SYNTHESIS, CONFORMATIONAL ANALYSIS, AND ANTI-ARRHYTHMIC PROPERTIES OF SELECTED 3-SELENA-7-AZABICYCLO[3.3.1]NONANES AND DERIVATIVES

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CHAPTER I

HISTORICAL

Myocardial infarction is the necrosis of heart tissue due to ischemia which is the obstruction of circulation to the heart. There are two serious consequences to this occlusion of coronary arteries and the resulting infarction.[71] One is the development of life-threatening arrhythmias and the other is the failure of the heart as a pump. The latter may also be the direct result of the arrhythmias.

The purpose of this study is to develop a novel class of antiarrhythmic agents with characteristics of being both potent and nontoxic. In addition, it would be of value to be able to label the agent with a radionuclide which would permit imaging of the heart in a noninvasive manner, thus giving indication of the extent of damage caused by a myocardial infarction and also to provide insight into the mechanism of its biological activity.

Arrhythmias and Heart Disease

Coronary heart disease culminating in myocardial infarction accounts for 650,000 deaths each year making this the leading cause of death in this country.[71] Cardiac arrest, initiated without warning, occurs over 300,000 times each year. These deaths, in most cases, are caused by ventricular fibrillation which may be preceded and precipitated by ventricular arrhythmias.[100]

Of myocardial infarction related deaths, 60-70% occur in the first hour after onset of symptoms. This is before many victims even reach the hospital. Most of these succumb as a result of ventricular tachycardias[71] which are rapid or accelerated heart rhythms originating within the ventricles. In fact, half of the deaths from myocardial infarction are the result of cardiac arrhythmias[41] with ventricular tachycardias being the most serious and life threatening.[24,100]

Following a myocardial infarction, nearly all patients exhibit ventricular tachycardia.[24] Of these, 70-80% require pharmacological therapy[71] since the mortality rate for myocardial infarction is two to three times higher when complicated with ventricular tachycardia.[24] There is also a link between ventricular tachycardia and coronary heart disease indicated by the fact that these arrhythmias are nearly always found in patients with advanced coronary heart disease.[24]

In addition to myocardial infarction, there are a number of other potential causes of cardiac arrhythmias. For example, all healthy adults have at one time or another experienced ventricular premature contractions which are the first signs of an arrhythmia. These most often occur after excessive ingestion of coffee or tea, heavy smoking, or emotional excitement.[24] Other causes of arrhythmias include hypokalemia, hypocalcemia, hyperthyroidism, hyperactivity of the sympathetic system, and hypoxia. The latter includes local ischemia in the heart tissue due to atherosclerosis in the coronary system.[116] Even one of the main drugs presently being used for the suppression of atrial arrhythmias, namely digitalis, can produce severe arrhythmias in an overdose.

Dog Models for the Study of Arrhythmias and Antiarrhythmics

For practical and ethical reasons, experimentation required in the study of arrhythmias and antiarrhythmic agents is not always feasible on human subjects. Consequently, this experimentation must be performed on animal subjects such as the dog. The dog is the model of choice since the ligation of the anterior descending coronary artery in this animal produces arrhythmias which have similar etiologies to certain types of ventricular arrhythmias which are found in man.[25] Moreover, the persistence of these arrhythmias makes repeated testing possible as well as simultaneous evaluation of drug activity and toxicity in some cases.[25]

Following the design and synthesis of the potential antiarrhythmic agents to be discussed later, the evaluation for biological activity was performed in the laboratory of Dr. Benjamin Scherlag of the Veterans Administration Medical Center in Oklahoma City. Under his supervision, the dogs were prepared according to standardized procedures.[52,101,102]

The method begins with anesthetizing the dog with sodium pentobarbital (30 mg/kg, iv).[101,102] The dog is then connected to an artificial breathing apparatus and a thoracotomy is performed at the fourth intercostal space. The left atrium is pulled back to expose the left anterior descending coronary artery. This artery is then closed off in two stages by a double ligature. The first ligature is drawn around the artery and a 20-gauge hypodermic needle. Once this is tied, the needle is removed, thus leaving the artery constricted but not completely occluded. After thirty minutes, the second ligature is tightened. This ligature completely and permanently closes the artery.

The resulting myocardial infarction gives rise to arrhythmias which

occur in two distinct phases.[56,101] There is an initial arrhythmic period immediately following the coronary occlusion which lasts for 20-30 minutes. This is a very serious and often fatal phase since these arrhythmias, which are attributed to re-entry mechanisms,[24,29,56] may degenerate into ventricular fibrillation leading to cardiac arrest and death.[35] This phase has its clinical counterpart in the pre-hospital phase of acute myocardial infarction.[57] The frequency of sudden death caused by ventricular fibrillation in this phase is greater than 50%.[56]

Assuming the dog survives this phase of arrhythmias, there is a quiescent period of up to several hours. This is followed by a second phase of arrhythmic activity which lasts from 24 to 48 hours[56,101] which corresponds to the coronary care, hospitalization phase in the clinical setting. The arrhythmias in this phase are attributed to increased automaticity of ventricular pacemakers.[56,102]

During this phase, reentrant ventricular arrhythmias may be induced by electrically pacing the dog heart with a low voltage DC current.[102] In this way, the arrhythmia may be studied as well as the response of the heart to antiarrhythmic agents.

Antiarrhythmic Agents

There are large number of antiarrhythmic agents in clinical use. However, all of these exhibit a variety of undesirable side effects, some even critical in certain instances. The most common side effects are cardiotoxicity, gastrointestinal complications, and adverse effects on the central nervous system.[111]

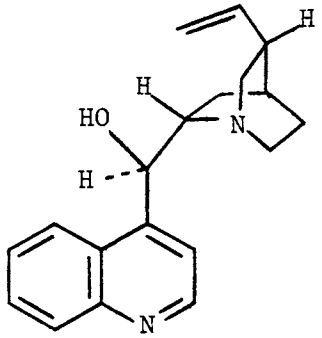
The treatments of arrhythmias are as varied as the causes. One simple treatment employed to terminate ventricular arrhythmia is a sharp

thump or blow to the pericardium. Since this treatment only succeeds occasionally, other, more harsh remedies must be used.

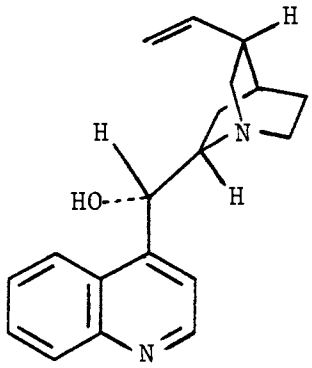
Cardioversion or the administration of a DC shock is effective in terminating a paroxysm of ventricular tachycardia in greater than 90% of all cases. However, it should not be used indiscriminately. The use of electric shock in the case of arrhythmias caused by digitalis intoxication may provoke fatal ventricular fibrillation. Other measures should also be used when the tachycardia is repetitive.[24,41]

There are a wide variety of drugs in use at the present time for the suppression and prevention of arrhythmias of different types. The earliest reported drug therapy for cardiac arrhythmias occurred in 1914 when an arrhythmia in a malarial patient, being treated with cinchona alkaloids (Figure 1), was converted to a normal sinus rhythm.[80] Later, it was found that each of these alkaloids had the ability to convert atrial fibrillation to normal sinus rhythm. Of the alkaloids in this group, quinidine (3) was the most potent and is still in wide usage in the treatment of atrial fibrillation[41,80] and also in the treatment of atrial and ventricular premature depolarization.[14] As mentioned earlier, all antiarrhythmic agents currently available exhibit undesired side effects. Quinidine and related compounds can promote nausea or vomiting, diarrhea, cramping abdominal pain, and headaches. This drug has also been known to produce ventricular tachycardia and fibrillation even at therapeutic doses.[41]

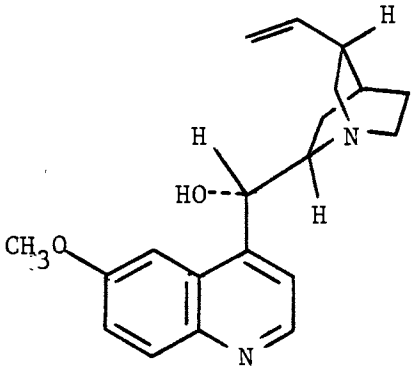
Another antiarrhythmic agent used in the treatment of atrial arrhythmias is atropine (5). This drug is used in the treatment and abolishment of sinus bradycardia.[14,41] Adverse side effects of atropine include dryness of the mouth, blurred vision, constipation, micturation



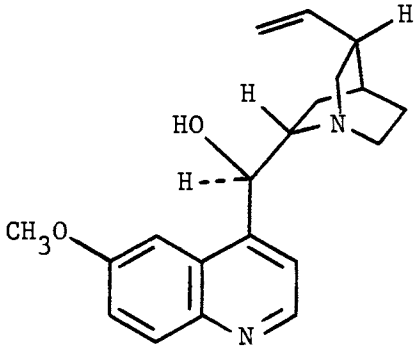
Cinchonidine (1)



Cinchonine (2)

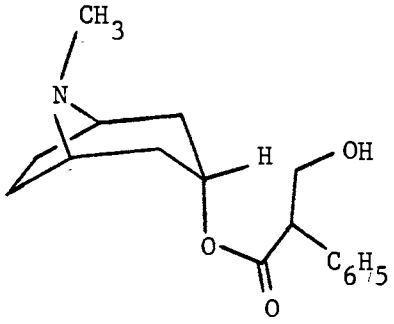


Quinidine (3)



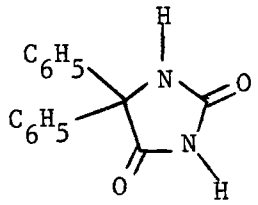
Quinine (4)

Figure 1. Selected Cinchona Alkaloids



disturbances, and minor aberrations of mental function.[41]

A very important family of antiarrhythmics is a group of glycosides which are extracts of the plant Digitalis Purpurea. The most common preparation is referred to as digoxin (6) and is used to control and convert sinus tachycardia and fibrillation.[14,41,115] Digoxin (6) and related systems 7-9 are shown in Figure 2. Of the side effects attendant to digitalis glycosides, the most common are headaches, gastrointestinal upset, and visual disturbances. Ironically, digitalis glycoides may even produce cardiac arrhythmias of virtually all types including the most dangerous ones such as ventricular tachycardia and ventricular fibrillation.



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For the treatment of arrhythmias induced by digitalis intoxication, the drug of choice is diphenylhydantoin (10, dilantin). It also has more than its share of side effects of which the most common are giddiness, ataxia, nystagmus, dysarthria, fatigue, gastrointestinal upset, hirsutism, hyperplasia of the gums, morbilliform rashes, hemorrhagic erythema multiform, blood dyscrasias, hepatitis, and pseudoxanthoma formation.[41]

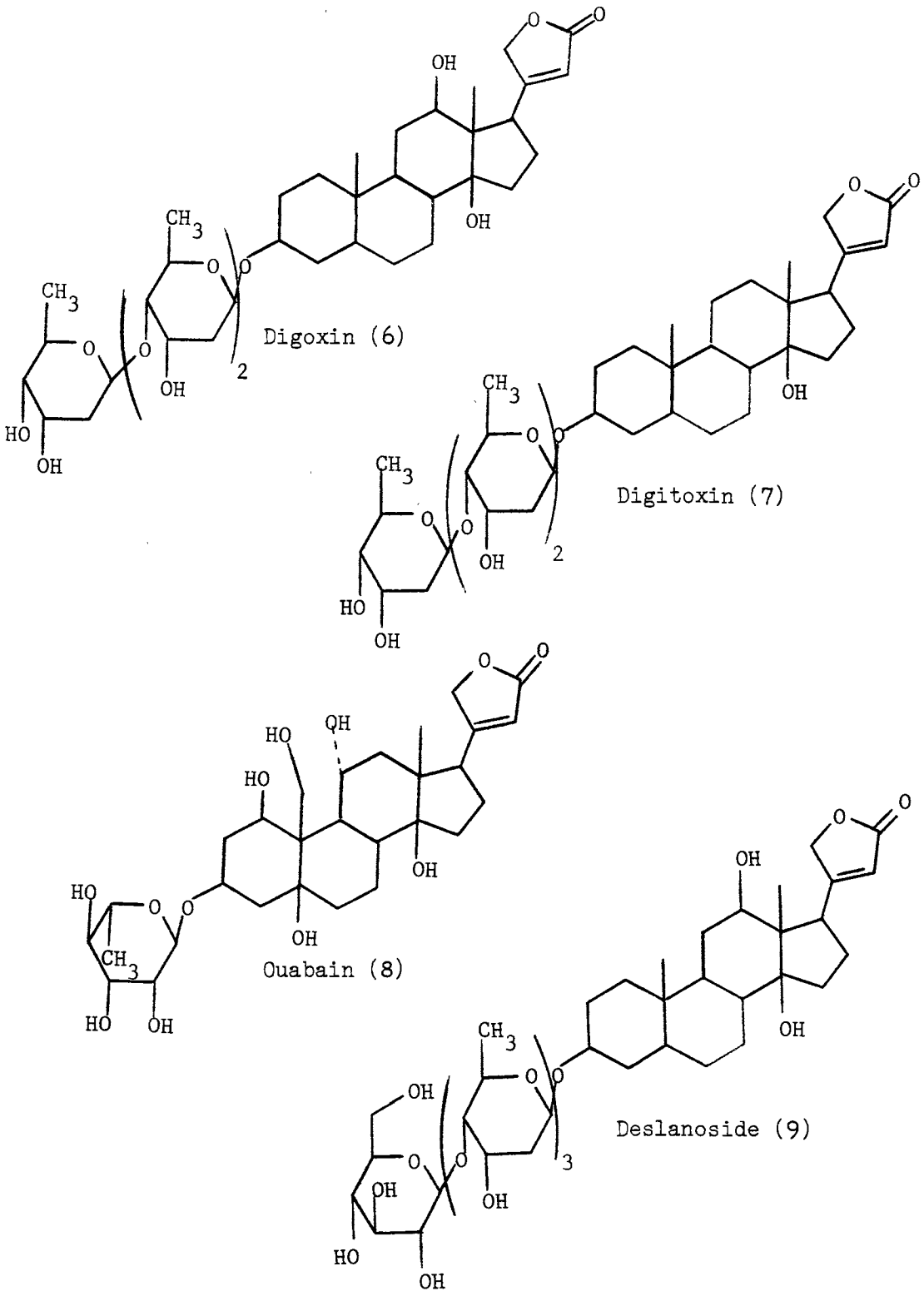
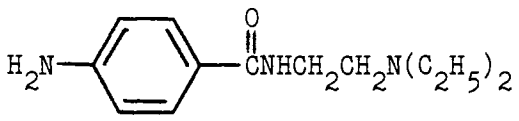


Figure 2. Selected Digitalis Glycosides

One very potent and much prescribed antiarrhythmic drug is procainamide (11, pronestyl). It is used in the suppression of premature ventricular contractions and ventricular tachycardia. The side effects related to this drug include anorexia, nausea, vomiting, diarrhea, weakness, giddiness. Also reported are occasional hallucinations, fevers, rashes, and hypotension.[41]



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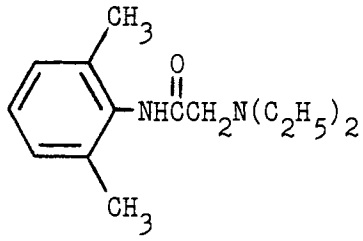

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Of all of the antiarrhythmic agents in clinical use at this time, lidocaine (12, xylocaine) may be the most important. It is usually the first drug administered to patients with acute myocardial infarction when serious arrhythmias are recognized.[41] Lidocaine is the preferred agent for the treatment of ventricular tachycardia arising from nearly any cause with the exception of digitalis intoxication.[24] It is for these reasons that the activities of the new potential antiarrhythmic agents to be discussed later are compared to that of lidocaine which is used as a standard.

Lidocaine (12), which is given intravenously, begins to act within a very few minutes. However, because of rapid metabolism, the blood

serum halflife of lidocaine is only 20 to 30 minutes. Lidocaine also has the disadvantage of being capable of producing sinus arrest due to depressed automaticity of the sinoatrial node tissue. The most alarming toxic reactions to lidocaine involve the central nervous system. These include muscular twitching, visual disturbances, tinnitus, paresthesias, dizziness, drowsiness, dysarthria, confusion, coma, convulsions, arterial hypotension, bradycardia, and respiratory arrest. There have also been complaints of intense feelings of apprehension and also intense euphoria.[41] Although these are substantial side effects, most are due to excessive doses or advanced liver disease.[41]

The group of antiarrhythmic drugs described is by no means all inclusive. There are many new potential antiarrhythmic agents exhibiting novel structures and mechanism of biological activity which are currently awaiting the completion of clinical trials.[6,80,84,111,116]

Radionuclides for Myocardial Imaging Studies

Although much is known about the etiology of cardiac arrhythmias, much remains undiscovered. After myocardial infarction, it is of interest to be able to determine the extent of damage. One method of assessing the damage is to perform exploratory open-heart surgery. It is of considerable importance to be able to make this determination via a less traumatic, nonsurgical technique. This may be done through the use of radionuclide tracer studies, or imaging, of the heart tissue. A large volume of work has been done in the area of designing and testing radioisotopically labelled compounds for use in this fashion.[27b,90] Many of these compounds are also of potential use in the detection of coronary artery disease.

There are two radiopharmaceutical methods which are used in the identification and quantitation of ischemic regions due to myocardial infarction.[90] One technique, referred to as cold spot imaging, employs labelled compounds which show greater uptake in normal tissue than in infarcted and ischemic regions, thus leading to indirect information about the type and extent of damage. The other approach, referred to as hot spot imaging, utilizes those labels which localize in the infarcted or damaged regions. Representatives of each group of myocardial imaging agents are found in Tables I and II.

Although each of the radioisotopes currently in use has characteristics of value to imaging studies, many also possess intrinsic traits which hinder their general utility. For example, many of the nuclides, such as ^{14}C and ^{3}H are beta particle emitters. Since these particles will not penetrate tissues of the body, these are limited mainly to in vitro studies.[27,90] Other nuclides, such as ^{13}N, ^{11}C, and ^{15}O are ultra-short lived positron emitters which require a nearby cyclotron. This greatly restricts general use since equipment of this type is not widely available.

Gamma emitting radioisotopes are the best suited for imaging studies since this nonparticle radiation will readily penetrate tissues. However, just being a gamma emitter is not enough to make a radioisotope a good candidate for imaging studies. The emission energy must be of sufficient power so as to be detectable (20 keV), and it must also be within an upper limit (510 keV) to obtain good quality images and also to avoid excessive patient radiation.[27a] It is for the latter reason that the use of ^{43}K on a routine basis is limited.

TABLE I

COLD-SPOT IMAGING AGENTS[90]

Radionuclide	Major Emissions	Half-life
Inorganic Salts		
^{43}KCl	γ β^-	22.4 h
^{81}RbCl	γ β^+	4.7 h
^{131}CsCl	x-ray	9.7 d
^{201}TlCl	γ	72 h
$^{13}NH_3$	β^+	10 m
^{99m}Tc Complexes	γ	6.1 h
Macroaggregated Albumin		
Human Serum Albumin		
Metabolites		
1-[^{14}C]Palmitic Acid	β^-	5730 y
1-[^{14}C]Oleic Acid		
16-[^{131}I]Iodo-9-Hexadecenoic Acid	γ β^-	8.05 d
18-Iodo-13-[^{123m}Te]Tellura-17-octadecenoic Acid[11,64a]	γ	119 d
18-[^{82}Br]Bromo-5-tellura-17-octadecenoic Acid[64b]	β^-	35.7 h
[^{13}N]l-Asparagine	β^+	10 m
Inert Gases		
^{133}Xe	γ β^-	5.3 d
^{81m}Kr	γ	13 s

TABLE II

HOT-SPOT IMAGING AGENTS[90]

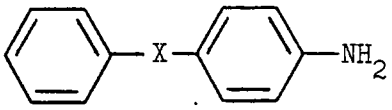
Radionuclide	Major Emissions	Half-life
[(E)-1-[^{123}I]Iodo-1-penten-5-yl]-triphenylphosphonium Iodide[109]	γ	13.3 h
Potassium [^{18}F]Fluoride	β^+	110 m
^{99m}Tc Complexes	γ	6.1 h
Tetracycline		
Glucoheptonate		
Pyrophosphate		
Metabolites		
[^{67}Ga]Gallium Citrate[28]	γ	78 h
[^{165}Er]Erbium Citrate	x-ray, γ	10.3 h
[^{203}Hg]Chlormerodrin	γ β^-	49.6 d
[^{203}Hg]phthaleins	γ β^-	49.6 d
[^{203}Hg]Fluoresceins	γ β^-	49.6 d

A short half-life is desirable so as to minimize the patient's radiation exposure. However, there are time requirements for synthesis and administration of the agent as well as for its in vivo accumulation and the collection of data. It is also preferable that the observed radioactivity does not drastically decrease during the imaging procedure.[27a] For this reason, some of the isotopes, which have short half-

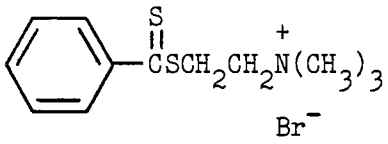
lives, such as ^{81m}Kr (13 s), ^{123}I (13.3 h), and ^{99m}Tc (6.1 h), must be produced immediately before use by the decay of other radioactive species. The precursors of these three are ^{81}Rb, ^{123}Xe, and ^{99}Mo, respectively.[27a,90]

In addition to having desirable physical characteristics, the radioisotope must also possess certain chemical traits. One such trait is that the nuclide must be able to be incorporated into an organic carrier molecule or be amenable to use in an inorganic form. Because of one restriction or another, of the 600 gamma-emitting nuclides, nine of them (^{131}I, ^{132}I, ^{125}I, ^{51}Cr, ^{99m}Tc, ^{22}Na, ^{85}Kr, ^{197}Hg, and ^{203}Hg) comprise greater than 70% of the radionuclides used as diagnostic radiotracers.[27a]

One very productive technique used in the development of novel compounds for use in radioactive tracing studies utilizes the concept of bioisosterism in the design of these compounds. The concept of isosterism, first proposed by Langmuir[69] in 1919, dealt with the similarities and substitution of atoms or groups of atoms with respect to electron number and arrangement.[20] Substitutions of this type should give new compounds which have properties similar to the parent compound. This idea was extended by Erlenmeyer[37] and Grimm[20b] to include atoms or groups of atoms which were similar in size or shape. For example, -NH-, $-CH_2-$, and -O- are close enough in group size and bond angles that compounds 13, 14, and 15 each exhibit similar antigen activity.[20c] This is a useful concept in the formation of radionuclide-containing molecules for use as imaging agents which should have similar biological functions as the parent compound. For example, ^{18}F may be incorporated into a molecule as a bioisosteric replacement of hydrogen.[27a] The



13 X = NH
14 X = CH_2
15 X = O



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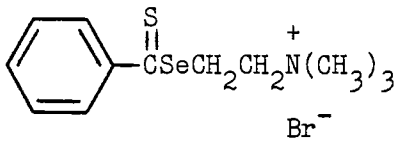

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isotope ^{82}Br may bioisosterically replace a methyl group.[20,27a]

One pair of bioisosteres which is currently receiving considerable attention is that of sulfur and selenium.[27a,63,122] These elements, being in the same chemical family, have the same valence electron configuration and are also similar in size and electronegativities, thus making them excellent bioisosteres. This is supported by the fact that compounds 16 and 17 share almost identical abilities to block axial transmission of nerve impulses.[23] Findings of this nature have led to the incorporation of the gamma emitting ^{75}Se in place of sulfur[23,96] (as well as $-CH_2-$,[96] -NH-,[97] and other isosteric groups[99]).

Selenium-75 possesses some characteristics which make it favorable for radionuclide studies. It has a half-life of 120 days which allows time for synthesis and handling. Selenium-75 is a gamma emitting isotope which gives 1.74 gamma rays per disintegration between 100 and 400

keV. Iodine-131, the most common of the foreign labels, gives only 0.91 gamma rays per disintegration. This, plus the fact that the beta particle absorbed dose is only about 7% of that for ^{131}I, indicates that smaller administered doses are required for imaging.[10] Selenium forms stable covalent bonds with carbon, giving organoselenium compounds greater stability in vivo than corresponding halogenated derivatives.[97] The ^{75}Se containing compounds may be synthesized directly from their nonradioactive counterparts by use of a neutron beam in a graphite reactor.[73] However, recent synthetic developments have led to more simple and cost-effective methods for introducing this radioisotope.[10,98]

Elemental selenium-75 may be reduced directly to the very useful nucleophile, $NaH^{75}Se$, by sodium borohydride according to the following equation.[10] The $NaH^{75}Se$ thus formed may then be treated with alkyl

$$^{75}Se + NaBH_4 + 3\ C_2H_5OH \longrightarrow NaH^{75}Se + B(OC_2H_5)_3 + 3\ H_2$$

halides, tosylates, or epoxides to form other useful nucleophiles of the type $R^{75}SeH$.

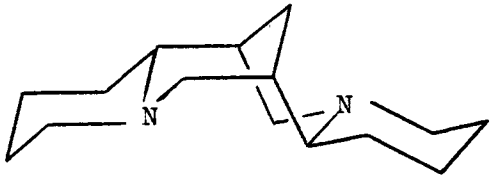
An improvement on this method involves the reduction of [^{75}Se]-selenous acid, instead of elemental selenium-75, with sodium hydride in the production of $NaH^{75}Se$.[98] Elemental selenium-75 is commercially available with a specific activity of only 1-2 mCi/mg Se, whereas $H_2{}^{75}SeO_3$ is available with a much greater specific activity of 0.1-2.3 Ci/mg Se. [^{75}Se]Selenous acid may be obtained for as little as $2.00/mCi while the price of ^{75}Se metal is closer to $30.00/mCi.[98] This

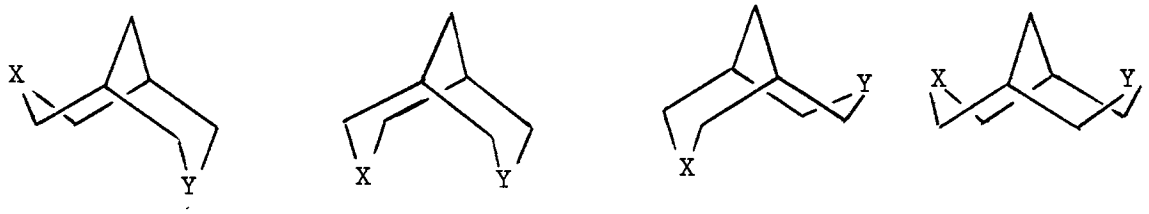
makes the use of $H_2{}^{75}SeO_3$ much more cost effective than ^{75}Se metal in the total synthesis of potential radionuclide imaging agents.

Bicyclo[3.3.1]nonanes and the Treatment of Arrhythmias

By 1949, sparteine (18), one of the lupine alkaloids, was known to have properties as a local anesthetic and also was able to cause a depression in heart action as well as circulation.[53] It was later found to have useful antiarrhythmic characteristics[32,93,107] and has actually been used in the management of various cardiac arrhythmias.[86] In one study, sparteine was found to be more potent as an antiarrhythmic agent than quinidine (3), diphenylhydantoin (10), procainamide (11), or lidocaine (12).[112] However, animals intoxicated with plants which produce sparteine showed symptoms of nervousness, difficulty in breathing, loss of muscular control, salivation, convulsions, and coma in extreme cases.[86]

The two central rings in sparteine (18) form the structural backbone of 3,7-diheterabicyclo[3.3.1]nonanes (19).[59] Several compounds of this type have been synthesized and were found to have antiarrhythmic activity.[6,93,94] These bicyclic systems are potentially an equilibrium mixture involving four different conformers as attested to by numerous



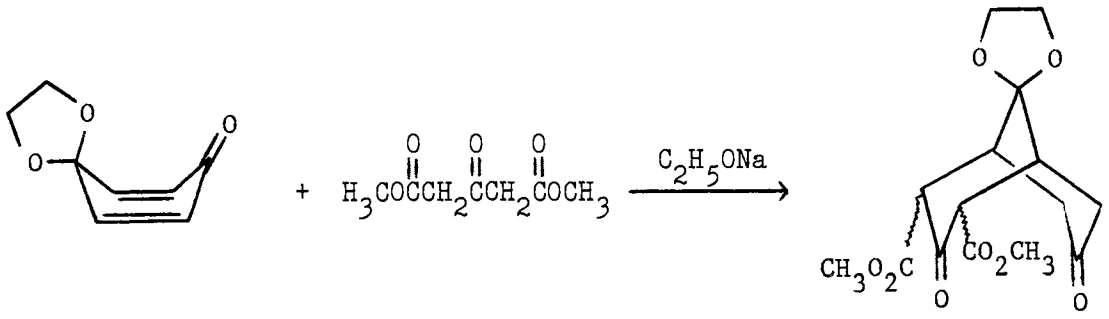


B-C C-C C-B B-B

19

publications in the area of conformational analysis.[121] The variety of choices for atoms X and Y, as well as ring substituents, gives rise to very diverse methods of syntheses.

Several reaction types are utilized in the syntheses of many types of bicyclo[3.3.1]nonanes. A double Michael addition of dimethyl acetonedicarboxylate to the dienone 20 gave the bicyclononane 21 in a yield of 86%.[59c] The α,α-annelation of the enamine 22 produced the phosphorus containing bicyclononane 23 (59%).[77]



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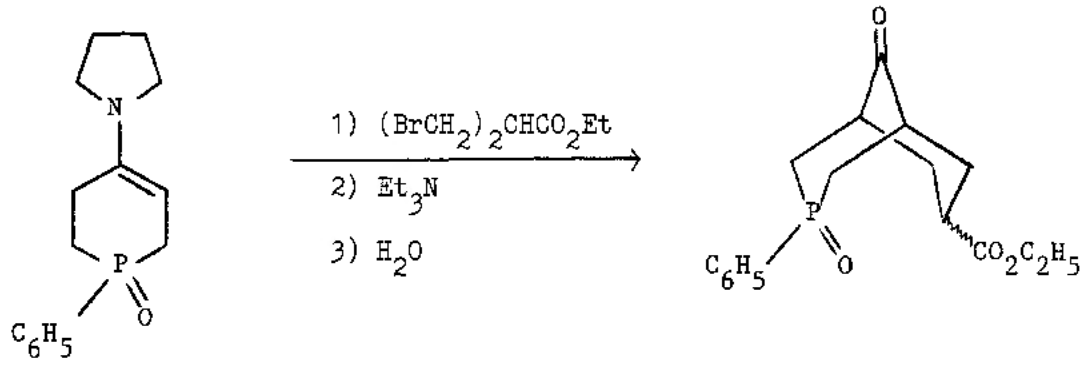
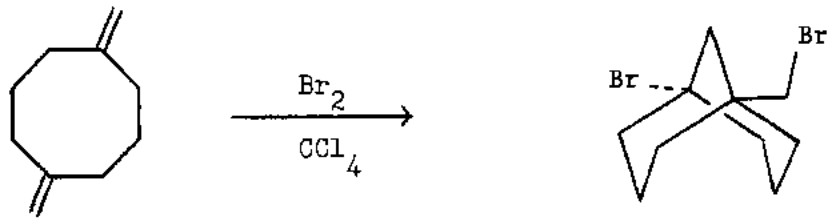


22 23

Other means of producing bicyclo[3.3.1]nonanes include several methods for bridging certain functionalized cyclooctanes. Bromination of 1,5-dimethylenecyclooctane (24) gave the bicyclononane dibromide 25 (80%).[16] Reaction of 24 with sulfuric acid produced the tertiary



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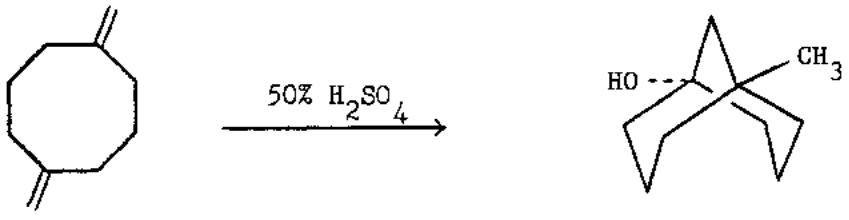
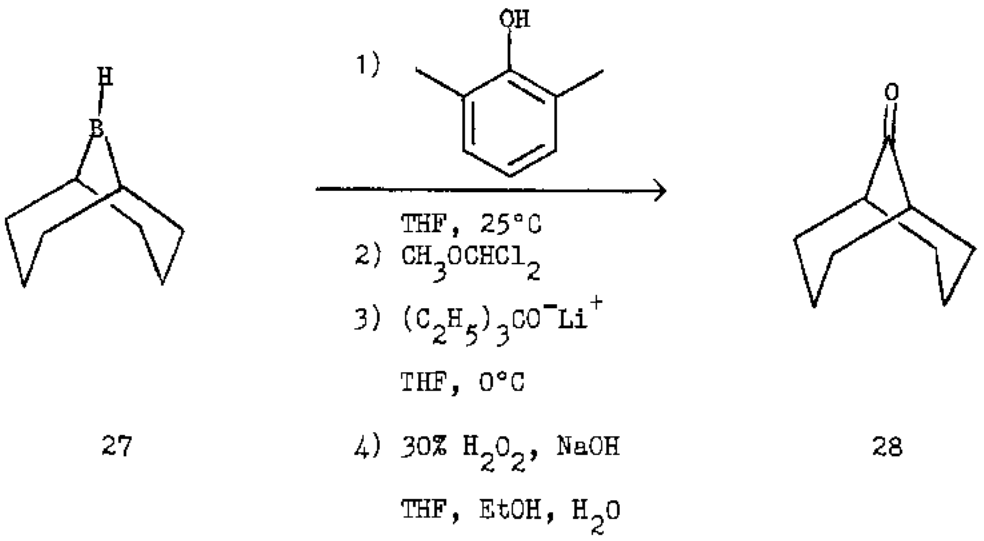


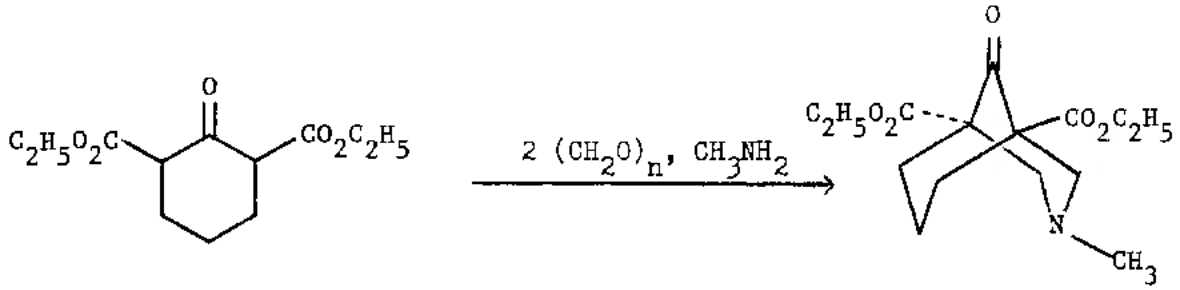
24 26

alcohol 26 (88%).[24] The intermediate 9-borabicyclononane (27), generated from 1,5-cyclooctadiene (91%), yielded bicyclononan-9-one (28).[22]



27 28

Of the various method of producing bicyclo[3.3.1]nonanes, the most versatile and widely used is the double Mannich reaction involving substituted cyclohexanones, an amine, and two or more equivalents of an aldehyde. One early paper in the area reports a yield of 80% for 3-methyl-3-azabicyclo[3.3.1]nonan-9-one dicarboxylate (29) from diethyl cyclohexanone-2,6-dicarboxylate.[17] Since that time, many bicyclo-

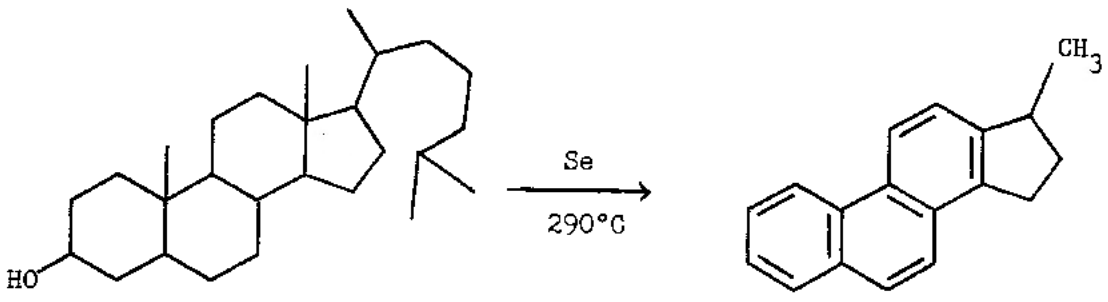


29

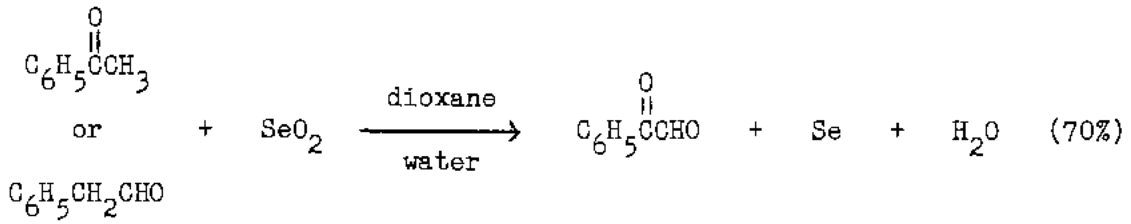
[3.3.1]nonanes have been synthesized with different combinations of heteroatoms in the 3- and 7- positions, such as nitrogen-nitrogen systems,[95] oxygen-nitrogen systems,[3,7] as well as sulfur-nitrogen systems.[5,8,34] The syntheses of the first reported bicyclo[3.3.1]nonanes with selenium incorporated into the ring at the 3-position are discussed in the next chapter.

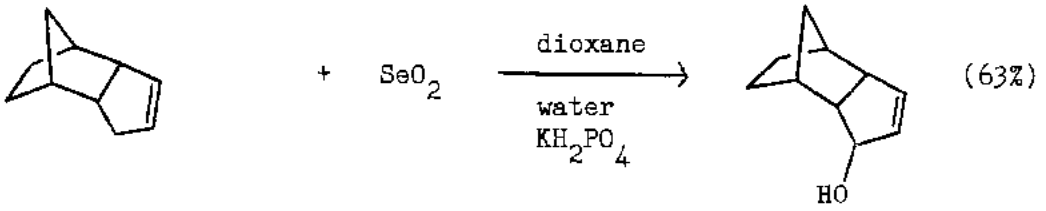
Current Organoselenium Chemistry

Although extensive organoselenium work was reported in the comprehensive reviews published by Bradt and co-workers[18] (1929-1933) before about 1973, there were only two selenium reagents which were in common usage by organic chemists.[104] These were elemental selenium and selenium dioxide. Elemental selenium was used mainly in the dehydrogenation of cyclic and acyclic hydrocarbons[91] such as in the dehydrogenation of cholesterol (30) to Diel's hydrocarbon (31).[39] Selenium dioxide was and is still used as an oxidizing agent for ketones and olefins.[92,119] Representative examples are shown in the following equations.

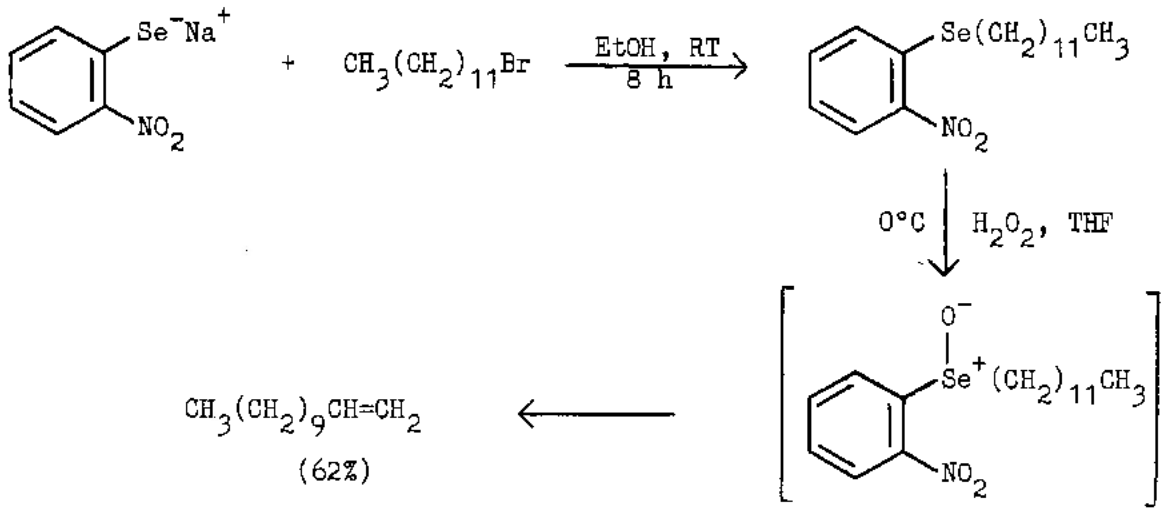


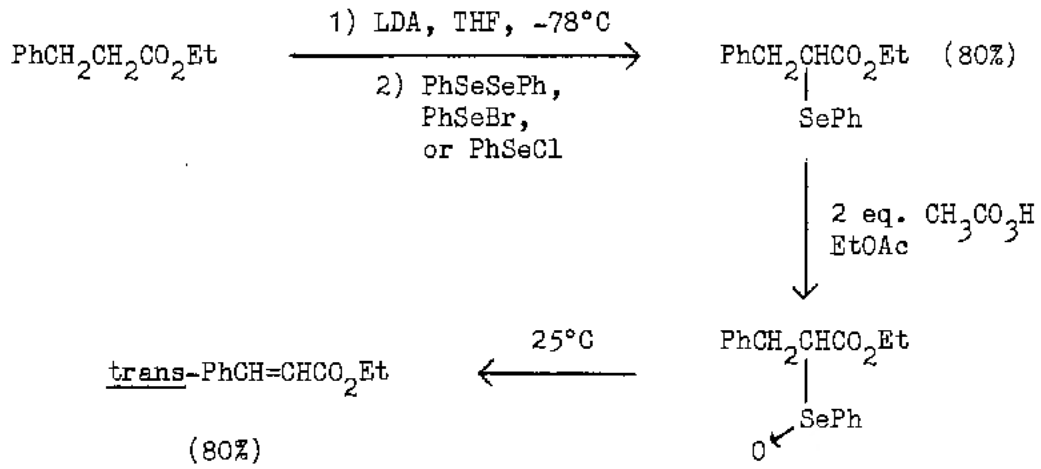
30 31





Since 1973, there have been major advances in the usefulness of selenium reagents which affect a variety of functional groups.[26,104] One of the most important functional group transformations is the introduction of unsaturation into saturated systems. These reaction sequences begin with the formation of an aryl alkyl selenoether primarily via attack of a selenophenylate anion on an alkyl halide, or the attack of an enolate anion on an aryl selenium halide or a diaryl diselenide. The

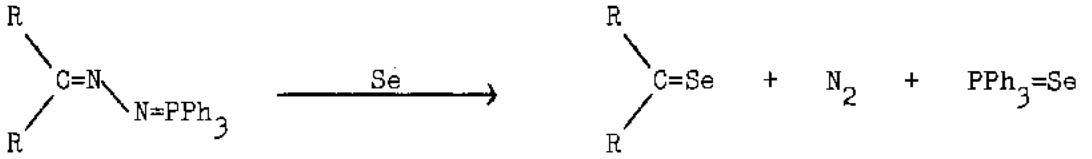




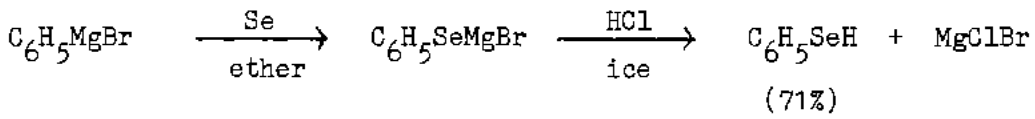
selenoether thus formed is oxidized to a selenoxide which then fragments to the unsaturated system as shown.[26a,105a]

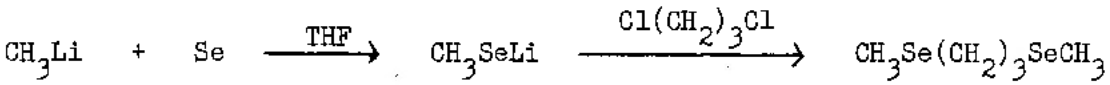
In addition to the use of selenium reagents to modify substrate molecules, methods for using selenium reagents for the purpose of incorporating selenium into target molecules have been known for well over 50 years.[18,91] Although techniques and the availability of certain reagents have changed, the basic starting material for these reactions is still elemental selenium. Elemental selenium may be used in its metallic form or it may be reduced to neutral and anionic nucleophilic reagents.

Elemental selenium undergoes an insertion reaction with phosphazines (32) to give sterically hindered selenoketones (33) in fair to good yields.[50,105b] Selenium will also insert into carbon-metal bonds in cases such as Grignard[40] and alkyl lithium reagents.[48] These organometallic selenides are very nucleophilic reagents and are generally formed in situ.

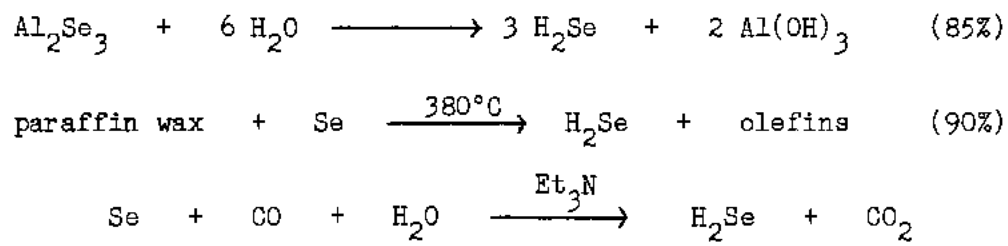


32 33 (66-85%)





One very useful reagent employed in the synthesis of organoselenium compounds is hydrogen selenide which may be prepared in several ways as shown below.[38,46,65,85,117] Because H_2Se is very air sensitive and extremely toxic, it is usually generated in situ. In order to circumvent the handling problems associated with handling H_2Se, a number of very useful synthons may be produced by the reduction of elemental selenium under various and quite convenient conditions.[19,62] These alkali selenides are extremely aggressive nucleophiles which may participate in most types of displacement reactions leading to target organoselenium molecules.



$$4\ NaBH_4 + 2\ Se + 7\ H_2O \longrightarrow 2\ NaHSe + Na_2B_4O_7 + 14\ H_2$$

$$NaBH_4 + Se + 3\ EtOH \longrightarrow NaHSe + B(OEt)_3 + 3\ H_2$$

$$2\ Na + Se \xrightarrow{NH_3} Na_2Se$$

$$Na + Se \xrightarrow{NH_3} Na_2Se_2$$

$$2\ NaBH_4 + 2\ Se + 6\ H_2O \longrightarrow Na_2Se_2 + 2\ H_3BO_3 + 7\ H_2$$

In comparison to sulfur analogs, H_2Se and the selenols, RSeH and ArSeH, are more acidic[81] and also more nucleophilic[89] than their sulfur counterparts.

Toxicity of Selenium Compounds

Selenium is one of the essential trace elements which is required for optimum health. Dietary deficiency of selenium has been indicated to increase the potential for developing cardiovascular disease and certain types of cancer.[43] It also appears that a deficiency of selenium may increase incidences of chronic arthritis.[43] Although beneficial in trace amounts, larger quantities of selenium and some of its compounds have been found to be quite toxic.[63,122] Little is actually known about the toxicity of these compounds, however, since no systematic study has been made.

Elemental selenium is relatively non-toxic. Although it appears from animal studies that some inorganic selenium compounds are metabolized,[72,87] elemental selenium has been found to pass unchanged through

dog intestine without observable effect on the dog.[63] Fine selenium dust and fumes have been found to be "irritating" to exposed workers.[122] In one particular case, some workers were exposed to dense selenium fumes which reportedly had an unpleasant, garlic-like odor and caused an intense irritation of the eyes, nose, and throat. The more severely exposed workers experienced immediate sneezing, coughing, nasal congestion, dizziness, inflammation of the eyes, and headaches. However, no selenium was detected in the urine. All workers were entirely well in three days with no persisting ill effects.[122]

Although elemental selenium appears to exhibit little systemic toxicity, hydrogen selenide is one of the most toxic substances known.[63] This gas has an extremely offensive odor (that of rotting radishes), but causes olfactory fatigue at a concentration of 0.0001 mg/l which makes it all the more hazardous.[63] The threshold limit for exposure has been set at 0.05 ppm Se by the American Conference of Governmental Industrial Hygienists.[63]

Selenium dioxide has been found to cause intense local irritation and inflammation as well as cause the developement of dermatitis. Some people can develop an allergy to selenium dioxide resulting in the swelling of their eyes when exposed even at a distance.[122] Sodium selenite and selenate have been shown to have a marked toxicity in animal studies.[122]

Few organoselenium compounds have been tested for toxicity and thus general trends and conclusion that can be drawn are also few. To date, no organoselenium compound has been found to be more toxic than the inorganic forms of the element.[122] Representative samples of toxicity data may be found in Table III.

TABLE III

TOXICITY OF SELECTED SELENIUM COMPOUNDS[122]

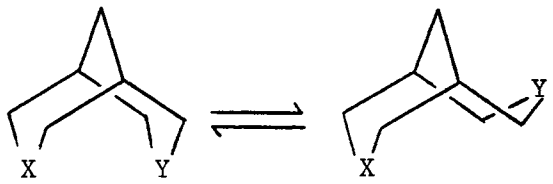
Selenium[a] Compound	mg Se/kg Body Weight
d,l-Selenocystine	4
Selenomethionine	4.25
n-Propylseleninic Acid	20-25
β-Seleninopropionic Acid	25-30
Sodium β,β'-Diselenodipropionate	25-30
Sodium β-Selenodipropionic Acid	>40
Sodium Selenite	3.25-3.50
Sodium Selenate	5.25-5.75

[a]Intraperitoneal administration of a minimum fatal dose to a rat.

CHAPTER II

RESULTS AND DISCUSSION

3,7-Diheterabicyclo[3.3.1]nonane systems 19 have intriguing stereochemical properties[34,59,88,95c,121] and, in some cases, valuable antiarrhythmic properties.[6,93] We have developed methods of preparation of selenium-containg derivatives, several of which also display antiarrhythmic action in dog models.[35,56,57,101,102]



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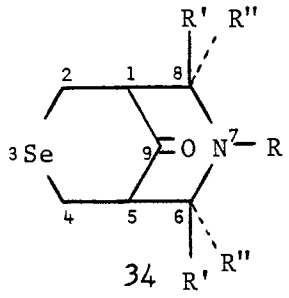
The principle objective of this research was to develop synthetic methodology to obtain substituted 3-selena-7-azabicyclo[3.3.1]nonanones 34, the corresponding nonanes 35, and the salts 36 and 37. Moreover, it was also an objective to screen these heterocycles for potential antiarrhythmic activity in dog models and to evaluate selected members of the above families for use as imaging agents for mapping infarcted areas of the heart in the animal models. For imaging purposes, the cold selenium would have to be replaced by the radioisotope ^{75}Se. Antiarrhythmic



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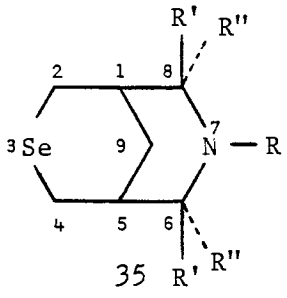

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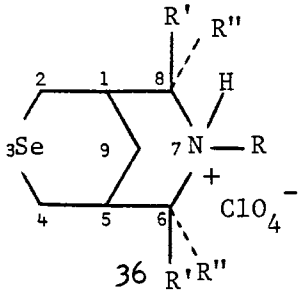

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a, R = $C_6H_5CH_2$-; R' = R" = H

b, R = 2-$C_4H_3SCH_2$-; R' = R" = H

c, R = $C_6H_5CH_2CH_2$-; R' = R" = H

d, R = 4-$CH_3OC_6H_4CH_2CH_2$-; R' = R" = H

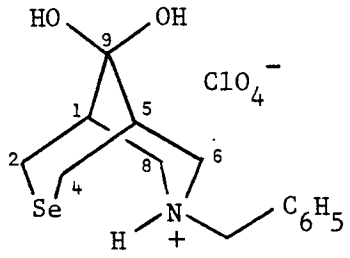
e, R = 3,4-$(CH_3O)_2C_6H_3CH_2CH_2$-; R' = R" = H

f, R' = C_6H_5-; R = R" = H

g, R' = 2-C_4H_3S-; R = R" = H

h, R' = 4-ClC_6H_4-; R = R" = H

i, R" = 4-ClC_6H_4-; R = R' = H



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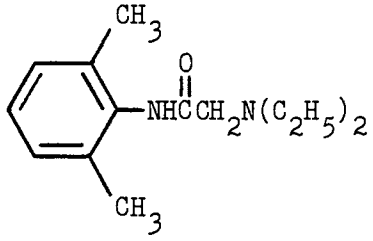
activity was evaluated in anesthetized dogs by Dr. Benjamin J. Scherlag of the Veterans Administration Medical Center in Oklahoma City. The

development of the imaging agent utilizing our synthetic techniques is currently in progress under the direction of Dr. G. Basmadjian of the University of Oklahoma College of Pharmacy in Oklahoma City.

Initially, it seemed logical that 4-selenanone (38) would be a key synthon for the preparation of the ketones 34 which, in turn, could be converted to the amines 35 and the salts 36 and 37. It was surprising to find that 4-selenanone had never been reported, although it is a parent six-membered ketone in the group VIa elements. Consequently, a de novo synthesis was completed for 4-selenanone (38) and a paper is in press on the work.[114a] In addition, the preparation has been submitted for possible inclusion in Inorganic Syntheses.[114b] One additional spin off from the work has been the recording of ^{77}Se NMR shifts for a variety of selenanones and related six-membered, selenium-containing ring systems.[115] These kinds of data appear to be of potential value for certain stereochemical designations in the six-membered rings.



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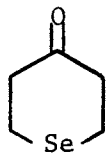

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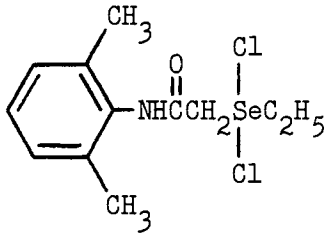

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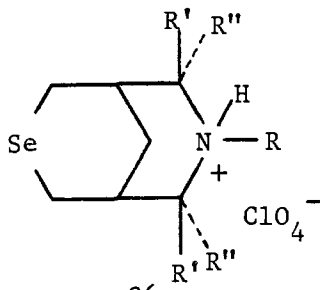
During the course of this investigation, the screening for antiarrhythmic activity in dogs by Dr. Scherlag required a standard agent with which to compare the action of the selenium compounds. Since lidocaine (12) is the most common clinical agent for the treatment of arrhythmias for victims of sudden heart attacks, we elected to synthesize a selenium-containing mimic of lidocaine. This was achieved with the complete structure characterization of 39.

Chemistry

Because of the favorable biological properties of several of the 3,7-diheterobicyclo[3.3.1]nonanes, and most notably 7-benzyl-3-thia-7-azabicyclo[3.3.1]nonane hydroperchlorate (40),[6] we wished to synthesize selenium-containing analogs of 40, namely 36 and 37, which, with ^{75}Se incorporation, could potentially be of use as myocardial imaging agents.



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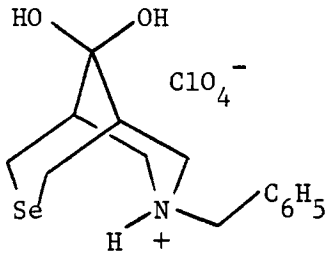

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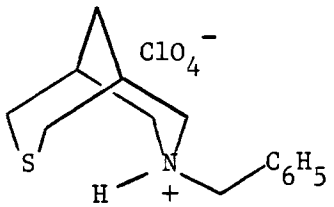

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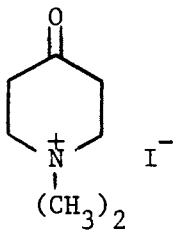

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Frequently, the synthetic routes leading to most of the 3,7-diheterabicyclo[3.3.1]nonanes begin with heterocyclic analogs of cyclohexanone. Therefore, 4-selenanone (38) was chosen as the selenium-containing synthon. Although a few substituted selenanones have been reported,[31,51,66,78,82] this parent compound was heretofore unknown and constituted a new member in the family of 4-heteracyclohexanones.[54,67,68]

The synthesis of 4-selenanone (38, Figure 3) was accomplished in a manner which bears a remote similarity to that for 4-thianone.[61] Elemental selenium was reduced in situ with an equivalent of sodium borohydride[62] to give sodium hydrogen selenide which attacked 1,1-dimethyl-4-piperidonium iodide (41) in a double S_N2 displacement of dimethylamine. The reduction was performed in ethanol at room temperature and produced a colorless solution to which the amine salt 41 was added. After 5 h at reflux, followed by partial evaporation of ethanol, an aqueous work-up gave a yellow-brown solid which was sublimed to give 4-selenanone (38) as a white crystalline solid (63%) which melted at 55.0-55.5°C. Other attempted syntheses met with varying degrees of success (Figure 3). Efforts to cyclize dicyanoethylselenide under Thorpe condensation conditions failed. In situ generation of H_2Se by reaction of aluminum selenide with water and sodium acetate followed by reaction with 1,1-dimethyl-4-piperidonium iodide (41) produced 4-selenanone in a yield of only 5%. Similarly, reaction of the iodide 41 with sodium selenide also resulted in a low yield of 4-selenanone (38, 5%). Better success was achieved by the generation of H_2Se via reaction of elemental selenium with paraffin wax at 400°C. The H_2Se thus formed was bubbled into methanolic sodium methoxide. Reaction of this solution with the iodide 41 gave 4-selenanone (38) in a yield of 40%. Because of the novelty of

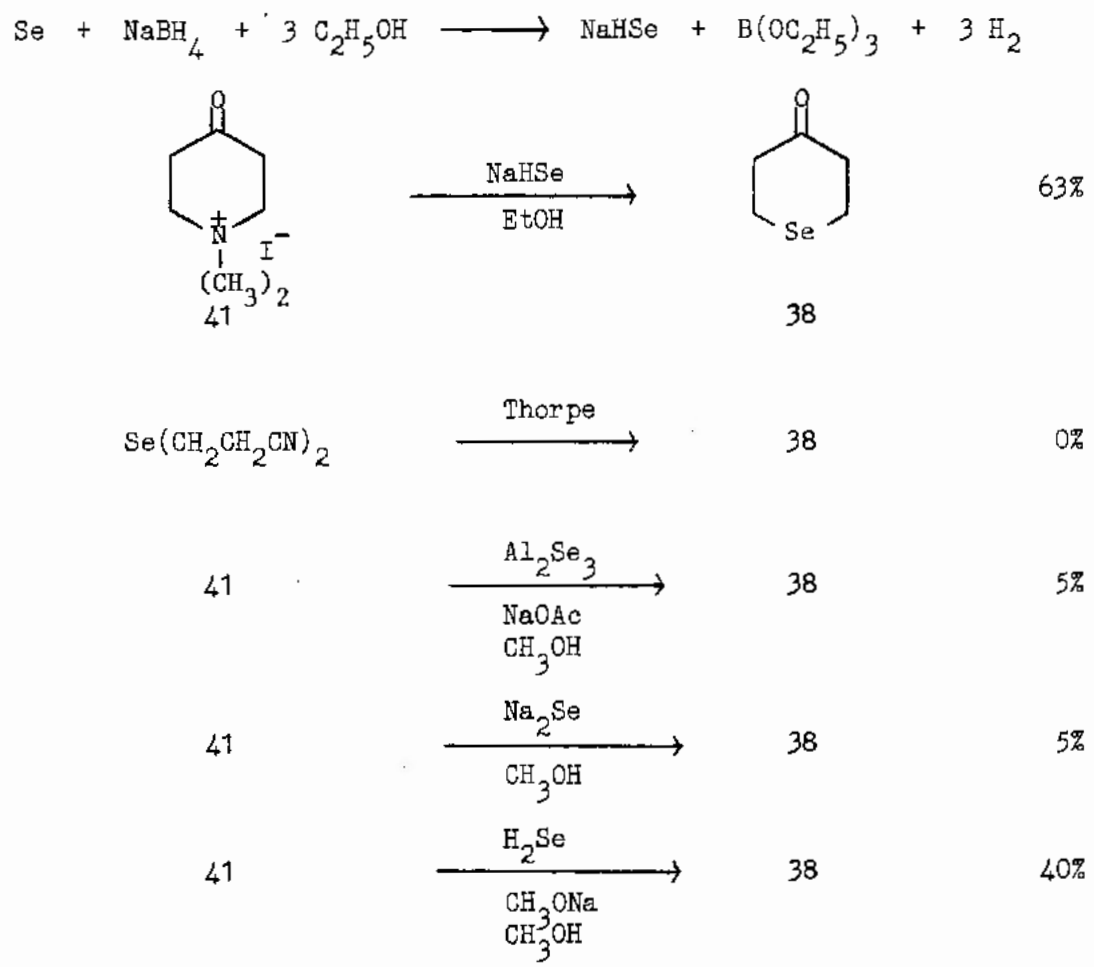
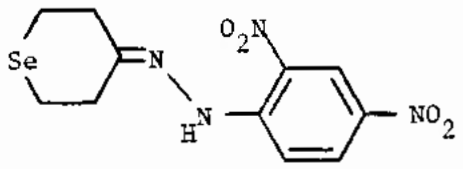


Figure 3. Synthesis of 4-Selenanone (38)

this compound, a single crystal X-ray diffraction analysis was performed which will be discussed later. For characterization purposes, the 2,4-DNP derivative 42 was prepared and melted at 167.0-167.5°C.



42

4-Selenanone (38) was then condensed in a double Mannich reaction with an excess of paraformaldehyde and one of several members of a series of primary amines which contained an aromatic ring (Figure 4). The amines chosen for this study were benzylamine, 2-aminomethylthiophene, phenethylamine, 4-methoxyphenethylamine, and 3,4-dimethoxyphenethylamine leading to 34a-e in yields of 43%, 47%, 22%, 35%, and 31%, respectively.

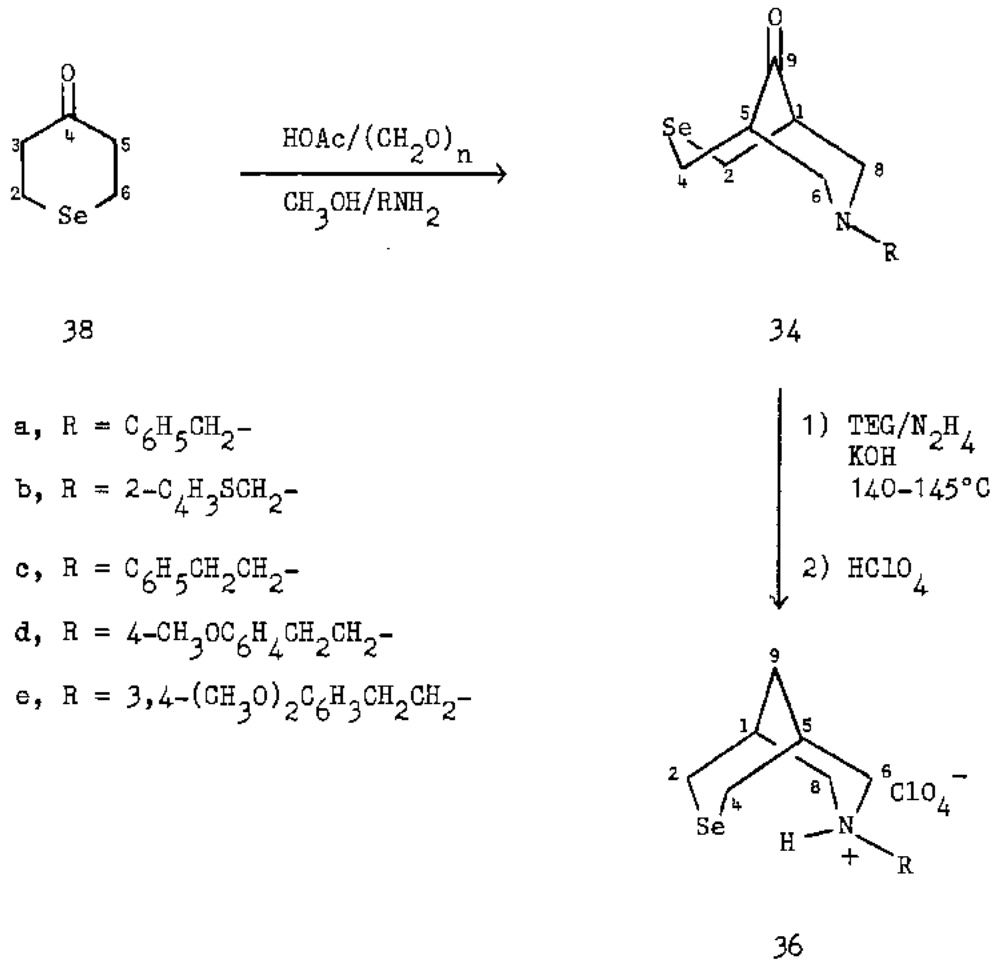
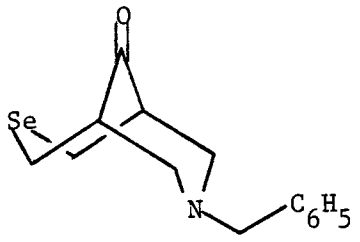
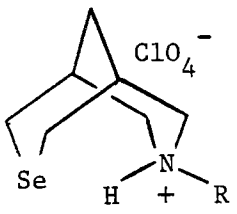


Figure 4. Synthesis of 7-Alkyl-3-selena-7-azabicyclo[3.3.1]nonanes

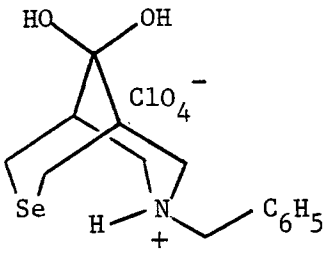
These 7-alkyl-3-selena-7-azabicyclo[3.3.1]nonan-9-ones 34a-e were subjected to Huang-Minlon modifications[79] of the Wolff-Kischner reduction. A typical reduction consisted of dissolving a bicyclic ketone 34 in triethylene glycol along with an excess of hydrazine and potassium hydroxide (Figure 4). Under a stream of nitrogen, the reaction mixture was heated to 140-145°C for 1.5-4 hours. During this time a small amount of water and excess hydrazine was distilled from the reaction mixture. After cooling the glycol solution, it was poured into cool water. The resulting mixture was extracted with ether. The ether extracts were dried and 60% perchloric acid was added very slowly. This precipitated an orange solid, which was recrystallized from methanol, ethanol, or 2-propanol, to give a pure hydroperchlorate salt of a 7-alkyl-3-selena-7-azabicyclo[3.3.1]nonane (36a-e).



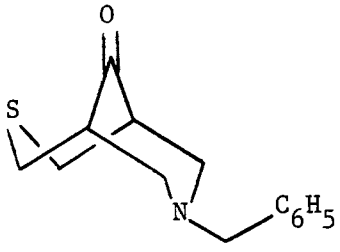
34a



36

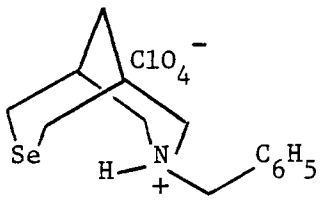


37

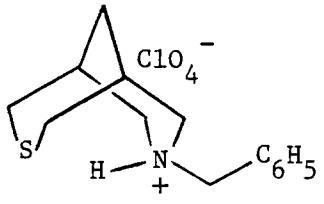


43

Ketone 34a was treated with 60% perchloric acid in ether to give the diol hydroperchlorate salt 37. This is reminiscent of other diols of 3,7-diheterabicyclo[3.3.1]nonan-9-one systems.[3,5a] In addition, ketone 34a was subjected to a single crystal X-ray diffraction analysis. The synthesis and X-ray diffraction analysis of ketone 43, the sulfur analog of 34a, was reported by Bailey and co-workers[6] as a precursor to compound 40. In that study, it was determined that solid ketone 43 existed in a chair-boat conformation with the sulfur atom in the boat ring. Due to the isosterism of selenium and sulfur and the very close similarities of the ^{13}C NMR data for all corresponding carbons (except those alpha to Se and S) of 34a and 43, a chair-boat conformation for 34a (selenium in the boat ring) was assumed. This assumption was verified by a single crystal X-ray diffraction analysis performed on 34a. Because of the close similarities in all the spectral data of compounds 34a-e, we feel that a chair-boat conformation is present in these systems with the selenium atom in a boat ring. Salt 36a, a representative member of family 36, was also subjected to a single crystal X-ray diffraction analysis which revealed a chair-chair conformation similar to that found by Bailey and co-workers for the sulfur analog 40[6] and with selenium in a chair ring.



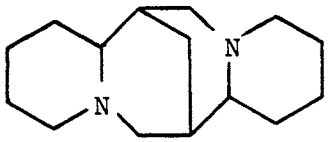
36a



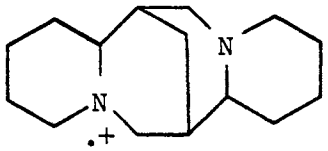
40

The biological activity of compounds 36a, 36c, and 37 were assayed in the laboratory of Dr. B. J. Scherlag of the Veterans Administration Medical Center, Oklahoma City. The results of these tests will be discussed below.

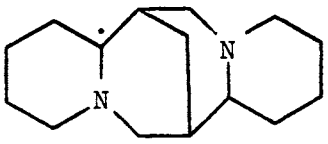
As previously indicated, these bicyclic heterocycles have the same structural backbone as the two internal rings of sparteine (18) and also in many cases share antiarrhythmic properties.[6,93] Sparteine (18) has been found to be metabolized in vitro, through postulated intermediates 44 and 45, to give alcohol 46.[49] Since it is possible that the metabo-



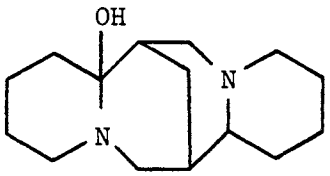
18



44



45

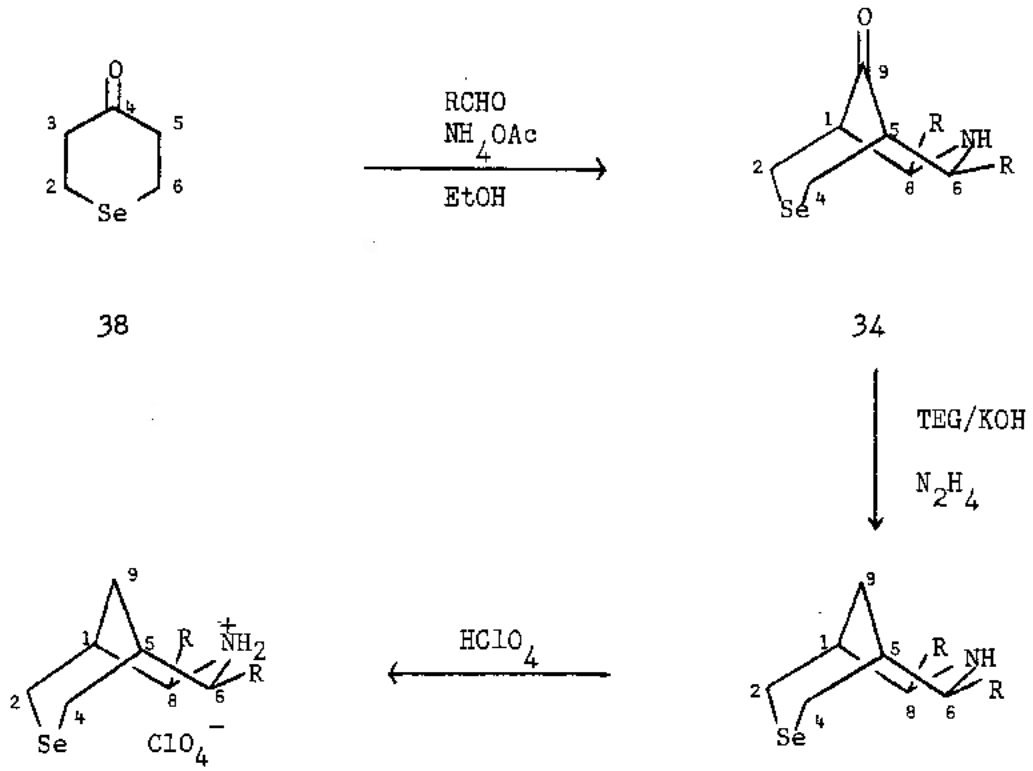


46

lism of 3,7-diheterabicyclo[3.3.1]nonanes may proceed in a similar manner, it was decided to synthesize several bicyclononanes 36f-i (page 29) which had aromatic rings substituted at C(6) and C(8) (flanking the

nitrogen atom). These aromatic rings would stabilize a radical generated alpha to nitrogen (and benzylic). The aromatic groups were chosen so as to enhance the stability of this radical.

The synthetic scheme for the 6,8-diaryl-3-selena-7-azabicyclo[3.3.1]nonanes in Figure 5 involve a double Mannich condensation of an aryl aldehyde and ammonium acetate with 4-selenanone (38). An ethanolic solution of 4-selenanone (38) was added to a warm solution of



38 34

36 35

f, R = C_6H_5-

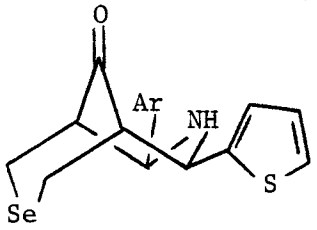
g, R = 2-C_4H_3S-

h, R = 4-ClC_6H_4-

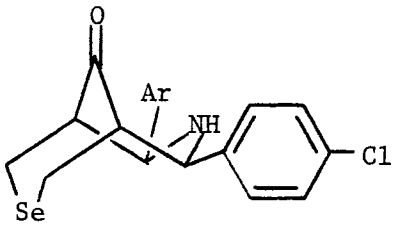
Figure 5. Synthesis of 6,8-Diaryl-3-selena-7-azabicyclo[3.3.1]nonanes

benzaldehyde and ammonium acetate in ethanol. After one hour, a small amount of ether was added and the resulting solution was refrigerated overnight. Work-up of the solid which formed gave 6,8-diphenyl-3-selena-7-azabicyclo[3.3.1]nonan-9-one (34g, 17%).

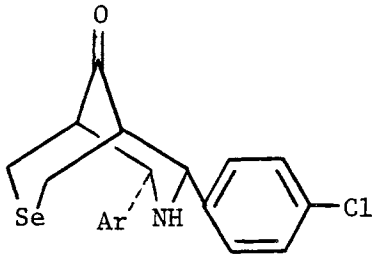
In the cases using 2-thiophenecarboxaldehyde and 4-chlorobenzaldehyde, a simpler, more crude method appeared to be advantageous. In these cases, a boiling solution of the aromatic aldehyde and 4-selenanone (38) in ethanol was poured into a boiling solution of ammonium acetate in ethanol. This was accomplished in open Erlenmeyer flasks on a hot plate. Unaccountably, in these cases, this procedure gave comparable yields (18% and 13%, respectively) of the bicyclic ketones (34g and 34h) with a less tedious work-up than the conditions used for the benzaldehyde run.



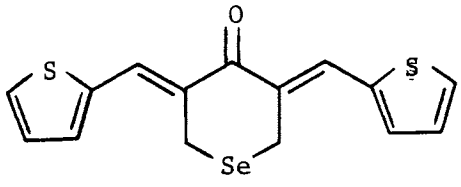
34g



34h



34i

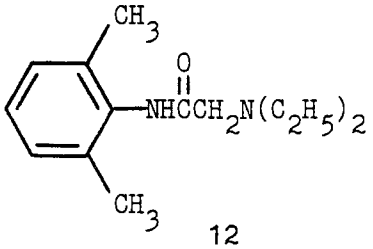


47

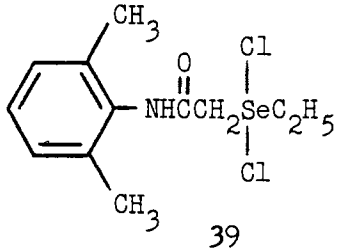
Evaporation of the mother liquor in the run using 2-thiophenecarboxaldehyde gave a dark orange-red oil which crystallized from absolute ethanol to give a small amount of an orange solid which was determined to be enone 47 based on NMR and elemental analyses. Addition of water to the mother liquor in the run using 4-chlorobenzaldehyde caused the formation of a precipitate which was determined to be ketone **34i**, an isomer of **34h**. The conformational analysis of **34h** and **34i** will be discussed in the NMR analysis section.

These bicyclic ketones (**34f-i**) were then subjected to reduction under Wolff-Kishner conditions. For example, ketone **34f** was dissolved in triethylene glycol and allowed to react with an excess of hydrazine and potassium hydroxide at a temperature of about 200°C for four hours (Figure 5). A precipitate formed upon pouring the reaction mixture into cold water. Recrystallization of the crude product gave a good yield (74%) of **35f**. The reductions of **34g**, **34h**, and **34i** were accomplished in a similar manner (67%, 47%, 59%, respectively). Hydroperchlorate salts **36f-i** of these amines were formed by treatment with 60% hydrochloric acid in either benzene or ether in the usual manner.

Since lidocaine (**12**) is the drug of choice in the treatment of ventricular tachycardia and also because it is the standard to which the



12



39

compounds above are compared in their assay of biological activity, we elected to synthesize the selenium-containing lidocaine analogue 39. The preparation of 39 (Figure 6) began with preparation of the synthon, diethyl diselenide (48). This was accomplished by a dissolving metal

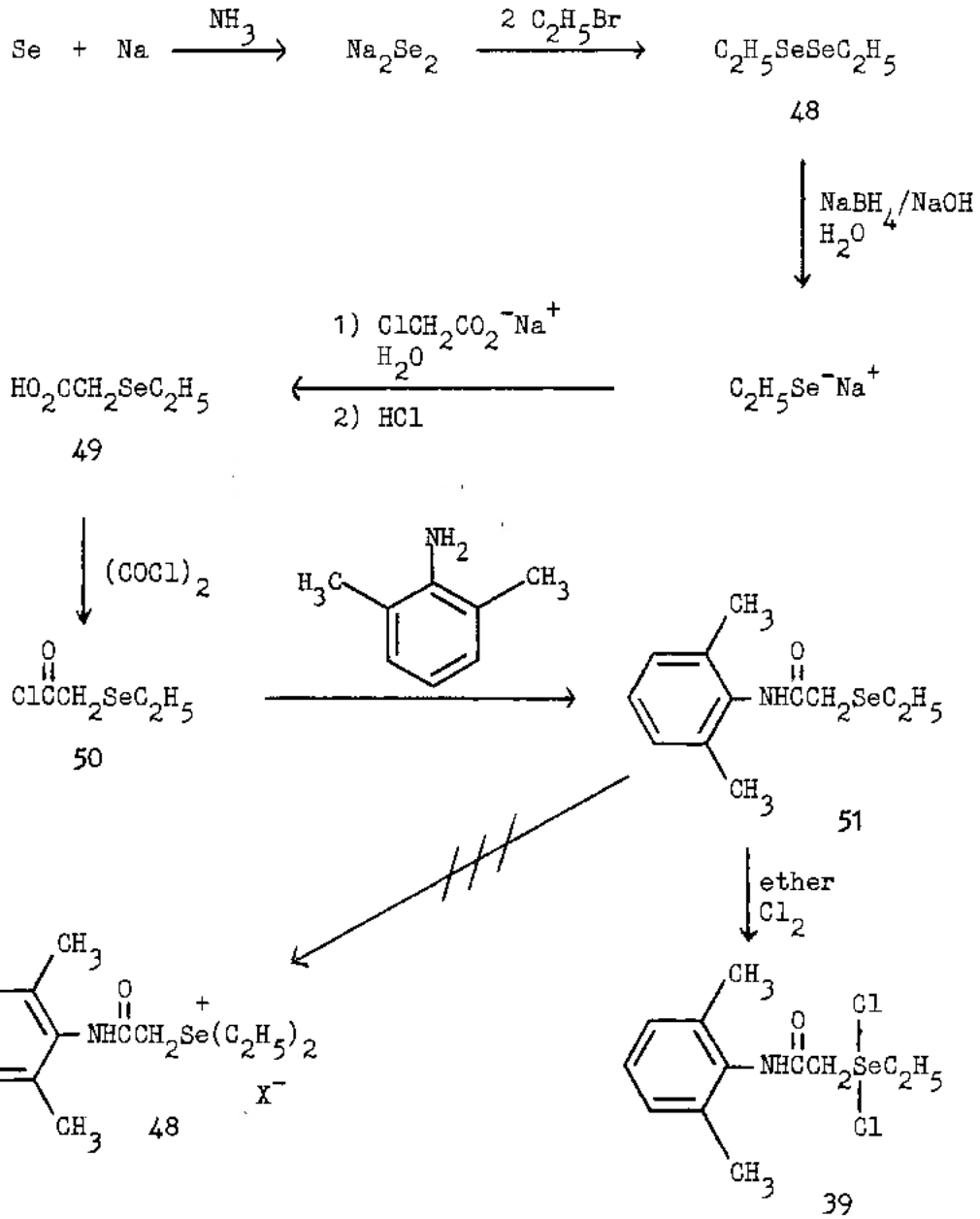


Figure 6. Synthesis of Selenalidocaine (39)

reduction of elemental selenium to disodium diselenide followed by addition of ethyl bromide to produce, after distillation, diethyl diselenide (48, 48%). Sodium borohydride reduction of diethyl diselenide (48) followed by addition of an aqueous solution of sodium chloroacetate gave, after acidification, 3-selenavaleric acid (49) in a yield of 76%.[13]

The acid chloride 50 could not be formed by reaction of acid 49 with thionyl chloride. Instead, this tranformation was accomplished with oxalyl chloride as the chlorinating agent to give 3-selenavaleryl chloride (50, 76%). Two equivalents of 2,6-dimethylaniline were added dropwise to an ether solution of 50 precipitating 2,6-dimethylaniline hydrochloride. Filtration of this solid and evaporation of the ether gave the amide 51 (71% after recrystallization).

In order to increase the water-solubility of the amide 51 and also more closely mimic lidocaine (12), attempts were made to ethylate selenium in 51 with ethyl bromide, ethyl iodide, and diethyl sulfate. However, each of these methods failed, and thus the dichloride derivative 39 was synthesized (Figure 6). Amide 51 was dissolved in ether and chlorine gas was bubbled through the solution with the immediate precipitation of dichloroselenide 39 (78%). A single crystal X-ray diffraction analysis was performed on 39.

NMR Analyses

In the characterization and structure elucidation of the compounds discussed above, NMR spectral analysis was indispensable. The elements examined were ^{1}H, ^{13}C, ^{15}N as well as ^{77}Se NMR.

The proton spectra of 4-selenanone (38) exhibited an A_2X_2 splitting

pattern appearing as two triplets, one at δ 2.82 for H(3,5) and one at δ 3.00 for H(2,6). Each of the triplets had a coupling constant of 6.1 Hz. The assignments were made by noting the reduction in the intensity of the triplet at δ 3.00 when the NMR sample was treated with D_2O and K_2CO_3, indicating the exchange of the protons adjacent to the carbonyl group.

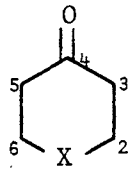
Carbon-13 resonances for 4-selenanone (38) appeared at 19.29, 43.68, and 209.28 ppm and were assigned to C(2,4), C(3,5), and C(4), respectively. Assignments were made by comparison with model compounds such as 4-thianone.[54] Resonances for 4-thianone are shown in Table IV along with those of other heteracyclohexan-4-ones.[54] Comparison of the shifts for the carbons alpha to the heteroatom seem to indicate that selenium is more electropositive than carbon as well as the other heteroatoms shown in the table.

Also recorded was the ^{77}Se NMR spectrum of 4-selenanone (38; this was done as well for the other compounds synthesized in this project). Selenium-77, one of the six stable isotopes of selenium, has a spin of one-half, and, although it has a sensitivity somewhat less than that of carbon (6.93×10^{-3} for selenium; 1.59×10^{-2} for carbon)[83], ^{77}Se has a natural abundance of 7.58% which allows for convenient observation.

Since ^{77}Se NMR is still a relatively new technique, there has not been complete agreement on a universal standard. Some of the suggested standards have been liquid $SeOCl_2$,[15] selenophene,[42,47] and dimethyl selenide.[83] All of the ^{77}Se shifts reported herein will be referenced <u>downfield</u> from dimethyl selenide. However, for routine use, diphenyl diselenide (481.0 ppm downfield from dimethyl selenide[83]) has been used as an <u>external</u>, secondary standard in the collection of ^{77}Se NMR spectra.

TABLE IV

^{13}C NMR DATA FOR SELECTED HETERACYCLOHEXAN-4-ONES[a,b]



X	C(2,6)	C(3,5)	C(4)	Other
Se (38)	19.3	43.7	209.3	
S	30.0	44.0	208.0	
O	67.7	42.8	206.2	
CH_2	27.1	41.9	211.3	25.1
NCH_3	55.3	41.0	207.1	45.4

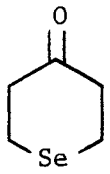
a. Spectra taken in $CDCl_3$; shifts (ppm) are downfield from internal Me_4Si.

b. ^{13}C shifts except those for X = Se were taken from reference 54.

Table V is a collection of ^{77}Se shifts for a selection of organoselenium compounds which includes that of 4-selenanone (38). It is of interest to note that H_2Se gives a ^{77}Se resonance at a very high field in view of the fact that CH_4, PH_3, NH_3, and H_2O give very high field resonances in ^{13}C, ^{31}P, ^{15}N, and ^{17}O NMR, respectively.[15]

TABLE V

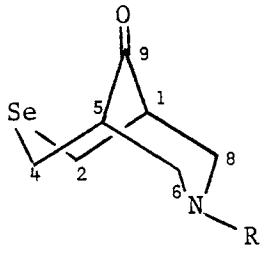
SELENIUM-77 SHIFTS OF SELECTED ORGANOSELENIUM COMPOUNDS[a]

Compound	Shift (ppm)
$(CH_3)_2Se$	0
$(\underline{n}\text{-}C_4H_9)_2Se$	167
$(\underline{n}\text{-}C_8H_{17})_2Se$	168
$(\underline{i}\text{-}C_3H_7)_2Se$	432
$(C_6H_5Se)_2$	481
H_2Se	-288[b]
 (38)	176.6

a. See reference 83.

b. Spectra taken in D_2O. All others taken in $CDCl_3$.

Proton resonances for the 7-alkyl-3-selena-7-azabicyclo[3.3.1]-nonan-9-ones (**34a-e**) were assigned by comparison with model compounds such as **43**[6] and **52**.[3] There was also heavy reliance upon integrations, splitting patterns, and coupling constants. The highest field resonance in the ^1H spectra of **34a** was a multiplet at δ 2.64-2.78 which integrated to four protons. This was assigned to H(2,4) due to the indication mentioned earlier that selenium appears to be electropositive relative to carbon. A two-proton singlet corresponding to H(10) (benzylic CH_2) was



a, R = $C_6H_5CH_2$-

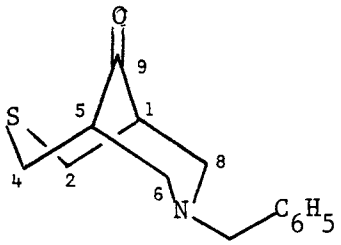
b, R = 2-$C_4H_3SCH_2$-

c, R = $C_6H_5CH_2CH_2$-

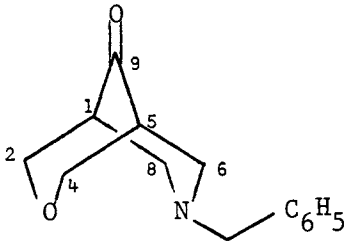
d, R = 4-$CH_3OC_6H_4CH_2CH_2$-

e, R = 3,4-$(CH_3O)_2C_6H_3CH_2CH_2$-

34



43



52

found at δ 3.59. This is in comparison with the corresponding protons in 43[6] and 52[3] which appear at δ 3.50 and 3.52, respectively. The ring protons next to the nitrogen atom in 34a appeared as a four-proton multiplet at δ 3.14-3.25. The corresponding resonance in 52 appears as peaks at δ 2.9-3.1.[3] A two-proton multiplet (or broad singlet) for H(1,5) was found at δ 3.02-3.14. The aromatic protons appeared as a five-proton multiplet at δ 7.24-7.50. Similar shifts were found for 34b. In 34c, 34d, and 34e, the resonances for H(1,5), H(2,4), and H(11) all appear under the same eight proton multiplet. These are centered at δ 2.72 , δ 2.65, and δ 2.70 for 34c, 34d, and 34e, respectively. Resonances for H(6,8) and H(10) also appear together as multiplets which are centered at δ 3.11, δ 3.05, and δ 3.10 for 34c, 34d, and 34e, respec-

tively. Other resonances are found in the experimental section.

Carbon-13 resonances of the bicyclic ketones 34a-e were assigned by comparison with the model ketone 43 and also with respect to the multiplicities found in the off-resonance spectra. In each case the most upfield carbon was determined to be C(2,4). Aliphatic carbon resonances for the model compound 43 and 52 as well as those for 34a-e are found in Table VI. More complete listings are found in the experimental section.

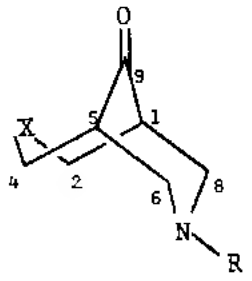
The ^{77}Se and ^{15}N shifts for bicyclononanones 34a-e have been collected in Table VII. The ^{77}Se shifts of salts 34a and 34b are similar to each other but are several parts per million downfield from the salts 34c, 34d, and 34e which also show similarities. This trend is also seen in the ^{15}N shifts.

The ^{13}C NMR spectra for 7-alkyl-3-selena-7-azabicyclo[3.3.1]nonane hydroperchlorate salts 36a-e were assigned by comparison with the spectra of model compounds 40[6] and 53,[3] which are the sulfur and oxygen analogs of 36a. Off-resonance ^{13}C spectra were also utilized in the assignments. A comparison of the shifts for the aliphatic carbons of these compounds is given in Table VIII with a more complete listing given in the experimental section. As before, the highest field resonance was that of C(2,4). With the exception of the C(2,4) peak, the spectra of 36a and 40 were almost identical.

The ^{77}Se and ^{15}N shifts for the salts 36a-e are collected in Table IX. Once again the corresponding shifts for 36a and 36b are further downfield than those of 36c, 36d, and 36e.

TABLE VI

ALIPHATIC ^{13}C SHIFTS FOR SELECTED 7-ALKYL-3-HETERA-7-AZABICYCLO[3.3.1]NONAN-9-ONES



34a, X = Se; R = $C_6H_5CH_2$-

b, X = Se; R = 2-$C_4H_3SCH_2$-

c, X = Se; R = $C_6H_5CH_2CH_2$-

d, X = Se; R = 4-$CH_3OC_6H_4CH_2CH_2$-

e, X = Se; R = 3,4-$(CH_3O)_2C_6H_3CH_2CH_2$-

43, X = S; R = $C_6H_5CH_2$-

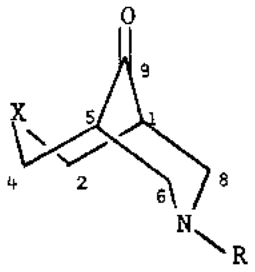
52, X = O; R = $C_6H_5CH_2$-

Compound	C(2,4)	C(1,5)	C(6,8)	C(10)	C(11)	C(9)	Other
34a	25.5	46.2	59.0	61.5	-	213.7	
34b	24.9	46.3	58.8	55.9	-	213.3	
34c	25.4	46.2	59.1	58.3	33.7	213.5	
34d	24.6	45.4	58.2	57.8	33.0	212.5	54.2
34e	25.4	46.2	59.1	58.6	33.2	213.8	55.7
43	34.6	47.1	58.4	61.4	-	212.8	
52[a]	73.3	49.5	57.5	61.1	-	211.5	

a. Thought to exist in a chair-chair conformation.[3]

TABLE VII

SELENIUM-77 AND NITROGEN-15 SHIFTS FOR SELECTED 7-ALKYL-3-HETERA-7-AZABICYCLO[3.3.1]NONAN-9-ONES



34a, X = Se; R = $C_6H_5CH_2$-

b, X = Se; R = 2-$C_4H_3SCH_2$-

c, X = Se; R = $C_6H_5CH_2CH_2$-

d, X = Se; R = 4-$CH_3OC_6H_4CH_2CH_2$-

e, X = Se; R = 3,4-$(CH_3O)_2C_6H_3CH_2CH_2$-

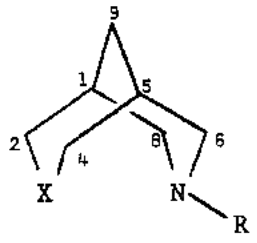
43, X = S; R = $C_6H_5CH_2$-

Compound	^{77}Se (ppm)	^{15}N (ppm)
34a	84.68	38.31
34b	86.28	40.31
34c	79.51	35.44
34d	78.81	35.43
34e	77.00	35.16
43[a]	-	37.36

a. Reference 6.

TABLE VIII

ALIPHATIC ^{13}C SHIFTS FOR SELECTED 7-ALKYL-3-HETERA-7-AZABICYCLO[3.3.1]NONANE HYDROPERCHLORATES



36a, X = Se; R = $C_6H_5CH_2$-

b, X = Se; R = 2-$C_4H_3SCH_2$-

c, X = Se; R = $C_6H_5CH_2CH_2$-

d, X = Se; R = 4-$CH_3OC_6H_4CH_2CH_2$-

e, X = Se; R = 3,4-$(CH_3O)_2C_6H_3CH_2CH_2$-

37, X = Se; R = $C_6H_5CH_2$-; 9,9-diol

40, X = S; R = $C_6H_5CH_2$-

53, X = O; R = $C_6H_5CH_2$-

Compound	C(2,4)	C(1,5)	C(6,8)	C(10)	C(11)[a]	C(9)	Other
36a	22.0	25.3	56.6	60.6	-	28.7	
36b	21.9	25.3	56.2	54.9	-	28.6	
36c	21.9	25.3	56.7	58.8	29.9	28.5	
36d	21.9	25.3	56.7	58.9	28.9	28.5	55.01
36e	22.0	25.3	56.7	58.9	29.4	28.5	55.4, 55.5
37	21.1	34.7	54.9	60.1	-	92.5	
40[b]	29.9	24.9	55.6	59.9	-	27.7	
53[c]	58.1	29.9	62.5	72.9	-	30.4	

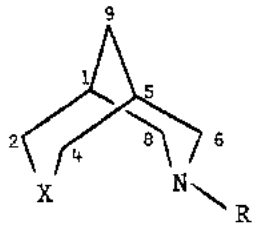
a. C(11) and C(9) may be reversed.

b. Reference 6.

c. Reference 3.

TABLE IX

SELENIUM-77 AND NITROGEN-15 SHIFTS FOR SELECTED 7-ALKYL-3-HETERA-7-AZABICYCLO[3.3.1]NONANE HYDROPERCHLORATES



36a, X = Se; R = $C_6H_5CH_2$-

b, X = Se; R = 2-$C_4H_3SCH_2$-

c, X = Se; R = $C_6H_5CH_2CH_2$-

d, X = Se; R = 4-$CH_3OC_6H_4CH_2CH_2$-

e, X = Se; R = 3,4-$(CH_3O)_2C_6H_3CH_2CH_2$-

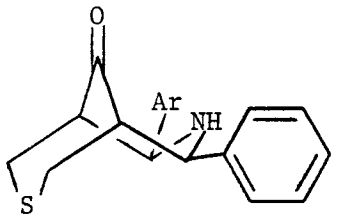
37, X = Se; R = $C_6H_5CH_2$-; 9,9-diol

40, X = S; R = $C_6H_5CH_2$-

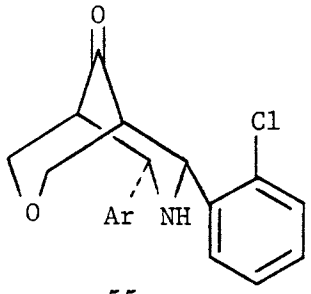
Compounds	^{77}Se (ppm)	^{15}N (ppm)
36a	96.61	51.56
36b	89.41	58.54
36c	88.42	48.25
36d	88.64	48.10
36e	88.35	48.03
37	62.39	51.88
40[a]	-	54.16

a. Reference 6.

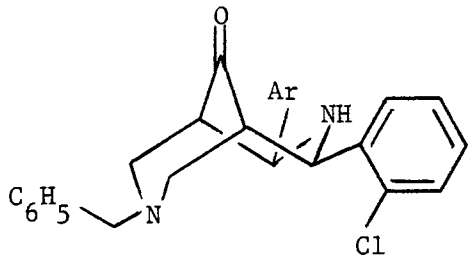
Compounds 54[34] and 55[3] were used as model compounds in the ^{13}C spectral analysis (Tables X and XI) of the 6,8-diaryl-3-selena-7-azabicyclo[3.3.1]nonan-9-ones (34f-i). Spectral data[108] of the isomeric ketones 56 and 57 were indispensable in the conformational analysis of the



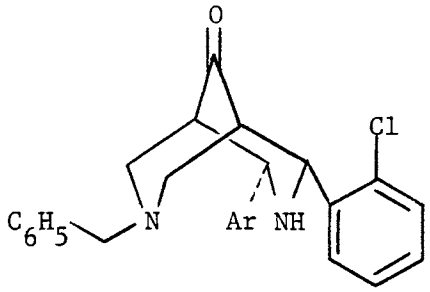
54



55



56



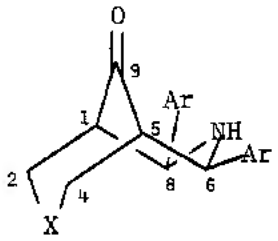
57

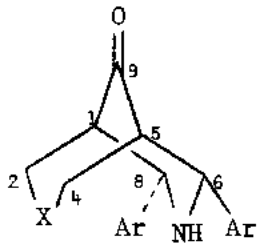
ketones 34f-i. The conformations of the isomers 56 and 57 were determined from spectral analysis as well as from an X-ray diffraction analysis which was performed on ketone 56.[108]

Similarities in the ^{13}C shifts indicated that ketones 34f, 34g, and 34h all had common conformations (Tables X) which were different from that of 34i. For example, the ^{13}C shifts for the carbon alpha to selenium in 34f, 34g, and 34h were 29.2, 29.3, 29.0 ppm, respectively, while the corresponding shift in 34i was 20.9 ppm. Comparison of the relative ^{13}C shifts of the corresponding carbons in ketones 56 and 57 as well as those for ketones 34h and 34i seem to indicate that the nitrogen-containing ring in 34h resides in a boat conformation whereas the corresponding ring in 34i is in a chair conformation. For example, the ^{13}C shifts for C(2,4) and C(1,5) in ketone 56 (chair-boat; 58.8 and 55.2 ppm, respectively) appear downfield relative to the corresponding shifts

TABLE X

ALIPHATIC ^{13}C SHIFTS OF SELECTED 6,8-DIARYL-3-HETERA-7-AZABICYCLO[3.3.1]NONAN-9-ONES





34f, X = Se; Ar = C_6H_5-

34g, X = Se; Ar = 2-C_4H_3S-

34h, X = Se; Ar = 4-ClC_6H_4-

54, X = S; Ar = C_6H_5-

56, X = $C_6H_5CH_2N$; Ar = 2-ClC_6H_4-

34i, X = Se; Ar = 4-ClC_6H_4-

55, X = O; Ar = 2-ClC_6H_4-

57, X = $C_6H_5CH_2N$; Ar = 2-ClC_6H_4-

Compound	C(2,4)	C(1,5)	C(6,8)	C(9)
34f	29.2	53.9	64.1	206.3
34g	29.3	54.6	59.1	212.5
34h	29.0	53.9	63.4	213.4
54[a]	37.4	55.0	63.5	212.7
56[b]	58.8	55.2	59.0	212.0
34i	20.9	51.5	63.8	212.9
55[c]	69.9	52.2	60.3	209.7
57[b]	55.5	50.9	62.1	212.2

a. Reference 34.
b. Reference 108.
c. Reference 3.

for ketone **57** (chair-chair; 55.5 and 50.9, respectively). Similarly, the shifts for C(2,4) and C(1,5) for ketone **34h** (29.0 and 53.9 ppm, respectively) are downfield relative to the corresponding carbons in ketone **34i** (20.9 and 51.5 ppm, respectively). Although to a lesser extent, the ^{13}C shifts for C(6,8) show a similar relationship. These findings seem to indicate that **34h** (and therefore **34f** and **34g**) exists in a chair-boat conformation with the nitrogen in the boat ring while **34i** resides in a chair-chair conformation.

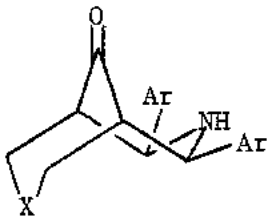
Comparison of the ^{15}N shifts (Table XI) of these compounds gives further credence to this conclusion. The ^{15}N shift for the secondary nitrogen in the 7-position of **56** (58.24 ppm) is downfield from that of **57** (54.45 ppm). A similar relationship exists between **34h** and **34i**. The ^{15}N shift for **34h** (62.84 ppm) is significantly downfield from that found for **34i** (44.24 ppm).

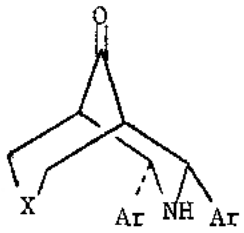
Perhaps one of the strongest pieces of evidence for a chair-chair conformation for the ketone **34i** is the drastic deshielding of selenium found in the ^{77}Se NMR spectrum (122.66 ppm for **34i** compared to 26.67 ppm for **34h**) indicating a hydrogen bond (Se...H-N) which could only be achieved if ketone **34i** resides in a chair-chair conformation. Unfortunately, there are no adequate selenane systems published whose known structure could serve as a model for our compounds.

Spectral data for the amines **35f-i** and salts **36f-i** are found in Tables XII and XIII and Tables XIV and XV, respectively. It is interesting that protonation of nitrogen four bonds removed from selenium causes the ^{77}Se signal to be shifted upfield one part per million in **36f** as compared to **35f**.

TABLE XI

SELENIUM-77 AND NITROGEN-15 SHIFTS FOR SELECTED 6,8-DIARYL-3-SELENA-7-AZABICYCLO[3.3.1]NONAN-9-ONES





34f, X = Se; Ar = C_6H_5-

34g, X = Se; Ar = 2-C_4H_3S-

34h, X = Se; Ar = 4-ClC_6H_4-

56, X = $C_6H_5CH_2N$; Ar = 2-ClC_6H_4-

34i, X = Se; Ar = 4-ClC_6H_4-

57, X = $C_6H_5CH_2N$; Ar = 2-ClC_6H_4-

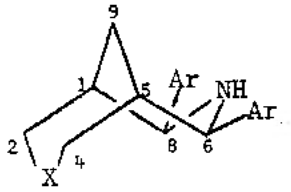
Compound	^{77}Se (ppm)	^{15}N (ppm)
34f	25.38	63.28
34g	30.60	67.09
34h	26.67	62.84
56[a]	-	58.24 (38.31)[b]
34i	122.66	44.24
57[a]	-	54.45 (46.90)[b]

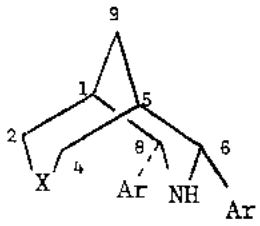
a. Reference 108.

b. ^{15}N shifts for the nitrogen in position 3.

TABLE XII

ALIPHATIC ^{13}C SHIFTS OF SELECTED 6,8-DIARYL-3-HETERA-7-AZABICYCLO[3.3.1]NONANES





35f, X = Se; Ar = C_6H_5-

35g, X = Se; Ar = 2-C_4H_3S-

35h, X = Se; Ar = 4-ClC_6H_4-

58, X = $C_6H_5CH_2N$; Ar = 2-ClC_6H_4-

35i, X = Se; Ar = 4-ClC_6H_4-

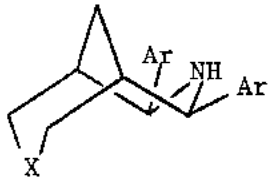
59, X = $C_6H_5CH_2N$; Ar = 2-ClC_6H_4-

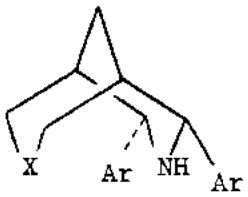
Compound	C(2,4)	C(1,5)	C(6,8)	C(9)
35f	25.1	34.5	62.0	27.2
35g	25.0	34.6	57.1	25.8
35h	25.1	33.8	60.9	26.9
58[a]	58.8	36.1	56.1	24.6
35i	17.7	30.4	64.0	35.0
59[a]	54.9	31.5	61.6	35.9

a. Reference 108.

TABLE XIII

SELENIUM-77 AND NITROGEN-15 SHIFTS OF SELECTED 6,8-DIARYL-3-SELENA-7-AZABICYCLO[3.3.1]NONANES





35f, X = Se; Ar = C_6H_5-

35g, X = Se; Ar = 2-C_4H_3S-

35h, X = Se; Ar = 4-ClC_6H_4-

58, X = $C_6H_5CH_2N$; Ar = 2-ClC_6H_4-

35i, X = Se; Ar = 4-ClC_6H_4-

59, X = $C_6H_5CH_2N$; Ar = 2-ClC_6H_4-

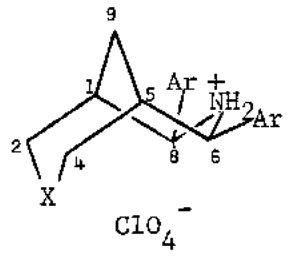
Compound	^{77}Se (ppm)	^{15}N (ppm)
35f	2.38	55.68
35g	4.05	60.10
35h	-0.79	55.37
58[a]	-	50.48 (38.14)[b]
35i	101.86	50.52
59[a]	-	53.80 (47.44)[b]

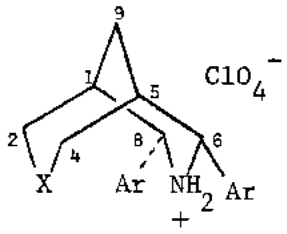
a. Reference 108.

b. ^{15}N shift for the nitrogen in position 3.

