: 9 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 7.70 (d, ^3J = 8.8, 2H, Ar), 6.91 (d, ^3J = 8.8, 2H, Ar), 6.18 (s, 1H, =CH), 3.90 (s, 2H, N-CH_2), 3.81 (s, 3H, OCH_3), 2.69 (s, 2H, =C-CH_2), 1.29 (s, 6H, 2×CH_3).

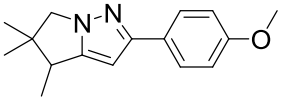
^{13}C NMR 159.2 (C), 155.5 (N=C), 146.3 (N-C), 127.3 (C), 126.7 (2×CH), 114.1 (2×CH), 96.1 (=CH), 61.2 (N-CH_2), 55.4 (OCH_3), 43.1 (H_3C-$\underline{C}$-CH_3), 39.0 (=C-$\underline{C}H_2$), 28.4 (2×CH_3).

GC-MS *m/z* (%): 242 (M^+, 100), 227 (44), 142 (16), 115 (15).

FTIR (KBr): 2959, 2938, 2872, 1611, 1520, 1428, 1244, 1173, 1029.

Anal. Calcd. for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56. Found: C, 74.58; H, 7.56; N, 11.48.

2-(4-Methoxyphenyl)-4,5,5-trimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25ap)



Yield: 205 mg (82 %), white solid. MP 74.5–75.5 °C.

Reaction time and purification: 3 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 7.71 (d, ^3J = 8.8, 2H, Ar), 6.90 (d, ^3J = 8.8, 2H, Ar), 6.18 (s, 1H, =CH), 3.91 (d, ^2J = 10.7, 1H, N-CH_2), 3.87 (d, ^2J = 10.7, 1H, N-CH_2), 3.80 (s, 3H, OCH_3), 2.88 (q, ^3J = 7.2, 1H, $\underline{H}$C-CH_3), 1.24 (s, 3H, CH_3), 1.19 (d, ^3J = 7.2, 3H, HC-$C\underline{H}_3$), 1.08 (s, 3H, CH_3).

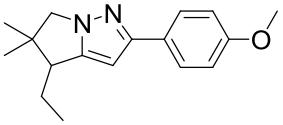
^{13}C NMR 159.1 (C), 155.0 (N=C), 151.3 (N-C), 127.3 (C), 126.6 (2×CH), 114.0 (2×CH), 95.1 (=CH), 61.0 (N-CH_2), 55.3 (OCH_3), 46.0 (H_3C-$\underline{C}$-CH_3), 42.1 ($H\underline{C}$-CH_3), 26.9 (CH_3), 22.7 (CH_3), 13.0 (HC-$\underline{C}H_3$).

GC-MS *m/z* (%): 256 (M^+, 100), 241 (32), 201 (41), 172 (31), 128 (18).

FTIR (KBr): 2962, 2873, 2838, 1610, 1519, 1427, 1244, 1174, 1030.

Anal. Calcd. for $C_{16}H_{20}N_2O$: C, 74.97; H, 7.86; N, 10.93. Found: C, 74.97; H, 7.64; N, 11.19.

4-Ethyl-2-(4-methoxyphenyl)-5,5-dimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25aq)



Yield: 195 mg (78 %), colorless oil.

Reaction time and purification: 3 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 7.63 (d, ^3J = 8.6, 2H, Ar), 6.84 (d, ^3J = 8.6, 2H, Ar), 6.17 (s, 1H, =CH), 3.82 (d, ^2J = 10.6, 1H, N-CH_2), 3.77 (d, ^2J = 10.6, 1H, N-CH_2), 3.75 (s, 3H, OCH_3), 2.57 (dd, ^3J = 10.6, ^3J = 4.6, 1H, HC-Et), 1.54–1.74 (m, 1H, $C\underline{H}_2CH_3$), 1.20–1.41 (m, 1H, $C\underline{H}_2CH_3$), 1.18 (s, 3H, CH_3), 1.05 (t, ^3J = 7.4, 3H, $CH_2C\underline{H}_3$), 1.05 (s, 3H, CH_3).

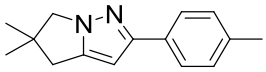
^{13}C NMR 159.3 (C), 154.9 (N=C), 150.1 (N-C), 127.4 (C), 126.7 (2×CH), 114.2 (2×CH), 96.5 (=CH), 61.1 (N-CH_2), 55.5 (OCH_3), 50.0 (HC-Et), 46.1 (H_3C-$\underline{C}$-CH_3), 27.9 (CH_3), 22.9 (CH_3), 21.8 ($\underline{C}H_2CH_3$), 13.0 ($CH_2\underline{C}H_3$).

GC-MS *m/z* (%): 270 (M^+, 100), 241 (43), 215 (24), 171 (51).

FTIR (film): 2962, 2873, 2836, 1613, 1522, 1433, 1246, 1173, 1032.

Anal. Calcd. for $C_{17}H_{22}N_2O$: C, 75.52; H, 8.20; N, 10.36. Found: C, 75.29; H, 7.92; N, 10.41.

5,5-Dimethyl-2-(4-methylphenyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25ar)



Yield: 193 mg (77 %), white solid. MP 101.0–103.0 °C.

Reaction time and purification: 9 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 7.66 (d, ^3J = 8.1, 2H, Ar), 7.17 (d, ^3J = 8.1, 2H, Ar), 6.22 (s, 1H, =CH), 3.90 (s, 2H, N-CH_2), 2.68 (s, 2H, =C-CH_2), 2.34 (s, 3H, Ph-CH_3), 1.28 (s, 6H, 2×CH_3).

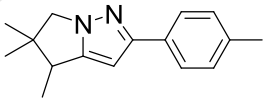
^{13}C NMR 155.6 (N=C), 146.2 (N-C), 137.1 (C), 131.6 (C), 129.4 (2×CH), 125.3 (2×CH), 96.3 (=CH), 61.1 (N-CH_2), 43.1 (H_3C-C-CH_3), 39.0 (=C-CH_2), 28.4 (2×CH_3), 21.4 (Ph-CH_3).

GC-MS *m/z* (%): 226 (M^+, 100), 211 (25), 171 (16), 141 (20), 115 (15).

FTIR (KBr): 2957, 2924, 2871, 1572, 1527, 1472, 1432, 1318, 1195.

Anal. Calcd. for $C_{15}H_{18}N_2$: C, 79.61; H, 8.02; N, 12.38. Found: C, 79.65; H, 8.07; N, 12.25.

4,5,5-Trimethyl-2-(4-methylphenyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25as)



Yield: 223 mg (89 %), white solid. MP 84.5–85.5 °C.

Reaction time and purification: 3 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 7.67 (d, ^3J = 8.0, 2H, Ar), 7.17 (d, ^3J = 8.0, 2H, Ar), 6.22 (s, 1H, =CH), 3.90 (d, ^2J = 10.8, 1H, N-CH_2), 3.86 (d, ^2J = 10.8, 1H, N-CH_2), 2.87 (q, ^3J = 7.2, 1H, H-CH_3), 2.34 (s, 3H, Ph-CH_3), 1.23 (s, 3H, CH_3), 1.18 (d, ^3J = 7.2, 3H, HC-CH_3), 1.07 (s, 3H, CH_3).

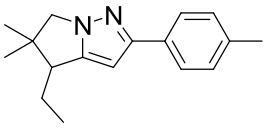
^{13}C NMR 155.2 (N=C), 151.3 (N-C), 137.0 (C), 131.6 (C), 129.3 (2×CH), 125.2 (2×CH), 95.4 (=CH), 61.0 (N-CH_2), 45.9 (H_3C-C-CH_3), 42.0 (HC-CH_3), 26.8 (CH_3), 22.6 (CH_3), 21.3 (Ph-CH_3), 13.0 (HC-CH_3).

GC-MS *m/z* (%): 240 (M^+, 100), 225 (36), 185 (81), 156 (29), 141 (17), 115 (15).

FTIR (KBr): 2965, 2926, 2865, 1623, 1466, 1430, 1309, 1189.

Anal. Calcd. for $C_{16}H_{20}N_2$: C, 79.96; H, 8.39; N, 11.66. Found: C, 80.10; H, 8.46; N, 11.57.

4-Ethyl-5,5-dimethyl-2-(4-methylphenyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25at)



Yield: 205 mg (82 %), colorless oil.

Reaction time and purification: 3 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 7.67 (d, ^3J = 7.9, 2H, Ar), 7.17 (d, ^3J = 7.9, 2H, Ar), 6.28 (s, 1H, =CH), 3.90 (d, ^2J = 10.6, 1H, N-CH_2), 3.85 (d, ^2J = 10.6, 1H, N-CH_2), 2.64 (dd, ^3J = 10.7, ^3J = 4.5, 1H, HC-Et), 2.34 (s, 3H, Ph-CH_3), 1.56–1.73 (m, 1H, CH_2CH_3), 1.35–1.55 (m, 1H, CH_2CH_3), 1.25 (s, 3H, CH_3), 1.12 (t, ^3J = 7.4, 3H, CH_2CH_3), 1.12 (s, 3H, CH_3).

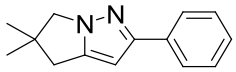
^{13}C NMR 155.2 (N=C), 150.1 (N-C), 137.1 (C), 131.7 (C), 129.4 (2×CH), 125.4 (2×CH), 96.8 (=CH), 61.2 (N-CH_2), 50.0 (HC-Et), 46.1 (H_3C-C-CH_3), 27.9 (CH_3), 22.9 (CH_3), 21.8 (CH_2CH_3), 21.4 (Ph-CH_3), 13.0 (CH_2CH_3).

GC-MS *m/z* (%): 254 (M^+, 100), 239 (25), 225 (62), 193 (34), 155 (56).

FTIR (film): 2963, 2932, 2873, 1523, 1459, 1434, 1325, 1192.

Anal. Calcd. for $C_{17}H_{22}N_2$: C, 80.27; H, 8.72; N, 11.01. Found: C, 80.53; H, 8.73; N, 11.06.

5,5-Dimethyl-2-phenyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25au)



Yield: 195 mg (78 %), white solid. MP 89.0–91.5 °C.

Reaction time and purification: 9 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 7.76–7.78 (m, 2H, Ph), 7.22–7.40 (m, 3H, Ph), 6.26 (s, 1H, =CH), 3.92 (s, 2H, N-CH_2), 2.71 (s, 2H, =C-CH_2), 1.31 (s, 6H, 2×CH_3).

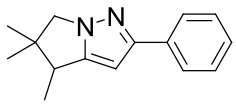
^{13}C NMR 155.7 (N=C), 146.4 (N-C), 134.5 (C), 128.7 (CH), 127.5 (2×CH), 125.5 (2×CH), 96.7 (=CH), 61.3 (N-CH_2), 43.2 (H_3C-C-CH_3), 39.1 (=C-CH_2), 28.5 (2×CH_3).

GC-MS *m/z* (%): 212 (M^+, 100), 197 (38), 171 (34), 157 (28), 128 (34).

FTIR (KBr): 2965, 2933, 2904, 2873, 1606, 1541, 1450, 1429, 1316, 1201.

Anal. Calcd. for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60; N, 13.20. Found: C, 78.81; H, 7.65; N, 13.08.

4,5,5-Trimethyl-2-phenyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25av)



Yield: 198 mg (79 %), colorless oil.

Reaction time and purification: 3 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 7.79–7.86 (m, 2H, Ph), 7.23–7.44 (m, 3H, Ph), 6.30 (s, 1H, =CH), 3.96 (d, ^2J = 10.8, 1H, N-CH_2), 3.92 (d, ^2J = 10.8, 1H, N-CH_2), 2.93 (q, ^3J = 7.2, 1H, HC-CH_3), 1.29 (s, 3H, CH_3), 1.23 (d, ^3J = 7.2, 3H, HC-CH_3), 1.12 (s, 3H, CH_3).

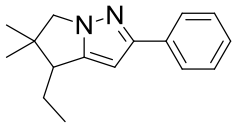
^{13}C NMR 155.2 (N=C), 151.4 (N-C), 134.5 (C), 128.7 (CH), 127.4 (2×CH), 125.5 (2×CH), 95.7 (=CH), 61.1 (N-CH_2), 46.0 (H_3C-C-CH_3), 42.2 (HC-CH_3), 26.9 (CH_3), 22.7 (CH_3), 13.1 (HC-CH_3).

GC-MS *m/z* (%): 226 (M^+, 100), 211 (43), 185 (32), 171 (98), 141 (43), 102 (20).

FTIR (film): 2964, 2932, 2873, 1605, 1541, 1455, 1430, 1316, 1293.

HRMS Calcd. for $C_{15}H_{19}N_2$: 227.1548. Found: 227.1557.

4-Ethyl-5,5-dimethyl-2-phenyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25aw)



Yield: 195 mg (78 %), colorless oil.

Reaction time and purification: 3 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 7.76–7.81 (m, 2H, Ph), 7.24–7.40 (m, 3H, Ph), 6.32 (s, 1H, =CH), 3.91 (d, ^2J = 10.7, 1H, N-CH_2), 3.87 (d, ^2J = 10.7, 1H, N-CH_2), 2.66 (dd, ^3J = 10.6, ^3J = 4.6, 1H, HC-Et), 1.58–1.72 (m, 1H, CH_2CH_3), 1.39–1.52 (m, 1H, CH_2CH_3), 1.26 (s, 3H, CH_3), 1.14 (t, ^3J = 7.3, 3H, CH_2CH_3), 1.12 (s, 3H, CH_3).

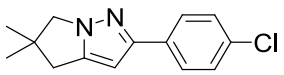
^{13}C NMR 155.1 (N=C), 150.2 (N-C), 134.5 (C), 128.7 (2×CH), 127.5 (CH), 125.5 (2×CH), 97.1 (=CH), 61.2 (N-CH_2), 49.9 (HC-Et), 46.1 (H_3C-C-CH_3), 27.8 (CH_3), 22.9 (CH_3), 21.8 (CH_2CH_3), 13.0 (CH_2CH_3).

GC-MS *m/z* (%): 240 (M^+, 100), 225 (31), 211 (67), 185 (41), 141 (52).

FTIR (film): 2963, 2933, 2873, 1605, 1537, 1460, 1431, 1324, 1194.

HRMS Calcd. for $C_{16}H_{21}N_2$: 241.1705. Found: 241.1697.

2-(4-Chlorophenyl)-5,5-dimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25ax)



Yield: 193 mg (77 %), white solid. MP 109.0–110.0 °C.

Reaction time and purification: 9 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 7.70 (d, ^3J = 8.5, 2H, Ar), 7.33 (d, ^3J = 8.5, 2H, Ar), 6.22 (s, 1H, =CH), 3.90 (s, 2H, N-CH_2), 2.70 (s, 2H, =C-CH_2), 1.29 (s, 6H, 2×CH_3).

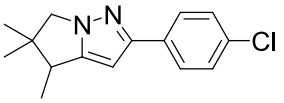
^{13}C NMR 154.4 (N=C), 146.6 (N-C), 133.1 (C), 133.0 (C), 128.8 (2×CH), 126.7 (2×CH), 96.7 (=CH), 61.2 (N-CH_2), 43.2 (H_3C-C-CH_3), 39.0 (=C-CH_2), 28.3 (2×CH_3).

GC-MS *m/z* (%): 246 (M^+, 100), 231 (32), 205 (26), 191 (20), 127 (24).

FTIR (KBr): 2956, 2926, 2866, 1506, 1431, 1320, 1199, 1086.

Anal. Calcd. for $C_{14}H_{15}ClN_2$: C, 68.15; H, 6.13; N, 11.35. Found: C, 68.02; H, 6.16; N, 11.06.

2-(4-Chlorophenyl)-4,5,5-trimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25ay)



Yield: 213 mg (85 %), white solid. MP 59.0–61.5 °C.

Reaction time and purification: 3 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 7.70 (d, ^3J = 8.5, 2H, Ar), 7.32 (d, ^3J = 8.5, 2H, Ar), 6.22 (s, 1H, =CH), 3.91 (d, ^2J = 10.9, 1H, N-CH_2), 3.87 (d, ^2J = 10.9, 1H, N-CH_2), 2.88 (q, ^3J = 7.2, 1H, HC-CH_3), 1.24 (s, 3H, CH_3), 1.18 (d, ^3J = 7.2, 3H, HC-CH_3), 1.07 (s, 3H, CH_3).

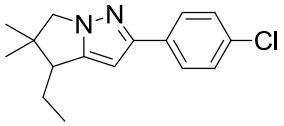
^{13}C NMR 153.9 (N=C), 151.6 (N-C), 133.0 (2×C), 128.8 (2×CH), 126.6 (2×CH), 95.8 (=CH), 61.0 (N-CH_2), 46.0 (H_3C-C-CH_3), 42.0 (HC-CH_3), 26.8 (CH_3), 22.6 (CH_3), 13.0 (HC-CH_3).

GC-MS *m/z* (%): 260 (M^+, 100), 245 (45), 205 (94), 176 (24), 141 (28).

FTIR (KBr): 2966, 2932, 2865, 1506, 1432, 1340, 1191, 1087.

Anal. Calcd. for $C_{15}H_{17}ClN_2$: C, 69.09; H, 6.57; N, 10.74. Found: C, 69.29; H, 6.66; N, 10.68.

4-Ethyl-2-(4-chlorophenyl)-5,5-dimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25az)



Yield: 190 mg (76 %), colorless oil.

Reaction time and purification: 3 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 7.71 (d, ^3J = 8.3, 2H, Ar), 7.33 (d, ^3J = 8.3, 2H, Ar), 6.29 (s, 1H, =CH), 3.89 (d, ^2J = 10.8, 1H, N-CH_2), 3.85 (d, ^2J = 10.8, 1H, N-CH_2), 2.65 (dd, ^3J = 10.7, ^3J = 4.5, 1H, HC-Et), 1.54–1.75 (m, 1H, CH_2CH_3), 1.31–1.53 (m, 1H, CH_2CH_3), 1.25 (s, 3H, CH_3), 1.11 (t, ^3J = 7.4, 3H, CH_2CH_3), 1.11 (s, 3H, CH_3).

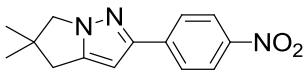
^{13}C NMR 153.8 (N=C), 150.3 (N-C), 133.0 (C), 132.9 (C), 128.8 (2×CH), 126.6 (2×CH), 97.1 (=CH), 61.1 (N-CH_2), 49.8 (HC-Et), 46.1 (H_3C-C-CH_3), 27.7 (CH_3), 22.8 (CH_3), 21.7 (CH_2CH_3), 12.9 (CH_2CH_3).

GC-MS *m/z* (%): 274 (M^+, 100), 245 (70), 219 (52), 175 (51).

FTIR (film): 2964, 2933, 2874, 1506, 1432, 1324, 1194, 1091.

Anal. Calcd. for $C_{16}H_{19}ClN_2$: C, 69.93; H, 6.97; N, 10.19. Found: C, 70.16; H, 6.81; N, 10.17.

5,5-Dimethyl-2-(4-nitrophenyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25ba)



Yield: 178 mg (71 %), yellow solid. MP 176.5–178.5 °C.

Reaction time and purification: 3 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 8.21 (d, ^3J = 8.9, 2H, Ar), 7.89 (d, ^3J = 8.9, 2H, Ar), 6.36 (s, 1H, =CH), 3.95 (s, 2H, N-CH_2), 2.74 (s, 2H, =C-CH_2), 1.33 (s, 6H, 2×CH_3).

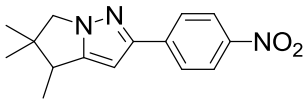
^{13}C NMR 153.0 (N=C), 147.1 (N-C), 146.8 (C), 140.7 (C), 125.7 (2×CH), 124.2 (2×CH), 97.9 (=CH), 61.3 (N-CH_2), 43.3 (H_3C-C-CH_3), 38.9 (=C-CH_2), 28.3 (2×CH_3).

GC-MS *m/z* (%): 257 (M^+, 100), 242 (38), 216 (18), 202 (21).

FTIR (KBr): 2964, 2939, 2874, 1600, 1511, 1344, 1314, 1107.

Anal. Calcd. for $C_{14}H_{15}N_3O_2$: C, 65.35; H, 5.88; N, 16.33. Found: C, 65.28; H, 5.78; N, 16.40.

4,5,5-Trimethyl-2-(4-nitrophenyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bb)



Yield: 223 mg (89 %), yellow solid. MP 154.0–155.5 °C.

Reaction time and purification: 0.5 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 8.20 (d, ^3J = 8.6, 2H, Ar), 7.90 (d, ^3J = 8.6, 2H, Ar), 6.35 (s, 1H, =CH), 3.94 (d, ^2J = 10.9, 1H, N-CH_2), 3.92 (d, ^2J = 10.9, 1H, N-CH_2), 2.94 (q, ^3J = 7.3, 1H, H-C-CH_3), 1.28 (s, 3H, CH_3), 1.23 (d, ^3J = 7.3, 3H, HC-CH_3), 1.11 (s, 3H, CH_3).

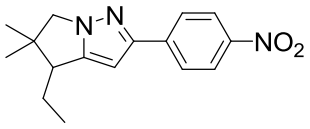
^{13}C NMR 152.6 (N=C), 152.1 (N-C), 146.8 (C), 140.8 (C), 125.6 (2×CH), 124.2 (2×CH), 97.0 (=CH), 61.2 (N-CH_2), 46.2 (H_3C-C-CH_3), 42.1 (HC-CH_3), 26.7 (CH_3), 22.6 (CH_3), 12.9 (HC-CH_3).

GC-MS *m/z* (%): 271 (M^+, 84), 256 (46), 216 (100), 170 (38), 115 (21).

FTIR (KBr): 2967, 2933, 2875, 1599, 1513, 1344, 1310, 1106.

Anal. Calcd. for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.51; H, 6.28; N, 15.56.

4-Ethyl-5,5-dimethyl-2-(4-nitrophenyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bc)



Yield: 218 mg (87 %), yellow solid. MP 99.5–101.0 °C.

Reaction time and purification: 0.5 h, preparative TLC (AcOEt/PE = 2:8).

^{1}H NMR 8.23 (d, ^3J = 9.0, 2H, Ar), 7.92 (d, ^3J = 9.0, 2H, Ar), 6.42 (s, 1H, =CH), 3.94 (d, ^2J = 10.9, 1H, N-CH_2), 3.90 (d, ^2J = 10.9, 1H, N-CH_2), 2.69 (dd, ^3J = 10.7, ^3J = 4.5, 1H, HC-Et), 1.58–1.79 (m, 1H, C$H_2$$CH_3$), 1.33–1.55 (m, 1H, C$H_2$$CH_3$), 1.28 (s, 3H, CH_3), 1.15 (t, ^3J = 7.3, 3H, CH_2CH_3), 1.15 (s, 3H, CH_3).

^{13}C NMR 152.6 (N=C), 150.8 (N-C), 146.9 (C), 140.8 (C), 125.7 (2×CH), 124.3 (2×CH), 98.3 (=CH), 61.3 (N-CH_2), 49.9 (HC-Et), 46.3 (H_3C-C-CH_3), 27.7 (CH_3), 22.8 (CH_3), 21.7 (C$H_2$$CH_3$), 12.9 ($CH_2CH_3$).

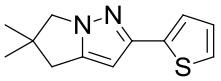
GC-MS *m/z* (%): 285 (M^+, 100), 270 (42), 256 (86), 230 (62), 186 (45), 140 (31).

FTIR (KBr): 2965, 2935, 2874, 2847, 1602, 1507, 1349, 1317, 1109.

Anal. Calcd. for $C_{16}H_{19}N_3O_2$: C, 67.35; H, 6.71; N, 14.73. Found: C, 67.36; H, 6.68; N, 14.57.

5,5-Dimethyl-2-(thiofen-2-yl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bd)

Yield: 110 mg (44 %), yellow solid. MP 84.9–85.9 °C.



Reaction time and purification: 7 h, HPFC (DCM).

^{1}H NMR 7.26 (d, ^3J = 2.6, 1H, Ar), 7.18 (d, ^3J = 4.7, 1H, Ar), 6.98–7.03 (m, 1H, Ar), 6.16 (s, 1H, =CH), 3.88 (s, 2H, N-CH_2), 2.67 (s, 2H, =C-CH_2), 1.28 (s, 6H, 2×CH_3).

^{13}C NMR 150.6 (N=C), 146.3 (N-C), 137.8 (C), 127.4 (CH), 123.9 (CH), 123.0 (CH), 96.7 (=CH), 61.2 (N-CH_2), 43.2 (H_3C-$\underline{C}$-CH_3), 38.9 (=C-$\underline{C}H_2$), 28.3 (2×CH_3).

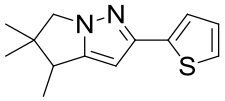
GC-MS *m/z* (%): 218 (M^+, 100), 203 (23), 177 (17), 134 (25).

FTIR (KBr): 2956, 2925, 2859, 1593, 1526, 1461, 1433, 1385, 1320, 1265, 1219, 1186, 1118, 1047.

HRMS Calcd. for $C_{12}H_{15}N_2S$: 219.0956. Found: 219.0941.

4,5,5-Trimethyl-2-(thiofen-2-yl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25be)

Yield: 203 mg (81 %), yellowish oil.



Reaction time and purification: 3 h, HPFC (DCM).

^{1}H NMR 7.26 (dd, ^3J = 3.6, ^4J = 1.1, 1H, Ar), 7.16 (dd, ^3J = 5.1, ^4J = 1.1, 1H, Ar), 7.00 (dd, ^3J = 5.1, ^3J = 3.6, 1H, Ar), 6.14 (s, 1H, =CH), 3.87 (d, ^2J = 10.7, 1H, N-CH_2), 3.83 (d, ^2J = 10.7, 1H, N-CH_2), 2.85 (q, ^3J = 7.2, 1H, $\underline{H}C$-CH_3), 1.21 (s, 3H, CH_3), 1.16 (d, ^3J = 7.2, 3H, HC-$C\underline{H}_3$), 1.05 (s, 3H, CH_3).

^{13}C NMR 151.4 (N=C), 150.0 (N-C), 137.8 (C), 127.3 (CH), 123.7 (CH), 122.8 (CH), 95.7 (=CH), 60.9 (N-CH_2), 45.9 (H_3C-$\underline{C}$-CH_3), 41.9 ($H\underline{C}$-CH_3), 26.7 (CH_3), 22.5 (CH_3), 12.9 (HC-$\underline{C}H_3$).

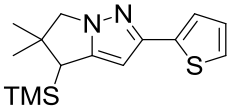
GC-MS *m/z* (%): 232 (M^+, 100), 217 (27), 191 (15), 177 (53), 147 (32), 108 (18).

FTIR (film): 2964, 2932, 2872, 1560, 1531, 1465, 1394, 1329, 1313, 1222, 1188, 1173, 1095, 1051.

HRMS Calcd. for $C_{13}H_{17}N_2S$: 233.1112. Found: 233.1116.

5,5-Dimethyl-2-(thiofen-2-yl)-4-trimethylsilyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bf)

Yield: 73 mg (29 %), yellow oil.



Reaction time and purification: 7.5 h at 110 °C, HPFC (DCM).

^{1}H NMR 7.28 (d, ^3J = 3.6, 1H, Ar), 7.18 (d, ^3J = 5.0, 1H, Ar), 7.02 (dd, ^3J = 5.0, ^3J = 3.6, 1H, Ar), 6.07 (s, 1H, =CH), 3.83 (bs, 2H, N-CH_2), 2.20 (s, 1H, HC-TMS), 1.31 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 0.15 (s, 9H, TMS).

^{13}C NMR 150.2 (N=C), 149.5 (N-C), 138.0 (C), 127.5 (CH), 123.9 (CH), 123.0 (CH), 96.1 (=CH), 62.0 (N-CH_2), 47.1 (H_3C-$\underline{C}$-CH_3), 40.1 (HC-TMS), 30.3 (CH_3), 26.5 (CH_3), -0.8 (TMS).

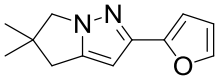
GC-MS *m/z* (%): 290 (M^+, 31), 275 (100), 73 (94), 45 (15).

FTIR (film): 2961, 2932, 2893, 2877, 1558, 1514, 1466, 1392, 1372, 1326, 1252, 1221, 1120, 1053.

HRMS Calcd. for $C_{15}H_{23}N_2SSi$: 291.1351. Found: 291.1349.

2-(Furan-2-yl)-5,5-dimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bg)

Yield: 153 mg (61 %), colorless oil.



Reaction time and purification: 6 h, HPFC (DCM/Et_2O = 7:1).

^{1}H NMR 7.39 (bs, 1H, Ar), 6.59 (d, ^3J = 2.6, 1H, Ar), 6.41 (bs, 1H, Ar), 6.17 (s, 1H, =CH), 3.86 (s, 2H, N-CH_2), 2.65 (s, 2H, =C-CH_2), 1.25 (s, 6H, 2×CH_3).

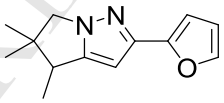
^{13}C NMR 149.6 (N=C), 147.5 (N-C), 145.8 (C), 141.2 (CH), 111.1 (CH), 104.7 (CH), 96.4 (=CH), 60.9 (N-CH_2), 43.1 (H_3C-C-CH_3), 38.6 (=C-CH_2), 28.0 (2×CH_3).

GC-MS *m/z* (%): 202 (M^+, 100), 187 (19), 161 (17), 147 (15), 118 (18), 89 (15).

FTIR (film): 2959, 2872, 1538, 1485, 1466, 1441, 1376, 1352, 1323, 1264, 1202, 1149, 1078, 1010.

HRMS Calcd. for $C_{12}H_{15}N_2O$: 203.1184. Found: 203.1167.

2-(Furan-2-yl)-4,5,5-trimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bh)



Yield: 238 mg (95 %), yellow oil.

Reaction time and purification: 3 h, HPFC (DCM/AcOEt = 10:1).

^{1}H NMR 7.38 (bs, 1H, Ar), 6.59 (d, ^3J = 3.3, 1H, Ar), 6.40 (d, ^3J = 3.3, 1H, Ar), 6.16 (s, 1H, =CH), 3.85 (d, ^2J = 10.7, 1H, N-CH_2), 3.82 (d, ^2J = 10.7, 1H, N-CH_2), 2.83 (q, ^3J = 7.2, 1H, HC-CH_3), 1.19 (s, 3H, CH_3), 1.13 (d, ^3J = 7.2, 3H, HC-CH_3), 1.02 (s, 3H, CH_3).

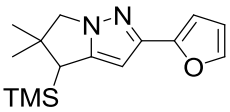
^{13}C NMR 150.7 (N=C), 149.5 (N-C), 147.0 (C), 141.0 (CH), 110.9 (CH), 104.4 (CH), 95.3 (=CH), 60.5 (N-CH_2), 45.8 (H_3C-C-CH_3), 41.6 (HC-CH_3), 26.3 (CH_3), 22.1 (CH_3), 12.5 (HC-CH_3).

GC-MS *m/z* (%): 216 (M^+, 100), 201 (25), 175 (16), 161 (52), 132 (39), 92 (16), 78 (16).

FTIR (film): 2964, 2934, 2872, 1540, 1483, 1469, 1455, 1375, 1338, 1316, 1197, 1149, 1079, 1009.

HRMS Calcd. for $C_{13}H_{17}N_2O$: 217.1341. Found: 217.1334.

2-(Furan-2-yl)-5,5-dimethyl-4-trimethylsilyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bi)



Yield: 63 mg (25 %), yellow oil.

Reaction time and purification: 10 h at 110 °C, HPFC (DCM/AcOEt = 15:1).

^{1}H NMR 7.40 (bs, 1H, Ar), 6.61 (d, ^3J = 3.3, 1H, Ar), 6.43 (d, ^3J = 3.3, 1H, Ar), 6.10 (s, 1H, =CH), 3.84 (d, ^2J = 10.7, 1H, N-CH_2), 3.81 (d, ^2J = 10.7, 1H, N-CH_2), 2.20 (s, 1H, HC-TMS), 1.30 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 0.15 (s, 9H, TMS).

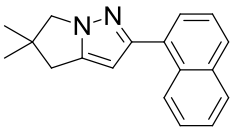
^{13}C NMR 149.9 (N=C), 149.1 (N-C), 147.3 (C), 141.4 (CH), 111.3 (CH), 104.8 (CH), 96.0 (=CH), 61.9 (N-CH_2), 47.2 (H_3C-C-CH_3), 40.0 (HC-TMS), 30.2 (CH_3), 26.5 (CH_3), -0.8 (TMS).

GC-MS *m/z* (%): 274 (M^+, 25), 259 (86), 73 (100), 45 (17).

FTIR (film): 2960, 2876, 1524, 1464, 1425, 1374, 1322, 1251, 1196, 1120, 1078, 1009.

HRMS Calcd. for $C_{15}H_{23}N_2OSi$: 275.1580. Found: 275.1584.

5,5-Dimethyl-2-(naphthalen-1-yl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bj)



Yield: 200 mg (80 %), white solid. MP 101.7–101.8 °C.

Reaction time and purification: 7 h, HPFC (AcOEt/PE = 1:4).

^{1}H NMR 8.58 (d, ^3J = 8.8, 1H, Ar), 7.85 (d, ^3J = 8.9, 1H, Ar), 7.81 (d, ^3J = 8.2, 1H, Ar), 7.68 (d, ^3J = 7.1, 1H, Ar), 7.42–7.52 (m, 3H, Ar), 6.25 (s, 1H, =CH), 3.99 (s, 2H, N-CH_2), 2.76 (s, 2H, =C-CH_2), 1.33 (s, 6H, 2×CH_3).

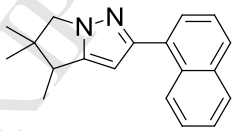
^{13}C NMR 155.2 (N=C), 145.5 (N-C), 134.1 (C), 132.7 (C), 131.6 (C), 128.4 (CH), 128.1 (CH), 127.0 (CH), 126.5 (CH), 126.3 (CH), 125.8 (CH), 125.5 (CH), 100.5 (=CH), 61.4 (N-CH_2), 43.2 (CH_3-C-CH_3), 39.2 (=C-CH_2), 28.5 (2×CH_3).

GC-MS *m/z* (%): 262 (M^+, 100), 230 (13), 178 (14), 152 (11).

FTIR (KBr): 3051, 2957, 2925, 2882, 1591, 1544, 1485, 1464, 1378, 1314, 1259, 1215, 1179, 1013.

Anal. Calcd. for $C_{18}H_{18}N_2$: C, 82.41; H, 6.92; N, 10.68. Found: C, 82.73; H, 6.96; N, 10.90.

4,5,5-Trimethyl-2-(naphthalen-1-yl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bk)



Yield: 230 mg (92 %), colorless oil.

Reaction time and purification: 4 h, HPFC (DCM).

^{1}H NMR 8.67 (d, ^3J = 8.3, 1H, Ar), 7.66–7.83 (m, 3H, Ar), 7.36–7.50 (m, 3H, Ar), 6.21 (s, 1H, =CH), 3.90 (d, ^2J = 10.6, 1H, N-CH_2), 3.85 (d, ^2J = 10.6, 1H, N-CH_2), 2.80 (q, ^3J = 7.2, 1H, H-CH_3), 1.12 (s, 3H, CH_3), 1.10 (d, ^3J = 7.2, 3H, HC-CH_3), 0.99 (s, 3H, CH_3).

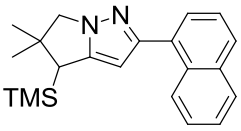
^{13}C NMR 154.4 (N=C), 150.3 (N-C), 133.9 (C), 132.5 (C), 131.3 (C), 128.1 (CH), 127.8 (CH), 126.7 (CH), 126.4 (CH), 125.9 (CH), 125.5 (CH), 125.2 (CH), 99.3 (=CH), 60.9 (N-CH_2), 45.7 (CH_3-C-CH_3), 41.8 (H-C-CH_3), 26.5 (CH_3), 22.4 (CH_3), 12.8 (HC-CH_3).

GC-MS *m/z* (%): 276 (M^+, 100), 261 (14), 221 (38), 191 (22), 152 (20).

FTIR (film): 3049, 2964, 2933, 2871, 1592, 1540, 1461, 1378, 1359, 1312, 1261, 1219, 1162, 1012.

HRMS Calcd. for $C_{19}H_{21}N_2$: 277.1705. Found: 277.1690.

5,5-Dimethyl-2-(naphthalen-1-yl)-4-trimethylsilyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bl)



Yield: 53 mg (21 %), yellow oil.

Reaction time and purification: 7.5 h at 110 °C, HPFC (DCM).

^{1}H NMR 8.60 (d, ^3J = 8.1, 1H, Ar), 7.86 (d, ^3J = 8.3, 1H, Ar), 7.81 (d, ^3J = 8.2, 1H, Ar), 7.70 (d, ^3J = 7.0, 1H, Ar), 7.44–7.52 (m, 3H, Ar), 6.17 (s, 1H, =CH), 3.94 (d, ^2J = 10.5, 1H, N-CH_2), 3.92 (d, ^2J = 10.5, 1H, N-CH_2), 2.29 (s, 1H, HC-TMS), 1.36 (bs, 6H, 2×CH_3), 0.18 (s, 9H, TMS).

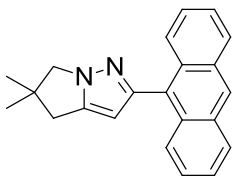
^{13}C NMR 154.7 (N=C), 148.5 (N-C), 134.2 (C), 132.7 (C), 131.7 (C), 128.4 (CH), 128.1 (CH), 127.0 (CH), 126.6 (CH), 126.3 (CH), 125.7 (CH), 125.5 (CH), 100.0 (=CH), 62.2 (N-CH_2), 47.2 (CH_3-C-CH_3), 40.2 (HC-TMS), 30.2 (CH_3), 26.7 (CH_3), -0.7 (TMS).

GC-MS *m/z* (%): 334 (M^+, 29), 319 (100), 73 (65), 45 (12).

FTIR (film): 3072, 2961, 2930, 2877, 1525, 1466, 1379, 1360, 1323, 1252, 1221, 1198, 1121, 1015.

HRMS Calcd. for $C_{21}H_{27}N_2Si$: 335.1944. Found: 335.1940.

2-(Anthracen-9-yl)-5,5-dimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bm)



Yield: 193 mg (77 %), yellow solid. MP 157.0–158.0 °C.

Reaction time and purification: 7 h, HPFC (AcOEt/PE = 1:4).

^{1}H NMR 8.47 (s, 1H, Ar), 8.04 (d, ^3J = 8.8, 2H, Ar), 8.00 (d, ^3J = 8.3, 2H, Ar), 7.43 (t, ^3J = 7.0, 2H, Ar), 7.41 (t, ^3J = 7.1, 2H, Ar), 6.20 (s, 1H, =CH), 4.08 (s, 2H, N-CH_2), 2.88 (s, 2H, =C-CH_2), 1.43 (s, 6H, 2×CH_3).

^{13}C NMR 152.6 (N=C), 145.7 (N-C), 131.6 (2×C), 131.4 (2×C), 130.1 (C), 128.4 (2×CH), 127.4 (CH), 127.2 (2×CH), 125.6 (2×CH), 125.2 (2×CH), 103.0 (=CH), 61.5 (N-CH_2), 43.5 (CH_3-$\underline{C}$-CH_3), 39.4 (=C-$\underline{C}H_2$), 28.6 (2×CH_3).

GC-MS *m/z* (%): 312 (M^+, 100).

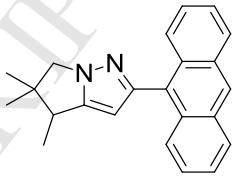
FTIR (KBr): 3049, 2961, 2928, 2881, 1601, 1539, 1463, 1370, 1318, 1266, 1233.

HRMS Calcd. for $C_{22}H_{21}N_2$: 313.1705. Found: 313.1698.

2-(Anthracen-9-yl)-4,5,5-trimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bn)

Yield: 230 mg (92 %), yellow solid. MP 117.9–118.4 °C.

Reaction time and purification: 3.5 h, HPFC (AcOEt/PE = 1:4).



^{1}H NMR 8.49 (s, 1H, Ar), 7.98–8.06 (m, 4H, Ar), 7.35–7.50 (m, 4H, Ar), 6.21 (s, 1H, =CH), 4.09 (bs, 2H, N-CH_2), 3.11 (q, ^3J = 7.2, 1H, $\underline{H}$C-CH_3), 1.40 (s, 3H, CH_3), 1.33 (d, ^3J = 7.2, 3H, HC-C$\underline{H}_3$), 1.24 (s, 3H, CH_3).

^{13}C NMR 152.1 (N=C), 150.8 (N-C), 131.6 (2×C), 131.5 (2×C), 130.2 (C), 128.4 (2×CH), 127.3 (CH), 127.2 (2×CH), 125.6 (2×CH), 125.2 (2×CH), 102.1 (=CH), 61.4 (N-CH_2), 46.5 (CH_3-$\underline{C}$-CH_3), 42.5 (H$\underline{C}$-CH_3), 27.0 (CH_3), 22.9 (CH_3) 13.2 (HC-$\underline{C}H_3$).

GC-MS *m/z* (%): 327 (M^+, 100), 241 (11), 202 (12).

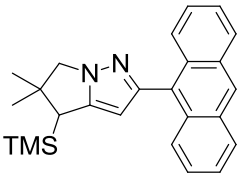
FTIR (KBr): 3051, 2966, 2935, 2875, 1537, 1467, 1379, 1315, 1172, 1096, 911.

Anal. Calcd. for $C_{23}H_{22}N_2$: C, 84.63; H, 6.79; N, 8.58. Found: C, 84.18; H, 7.00; N, 8.25.

2-(Anthracen-9-yl)-5,5-dimethyl-4-trimethylsilyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bo)

Yield: 58 mg (23 %), yellow oil.

Reaction time and purification: 8 h at 110 °C, HPFC (DCM/hexane = 3:1).



^{1}H NMR 8.50 (s, 1H, Ar), 8.06 (d, ^3J = 8.6, 2H, Ar), 8.02 (d, ^3J = 8.6, 2H, Ar), 7.40–7.52 (m, 4H, Ar), 6.17 (s, 1H, =CH), 4.07 (d, ^2J = 10.5, 1H, N-CH_2), 4.04 (d, ^2J = 10.5, 1H, N-CH_2), 2.42 (s, 1H, HC-TMS), 1.47 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 0.25 (s, 9H, TMS).

^{13}C NMR 152.0 (N=C), 148.7 (N-C), 131.6 (2×C), 131.4 (2×C), 130.2 (C), 128.4 (2×CH), 127.3 (CH), 127.1 (2×CH), 125.6 (2×CH), 125.2 (2×CH), 102.5 (=CH), 62.2 (N-CH_2), 47.4 (CH_3-$\underline{C}$-CH_3), 40.3 (HC-TMS), 30.5 (CH_3), 26.8 (CH_3), -0.7 (TMS).

GC-MS *m/z* (%): 384 (M^+, 100), 369 (99), 73 (94), 45 (12).

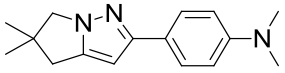
FTIR (film): 3051, 2959, 2874, 1522, 1447, 1347, 1315, 1251, 1118, 1013.

HRMS Calcd. for $C_{25}H_{29}N_2Si$: 385.2100. Found: 385.2108.

5,5-Dimethyl-2-(4-dimethylaminophenyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bp)

Yield: 200 mg (80 %), orange solid. MP 136.1–137.0 °C.

Reaction time and purification: 7 h, HPFC (DCM /AcOEt = 1:1).



^{1}H NMR 7.65 (d, ^3J = 8.8, 2H, Ar), 6.73 (d, ^3J = 8.8, 2H, Ar), 6.15 (s, 1H, =CH), 3.89 (s, 2H, N-CH_2), 2.95 (s, 6H, N(CH_3)$_2$), 2.68 (s, 2H, =C-CH_2), 1.29 (s, 6H, 2×CH_3).

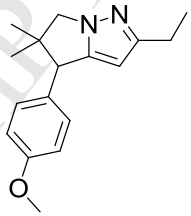
^{13}C NMR 156.2 (N=C), 150.2 (C), 146.1 (N-C), 126.4 (2×CH), 123.2 (C), 112.7 (2×CH), 95.6 (=CH), 61.2 (N-CH_2), 43.1 (H_3C-C-CH_3), 40.7 ($N(CH_3)_2$), 39.1 (=C-CH_2), 28.5 (2×CH_3).

GC-MS *m/z* (%): 255 (M^+, 100).

FTIR (KBr): 2952, 2922, 2899, 2884, 2866, 2809, 1614, 1529, 1434, 1360, 1320, 1230, 1203, 1167.

HRMS Calcd. for $C_{16}H_{22}N_3$: 256.1814. Found: 256.1806.

2-Ethyl-4-(4-methoxyphenyl)-5,5-dimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bq)



Yield: 208 mg (83 %), colorless oil.

Reaction time and purification: 5 h, HPFC (DCM/AcOEt = 5:1).

^{1}H NMR 7.04 (d, ^3J = 8.5, 2H, Ar), 6.85 (d, ^3J = 8.5, 2H, Ar), 5.76 (s, 1H, =CH), 3.96 (s, 1H, HC-Ar), 3.94 (d, ^2J = 10.4, 1H, N-CH_2), 3.88 (d, ^2J = 10.4, 1H, N-CH_2), 3.78 (s, 3H, OCH_3), 2.68 (q, ^3J = 7.6, 2H, CH_2CH_3), 1.33 (s, 3H, CH_3), 1.27 (t, ^3J = 7.6, 3H, CH_2CH_3), 0.74 (s, 3H, CH_3).

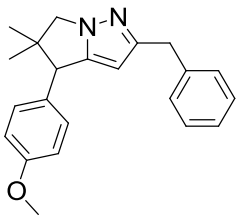
^{13}C NMR 158.9 (N=C), 158.8 (C), 148.2 (N-C), 130.1 (C), 129.6 (2×CH), 113.7 (2×CH), 97.9 (=CH), 60.6 (N-CH_2), 55.3 (HC-Ar), 53.5 (OCH_3), 47.6 (CH_3-C-CH_3), 27.4 (CH_3), 24.2 (CH_3), 22.3 (CH_2CH_3), 14.0 (CH_2CH_3).

GC-MS *m/z* (%): 270 (M^+, 43), 215 (100), 199 (23), 171 (15), 159 (17), 128 (20).

FTIR (film): 3025, 2958, 2932, 2874, 2835, 1612, 1513, 1461, 1248, 1178, 1032.

HRMS Calcd. for $C_{17}H_{23}N_2O$: 271.1810. Found: 271.1808.

2-Benzyl-4-(4-methoxyphenyl)-5,5-dimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25br)



Yield: 208 mg (83 %), colorless oil.

Reaction time and purification: 5 h, HPFC (DCM/AcOEt = 6:1).

^{1}H NMR 7.26–7.31 (m, 4H, Ph), 7.13–7.21 (m, 1H, Ph), 7.01 (d, ^3J = 8.7, 2H, Ar), 6.83 (d, ^3J = 8.7, 2H, Ar), 5.70 (s, 1H, =CH), 4.00 (bs, 2H, N-CH_2), 3.96 (d, ^2J = 10.4, 1H, CH_2-Ph), 3.94 (s, 1H, HC-Ar), 3.89 (d, ^2J = 10.4, 1H, CH_2-Ph), 3.78 (s, 3H, OCH_3), 1.32 (s, 3H, CH_3), 0.74 (s, 3H, CH_3).

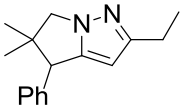
^{13}C NMR 159.0 (C), 156.1 (N=C), 148.6 (N-C), 140.5 (C), 130.0 (C), 129.8 (2×CH), 129.0 (2×CH), 128.6 (2×CH), 126.2 (CH), 113.9 (2×CH), 99.3 (=CH), 60.8 (N-CH_2), 55.4 (HC-Ar), 53.7 (OCH_3), 47.8 (CH_3-C-CH_3), 35.8 (CH_2-Ph), 27.5 (CH_3), 24.3 (CH_3).

GC-MS *m/z* (%): 332 (M^+, 41), 277 (100), 199 (17), 185 (20), 91 (33).

FTIR (film): 3027, 2958, 2931, 2873, 2836, 1612, 1511, 1463, 1247, 1178, 1033.

HRMS Calcd. for $C_{22}H_{25}N_2O$: 333.1967. Found: 333.1951.

2-Ethyl-5,5-dimethyl-4-phenyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bs)



Yield: 228 mg (91 %), colorless oil.

Reaction time and purification: 5 h, HPFC (AcOEt/PE = 1:3).

^{1}H NMR 7.23–7.36 (m, 3H, Ph), 7.12 (d, ^3J = 6.9, 2H, Ph), 5.78 (s, 1H, =CH), 4.01 (s, 1H, HC-Ph), 3.96 (d, ^2J = 10.4, 1H, N-CH_2), 3.91 (d, ^2J = 10.4, 1H, N-CH_2), 2.69 (q, ^3J = 7.6, 2H, CH_2CH_3), 1.36 (s, 3H, CH_3), 1.27 (t, ^3J = 7.6, 3H, CH_2CH_3), 0.75 (s, 3H, CH_3).

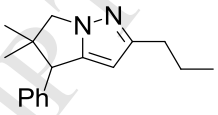
^{13}C NMR 159.1 (N=C), 148.1 (N-C), 138.3 (C), 128.8 (2×CH), 128.5 (2×CH), 127.4 (CH), 98.1 (=CH), 60.8 (N-CH_2), 54.4 (HC-Ph), 47.8 (CH_3-C-CH_3), 27.7 (CH_3), 24.4 (CH_3), 22.5 (CH_2CH_3), 14.1 (CH_2CH_3).

GC-MS *m/z* (%): 240 (M^+, 52), 199 (21), 185 (100), 115 (18).

FTIR (film): 3062, 3029, 2964, 2873, 1949, 1729, 1602, 1536, 1494, 1465, 1382, 1309, 1143, 1076.

HRMS Calcd. for $C_{16}H_{21}N_2$: 241.1705. Found: 241.1688.

5,5-Dimethyl-4-phenyl-2-propyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bt)



Yield: 205 mg (82 %), colorless oil.

Reaction time and purification: 5 h, HPFC (AcOEt/PE = 1:3).

^{1}H NMR 7.27–7.34 (m, 3H, Ph), 7.10–7.14 (m, 2H, Ph), 5.77 (s, 1H, =CH), 4.02 (s, 1H, HC-Ph), 3.95 (d, ^2J = 10.4, 1H, N-CH_2), 3.91 (d, ^2J = 10.4, 1H, N-CH_2), 2.60–2.65 (m, 2H, $CH_2CH_2CH_3$), 1.64–1.75 (m, 2H, CH_2CH_3), 1.36 (s, 3H, CH_3), 0.98 (t, ^3J = 7.4, 3H, CH_2CH_3), 0.74 (s, 3H, CH_3).

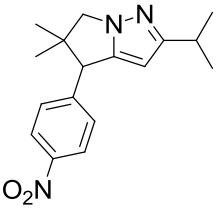
^{13}C NMR 157.7 (N=C), 148.0 (N-C), 138.3 (C), 128.8 (2×CH), 128.5 (2×CH), 127.4 (CH), 98.7 (=CH), 60.8 (N-CH_2), 54.4 (HC-Ph), 47.8 (CH_3-C-CH_3), 31.4 ($CH_2CH_2CH_3$), 27.7 (CH_3), 24.4 (CH_3), 23.2 (CH_2CH_3), 14.2 (CH_2CH_3).

GC-MS *m/z* (%): 254 (M^+, 24), 226 (100), 213 (23), 199 (91), 115 (31), 59 (17), 45 (20).

FTIR (film): 3027, 2962, 2925, 2871, 1947, 1731, 1652, 1536, 1494, 1456, 1382, 1076.

HRMS Calcd. for $C_{17}H_{23}N_2$: 255.1861. Found: 255.1845.

5,5-Dimethyl-4-(4-nitrophenyl)-2-(prop-2-yl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bu)



Yield: 220 mg (88 %), yellow oil.

Reaction time and purification: 5 h, HPFC (AcOEt/PE = 1:3).

^{1}H NMR 8.20 (d, ^3J = 8.6, 2H, Ar), 7.31 (d, ^3J = 8.6, 2H, Ar), 5.79 (s, 1H, =CH), 4.13 (s, 1H, HC-Ph), 3.99 (d, ^2J = 10.6, 1H, N-CH_2), 3.96 (d, ^2J = 10.6, 1H, N-CH_2), 3.00 (sep, ^3J = 6.9, 1H, HC-$(CH_3)_2$), 1.40 (s, 3H, CH_3), 1.29 (d, ^3J = 6.9, 6H, HC-$(CH_3)_2$), 0.77 (s, 3H, CH_3).

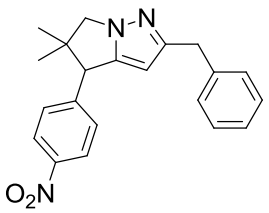
^{13}C NMR 164.3 (N=C), 147.6 (C), 146.5 (C), 146.2 (C), 129.7 (2×CH), 123.8 (2×CH), 97.0 (=CH), 60.7 (N-CH_2), 54.2 (HC-Ar), 48.2 (CH_3-C-CH_3), 28.8 (HC-$(CH_3)_2$), 27.8 (CH_3), 24.5 (CH_3), 23.2 (CH_3), 23.1 (CH_3).

GC-MS *m/z* (%): 299 (M^+, 51), 284 (37), 258 (42), 244 (100), 163 (21), 151 (23), 129 (20), 43 (31).

FTIR (film): 2362, 2338, 1642, 1597, 1516, 1388, 1343, 1088.

HRMS Calcd. for $C_{17}H_{22}N_3O_2$: 300.1712. Found: 300.1721.

2-Benzyl-5,5-dimethyl-4-(4-nitrophenyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bv)



Yield: 205 mg (82 %), yellow oil.

Reaction time and purification: 5 h, HPFC (AcOEt/PE = 1:3).

^{1}H NMR 8.17 (d, ^3J = 8.7, 2H, Ar), 7.25–7.30 (m, 6H, Ar+Ph), 7.17–7.22 (m, 1H, Ph), 5.72 (s, 1H, =CH), 4.11 (s, 1H, HC-Ar), 3.97–4.02 (m, 4H, N-CH_2 + CH_2-Ph), 1.39 (s, 3H, CH_3), 0.76 (s, 3H, CH_3).

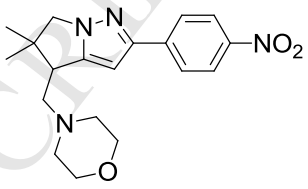
^{13}C NMR 156.8 (N=C), 147.5 (C), 146.9 (C), 145.9 (N-C), 140.2 (C), 129.6 (2×CH), 129.0 (2×CH), 128.7 (2×CH), 126.4 (CH), 123.8 (2×CH), 99.5 (=CH), 60.8 (N-CH_2), 54.2 (HC-Ar), 48.2 (CH_3-C-CH_3), 35.8 (CH_2-Ph), 27.7 (CH_3), 24.4 (CH_3).

GC-MS *m/z* (%): 347 (M^+, 91), 321 (20), 306 (21), 292 (100), 256 (27), 246 (22), 214 (34), 184 (31), 168 (23), 128 (20), 115 (30), 91 (57), 65 (22).

FTIR (film): 3029, 2971, 2925, 2873, 1660, 1600, 1517, 1444, 1346, 1106, 1014.

HRMS Calcd. for $C_{21}H_{22}N_3O_2$: 348.1712. Found: 348.1692.

5,5-Dimethyl-4-(4-morpholinomethyl)-2-(4-nitrophenyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bw)



Yield: 210 mg (84 %), orange solid. MP 194.2–194.4 °C.

Reaction time and purification: 2 h, recrystallization (Et_2O).

^{1}H NMR 8.23 (d, ^3J = 8.6, 2H, Ar), 7.92 (d, ^3J = 8.6, 2H, Ar), 6.44 (s, 1H, =CH), 3.95 (bs, 2H, N-CH_2), 3.73–3.80 (m, 4H, O-CH_2), 3.11 (t, ^3J = 7.6, 1H, HC-CH_2), 2.41–2.67 (m, 6H, N-CH_2), 1.38 (s, 3H, CH_3), 1.16 (s, 3H, CH_3).

^{13}C NMR 152.9 (N=C), 149.8 (N-C), 147.0 (C), 140.8 (C), 125.8 (2×CH), 124.3 (2×CH), 98.5 (=CH), 67.3 (2×O-CH_2), 62.0 (N-N-CH_2), 57.5 (HC-CH_2), 54.2 (2×N-CH_2), 46.1 (H_3C-C-CH_3), 44.1 (HC-CH_2), 27.3 (CH_3), 22.9 (CH_3).

