SYNTHESIS AND CHARACTERIZATION OF ORGANOPHOSPHORUS COMPOUNDS

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER OF PHILOSOPHY (M. PHIL.) IN CHEMISTRY

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Department of Chemistry

THESIS ACCEPTANCE LETTER

The thesis titled "Synthesis and Characterization of Organophosphorus Compounds" submitted by Hemshankar Saha Roy, Roll No. 040503106P, Registration No. 0405031, Session-April 2005 has been accepted as satisfactory in partial fulfilment of the requirement for the degree of Masters of Philosophy (M. Phil.) in Chemistry on November 23, 2009.

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Author

(Hemshankar Saha Roy)

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Chapter 1

INTRODUCTION

INTRODUCTION

Compounds containing P—C linkages are usually known as organophosphorus compounds. The term 'Organophosphorus compounds' are reserved for compounds containing phosphorous and carbon. The most important organophosphorus compounds are phosphate esters which are based on P—O—C linkages. Phosphorus chemistry is dominated by oxyphosphorus compounds[1], all of which contain phosphorus-oxygen linkages. Most of these are usually known as phosphates. Almost all naturally occurring phosphorus compounds contain phosphorus-oxygen linkages and those of biochemical importance are organic phosphate esters which contain phosphorus-oxygen-carbon linkages. Organophosphorus compounds which are based on phosphorous–carbon linkages constitute the second most important group and those containing phosphorous-nitrogen linkages are probably the third. Widespread phosphorous compounds on earth and phosphoric acid are the most important industrial commodity based on phosphorous. The organic phosphate ester known as deoxyribonucleic acid (DNA) is present in all life forms and lies at the heart of biochemistry and genetics. It is the most studied phosphorus compound and is probably the most crucial phosphorus compound as far as the survival and development of the human race concerned.

Although inorganic phosphorus compounds remain by far the most important commercially, the chemistry of organophosphorus compound has evolved rapidly and now represents a sizeable and explosively expanding part of the whole. There are four major classes of phosphorus compounds:

i) Oxyphosphorus compounds, which contain covalent P—O linkages.

ii) Organophosphorus (carbophosphorus) compounds which contain P—C linkages.

iii) Azaphosphorus compounds which contain P—N linkages.

iv) Metallophosphorus compounds which contain P-metal linkages.

It will sometimes be useful to classify phosphorous compound in accordance with the presence of two characteristics bonds e.g.

C - P - O Organo-oxyphosphorus compound

N - P - O Aza-oxyphosphorus compound

M - P - O	Metallo-oxyphosphorus compound
N - P - C	Aza-organophosphorus compound
M - P - C	Metallo-organophosphorus compound
M - P - N	Metallo-azaphosphorus compound.

The application of phosphorous compounds are of diverse nature. The commercial production of orthophosphates and polyphosphates greatly exceeds that of all other compounds of phosphorus. Phosphate esters, although produced in smaller quantities, have very diverse but important applications. Substituted phosphates, particularly phosphonates and thioated derivatives also have a considerable number of current uses. Prominent amongst these are in pesticides, heavy metal extraction, oil additives and polymers of various kinds. Industrially produced natural products such as casein and lethicin have a growing number of applications in food products and other areas.

The utilization of phosphorus containing organophosphorus compounds are as follows:

(i) Food technology
(ii) Animal foodstuffs
(iii) Industrial phosphate esters
(iv) Pesticides
(v) Medicinal compounds
(vi) Synthetic polymers and fire retardants
(vii) Natural products.

In food technology

Phosphates[2-7] are present in most natural foods, particularly meat, milk and dairy products, fruits and cereals. Further addition of phosphates is frequently made in the processing of foods for a variety of purposes which include for increasing nutritive value, for complexing of undesirable metal ions, preservation, prevention of caking, leavening action, colour development or stabilization.

The major phosphorus–containing products in current use as food additives may be listed as:

(i) Inorganic salts – ortho, pyro and polyphosphates, mostly of Na, K or Ca.

(ii) Bipolymer phosphates – casein, lactalbumins phosphates, starch phosphates, lecithin.

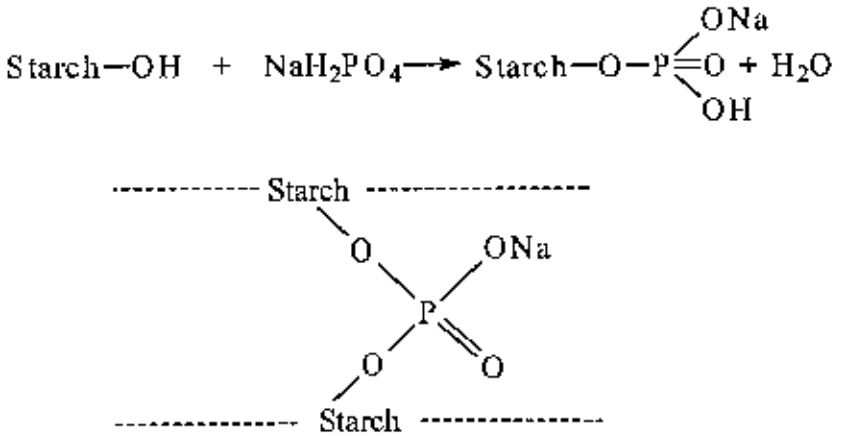
Medicinal supplementation of phosphorus is usually with casein, orthophosphates of glycerophosphates of Na, K, Mg or Ca. The applications of phosphorous compounds are exceedingly numerous in the field of food technology snch as in milk and dairy products, meat and fish, fruit and vegetables, beverages, leavening agents, biopolymer phosphates etc.

The chief mineral constituents of milk are phosphorus and calcium together with Na, K, Mg and minor qnantities are citric acid and a great deal of water. The phosphorus content (about 0.95 g of P/liter in cows milk) is distributed between more than 50 different compounds both organic and inorganic. Most abundant and important of these are the casein phosphoproteins, calcium phosphates and the phospholipids. Other phosphorous compounds present in much smaller quantities are most of the vitamins, various nucleic acids, enzymes, sugarphosphates and protcose peptones (phosphoglycopeptides).

About 2.0% of $H_2PO_4^-$ anions are present in natural citrus fruit juices as well as about 0.02% glucose-6-phosphate and other sugar phosphates. Other phosphorus compounds present in relatively minor quantities are nucleic acids, ATP, phospholipids and B group vitamins. Very useful effects are observed by treatment of fruit and vegetables with added phosphates. These include stabilization against bacteria and rancidity enhancement of colour and desirable effects on tenderness and firmness. For example, small additions of $Na_4P_2O_7$ to peas and beans prior to canning lead to a more tender product due to the sequestering of calcium ions.

The addition of sodium polyphosphates stabilizes the colour of strawberries, tomatoes, cherries etc. and the use of such compounds prior to canning or freezing will help to keep vegetables green[8]. Pyrophosphates such as $Na_2H_2P_2O_7$ are used to counteract the blackening of raw potato or apple juice which is due to the oxidation of diphenolic compounds in the presence of heavy metal ions. The latter are removed by complexing with the pyrophosphate ions.

Starch phosphates[9,10] are being increasingly used in manufacturing since they promote thickening without gelly form. Starch phosphates have a fairly low degree of $-OPO_3$ substitution for – OH and are obtained by heating starch with phosphoric acid at about 60°C. Some natural potato starch already contain a few phosphate ester groups.



Scheme -1

Sodium dihydrogen phosphate reacts with starch to give a monoester salt, while sodium trimetaphosphate reacts to produce cross linked diester. Cross-linked varieties of these kinds are more stable towards heat, agitation and acidity than monoester salts.