TABLE XIV

ALIPHATIC ^{13}C SHIFTS OF SELECTED 6,8-DIARYL-3-HETERA-7-AZABICYCLO[3.3.1]NONANE HYDROPERCHLORATES





36f, X = Se; Ar = C_6H_5-

36g, X = Se; Ar = 2-C_4H_3S-

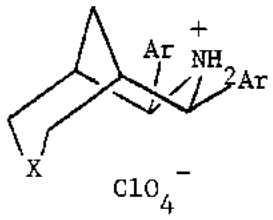
36h, X = Se; Ar = 4-ClC_6H_4-

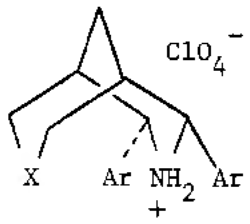
36i, X = Se; Ar = 4-ClC_6H_4-

Compound	C(2,4)	C(1,5)	C(6,8)	C(9)
36f	23.5	31.2	61.5	26.6
36g	23.5	32.5	56.1	26.2
36h	23.5	31.1	60.6	26.5
36i	17.7	29.7	63.7	32.0

TABLE XV

SELENIUM-77 AND NITROGEN-15 SHIFTS OF SELECTED 6,8-DIARYL-3-SELENA-7-AZABICYCLO[3.3.1]NONANE HYDROPERCHLORATES





36f, X = Se; Ar = C_6H_5-

36g, X = Se; Ar = 2-C_4H_3S-

36h, X = Se; Ar = 4-ClC_6H_4-

36i, X = Se; Ar = 4-ClC_6H_4-

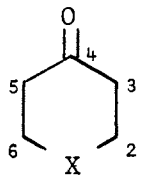
Compound	^{77}Se (ppm)	^{15}N (ppm)
36f	1.16	57.91
36g	5.11	62.39
36h	2.25	57.67
36i	74.96	49.57

X-Ray Data

A single crystal X-ray diffraction study of 4-selenanone (38, Tables XVI-XVIII) revealed that in the solid state the molecule assumes a chair conformation (Figure 7) as has been observed for six-membered rings such as cyclohexanone,[33] tetrahydropyran-4-one,[1] and 4-thianone.[103] However, comparison of the dihedral angles (Table XVII) of 4-

TABLE XVI

BOND DISTANCES (Å) AND ANGLES (°) FOR 1-HETERACYCLOHEXAN-4-ONES



Bond	CH_2[a]	O[b]	S[c]	Se[d]
X-C(2)	1.545	1.41	1.804(3)	1.92(2)
C(6)-X				1.93(2)
C(2)-C(3)	1.542(2)	1.53	1.527(3)	1.56(3)
C(5)-C(6)				1.56(3)
C(3)-C(4)	1.503(4)	1.51	1.527(3)	1.46(3)
C(4)-C(5)				1.49(2)
C(4)-O	1.229(3)	1.222	1.223(5)	1.17(2)
C-H	1.088(2)	1.096	1.116(6)	
X-C(2)-C(3)	110.8(0.2)	113.5	113.2(4)	112.2(11)
C(5)-C(6)-X				111.1(13)
C(2)-C(3)-C(4)	111.5(0.1)	110.5	112.5(10)	115.8(18)
C(4)-C(5)-C(6)				115.5(14)
C(3)-C(4)-C(5)	115.3(0.1)	116.0	118.9(11)	118.2(16)
C(6)-X-C(2)	110.8(0.2)	113.0	97.0(19)	95.0(9)
H-C-H	106.0(0.9)	109.5	111.3(15)	

a. Electron Diffraction: reference 33.
b. Microwave: reference 1.
c. Electron Diffraction: reference 103.
d. X-ray Diffraction: reference 114.

TABLE XVII

DIHEDRAL ANGLES OF SELECTED 1-HETERACYCLOHEXAN-4-ONES

Dihedral Angles (°)	CH_2[a]	S[b]	Se[c]
X-C(2)-C(3)-C(4)	53.0	57.1(16)	57.0(20)
C(4)-C(5)-C(6)-X			58.6(18)
C(2)-C(3)-C(4)-C(5)	51.7	51.0(15)	53.1(22)
C(3)-C(4)-C(5)-C(6)			54.4(23)
C(6)-X-C(2)-C(3)	56.3	58.0(29)	53.5(18)
C(5)-C(6)-X-C(2)			54.2(12)

a. Electron diffraction: reference 33.
b. Electron diffraction: reference 103.
c. X-ray diffraction: reference 114.

selenanone (38) with the 56° observed for cyclohexane indicates that the former ring is somewhat puckered. Comparison with the dihedral angles found for 4-thianone[103] shows that the puckering in 38 is achieved by slightly greater bending of the C-Se-C and of the ring and slight flattening at the carbonyl end. Tables XVI and XVII compare the bond distances, bond angles, and dihedral angles of 4-selenanone (38) with those of cyclohexanone, tetrahydropyran-4-one, and 4-thianone where data was available. The bond angles and distances for 4-selenanone (38) are comparable to others in the literature.[122]

TABLE XVIII

CRYSYAL DATA FOR 4-SELENANONE (38)

Molecular Formula	C_5H_8OSe
Molecular Weight	163.1
Space Group	$P2_1/n$
Cell Dimensions	
<u>a</u>	6.949(4)Å
<u>b</u>	5.620(3)
<u>c</u>	16.926(12)
α	90.0°
β	112.03(5)
γ	90.0
Volume	612.8(6)Å^3
F(000)	320
μMoK_α	59.47 cm^{-1}
μMoK_α	0.71069 Å
D_{calc}	1.767 g cm^{-3}
Z	4
Number of reflections observed	812
R	8.1%

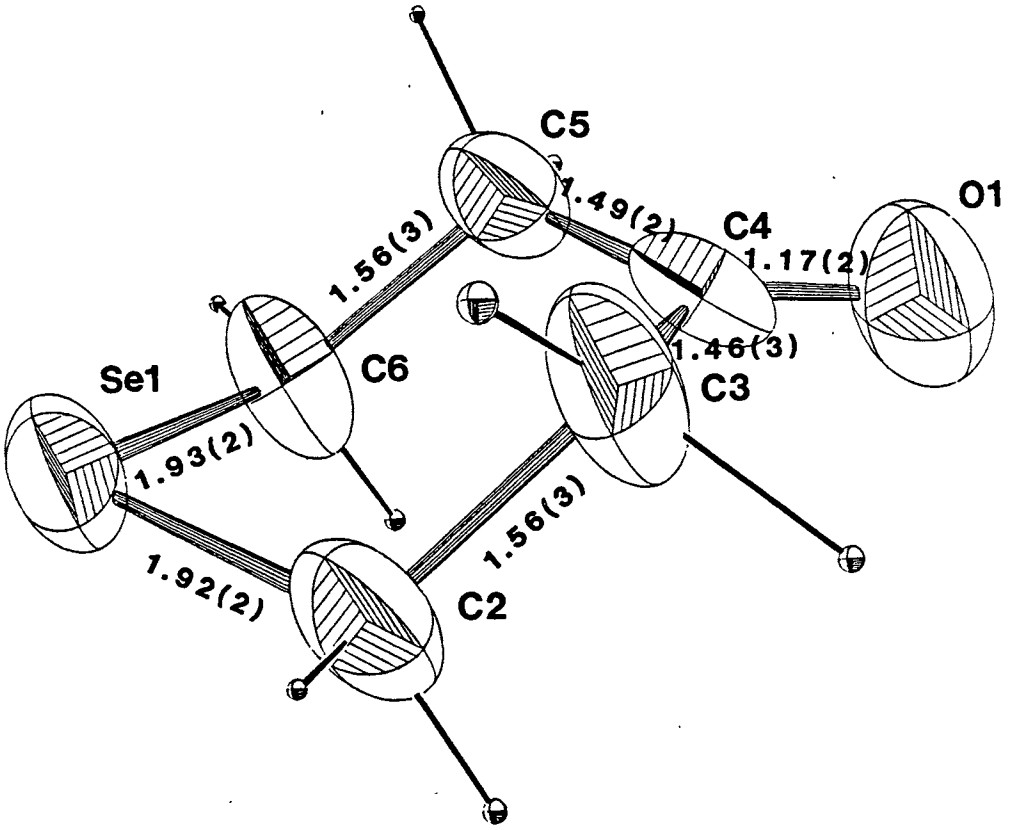
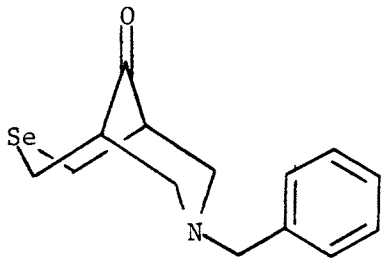


Figure 7. Perspective view of 4-selenanone (38)

7-Benzyl-3-selen-7-azabicyclo[3.3.1]nonan-9-one (34a) crystallized with two molecules per asymmetric unit, both of which displayed chair-boat (CB) conformations with the selenium-containing ring in a boat conformation and the nitrogen-containing ring in a chair form (Figure 8). This is similar to the conformation observed for the 3-thia analog 43.[6] Differences between the sulfur and selenium analogs may be interpreted in light of the larger covalent radius of selenium (1.16 Å as



34a

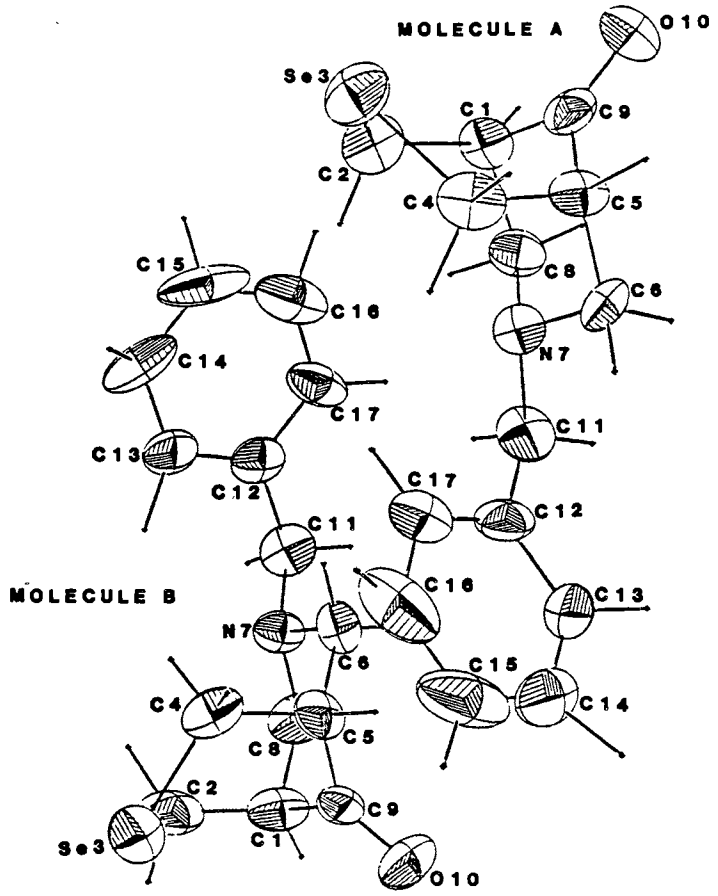


Figure 8. Perspective view of 7-benzyl-3-selena-7-azabicyclo[3.3.1]nonan-9-one (34a)

compared to 1.02 Å for sulfur)[88] and the resulting longer bond lengths (Se-C av. 1.94(1) Å as compared to S-C av. 1.810(4) Å). This manifests itself most prominently in **43a** in the torsion angles [C(9)-C(1)-C(2)-Se(3); C(9)-C(5)-C(4)-Se(3)] relating the conformation of the two ends of the boat. In **43**, these torsion angles are small in magnitude (2.6-3.9°) whereas in **34a**, the comparable torsion angles are significantly greater (45.5-47.2°) indicating a flattening of the selenium end of the boat compared to the sulfur containing boat. This flattening also manifests itself in the Se(3)-C(9) distance [2.901(13) Å, 2.886(13) Å] in **34a** which is larger than the S(3)-C(9) distance [2.831(4) Å, 2.802(4) A] in **43** by an amount approximately equal to the difference in covalent radii. The nitrogen-containing ring in **34a** displays larger [C(9)-C(5)-C(6)-N(7); C(9)-C(1)-C(8)-N(7)] torsion angles (67.7-68.8°) as compared to 58.7-59.1° for **43**, indicating a greater downward bend of the C(6)-N(7)-C(8) plane of the nitrogen-containing ring in **34a**. Thus, substitution of selenium for sulfur resulted in flattening of the selenium containing ring and a greater deviation from planarity for the nitrogen containing ring. Bond lengths, bond angles, and torsion angles are found in Tables XIX, XX, XXI, respectively.

TABLE XIX

BOND DISTANCES (Å) FOR 7-BENZYL-3-SELENA-7-AZABICYCLO[3.3.1]NONAN-9-ONE (34a)

	Molecule A	Molecule B
C(1)-C(2)	1.53(2)	1.51(3)
C(2)-Se(3)	1.93(1)	1.95(2)
Se(3)-C(4)	1.97(1)	1.91(1)
C(4)-C(5)	1.53(2)	1.49(2)
C(5)-C(6)	1.53(2)	1.53(2)
C(6)-N(7)	1.45(2)	1.44(2)
N(7)-C(8)	1.45(2)	1.46(2)
C(8)-C(1)	1.55(2)	1.57(2)
C(1)-C(9)	1.50(2)	1.49(2)
C(5)-C(9)	1.52(2)	1.51(2)
C(9)-O(10)	1.19(2)	1.22(2)
N(7)-C(11)	1.45(2)	1.48(2)
C(11)-C(12)	1.50(2)	1.50(2)
C(12)-C(13)	1.41(3)	1.35(2)
C(13)-C(14)	1.37(2)	1.37(2)
C(14)-C(15)	1.34(4)	1.40(3)
C(15)-C(16)	1.36(3)	1.36(4)
C(16)-C(17)	1.37(2)	1.35(2)
C(17)-C(12)	1.37(2)	1.37(2)

TABLE XX

BOND ANGLES (°) FOR 7-BENZYL-3-SELENA-7-AZABICYCLO[3.3.1]NONAN-9-ONE (34a)

	Molecule A	Molecule B
C(1)-C(2)-Se(3)	113.0(9)	112.1(12)
C(2)-Se(3)-C(4)	95.3(5)	90.5(6)
Se(3)-C(4)-C(5)	111.0(8)	114.4(9)
C(4)-C(5)-C(6)	111.3(10)	112.2(12)
C(5)-C(6)-N(7)	108.9(11)	112.3(11)
C(6)-N(7)-C(8)	110.8(10)	110.1(11)
N(7)-C(8)-C(1)	109.6(9)	110.3(10)
C(8)-C(1)-C(2)	111.0(11)	108.6(12)
C(2)-C(1)-C(9)	113.3(9)	113.4(11)
C(4)-C(5)-C(9)	114.6(11)	112.6(11)
C(8)-C(1)-C(9)	105.5(11)	106.1(11)
C(6)-C(5)-C(9)	106.6(9)	105.3(9)
C(1)-C(9)-C(5)	113.0(19)	113.4(12)
C(1)-C(9)-O(10)	123.4(12)	123.6(11)
C(5)-C(9)-O(10)	123.5(13)	122.8(13)
C(6)-N(7)-C(11)	113.7(11)	113.8(10)
C(8)-N(7)-C(11)	110.9(9)	110.7(9)
N(7)-C(11)-C(12)	111.3(10)	111.8(10)
C(11)-C(12)-C(13)	119.7(13)	120.2(13)
C(11)-C(12)-C(17)	123.2(13)	118.6(13)
C(12)-C(13)-C(14)	118.8(16)	120.2(14)
C(13)-C(14)-C(15)	123.2(19)	118.6(18)

Table XX (Continued)

C(14)-C(15)-C(16)	118.0(19)	119.8(16)
C(15)-C(16)-C(17)	121.5(18)	120.9(18)
C(16)-C(17)-C(12)	121.3(15)	119.3(17)
C(17)-C(12)-C(13)	117.2(13)	121.2(13)

TABLE XXI

TORSION ANGLES (°) FOR 7-BENZYL-3-SELENA-7-AZABICYCLO[3.3.1]NONAN-9-ONE (34a)

	Molecule A	Molecule B
C(1)-C(2)-Se(3)-C(4)	57.9	60.0
C(2)-Se(3)-C(4)-C(5)	55.8	58.5
Se(3)-C(4)-C(5)-C(6)	126.2	128.2
C(4)-C(5)-C(6)-N(7)	76.5	76.5
C(5)-C(6)-N(7)-C(8)	74.9	73.7
C(6)-N(7)-C(8)-C(1)	75.4	71.4
N(7)-C(8)-C(1)-C(2)	74.6	73.9
C(8)-C(1)-C(2)-Se(3)	125.9	130.5
C(1)-C(9)-C(5)-C(4)	78.6	76.4
C(5)-C(9)-C(1)-C(2)	77.1	74.1
C(1)-C(9)-C(5)-C(6)	70.0	70.1
C(5)-C(9)-C(1)-C(8)	68.8	70.6
Se(3)-C(2)-C(1)-C(9)	46.3	46.5
Se(3)-C(4)-C(5)-C(9)	45.5	47.2
N(7)-C(8)-C(1)-C(9)	67.8	67.7
N(7)-C(6)-C(5)-C(9)	68.2	68.8
C(2)-C(1)-C(9)-O(10)	126.7	131.4
C(4)-C(5)-C(9)-O(10)	126.3	128.0
C(8)-C(1)-C(9)-O(10)	122.2	119.9
C(6)-C(5)-C(9)-O(10)	122.1	119.6
C(1)-C(8)-N(7)-C(11)	168.3	173.5
C(5)-C(6)-N(7)-C(11)	169.1	173.6

Table XXI (Continued)

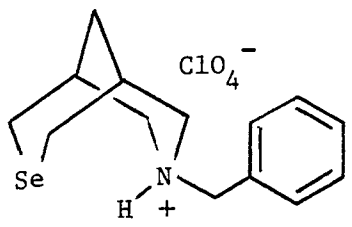
C(8)-N(7)-C(11)-C(12)	168.7	174.5
C(6)-N(7)-C(11)-C(12)	78.8	74.9
N(7)-C(11)-C(12)-C(13)	140.3	72.3
N(7)-C(11)-C(12)-C(17)	68.5	134.0

TABLE XXII

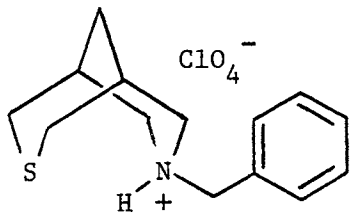
CRYSTAL DATA FOR 7-BENZYL-3-SELENA-7-AZABI-CYCLO[3.3.1]NONAN-9-ONE (34a)

Molecular Formula	$C_{14}H_{17}NOSe$
Molecular Weight	294.10
Space group	P1
Cell Dimensions	
a	12.298(3) Å
b	10.070(2)
c	11.156(4)
α	85.94(3)°
β	92.10(3)°
γ	104.81(2)°
Volume	1332.1(7) $Å^3$
Z	4
F(000)	600
μMoK_α	27.72 cm^{-1}
μMoK_α	0.71069 Å
Density (calculated)	1.466 g cm^{-3}
Number of Reflections Observed	2207
R	6.5%

A single-crystal X-ray diffraction analysis was also undertaken to investigate the conformation of the ring system of 7-benzyl-3-selena-7-azabicyclo[3.3.1]nonane hydroperchlorate (36a). This molecule is the selenium analog of the sulfur containing molecule, 7-benzyl-3-thia-7-azabicyclo[3.3.1]nonane (40), whose crystal structure has been reported.[6] The two structures are isomorphous. Both are found to exist in a chair-chair conformation in the solid state (Figure 9) and both are salts in which the proton from the perchlorate has been transferred to the nitrogen atom in the bicyclic ring. Bond lengths, bond angles and torsion angles are given in Tables XXIII, XXIV, and XV for 36a. A packing diagram is shown in Figure 10.



36a



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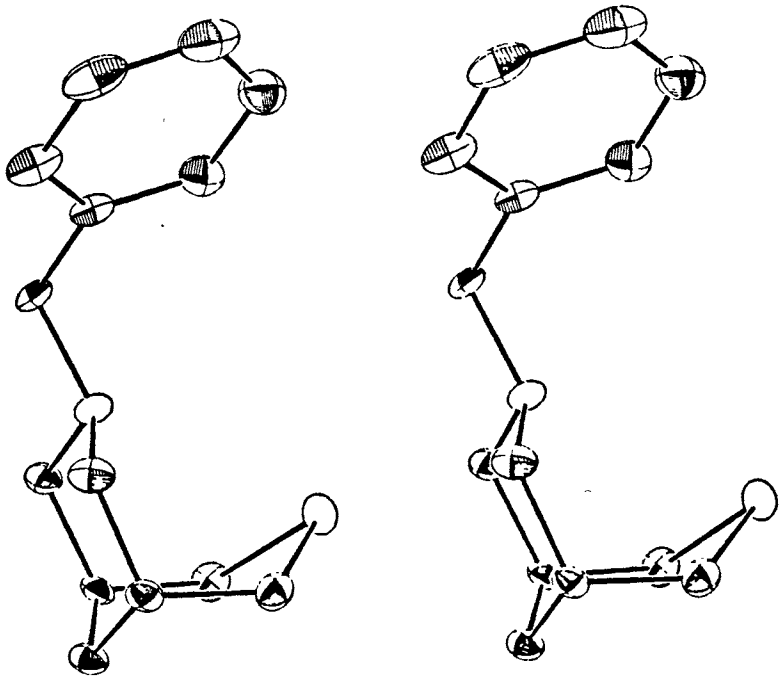


Figure 9. Stereo drawing of 7-benzyl-3-selena-7-azabicyclo[3.3.1]nonane hydroperchlorate (36a)

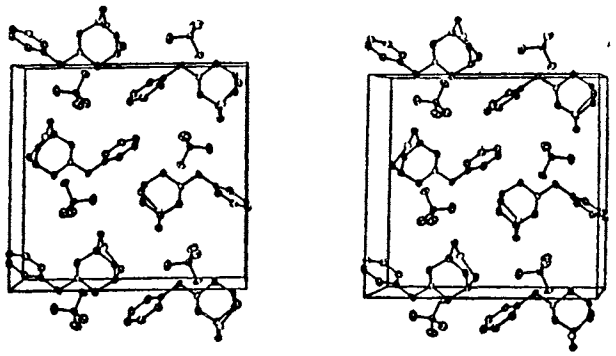


Figure 10. Stereo drawing of the packing of 7-benzyl-3-selena-7-azabicyclo[3.3.1]nonane hydroperchlorate (36a)

An intramolecular hydrogen bond between the selenium and the nitrogen is indicated from the interatomic distances. The distance between N(7) and Se(3) in 36a (Figure 9) is 3.116(5) Å which is significantly shorter than the calculated value of 3.5 Å which is the theoretical van der Waals distance between selenium and nitrogen.[88] The geometry around the selenium is not ideal for hydrogen bonding, however, with the Se(3)...H(7)-N(7) angle being 113.1(2)° rather than the expected 180.0°. On the other hand, the Se(3)...H(7) distance of 2.450(7) Å is also much shorter than expected from the sum of the van der Waals radii of 3.2 Å for selenium and hydrogen. The Se(3)...H(7)-N(7) bond may even be stronger than in the sulfur compound.

The C-Se bond lengths found in this structure are 1.965(7) Å, and 1.947(7) Å. These are close to the range of C-Se [1.98(3) Å] given by Sutton,[113] and about 0.014 Å longer than the comparable distances in the sulfur containing compound. The C-N bond lengths are slightly lengthened due to the protonation of the nitrogen.

The angles between planes 1, 2, 3, 4, and 5 (Figure 11) are similar to the sulfur analog except for the angle between planes 1 and 2, which is 10 degrees larger in the selenium compound. One might expect that the replacement of the sulfur with selenium and the resultant increase in van der Waals radii could cause an increase in ring flattening observed in the seleium compound. Also, the bond angles and torsion angles in the selenium compound are very close to those in the sulfur compound with the exception of the expected changes around the selenium atom.

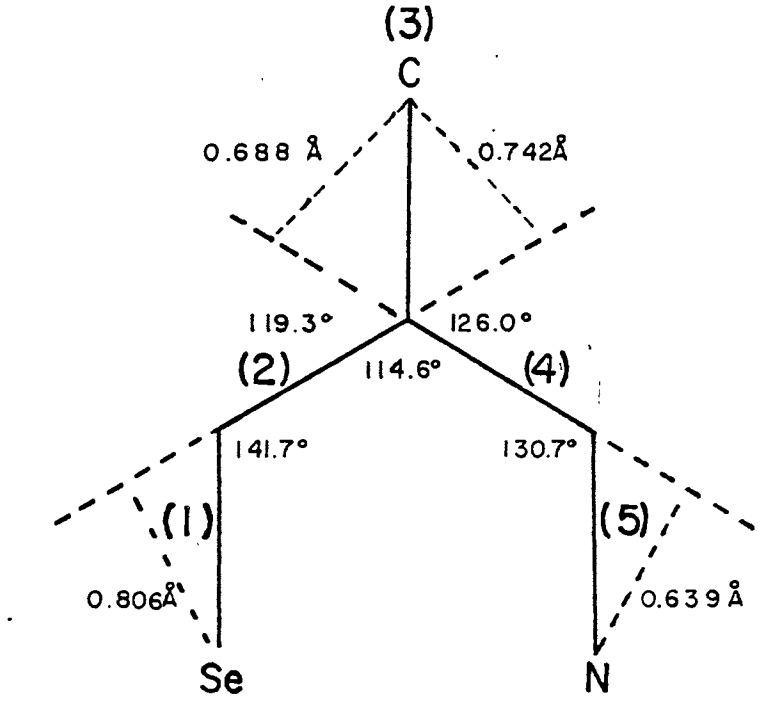


Figure 11. View of the molecular planes of 7-benzyl-3-selena-7-azabicyclo[3.3.1]nonane hydroperchlorate (36a)

TABLE XXIII

BOND DISTANCES (Å) FOR 7-BENZYL-3-SELENA-7-AZABICYCLO[3.3.1]NONANE HYDROPERCHLORATE (36a)

Bond	Distance (Å)[a]
C(1)-C(2)	1.531(10)
C(2)-Se(3)	1.947(7)
Se(3)-C(4)	1.965(7)
C(4)-C(5)	1.520(10)
C(5)-C(6)	1.519(8)
C(6)-N(7)	1.504(8)
N(7)-C(8)	1.512(9)
C(8)-C(1)	1.515(8)
C(1)-C(9)	1.522(9)
C(5)-C(9)	1.511(10)
N(7)-C(10)	1.481(8)
C(10)-C(11)	1.503(8)
C(11)-C(12)	1.382(10)
C(12)-C(13)	1.400(11)
C(13)-C(14)	1.394(10)
C(14)-C(15)	1.376(11)
C(15)-C(16)	1.392(9)
C(16)-C(11)	1.392(10)

a. Value in parentheses are estimated standard deviations (E.S.D.'s) in the significant figures.

TABLE XXIV

BOND ANGLES (°)[a] FOR 7-BENZYL-3-SELENA-7-AZABICYCLO[3.3.1]NONANE HYDROPERCHLORATE (36a)

C(1)-C(2)-Se(3)	113.5(4)
C(2)-Se(3)-C(4)	96.8(3)
Se(3)-C(4)-C(5)	115.5(4)
C(4)-C(5)-C(6)	114.7(6)
C(5)-C(6)-N(7)	110.7(6)
C(6)-N(7)-C(8)	111.9(5)
N(7)-C(8)-C(1)	112.3(6)
C(8)-C(1)-C(2)	114.2(6)
C(2)-C(1)-C(9)	112.7(6)
C(4)-C(5)-C(9)	112.5(6)
C(8)-C(1)-C(9)	109.0(5)
C(6)-C(5)-C(9)	109.1(5)
C(1)-C(9)-C(5)	111.8(6)
C(6)-N(7)-C(10)	108.9(5)
N(7)-C(10)-C(11)	110.2(5)
C(10)-C(11)-C(12)	119.8(7)
C(10)-C(11)-C(16)	119.8(7)
C(11)-C(12)-C(13)	119.3(8)
C(12)-C(13)-C(14)	119.8(8)
C(13)-C(14)-C(15)	121.4(7)
C(14)-C(15)-C(16)	119.8(8)
C(15)-C(16)-C(11)	118.8(7)
C(16)-C(11)-C(12)	120.8(6)

a. E.S.D.'s in the significant figures are given in parentheses.

TABLE XXV

TORSION ANGLES (°)[a] FOR 7-BENZYL-3-SELENA-7-AZABICYCLO-[3.3.1]NONANE HYDROPERCHLORATE (36a)

C(1)-C(2)-Se(3)-C(4)	-42.5(5)
C(2)-Se(3)-C(4)-C(5)	42.4(5)
Se(3)-C(4)-C(5)-C(6)	67.3(7)
C(4)-C(5)-C(6)-N(7)	-69.6(7)
C(5)-C(6)-N(7)-C(8)	-55.2(7)
C(6)-N(7)-C(8)-C(1)	54.0(7)
N(7)-C(8)-C(1)-C(2)	73.1(7)
C(8)-C(1)-C(2)-Se(3)	-65.6(7)
C(1)-C(9)-C(5)-C(4)	68.6(7)
C(5)-C(9)-C(1)-C(2)	-70.2(7)
C(1)-C(9)-C(5)-C(6)	-59.9(7)
C(5)-C(9)-C(1)-C(8)	57.7(7)
Se(3)-C(2)-C(1)-C(9)	59.6(6)
Se(3)-C(4)-C(5)-C(9)	-58.2(6)
N(7)-C(8)-C(1)-C(9)	-54.0(7)
N(7)-C(6)-C(5)-C(9)	57.6(7)
C(1)-C(8)-N(7)-C(10)	176.7(6)
C(5)-C(6)-N(7)-C(10)	-179.8(9)
C(8)-N(7)-C(10)-C(11)	64.0(7)
C(6)-N(7)-C(10)-C(13)	-171.6(6)
N(7)-C(10)-C(11)-C(13)	-116.3(7)
N(7)-C(10)-C(11)-C(16)	63.4(8)

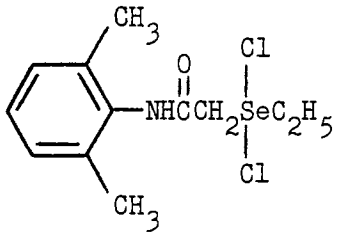
a. E.S.D.'s in the significant figures are given in parentheses.

TABLE XXVI

CRYSTAL DATA FOR 7-BENZYL-3-SELENA-7-AZABICYCLO[3.3.1]NONANE HYDROPERCHLORATE (36a)

Molecular Formula	$C_{14}H_{20}NSe \cdot ClO_4$
Molecular Weight	380.41 g/mole
Linear Absorption Coeffecient	44.56 cm^{-1}
Space Group	$P2_12_12_1$
Cell Dimensions	
a	14.692(4) Å
b	15.950(1) Å
c	6.646(1) Å
Volume	1557.41 $Å^3$
Z	4
Density (calculated)	1.62 g/cm^3
Cell Determination	36 reflections used
Data Collection Range	$0<2\theta<60$
Radiation	Mo K_α
Standards	3, remeasured every 200 reflections
Temperature of Date Collection	138±2K
Number of Reflections Measured	1843
Number of Reflections Observed [$I>2\sigma(I)$]	1766
Structure Refinement	Full Matrix Least Squares (SHELX) (4)
Refinement of Hydrogens	Isotropic
Final Difference Fourier Map Maximum Density	0.384
Final R	0.0552
Rw	0.0538

A single crystal X-ray diffraction analysis of the selenium containing lidocaine derivative **39** was made. The coordination about the selenium atom was found to be trigonal bipyramidal with the free electron pair occupying one of the positions in the basal plane (Figure 12). This seems to agree with previously found structures of selenium bound with chlorine[2,45,75,76,120] and with bromine[9,12,74] and with coordination number of four. Bond distances, bond angles and torsion angles are given Tables XXVII, XXVIII and XXIX. The deviation of the Cl-Se-Cl angle from the ideal value of 180° is very slight: 1.14(7)°. The Cl-Se-C angles differ from 90° value by less than 2°. The C-Se-C angle was found to be 100.4(4)° which compares with 106.5 and 108° for di-*p*-tolylselenium dichloride and dibromide, respectively.[76] The Se-Cl distances of 2.359(2) Å and 2.389(2) Å agree with those found previously.[76,120] The Se-C distances were found to be 1.972(9) Å [Se(1)-C(16)] and 1.942(7) Å [Se(1)-C(15)]. The latter seems somewhat short compared to distances in similar compounds[76,120] as well as the weighted average distance in non-aromatic compounds [0.98(2) Å].[55]. The non-planarity of the peptide group [-NHC(O)-] is described according to Winkler and Dunitz[118] X_C=-0.5°, t=174°, X_N=-21°.



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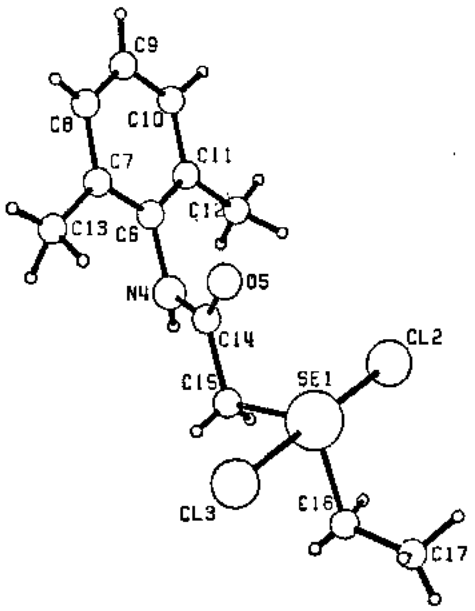


Figure 12. Perspective view of selenalidocaine dichloride (39)

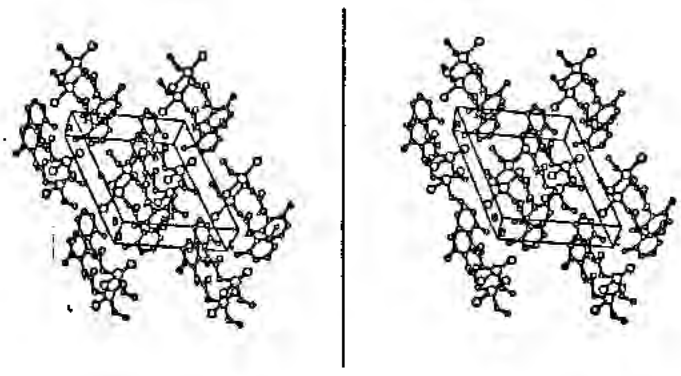


Figure 13. Stereoscopic view of the crystal packing of selenalidocaine dichloride (39)

The hydrogen bonding is observed between O(5) and N(4) of the next molecule. The O...N distance is 2.949(10) Å and O...H distance is 1.98(11) Å and the O-H-N angle is 165(7)°. There seems to be certain strain in the molecule caused by the tendency of the peptide group to align itself to allow for the best H-bonding on one hand and by the packing forces on the other hand (Figures 13). The angle between the plane of C-Se-C bonds and peptide group is 21°. The angle between the peptide group and the plane of six-membered ring is 60° (Table XXIX).

TABLE XXVII

BOND DISTANCES (Å) FOR SELENALIDOCAINE DICHLORIDE (39)

Se(1)-Cl(2)	2.359(2)
Se(1)-Cl(3)	2.389(2)
Se(1)-C(15)	1.942(7)
Se(1)-C(16)	1.972(9)
N(4)-C(6)	1.445(9)
N(4)-C(14)	1.342(10)
O(5)-C(14)	1.216(12)
C(6)-C(7)	1.413(9)
C(6)-C(11)	1.400(9)
C(7)-C(8)	1.396(10)
C(7)-C(13)	1.499(10)
C(8)-C(9)	1.384(10)
C(9)-C(10)	1.367(11)
C(10)-C(11)	1.404(10)
C(11)-C(12)	1.487(11)
C(14)-C(15)	1.517(11)
C(16)-C(17)	1.488(13)

TABLE XXVIII

BOND ANGLES (°) FOR SELENALIDOCAINE DICHLORIDE (39)

Se(1)-C(15)-C(14)	106.2(6)
Se(1)-C(16)-C(17)	109.3(8)
Cl(2)-Se(1)-C(15)	89.3(2)
Cl(2)-Se(1)-C(16)	90.2(2)
Cl(3)-Se(1)-C(15)	91.8(2)
Cl(3)-Se(1)-C(16)	89.4(2)
N(4)-C(6)-C(7)	119.7(5)
N(4)-C(6)-C(11)	117.1(6)
N(4)-C(14)-O(5)	126.0(8)
N(4)-C(14)-C(15)	113.5(8)
O(5)-C(14)-C(15)	120.5(7)
C(6)-N(4)-C(14)	120.9(7)
C(6)-C(7)-C(8)	116.5(6)
C(6)-C(7)-C(13)	122.2(6)
C(6)-C(11)-C(10)	117.4(6)
C(6)-C(11)-C(12)	121.7(7)
C(7)-C(8)-C(9)	120.9(7)
C(8)-C(7)-C(13)	121.2(6)
C(8)-C(9)-C(10)	121.7(7)
C(9)-C(10)-C(11)	120.3(7)
C(10)-C(11)-C(12)	120.9(7)

TABLE XXIX

TORSION ANGLES (°) FOR SELENALIDOCAINE DICHLORIDE (39)

Se(1)-C(15)-C(14)-N(4)	158.1(5)
C(6)-N(4)-C(14)-C(15)	-175.5(5)
C(7)-C(6)-N(4)-C(14)	-67.8(8)
C(11)-C(6)-N(4)-C(14)	110.3(8)
C(14)-C(15)-Se(1)-C(16)	-169.9(5)
C(15)-Se(1)-C(16)-C(17)	-176.7(6)

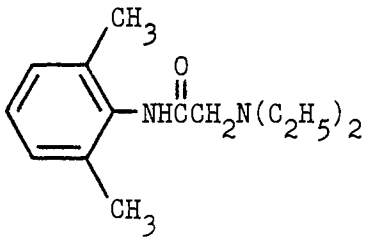
TABLE XXX

CRYSTAL DATA FOR SELENALIDOCAINE DICHLORIDE (39)

Molecular Formula	$C_{12}H_{17}NOSeCl_2$
Molecular Weight	351 g/mole
Space Group	$P2_1$
Cell Dimension	
a	13.622(10) Å
b	4.733(3)
c	12.284(8)
β	113.36(4)
Volume	727 $Å^3$
Z	2
Density (Calculated)	1.56 g/cm^3
Cell Determination	48 reflections used
Data Collection Range	$0<2\theta<53°$
Radiation	MoK_α
Standards	3, monitored every 7200 s of X-ray exposure
Temperature of Data Collection	138±2 K
Number of Reflections Measured	1688
Number of Reflections Observed [$I>2\sigma(I)$]	1388
Structure Refinement	Full Matrix Least Squares (SHELX)
Refinement of Hydrogens	Isotropic
Final Defference Fourier Map Maximum Density	0.52
Final R	0.038

Biological Data

The antiarrhythmic activity of selected members of the family of 3-selena-7-azabicyclo[3.3.1]nonanes was assessed by Dr. B. J. Scherlag of the Veterans Administration Medical Center in Oklahoma City using the 24-hour infarcted dog model described in Chapter I. In these tests, the extent of the activity of each compound was compared to that of the control drug lidocaine (12). The compounds tested were the hydroperchlorates 36a, 36c, 36f, 37, and the selenium-containing, lidocaine mimic 39.



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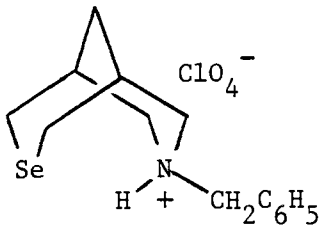
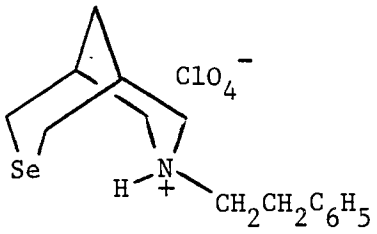
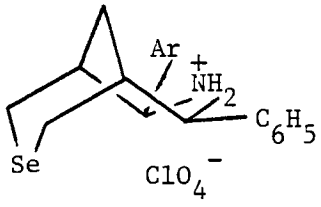


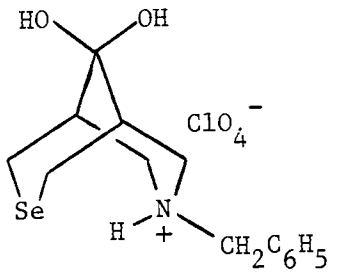
36a



36c



36f



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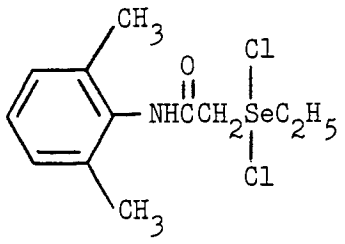
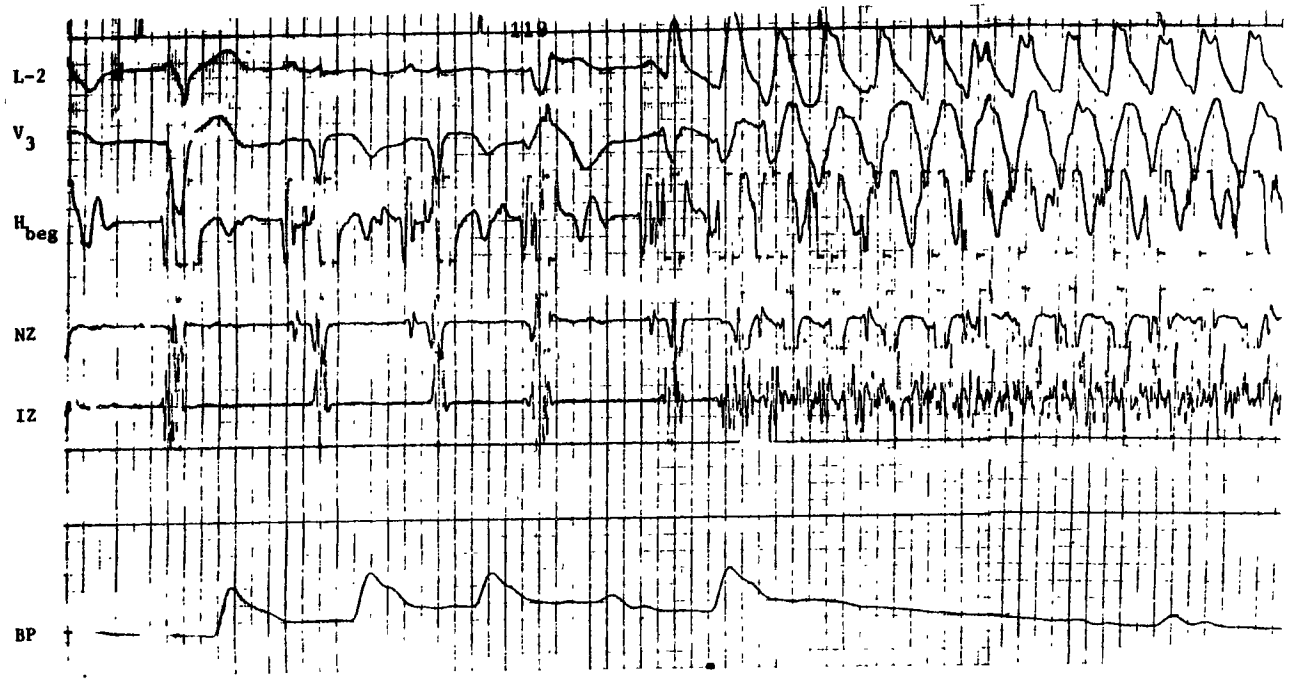


39

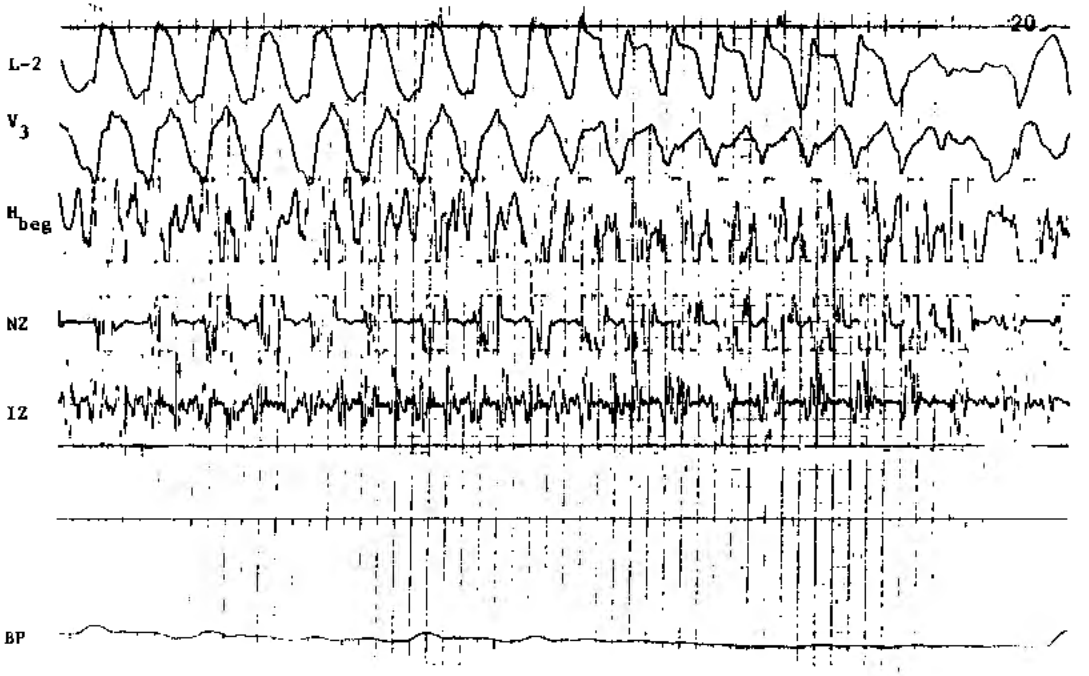
A series of electrograms were used in each case to monitor and record the results of the tests. Very brief examples of the electrograms taken in the assay of 36a are found in Figures 14-16. In each of these Figures, a series of five electrograms are shown. The uppermost electrogram was taken from a standard limb lead referred to as L-2. The second lead, referred to as V_3, was taken from a lead on the chest wall. The third originated from a lead in the His bundle. The fourth electrogram was taken from a composite electrode recorded from the posterior epicardial surface of the left ventricle in contact with a normal zone. The last electrogram is from a composite electrode recording from the anterior epicardial surface overlying the infarct zone. The tracing at the bottom is a recording of the arterial blood pressure.

In the electrograms displayed in Figure 14, the first and fourth beats shown give a representation of isolated ectopic beats which are common in dogs with a 24 hour myocardial infarction. The second and third beats represent the normal sinus rhythm and show normal tracings in each of the electrograms. The last tracing in Figure 14 indicates that the mean blood pressure during the normal sinus rhythm was 170 mmHg in this particular dog.



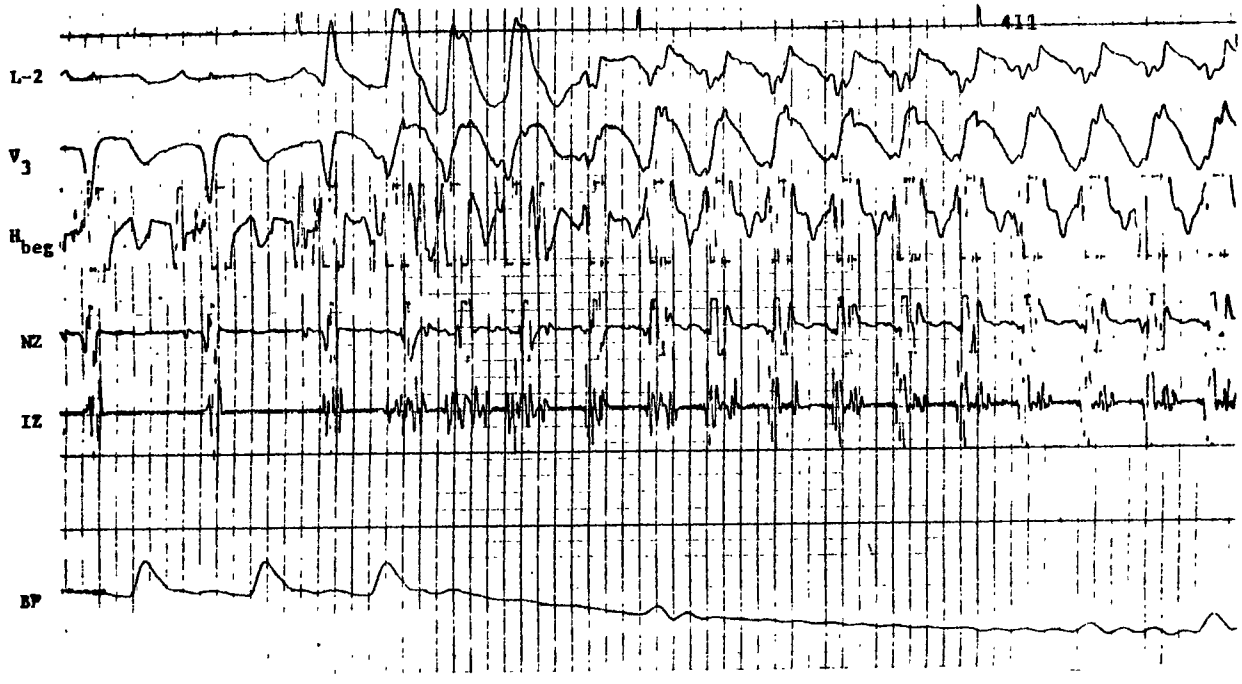
L-2: Limb electrode
V_3: Chest wall electrode
H_{beg}: His bundle electrogram
NZ: Normal zone electrogram
IZ: Infarct zone electrogram
BP: Blood pressure

Figure 14. Electrogram recorded for a control



L-2:	Limb electode	NZ:	Normal zone electrogram
V_3:	Chest wall electrode	IZ:	Infarct zone electrogram
H_{beg}:	His bundle electrogram	BP:	Blood pressure

Figure 15. Electrogram recorded after administration of lidocaine (12)



L-2:	Limb electrode	NZ:	Normal zone electrogram
V_3:	Chest wall electrode	IZ:	Infarct zone electrogram
H_{beg}:	His bundle electrogram	BP:	Blood pressure

Figure 16. Electrogram recorded after administration of 7-benzyl-3-selena-7-azabicyclo[3.3.1]nonane hydroperchlorate (36a)

After the fourth beat, two stimulated beats delivered from an electrical pacemaker induced a rapid (450 beats per minute), spontaneous, ventricular tachycardia (VT) due to a reentrant mechanism. If electrical cardioversion had not been used, this VT would probably have deteriorated into ventricular fibrillation and sudden death. At this VT rate, the heart could not efficiently pump blood which resulted in a drop in blood pressure to the dangerously low level of 50 mmHg. During the VT, the first four electrograms show each of the heart beats as unique electrical events. However, in the fifth electrogram (originating from the damaged area caused by the infarction) continuous electrical activity is seen.

Lidocaine (12) was then administered to the dog in a dose of four mg/Kg and the same VT as above was reinduced. Figure 15 shows a segment of a series of electrograms which were recorded during the VT. The rate of the VT is shown to have been reduced to 375 beats per minute. Although the VT was slowed, the blood pressure still fell to 50 mm Hg which was probably due to a depressant action of lidocaine on cardiac contractility. Continuous electrical activity was again apparent in the fifth electrogram which was recorded from the infarct zone.

After a lapse of sufficient time for the action of lidocaine to fade (about 30 minutes), ventricular pacing induced the same VT as in the control state (Figure 14) indicating the dissipation of the drugs effects. 7-Benzyl-3-selena-7-azabicyclo[3.3.1]nonane hydroperchlorate (36a) was then administered in a dose of 3 mg/kg as a solution in a minimum of 50% ethanol. Within about two minutes, the mean blood pressure increased from 170 mmHg to 200 mmHg. Ventricular tachycardia was then induced as before; however, the rate was greatly reduced from 450 beats per minute found in the control to 330 beats per minute with 36a

present. During the VT, the blood pressure fell to only 100 mmHg. In the electrogram taken from the infarct zone (fifth tracing), continuous electrical activity was no longer observed. This indicates the possibility that salt 36a may act specifically on the tissue which has been damaged by a myocardial infarction rather than in the general manner observed for lidocaine (12). Results such as these indicate that 36a has a more potent inhibitory effect on ventricular tachycardia than the commercially available, lidocaine (12). The results of similar tests on the salts 36c, 36f, and 37 as well as those of the selenium-containing lidocaine derivative 39 have been collected in Table XXXI.

As indicated in Table XXXI, salt 36c exhibits a marked ability to reduce the ventricular rate at both the 3 mg/kg and the 6 mg/kg dosage. The ventricular tachycardia which was induced after the administration of 36c was not sustained but reverted back to a normal sinus rhythm. Salt 36c also shows a blood pressure increase at both dose levels. Salt 36f was also found to have significant activity in the reduction of the rate of ventricular tachycardia. However, no significant hemodynamic effect was observed. Diol 37, although active, exhibited a pro-arrhythmic effect (generation of a new arrhythmia at 390 beats per minute) at a dose of 6 mg/kg. The selenium-containing lidocaine mimic (39) showed activity, but only at the 6 mg/kg dose. There was also a more dramatic decrease in the blood pressure during the ventricular tachycardia.

From these results as well as those obtained by Bailey and coworkers,[6] several structure-activity relationships are implicated. Bailey and coworkers showed that a carbonyl (sp^2 carbon) in the 9-position of the bicyclononanes drastically reduced the antiarrhythmic

activity. Although the 9,9-diol 37 was shown to be somewhat active, a methylene (sp^3 carbon) in the 9-position was necessary for optimal activity. It also appears that the N-alkylbicyclononanes (such as 36a and 36c) are more active than the 6,8-diarylbicyclononanes (such as 36f).

Because of the favorable response in the biological testing of 36a, we are anxiously awaiting the completion of the synthesis of [^{75}Se]36a, now in progress. This labelled compound could potentially be very useful as a cardiac imaging agent by providing for a nonsurgical technique for the determination of the extent and location of damage caused by a myocardial infarction.

We are also interested to find how the conformation of these bicyclononanes influence their biological activity. The assays of the salts 36h (chair-boat) and 36i (chair-chair) should be instrumental in determining which conformation is most condusive for antiarrhythmic activity.

TABLE XXXI[a]

BIOLOGICAL DATA FOR SELECTED ORGANOSELENIUM COMPOUNDS

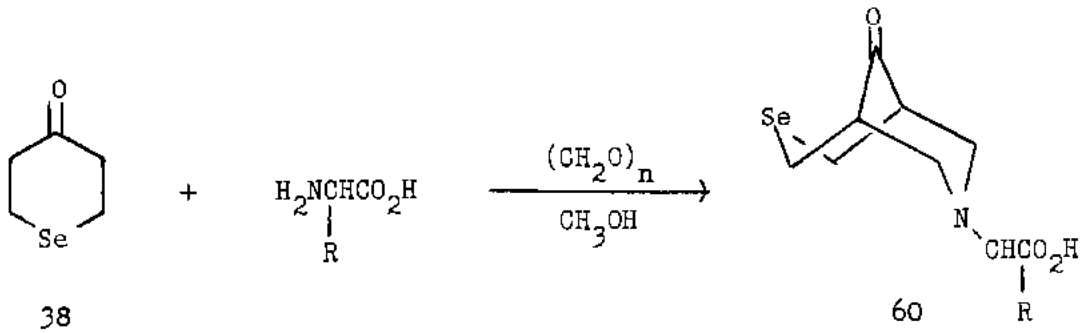
Compound	Normal[b]		Control[c]		Dosage					
					3 mg/kg			6 mg/kg		
	NSR[d]	BP	SVT[e]	BP	SVT	BP (no VT)	BP (VT)	SVT	BP (no VT)	BP (VT)
12[f]	171	170	450	50	375		50			
36a	171	170	450	50	330	230	100			
12	180	155	390	50	360	150	45	330		40
39	180	155	390	50	390	130	40	370		35
37	150	140	290	80	270	130	40	270	130	60
36c	150	160	330	70	240[g]	125		270[g]	150	
36f	170	150	330	70	300	125	70	280	125	75
37	170	160	330	70	300	125	85	310	125	70

a. Each division represents tests performed on separate dogs.
b. Data recorded before induction of ventricular tachycardia.
c. Recorded before administration of the compound.
d. Normal sinus rhythm.
e. Sustained ventricular tachycardia.
f. Administered at a 4 mg/kg dose.
g. Nonsustained ventricular tachycardia.

Suggestions for Future Work

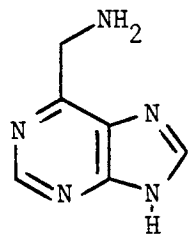
One very important aspect in the design and synthesis of bicyclononanes for the treatment of arrhythmias is that of hydrophilicity. Good water solubility would be an asset in the administration of these compounds since they must ultimately travel in the bloodstream. It was for this reason that the sulfur-containing salt 36b was synthesized. This salt (36b) contains the bioisosteric replacement of the N-benzyl group (as in 36a) with the N-thiophenemethyl group. The methoxy groups of 36d and 36e were added to the phenyl ring of salt 36c in order to increase the water-solubility of these salts.

The syntheses of the salts 36a-e utilized primary amines which were nearly insoluble in water. Starting amines with a greater water solubility should enhance the water-solubility of the final products. The amino acids are one type of very hydrophilic amines which could be used as the nitrogen donor in the double Mannich reaction in the formation of bicyclo[3.3.1]nonanes 60. These amines are also readily availably and fairly inexpensive. The use of amino acids may also eliminate the need for an acid catalyst such as acetic acid which is used in the syntheses of 34e-e. Racemic mixtures of the amino acids,

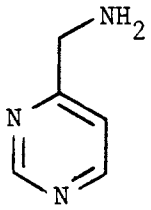


38 60

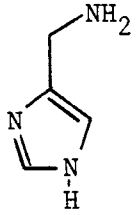
which are less expensive than either the pure d or pure l amino acids, could be used since in the Wolff-Kishner reduction of 60, epimerization would surely occur. Since it is unknown if the carboxylic acid function would survive the rather severe conditions of the Wolff-Kishner reduction, it may be protected as the tertiary butyl ester.



61a

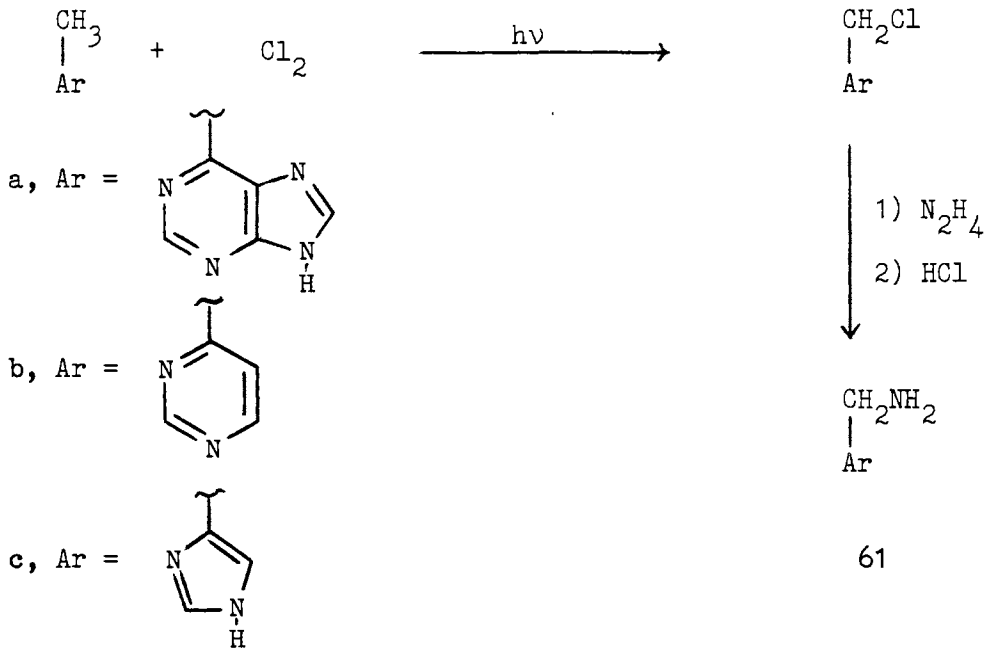


61b



61c

Another alternative in the use of water soluble amines is the use of amine functions which have been attached to nitrogen containing aromatic rings such as 6-aminomethylpurine (61a), 4-aminomethylpyrimidine (61b), and 4-aminomethylimidazole (61c). These should participate in the double Mannich reaction in a manner similar to benzylamine but in contrast to benzylamine, each should be very water soluble. These amines (61a-c) may be synthesized from the readily available, low-cost, starting materials 6-methylpurine, 4-methylpyrimidine, and 4-methylimidazole. Chlorination of the methyl groups of these starting materials may be accomplished with the use of chlorine gas in the presence of ultraviolet light. The transformation of toluene to benzyl chloride in this manner proceeds in a yield of 92.5%.[44a] A Gabriel synthesis utilizing the potassium salt of phthalimide may then be used in the aminolysis of the alkyl chloride to give the intermediate N-alkylphthal-



imide which is then destroyed by treatment with hydrazine and hydrochloric acid. Aminolysis of benzyl chloride using this method yields benzylamine in a yield of 94%.[44b] The the bicyclo[3.3.1]nonanes formed using these amines (61a-c) should have a much greater water solubility than other N-alkylbicyclononanes (36a-e) which have been discussed.

Since amino acids, purine, pyrimidine, and imidazole are all common to the body, their presence in bicyclononanes of interest may lessen whatever toxic effects these bicyclononanes may have on the body.

CHAPTER III

EXPERIMENTAL SECTION

General Information

All reactions were performed under a nitrogen atmosphere with magnetic stirring unless otherwise specified. Melting points were determined with a Thomas Hoover capillary apparatus and were uncorrected. Infrared spectra were obtained on KBr pellets (oils-films) with a Perkin-Elmer 681 IR spectrophotometer. The ^{13}C NMR spectra were obtained at 25.20 MHz on a Varian XL-100(15) NMR spectrometer equipped with a Nicolet TT-100 PFT accessory. Several ^{13}C NMR spectra were also obtained at 75.4 MHz on a Varian XL-300 NMR spectrometer. All ^{1}H, ^{15}N, and ^{77}Se NMR spectra were obtained on a Varian XL-300 NMR spectrometer at 299.99 MHz, 30.41 MHz, and 57.22 MHz, respectively. The ^{1}H and ^{13}C shifts are reported in delta or parts per million downfield from $(CH_3)_4Si$ as an internal standard. All ^{15}N shifts are reported in parts per million downfield from liquid NH_3 (25°C) using $^{15}NH_4NO_3$ (19.73 ppm) as an external secondary standard. All ^{77}Se shifts are reported in parts per million downfield from $(CH_3)_2Se$ (0°C) using $(C_6H_5Se)_2$ (481.0 ppm) as an external secondary standard. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tennessee.

Residues from the reactions to be described were disposed of in Clorox bleach. Reaction flasks, which were frequently coated with red

amorphous selenium during the course of the reactions or work-up procedures, were rinsed with Clorox bleach before washing to remove selenium.

1,1-Dimethyl-4-piperidonium Iodide (41)

A solution of freshly distilled 1-methyl-4-piperidone (15.0 g, 0.133 mol) in 300 mL of anhydrous ether was placed in a 500-mL, round-bottomed flask equipped with a condenser and a magnetic stirring bar. Iodomethane (20.0 g, 0.141 mol) was added in one portion and the resulting solution was stirred for 2 h and then heated at reflux for an additional 20 h. During this time a dense, white solid formed which was suction filtered and dried under vacuum (aspirator) to give 31.0 g (91.4%) of 41 as a white powdery solid: mp 186-188°C (dec)(lit.[21] mp 186-189°C); IR (KBr) cm^{-1} 1720 (C=O); ^{13}C NMR (DMSO-$\underline{d}_6$) ppm 35.2 [q, $N(CH_3)_2$], 51.1 [t, C(3,5)], 60.1 [t, C(2,6)], 201.3 [s, C(4)]. This solid was used without further purification in the synthesis of 4-selenanone (38). However, this salt may be recrystallized from methanol with a molecule of methanol retained as a hemiketal (mp 196°C with decomposition, lit.[21] mp 189-190°C). The hemiketal may be satisfactorily used in the preparation of 4-selenanone (38).

4-Selenanone (38)

Powdered elemental selenium (4.35 g, 55.1 mg-at.) and $NaBH_4$ (4.0 g, 106 mmol) were placed in a 1-L, three-necked, round-bottomed flask which was equipped with a condenser, a magnetic stirring bar, and a nitrogen inlet. The effluent gases are passed through a series of three traps; a blank, one containing Clorox bleach, and one containing a saturated solution of potassium hydroxide in 95% ethanol. Absolute ethanol (500

mL) was added to the flask and the resulting mixture was stirred at RT for 30 min. Heating at reflux for an additional 2 h gave a colorless suspension. This resulted in the formation of the reactive species which was presumably NaHSe.[62] The boiling process was to complete the reaction and to destroy excess sodium borohydride. The salt, 41 (12.75 g, 50.0 mmol) was then added in 2-3 g portions over 20 min (the color of the suspension changed to yellow almost immediately). Reflux was continued for 5 h after which time the resulting dark purple solution was cooled to RT. The volume of this solution was reduced to 100 mL by rotary evaporation. The residue was diluted with water (125 mL) and extracted with ether (5 X 40 mL). The combined extracts were washed with two 30-mL portions of a saturated sodium chloride solution and dried (K_2CO_3). Rotary evaporation of the ether gave a dark yellow oil which was quickly transferred to a sublimation apparatus where it solidified. Sublimation of this solid (50°C/0.1 mm Hg) gave 38 (5.1 g, 63%) as a white crystalline solid: mp 55.0-55.5°C; IR (KBr) cm^{-1} 1700 (C=O); ^1H NMR ($CDCl_3$) δ 2.82 [t, 4 H, H(2,6), J = 6.1 Hz], 3.00 [t, 4 H, H(3,5), J = 6.1 Hz]; ^{13}C NMR ($CDCl_3$) ppm 19.3 [C(2,6)], 43.7 [C(3,5)], 209.3 [C(4)]; ^{77}Se NMR ($CDCL_3$) ppm 176.6 [Se(1)]. Anal. Calcd for C_5H_8OSe: C, 36.81; H, 4.94; Se, 48.44. Found: C, 36.79; H, 4.87; Se, 48.33.

A second sublimation may be necessary since the first sublimation may give a slightly yellow product. Pure 4-selenanone appears to be stable in air and to light but storage in capped, dark bottle in a cool place is recommended. Slight impurities cause its rapid decomposition. 4-Selenanone (38) will sublime slowly even at room temperature and atmospheric pressure. Close work with this solid may cause minor eye

irritation and care should be exercised in all handling procedures.

4-Selenanone-2,4-dinitrophenylhydrazone (42)

Ketone 38 (0.25 g, 1.5 mmol) was added to a warm solution of 2,4-dinitrophenylhydrazine (0.5 g, 2.5 mmol) and conc HCl (1 mL) in absolute ethanol. Warming was continued until the ketone had dissolved. Upon slow cooling, an orange solid formed which was recrystallized (absolute ethanol) to give orange needles of 42: mp 167.0-167.5°C; IR (KBr) cm^{-1} 3325 (N-H); ^{1}H NMR ($CDCL_3$) δ 2.80-3.20 [m, 9 H, H(2,6) and NH], 7.99 [d, 1 H, H(6'), J = 9.0 Hz], 8.33 [dd, 1 H, H(5'), J = 1.5, 9.0 Hz], 9.13 [d, 1 H, H(3'), J = 1.5 Hz]; ^{13}C NMR ($CDCl_3$) ppm 16.1 [C(2)], 18.2 [C(6)], 30.0 [C(3)], 35.3 [C(5)], 116.2, 123.2, 129.1, 129.8, 137.7, 144.9, 158.2 [Ar-C and C(4)]; ^{77}Se NMR ($CDCl_3$) ppm 175.66 [Se(1)]. Anal. Calcd for $C_{11}H_{12}N_4O_4Se$: C, 38.50; H, 3.52; N, 16.33; Se, 23.01. Found: C, 38.37; H, 3.80; N, 16.35; Se, 23.23.

7-Benzyl-3-selena-7-azabicylo[3.3.1]nonan-9-one (34a)

Benzylamine (0.67 g, 6.26 mmol) and glacial acetic acid (0.38 g, 6.33 mmol) were dissolved in dry methanol (30 mL). Paraformaldehyde (1.5 g, 50 mmol) was added and the resulting mixture was brought to reflux under an atmosphere of nitrogen. 4-Selenanone (38, 1.00 g, 6.13 mmol) was then added in one portion which quickly turned the solution yellow. Reflux was continued under nitrogen in the dark for 5 h. The resulting deep red solution was then allowed to cool to room temperature and was stirred for an additional 18 h. The methanol was evaporated (aspirator) and the orange residual oil was partitioned between ether (50 mL) and water (50 mL). The ether layer was discarded and the

aqueous layer was made basic with KOH (85%, 1.2 g, 18.2 mmol). This solution was extracted with ether (5 x 40 mL). The combined extracts were dried (K_2CO_3) and evaporated (aspirator) to give an oil which was digested on a steam bath with Skelly B (50 mL). Evaporation gave a light yellow oil which solidified upon standing. This solid was recrystallized (95% ethanol) to give 34a (0.78 g, 43%) as white needles: mp 155.5-157.0°C (dec); IR (KBr) cm^{-1} 1726 (C=O); ^1H NMR ($CDCl_3$) δ 2.71 [m, 4 H, H(2,4)], 3.08 [m, 2 H, H(1,5)], 3.20 [m, 4 H, H(6,8)], 3.57 [s, 2 H, H(10)], 7.32 [m, 5 H, ArH]; ^{13}C NMR ($CDCl_3$) ppm 25.5 [t, C(2,4)], 46.2 [d, C(1,5)], 59.0 [t, C(6,8)], 61.5 [t, C(10)], 127.1 [d, C(4')], 128.2 (d) and 128.6 (d) [C(2',3',5',6')], 138.0 [s, C(1')], 213.8 [s, C(9)]; ^{15}N NMR ($CDCl_3$) ppm 38.31 [N(7)]; ^{77}Se NMR ($CDCl_3$) ppm 84.68 [Se(3)].

7-Benzyl-3-selena-7-azabicyclo[3.3.1]nonan-9,9-diol Hydroperchlorate (37)

Ketone 34a (0.65 g, 2.2 mmol) was dissolved in dry benzene (250 mL). Perchloric acid (60%, 1.0 g, 6.0 mmol) was added dropwise very slowly with cooling and swirling. This precipitated an orange solid which adhered to the side of the flask. The benzene was decanted and the solid was recrystallized (95% ethanol) to give the diol hydroperchlorate 37 (0.62 g, 68.3%) as white needles: mp 214.0-216.0°C (dec); ^1H NMR (DMSO-$\underline{d}_6$) δ 2.43 [br s, 2 H, $H(2,4)_{ax}$], 2.72 [br d, 2 H, $H(2,4)_{eq}$], 3.22-3.50 [m, 6 H, $H(6,8)_{ax}$, H(1,5), O$\underline{H}$], 3.50-3.64 [m, 2 H, $H(6,8)_{eq}$], 4.35 [d, 2 H, H(10)], 7.40-7.70 [m, 5 H, ArH], 9.20 [br s, 1 H, H(7)]; ^{13}C NMR (DMSO-$\underline{d}_6$) ppm 21.1 [C(2,4)], 34.7 [C(1,5)], 54.9 [C(6,8)], 60.1 [C(10)], 92.5 [C(9)], 129.2, 129.7, 130.0, 130.5 [ArC]; ^{15}N NMR (DMSO-$\underline{d}_6$)

ppm 51.88 [N(7)]; ^{77}Se NMR (DMSO-d_6) ppm 62.39 [Se(3)].

7-Benzyl-3-selena-7-azabicyclo[3.3.1]nonane Hydroperchlorate (36a)

A solution was made of 34a (2.0 g, 6.8 mmol) and hydrazine (95%, 5.0 g, 148 mmol) in triethylene glycol (40 mL). Potassium hydroxide (85%, 10.0 g, 152 mmol) was added and the resulting mixture was heated to 140°C in an oil bath under a nitrogen atmosphere for 12 h. After cooling to room temperature, the solution was poured into water (200 mL) and the resulting suspension was extracted with ether (5 x 40 mL). The combined extracts were dried overnight (K_2CO_3) and cooled to 0°C. Perchloric acid (60%, 2.0 g, 11.9 mmol) was added dropwise. The yellow-orange solid which formed was filtered and recrystallized (methanol) to give 36a (1.94 g, 75%) as white needles: mp 161.0-162.0°C (dec); ^{1}H NMR (DMSO-d_6) δ 1.75 [d, 1 H, H(9), J = 13.7 Hz], 1.88 [d, 1 H, H(9), J = 13.6 Hz], 2.41 [br s, 2 H, H(1,5)], 2.64 [d, 2 H, $H(2,4)_{ax}$, J = 12.21 Hz], 3.19 [d, 2 H, $H(2,4)_{eq}$, J = 12.10 Hz], 3.42 [d, 2 H, $H(6,8)_{ax}$], 3.61 [d, 2 H, $H(6,8)_{eq}$, J = 11.83 Hz], 4.32 [d, 2 H, H(10), J = 5.75 Hz]; ^{13}C NMR (DMSO-d_6) ppm 22.0 [C(2,4)], 25.3 [C(1,5)], 28.7 [C(9)], 56.6 [C(6,8)], 60.6 [C(10)], 128.9, 129.3, 129.8, 130.0 [ArC]; ^{15}N NMR (DMSO-d_6) ppm 51.56 [N(7)]; ^{77}Se NMR (DMSO-d_6) ppm 96.61 [Se(3)]. Anal. Calcd for $C_{14}H_{20}ClNO_4Se$: C, 44.14; H, 5.30; N, 3.68; Cl, 9.32; Se, 20.75. Found: C, 44.45; H, 5.38; N, 3.61; Cl, 9.52; Se, 20.67.

7-(2-Thiophene)methyl-3-selena-7-azabicyclo[3.3.1]nonan-9-one (34b)

A solution was made of 2-aminomethylthiophene (1.39 g, 12.3 mmol) and glacial acetic acid (1.10 g, 18.3 mmol) in methanol (60 mL) in a 150 mL, three-necked, round-bottomed flask eqipped with a water-cooled

condenser. To this solution was added paraformaldehyde (3.0 g, 100 mmol) and the resulting mixture was heated to reflux. Ketone 38 (2.00 g, 12.3 mmol) was add and reflux was continued for 5 h. After allowing the resulting red solution to cool to room temperature, the methanol was evaporated (aspirator) to give a red oil. This oil was partitioned between water and ether (100 mL: 30 mL). The ether portion was discarded and the aqueous layer was made basic by the addition of NaOH (1.5 g, 37.5 mmol). The resulting yellow suspension was extracted with ether (5 x 40 mL). The combined extracts were washed with water (2 x 30 mL) and dried (K_2CO_3). Evaporation of the ether gave a brown oil which was digested in boiling Skelly B (3 x 100 mL). Evaporation of the Skelly B gave 1.72 g of **34b** as a colorless viscous oil (47%): IR (film) cm^{-1} 1710 (C=O); ^1H NMR ($CDCl_3$) δ 2.60-2.74 [m, 4 H, H(2,4)], 3.02-3.18 [m, 4 H, H(1,5), $H(6,8)_{ax}$], 3.27 [dd, 2 H, $H(6,8)_{eq}$, J = 11.7 Hz, 3.4 Hz], 3.75 [s, 2 H, H(10)], 6.80-7.30 [m, 3 H, ArH]; ^{13}C NMR ($CDCl_3$) ppm 24.8 [C(2,4)], 46.0 [C(1,5)], 55.6 [C(10)], 58.5 [C(6,8)], 124.9 [C(4')], 125.5 [C(2')], 126.1 [C(3')], 141.4 [C(1')], 212.9 [C(9)]; ^{15}N NMR ($CDCl_3$) ppm 40.31 [N(7)]; ^{77}Se NMR ($CDCl_3$) ppm 86.28 [Se(3)].

7-(2-Thiophene)methyl-3-selena-7-azabicyclo[3.3.1]nonane Hydroperchlorate (36b)

Ketone **34b** (1.0 g, 3.33 mmol) and anhydrous hydrazine (95%, 2.0 g, 5.94 mmol) were dissolved in triethylene glycol (40 mL) in a 60 mL jacketed flask which was equipped for distillation. Potassium hydroxide (85%, 3.0 g, 45.5 mmol) was added and the resulting mixture was heated with stirring to 140-145°C by boiling xylene in the jacket of the reaction vessel. Heating was continued for 4 h after which time the reac-

tion mixture was cooled to room temperature and was poured into cool water (150 mL). The resulting suspension was extracted with ether (5 x 40 mL) and the combined extracts were dried (K_2CO_3). After filtration of the desiccant, 60% $HClO_4$ (1.0 g, 6.0 mmol) was added dropwise very slowly causing an orange solid to form. The ether was decanted and the solid was recrystallized twice (isopropyl alcohol, decolorizing carbon) to give 0.88 g of salt **36b** as white needles (68%): mp 141.0-141.5°C; ^{1}H NMR (DMSO-$\underline{d}_6$) δ 1.74 [d, 1 H, H(9), J = 13.6 Hz], 1.86 [d, 1 H, H(9), J = 13.6 Hz], 2.43 [br s, 2 H, H(1,5)], 2.64 [d, 2 H, $H(2,4)_{ax}$, J = 12.0 Hz], 3.19 [d, 2 H, $H(2,4)_{eq}$, J = 11.3 Hz], 3.35 [m, 2 H, $H(6,8)_{ax}$], 3.62 [d, 2 H, $H(6,8)_{eq}$, J = 12.7 Hz], 4.53 [d, 2 H, H(10), J = 5.3 Hz], 7.16 [dd, 1 H, H(3'), J = 5.1 Hz, 3.7 Hz], 7.36 [d, 1 H, H(2'), J = 3.3 Hz], 7.75 [d, 1 H, H(4'), J = 5.1 Hz], 9.24 [br s, 1 H, H(7)]; ^{13}C NMR (DMSO-$\underline{d}_6$) ppm 21.9 [t, C(2,4)], 25.3 [d, C(1,5)], 28.6 [t, C(9)], 54.9 [t, C(10)], 56.1 [t, C(6,8)], 127.2 [d, C(4')], 129.3 [d, C(2')], 130.5 [s, C(1')], 131.8 [d, C(3')]; ^{15}N NMR (DMSO-$\underline{d}_6$) ppm 58.54 [N(7)]; ^{77}Se NMR (DMSO-$\underline{d}_6$) ppm 89.41 [Se(3)]. Anal. Calcd for $C_{12}H_{18}ClNO_4SSe$: C, 37.27; H, 4.69; N, 3.62; Se, 20.42. Found: C, 37.30; H, 4.76; N, 3.60; Se, 20.10.

7-Phenethyl-3-selena-7-azabicyclo[3.3.1]nonan-9-one (34c)

A 100-mL, three-necked, round-bottomed flask equipped with a condenser was charged with a solution of phenethylamine (1.48 g, 12.3 mmol) and glacial acetic acid (0.85 g, 14.2 mmol) in methanol (60 mL). Paraformaldehyde (3.0 g, 100 mmol) was added and the resulting mixture was heated to reflux with magnetic stirring under an atmosphere of nitrogen. Ketone **38** (2.00 g, 12.3 mmol) was added and reflux was continued for 5 h

resulting in an orange solution. The methanol was evaporated (aspirator) and the resudual orange oil was mixed with water (200 mL). This aqueous mixture was made basic by addition of NaOH (2.0 g, 50 mmol) and was then extracted with ether (5 X 40 mL). The combined extracts were washed with saturated brine and dried (K_2CO_3). Evaporation (aspirator) gave a brown residue which was digested in boiling Skelly B (150 mL). Evaporation of the Skelly B gave a solid which was recrystallized (ethanol) to give 0.82 g (22%) of 34c as a light tan solid: mp 91-92°C; IR (KBr) cm^{-1} 1710 (C=O); ^1H NMR ($CDCl_3$) δ 2.62-2.83 [m, 8 H, H(2,4,1,5, 11)], 3.02-3.20 [m, 6 H, H(6,8,10)], 7.16-7.38 [m, 5 H, Ar-H]; ^{13}C NMR ($CDCl_3$) ppm 25.4 [t, C(2,4)], 33.7 [t, C(11)], 46.2 [d, C(1,5)], 58.3 [t, C(10)], 59.1 [t, C(6,8)], 125.9 [s, C(4')], 128.1 [d, C(2',6') or C(3',5')], 128.4 [d, C(3',5') or C(2',6')], 139.7 [s, C(1')], 213.5 [s, C(9)]; ^{15}N NMR ($CDCl_3$) ppm 35.44 [N(7)]; ^{77}Se NMR ($CDCl_3$) ppm 79.51 [Se(3)].

7-Phenethyl-3-selena-7-azabicyclo[3.3.1]nonane Hydroperchlorate (36c)

A 60-mL, two-necked, round-bottomed, jacketed flask was charged with a mixture of ketone 34c (1.3 g, 4.2 mmol), N_2H_4 (95%, 2.0 g, 59 mmol), and KOH (85%, 6.0 g, 91 mmol) in triethylene glycol (40 mL). The flask was equipped for simple distillation under a rapid stream of nitrogen. The reaction mixture was heated to 140-145°C by boiling xylene contained in the jacket. Heating was continued under a nitrogen stream for 5 h. During this time, a small amount of water and hydrazine distilled out. The resulting clear, light brown solution was cooled in a water bath to room temperature and was then poured into ice-water (200 mL). The white suspension which formed was extracted with ether (5 X 40

mL). The combined ether extracts were washed with brine (30 mL) and dried (K_2CO_3) overnight. After filtering out the desiccant, this ether solution was cooled to 0-5°C in an ice bath and 60% $HClO_4$ (1.0 g, 6.0 mmol) was added dropwise very slowly. After stirring overnight, the resulting orange precipitate was filtered and recrystallized (methanol, decolorizing carbon) to give 0.67 g (40%) of **36c** as white plates: mp 249-250°C (dec.); ^{1}H NMR (DMSO-d_6) δ 1.73 [br d, 1 H, H(9), J = 14.0 Hz], 1.89 [br d, 1 H, H(9), J = 13.8 Hz], 2.41 [br s, 2 H, H(1,5)], 2.64 [d, 2 H, $H(2,4)_{ax}$, J = 12.1 Hz], 3.07 [t, 2 H, H(11), J = 7.9 Hz] 3.20 [d, 2 H, $H(2,4)_{eq}$, J = 12.2 Hz], 3.33 [m, 4 H, $H(10)(6,8)_{ax}$], 3.86 [d, 2 H, $H(6,8)_{eq}$, J = 12.3 Hz], 7.28-7.50 [m, 5 H, Ar-H], 8.89 [br s, 1 H, H(7)]; ^{13}C NMR (DMSO-d_6) ppm 21.9 [t, C(2,4)], 25.3 [d, C(1,5)], 28.5 [t, C(9) or C(11)], 29.9 [t, C(11) or C(9)], 56.7 [y, C(6,8)], 58.8 [t, C(10)], 126.8 [d, C(4')], 128.5 [d, C(2',6',3',5')], 136.2 [s, C(1')]; ^{15}N NMR (DMSO-d_6) ppm 48.25 [N(7)]; ^{77}Se NMR (DMSO-d_6) ppm 88.42 [Se(3)]. Anal. Calcd. for $C_{15}H_{22}ClNO_4Se$: C, 45.64; H, 5.62; N, 3.55; Se, 20.00. Found: C, 45.77; H, 5.80; N, 3.48; Se, 19.85.

7-p-Methoxyphenethyl-3-selena-7-azabicyclo[3.3.1]nonan-9-one (34d)

A 100-mL, three-necked, round-bottomed flask, equipped with a condenser and a magnetic stirring bar, was charged with a solution of p-methoxyphenethylamine (0.93 g, 6.16 mmol) and glacial acetic acid (0.50 g, 8.33 mmol) in methanol (40 mL). Paraformaldehyde (1.50 g, 50.0 mmol) was added and the resulting mixture was heated to reflux under an atmosphere of nitrogen. Ketone **38** (1.00 g, 6.13 mmol) was added in one portion and reflux was continued for 4 h. The methanol was evaporated (aspirator) from the resulting orange solution to give a very viscous

red oil. This oil was dissolved in water (150 mL) and KOH (85%, 1.0 g, 15.2 mmol) was added to make the solution very basic. The resulting yellow suspension was extracted with ether (5 X 40 mL). The combined extracts were washed with water (30 mL) and dried (K_2CO_3). Evaporation of the ether (aspirator) gave 0.72 g (35%) of 34d as a light yellow oil: IR (neat) cm^{-1} 1723 (C=O); ^1H NMR ($CDCl_3$) δ 2.50-2.80 [m, 8 H, H(1,5,2,4,11)], 2.96-3.14 [m, 6 H, H(6,8,10)], 3.71 [s, 3 H, $OC\underline{H}_3$], 6.72-6.90 [m, 2 H, H(3',5')], 7.00-7.16 [m, 2 H, H(2',6')]; ^{13}C NMR ($CDCl_3$) ppm 24.6 [C(2,4)], 32.0 [C(11)], 45.4 [C(1,5)], 54.2 [OCH_3], 57.8 [C(10)], 58.2 [C(6,8)], 112.8 [C(3',5')], 128.5 [C(2',6')], 130.9 [C(1')], 156.9 [(C(4')], 212.5 [C(9)]; ^{15}N NMR ($CDCl_3$) ppm 35.43 [N(7)]; ^{77}Se NMR ($CDCl_3$) 78.81 [Se(3)].

7-p-Methoxyphenethyl-3-selena-7-azabicyclo[3.3.1]nonane Hydroperchlorate (36d)

A two-necked, 60-mL, jacketed flask equipped for simple distillation was charged with a suspension of ketone 34d (0.65 g, 1.92 mmol), hydrazine (95%, 1.00 g, 29.7 mmol), and potassium hydroxide (85%, 3.0 g, 45.5 mmol) in triethylene glycol (25 mL). Under a rapid stream of nitrogen, the suspension was heated to 140-145°C by boiling xylene in the jacket of the flask. Stirring was continued at this temperature for 3 h during which time a small amount of water and excess hydrazine was distilled from the reaction mixture. After cooling to room temperature, the resulting solution was dilluted with water (100 mL) and was extracted with ether (5 X 40 mL). The combined ether extracts were dried (K_2CO_3) overnight and 60% perchloric acid (0.5 g, 3.0 mmol) was added very slowly. This precipitated an orange solid. The ether was

decanted and the solid was recrystallized (abs. ethanol) with the aid of decolorizing carbon to give 0.58 g (71%) of salt 36d as white needles: mp 208.5-209.0°C; ^{1}H NMR (DMSO-$\underline{d}_6$) δ 1.73 [br d, 1 H, H(9), J = 14 Hz], 1.90 [br d, 1 H, H(9), J = 14 Hz], 2.42 [br s, 2 H, H(1,5)], 2.65 [d, 2 H, $H(2,4)_{ax}$, J = 12 Hz], 3.02 [t, 2 H, H(11), J = 7 Hz], 3.22 [d, 2 H, $H(2,4)_{eq}$, J = 12 Hz], 3.30 [m, 2 H, H(10)], 3.36 [d, 2 H, H(6,8), J = 12 Hz], 3.76 [s, 3 H, OCH_3], 3.86 [d, 2 H, $H(6,8)_{eq}$, J = 12 Hz], 6.97 [d, 2 H, H(3',5'), J = 9 Hz], 7.32 [d, 2 H, H(2',6'), J = 9 Hz], 8.92 [br s, 1 H, H(7)]; ^{13}C NMR (DMSO-$\underline{d}_6$) ppm 21.9 [t, C(2,4)], 25.3 [d, C(1,5)], 28.5 [t, C(9) or C(11)], 28.9 [t, C(11) or C(9)], 55.0 [q, OCH_3], 56.7 [t, C(6,8)], 58.9 [t, C(10)], 114.0 [d, C(3',5')], 127.7 [s, C(1')], 129.6 [d, C(2',6')], 158.1 [s, C(4')]; ^{15}N NMR (DMSO-$\underline{d}_6$) ppm 48.10 [N(7)]; ^{77}Se NMR (DMSO-$\underline{d}_6$) ppm 88.64 [Se(3)]. Anal. Calcd. for $C_{16}H_{24}ClNO_5Se$: C, 45.24; H, 5.69; N, 3.30; Se, 18.59. Found: C, 45.42; H, 5.80; N, 3.30; Se, 18.46.

7-(3,4-Dimethoxy)phenethyl-3-selena-7-azabicyclo[3.3.1]nonan-9-one (34e)

A 150 mL three-necked, round-bottomed flask was charged with a solution of 3,4-dimethoxyphenethylamine (2.23 g, 12.3 mmol) and glacial acetic acid (1.0 g, 16.6 mmol) in methanol (60 mL). Paraformaldehyde (3.0 g, 100 mmol) was added and the resulting mixture was heated to boiling. 4-Selenanone (38, 2.00g, 12.3 mmol) was added and reflux was continued for 4 hours. The resulting brown solution was evaporated (aspirator) to a brown oil. This oil was added to water (150 mL) and the mixture which formed was extracted with ether (4 x 50 mL). The combined extracts were washed with water (30 mL) and dried (K_2CO_3). Evaporation (aspirator) gave a dark brown oil which was digested in

boiling Skelly B (3 x 100 mL). Evaporation of the Skelly B gave 1.4 g of ketone 34e as a pale yellow viscous oil (31%): IR (neat) cm^{-1} 1730 (C=O); ^{1}H NMR ($CDCl_3$) δ 2.60-2.80 [m, 8 H, H(2,4,1,5,11)], 3.00-3.20 [m, 6 H, H(6,8,10)], 3.80 [s, 3 H, OCH_3], 3.84 [s, 3 H, OCH_3], 7.70-7.90 [m, 3 H, ArH]; ^{13}C NMR ($CDCl_3$) ppm 25.4 [C(2,4)], 33.2 [C(11)], 46.2 [C(1,5)], 55.7 [both OCH_3], 58.6 [C(10)], 59.1 [C(6,8)], 111.3, 112.0, 120.5, 132.8 [C(1')], 141.2, 148.7, 213.8 [C(9)]; ^{15}N NMR ($CDCl_3$) ppm 35.16 [N(7)]; ^{77}Se NMR ($CDCl_3$) ppm 77.00 [Se(3)].

7-(3,4-Dimethoxy)phenethyl-3-selena-7-azabicyclo[3.3.1]nonane Hydroperchlorate (36e)

A 60 mL, two-necked, jacketed flask which was equpped for distillation, was charged with solution of ketone 34e (1.10 g, 3.00 mmol), anhydrous hydrazine (95%, 2.00 g, 5.94 mmol), and potassium hydroxide (85%, 3.0 g, 45.5 mmol) in triethylene glycol (40 mL). This solution was heated to 140-145°C by boiling xylene in the jacket of the reaction flask. Heating was continued for 4 h during which time a small amount of water and excess hydrazine distilled out. The reaction mixture, which had turned brown, was cooled and poured into cool water (150 mL). The resulting suspension was extracted with ether (4 x 50 mL). The combined extracts were washed with water (40 mL) and dried (K_2CO_3). Perchloric acid (60%, 1.0 g, 6.0 mmol) was added to the ether solution dropwise very slowly. This precipitated a white solid which rapidly turned orange. The ether was decanted and the solid was recrystallized twice from absolute ethanol (decolorizing carbon) to give 0.92 g (68%) of salt 36e as a white crystalline solid: mp 162-163°C; ^{1}H NMR (DMSO-d_6) δ 1.74 [d, 1 H, H(9), J = 13 Hz], 1.92 [d, 1 H, H(9), J =

13 Hz], 2.42 [br s, 2 H, H(1,5)], 2.65 [d, 2 H, $H(2,4)_{ax}$, J = 12 Hz], 3.02 [t, 2 H, H(11)], 3.22 [d, 2 H, $H(2,4)_{eq}$, J = 12 Hz], 3.36 [m, 4 h, H(10) and $H(6,8)_{ax}$], 3.76 [s, 3 H, OCH_3], 3.80 [s, 3 H, OCH_3], 3.87 [d, 2 H, $H(6,8)_{eq}$, J = 12 Hz], 6.88-7.02 [m, 3 H, ArH], 8.88 [br s, 1 H, H(7)]; ^{13}C NMR (DMSO-d_6) ppm 22.0 [C(2,4)], 25.3 [C(1,5)], 28.5 [C(11) or C(9)], 29.4 [C(9) or C(11)], 55.4 [OCH_3], 55.5 [OCH_3], 56.7 [C(6,8)], 58.9 [C(10)], 112.0, 112.3, 120.6, 128.3 [C(1')], 147.7 [C(3') or C(4')], 148.8 [C(3') or C(4')]; ^{15}N NMR (DMSO-d_6) ppm 48.03 [N(7)]; ^{77}Se NMR (DMSO-d_6) ppm 88.35 [Se(3)]. Anal. Calcd for $C_{17}H_{26}ClNO_6Se$: C, 44.90; H, 5.76; N, 3.08. Found: C, 44.86; H, 5.86; N, 3.04.

6,8-Diphenyl-3-selena-7-azabicyclo[3.3.1]nonan-9-one (34f)

A 50-mL, two-necked, jacketed flask was charged with a solution of dry ammonium acetate (2.31 g, 30.0 mmol) in absolute ethanol (30 mL) which was warmed to 65°C by refluxing methanol in the jacket. A solution of ketone 38 (2.45 g, 15.0 mmol) and benzaldehyde (3.18 g, 30.0 mmol) in absolute ethanol (15 mL) was added in one portion. The resulting solution was stirred under nitrogen at 65°C for 45 min. After cooling the reaction mixture to about 30-40°C, ether (15 mL) was added and stirring was continued for 10 min. Cooling (5°C) overnight resulted in the formation of a yellow solid which was filtered and recrystallized (ethanol) to give 0.89 g (17%) of ketone 34f as white needles: mp 207.0-208.5°C (dec); IR (KBr) cm^{-1} 3320 (N-H), 1730 (C=O); ^1H NMR ($CDCl_3$) δ 1.77 [br s, 1 H, H(7)], 2.84 [br d, 4 H, H(2,4), J = 8 Hz], 3.59 [m, 2 H, H(1,5)], 5.04 [m, 2 H, H(6,8)], 7.20-7.50 [m, 10 H, ArH]; ^{13}C NMR ($CDCl_3$) ppm 29.2 [C(2,4)], 54.0 [C(1,5)], 64.2 [C(6,8)], 144.4 [C(1')], 127.0 [C(3',5') or C(2',6')], 127.9 [C(4')], 128.7 [C(2',6') or

C(3',5)]; ^{15}N NMR ($CDCl_3$) ppm 63.28 [N(7)]; ^{77}Se NMR ($CDCl_3$) ppm 25.38 [Se(3)]. Anal. Calcd for $C_{19}H_{19}NOSe$: C, 64.02; H, 5.38; N, 3.93; Se, 22.17. Found: C, 63.86; H, 5.45; N, 3.81; Se, 21.90.

6,8-Diphenyl-3-selena-7-azabicyclo[3.3.1]nonane (35f)

Ketone **34f** (0.89 g, 2.5 mmol) and hydrazine (95%, 3.0 g, 89 mmol) was dissolved in triethylene glycol (40 mL). This solution was placed in a 60-mL, two-necked, jacketed flask which was equipped for simple distillation under a rapid stream of nitrogen. Water was boiled in the jacket which heated the reaction mixture to about 100°C. The solution was stirred at this temperature for 2 h. Potassium hydroxide (85%, 1.0 g, 15 mmol) was added and the temperature was increased to about 207° by boiling tetralin in the jacket. As the temperature increased, nitrogen was produced. After stirring at this temperature for 4 h, 3 mL of water and excess hydrazine had distilled out. The reaction mixture was cooled to 60-70°C and was then poured into ice-water (200 mL). A white precipitate immediately formed. After refrigerating this mixture overnight, the solid was filtered and dried on the filter paper. This solid was recrystallized (ether, decolorizing carbon) to give 0.63 g (74%) of amine 35f as white needles: mp. 193.5-195.0°C (dec); IR (KBr) cm^{-1} 3250 (N-H); ^{1}H NMR (C_6D_6) δ 0.83 [dt, 1 H, H(9), J = 12.0, 1.5 Hz], 1.34 [m, 1 H, H(7)], 1.78 [m, 2 H, H(1,5)], 2.00 [dd, 2 H, $H(2,4)_{ax}$, J = 12.0, 1.5 Hz], 2.33 [m, 1 H, H(9)], 2.84 [dd, 2 H, $H(2,4)_{eq}$, J = 12.0, 2.0 Hz], 4.34 [d, 2 H, H(6,8), J = 2.0 Hz], 7.1-7.4 [m, 10 H, ArH]; ^{13}C NMR (C_6D_6 @ 50°C) ppm 25.1 [C(2,4)], 27.2 [C(9)], 34.5 [C(1,5)], 62.0 [C(6,8)], 126.9 [C(2') or C(3')], 127.2 [C(4')], 128.7 [C(3') or C(2')], 151.9 [C(1'); ^{15}N NMR (C_6D_6) ppm 55.68 [N(7)]; ^{77}Se NMR (C_6D_6 @ 50°C)

ppm 2.38 [Se(3)]. Anal. Calcd for $C_{19}H_{21}NSe$: C, 66.66; H, 6.18; N, 4.09; Se, 23.06. Found: C, 66.82; H, 6.34; N, 3.97; Se, 22.82.

6,8-Diphenyl-3-selena-7-azabicyclo[3.3.1]nonane Hydroperchlorate (36f)

A solution was made of amine 35f (0.63 g, 1.8 mmol) in benzene (100 mL) in a 250-mL Erlenmeyer flask. Perchloric acid (60%, 1.0 g, 6.0 mmol) was added dropwise very slowly with swirling. The resulting mixture was allowed to stand at room temperature with occasional swirling for 3 h. The orange solid which formed was filtered and recrystallized (methanol) to give 0.62 g (78%) of salt 36f as white needles: mp 288.0-289.0°C (dec, sealed tube); ^{1}H NMR (DMSO-d_6) δ 1.78 [br d, 1 H, H(9), J = 13.0 Hz], 2.36 [br d, 2 H, $H(2,4)_{ax}$, J = 13.0 Hz], 2.59 [m, 3 H, H(1,5) and H(9)], 3.16 [dd, 2 H, $H(2,4)_{eq}$, J = 12.0, 2.0 Hz], 4.73 [br d, 2 H, H(6,8), J = 3.0 Hz], 7.19-7.70 [m, 10 H, ArH], 8.72 [m, 1 H, $H(7)_{ax}$], 9.67 [m, 1 H, $H(7)_{eq}$]; ^{13}C NMR (DMSO-d_6) ppm 23.5 [C(2,4)], 26.6 [C(9)], 31.2 [C(1,5)], 61.5 [C(6,8)], 128.5, 128.7, 128.6, 137.0 [C(1')]; ^{15}N NMR (DMSO-d_6) ppm 57.91 [N(7)]; ^{77}Se NMR (DMSO-d_6) ppm 1.16 [Se(3)]. Anal. Calcd for $C_{19}H_{22}ClNO_4Se$: C, 51.54; H, 5.01; N, 3.16; Se, 17.83. Found: C, 51.52; H, 4.94; N, 3.34; Se, 17.65.

6,8-Di(2-thiophene)-3-selena-7-azabicyclo[3.3.1]nonan-9-one (34g)

A solution of 2-thiophenecarboxaldehyde (1.38 g, 12.3 mmol) and dry ammonium acetate (0.94 g, 12.3 mmol) in absolute ethanol (20 mL) was heated to boiling in a 50-mL Erlenmeyer flask on a hot plate. To this was added a hot solution of freshly sublimed ketone 38 (1.00 g, 6.13 mmol) in absolute ethanol (15 mL). Boiling was continued for 10 min

with ethanol being added to keep the volume constant. During this time the colorless solution turned yellow. The flask was removed from the hot plate, was stoppered, and was allowed to stand at room temperature for 3 days. The resulting dark red solution was decanted from the yellow solid which had formed during this time. The solid was taken up in benzene (100 mL) and was treated with decolorizing carbon. Filtration followed by evaporation (aspirator) gave a light brown solid which was recrystallized (methanol) to give 0.40 g (18%) of ketone 34g as a light yellow solid: mp 155-161°C (dec); IR (KBr) cm^{-1} 3260 (N-H), 1723 (C=O); ^{1}H NMR ($CDCl_3$) δ 2.16 [br s, 1 H, H(7)], 2.80 [m, 4 H, H(1,5) and $H(2,4)_{ax}$], 3.57 [d, 2 H, $H(2,4)_{eq}$, J = 10.03 Hz], 5.32 [d, 2 H, H(6,8), J = 3.96 Hz], 6.90-7.40 [m, 6 H, Ar-H]; ^{13}C NMR ($CDCl_3$) ppm 29.3 [C(2,4)], 54.6 [C(1,5)], 59.1 [C(6,8)], 123.7, 124.8, 126.3 [C(2',3', 4')], 147.0 [C(1')], 212.5 [C(9)]; ^{15}N NMR ($CDCl_3$) ppm 67.09 [N(7)]; ^{77}Se NMR ($CDCl_3$) ppm 30.60 [Se(3)].

The dark red mother liquor which was decanted earlier was allowed to evaporate. The residue was recrystallized (absolute ethanol, decolorizing carbon) to give a small amount of enone 47 as a yellow-orange solid: mp 138-141°C (dec); ^{1}H NMR ($CDCl_3$) δ 2.19 [d, 4 H, H(2,6), J = 6.0 Hz], 7.14 [dd, 2 H, H(11)], 7.36 [d, 2 H, H(12), J = 4.0 Hz], 7.55 [d, 2 H, H(7), J = 6.0 Hz], 7.78 [br s, 2 H, H(10)]; ^{13}C NMR ($CDCl_3$) ppm 18.7 [t, C(2,6)], 131.2 [s, C(3,5)], 138.1 [s, C(8,14)], 190.4 [s, C(4)], 127.3 (d), 128.7 (d), 129.5 (d), 133.0 (d); ^{77}Se NMR ($CDCl_3$) ppm 200.35 [Se(3)]. Anal. Calcd. for $C_{15}H_{12}OS_2Se$: C, 51.28; H, 3.44; S, 18.25; Se, 22.47. Found: C, 50.92; H, 3.65; S, 18.40; Se, 22.76.

6,8-Di(2-thiophene)-3-selena-7-azabicyclo[3.3.1]nonane (35g)

Ketone 34g (1.00 g, 2.71 mmol) and anhydrous hydrazine (95%, 1.0 g, 30 mmol) were dissolved in triethylene glycol (40 mL) which was contained in a 60 mL, two-necked, jacketed flask which was equipped for distillation. By boiling water in the jacket, the reaction mixture was heated to 100°C and stirred at this temperature for 2 h. Potassium hydroxide (85%, 2.0 g, 30 mmol) was added in one portion and the water in the jacket then replaced by xylene which when boiled, brought the temperature of the reaction mixture to 140-145°C. Stirring was continued at this temperature for 5 hours. After cooling to room temperature, the reaction mixture was poured into ice-cold water (200 mL) after which a precipitated immediately formed. This mixture set aside at room temperature overnight and then filtered. The filtrate was taken up in boiling benzene and treated with decolorizing carbon. The benzene was evaporated (aspirator) and the residue was recrystallized in 95% ethanol to give 0.64 g (67%) of 35g as a light tan solid: mp 183-185°C (dec); IR (KBr) cm^{-1} 3270 (N-H); ^{1}H NMR ($CDCl_3$) δ 1.28 [d, 1 H, H(9), J = 13 Hz], 1.78 [br s, 1 H, H(7)], 2.18 [br s, 2 H, H(1,5)], 2.32 [d, 2 H, $H(2,4)_{ax}$, J = 12 Hz], 2.50 [m, 1 H, H(9)], 3.20 [dd, 2 H, $H(2,4)_{eq}$, J = 13 Hz, 2 Hz], 4.79 [d, 2 H, H(6,8), J = 4 Hz], 6.96 [dd, 2 H, ArH], 7.01 [2 H, d, ArH], 7.21 [d, 2 H, ArH]; ^{13}C NMR ($CDCl_3$) ppm 25.0 [C(2,4)], 25.8 [C(9)], 34.6 [C(1,5)], 57.1 [C(6,8)], 122.2 [C(4')], 122.6 [C(2')], 126.1 [C(3')], 150.7 [C(1')]; ^{15}N NMR ($CDCl_3$) ppm 60.10 [N(7)]; ^{77}Se NMR ($CDCl_3$) ppm 4.05 [Se(3)].