GC-MS *m/z* (%): 355 (M^+, 5), 213 (31), 207 (27), 166 (21), 137 (33), 123 (29), 109 (36), 97 (100), 81 (27), 67 (44), 43 (36), 41 (59).

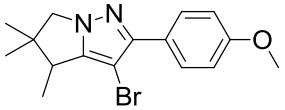
FTIR (KBr): 2968, 2923, 1652, 1601, 1514, 1455, 1418, 1344, 1263, 1114.

HRMS Calcd. for $C_{19}H_{25}N_4O_4$: 357.1927. Found: 357.1937.

4. Bromination of dimethylated dihydropyrrolo[1,2-*b*]pyrazoles with NBS

The bicyclic compound **25as** or **25ax** (200 mg) was dissolved in chloroform (10 mL) and 1.05 eq NBS was added. The mixture was stirred at room temperature, diluted with $CHCl_3$ (10 mL), washed with water (3×15 mL), dried over $MgSO_4$ and concentrated in vacuo. Brown solids were purified by a column chromatography.

3-Bromo-2-(4-methoxyphenyl)-4,5,5-trimethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bx)



Yield: 230 mg (83 %), white solid. MP 45.4–45.5 °C.

Reaction time and purification: 90 min, HPFC (DCM/AcOEt = 40:1).

^{1}H NMR 7.81 (d, ^3J = 8.8, 2H, Ar), 6.94 (d, ^3J = 8.8, 2H, Ar), 3.90 (d, ^2J = 10.6, 1H, N-CH_2), 3.85 (d, ^2J = 10.6, 1H, N-CH_2), 3.81 (s, 3H, OCH_3), 2.91 (q, ^3J = 7.3, 1H, HC-CH_3), 1.26 (d, ^3J = 7.3, 3H, HC-CH_3), 1.24 (s, 3H, CH_3), 1.12 (s, 3H, CH_3).

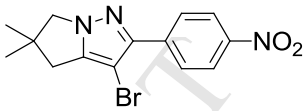
^{13}C NMR 159.5 (C), 151.8 (N=C), 148.8 (C), 128.9 (2×CH), 125.7 (C), 113.8 (2×CH), 85.2 (C-Br), 61.5 (N-CH_2), 55.3 (OCH_3), 45.6 (H_3C-C-CH_3), 42.6 (HC-CH_3), 27.4 (CH_3), 22.5 (CH_3), 12.2 (HC-CH_3).

GC-MS *m/z* (%): 336 (M^++1, 100), 334 (100), 279 (13), 255 (17), 171 (91), 128 (31).

FTIR (KBr): 2967, 2937, 2876, 2837, 1613, 1579, 1527, 1450, 1433, 1392, 1375, 1301, 1267, 1248, 1178, 1109, 1036, 1016, 1007.

HRMS Calcd. for $C_{16}H_{20}N_2OBr$: 335.0759. Found: 335.0750.

3-Bromo-5,5-dimethyl-2-(4-nitrophenyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25by)



Yield: 277 mg (85 %), white solid. MP 159.5–161.3 °C.

Reaction time and purification: 3 h, HPFC ($CHCl_3$).

^{1}H NMR 8.25 (d, ^3J = 8.6, 2H, Ar), 8.11 (d, ^3J = 8.6, 2H, Ar), 3.99 (s, 2H, N-CH_2), 2.74 (s, 2H, =C-CH_2), 1.35 (s, 6H, 2×CH_3).

^{13}C NMR 149.6 (N=C), 147.3 (N-C), 146.7 (C), 139.5 (C), 127.8 (2×CH), 123.8 (2×CH), 86.7 (C-Br), 62.5 (N-CH_2), 43.0 (H_3C-C-CH_3), 38.6 (=C-CH_2), 28.4 (2×CH_3).

GC-MS *m/z* (%): 337 (M^++1, 100), 335 (99), 320 (15), 256 (70), 210 (29), 126 (33), 76 (16), 41 (27).

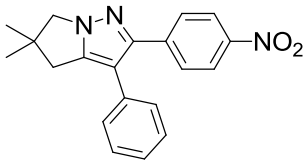
FTIR (KBr): 2962, 2936, 2870, 1599, 1506, 1448, 1389, 1371, 1341, 1321, 1266, 1183, 1111, 1004.

HRMS Calcd. for $C_{14}H_{15}N_3O_2Br$: 336.0348. Found: 336.0352.

5. Suzuki-Miyaura cross-coupling product **25bz**

Compound **25by** (0.59 mmol, 200 mg), 1.5 eq. phenylboronic acid (0.89 mmol), 2 mol% $Pd(PPh_3)_4$ (0.012 mmol, 14 mg) and 3 eq. 2M solution of K_2CO_3 (1.78 mmol, 247 mg) were mixed in DMF (10 mL) and the reaction mixture was heated to reflux. The reaction process was monitored by TLC (AcOEt). The mixture was filtered, diluted with DCM (25 mL) and extracted with water (10 mL). Organic layer was dried over $MgSO_4$ and evaporated in vacuo. The crude product was purified by a column chromatography.

5,5-Dimethyl-2-(4-nitrophenyl)-3-phenyl-5,6-dihydro-4*H*-pyrrolo[1,2-*b*]pyrazole (25bz)



Yield: 154 mg (78 %), yellow solid. MP 142.6–142.7 °C.

Reaction time and purification: 5.5 h, HPFC ($CHCl_3$).

^{1}H NMR 8.13 (d, ^3J = 9.0, 2H, Ar), 7.68 (d, ^3J = 9.0, 2H, Ar), 7.31–7.35 (m, 2H, Ph), 7.25–7.29 (m, 1H, Ph), 7.20–7.22 (m, 2H, Ph), 4.00 (s, 2H, N-CH_2), 2.82 (s, 2H, =C-CH_2), 1.36 (s, 6H, 2×CH_3).

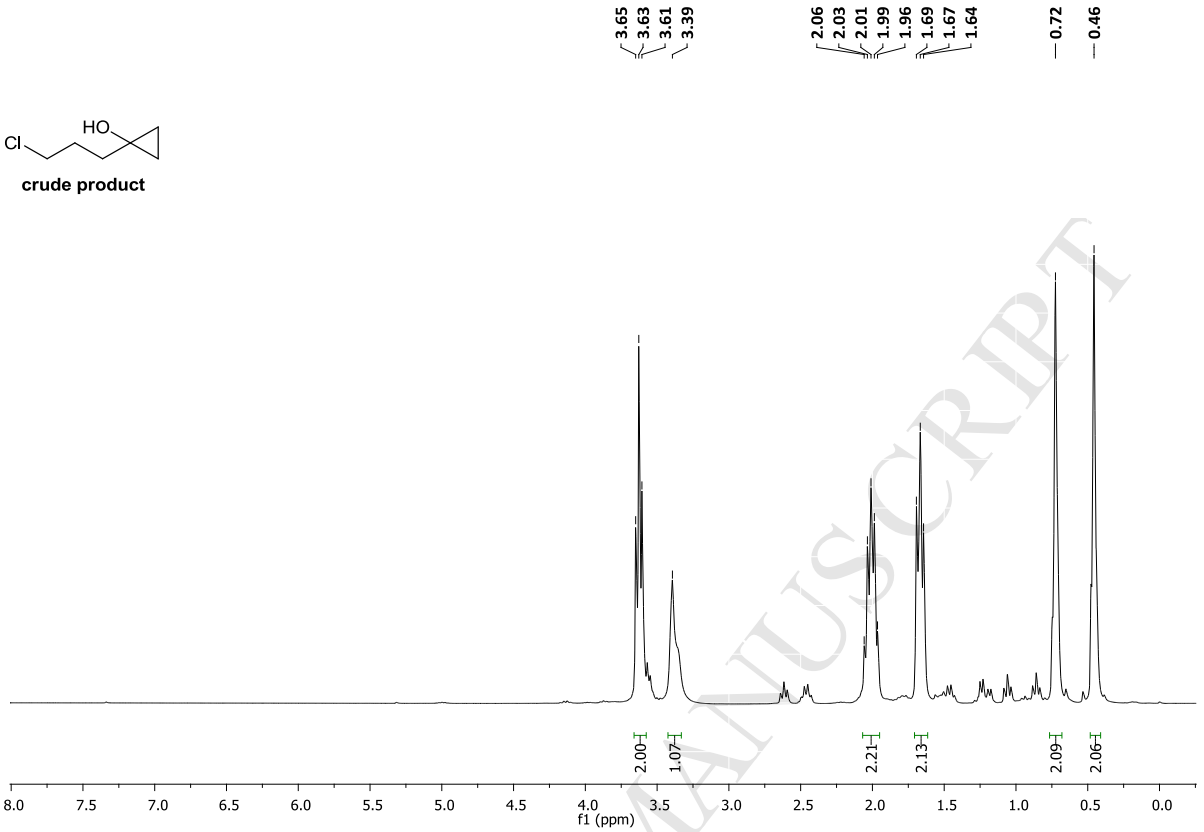
^{13}C NMR 150.2 (N=C), 147.1 (N-C), 145.4 (C), 141.2 (C), 133.4 (C), 128.9 (2×CH), 128.9 (2×CH), 128.6 (2×CH), 126.9 (CH), 123.8 (2×CH), 115.3 (C), 61.6 (N-CH_2), 43.3 (H_3C-C-CH_3), 39.1 (=C-CH_2), 28.5 (2×CH_3).

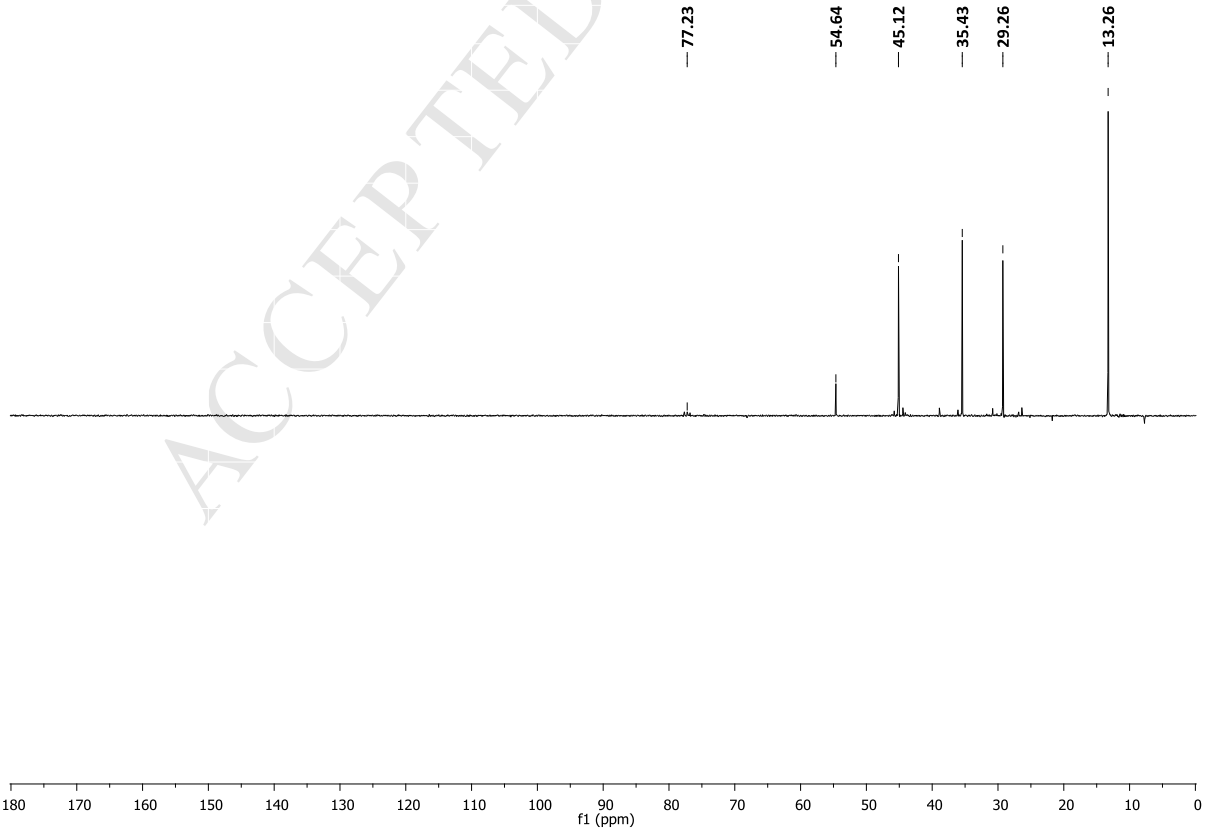
GC-MS *m/z* (%): 333 (M^+, 100), 318 (18), 202 (15).

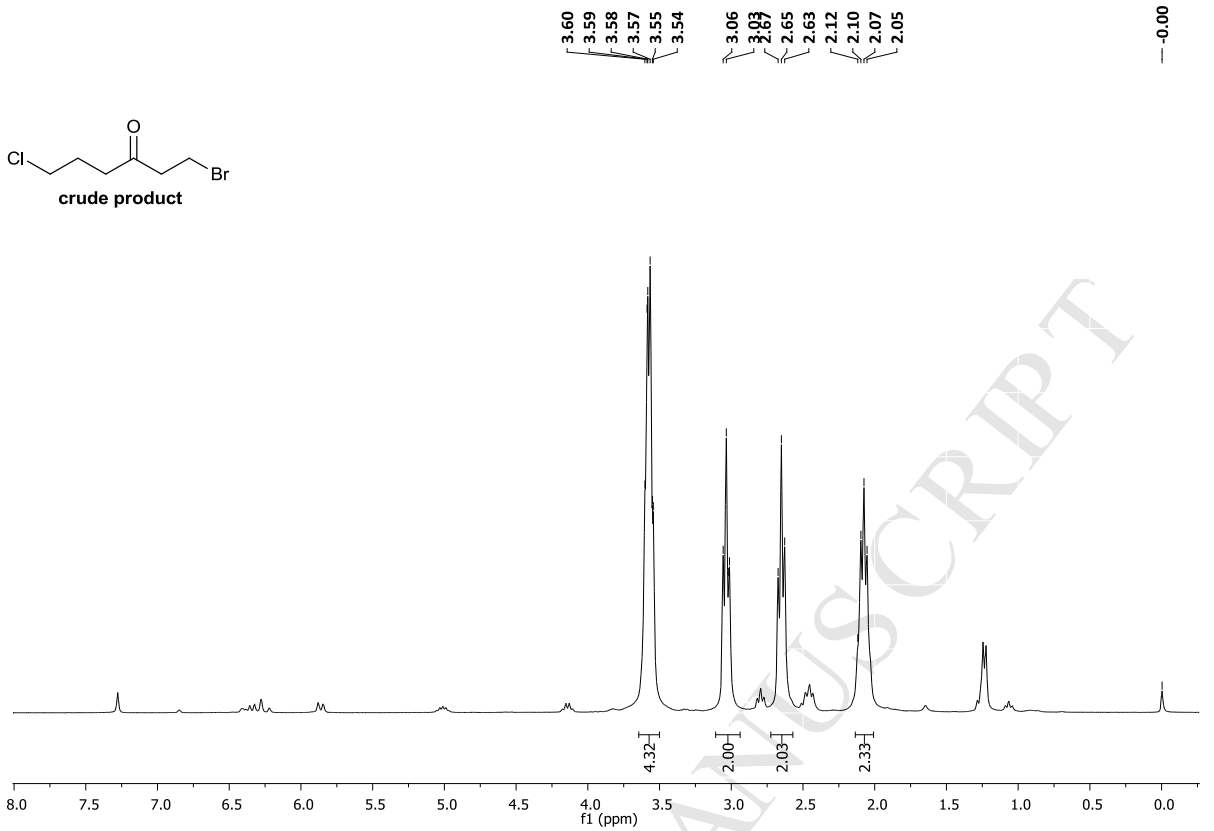
FTIR (KBr): 2960, 2926, 2868, 1597, 1514, 1426, 1342, 1319, 1176, 1104.

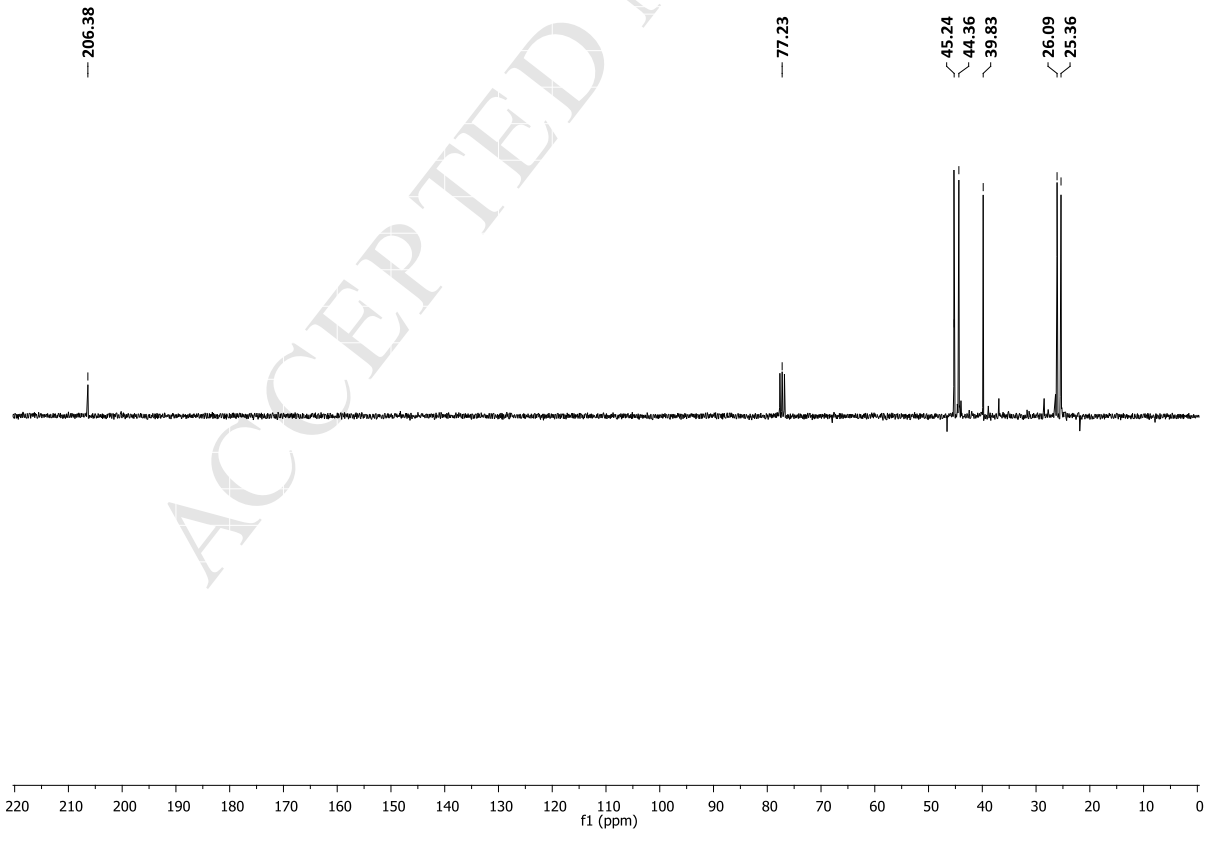
HRMS Calcd. for $C_{20}H_{20}N_3O_2$: 334.1556. Found: 334.1554.

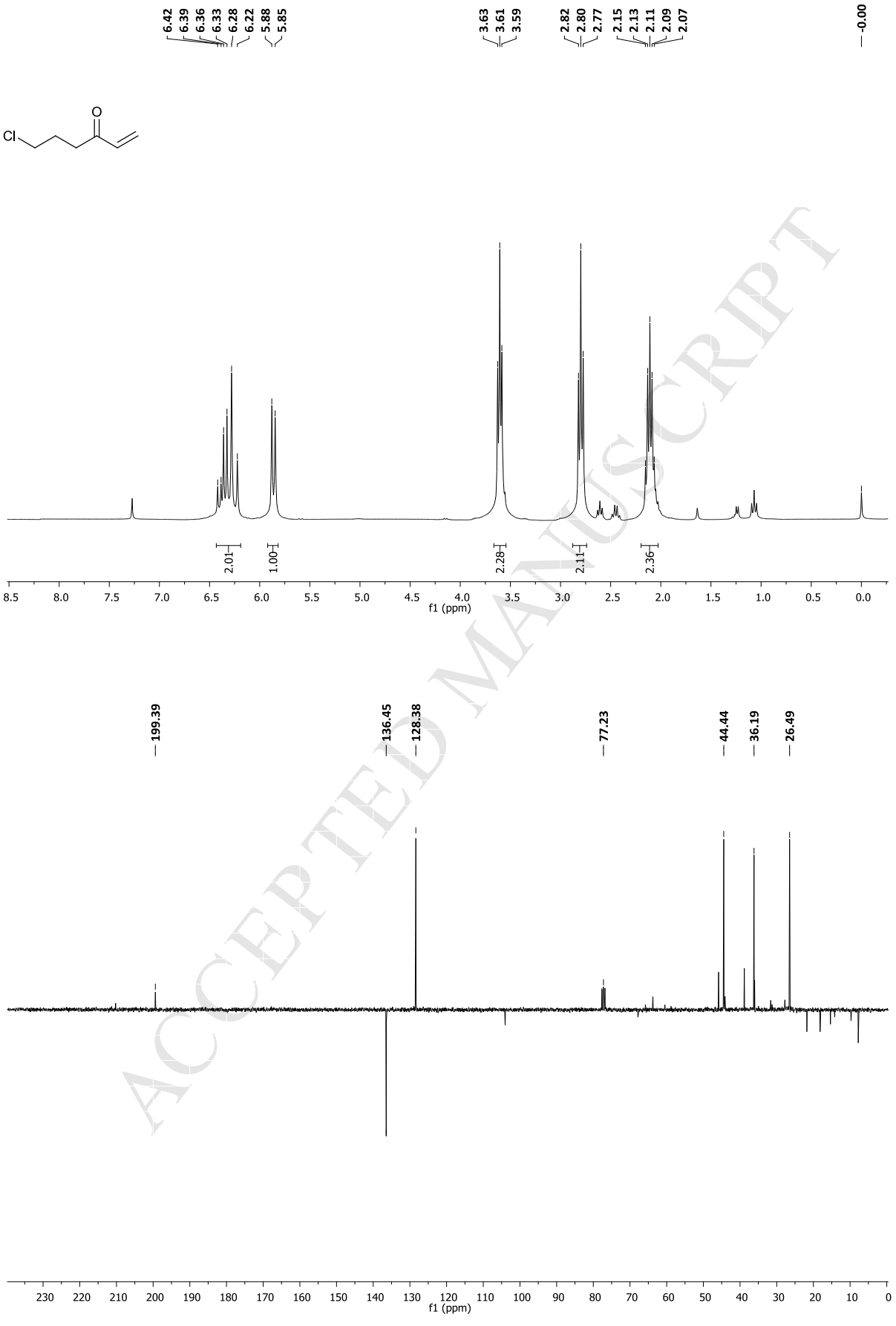
6. ^{1}H and ^{13}C NMR spectra of all intermediates and final products