Corn starch processed with cyclic sodium trimetaphosphate is used to make cold-water jellies. Phosphorylated varieties of this kind are resistant to hydrolysis and degradation probably due to cross-linking and are used as thickening agents in cooked foods.

Sugar phosphates used in foods are relatively few in number, they include the improvement of the crispness of breakfast cereals[11] and the flavor of alcoholic beverages[12].

Phospholipids such as lecithin which is available in various grades is widely used in the food industry as a surfactant, an emulsifier and an anti-oxidant.[13-16] Lecithin is used in baking, where it acts as an emulsifier, a wetting agent to reduce mixing time, a parting agent to affect cleaner and easier release from moulds and an anti-oxidant to stabilize vegetable and animal fats. Dough–handling properties are improved with

lecithin and other improvements are secured in biscuits, pies, cakes and waffles. Lecithin improves the cheese yield from milk.[17] It is also introduced into foods in the form of egg yolk where it may act as an emulsifier as in mayonnaise and salad dressings.

Synthetic organophosphorus compounds are used in foodprocessing, the use of poly-substituted tri-arylphosphine compounds as anti-oxidants and poly (*p*-diphenyl phosphino)styrene retards the formation of peroxides in sunflower oil.[18]

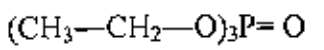
In Animal foodstuffs

The phosphorus contents of most animal foodstuffs are not particularly high and the more restricted variety of their diet makes animals much more prone to phosphorus deficiency than humans.[19-26] Phosphorus deficiency is the most wide spread and economically important of all mineral deficiencies affecting grazing livestock.
Phosphorous is absorbed as soluble phosphate in the duodenum. The amount of absorption of phosphorus from the dietary input is influenced by many factors. These include the type of food, animal age, internal pH, and the intake of other elements such as Ca, Fe, Al, K, Mg, and Zn. Excessive Fe, Mg, Al in the animal diet is known to reduce the absorption of phosphorus by forming insoluble phosphates. Mono- and di-calcium phosphates are added to from animal foodstuff to guard against dietary deficiency of phosphorus. Stock feed di-calcium phosphate, $CaHPO_4.2H_2O$ can be made from calcium hydroxide and most wet-process phosphoric acid. Apart from possible reduction of phosphorus absorption, the Fe, Al, and Mg salt impurities do not seem to be harmful to animals.

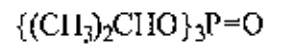
Disodium phosphate, Na_2HPO_4, ammonium phosphate or urea phosphate $CO(NH_2)_2.H_3PO_4$ may also be used as supplements to animal feeding compositions. Pyrophosphates and potassium orthophosphates are sometimes incorporated into pet foods. Ammonium phosphates are used in cattle foods.
Lecithin and dehydrated casein are also used as animal food supplements. A useful animal food supplement can be obtained by adding phosphoric acid to molasses. The acid reduces the viscosity of the latter as well as increasing its nutrient value.

In Industrial phosphate esters

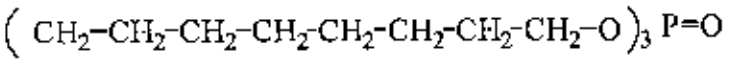
Though phosphorous compounds have enormous importance in biochemistry, phosphates esters[27-29] may have many technological applications. Some of the more important industrial products are listed below:



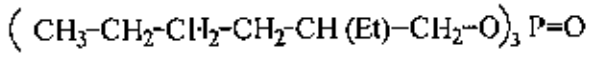
Triethyl phosphate
(1)



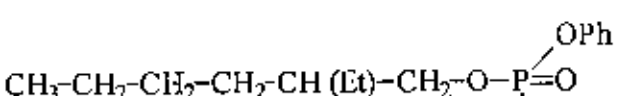
Tri-isopropylphosphate
(2)



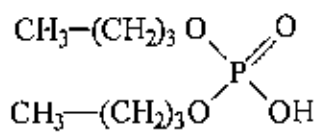
Tri-octylphosphate
(3)



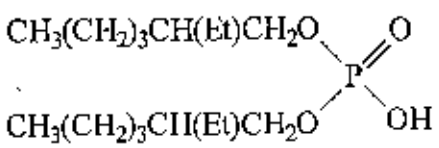
Tris-(2-ethylhexyl)phosphate
(4)



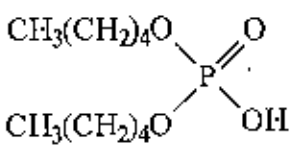
2-ethylhexyldiphynylphosphate
(5)



dibutyl hydrogen phosphate
(6)



bis-(2-ethylhexyl)hydrogenphosphate
(7)



diamylhydrogenphosphate
(8)

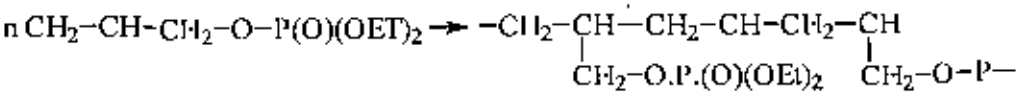
Tributyl phosphate and related esters such as di-butylphosphate $(Bu^nO)_2P(O)OH$ (DBP) and bis-2-ethylhexyl phosphate (HDEP) have important uses in the extraction of rare earth, actinide and other heavy metals from mineral resources and their recovery from waste products of the atomic energy industry. A solution of TBP in kerosine can. be used for solvent extraction of uranium and thorium and other rare earths from their mixtures in a 10% aqueous solution in nitric acid. The metal complexes such as $UO_2(NO_3)_2\{(BuO)_3PO\}_2$, which are formed on mixing the

aqueous and kerosene phases can be successively removed from the latter, in which they are soluble (a)

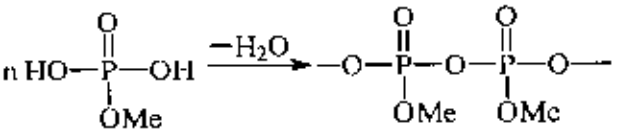
UO_2^{++} aq. + $2NO_3^-$ + 2TBP org ⇆ $UO_2(NO_3)_2$. 2TBP org aq. ... ... (a)

Difference of the extraction coefficients with different cations may be utilised in the separation of Uranium, transition metals and rare earths. This is a well established method for the extraction of uranium in the processing of nuclear fuels. Hafnium can also be separated from zirconium by this technique using TBP.

Tributyl phosphate TBP is still widely used for the purification of uranium for nuclear reactors and in the re-processing of spent nuclear fuels. Certain phosphate esters can be polymerized to give polymers on their own account (homopolymers) with the phosphorus atom either in the side chain (13) or in the main chain (14). Natural polymers of the latter type include the nucleic acids and the techoic acids.