6,8-Di(2-thiophenyl)-3-selena-7-azabicyclo[3.3.1]nonane Hydroperchlorate (36g)

A solution was made of amine 35g (0.5 g, 1.4 mmol) in benzene (200 mL) and isopropyl alcohol (10 mL). To this solution was added 60% $HClO_4$ (0.5 g, 3.0 mmol) dropwise slowly causing a white precipitate to form. This precipitate quickly became yellow. The solvent was decanted and the solid was recrystallized twice (isopropyl alcohol, decolorizing carbon) to give 0.4 g (63%) of salt 36g as white needles: mp 285°C (dec); ^{1}H NMR (DMSO-d_6) δ 1.78 [d, 1 H, H(9), J = 14 Hz], 2.36 [d, 2 H, $H(2,4)_{ax}$, J = 14 Hz], 2.44 [m, 1 H, H(9)], 2.66 [br s, 2 H, H(1,5)], 3.19 [dd, 2 H, $H(2,4)_{eq}$, J = 12 Hz, 3 Hz], 5.07 [m, 2 H, H(6,8)], 7.16 [dd, 2 H, H(3')], 7.43 [d, 2 H, H(2')], 7.69 [dd, 2 H, H(4')], 9.36 [br s, 1 H, H(7)], 9.61 [br s, 1 H, H(7)]; ^{13}C NMR (DMSO-d_6) ppm 23.5 [C(2,4)], 26.2 [C(9)], 32.5 [C(1,5)], 56.1 [C(6,8)], 127.3 [C(2') or C(4')], 127.6 [C(4') or C(2')], 129.2 [C(3')], 138.9 [C(1')]; ^{15}N NMR (DMSO-d_6) ppm 62.39 [N(7)]; ^{77}Se NMR (DMSO-d_6) ppm 5.11 [Se(3)]. Anal. Calcd for $C_{15}H_{18}ClNO_4S_2Se$: C, 39.61; H, 3.99; N, 3.08; S, 14.10; Se, 17.36. Found: C, 39.81; H, 3.97; N, 3.10; S, 14.35; Se, 17.18.

6,8-Di(4-chlorophenyl)-3-selena-7-azabicyclo[3.3.1]nonan-9-one (34h) and (34i)

A solution of dry ammonium acetate (0.94 g, 12.3 mmol) and p-chlorobenzaldehyde (1.73 g, 12.3 mmol) in absolute ethanol (20 mL) was heated to boiling in a 50-mL Erlenmeyer flask on a hot plate. To this solution was added a boiling solution of freshly sublimed ketone 38 (1.00 g, 6.13 mmol) in absoute ethanol (15 mL). The combined solutions

were boiled for 10 min with ethanol being added to keep the volume constant. During this time the colorless solution became light yellow. The flask was then removed from the hot plate and stoppered. The reaction mixture was allowed to stand at room temperature for 3 days, during which time the solution turned dark redish-brown and a yellow solid formed. The liquid was decanted and the solid was dissolved in benzene (100 mL). This solution was treated with decolorizing carbon and was filtered. Evaporation (aspirator) of the benzene gave a light brown solid which was recrystallized (absolute ethanol) giving 0.33 g (13%) of ketone **34h** as a light tan solid: mp 219-220°C (dec); IR (KBr) cm^{-1} 3280 (N-H), 1722 (C=O); ^{1}H NMR ($CDCl_3$) δ 1.70 [br s, 1 H, H(7)], 2.69 [m, 4 H, H(1,5) and $H(2,4)_{ax}$], 3.56 [d, 2 H, $H(2,4)_{eq}$, J = 10.20 Hz], 4.99 [d, 2 H, H(6,8), J = 4.07 Hz], 7.30-7.40 [m, 8 H, Ar-H]; ^{13}C NMR ($CDCl_3$) ppm 29.0 [C(2,4)], 53.9 [C(1,5)], 63.4 [C(6,8)], 128.2 [C(2',6') or C(3',5')], 128.8 [C(3',5') or C(2',6')], 133.7 [C(4')], 142.5 [C(1')], 213.4 [C(9)]; ^{15}N NMR ($CDCl_3$) ppm 62.84 [N(7)]; ^{77}Se NMR ($CDCl_3$) ppm 26.67 [Se(3)].

Addition of water (10 mL) to the original mother liquor caused the precipitation of a dense brown solid. After allowing this mixture to stand at room temperature overnight, the solid was filtered and recrystallized (ethanol, decolorizing carbon) to give 0.2 g (7%) of **34i** (isomeric with **34h**) as a light tan solid: mp 168-171°C (dec); IR (KBr) cm^{-1} 3315 (N-H), 1710 (C=O); ^{1}H NMR ($CDCl_3$) δ 2.68-2.90 [m, 2 H, $H(2,4)_{ax}$], 2.83 [br s, 2 H, H(1,5)], 3.06-3.18 [m, 2 H, $H(2,4)_{eq}$], 4.48 [br s, 2 H, H(6,8)], 7.30-7.60 [m, 8 H, ArH]; ^{13}C NMR ($CDCl_3$) ppm 20.9 [t, C(2,4)], 51.5 [d, C(1,5)], 63.8 [d, C(6,8)], 127.7 [d, C(2') or C(3')], 128.8 [d, C(3') or C(2')], 133.4 [s, C(4')], 137.6 [s, C(1')], 212.9 [s, C(9)];

^{15}N NMR ($CDCl_3$) ppm 44.24 [N(7)]; ^{77}Se NMR ($CDCl_3$) ppm 122.66 [Se(3)].

6,8-Di(4-chlorophenyl)-3-selena-7-azabicyclo[3.3.1]nonane (35h)

Ketone **34h** (2.00 g, 4.71 mmol), anhydrous hydrazine (95%, 2.0 g, 60 mmol), and triethylene glycol (35 mL) were placed in a 60-mL, two-necked, jacketed, round-bottomed flask along with a magnetic stirring bar. The contents of the flask were heated to 100°C under a stream of nitrogen by boiling water in the jacket of the reaction flask. Stirring at this temperature was continued for 3 h after which time potassium hydroxide (85%, 5.0 g, 76 mmol) was added in one portion. The reaction mixture was then heated to 140-145°C by boiling xylene in the jacket. After 4 h at this temperature, the resulting solution was cooled (60-70°C) and was poured into water (100 mL) which precipitated a cream-colored solid. This solid was filtered and washed with water. Recrystallization (twice, absolute ethanol, decolorizing carbon) gave **35h** as a light tan solid (0.91g, 47%): mp 179-180°C (dec); IR (KBr) cm^{-1} 3260 (N-H); ^1H NMR ($CDCl_3$) δ 1.30 [d, 1 H, H(7), J = 12 Hz], 1.74 [br s, 1 H, H(7)], 2.04 [br s, 2 H, (1,5)], 2.28 [br d, 2 H, $H(2,4)_{ax}$, J = 12 Hz], 2.48 [m, 1 H, H(9)], 3.17 [dd, 2 H, $H(2,4)_{eq}$, J = 12 Hz, 4 Hz], 4.43 [d, 2 H, H(6,8), J = 5 Hz], 7.26-7.50 [m, 8 H, ArH]; ^{13}C NMR ($CDCl_3$) ppm 25.1 [C(2,4)], 26.9 [C(9)], 33.8 [C(1,5)], 60.9 [C(6,8)], 127.9, 128.6, 132.6 [C(4')], 145.7 [C(1')]; ^{15}N NMR ($CDCL_3$) ppm 55.37 [N(7)]; ^{77}Se NMR ($CDCl_3$) ppm -0.79 [Se(3)].

6,8-Di(4-chlorophenyl)-3-selena-7-azabicyclo[3.3.1]nonane Hydroperchlorate (36h)

Amine 35h (1.00 g, 2.43 mmol) was dissolved in ether (200 mL) in a

500-mL, round-bottomed flask. Perchloric acid (60%, 1.0 g, 6.0 mmol) was added slowly with vigorous swirling. The resulting mixture was allowed to stand for 24 h with occasional swirling. The yellow-orange solid which formed was filtered and recrystallized (twice, absolute ethanol, decolorizing carbon) to give 36**h** as a white powder (0.46 g, 37%): mp 272-274°C (dec); ^{1}H NMR (DMSO-d_6) δ 1.77 [d, 1 H, H(9), J = 12.9 Hz], 2.36 [d, 2 H, $H(2,4)_{ax}$, J = 10.8 Hz], 2.53 [m, 2 H, H(1,5)], 3.14 [d, 2 H, $H(2,4)_{eq}$, J = 10.5 Hz], 3.38 [br s, 1 H, H(9)], 4.76 [br s, 2 H, H(6,8)], 7.50-7.75 [m, 8 H, ArH], 8.77 [br s, 1 H, H(7)], 9.59 [br s, 1 H, H(7)]; ^{13}C NMR (DMSO-d_6) ppm 23.5 [C(2,4)], 26.5 [C(9)], 31.1 [C(1,5)], 60.6 [C(6,8)], 128.5, 130.9, 133.8 [C(4')], 136.1 [C(1')]; ^{15}N NMR (DMSO-d_6) ppm 57.67 [N(7)]; ^{77}Se NMR (DMSO-d_6) ppm 2.25 [Se(3)]. Anal. Calcd. for $C_{19}H_{20}Cl_3NO_4Se$: C, 44.60; H, 3.94; N, 2.47; Se, 15.43. Found: C, 44.53; H, 3.84; N, 2.74; Se, 14.90.

6,8-Di(4-chlorophenyl)-3-selena-7-azabicyclo[3.3.1]nonane (35i)

Ketone **34i** (2.00 g, 4.71 mmol), anhydrous hydrazine (95%, 2.0 g, 60 mmol), and triethylene glycol (35 mL) were placed in a 60-mL, two-necked, jacketed, round-bottomed flask along with a magnetic stirring bar. This mixture was heated to 100°C by boiling water in the jacket of the reaction flask. Stirring at this temperature under a stream of nitrogen was continued for 2 h at which time potassium hydroxide (85%, 5.0 g, 76 mmol) was added. The temperature of the resulting mixture was increased to 140-145°C by boiling xylene in the jacket of the reaction flask. After stirring at this temperature for 3 h, the resulting solution was cooled (60-70°C) and was poured into water (100 mL). This precipitated a light yellow solid which was filtered and washed with

water. This solid was recrystallized (absolute ethanol, decolorizing carbon) to give 35i as a white powder (1.14 g, 59%): mp 163-165°C (dec); IR (KBr) cm^{-1} 3290 (N-H); ^{1}H NMR ($CDCl_3$) δ 2.04 [br s, 2 H, H(1,5)], 2.18 [d, 1 H, H(9), J = 14 Hz], 2.25 [d, 2 H, $H(2,4)_{ax}$, J = 12 Hz], 2.36 [d, 1 H, H(9), J = 13 Hz], 2.59 [br s, 1 H, H(7)], 3.04 [dd, 2 H, $H(2,4)_{eq}$, J = 12 Hz, 4 Hz], 4.50 [d, 2 H, H(6,8), J = 3 Hz], 7.32-7.52 [m, 8 H, ArH]; ^{13}C NMR ($CDCl_3$) ppm 17.7 [C(2,4)], 30.4 [C(1,5)], 35.0 [C(9)], 64.0 [C(6,8)], 127.9, 128.5, 132.6 [C(4')], 141.1 [C(1')]; ^{15}N NMR ($CDCl_3$) ppm 50.52 [N(7)]; ^{77}Se NMR ($CDCl_3$) ppm 101.86 [Se(3)].

6,8-Di(4-chlorophenyl)-3-selena-7-azabicyclo[3.3.1]nonane Hydroperchlorate (36i)

Amine 35i (1.00 g, 2.43 mmol) was dissolved in ether (200 mL) in a 500-mL, round-bottomed flask. Perchloric acid (60%, 1.0 g, 6.0 mmol) was added slowly with swirling. The resulting mixture was allowed to stand at room temperature for 24 h with occasional swirling. The orange solid which formed was filtered and recrystallized (absolute ethanol, decolorizing carbon) to give 36i (0.36 g, 29%) as white needles: mp 264-265°C (dec); ^{1}H NMR (DMSO-d_6) δ 2.16 [d, 1 H, H(9), J = 12.1 Hz], 2.29 [d, 2 H, $H(2,4)_{ax}$, J = 12.7 Hz], 2.50 [m, 3 H, H(1,5), H(9)], 3.13 [d, 2 H, $H(2,4)_{eq}$, J = 12.3 Hz], 5.07 [d, 2 H, H(6,8), J = 8.5 Hz], 7.58-7.90 [m, 8 H, ArH], 9.18 [br s, 1 H, H(7)], 10.46 [br s, 1 H, H(7)]; ^{13}C NMR (DMSO-d_6) ppm 17.7 [C(2,4)], 29.7 [C(1,5)], 32.0 [C(9)], 63.7 [C(6,8)], 128.6, 128.9, 133.2 [C(4')], 134.5 [C(1')]; ^{15}N NMR (DMSO-d_6) ppm 49.57 [N(7)]; ^{77}Se NMR (DMSO-d_6) ppm 74.96 [Se(3)]. Anal. Calcd. for $C_{19}H_{20}Cl_3NO_4Se.C_2H_5OH$: C, 45.22; H, 4.70; N, 2.51; Se, 14.16. Found: C, 44.93; H, 4.39; N, 2.58; Se, 14.43.

Diethyl Diselenide (48)

Ammonia (500 mL) was condensed into a 1-l, round-bottomed, three-necked flask which was equipped with a gas inlet and a dry ice/acetone condenser. Freshly cut sodium metal (8.0 g at., 348 mmol) was added to the ammonia in small pieces over 30 min to give a very dark blue solution. After 30 min, selenium metal (27.7 g at., 350 mmol) was then added slowly in 5 g portions over 1 h. During this addition, the dark blue color of the sodium solution turned progressively to purple, light pink, light brown, and finally very dark green. This green solution was stirred for an additional hour. Ethyl bromide (90 g, 830 mmol) was added dropwise over 1 h. The ammonia was allowed to boil away overnight and the residue was taken up in ether (350 mL). The ether was then washed with water (50 mL) and dried (K_2CO_3). Evaporation (aspirator) and distillation of the residue gave 36.0 g (48%) of the diselenide 48 as an orange oil: bp 60-70°C/5 mm Hg (lit.[19] 75°C/14 mm Hg); ^{1}H NMR ($CDCl_3$) δ 1.46 [t, 6 H, C(2), J = 7.46 Hz], 2.90 [q, 4 H, C(1), J = 7.43 Hz]; ^{13}C NMR ($CDCl_3$) ppm 16.4 [q, C(2)], 23.0 [t, C(1)].

3-Selenavaleric Acid (49)

A solution of diethyl diselenide (48, 25.0 g, 115 mmol) in 95% ethanol (35 mL) was placed in a 250-mL, three-necked, round-bottomed flask equipped with magnetic stirring, a reflux condenser and two addition funnels, one carrying a nitrogen inlet. A solution of NaOH (5.0 g, 217 mmol) and $NaBH_4$ (10.0 g, 265 mmol) in water (80 mL) was added dropwise. The resulting solution was heated to boiling and was stirred at reflux until the orange color disappeared (1 h). After cooling this

colorless solution to 0°C in an ice bath, a solution of $ClCH_2CO_2H$ (21.8 g, 229 mmol) and Na_2CO_3 (12.2 g, 114 mmol) in water (75 mL) was added dropwise. After stirring at room temperature for 18 h, the reaction mixture cooled to 0°C and was acidified with conc HCl (40 mL) and was extracted with ether (4 X 50 mL). The combined extracts were washed with water (50 mL) and dried (Na_2SO_4). Evaporation (aspirator) of the ether gave a light yellow oil and a white solid. The solid was filtered and the oil was distilled to give acid 49 (29.2 g, 76%) as a light yellow oil: bp 89-94°C/1.0 mm Hg (lit[13] bp 85-86°C/0.6 mm Hg); ^{1}H NMR ($CDCl_3$) δ 1.43 [t, 3 H, H(5), J = 7.51 Hz], 2.80 [q, 2 H, H(4), J = 7.49 Hz], 3.19 [s, 2 H, H(2)], 11.77 [s, 1 H, CO_2H]; ^{13}C NMR ($CDCl_3$) ppm 15.1 [C(5)], 19.3 [C(4)], 21.4 [C(2)], 178.5 [C(1)]; ^{77}Se NMR ($CDCl_3$) ppm 96.29 [Se(3)].

3-Selenavaleryl Chloride (50)

A 25-mL, two-necked, conical flask which was equipped with magnetic stirring and a condenser, was charged with oxalyl chloride (7.30 g, 56.7 mmol). Acid 49 (4.75 g, 28.3 mmol) was added cautiously with cooling. Once the initial, vigorous reaction had subsided, the solution was heated to reflux and stirred at this temperature for 4 h. The reaction flask was then equipped for vacuum distillation and the excess oxalyl chloride was distilled under aspirator vacuum. The residual oil was then distilled under high vacuum to give 4.0 g (76%) of acid chloride 50 as a light yellow oil: bp. 25-33°C/0.25 mm Hg (lit.[13] 75-76°C/15 mm Hg); ^{1}H NMR ($CDCl_3$) δ 1.44 [t, 3 H, H(5), J = 6 Hz], 2.83 [q, 2 H, H(4), J = 6 Hz], 3.64 [s, 2 H, H(2)]; ^{13}C NMR ($CDCl_3$) ppm 14.9 [C(5)], 19.7 [C(4)], 33.1 [C(2)], 169.8 [C(1)]; ^{77}Se NMR ($CDCl_3$) ppm 5.06 [Se(3)].

3-Selenavalero-o-xylidide (51)

Acid chloride 50 (4.00 g, 21.6 mmol) was dissolved in anhydrous ether (70 mL) in a 250-mL Erlenmeyer flask. This solution was cooled to 0°C in an ice bath and 2,6-dimethylaniline (5.30 g, 43.8 mmol) was added dropwise very slowly with swirling. A dense white precipitate formed immediately. This mixture was allowed to stand at room temperature with occasional stirring for 1 h. The solid 2,6-dimethylaniline hydrochloride was filtered and ice-water (100 mL) was cautiously. The layers were separated and the aqueous layer was extracted with ether (2 x 75 mL). The combined ether portions were dried (K_2CO_3) and evaporated (aspirator) to give a 4.12 g (71%) of amide 51 as white needles: mp 93.0-94.0°C; ^{1}H NMR ($CDCl_3$) δ 1.38 [t, 3 H, H(5), J = 7.5 Hz], 2.13 [s, 6 H, $ArCH_3$], 2.70 [q, 2 H, H(4), J = 7.5 Hz], 3.28 [s, 2 H, H(2)], 6.97 [m, 3 H, ArH], 7.90 [br s, 1 H, N-H]; ^{13}C NMR ($CDCl_3$) ppm 15.3 [C(5)], 18.3 [$ArCH_3$], 19.2 [C(4)], 25.5 [C(2)], 127.2 [C(4')], 128.1 [C(3',5')], 133.6 [C(2',6')], 135.2 [C(1')], 168.2 [C(1)]. Anal. Calcd for $C_{12}H_{17}NOSe$: C, 53.31; H, 6.34; N, 5.19; Se, 29.23. Found: C, 53.06; H, 6.45; N, 5.10; Se, 29.44.

3-Selenavalero-o-xylidide Dichloride (39)

A solution of amide 51 (0.5 g, 1.80 mmol) in anhydrous ether (100 mL) was placed in a 250-mL Erlenmeyer flask. Chlorine gas was bubbled through the solution. This immediately precipitated a white solid. Bubbling was continued until no more solid formed. The solid was filtered to give 0.48 g (78%) of dichloride 39 as a white crystalline solid: mp 142.0-143.0°C (dec); ^{1}H NMR ($CDCl_3$) δ 1.74 [t, 3 H, H(5)],

2.50 [s, 6 H, $ArCH_3$], 3.98 [q, 2 H, H(4)], 4.36 [br s, 2 H, H(2)], 7.40 [m, 3 H, ArH], 9.98 [br s, 1 H, N-H]; ^{13}C NMR ($CDCl_3$) ppm 10.2 [C(5)], 18.3 [$ArCH_3$], 53.9 [C(4)], 62.8 [C(2)], 126.8 [C(4')], 127.7 [C(3',5')], 133.9 [C(1')], 134.9 [C(2',6')], 161.9 [C(1)]; ^{77}Se NMR ($CDCl_3$) ppm 590.06 [Se(3)]. Anal. Calcd for $C_{12}H_{17}Cl_2NOSe$: C, 42.22; H, 5.02; N, 4.11; Cl, 20.79; Se, 23.15. Found: C, 42.26; H, 4.96; N, 4.06; Cl, 20.68; Se, 22.99.

Experimental for X-ray Data Collection for 4-Selenanone (38)

Experimental parameters for the study of 4-selenanone (38) are found in Table XVIII. A single crystal of 4-selenanone (38, 0.2 x 0.2 x 0.4 mm) was sealed in a capillary and mounted on a Syntex P3 automated diffractometer. Unit cell dimensions (Table XVIII) were determined by least squares refinement of the best angular position for fifteen independent reflections ($2\theta>15°$) during normal allignment procedures using molybdenum radiation ($\lambda = 0.71069$ Å). Data (2339 points) were collected at room temperature using a variable scan rate, a θ-2θ scan mode and a scan width of 1.2° below $K\alpha_1$ and 1.2° above $K\alpha_2$ to a maximum 2θ value of 116°. Backgrounds were measured at each side of the scan for a combined time equal to the total scan time. The intensities of three standard reflections were remeasured after every 97 reflections and as the intensities of these reflections showed less than 8% variation, corrections for decomposition were deemed unnecessary. Data were corrected for Lorentz, polarization and background effects. After removal of redundant and space group forbidden data, 812 reflections were considered observed [$I>3.0\sigma(I)$]. The structure was solved from a Patterson synthesis to locate the heavy atom. Successive least squares/ difference

Fourier cycles allowed location of the remainder of the non- hydrogen atoms. Refinement of scale factor, positional and anisotropic thermal parameters[108] for all non-hydrogen atoms was carried out to convergence. Hydrogen positional parameters were determined from a difference Fourier synthesis. These hydrogen positional parameters and the associated isotropic thermal parameters were refined along with non-hydrogen parameters in the final cycles of refinement. The final cycle of refinement [function minimized $\Sigma(|F_o| - |F_c|)^2$] led to a final agreement factor, R = 8.1% [$R = (\Sigma||F_o| - |F_c||/|F_o|) \times 100$]. Anomalous dispersion corrections were made for selenium. Scattering factors were taken from Cromer and Mann.[30] Unit weights were used throughout.

Experimental for X-ray Data Collection for 7-Benzyl-3-Selena-7-aza-bicyclo[3.3.1]nonan-9-one (34a)

A crystal of 7-benzyl-3-selena-7-azabicyclo[3.3.1]nonan-9-one (34a) was sealed in a capillary and mounted on a Syntex P3 automated diffractometer. Unit cell dimensions (Table XXII) were determined by least squares refinement of the best angular positions for fifteen independent reflections ($2\theta > 15°$) during normal allignment procedures using molybdenum radiation ($\lambda = 0.71069$ Å). Data (7756 points) were collected at room temperature using a variable scale rate, a θ-2θ scan mode and a scan width of 1.2° below $K\alpha_1$ and 1.2° above $K\alpha_2$ to a maximum 2θ value of 90.6°. Backgrounds were measured at each side of the scan for a combined time equal to the total scan time. The intensities of three standard reflections were remeasured after every 97 reflections and as the intensities of these reflections showed less than 6% variation, corrections for decomposition were deemed unnecessary. Data were

corrected for Lorentz, polarization and background effects. After removal of redundent data, 2207 points were considered observed [$I>3.0\,\sigma(I)$]. The structure was solved using MULTAN80.[70] Refinement of scale factor, positional and anisotropic thermal parameters for all non-hydrogen atoms was carried out to convergence. Hydrogen atom positions were determined from a difference Fourier synthesis. These positions were included in the final cycles of refinement but were held invariant.[108] The final cycle of refinement [function minimized $\Sigma(|F_o| - |F_c|)^2$] led to a final agreement factor, R = 6.5% [$R = (\Sigma||F_o| - |F_c||/|F_o|) \times 100$]. Anomalous dispersion corrections were made for selenium. Scattering factors were taken from Cromer and Mann.[30] Unit weights were used until the final cycles of refinement when a weight = $1/\sigma F$ was introduced.

Experimental for X-ray Data Collection for 7-Benzyl-3-Selena-7-aza-bicyclo[3.3.1]nonane Hydroperchlorate (36a)

Preliminary investigations indicated that the crystal system of **36a** was orthorhombic. Observations of reflection conditions (h00: h=2n, 0k0: k=2n, 00l: l=2n) uniquely determined the space group $P2_12_12_1$. Unit cell dimensions were refined by a least-squares fit of the $\pm$ 2θ values of 36 reflections distributed throughout reciprocal space (Table XXVI). Lattice parameter and intensity data were collected on an Enraf Nonius CAD-4 automatic X-ray diffractometer fitted with a liquid N_2 low temperature device, using Molybdenum K radiation (λ = 0.71069 A). A θ-2θ scan technique was employed using variable scan width and variable scan speed. Maximum scan time for a reflection was 90 seconds with two-thirds of the time spent on the reflection; the remaining time was

divided equally between the high and low backgrounds. The receiving aperature, which had a variable width of (4.0 + 0.86θ) mm and a constant height of 5 mm, was located 173 mm from the crystal. The intensities of three reflections, remeasured after every 200 reflections showed no significant variation during the time of data collection.

The position of the selenium atom was determined by a Patterson synthesis. The rest of the structure was determined by difference Fourier syntheses and refined by a full matrix least squares routing using anisotropic thermal parameters for the non-hydrogen atoms.[105] All of the hydrogen atoms were located from a difference Fourier map and were refined isotropically. Scattering factors were obtained from "International Tables for X-ray Crystallography".[58] The refinement converged to a final $R = (\Sigma||Fo|-|Fc||/|Fo|)$ of 0.0552 for 1766 observed reflections. An analysis of the variance after refinement of the data revealed no systematic variance of $\Sigma\omega|Fo|-|Fc|$ with either $\sin\theta$ or F.

Experimental for X-ray Data Collection for 3-Selenavalero-o-xylidide Dichloride (39)

A crystal with approximate dimensions of 0.08 x 0.09 x 0.31mm was used for data collection. The crystal data are given in Table XXX. The reflections were measured on a Nonius CAD-4 automatic diffractometer with liquid N_2 device using MoK_α radiation (λ = 0.71069 A). The θ-2θ scan technique was used, maximum scan time per reflection was 60 s with 2/3 of the time spent scanning the peak and the remaining 1/3 divided dqually between the high and low θ backgrounds.

The position of the Se atom was determined using a Patterson synthesis with the y coordinate arbitrarily assigned. Positions of other

atoms including all of the hydrogen atoms were determined by difference Fourier syntheses and subsequently refined with anisotropical thermal parameters (except the hydrogens which were kept isotropic) by full matrix least-squares with the SHELX program. The final difference-Fourier map had a maximum density of 0.52 e $Å^{-3}$ close to the Se-atom. The final R factor was 0.038. The space group is polar and the centro-symmetrically related coordinates refined to a larger R-value (0.042). Scattering factor for Se atom was taken from the International Tables for X-ray Crystallography.[58]

PLATE I. IR SPECTRUM OF **34a**

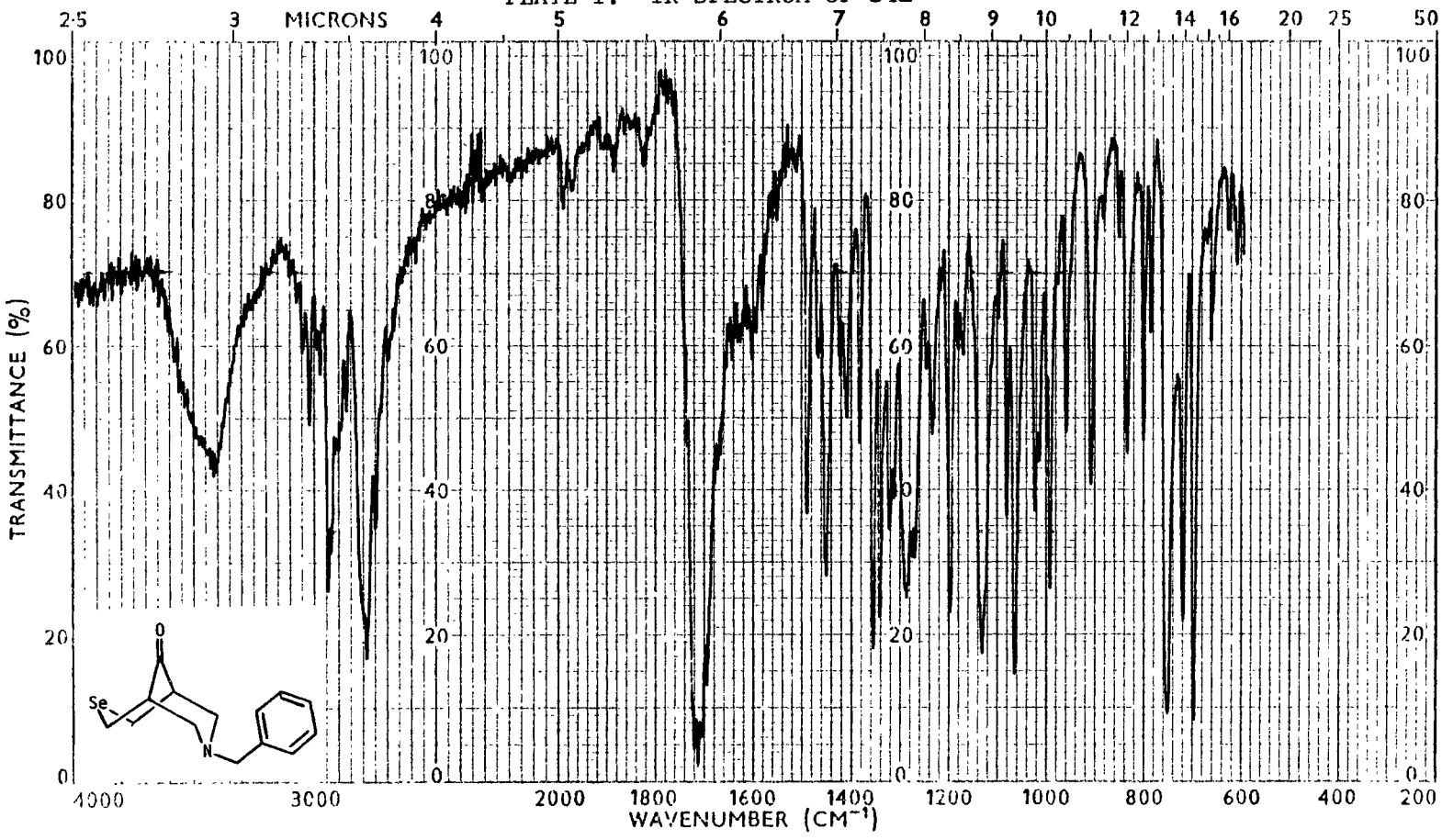
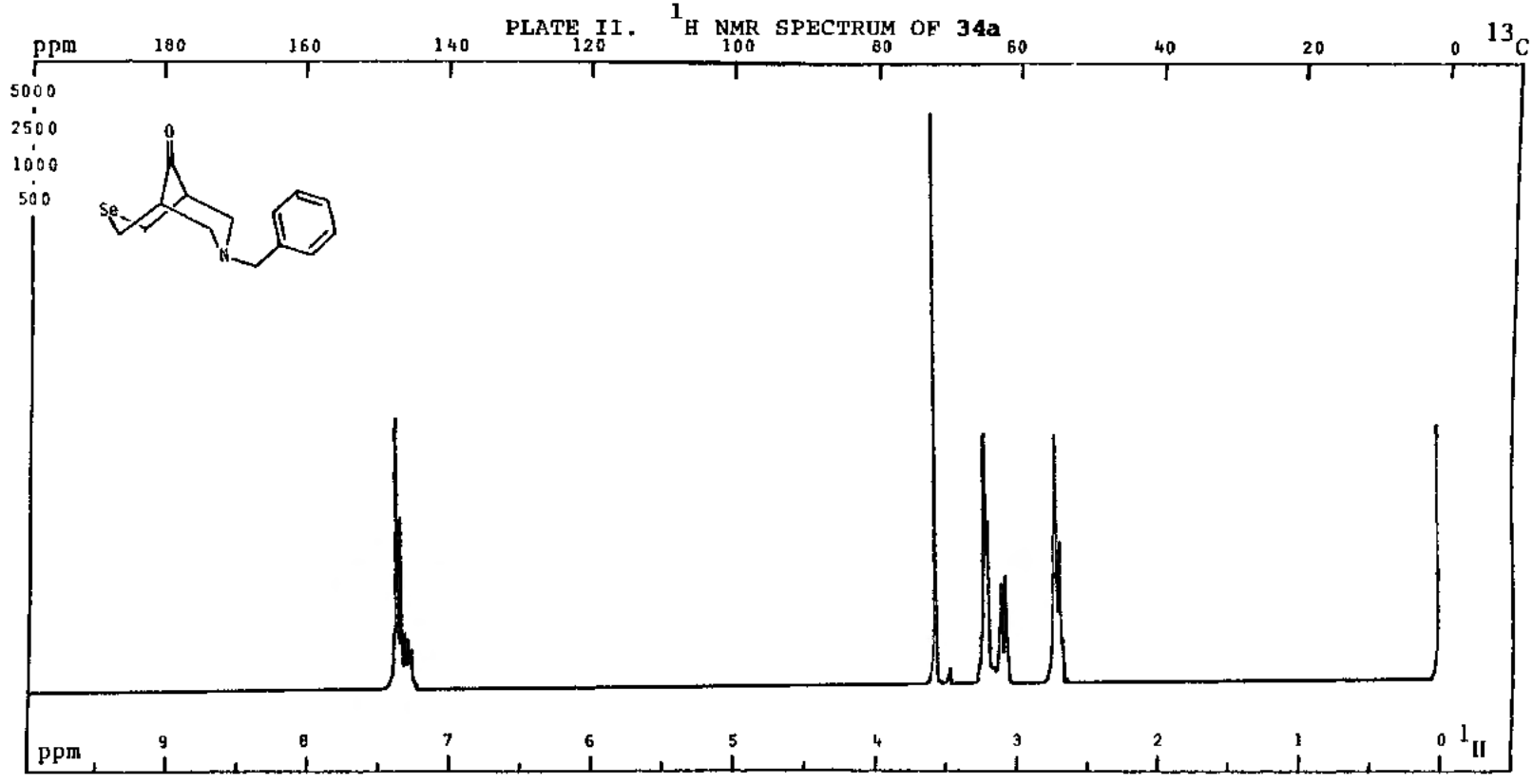


PLATE II. ^{1}H NMR SPECTRUM OF **34a**

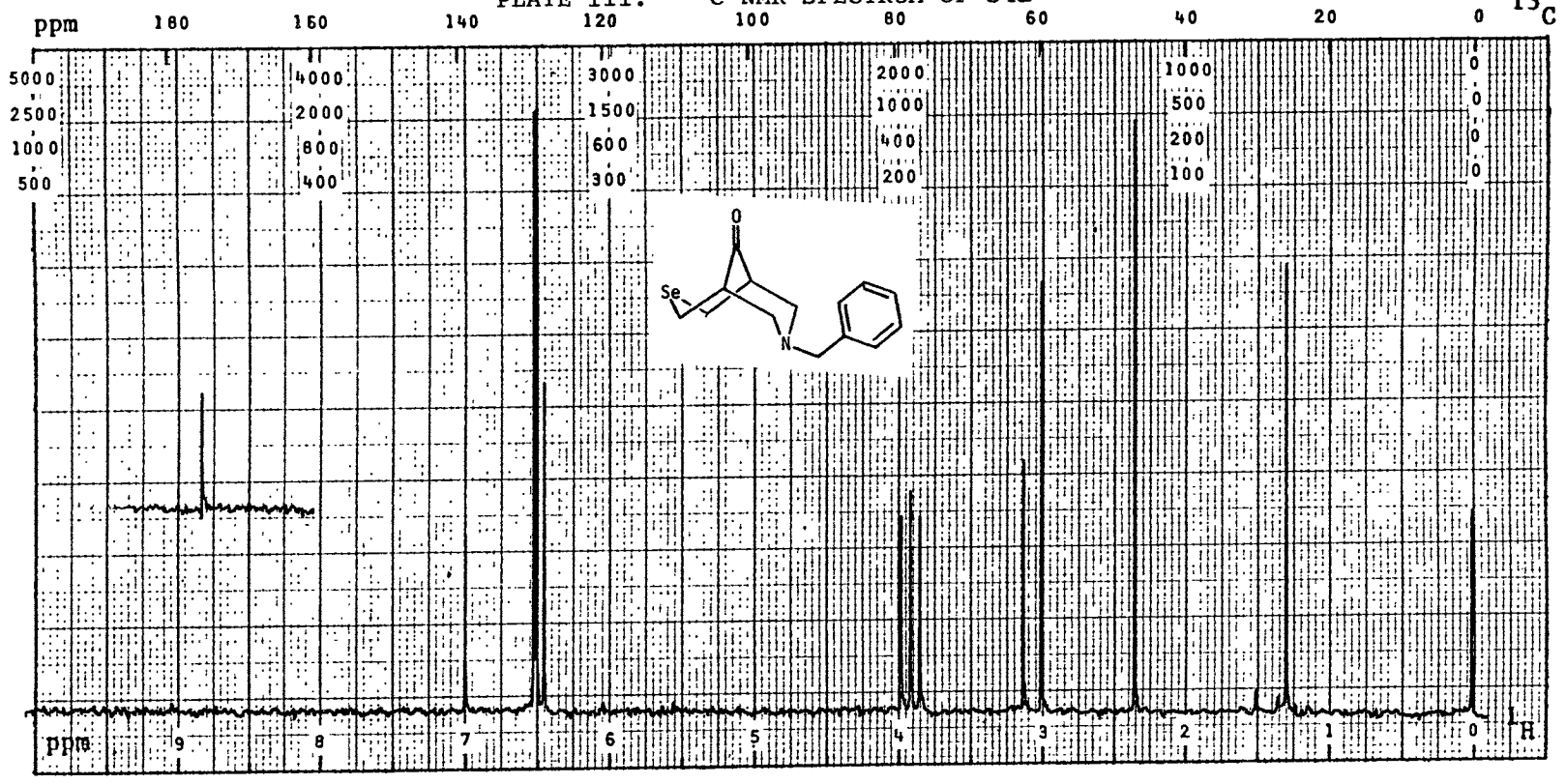


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 2999.4Hz; T: 25 °C; NT: 16 .

Size: 12 K; PW/RF: 8 µs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ;D1,D5: 0.500 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE III. ^{13}C NMR SPECTRUM OF **34a**

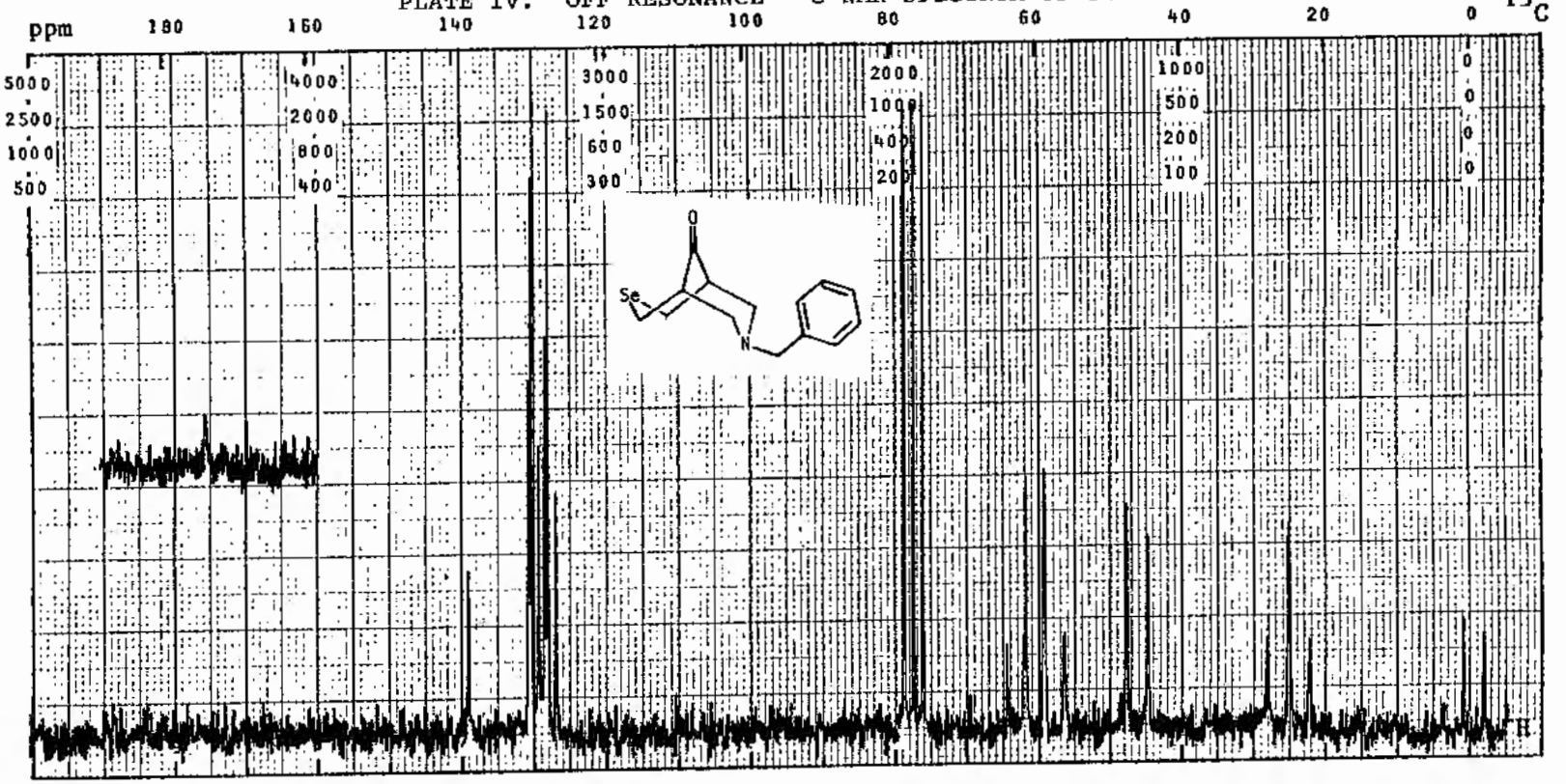


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 6000 Hz; T: 28 °C; NT: 3924 .

Size: 8 K; PW/RF: 10 µs/dB; TO: 35101 Hz; FB: 3 K Hz; Lock: ^2D ; D1,D5 : 5 s.

DC: Y, N ; Gated Off: A or D ; DO: 45316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE IV. OFF RESONANCE ^{13}C NMR SPECTRUM OF **34a**

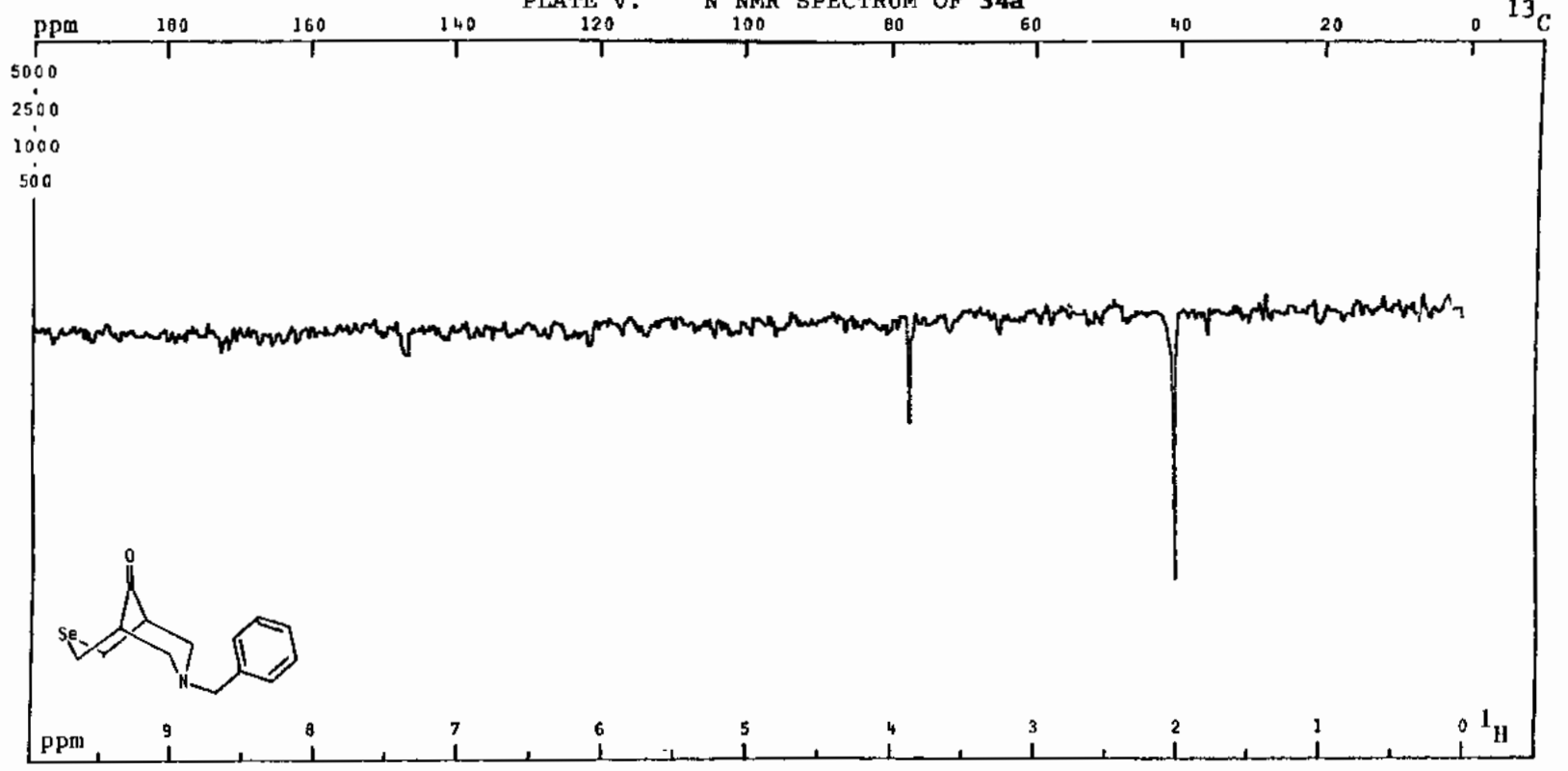


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 6000 Hz; T: 28 °C; NT: 4000 .

Size: 8 K; PW/RF: 10 µs/dB; TO: 35101 Hz; FB: 3 K Hz; Lock: ^2D ; D1,D5 : 5 s.

DC: Y, N ; Gated Off: A or D ; DO: 46316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz

PLATE V. ^{15}N NMR SPECTRUM OF **34a**

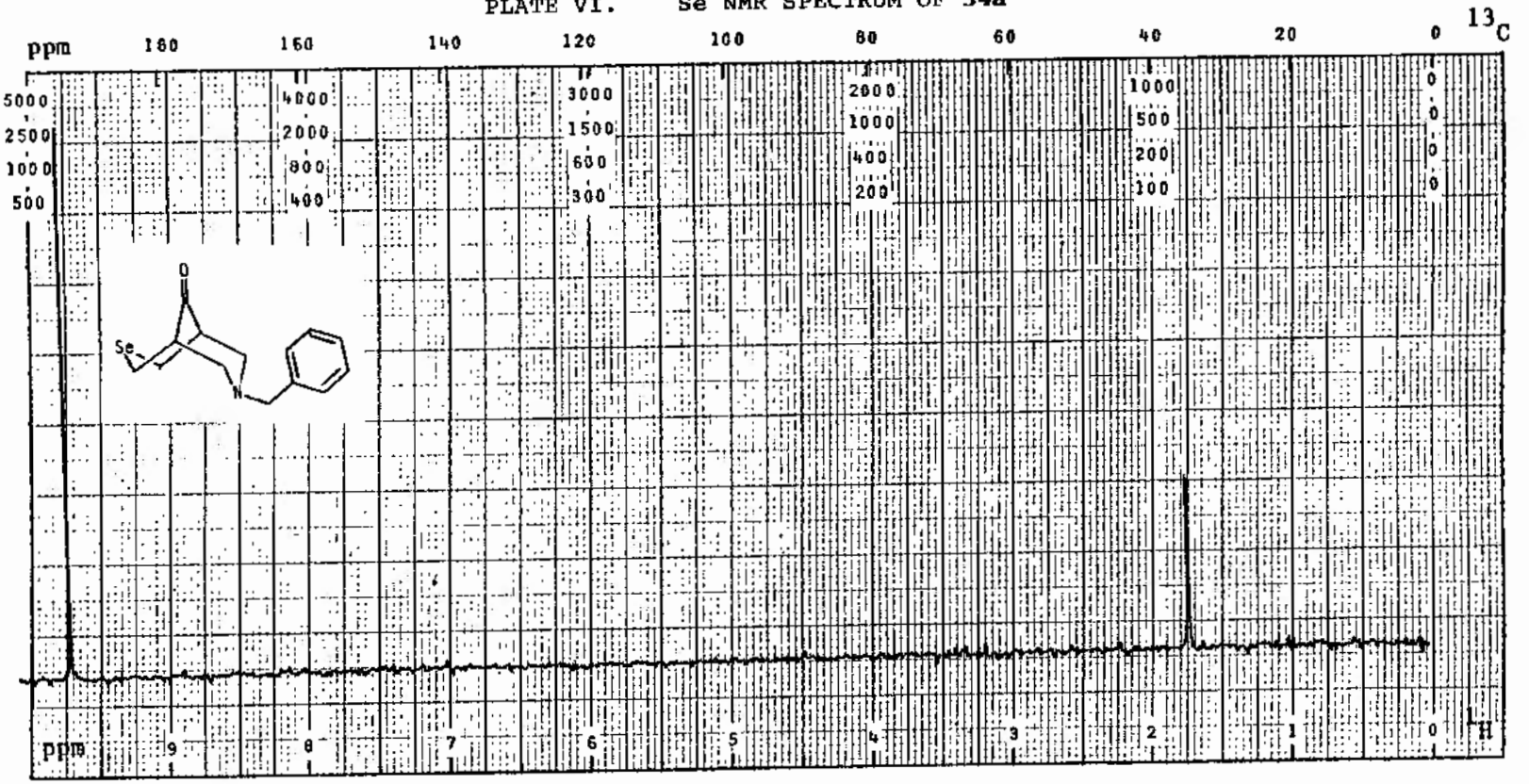


PFT X CW _ ; **Solvent:** $CDCl_3$; SF: 30.406 MHz; WC:3040.6 Hz; T: 25 °C; NT: 72,000 .

Size: 12K; PW/RF: 40 µs/dB; TO: - 11600 Hz; FB: Hz; Lock: ^{2}D ;D1,D5: 8.00 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE VI. ^{77}Se NMR SPECTRUM OF **34a**



PFT X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 160 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^2D ; D1,D5 : 25 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE VII. IR SPECTRUM OF **34b**

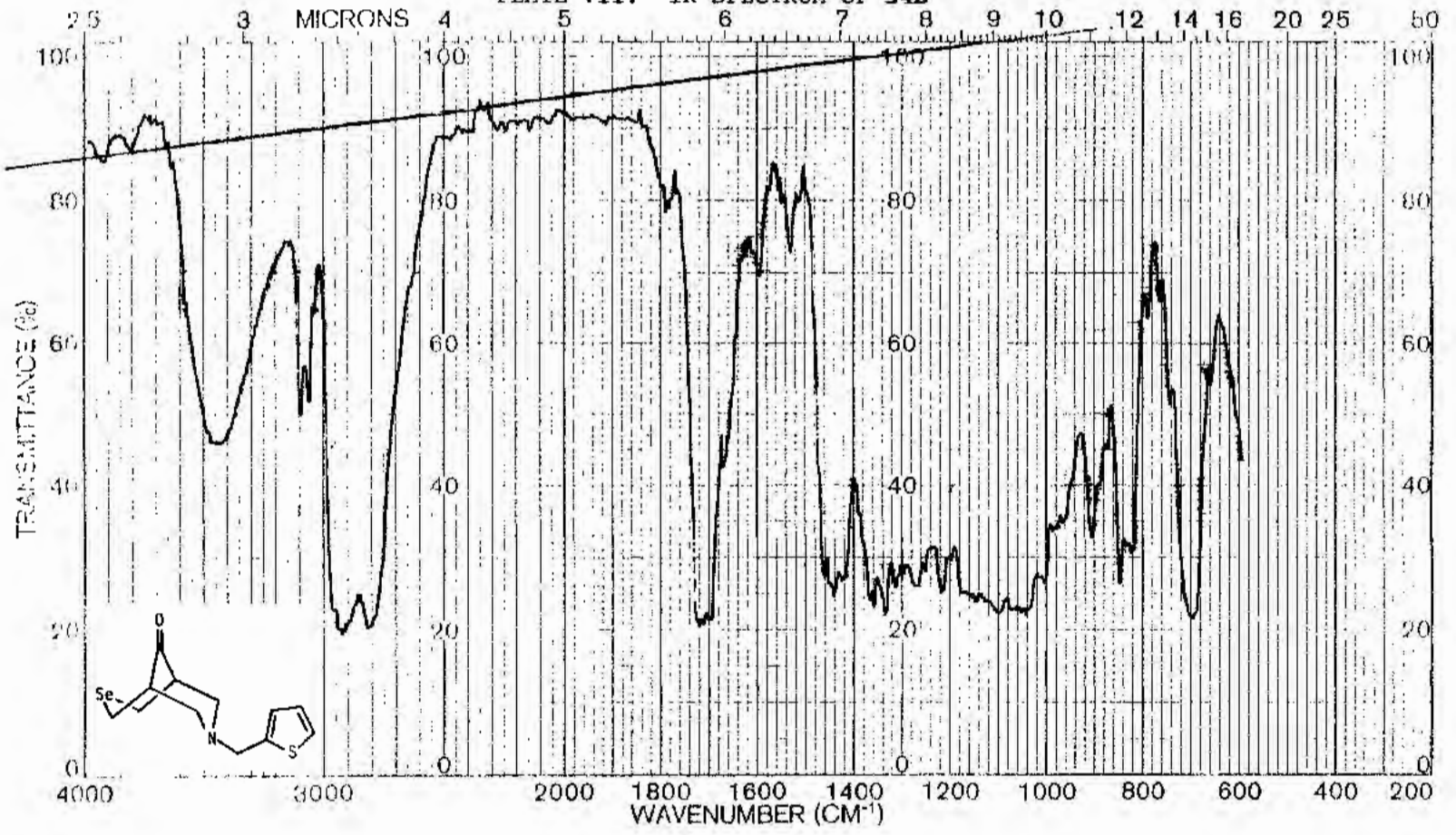
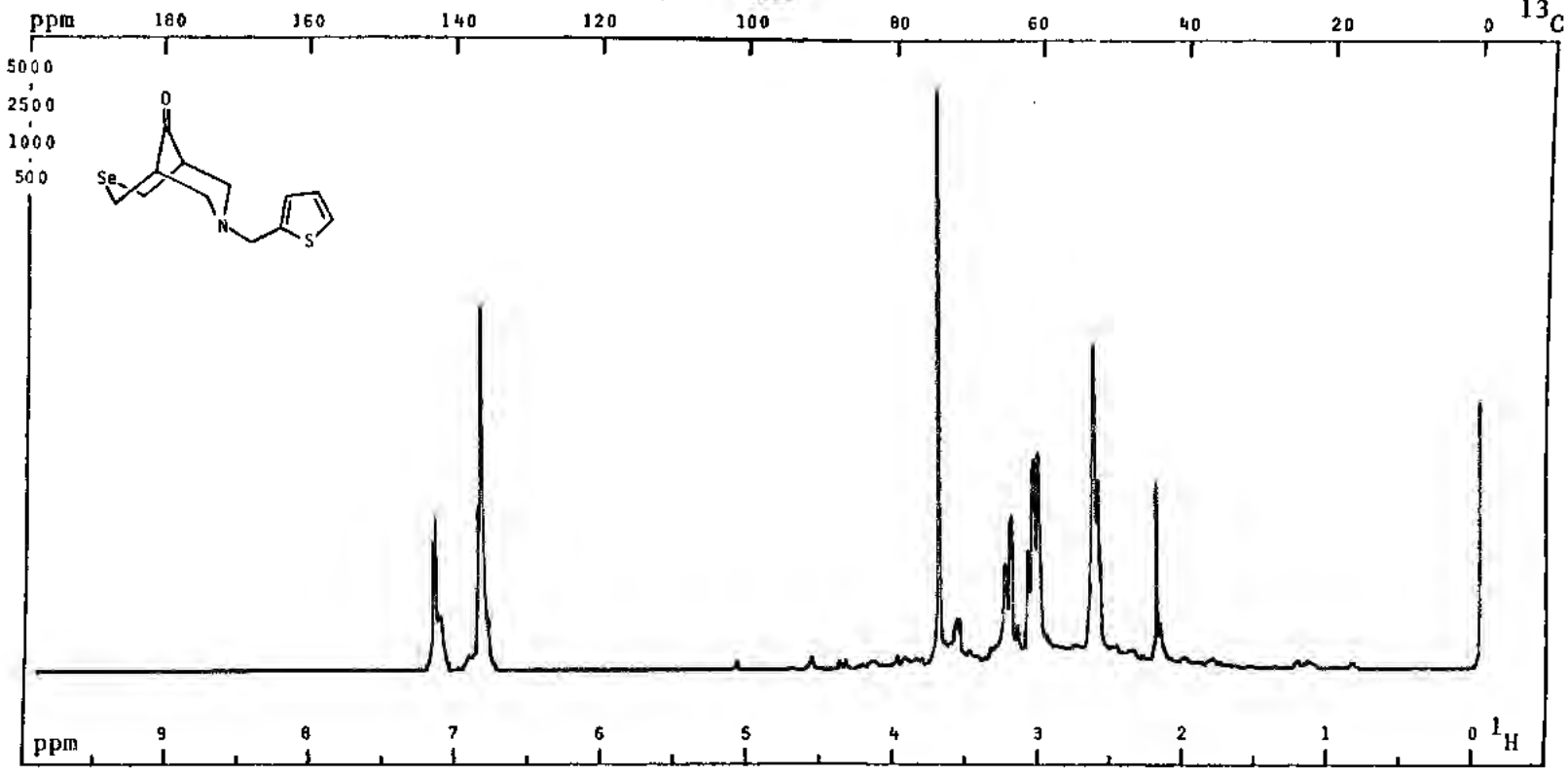


PLATE VIII. ^{1}H NMR SPECTRUM OF **34b**

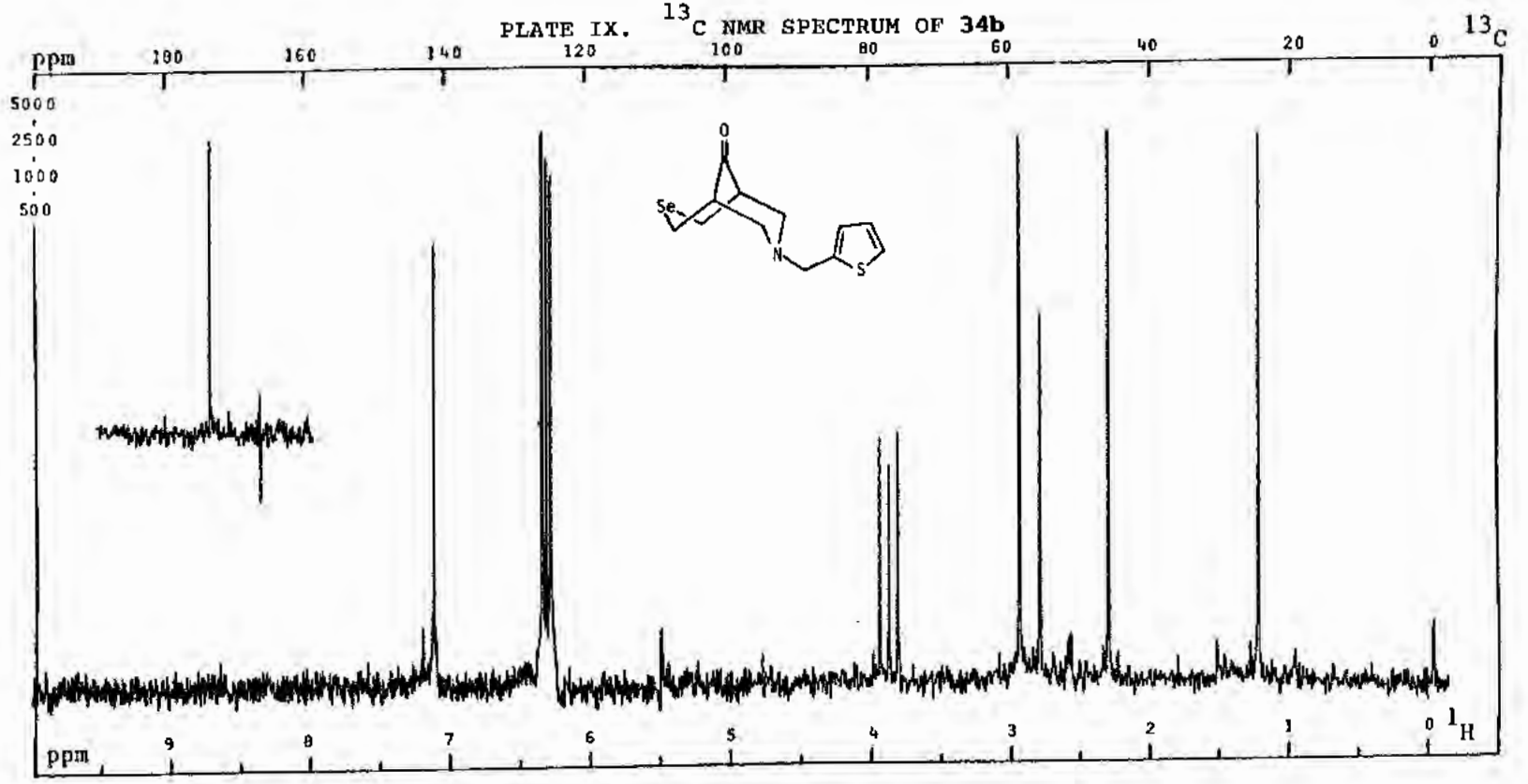


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 16 .

Size: 12K; PW/RF: 5 µs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE IX. ^{13}C NMR SPECTRUM OF **34b**

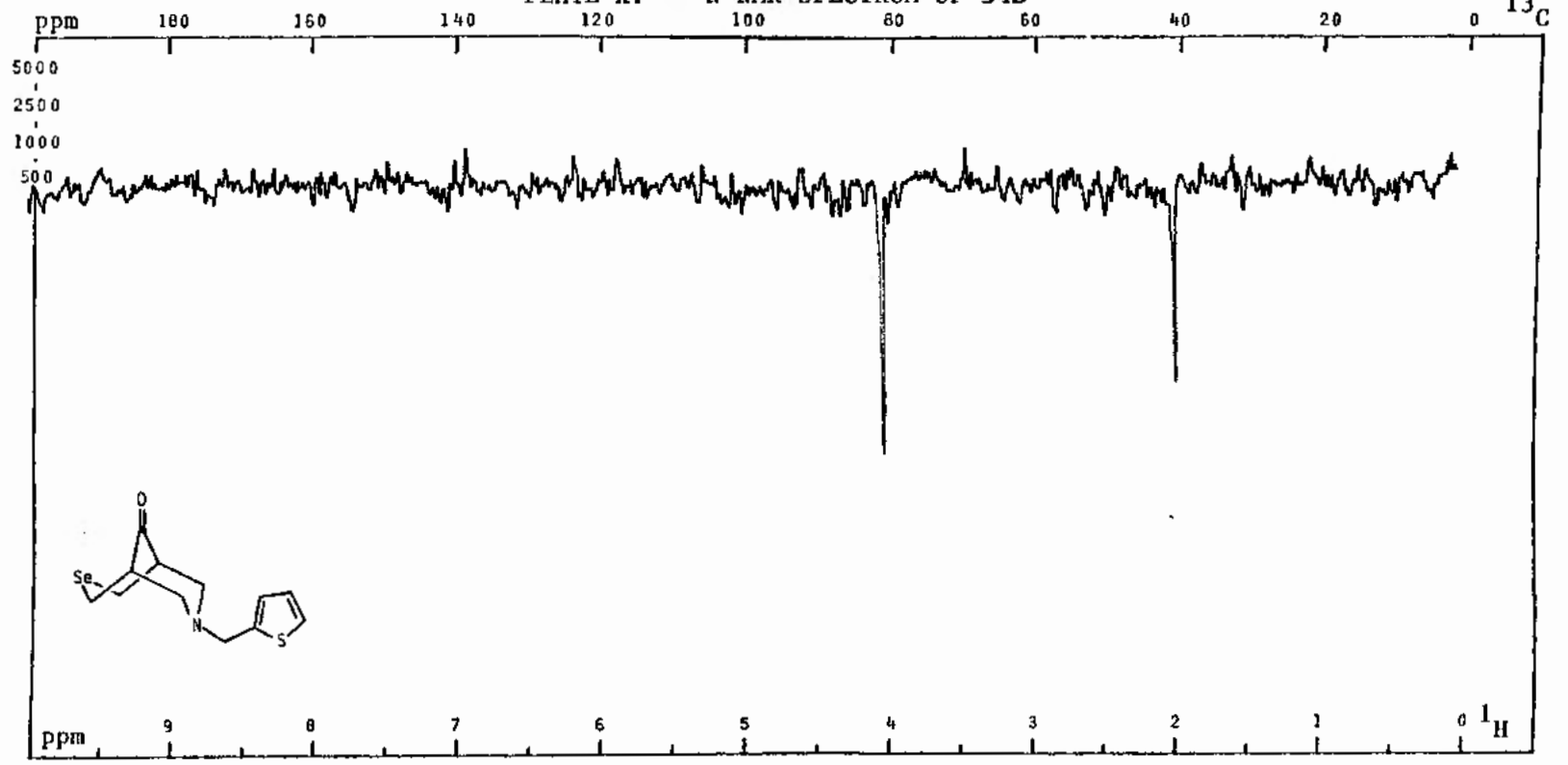


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 6000 Hz; T: 28 °C; NT: 3000 .

Size: 8 K; PW/RF: 10 µs/dB; TO: 35101 Hz; FB: 3K Hz; Lock: ^{2}D ; D1,D5: 5 s.

DC: Y, N ; Gated Off:A or D ; DO: 45316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE X. ^{15}N NMR SPECTRUM OF **34b**

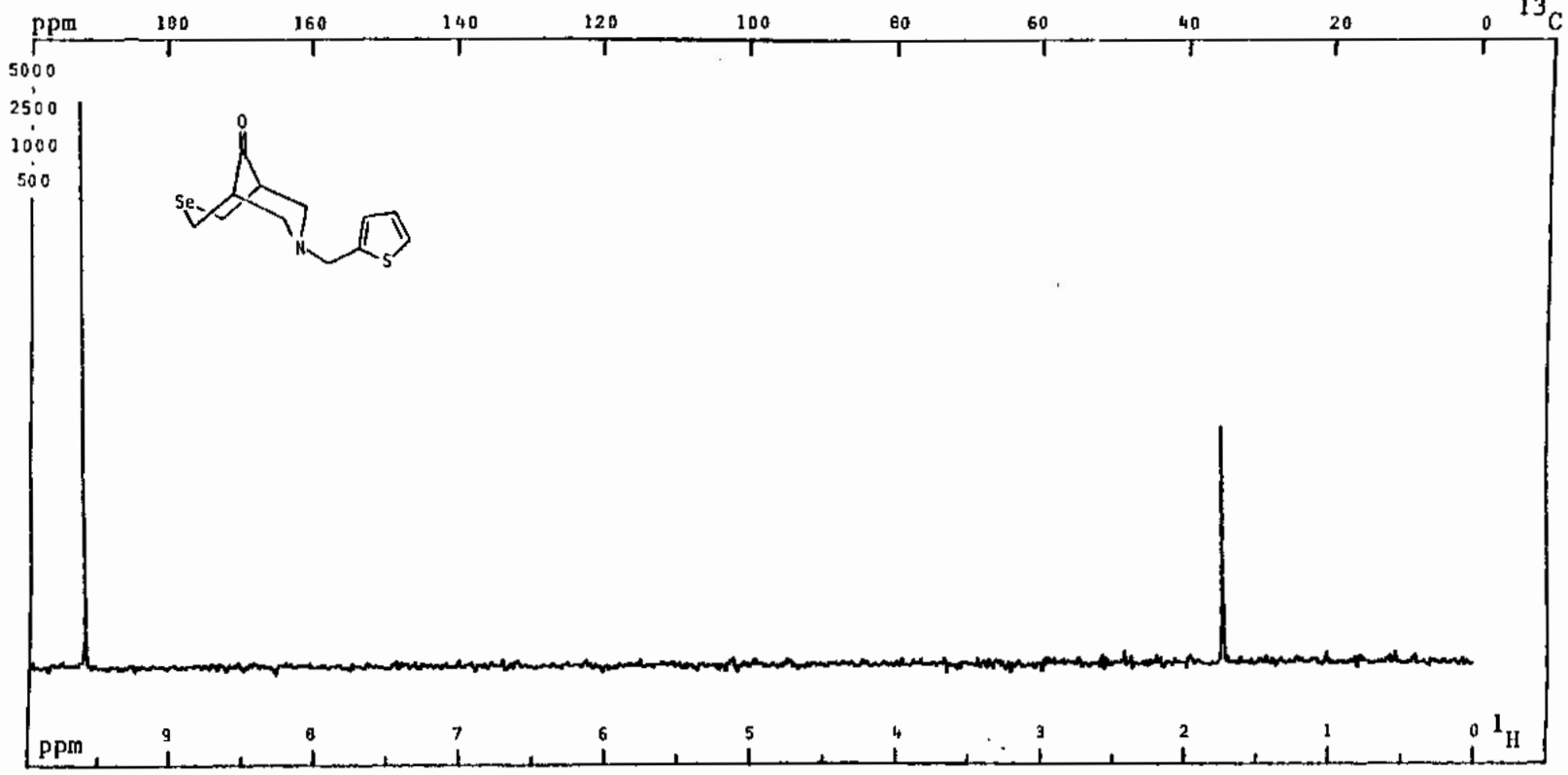


PFTX_ CW _ ; Solvent: $CDCl_3$; SF: 30.406 MHz; WC: 3040.6 Hz; T: 25 °C; NT: 5600 .

Size: 10 K; PW/RF: 40.0 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 8 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XI. ^{77}Se NMR SPECTRUM OF **34b**



PFTX_ CW _ : Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 20

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^2D ; D1,D5: 18 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE XII. IR SPECTRUM OF **34c**

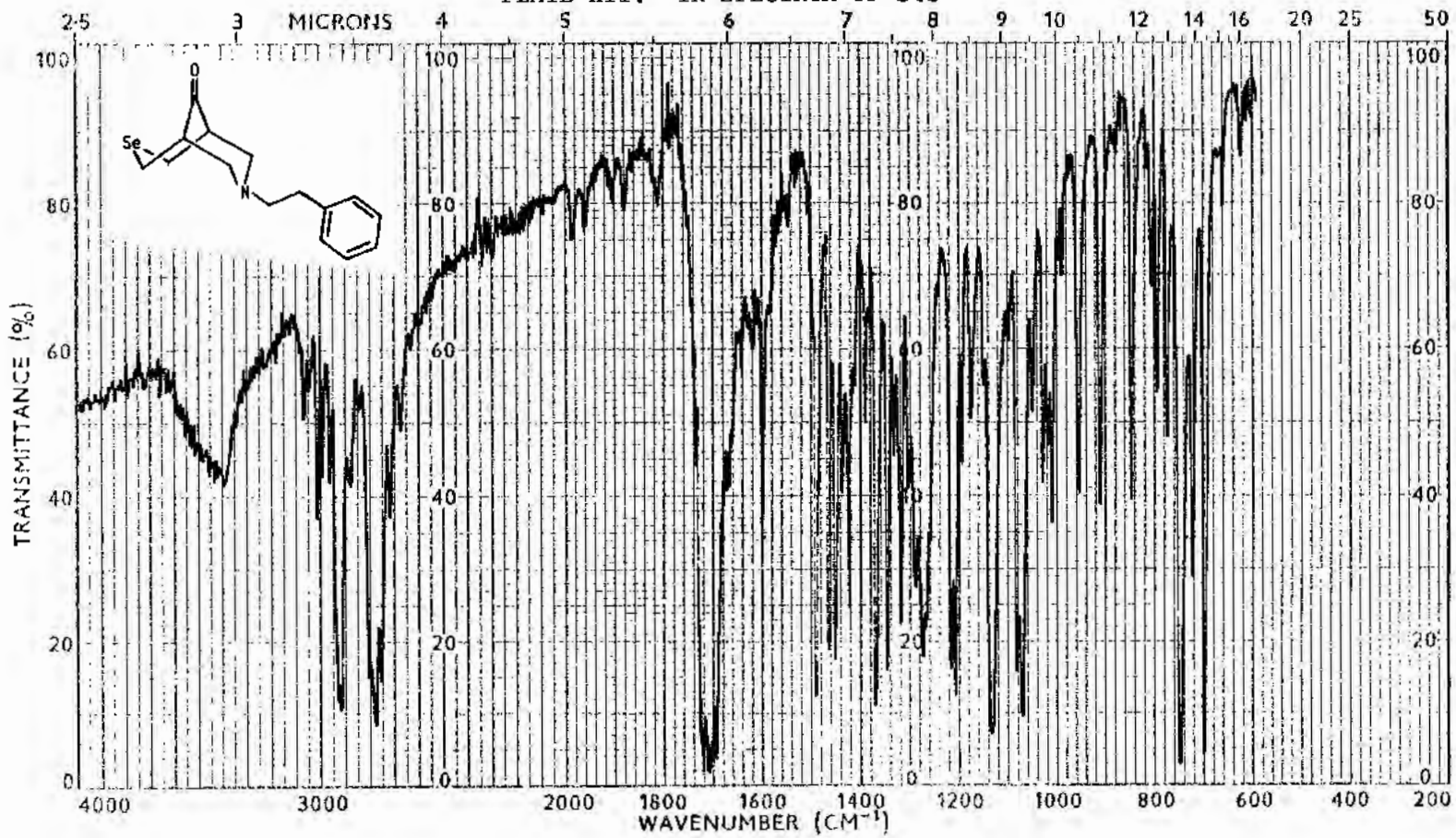
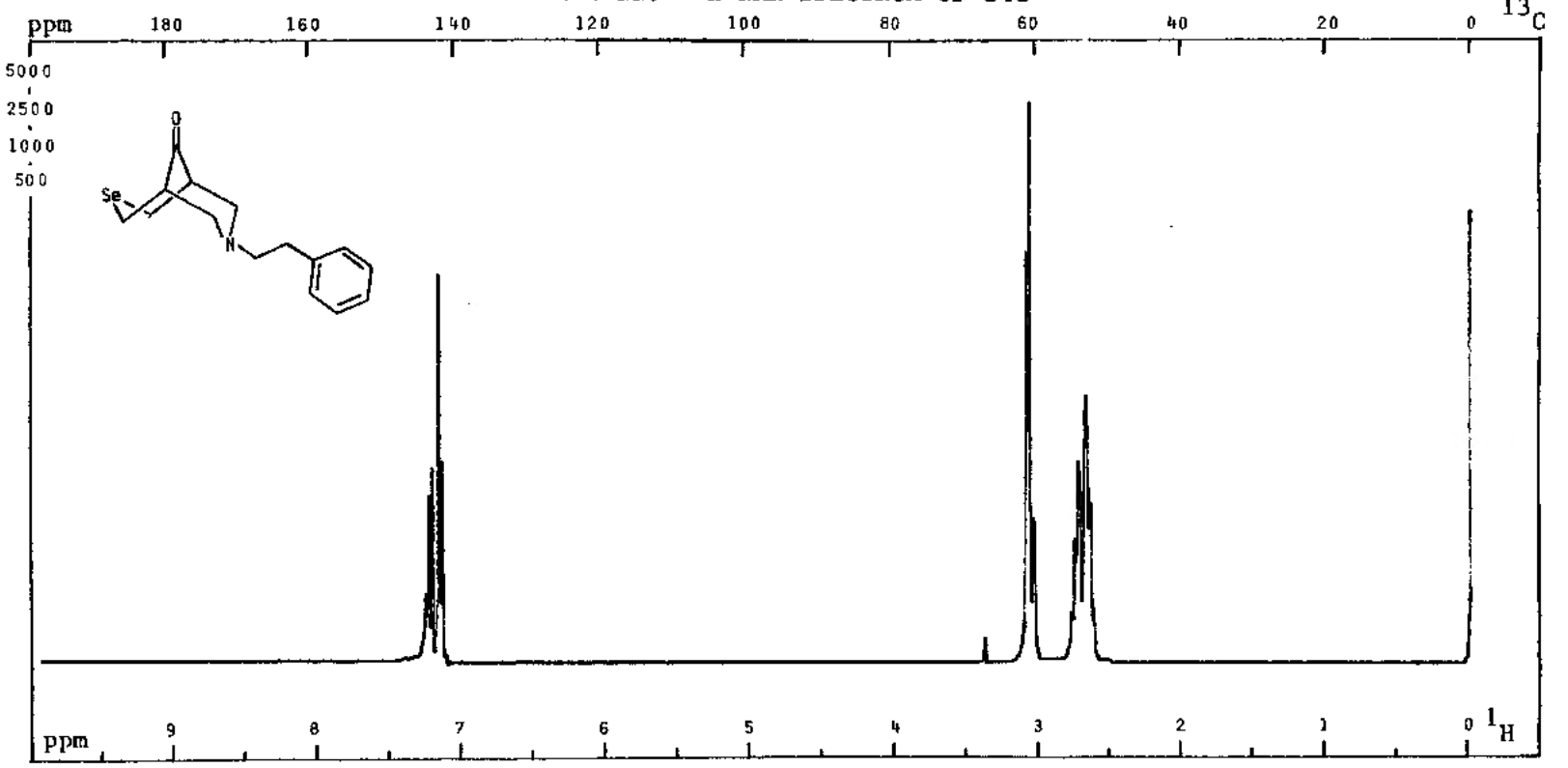


PLATE XIII. ^{1}H NMR SPECTRUM OF **34c**

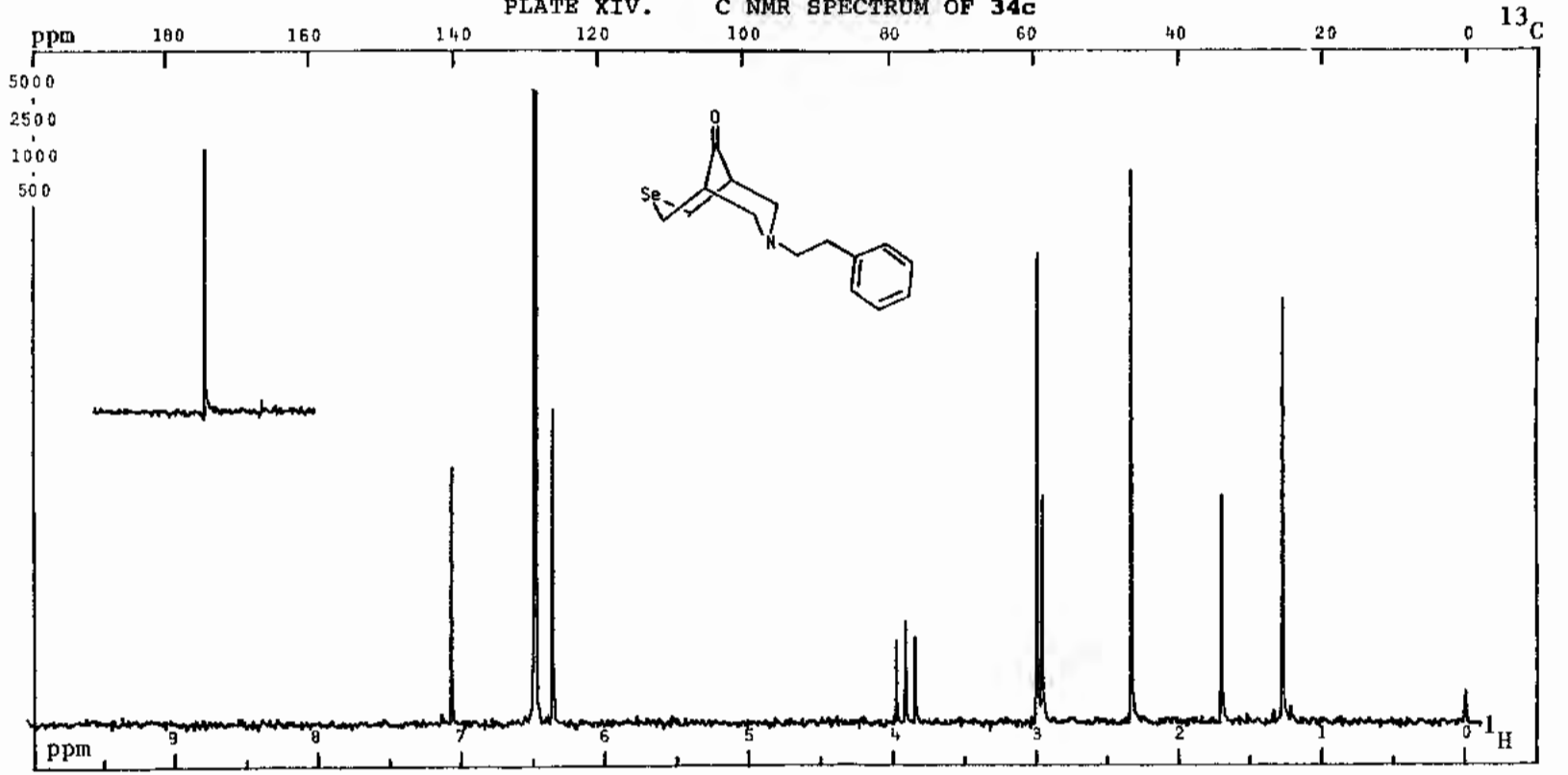


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 12

Size: 12 K; PW/RF: 5 µs/dB; SO: 0 Hz; FB: Hz; Lock: ^{2}D ; Delay: 0.500 s

DC: N ; Gated Off: ; Offset: Hz; RF: W/dB; NBW: Hz; LB:

PLATE XIV. ^{13}C NMR SPECTRUM OF **34c**

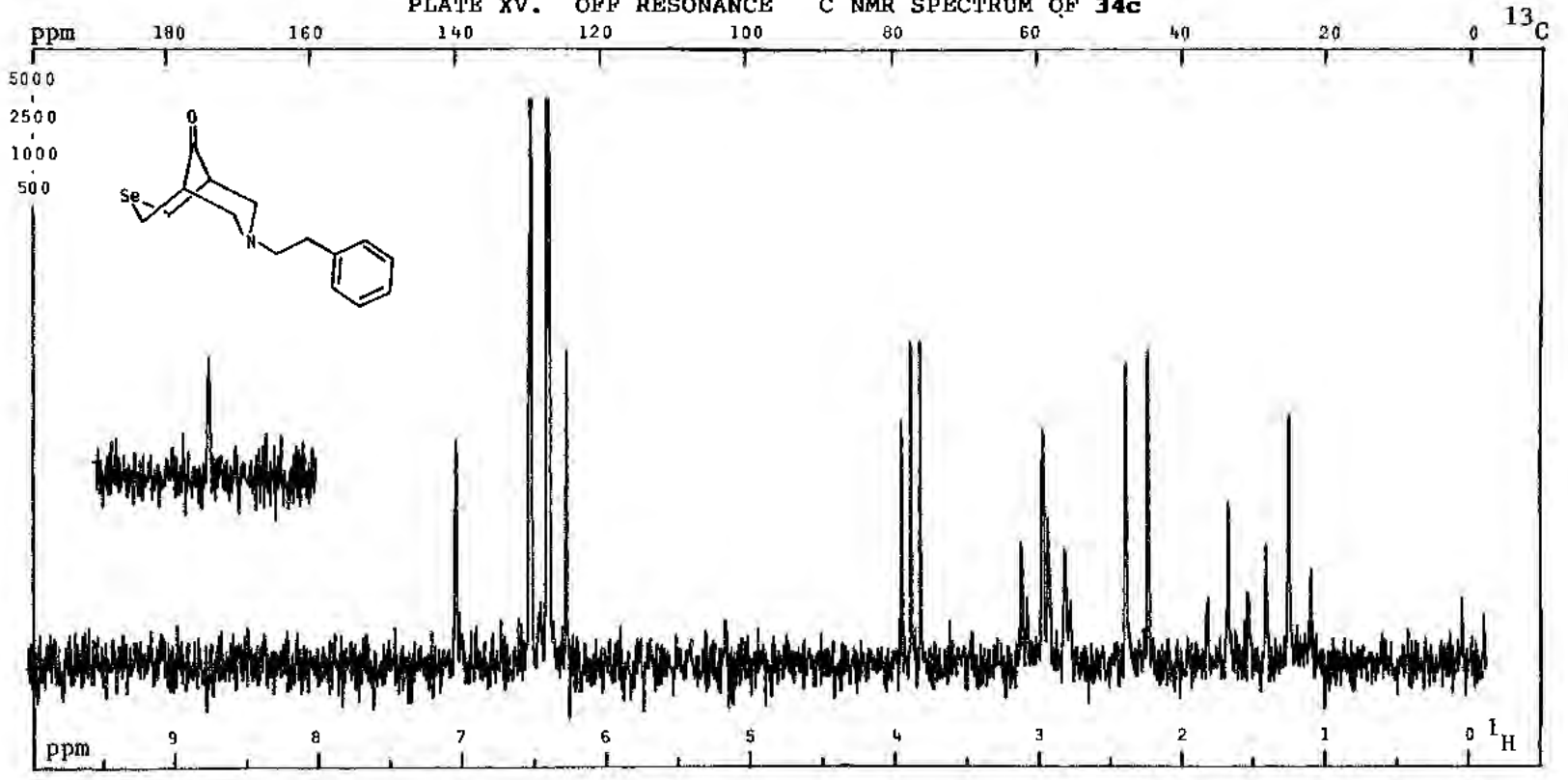


PFT X CW ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 6000 Hz; T: 28 °C; NT: 1398

Size: 8 K; PW/RF: 10 µs/dB; SO: 35101 Hz; FB: 3K Hz; Lock: ^{2}D ; Delay: 5 s.

DC: Y ; Gated Off: ; Offset: 45316 Hz; RF: 7.5 W/dB; NBW: Hz; LB:

PLATE XV. OFF RESONANCE ^{13}C NMR SPECTRUM OF **34c**

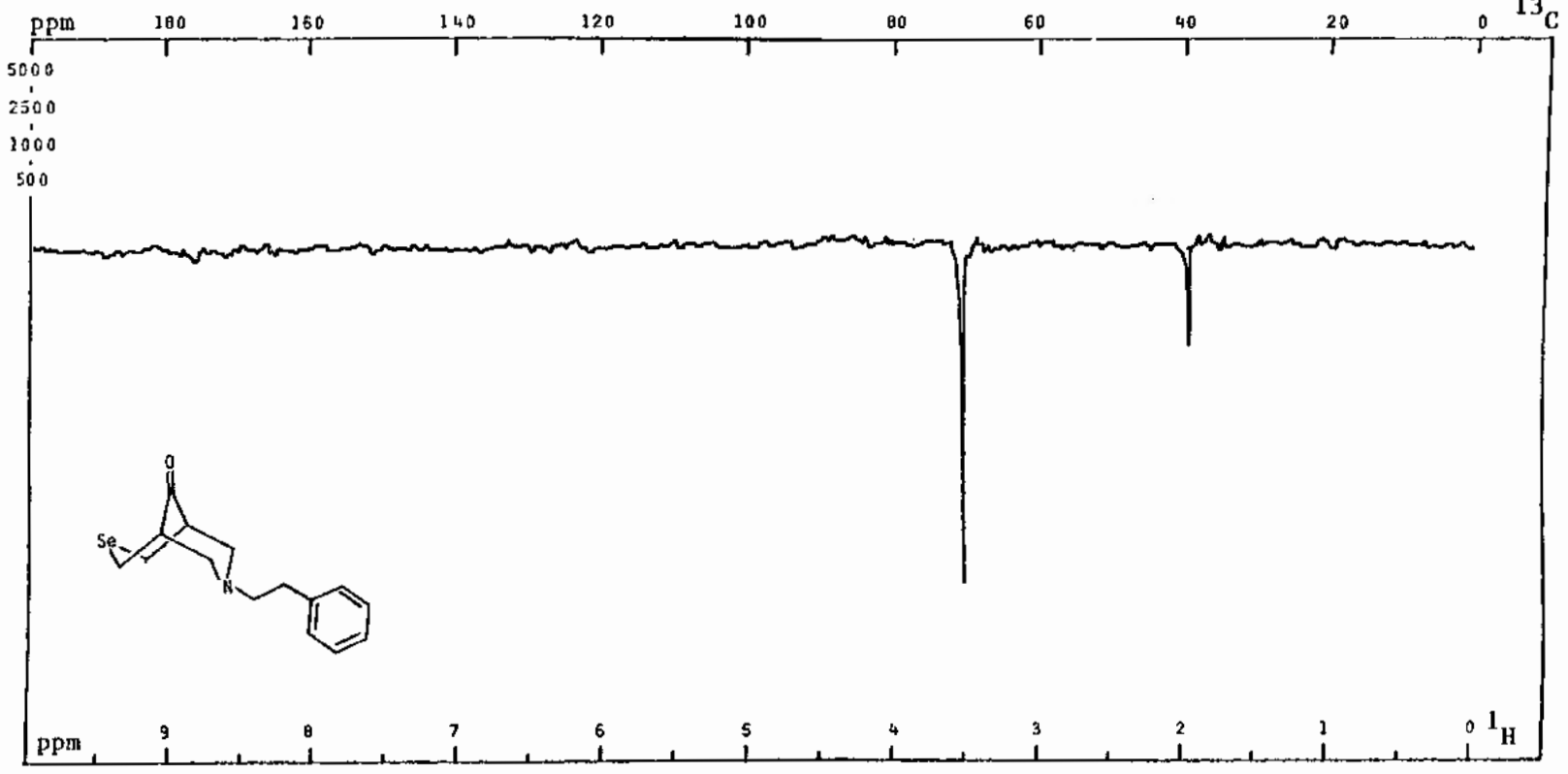


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 6000 Hz; T: 28 °C; NT: 3000 .

Size: 8 K; PW/RF: 7.5 μs/dB; SO: 35101 Hz; FB: 3K Hz; Lock: ^{2}D ; Delay: 5 s.

DC: Y ; Gated Off: ; Offset: 45316 Hz; RF: 7.5W/dB; NBW: Hz; LB: .

PLATE XVI. ^{15}N NMR SPECTRUM OF **34c**

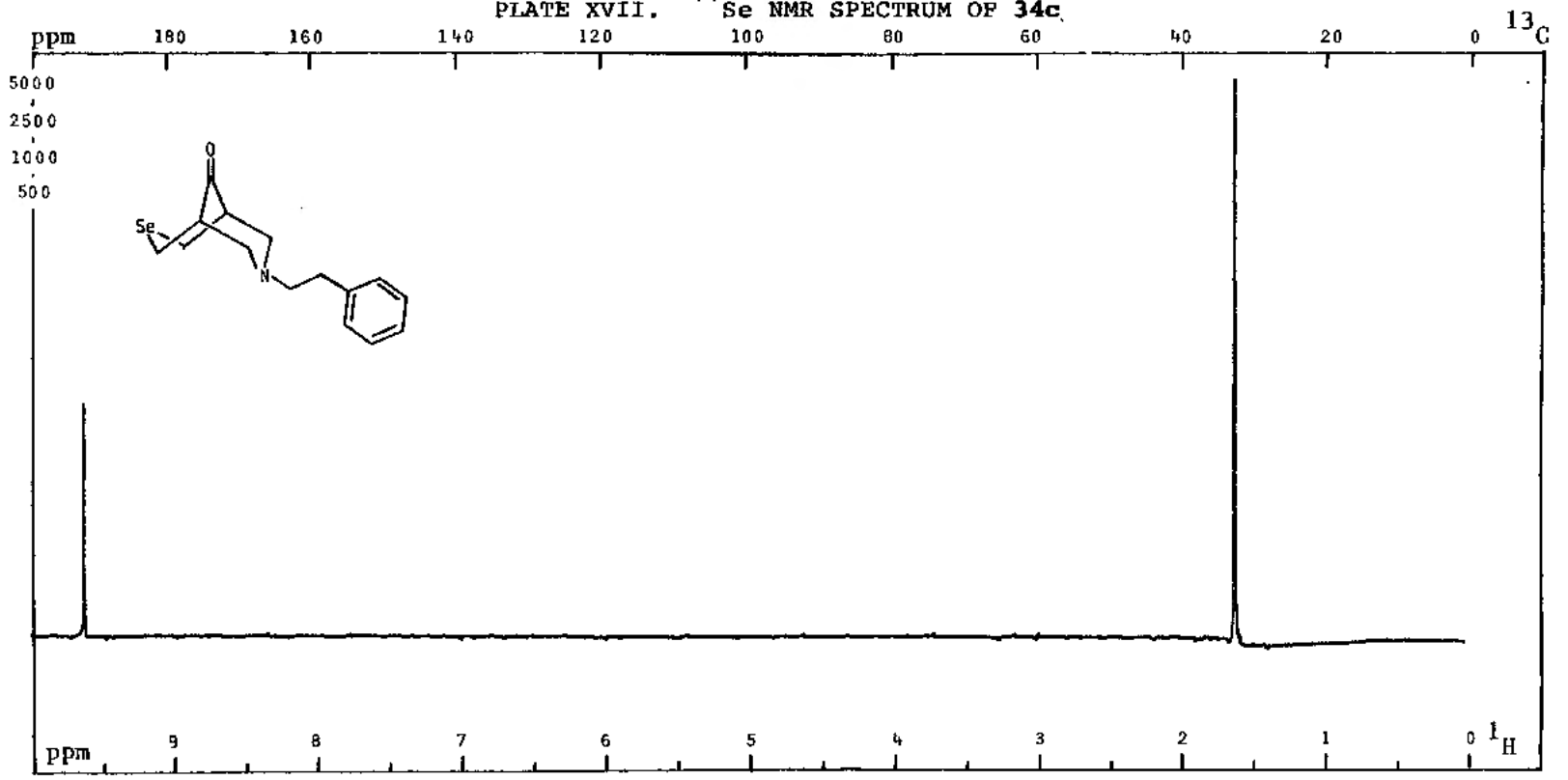


PFT$\underline{X}$ CW $\underline{\ }$; Solvent: $CDCl_3$; SF: 30.406 MHz; WC: 3040.6Hz; T: 25 °C; NT:6800 .

Size: 12 K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 8 s.

DC: Y, $\underline{N}$; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XVII. ^{77}Se NMR SPECTRUM OF **34c**



PFT X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC:28610 Hz; T: 25 °C; NT: 300 .

Size: 32K; PW/RF: 35 µs/dB; SO: 500 Hz; FB: Hz; Lock: ^2D ; Delay: 25 s.

DC: Y ; Gated Off: ; Offset: 0 Hz; RF: 20 W/dB; NBW: Hz; LB: .

PLATE XVIII. IR SPECTRUM OF **34d**

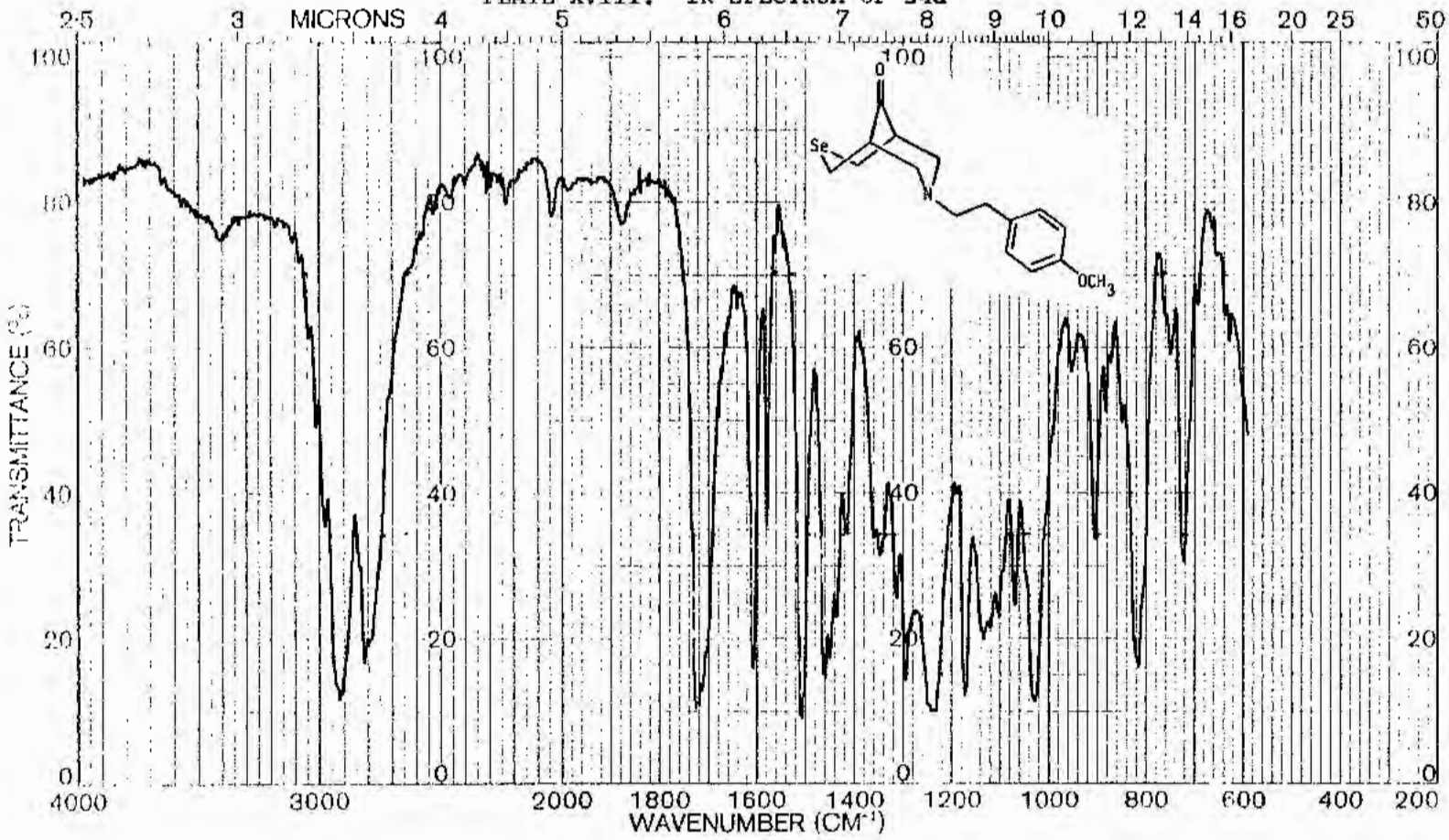
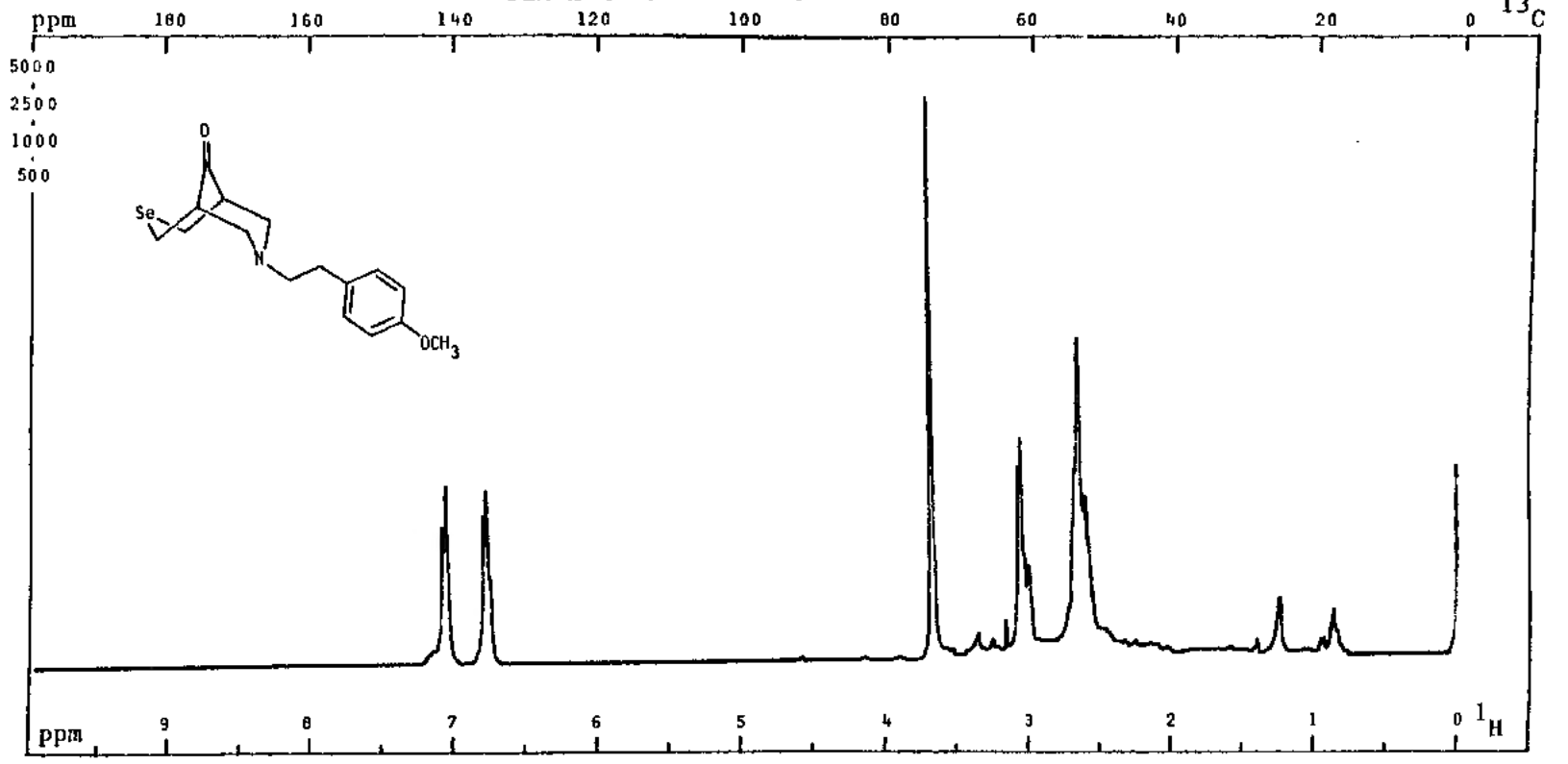


PLATE XIX. ^{1}H NMR SPECTRUM OF **34d**

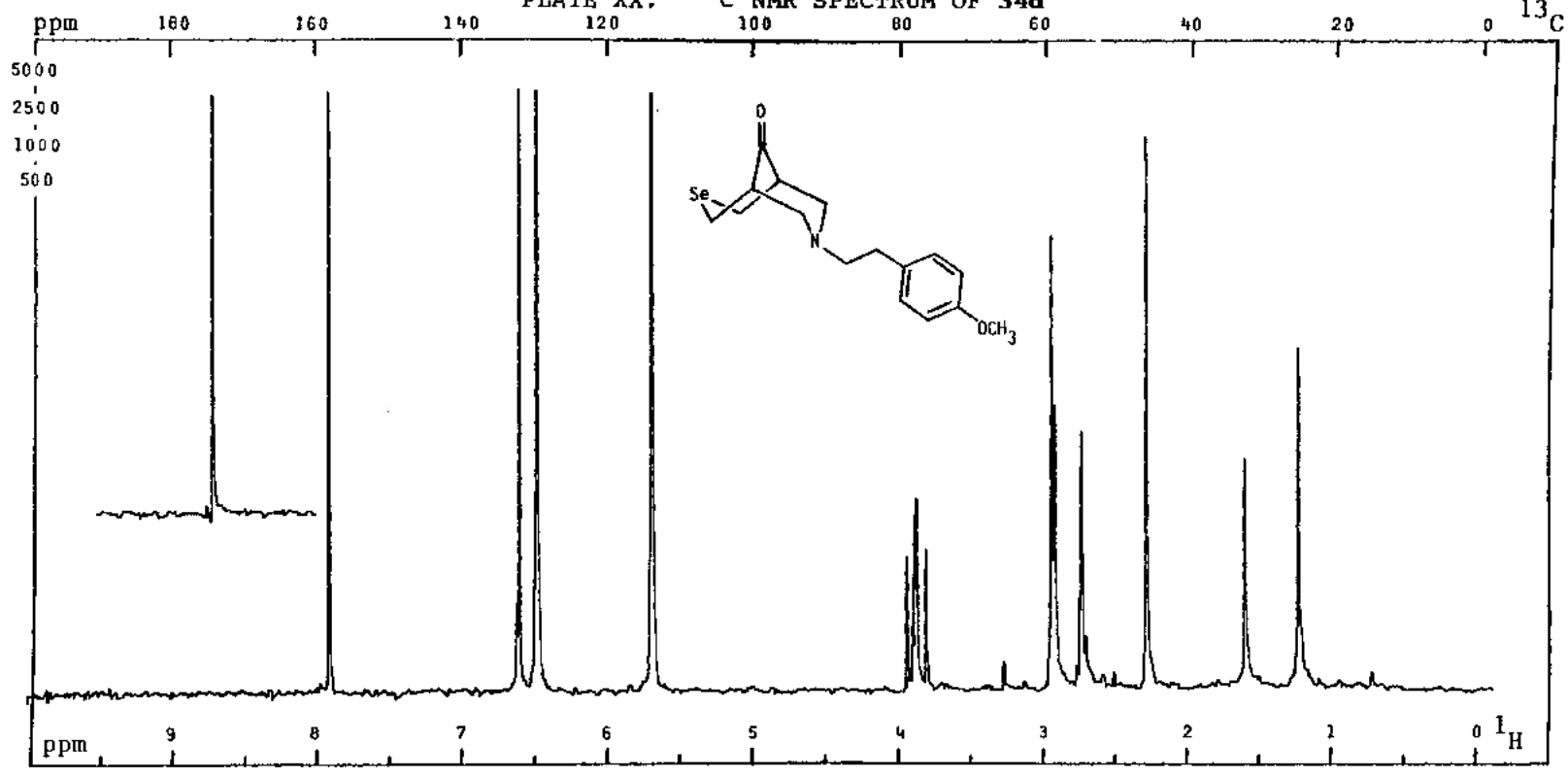


PFTX CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 12

Size: 12 K; PW/RF: 5 µs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XX. ^{13}C NMR SPECTRUM OF **34d**

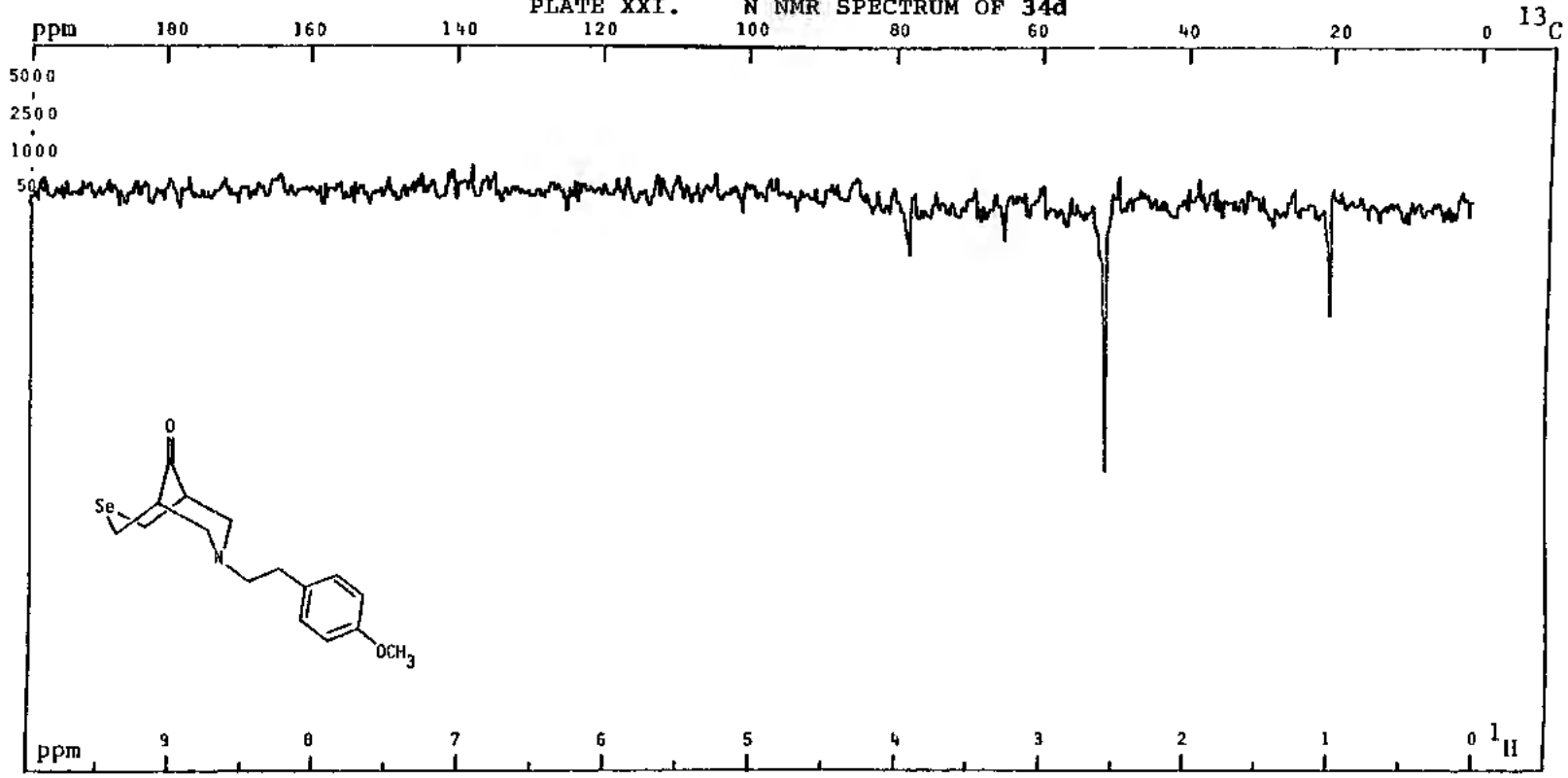


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 6000 Hz; T: 28 °C; NT: 8600 .