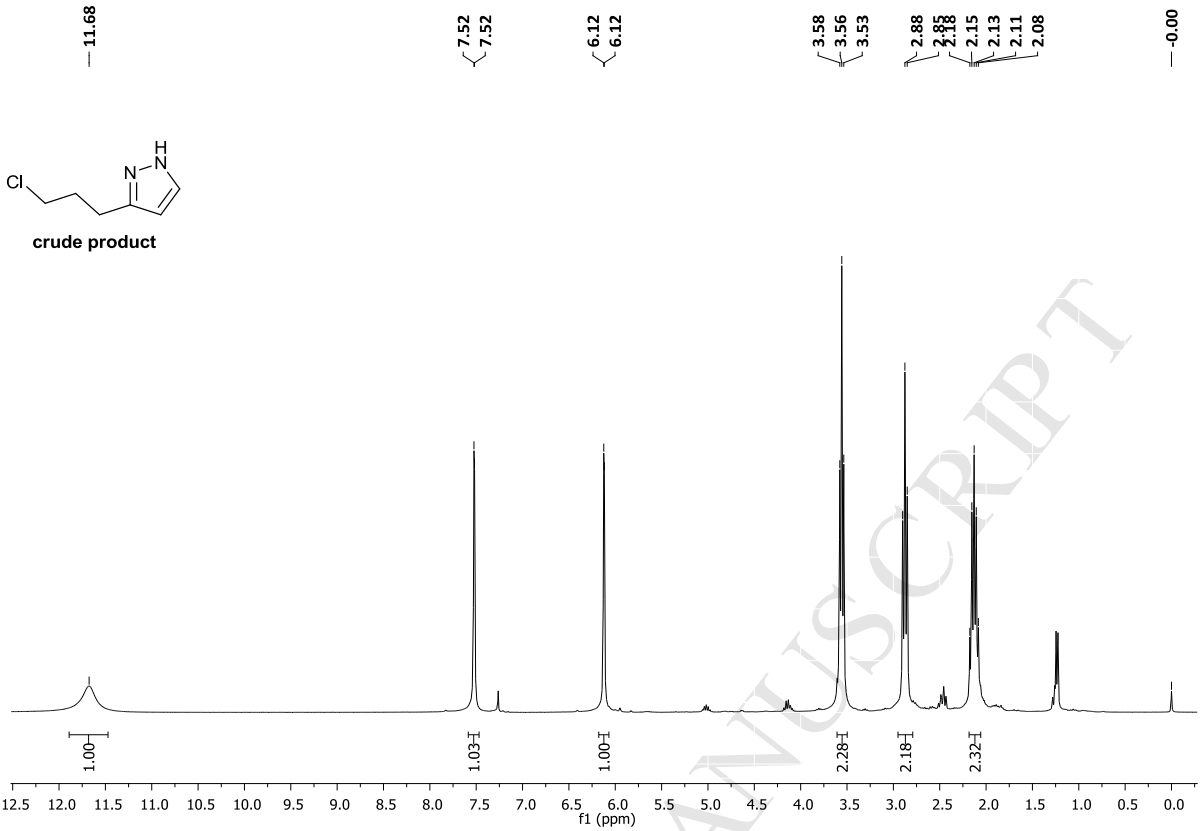


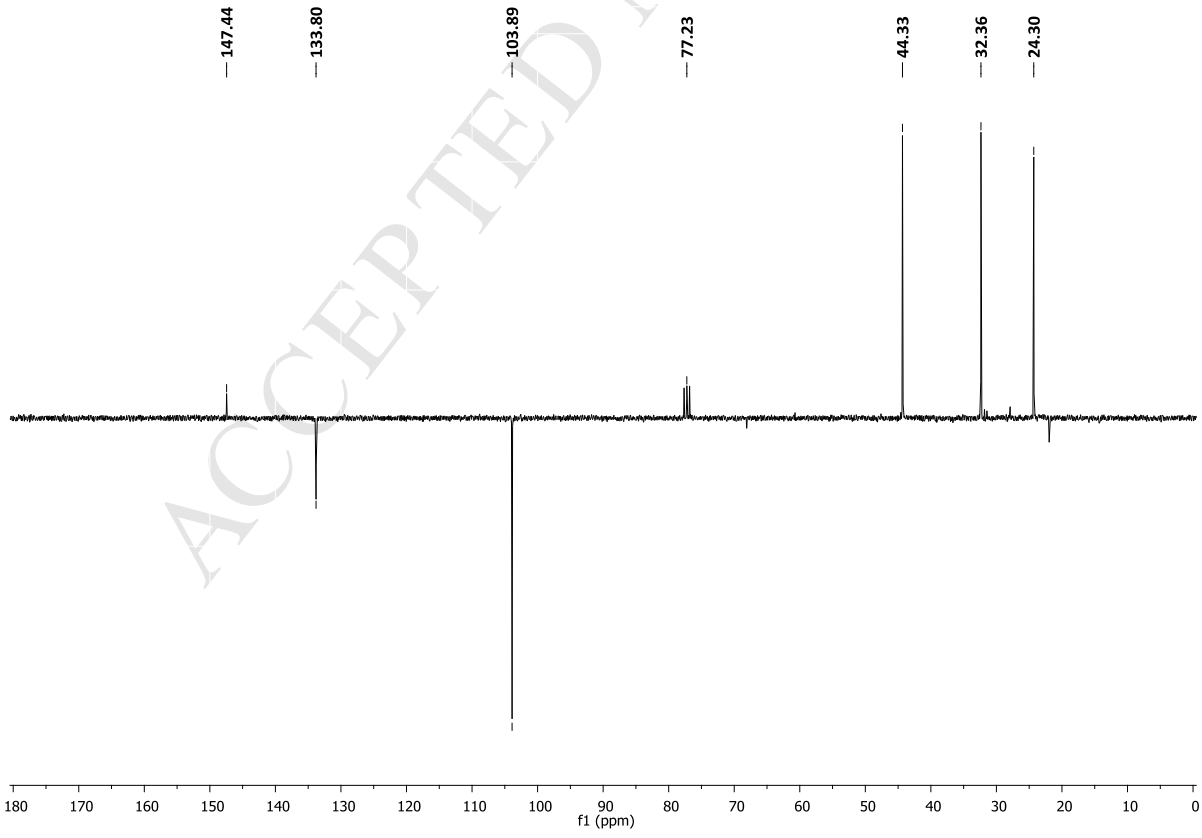


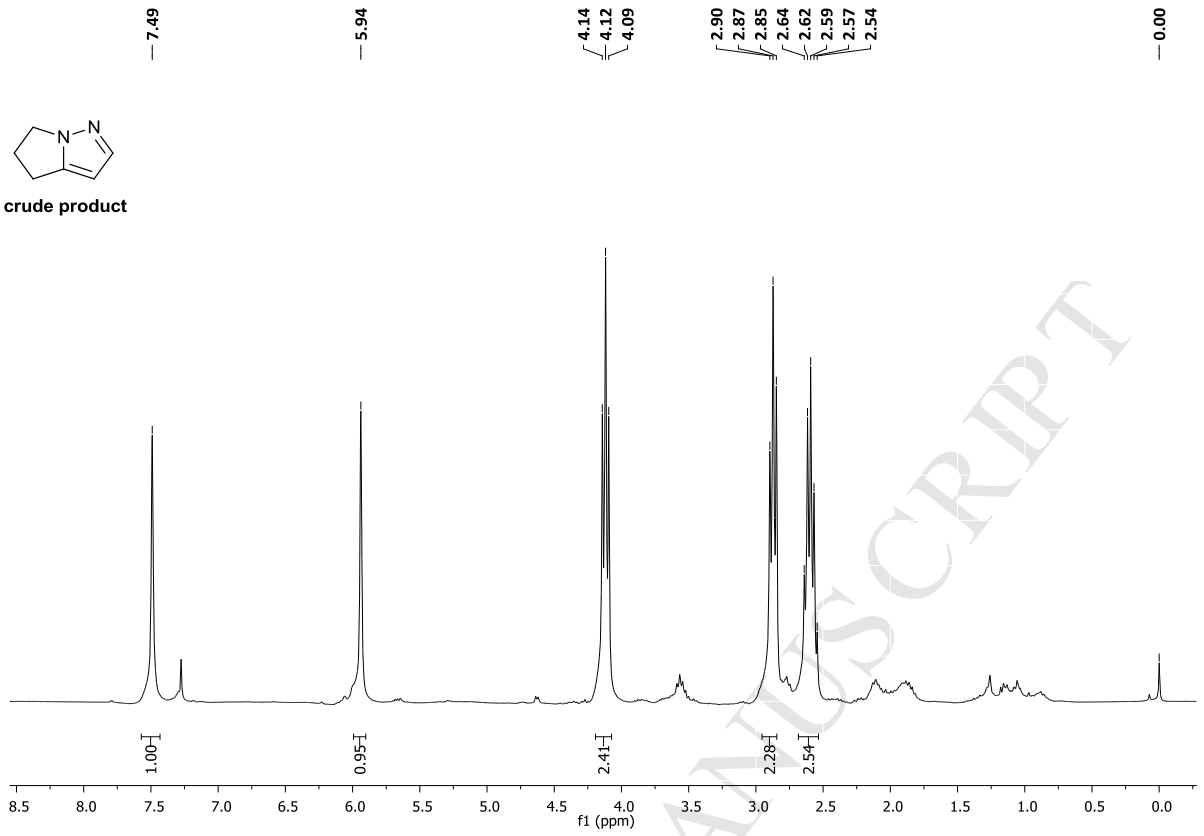


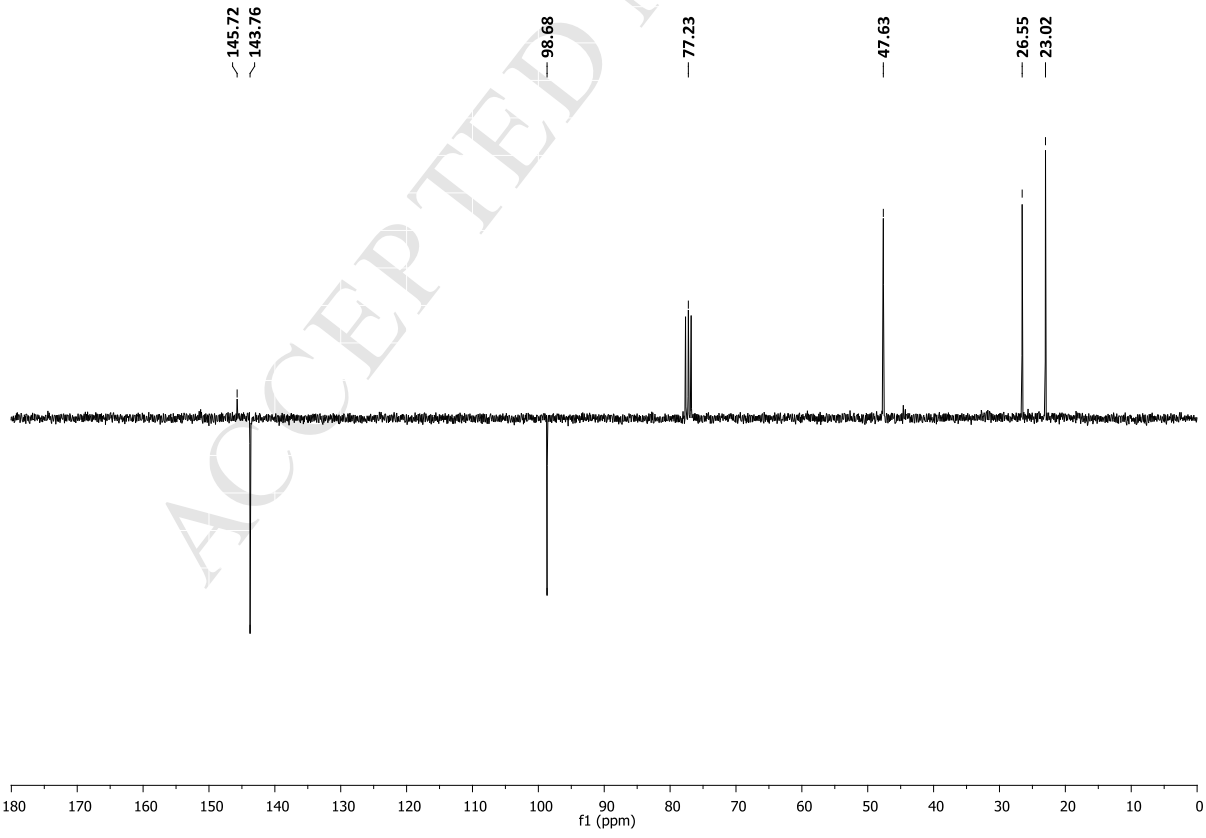


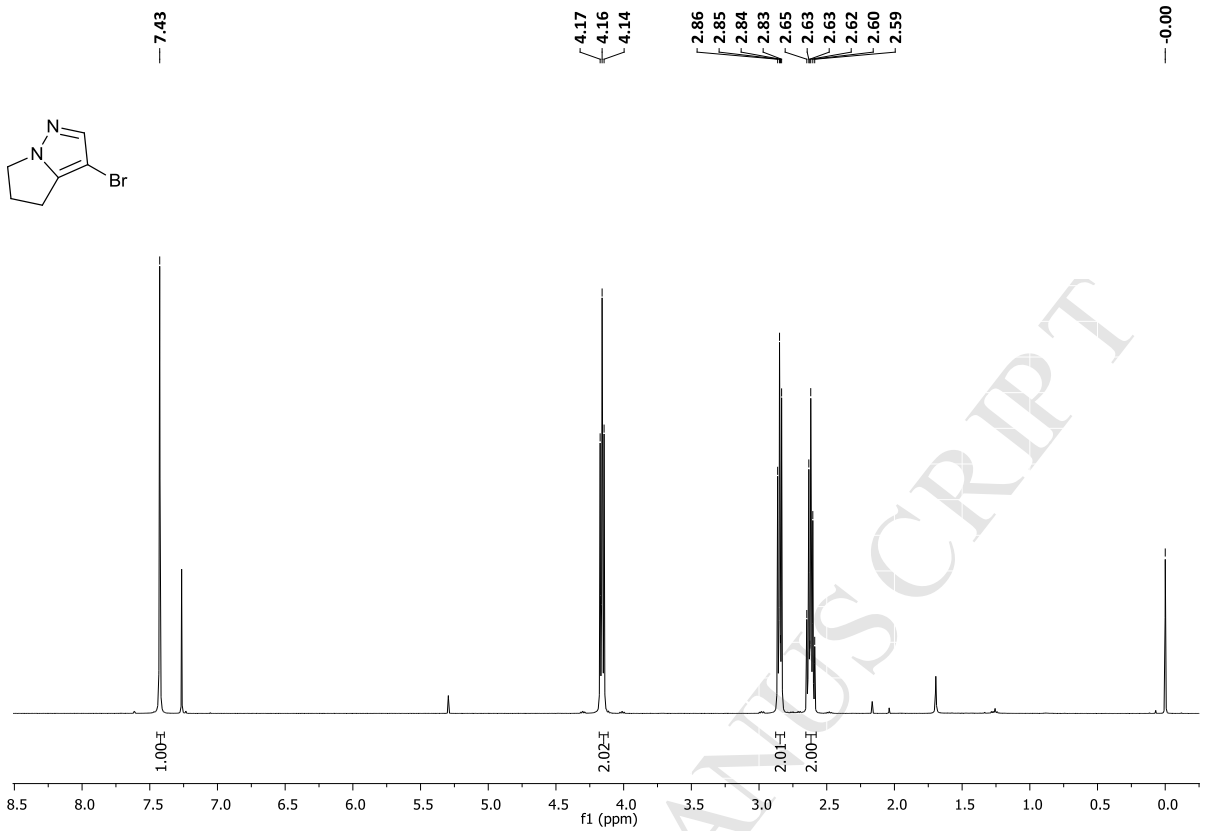


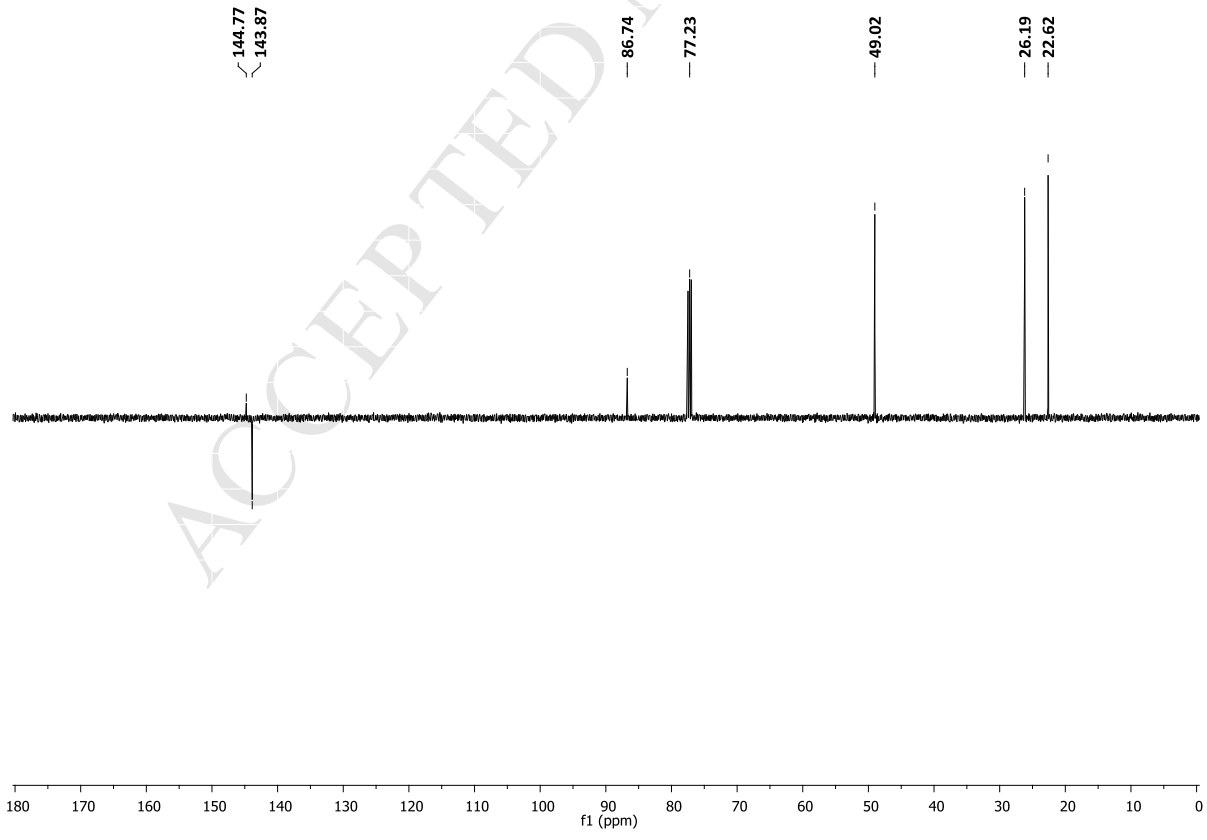


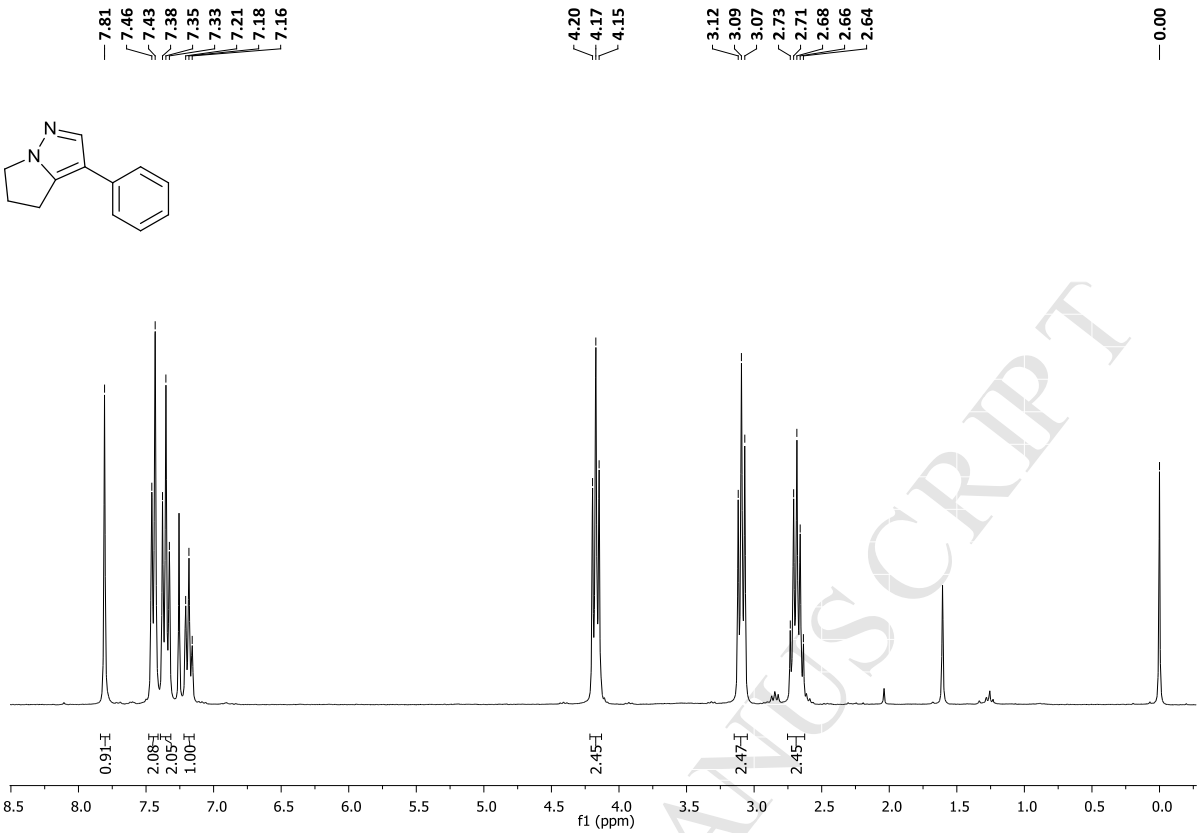


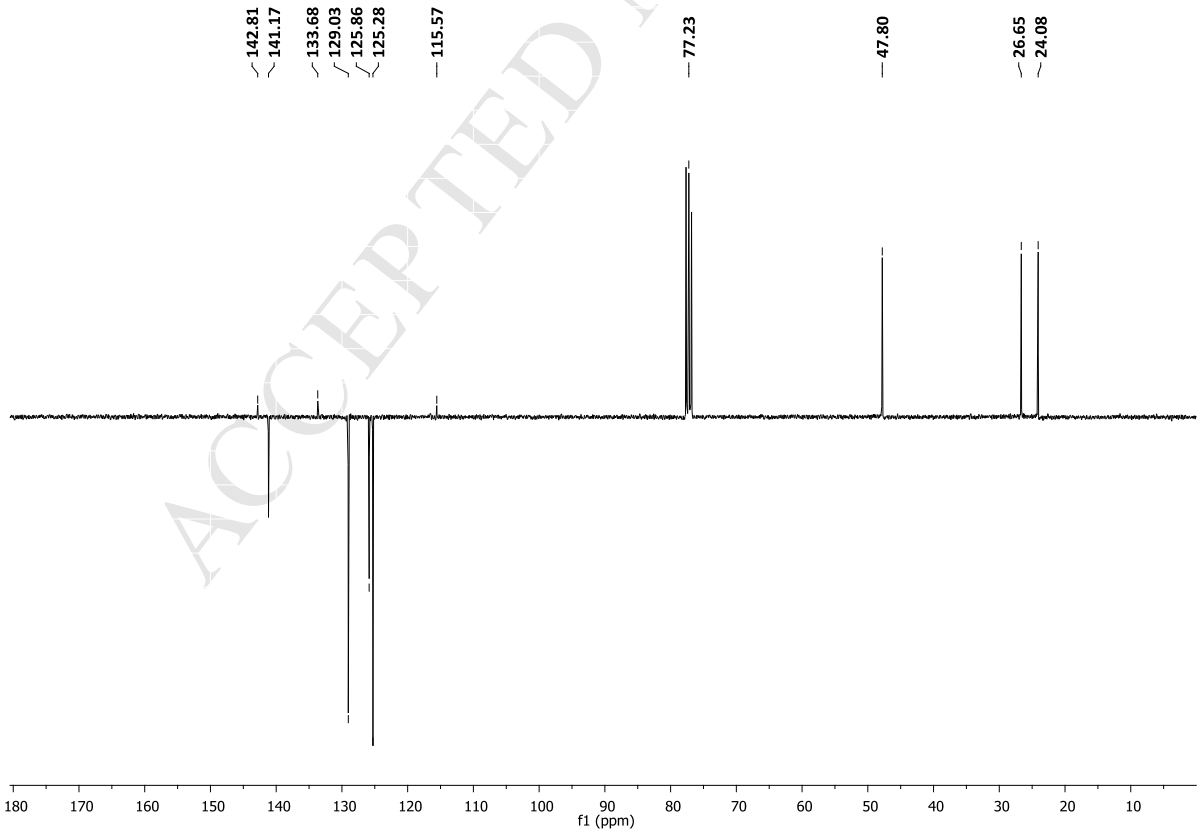


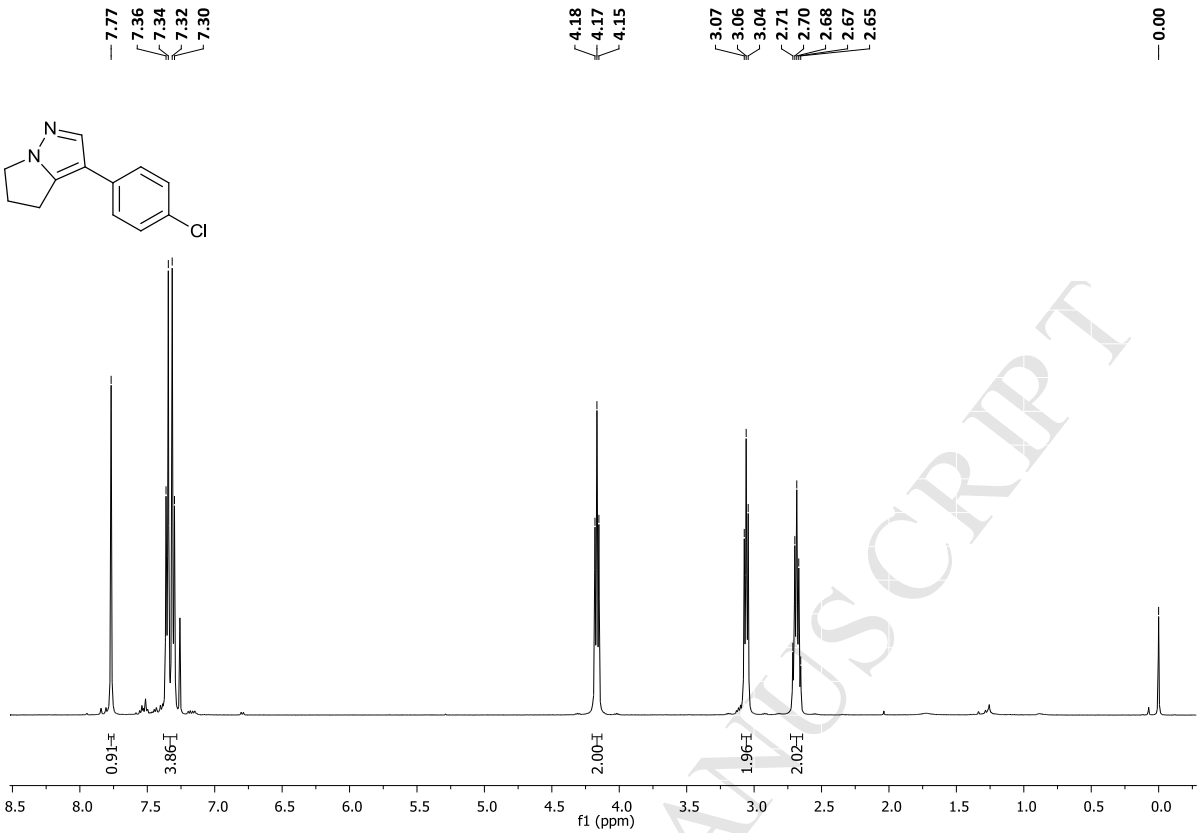


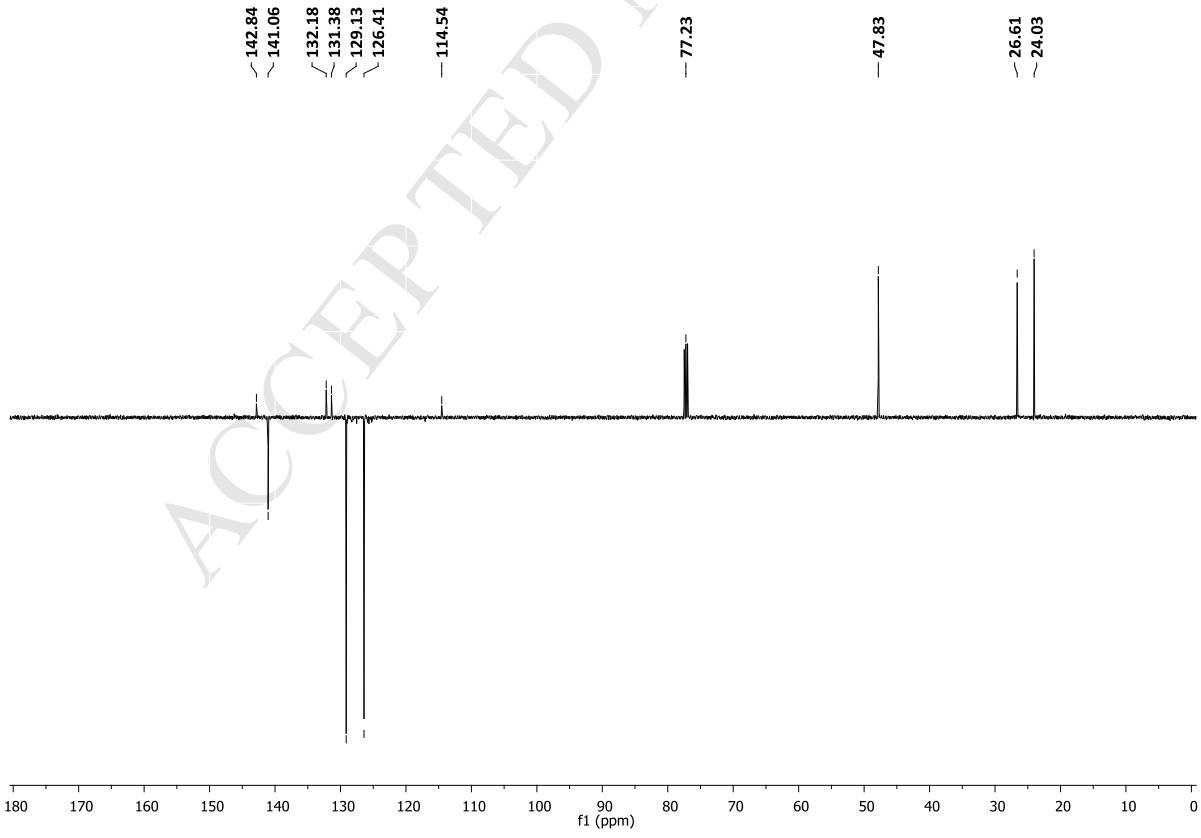


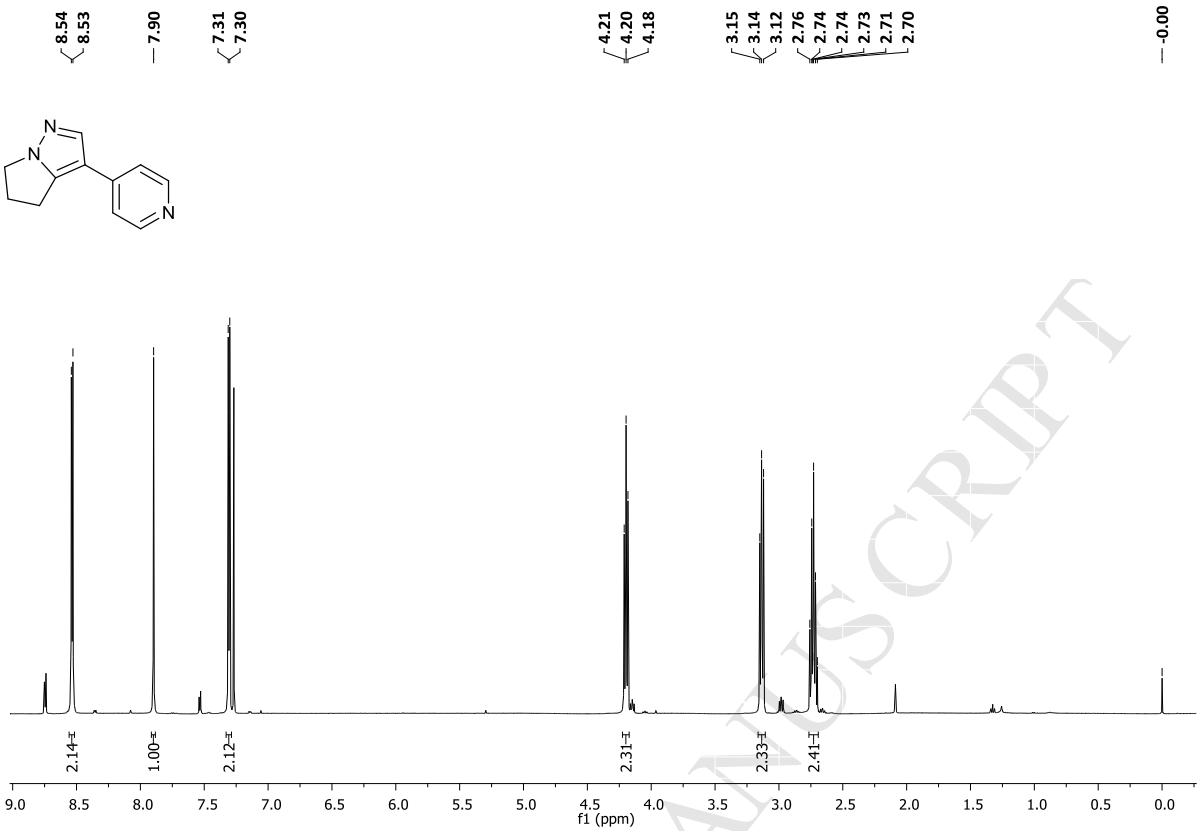


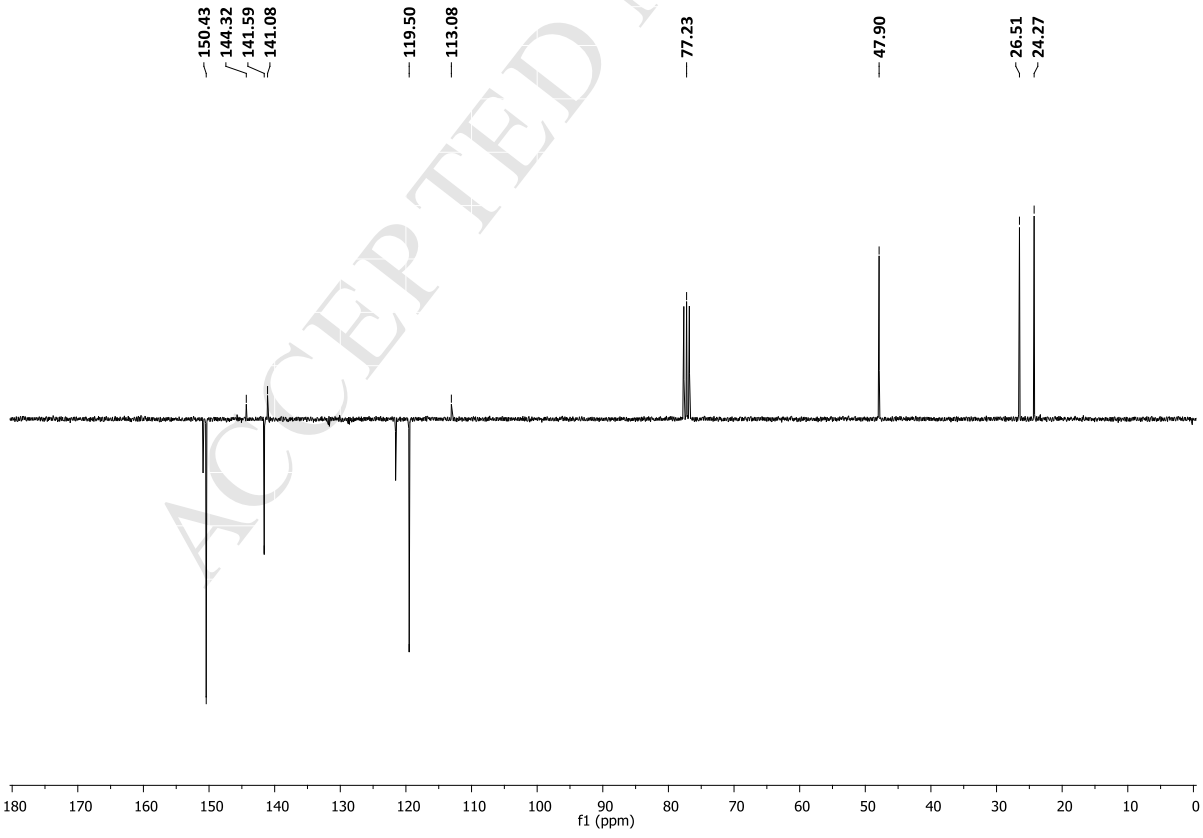


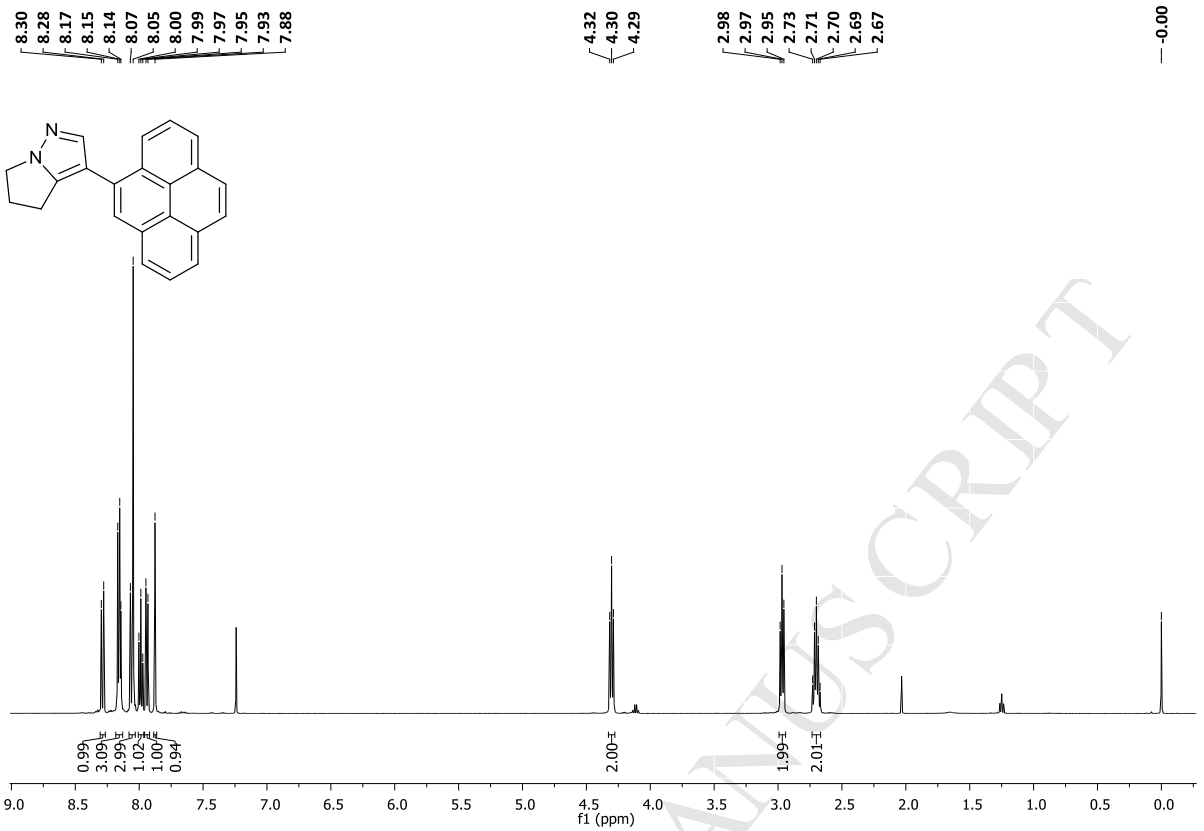


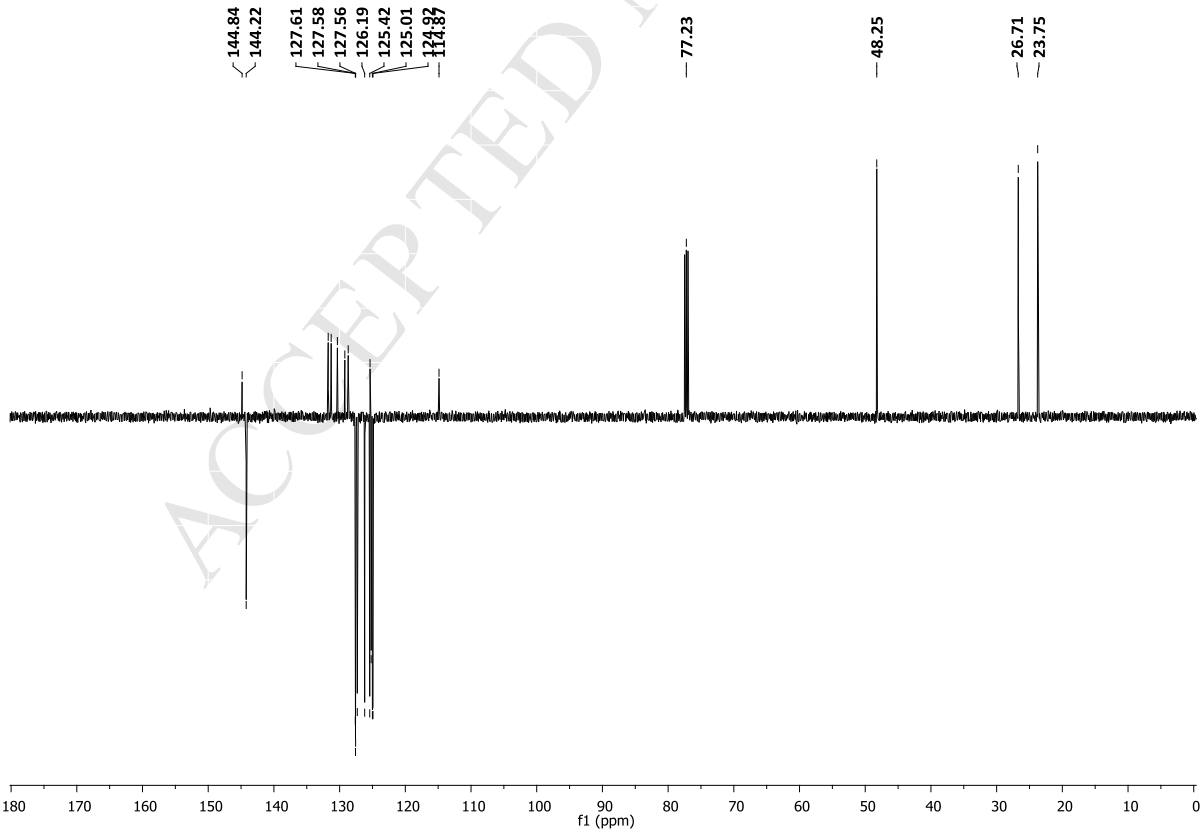


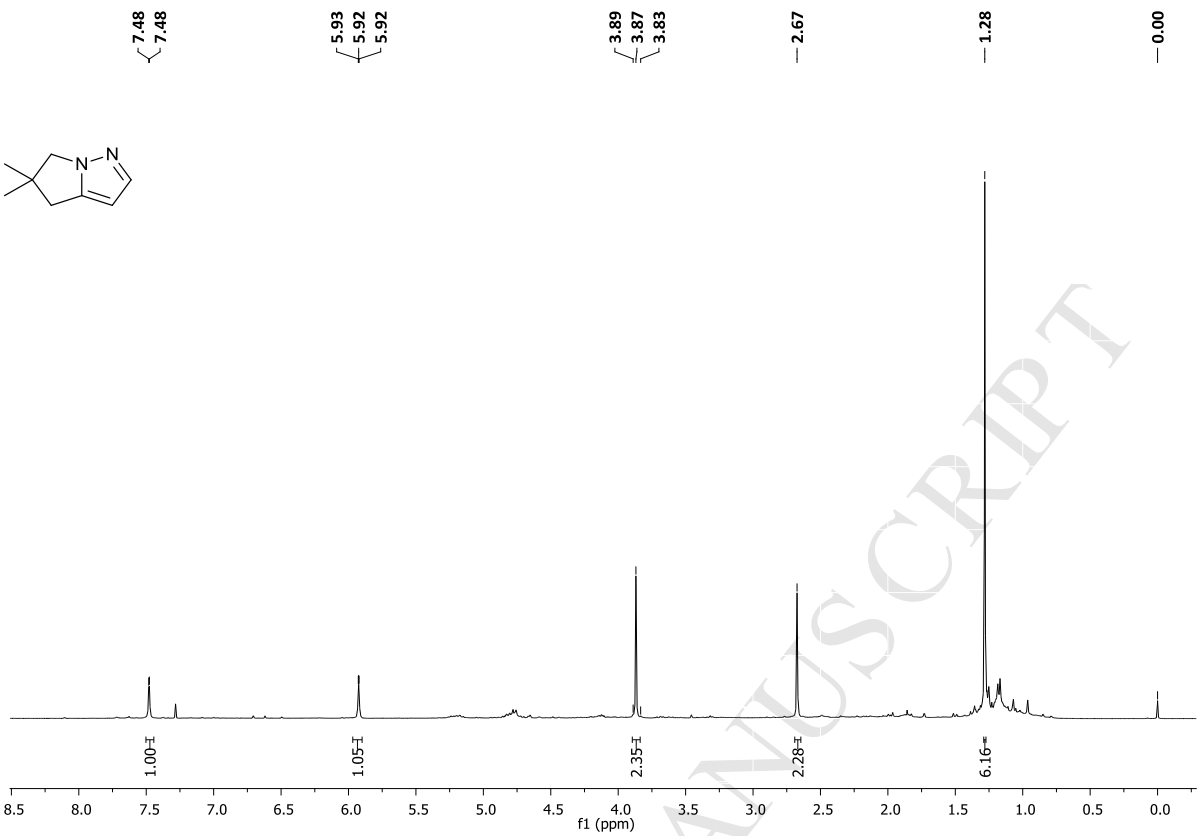


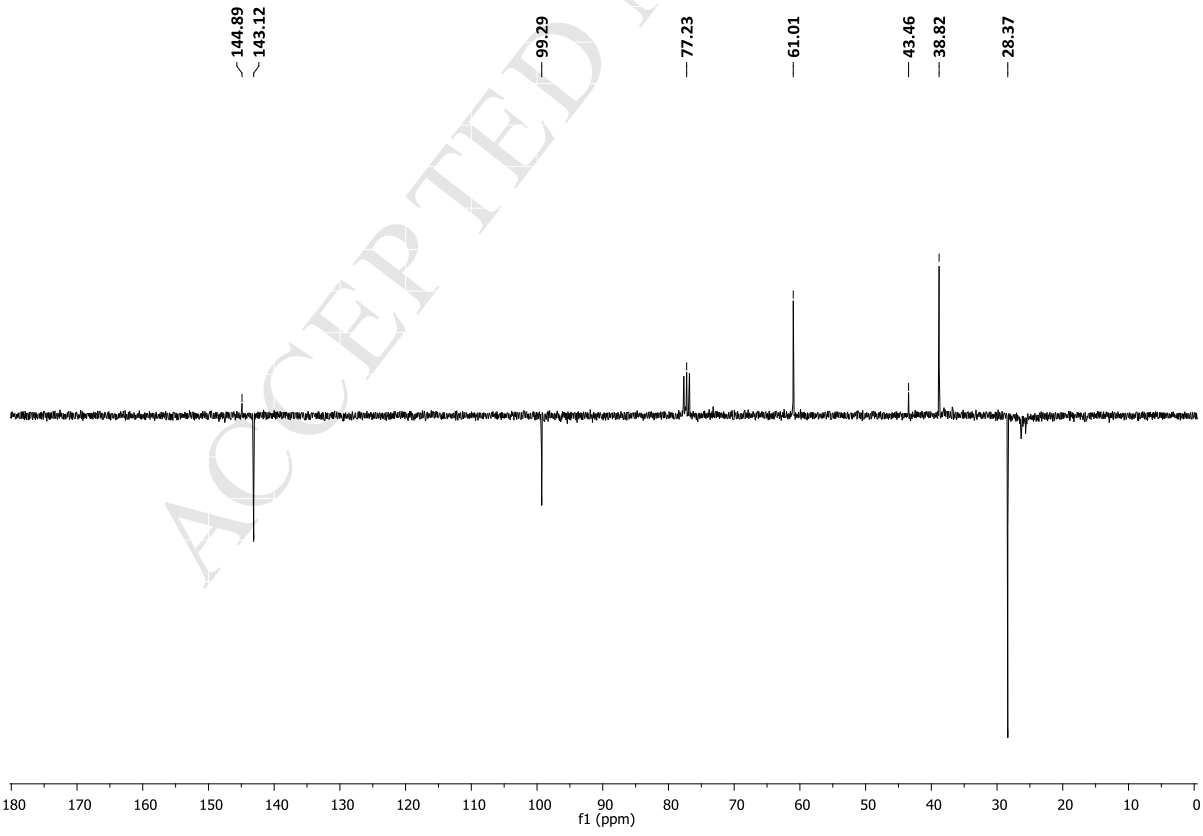


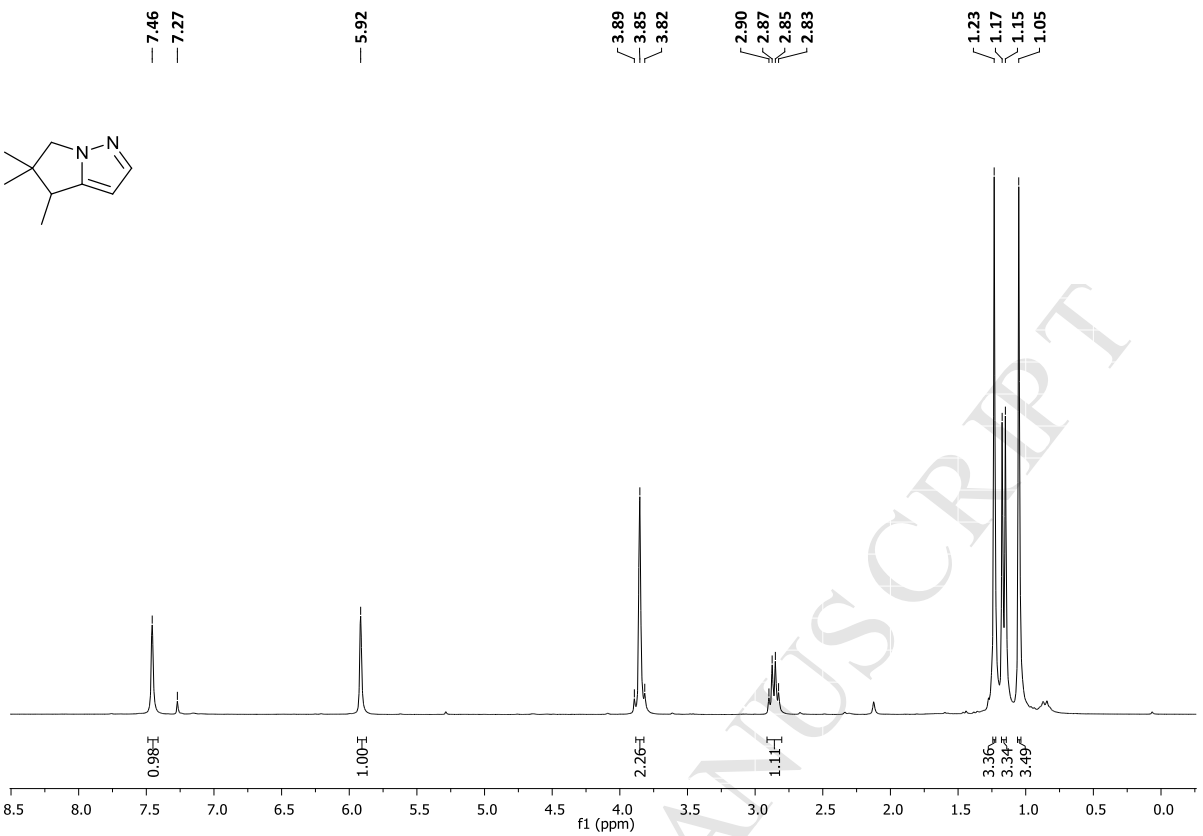


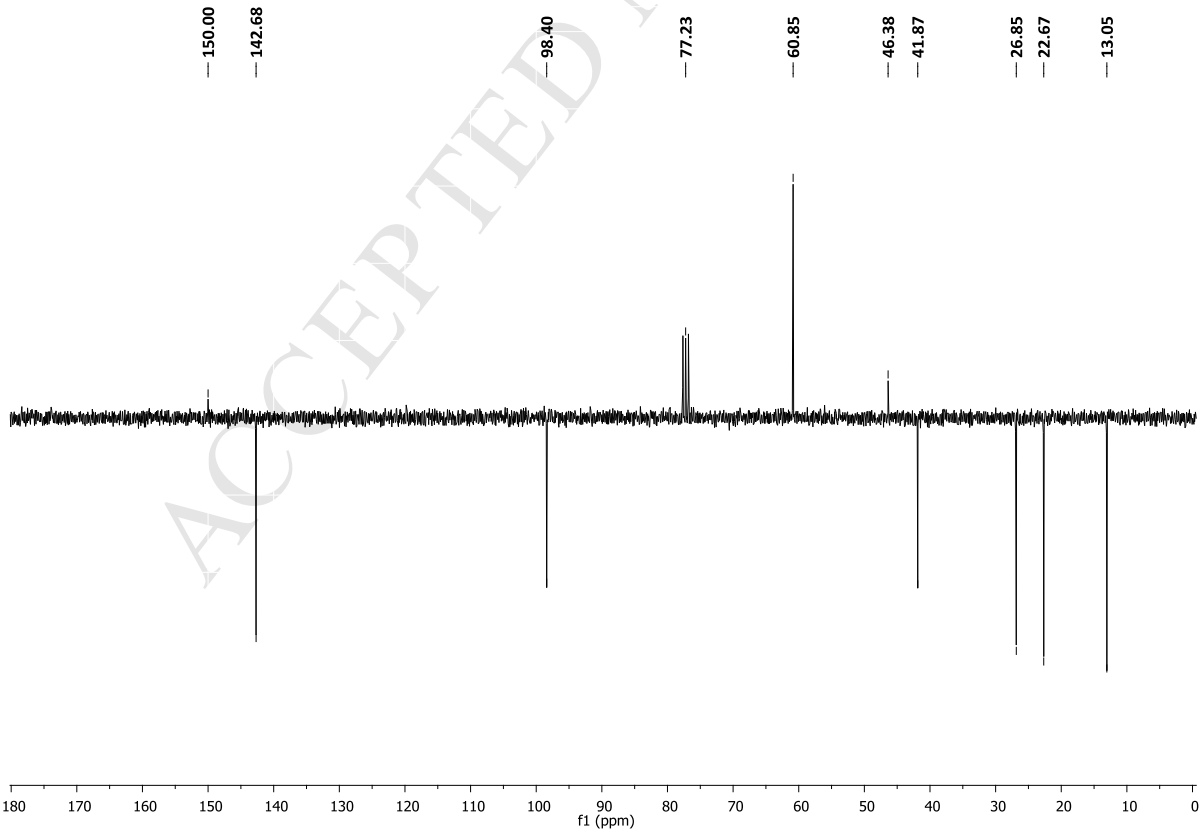


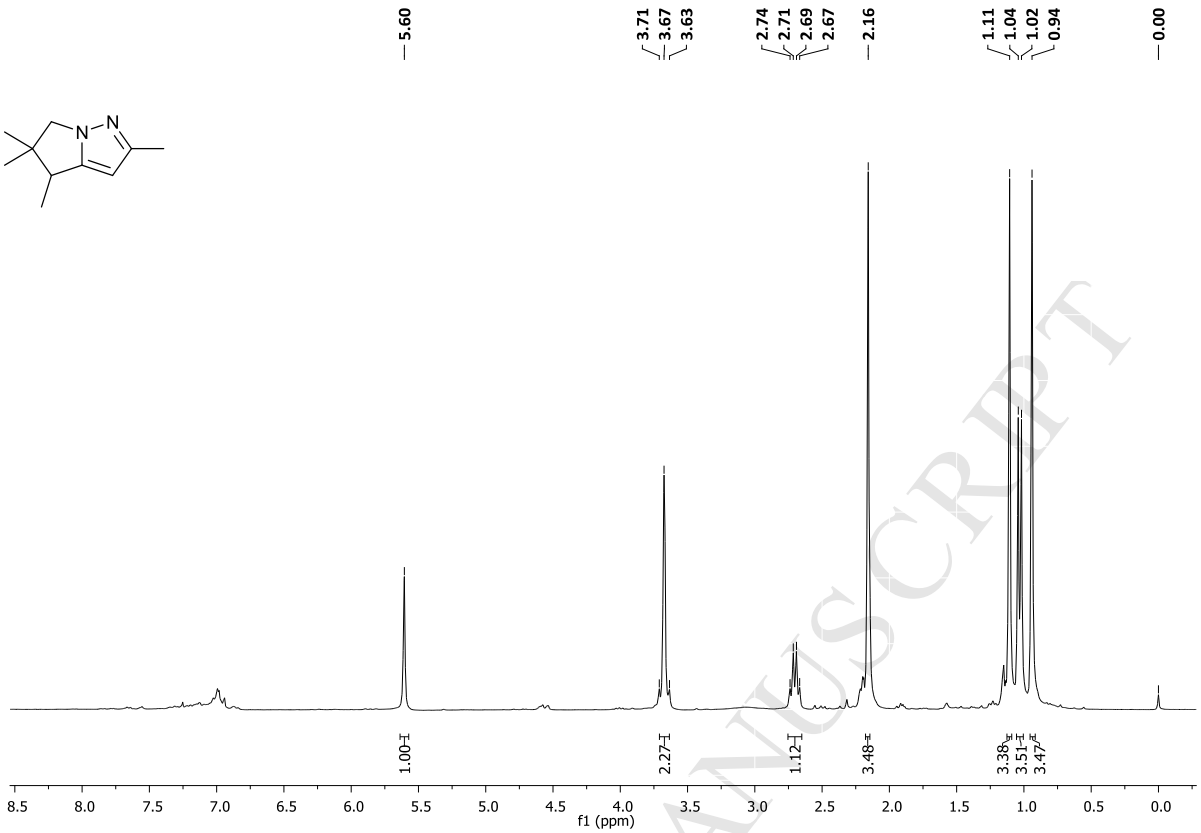


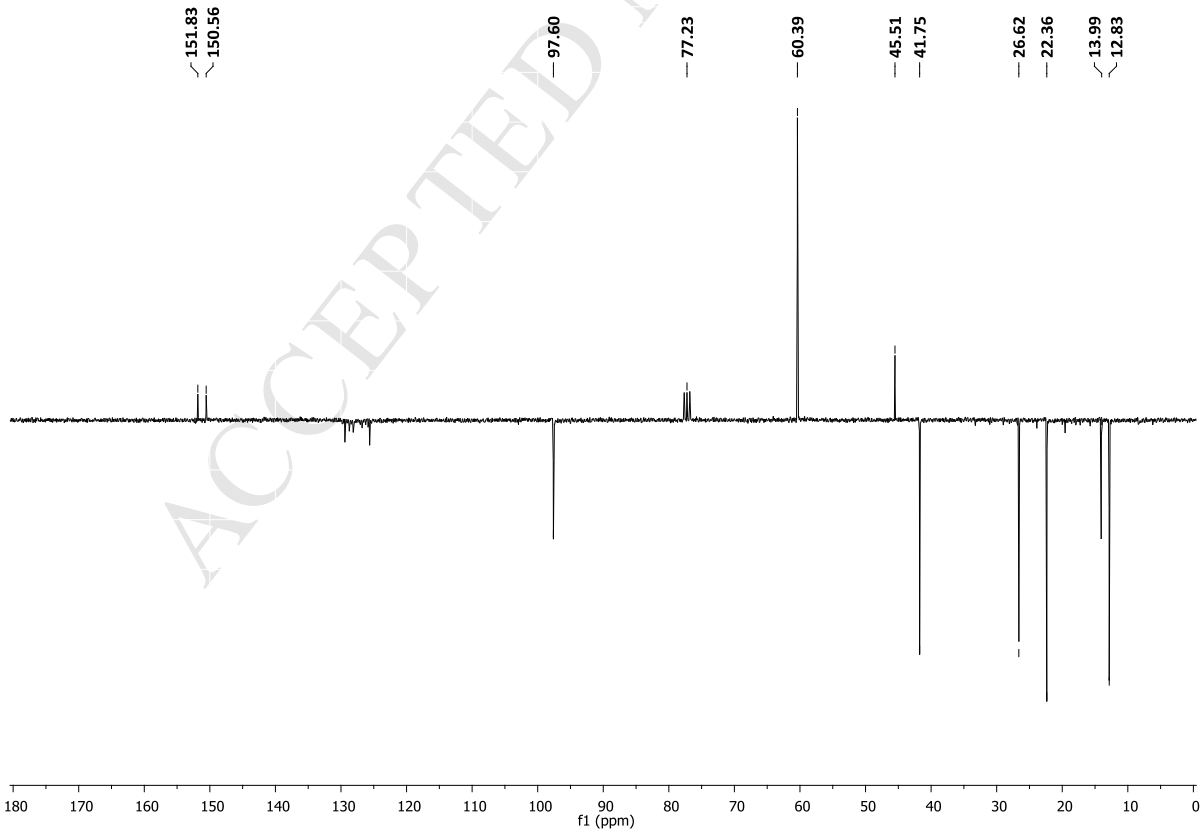


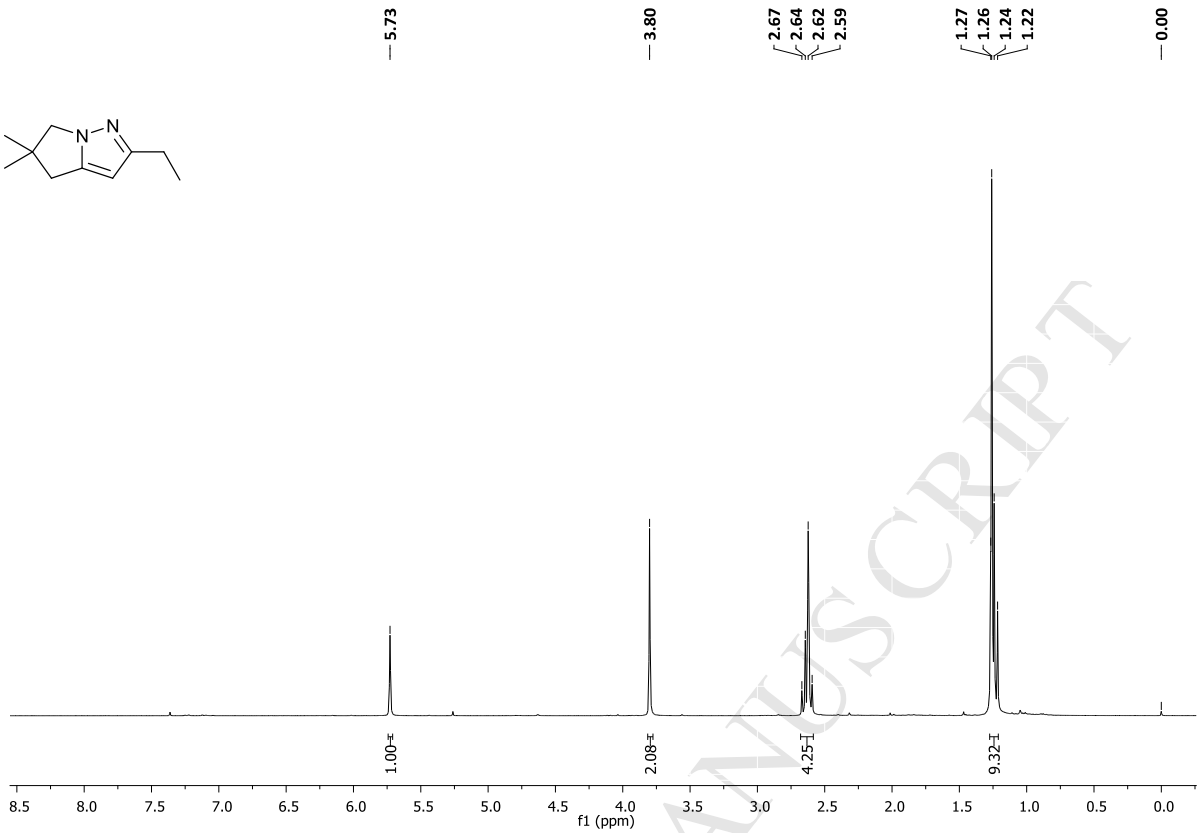


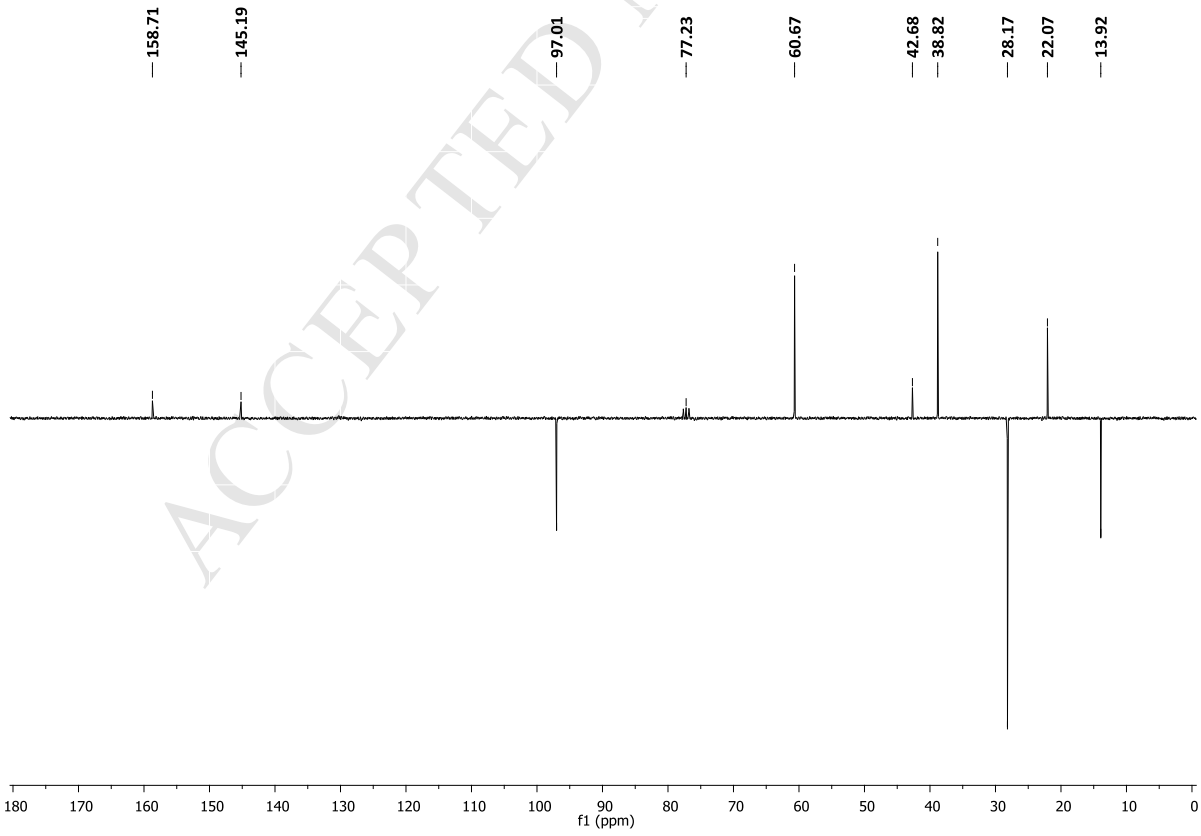