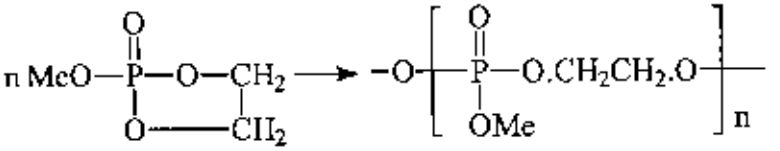


(9)



(10)

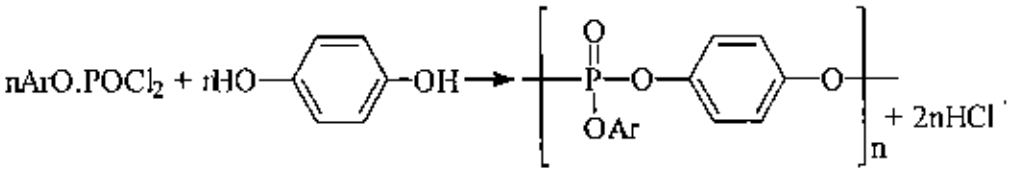
Some 5- and 6-membered ring phosphate esters can be polymerized as methyl ethylene phosphate (11)



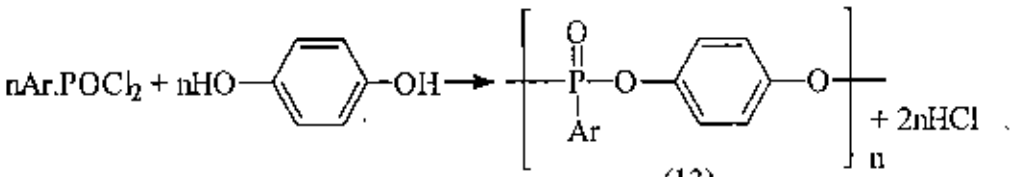
(11)

Tris allyl phosphate $(CH_2{=}CH\text{-}CH_2O)_3PO$, will give rise to a clear hard cross-linked polymer. Polymerized allyl or vinyl phosphates have not generally led to successful commercial products.

High molecular weight polymers or relatively short chain oligomers can be prepared by the reaction of $POCl_3$ or aromatic derivatives $ArPOCl_2$ with some dihydric phenols (12).



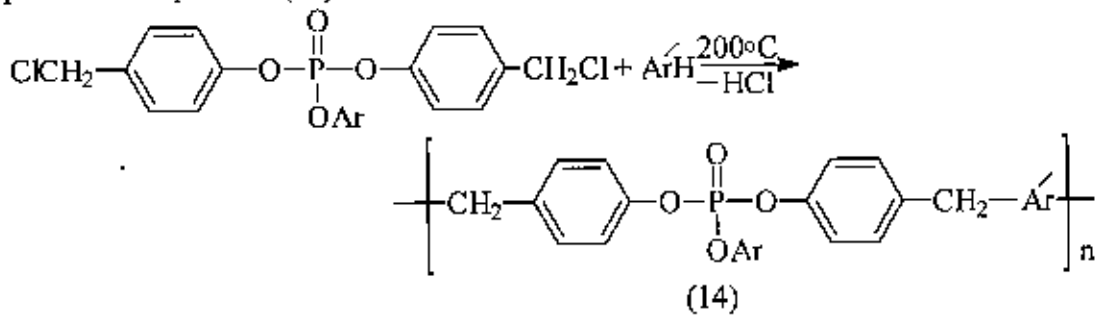
Products of type (16), first obtained about 40 years ago as 'phoryl resins' have good flame resistance, high transparency and hardness but they lack resistance to hydrolysis because of the P-O-C linkages are present. similar polymers based on phosphonates (13).



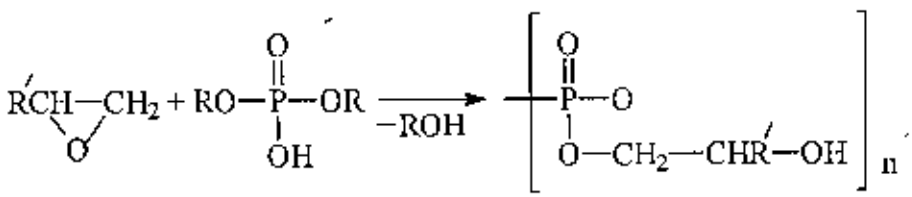
(13)

are somewhat more stable, but satisfactory stability towards hydrolysis is achieved with chains based on P-C linkages.

The Friedel-Crafts reaction can be used to prepare some polymeric phosphate esters (14) while others can be prepared by co-polymerization of dialkyl hydrogen phosphates with epoxides (15)



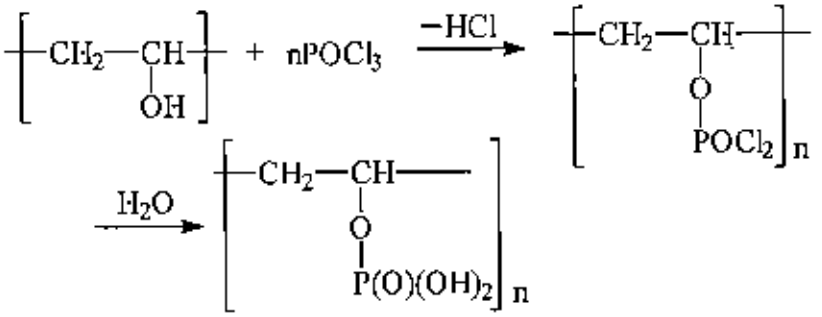
(14)



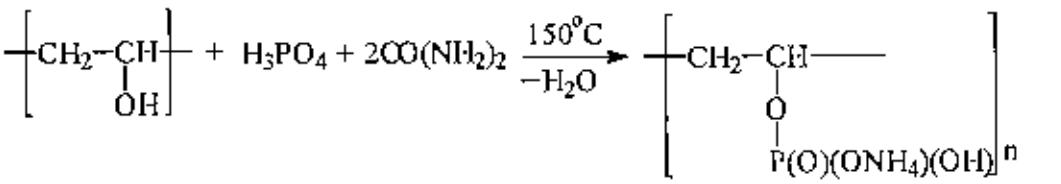
(15)

Polyvinyl alcohol can be wholly or partially converted to polyvinyl phosphate by the action of $POCl_3$ followed by hydrolysis (16). Heating of the polyacid product leads to a cross linked polymer which resists hydrolysis by dilute acids and bases.

The mono ammonium salt is obtained by the action of phosphoric acid and urea on polyvinyl alcohol (17).



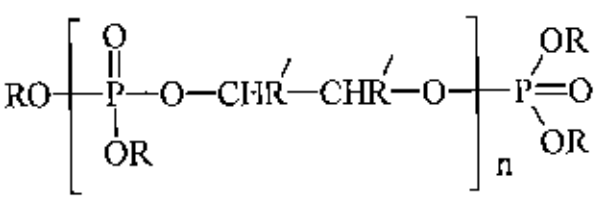
(16)



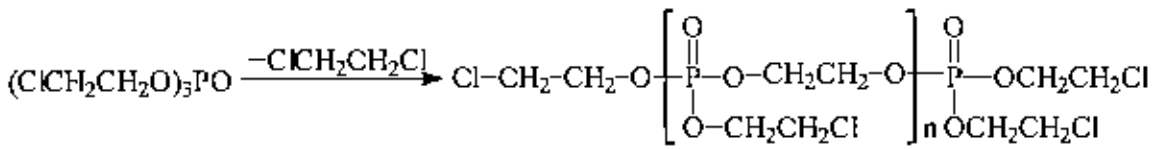
(17)

In current practice, polymeric phosphate esters are used almost exclusively as additives to modify the properites of established organic non-phosphorus polymers. This may be achieved either by co-polymerization, chemical bonding to the preformed organic polymer, or in some cases merely by physical incorporation.

Various oligomers of the type (18a) have been patented as flame retardant additives for poly urethane foams. One such material can be obtained from tris (2-chloroethyl) phosphate[31] (18b).



18(a) If R,Ŕ = Short chain alkyl



18 (b)

Highly polymerised mono-and diesters have been patented as rust preventing polymers.[32]

In Pesticides

One of the very important application of organophosphorus compounds is in pesticides[33-51] Two main groups of pesticides are insecticides and herbicides. There are also other crop-protection agents such as fungicides, acaricides, rodenticides, bactericides etc.