Size: 8 K; PW/RF: 14 µs/dB; TO: 35101 Hz; FB: 3K Hz; Lock: ^{2}D ; D1,D5: 6 s.

DC: Y, N ; Gated Off: A or D ; DO: 45316 Hz; RF(Power): 7.5W/dB; NBW: Hz; LB: Hz.

PLATE XXI. ^{15}N NMR SPECTRUM OF **34d**

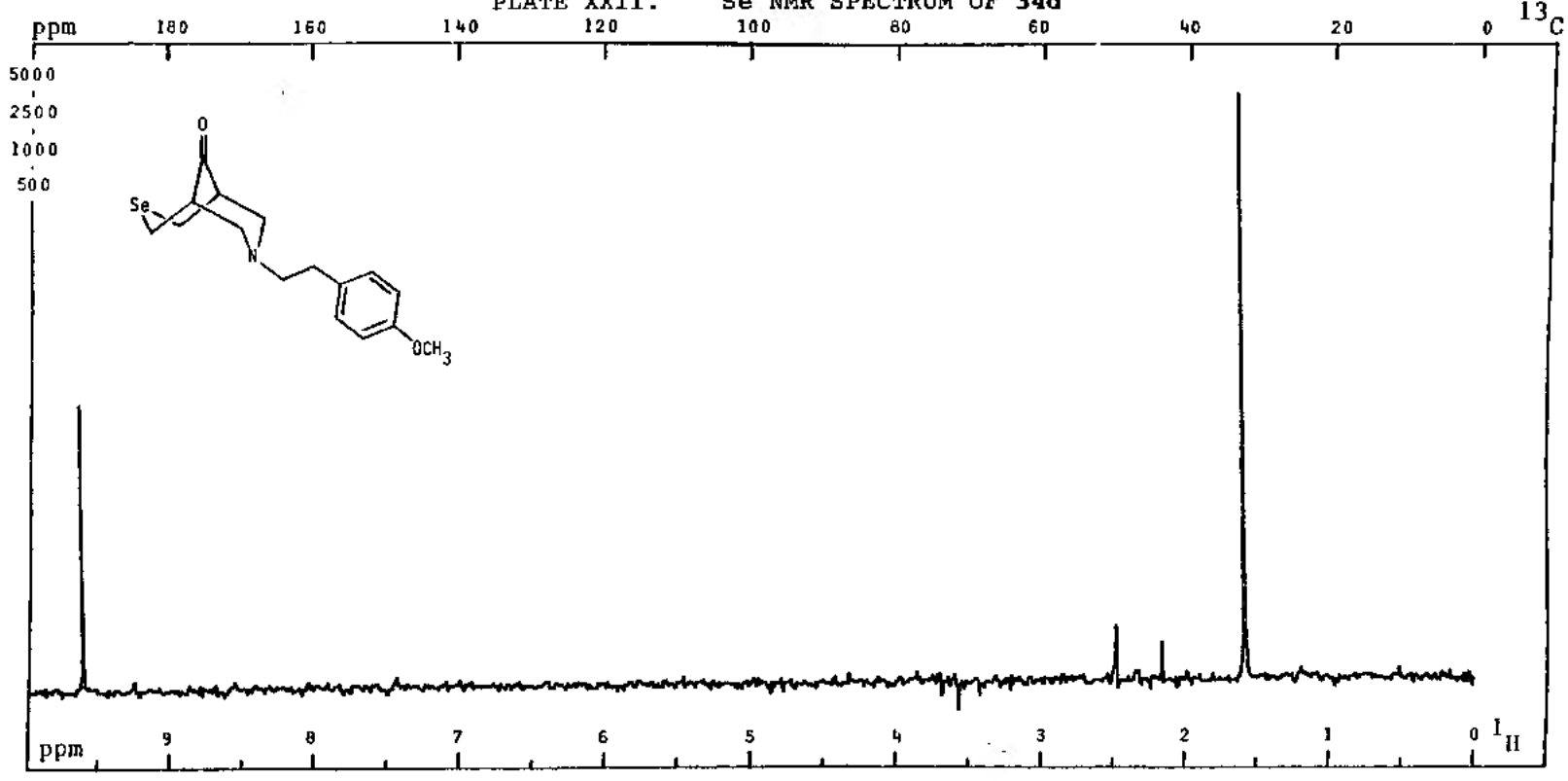


PFT X CW _ ; Solvent: $CDCl_3$; SF: 30.406 MHz; WC: 3040.6 Hz; T: 25 °C; NT: 10000 .

Size: 12 K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 8 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XXII. ^{77}Se NMR SPECTRUM OF **34d**



PFT X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 40

Size: 32 K; PW/RF: 35 µs/dB; TD: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 25 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE XXIII: IR SPECTRUM OF **34e**

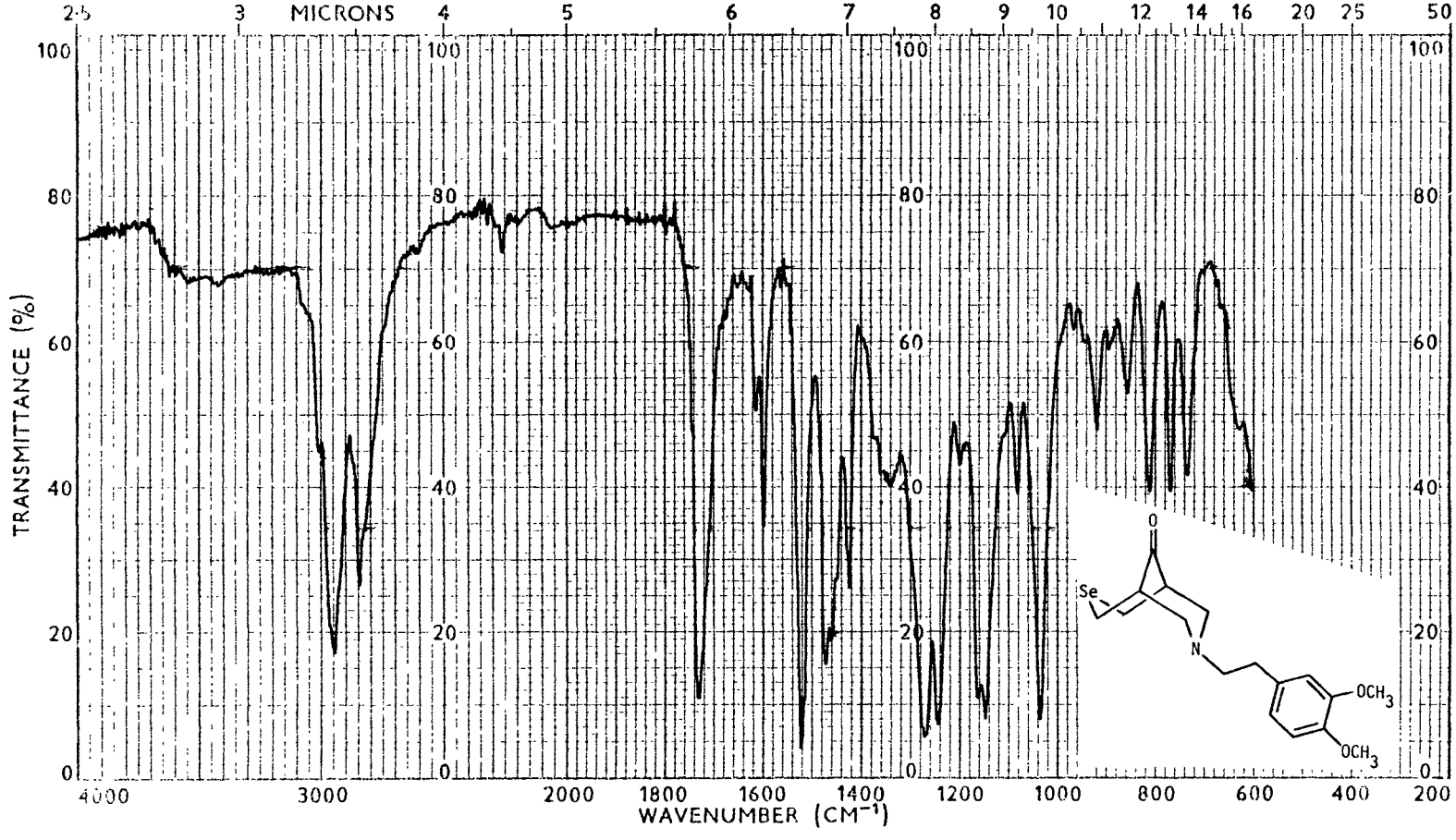
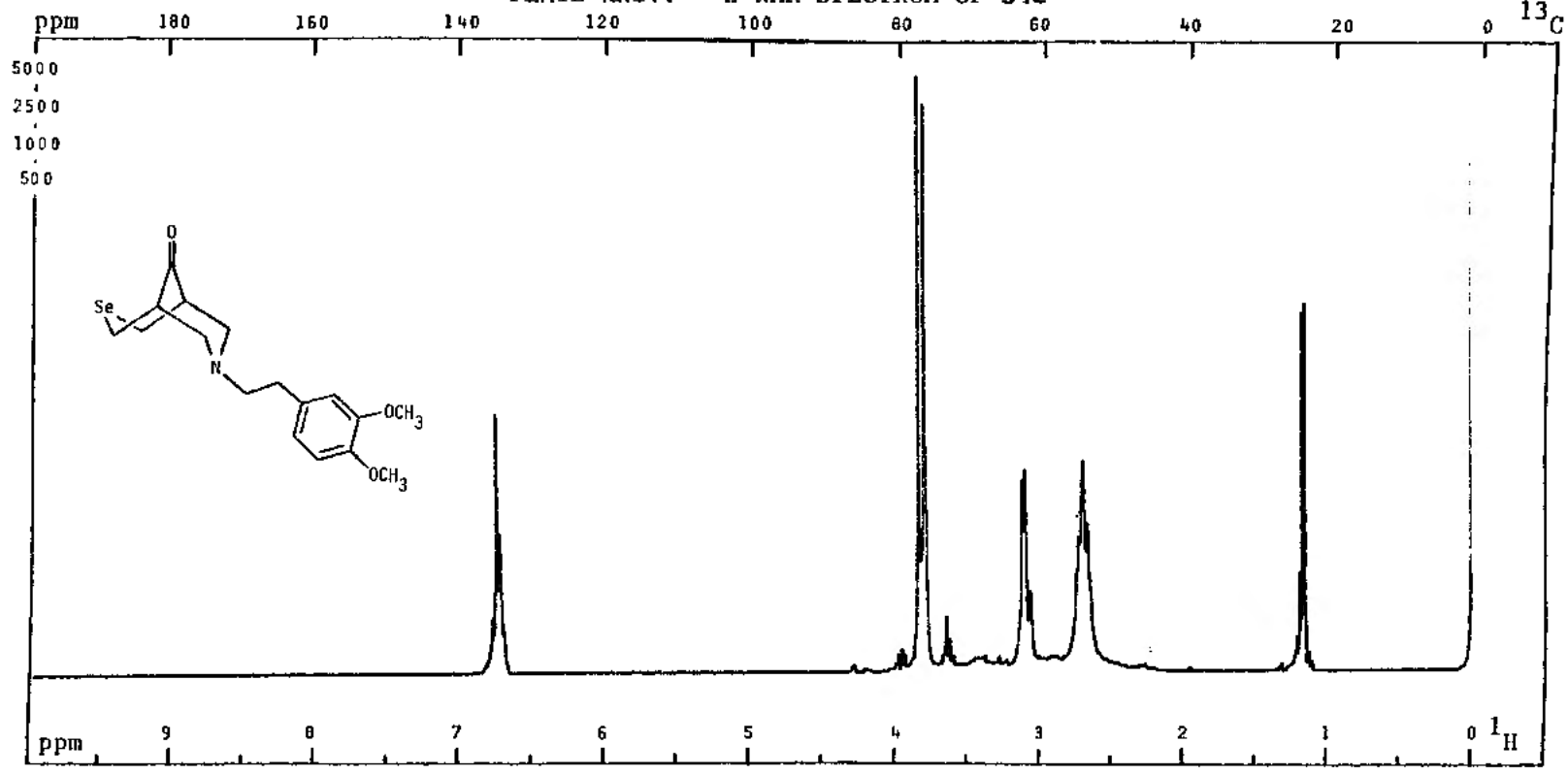


PLATE XXIV. ^{1}H NMR SPECTRUM OF **34e**

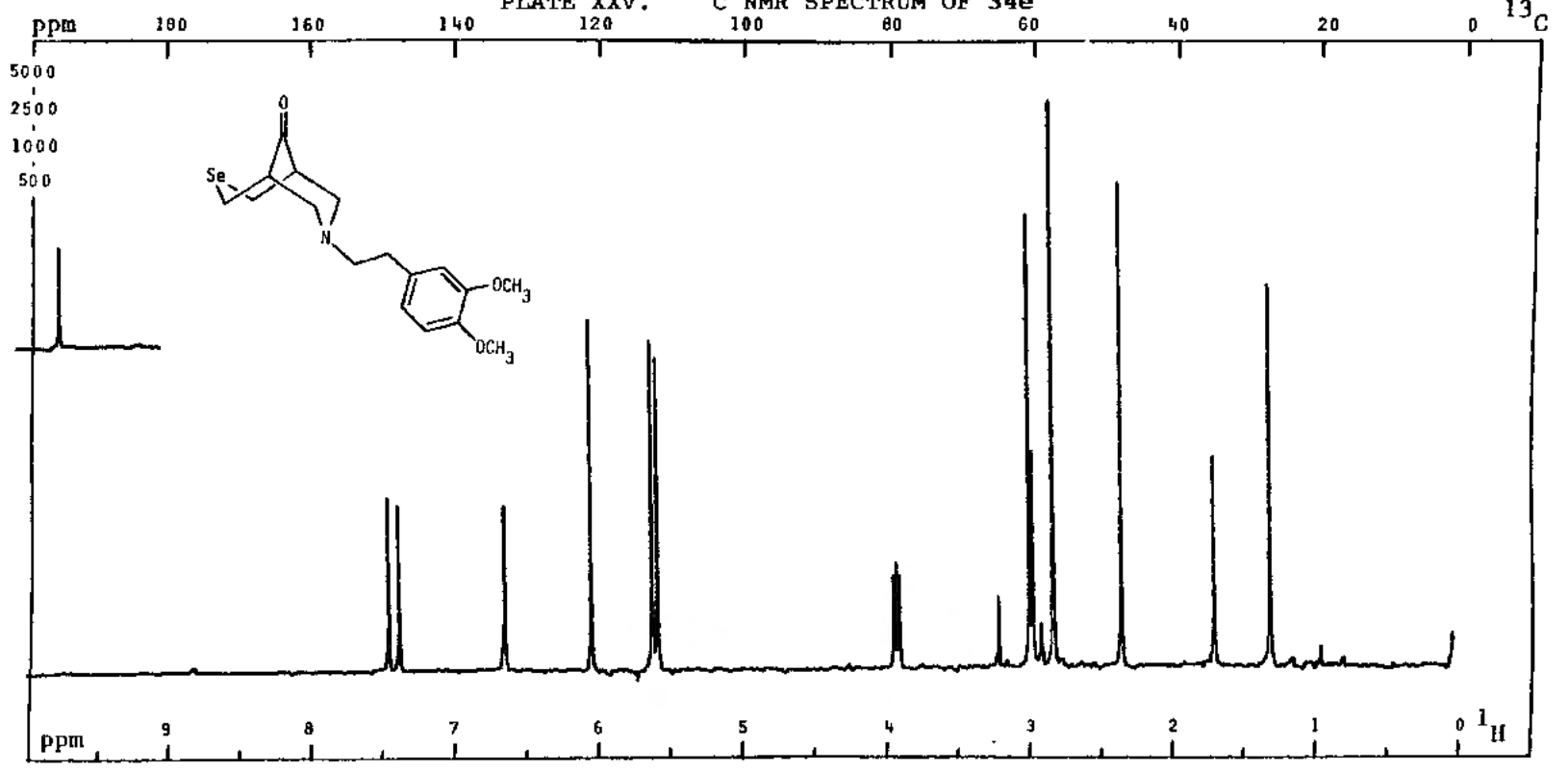


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 16 .

Size: 12K; PW/RF: 5 µs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XXV. ^{13}C NMR SPECTRUM OF 34e

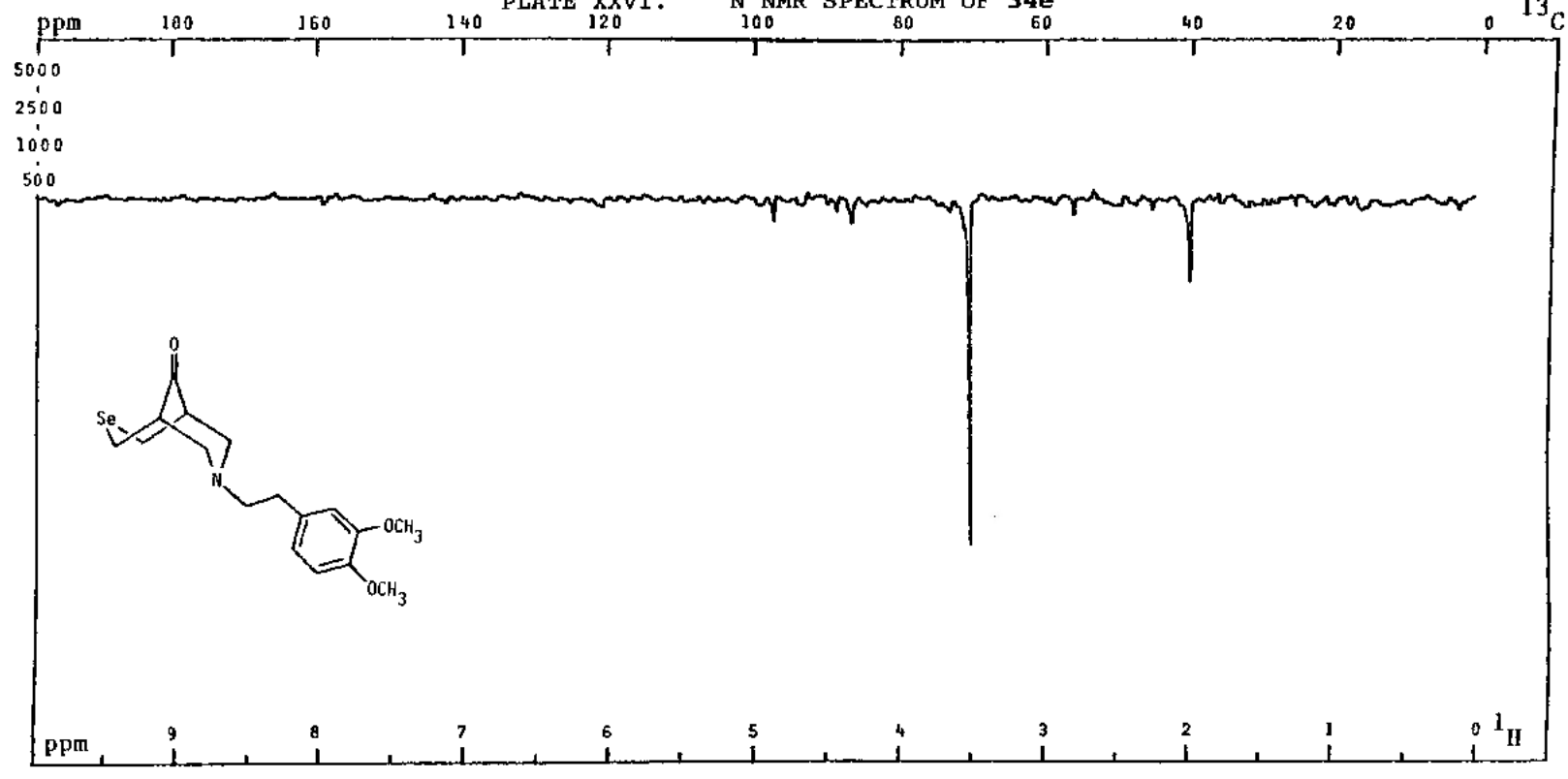


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 6000 Hz; T: 28 °C; NT: 6000 .

Size: 8 K; PW/RF: 14 µs/dB; TO:35101 Hz; FB: 3K Hz; Lock: ^2D ;D1,D5: 6 s.

DC: Y, N ; Gated Off:A or D ; DO: 45316 Hz; RF(Power): 7.5W/dB; NBW: Hz; LB: Hz.

PLATE XXVI. ^{15}N NMR SPECTRUM OF **34e**

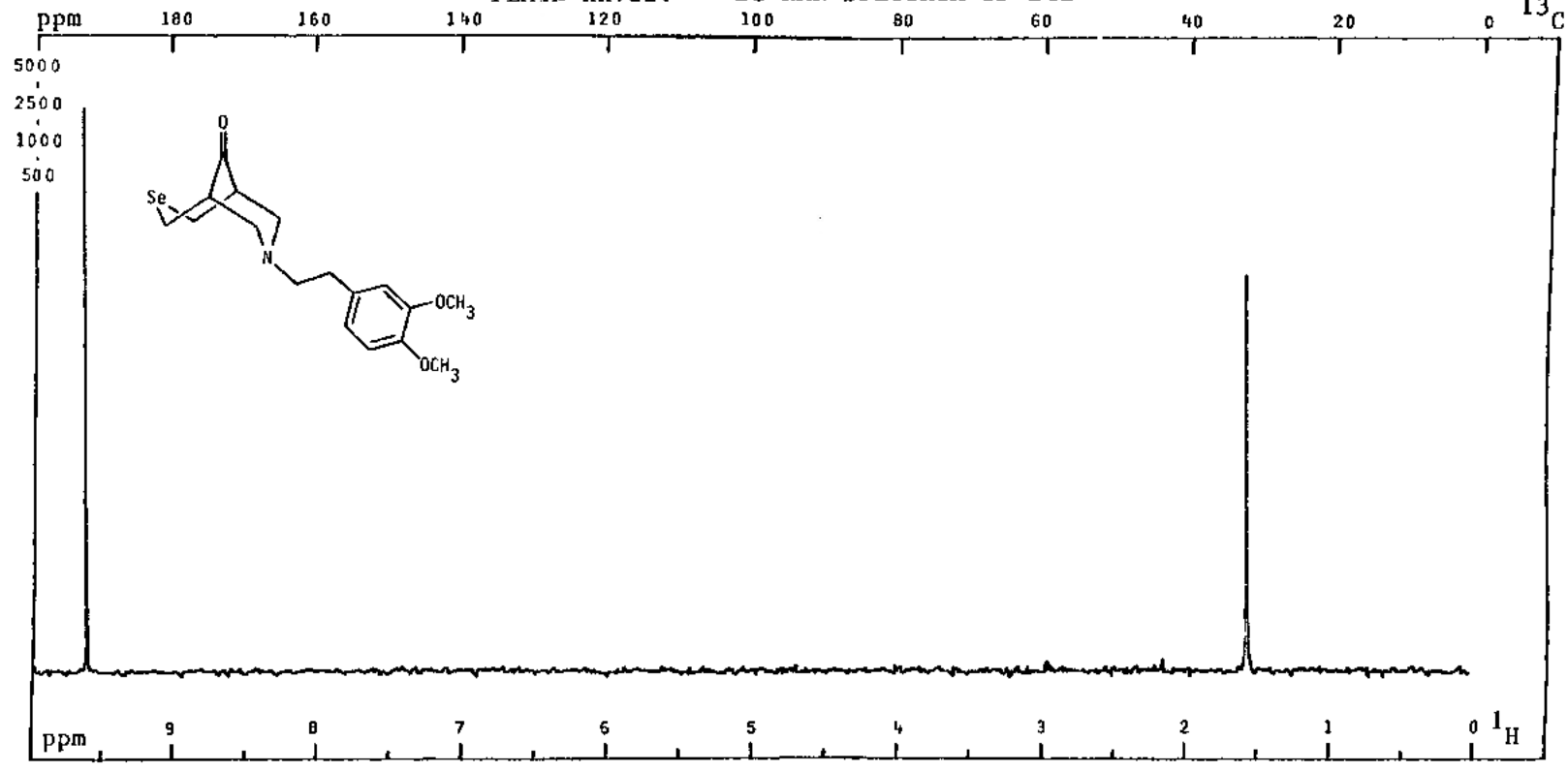


PFT X CW _ ; Solvent: $CDCl_3$; SF: 30.406 MHz; WC: 3040,6 Hz; T: 25 °C; NT: 25000 .

Size: 12 K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^2D ; D1,D5: 8 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XXVII. ^{77}Se NMR SPECTRUM OF **34e**



PFT X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 2132 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 25 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE XXVIII. IR SPECTRUM OF **34f**

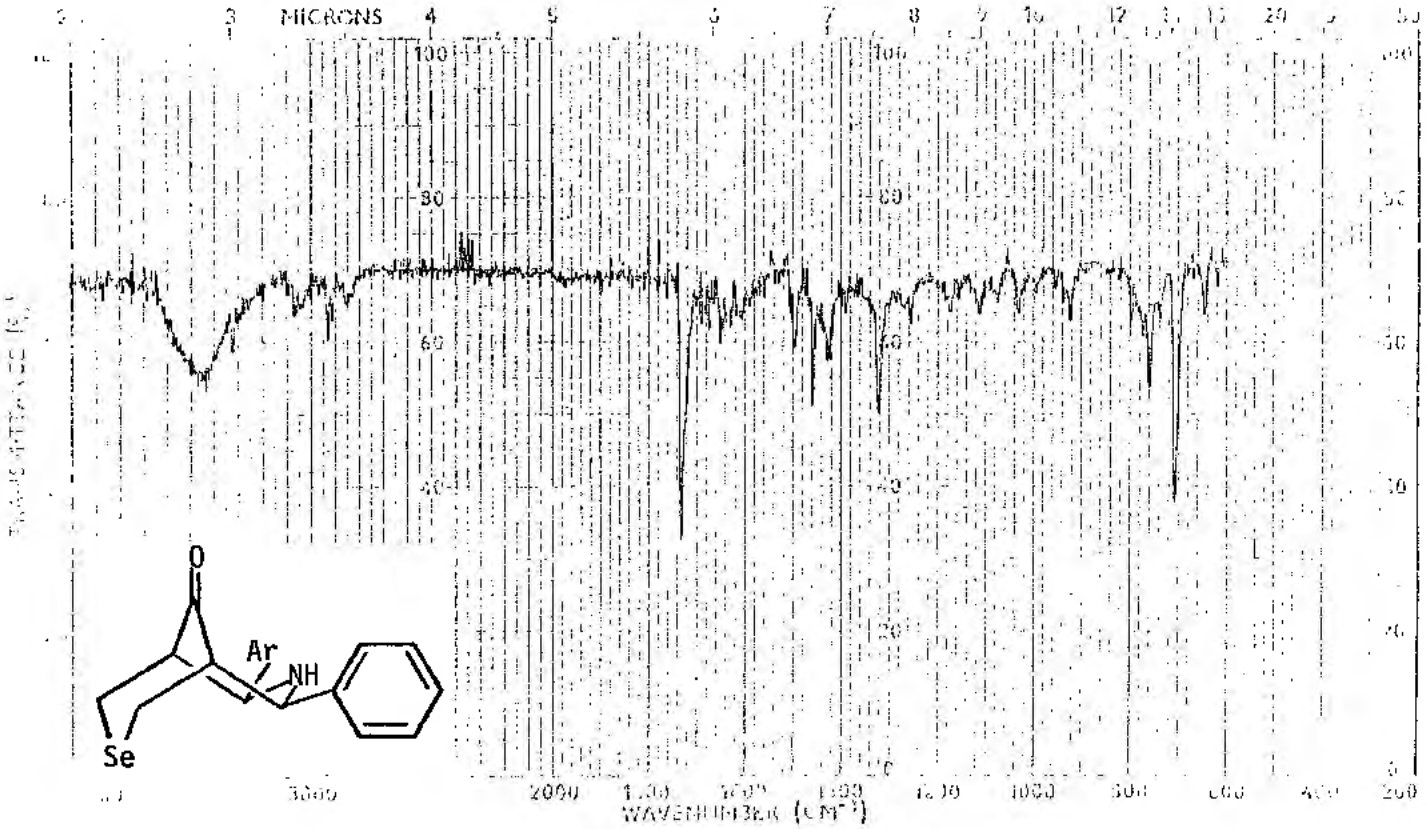
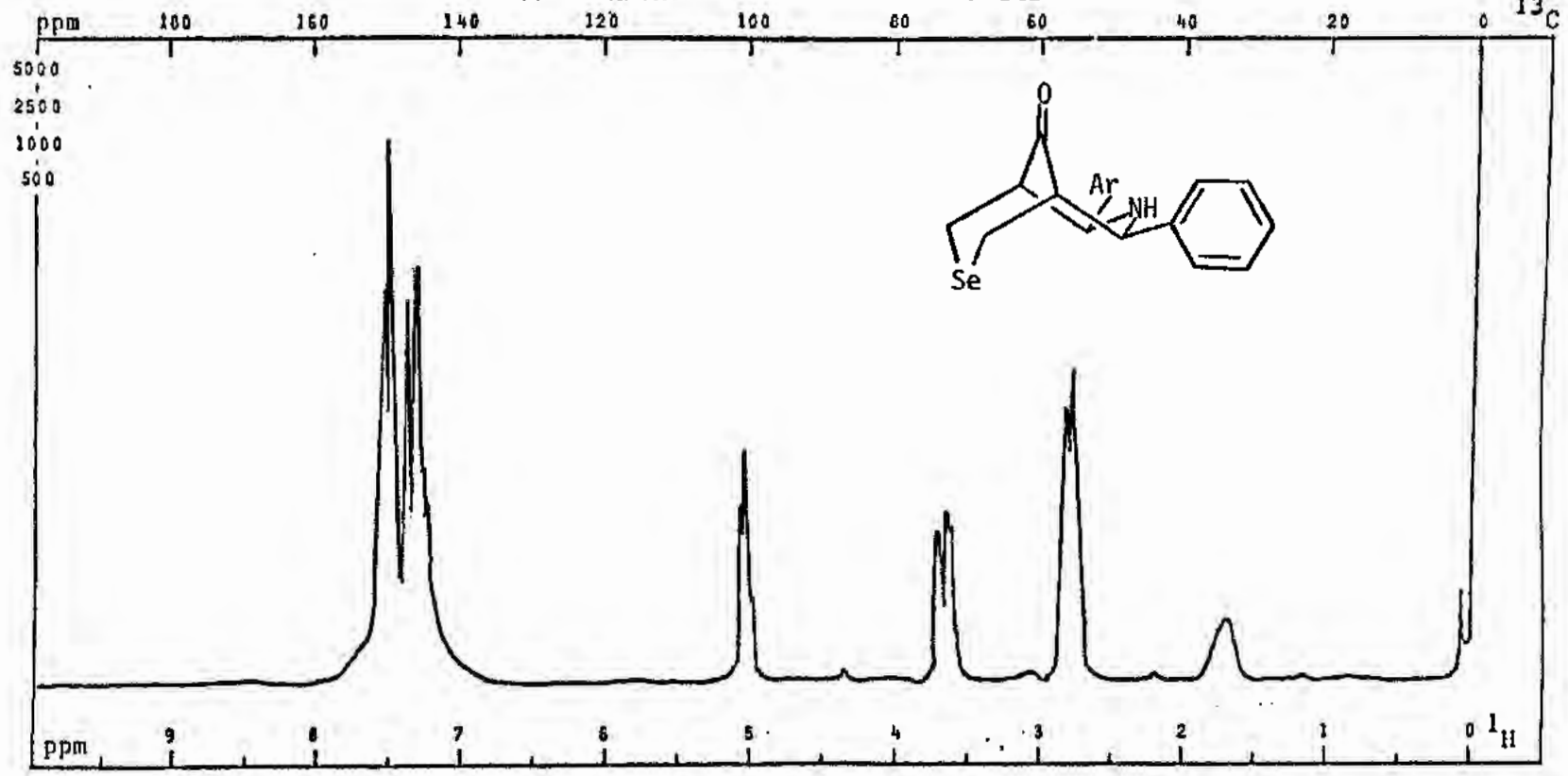


PLATE XXIX. ^{1}H NMR SPECTRUM OF **34f**

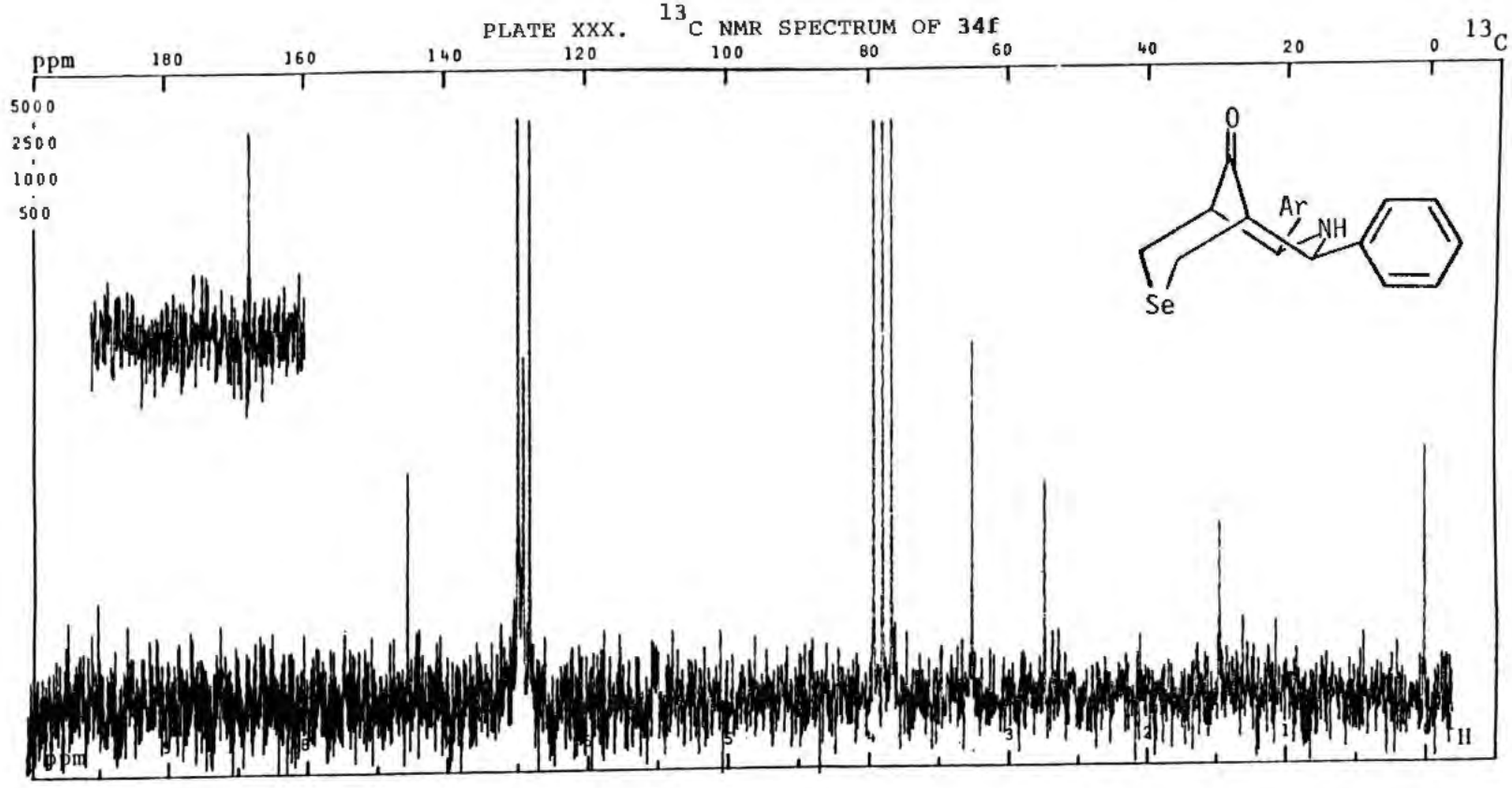


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 24

Size: 12 K; PW/RF: 5 µs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XXX. ^{13}C NMR SPECTRUM OF **34f**

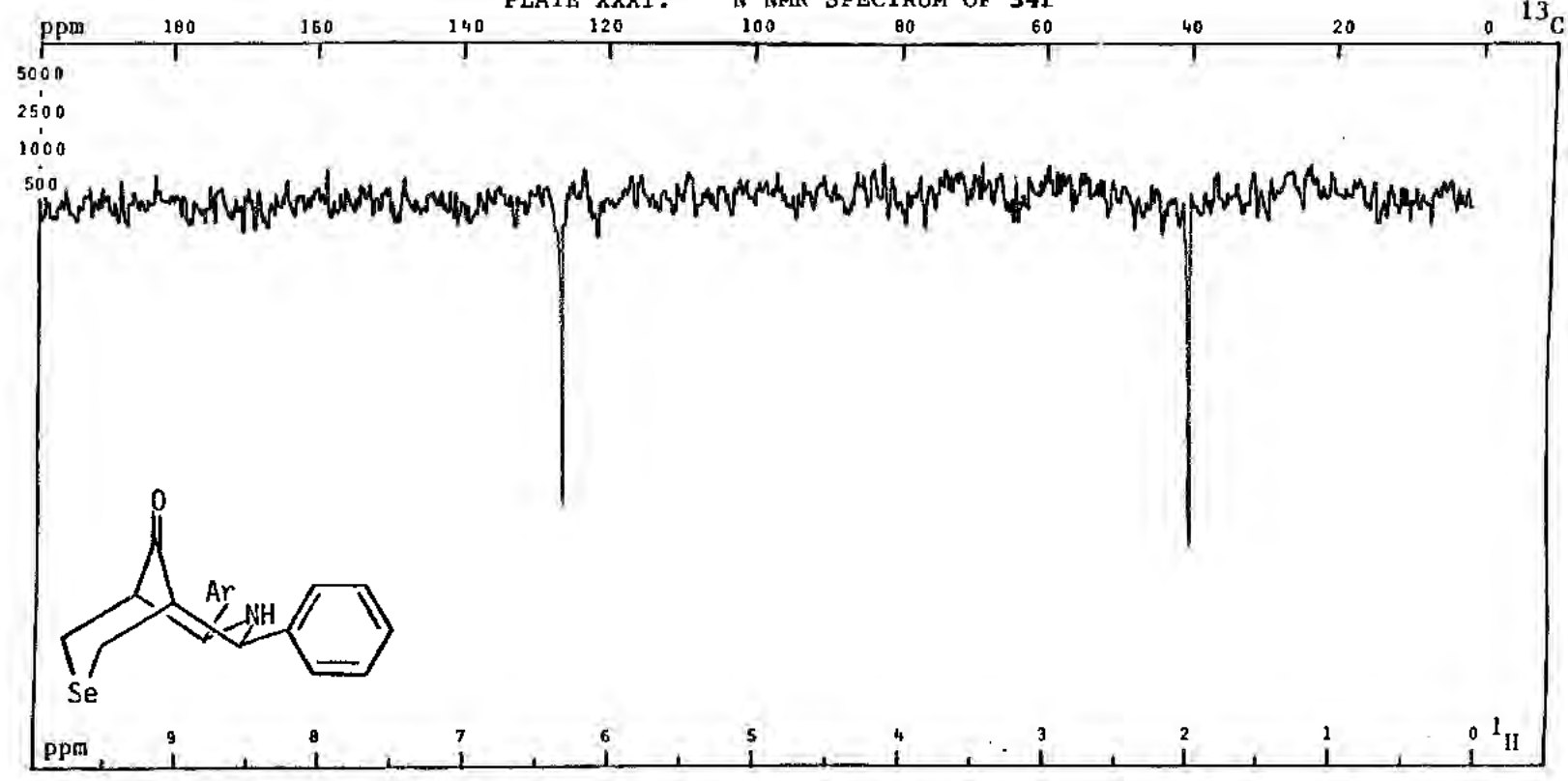


PFT X _ CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 6000 Hz; T: 28 °C; NT: 928

Size: 8 K; PW/RF: 10 µs/dB; TO: 35101 Hz; FB: 3K Hz; Lock: ^2D ;D1,D5: 5 s.

DC: Y, N ; Gated Off:A or D ; DO: 45316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE XXXI. ^{15}N NMR SPECTRUM OF **34f**

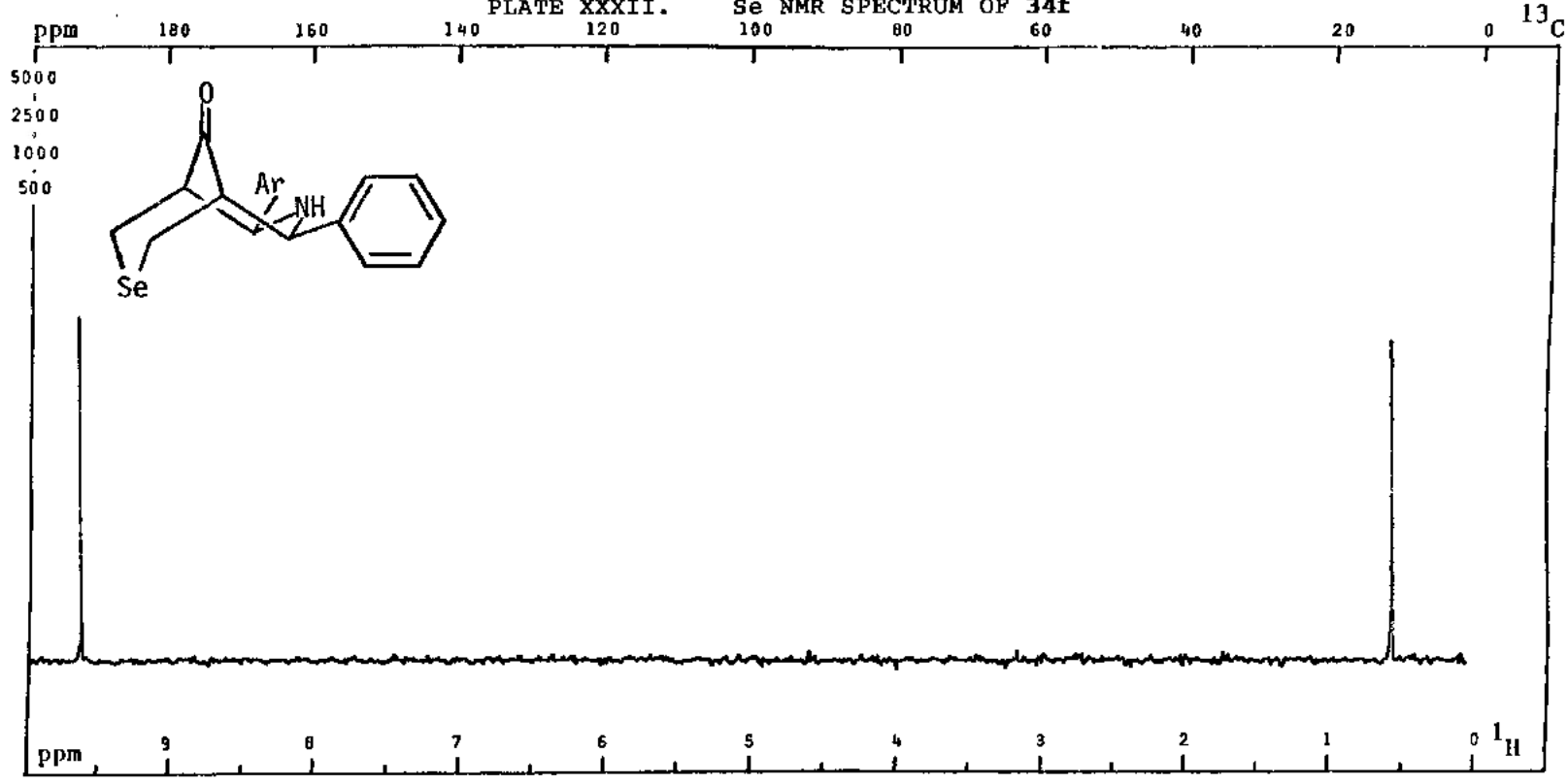


PFT X CW _ ; Solvent: $CDCl_3$; SF:30.406 MHz; WC: 3040.6Hz; T: 25 °C; NT:15800

Size: 12_K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^2D ;D1,D5: 8 s.

DC: Y, N ; Gated Off:A or D ; DO: 0 Hz; RF(Power): 0 W/dB; NBW: Hz; LB: Hz.

PLATE XXXII. ^{77}Se NMR SPECTRUM OF **34f**



PFT: X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 1000

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 15 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NDW: Hz; LB: Hz.

PLATE XXXIII. IR SPECTRUM OF **34g**

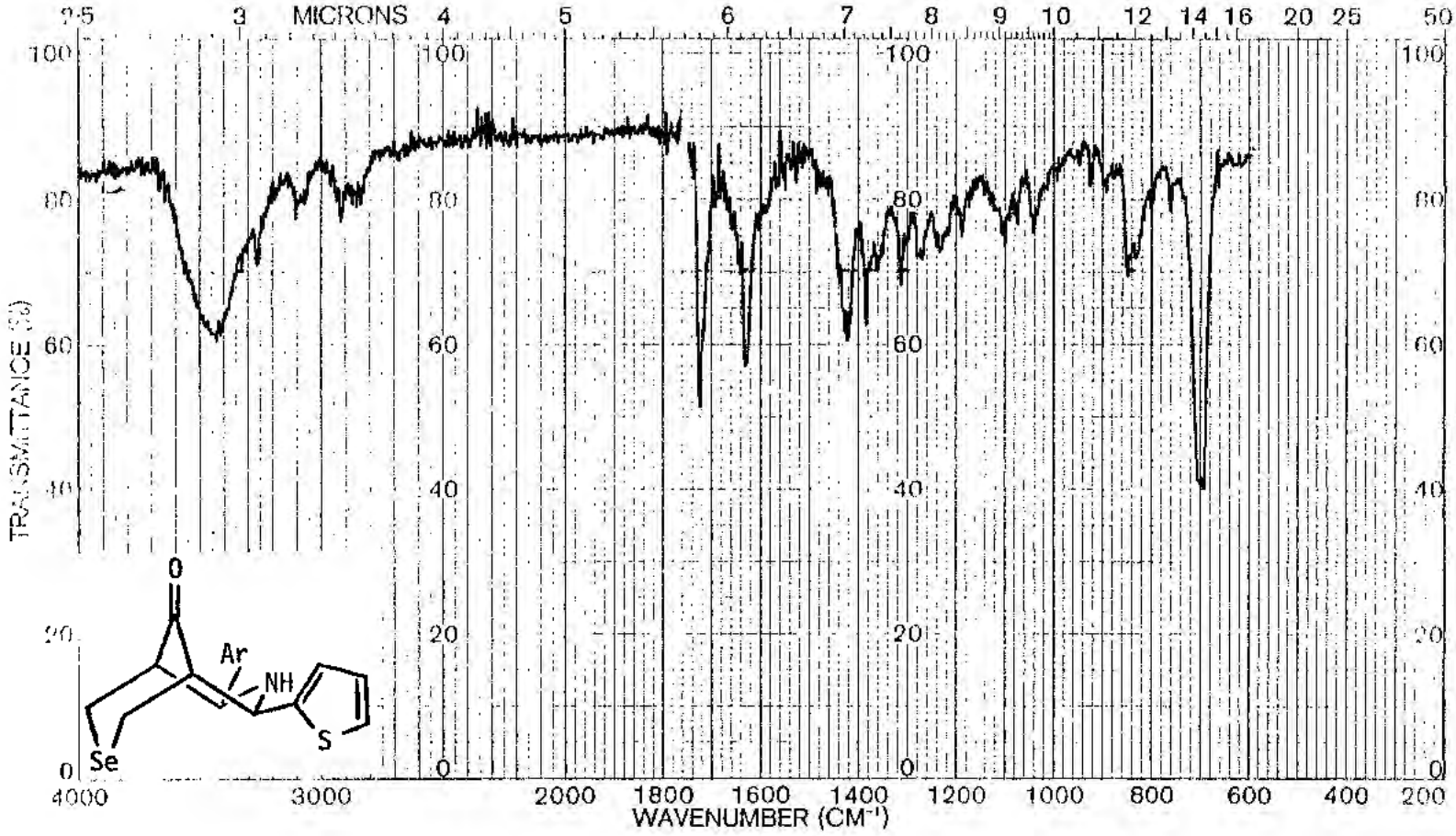
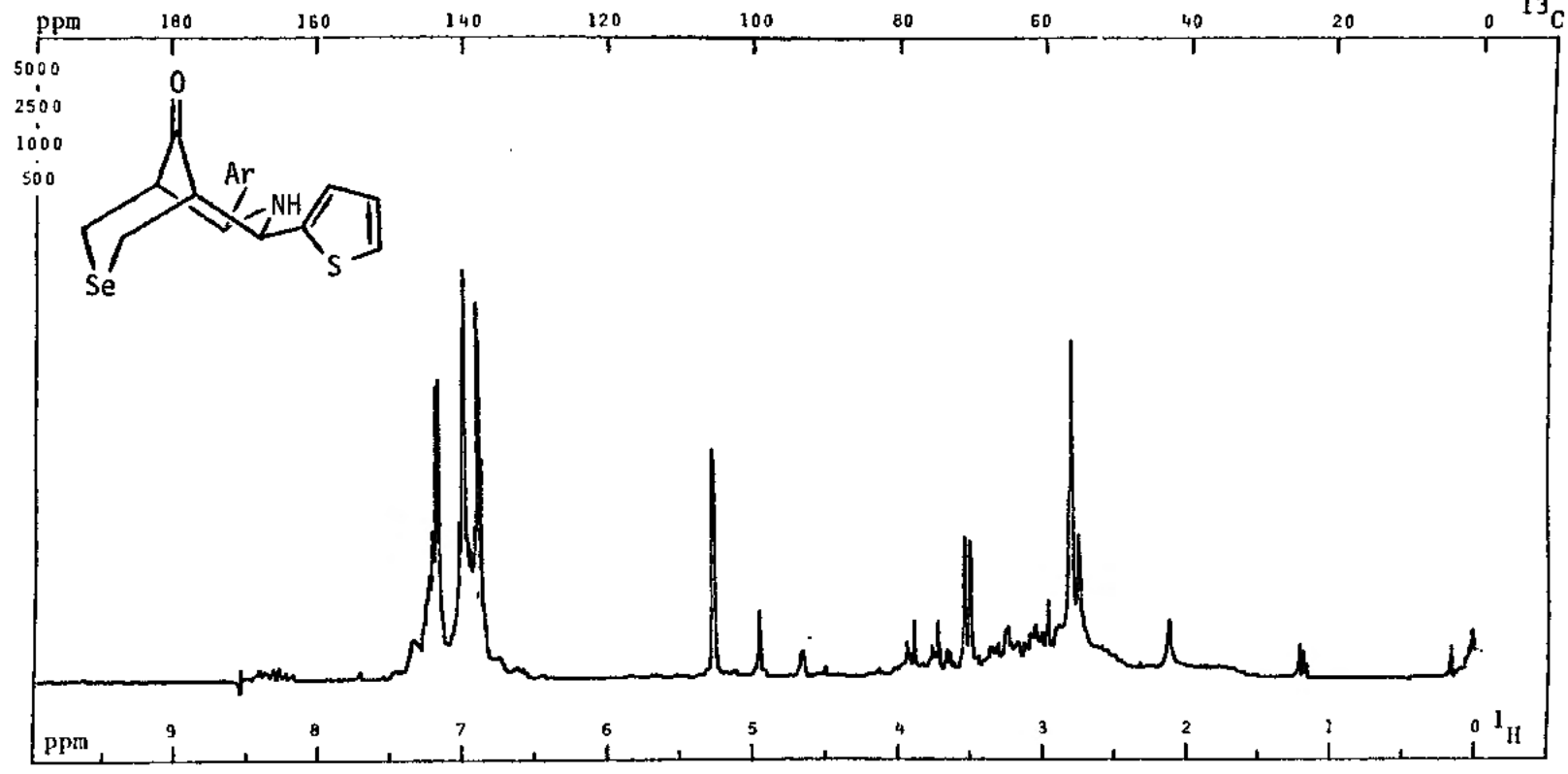


PLATE XXXIV. ^{1}H NMR SPECTRUM OF **34g**

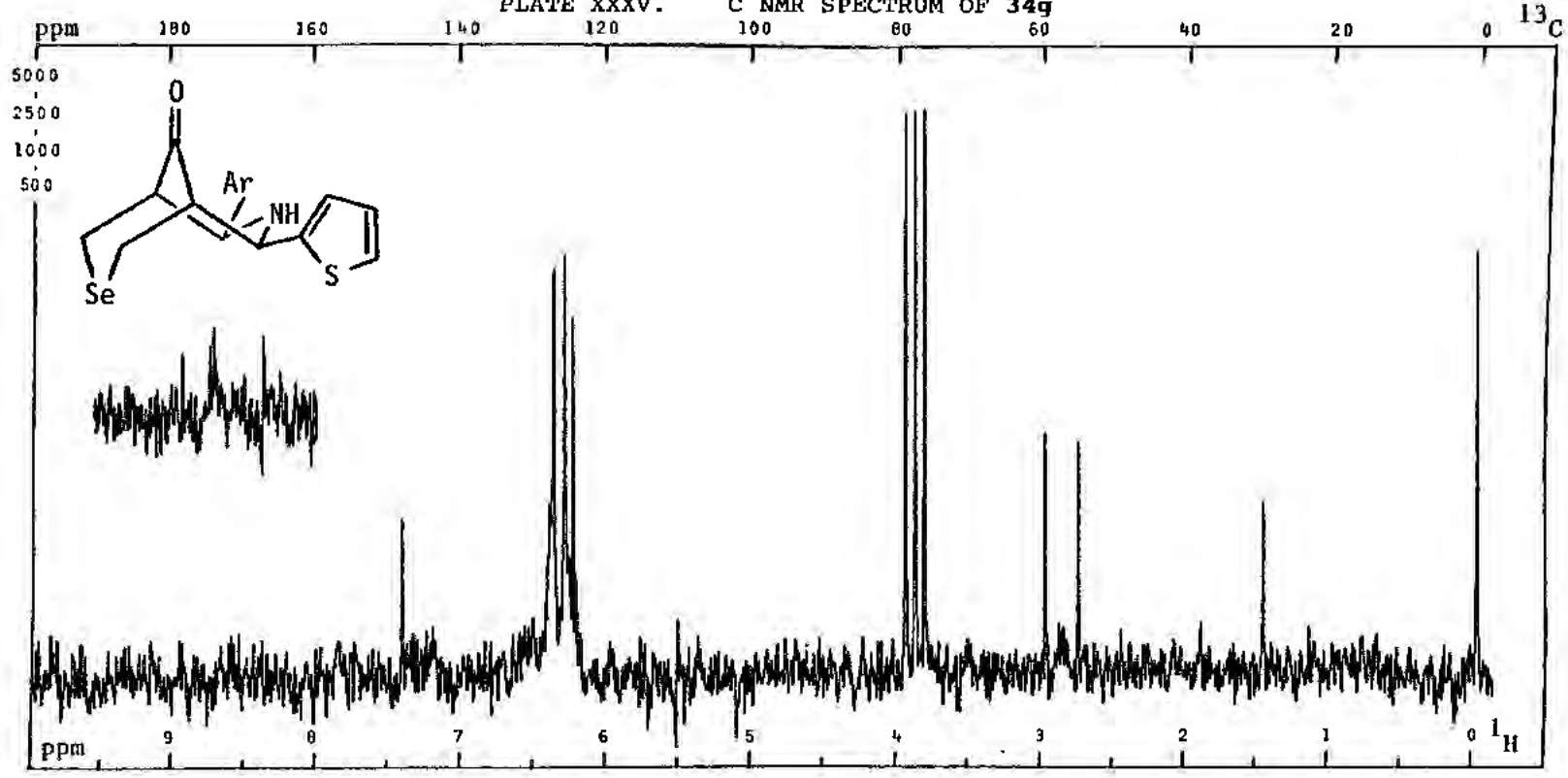


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 16 .

Size: 12 K; PW/RF: 5 µs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XXXV. ^{13}C NMR SPECTRUM OF **34g**

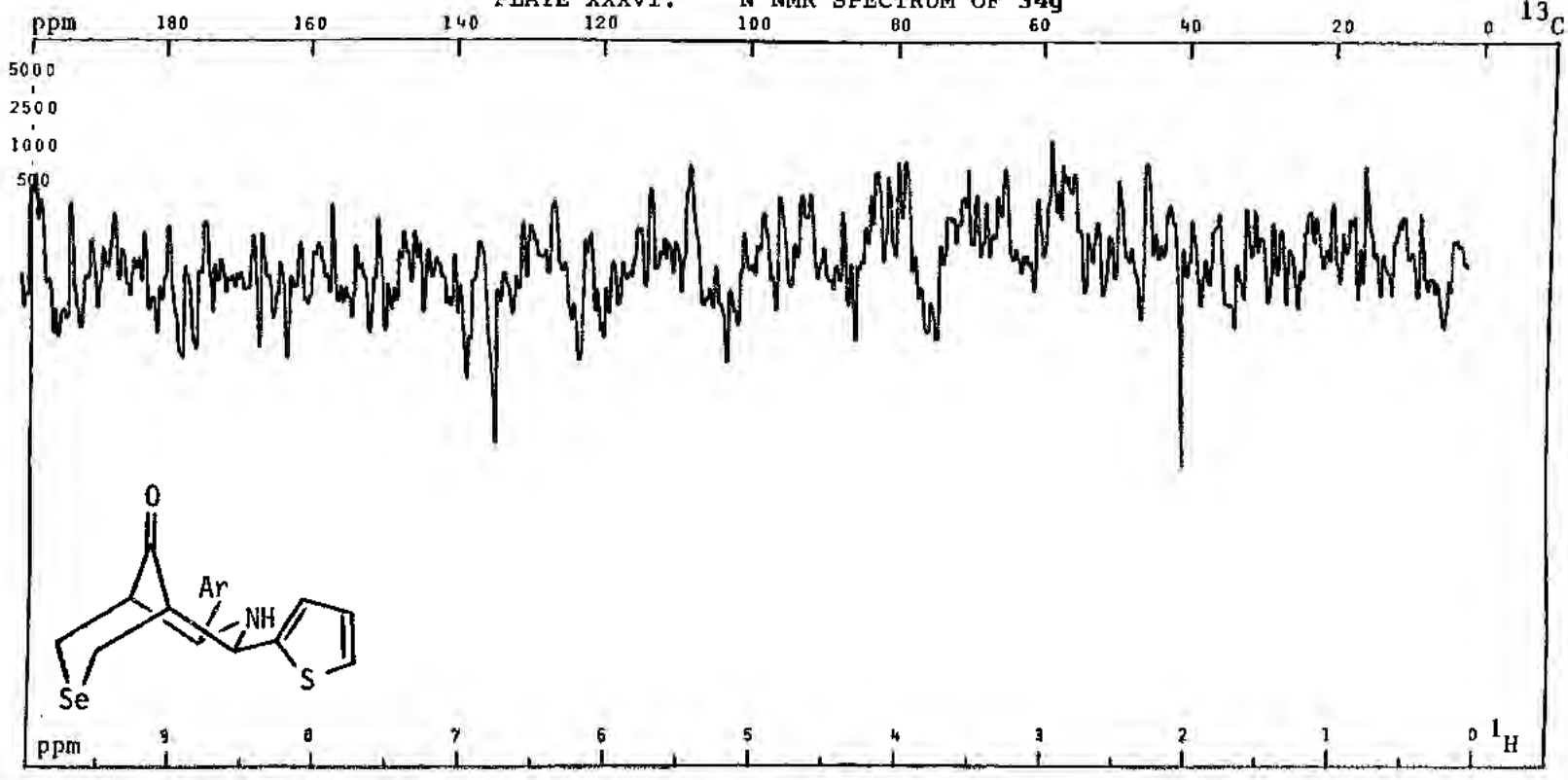


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 6000 Hz; T: 28 °C; NT: 1740 .

Size: 8 K; PW/RF: 10 μs/dB; TO: 35101 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 5 s.

DC: Y, N ; Gated Off:A or D ; DO: 45316 Hz; RF(Power):7.51 W/dB; NBW: Hz; LB: Hz.

PLATE XXXVI. ^{15}N NMR SPECTRUM OF **34g**

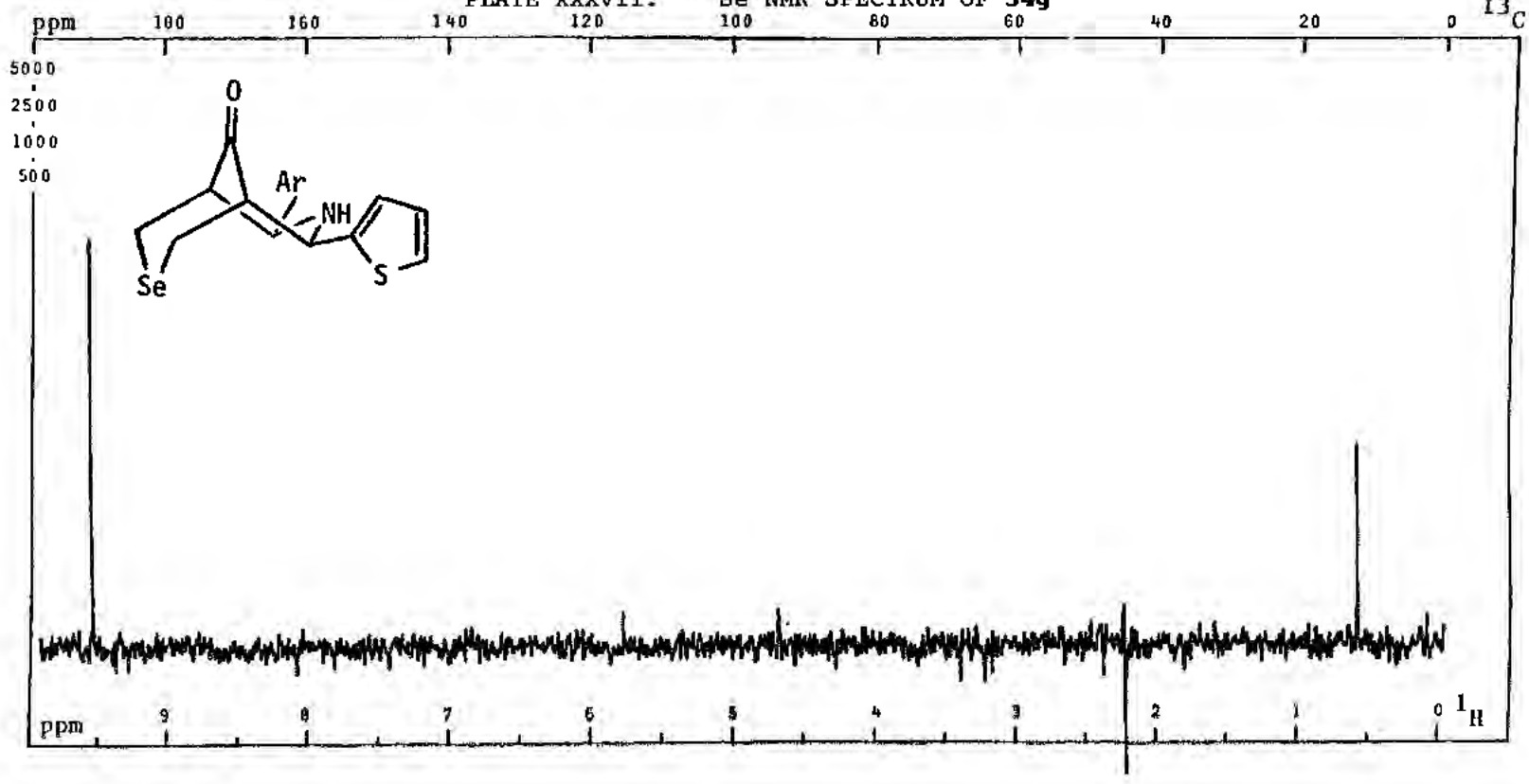


PFT X CW _ ; Solvent: $CDCl_3$; SF: 30.406 MHz; WG: 3040.6Hz; T: 25 °C; NT: 6200 .

Size: 12K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^2D ;D1,D5: 8 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XXXVII. ^{77}Se NMR SPECTRUM OF **34g**



PFT X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 176 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 18 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE XXXVIII. IR SPECTRUM OF **34h**

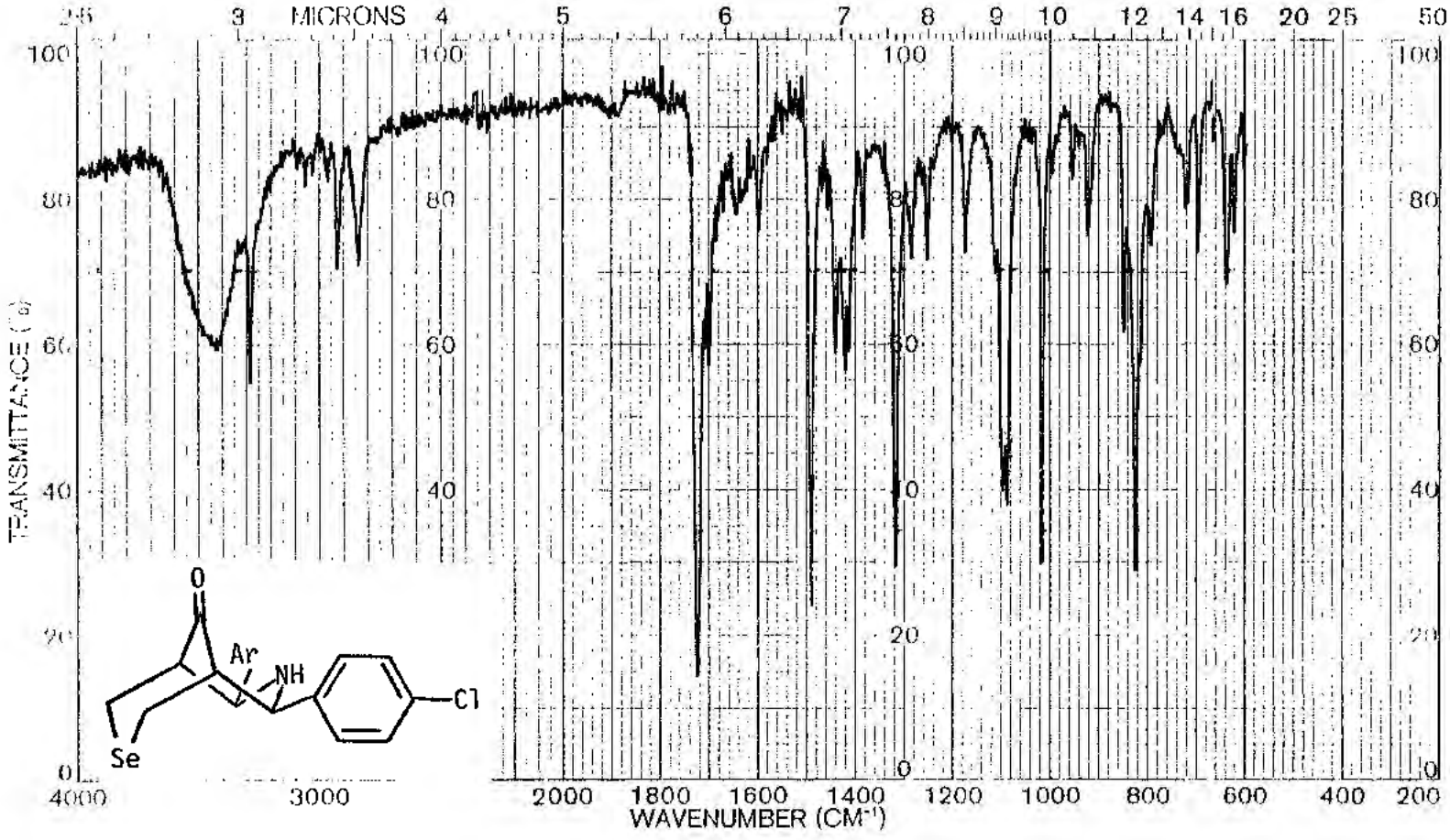
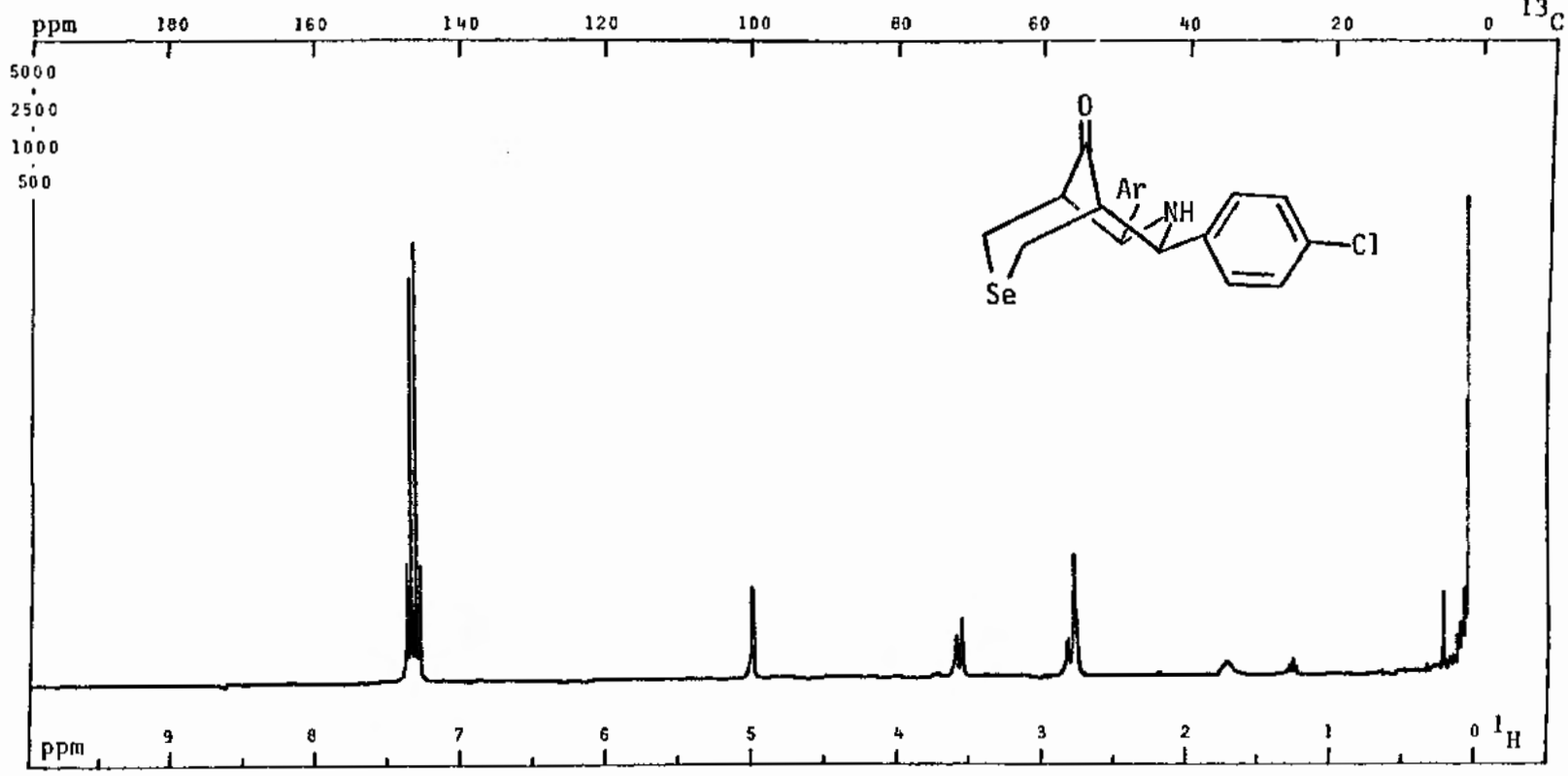


PLATE XXXIX. ^{1}H NMR SPECTRUM OF **34h**

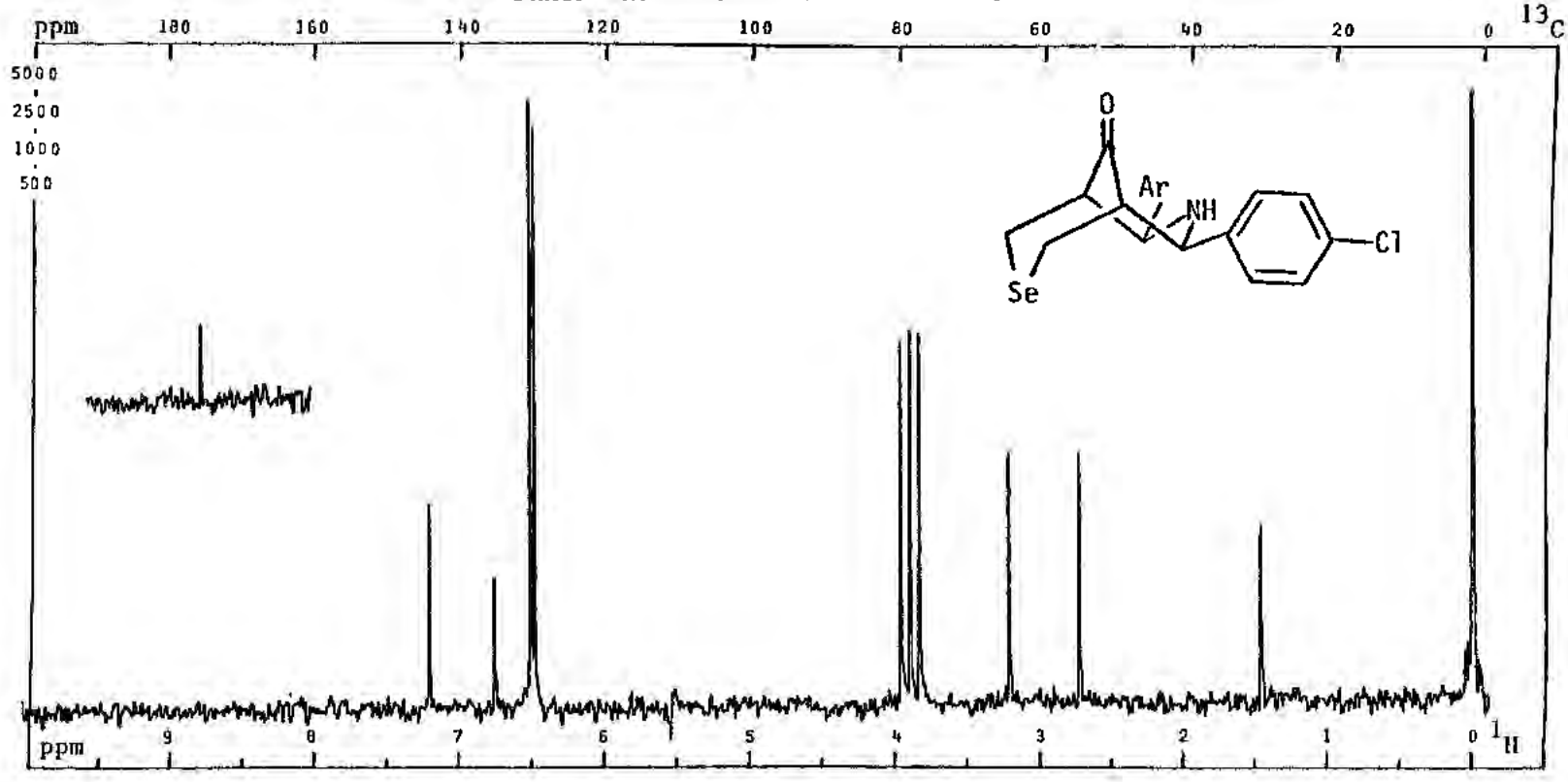


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 16 .

Size: 12 K; PW/RF: 5 µs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XL. ^{13}C NMR SPECTRUM OF **34h**

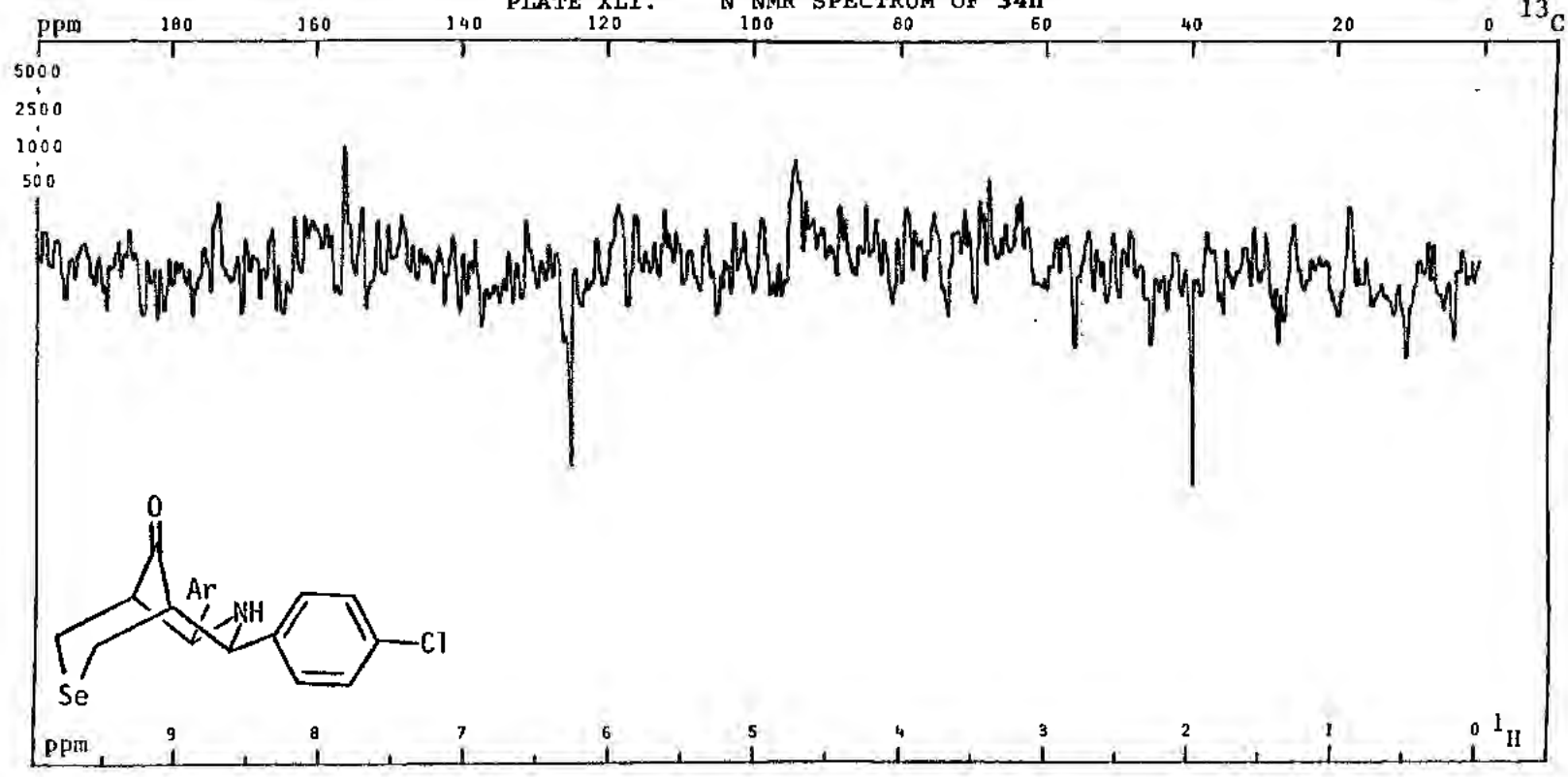


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 6000 Hz; T: 28 °C; NT: 1000 .

Size: 8 K; PW/RF: 10 µs/dB; TO: 35101 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 5 s.

DC: Y, N ; Gated Off: A or D ; DO: 45316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE XLI. ^{15}N NMR SPECTRUM OF **34h**

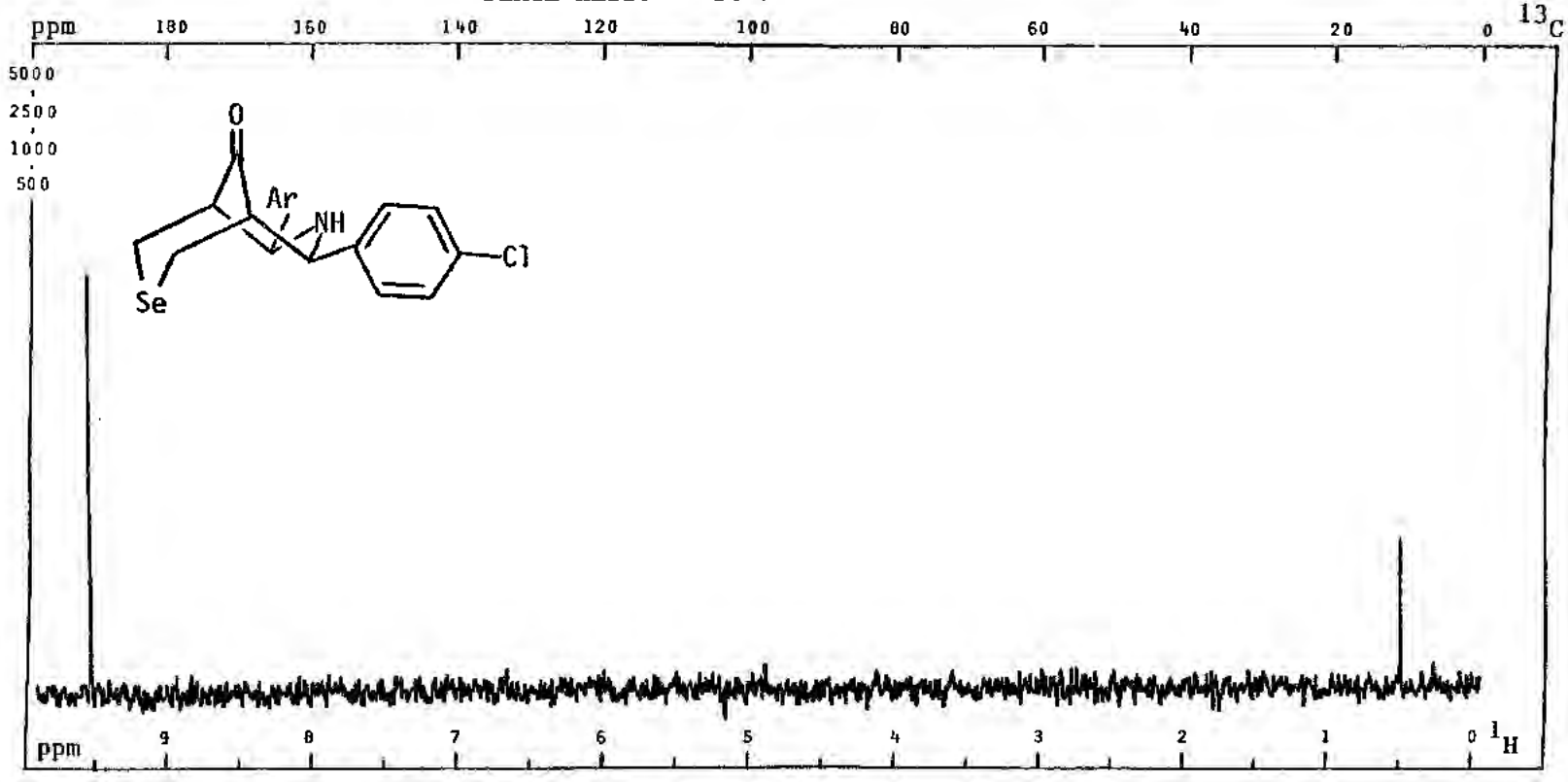


PFT X CW _ ; Solvent: $CDCl_3$; SF: 30.406 MHz; WC:3040.6 Hz; T: 25 °C; NT: 6000 .

Size: 12K; PW/RF: 40 µs/dB; TO: -1160Hz; FB: Hz; Lock: ^2D ;D1,D5:8 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XLII. ^{77}Se NMR SPECTRUM OF **34h**



PFTX_ CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 100 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 18 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE XLIII. IR SPECTRUM OF **34i**

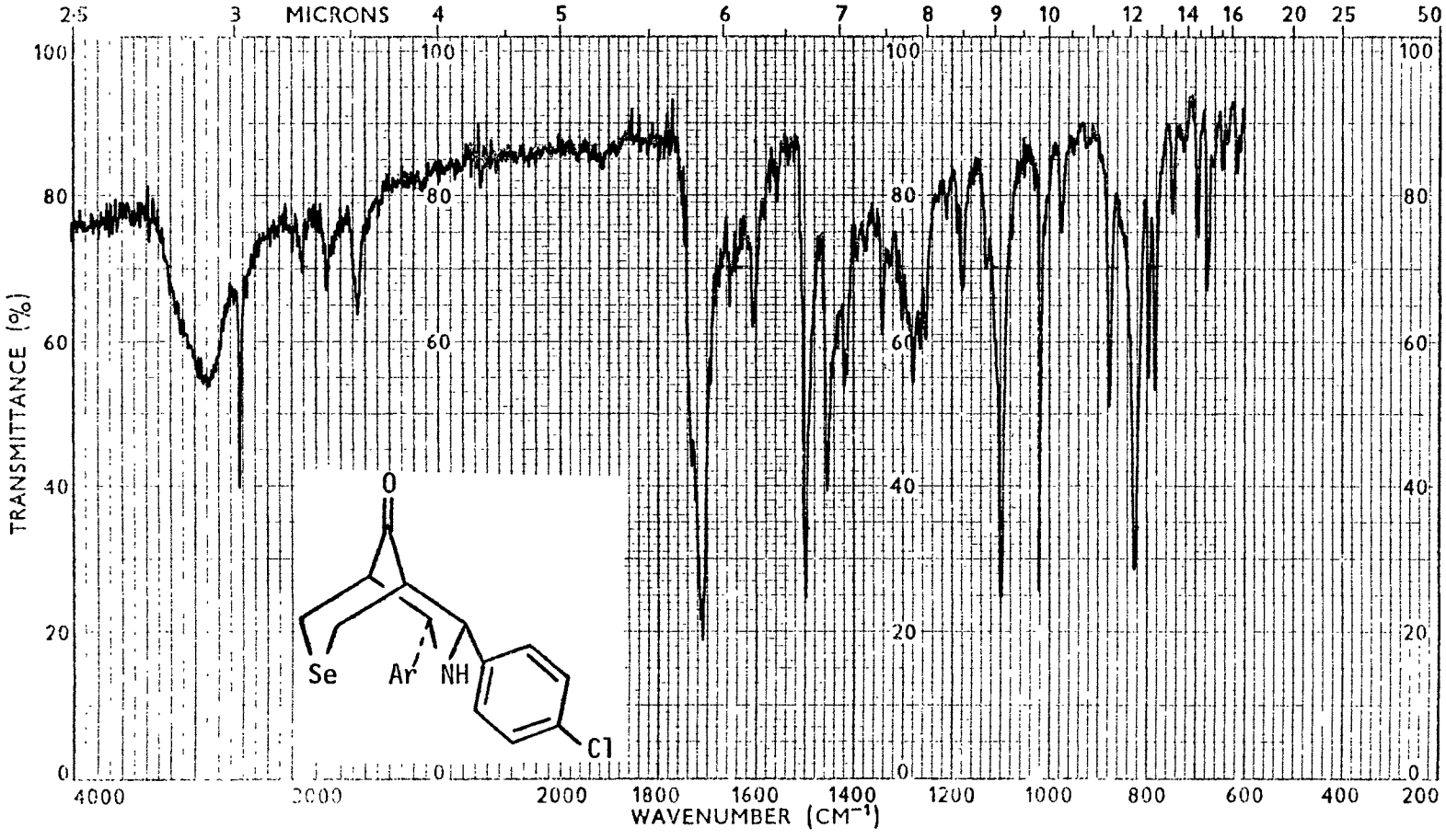
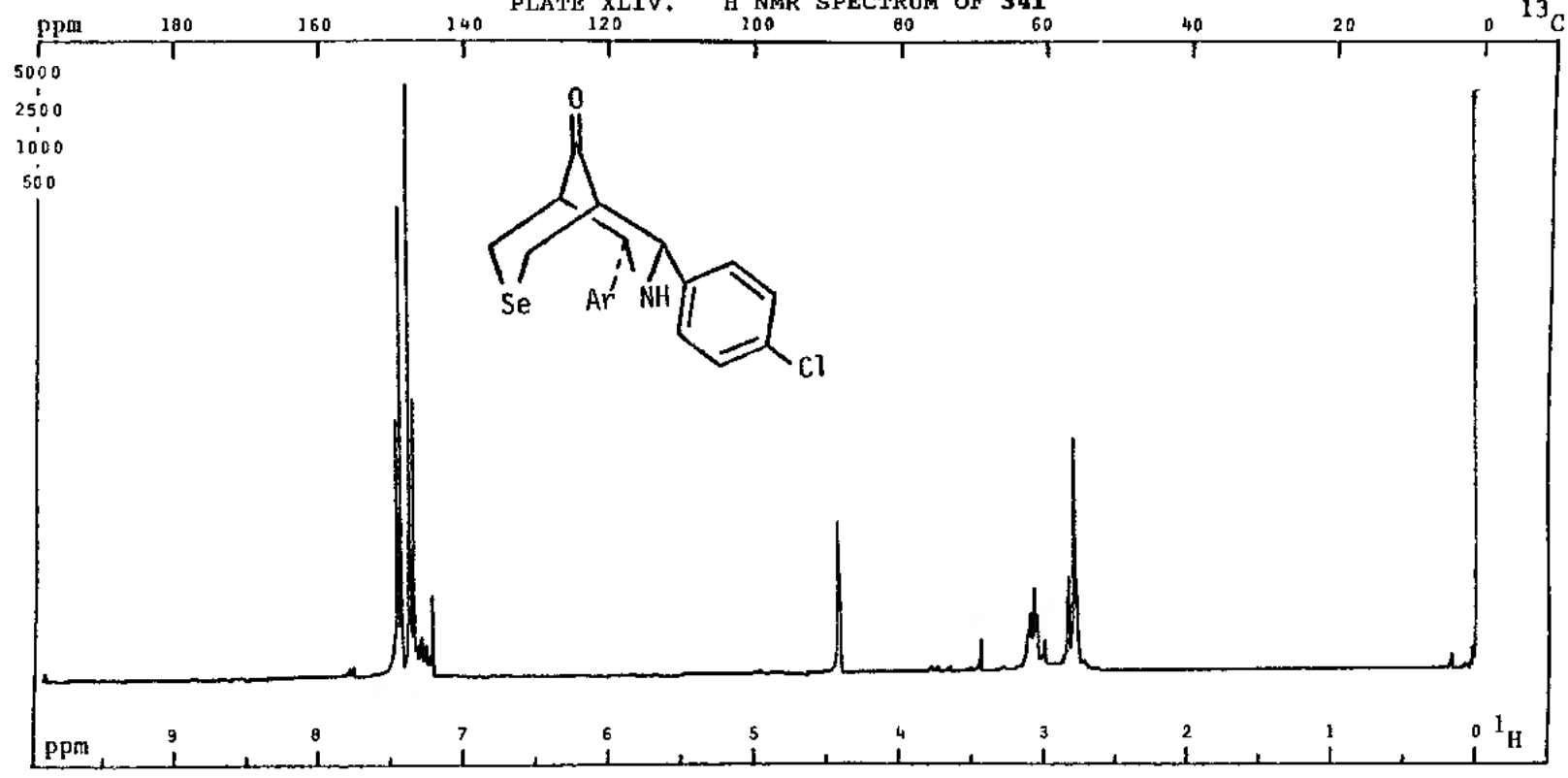


PLATE XLIV. ^{1}H NMR SPECTRUM OF **34i**

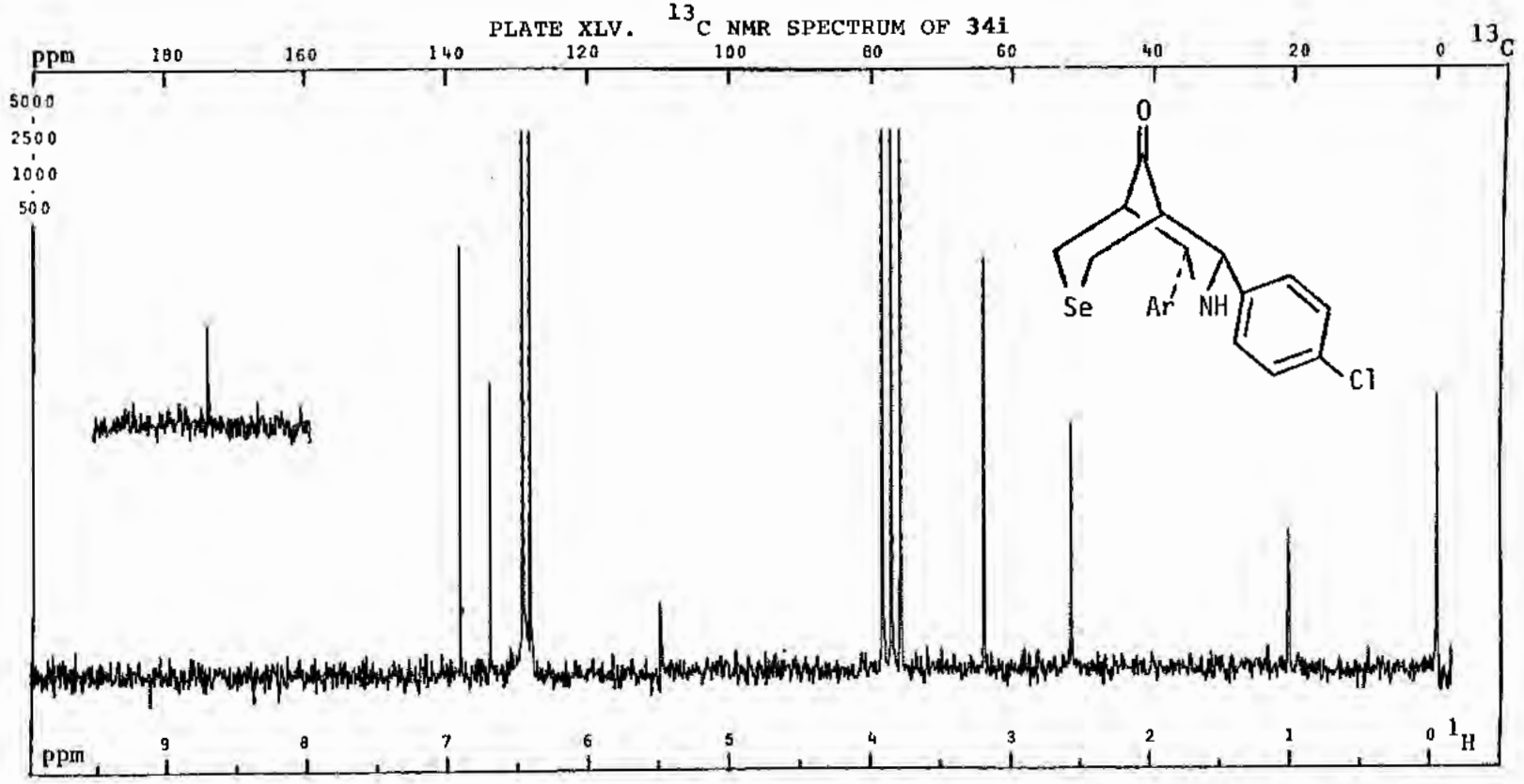


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 8

Size: 12 K; PW/RF: 5 μs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XLV. ^{13}C NMR SPECTRUM OF **34i**

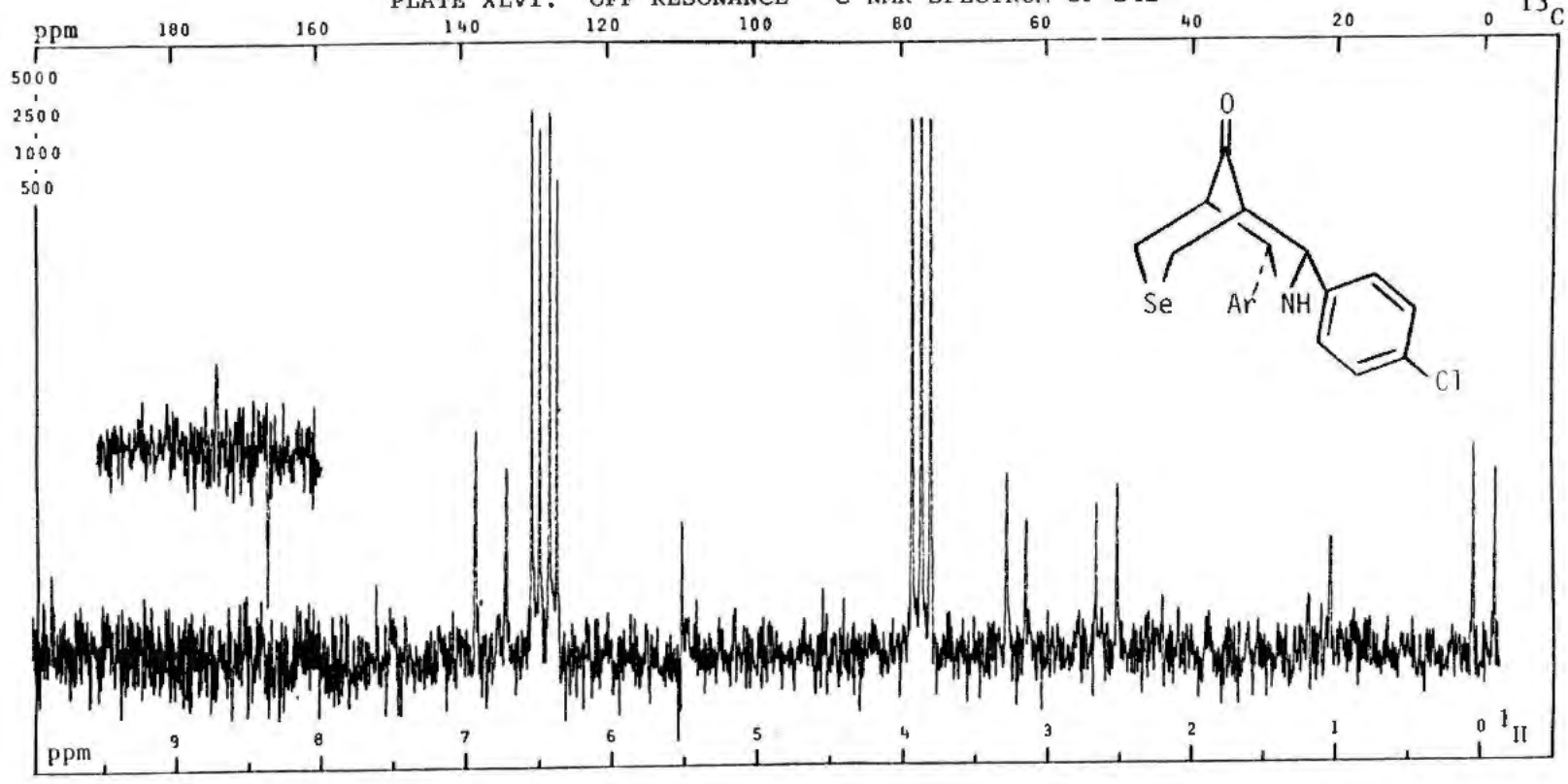


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 6000 Hz; T: 28 °C; NT: 1000 .

Size: 8 K; PW/RF: 10 µs/dB; TO:35101 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 5 s.

DC: Y, N ; Gated Off:A or D ; DO: 45316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE XLVI. OFF RESONANCE ^{13}C NMR SPECTRUM OF **34i**

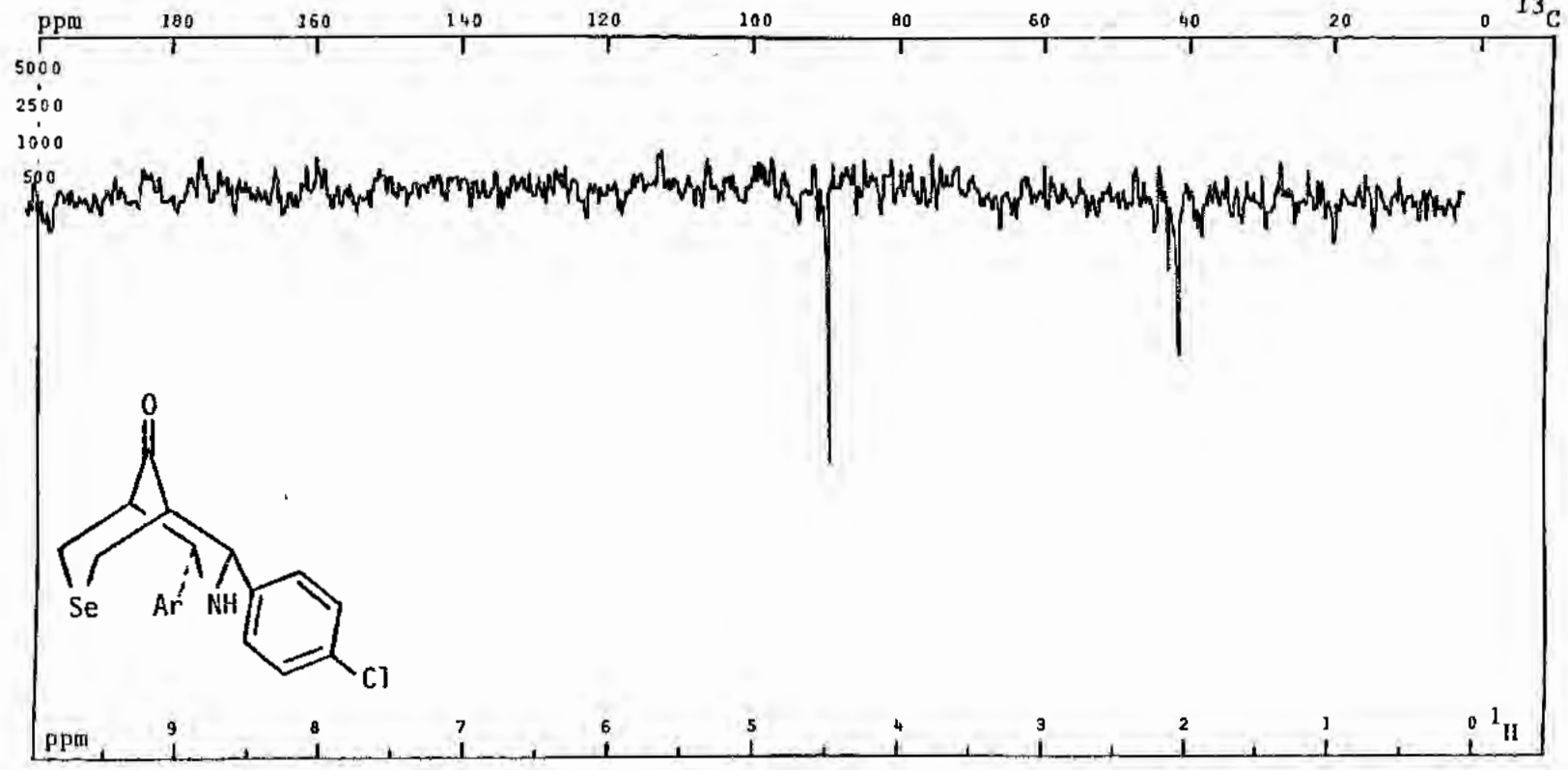


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 6000 Hz; T: 28 °C; NT: 1000

Size: 8 K; PW/RF: 10 µs/dB; TO: 35101 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 5 s.