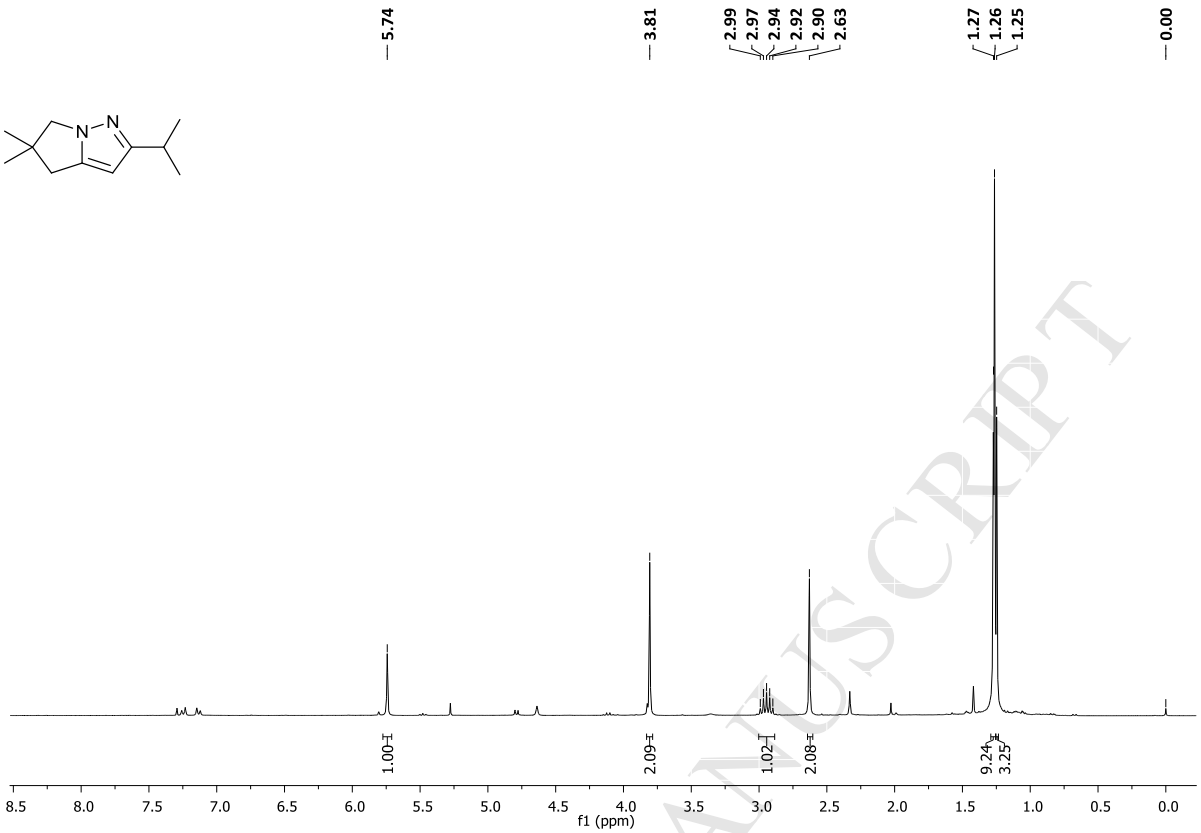


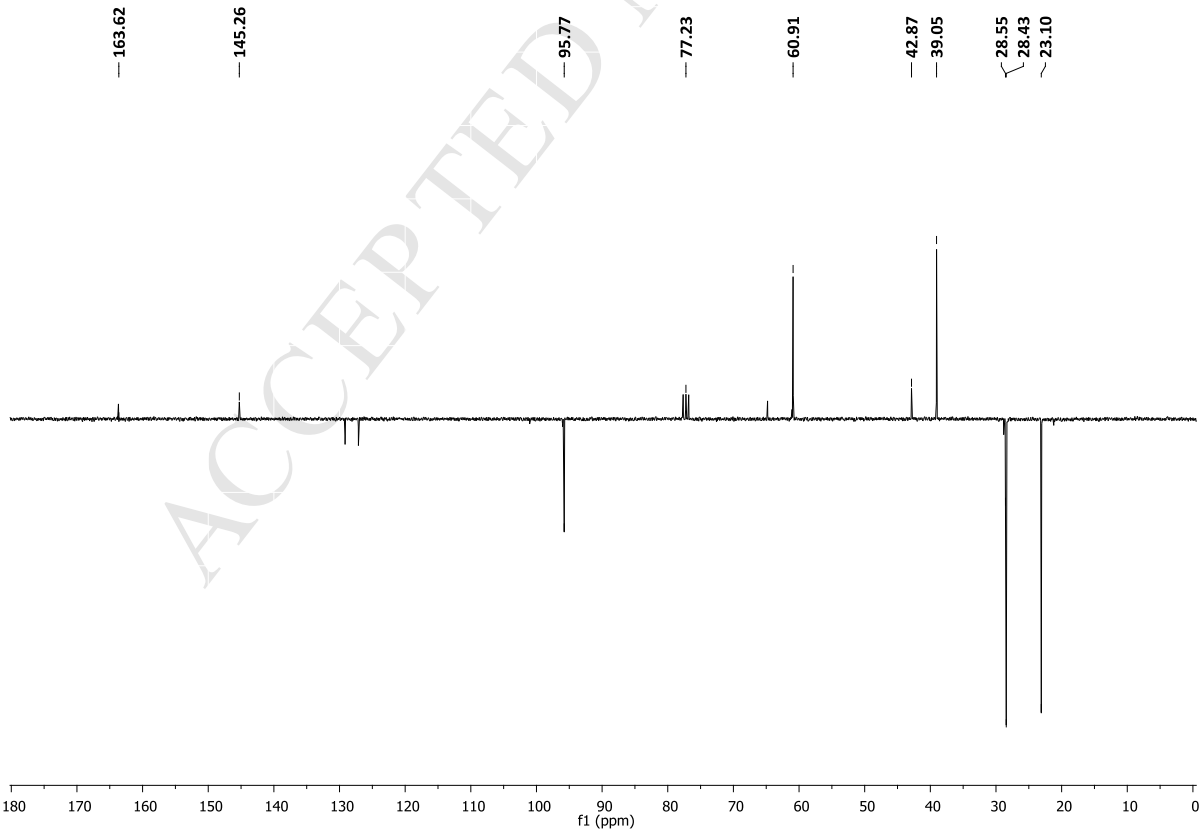


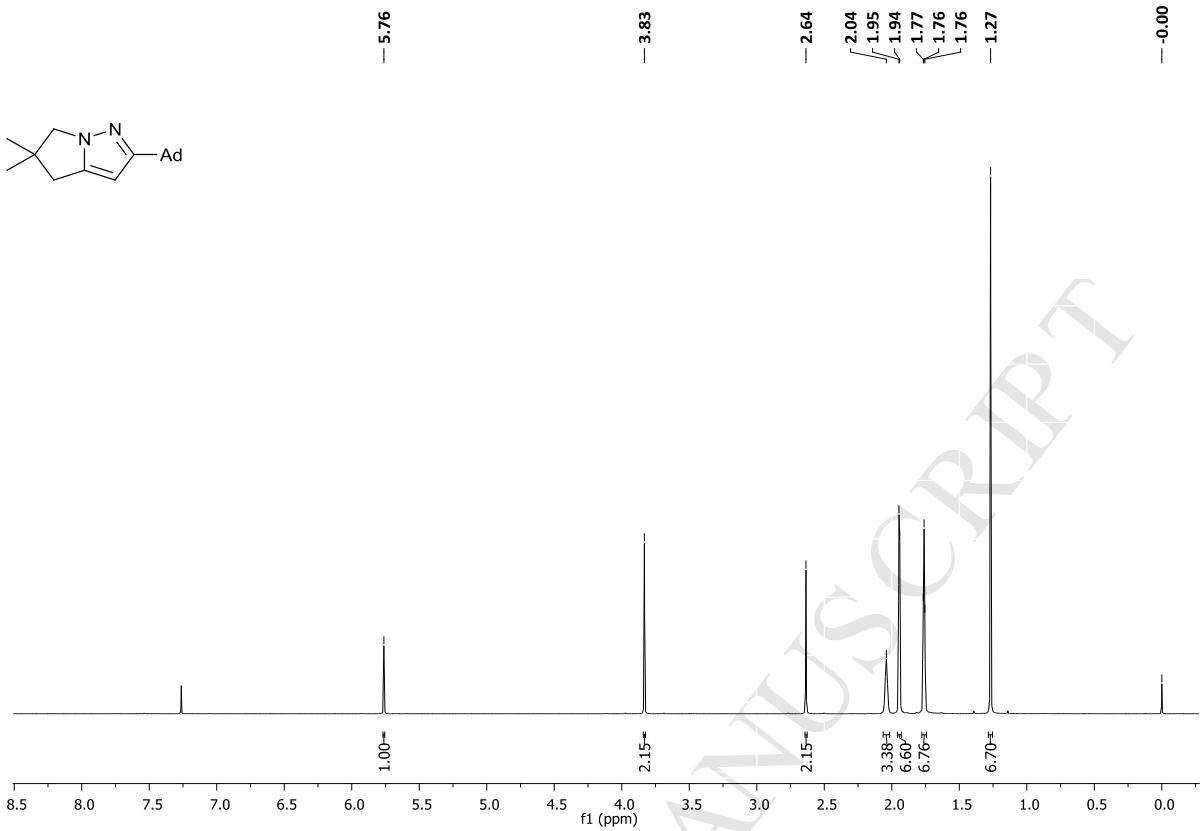


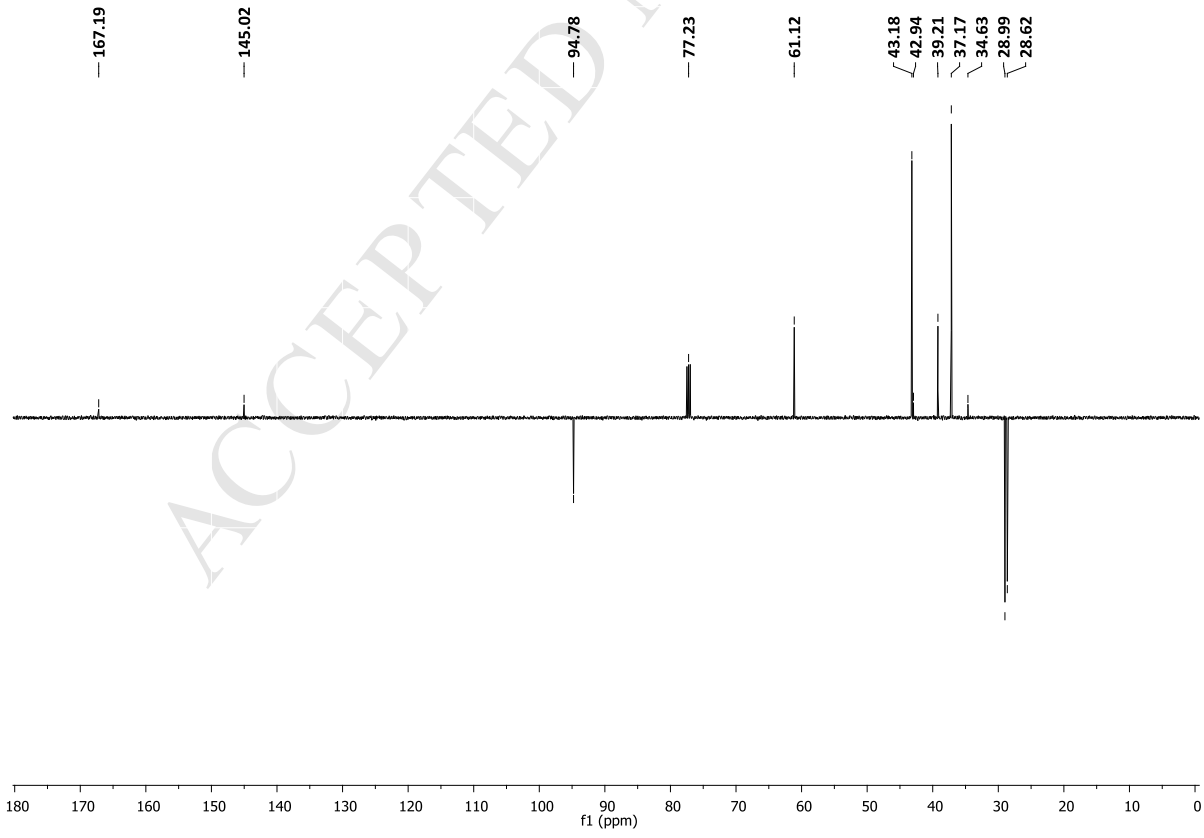


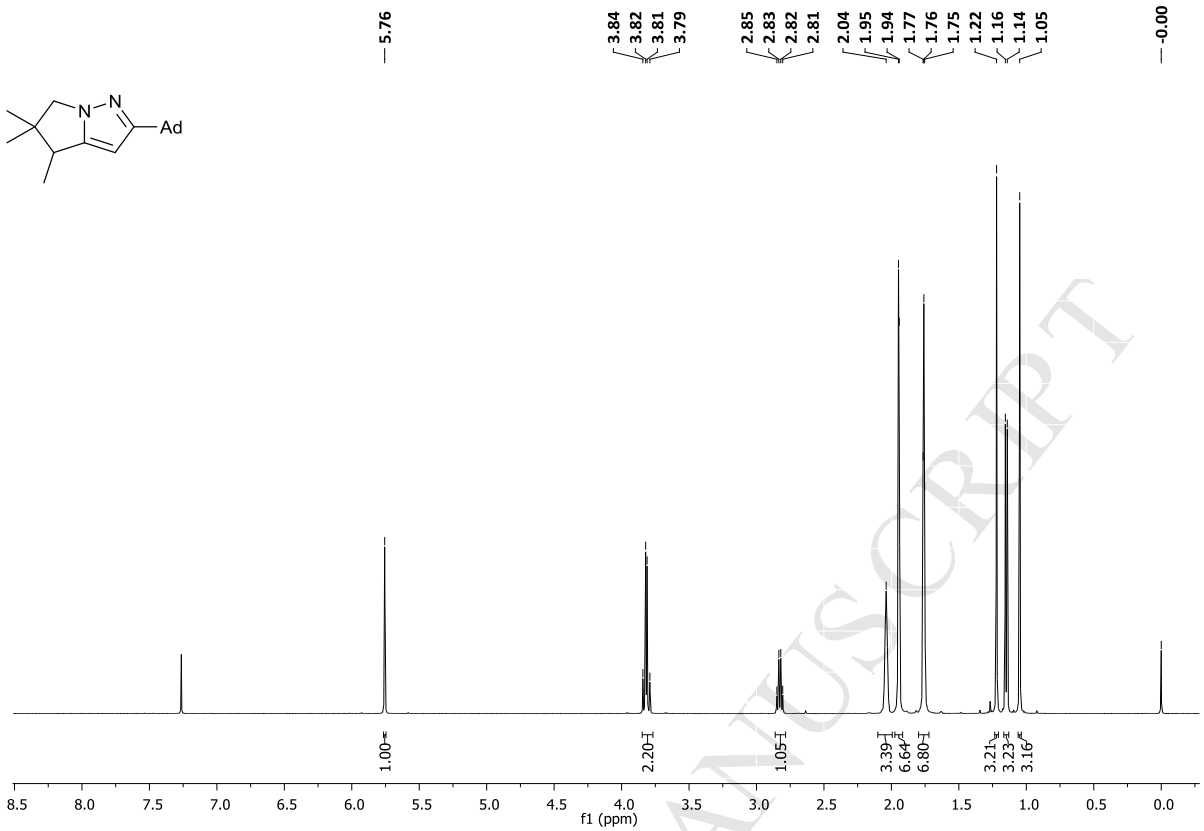


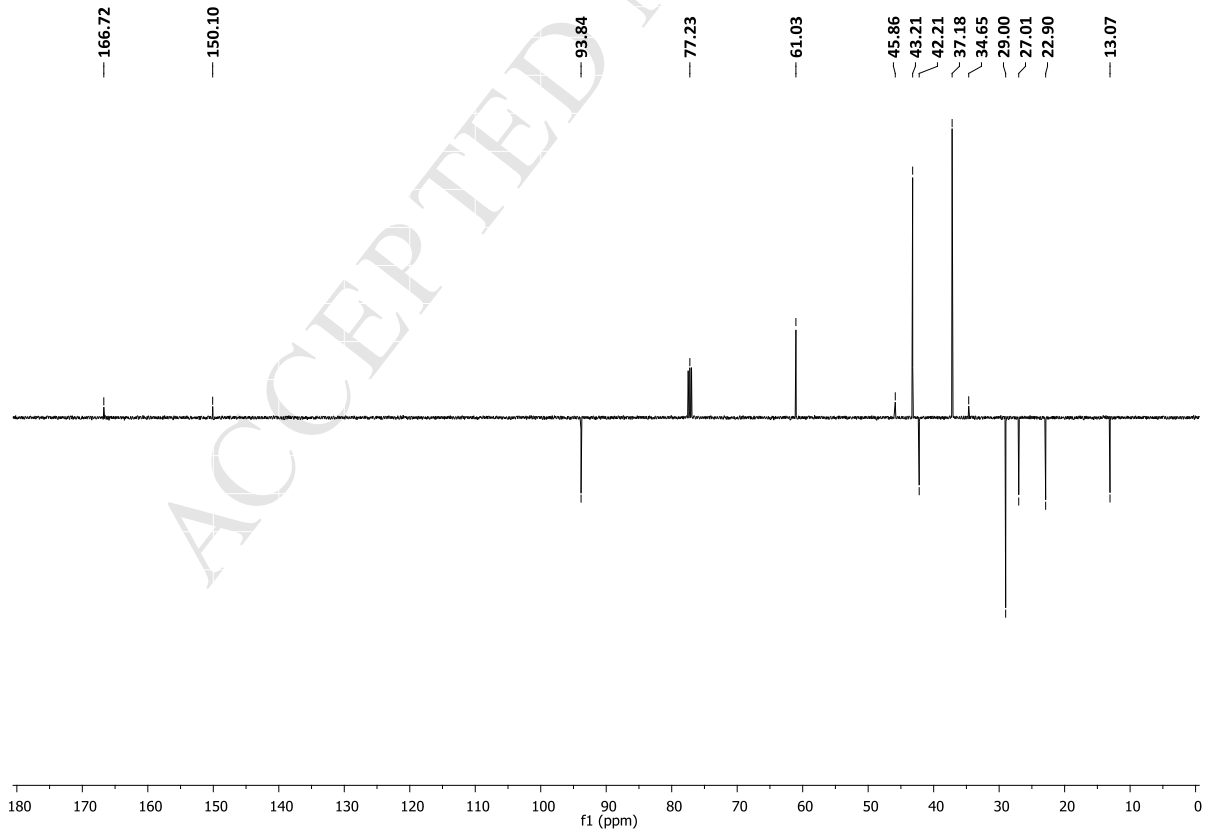


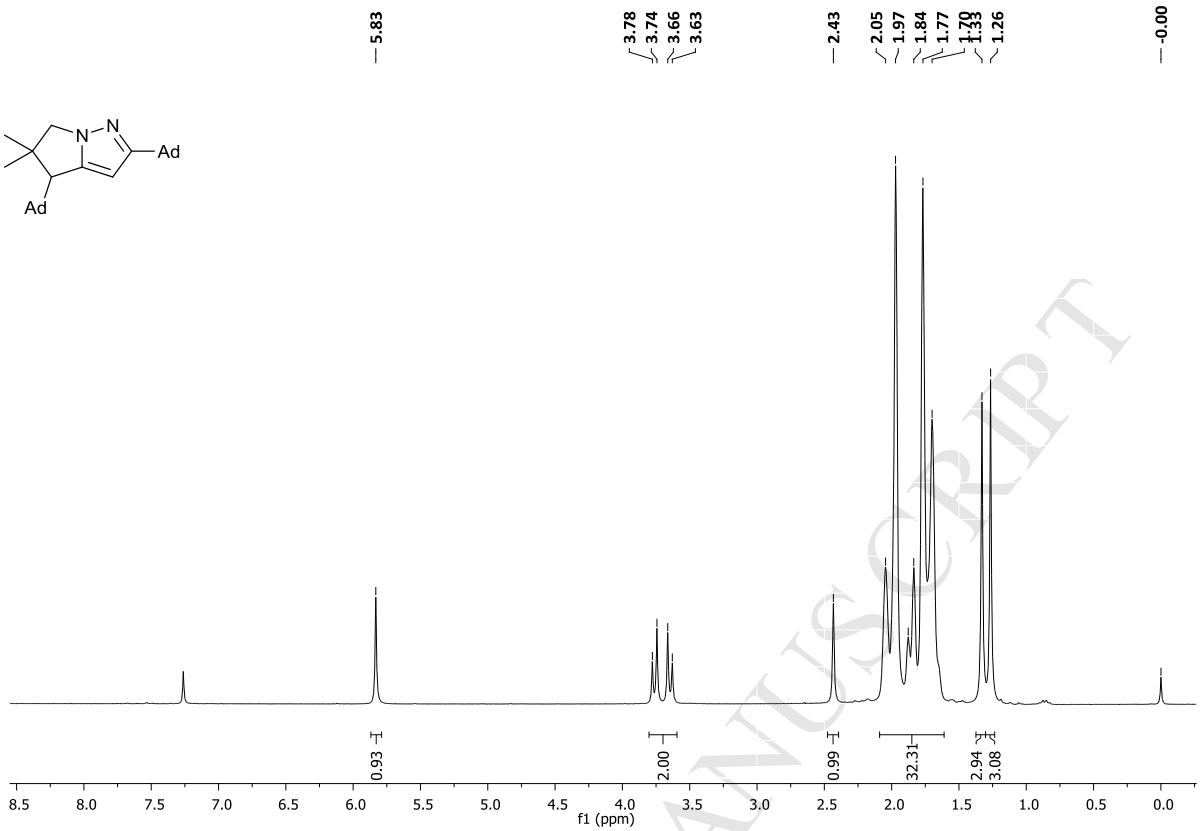


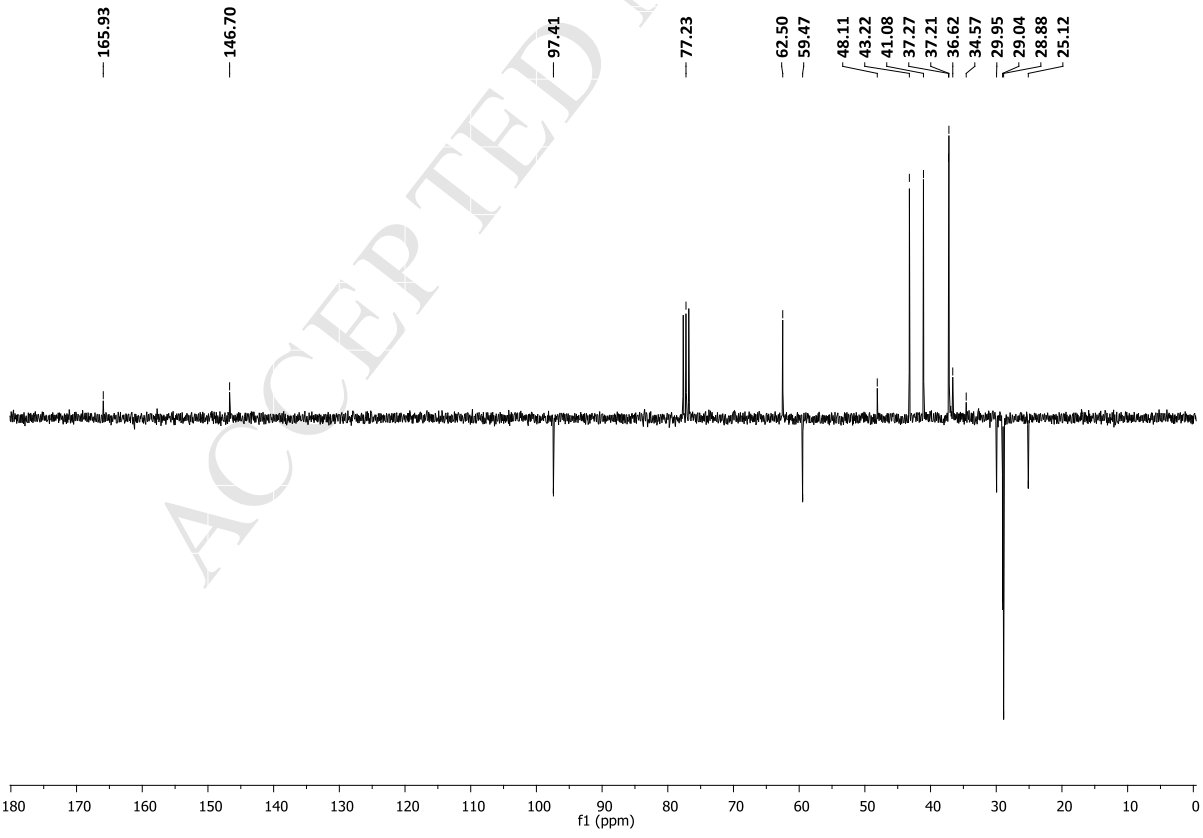


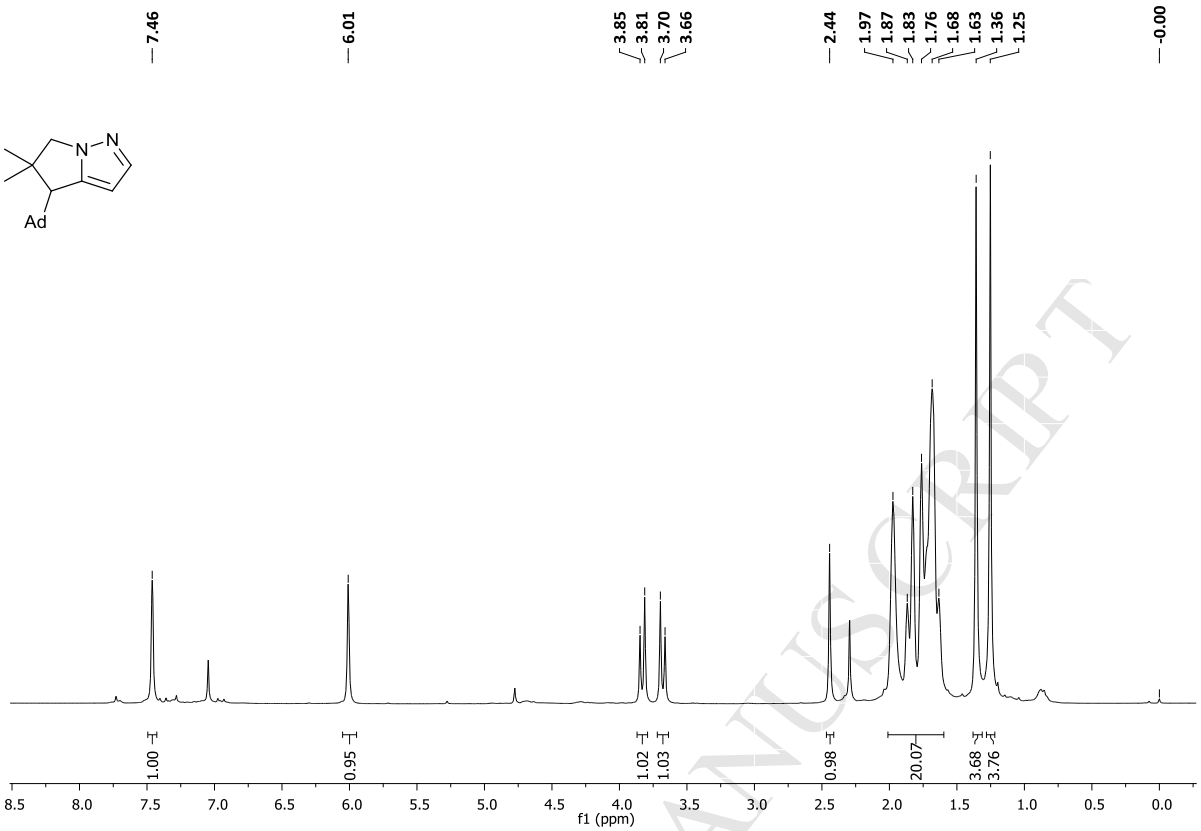


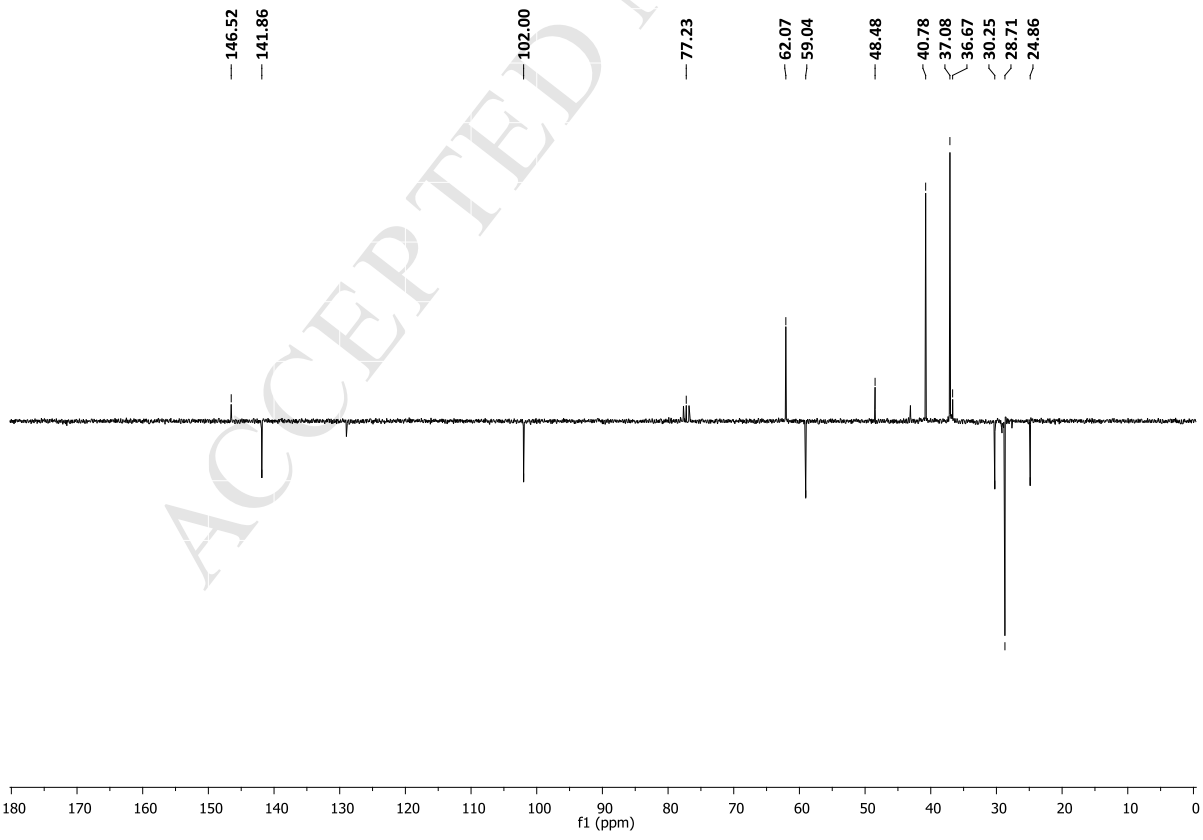


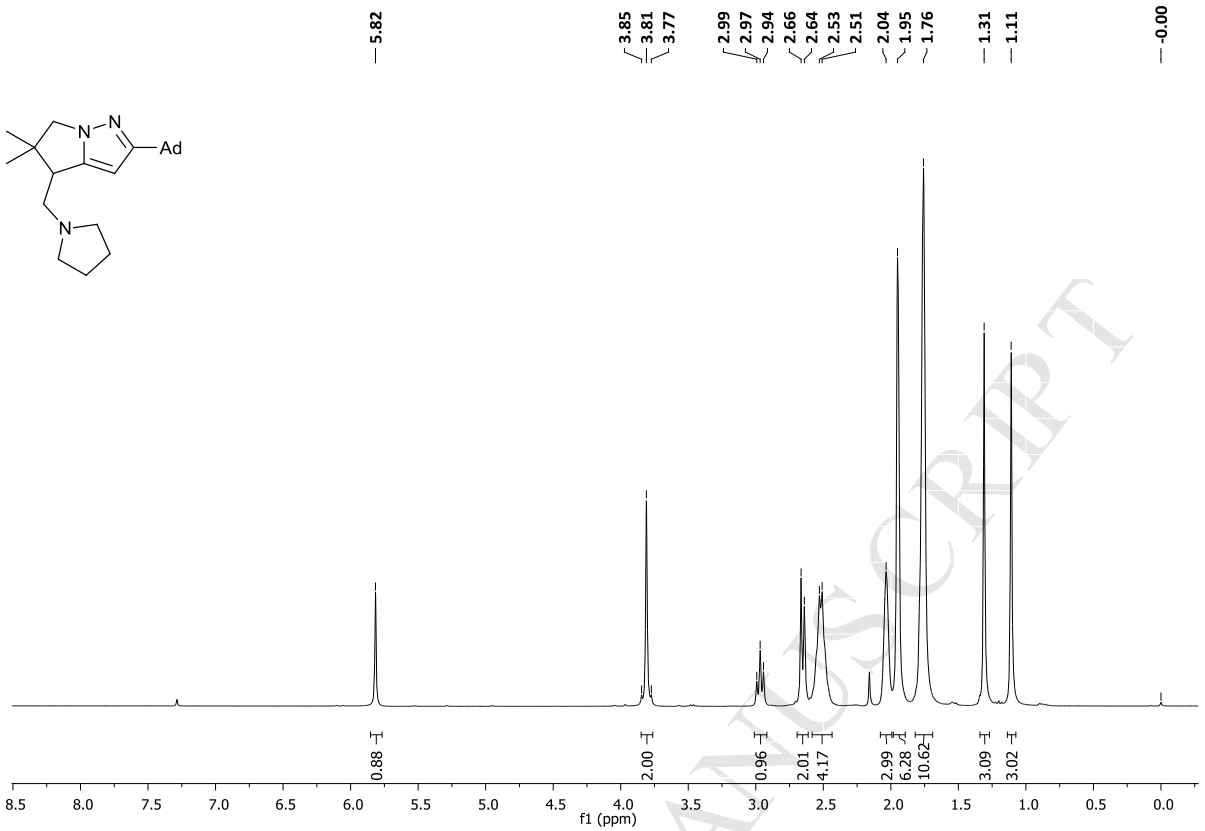


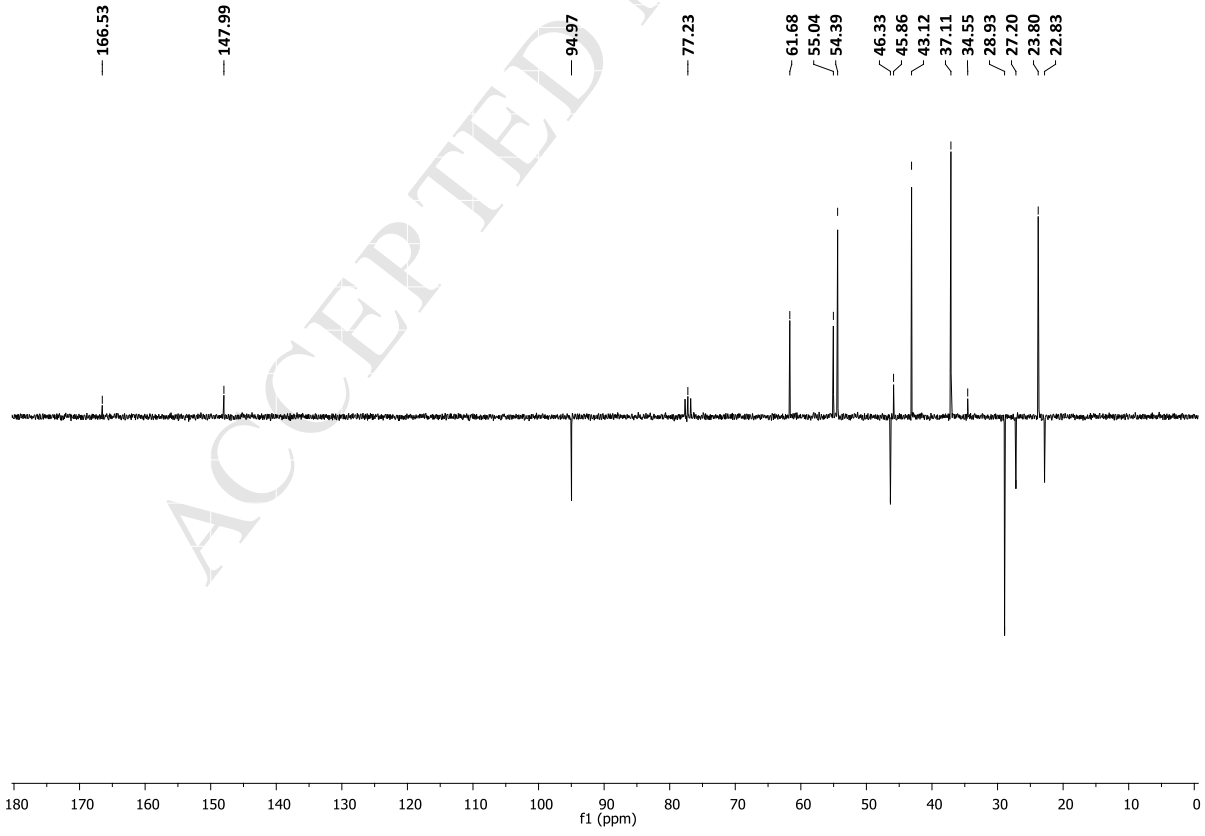


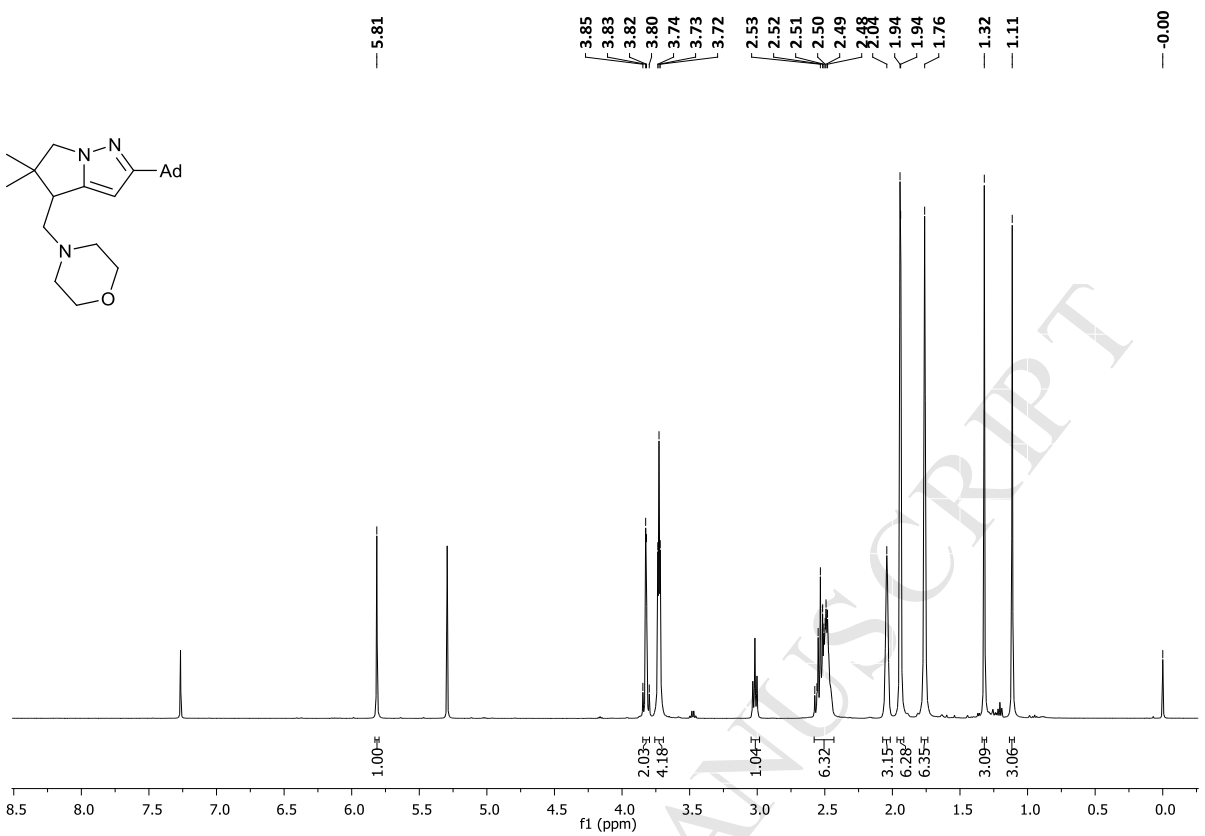


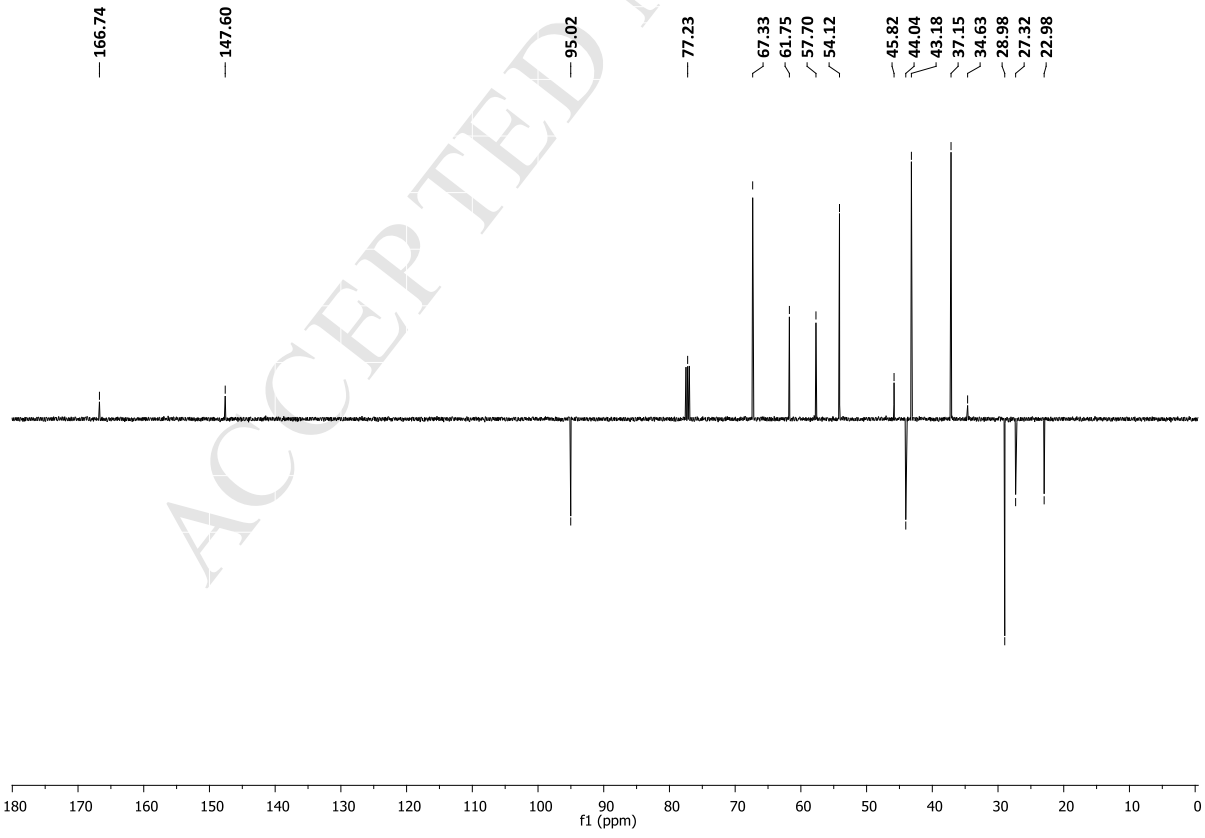


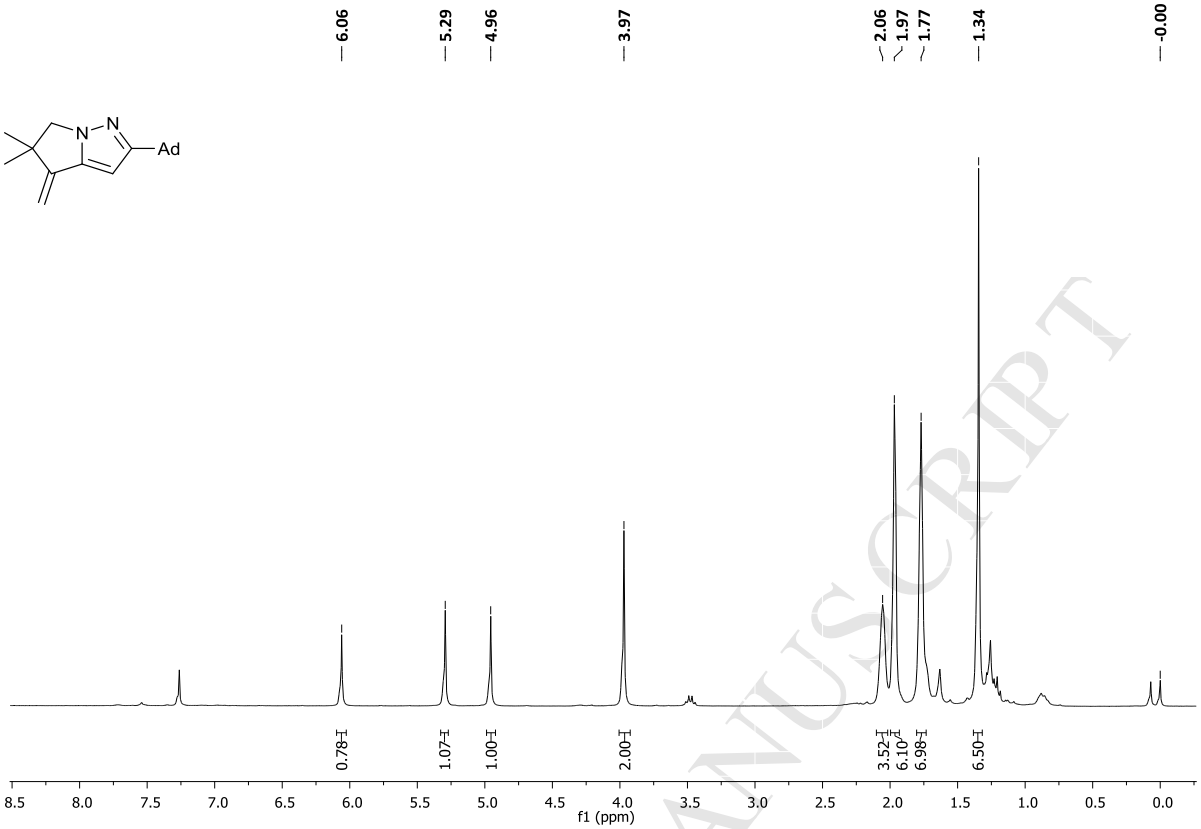


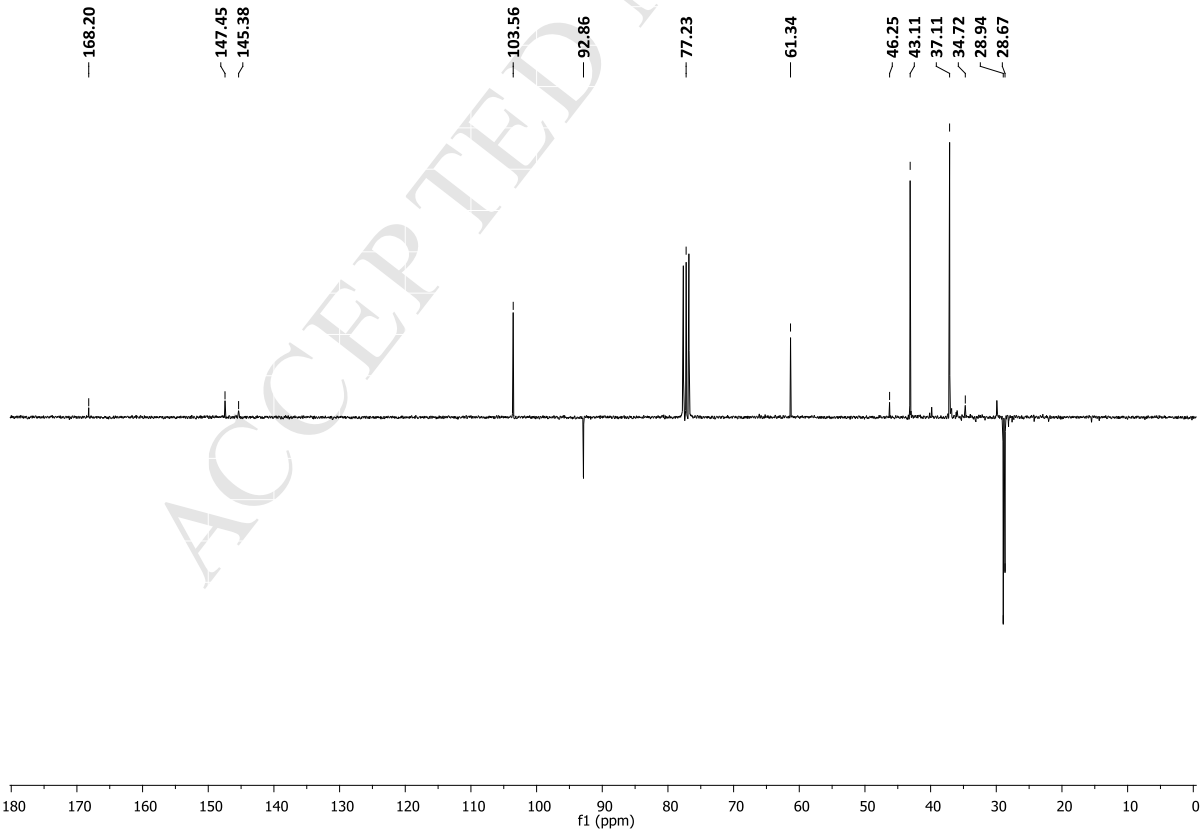


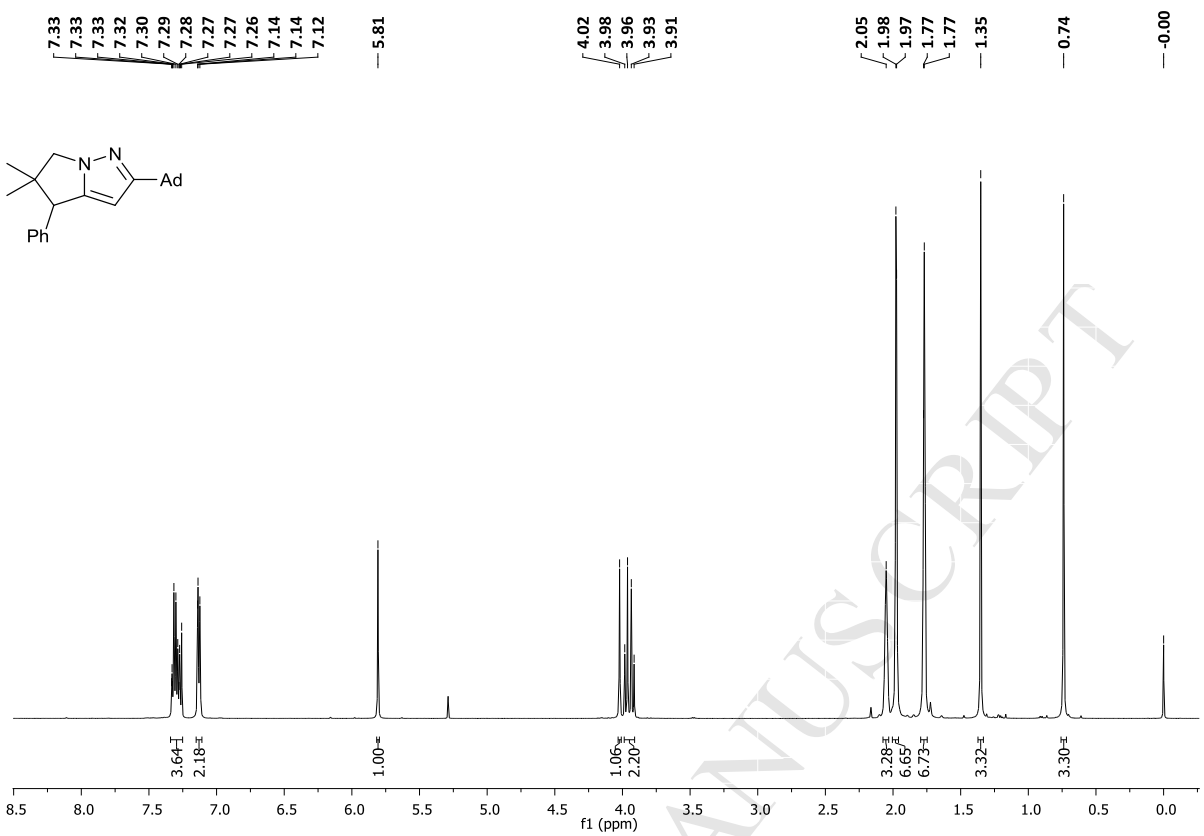


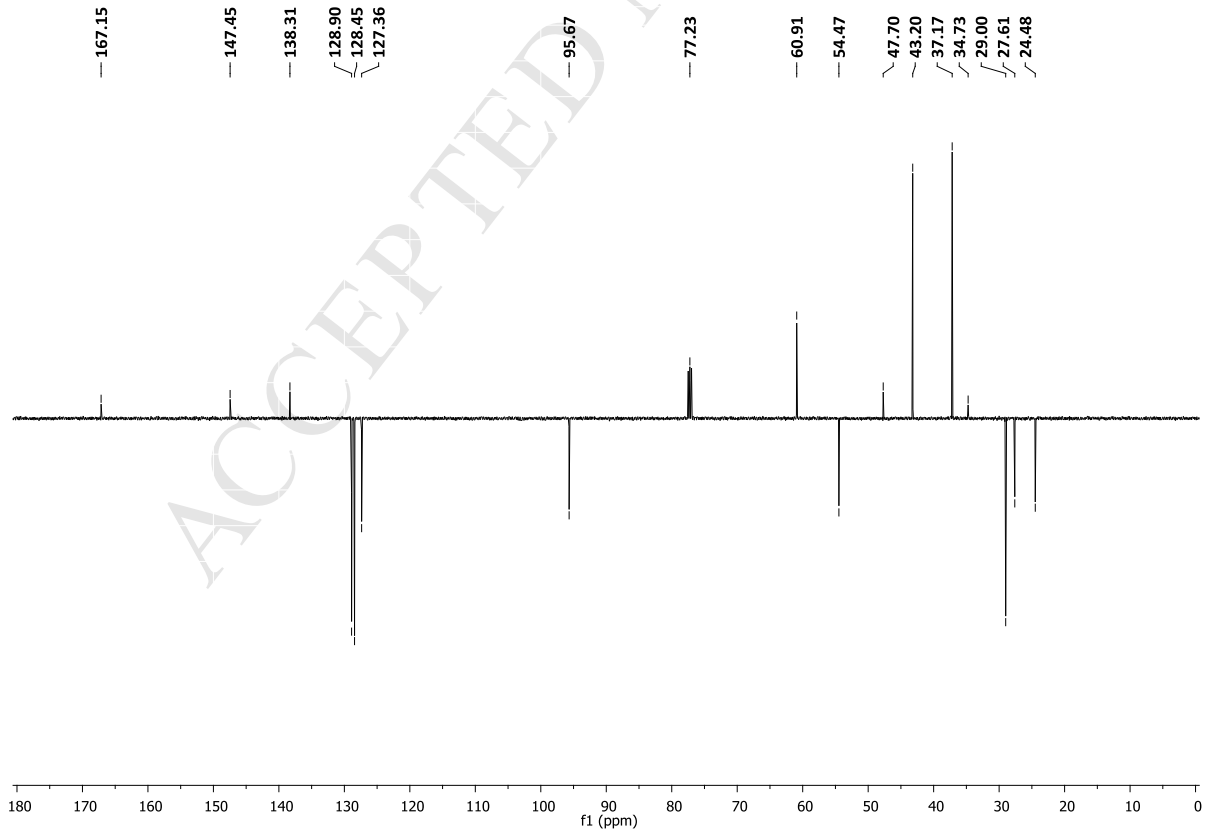


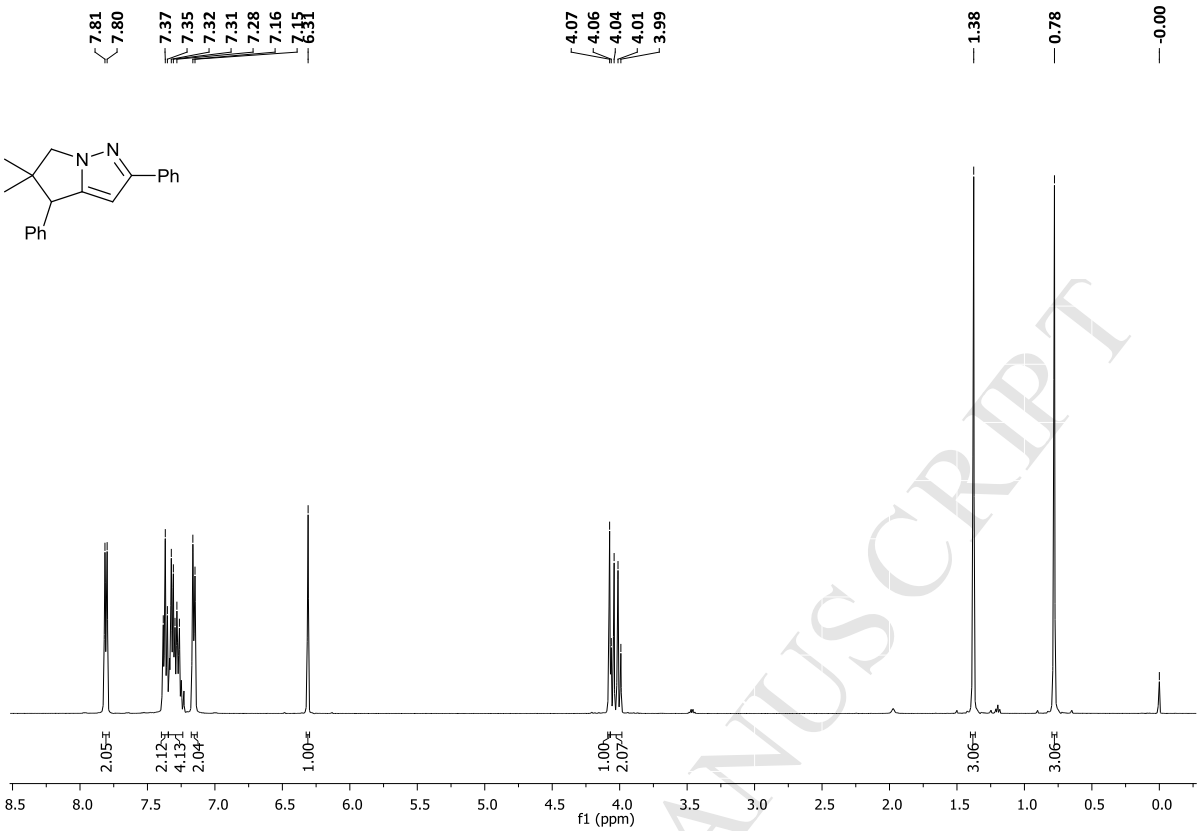


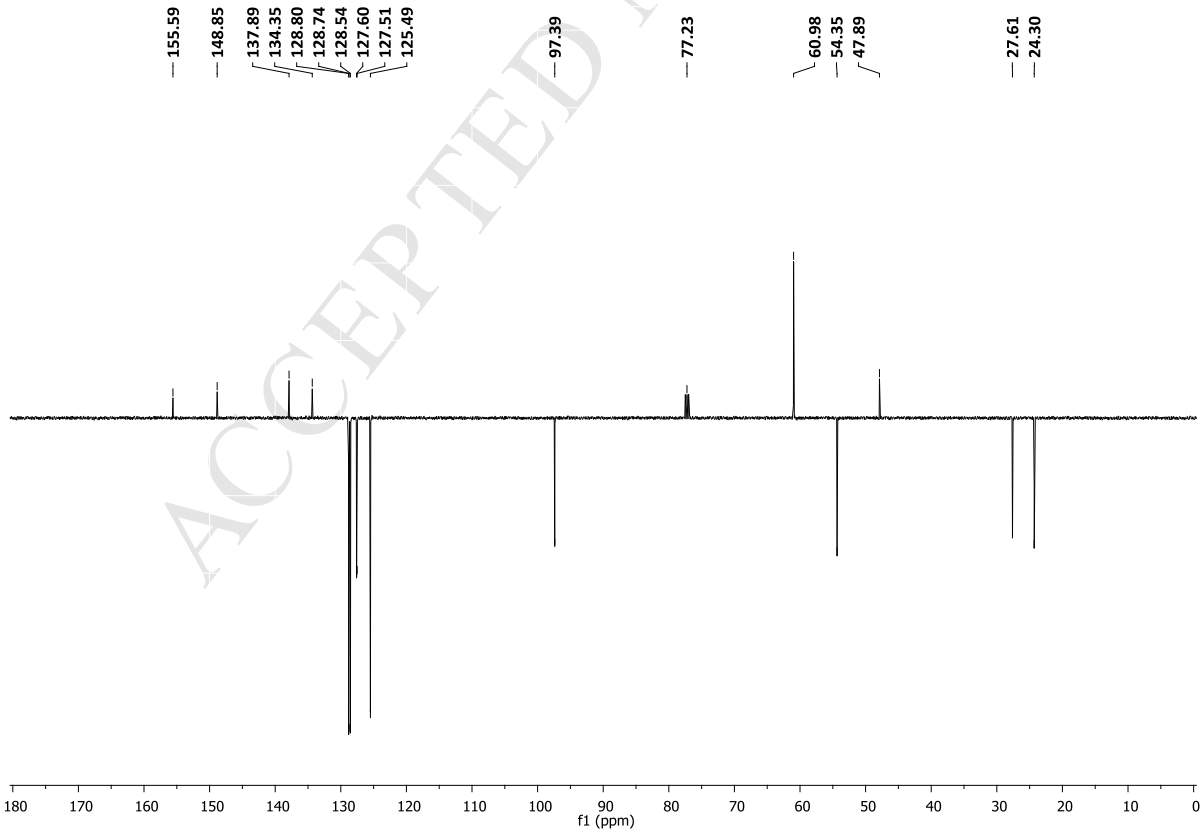


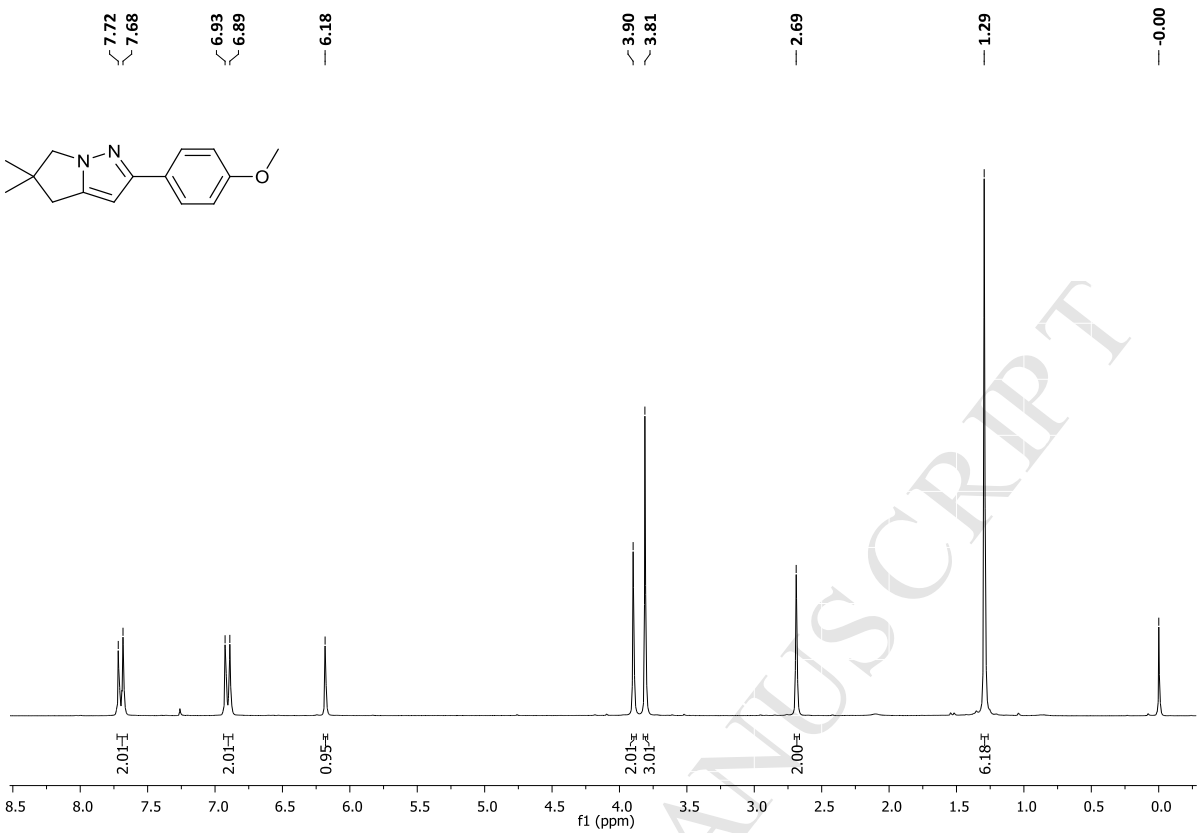


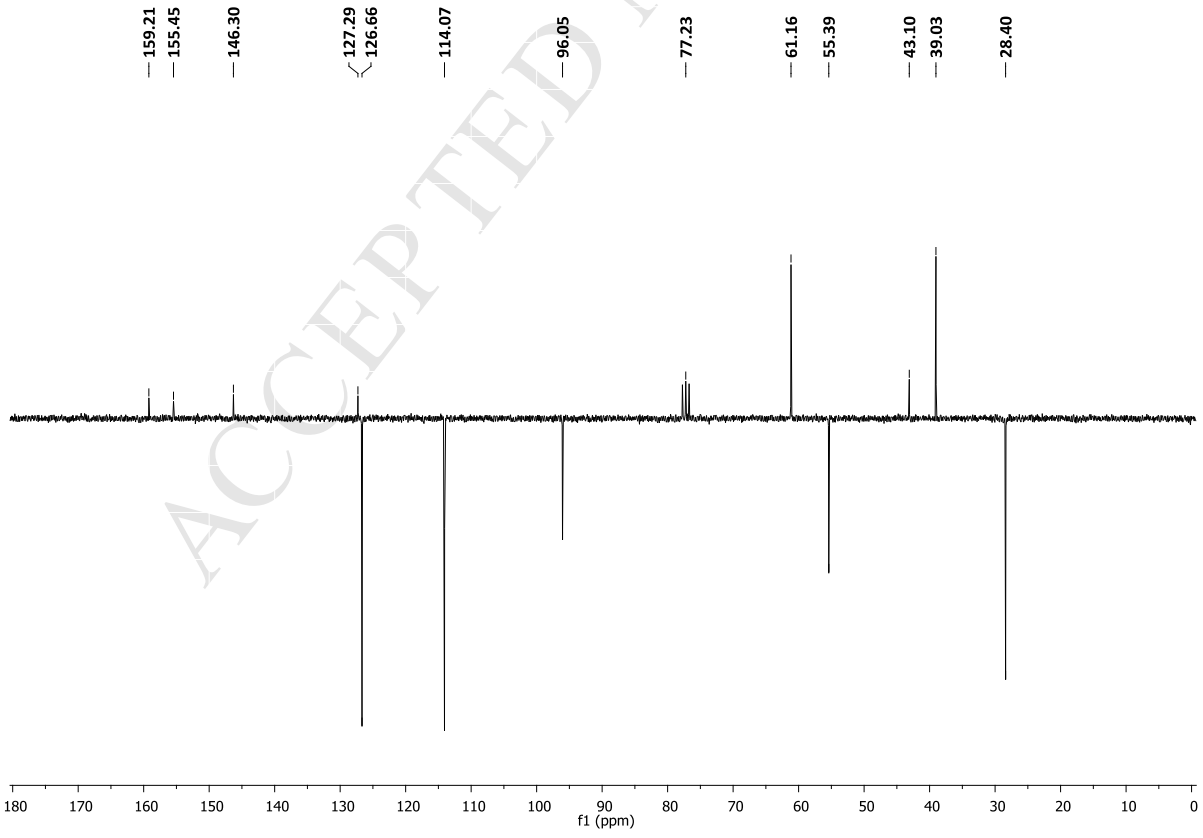