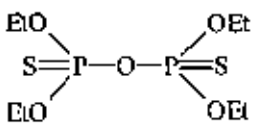
Some pesticides are very specific in action and may be effective against only one or two species, while other may be broad spectrum and effective against wide range of pests.

Pesticidal compounds sometimes have more than one function and may act as both insecticides and herbicides or as insecticides and fungicides.

The ideal insecticide needs to be highly toxic to the insect pest concerned but at the same time be non-toxic to the operator, the plant and the crop consumer. Persistence in action and cheapness are also necessary. A high persistence is desirable if used early in the growing season and low persistence if applied later.

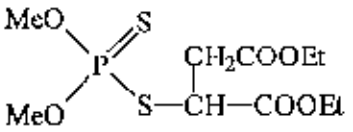
Many insecticides are also classed as acaricides and nematocides. Acaricides deal particularly with mites which attack plants and nematocide deals particularly with leaf, stem and root parasites known as nematodes. Besides, carbamates and organic chlorine compounds, other commercially important insecticide belong to organophosphorus compounds.

Some typical organphosphorus insecticides are listed below:



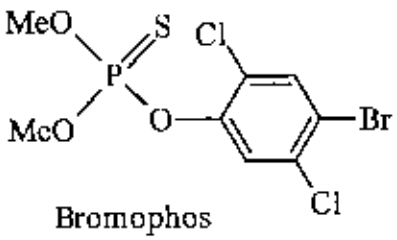
Sulphotepp

(19)



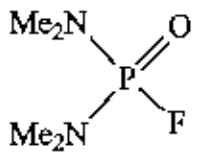
Malathion

(20)



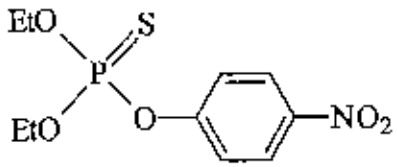
Bromophos

(21)



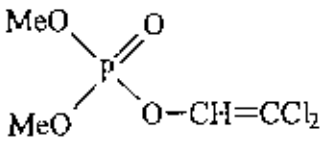
Dimetox

(22)



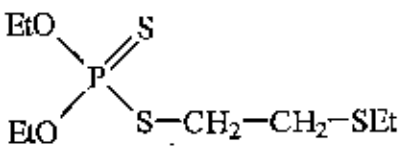
Parathion

(23)



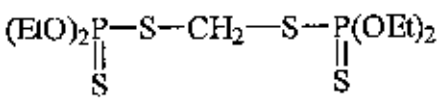
Dichlorovos

(24)



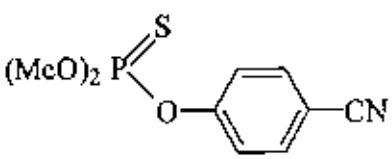
Disulphoton

(25)



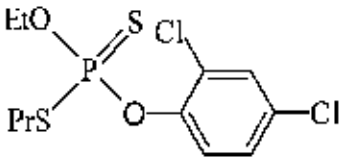
Ethion

(26)



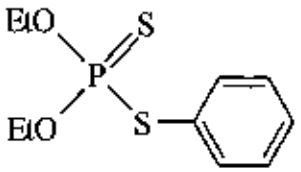
Cyanophos

(27)



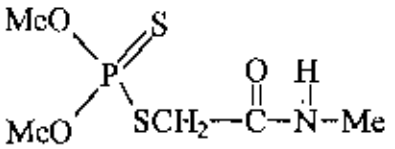
Prothiphos

(28)



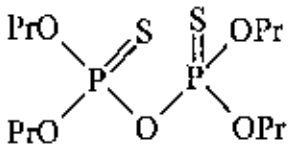
Fonophos

(29)



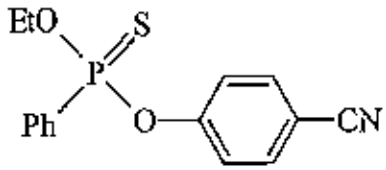
Dimethoate

(30)



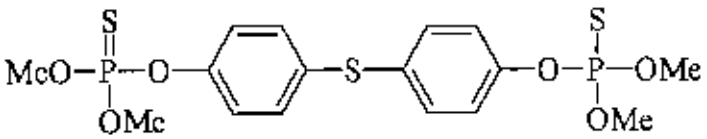
Aspon

(31)



Cyanofenfos

(32)



Temephos

(33)

Several thousands organophosphorus compounds are known to act as insecticides and about 250 of these are manufactured commercially. New compounds are constantly being patented.

Organophosphorus compounds owe their activity to their capacity to phosphorylate and intibit the action of cholinesterase, although in some instances the inhibition of other vital enzymes is believed to be involved.

Organophosphorus compounds show wide range of properties, some being highly specific in action while others are effective against a wide range of pests. Some of the compounds are also extremely toxic to humans. Others are relatively harmless and almost non-toxic to humans. Thio-derivatives are often considerably less toxic to mammals than their oxy analogues although their insecticidal activity is not diminished. Some compounds are non-toxic 'in vitro' but are converted to insect metabolism. Organophosphorus insecticides are generally rapid acting, highly

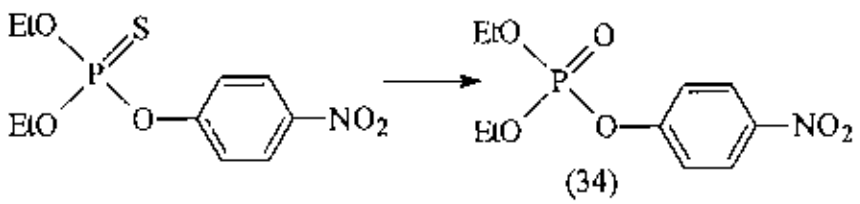
effective in small concentrations and have a low persistence, being easily broken down afterwards to non-toxic materials. Persistence of organophosphorus insecticides is related to water solubility, vapour pressure and hydrolytic stability, properties which can vary greatly from one insecticide to another. One technical process used to prepare TEPP was the chlorination of trialkyl phosphates with thionyl chloride (I), but the product is now almost obsolete because of its hydrolytic instability as well as toxicity.

$$2(RO)_3PO + SOCl_2 \rightarrow (RO)_2P(O)\text{–}O\text{–}P(O)(OR)_2 + SO_2 + 2RCl \qquad (I)$$

The highly toxic parathion (23) discovered in 1944 by Schrader, has a water solubility of 24 PPm and can be made by reaction (II). It has a greater hydrolytic stability than TEPP and is consequently more persistent in action.

$$(EtO)_2PSCl + NaOC_6H_4NO_2 \rightarrow (EtO)_2P(S)(OC_6H_4NO_2) + NaCl \qquad (II)$$

Conversion to a phosphoryl derivative is necessary for insecticidal action in order that phosphorylating action can ensure and the compound become active. In the case of parathion this may happen by thiono to thiolo isomerisation (34).



(34)

Parathion itself is less toxic but without phosphorylation it can't be active as insecticidal action.

In Medicinal Compounds

Organophosphorus compounds have some uses in medicinal compounds. Some inorganic phosphorus compounds[52-53] such as inorganic phosphate salts have long been established medicinal uses. These include stomach antacids such as hydrated

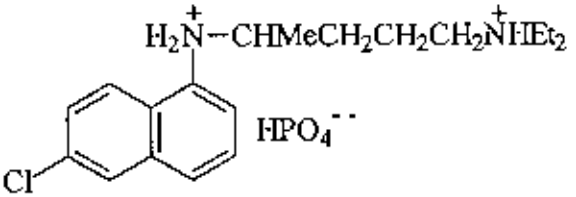
magnesium phosphate and aqueous suspensions of composition $AlPO_4.XH_2O$ (Phosphagel). Mixtures of Na_2HPO_4/KH_2PO_4 can be used for the treatment of phosphatemia (Phosphorus deficiency)

The wide variety nature of diets in western countries prevents the occurrence of phosphatemia which is quite rare in humans, An excess of phosphorus in the diet however, may lead to a reduced absorption of other essential trace elements and hence a deficiency of them may be observed. Phosphate salts make the urine more acidic and prevent the deposition of calcium salts as urinary stones.

