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Synthesis of Methyl 3-(pyrrolidin-1-yl) acrylate and its Complexation with Organotin(IV)halides

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Abstract

Organotin compounds have been receiving increasing attention in inorganic and metal-organic chemistry due to their important industrial, pharmaceutical and environmental applications. These compounds have been found to exhibit wide-ranging biocidalactivities, such as fungicidal, miticidal, molluscicidal and are used as marine antifoulingagents, surface disinfectants and wood preservatives.The reactivity and applications of organotin derivatives are affected mainly by the number and nature of the C-Sn bonds. In the present work, enamines have been explored as a potential ligand for the synthesis of organotin(IV) complexes. The complexes were well characterized by IR, ^{1}H-NMR, ^{13}C-NMR,^{119}Sn- NMR. The proposed geometry of the synthesized complexes is octahedral.

INTRODUCTION

Organotin compounds

Organotin compounds have been receiving increasing attention in inorganic and metal-organic chemistry due to their important industrial, pharmaceutical and environmental applications. Also known as stannanes, these are chemical compounds having covalent bond between tin and hydrocarbon substituents. In these compounds, tin is generally present in II or IV oxidation states. Depending on the number of alkyl (R) or aryl (Ar) moieties, the organotin compounds are classified as mono-, di-, tri- and tetraorganotin(IV) compounds. The anion is usually chloride, fluoride, oxide, hydroxide, a carboxylate or a thiolate.[1] Although tin atom may exist either in the Sn^{2+} or in the Sn^{4+} oxidation state, almost all stable organotin compounds have a tetravalent structure because tin(II) compounds are readily oxidized to tin(IV) state. Solutions of tin(II) compounds that do not contain sufficiently strong electron-donor species are rapidly oxidized with atmospheric oxygen.[2] Depending upon the co-ordination number of the tin atom, tin(IV) complexes may have tetrahedral (four-co-ordinated), trigonalbipyramidal (five-coordinated) or octahedral (six-coordinated) geometry. The reactivity and applications of organotin derivatives are affected mainly by the number and nature of the C-Sn bonds.

Enamines

Enamines are the species generated in situ that have an amino moiety bonded to a doubly bonded carbon.Enamine is an unsaturated compound derived by the condensation of an aldehyde or ketone with a secondary amine.(as shown in scheme 1) They are versatile intermediates. The word enamine is derived from the affix en and the root of amine. Enamines are considered to be nitrogen analogs of enol. If one of the nitrogen substituents is a hydrogen atom then it is the tautomeric form of an imine. The enamine-imine tautomerism may be considered analogous to the keto-enoltautomerism. In both cases, a hydrogen atom switches its location between the nitrogen and the second carbon atom.

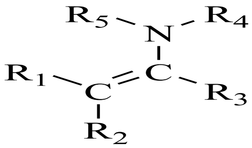
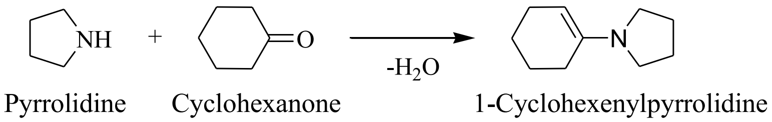


Figure 1.1 General structure of enamine



Scheme 1.1 Synthesis of 1-Cyclohexenylpyrrolidine

Enamines are both good nucleophiles and good bases. Their behavior as carbon-based nucleophiles is explained with reference to the following resonance structures.

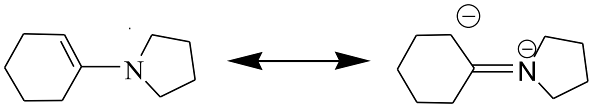


Figure 1.2 Resonating Structure of 1-Cyclohexenylpyrrolidine

They have also been shown to offer a greater selectivity with less side reactions. There is a gradient of reactivity among different enamine types, with a greater reactivity offered by ketone enamines than their aldehyde counterparts. Cyclic ketone enamines follow a reactivity trend where the five membered ring is the most reactive due to its maximally planar conformation at the nitrogen. This trend has been attributed to the amount of p-character on the nitrogen lone pair orbital- the higher p character corresponding to a greater nucleophilicity because the p-orbital would allow for donation into the alkene π- orbital. Analogously, if the N lone pair participates in stereoelectronic interactions on the amine moiety, the lone pair will pop out of the plane (will pyramidalize) and compromise donation into the adjacent π C-C bond. There are many ways to modulate enamine reactivity in addition to altering the steric/electronics at the nitrogen center including changing temperature, solvent, amounts of other reagents, and type of electrophile. Tuning these parameters allows for the preferential formation of E/Z enamines and also affects the formation of the more/less substituted enamine from the ketone starting material.

N lone pair donates effectively into the pi system

N lone pair cannot effectively interact with the pi system

Figure 1.3

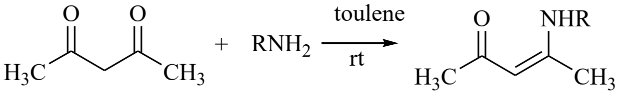
Enamines represent an important class of reactive intermediates in organic synthesis. They have high impacts as synthons for synthesis of various heterocyclic and biologically active analogues including anticonvulsant[3], anti-inflammatory (p-arylamidoacrylic acids)[4] and anti-tumor agents.[5] Enamines are frequently used as a potential building block to access several types of heterocyclic ring systems such as 1,4-dihydropyridines, pyrroles, oxazoles, pyridinones, quinolines, dibenzodiazepines, tetrahydrobenzoxazines, tetronic acids, azasteroids, (1H)-pyridin-2-one, pyrazolo-[1,5-α]- pyrimidine and isoxazole derivatives, which are well-known as anti-inflammatory, antitumor, antibacterial, and anti convulsant activities.[6] Realizing the wide spectrum of usage of enamines, there is a quest for the development of simple and high yielding process for the synthesis of various enamines.

2.REVIEW OF LITERATURE

Synthesis of enamines: Several methods were reported for the synthesis of enamines.