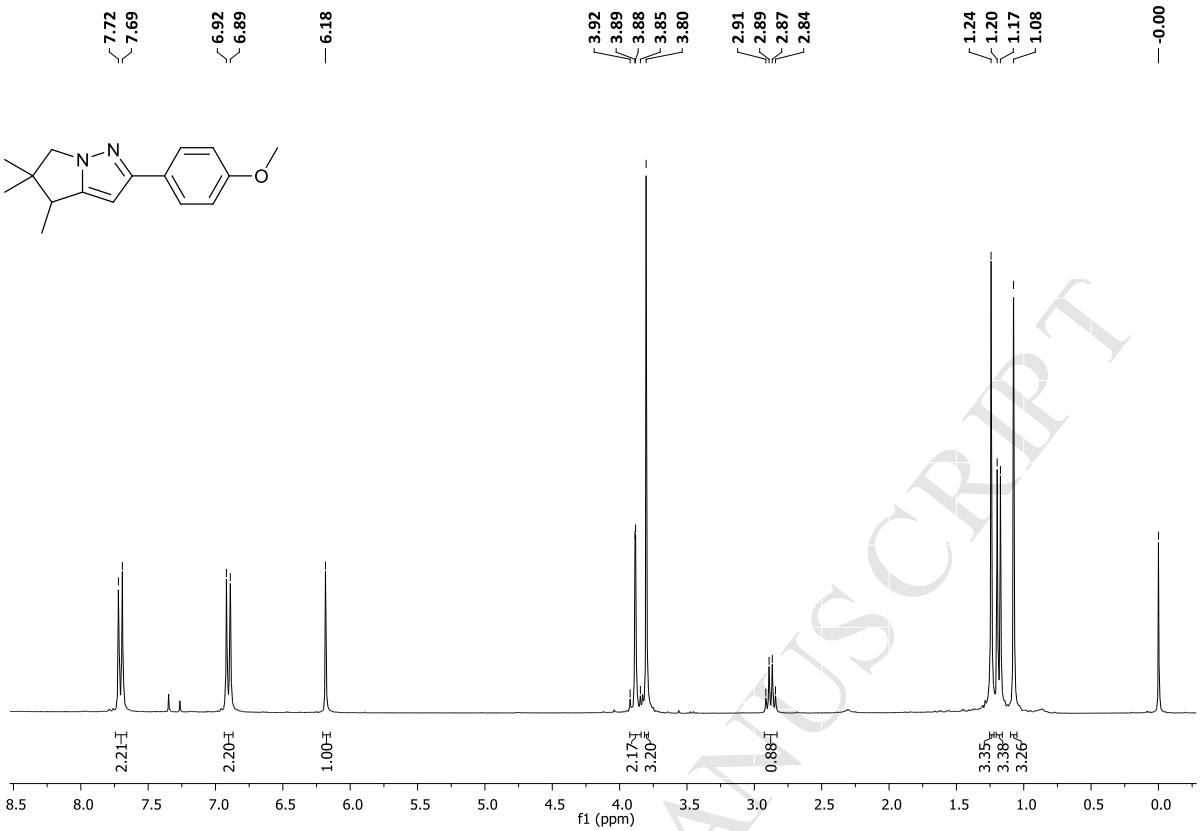


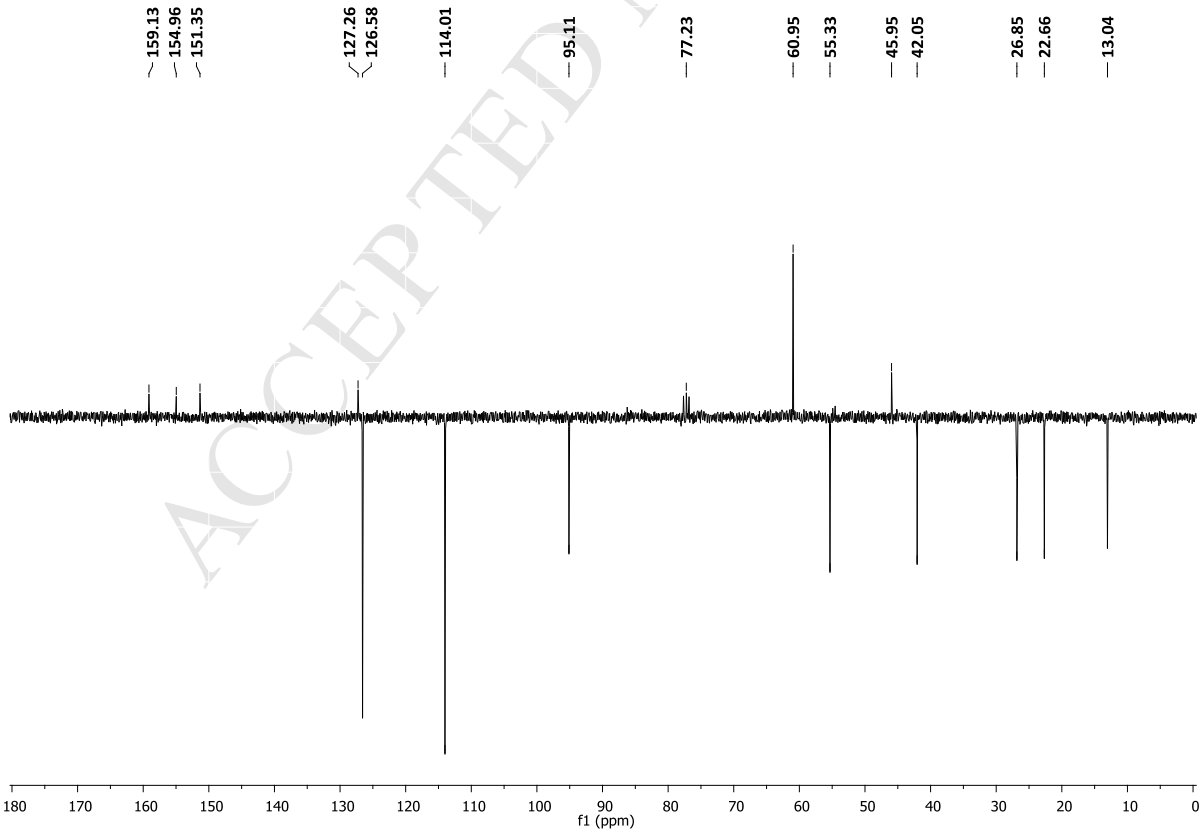


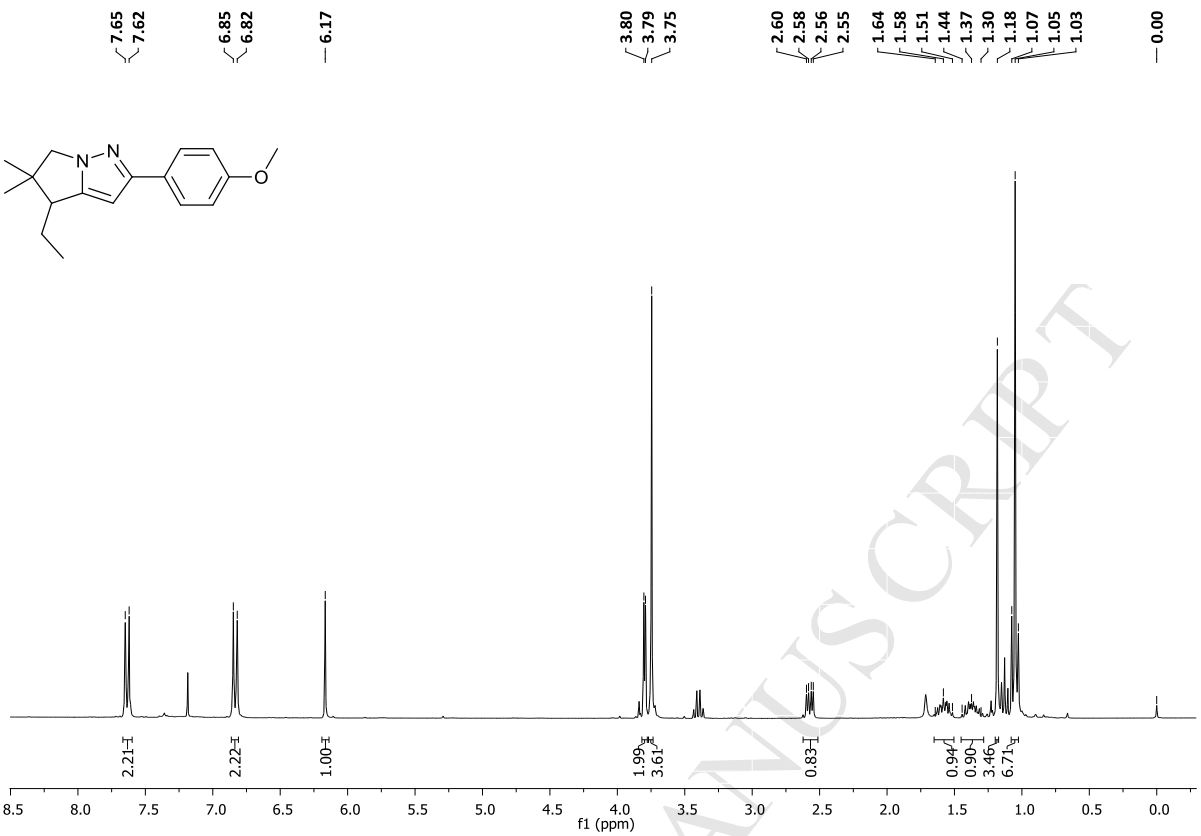


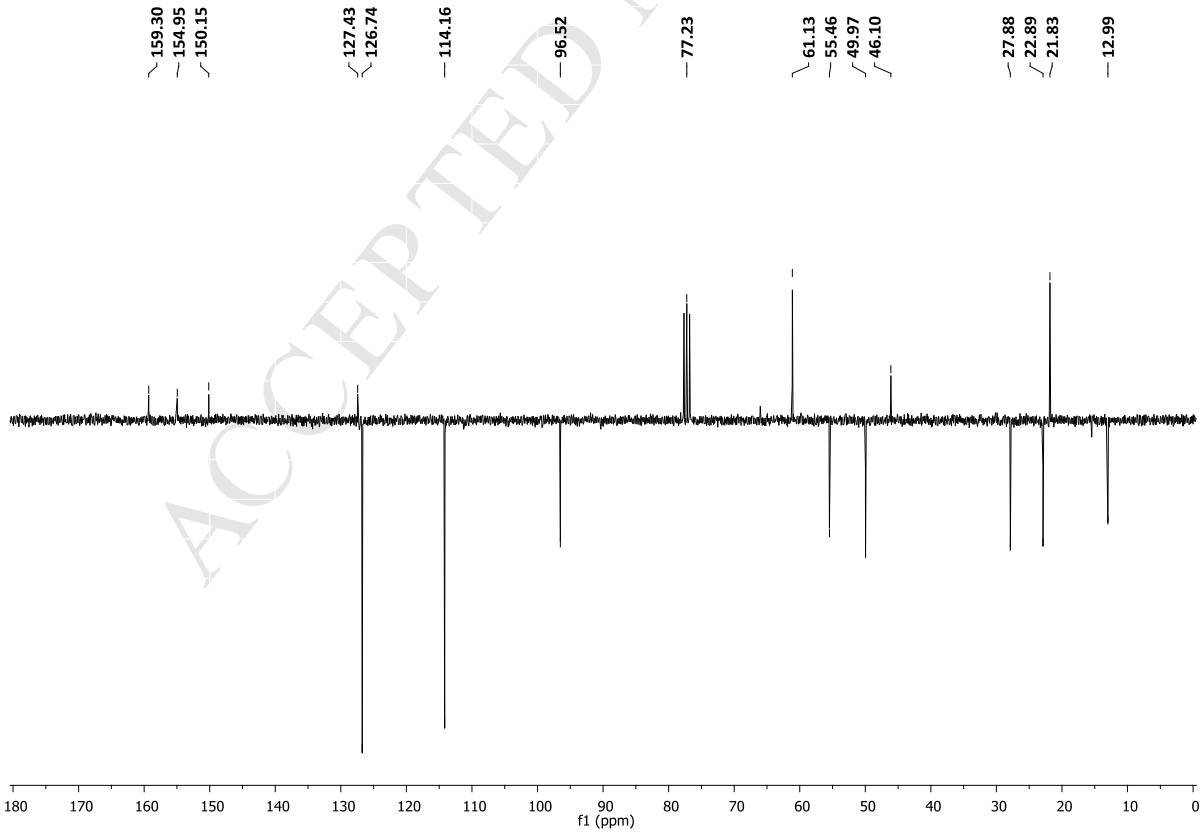


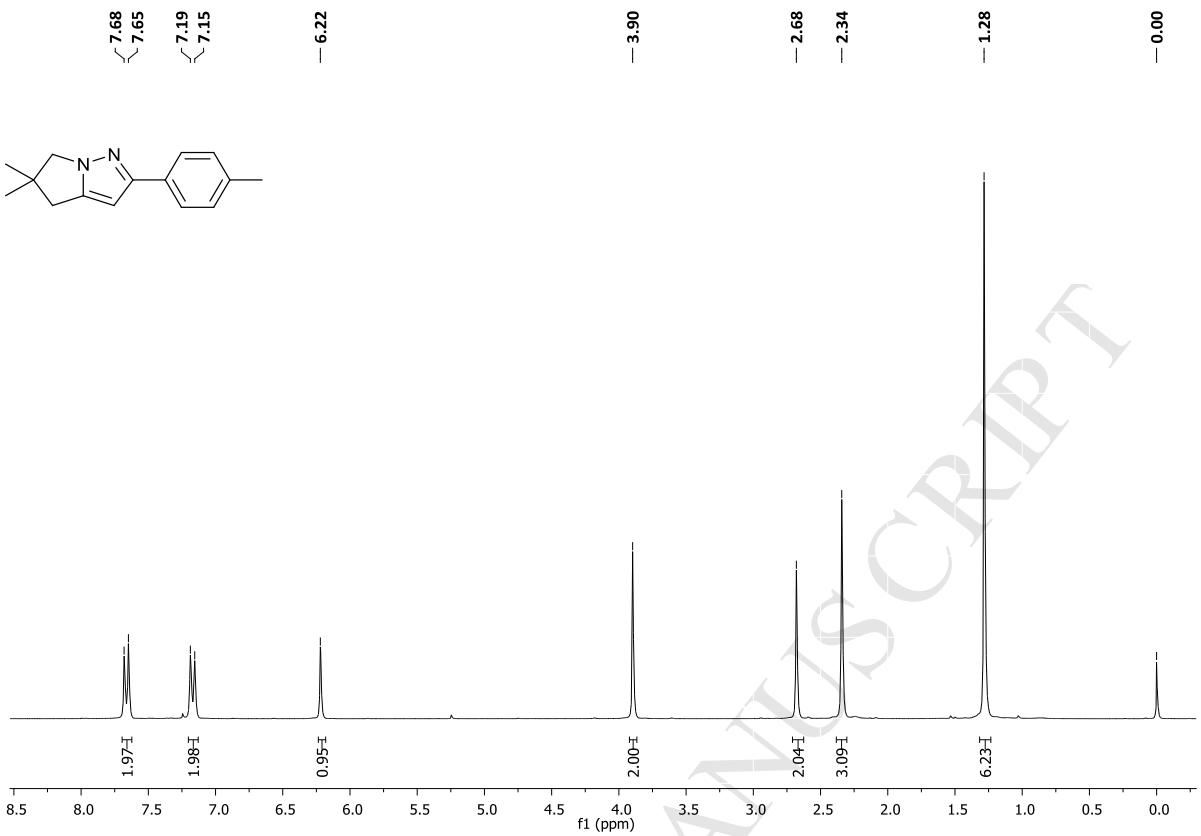


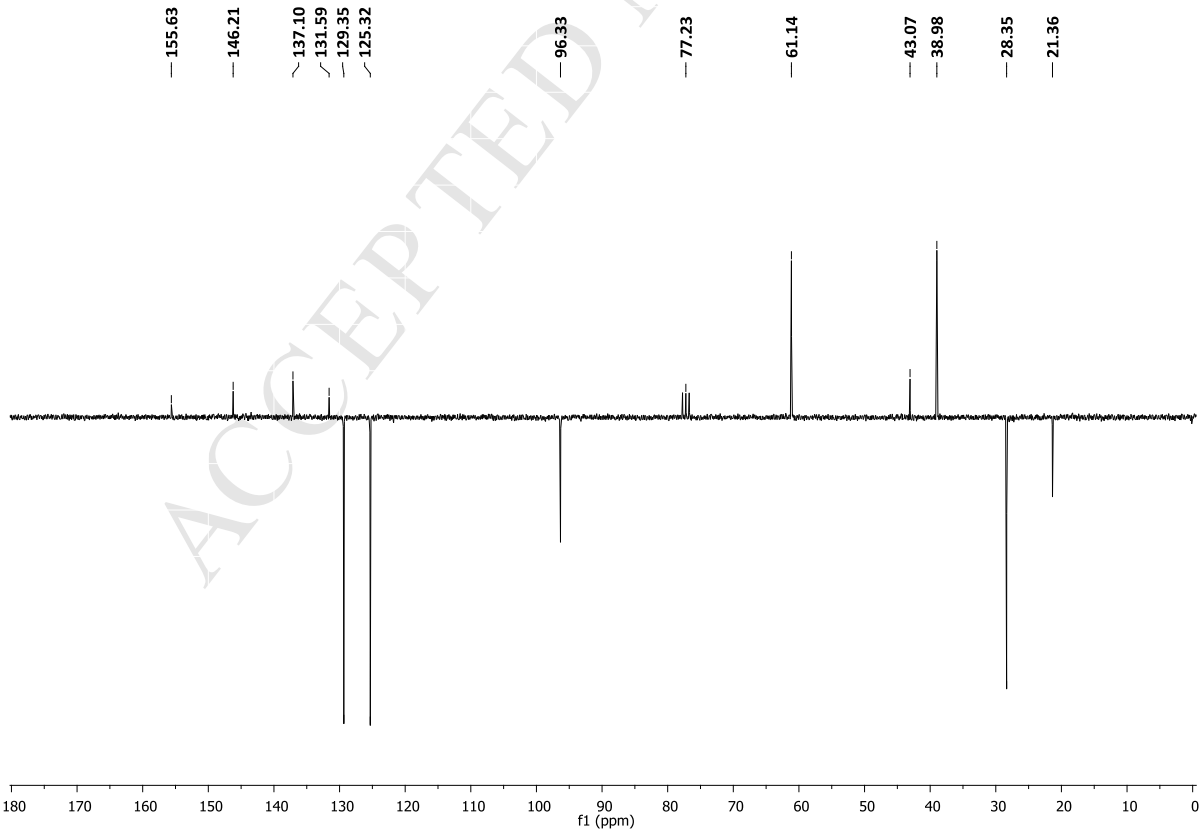


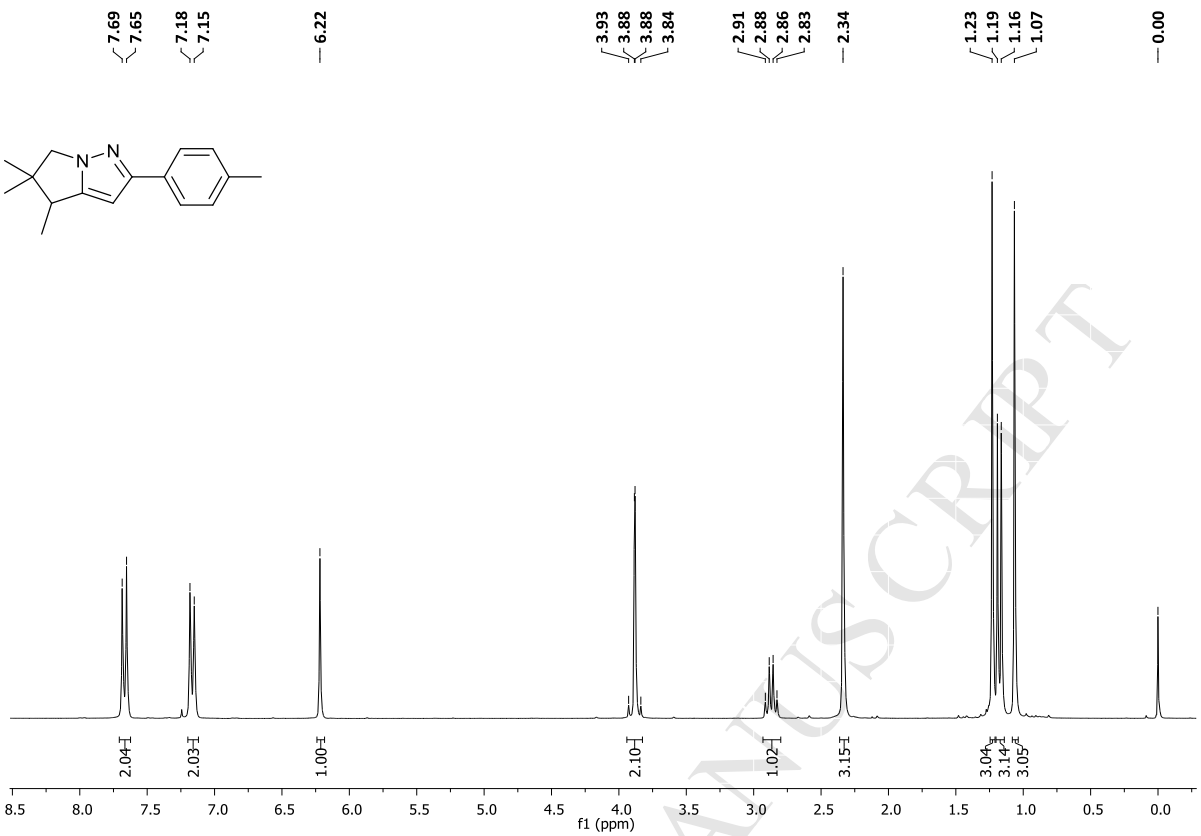


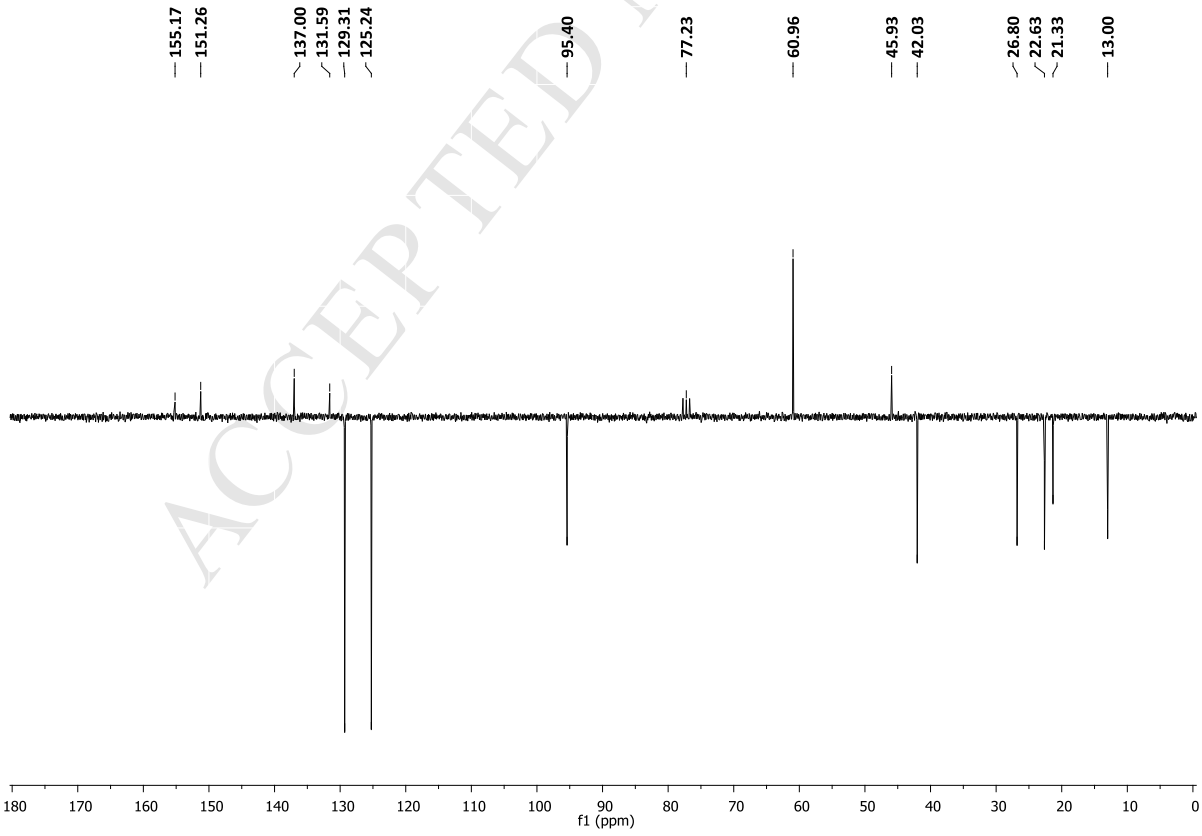


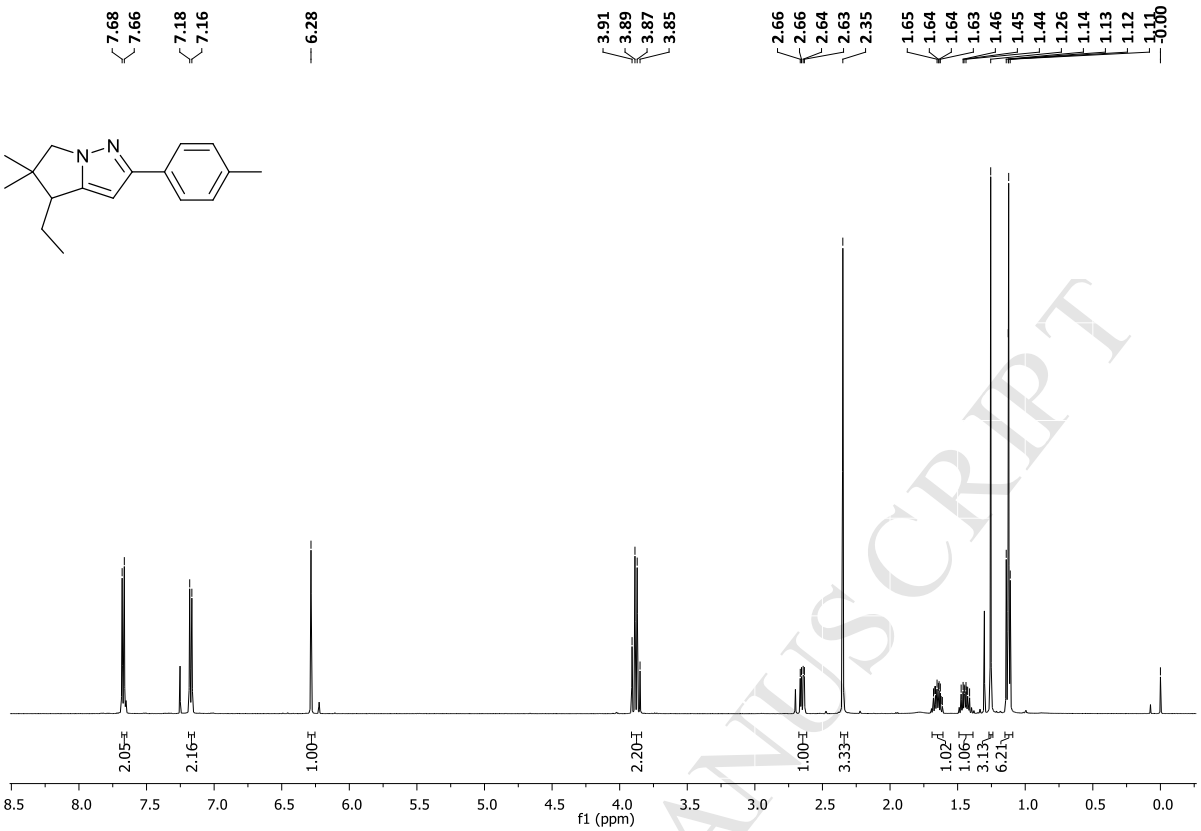


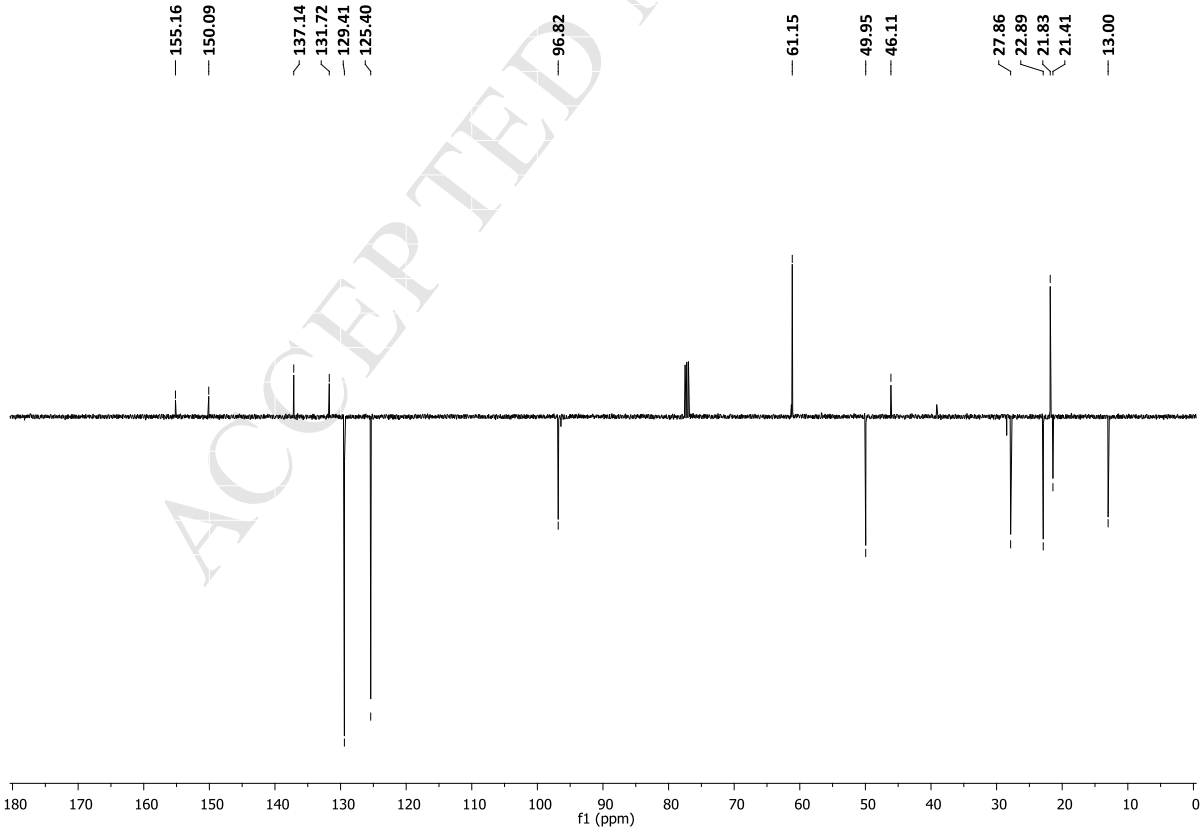


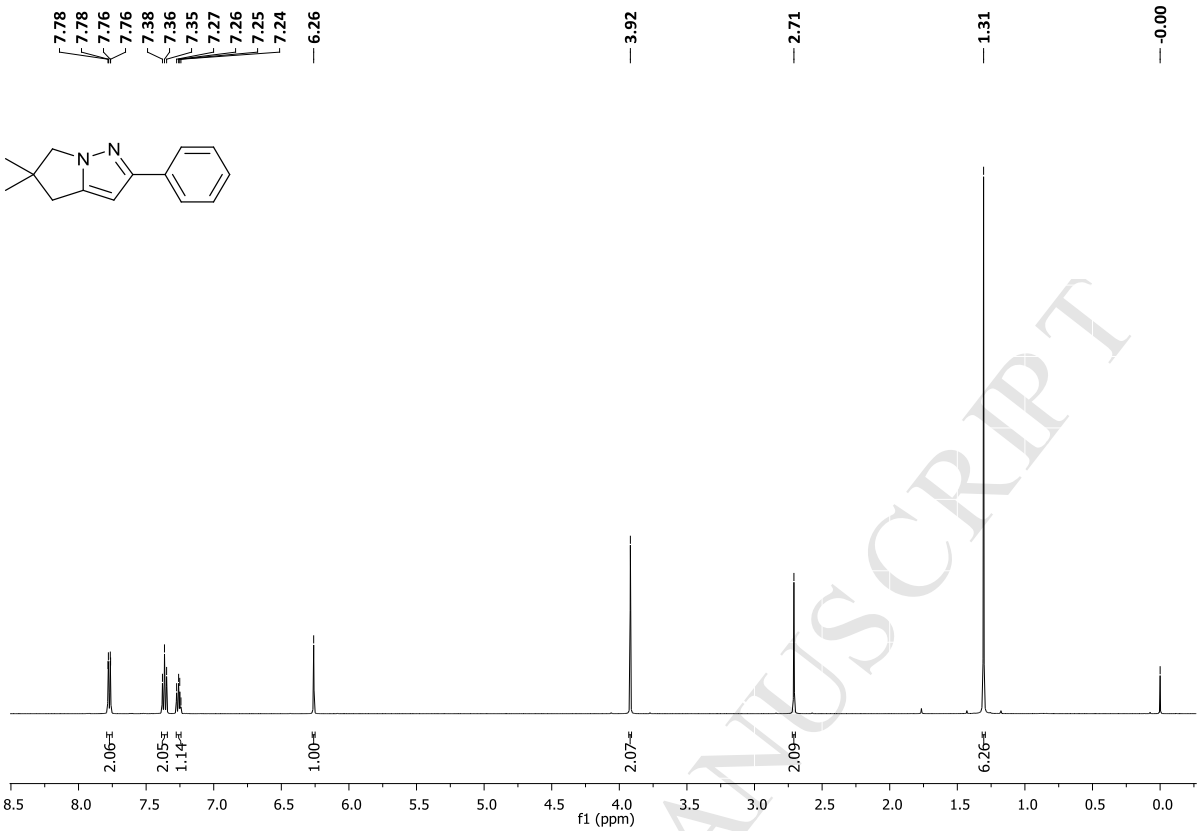


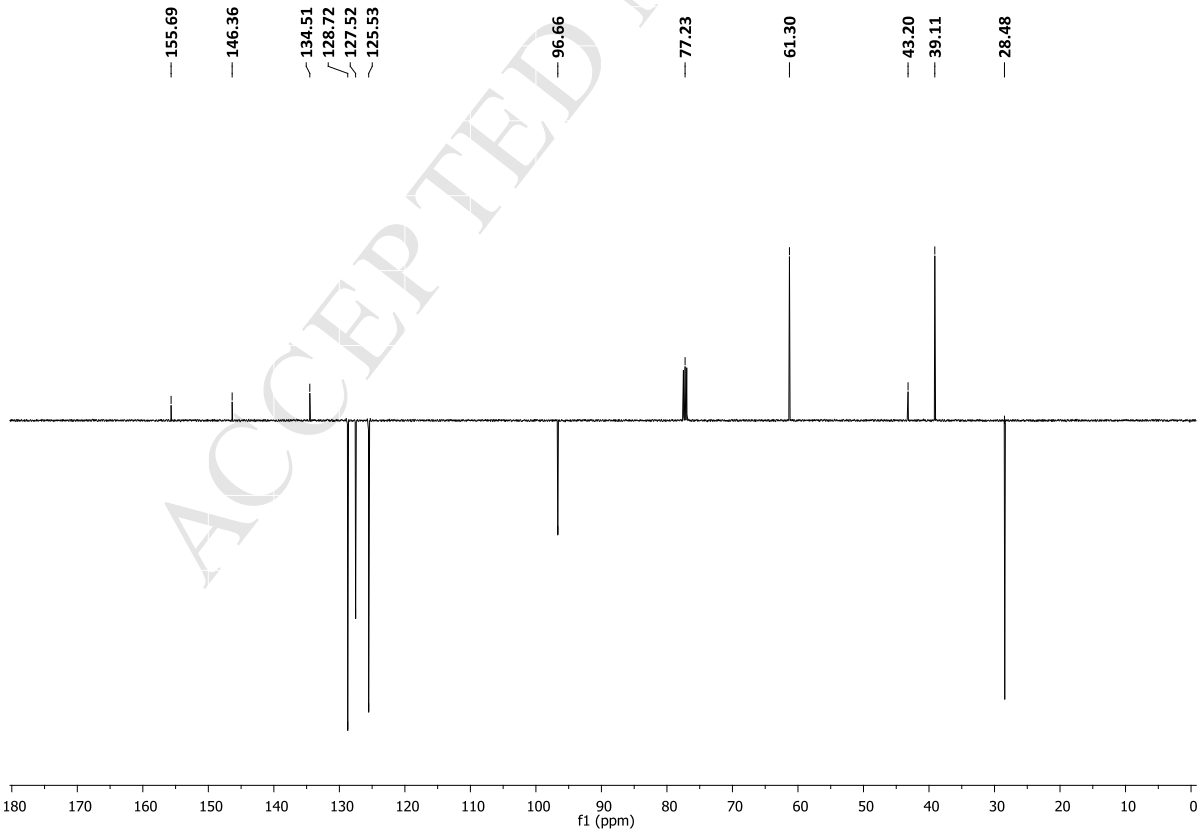


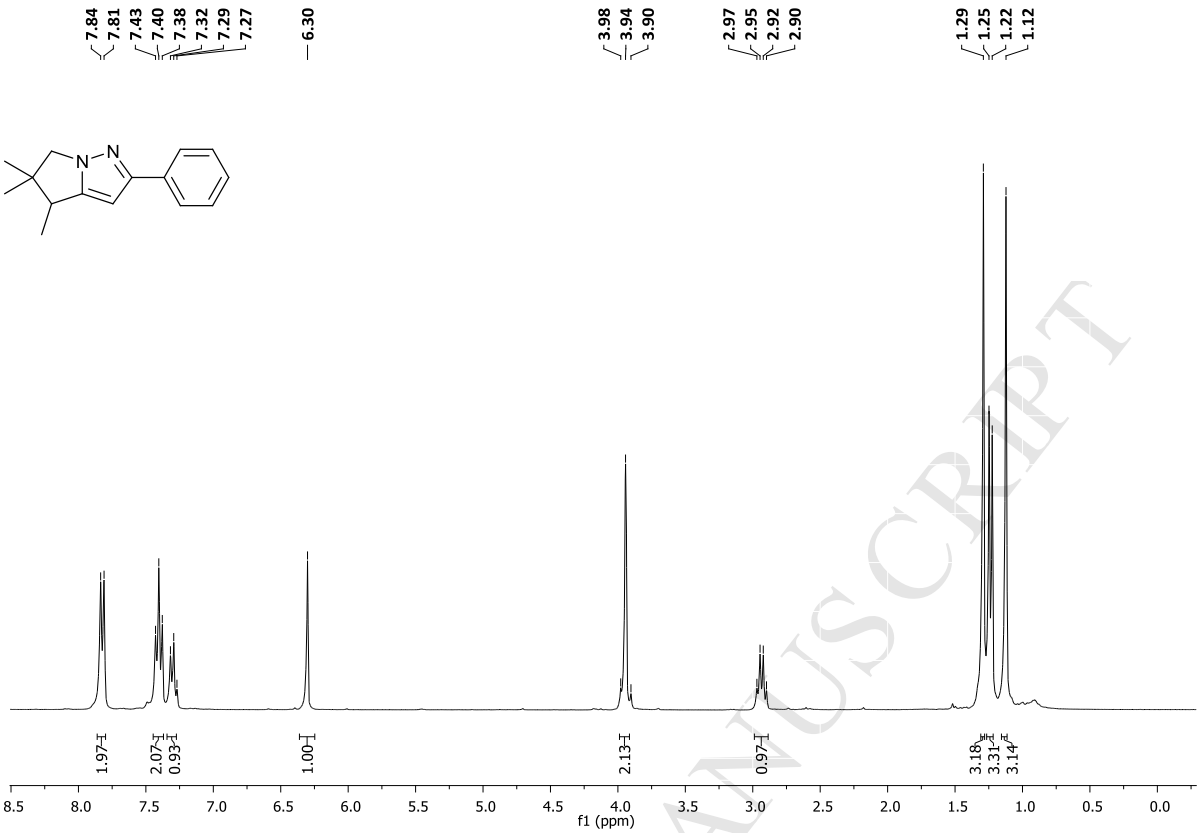


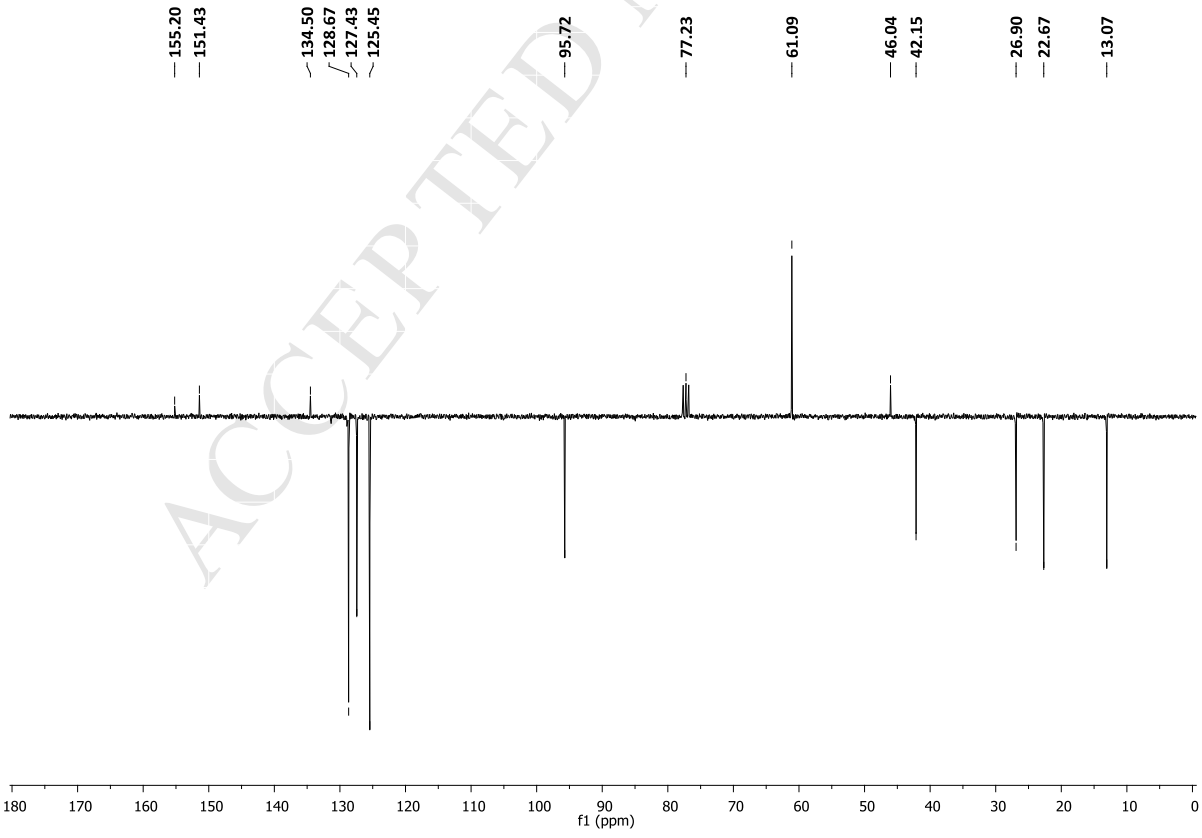


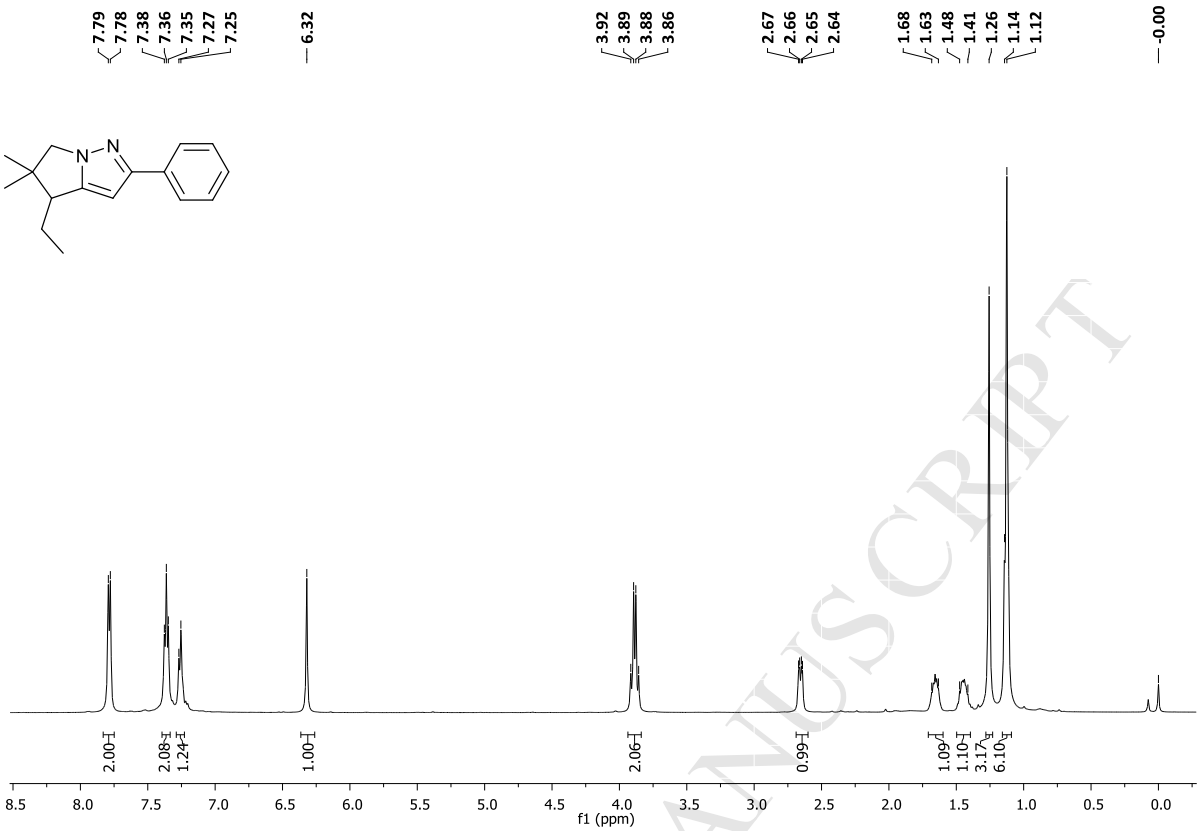


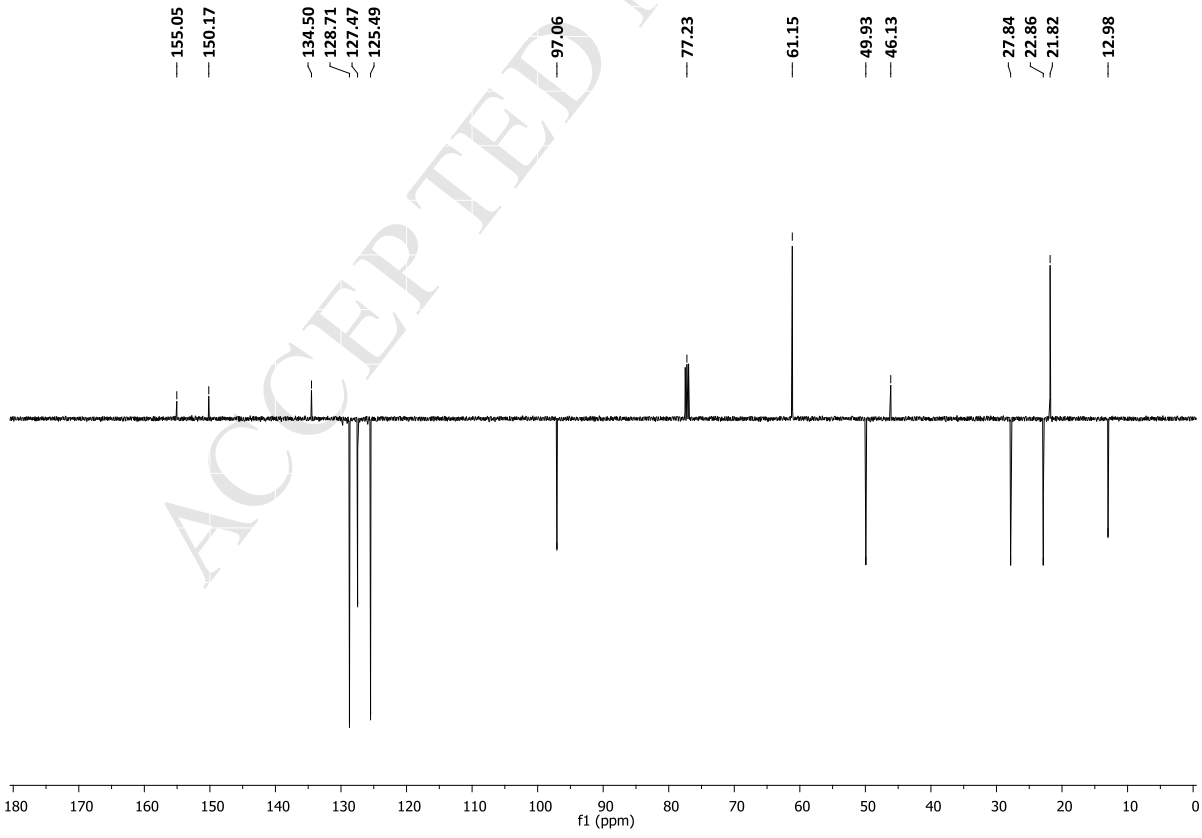


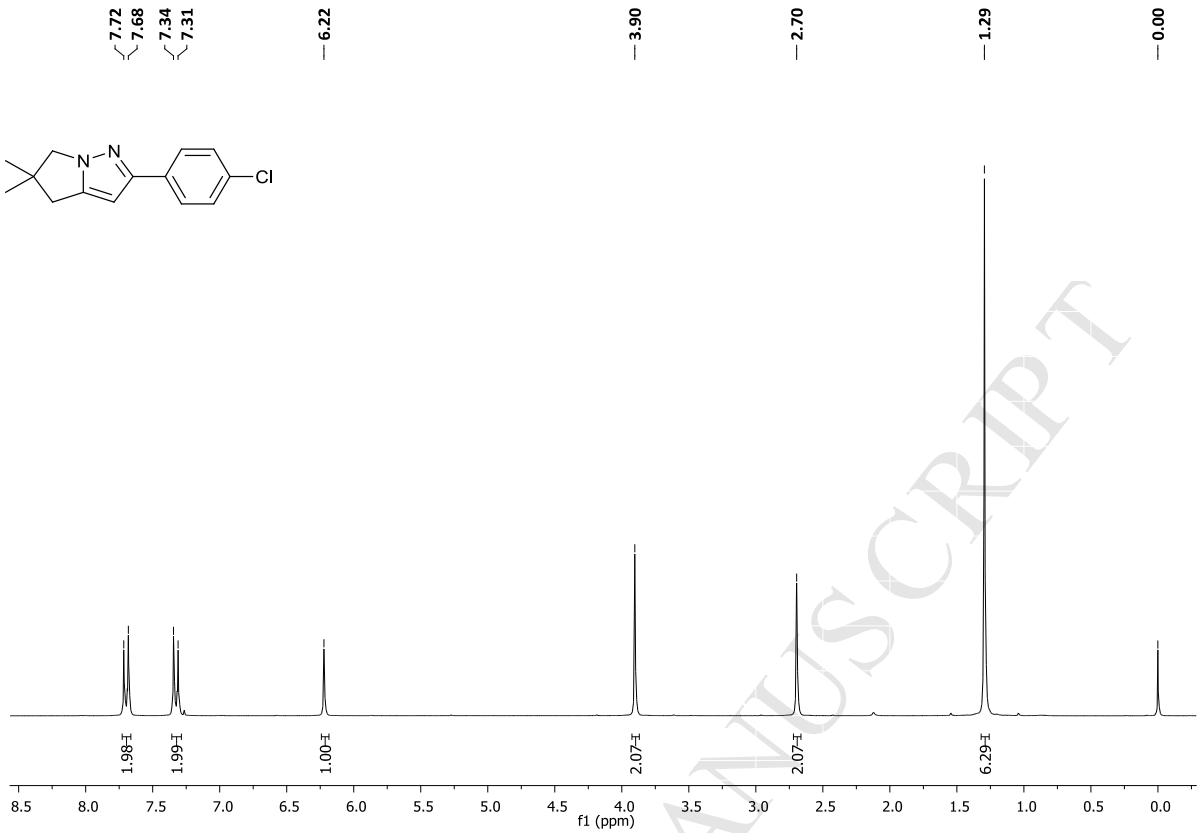


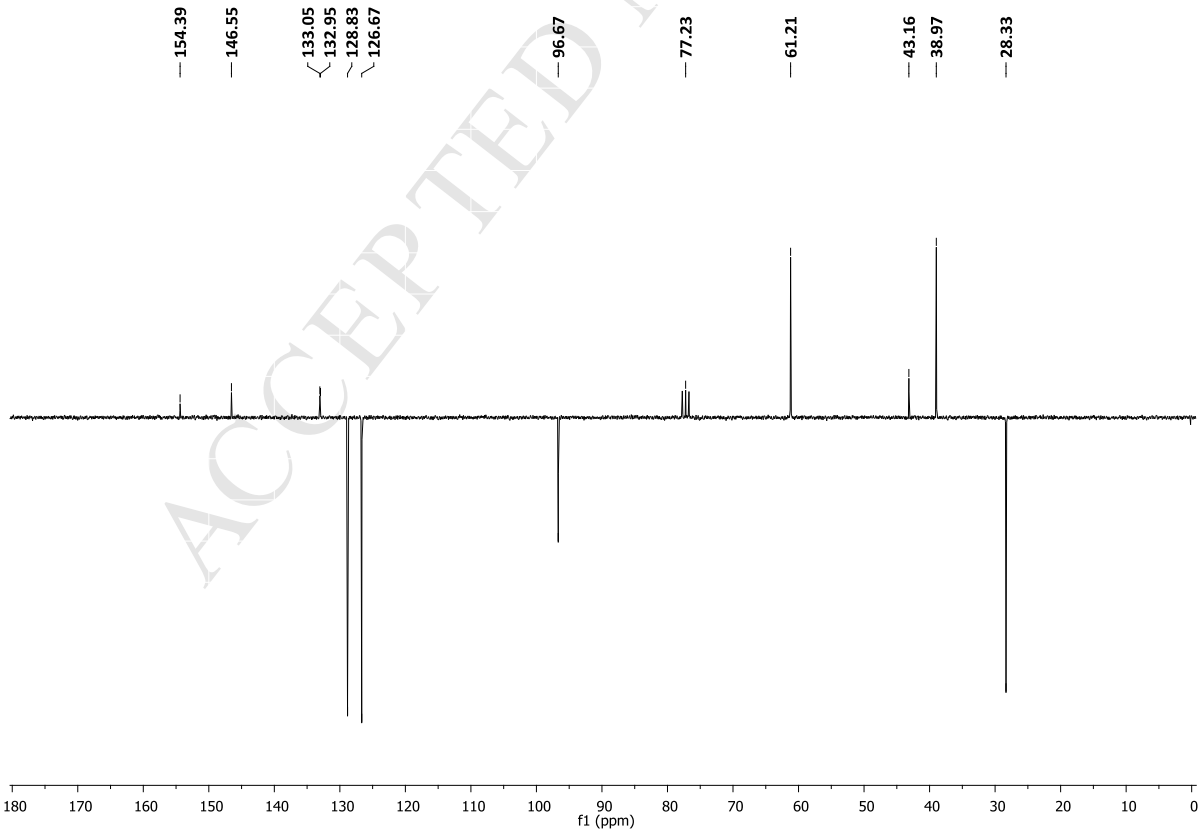


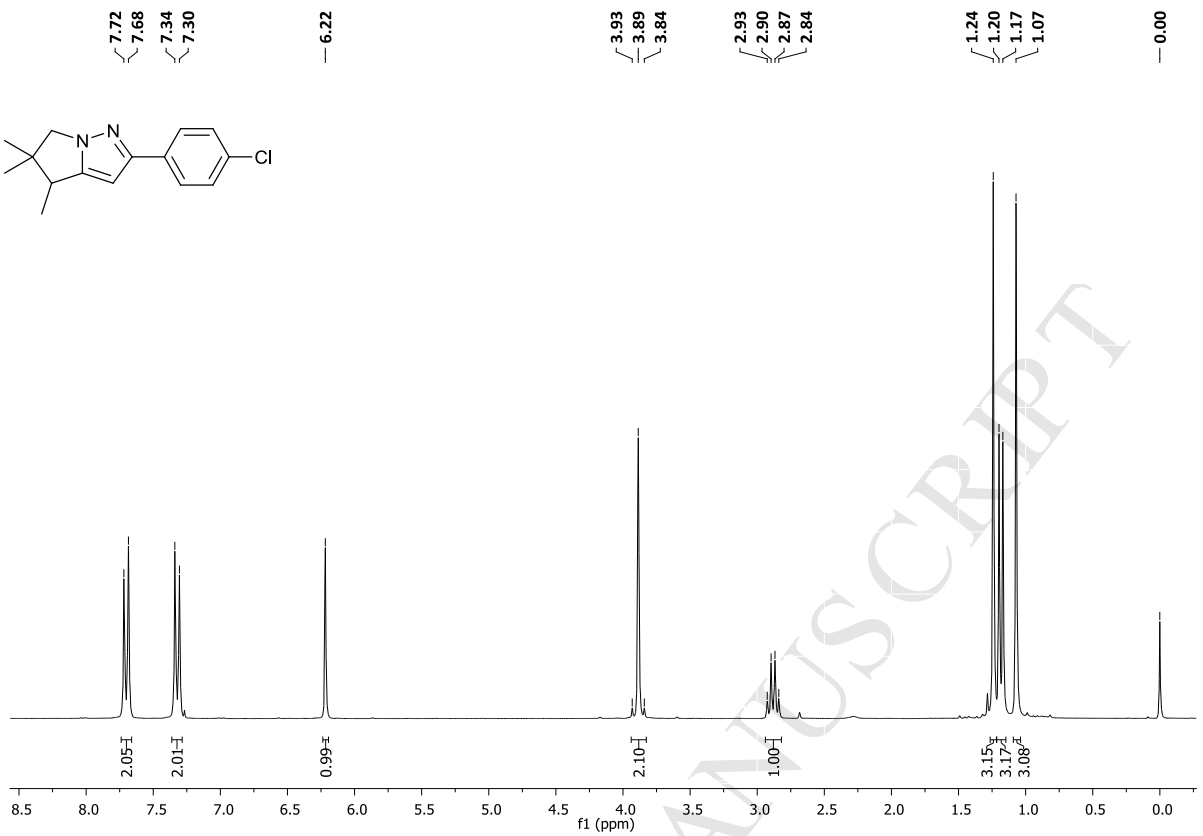


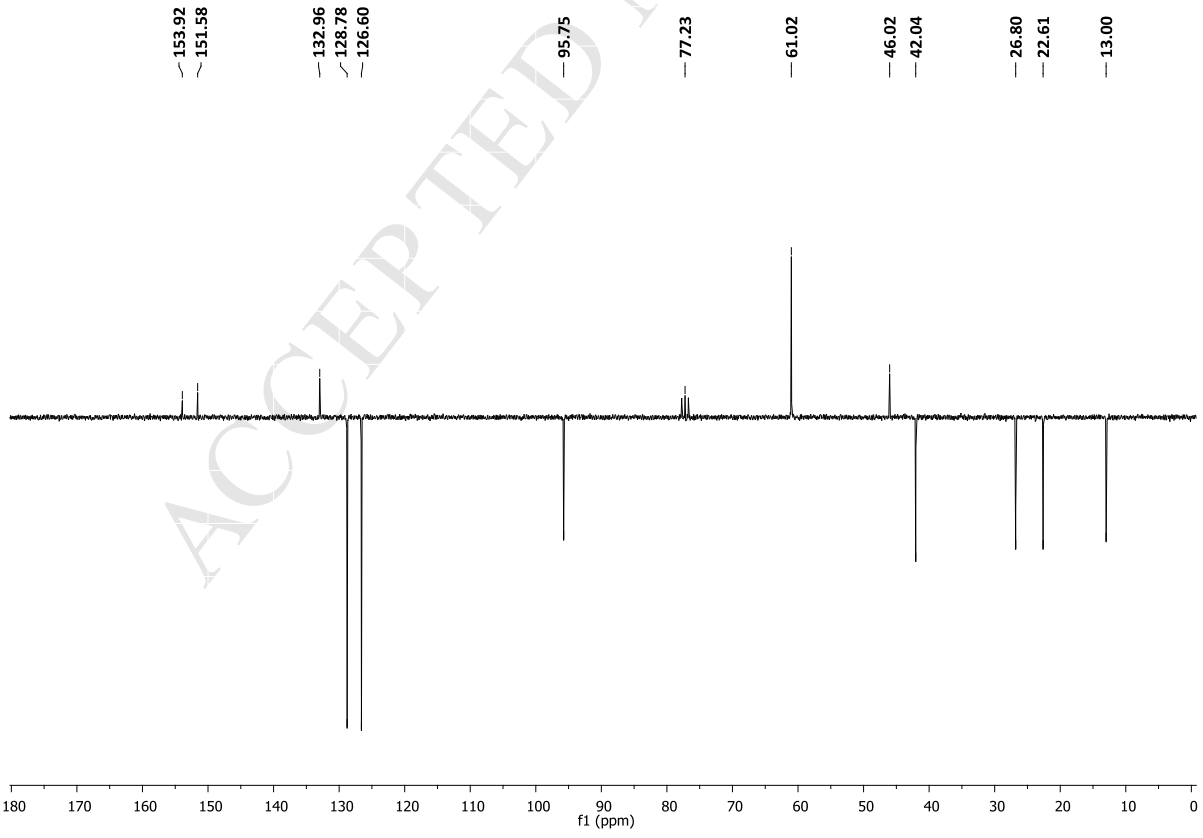


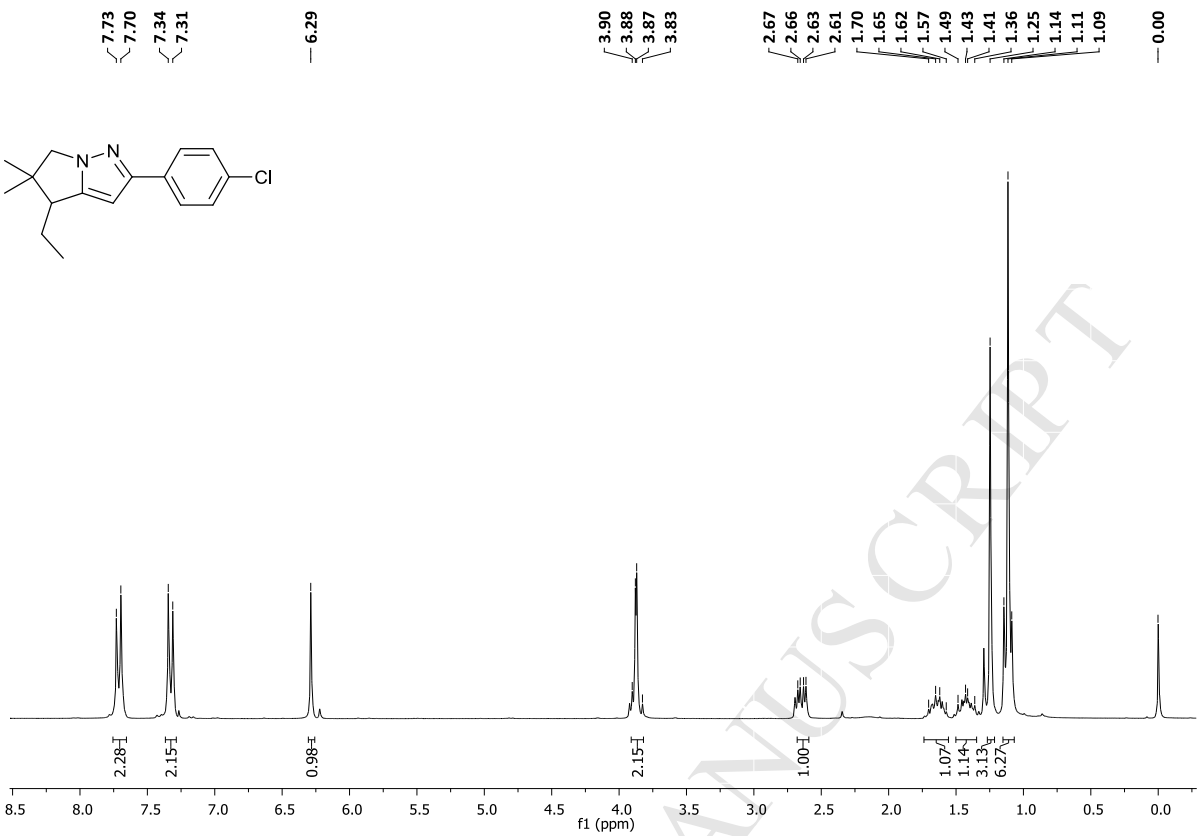


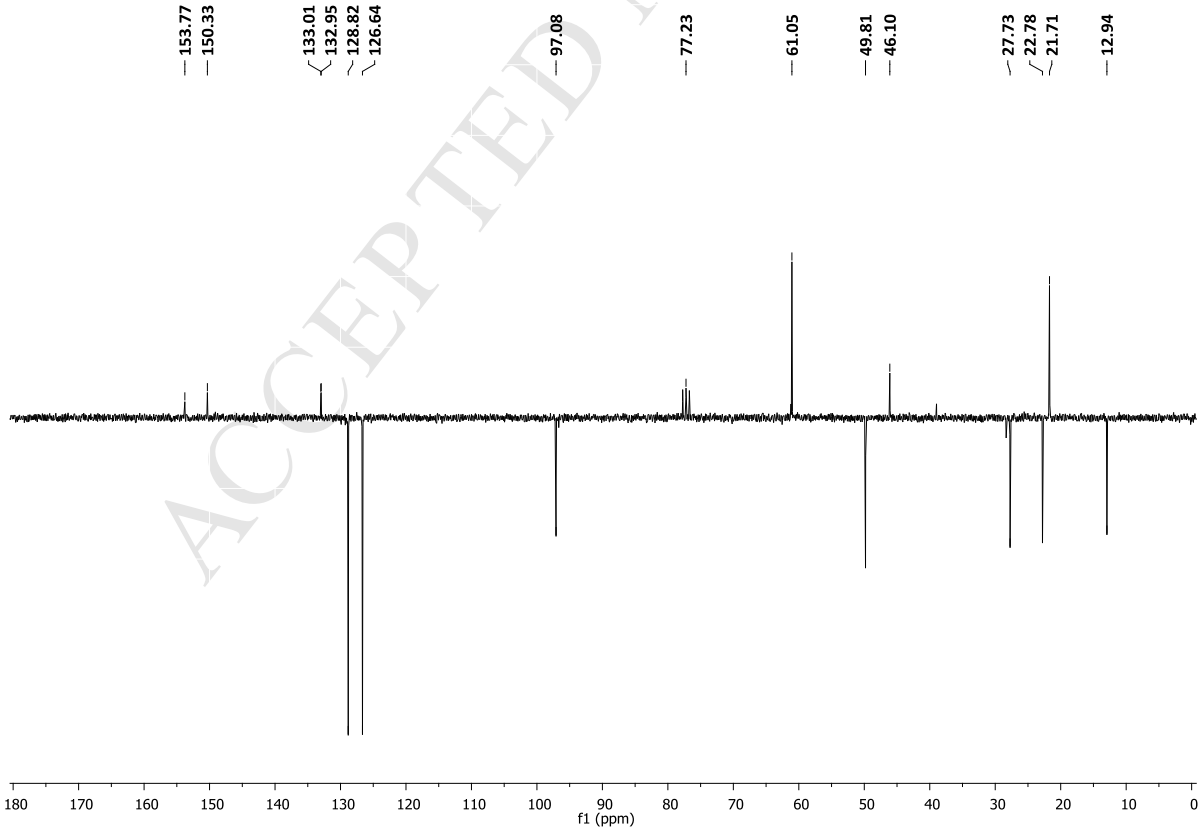