Various calcium phosphates are used in artificial bone formulations in dental practice and in toothpaste formulations. Amorphous zirconium phosphate α–$Zr(HPO_4)_2$ is an excellent sorbant for use in renal dialysis.[54]

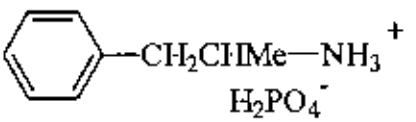
Radioactive $Cr^{32}PO_4$ is a neoplastic suppressant and is much used in cancer treatment. The heteropolyanion $P_2W_{18}O_{62}^{6-}$ is a potent inhibitor of viral DNA but other more complex anions of this type may prove to be more useful. Rodioactive ^{32}P has various uses in medicine.

A number of well known phosphate salts of organic drugs[55-56] are prescribed as medicines.This is because the phosphate generally causes less disturbance to physiological pH, it may have a more suitable solubility, or merely because it is the salt most conveniently prepared and purified. Examples are:



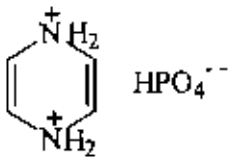
Chloroquinephosphate

(35)



Amphetamine phosphate

(36)

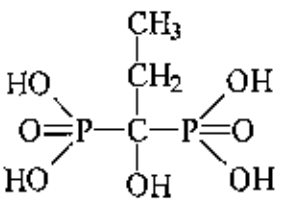


Piperezíae phosphate

(37)

Chloroquinephosphate is used as anti-malarial drug, amphetomine phosphate is used as anti-depressant and piperazine phostate is used as anthelmentic drug.

Ethane-1-hydroxy-1,1- diphosphonate (EHDP) (38) and related compounds such as (39) inhibit bone resorption and are used in the treatment of bone disease.Complexes of the diphosphonic acid with x-ray emitting isotopes of technitium are useful for medical diagnostic work since they concentrate in the bone.



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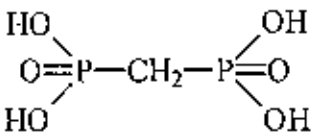
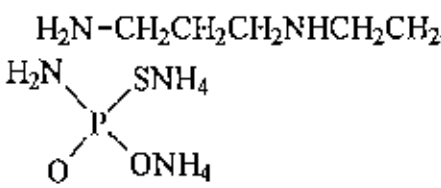
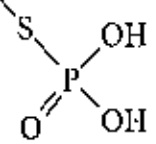


(39)

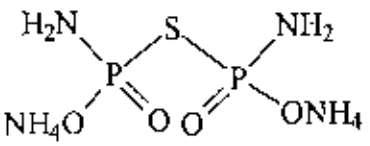
A number of phosphorothioates show anti-radiation activity and are excellent radioprotective agents. Some of these compounds are listed below.



(40)

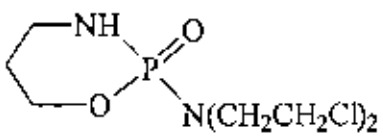


(41)



(42)

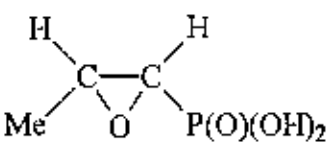
In the recent years an important advance was made in the discovery of the carcinostatic properties of cyclophosphamide (43) and its derivatives.



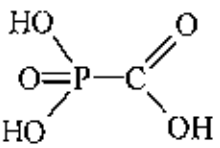
(43)

Phosphonomycin (44), Phosphonoformic acid (PFA) (45) and phosphonoacetic acid (PAA) (46) are among the earlier compounds found to have anti-viral properties. Phosphonoacetic acid is active against Herpes Virus and Marek's disease, while

phosphonomycin shows anti-bilharziosic and anti leprosy properties as well as functioning as a broad spectrum actibiotic.[57-59]



(44)



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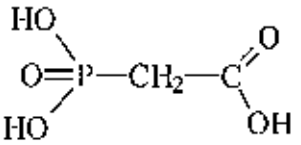
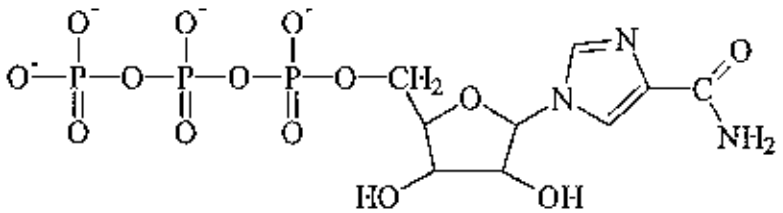
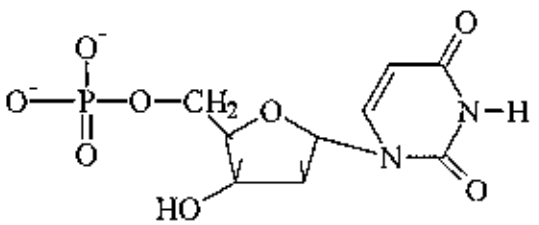


(46)

Much studied ribavirin (47) known since 1972 and 5-Fluro-2-deoxyuridine- 5-phosphate (48) is an anti-cancer drug. [60, 61,62]

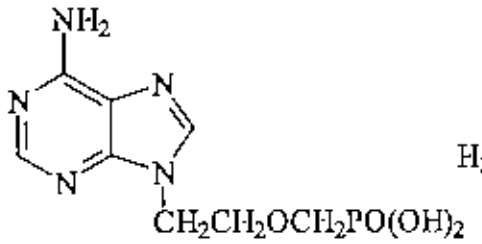


(47)

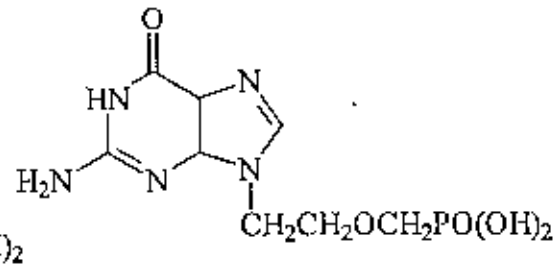


(48)

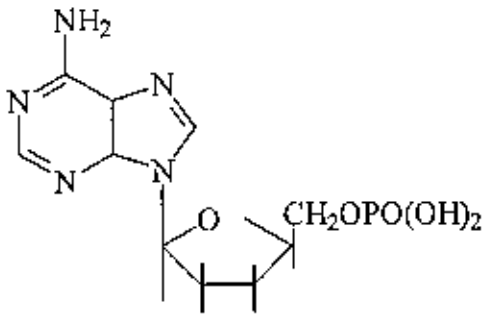
The three phosphonates (48-50) show strong activity against HSV or HIV and (51) is typical of the 2,3 di-deoxynucleotide derivatives which have antiviral activity.