DC: Y, N ; Gated Off: A or D ; DO: 46316 Hz; RF(Power): 7.5W/dB; NBW: Hz; LB: Hz.

PLATE XLVII. ^{15}N NMR SPECTRUM OF **34i**

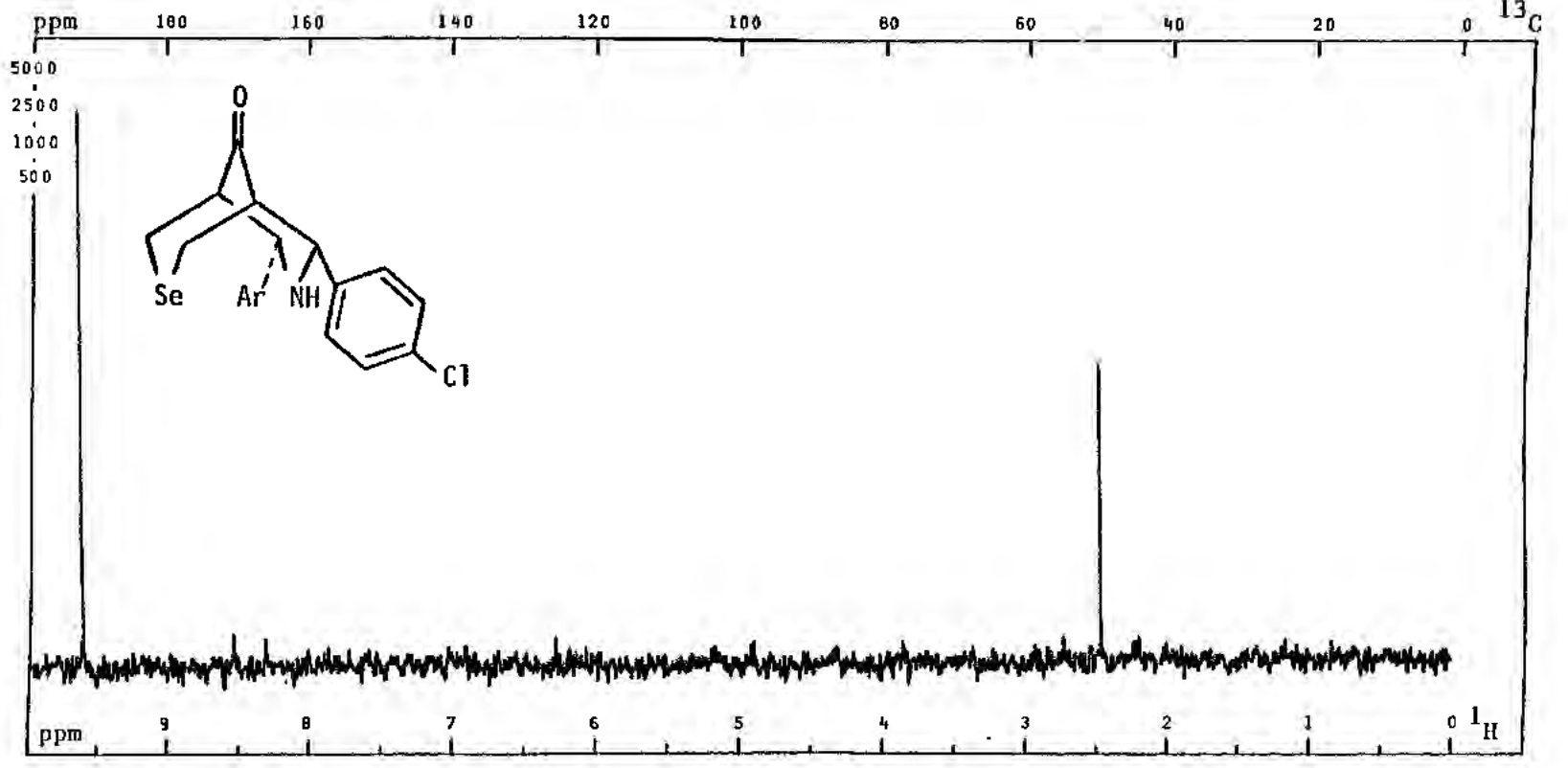


PFT X CW _ ; Solvent: $CDCl_3$; SF: 30.406 MHz; WC: 3040 Hz; T: 25 °C; NT: 11500 .

Size: 12K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^2D ; D1,D5: 8 s.

DC: Y, N ; Gated Off:A or D ; DO: -11600 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE XLVIII. ^{77}Se NMR SPECTRUM OF 34i



PFT X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 60 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 20 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE XLIX. IR SPECTRUM OF **35f**

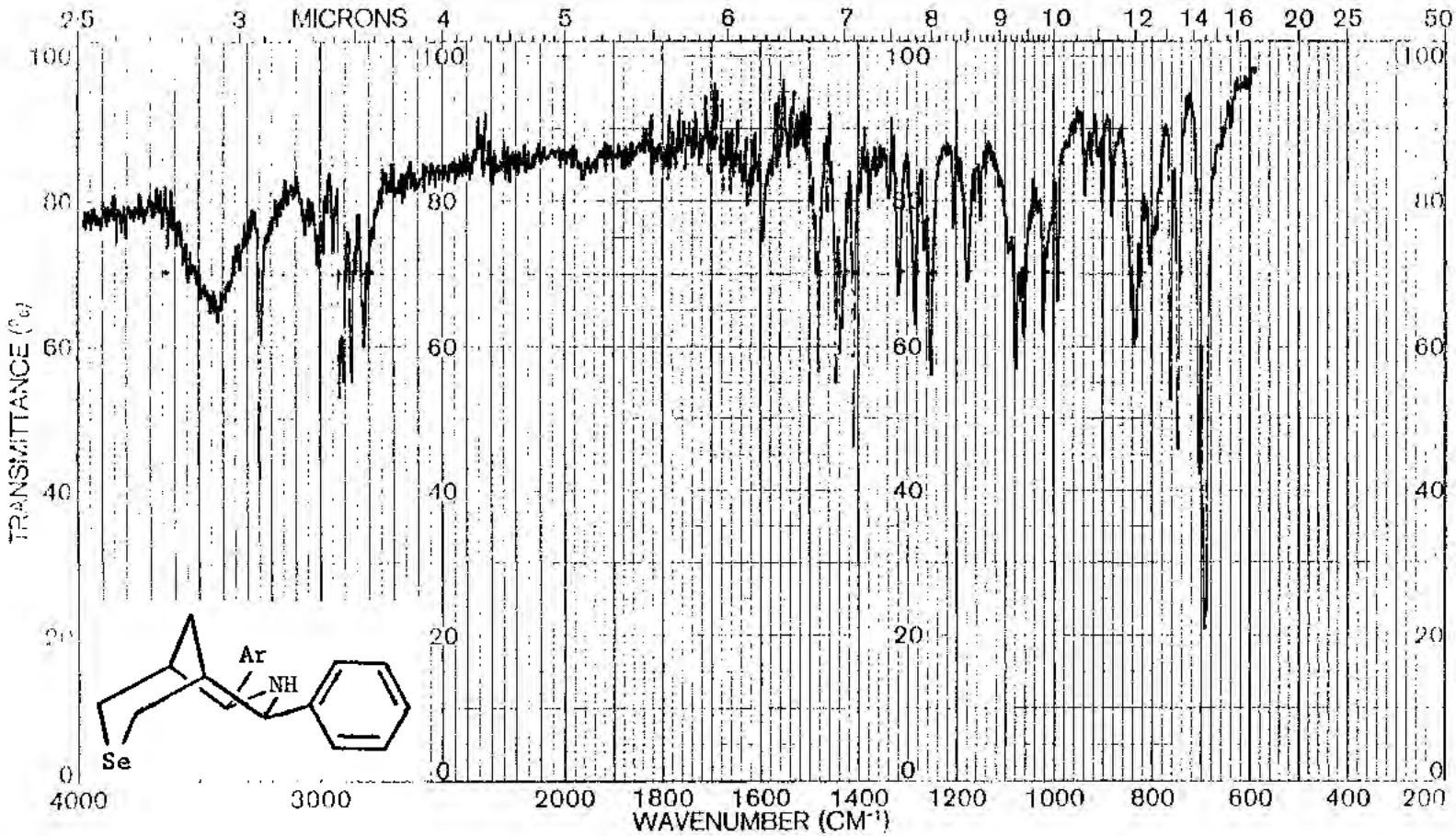
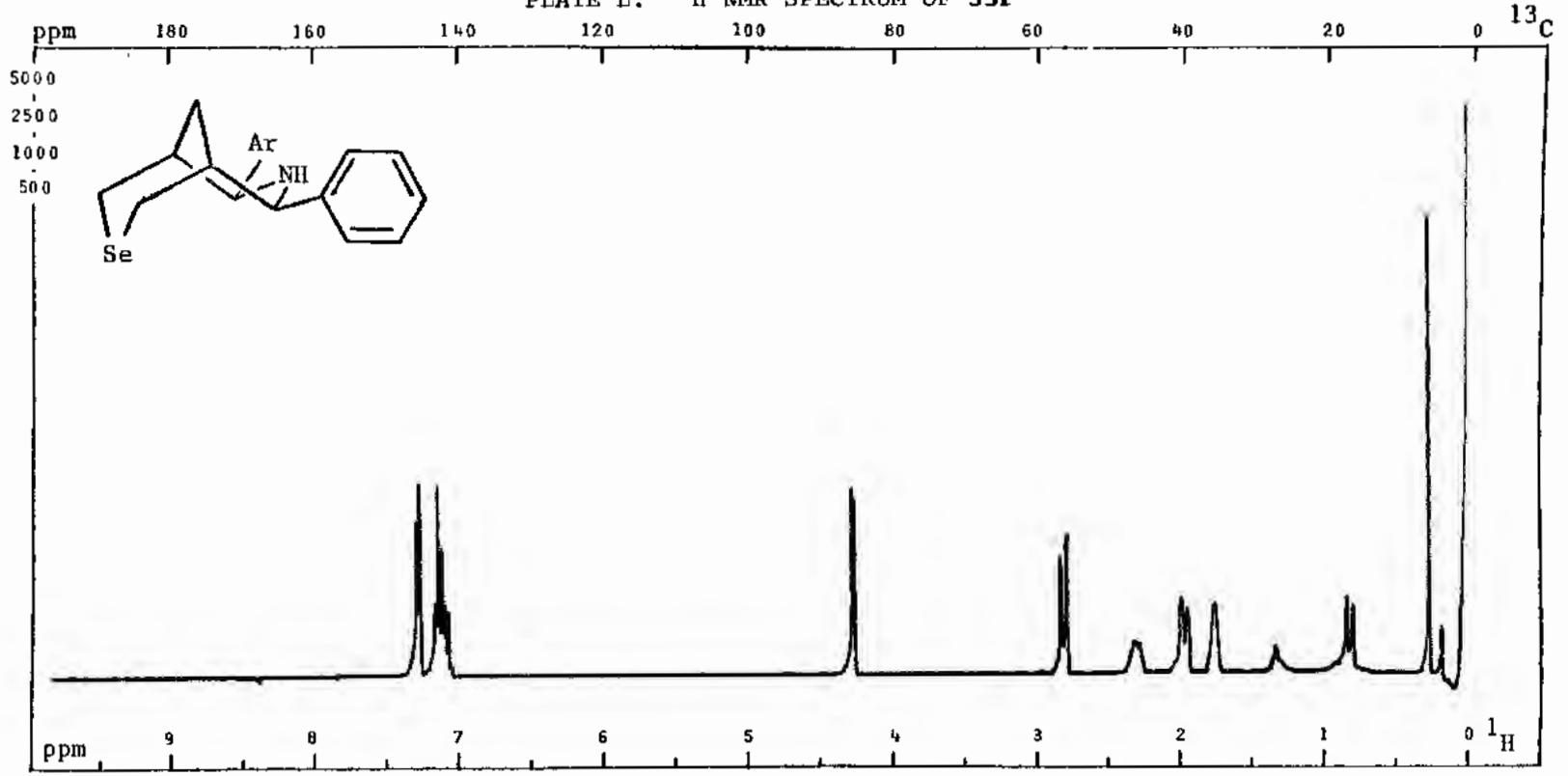


PLATE L. ^{1}H NMR SPECTRUM OF **35f**

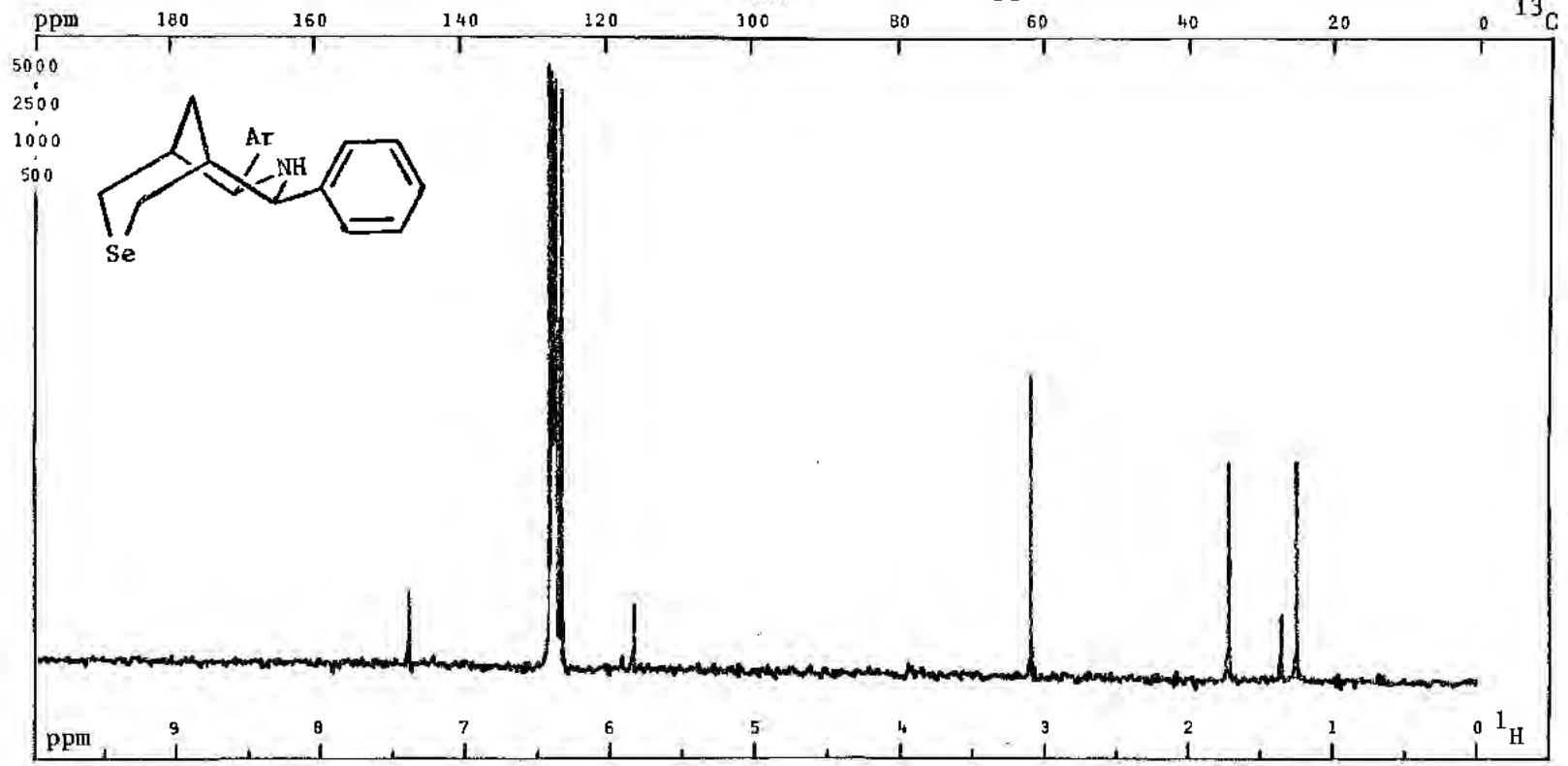


PFT X CW _ ; Solvent: C_6D_6 ; SF: 299.94 MHz; WC: 3000 Hz; T: 50 °C; NT: 200 .

Size: 12 K; PW/RF: 6 μs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0.5 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LI. ^{13}C NMR SPECTRUM OF 35f

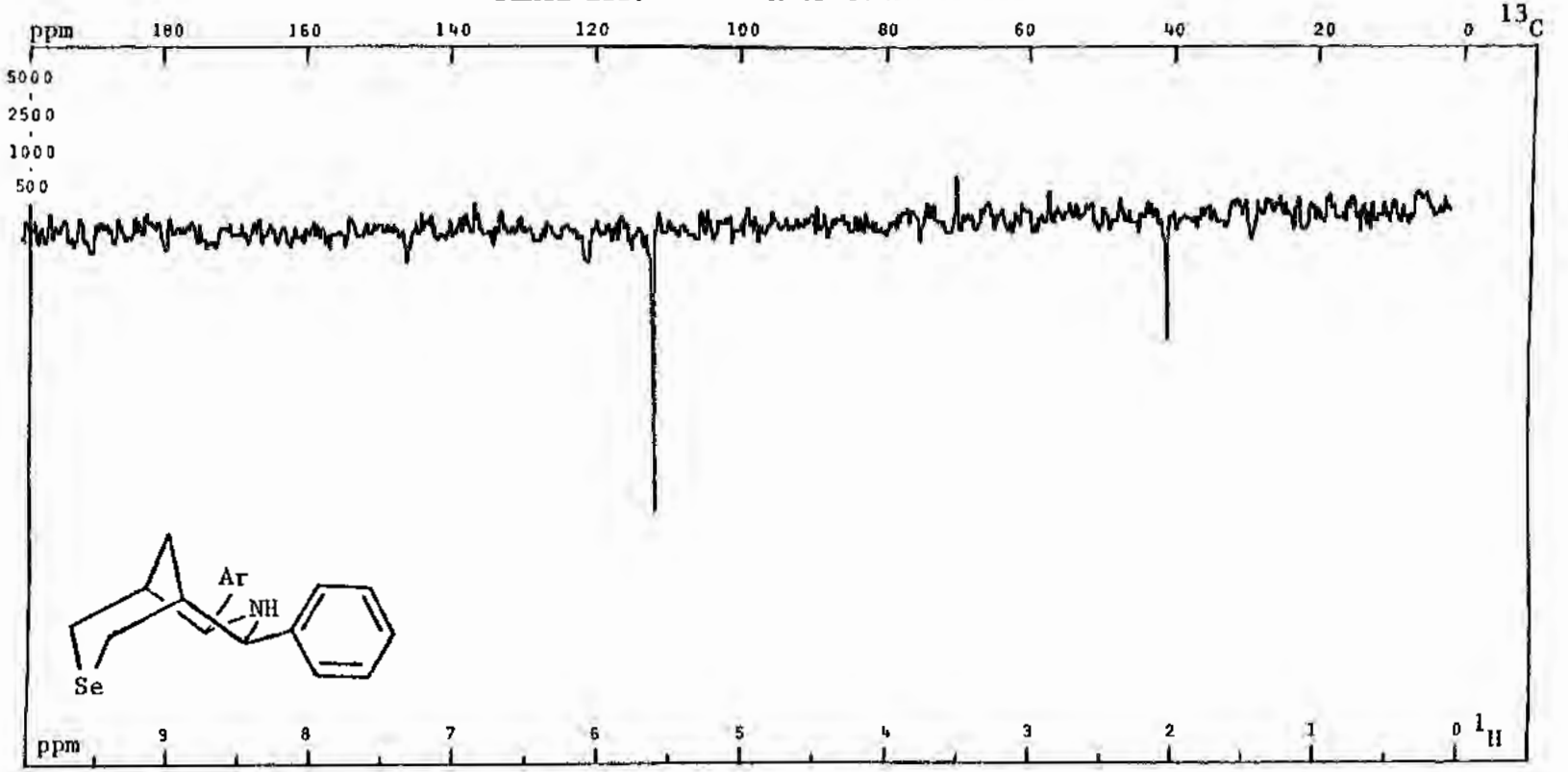


PFT X CW _ ; Solvent: C_6D_6 ; SF: 75.43 MHz; WC: 15085 Hz; T: 50 °C; NT: 240 .

Size: 20 K; PW/RF: 12 µs/dB; SO: 1000 Hz; FB: Hz; Lock: ^{2}D ; Delay: 4 s.

DC: Y ; Gated Off: ; Offset: 0 Hz; RF: 20 W/dB; NBW: Hz; LB: .

PLATE LII. ^{15}N NMR SPECTRUM OF 35f

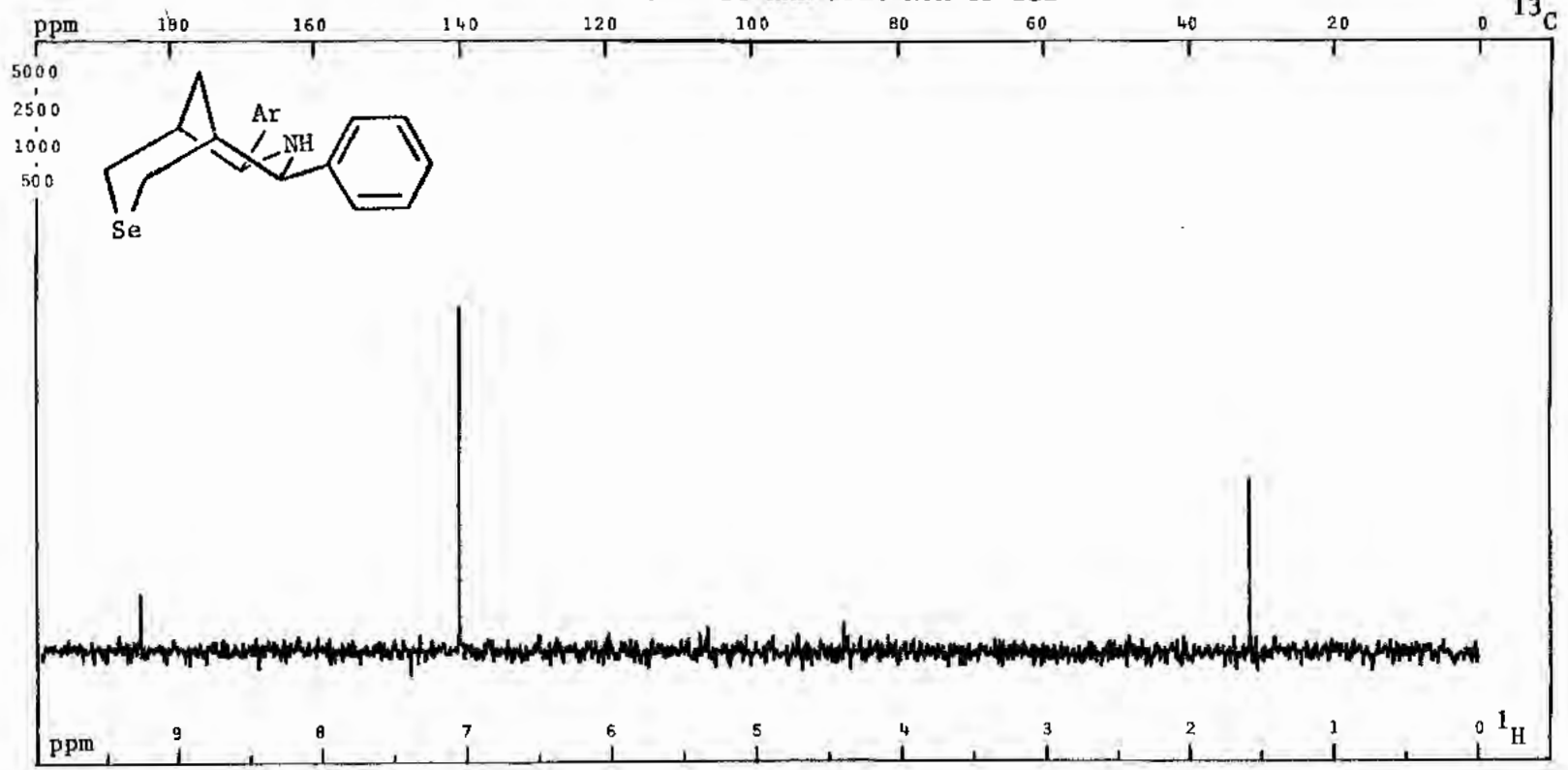


PFTX_ CW _ ; Solvent: C_6D_6 ; SF: 30.406 MHz; WC: 3040.6 Hz; T: 50 °C; NT: 13600

Size: 12 K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 8 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LIII. ^{77}Se NMR SPECTRUM OF **35f**



PFT X CW _ ; Solvent: C_6D_6 ; SF: 57.22 MHz; WC: 50000 Hz; T: 50 °C; NT: 200 .

Size: 32 K; PW/RF: 35 µs/dB; SO: 500 Hz; FB: Hz; Lock: ^{2}D ; Delay: 25 s.

DC: Y ; Gated Off: ; Offset: 0 Hz; RF: 20 W/dB; NBW: Hz; LB: .

PLATE LIV. IR SPECTRUM OF **35g**

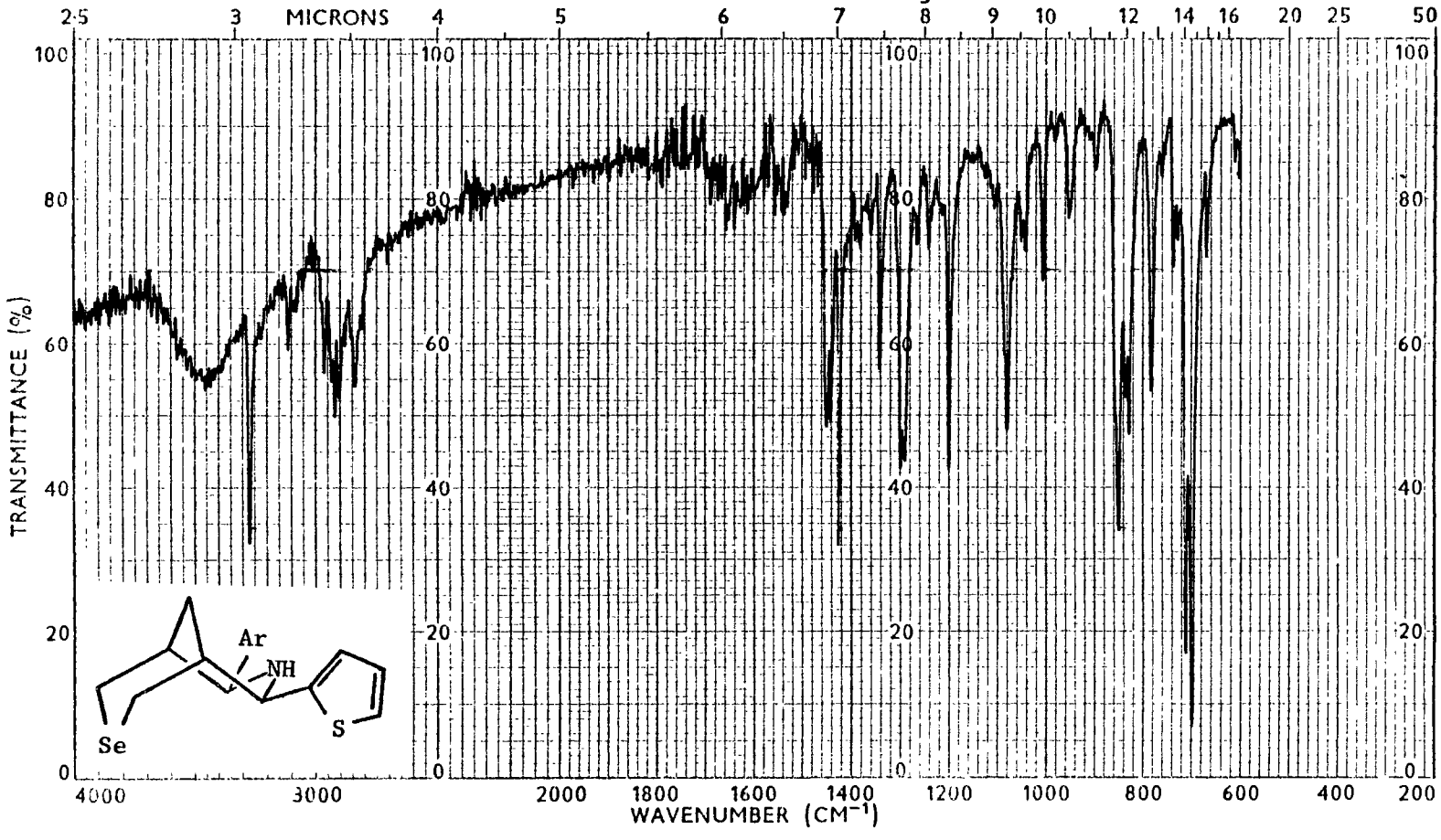
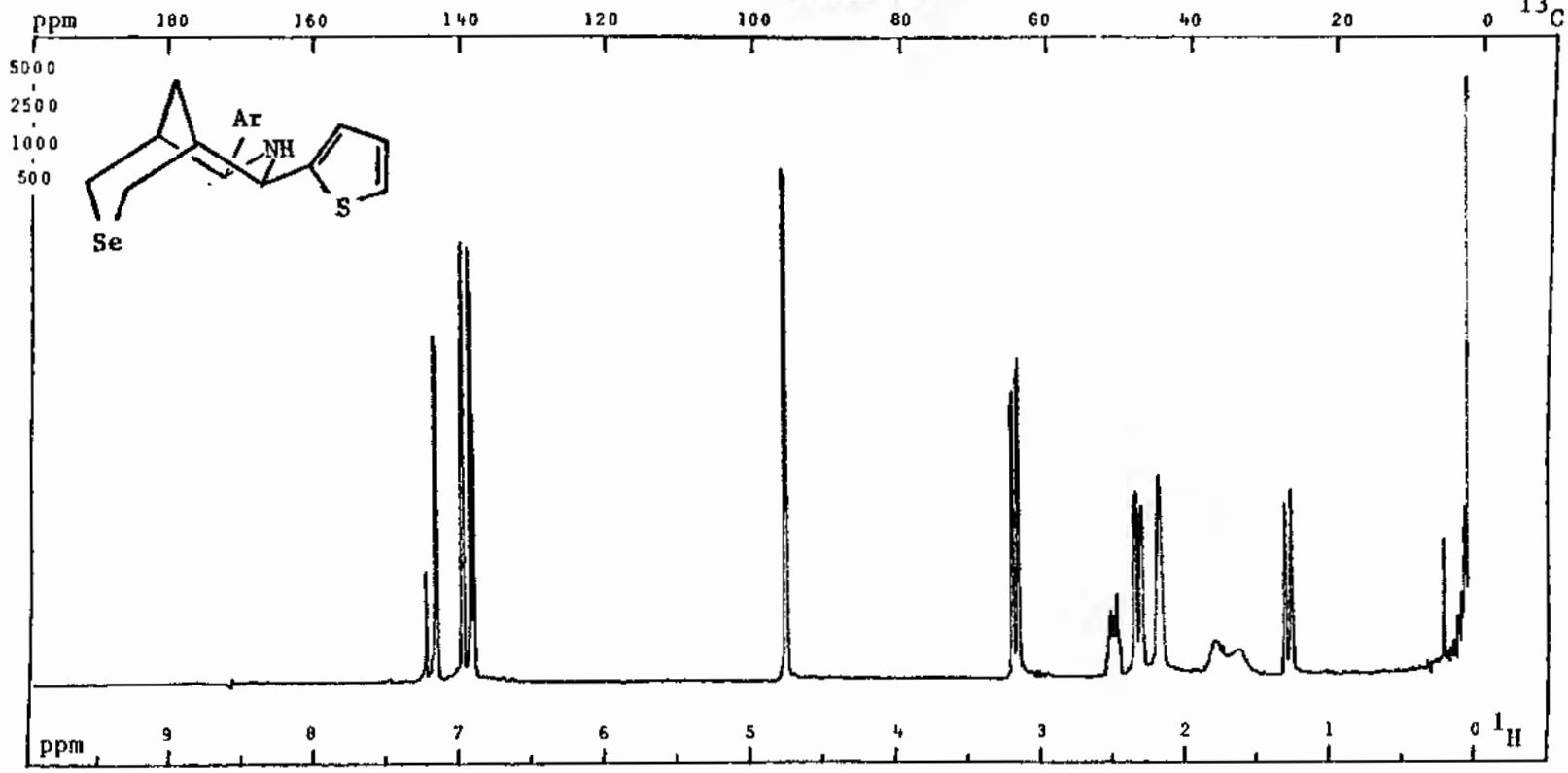


PLATE LV. ^{1}H NMR SPECTRUM OF 35g

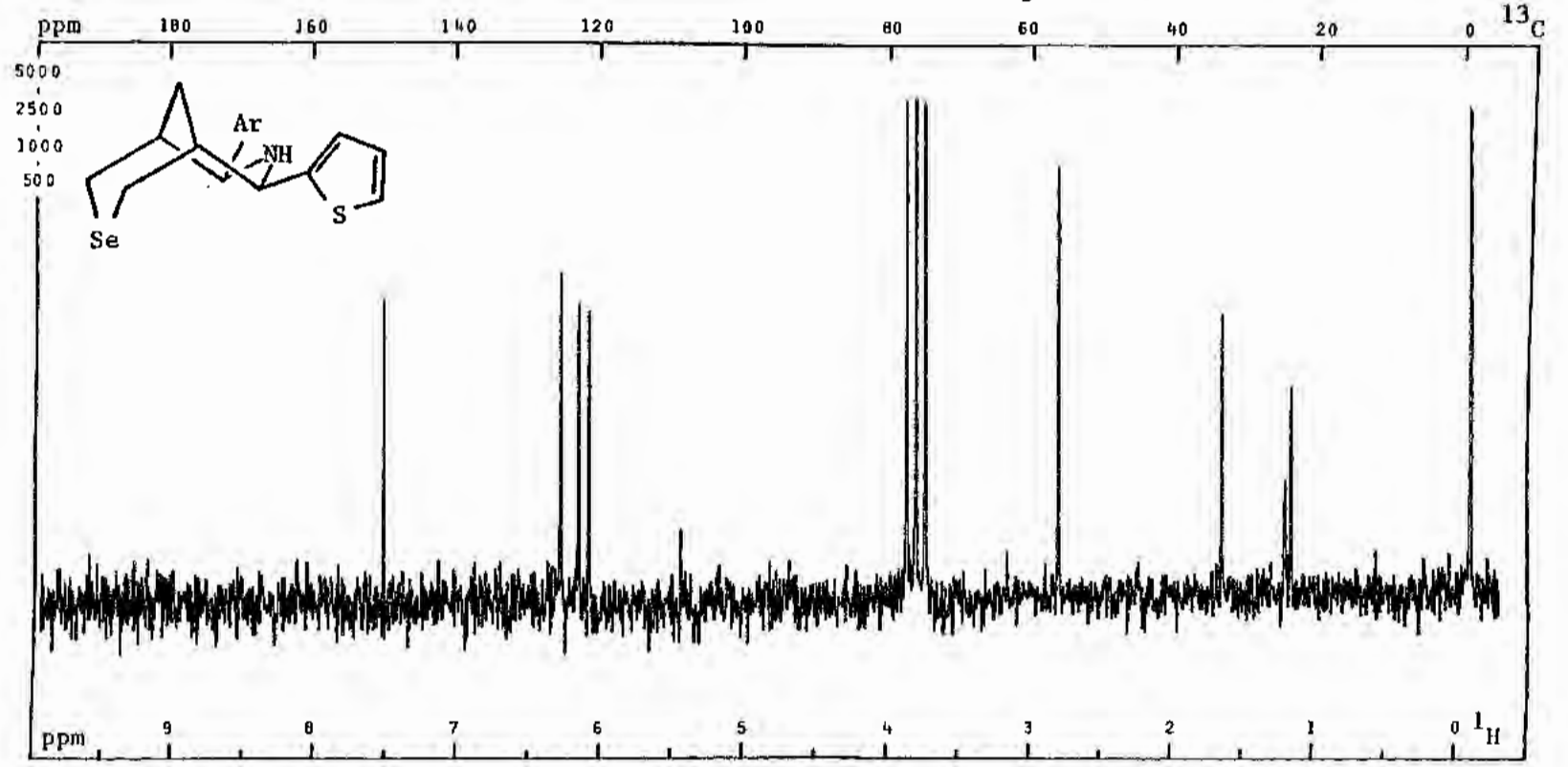


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 3000 Hz; T: 22 °C; NT: 16 .

Size: 12 K; PW/RF: 7 μs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LVI. ^{13}C NMR SPECTRUM OF 35g

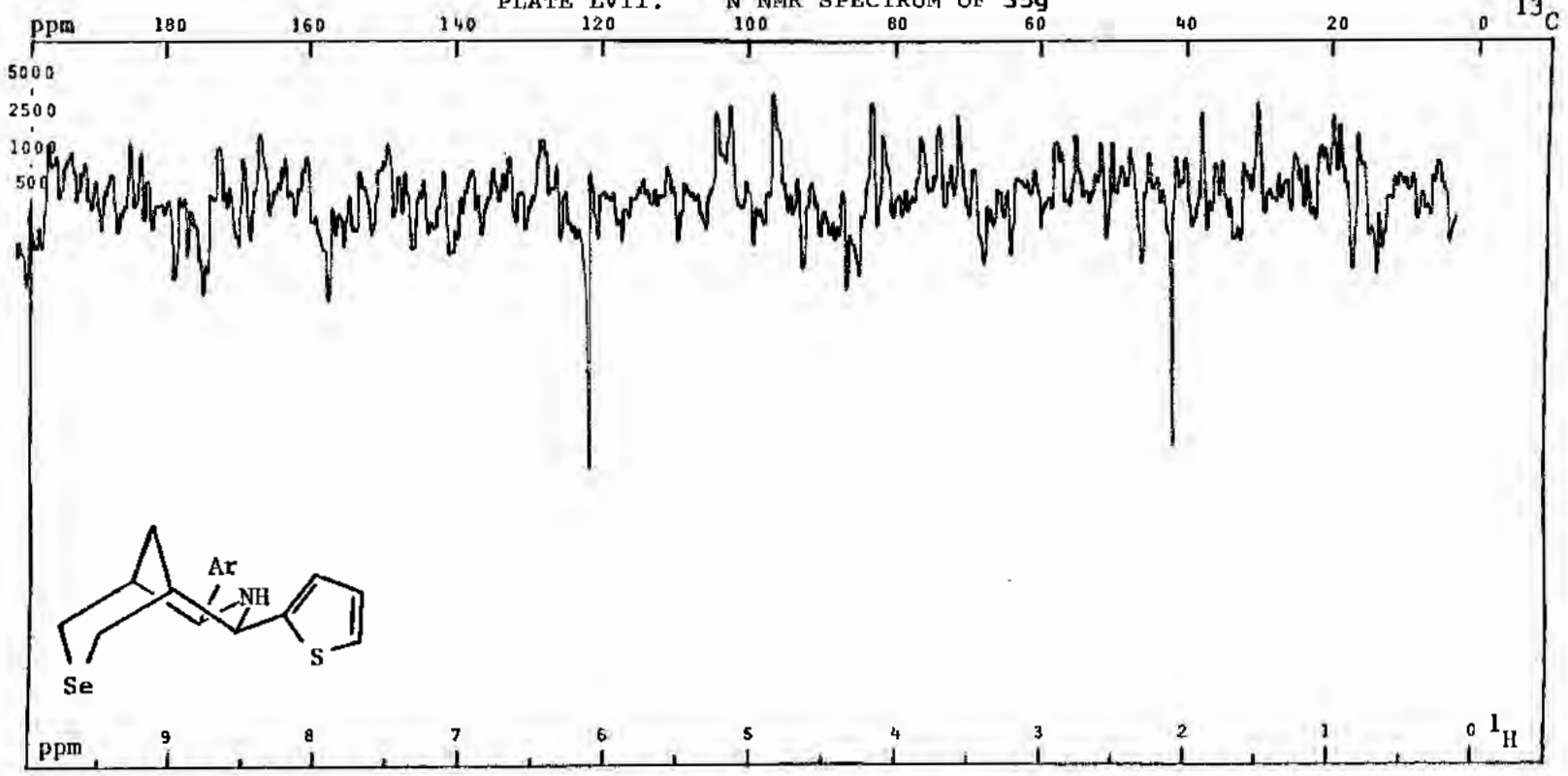


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 2648 .

Size: 8 K; PW/RF: 10 µs/dB; TO: 35101 Hz; FB: Hz; Lock: ^2D ; D1,D5: 5 s.

DC: Y, N ; Gated Off: A or D ; DO: 45316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE LVII. ^{15}N NMR SPECTRUM OF 35g

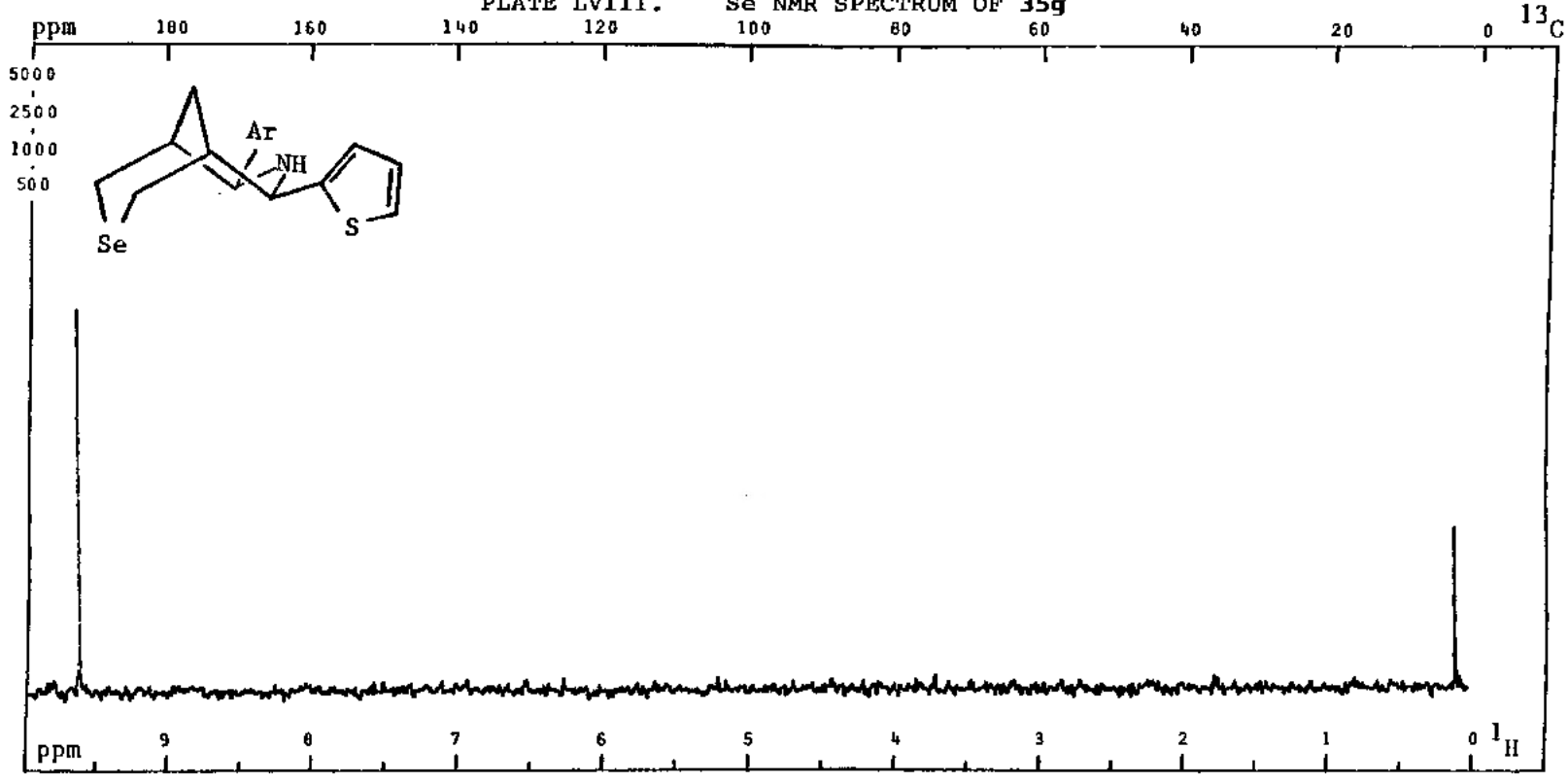


PFTX_ CW _ ; Solvent: $CDCl_3$; SF: 30.406 MHz; WC: 3040.6 Hz; T: 25 °C; NT: 9600 .

Size: 12 K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^2D ; D1,D5: 8 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LVIII. ^{77}Se NMR SPECTRUM OF 35g



PFT X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 200 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 15 s.

DC: Y, N ; Gated Off:A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE LIX. IR SPECTRUM OF **35h**

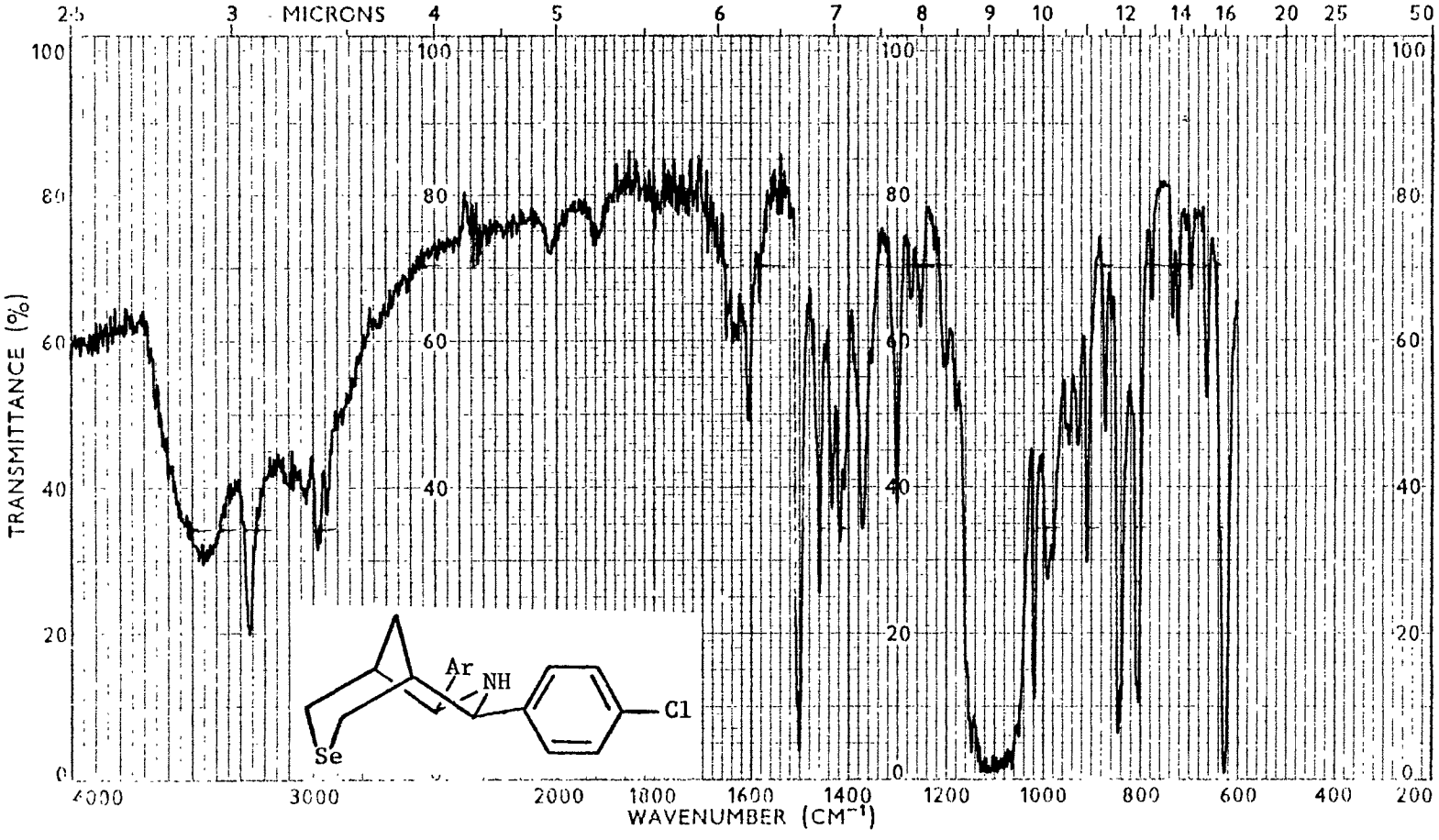
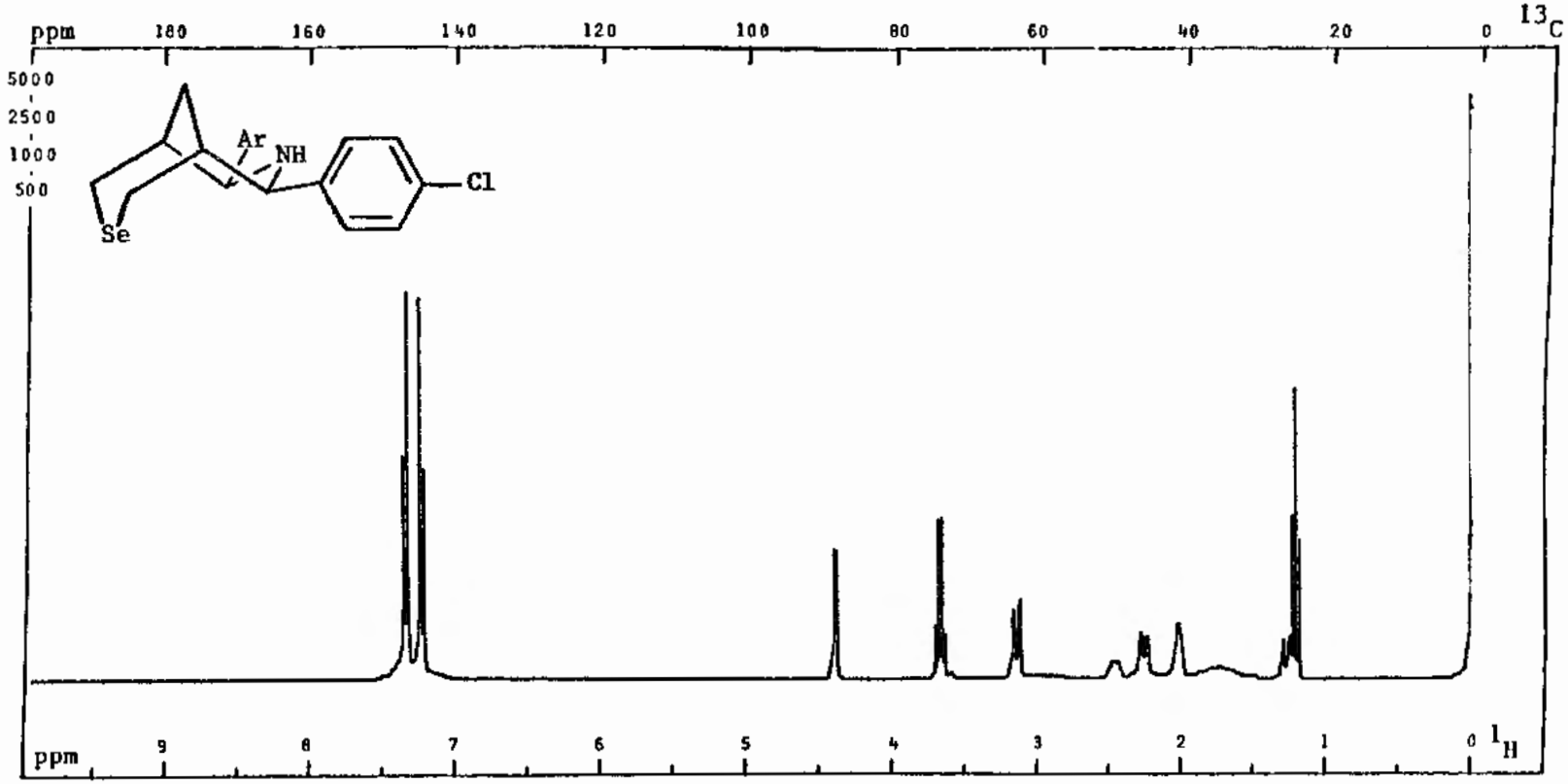


PLATE LX. ^{1}H NMR SPECTRUM OF 35h

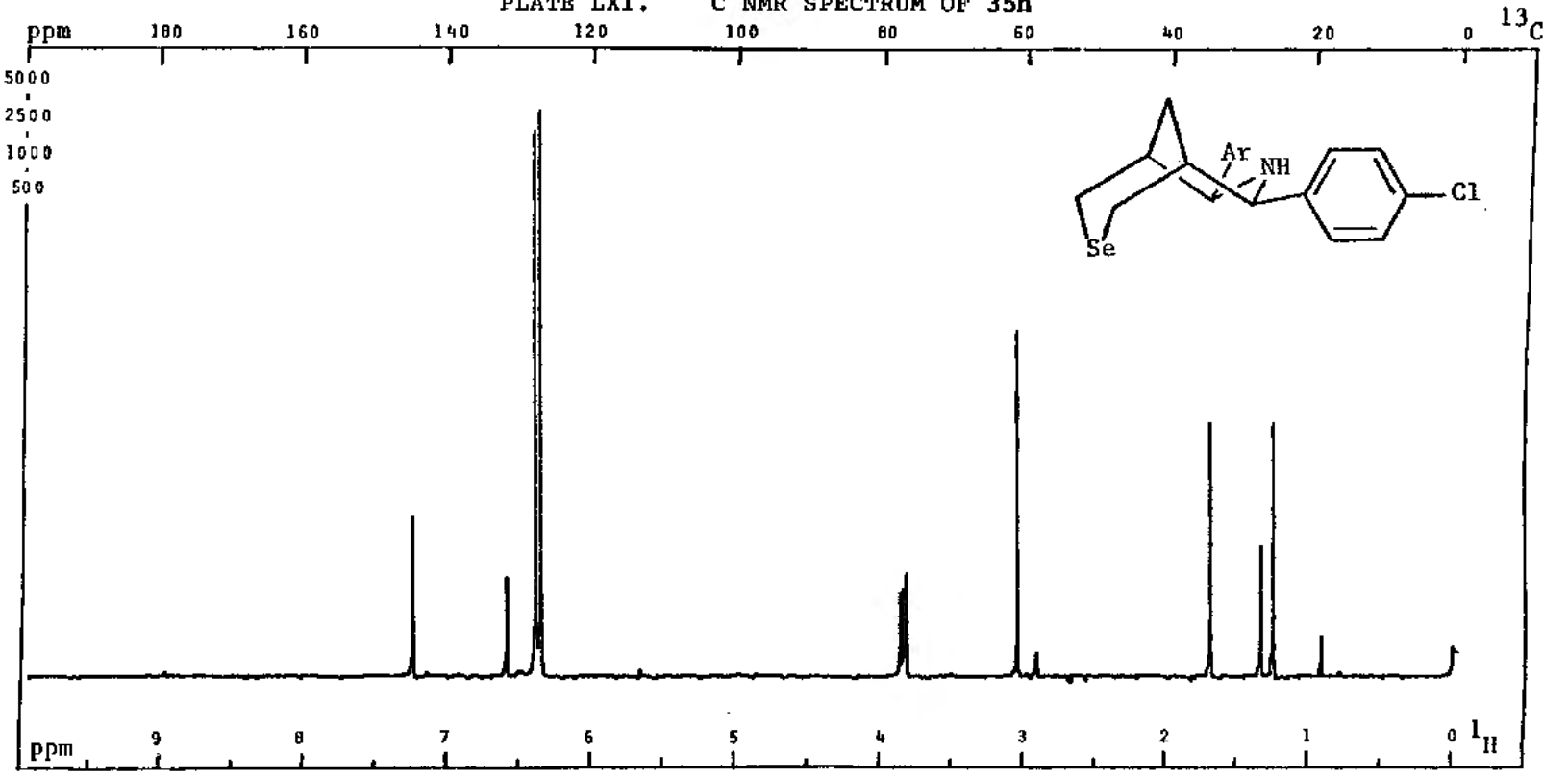


PFTX_ CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 8 .

Size: 12 K; PW/RF: 5 µs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LXI. ^{13}C NMR SPECTRUM OF 35h

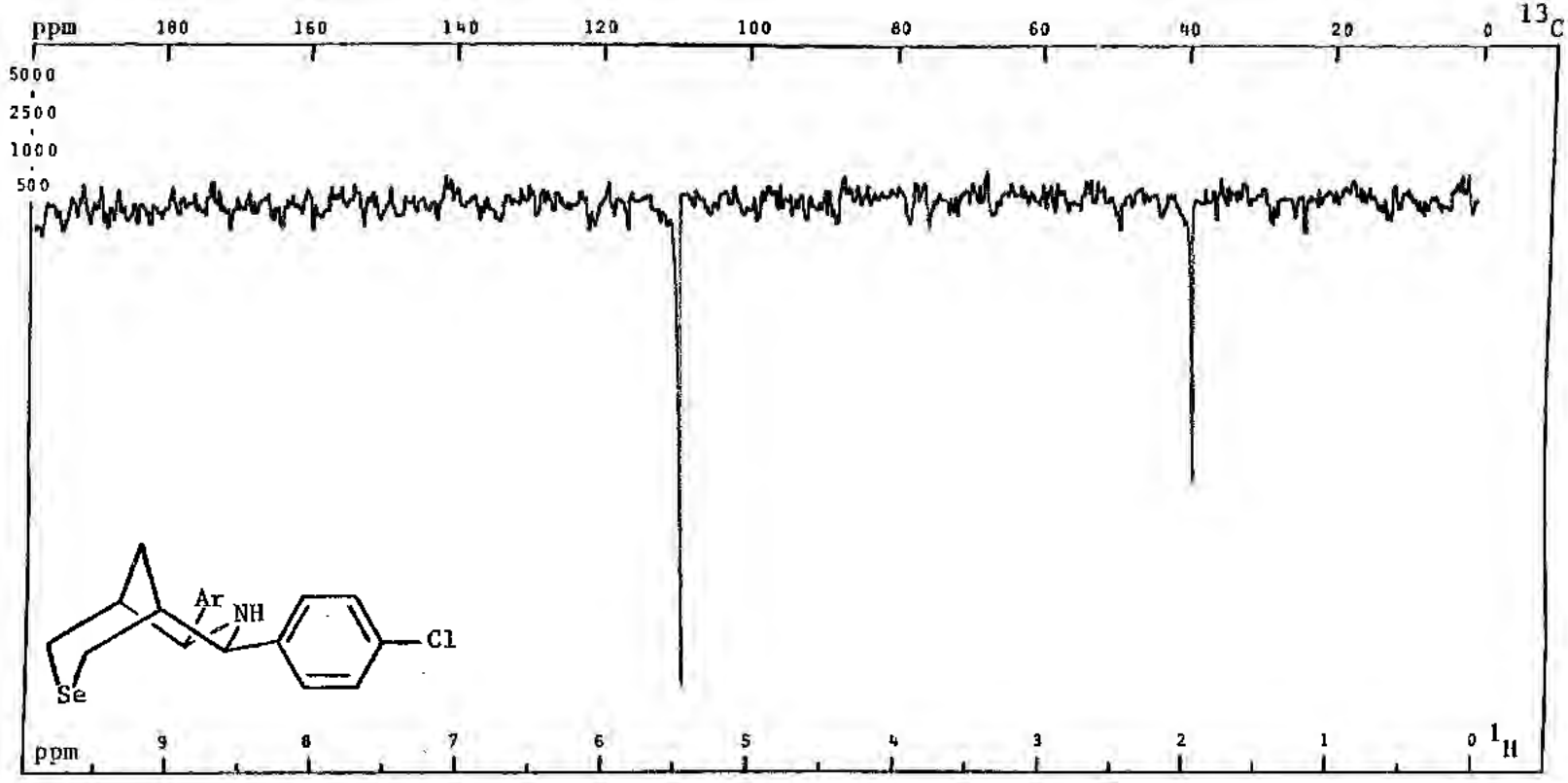


PFT X CW _ ; Solvent: $CDCl_3$; SF: 75.4 MHz; WC:15085 Hz; T: 25 °C; NT: 80 .

Size: 16 K; PW/RF: 12 μs/dB; TO: 1000 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 4 s.

DC: Y, N ; Gated Off:A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE LXII. ^{15}N NMR SPECTRUM OF **35h**

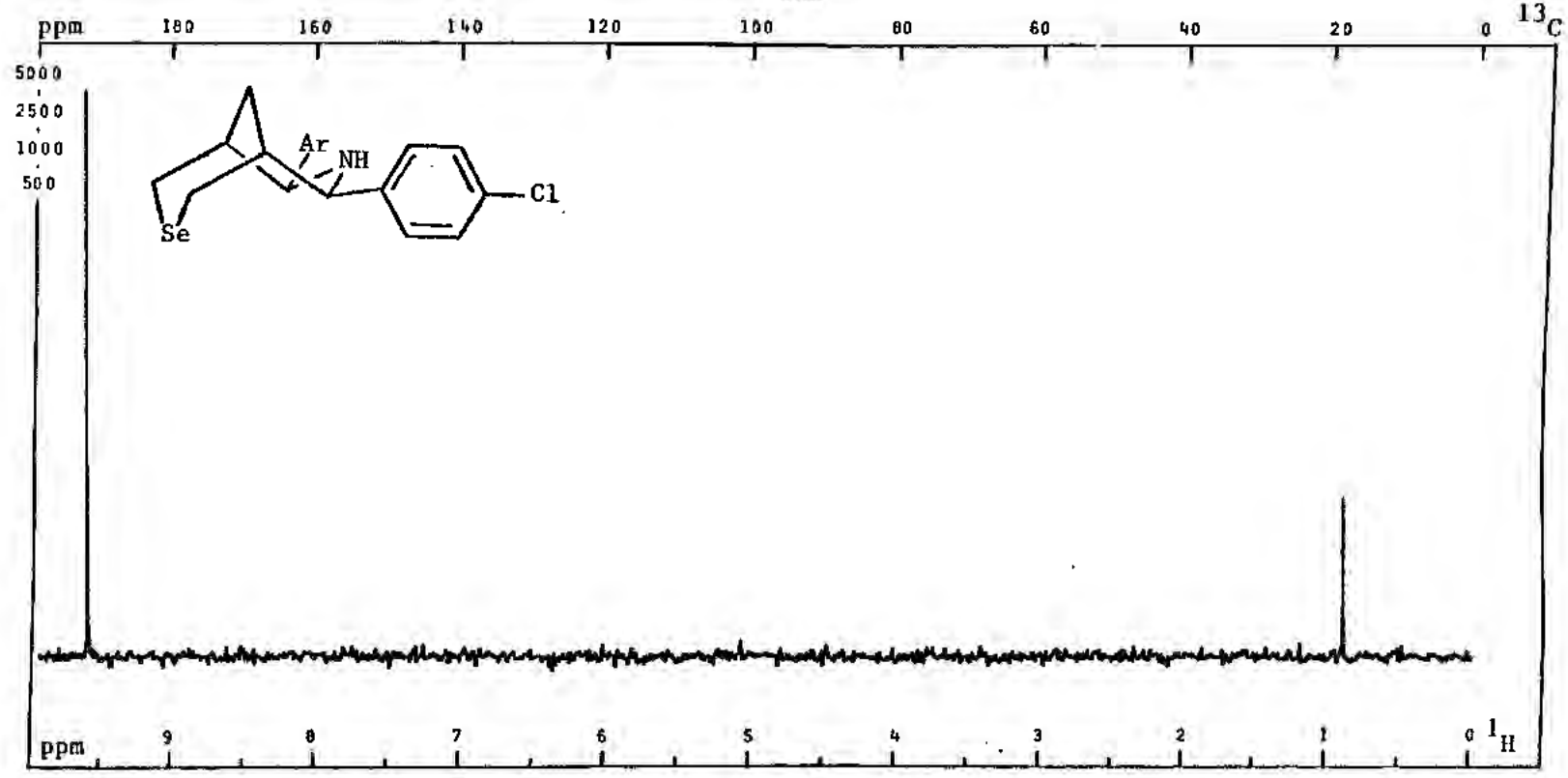


PFT X CW _ : Solvent: $CDCl_3$; SF: 30.406 MHz; WC: 3040.6 Hz; T: 25 °C; NT: 6000 .

Size: 12 K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 8 s.

DC: Y, N ; Cated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LXIII. ^{77}Se NMR SPECTRUM OF 35h



PFTX__ CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 40

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^2D ; D1,D5: 15 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE LXIV. IR SPECTRUM OF **35i**

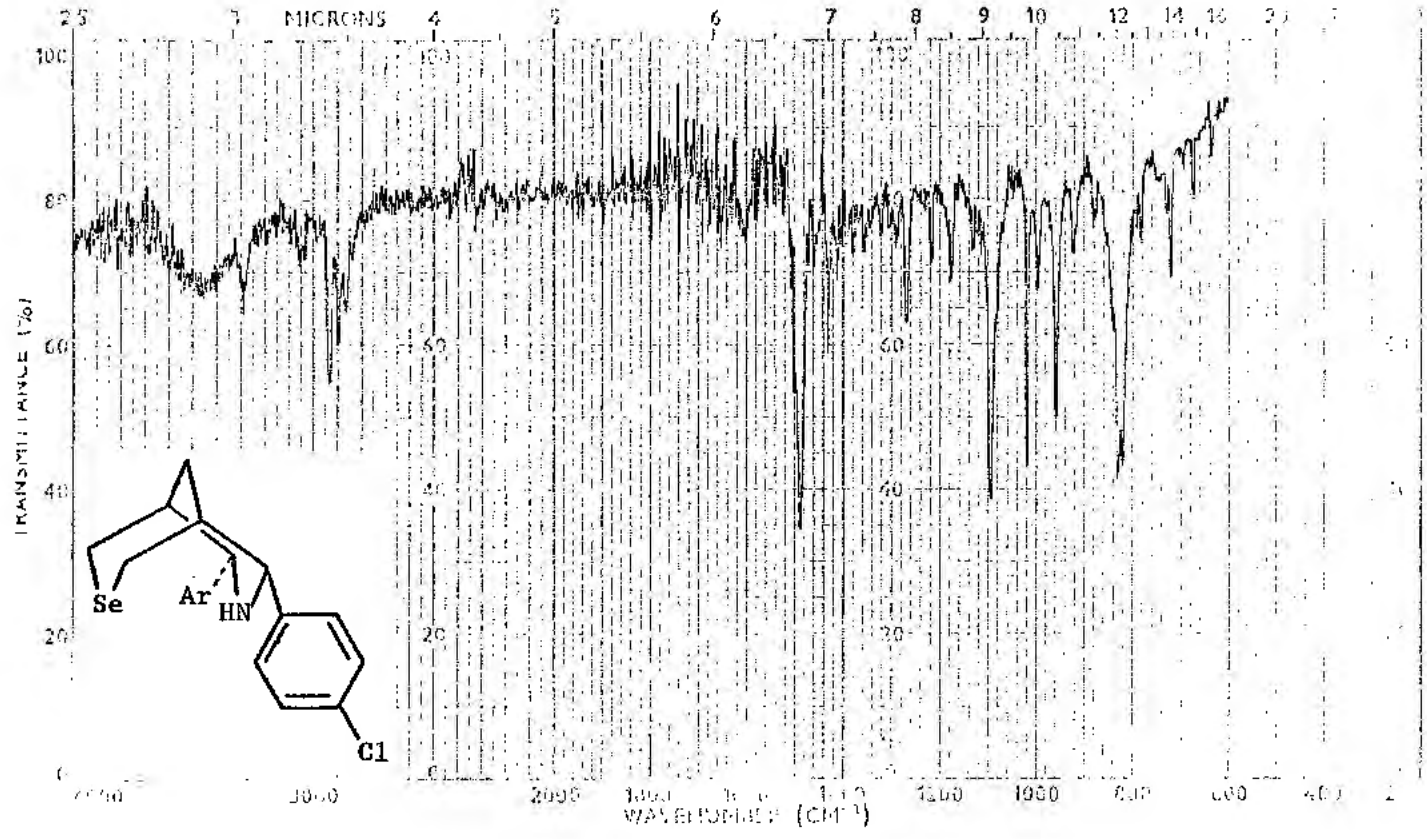
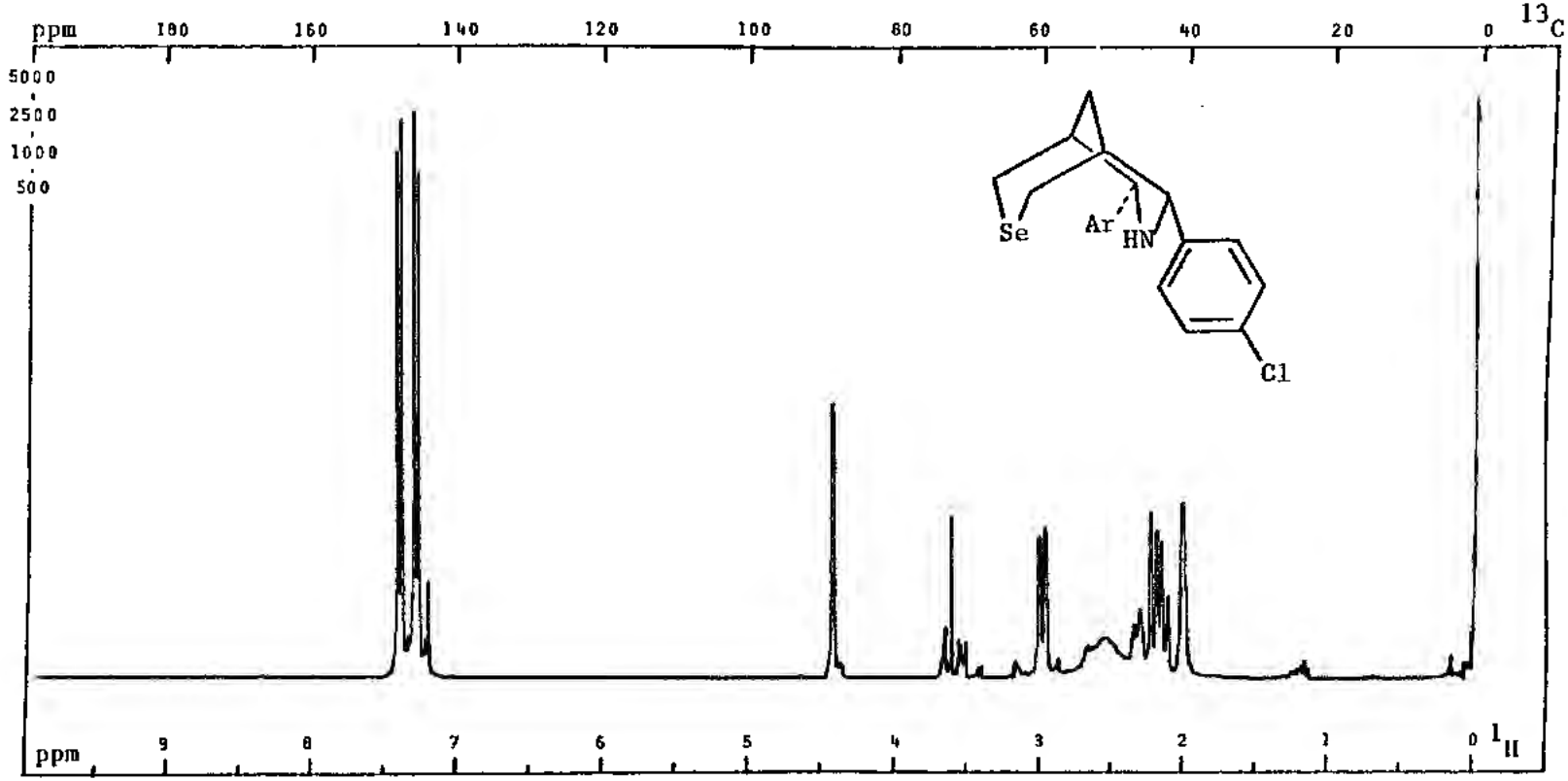


PLATE LXV. ^{1}H NMR SPECTRUM OF 35i

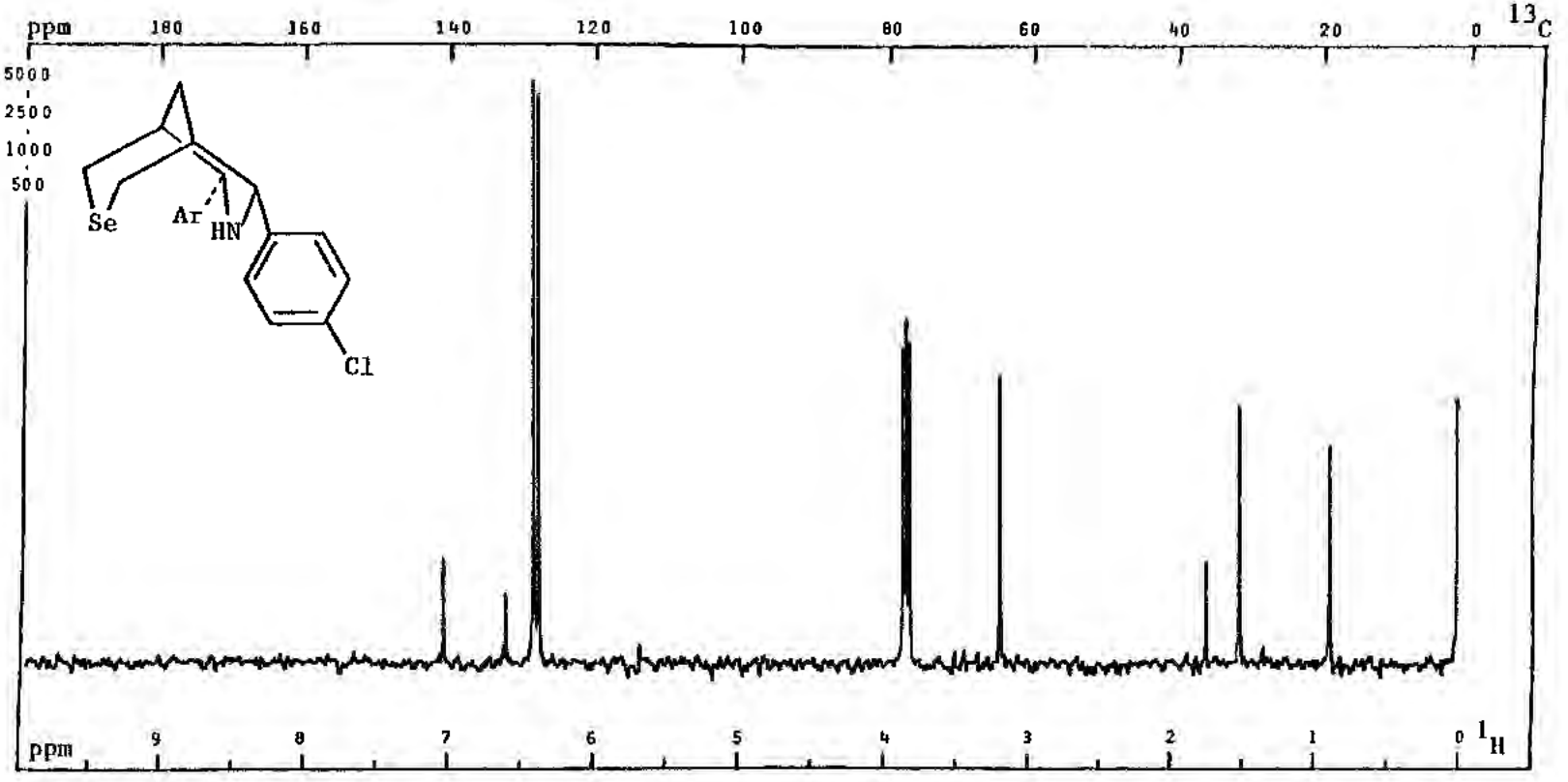


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT 8

Size: 12 K; PW/RF: 5 µs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LXVI. ^{13}C NMR SPECTRUM OF **35i**

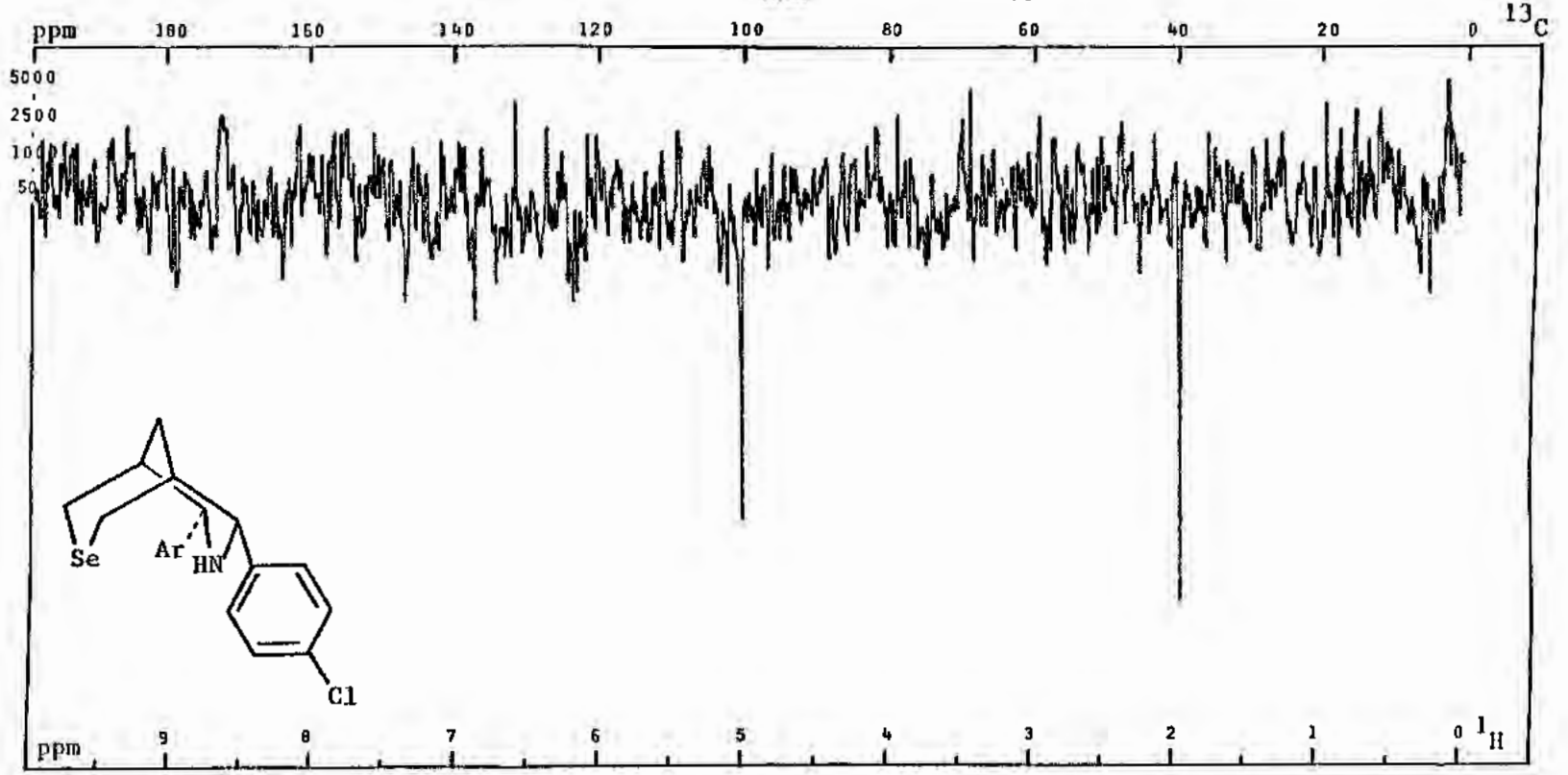


PFT X CW _ ; Solvent: $CDCl_3$; SF: 75.4 MHz; WC: 15085 Hz; T: 25 °C; NT: 240 .

Size: 16 K; PW/RF: 12 µs/dB; TO: 1500 Hz; FB: Hz; Lock: ^2D ; D1,D5: 4 s.

DC: X, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE LXVII. ^{15}N NMR SPECTRUM OF 35i

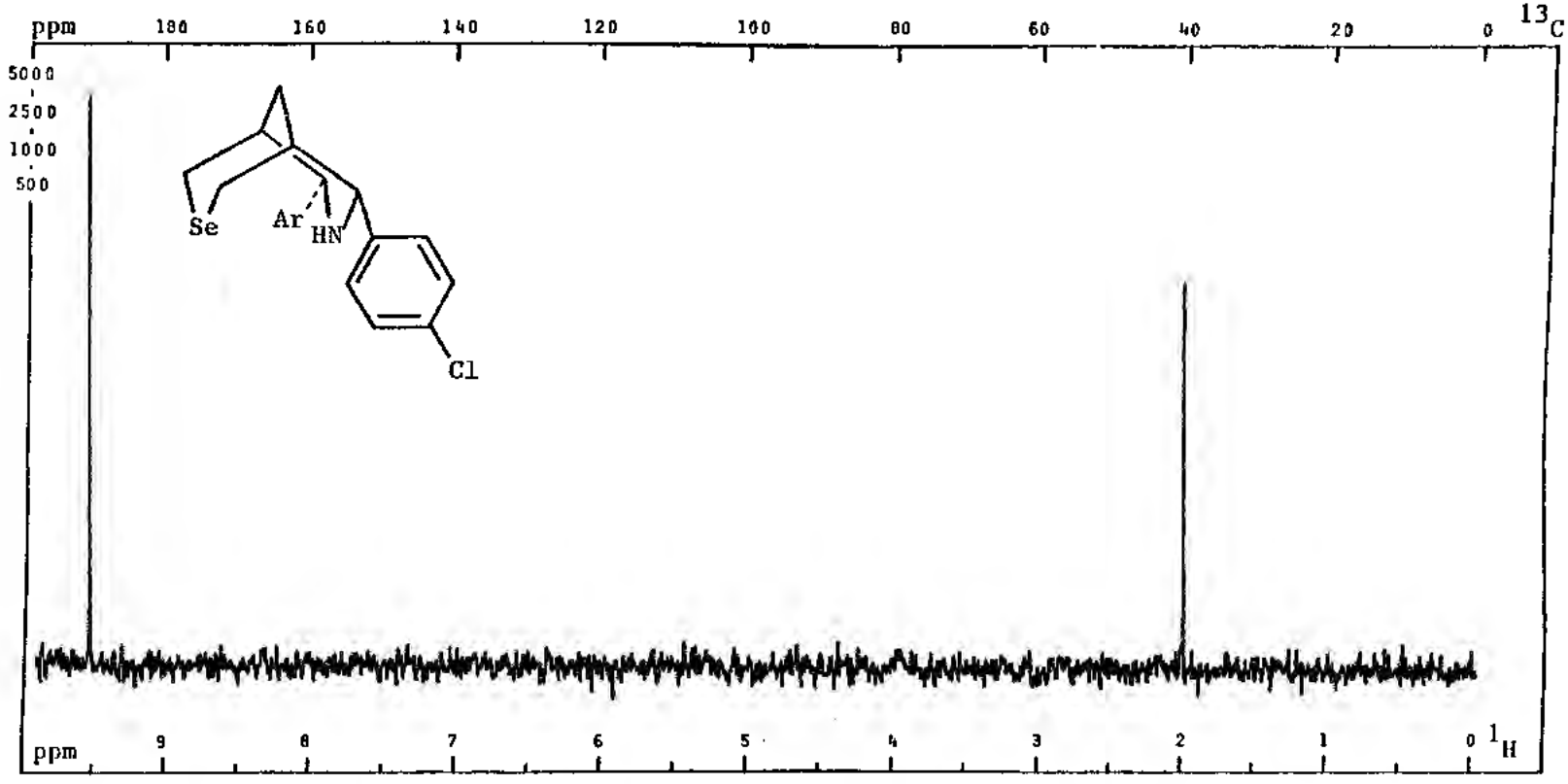


PFT X CW _ : Solvent: $CDCl_3$; SF: 30.406 MHz; WC:3040.6 Hz; T: 25 °C; NT: 6000

Size: 12 K; PW/RF: 40 µs/dB; TO:-11600 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 8 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LXVIII. ^{77}Se NMR SPECTRUM OF **35i**



PFT X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 200 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 0 Hz; FB: Hz; Lock: ^2D ;D1,D5: 15 s.

DC: Y, N ; Gated Off:A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE LXIX. IR SPECTRUM OF **36a**

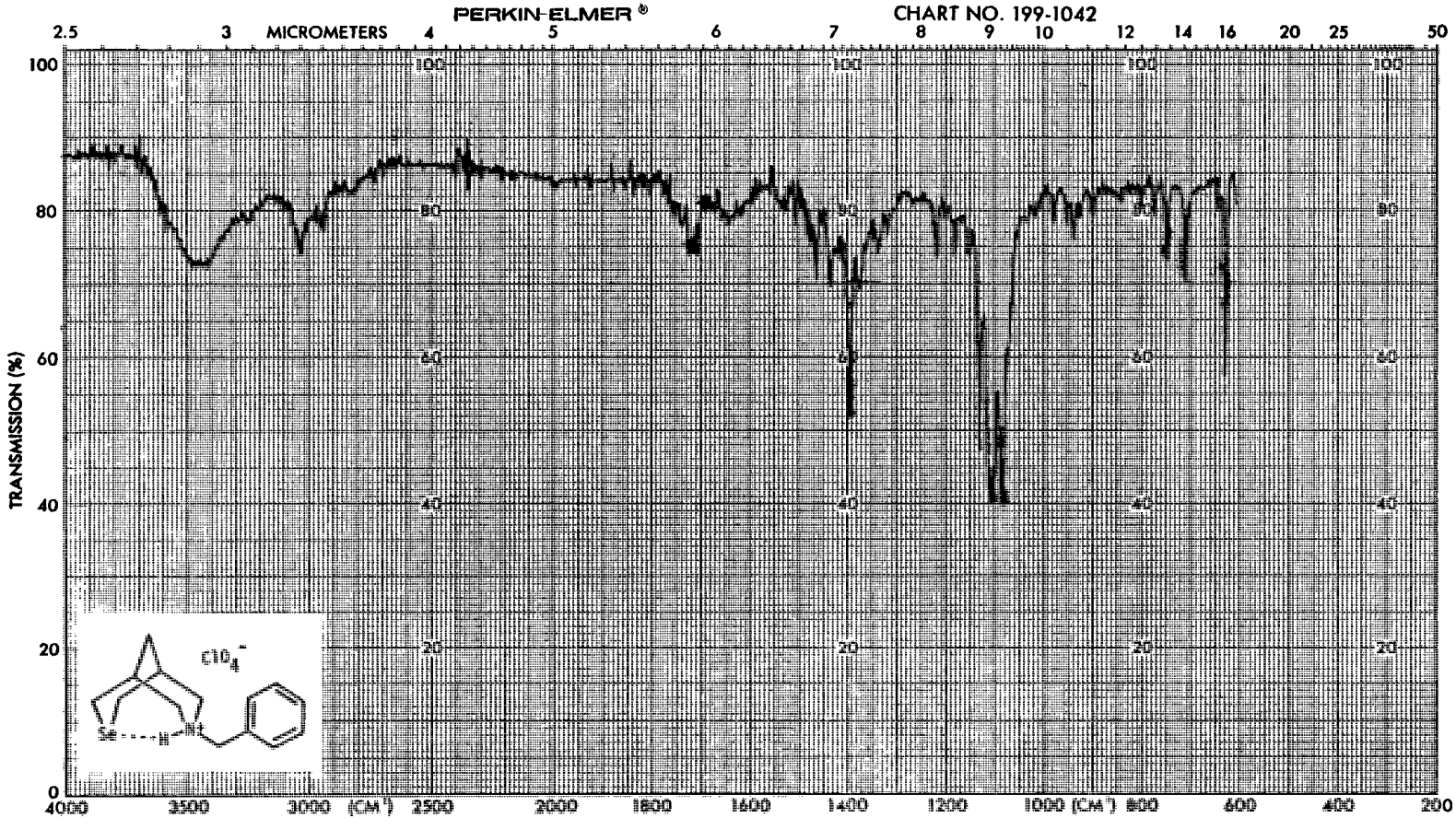
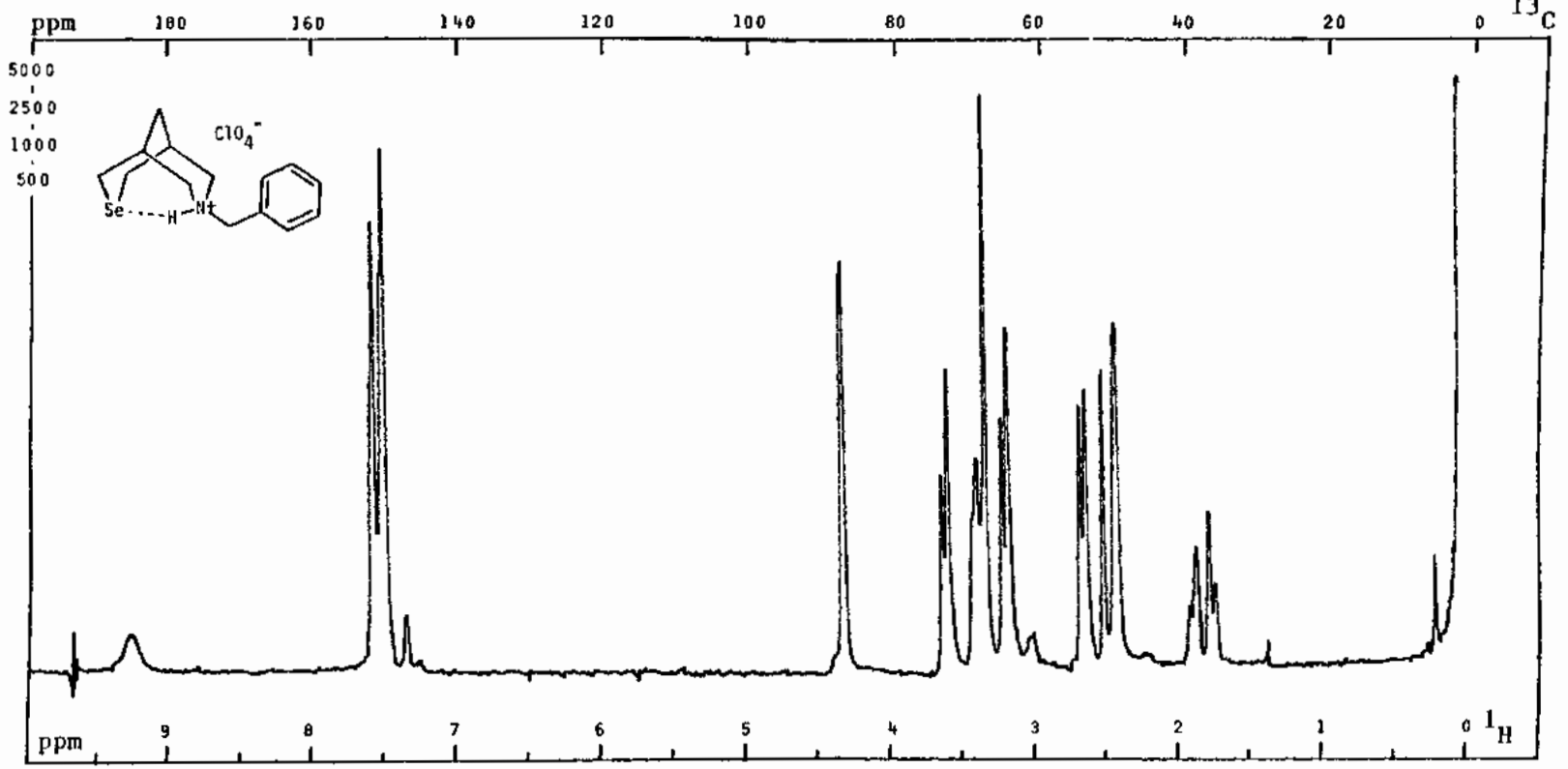


PLATE LXX. ^{1}H NMR SPECTRUM OF **36a**

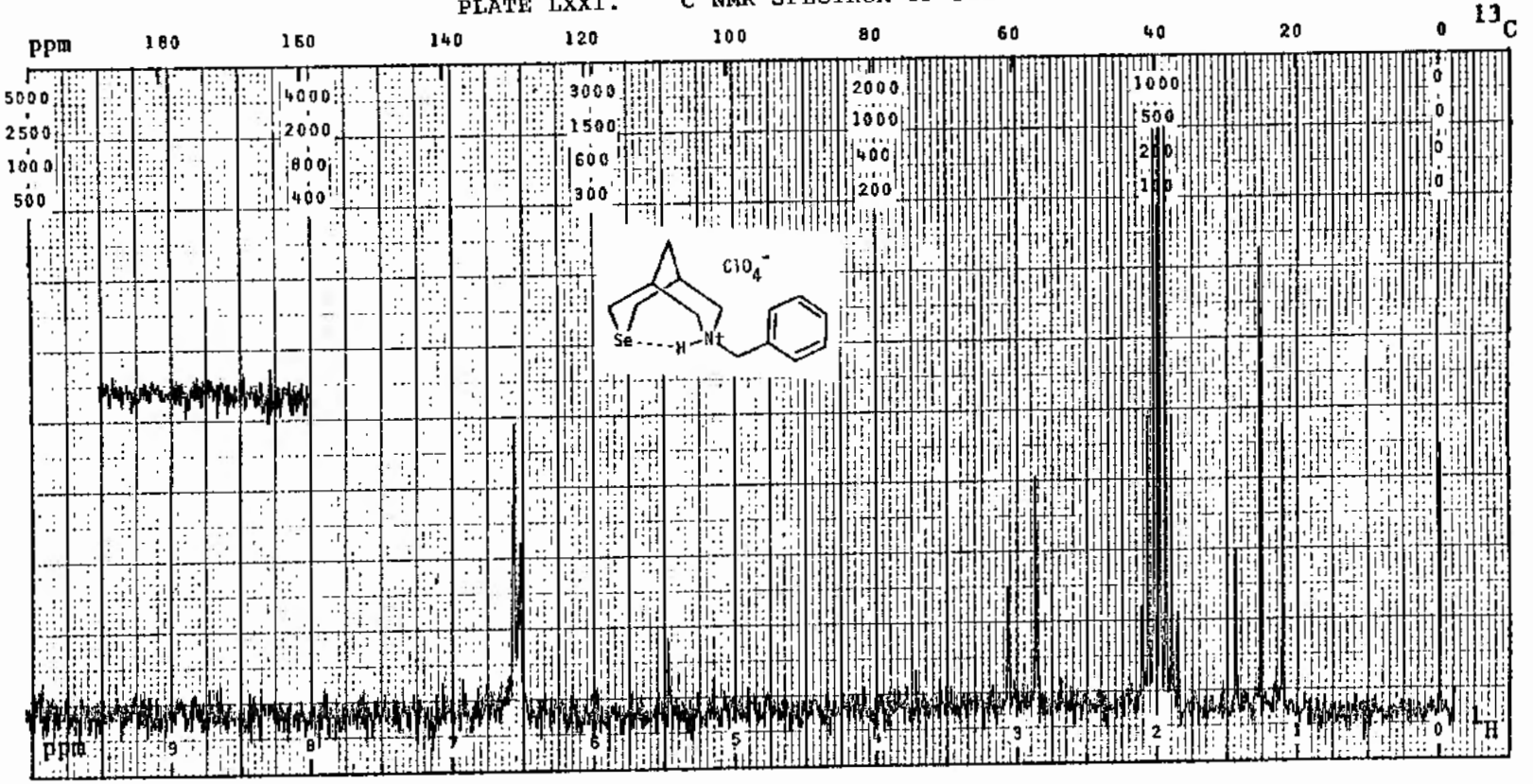


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 299.94 MHz; WC: 3000 Hz; T: 28 °C; NT: 24

Size: 12K; PW/RF: 5 μs/dB; TO: 1500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LXXI. ^{13}C NMR SPECTRUM OF 36a

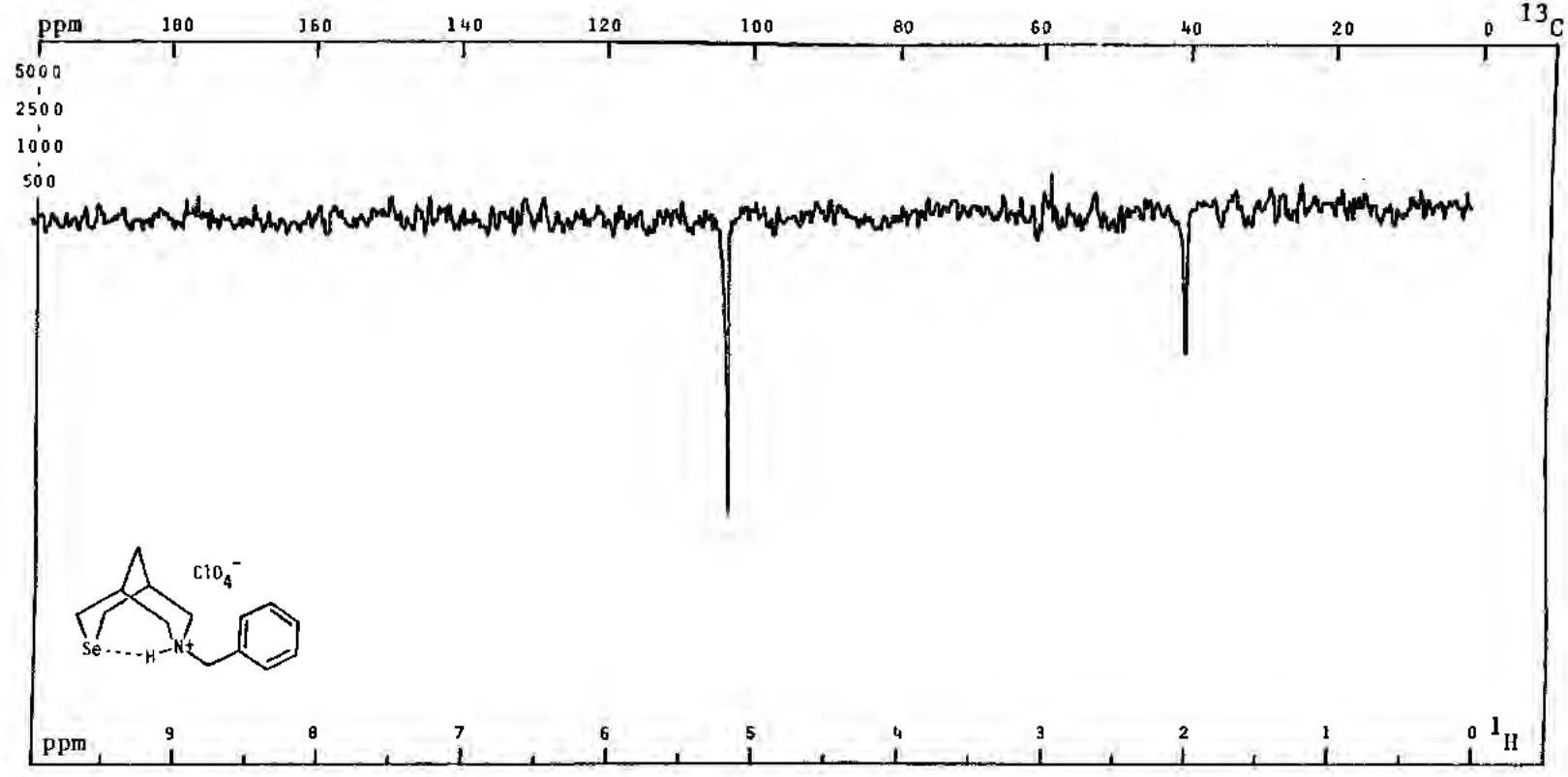


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 25.2 MHz; WC:6000 Hz; T: 28 °C; NT:4000 .

Size: 8 K; PW/RF: 10 µs/dB; TO: 35201 Hz; FB: Hz; Lock: ^2D ; D1,D5 : 5 s.

DC: Y, N ; Gated Off: A or D ; DO: 45316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE LXXII. ^{15}N NMR SPECTRUM OF **36a**

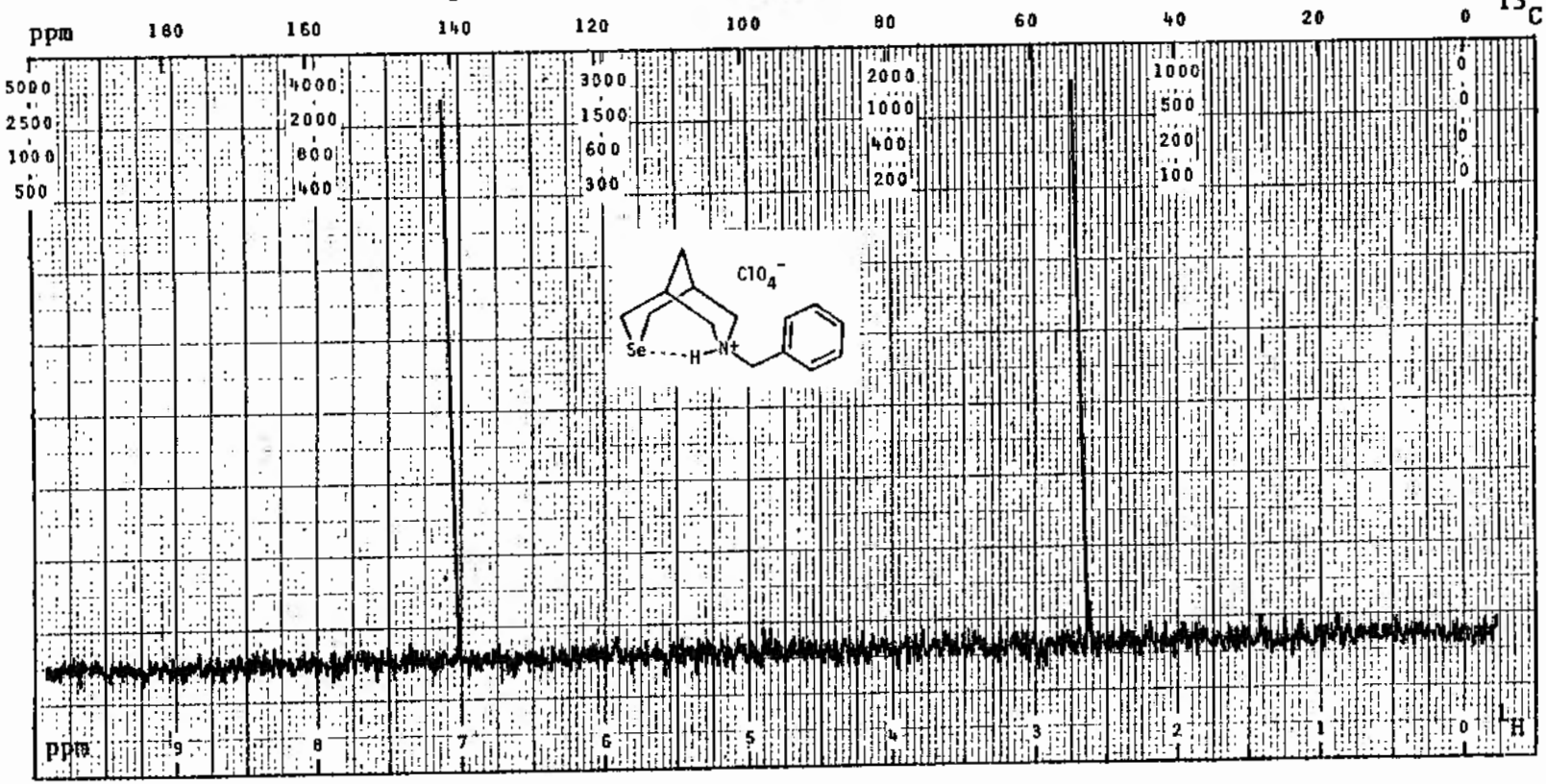


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 30.401 MHz; WC: 3040.6Hz; T: 25 °C; NT: 13400 .