(1) Reaction of 1,3-dicarbonyl compounds with amines:

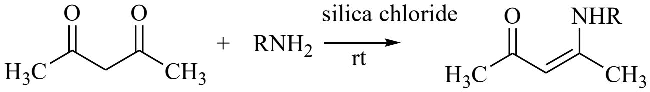
a) Reaction of 1,3-dicarbonyl compounds with amines in presence of solvent.[7] (Scheme 2.1)



pentan-2,4-dione 4-amino-3-penten-2-one

Scheme 2.1 Synthesis of 4-amino-3-penten-2-one

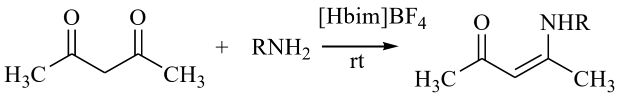
b) Reaction of 1,3-dicarbonyl compounds with amines in heterogeneous medium by using silica chloride.[8] (Scheme 2.2)



pentan-2,4-dione 4-amino-3-penten-2-one

Scheme 2.2 Synthesis of 4-amino-3-penten-2-one

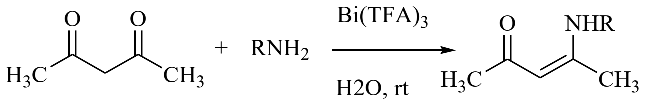
c) Reaction of 1,3-dicarbonyl compounds with amines by using ionic liquid.[8,9] (Scheme 2.3)



pentan-2,4-dione 4- amino-3-pentene-2-one

Scheme 2.3 Synthesis of 4-amino-3-penten-2-one

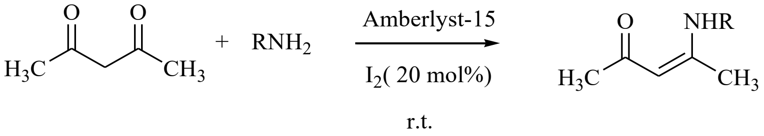
d) Reaction of 1,3-dicarbonyl compounds with amines by using bismuth catalyst[10] (Scheme 2.4)



pentan-2,4-dione 4-amino-3-penten-2-one

Scheme 2.4 Synthesis of 4-amino-3-penten-2-one

e) Reaction of 1,3-dicarbonyl compounds with amines by using Amberlyst-15 catalyst[11] or iodinecatalyst.[12] (Scheme 2.5)

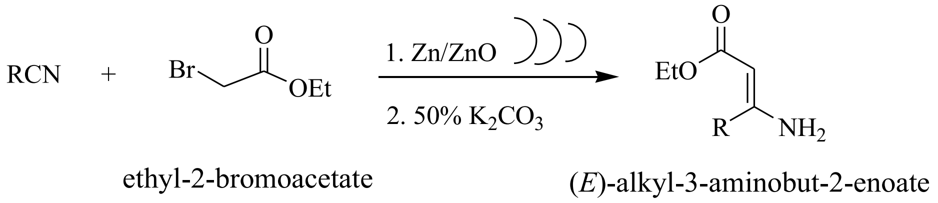


pentan-2,4-dione 4-amino-3-penten-2-one

Scheme 2.5 Synthesis of 4-amino-3-penten-2-one

(2) From nitriles by sonochemical method

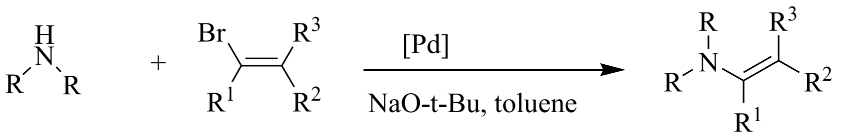
Enamines have also been obtained from nitriles on reaction with α-bromoester in presence of zinc/zinc oxide powder under sonochemical conditions.[13] (Scheme 2.6)



Scheme 2.6 Synthesis of (*E)*-alkyl-3-aminobut-2-enoate

(3) By coupling reaction

Barluenga et al. reported first time on the cross-coupling of alkenyl bromide and non-aromatic secondary amines leads to the enamines.[14] (Scheme 2.7)



Scheme 2.7 Synthesis of Enamine

Complexation of Enamine with organotin(IV) halides

Enamines have also been used as ligands for the complexation with various metals. However, very few reports have been obtained regarding the complexation. The literature survey shows that the mode of coordination to metal is either through nitrogen or through the π–system of the carbon–carbon double bond.[15]

Enamines have been used to form volatile chelate metal complexes with $PdCl_2$ in amine medium to form palladiuim*β*-ketoiminate.[16]

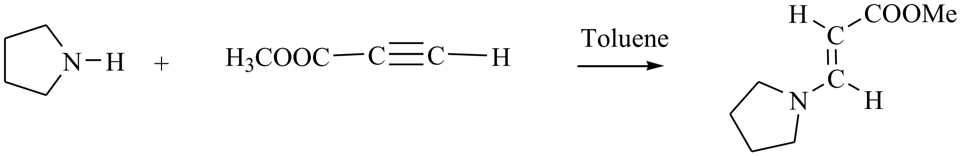
Mazzarella*et. al.*,[15] used a secondary enamines as ligands and synthesize various complexes with group (VIII) metals i.e. Fe(II), Co(II), Ni(II). In these complexes, the donor atoms are enaminic nitrogen and no coordination through carbon. The coordination geometry around the metal atom was found to be octahedral.

Some palladium(II) and platinum(II) complexes with enamine have also been reported where the enamine ligand is coordinated to the metal centre through nucleophilic carbon atom of enamineand represent monodentatebehavior of enamine.[17]

Huo*et. al*.,[18]prepared an octahedral iridium(III) complexes. In these complexes asymmetric enamine/ H- bonding dual activation catalyst nature was observed.