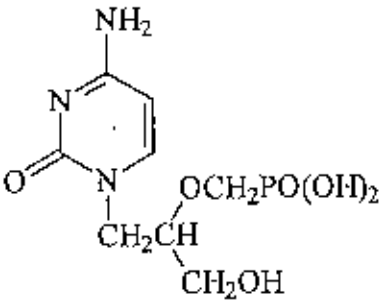
(49)



(50)

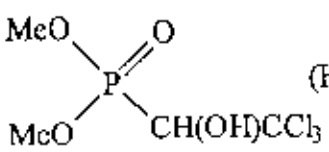


(51)

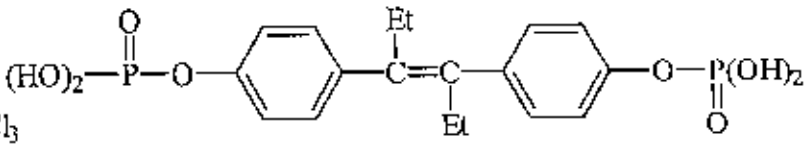


(52)

Metrifonate (53) is used for the treatment of urinary tract infections and diethylstilbestrol bisphosphate (54) can be used in the treatment of prostatic carcinoma.



(53)



(54)

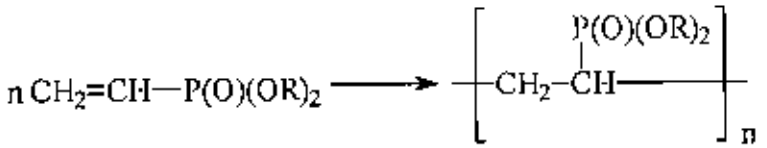
In synthetic polymers and fire retardants

Application of phosphorous containing synthetic material or synthetic polymer has many considerable advantages. Numerous polymerized products containing P are based on P-C linkages and are generally more difficult to prepare than those based on P-O-C linkages.

Some phosphorus containing monomers can be self condensed to form homo-polymers, while others can be co-polymerized with a non-phosphorous containing monomer. Desirable commercial properties are sought in polymers of the latter type, which employ a minimal amount of the usually more expensive phosphorous compound.

The major application of organophosphorous polymer has so far been in flame proofing and fire –retardancy but they have also found an important role in the modification of the properties of established non-phosphorous polymers. In addition, growing applications lie in the areas of ion-exchange materials, surface additives, catalysts and tooth preservation agents.

Polymerized phosphates constitute the most studied group of organophosphorus polymers, although in some cases the P-C linkages may be confined to the side chains. Among the methods which have been used for homopolymer formation are the heating of vinyl or allyl phosphonates (55) or vinyl or allyl esters of phosphonic acids (56).



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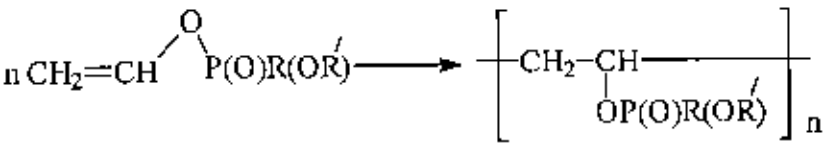
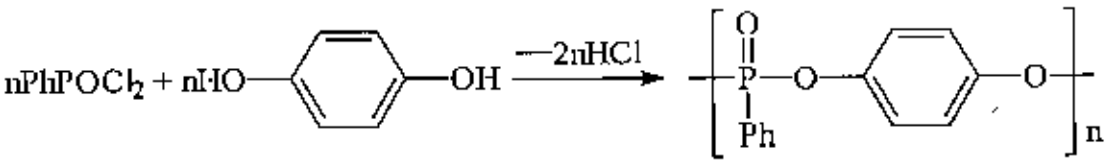


(56)

Methods used to obtain phosphonate copolymers include transesterification reactions between suitable diols and phosphonyl dichlorides(57) or phosphonate esters (58) or reaction of the latter with dihalides (59)



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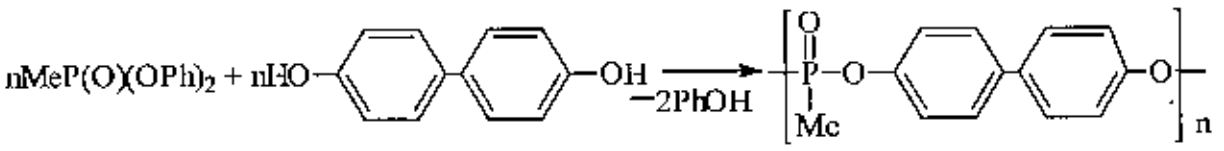
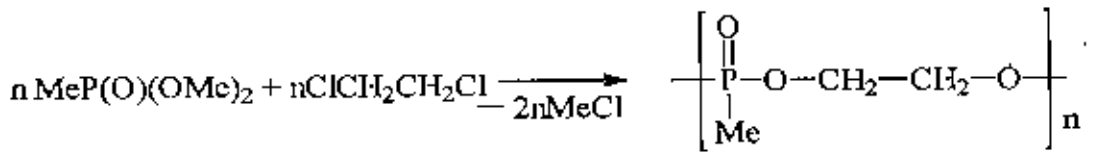
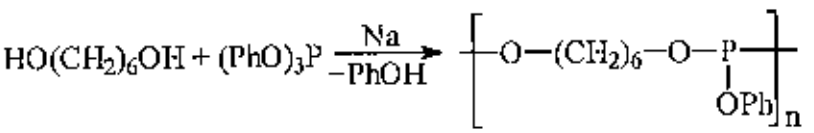


(58)



(59)

A limited number of polymerised phosphites have been made by reactions between phenyl phosphites and various diols. Typical examples of copolymers are 60-62.



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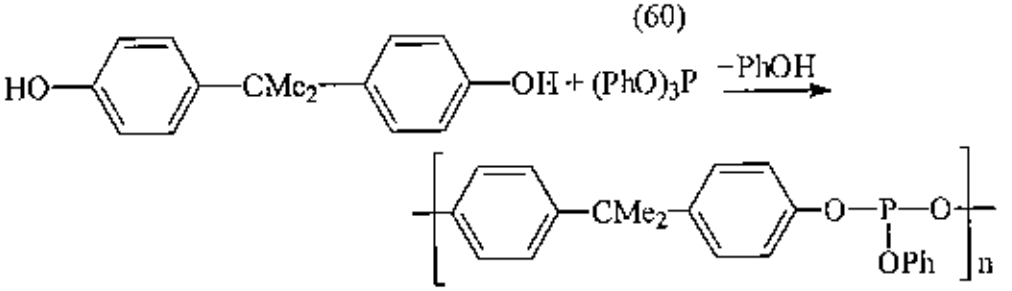
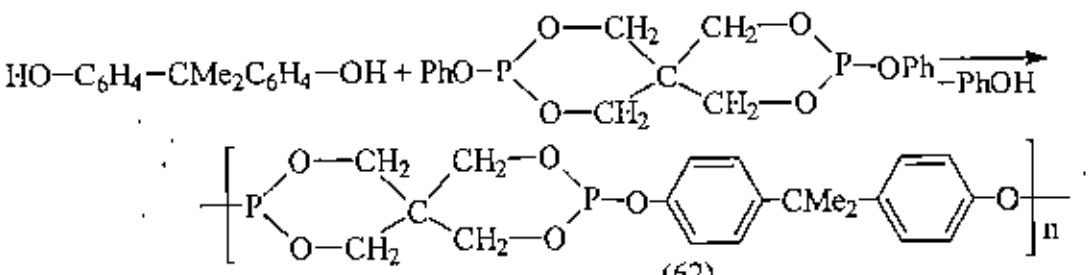
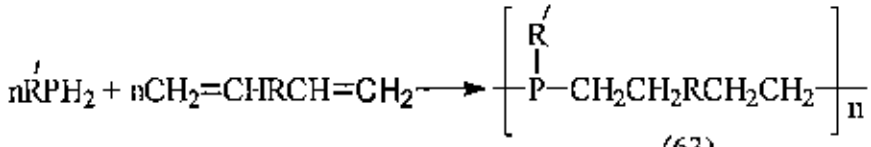


(61)



(62)

Phosphine copolymers can be obtained by heating primary phosphines with non-conjugated dienes (63) or condensing them with diisocyanates (64) or by reacting aryl phosphonous dihalides with certain hydrocarbons (65).