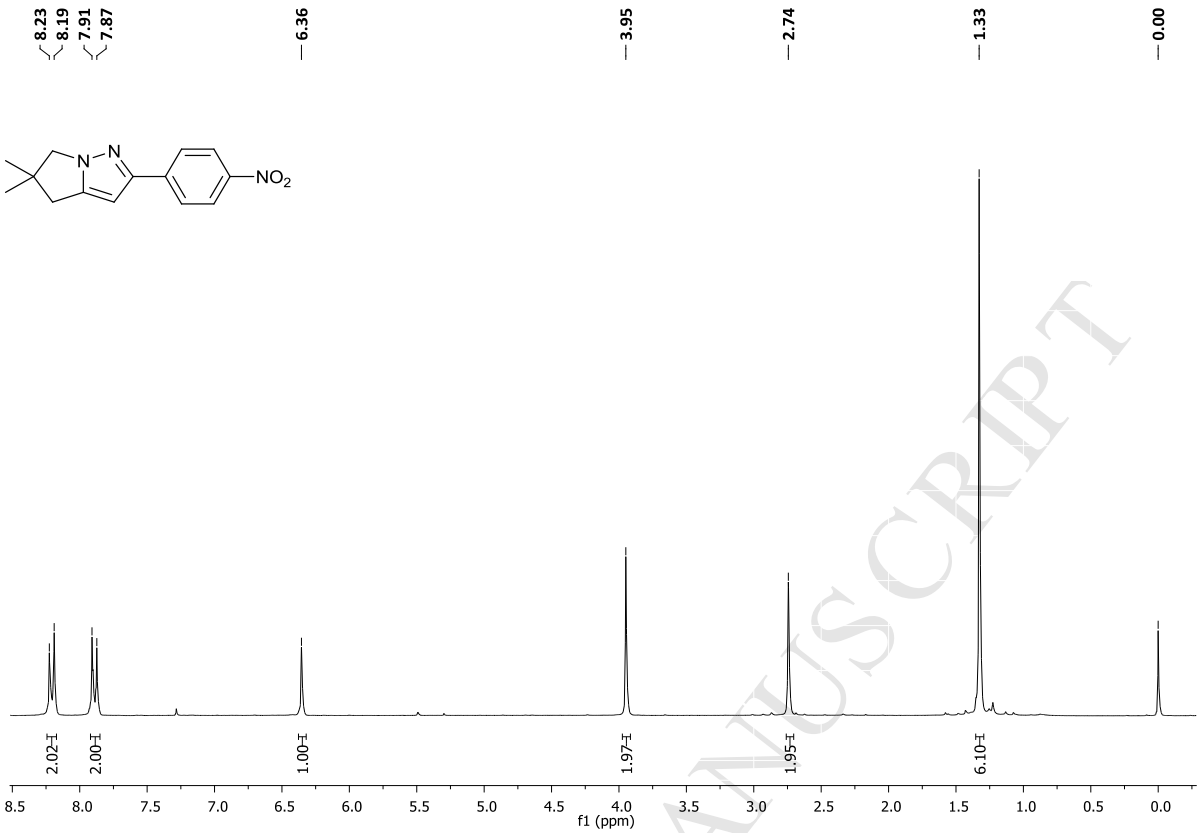


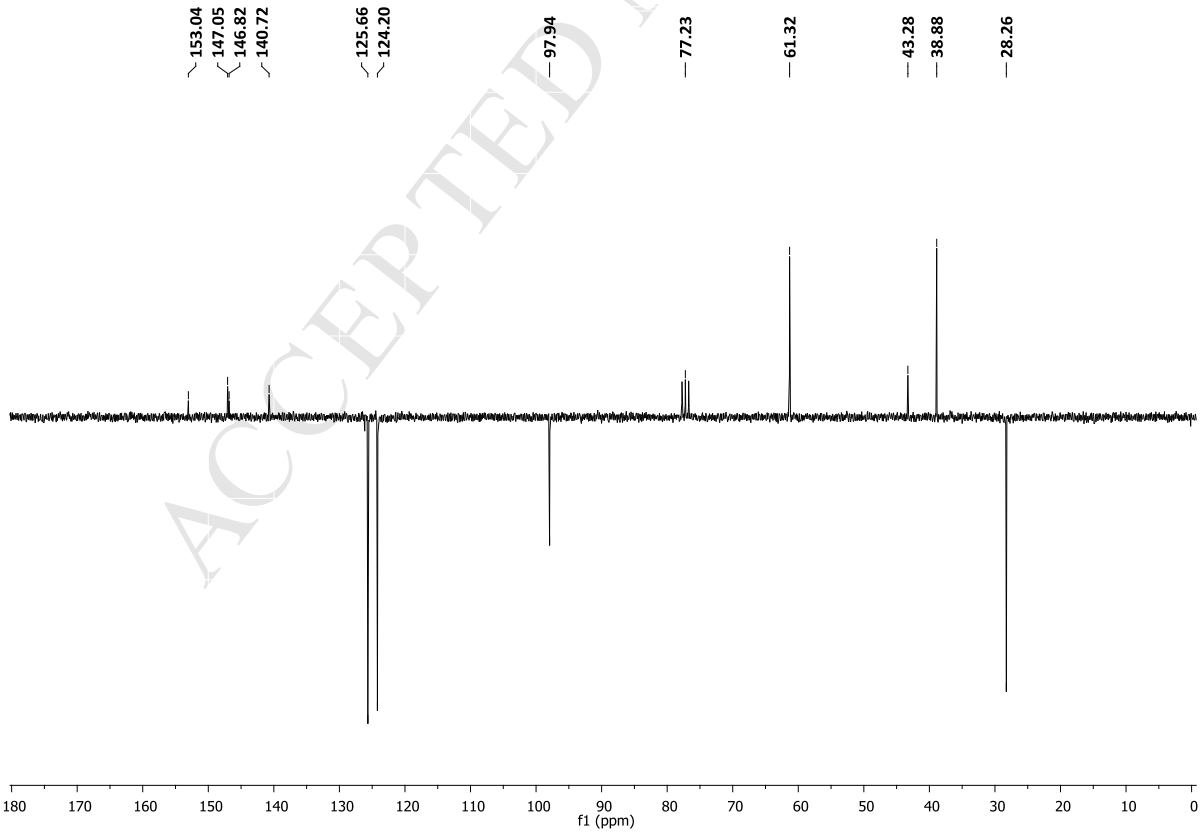


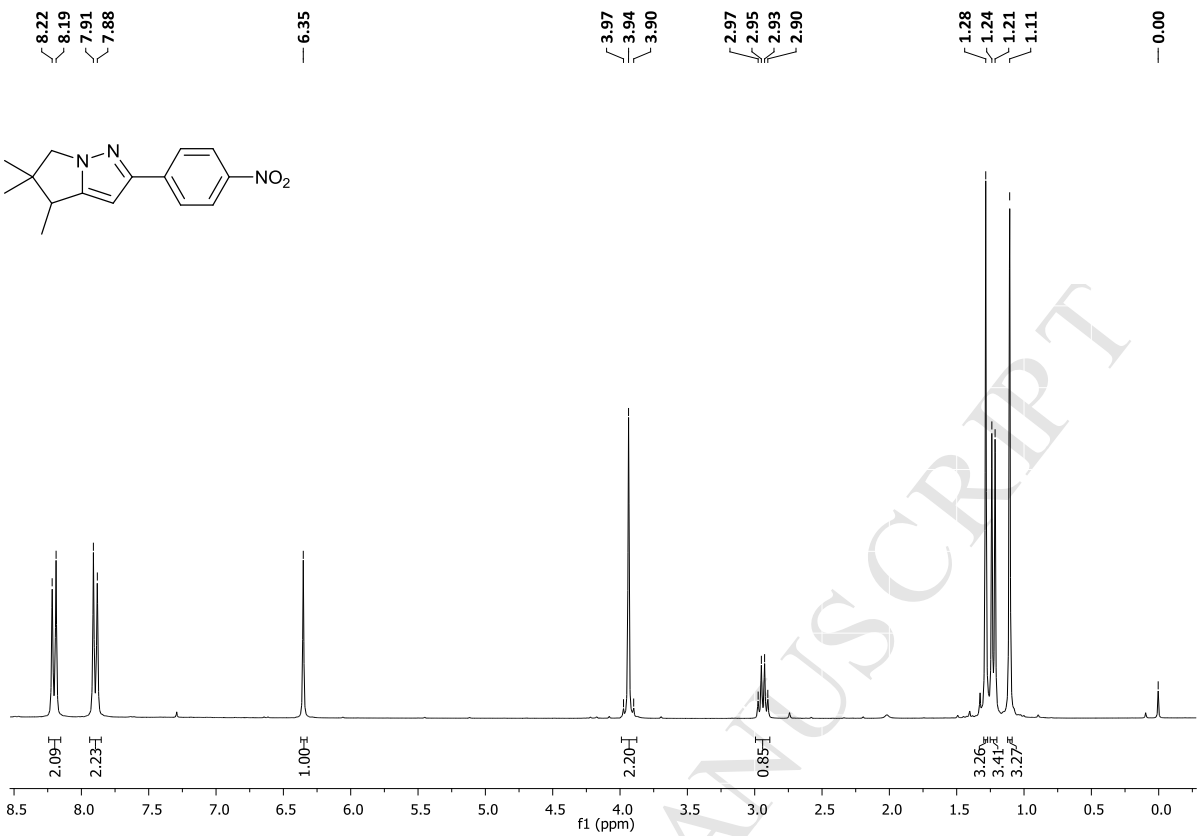


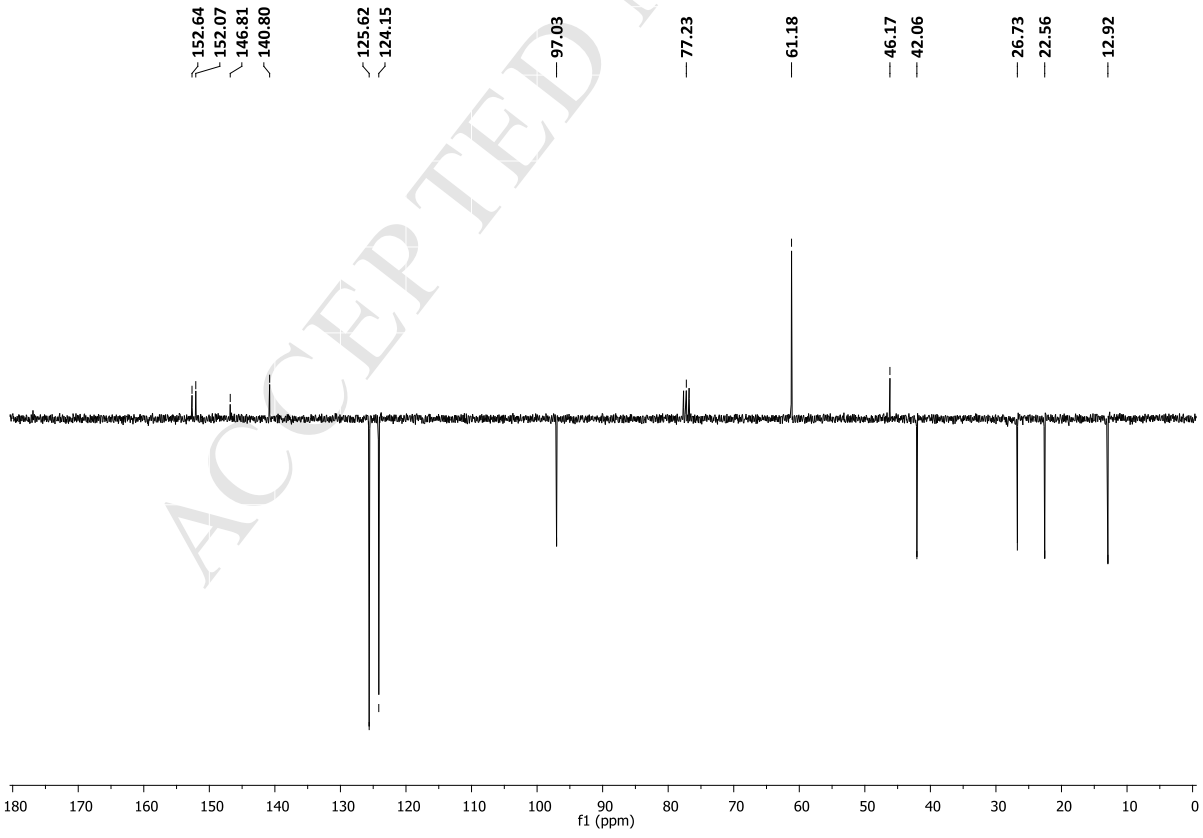


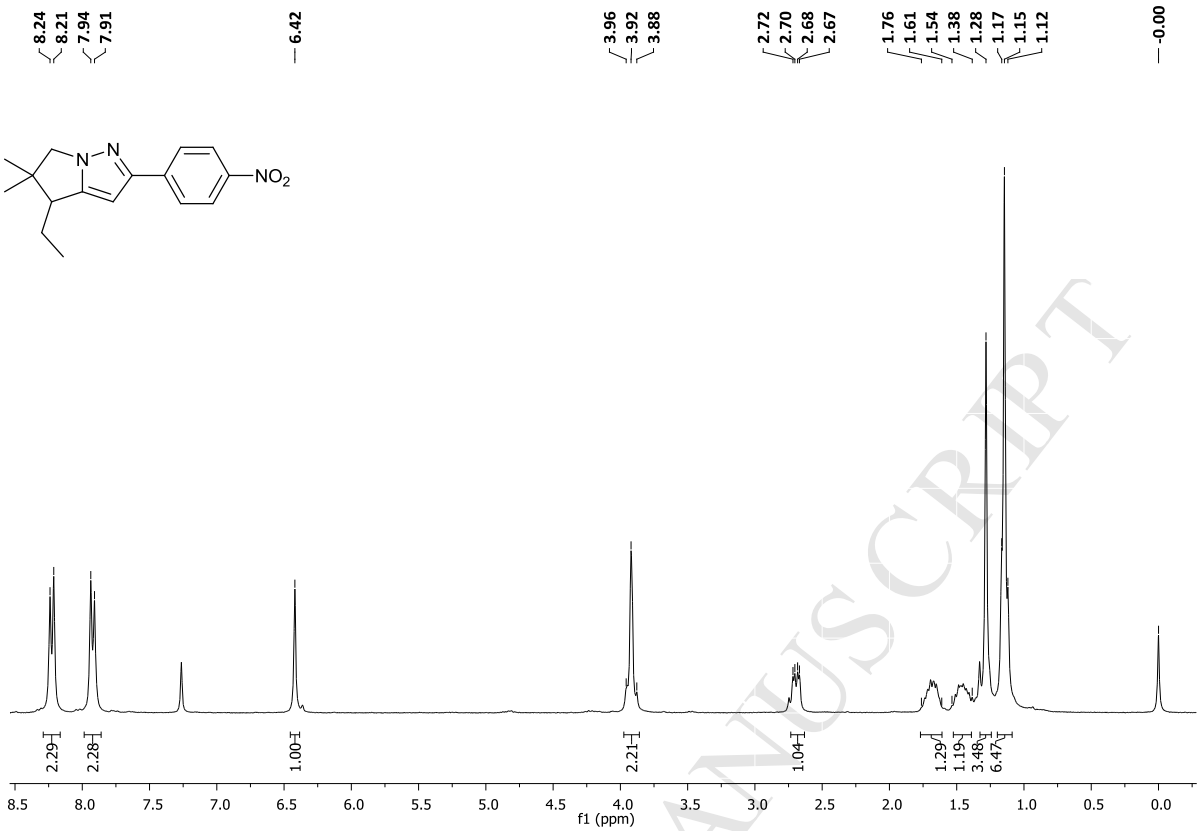


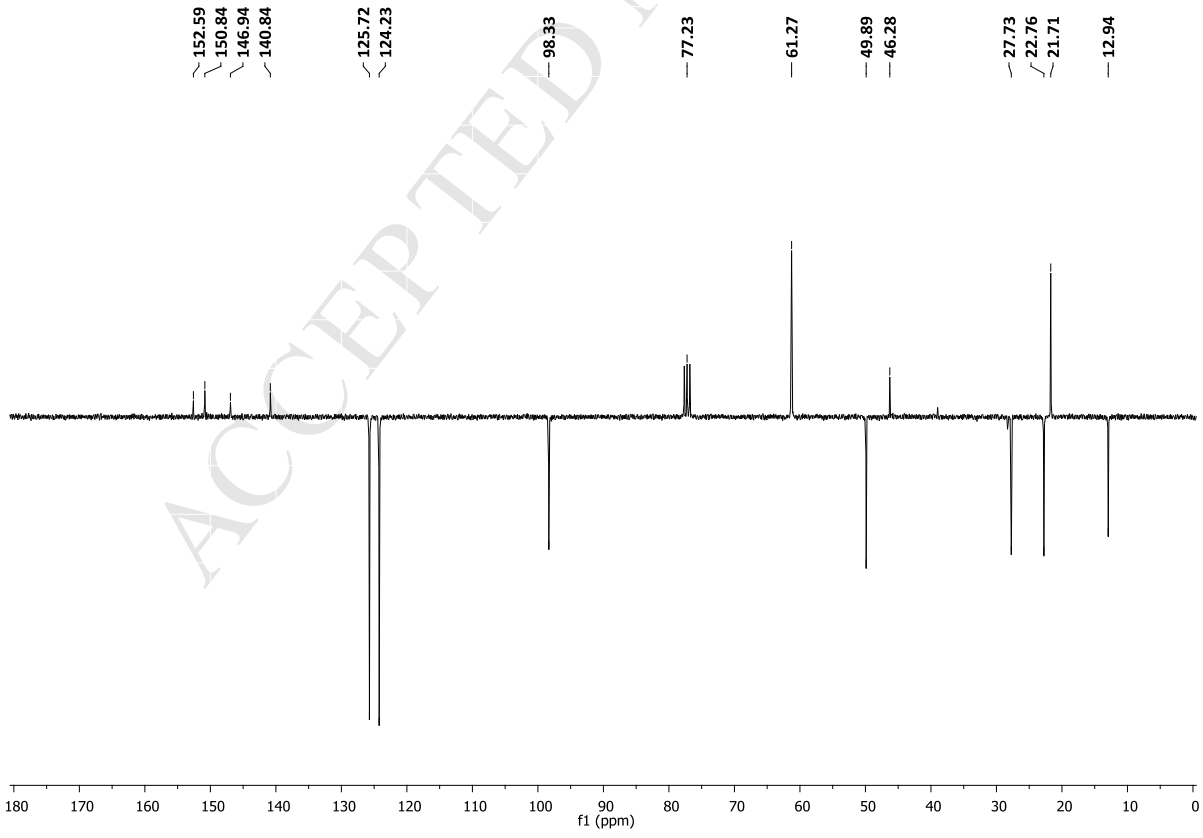


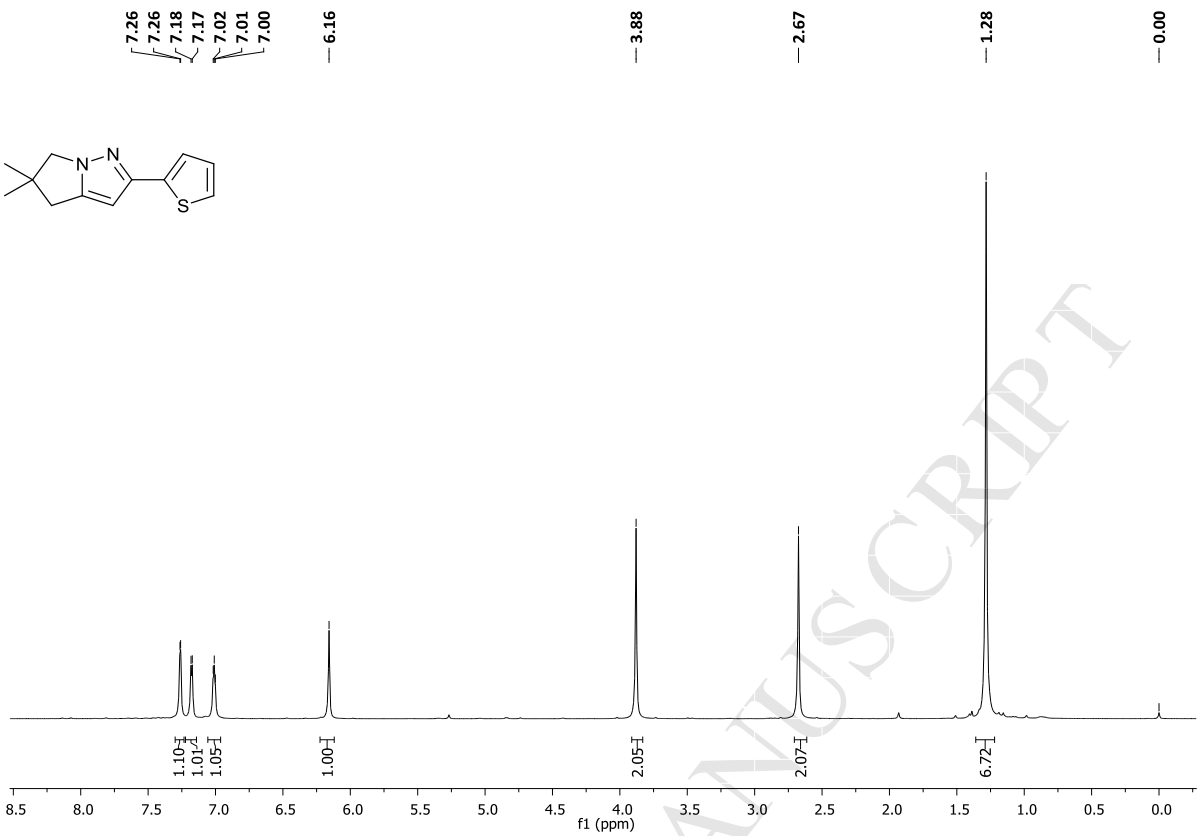


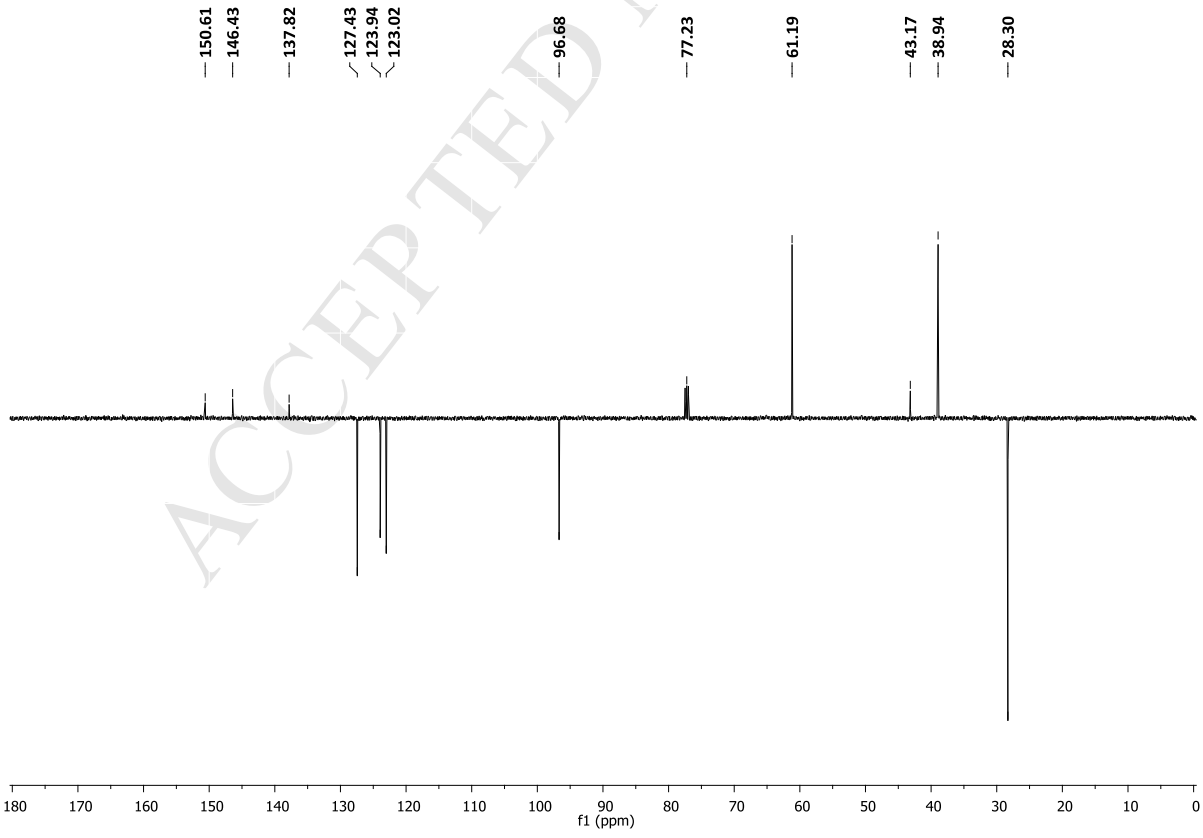


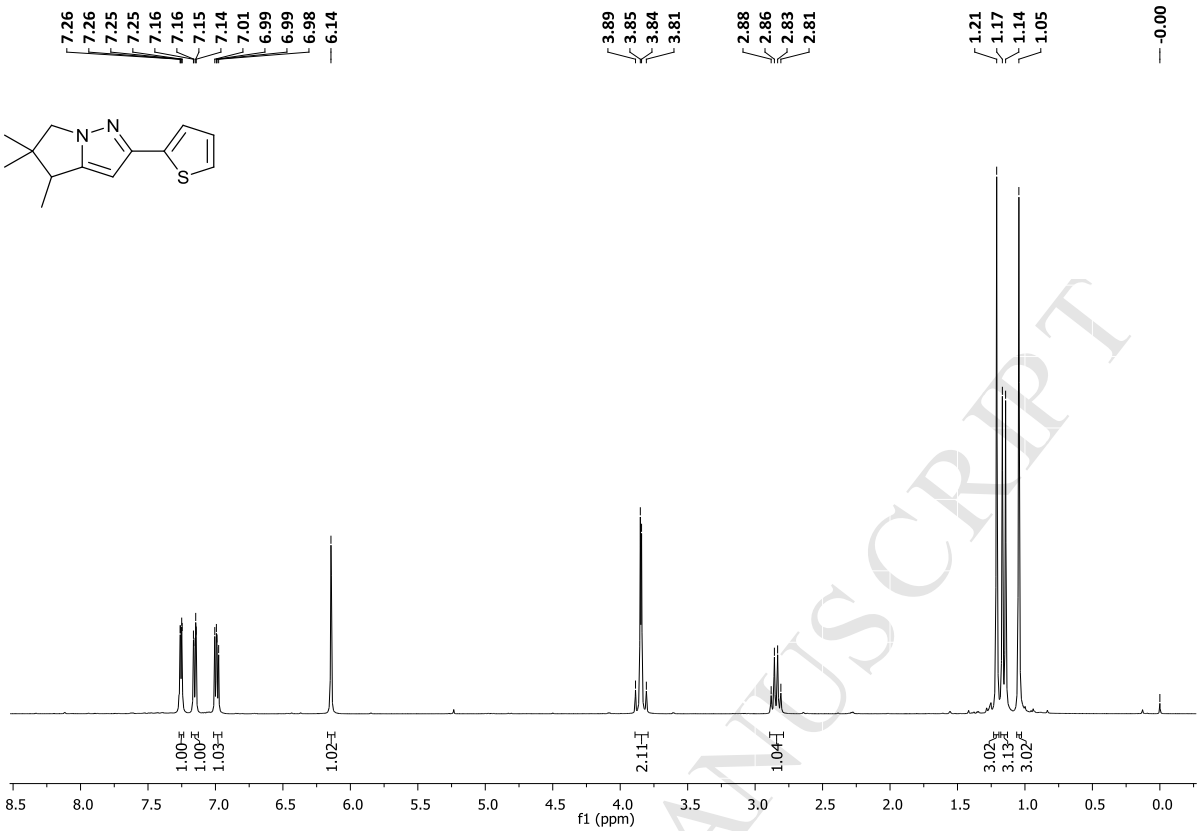


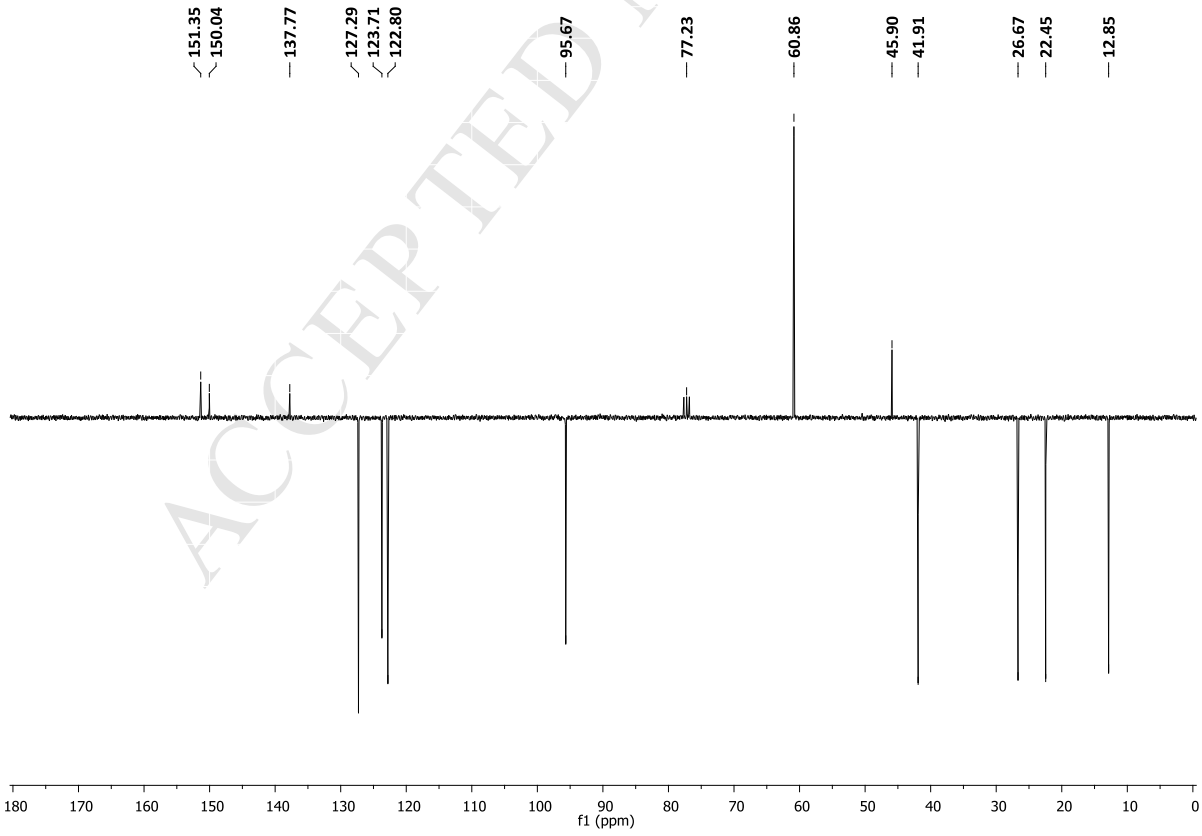


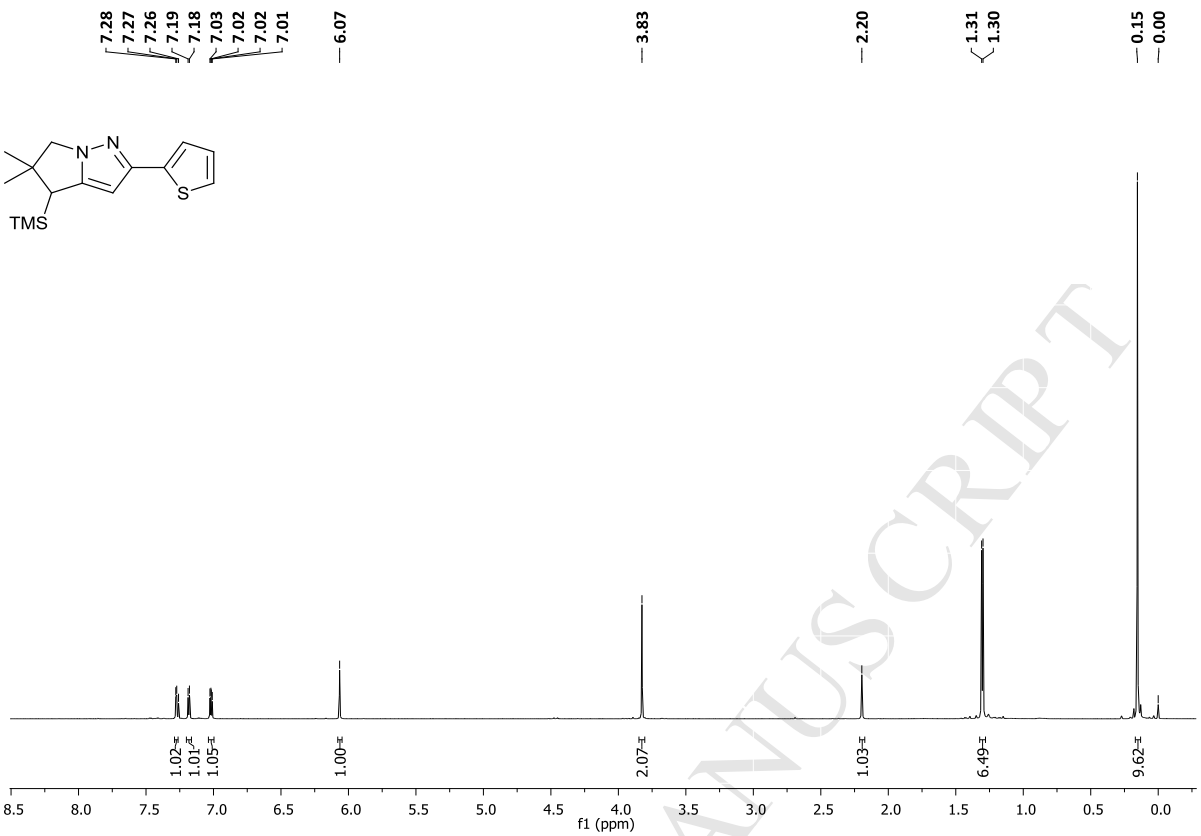


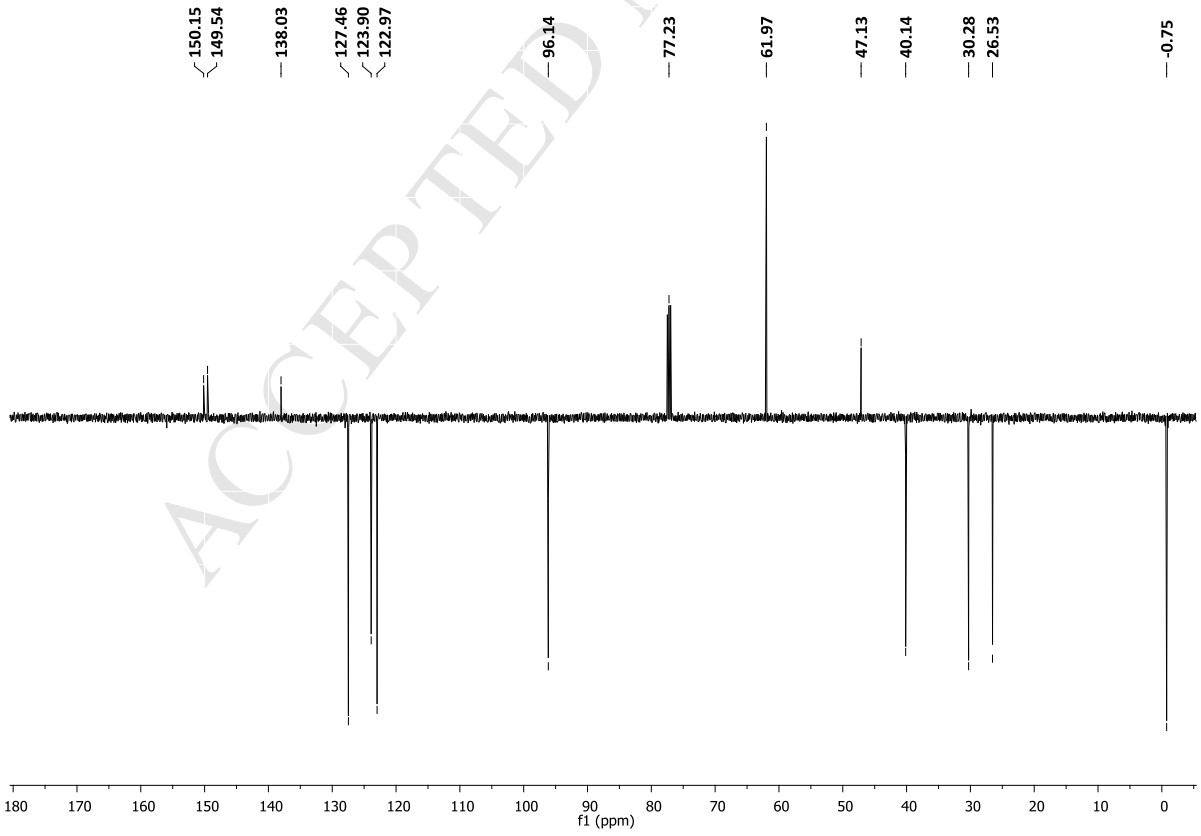


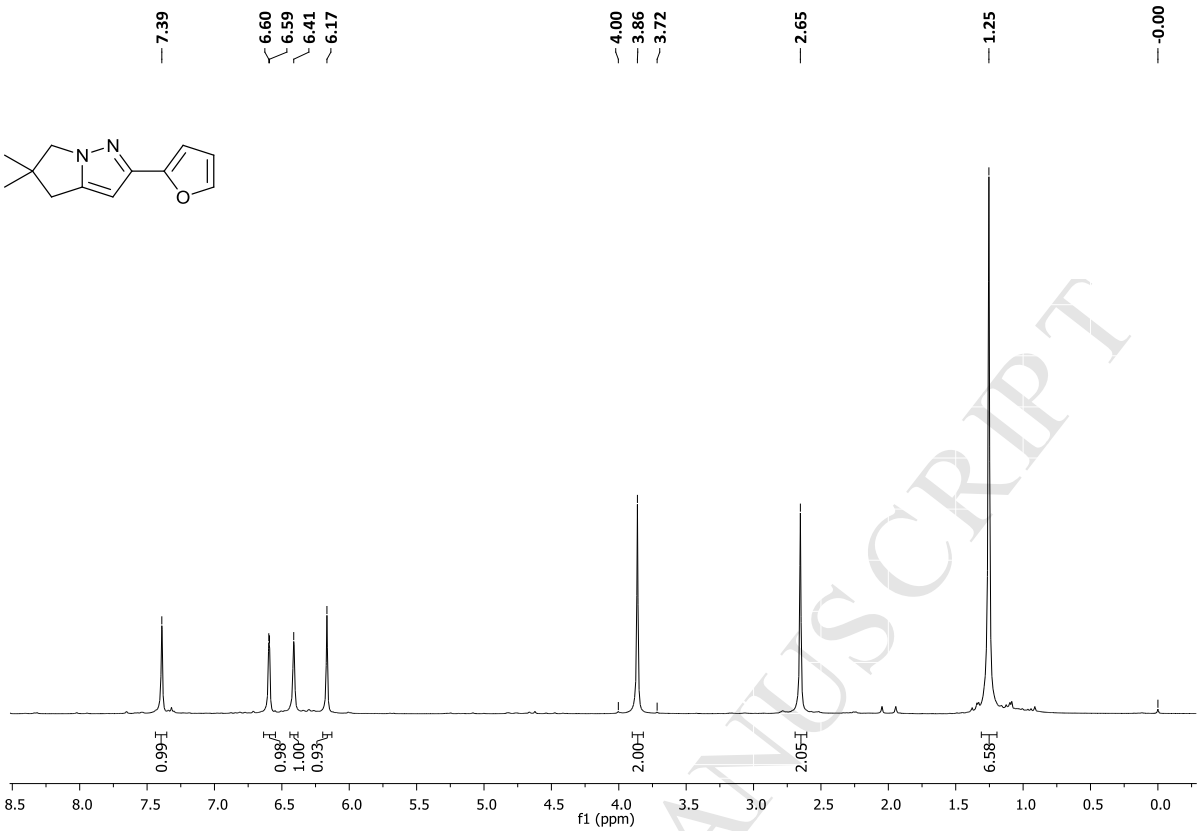


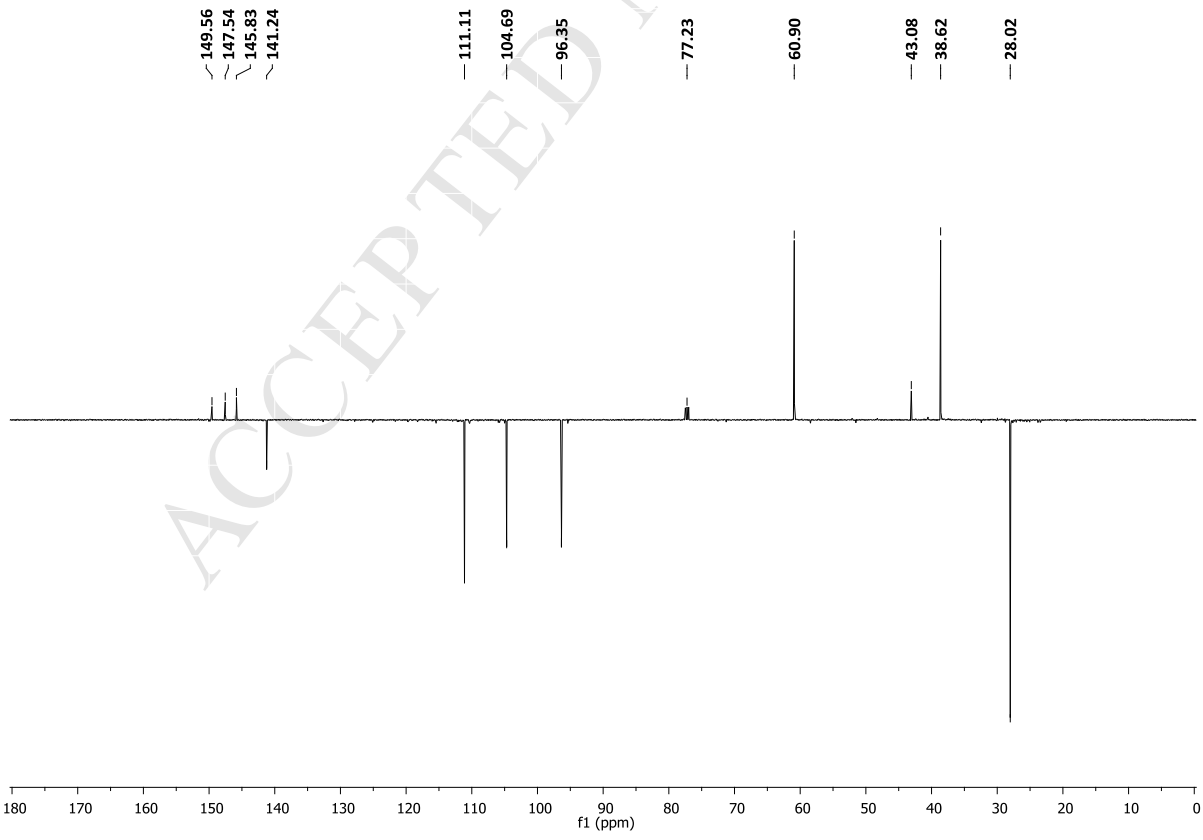


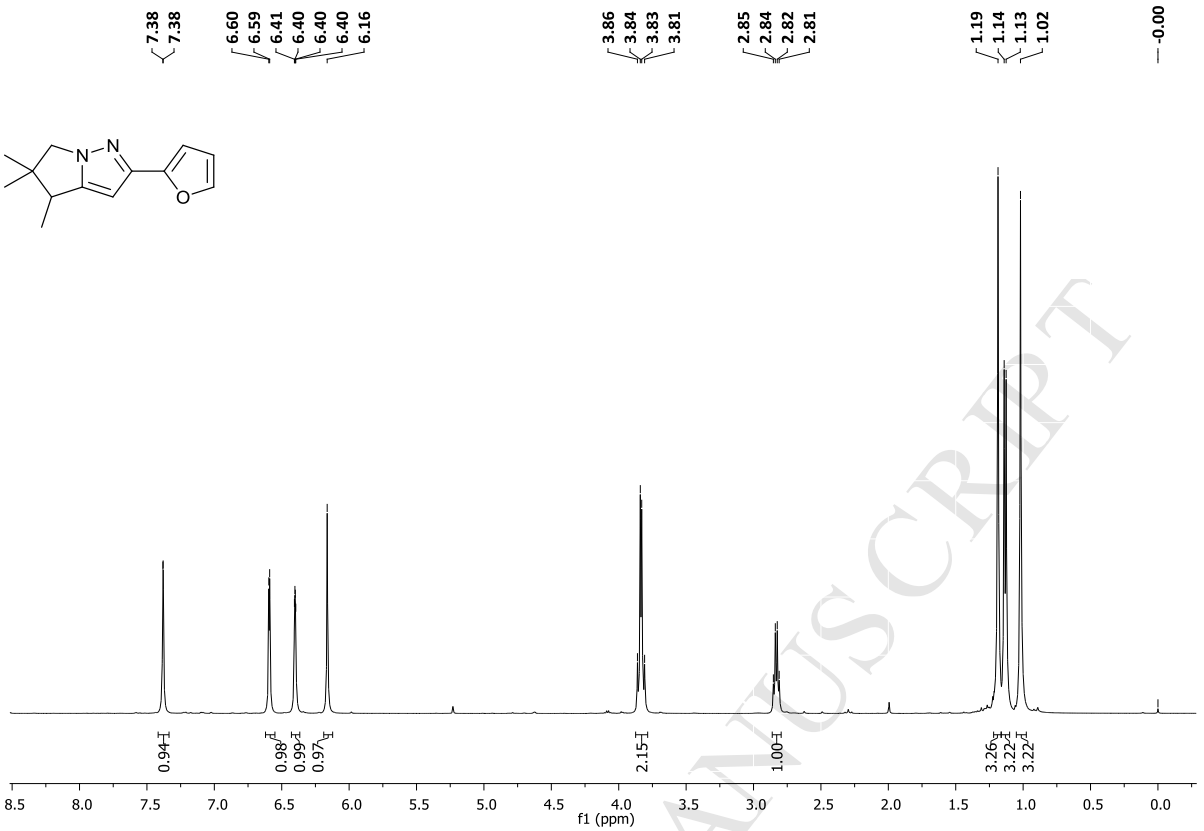


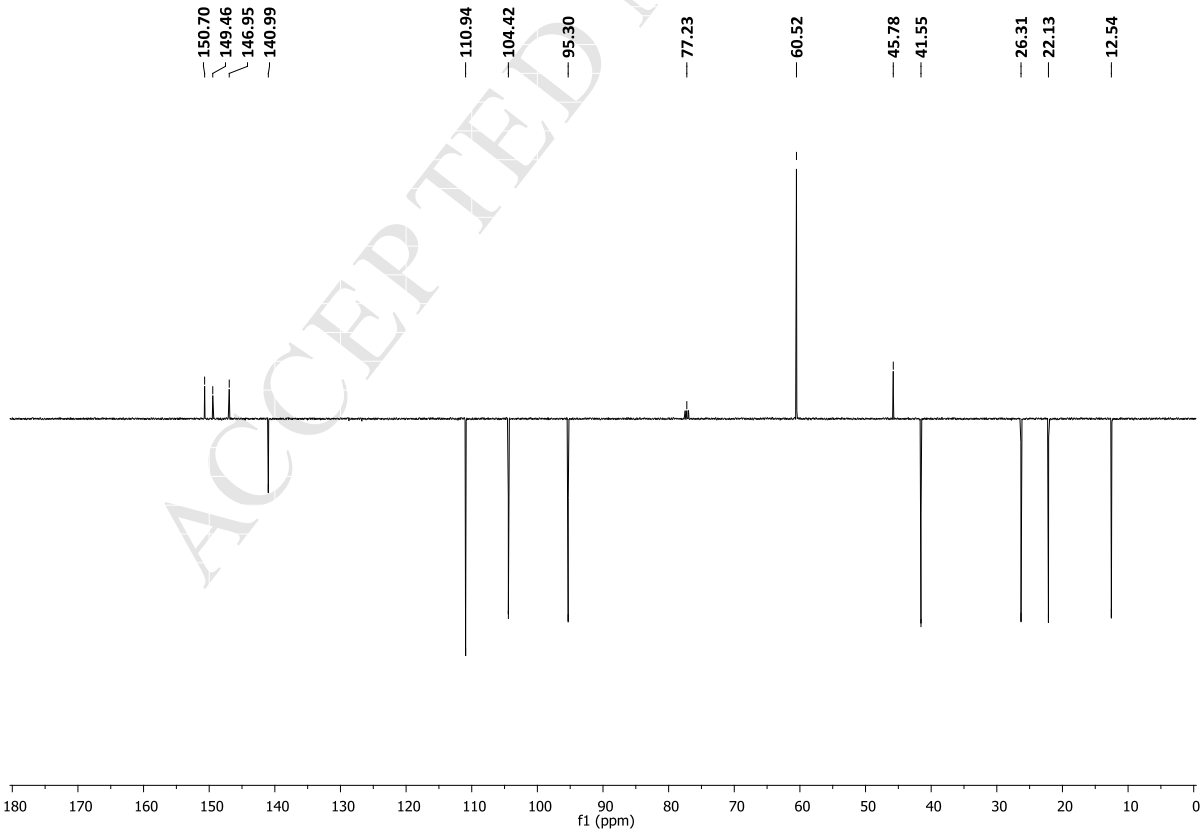


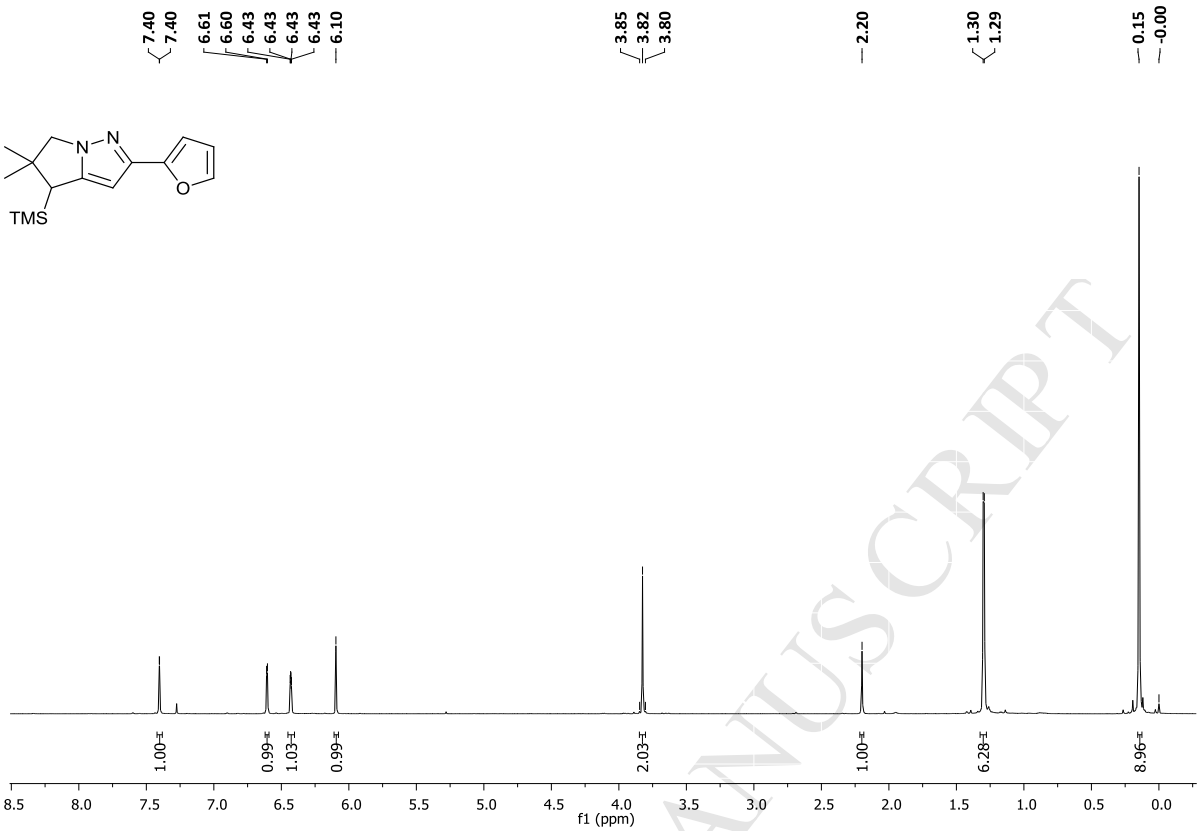


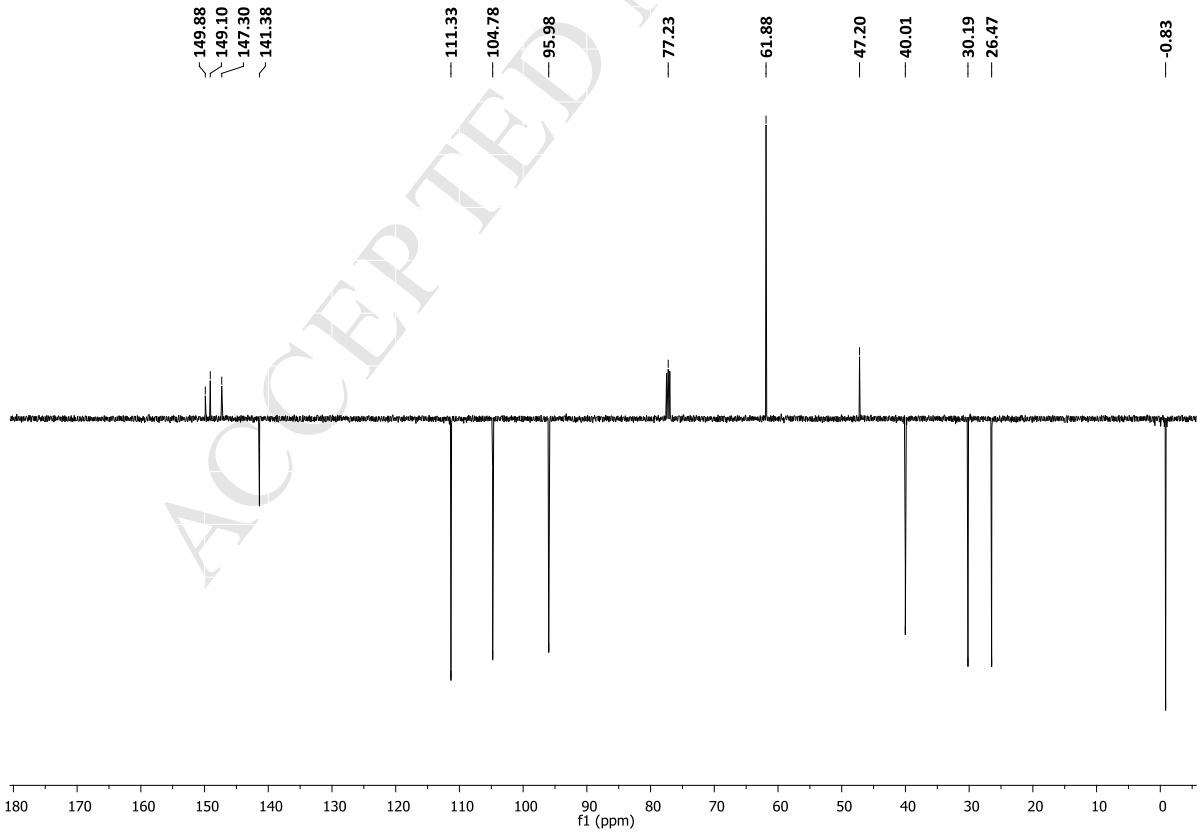


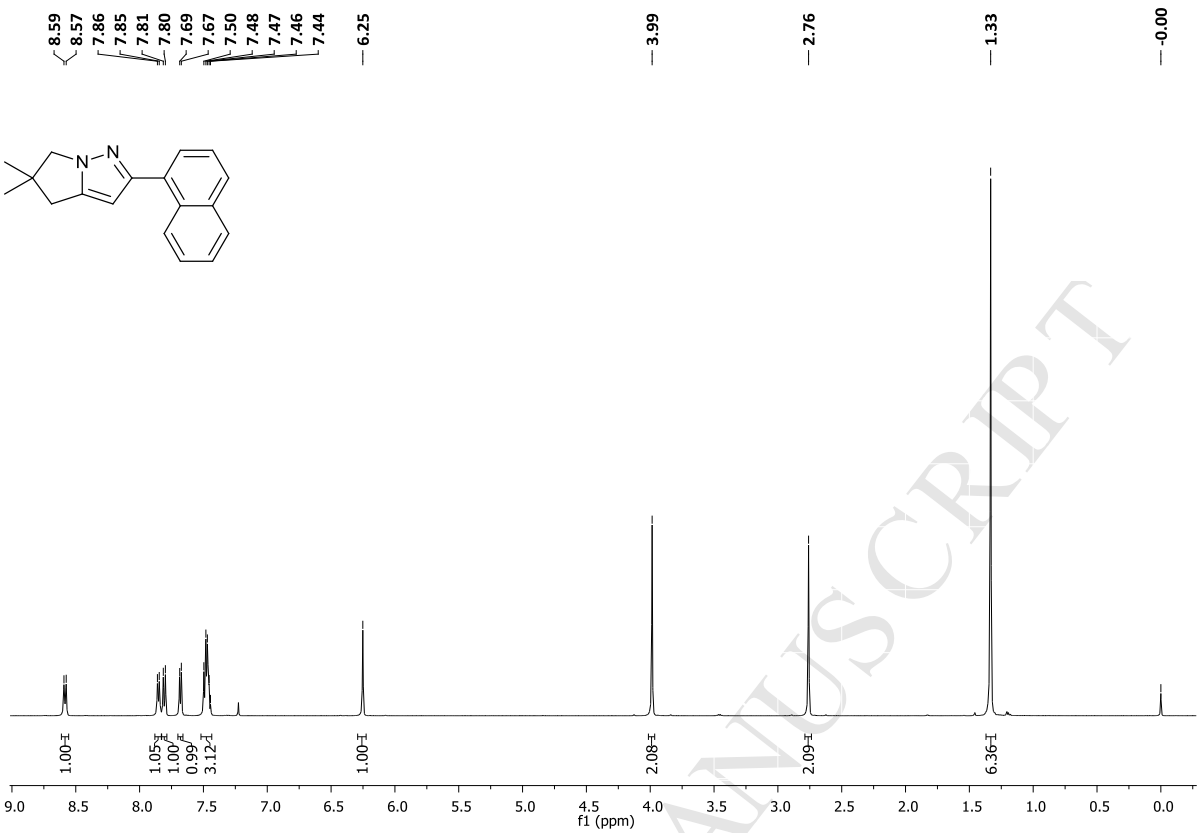


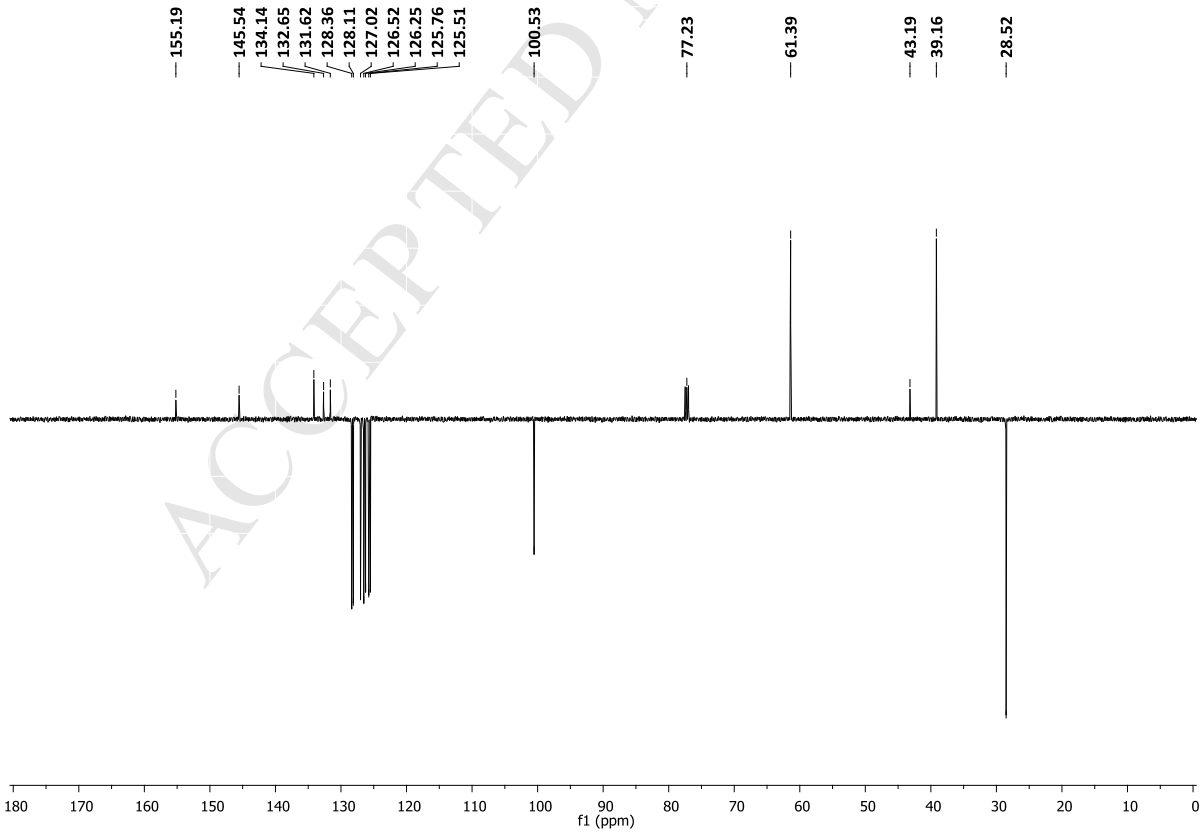


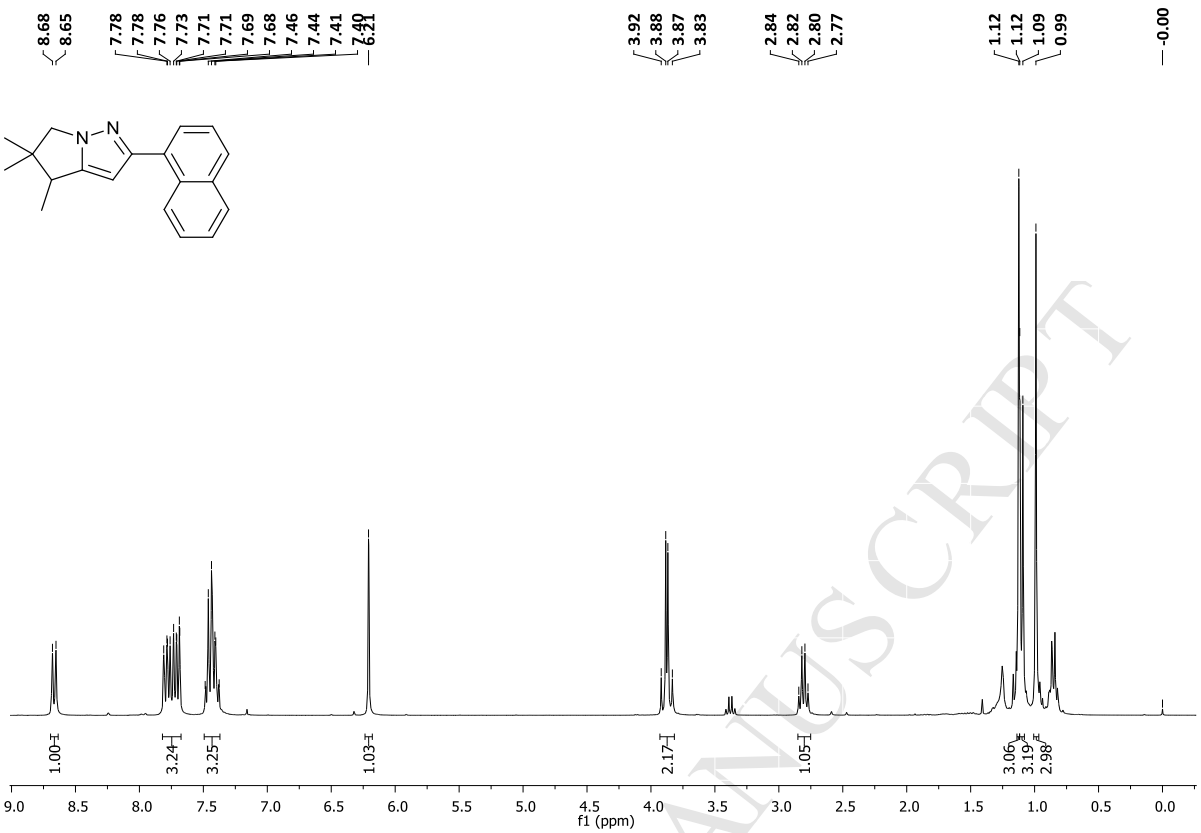


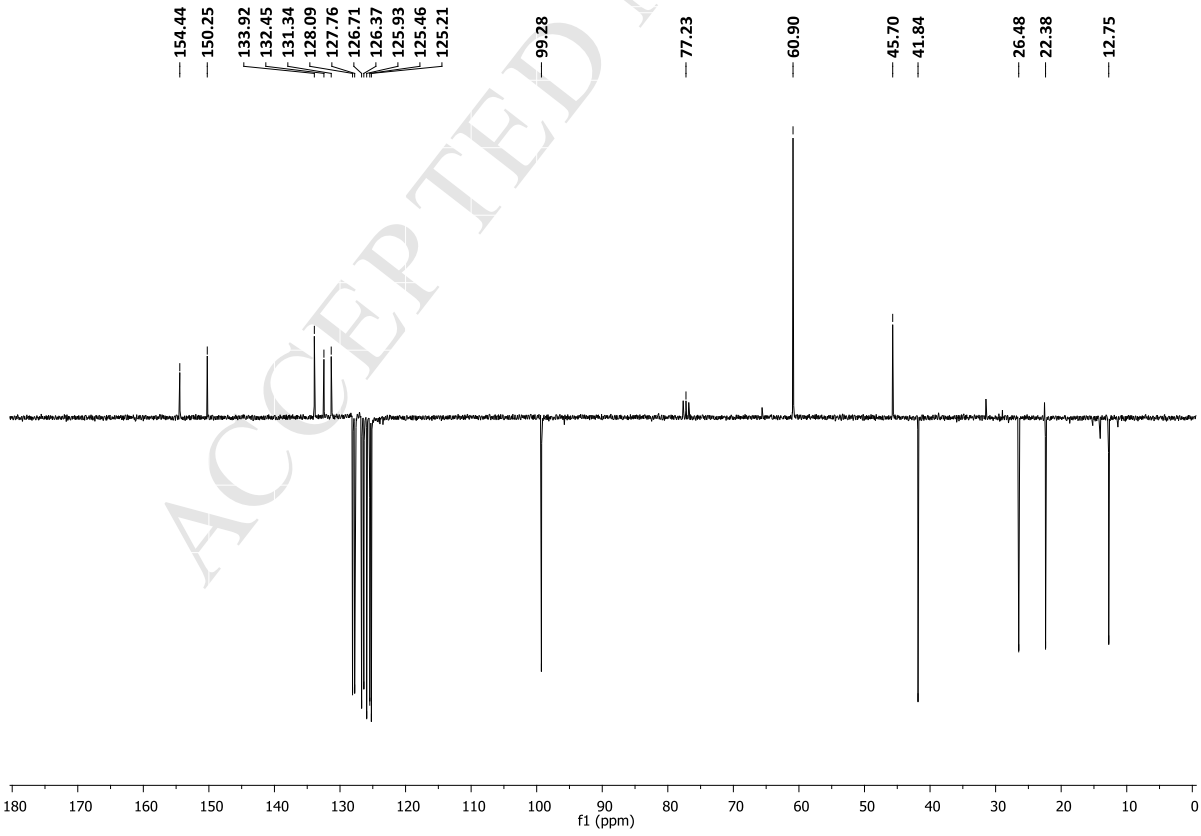