3. OBJECTIVES

1. To synthesize methyl-3-(pyrrolidin-1-yl)acrylate from pyrrolidine and methyl propiolate.[19] (Scheme 3.1)



1

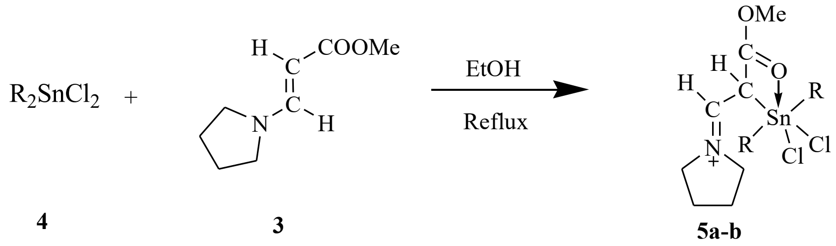
2

3

Pyrrolidine methyl propiolate methyl 3-(pyrrolidin-1-yl)acrylate

Scheme 3.1 Synthesis of methyl 3-(pyrrolidin-1-yl)acrylate

2. To synthesize the co-ordination complexes of methyl-3-(pyrrolidin-1-yl)acrylate with organotin(IV) halides. (Scheme 3.2)



R= Cl, Ph methyl 3-(pyrrolidin-1-yl)acrylate

2-(methyl 3-(1-pyrrolidino)acrylato) dialkyltin(IV)dichloride

5a-b	a	b
R	Cl	Ph

Scheme 3.2 Reaction of tin(IV) halides with methyl 3-(pyrrolidin-1-yl)acrylate.

3. To characterize the products by IR, ^{1}H NMR, ^{13}C NMR, and ^{119}Sn NMR techniques

4.METHOLODOGY

4.1Materials

Pyrrolidine, methyl propiolate and tin(IV) chlorides were purchased from Sigma Aldrich and were used as such. Enamine was prepared according to the published method.Solvents were dried by standard methods and all reactions were carried out under anhydrous conditions in nitrogen atmosphere in oven-dried glasswares.

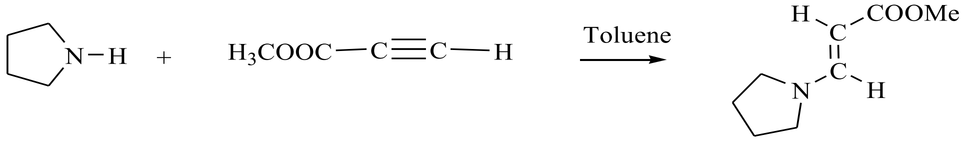
4.2 Instrumentation

Melting points were determined on a Paramount apparatus. The IR spectra were scanned on AGILENT Tech, CARY660 spectrometer using KBr pellets. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-300 NMR spectrometer at 300.00 MHz/400 MHz frequency respectively in DMSO-d_6 using TMS as internal reference. The ^{119}Sn NMR spectra were recorded on a BrukerAvance II 400 NMR spectrometer at 149.12 MHz in DMSO using $SnMe_4$ as external reference.

4.3 General Procedure

4.3.1 Synthesis of methyl 3-(pyrrolidin-1-yl)acrylate

A solution of methyl propiolate (5.6 mmol 0.5 mL in 10mL toluene) was taken in a 100 mL R.B. flask and cooled to 0° C. To it was added a solution of pyrrolidine (5.6 mmol 0.5 mL in 5 mL toluene) dropwise with continuous stirring and the whole reaction mixture was maintained at 0° C, where by an intense yellow color developed. The reaction was completed in 2–3 hrs [monitored by TLC [solvent/EtOAc/hexane, 50:50 v/v %].



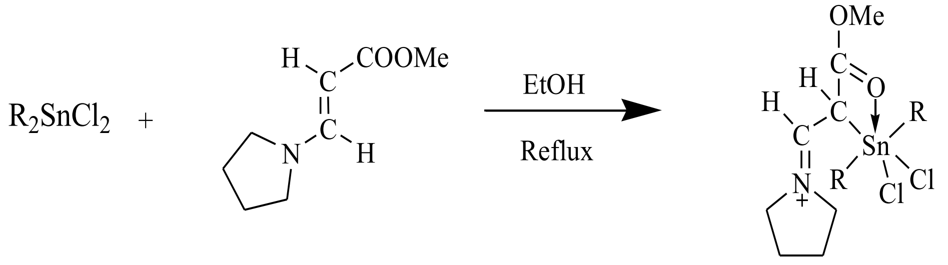
1 **2** **3**

Pyrrolidine methyl propiolate methyl 3-(pyrrolidin-1-yl)acrylate

Scheme 4.3.1 Synthesis of methyl 3-(pyrrolidin-1-yl)acrylate

4.3.2 Reaction of tin(IV) halides with methyl 3-(pyrrolidin-1-yl)acrylate

To an ethanolic solution of tin(IV) halide (in 10 mL ethanol) taken in a 100 mL RB flask was added a solution of enamine (in 5 mL ethanol) slowly with constant stirring. The mixture was stirred at r.t. for about 30 min. followed by refluxing for 3 hrs under anhydrous conditions. A clear solution resulted which was concentrated to about half the volume and left in the refrigerator (~ -20°C) overnight. Solid product deposited which was separated, washed with a small volume (~ 2 mL) of cold ethanol and dried. The mother liquor on concentration and cooling afforded a second crop of the product.



4 3 5a-b

R= Cl, Ph methyl 3-(pyrrolidin-1-yl)acrylate

2-(methyl 3-(1-pyrrolidino)acrylato) dialkyltin(IV)dichloride

5a-b	**a**	**b**
R	Cl	Ph

Scheme 4.3.2 Reaction of tin(IV) halides with methyl 3-(pyrrolidin-1-yl)acrylate.

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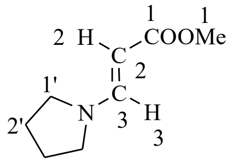
5.RESULTS AND DISCUSSION

able 5.1 physical data for the compounds.