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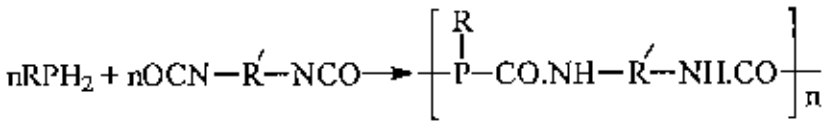
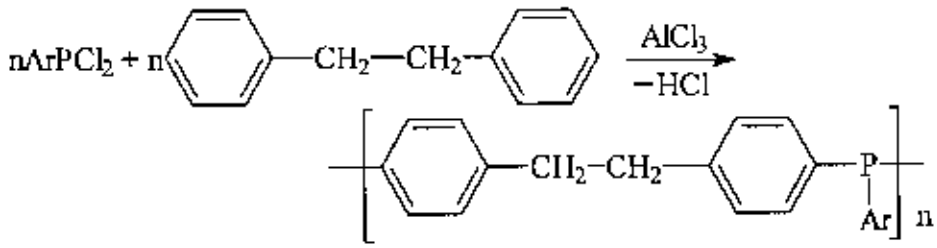
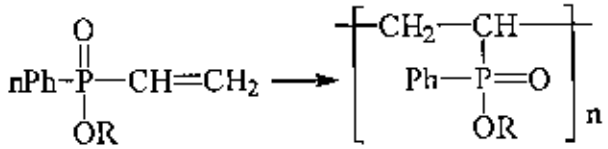


(64)

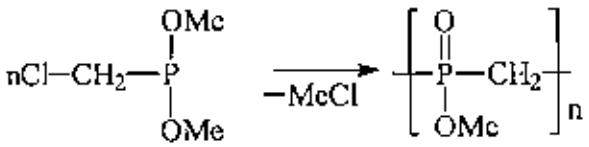


(65)

High molecular weight polyphosphinate homopolymers are obtained by heating phenyl (vinyl) phosphinic acid or its esters (66). When certain phosphinates are heated, Arbusov rearrangements takes place, followed by condensation to give polymers with phosphorus in the main chain (67).



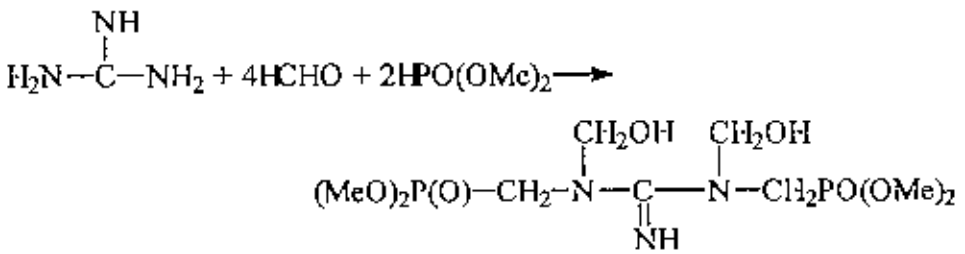
(66)



(67)

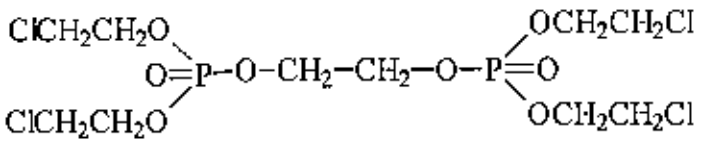
A permanent or semi-permanent fire resistance of paper, wood, plastics, fabrics etc. can be obtained when the fire retardant can be chemically bonded to, or physically incorporated in an insoluble form in these highly polymeric materials. In the case of synthetic materials, the most intimate bonding is usually obtained by

copolymerization with a fire retardant monomer or short chain oligomer. Alternatively, it may be possible to attach the phosphorus compound by a suitable reaction with the preformed polymer. There are now several hundred organophosphorus or organic phosphate fire retardants are available for application. Although most of these are considerably more expensive than ammonium phosphate, their use is often commercially justified, particularly with high quality fabrics. Their mode of action in many cases is probably at least partially similar to that of ammonium phosphate.Flame and grease resistance can be imparted to cotton fibers by carrying out reaction (68) in their presence but there is some loss of strength.

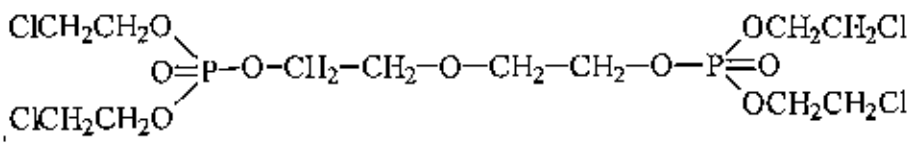


(68)

Two other commercial organic phosphates of the additive type are 'Thermolin 101' (68a) and ' phosgard 1227' (68b).



68 (a)



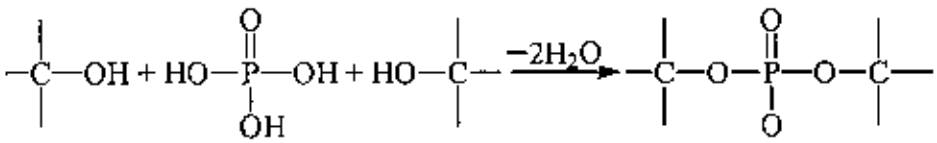
68 (b)

In natural products

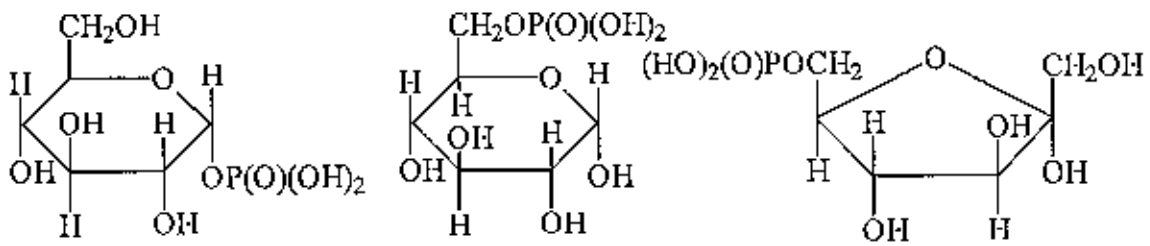
Natural products in the form of biopolymers are very much important as these are mostly phosphorus containing organic compounds. All nucleic acids are phosphate esters, only some varieties of proteins, lipids, polysaccharides are found in phosphorylated form, and these may be termed phosphoproteins, phospholipids and

phosphosaccharides respectively. Phosphorylated forms are intimately involved in the function of the all-important type of proteins known as enzymes.

The four types of biopolymer are frequently encountered in nature as intimately linked of considerable complexity. These associated units are known as lipoproteins, glycoproteins, proteoglycans, glycolipids, nucleoproteins etc. Phosphate groups when present in either biopolymer may also act as bridging groups.