Size: 12 K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^2D ;D1,D5: 8.00 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LXXIII. ^{77}Se NMR SPECTRUM OF 36a



PFT X CW _ ; Solvent: DMSO-d_6 ; SF:57.22 MHz; WC: 50,000Hz; T:25 °C; NT:80 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^2D ; D1,D5 : 20.0 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE LXXIV. IR SPECTRUM OF **36b**

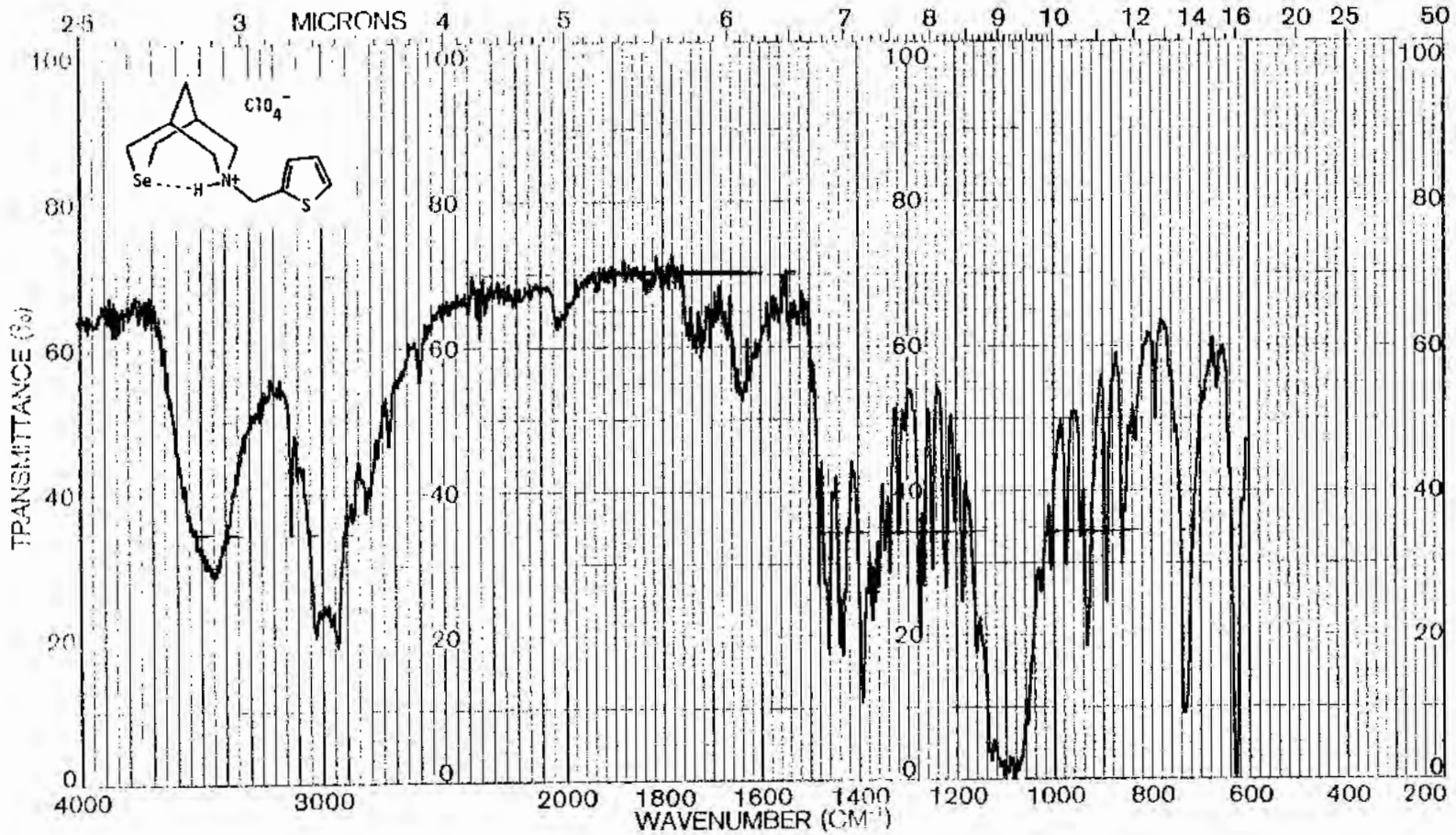
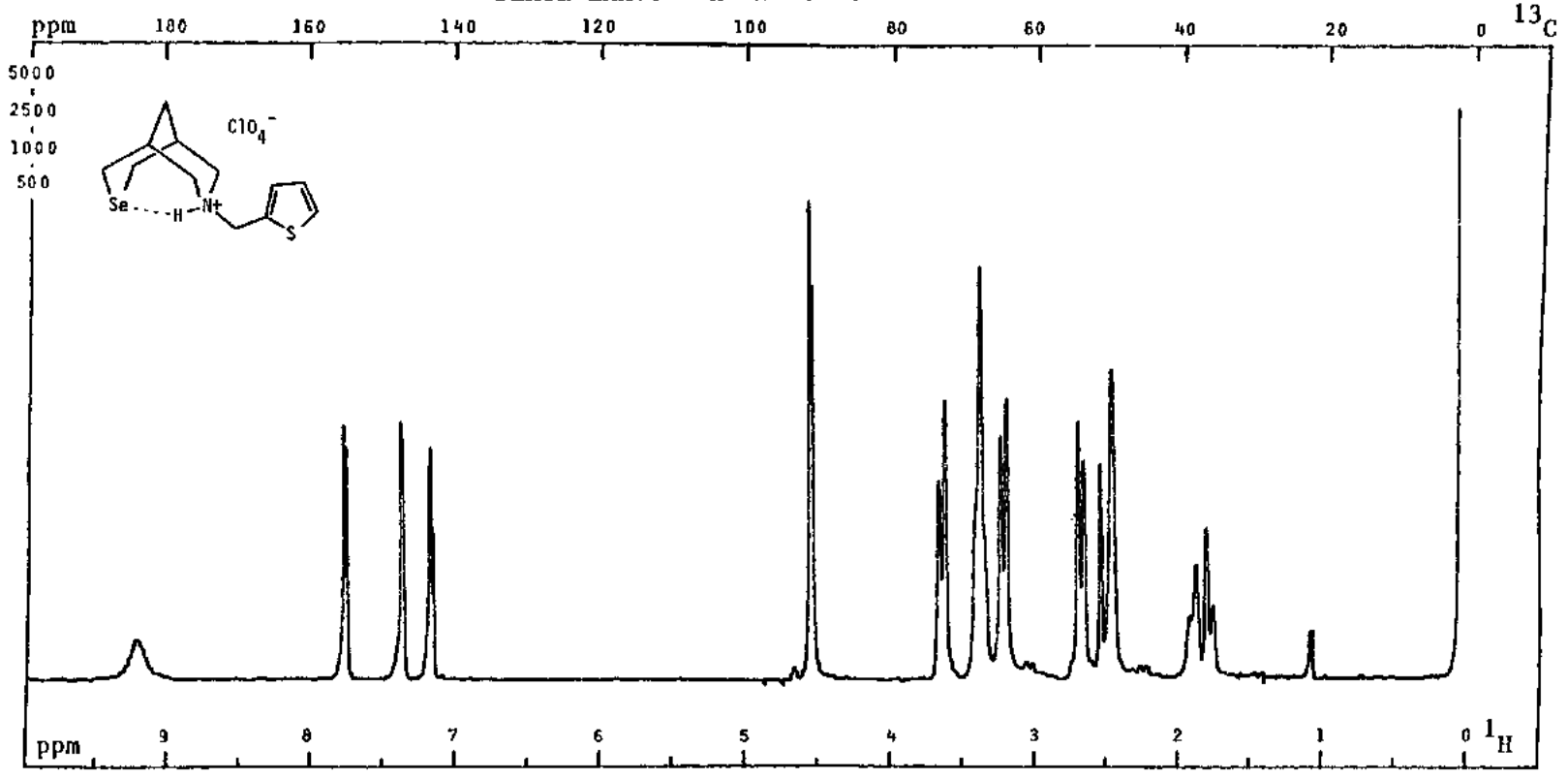


PLATE LXXV. ^{1}H NMR SPECTRUM OF **36b**

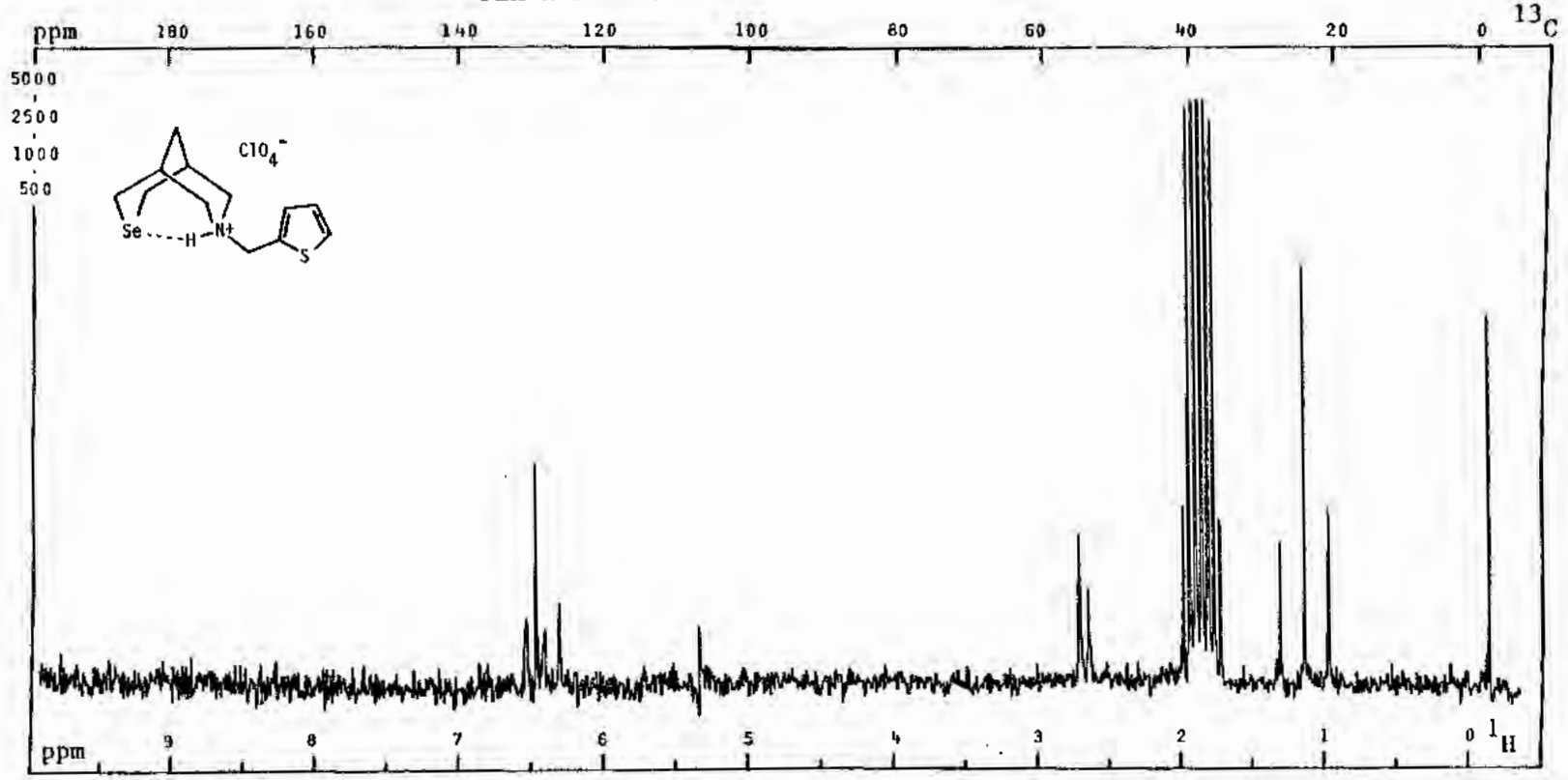


PFT X CW _ ; Solvent: dmso-d_6 ; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 8 .

Size: 12 K; PW/RF: 5 µs/dB; TO: 1500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LXXVI. ^{13}C NMR SPECTRUM OF 36b

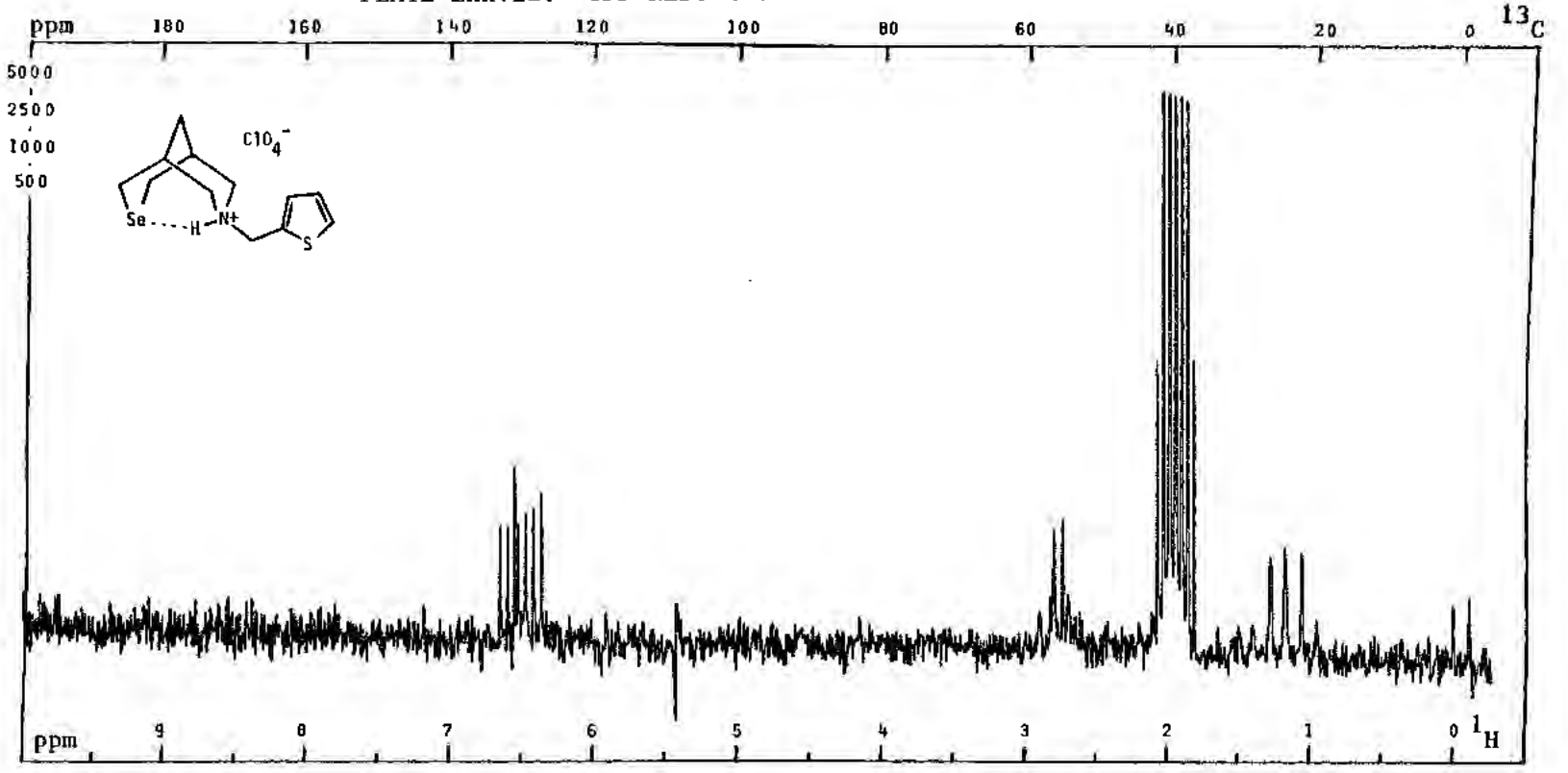


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 1000 .

Size: 8 K; PW/RF: 10 µs/dB; TO: 35201 Hz; FB: Hz; Lock: ^2D ; D1,D5: 5 s.

DC: Y, N ; Gated Off:A or D ; DO: 45316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE LXXVII. OFF RESONANCE ^{13}C NMR SPECTRUM OF **36b**

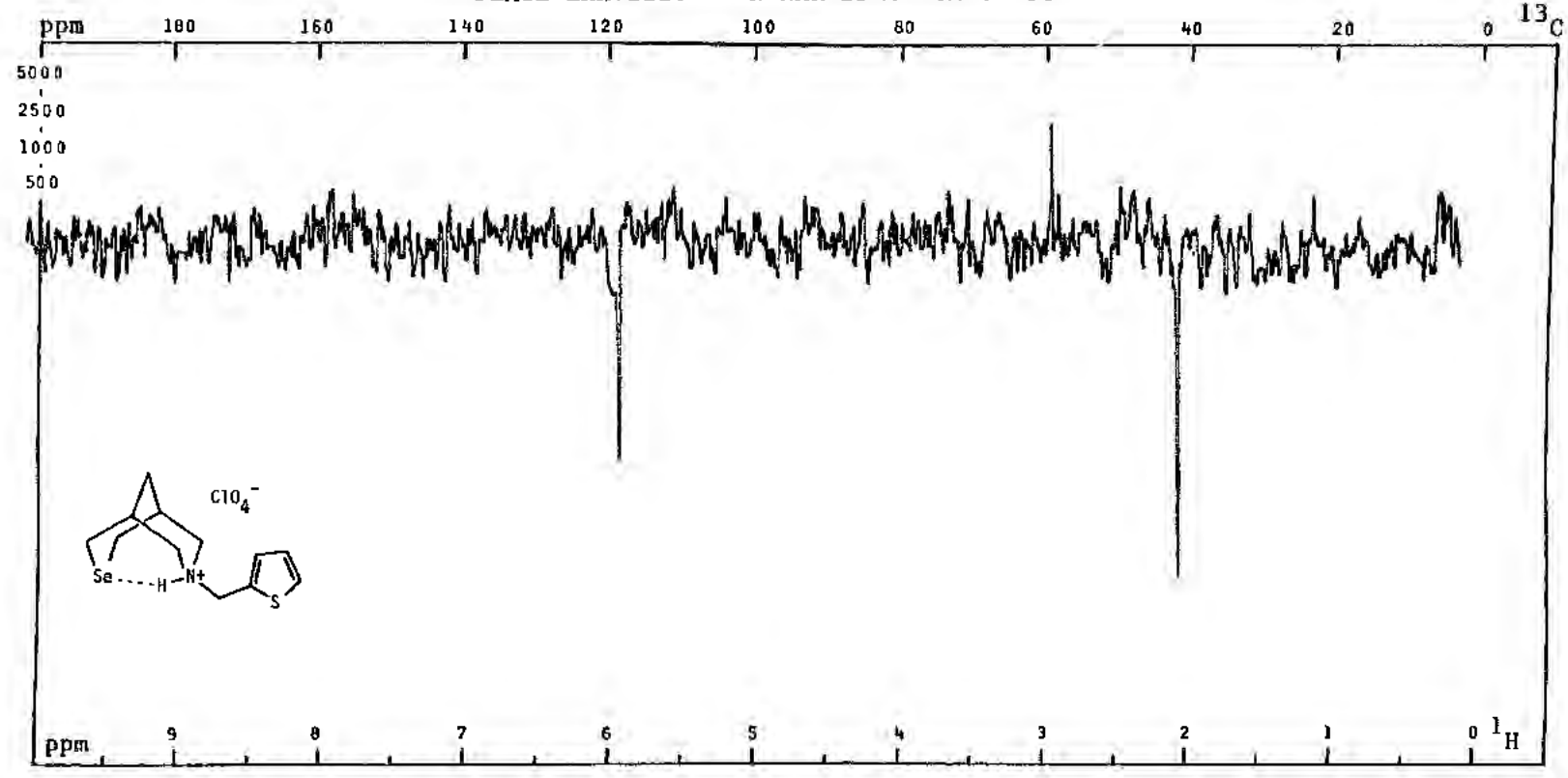


PFT X CW _ ; Solvent: $DMSO-d_6$; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 2000 .

Size: 8 K; PW/RF: 10 μs/dB; TO: 35201 Hz; FB: Hz; Lock: ^2D ; D1,D5: 5 s.

DC: Y, N ; Gated Off: A or D ; DO: 46316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE LXXVIII. ^{15}N NMR SPECTRUM OF **36b**

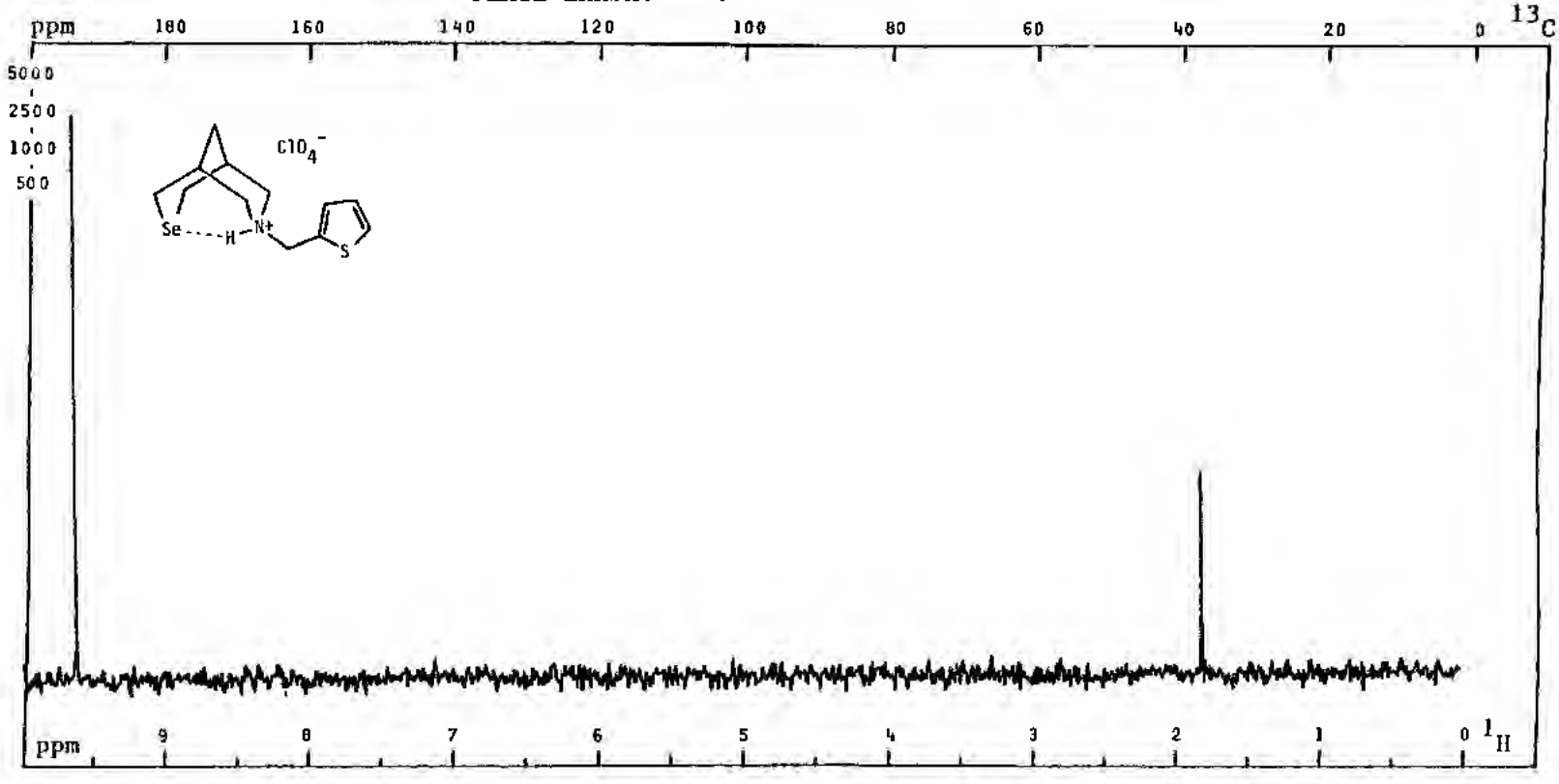


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 30.406 MHz; WC: 3040.6 Hz; T: 25 °C; NT: 4200 .

Size: 12 K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^2D ; D1,D5: 8 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LXXIX. ^{77}Se NMR SPECTRUM OF **36b**



PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 104 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^2D ; D1,D5: 20 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE LXXX. IR SPECTRUM OF **36c**

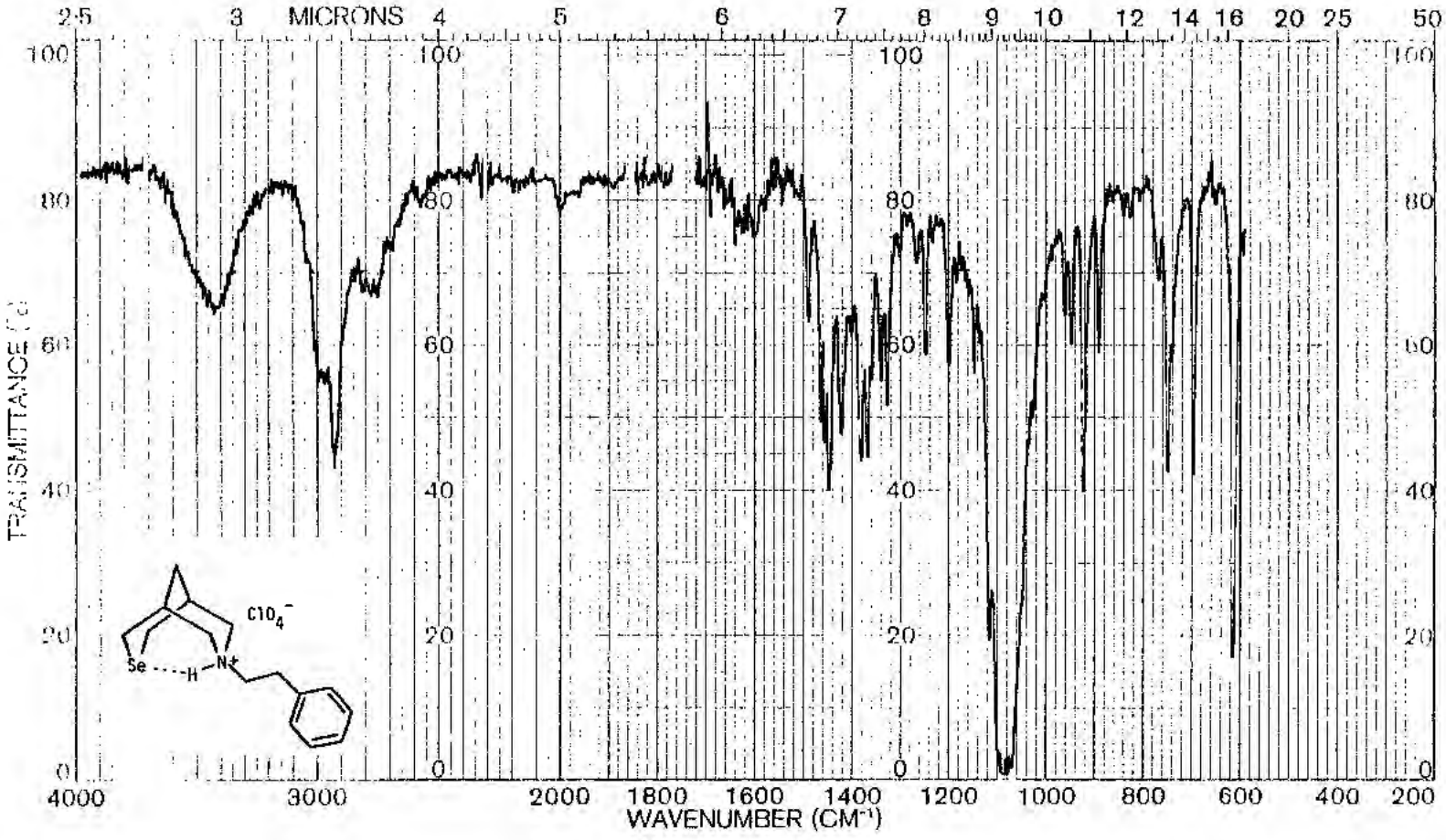
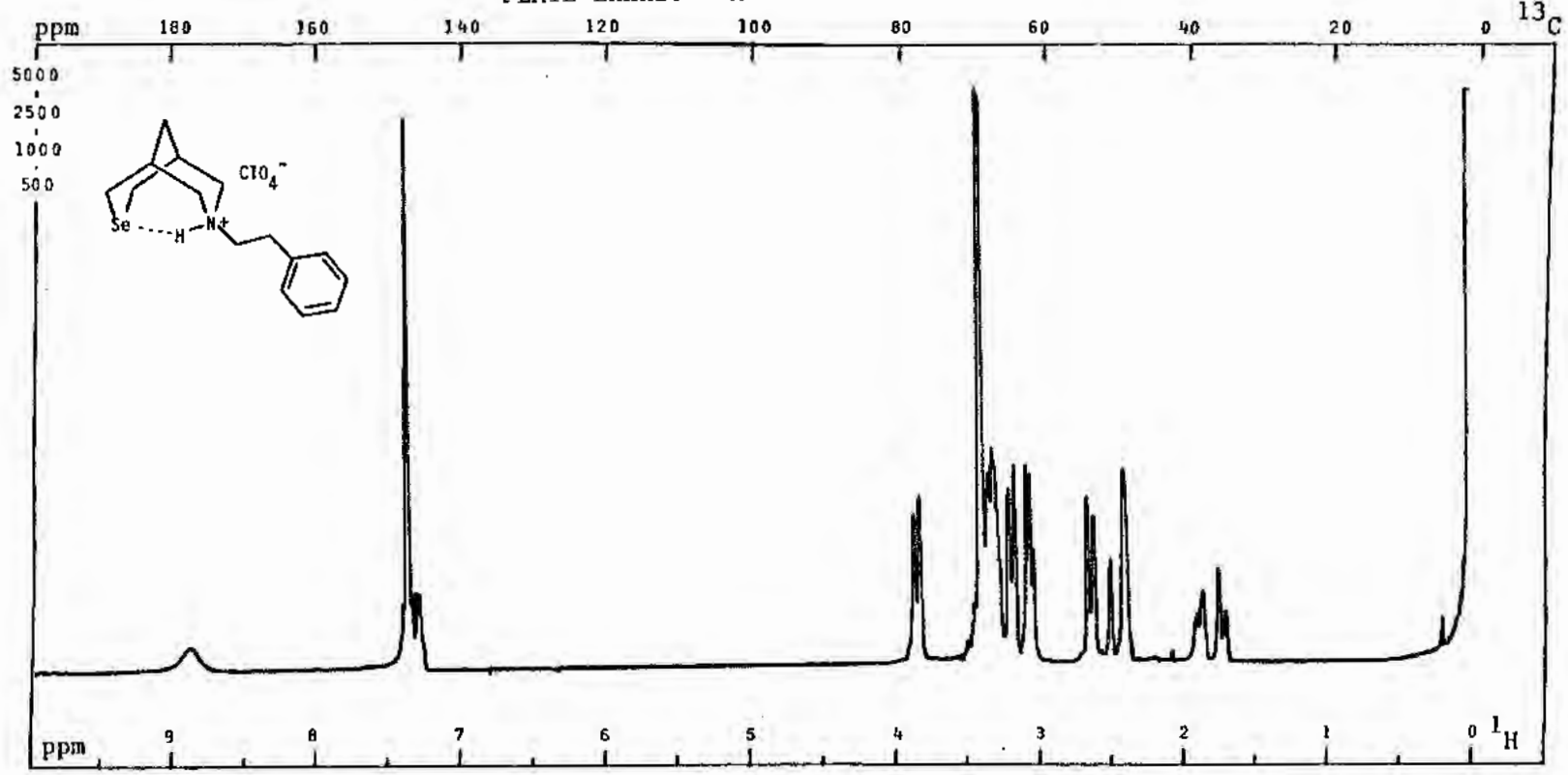


PLATE LXXXI. ^{1}H NMR SPECTRUM OF **36c**

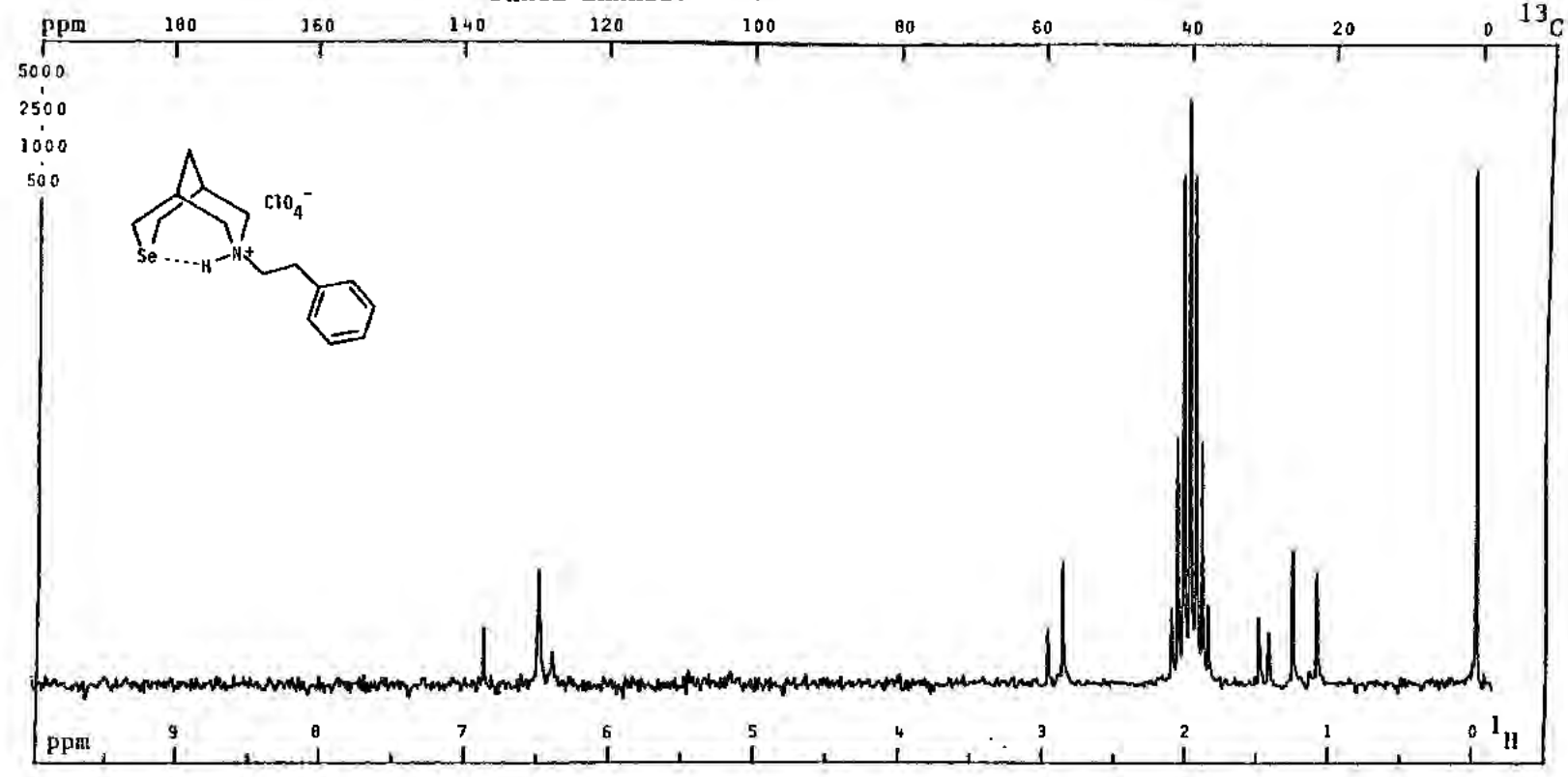


PFTX_ CW _ ; Solvent: DMSO-d_6 ; SF: 299.94MHz; WC: 3000 Hz; T: 25 °C; NT: 16

Size: 12 K; PW/RF: 8 µs/dB; TO: 1500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LXXXII. ^{13}C NMR SPECTRUM OF **36c**

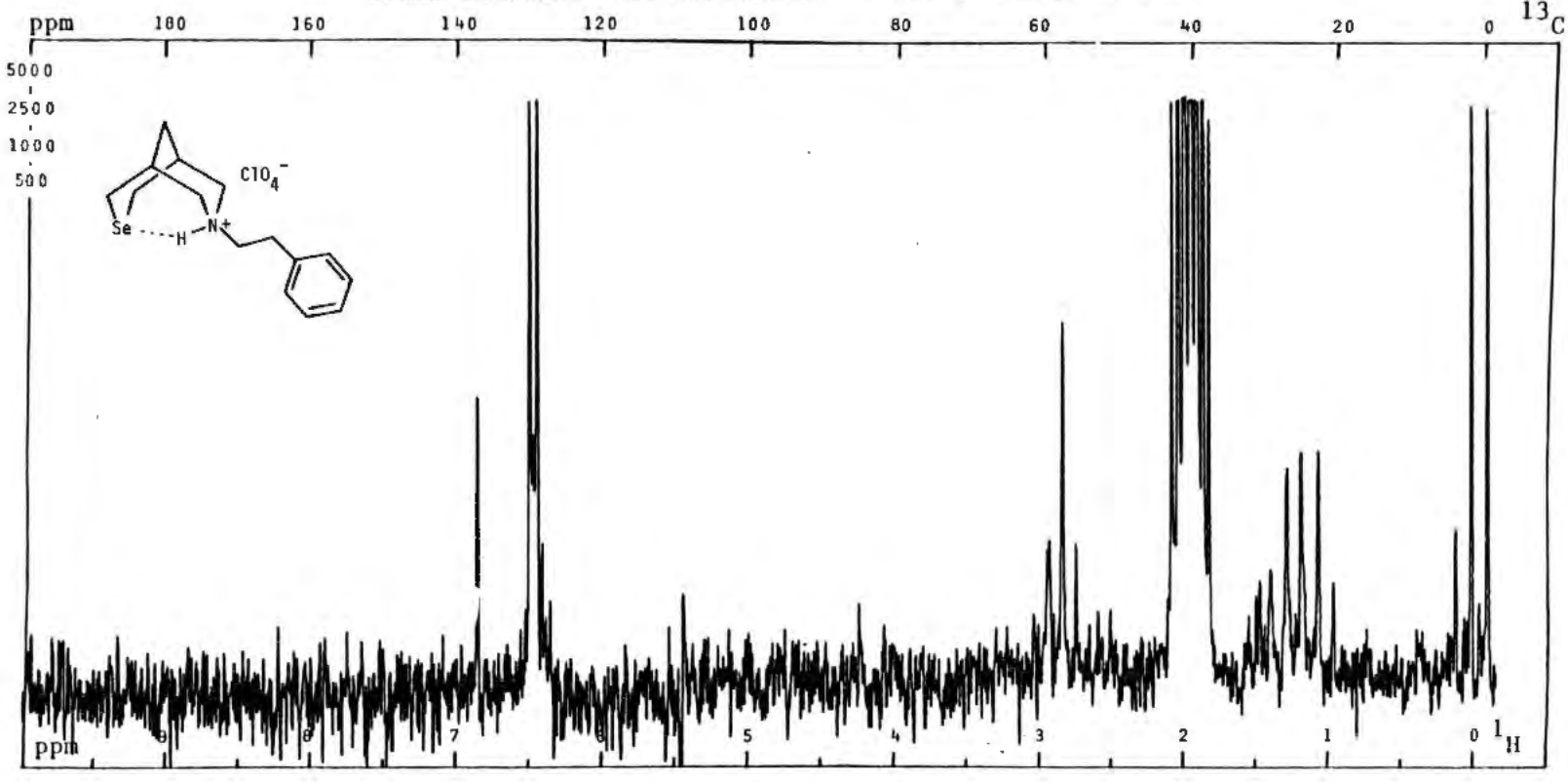


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 6168 .

Size: 8 K; PW/RF: 10 µs/dB; TO: 35101 Hz; FB: 3K Hz; Lock: ^2D ; D1,D5: 5 s.

DC: Y, N ; Gated Off:A or D ; DO: 45316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE LXXXIII. OFF RESONANCE ^{13}C NMR SPECTRUM OF **36c**

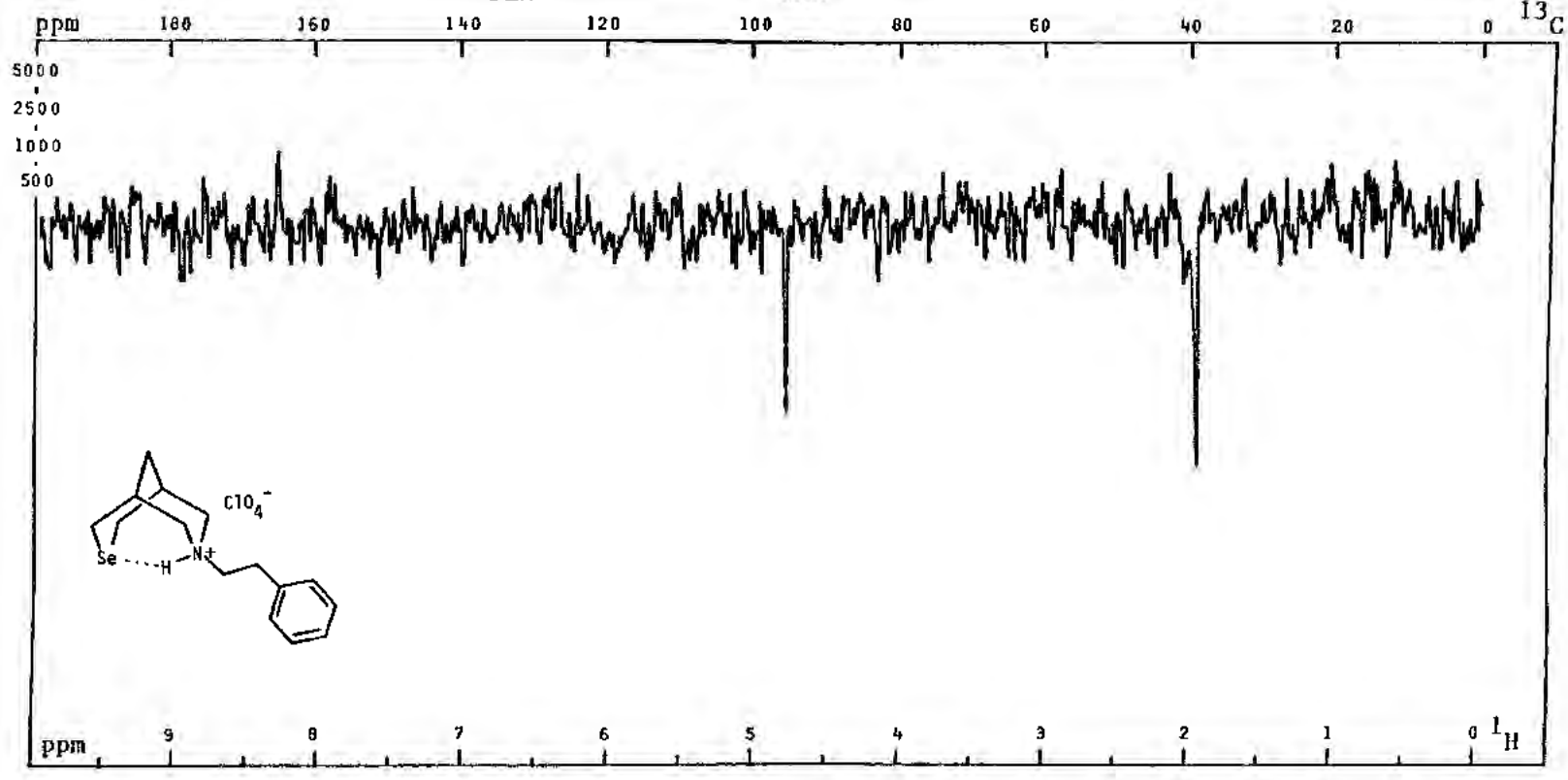


PFT X CW _ ; Solvent: $DMSO-d_6$; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 1600

Size: 8 K; PW/RF: 10 μs/dB; TO: 35201 Hz; FB: 3K Hz; Lock: ^2D ; D1,D5: 5 s.

DC: Y, N ; Gated Off: A or D ; DO: 46316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE LXXXIV. ^{15}N NMR SPECTRUM OF **36c**

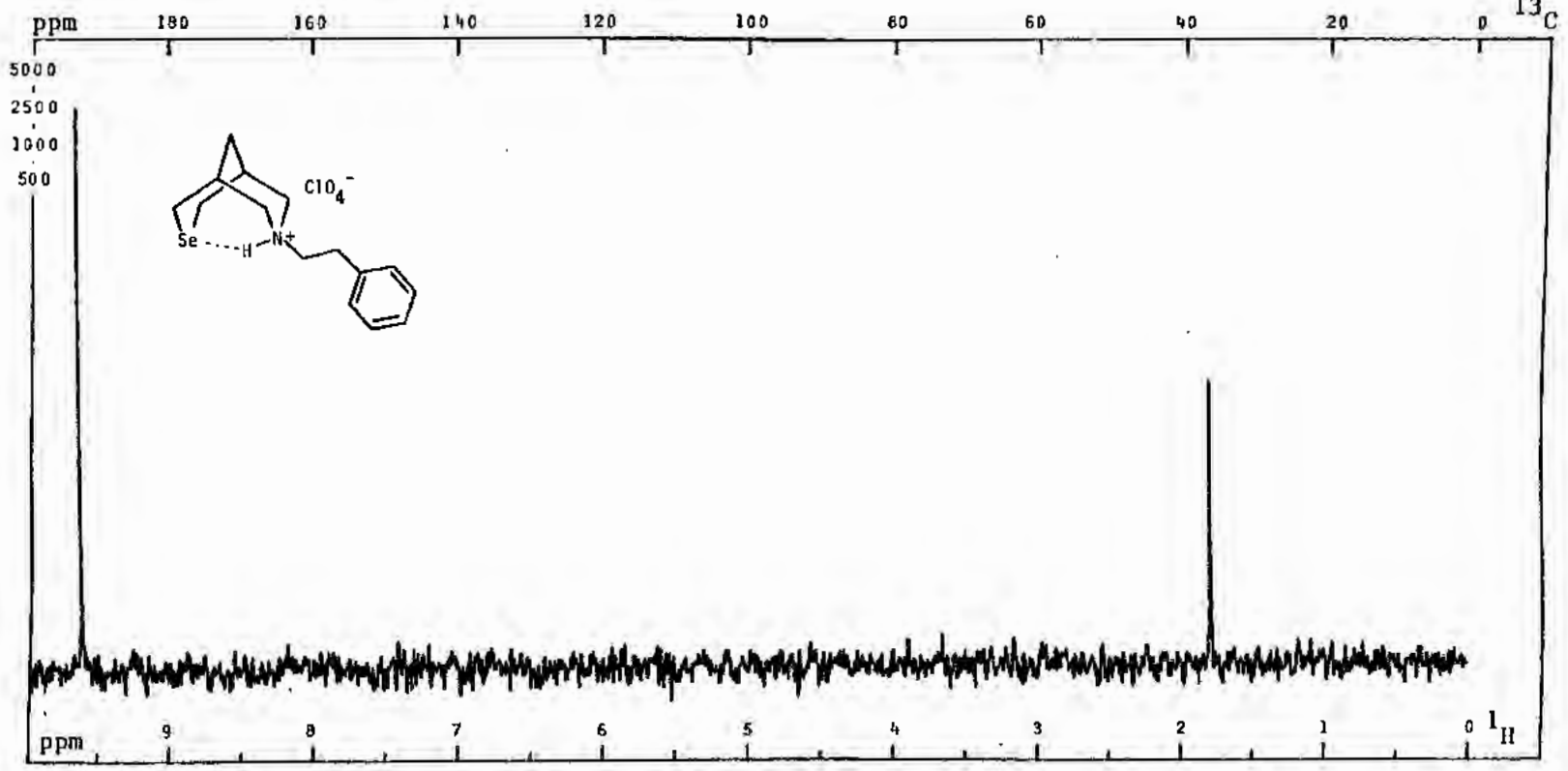


PFT X CW _ ; Solvent:DMSO-d_6 ; SF: 30.406 MHz; WC:3040.6 Hz; T:25 °C; NT: 6000 .

Size: 12 K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^{2}D ;D1,D5: 8 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LXXXV. ^{77}Se NMR SPECTRUM OF **36c**



PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 57.22 MHz; WC:28610 Hz; T: 25 °C; NT: 108

Size:32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^2D ;D1,D5: 15 s.

DC: Y, N ; Gated Off:A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE LXXXVI. IR SPECTRUM OF **36d**

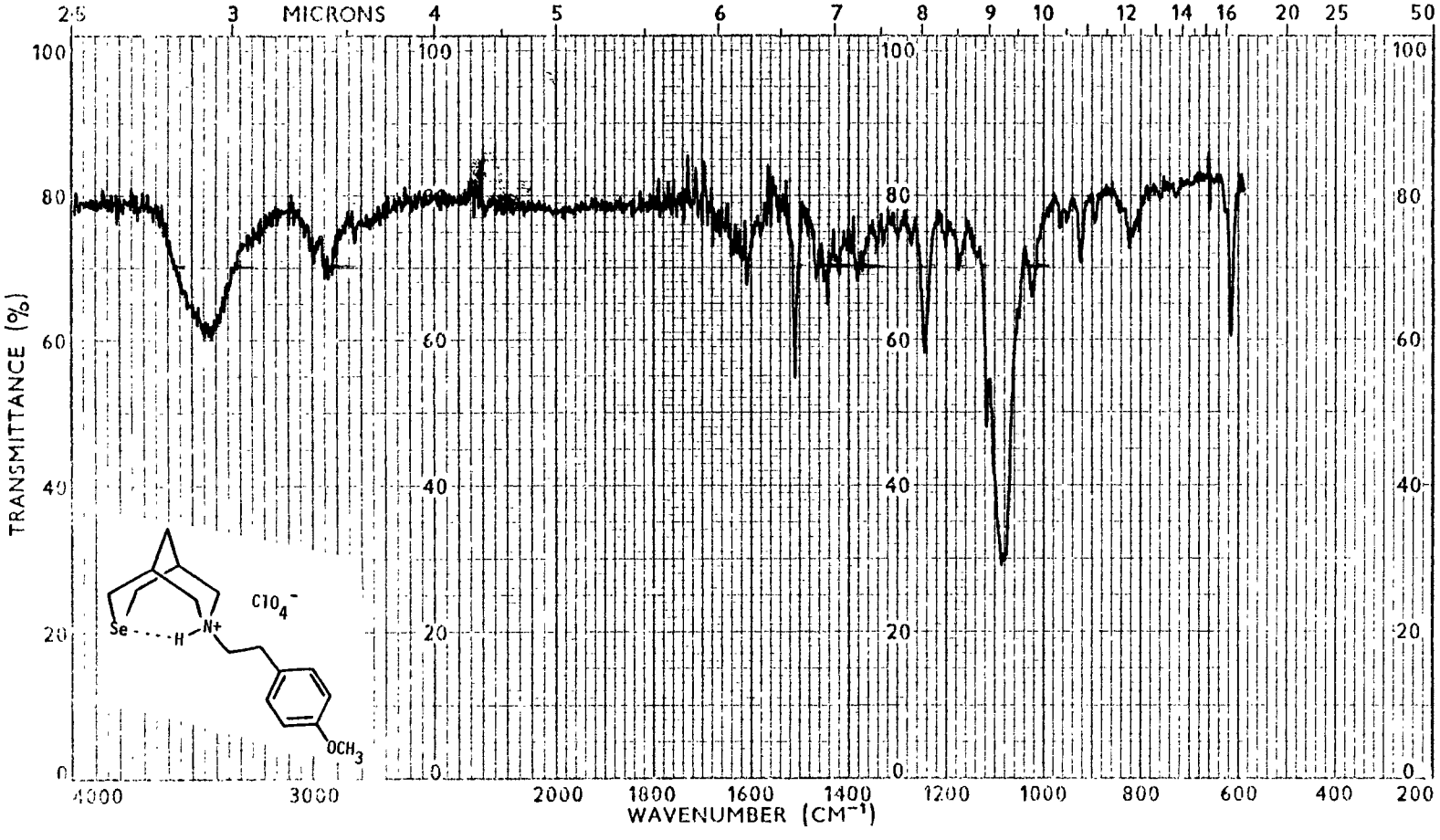
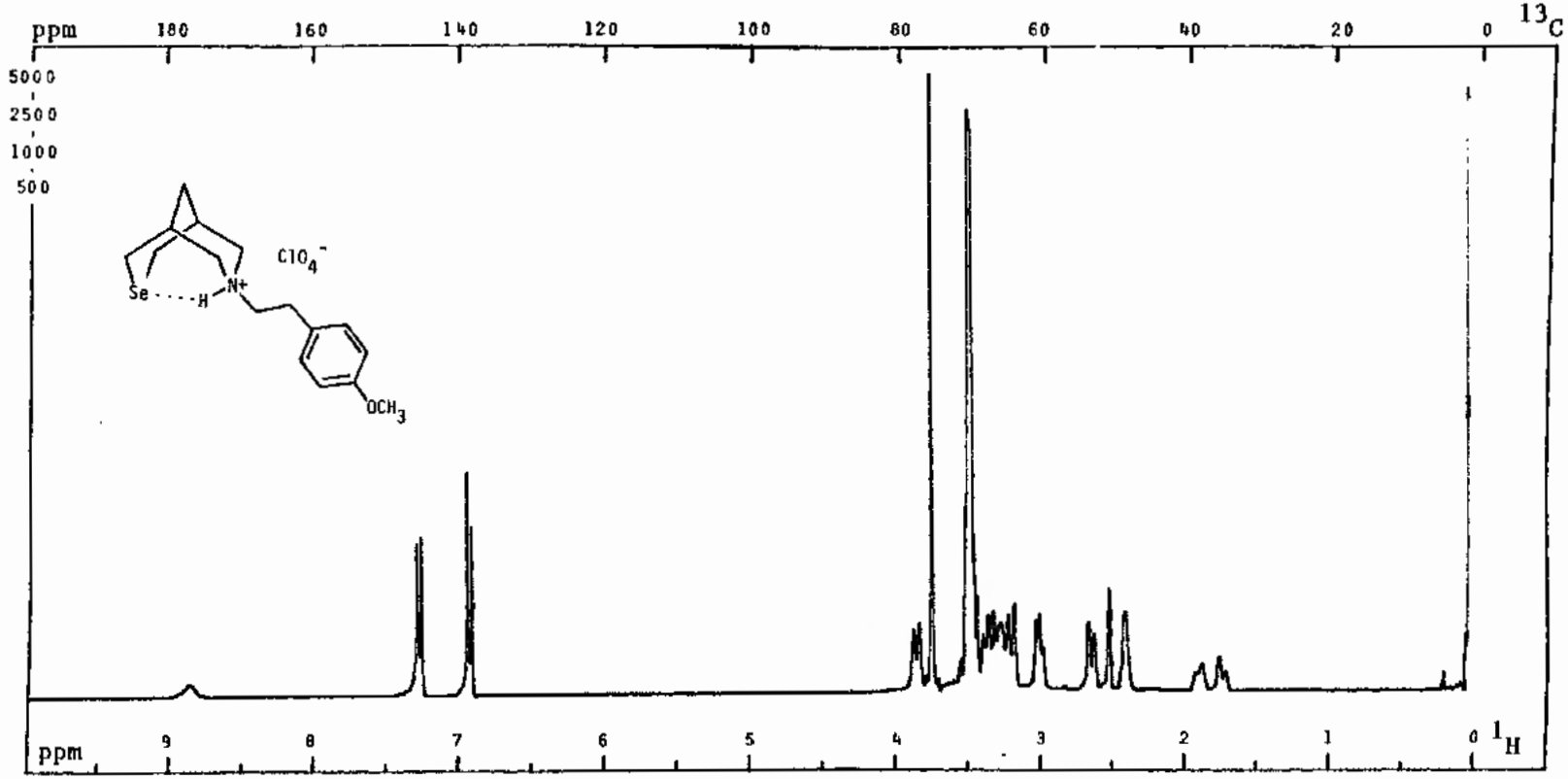


PLATE LXXXVII. ^{1}H NMR SPECTRUM OF **36d**

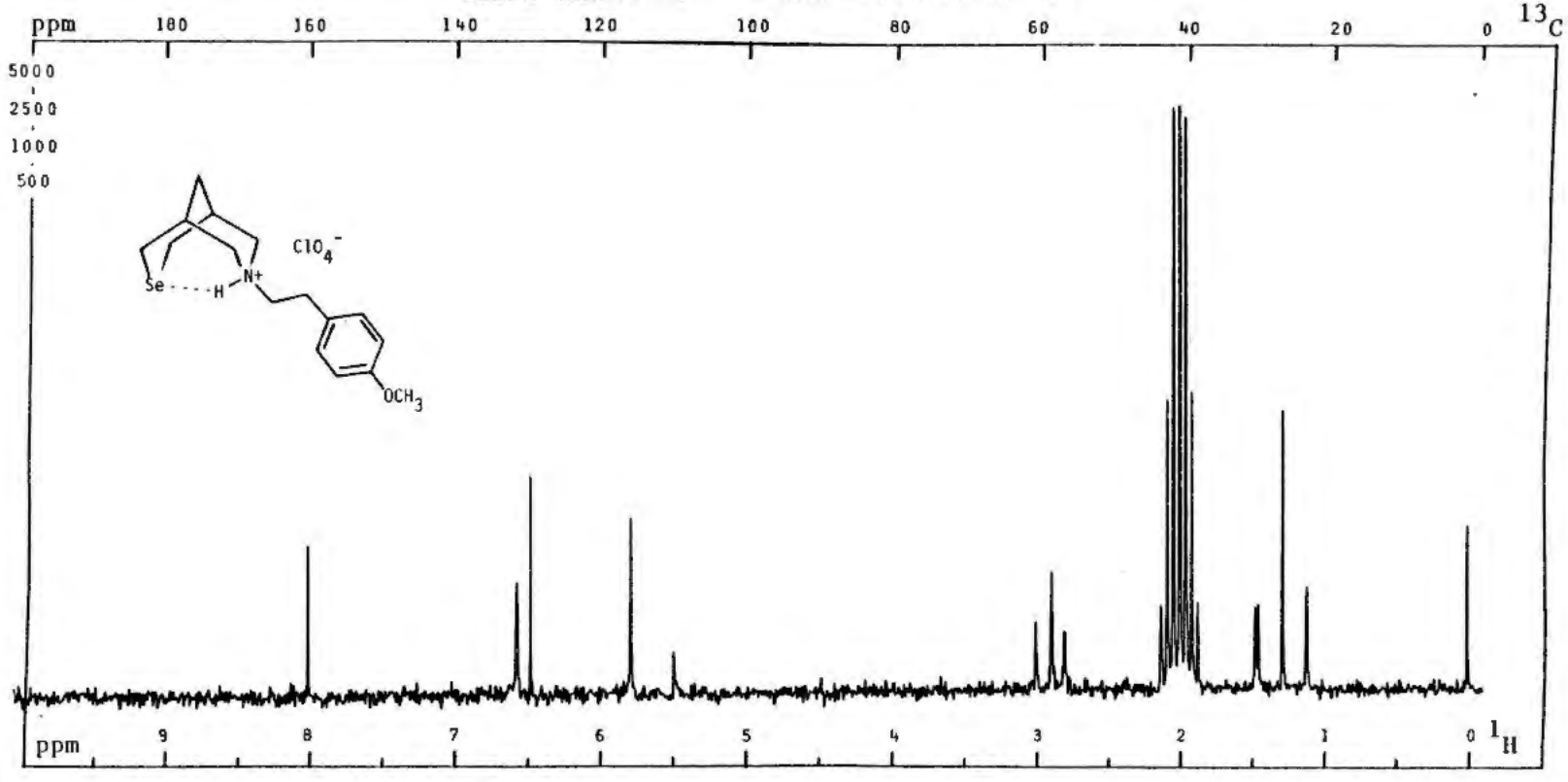


PFT X CW _ ; Solvent: DMS)-d_6 ; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 16

Size: 12K; PW/RF: 5 µs/dB; TO: 1500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE LXXXVIII. ^{13}C NMR SPECTRUM OF **36d**

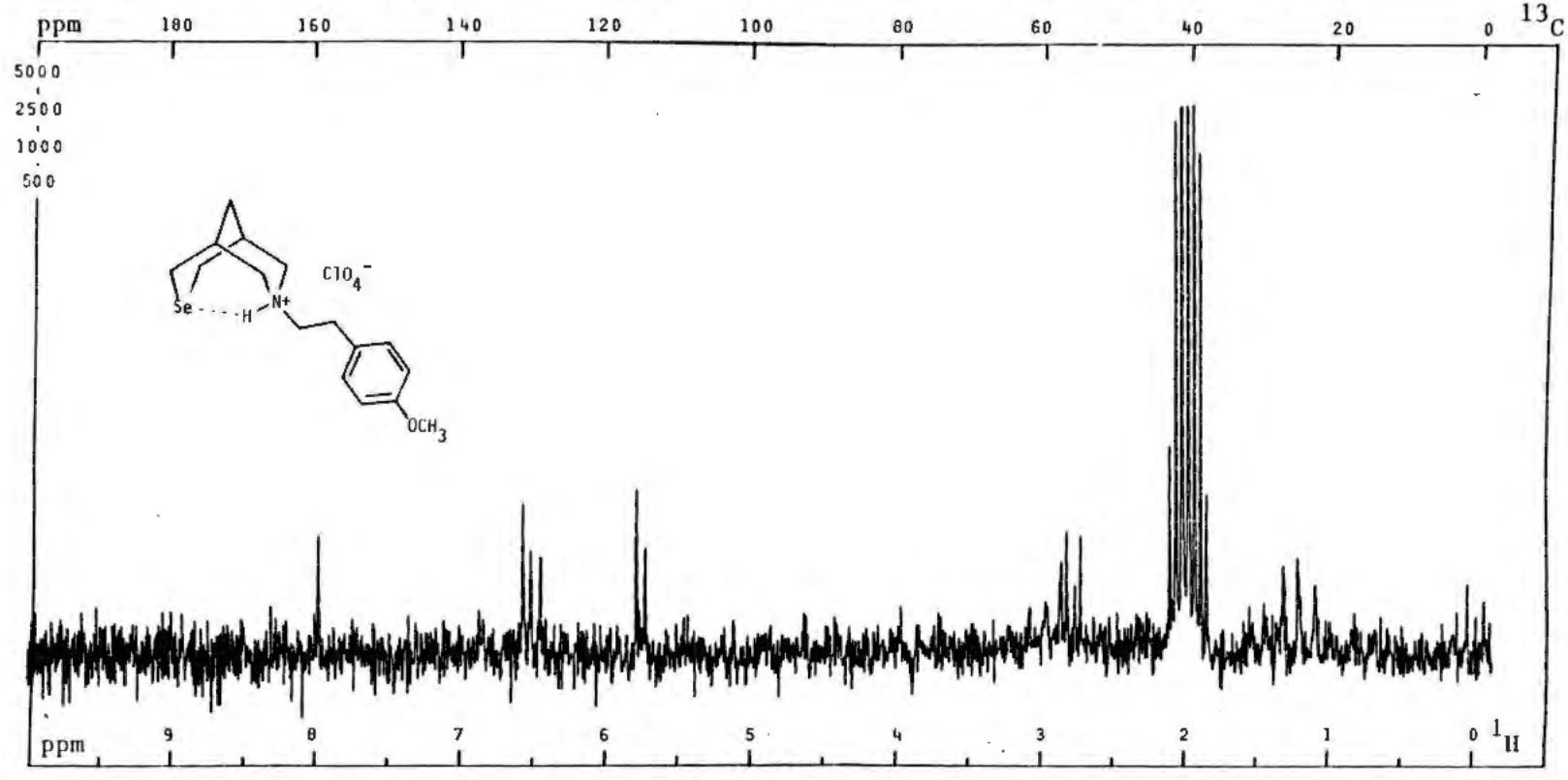


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 6000 .

Size: 8 K; PW/RF: 14 µs/dB; TO: 35101 Hz; FB: 3K Hz; Lock: ^{2}D ; D1,D5: 6 s.

DC: Y, N ; Gated Off:A or D ; DO: 45316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE LXXXIX. OFF RESONANCE ^{13}C NMR SPECTRUM OF **36d**

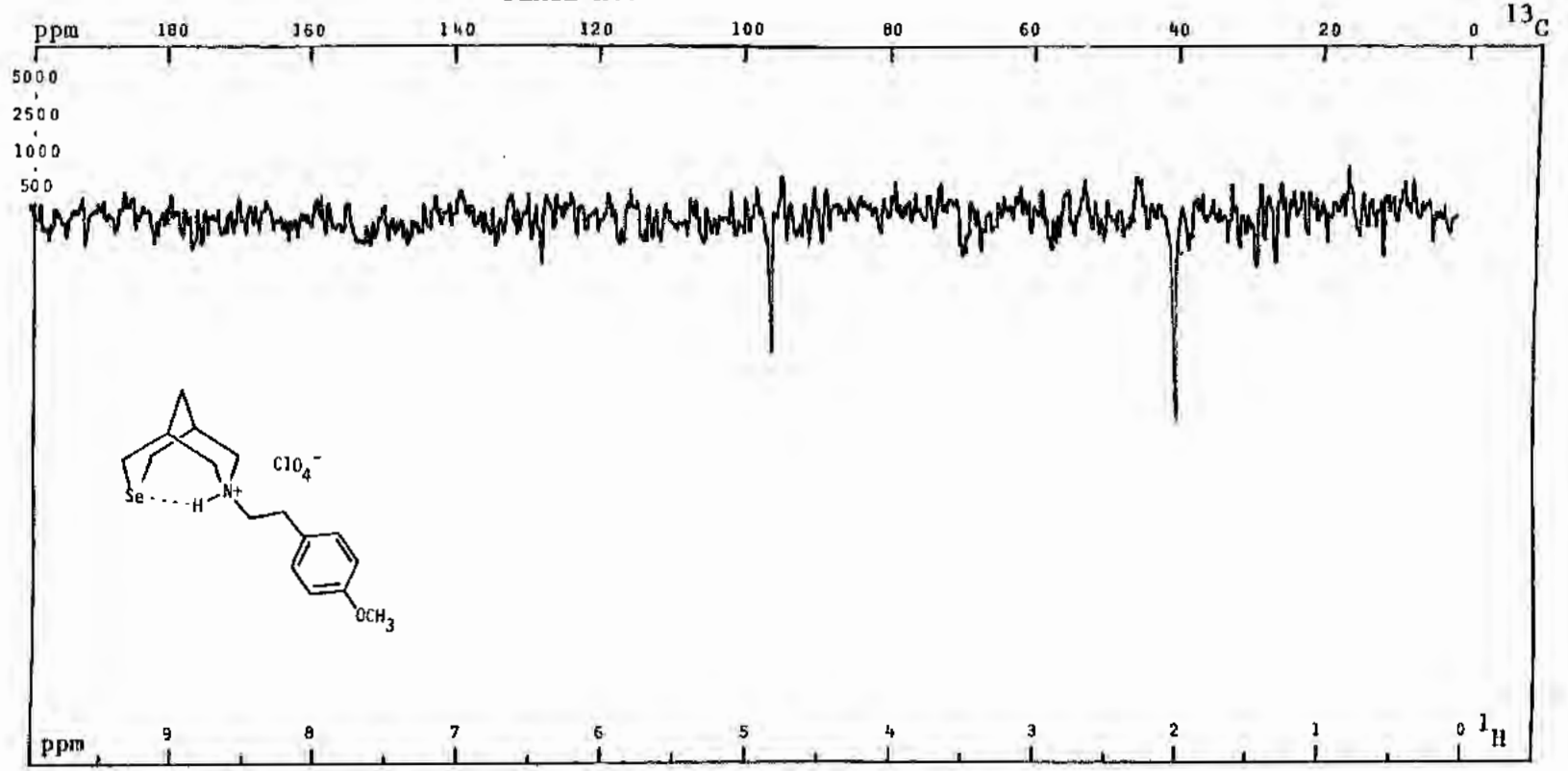


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 3000 .

Size: 8 K; PW/RF: 14 µs/dB; TO: 35101 Hz; FB: 3K Hz; Lock: ^2D ; D1,D5: 6 s.

DC: Y, N ; Gated Off:A or D ; DO: 46316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE XC. ^{15}N NMR SPECTRUM OF **36d**

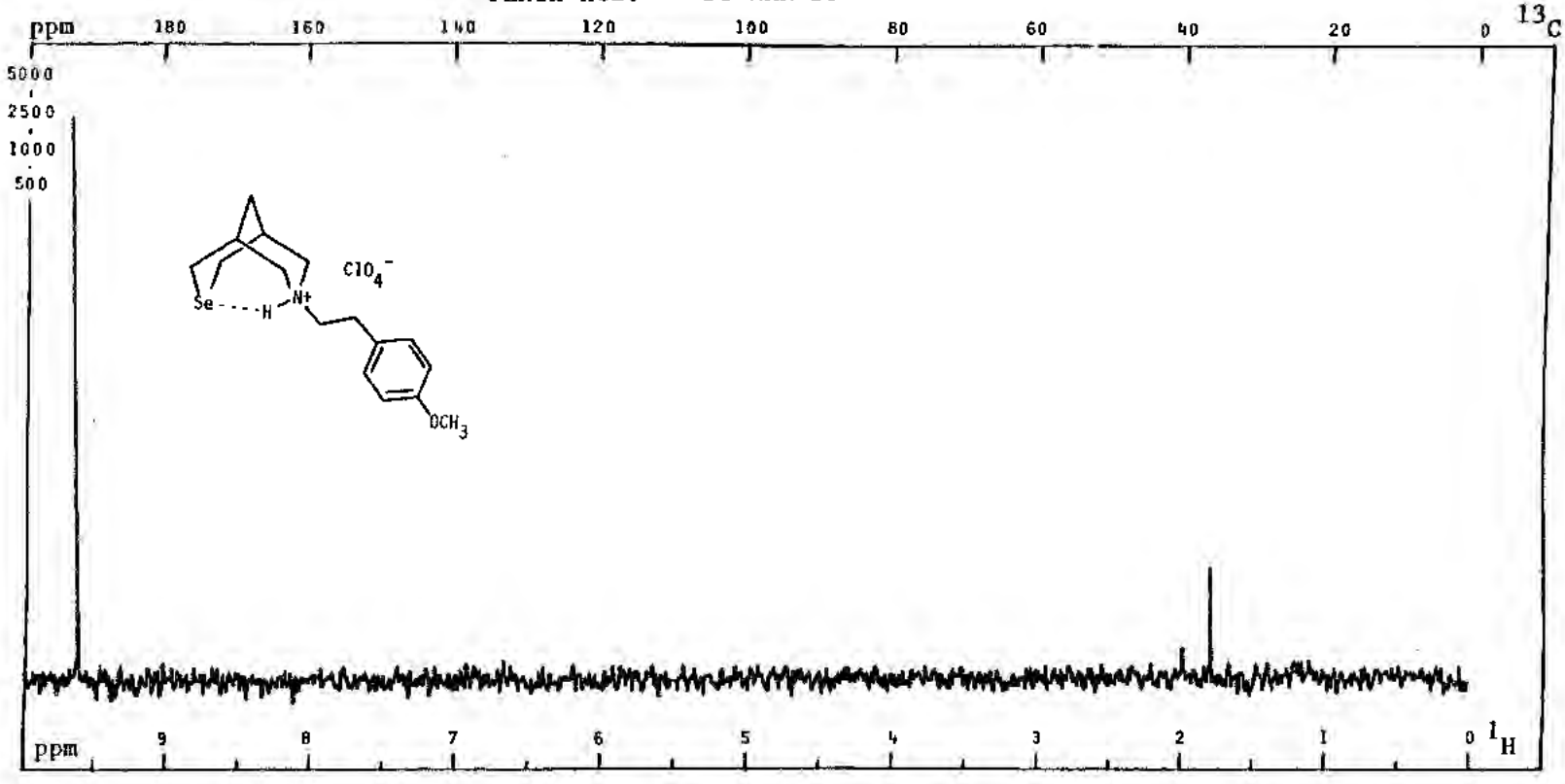


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 30.406 MHz; WC: 3040.6Hz; T: 25 °C; NT: 7200 .

Size: 12 K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 8 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XCI. ^{77}Se NMR SPECTRUM OF **36d**



PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 48

Size: 32K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 25 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE XCII. IR SPECTRUM OF **36e**

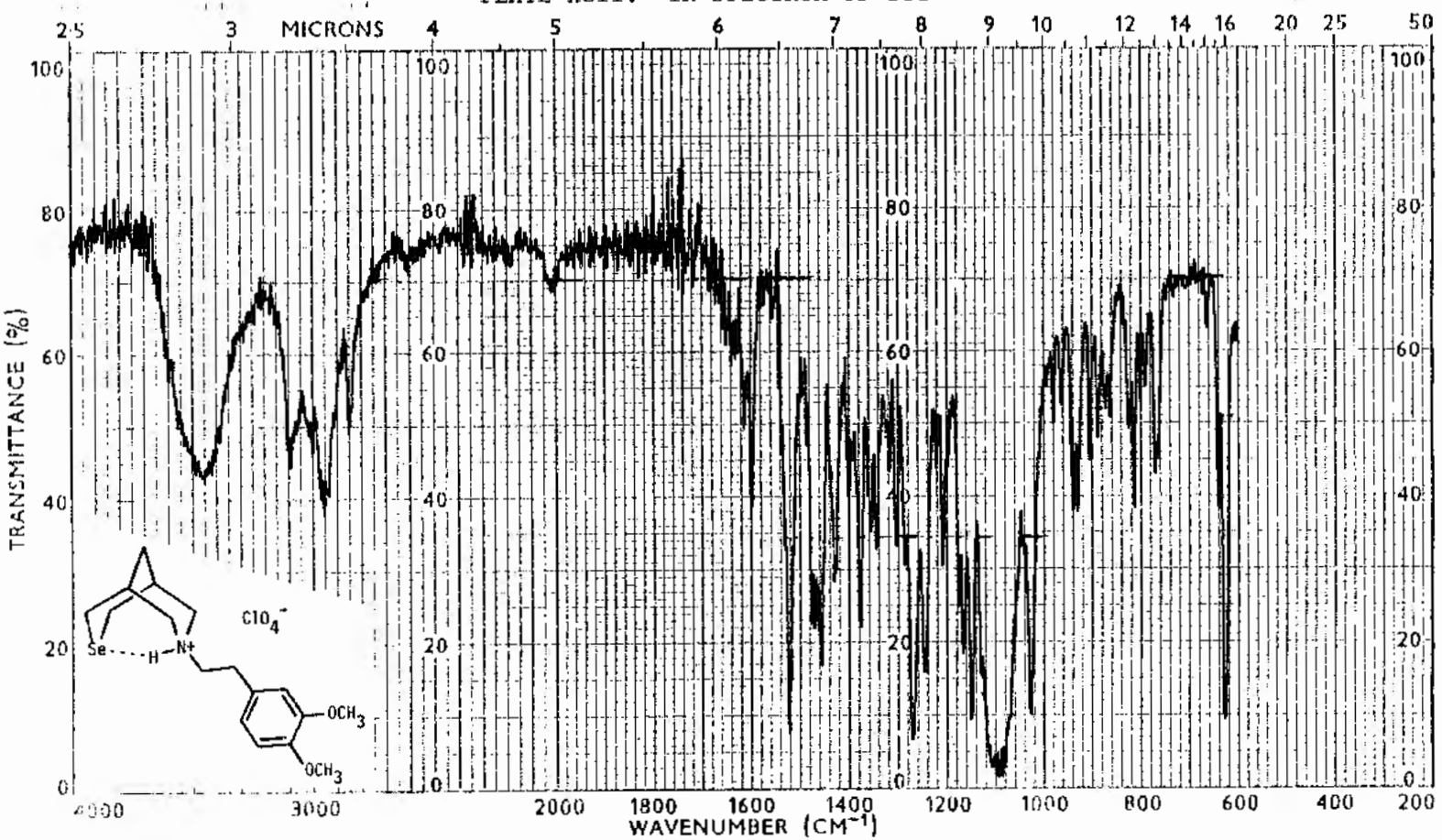
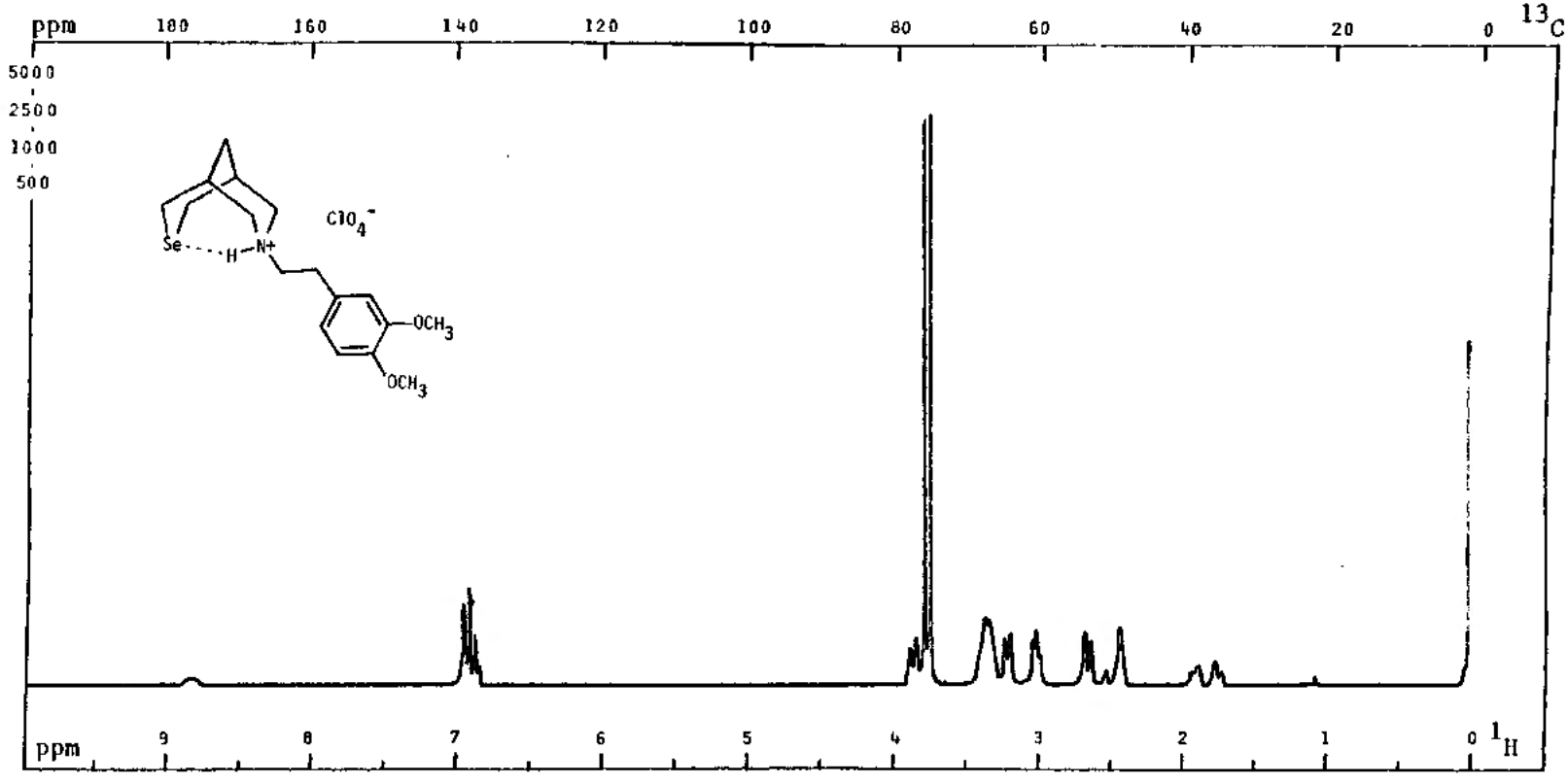


PLATE XCIII. ^{1}H NMR SPECTRUM OF **36e**

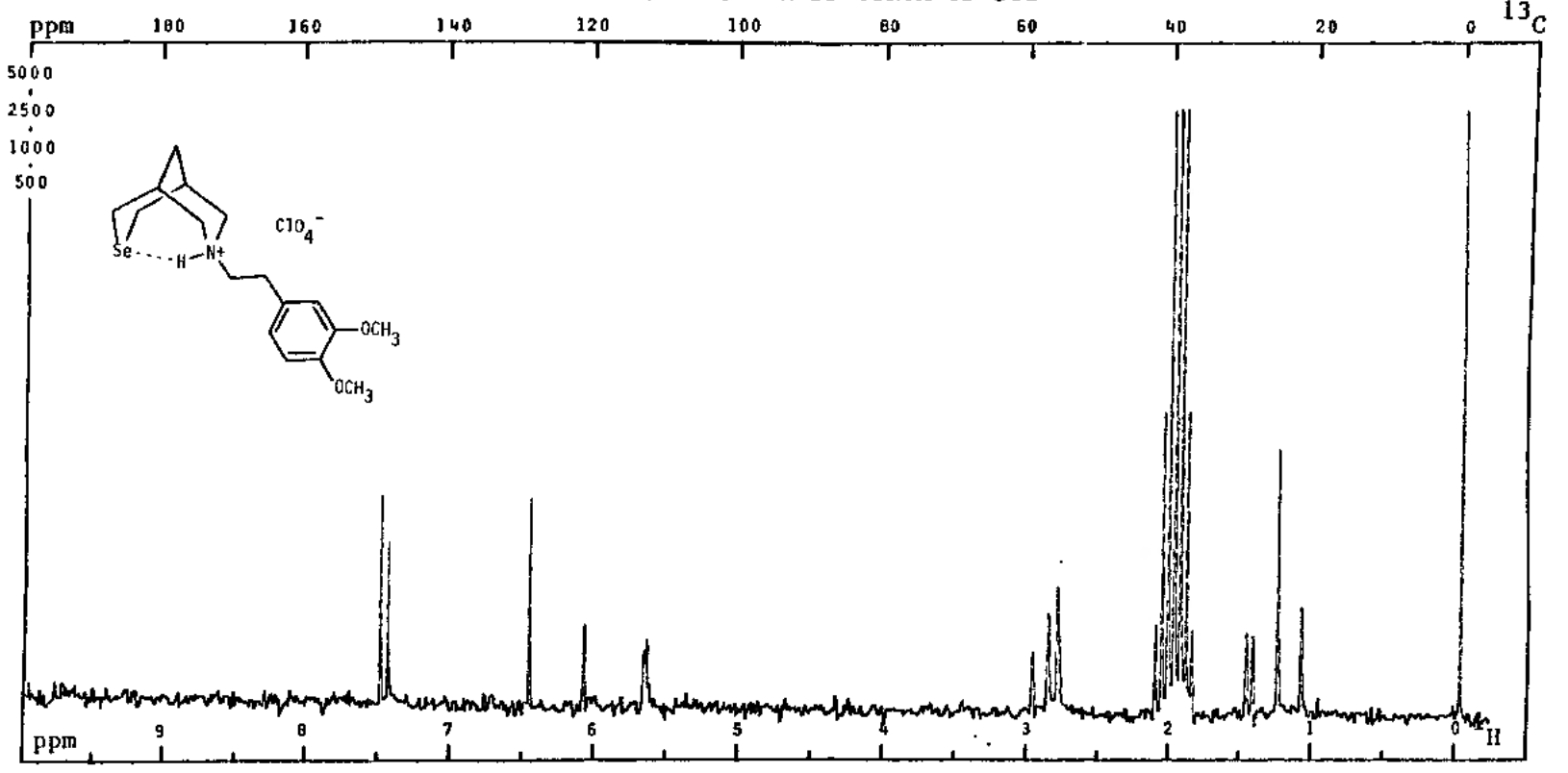


PFT X CW _ : Solvent: DMSO-d_6 ; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 16

Size: 12 K; PW/RF: 7 µs/dB; TO: 1500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XCIV. ^{13}C NMR SPECTRUM OF 36e

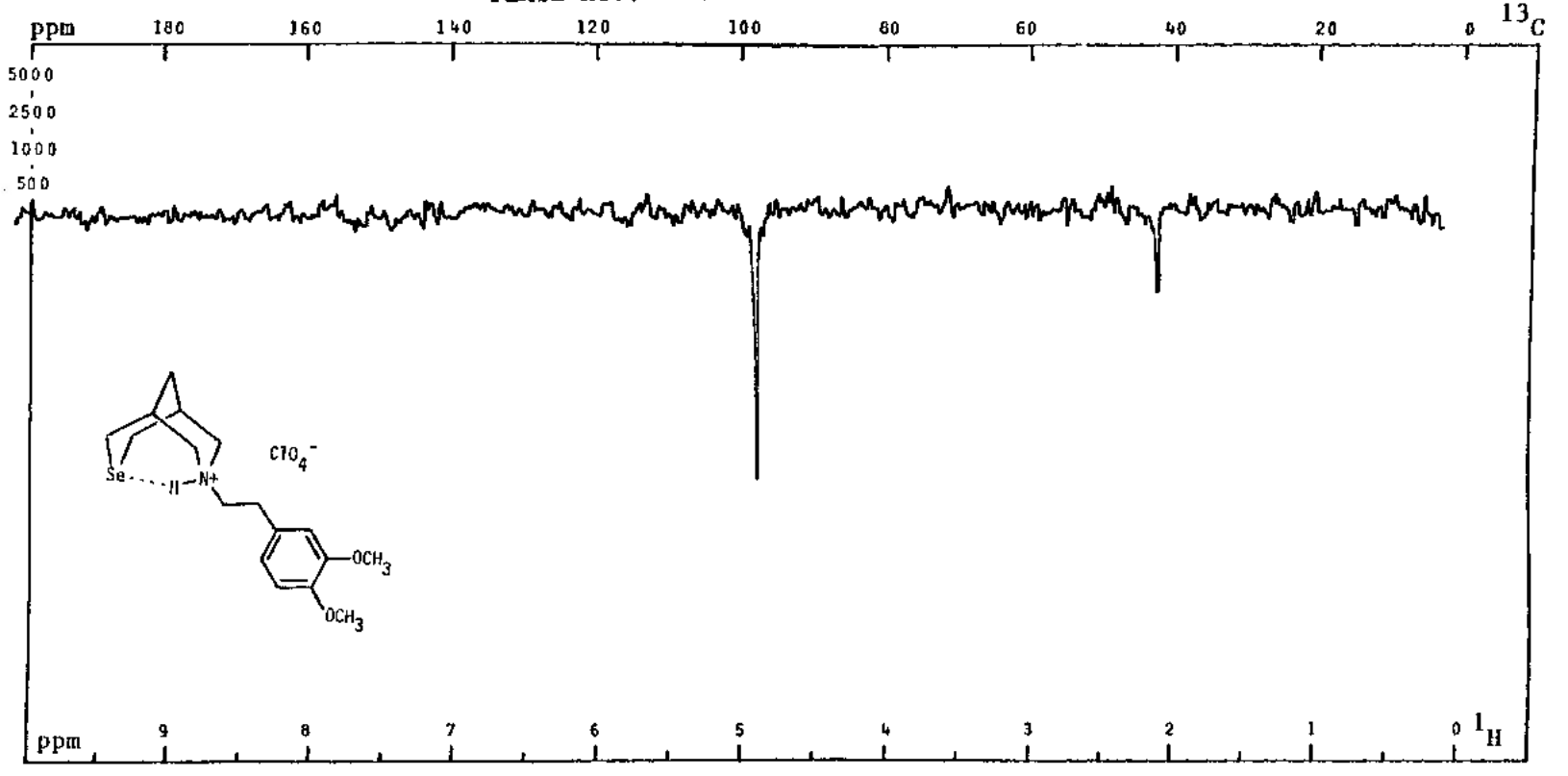


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 3396

Size: 8 K; PW/RF: 10 µs/dB; TO: 35101 Hz; FB: 3K Hz; Lock: ^2D ;D1,D5: 5 s.

DC: Y, N ; Gated Off:A or D ; DO: 45316 Hz; RF(Power): 7.5W/dB; NBW: Hz; LB: Hz.

PLATE XCV. ^{15}N NMR SPECTRUM OF **36e**

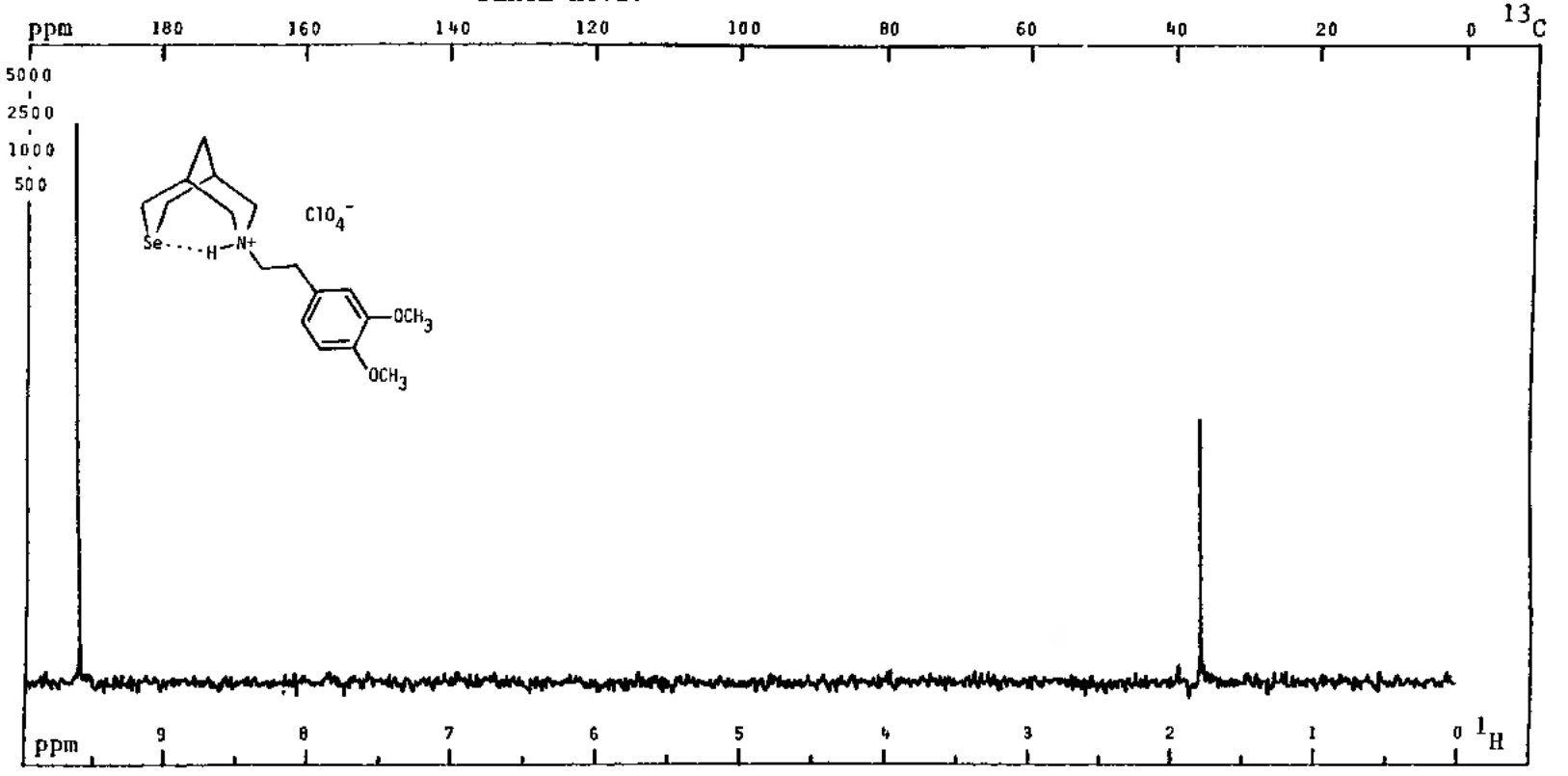


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 30.406MHz; WC: 3040.6Hz; T: 25 °C; NT: 21721 .

Size: 12 K; PW/RF: 40 µs/dB; TO:-11600 Hz; FB: Hz; Lock: ^2D ;D1,D5: 8 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XCVI. ^{77}Se NMR SPECTRUM OF **36e**



PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 152 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 15 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE XCVII. IR SPECTRUM OF **36f**

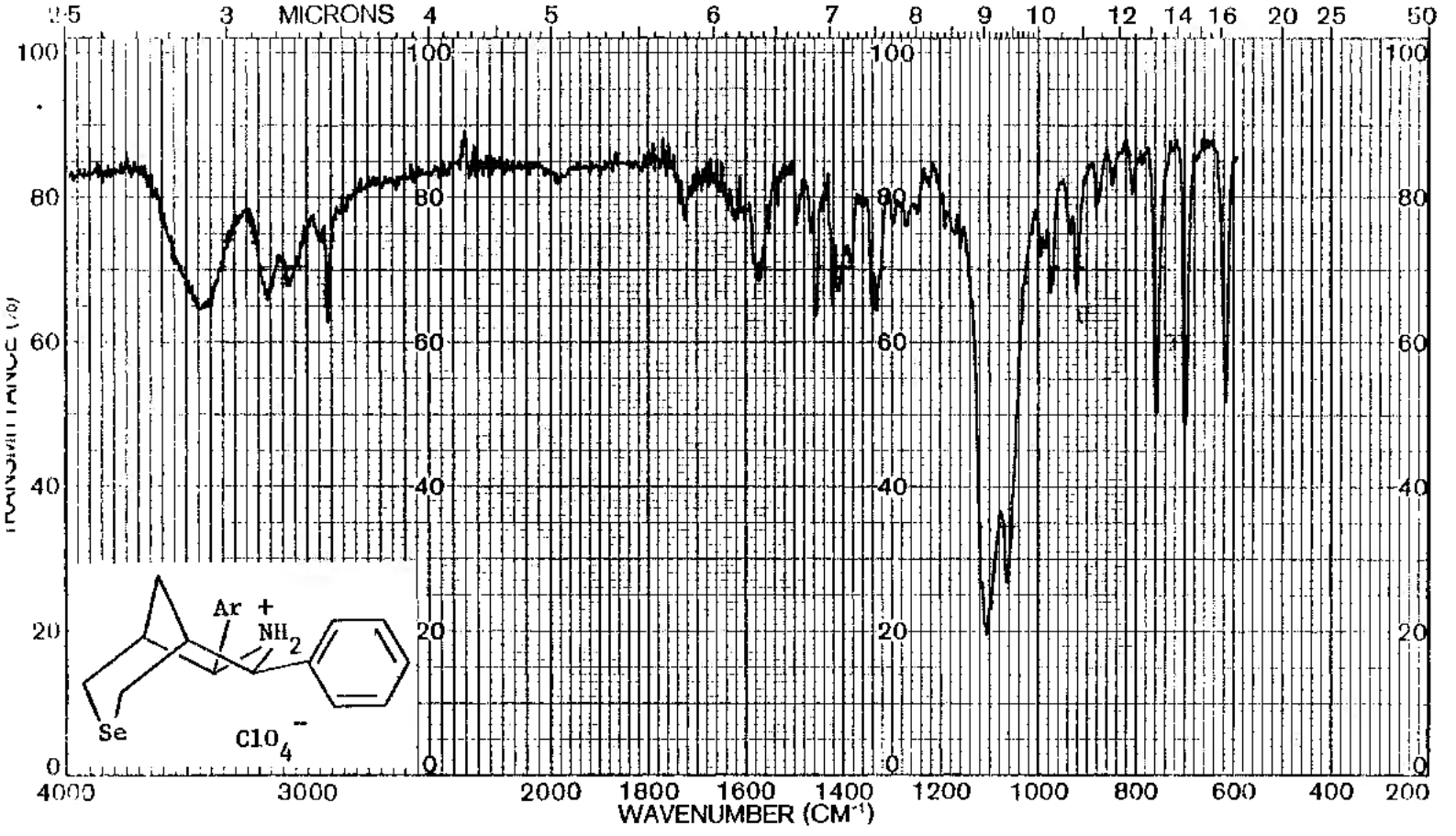
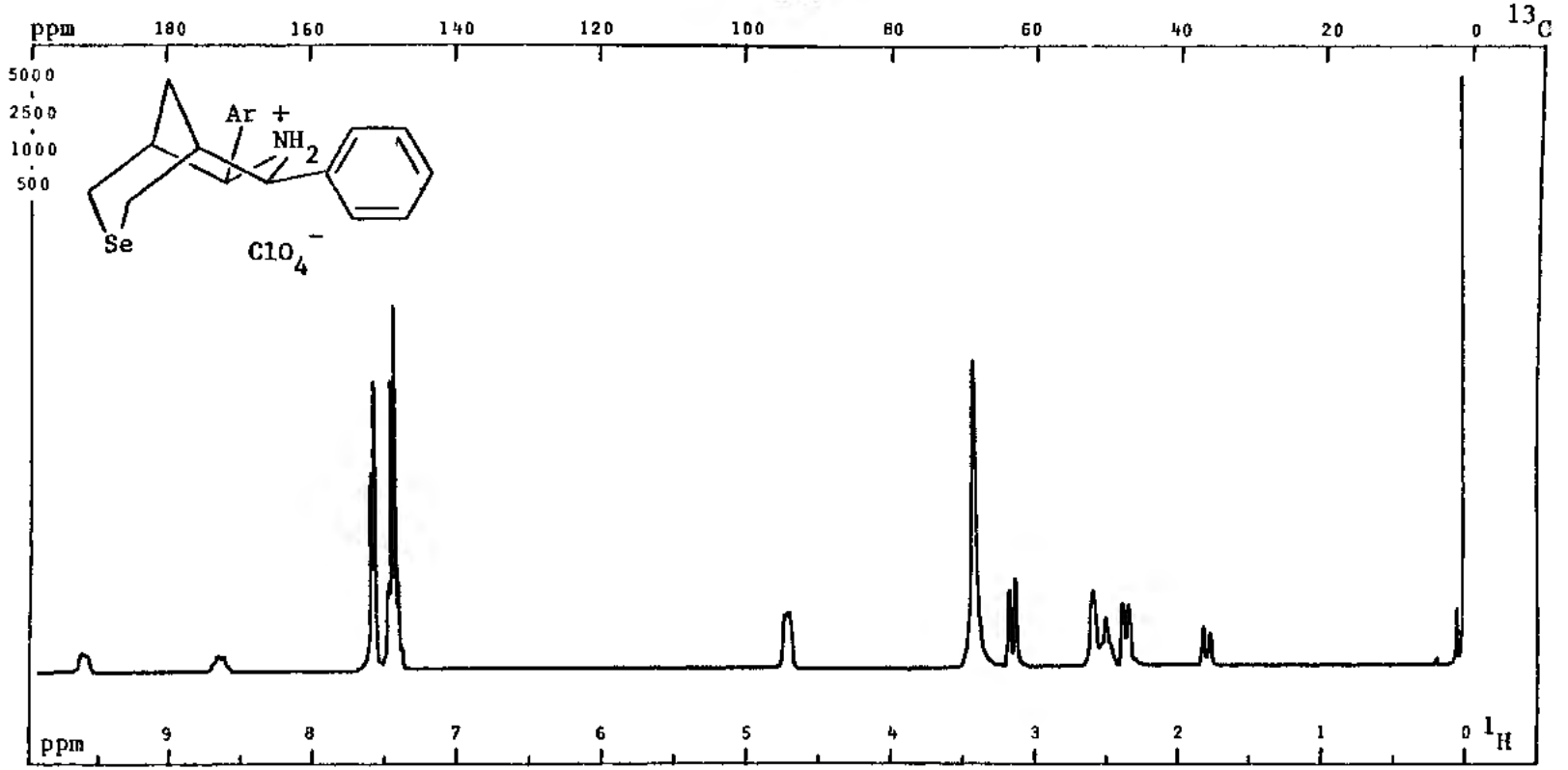


PLATE XCVIII. ^{1}H NMR SPECTRUM OF **36f**

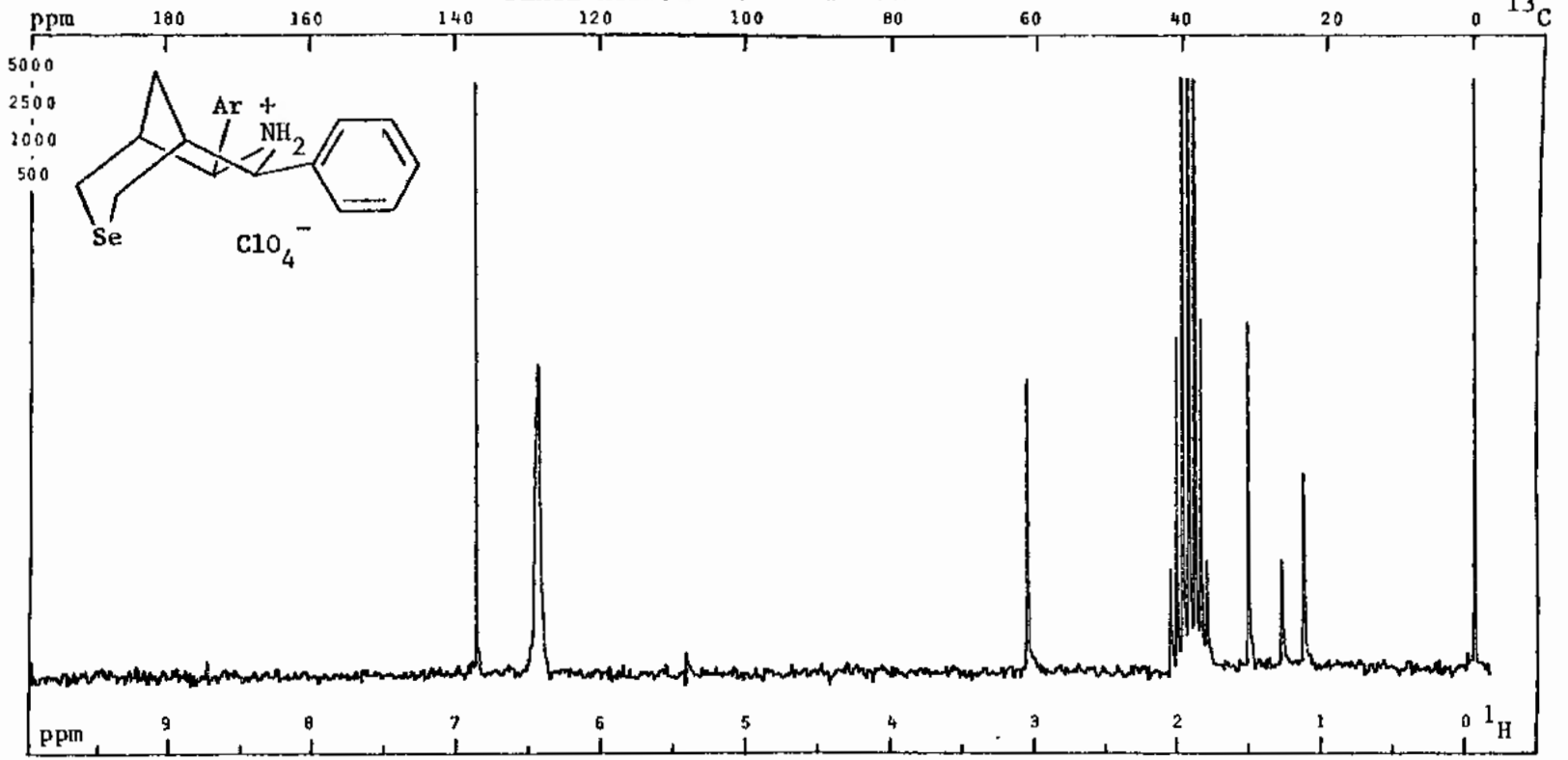


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 16 .

Size: 12 K; PW/RF: 5 µs/dB; TO: 1500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0.5 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE XCIX. ^{13}C NMR SPECTRUM OF **36f**

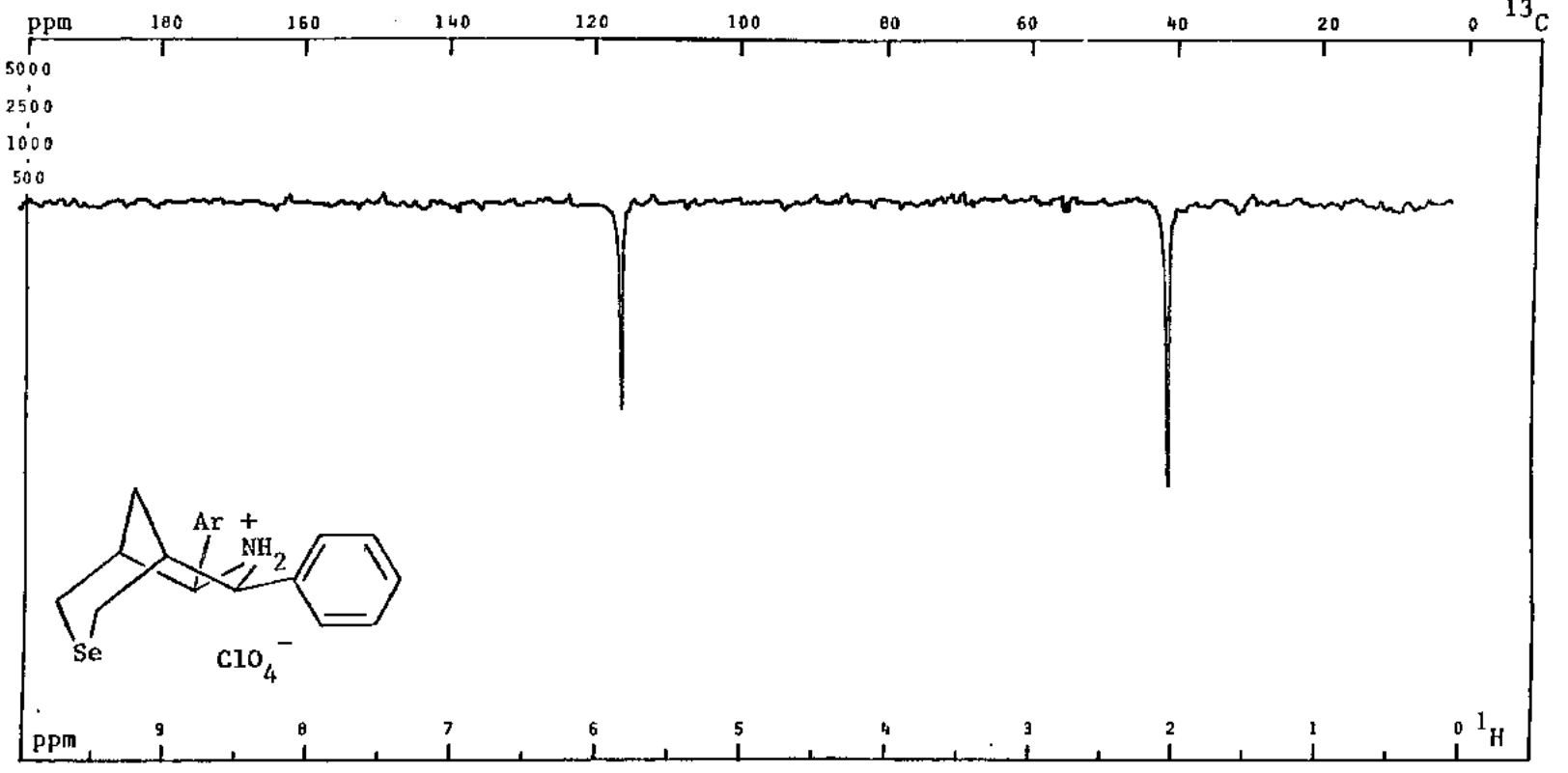


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 5510 .