Coco ound	**Molecular formula**	**Yield (%)**	**Color**	**Appearance**	**Melting Point**
3	$C_8H_{13}NO_2$	91	pale yellow	Solid	119-120 ^{0}C
5a	$C_8H_{13}NO_2SnCl_4$	66	white	Solid	135-136 ^{0}C
5b	$C_{20}H_{23}NO_2SnCl_2$	61	white	Solid	194-195 ^{0}C

Table 5.2 Spectral data of the compounds 3, 5a-b



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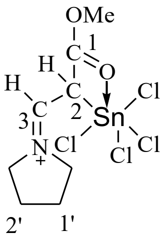
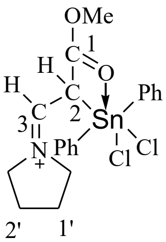


5a



5b

Compound	**IR**ν_{max} (cm^{-1})	^{1}**H NMR** (δ= ppm, *J*= Hz) (DMSO-d_6, δ= ppm, *J*= Hz)	^{13}**C NMR** (δ= ppm) (DMSO-d_6, δ= ppm)	^{119}**Sn NMR** (DMSO-d_6, δ= ppm)
3	1150(C-O)$_{str.}$ 1691(C=C)$_{str.}$ 1597(C=O)$_{str}$	δ 7.57(d,$^{3}J_{HH}$=12.9, 1H, H-3), δ 4.33(d,$^{3}J_{HH}$=12.9, 1H,H-2), δ 3.49(s, 3H, -OCH$_3$), δ 3.02(t, J=5.2 Hz, 4H, H-1′), δ 1.84(t, J=5.2 Hz, 4H, H-2′)	---	---
5a	1041(C-O)$_{str.}$ 1729(C=O)$_{str.}$ 546(Sn-C)$_{str}$	δ 8.56(b, unresolved doublet, 1H, H-3), δ 4.31(d,$^{3}J_{HH}$=6.8, 1H,H-2), δ 3.86(s, 3H, -OCH$_3$), δ 3.39(t, J=6.8 Hz, 4H, H-1′),	164.5(C=O), 133.9(C3), 56.6(OCH$_3$), 45.4(C1′), 24.2(C2′)	- 623.93, - 666.97

δ 0.99(t, J=6.8 Hz, 4H, H-2′)

5b δ 8.56(b,unresolved doublet, 1H, H-3), 169.0(C=O), 149.3(C3),

- 391.93

--- δ 4.33(d,$^{3}J_{HH}$=3.2, 1H,H-2), 127.6(Ph), 83.6(OCH_3),

δ 3.88(s, 3H, $-OCH_3$), 45.0(C1′), 24.6(C2′)

δ 3.43(t, 4H, H-1′),

δ 1.01(t, J=6.8 Hz, 4H, H-2′)

5.3 Spectral Characterization

IR

The ligand (enamine) **3** exhibit strong C=O stretching vibration absorption band at 1597 cm^{-1} and C-O group stretching vibration absorption bands are observed in the expected region of 1150-1100 cm^{-1}.While in organotin complexes, **5a-b** C=O stretching vibration absorption band shifts to higher frequency at 1729 cm^{-1} due to higher double character of C=O bond. This substantial increase in υ(C=O) stretching frequency confirms the coordination through the carbonyl oxygen. C-O stretching vibration in complexes are observed at 1080-1041 cm^{-1}.

^{1}H NMR

In ligand (enamine) **3**, H2 and H3 gives doublet at δ 7.57 and 4.33 ppm respectively. Those two protons shows vinylic coupling. Protons of methoxy group (OCH_3) gives a singlet at δ 3.49 ppm. Proton H-1′ and H-2′ shows triplet at δ 3.02 and 1.84 ppm respectively.

A remarkable feature of the ^{1}H NMR spectrum of the tin(IV) complexes **5a-b**, is broadening and downfield shifting of the signal of the vinylic proton. It indicates that the enamine acts as a bidentate ligand and forms chelate with Sn(IV) atom by co-ordinating through the carbonyl oxygen atom. The chemical shift of the other protons remain almost unaffected.

^{13}C NMR

In ^{13}C NMR of complex **5a-b**, the carbonyl carbon C=O gives a signal at δ 169.0-164.5 ppm. In **5b**, C2 is shielded due to conjugation of the lone pair of nitrogen and hence resonates upfield as compared to the C3 and the signal appears atδ 149.3-133.9 ppm. In the case of **5a-b** carbon 1′ and carbon 2′gives signal at δ 45.4 ppm and δ 24.6-24.2 ppm respectively.

^{119}Sn NMR

^{119}Sn NMR is strongly dependent on the coordination number of the tin atom and an increase in the co-ordination number produces a large upfield shift. The ^{119}Sn NMR spectra of the synthesized complexes **(5a-b)** exhibit two sharp peaks in the region -391.93 to -666.97 ppm as shown in Table 5.2. These values indicate hexa-coordination of the Sn atom.

The presence of two ^{119}Sn NMR peaks indicates that probably there exists a fluxional type of co-ordination between enamine and the tin atom resulting from pseudorotation (as shown in Figure 5.3.1).

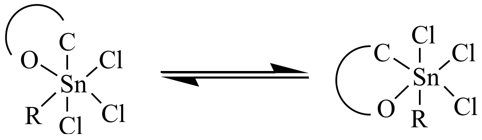
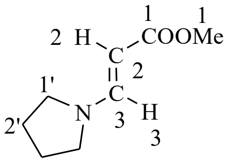


Figure 5.3.1



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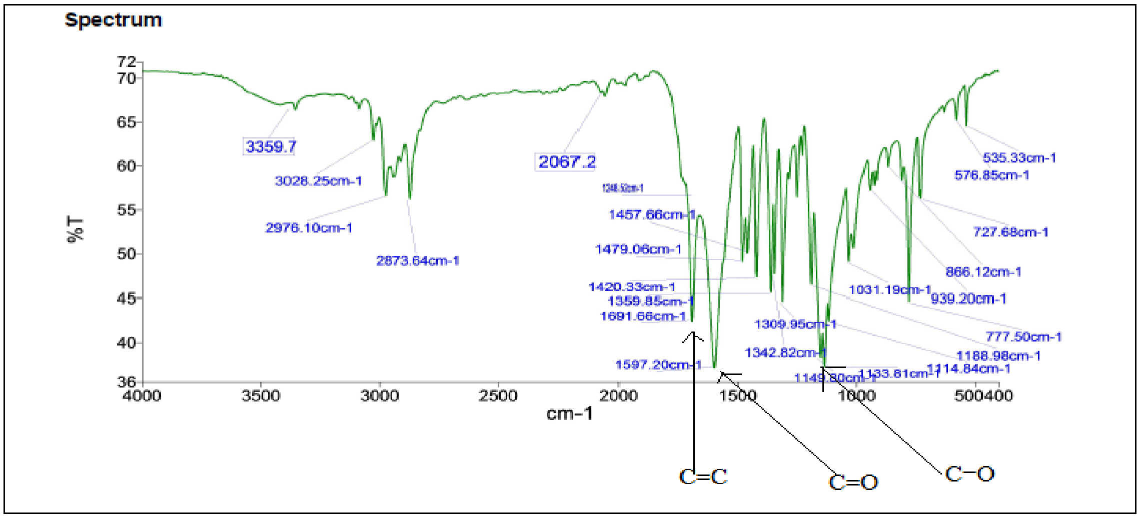
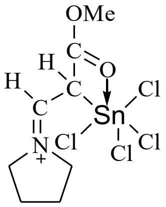


Figure 5.3.2 The IR spectrum of methyl 3-(pyrrolidin-1-yl)acrylate**(3)**.