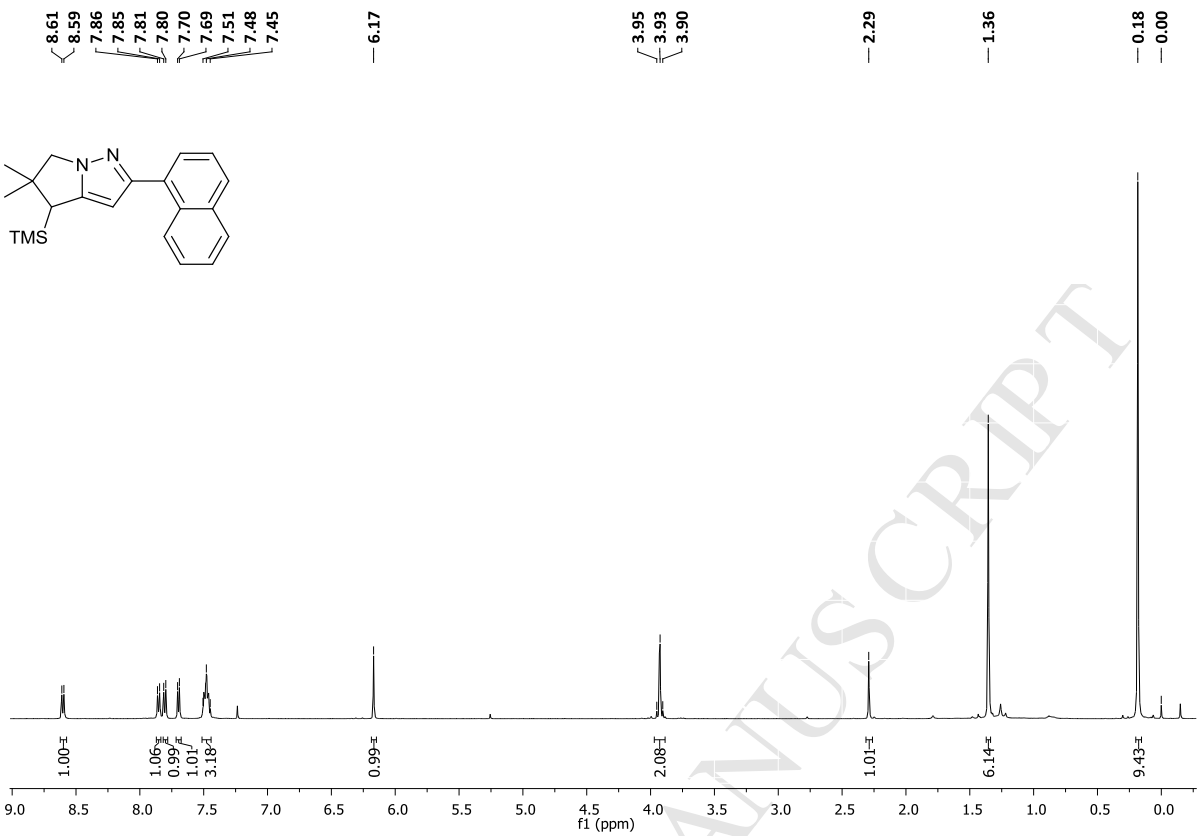


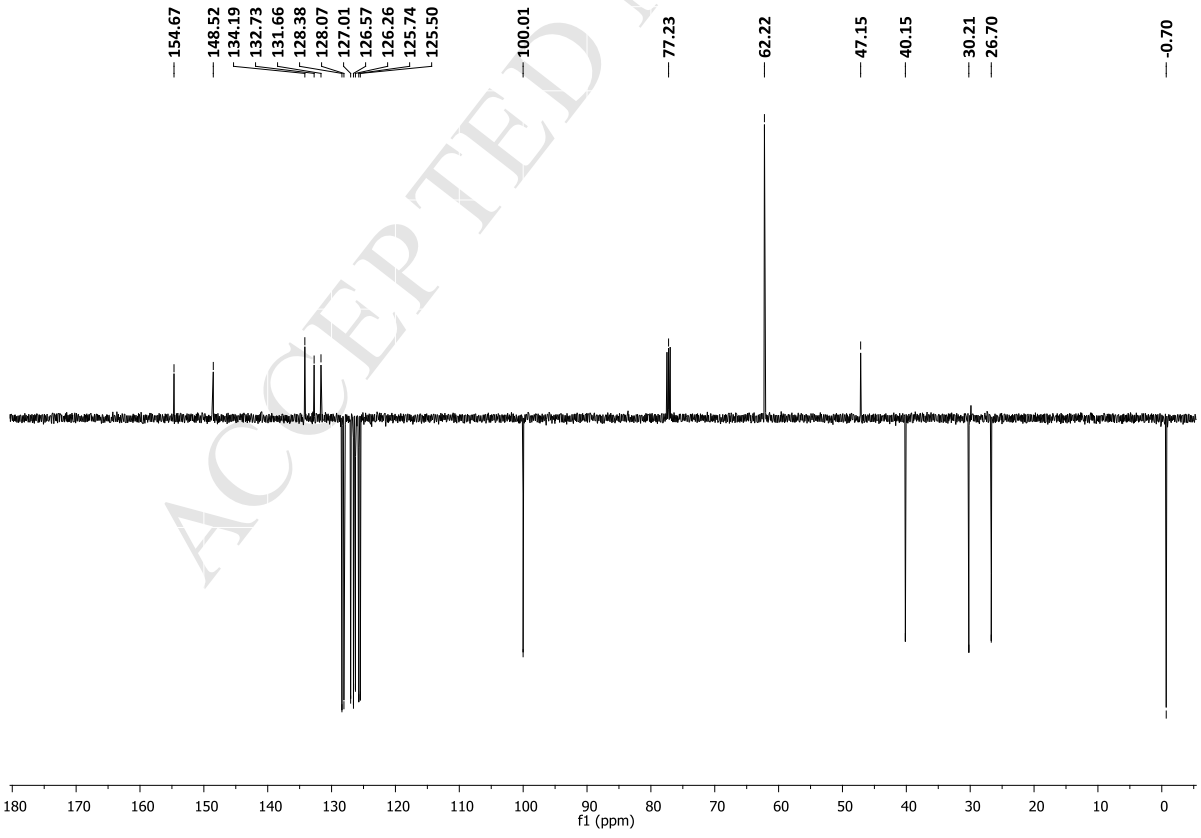


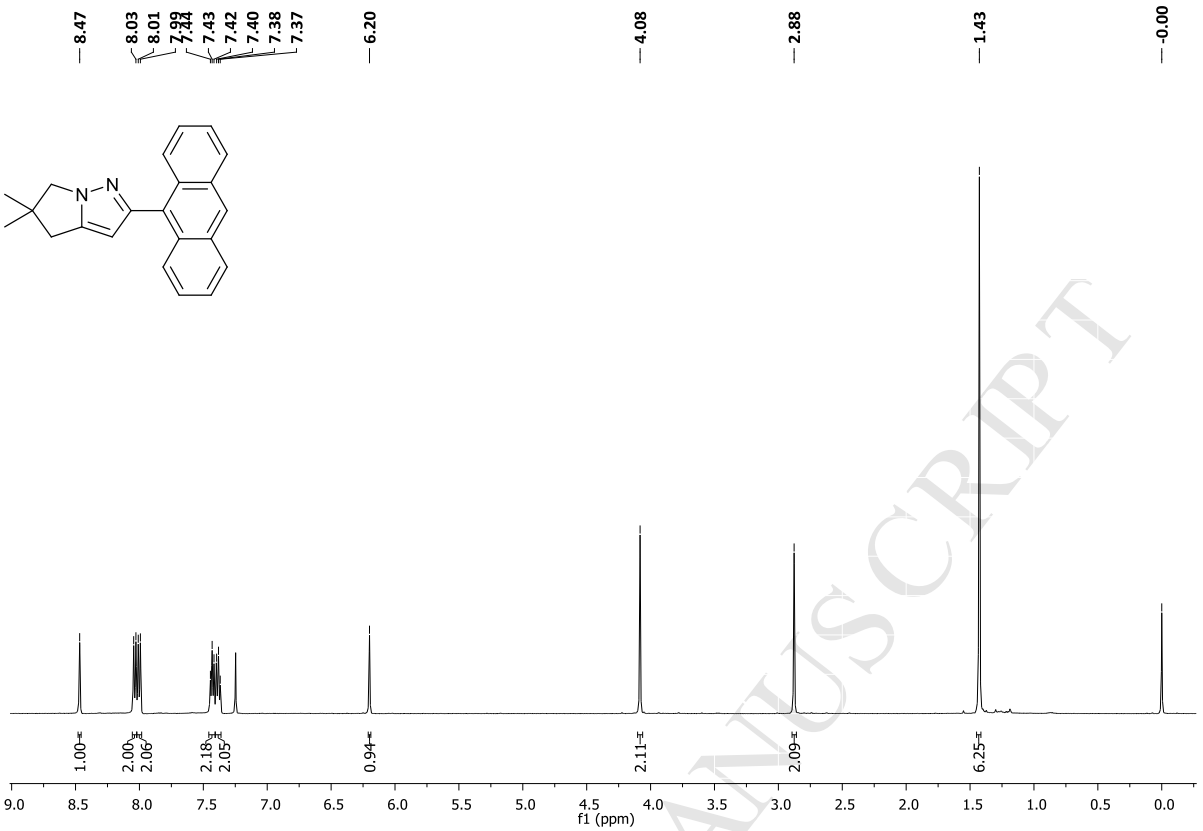


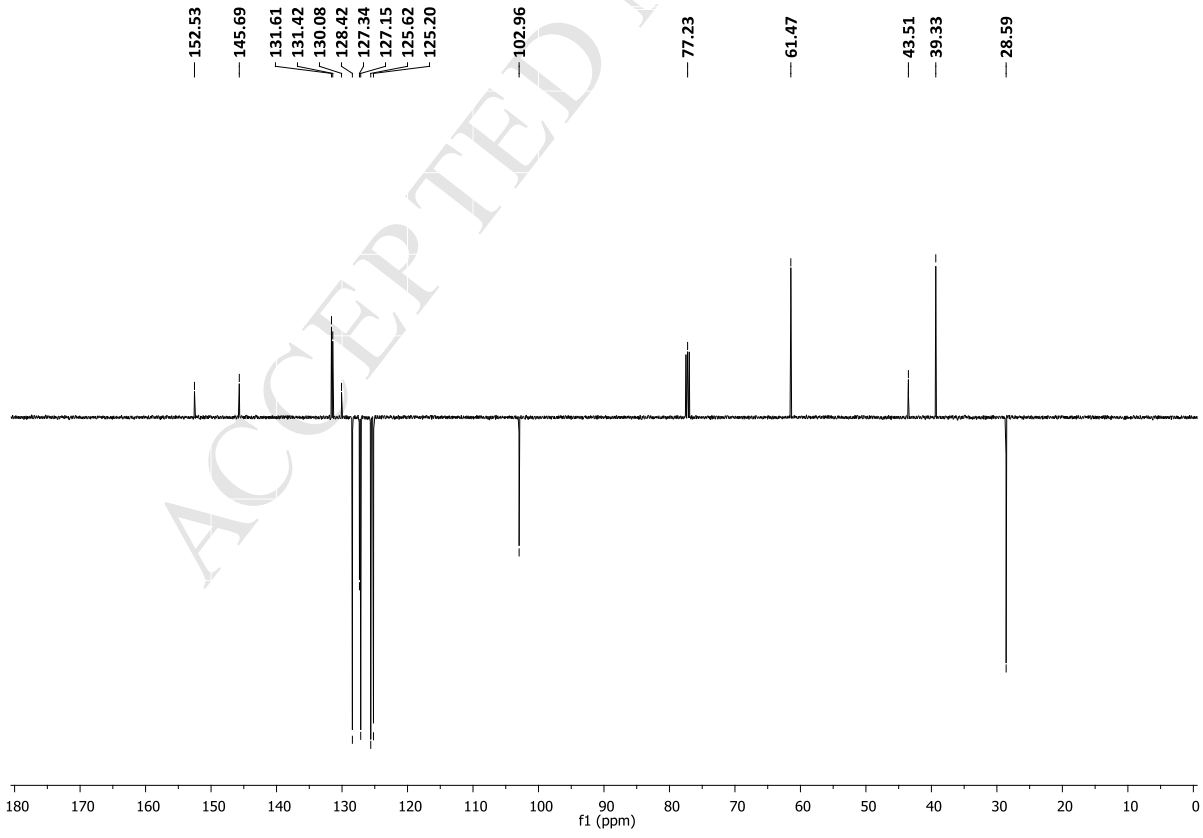


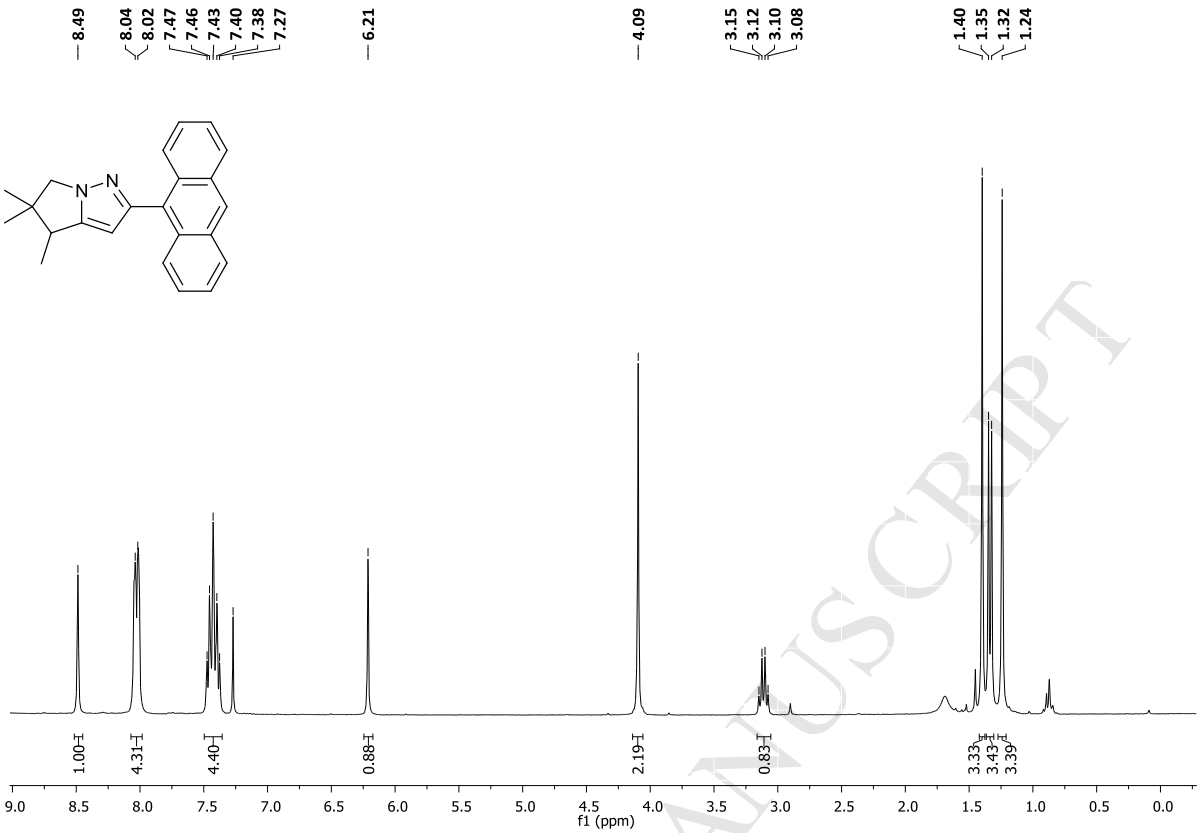


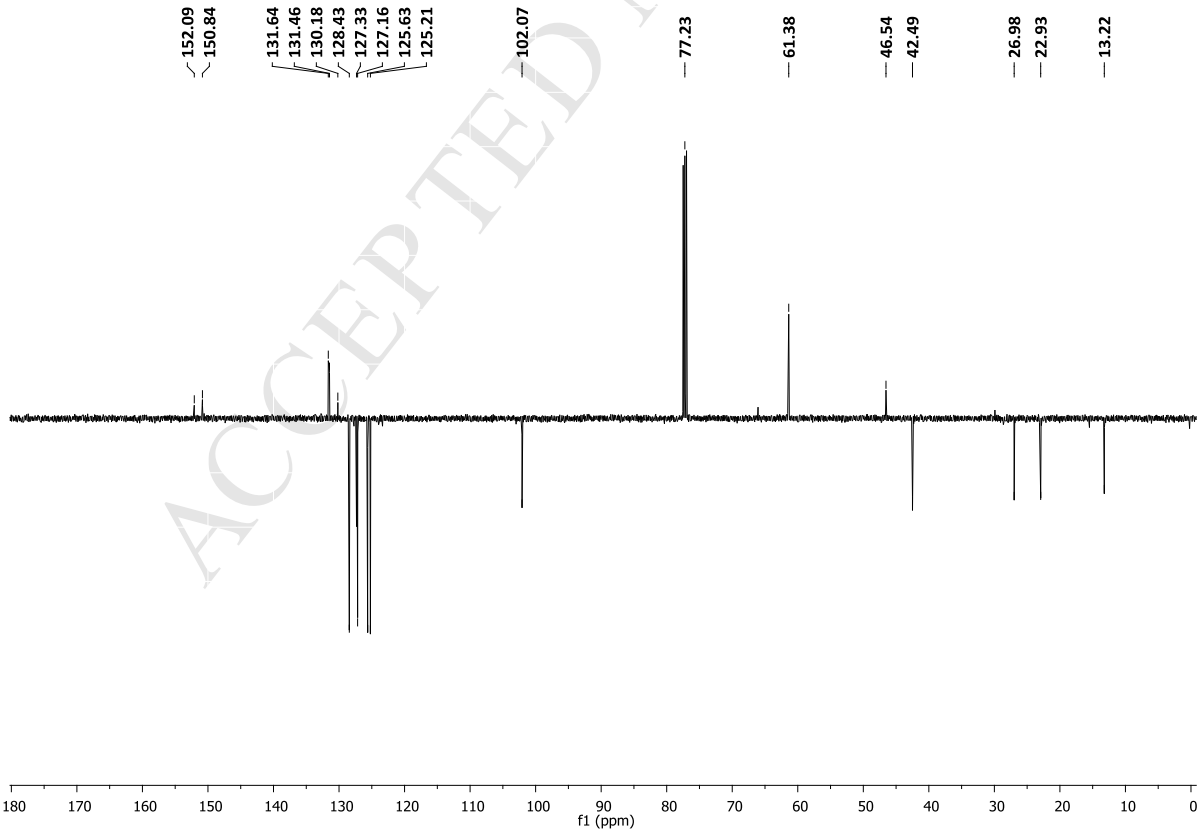


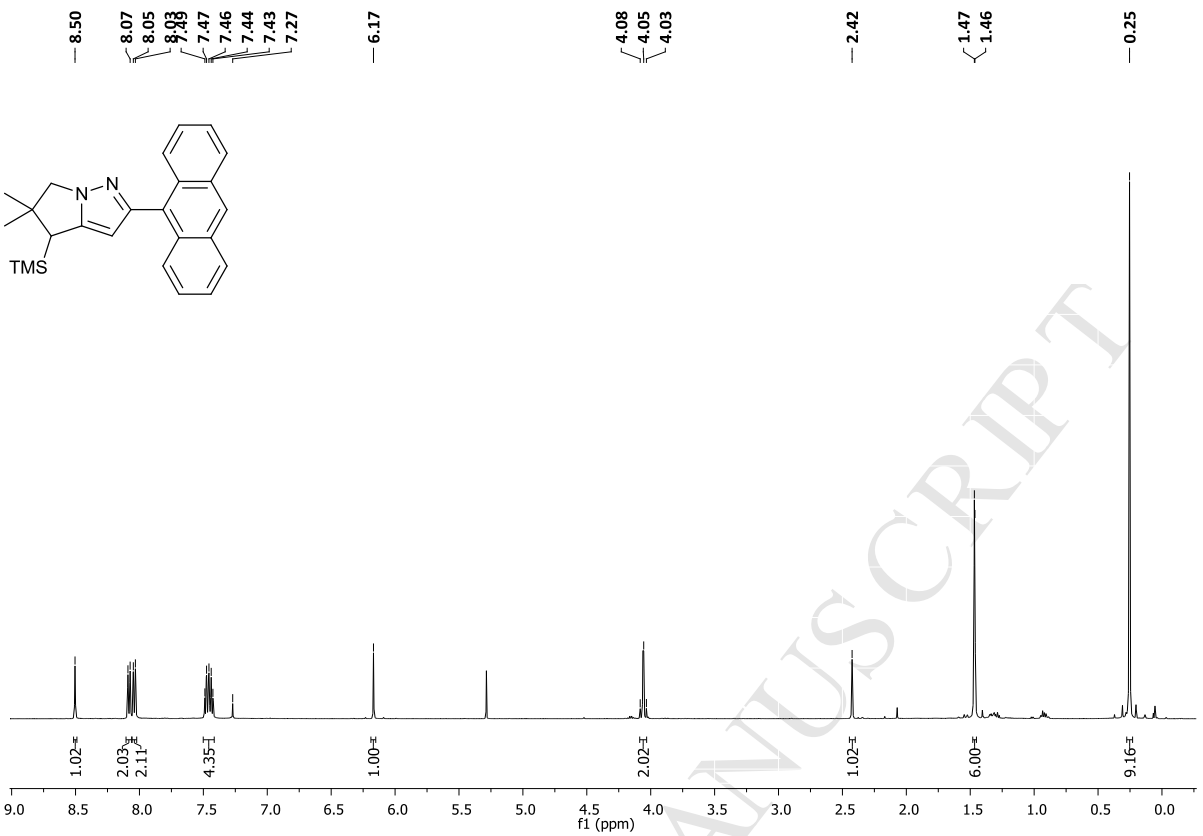


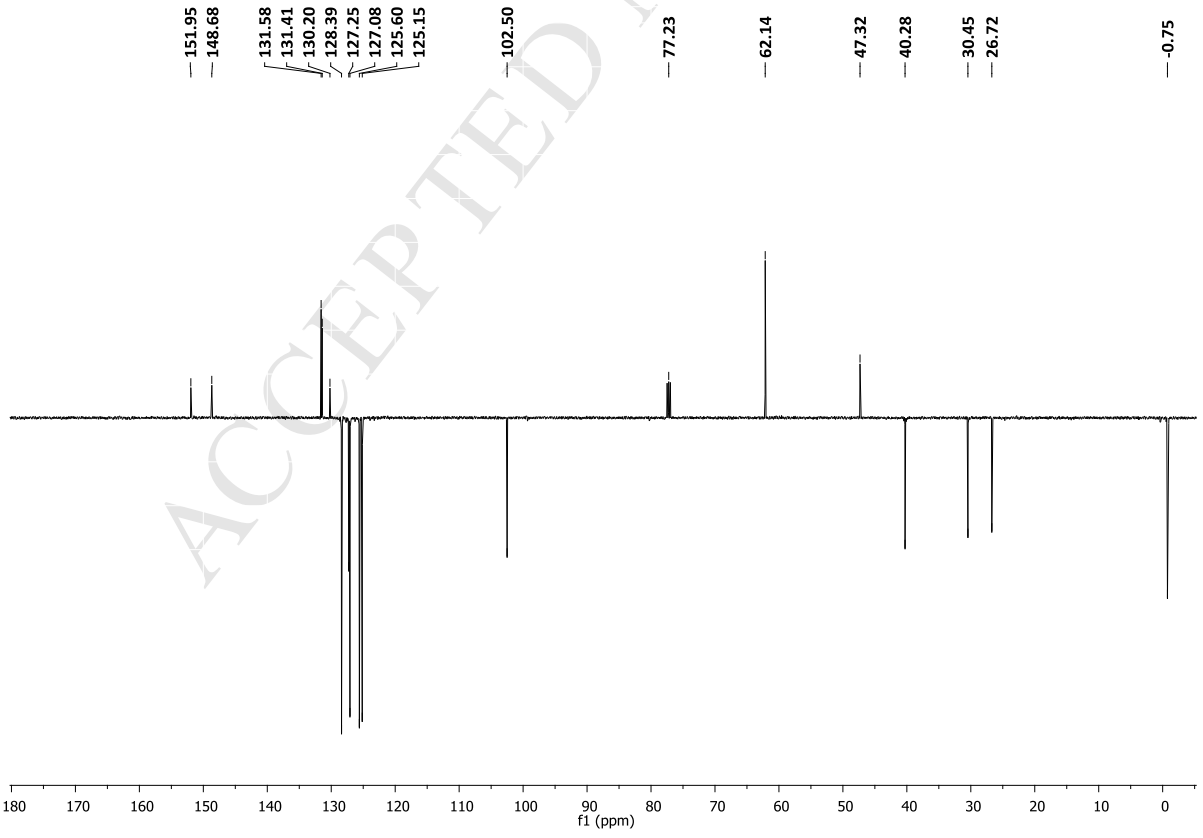


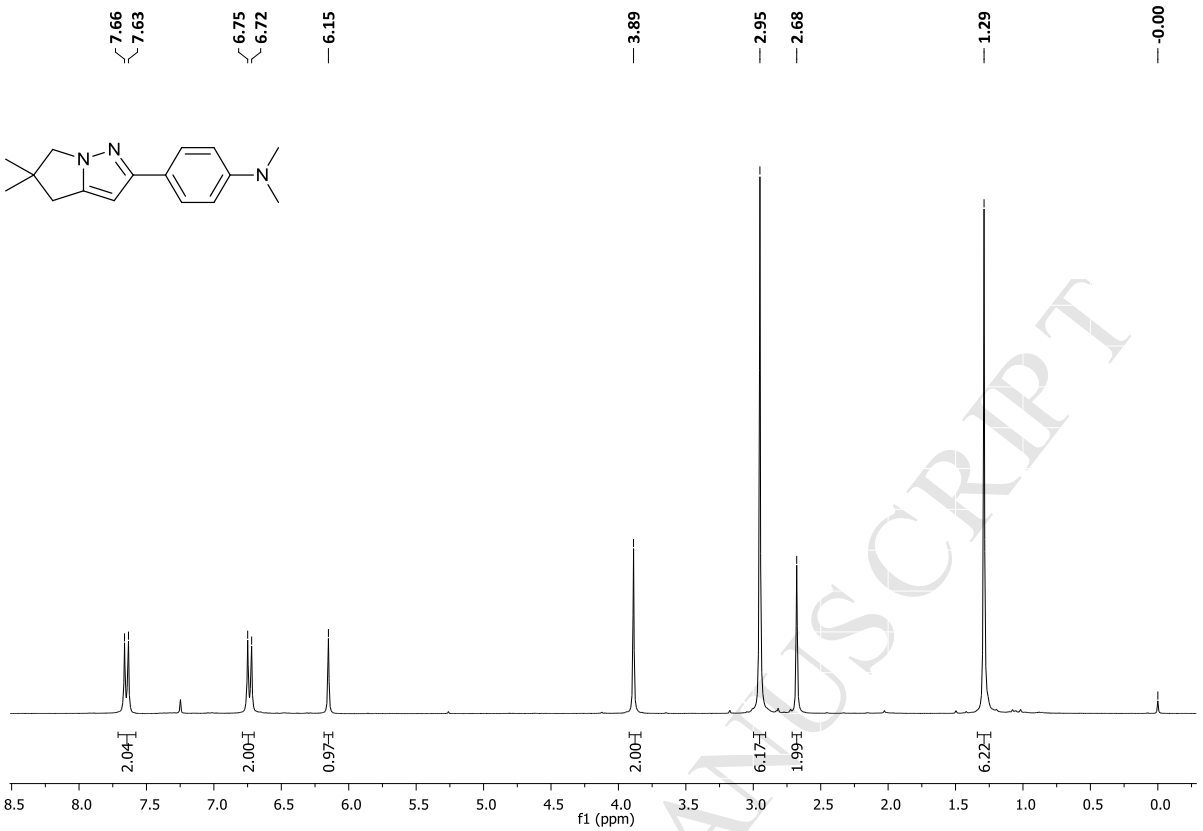


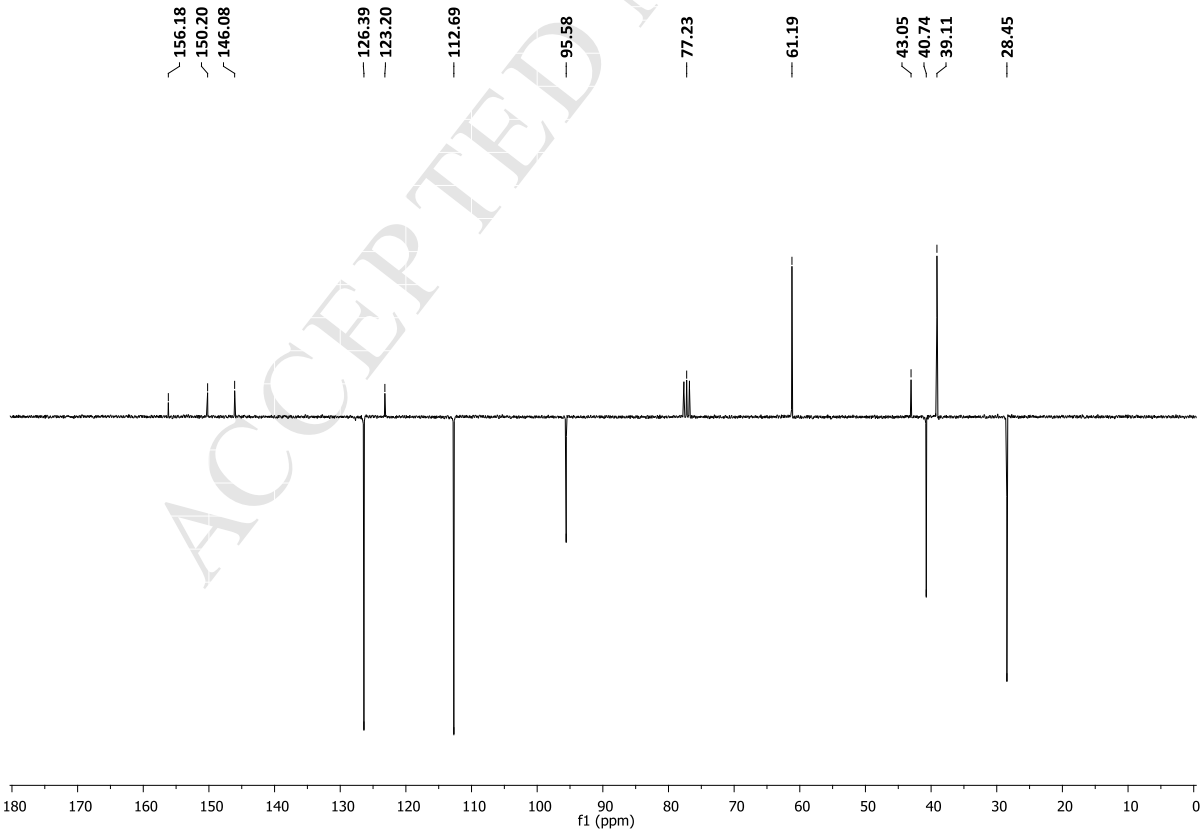


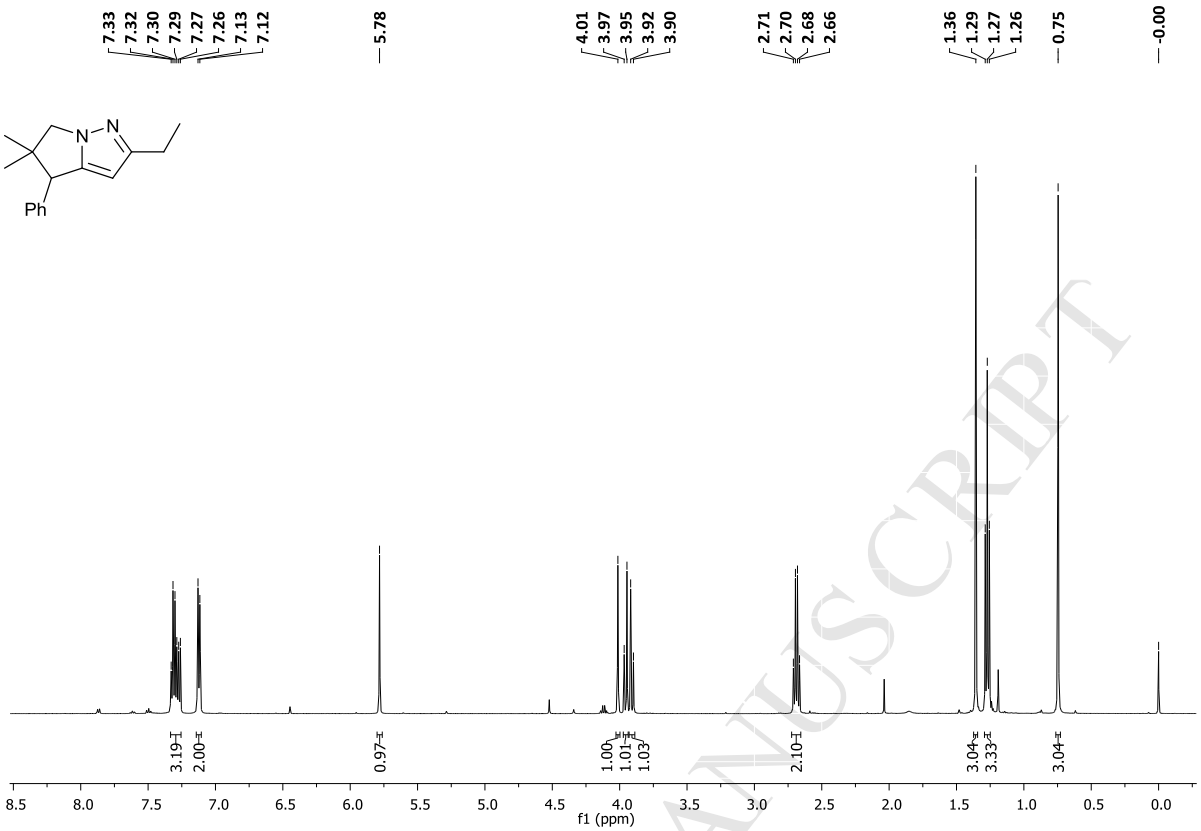


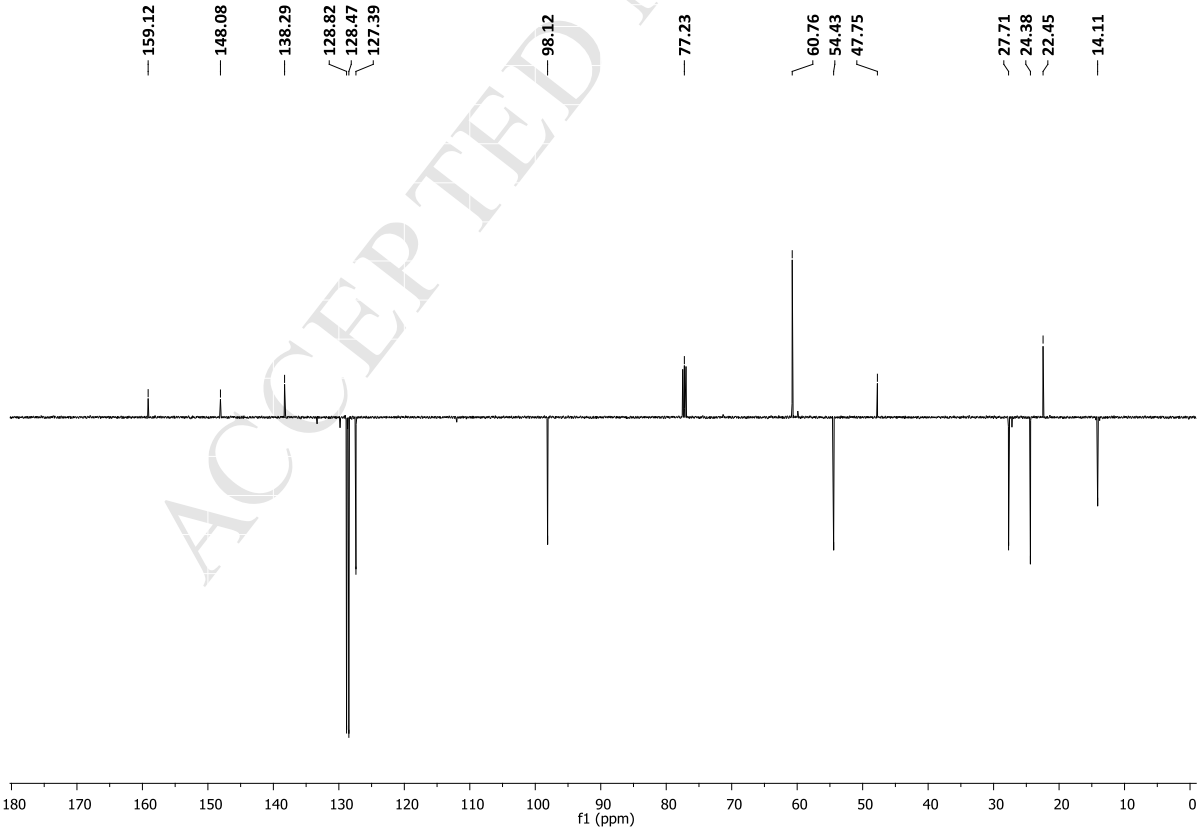


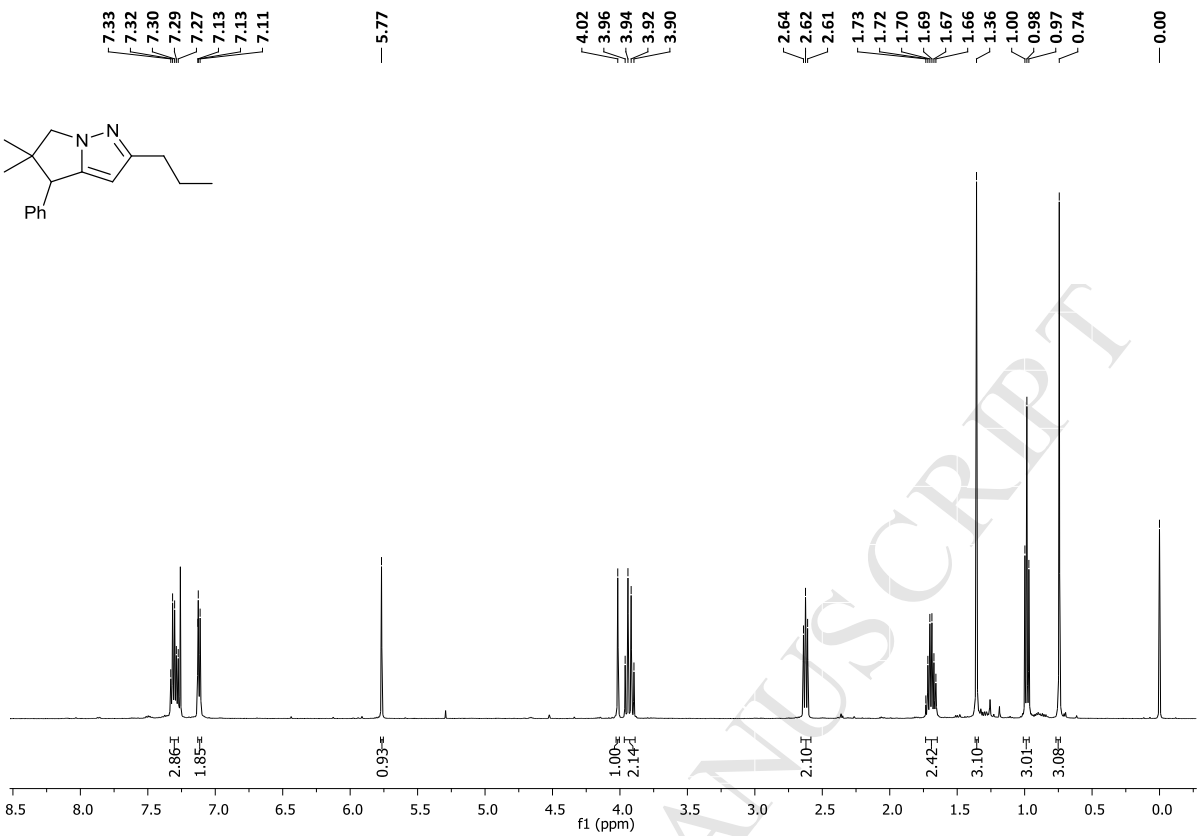


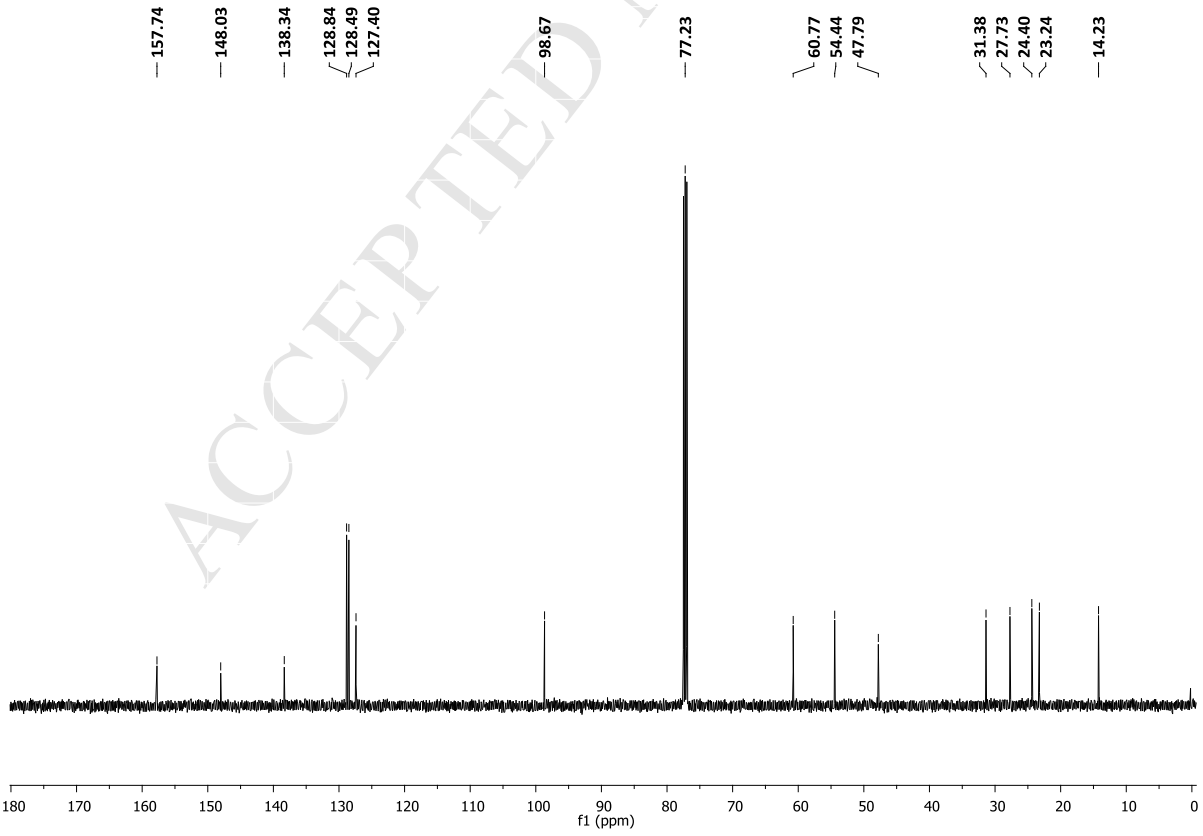


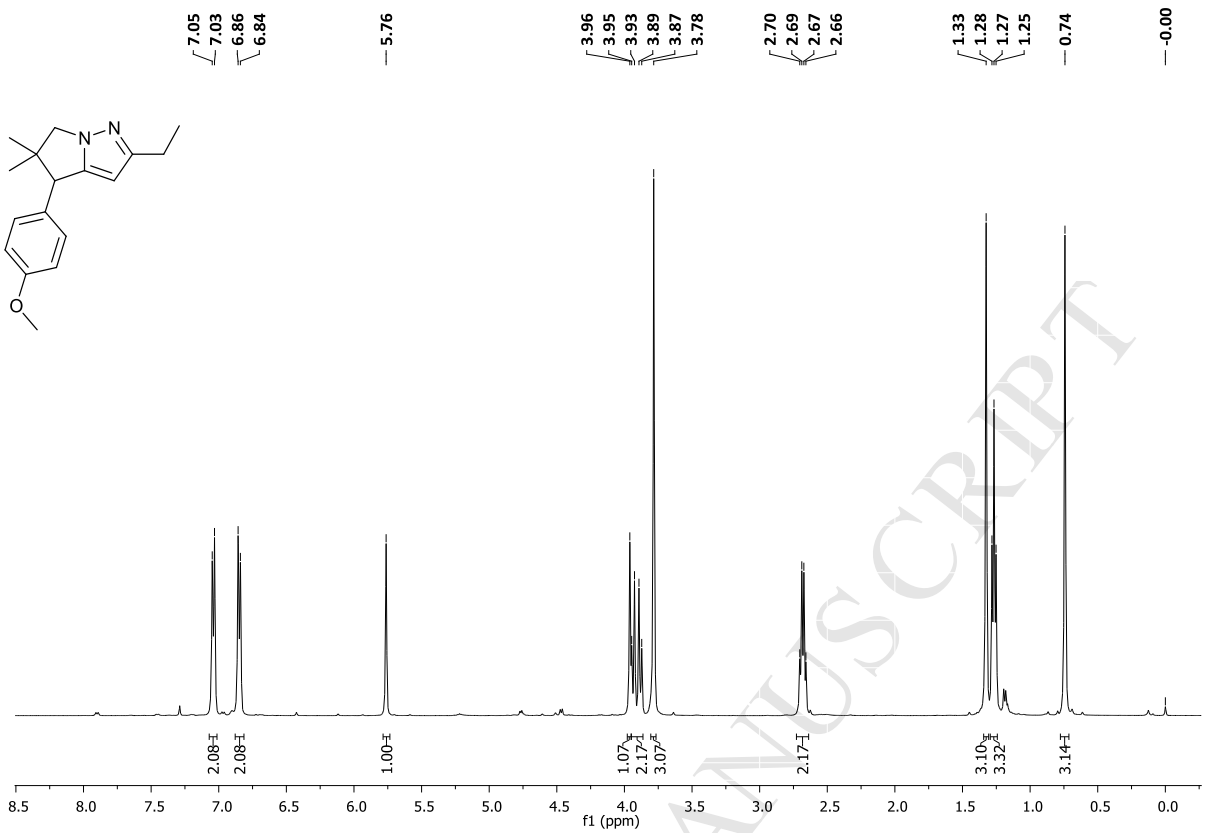


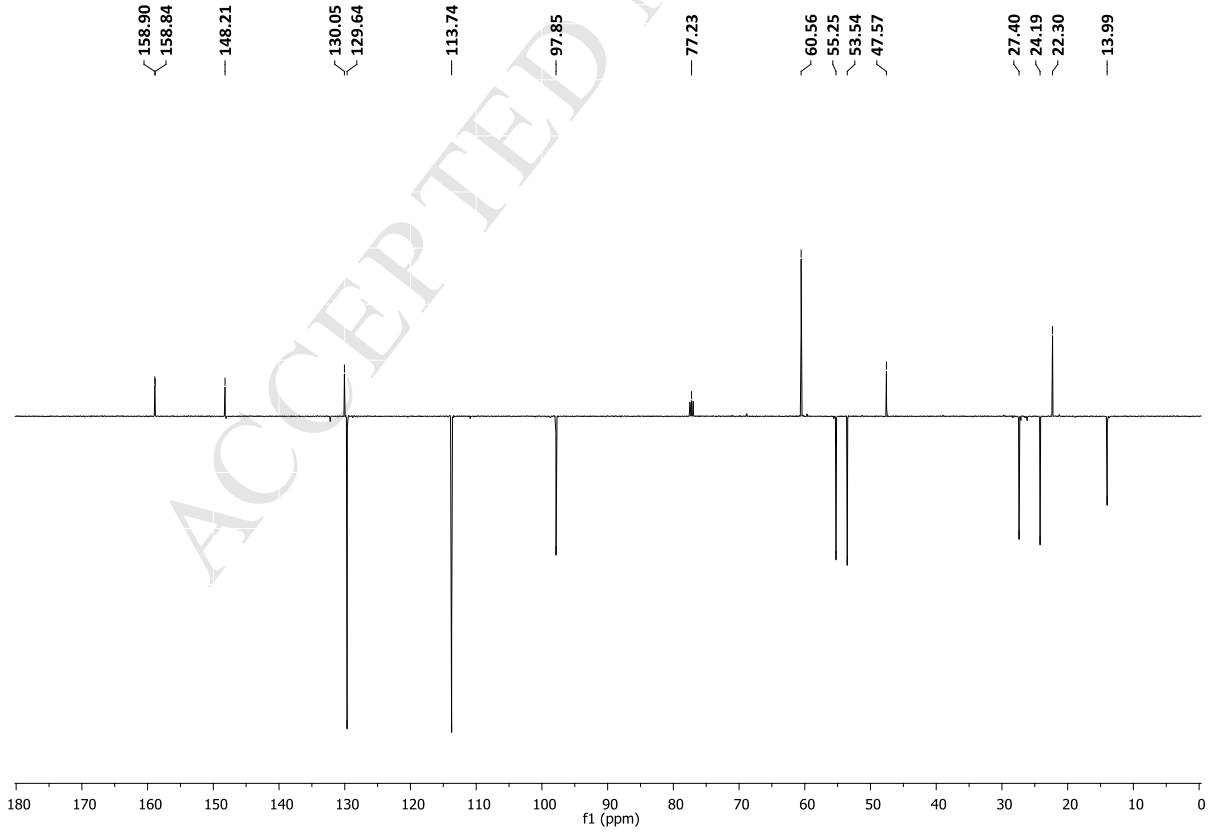


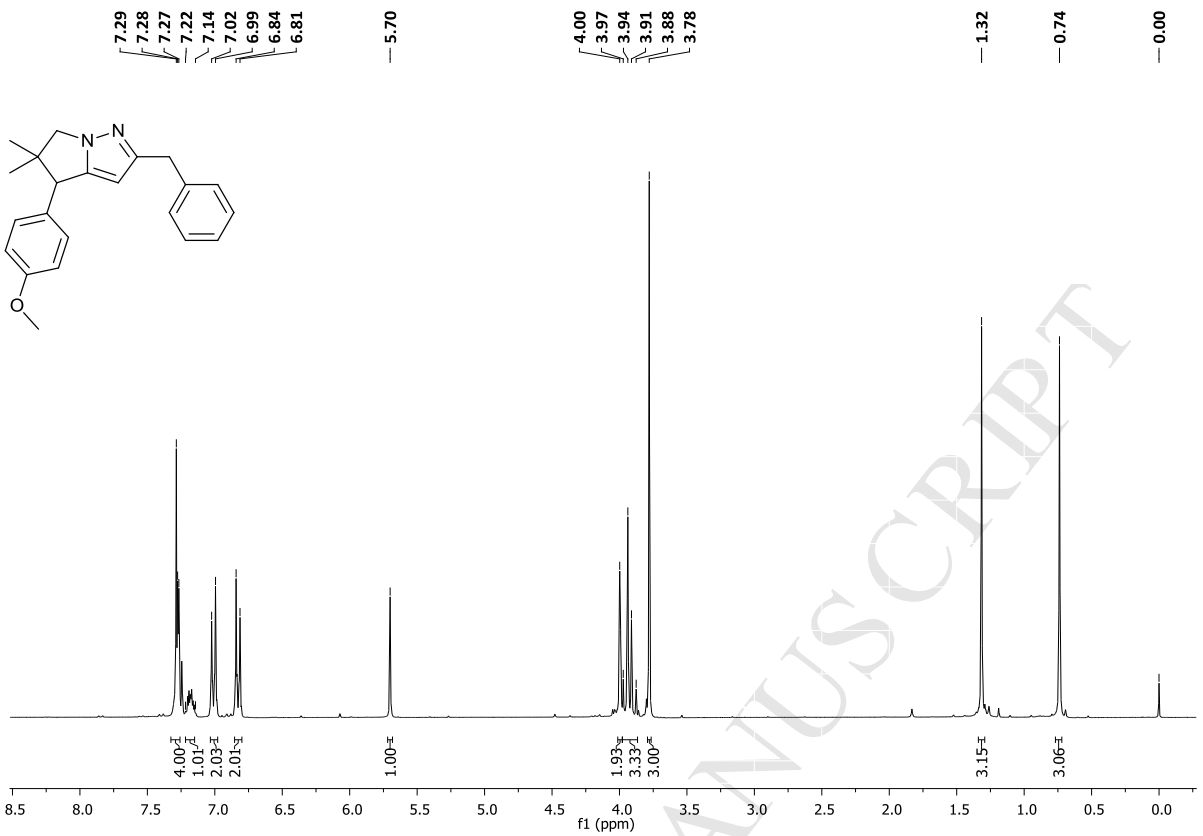


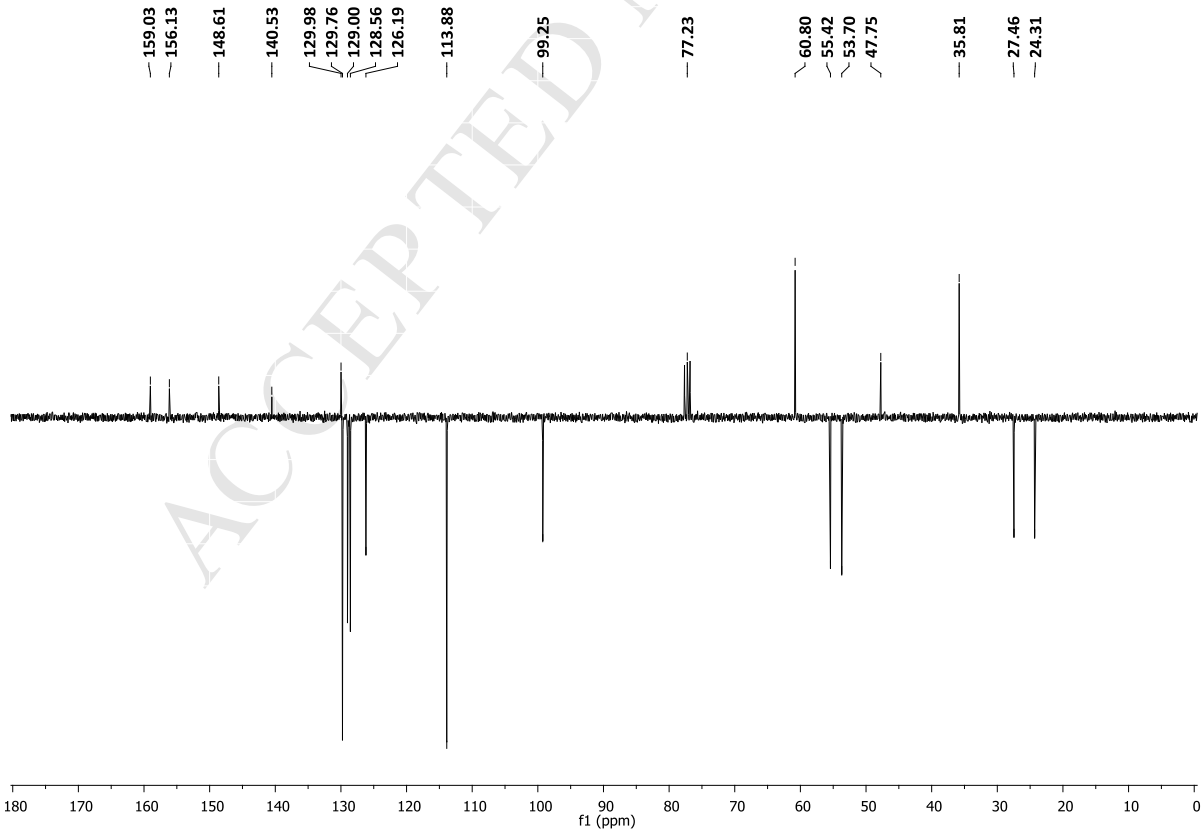


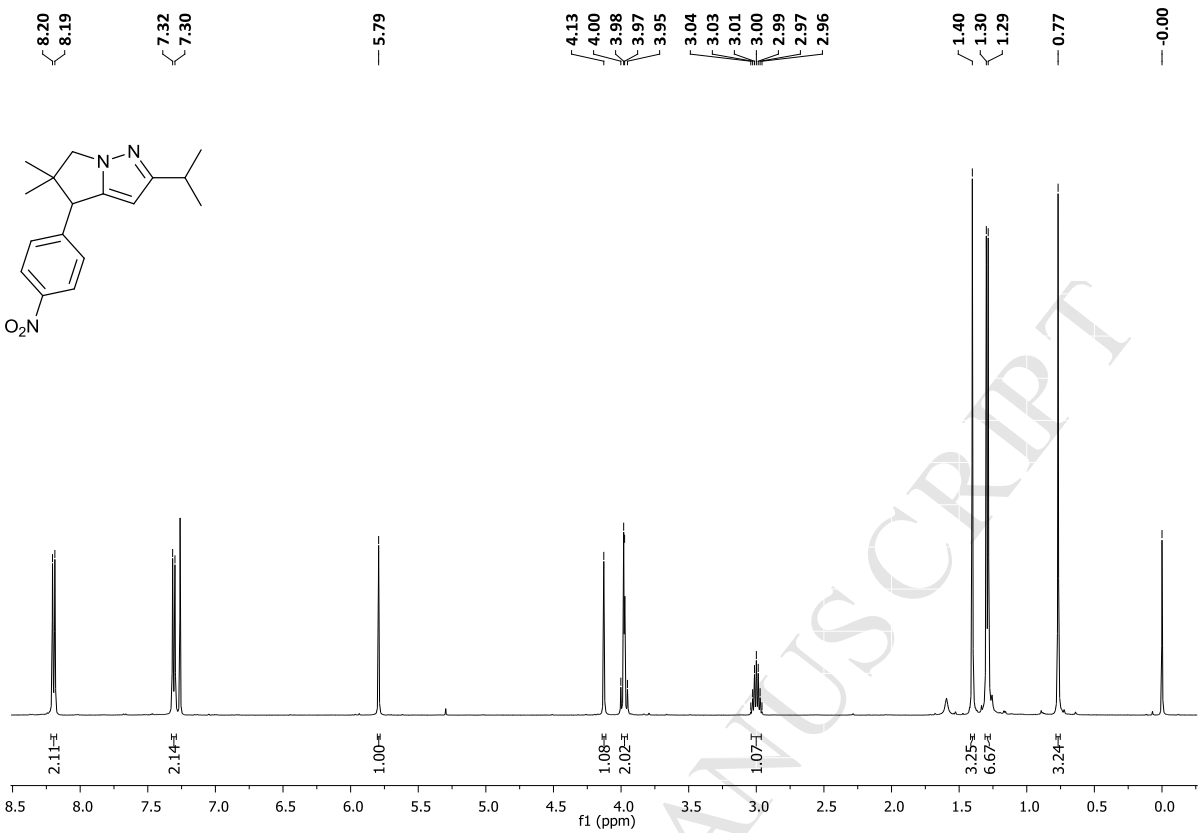


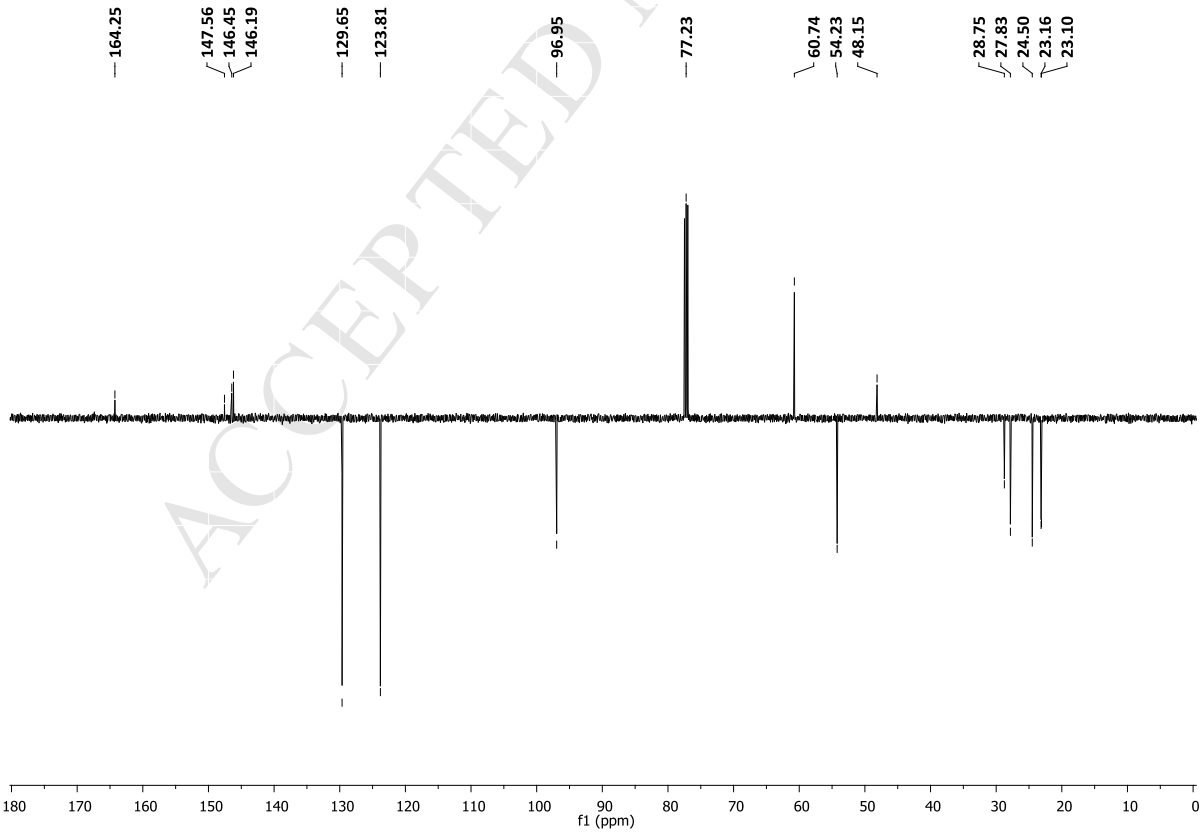


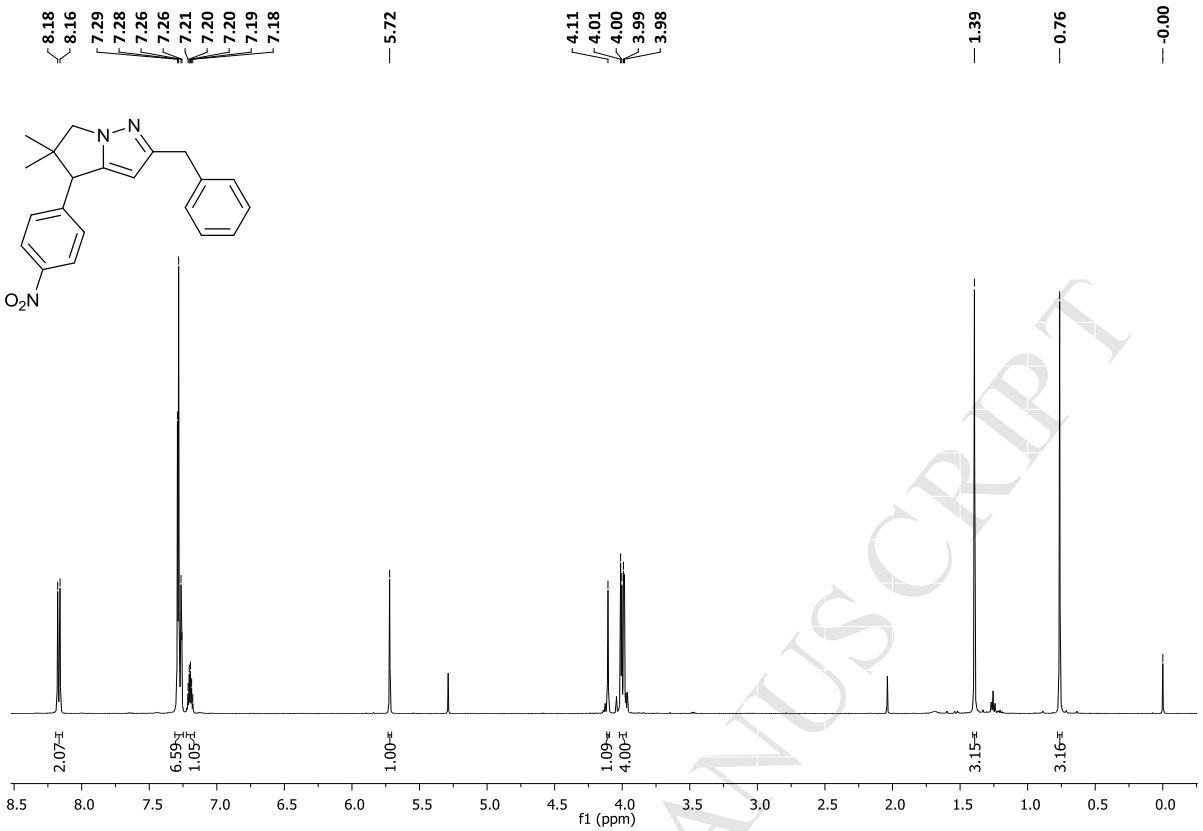


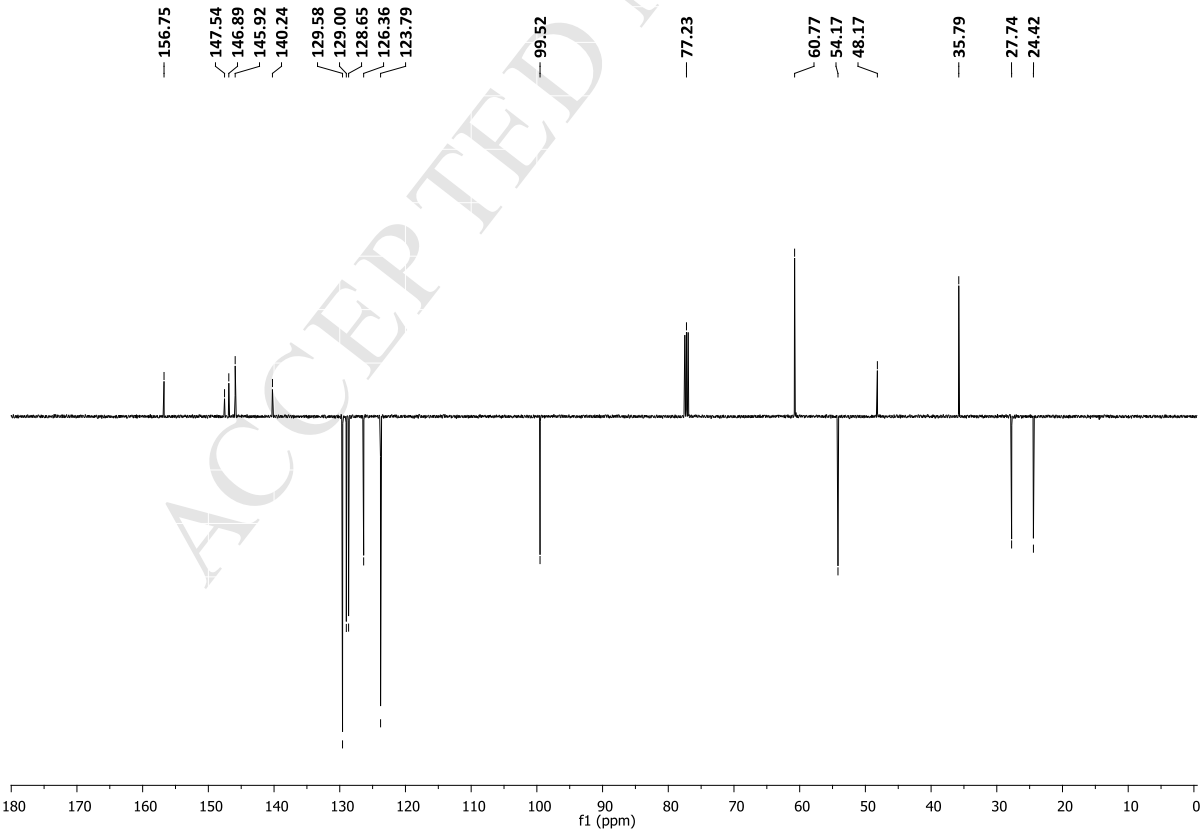