Size: 8 K; PW/RF: 10 μs/dB; TO: 35201 Hz; FB: Hz; Lock: ^2D ;D1,D5: 5 s.

DC: Y, N ; Gated Off:A or D ; DO: 45316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE C. ^{15}N NMR SPECTRUM OF **36f**

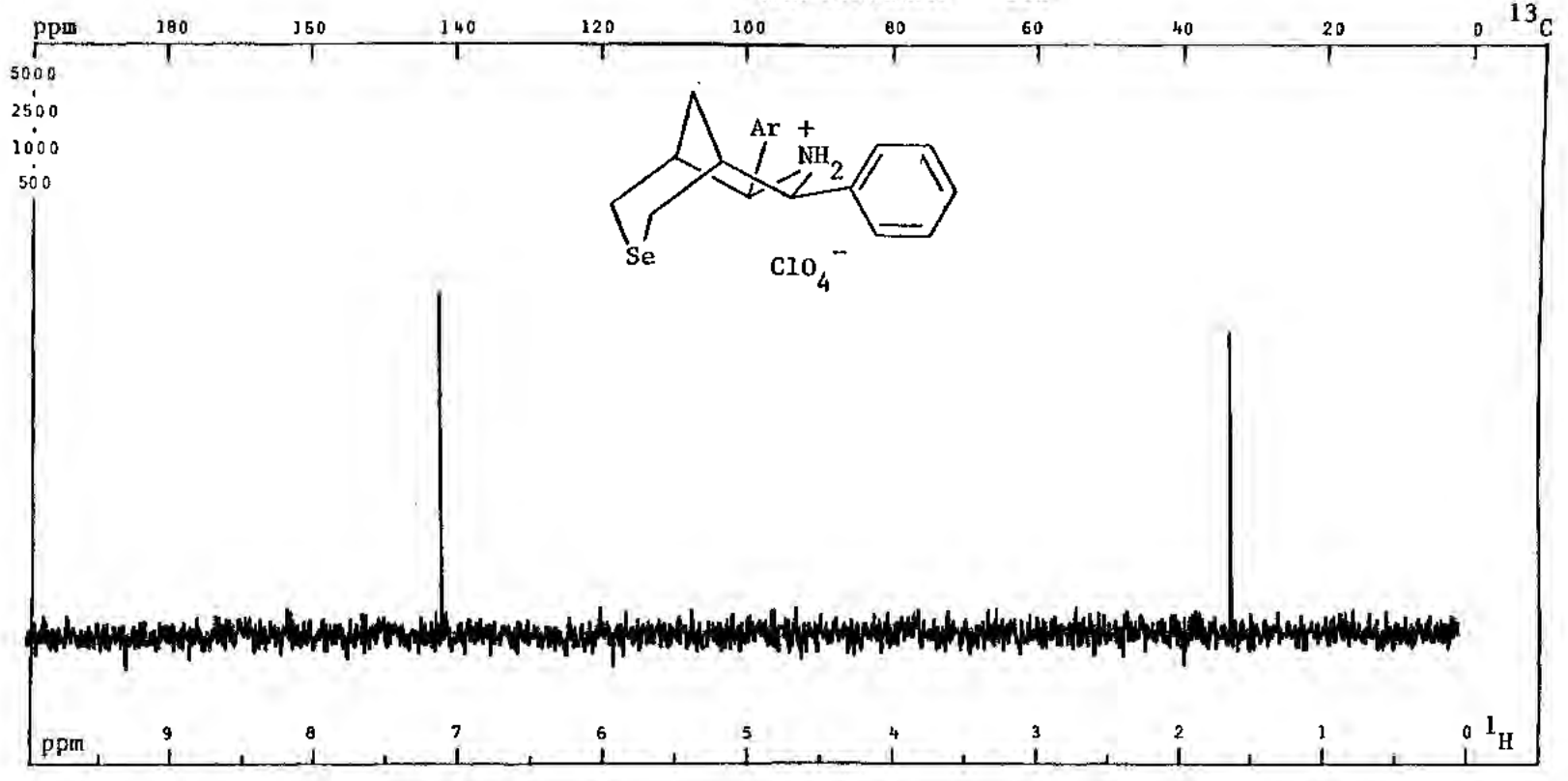


PFT X CW _ ; Solvent: DMSO-d_6; SF: 30.406 MHz; WC: 3040.6 Hz; T: 25 °C; NT: 15800 .

Size: 12 K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^2D ; D1,D5: 8 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE CI. ^{77}Se NMR SPECTRUM OF **36f**



PFT X CW _ ; Solvent: DMSO-d_6 ; SF:57.22 MHz; WC:50000 Hz; T: 25 °C; NT: 112 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ;D1,D5: 15 s.

DC: Y, N ; Gated Off:A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE CII. IR SPECTRUM OF **36g**

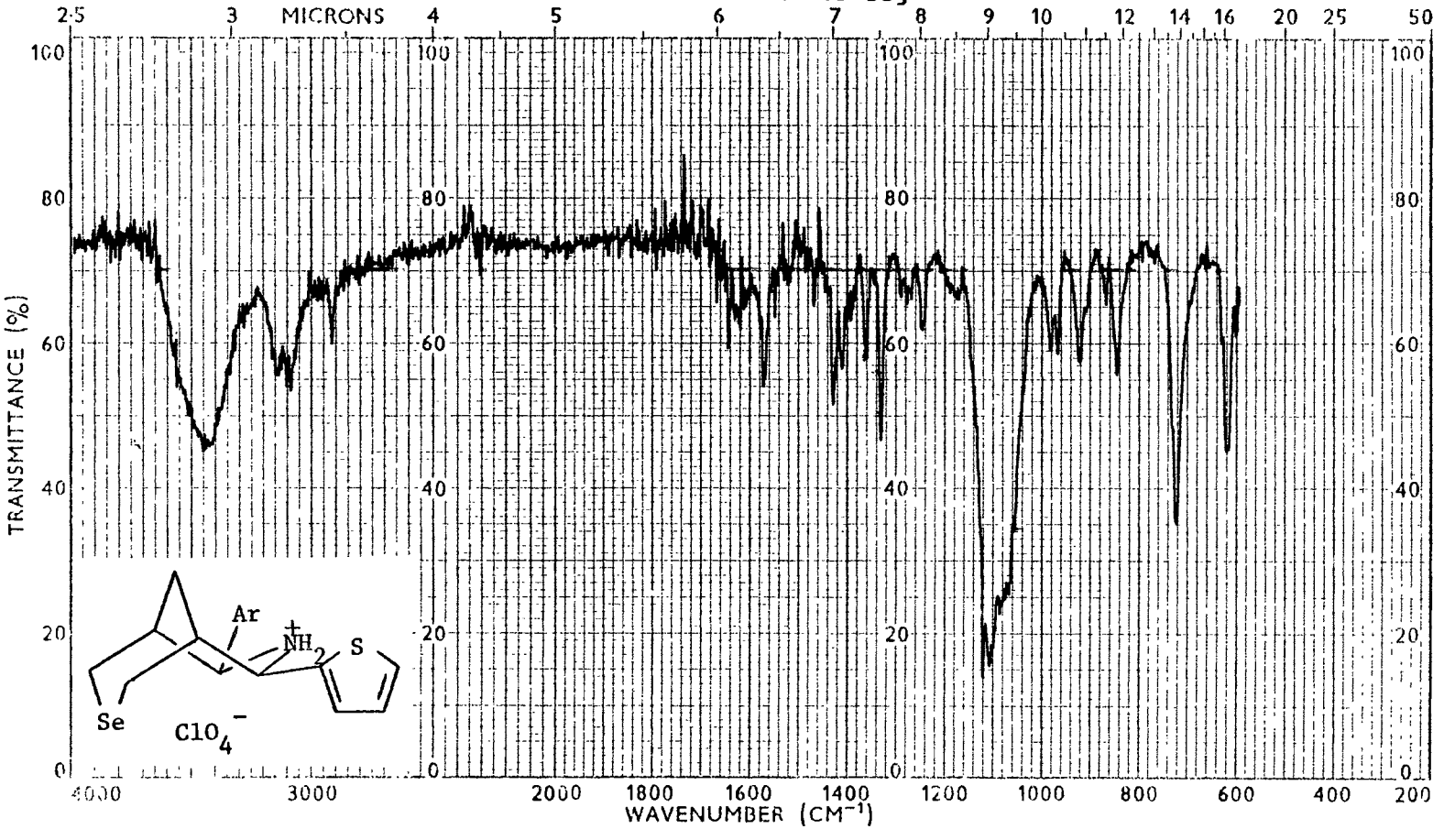
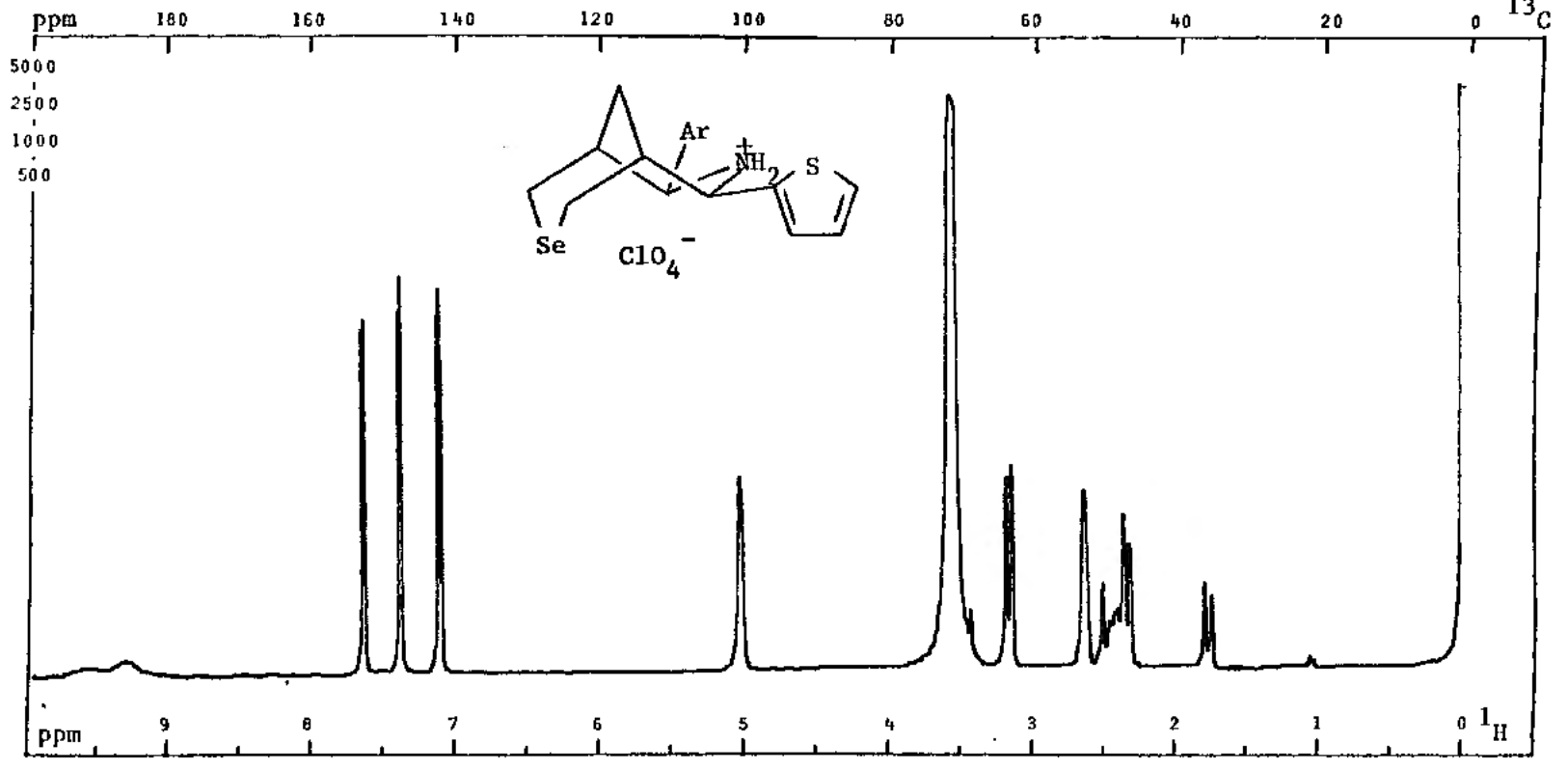


PLATE CIII. ^{1}H NMR SPECTRUM OF **36g**

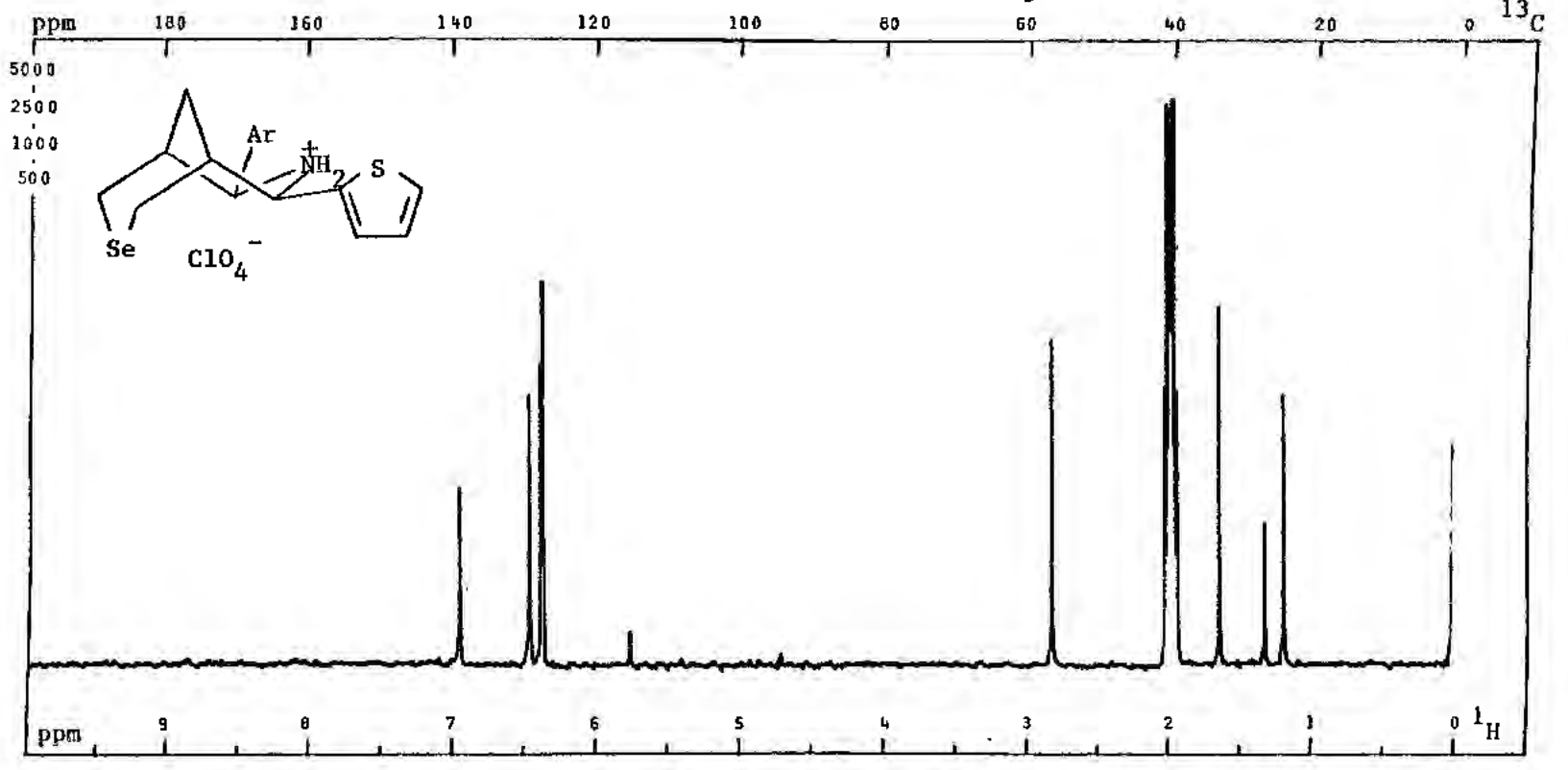


PFT X CW _ ; Solvent: DMSO-d_6 SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 16

Size: 12K; PW/RF: 5 µs/dB; TO: 1500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE CIV. ^{13}C NMR SPECTRUM OF **36g**

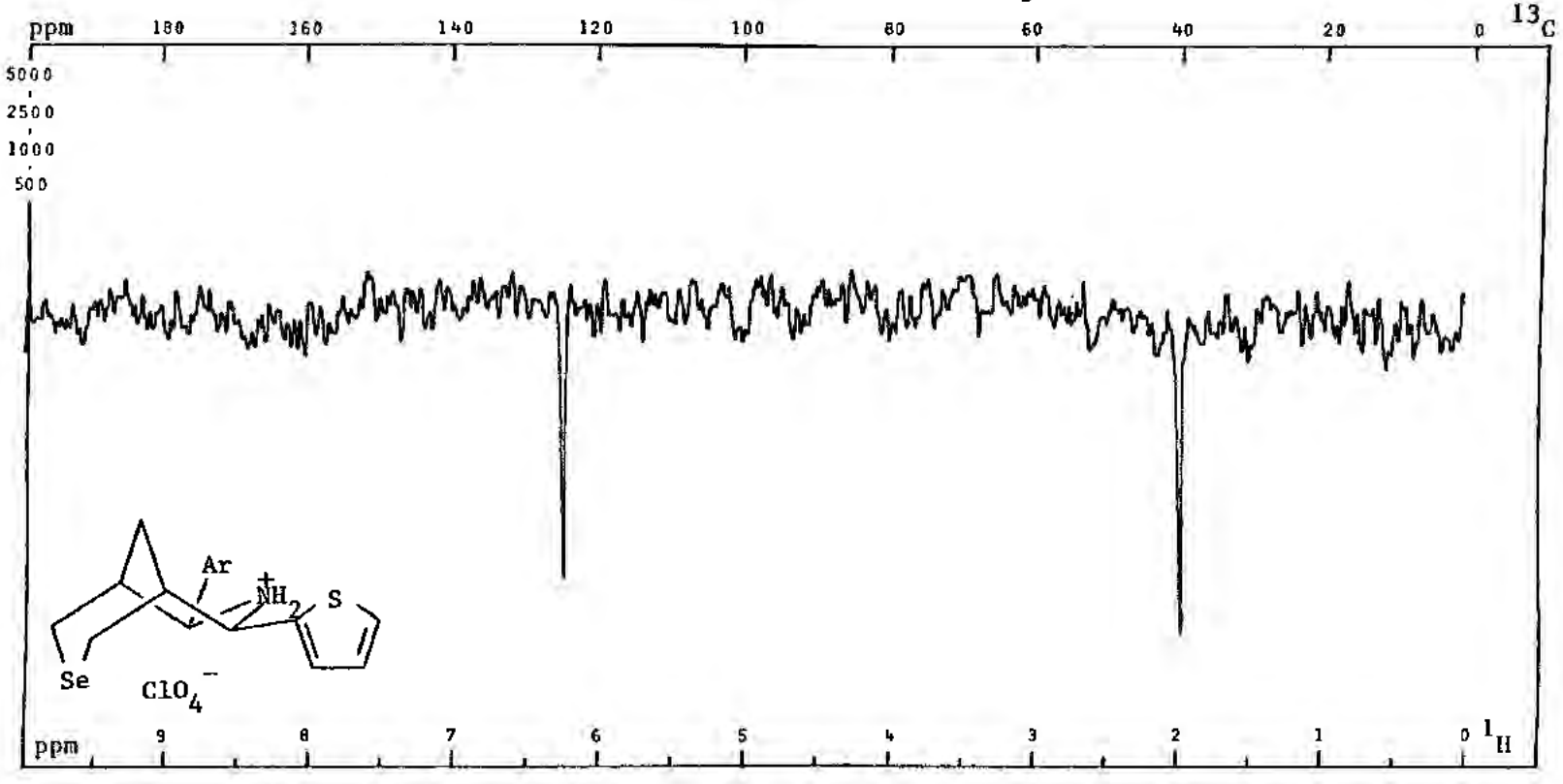


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 75.4 MHz; WC: 15085 Hz; T: 25 °C; NT: 1240 .

Size: 16 K; PW/RF: 12 µs/dB; TO: 1500 Hz; FB: Hz; Lock: ^2D ; D1,D5: 4 s.

DC: Y, N ; Gated Off:A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE CV. ^{15}N NMR SPECTRUM OF **36g**

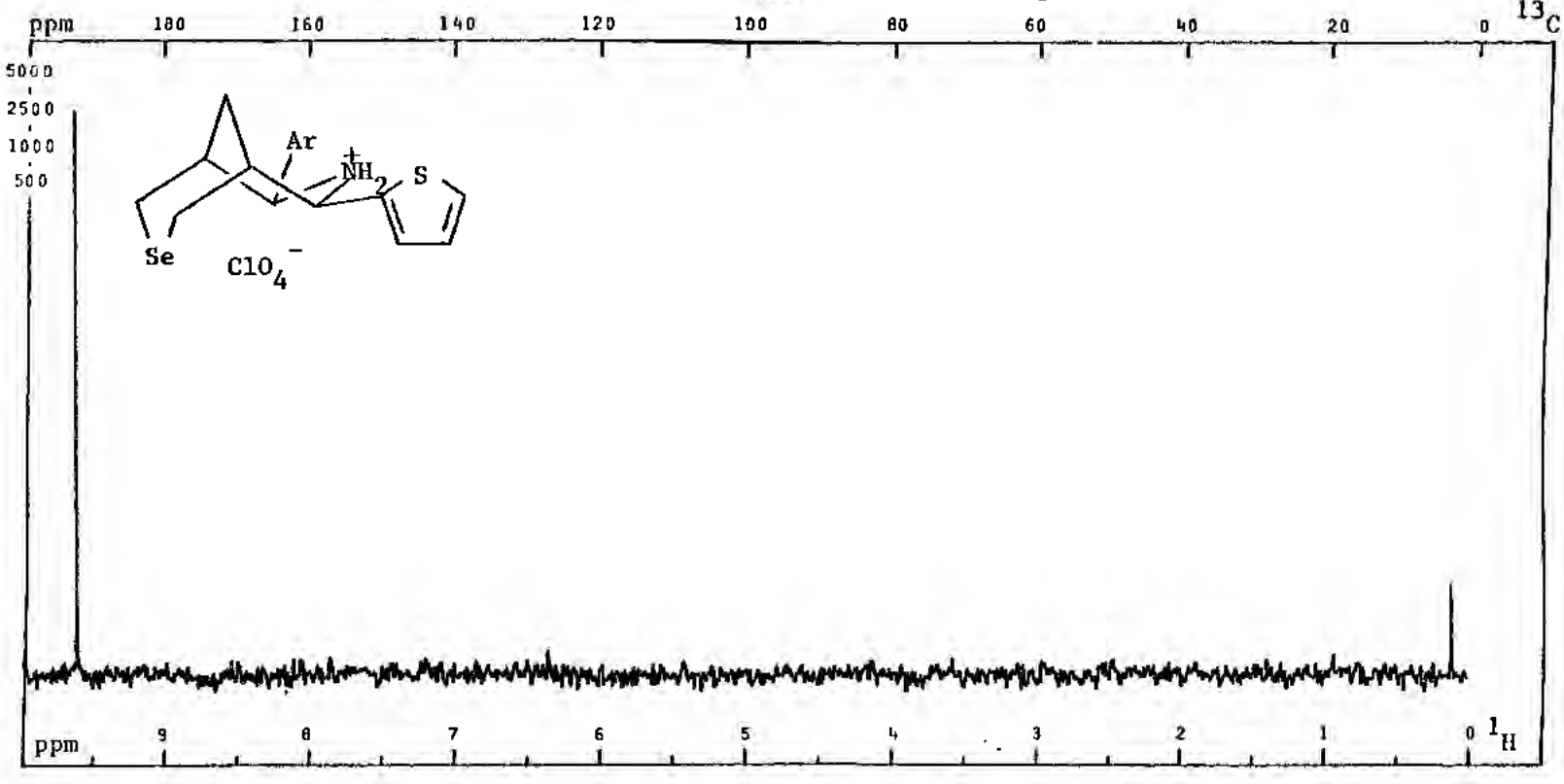


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 30.406 MHz; WC: 3040.6 Hz; T: 25 °C; NT: 6000 .

Size: 12K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^2D ; D1,D5: 8 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE CVI. ^{77}Se NMR SPECTRUM OF **36g**



PFTX_ CW _ ; Solvent: DMSO-d_6; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 40 .

Size: 32K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 25 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE CVII. IR SPECTRUM OF **36h**

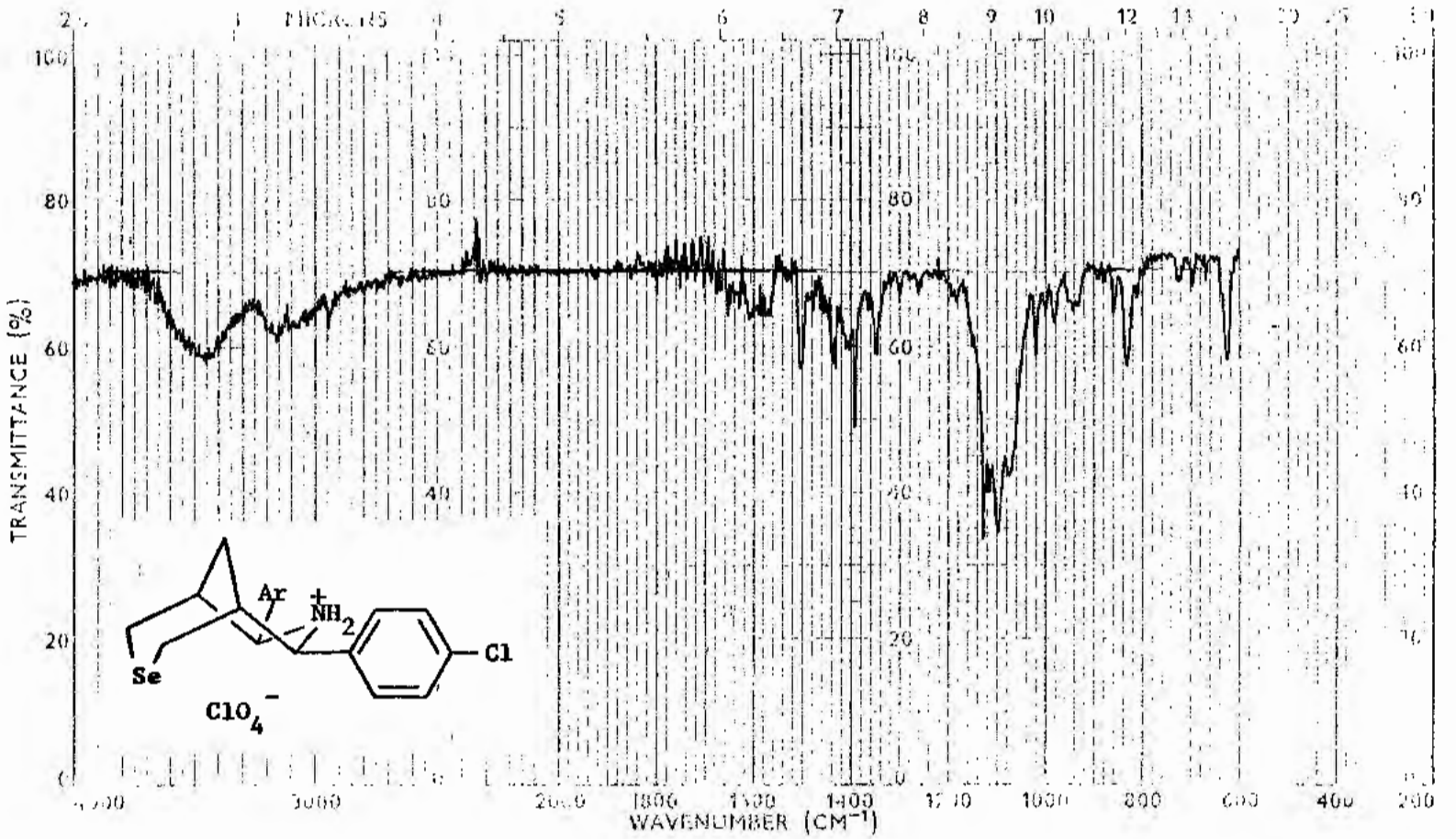
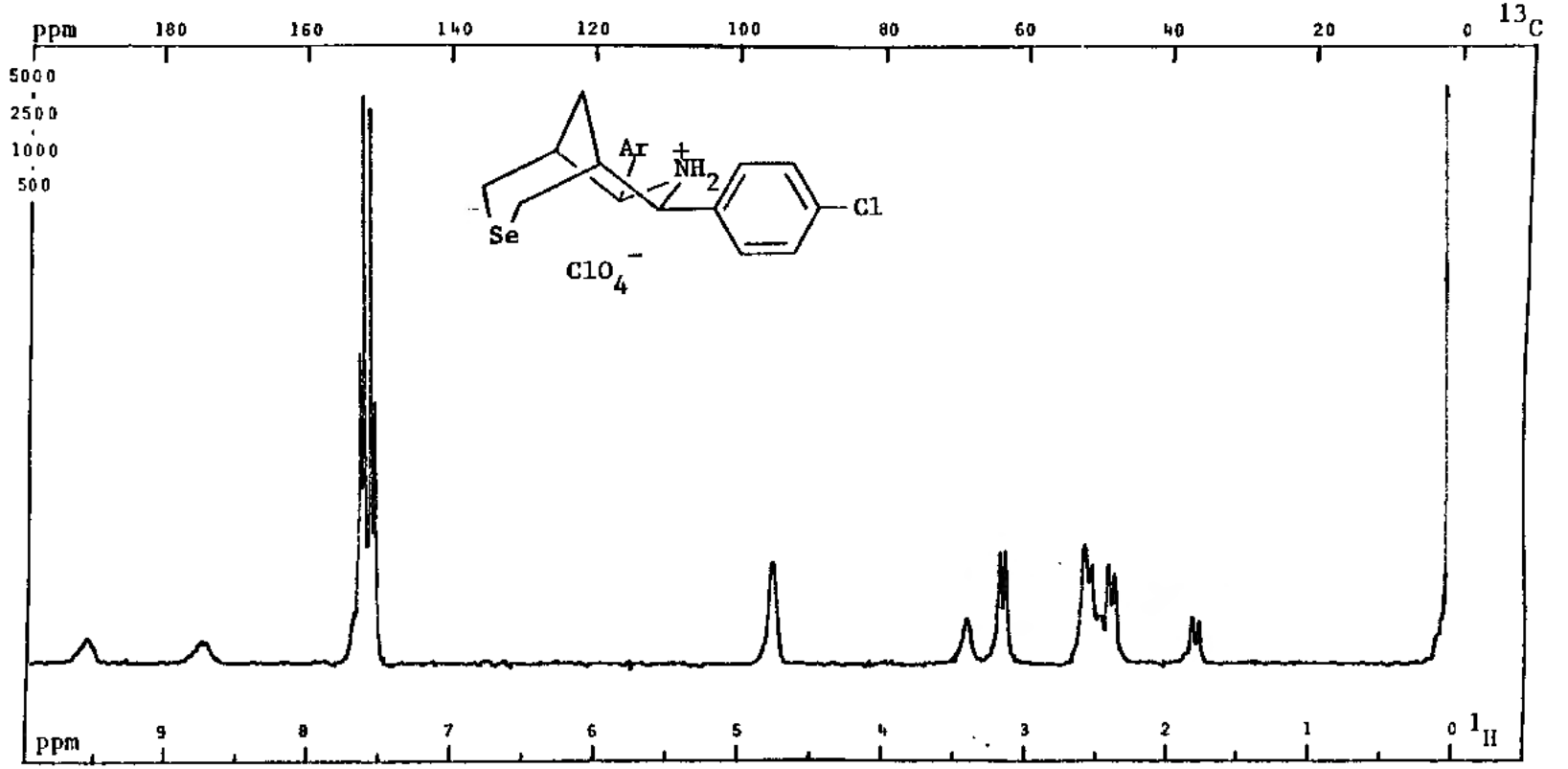


PLATE CVIII. ^{1}H NMR SPECTRUM OF 36h

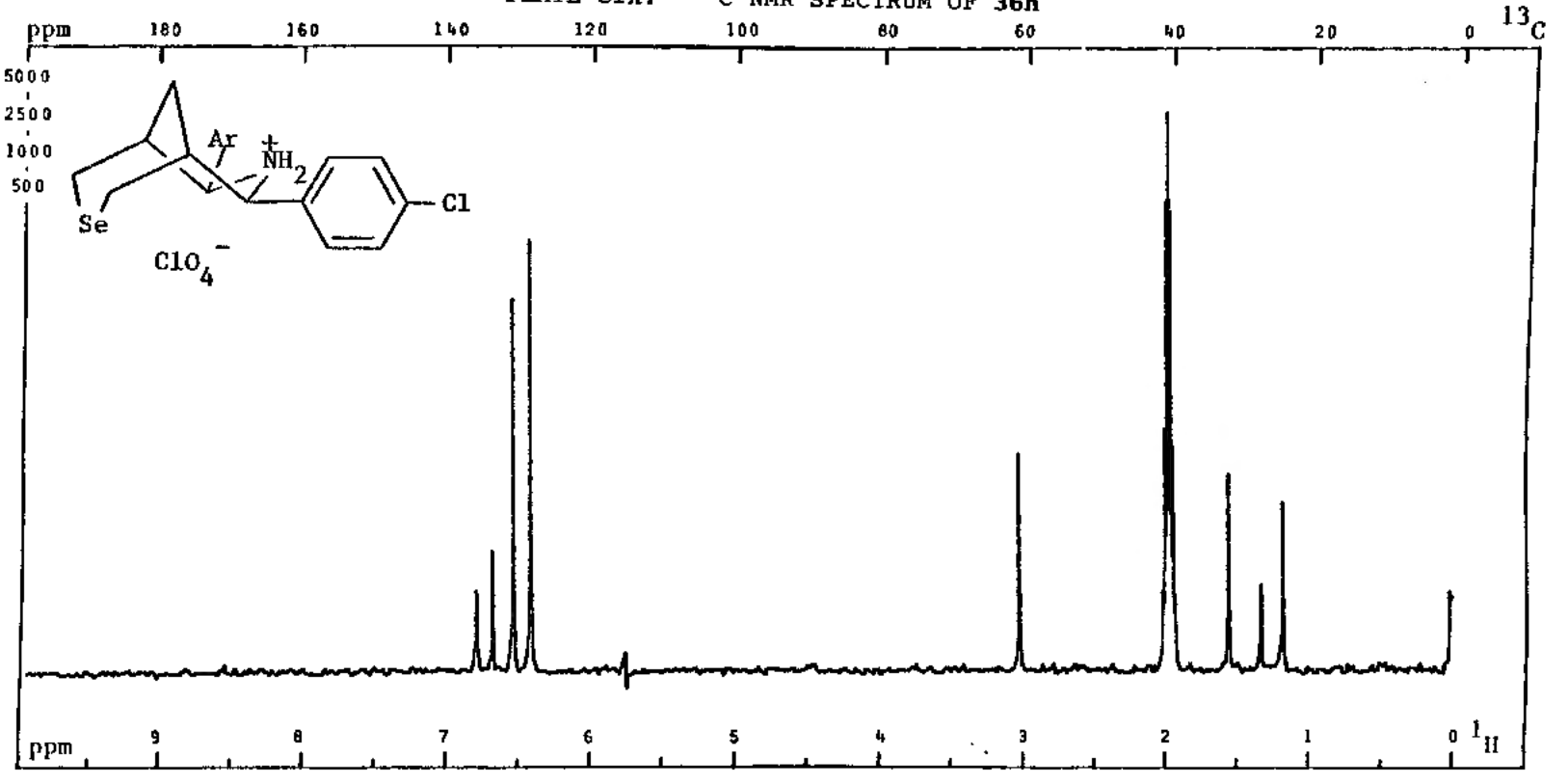


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 299.94 MHz; WC:3000 Hz; T: 25 °C; NT: 1360 .

Size: 12 K; PW/RF: 70 µs/dB; TO: 1500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE CIX. ^{13}C NMR SPECTRUM OF **36h**

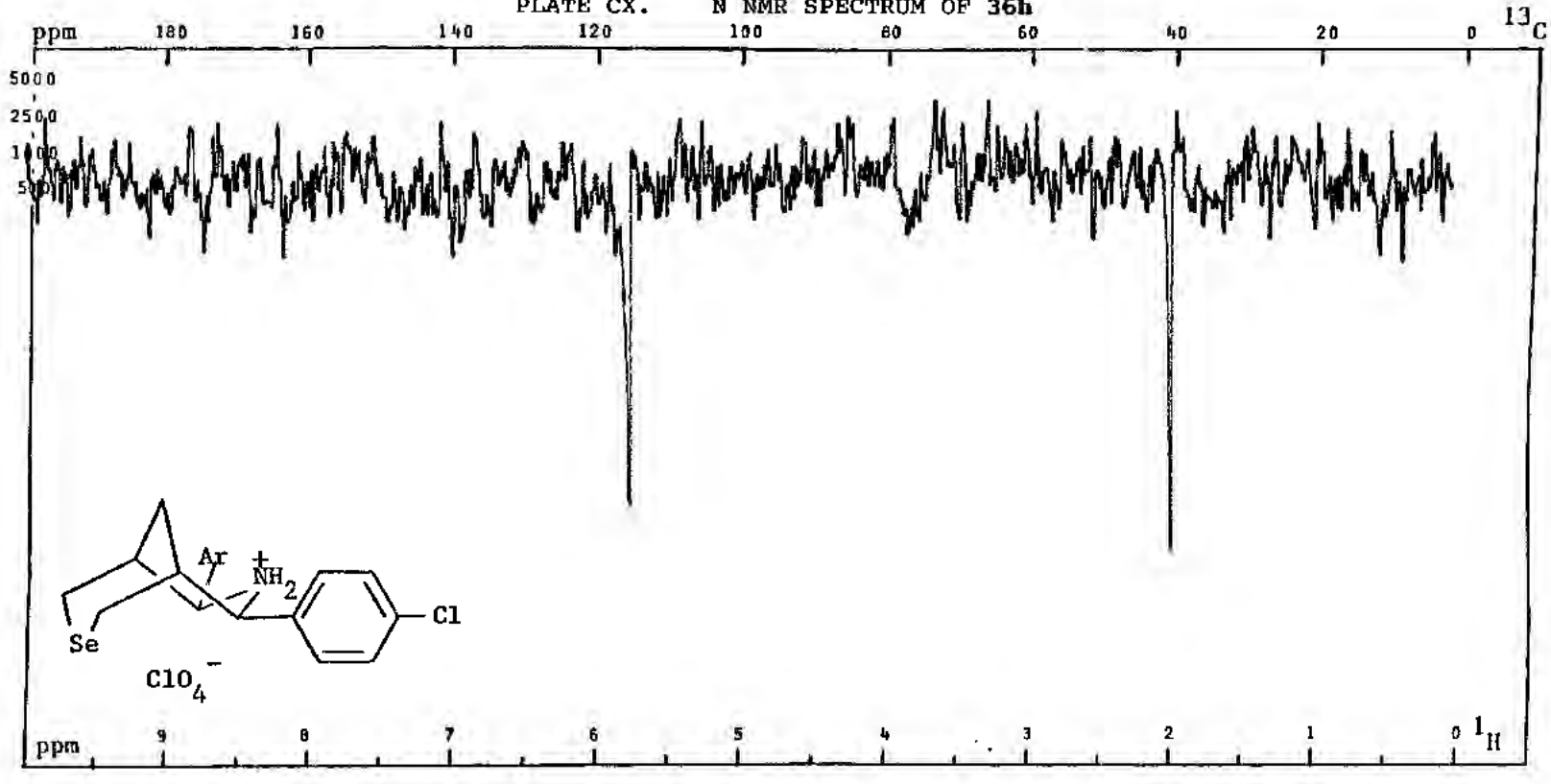


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 75.4 MHz; WC: 15000 Hz; T: 25 °C; NT: 80 .

Size: 16K; PW/RF: 12 μs/dB; TO: 1500 Hz; FB: Hz; Lock: ^2D ; D1,D5: 4 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE CX. ^{15}N NMR SPECTRUM OF **36h**

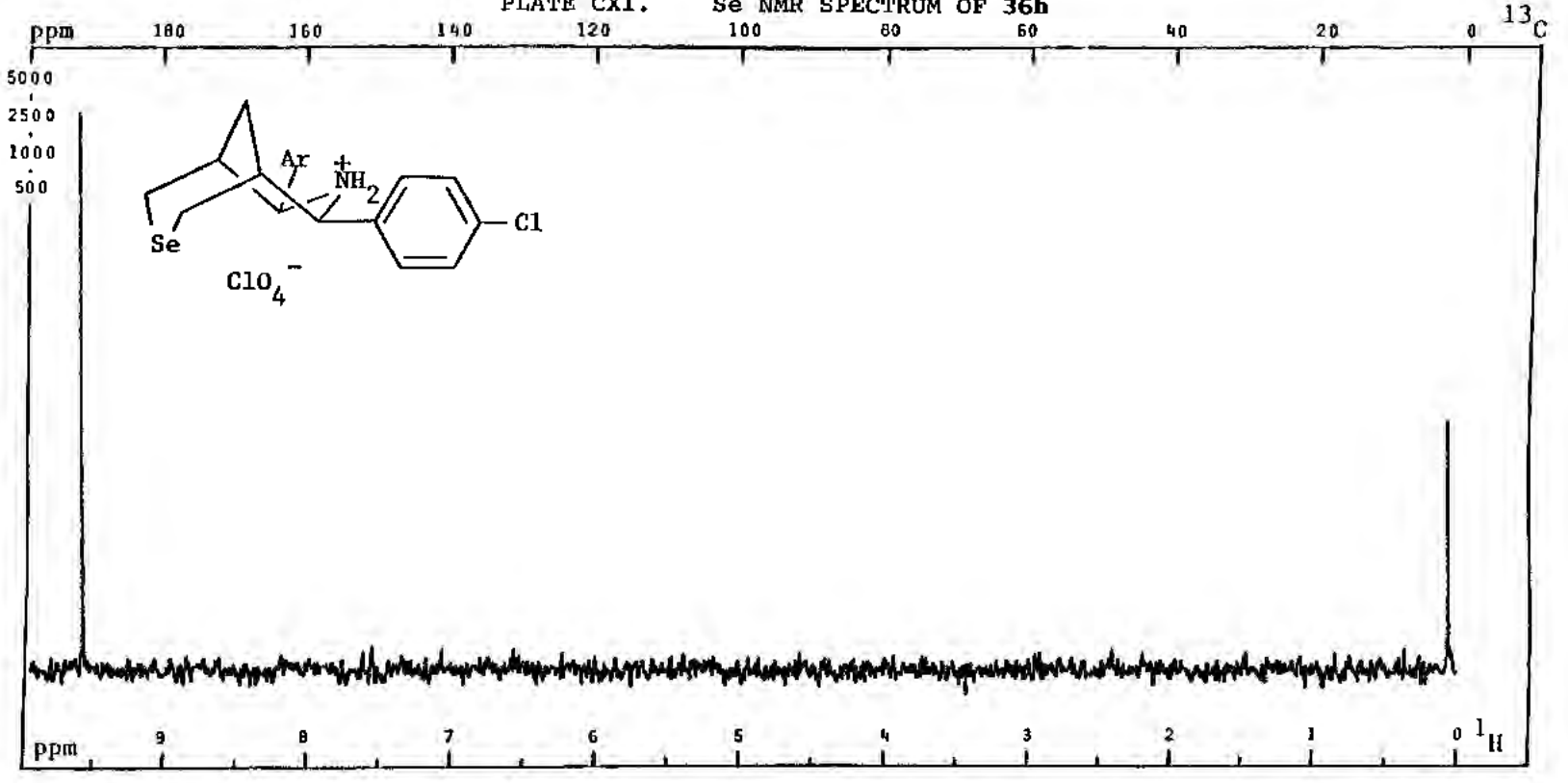


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 30.406 MHz; WC: 3040.6 Hz; T: 25 °C; NT: 6000 .

Size: 12 K; PW/RF: 40 μs/dB; TO: -11600 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 8 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 0 W/dB; NBW: Hz; LB: Hz.

PLATE CXI. ^{77}Se NMR SPECTRUM OF **36b**



PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 57.22 MHz; WC: 28610Hz; T: 25 °C; NT: 160 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 15 s.

DC: Y, N ; Gated Off:A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE CXII. IR SPECTRUM OF **36i**

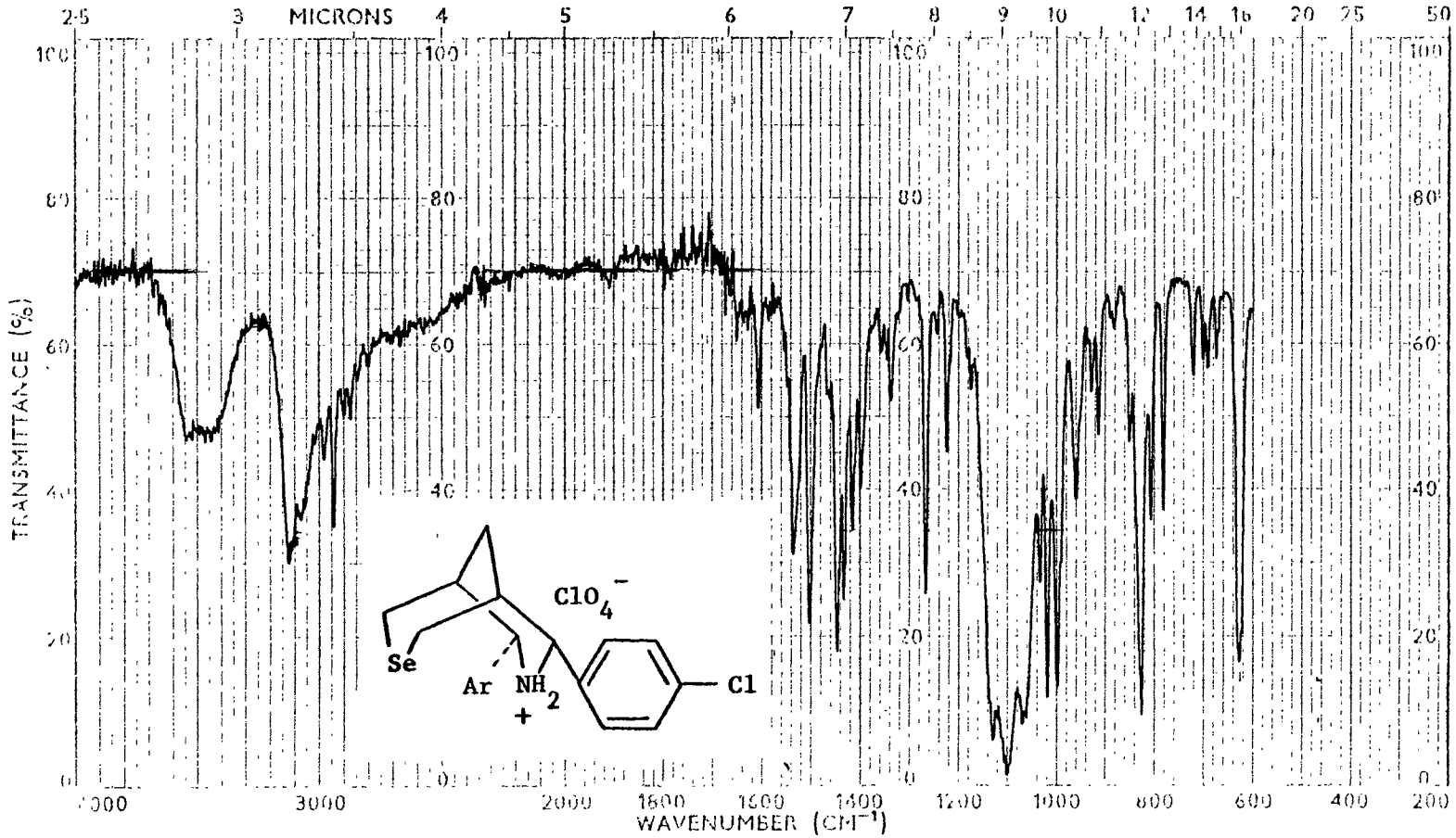
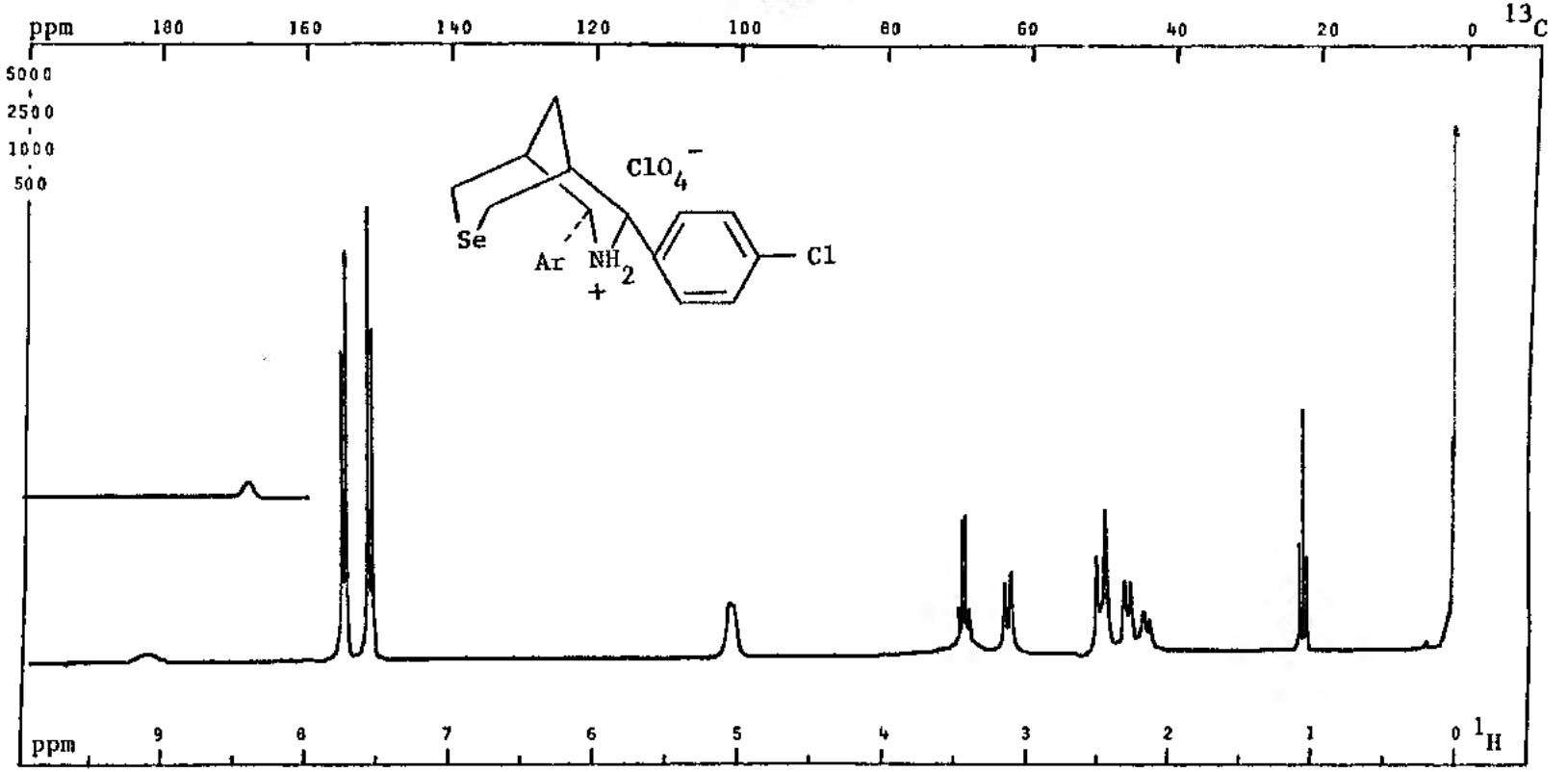


PLATE CXIII. ^{1}H NMR SPECTRUM OF 36i

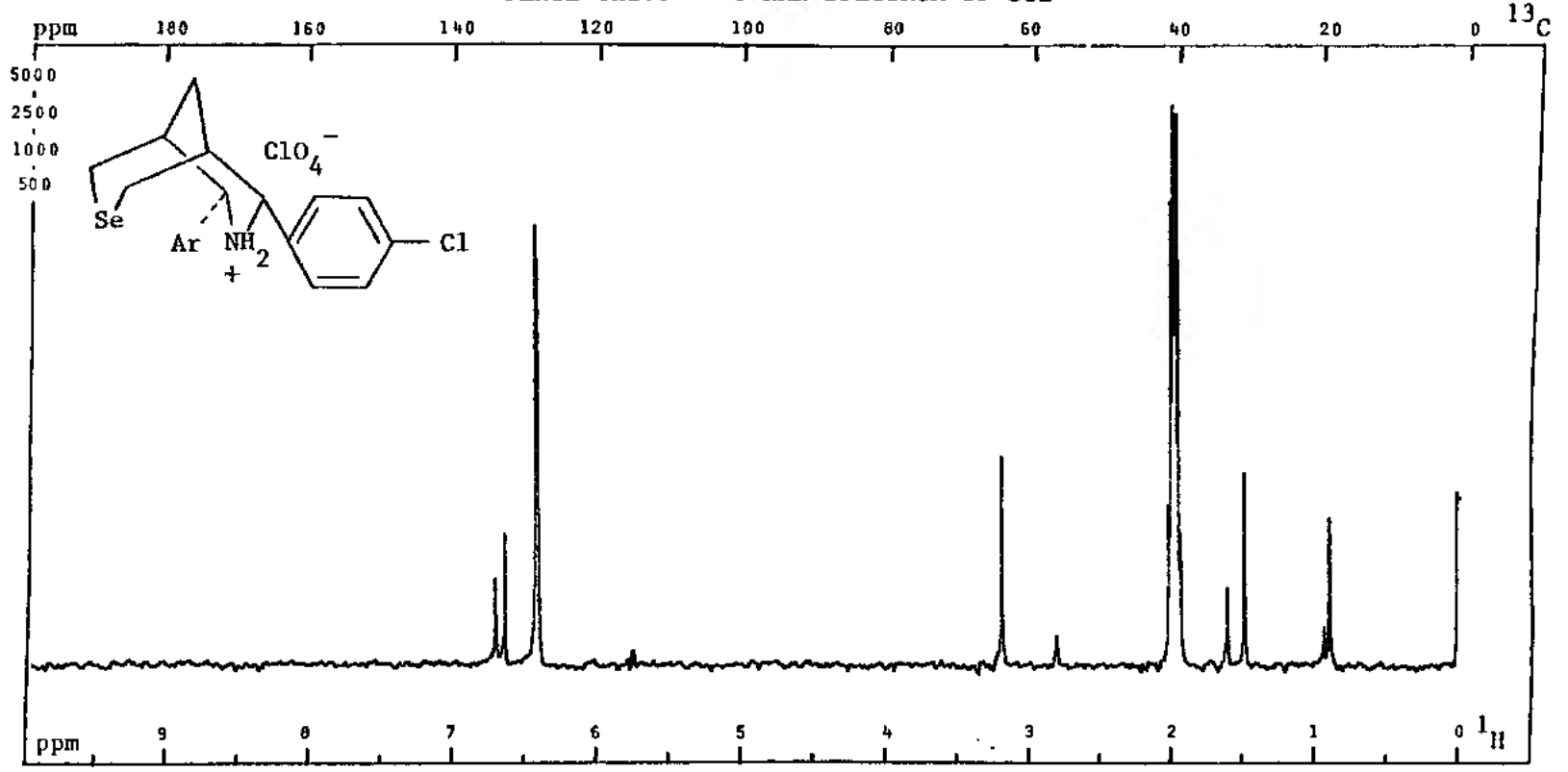


PFT X CW _ ; Solvent: DMSO-d_6; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 8 .

Size: 12 K; PW/RF: 5 µs/dB; TO: 1500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 0 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE CXIV. ^{13}C NMR SPECTRUM OF **36i**

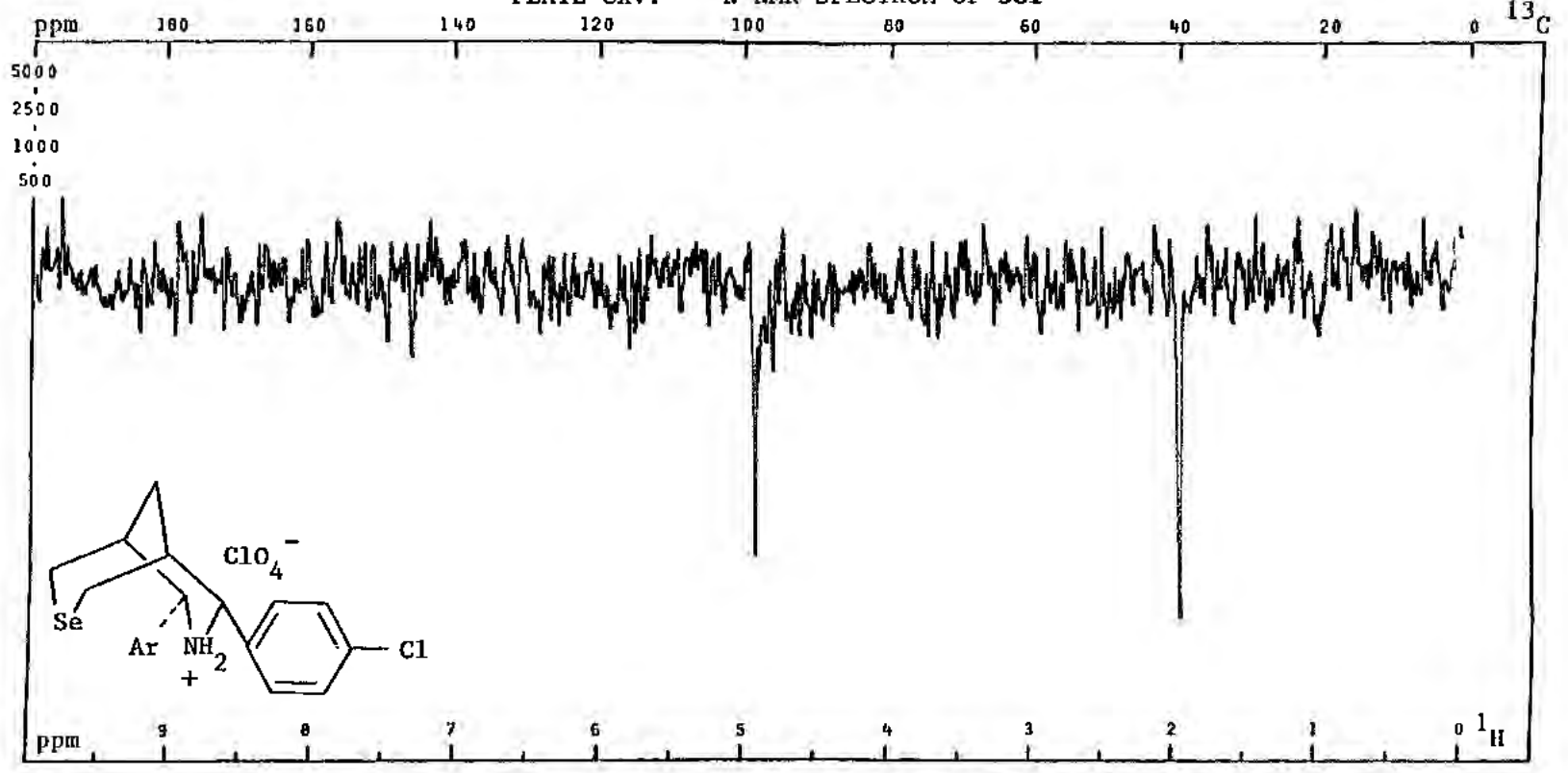


PFT X CW _ ; Solvent: DMSO-d_6; SF: 75.4 MHz; WC: 15085 Hz; T: 25 °C; NT: 240 .

Size: 16K; PW/RF: 12 µs/dB; TO: 1500 Hz; FB: Hz; Lock: ^2D ; D1,D5: 4 s.

DC: Y, N ; Gated Off:A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE CXV. ^{15}N NMR SPECTRUM OF **36i**

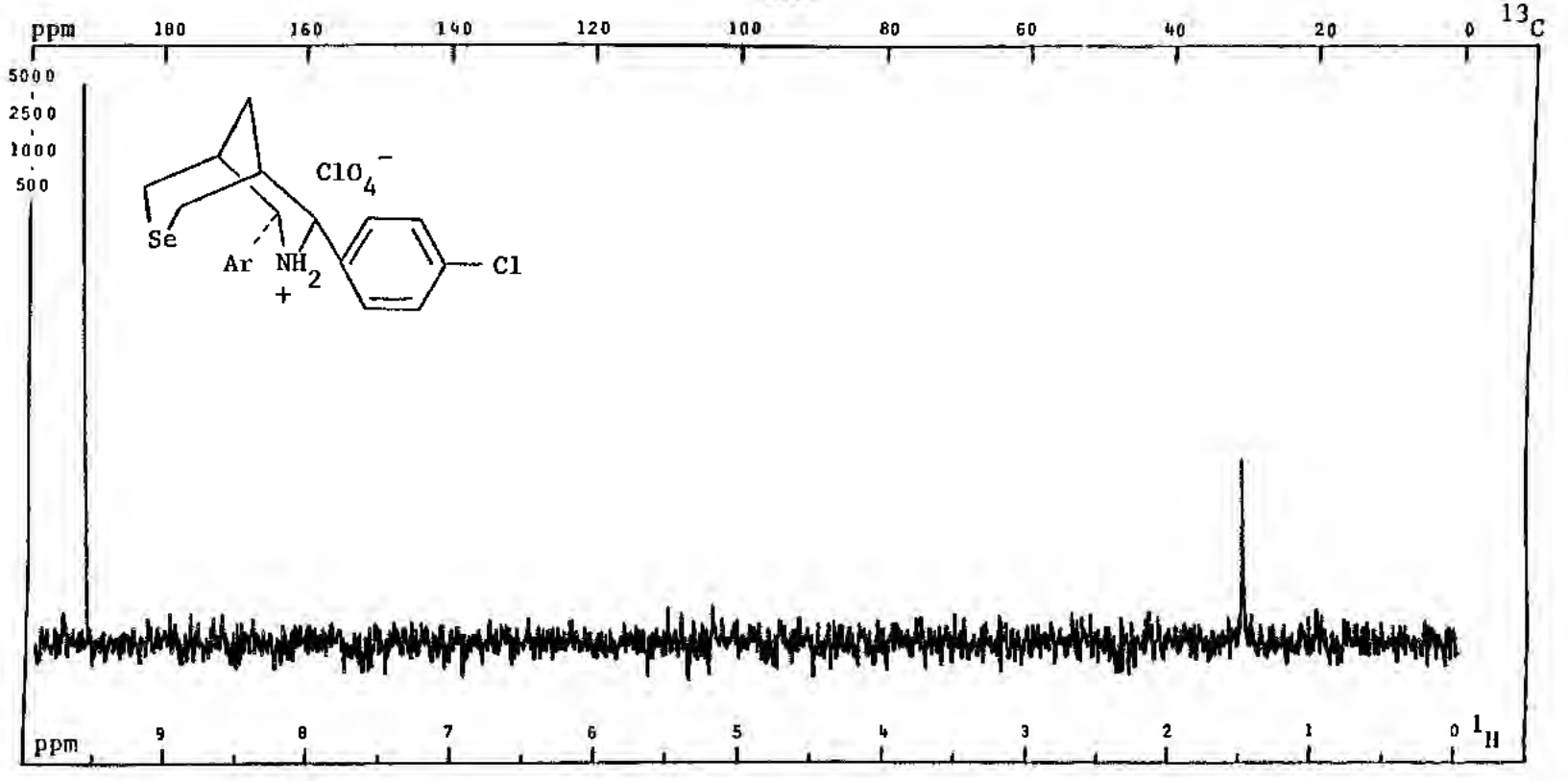


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 30.406 MHz; WC: 3040.6 Hz; T: 25 °C; NT: 6000

Size: 12 K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 8 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE CXVI. ^{77}Se NMR SPECTRUM OF **36i**



PFT/ CW _ ; Solvent: DMSO-d_6 ; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 200 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 15 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE CXVII. IR SPECTRUM OF **37**

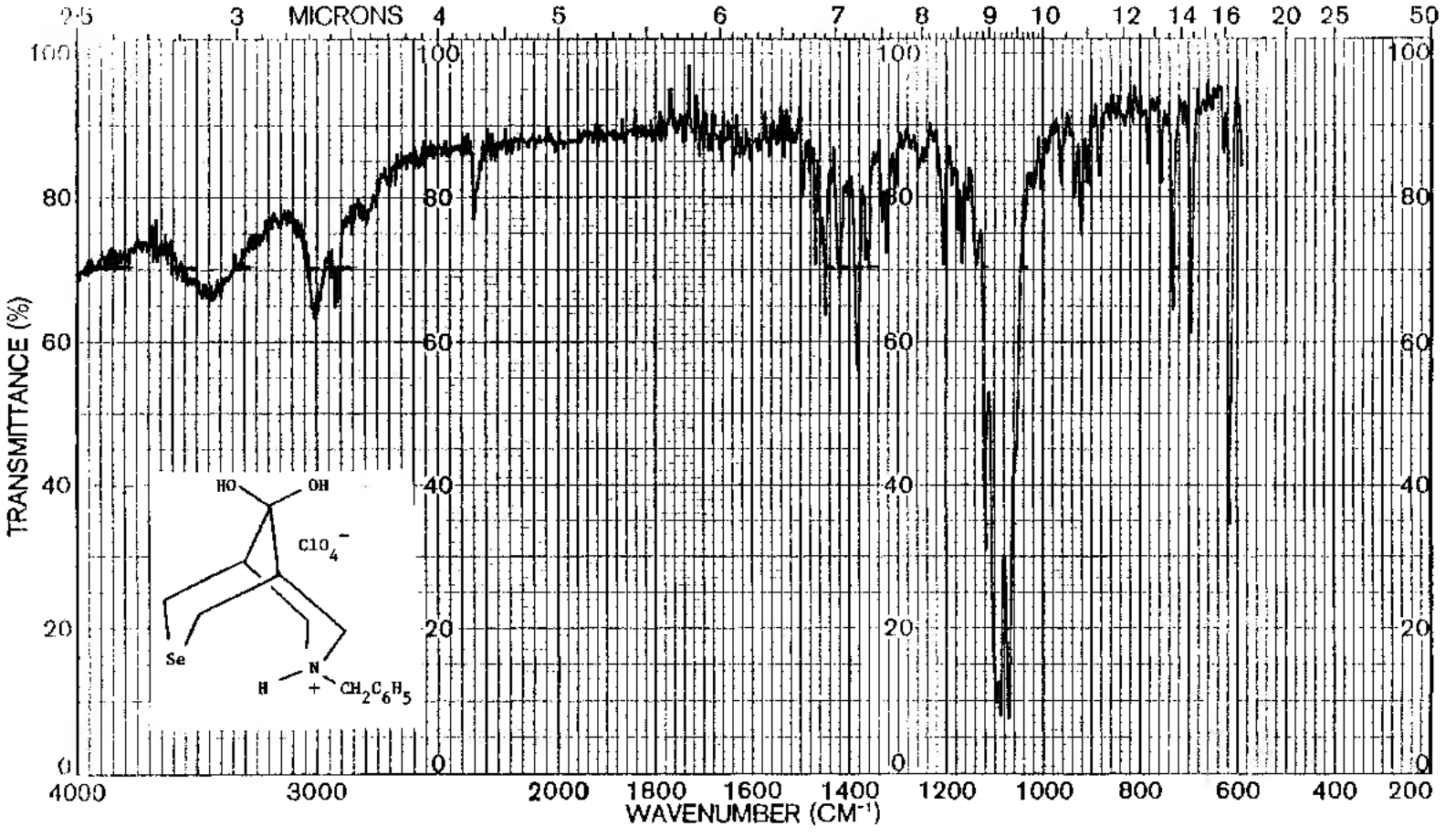
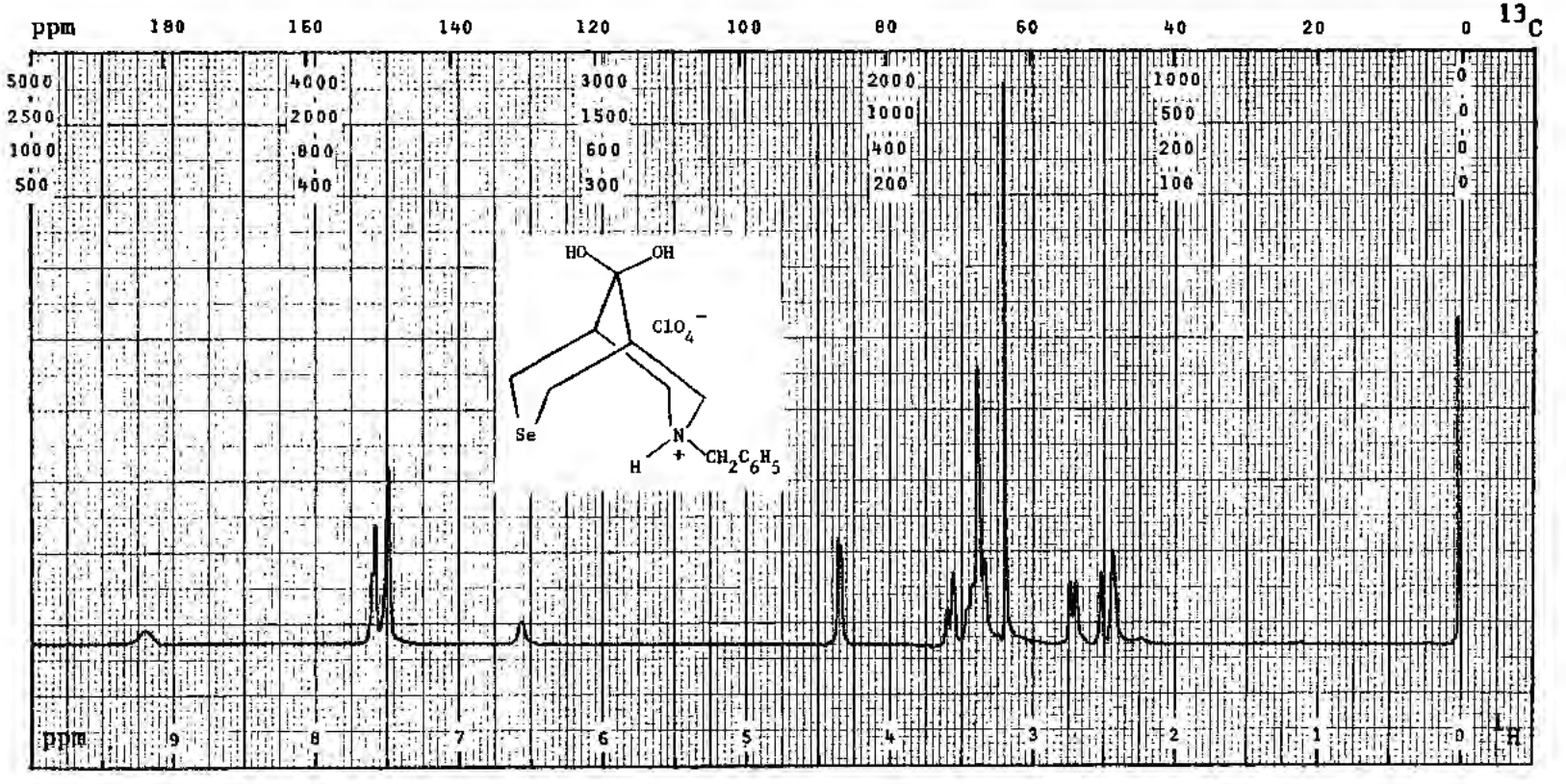


PLATE CXVIII. ^{1}H NMR SPECTRUM OF **37**

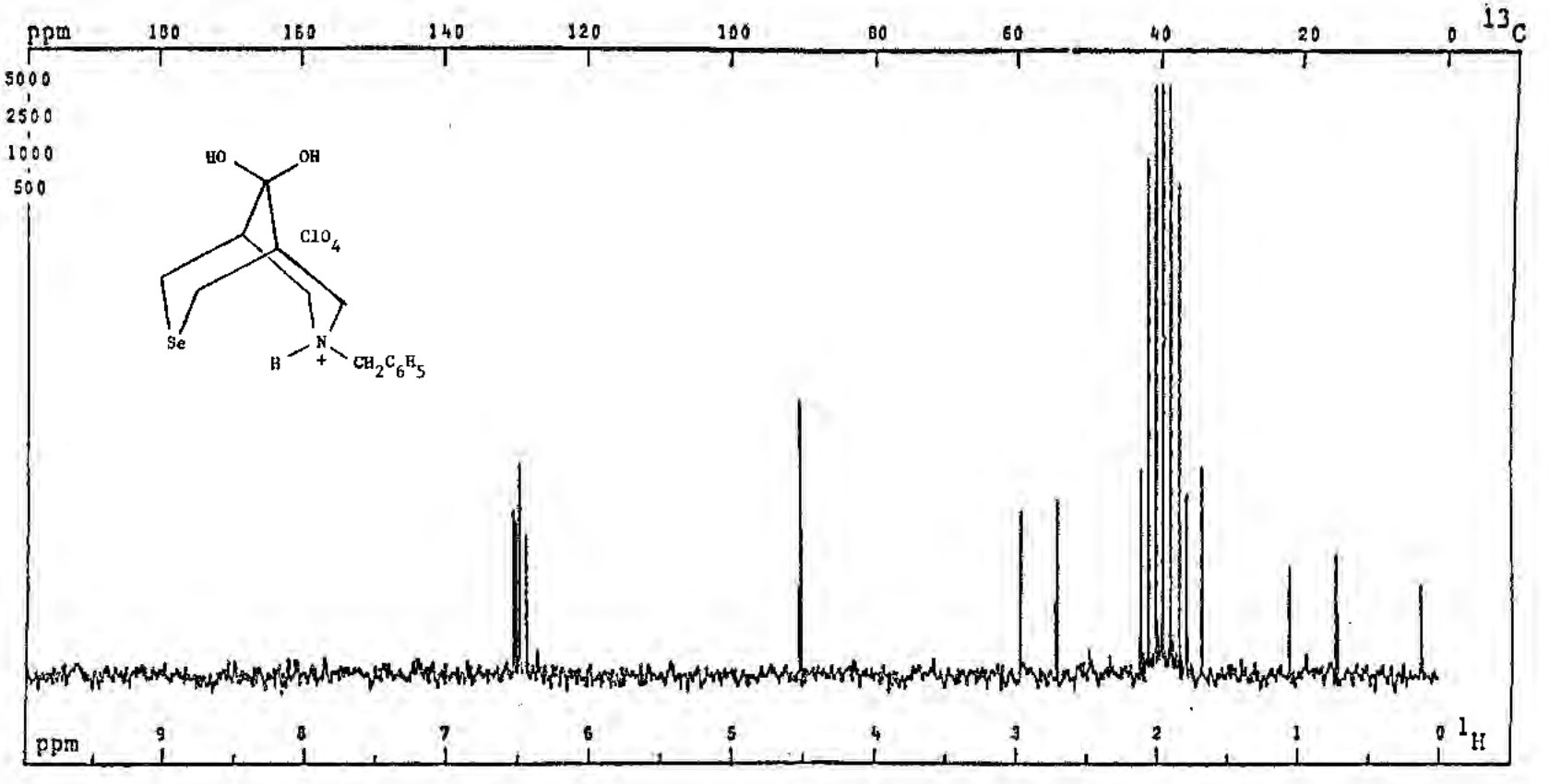


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 299.94MHz; WC: 3000 Hz; T: 25 °C; NT: 4 .

Size: 12 K; PW/RF: 5 µs/dB; SO: 1500 Hz; FB: Hz; Lock: ^{2}D ; Delay: 0.5 s.

DC: N ; Gated Off: ; Offset: Hz; RF: W/dB; NBW: Hz; LB: .

PLATE CXIX. ^{13}C NMR SPECTRUM OF 37

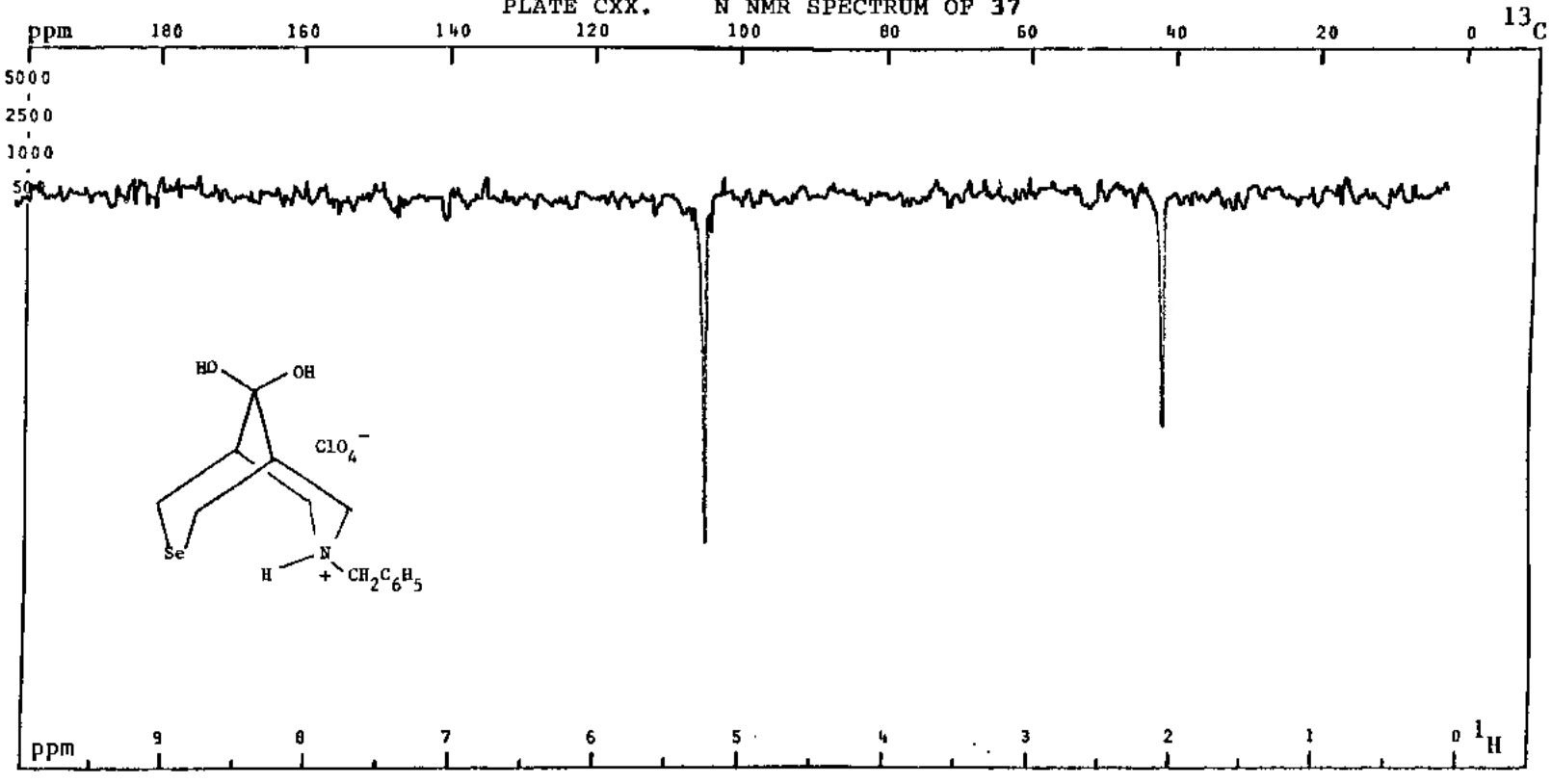


PFT _ CW X ; Solvent: DMSO-d_6 ; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 800 .

Size: 8 K ; PW/RF: 5 µs/dB; TO: 35201 Hz; FB: 3K Hz; Lock: ^2D ; D1,D5: 10 s.

DC: Y, N ; Gated Off:A or D ; DO: 45316 Hz; RF(Power): 7.5 W/dB; NBW: Hz; LB: Hz.

PLATE CXX. ^{15}N NMR SPECTRUM OF **37**

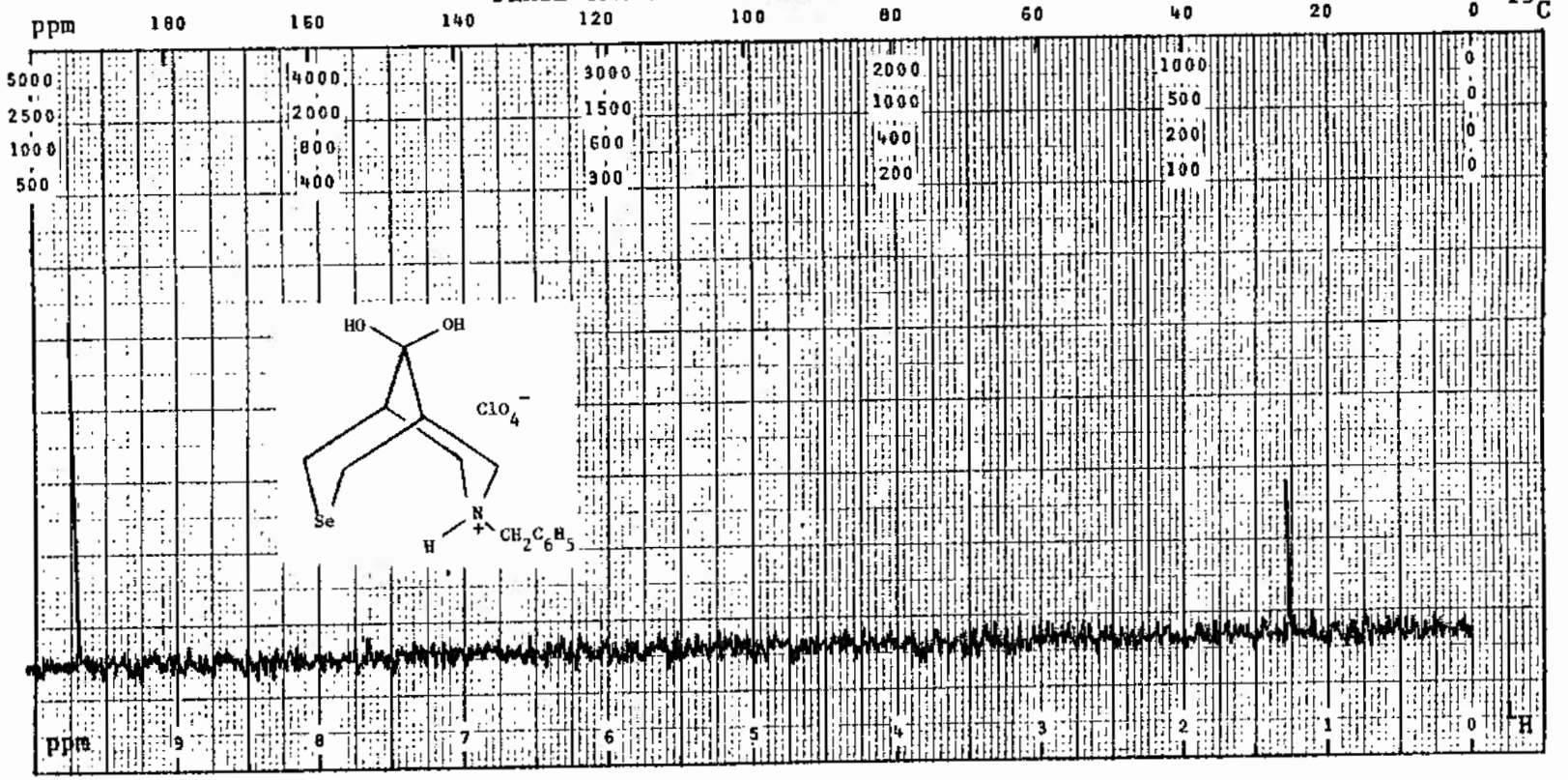


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 30.406 MHz; WC: 3040.6 Hz; T: 25 °C; NT: 15800

Size: 12K; PW/RF: 40 µs/dB; TO: -11600 Hz; FB: Hz; Lock: ^2D ; D1,D5: 8 s.

DC: Y, N ; Gated Off:A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE CXXI. ^{77}Se NMR SPECTRUM OF **37**



PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 88 .

Size: 32 K; PW/RF: 35 μs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5 : 25 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE CXXII. IR SPECTRUM OF **38**

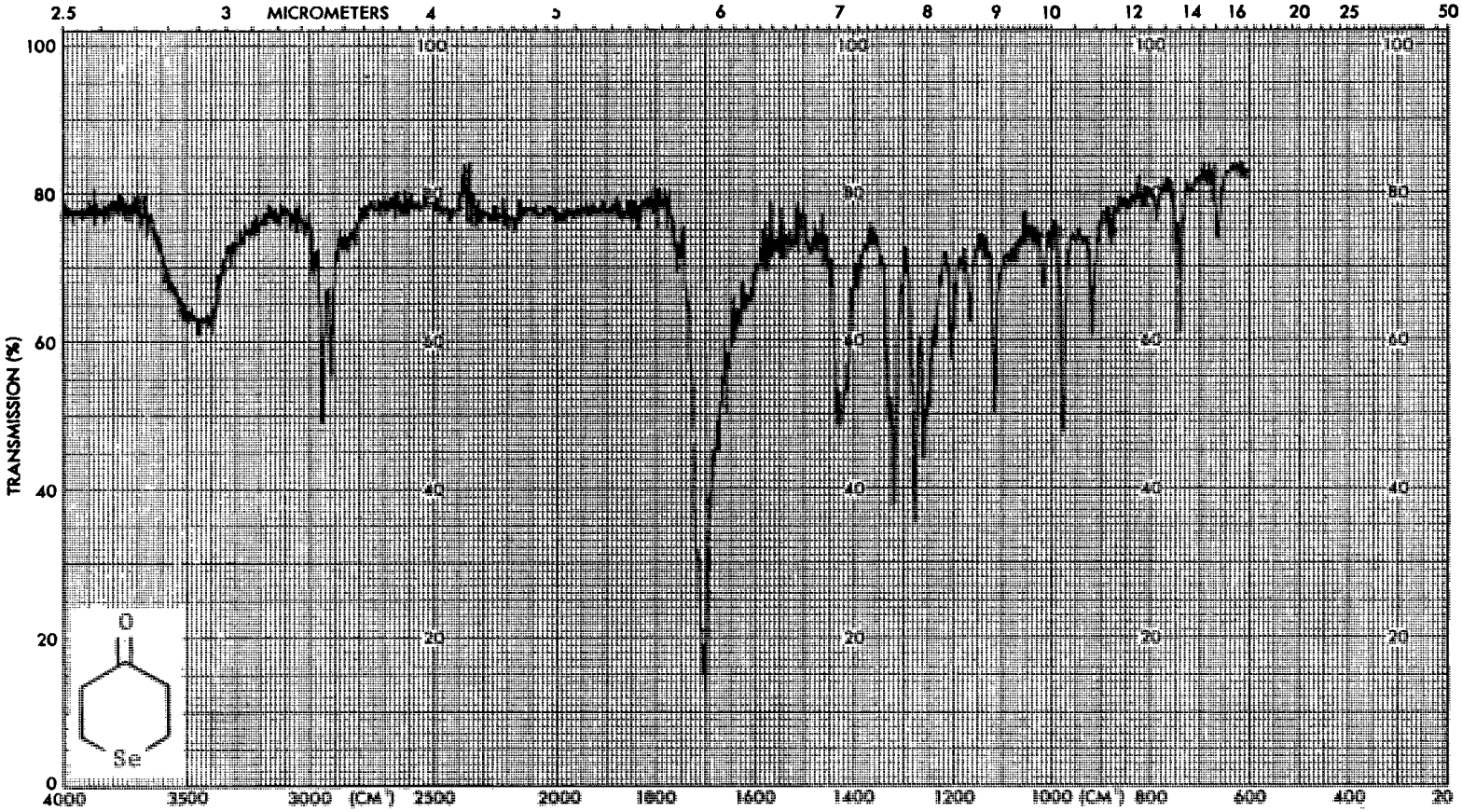
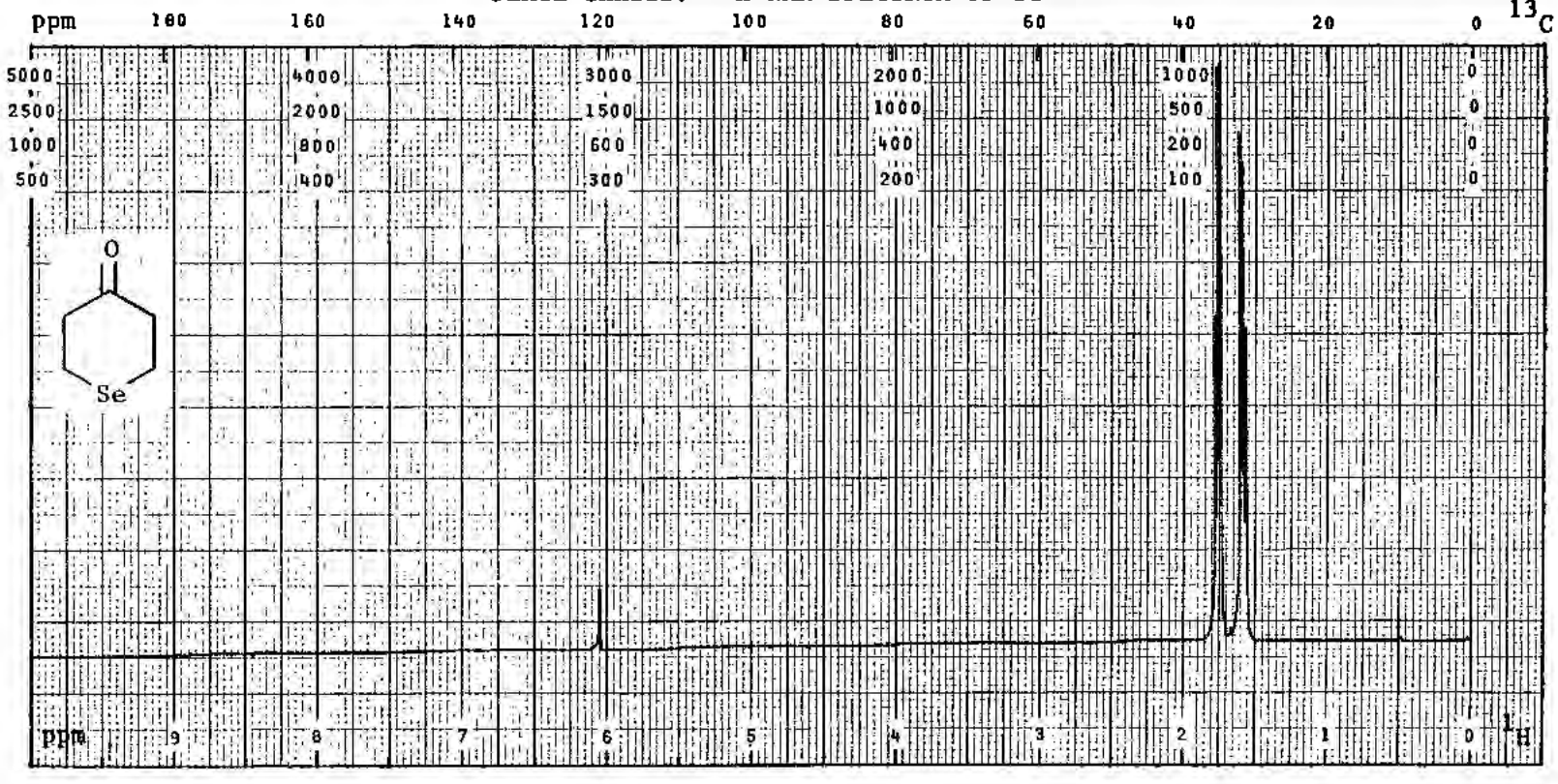


PLATE CXXIII. ^{1}H NMR SPECTRUM OF **38**

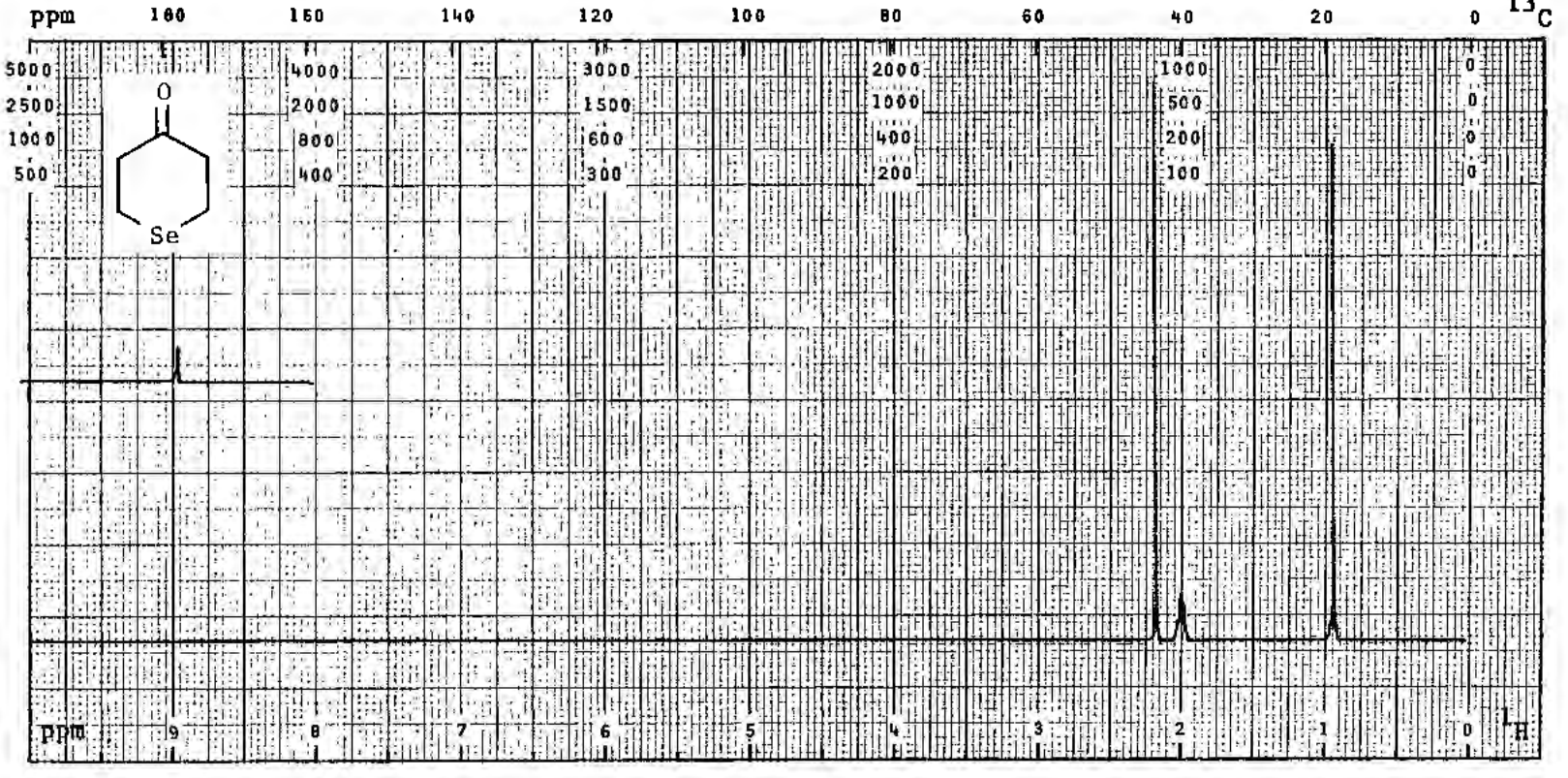


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 4

Size: 12K; PW/RF: 5.1 μs/dB; SO: 200 Hz; FB: Hz; Lock: ^{2}D ; Delay: 0.500 s.

DC: N ; Gated Off: ; Offset: Hz; RF: W/dB; NBW: Hz; LB:

PLATE CXXIV. ^{13}C NMR SPECTRUM OF **38**

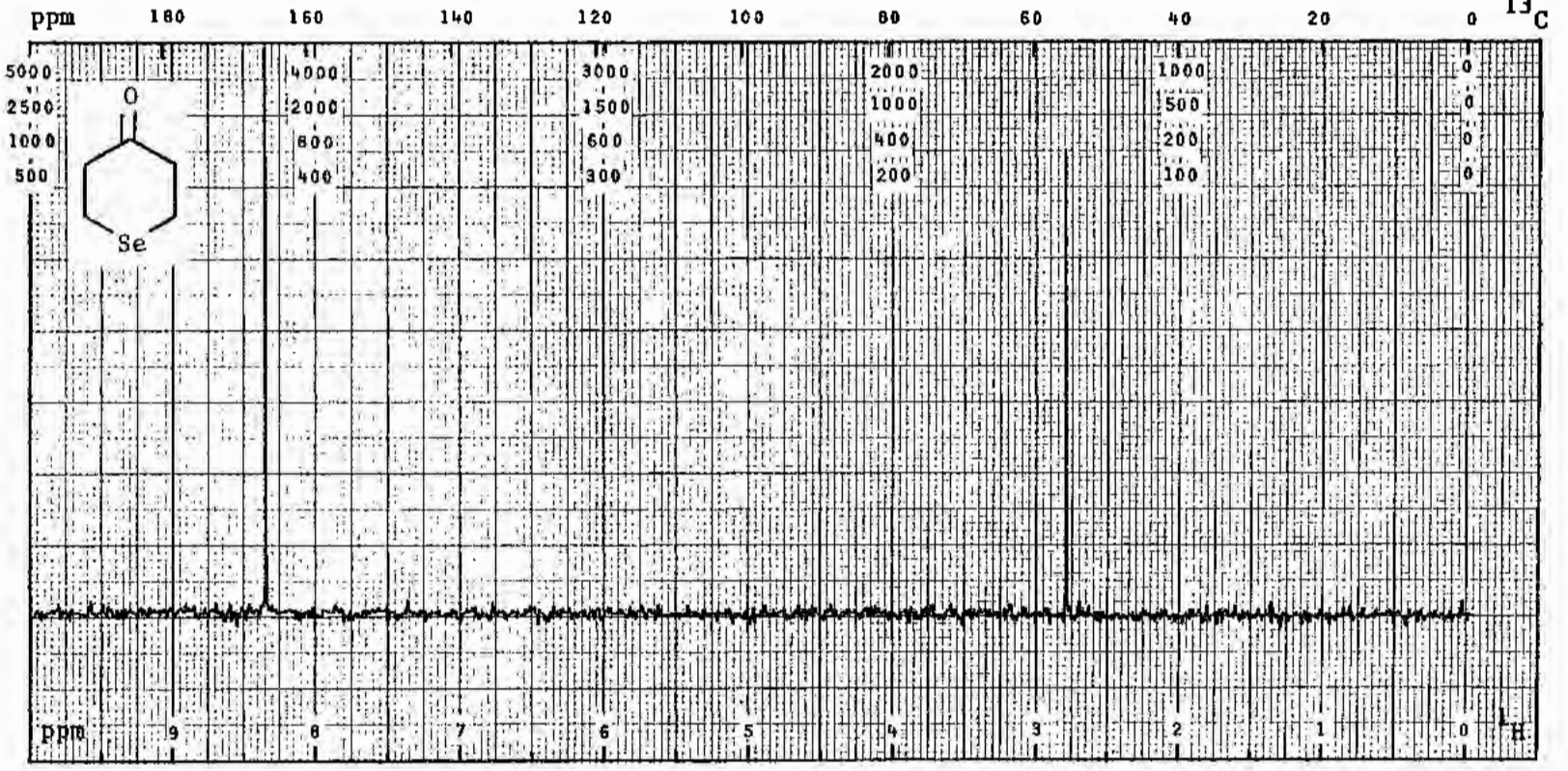


PFTX_ CW _ ; Solvent: DMSO-d_6 ; SF: 24.2 MHz; WC: 6000 Hz; T: 28 °C; NT: 4000 .

Size: 8 K; PW/RF: 10 µs/dB; SO: 35101 Hz; FB: Hz; Lock: ^{2}D ; Delay: 5 s.

DC: Y ; Gated Off: ; Offset: 45316 Hz; RF: 7.5 W/dB; NBW: Hz; LB: .

PLATE CXXV. ^{77}Se NMR SPECTRUM OF **38**

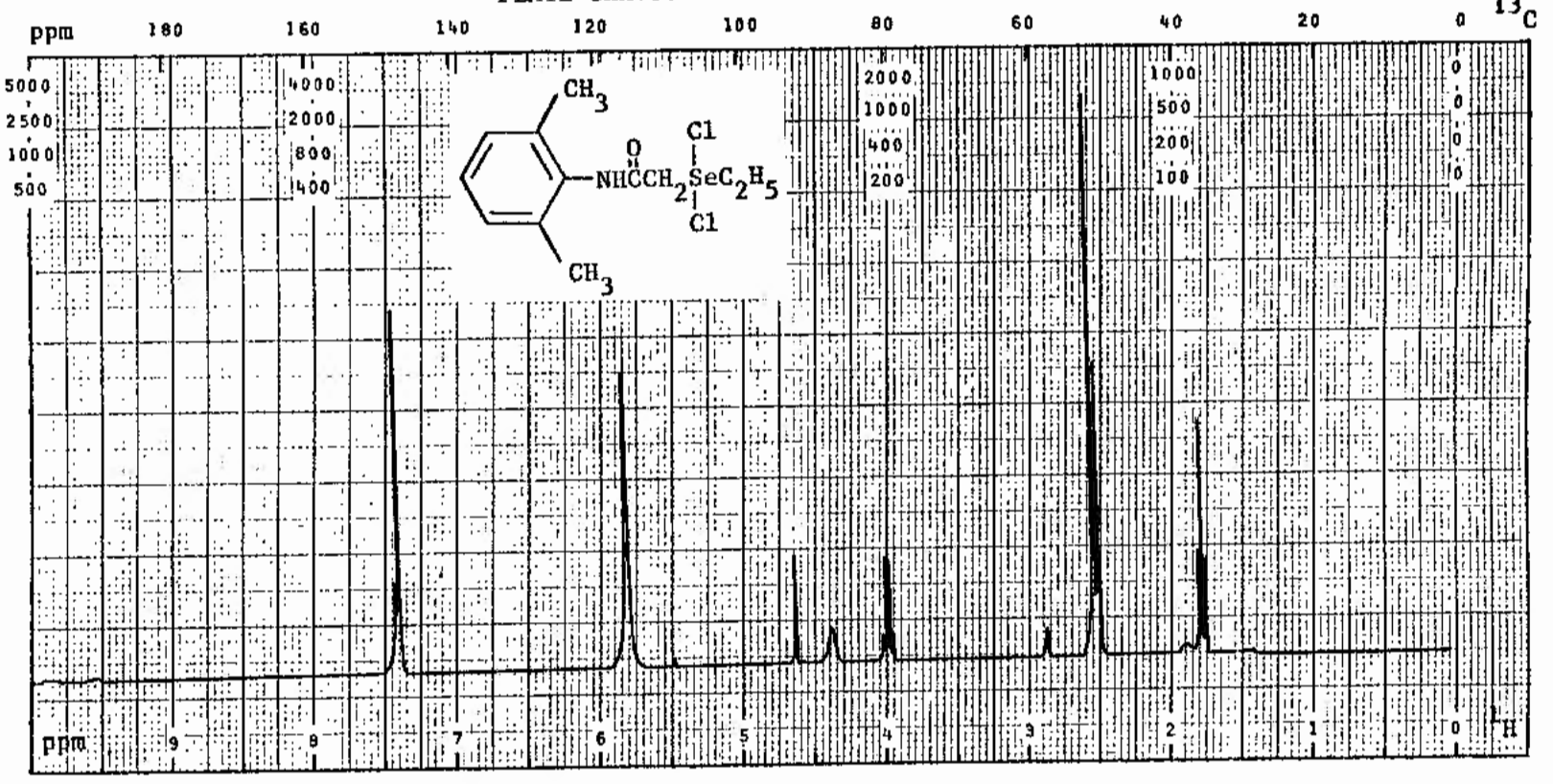


PFT X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 500 Hz; T: 25 °C; NT: 32

Size: 32 K; PW/RF: 35.0 µs/dB; SO: 500 Hz; FB: Hz; Lock: ^2D ; Delay: 25.0 s.