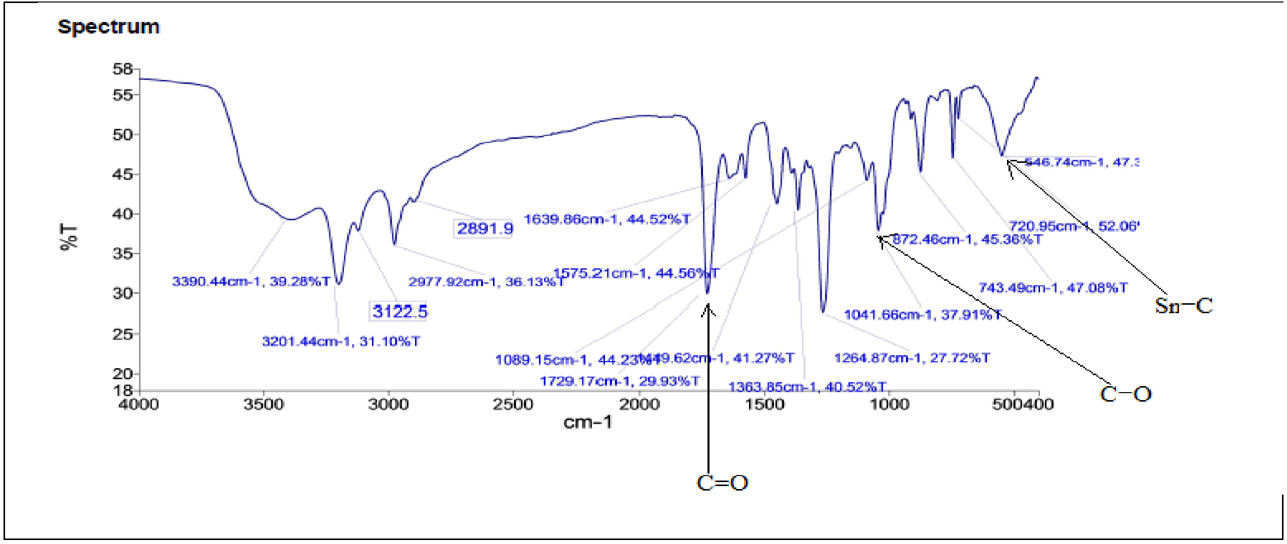
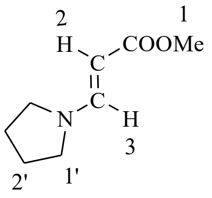


Figure 5.3.3 The IR spectrum of 2-(methyl 3-(1-pyrrolidino)acrylato) tin(IV)tetrachloride **(5a)**.



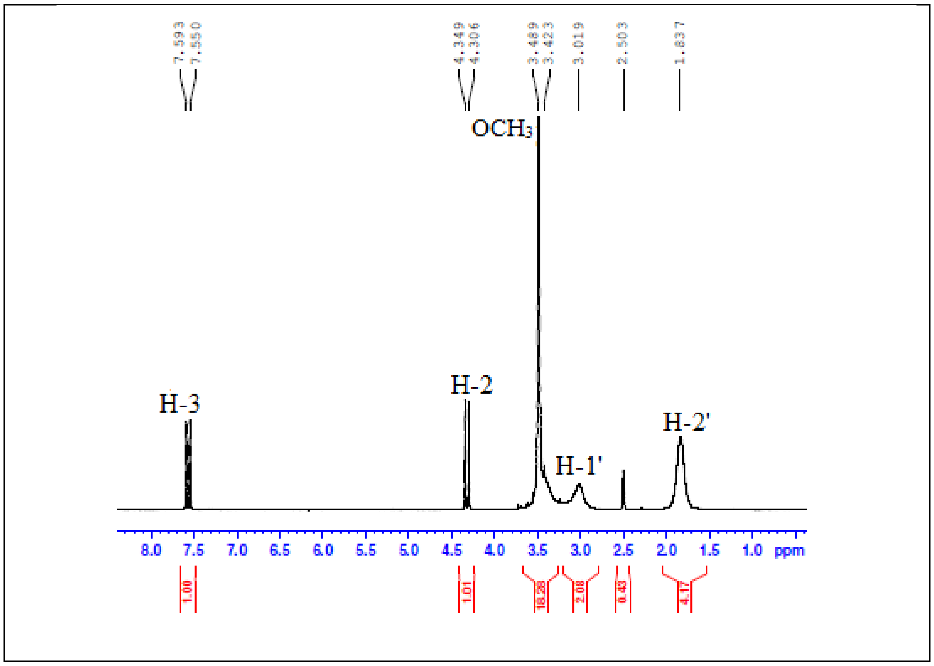


Figure 5.3.4 The ^{1}H NMR spectrum of methyl 3-(pyrrolidin-1-yl)acrylate**(3)**.