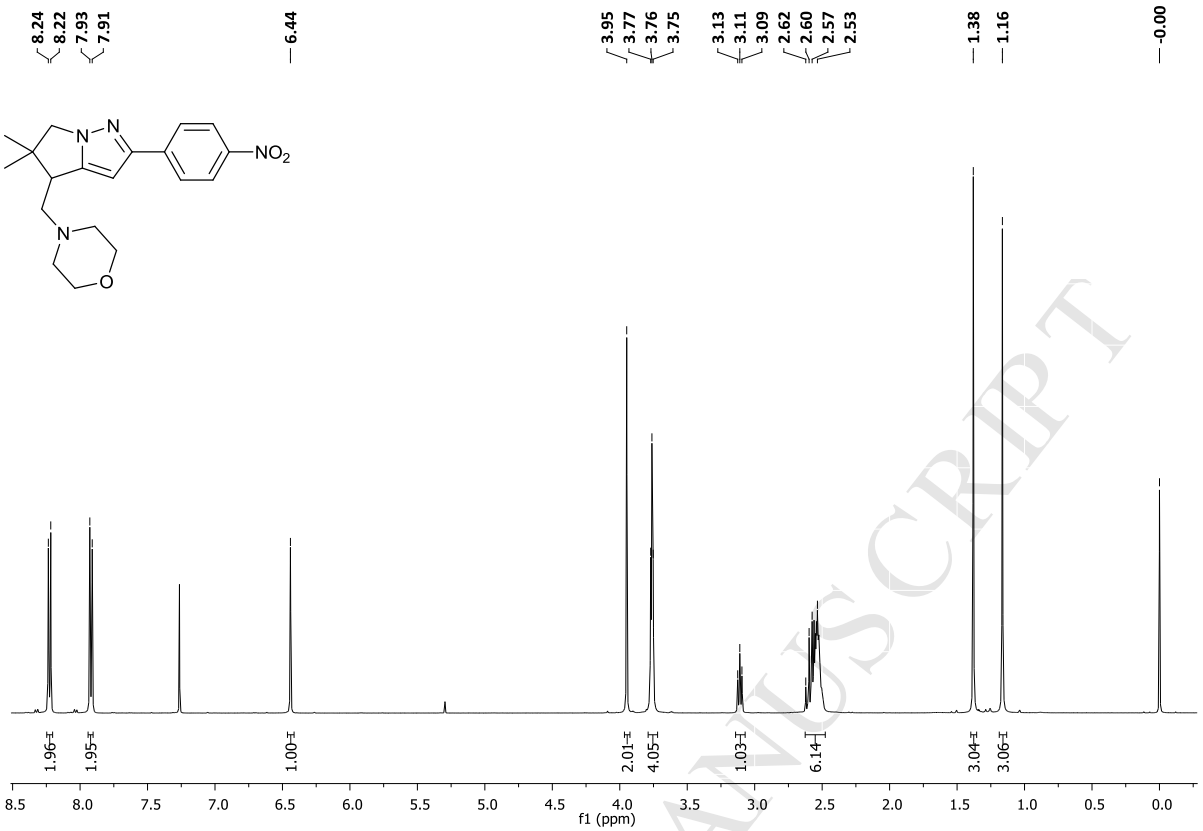


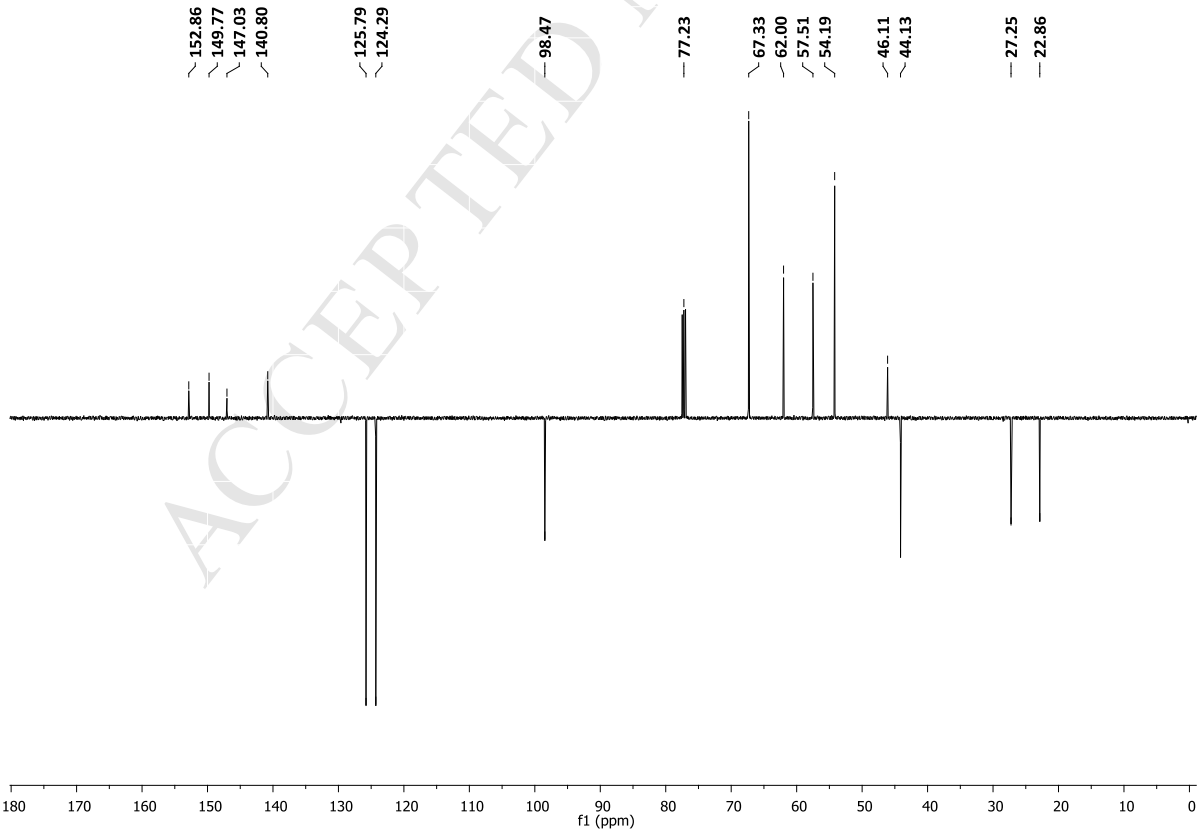


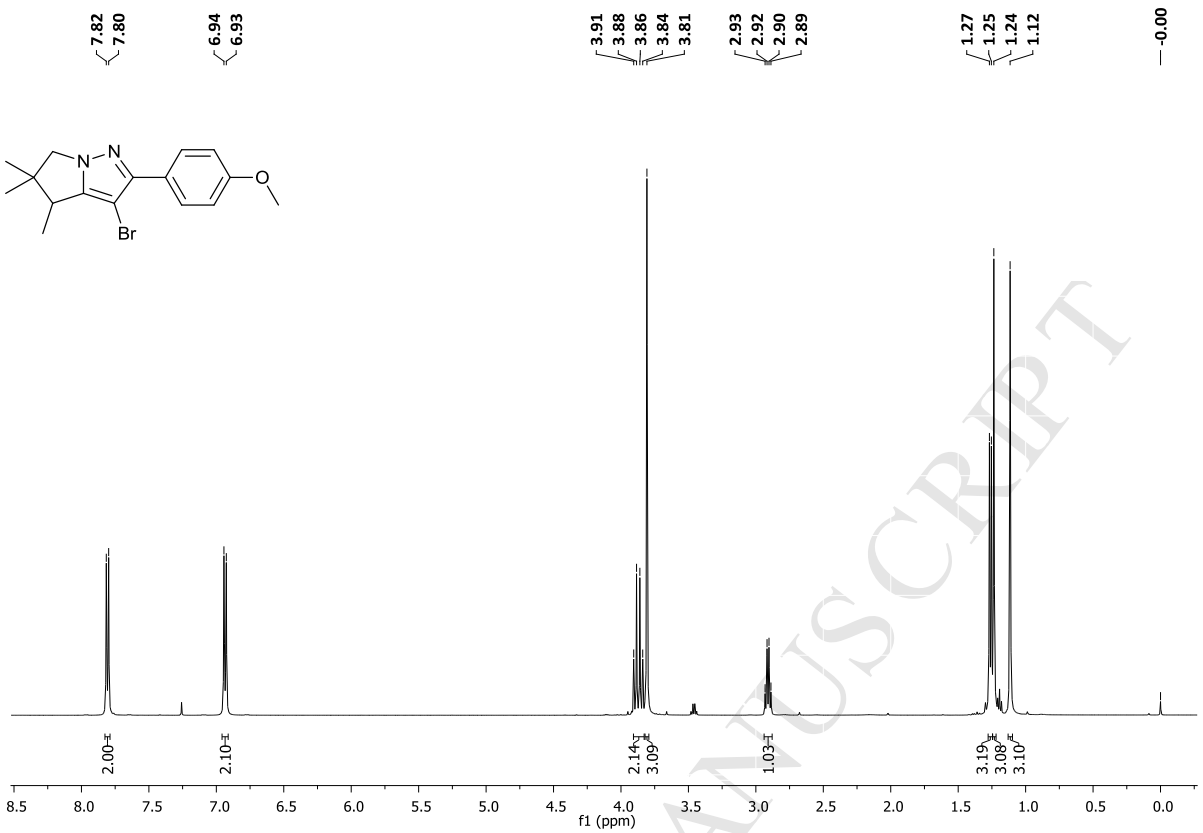


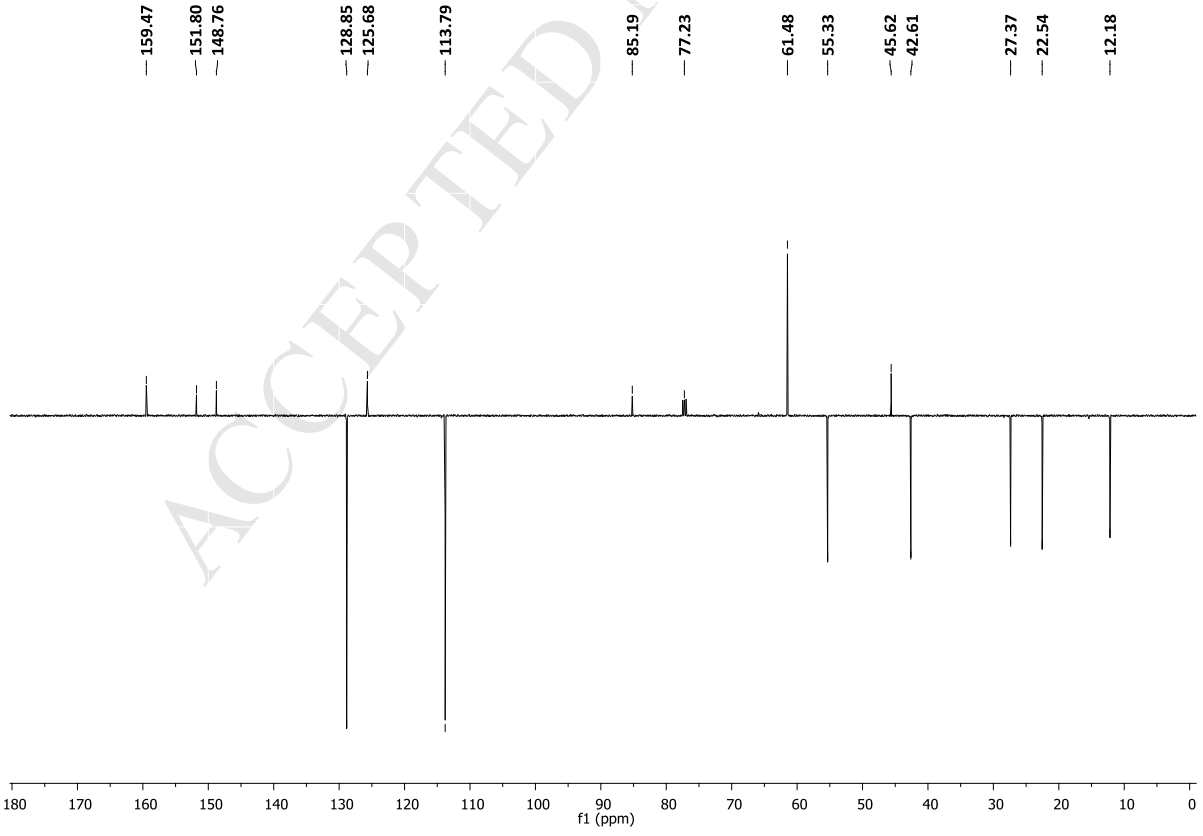


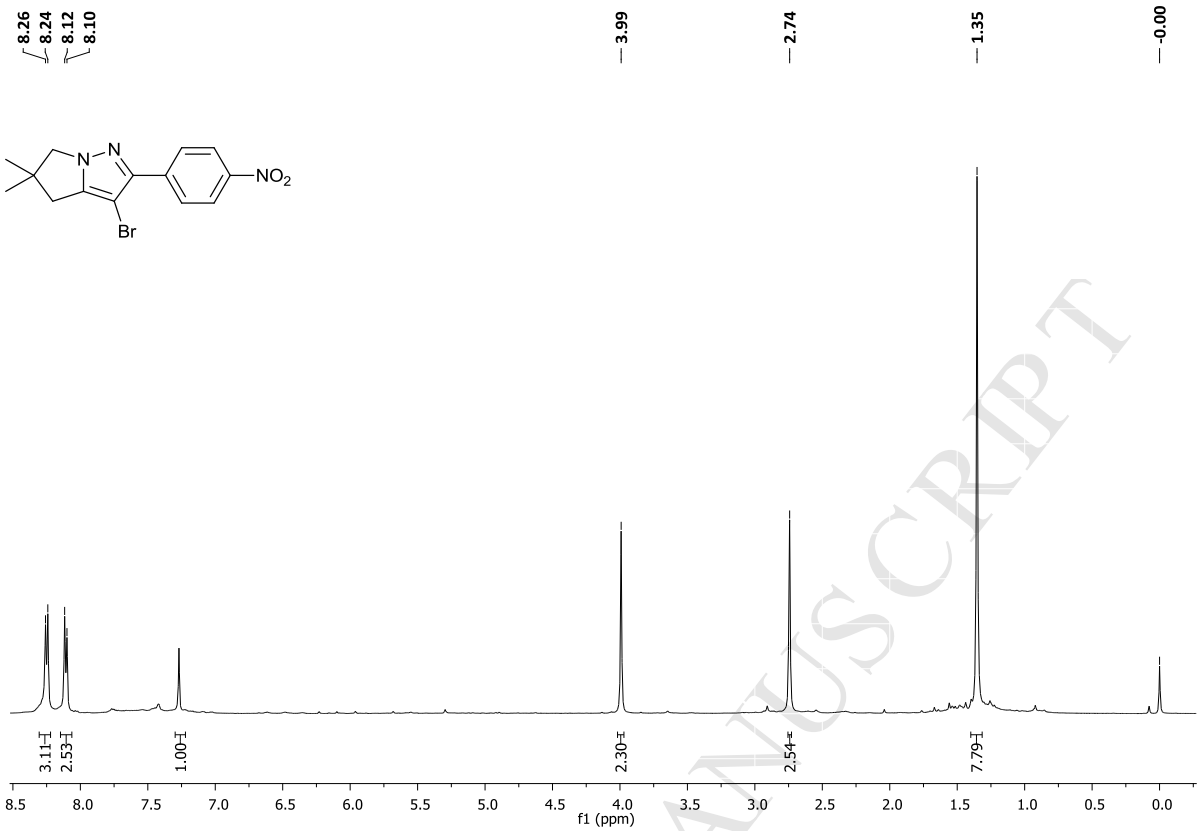


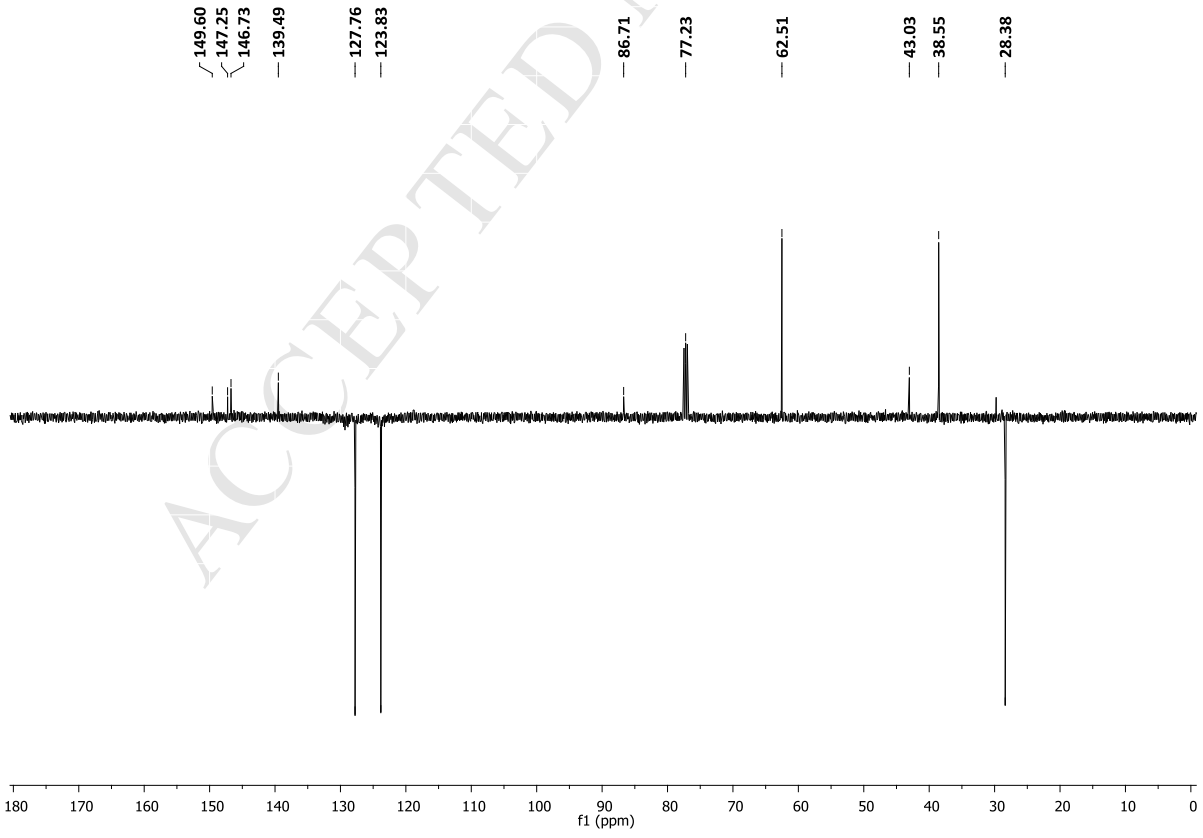


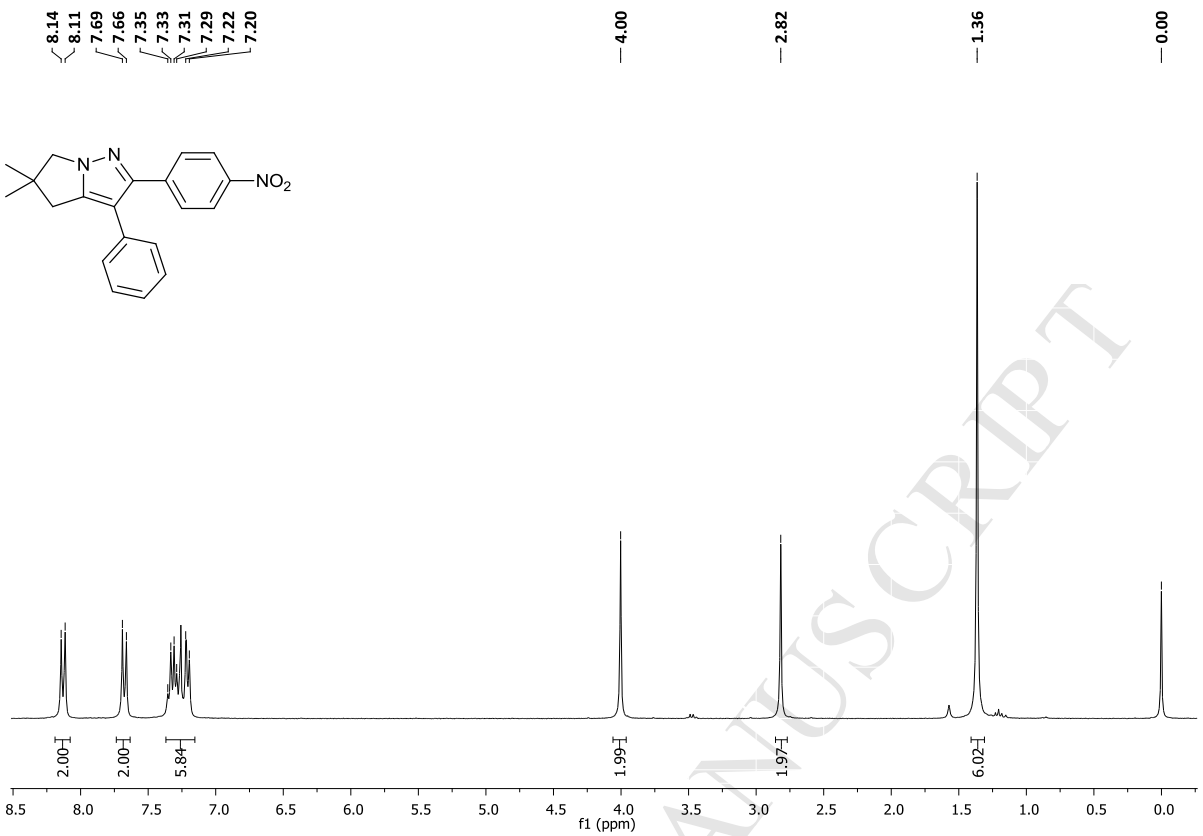


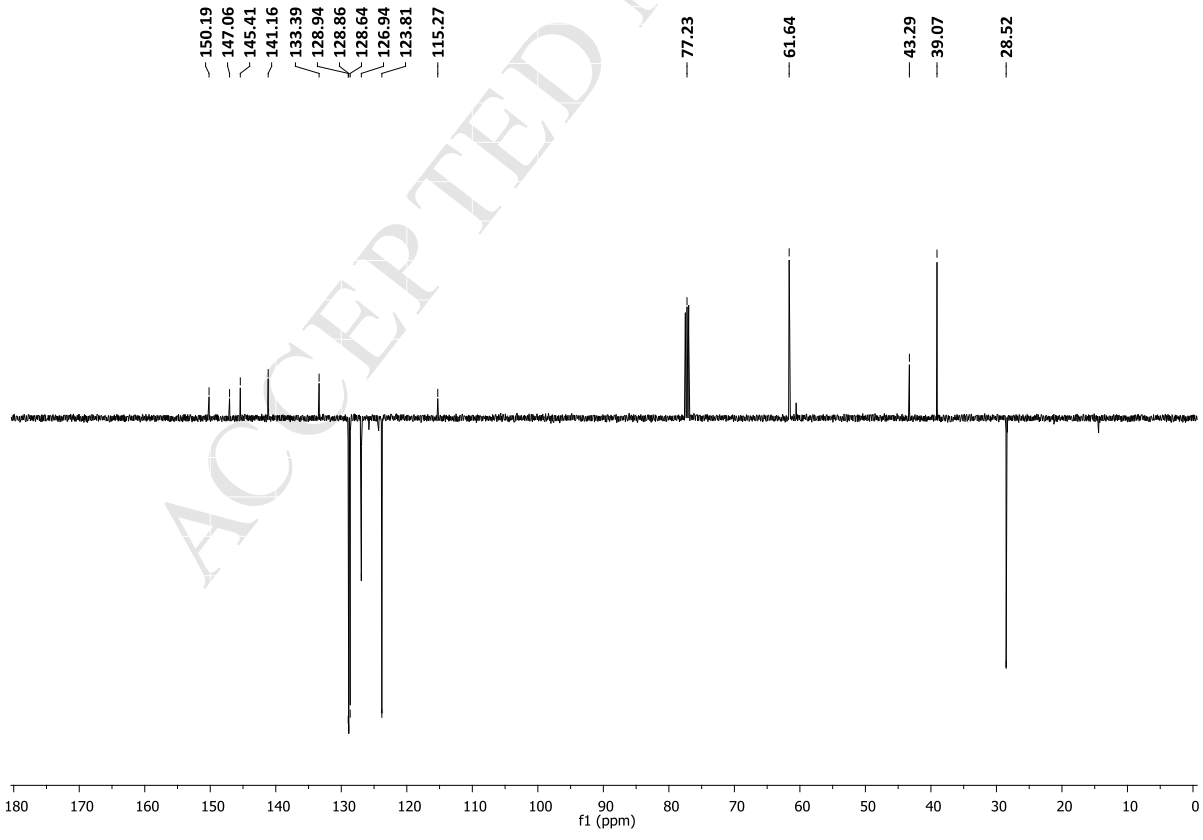






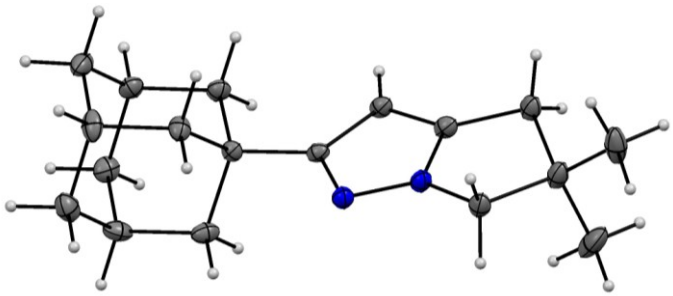




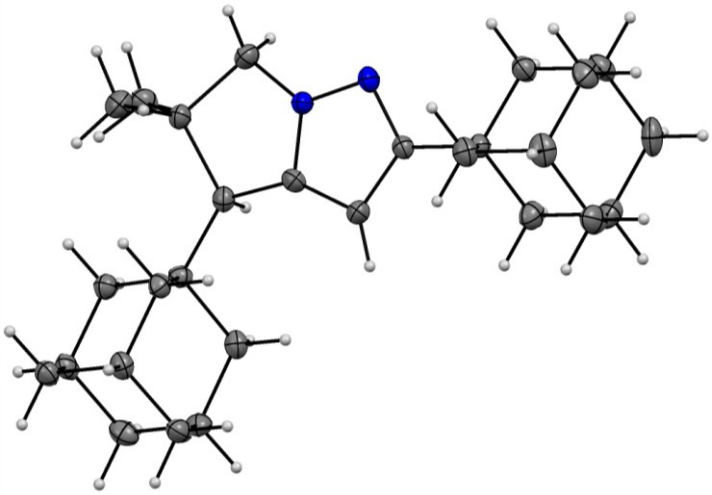


7. Crystal structures of **25af**,**ah**,**an**,**ba**,**bj**,**bp**

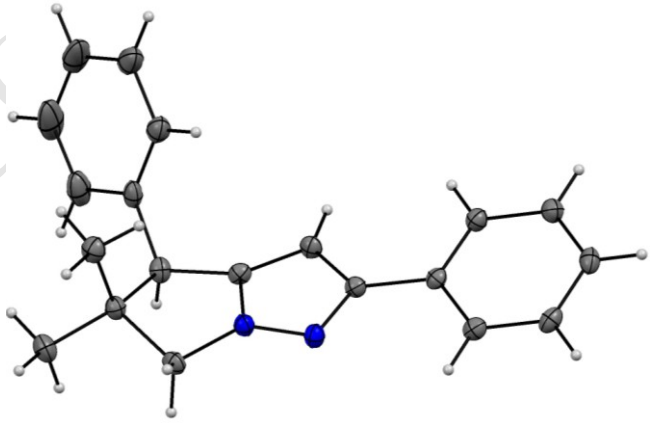
ORTEP representation of **25af** – CCDC 908394



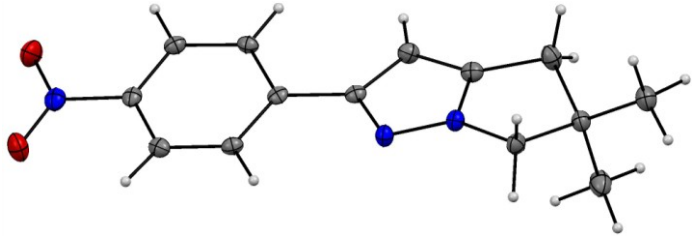
ORTEP representation of **25ah** – CCDC 908395



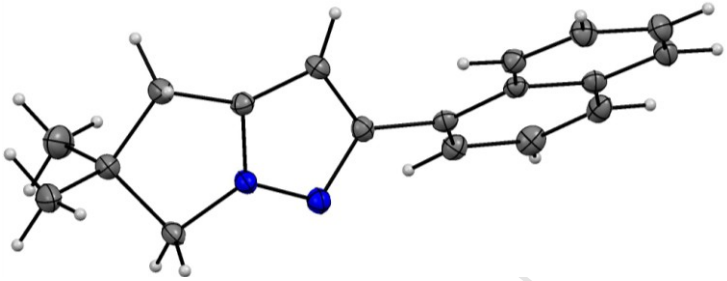
ORTEP representation of **25an** – CCDC 908397



ORTEP representation of **25ba** – CCDC 908398



ORTEP representation of **25bj** – CCDC 908400



ORTEP representation of **25bp** – CCDC 908402