DC: Y ; Gated Off: ; Offset: 0 Hz; RF: 20 W/dB; NBW: Hz; LB:

PLATE CXXVI. ^{1}H NMR SPECTRUM OF 39

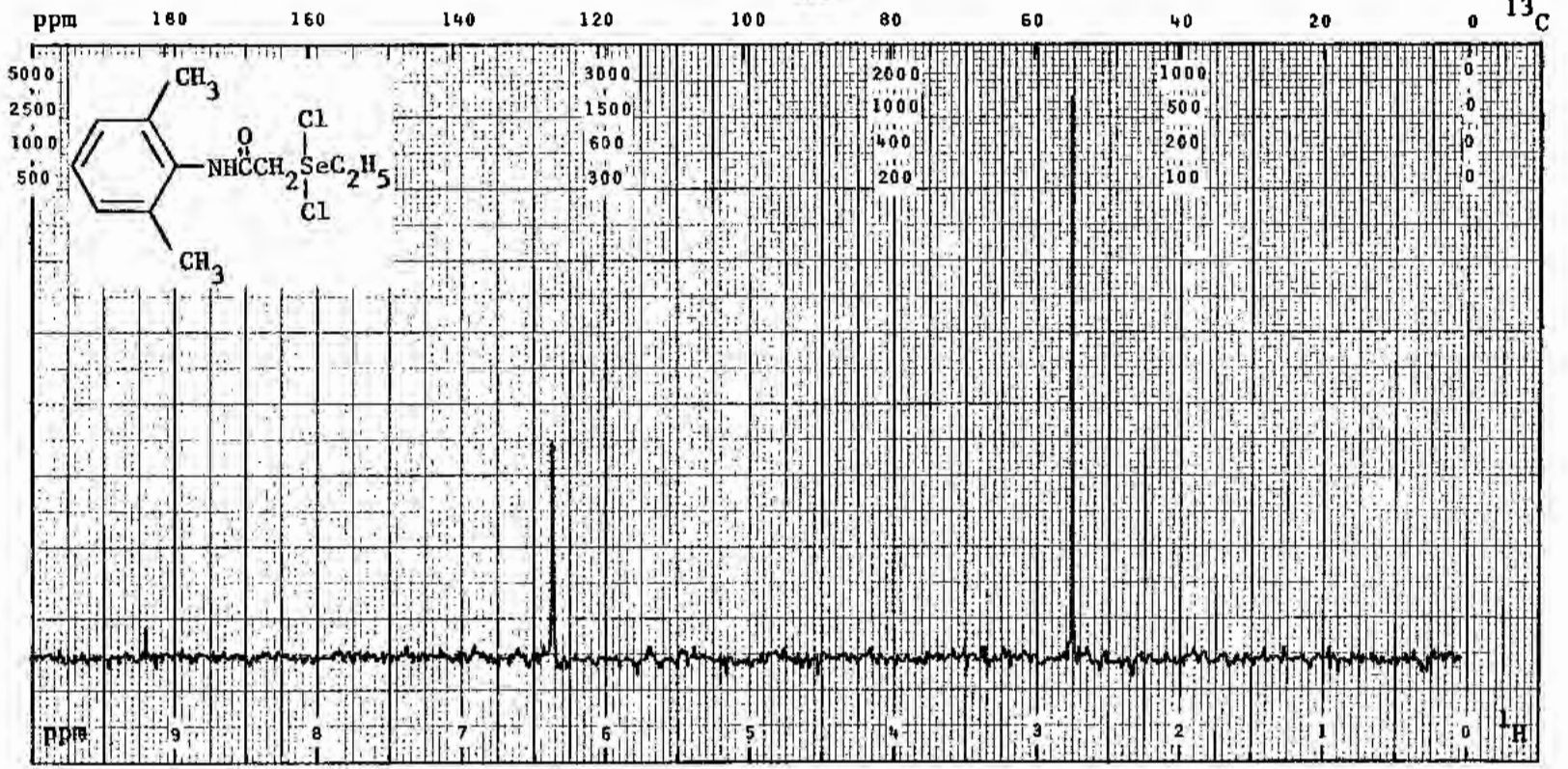


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 20 .

Size: 12 K; PW/RF: 5 µs/dB; TO: 1500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5 : 0.5 s.

DC: Y, N ; Cated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz.

PLATE CXXVIII. ^{77}Se NMR SPECTRUM OF 39



PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 57.22 MHz; WC:17166 Hz; T: 25 °C; NT: 40 .

Size: 32 K; PW/RF: 35 µs/dB; SO: 500 Hz; FB: Hz; Lock: ^{2}D ; Delay: 15 s.

DC: Y ; Gated Off: ; Offset: 0 Hz; RF: 20 W/dB; NBW: Hz; LB: .

PLATE CXXIX. IR SPECTRUM OF 41

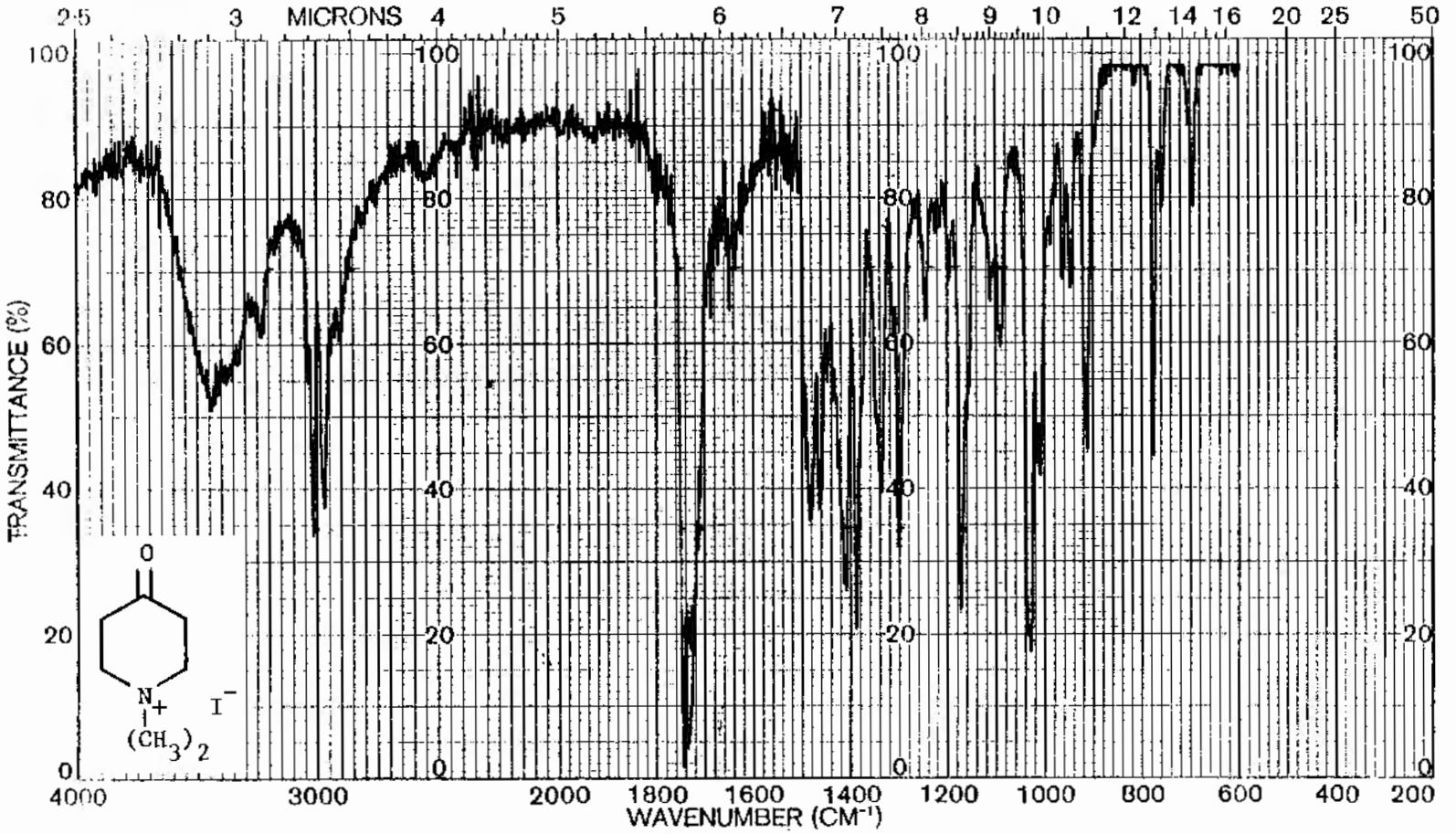
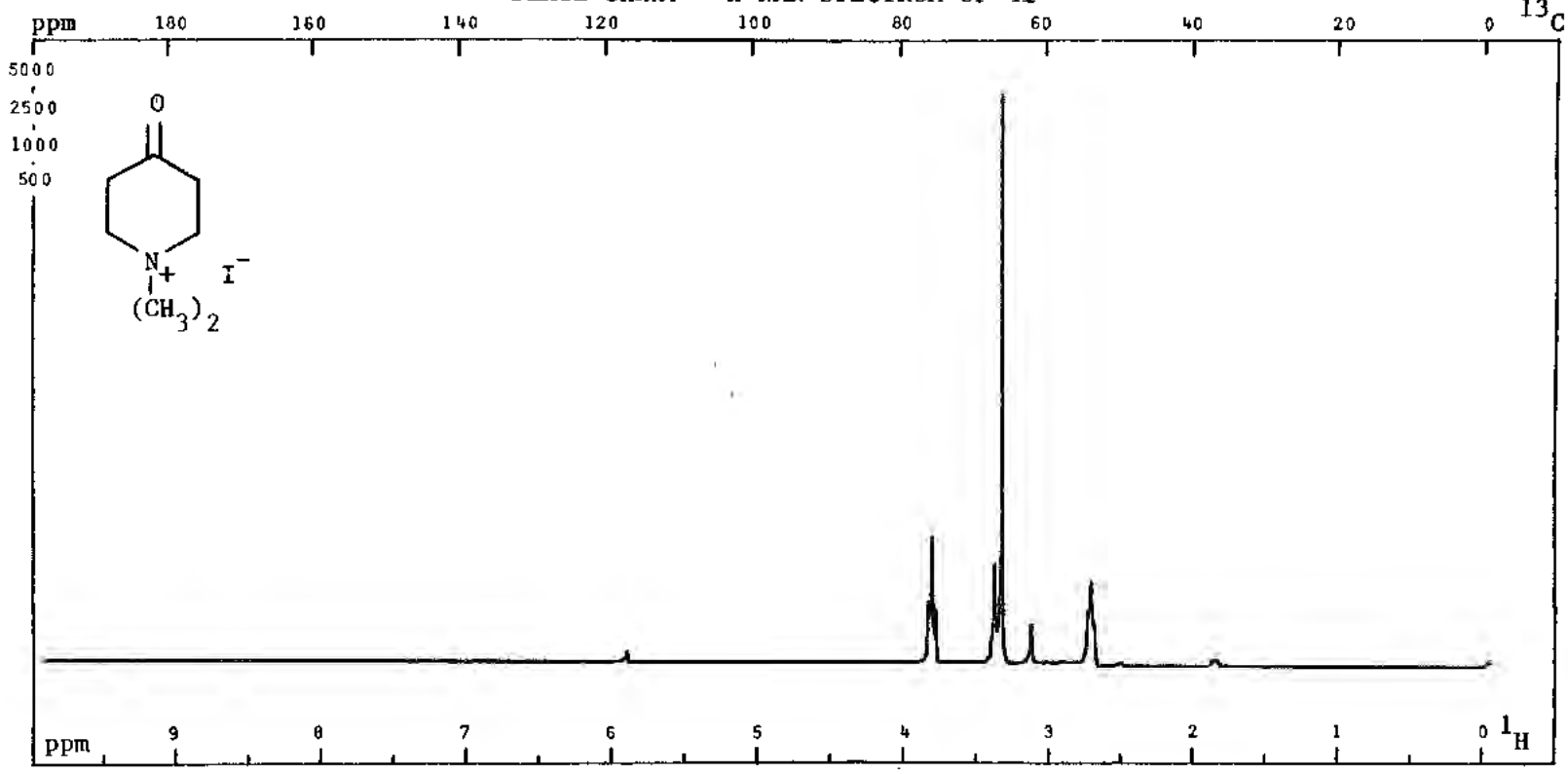


PLATE CXXX. ^{1}H NMR SPECTRUM OF **41**

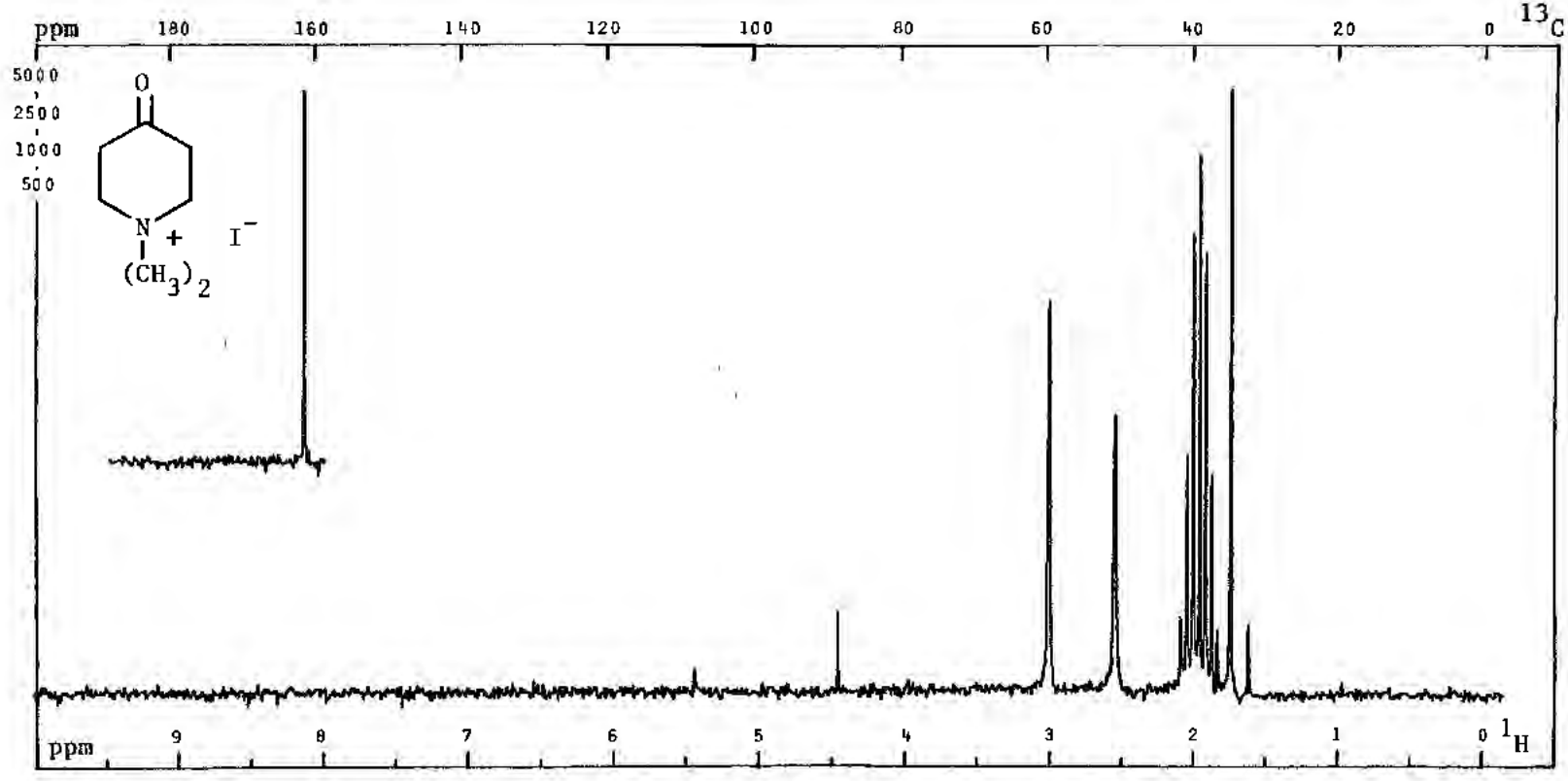


PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 4 .

Size: 12 K; PW/RF: 3.0 µs/dB; SO: 100 Hz; FB: Hz; Lock: ^{2}D ; Delay: 0.500 s.

DC: ; Gated Off: ; Offset: Hz; RF: W/dB; NBW: Hz; LB: .

PLATE CXXXI. ^{13}C NMR SPECTRUM OF **41**

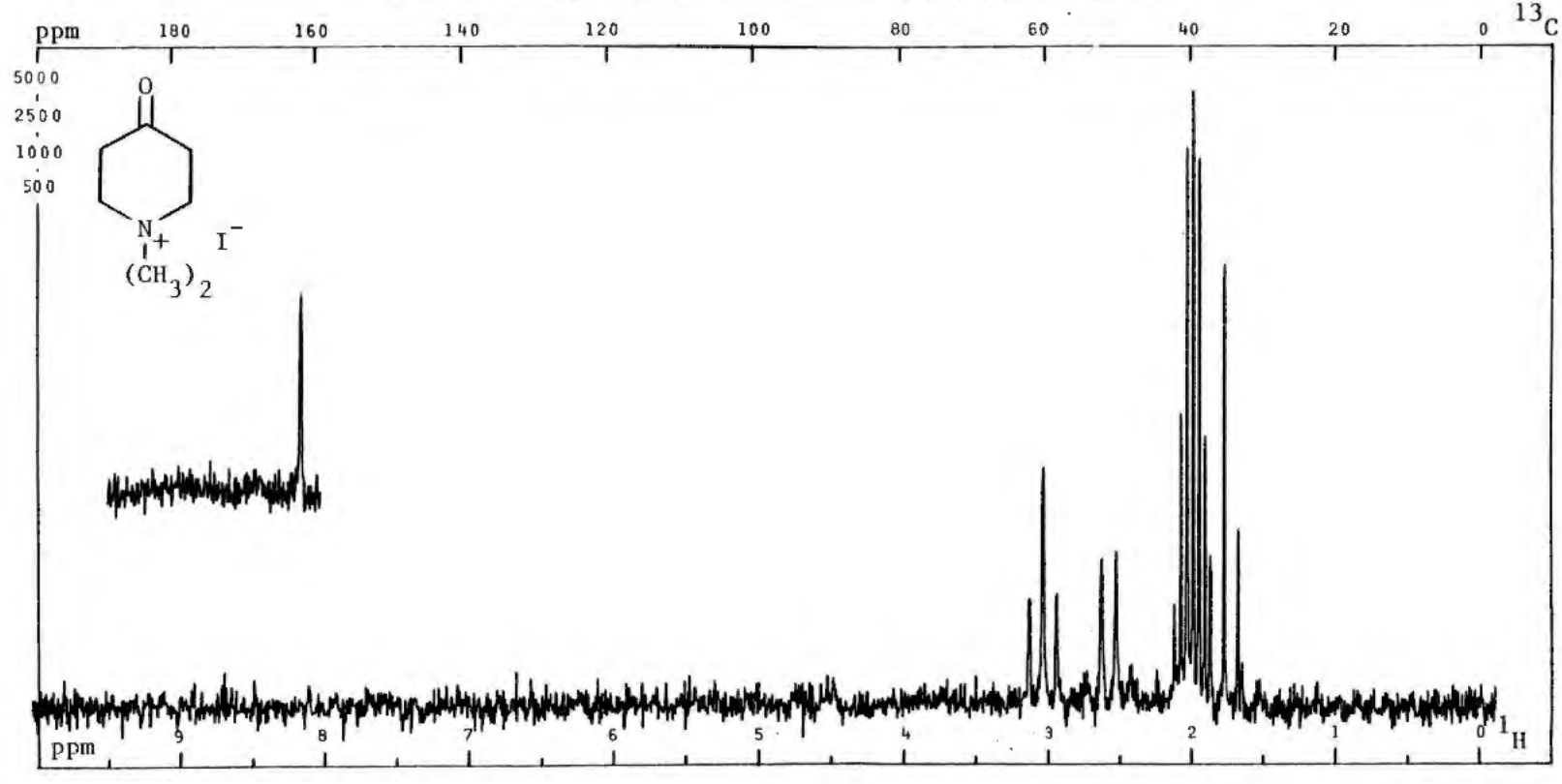


PFT X CW _ ; Solvent: DMSO-d6 ; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 1370 .

Size: 8 K; PW/RF: 10 µs/dB; SO: 35201 Hz; FB: 3K Hz; Lock: ^{2}D ; Delay: 5 s.

DC: Y ; Gated Off: ; Offset: 45316 Hz; RF: 7.5 W/dB; NBW: Hz; LB: .

PLATE CXXXII. OFF RESONANCE ^{13}C NMR SPECTRUM OF **41**



PFT X CW _ ; Solvent: DMSO-d_6 ; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 2000 .

Size: 8 K; PW/RF: 10 µs/dB; SO: 35201 Hz; FB: 3 K Hz; Lock: ^{2}D ; Delay: 5 s.

DC: Y ; Gated Off: ; Offset: 46316 Hz; RF: 7.5 W/dB; NBW: Hz; LB: .

PLATE CXXXIII. IR SPECTRUM OF **42**

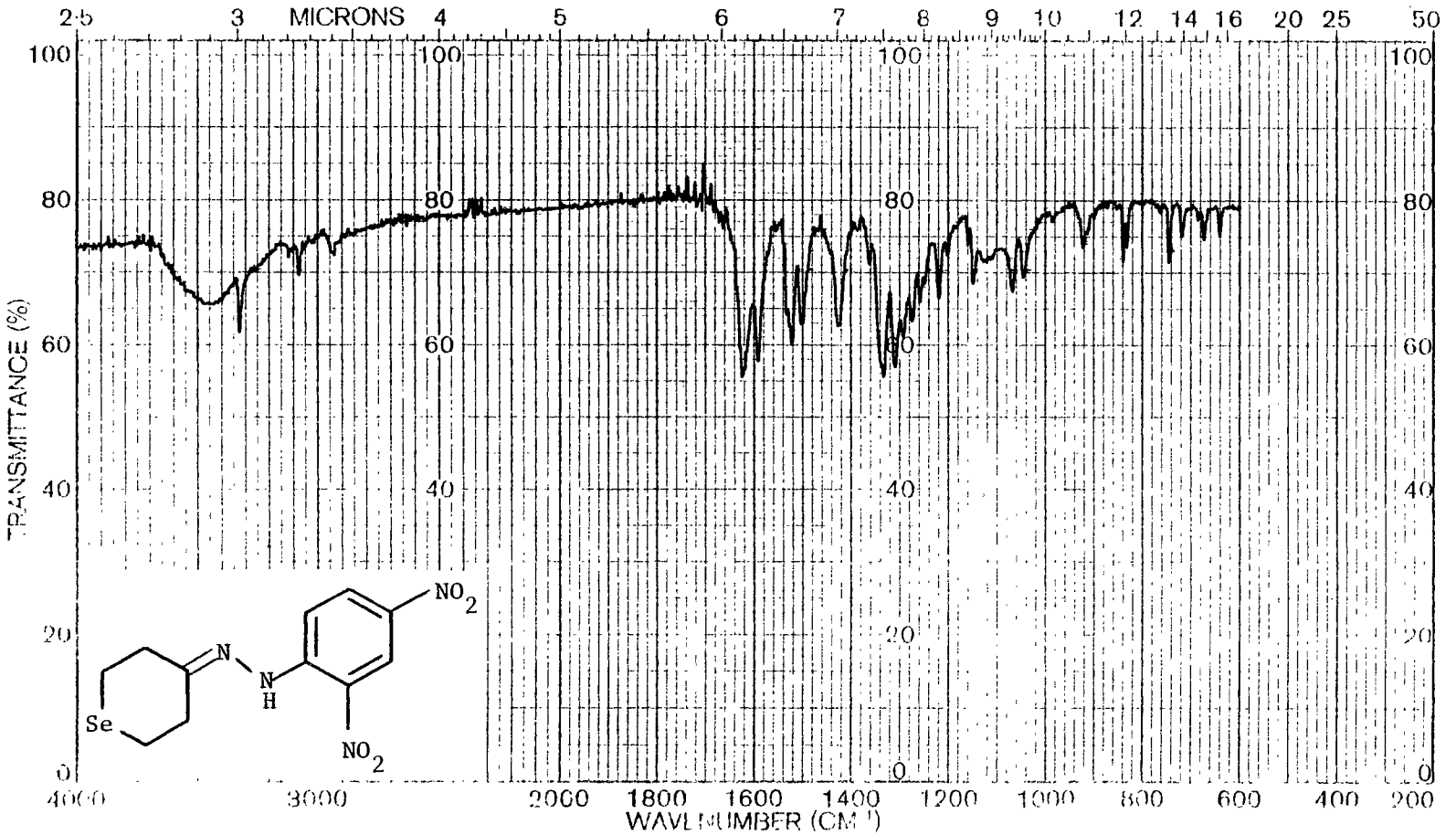
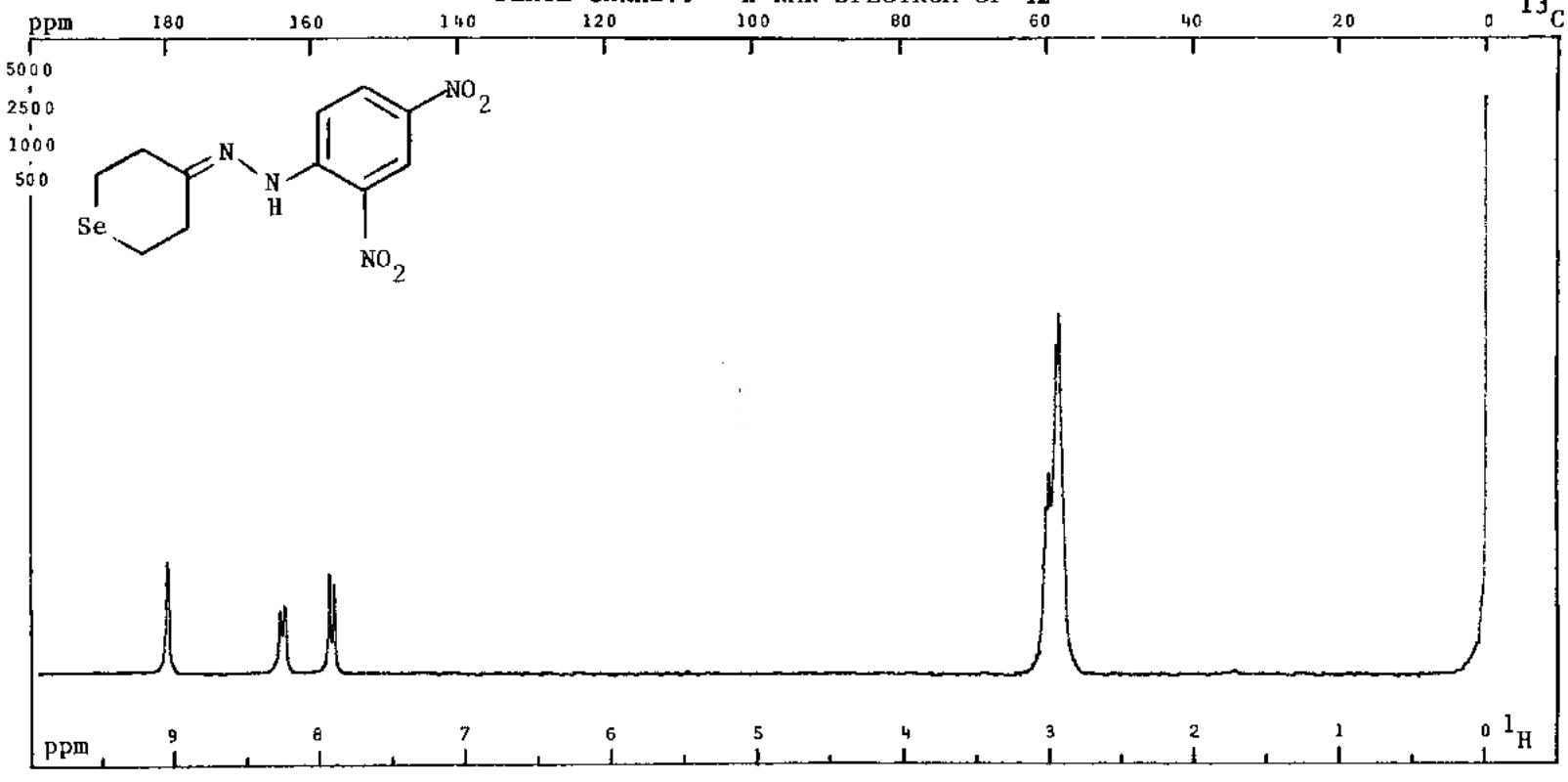


PLATE CXXXIV. ^{1}H NMR SPECTRUM OF **42**

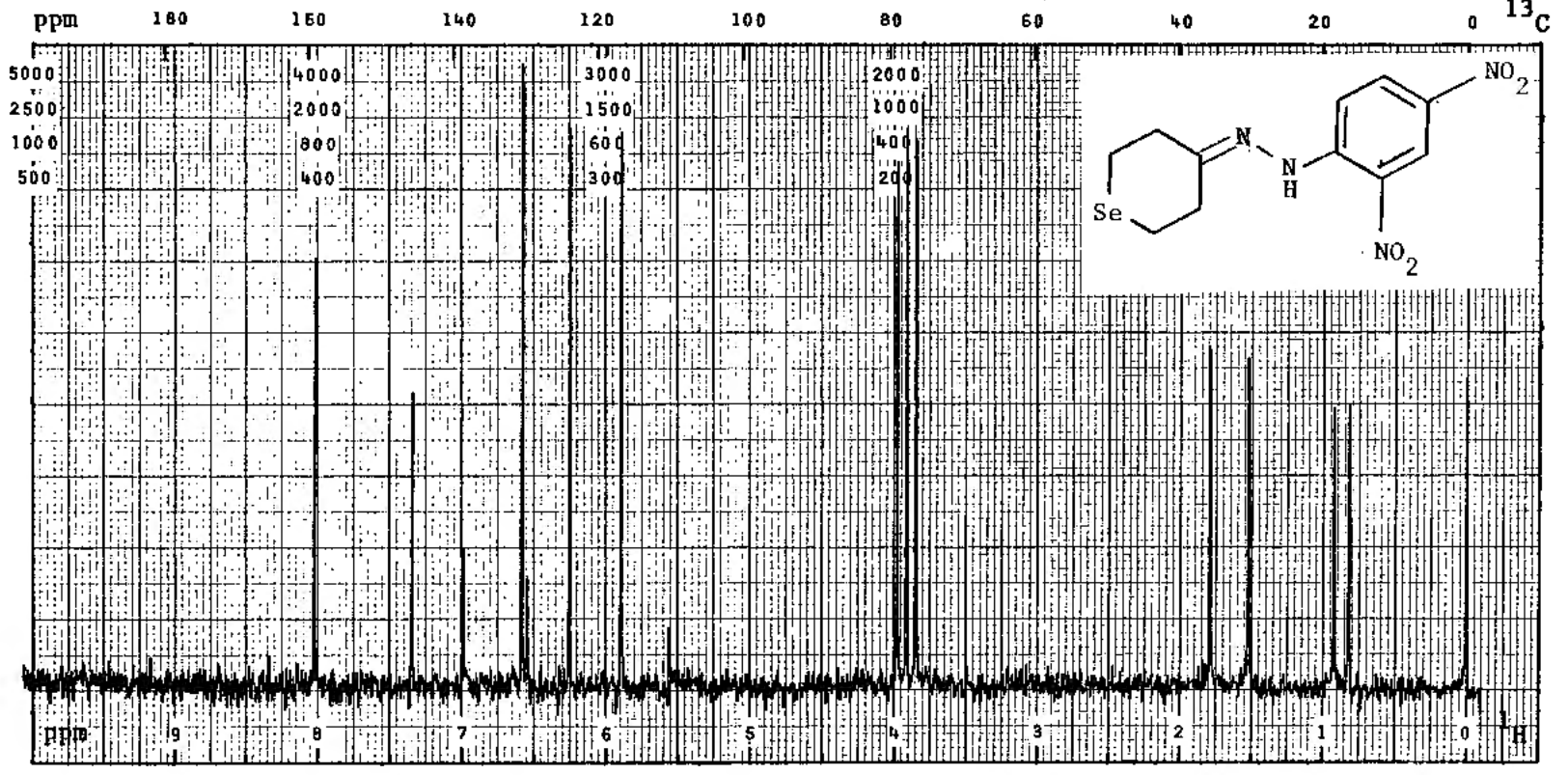


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 500 Hz; T: 25 °C; NT: 8 .

Size: 12 K; PW/RF: 90 µs/dB; SO: 0 Hz; FB: Hz; Lock: ^{2}D ; Delay: 0 s.

DC: ; Gated Off: ; Offset: Hz; RF: W/dB; NBW: Hz; LB: .

PLATE CXXXV. ^{13}C NMR SPECTRUM OF 42

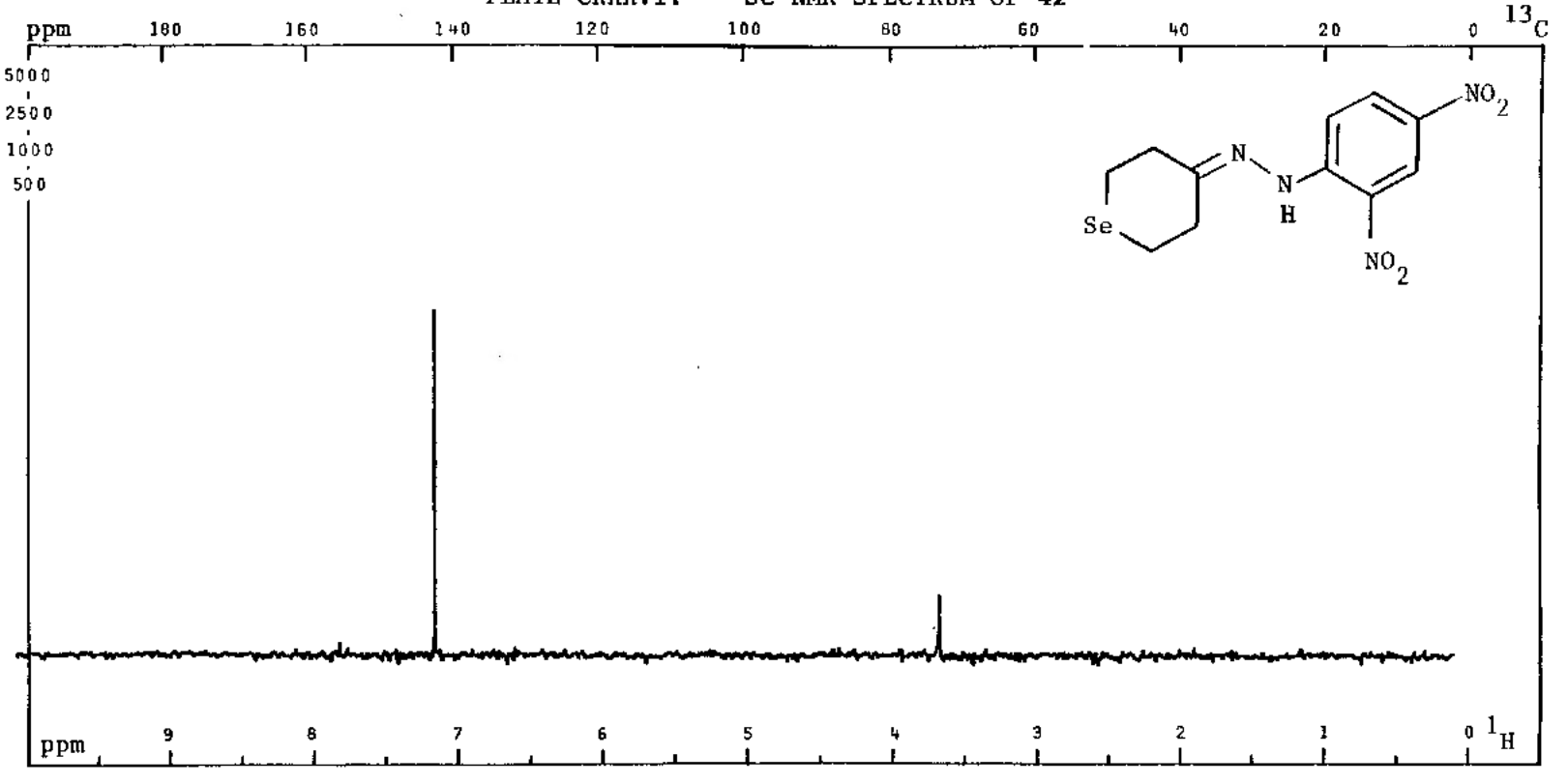


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 5000

Size: 18 K; PW/RF: 10 µs/dB; SO: 35101 Hz; FB: 3 Hz; Lock: ^2D ; Delay: 5 s.

DC: Y ; Gated Off: ; Offset: 45316 Hz; RF: 7.0 W/dB; NBW: Hz; LB:

PLATE CXXXVI. ^{77}Se NMR SPECTRUM OF 42



PFT X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 50,000 Hz; T: 25 °C; NT: 48 .

Size: 32 K; PW/RF: 35 µs/dB; SO: 500 Hz; FB: Hz; Lock: ^2D ; Delay: 25 s.

DC: Y ; Gated Off: ; Offset: 0 Hz; RF: 20 W/dB; NBW: Hz; LB: .

PLATE CXXXVII. IR SPECTRUM OF **47**

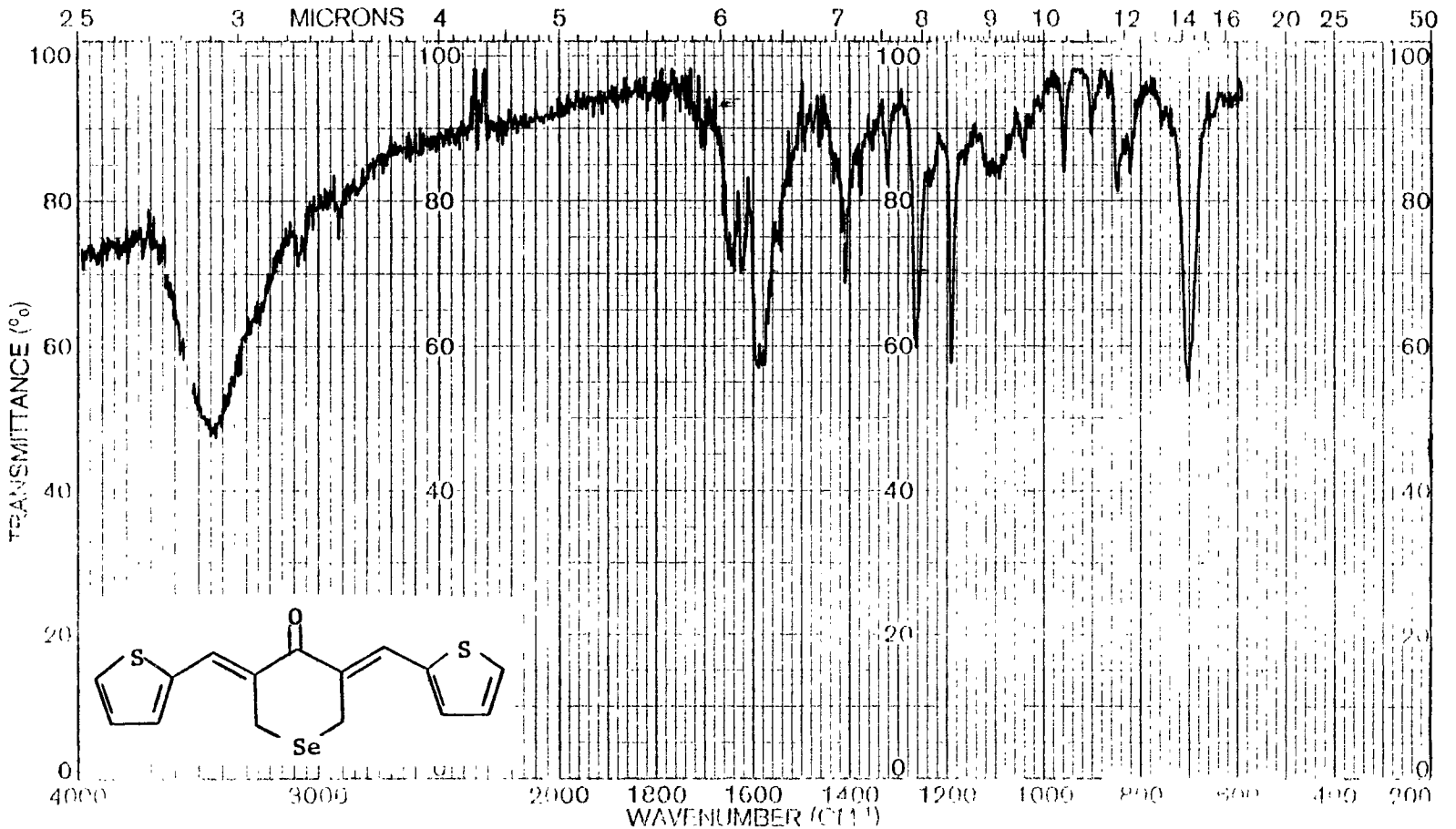
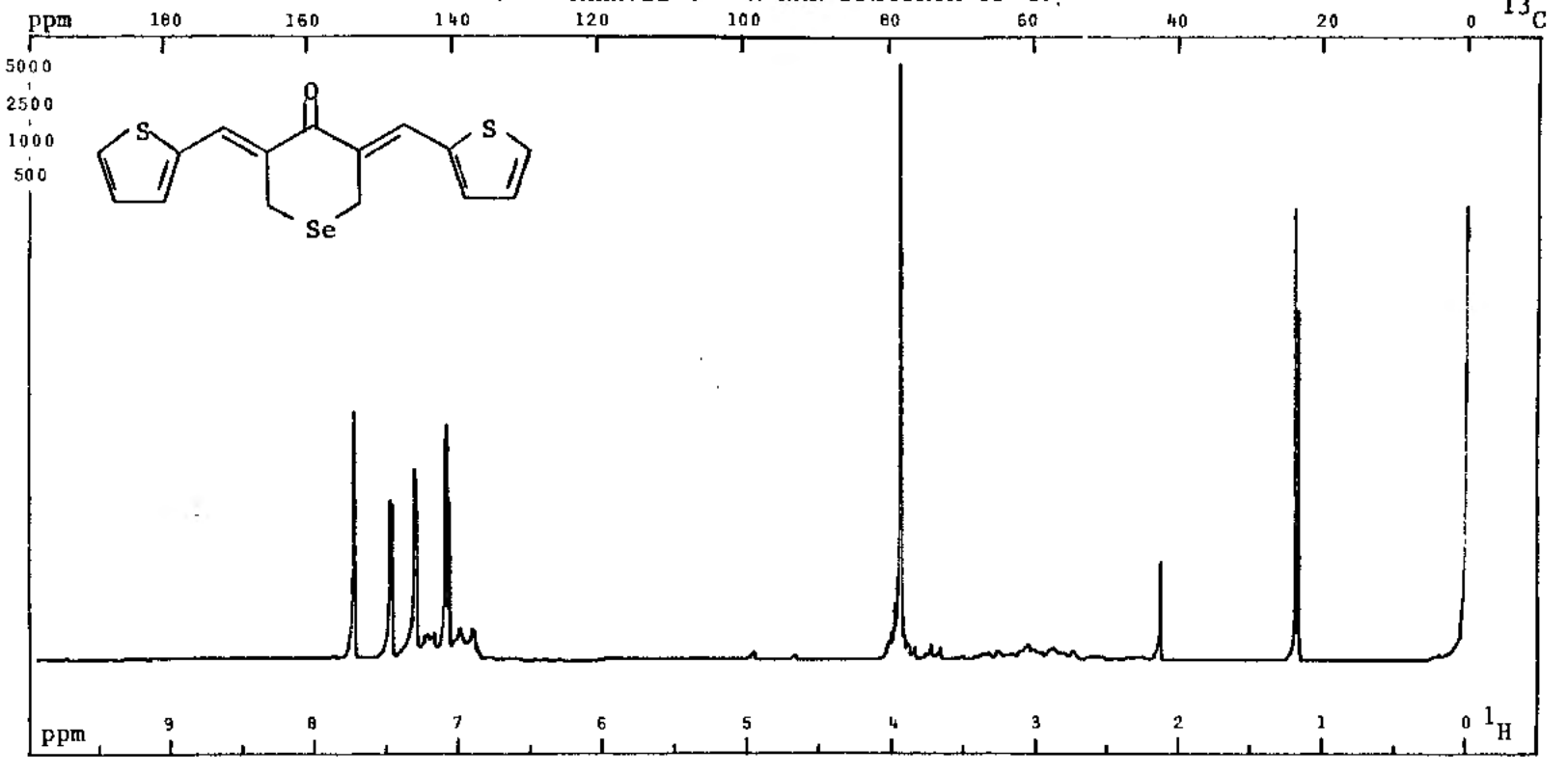


PLATE CXXXVIII. ^{1}H NMR SPECTRUM OF **47**.

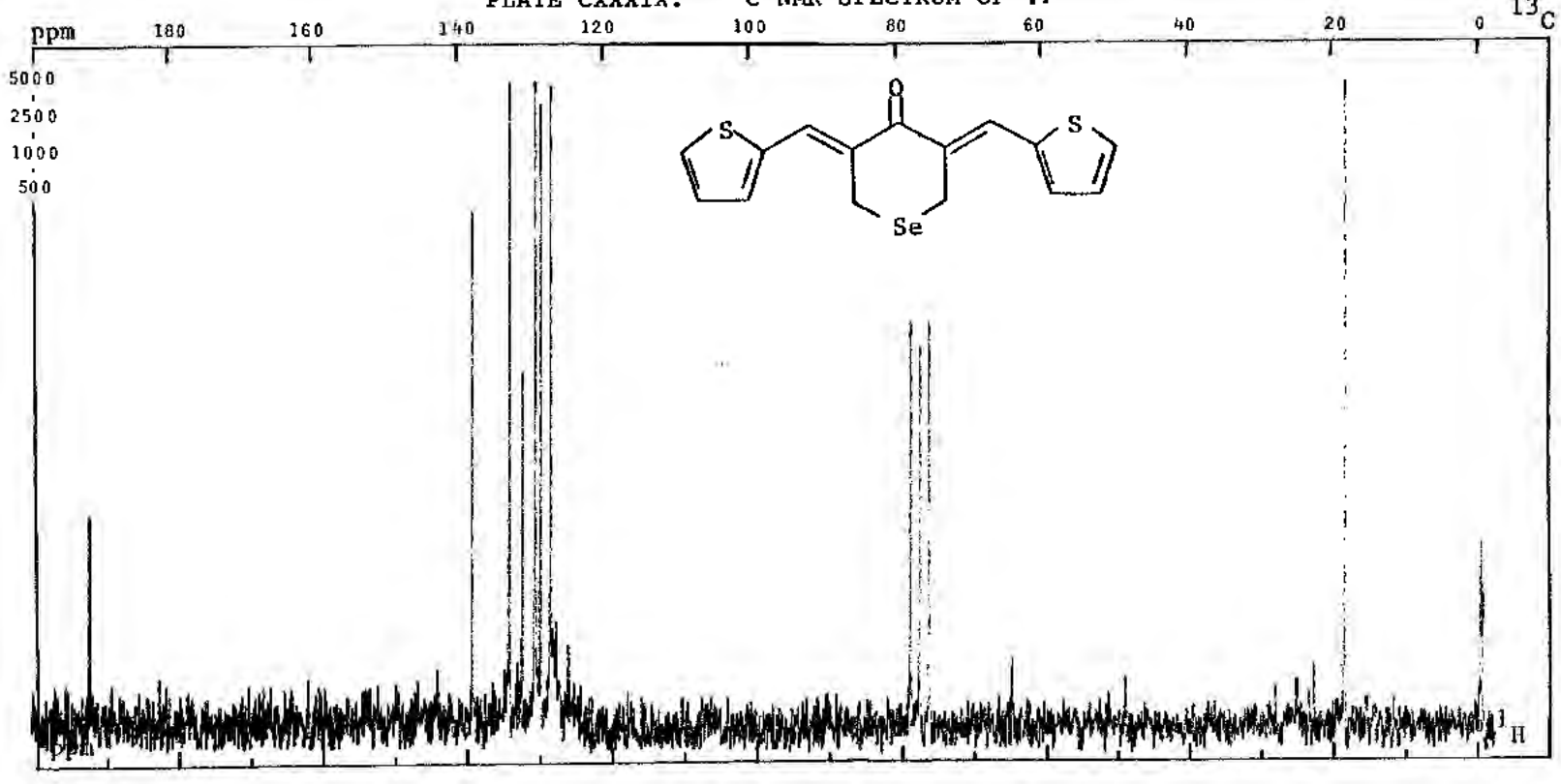


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC:3000 Hz; T: 25 °C; NT: 12 .

Size: 12K; PW/RF: 5 µs/dB; SO: 0 Hz; FB: Hz; Lock: ^{2}D ; Delay: 0.5 s.

DC: N ; Gated Off: ; Offset: Hz; RF: W/dB; NBW: Hz; LB: .

PLATE CXXXIX. ^{13}C NMR SPECTRUM OF **47**

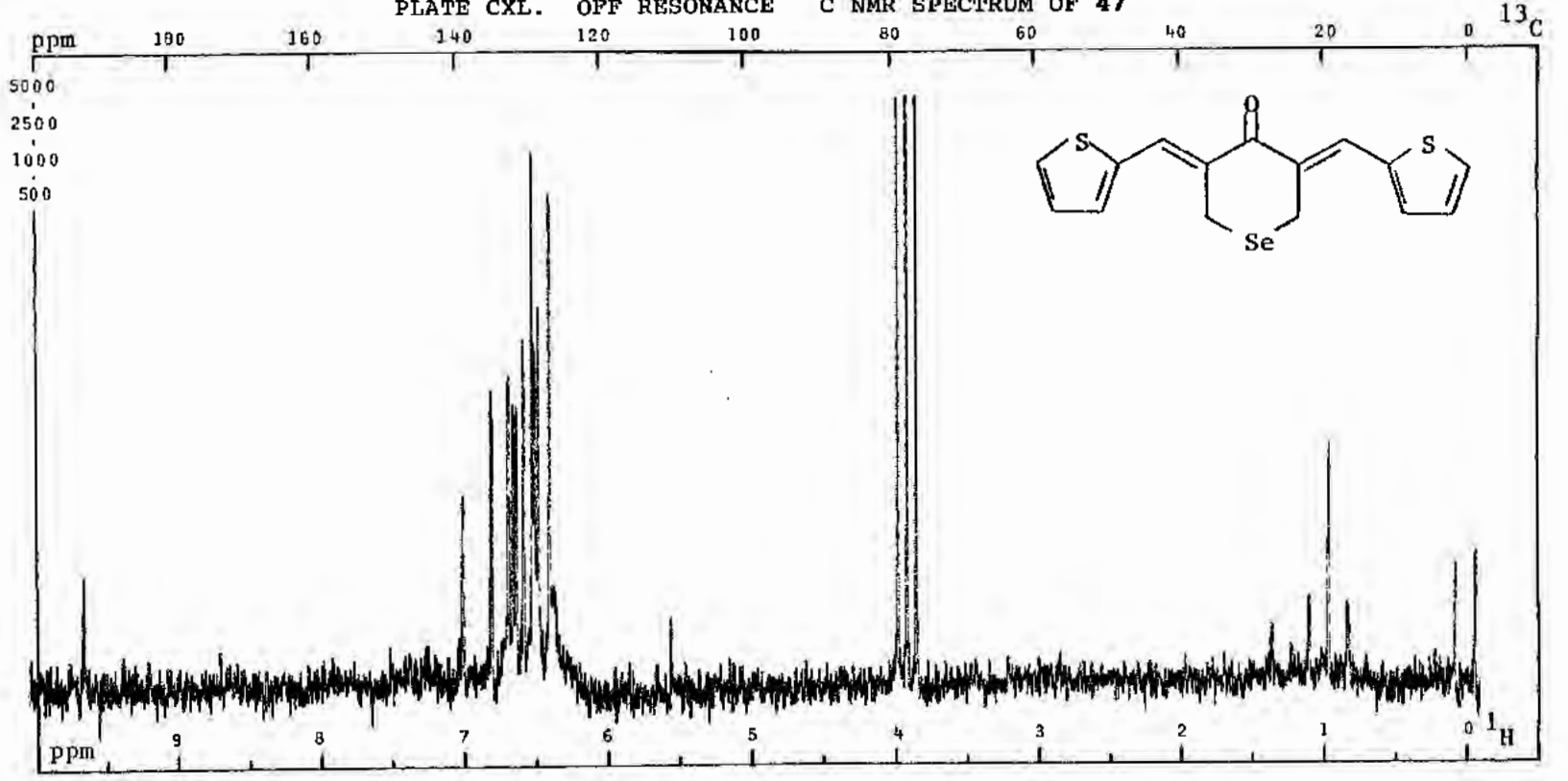


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 5000 .

Size: 8 K; PW/RF: 10 µs/dB; SO: 35101 Hz; FB: Hz; Lock: ^{2}D ; Delay: 5 s.

DC: Y ; Gated Off: ; Offset: 45316 Hz; RF: 7.5W/dB; NBW: Hz; LB: .

PLATE CXL. OFF RESONANCE ^{13}C NMR SPECTRUM OF **47**

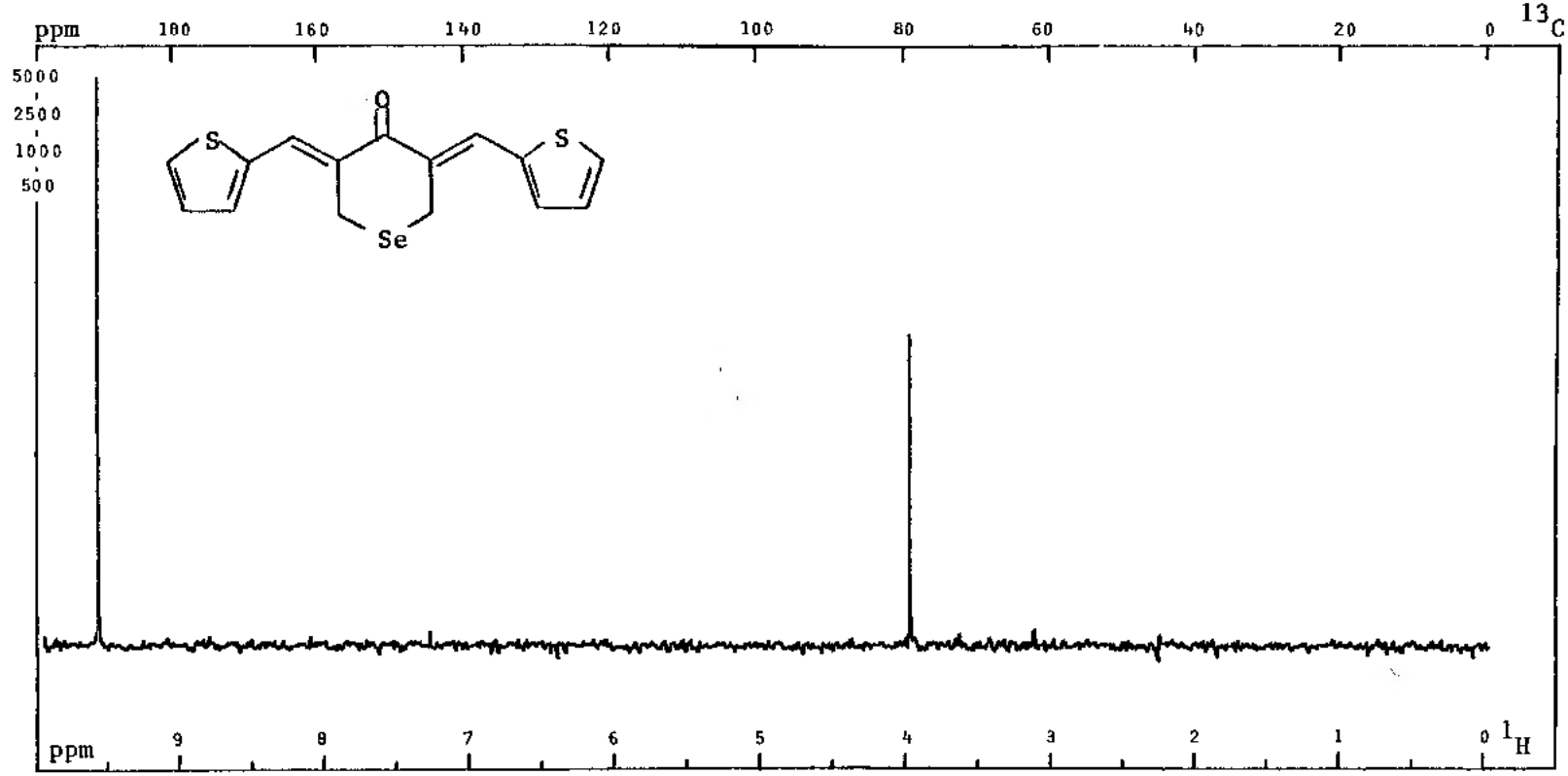


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 8400 .

Size: 8 K; PW/RF: 10 µs/dB; SO: 35101 Hz; FB: Hz; Lock: ^{2}D ; Delay: 5 s.

DC: Y ; Gated Off: ; Offset: 46316 Hz; RF: 7.5 W/dB; NBW: Hz; LB: .

PLATE CXLI. ^{77}Se NMR SPECTRUM OF **47**

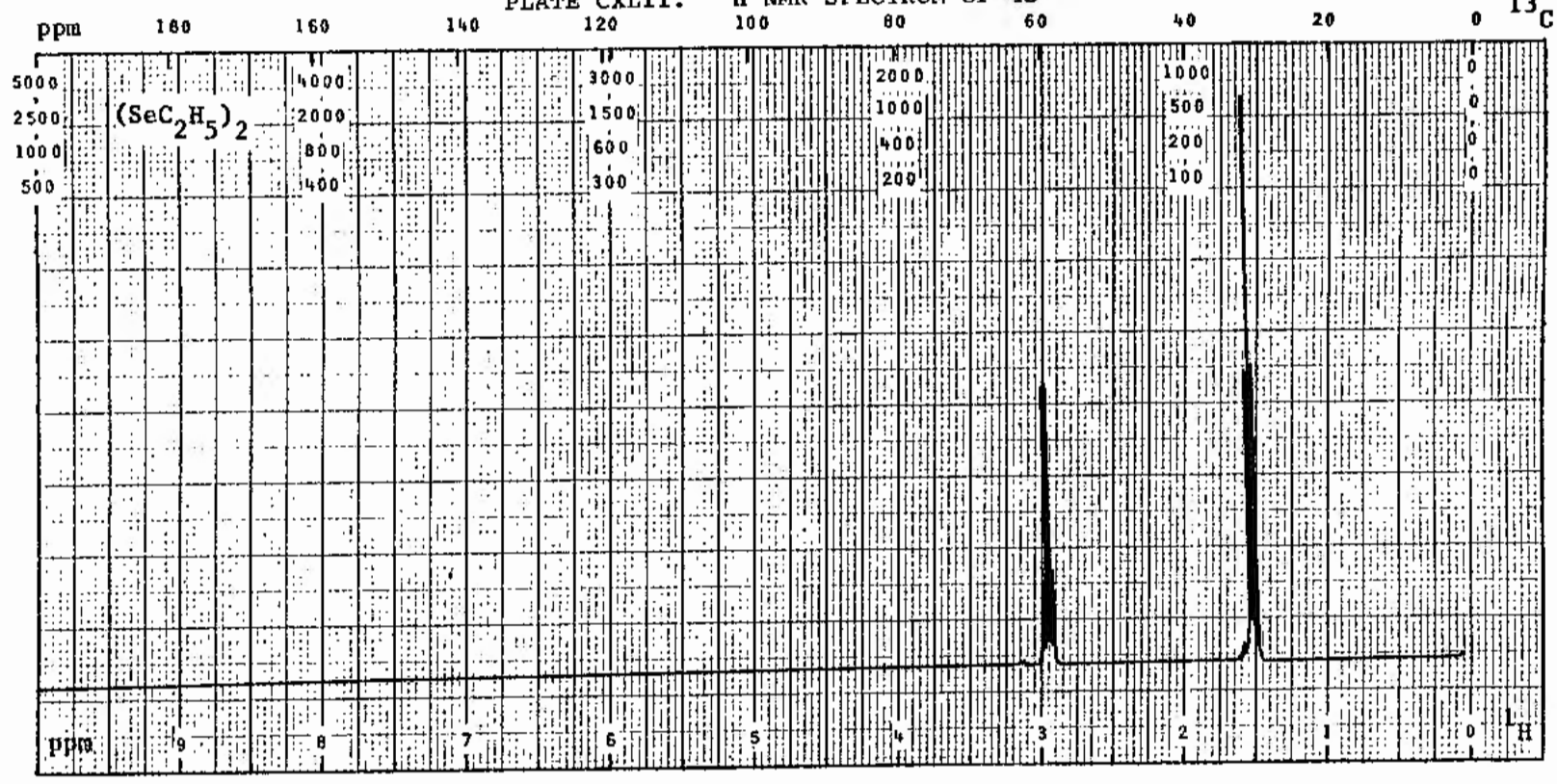


PFT X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 120 .

Size: 32 K; PW/RF: 35 µs/dB; SO: 500 Hz; FB: Hz; Lock: ^2D ; Delay: 20 s.

DC: Y ; Gated Off: ; Offset: 0 Hz; RF: 20 W/dB; NBW: Hz; LB: .

PLATE CXLII. ^{1}H NMR SPECTRUM OF **48**

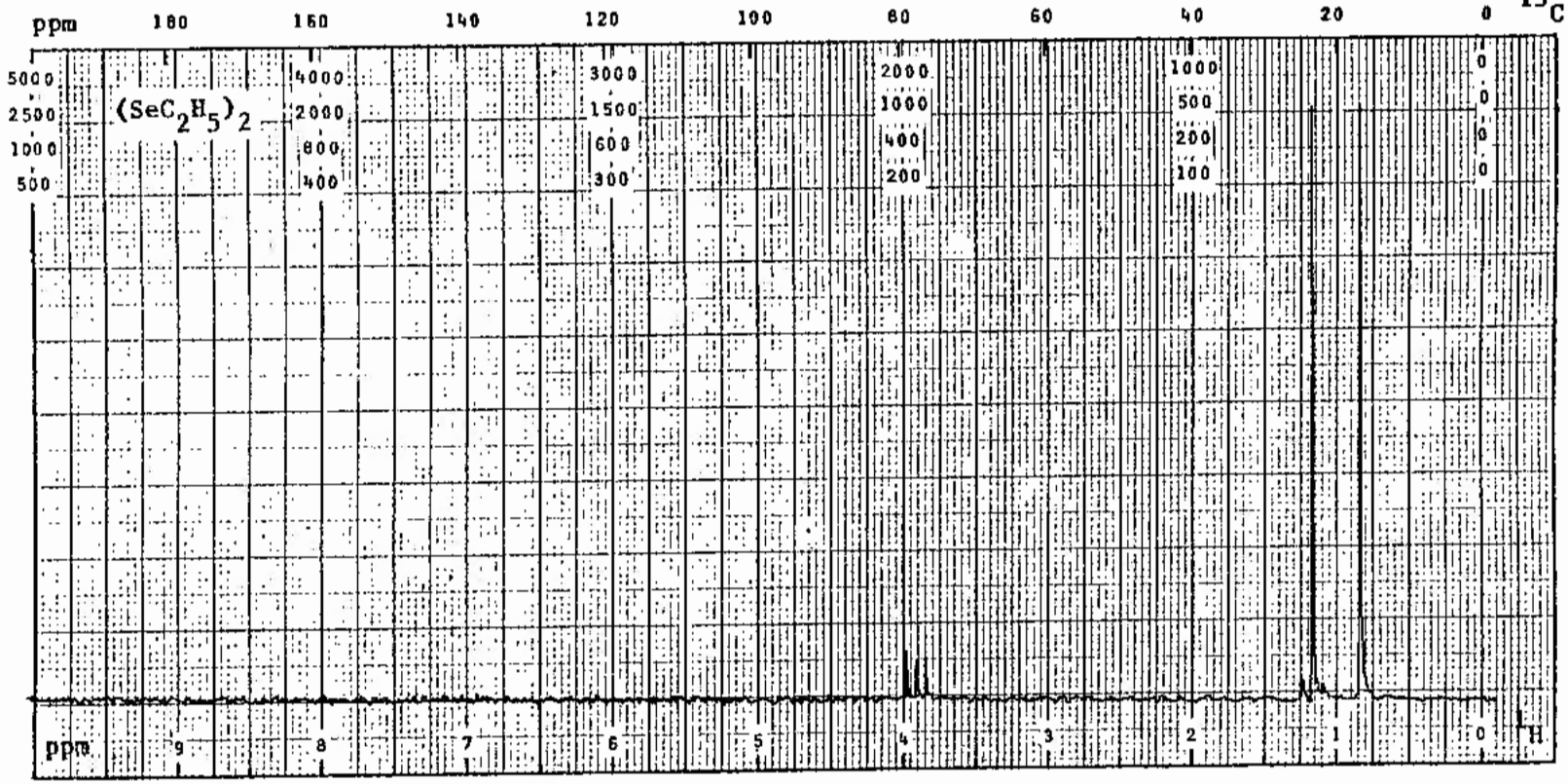


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 8

Size: 12 K; PW/RF: 5 μs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ; D1,D5 : 0.5 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz

PLATE CXLIII. ^{13}C NMR SPECTRUM OF 48

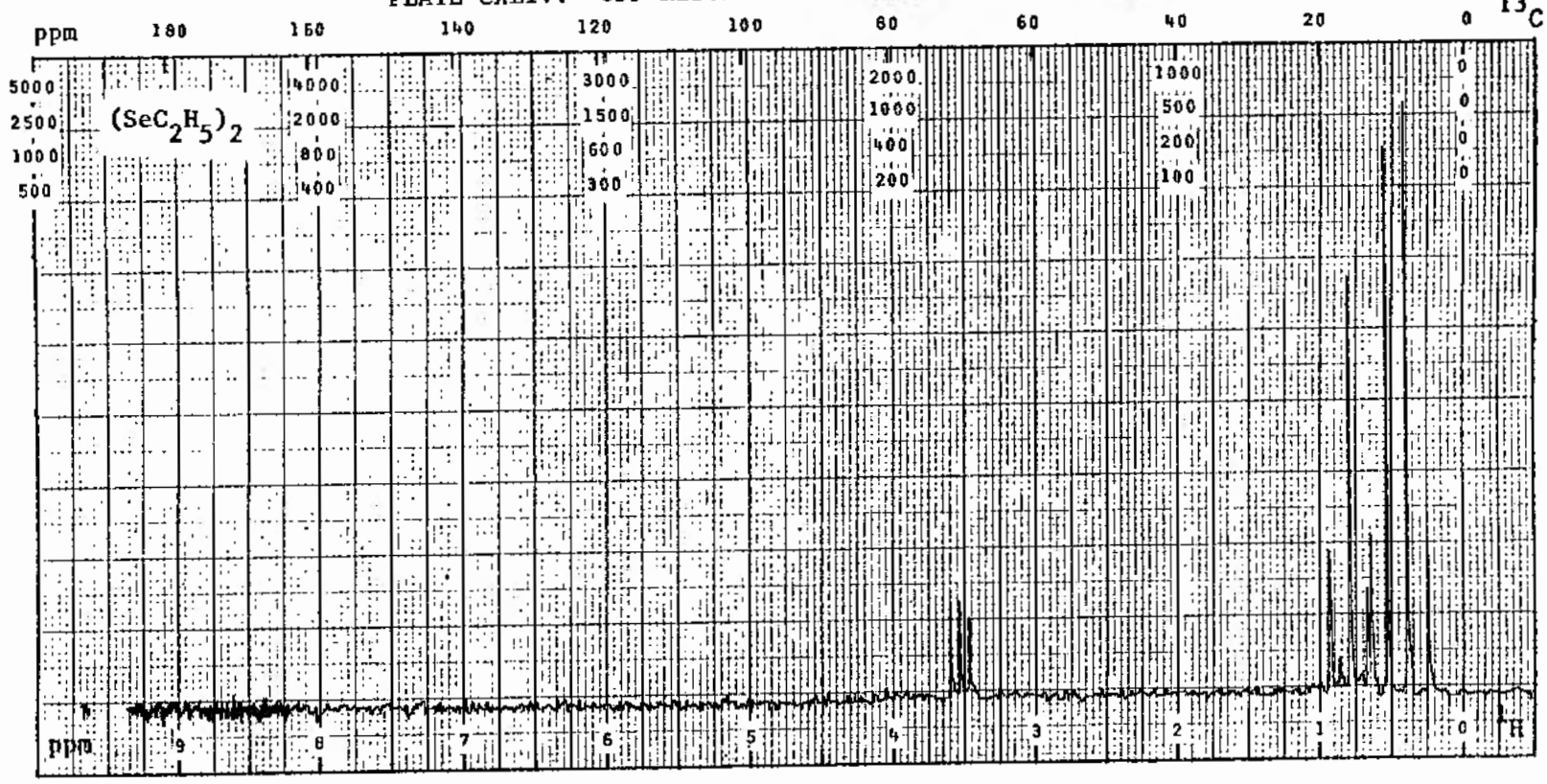


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 Mhz; WC: 5000 Hz; T: 28 °C; NT: 1000 .

Size: 8 K; PW/RF: 14 µs/dB; TO:35101 Hz; FB: Hz; Lock: ^2D ; D1,D5 : 5 s.

DC: Y, N ; Gated Off: A or D ; DO: 45316 Hz; RF(Power): 7.5W/dB; NBW: Hz; LB: Hz

PLATE CXLIV. OFF RESONANCE ^{13}C NMR SPECTRUM OF **48**

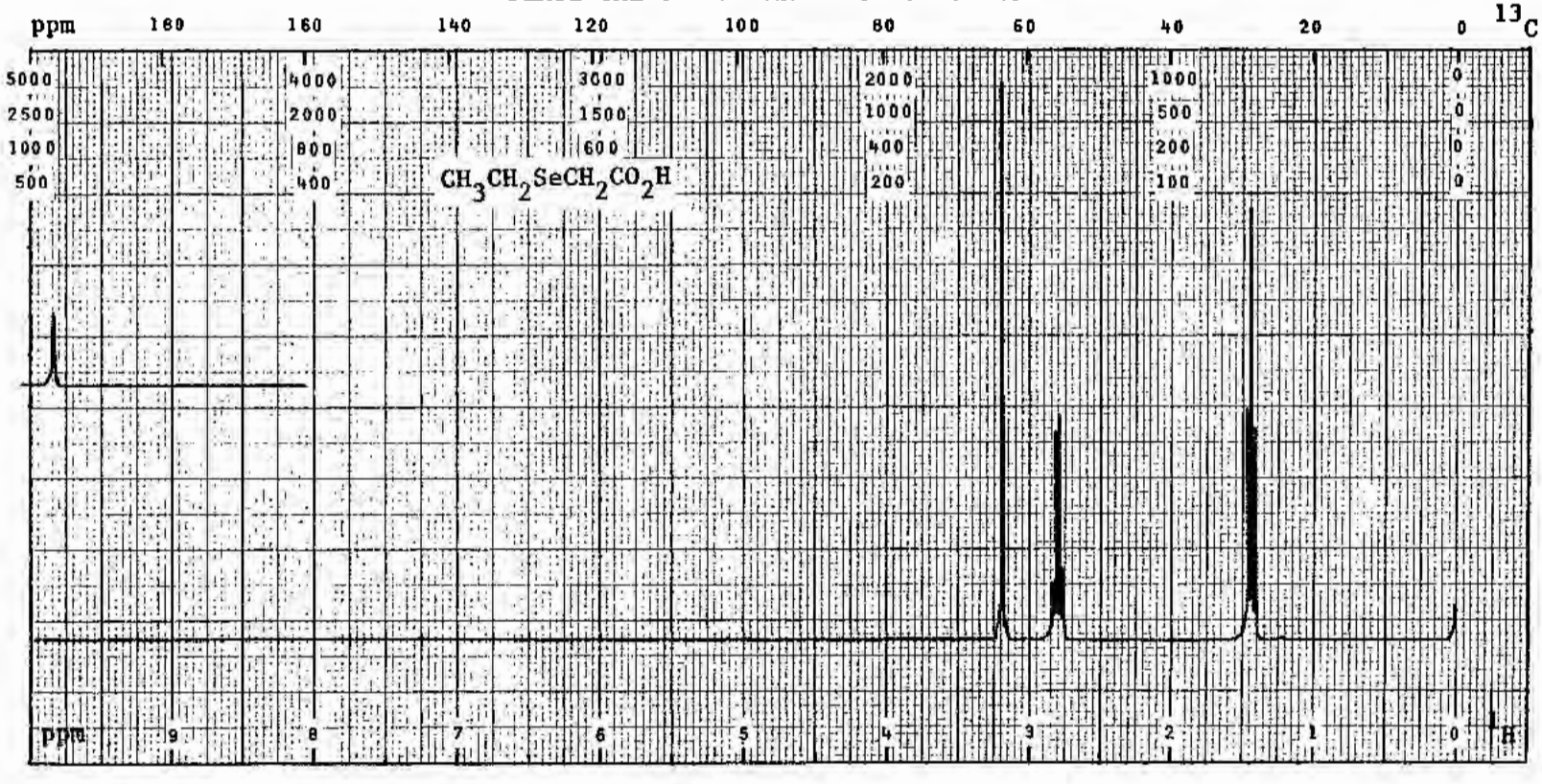


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 3000 Hz; T: 28 °C; NT: 2000 .

Size: 8 K; PW/RF: 14 μs/dB; TO: 35101 Hz; FB: Hz; Lock: ^2D ; D1,D5 : 5 s.

DC: X, N ; Gated Off: A or D ; DO: 46316 Hz; RF(Power): 7.W/dB; NBW: Hz; LB: Hz.

PLATE CXLV. ^{1}H NMR SPECTRUM OF 49

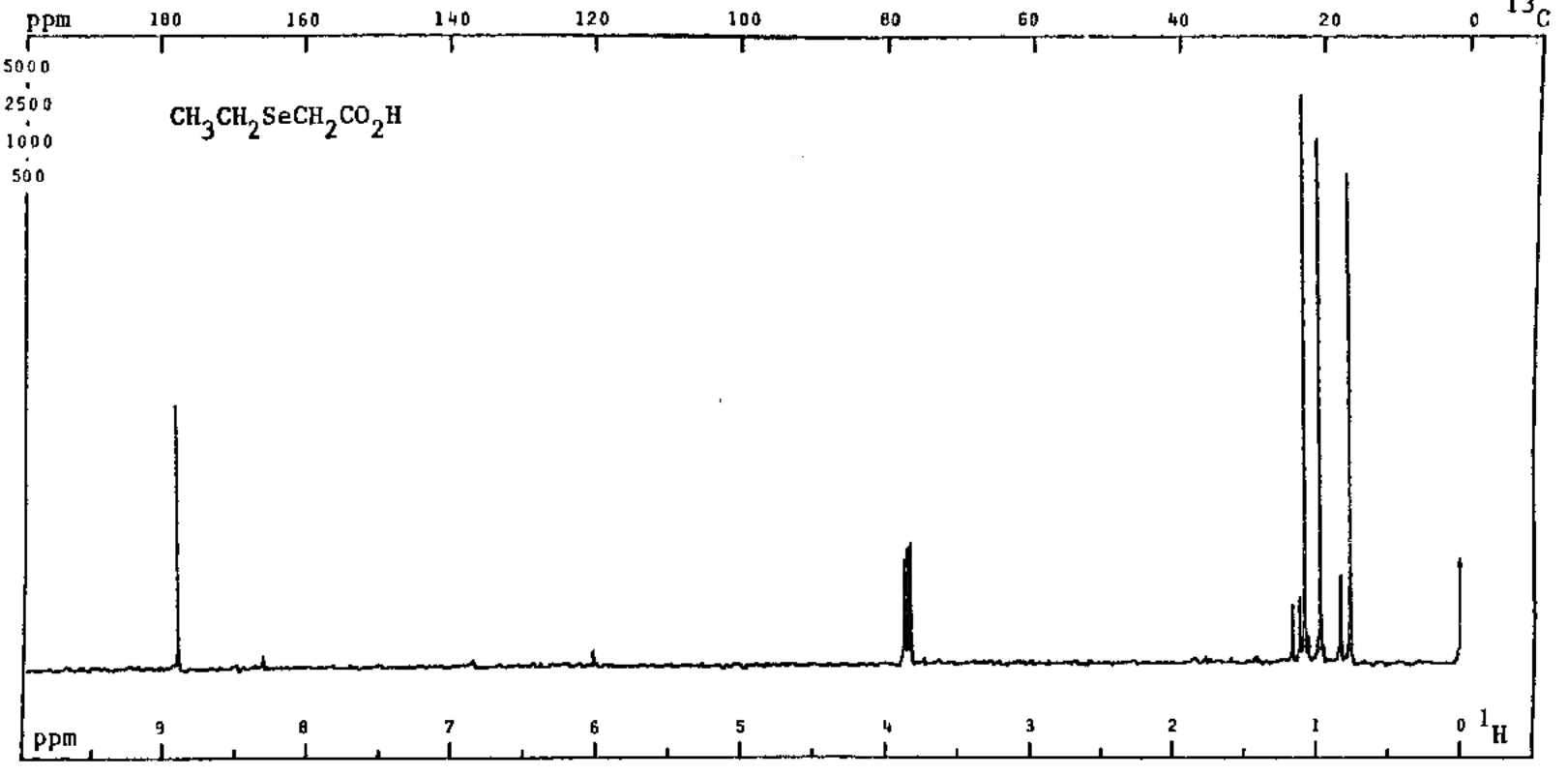


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 4 .

Size: 12 K; PW/RF: 5 µs/dB; SO: 0 Hz; FB: Hz; Lock: ^{2}D ; Delay: .05 s.

DC: N ; Gated Off: ; Offset: Hz; RF: W/dB; NBW: Hz; LB: .

PLATE CXLVI. ^{13}C NMR SPECTRUM OF 49

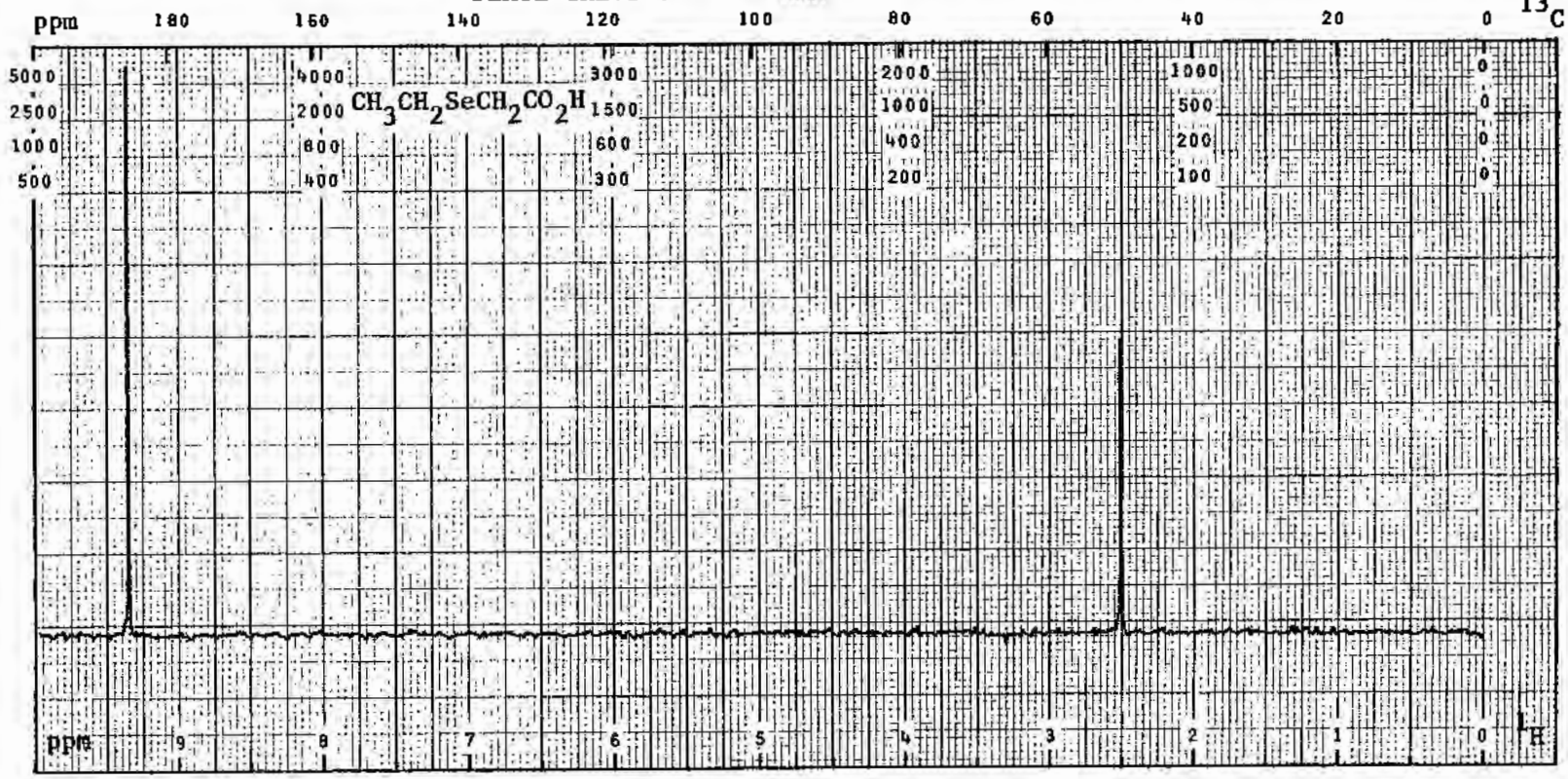


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 40 .

Size: 16 K; PW/RF: 12 µs/dB; TO: 1500 Hz; FB: Hz; Lock: ^2D ; D1,D5: 4 s.

DC: Y, N ; Gated Off:A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE CXLVII. ^{77}Se NMR SPECTRUM OF **49**

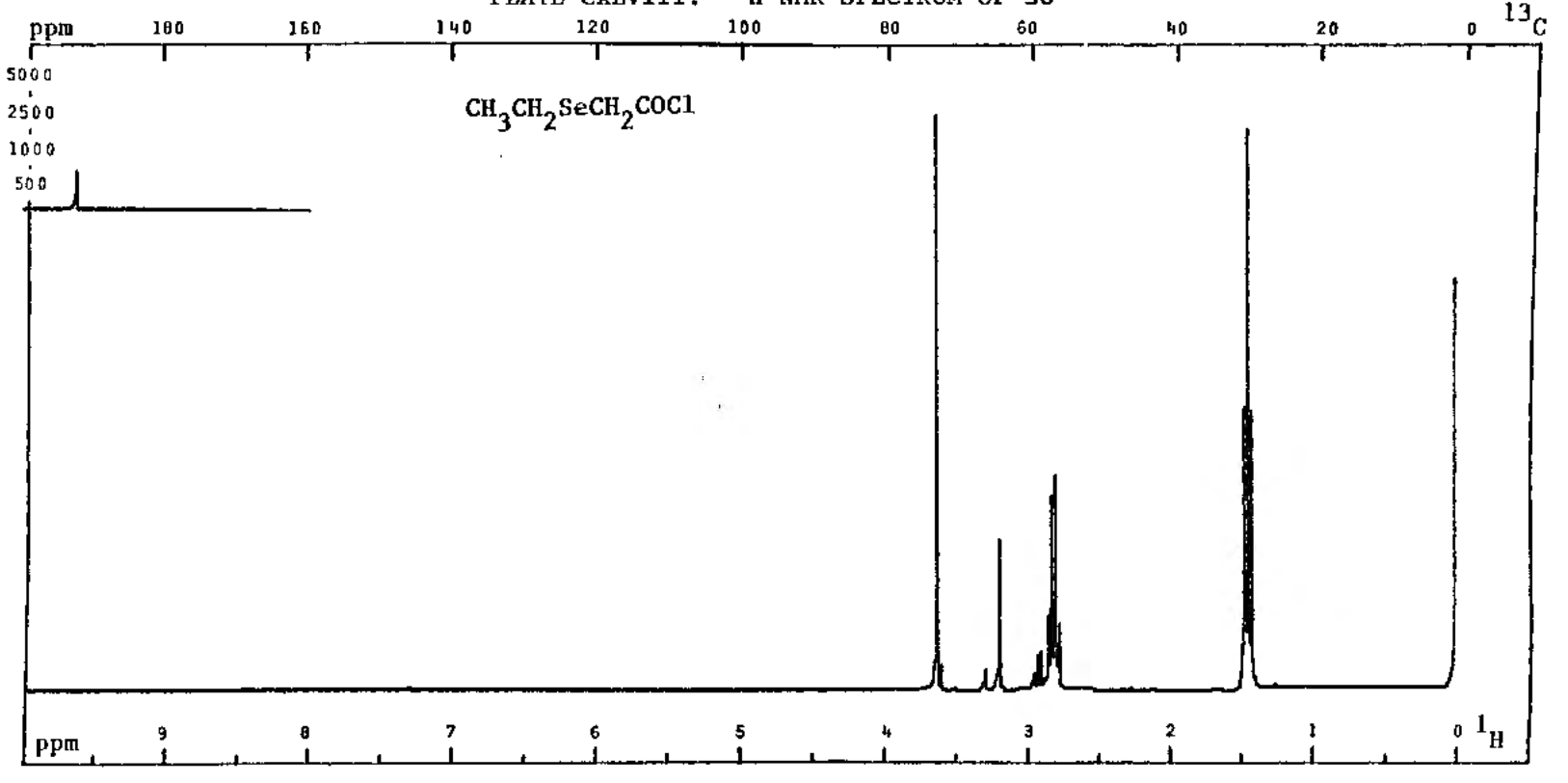


PFT X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 17166 Hz; T: 25 °C; NT: 20 .

Size: 32 K; PW/RF: 35 μs/dB; SO: 500 Hz; FB: Hz; Lock: ^{2}D ; Delay: 20 s.

DC: Y ; Gated Off: ; Offset: 0 Hz; RF: 20 W/dB; NBW: Hz; LB: .

PLATE CXLVIII. ^{1}H NMR SPECTRUM OF 50

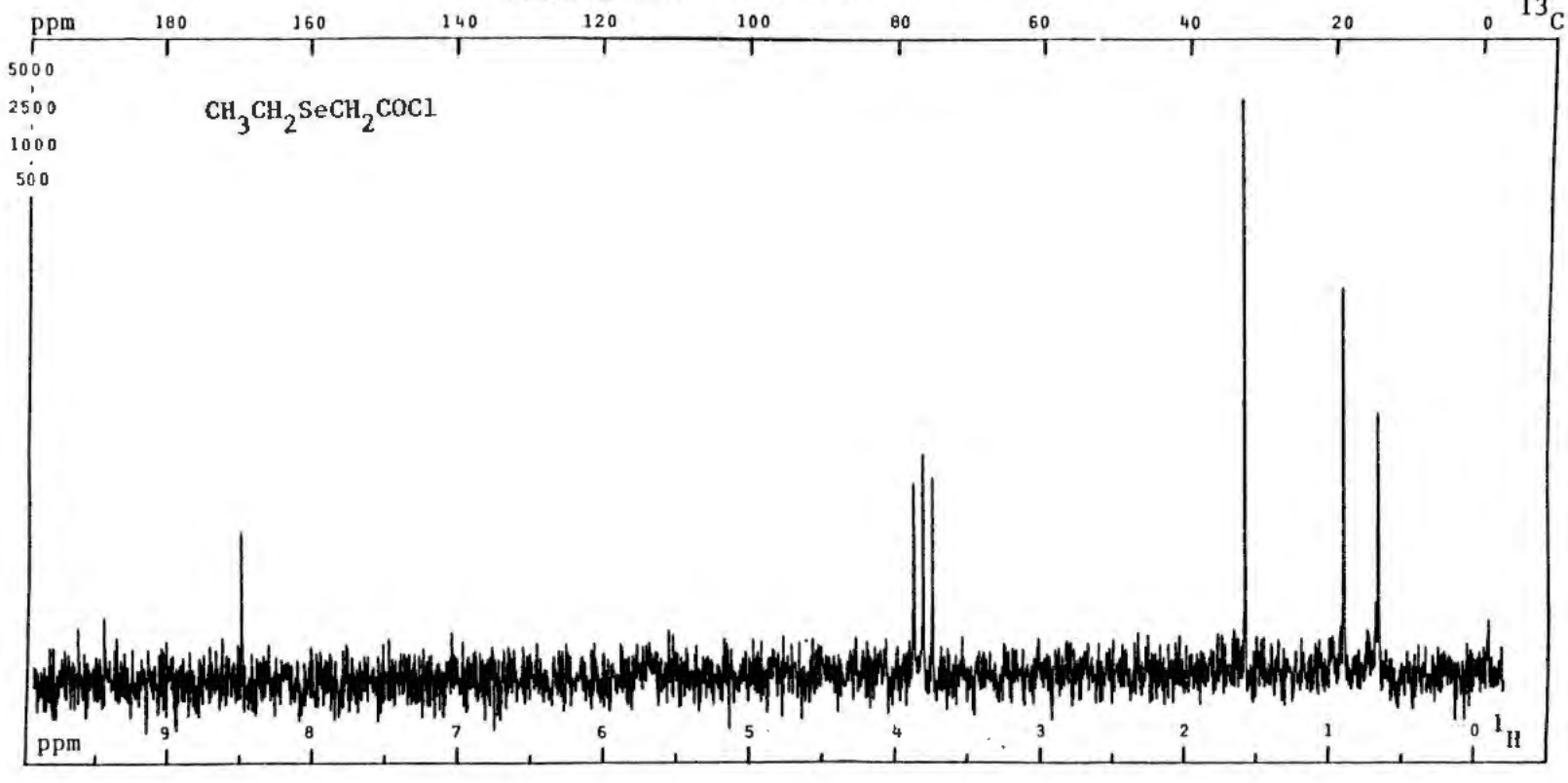


PFT X CW _ ; Solvent: $CDCl_3$; SF: 299.94 MHz; WC:3000 Hz; T: 25 °C; NT: 16

Size: 12K; PW/RF: 5 µs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ;D1,D5: 0 s.

DC: Y, N ; Gated Off:A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE CXLIX. ^{13}C NMR SPECTRUM OF **50**

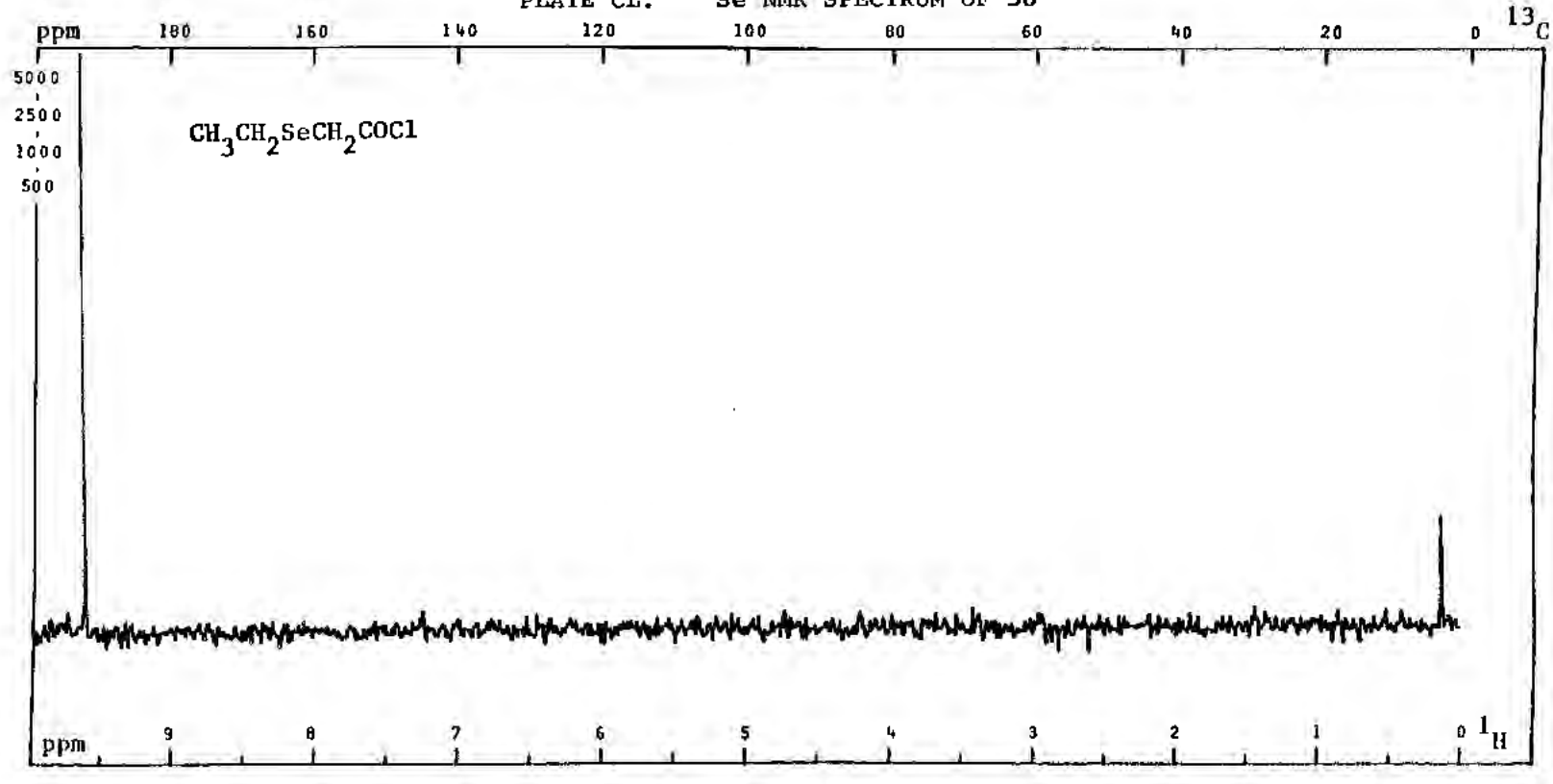


PFT X CW _ ; Solvent: $CDCl_3$; SF: 25.2 MHz; WC: 5000 Hz; T: 28 °C; NT: 750 .

Size: 8 K; PW/RF: 14 µs/dB; TO: 35101 Hz; FB: Hz; Lock: ^2D ; D1,D5: 5 s.

DC: Y, N ; Gated Off: A or D ; DO: 45316 Hz; RF(Power): 7.5W/dB; NBW: Hz; LB: Hz.

PLATE CL. ^{77}Se NMR SPECTRUM OF **50**

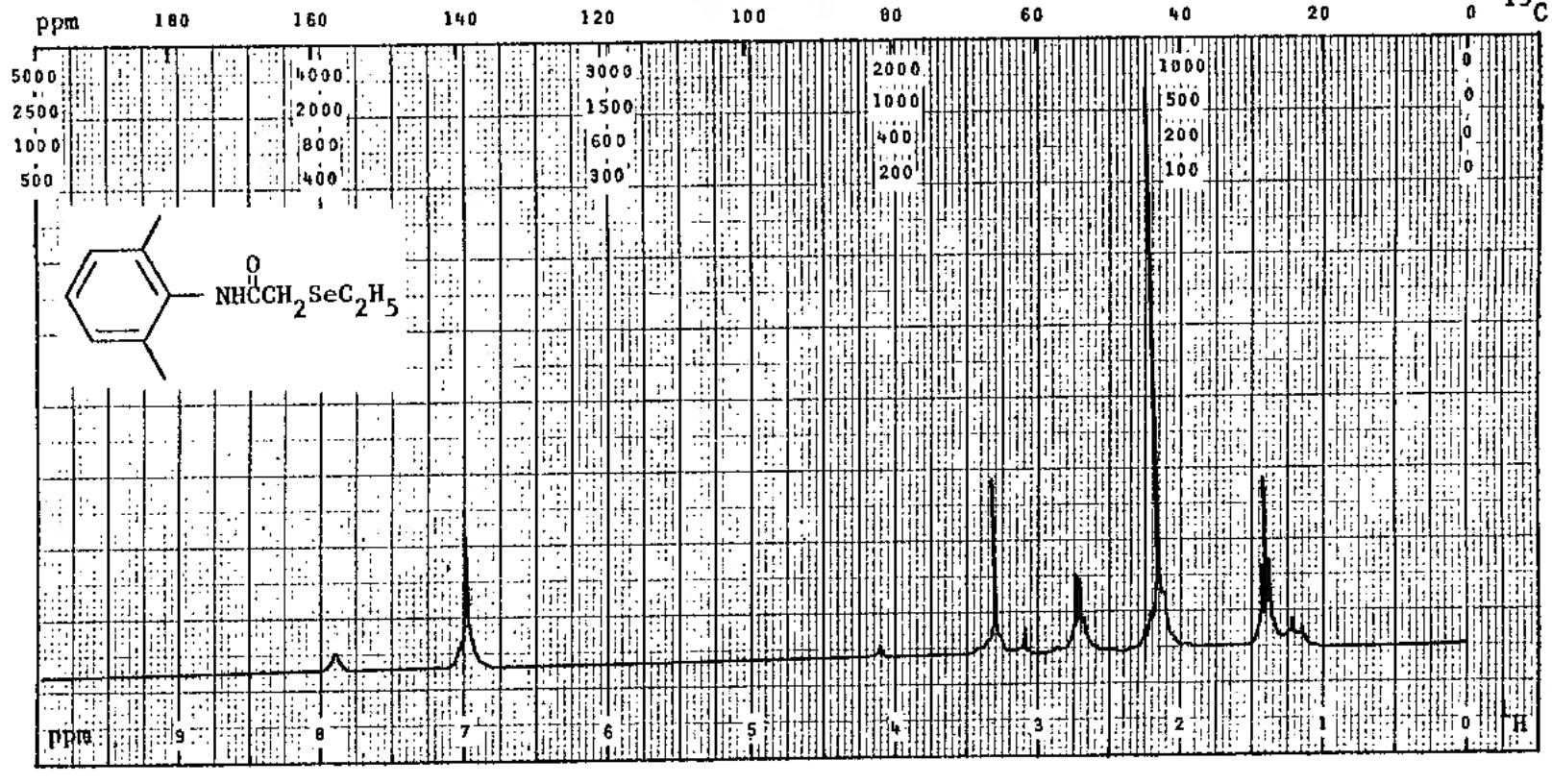


PFT X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 56 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 25 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE CLI. ^{1}H NMR SPECTRUM OF 51

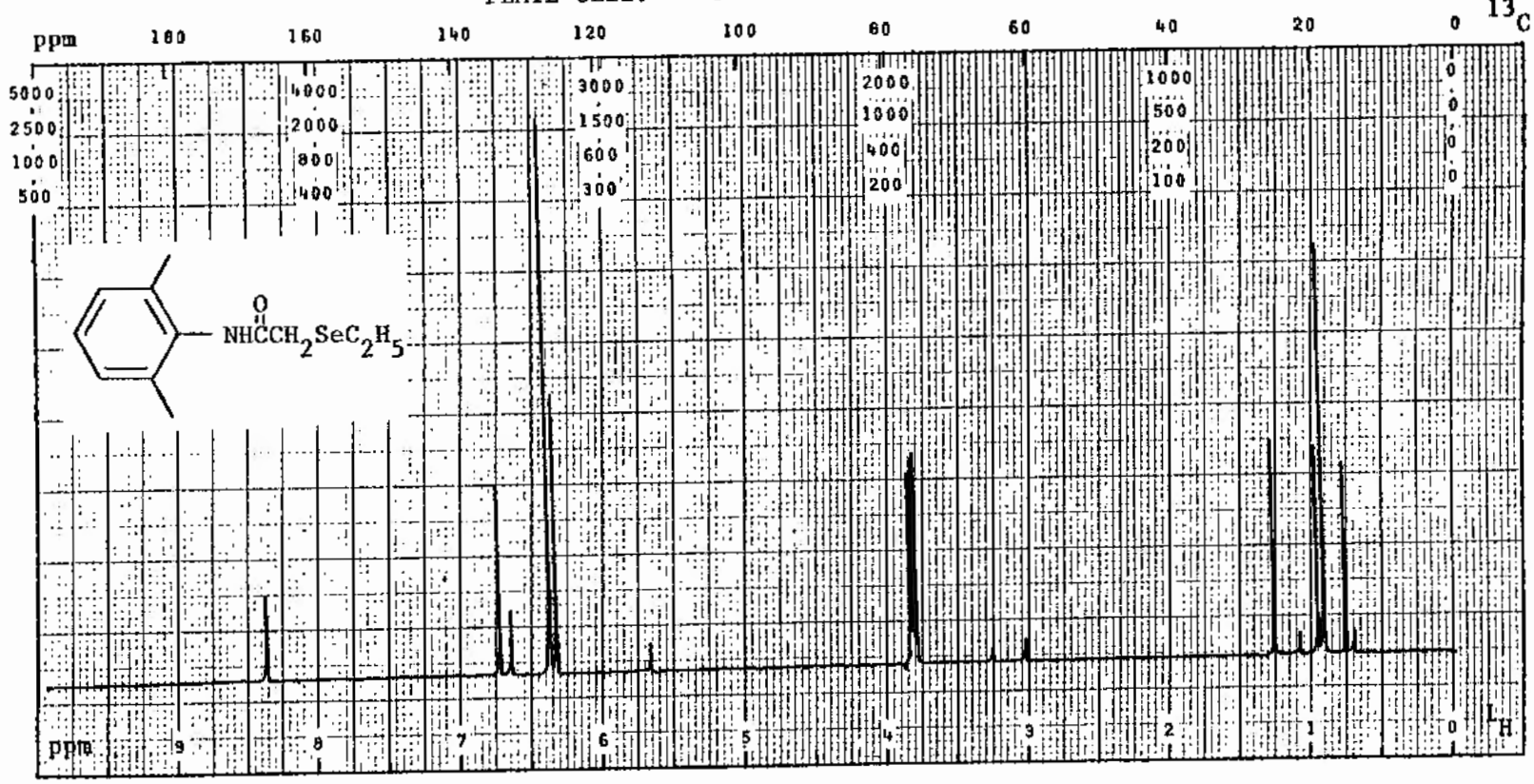


PFTX_ CW _ ; Solvent: $CDCl_3$; SF:299.94 MHz; WC: 3000 Hz; T: 25 °C; NT: 40 .

Size: 8 K; PW/RF: 10 µs/dB; TO: 0 Hz; FB: Hz; Lock: ^{2}D ; D1,D5 : 0.5 s.

DC: Y, N ; Gated Off: A or D ; DO: Hz; RF(Power): W/dB; NBW: Hz; LB: Hz

PLATE CLII. ^{13}C NMR SPECTRUM OF 51

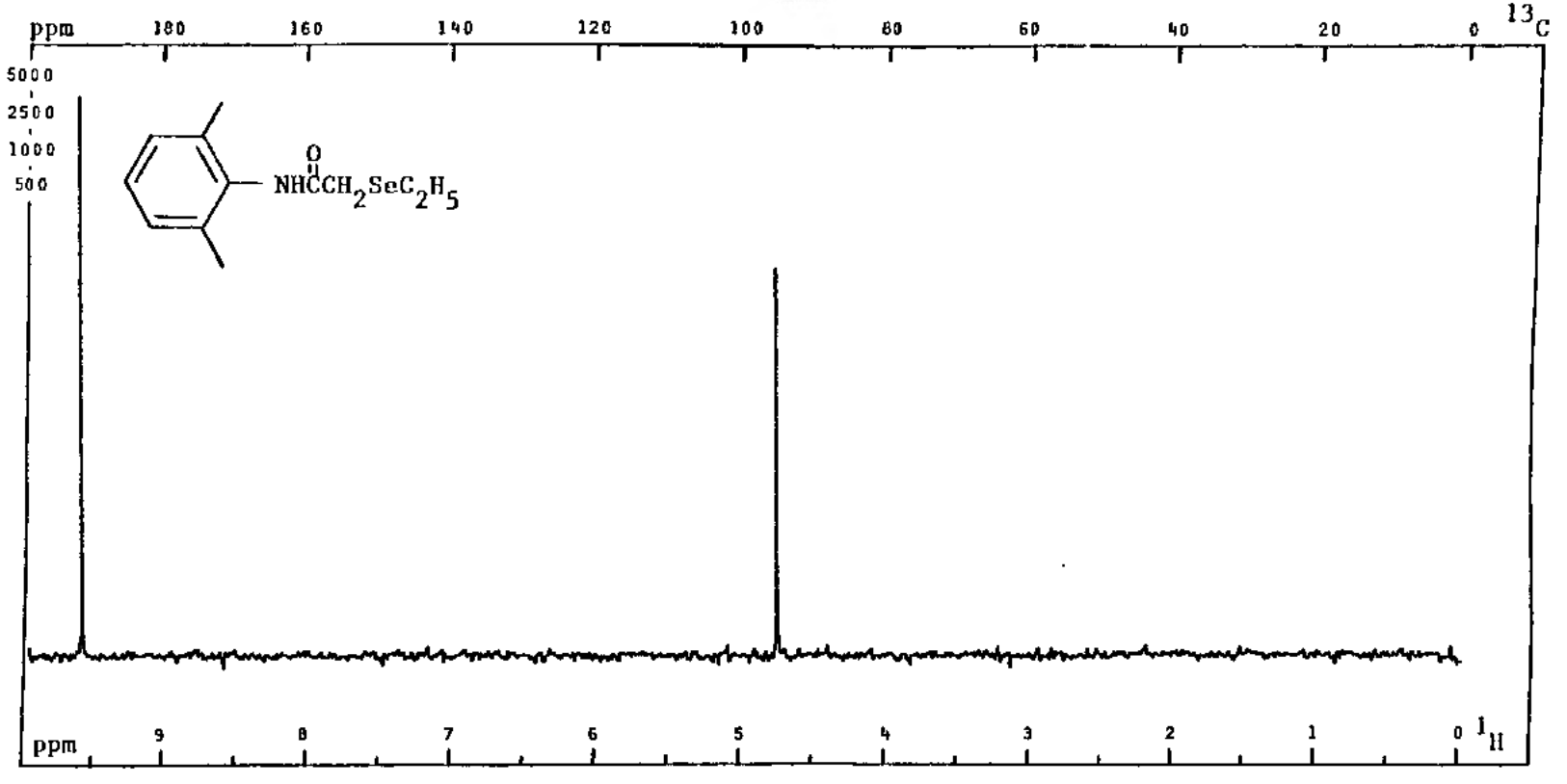


PFT X CW _ ; Solvent: $CDCl_3$; SF: 75.4 MHz; WC: 15000 Hz; T: 28 °C; NT: 280 .

Size: 20 K; PW/RF: 12 µs/dB; TO: 1000 Hz; FB: Hz; Lock: ^{2}D ; D1,D5 : 5 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

PLATE CLIII. ^{77}Se NMR SPECTRUM OF 51



PFT X CW _ ; Solvent: $CDCl_3$; SF: 57.22 MHz; WC: 28610 Hz; T: 25 °C; NT: 80 .

Size: 32 K; PW/RF: 35 µs/dB; TO: 500 Hz; FB: Hz; Lock: ^{2}D ; D1,D5: 15 s.

DC: Y, N ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 20 W/dB; NBW: Hz; LB: Hz.

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