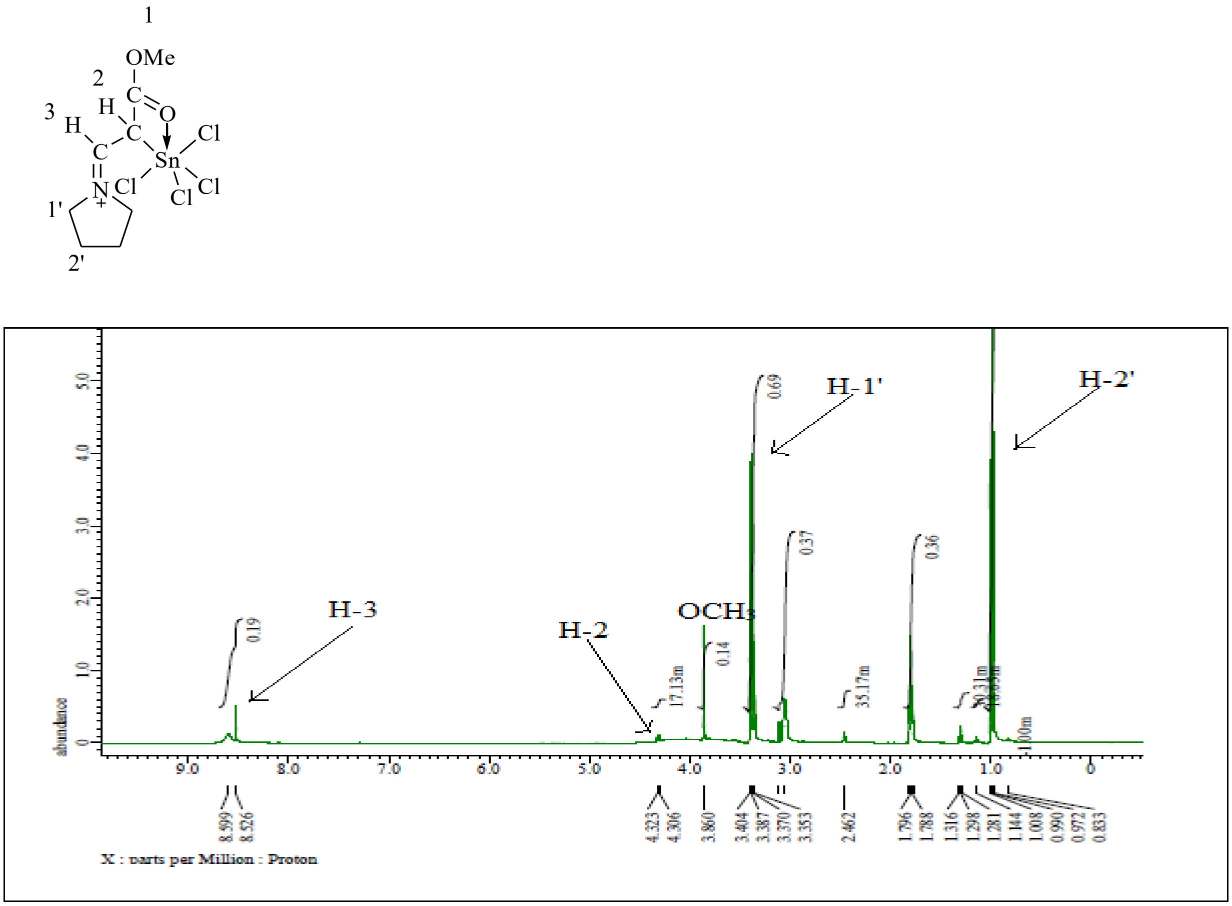


Figure 5.3.5 The ^{1}H NMR spectrum of 2-(methyl 3-(1-pyrrolidino)acrylato) tin(IV)tetrachloride **(5a)**.

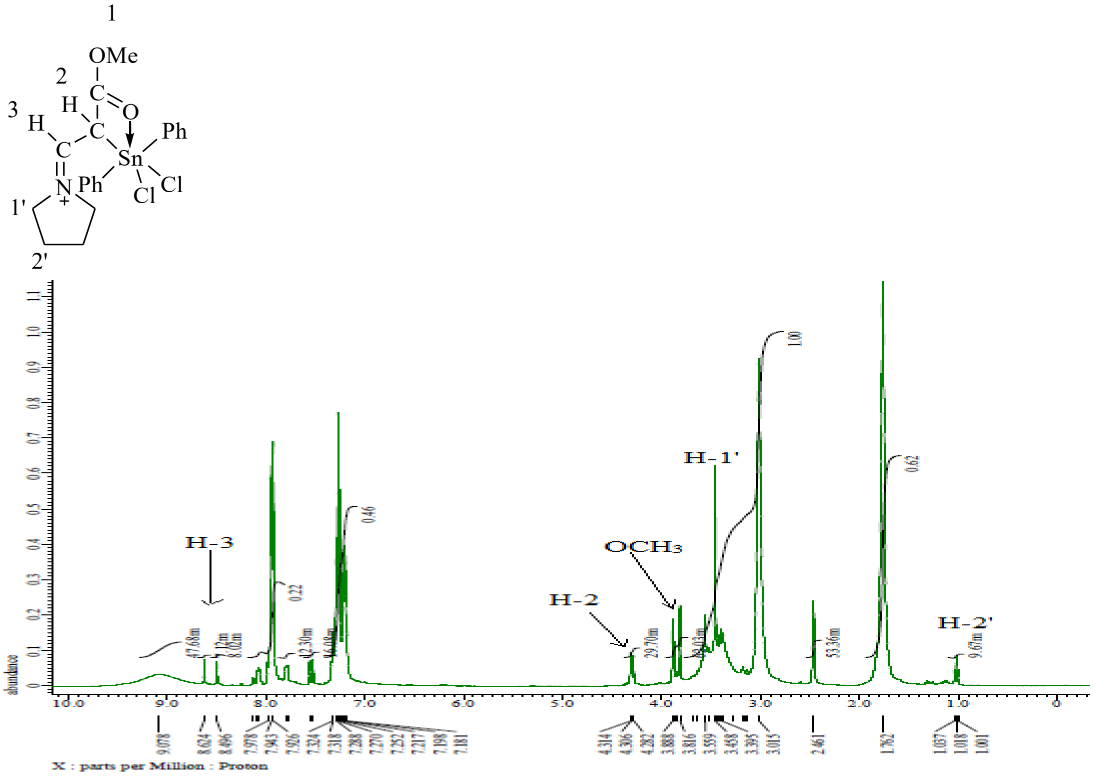
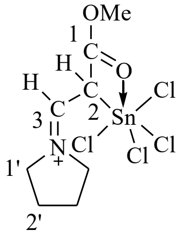


Figure 5.3.6 The ^{1}H NMR spectrum of 2-(methyl 3-(1-pyrrolidino)acrylato) diphenyltin(IV)dichloride **(5b)**.



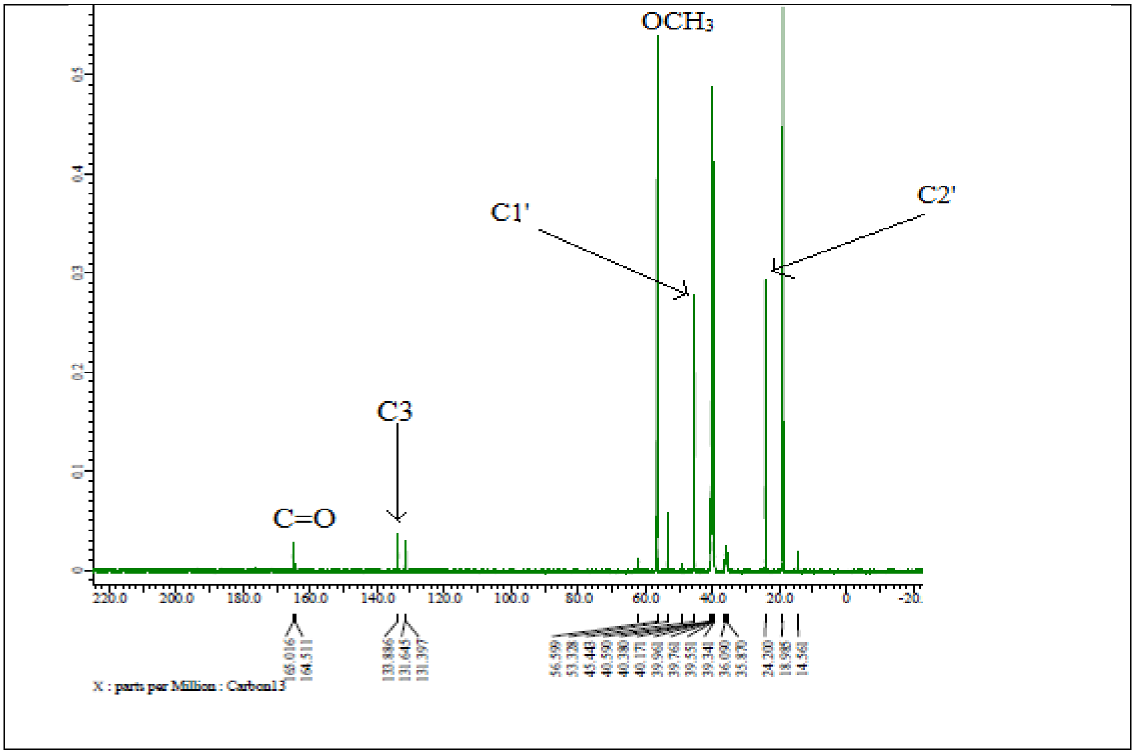
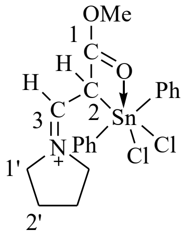


Figure 5.3.7 The ^{13}C NMR spectrum of 2-(methyl 3-(1-pyrrolidino)acrylato) tin(IV)tetrachloride **(5a)**.



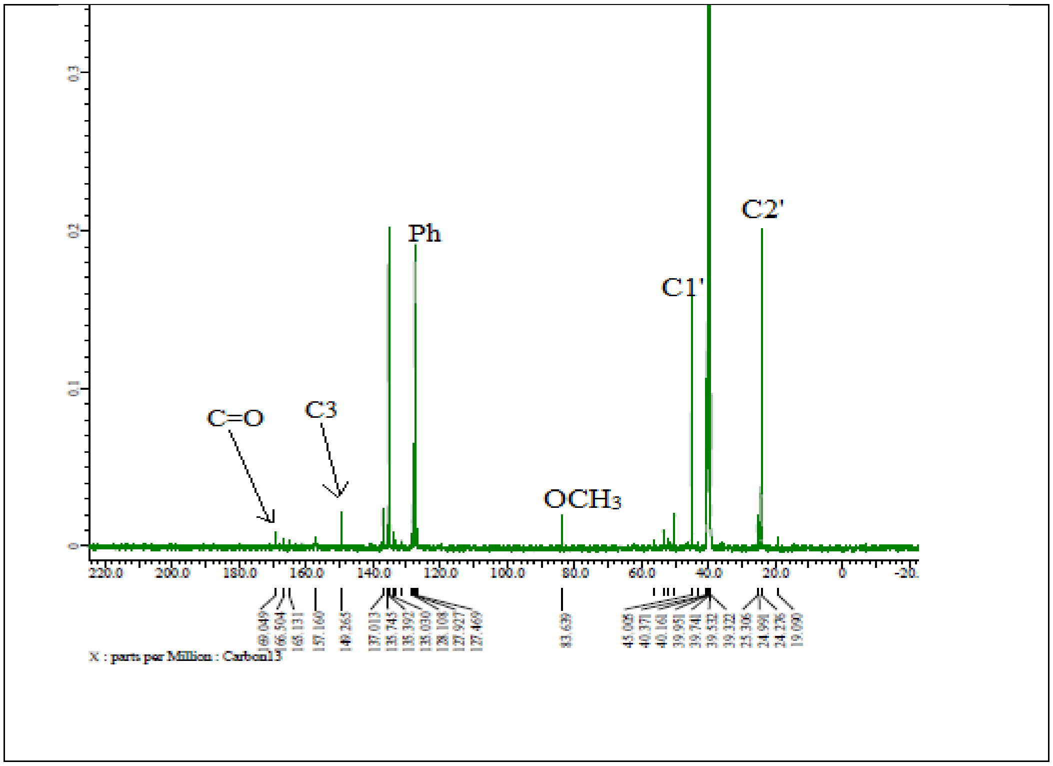
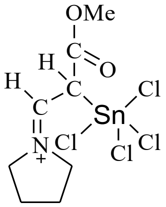


Figure 5.3.8 The ^{13}C NMR spectrum of 2-(methyl 3-(1-pyrrolidino)acrylato) diphenyltin(IV)dichloride **(5b)**.



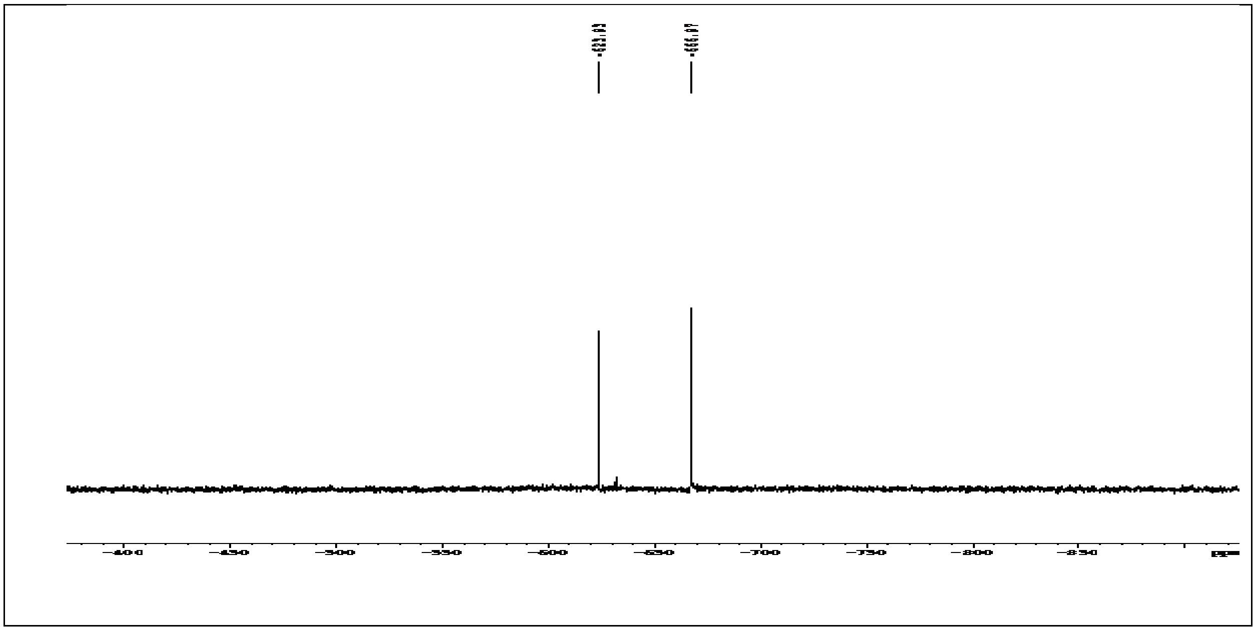
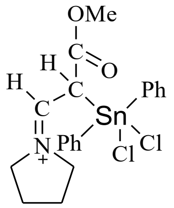


Figure 5.3.9 The ^{119}Sn NMR spectrum of 2-(methyl 3-(1-pyrrolidino)acrylato) tin(IV)tetrachloride **(5a)**.



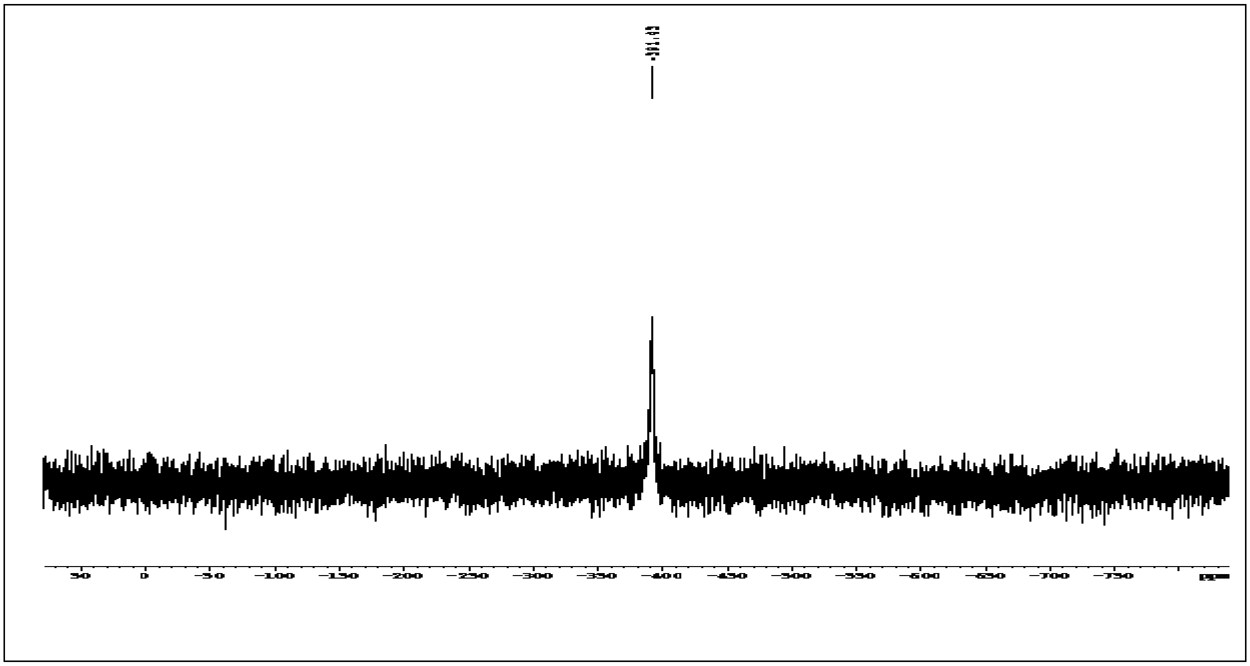


Figure 5.3.10 The ^{119}Sn NMR spectrum of 2-(methyl 3-(1-pyrrolidino)acrylato) diphenyltin(IV)dichloride **(5b)**.

CONCLUSION

The present work deals with the synthesis of methyl 3-(pyrrolidin-1-yl)acrylate and its complexation with tin tetrachloride and diphenyltin dichloride. The proposed geometry of both the complexes is octahedral.

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