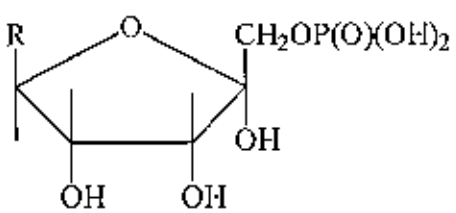


The monosaccharide found in living system are mostly mono and di-phosphate esters. of greatest importance in animal metabolism are the three esters, (69) which also occur in plant life, particularly fruit. They have high water solubilities and high acid strengths. Individual glucose phosphates vary greatly in their hydrolytic behaviour.



(69)

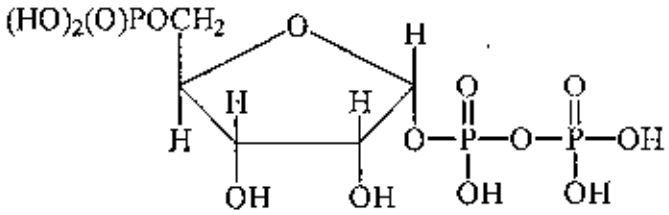
Amongst the ribose phosphates, ribose-5-phosphate (70) is utilized in forming the all important nucleotides.



R= bose 5 phosphate

(70)

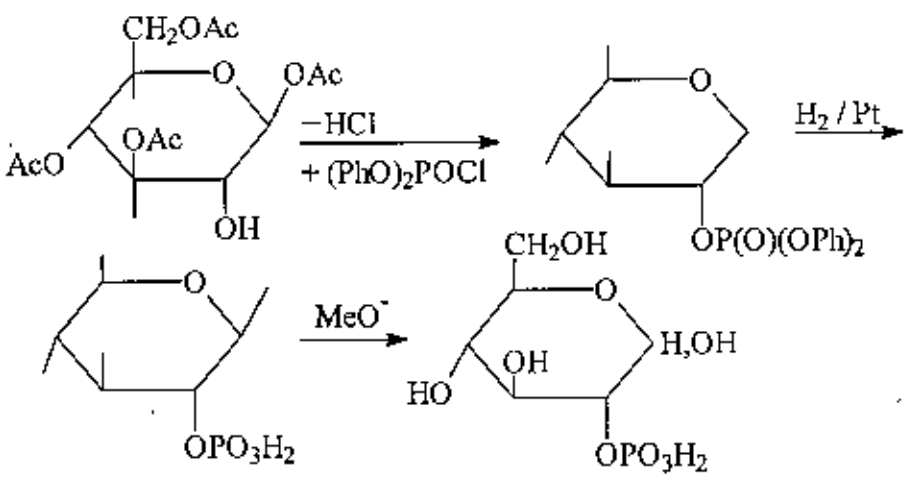
An important compound in biochemistry is 5 – Phosphoribosyl – 1– pyrophosthate PRPP (65). This compound is involved in the biosynthesis of amino acids and NAD.



(71)

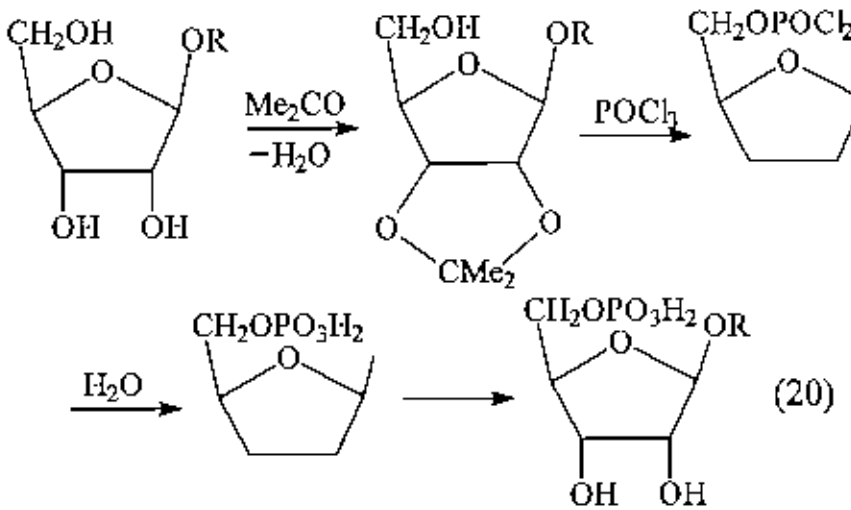
Saccharide phosphate esters can be isolated from natural sources or produced by chemical synthesis. Fructose 1 : 6 diphosphate can be isolated from yeast and glucose – 1 – phosphate can be obtained by phosphorolysis of glycogen. For preparation of bulk quantities, chemical methods of synthesis are usually to be preferred although they are not always available. As a result of studies over the past few decades, a wide variety of suitable phosphorylating agents have become available for treating both simple sugars and nucleotides.[63-65] The most widely used phosphorylating agents diphenyl phosphorochloridate $(PhO)_2POCl$ and dibenzyl phosphorochloridate $(PhCH_2O)_2$ POCl, are normally used in pyridine solution.

Simple monosaccharides such as D-glucose – 6 – phosphate can be prepared by direct phosphorylation of the unprotected sugar. In general, however, the sugar -OH groups have to be protected while phosphorylation can be carried out at the desired position, and the protective groups afterwards to be removed. Glucose–2–phosphate can be formed according to scheme (2).



(Scheme - 2)

In some cases phosphoryl chloride is a satisfactory phosphorylating agent (Scheme-3).

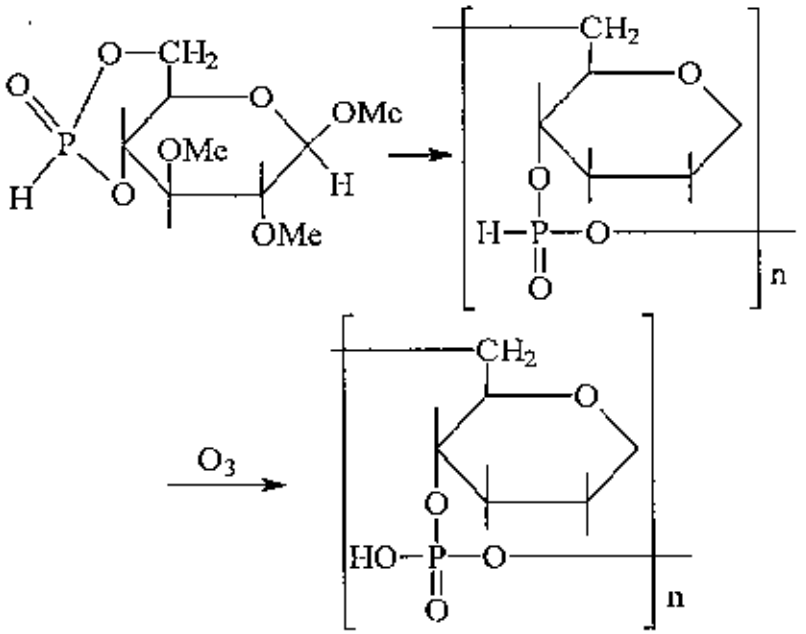


(Scheme –3)

Polysaccharides are widely distributed in plants and animals. They are present both as structural materials as in cellulose and as food storage compound such as starch and glycogen. Phosphorylated polysaccharides, phosphorylation with consequent modification of properties is possible in principle for any polysaccharide. Phosphopolysaccharides (Polysaccharide phosphate esters) of this kind occur frequently in living systems and in a number of important technological products. Many bacterial polysaccharides contain phosphate ester groups, these include the teichoic acids.

A considerable number of phosphosaccharides have been characterised by NMR, mass spectra, chromatography or other techniques. Many of these phosphosaccharides have however been obtained only in minimal amounts via biochemical processes and satisfactory chemical means for their bulk preparation are not yet available.

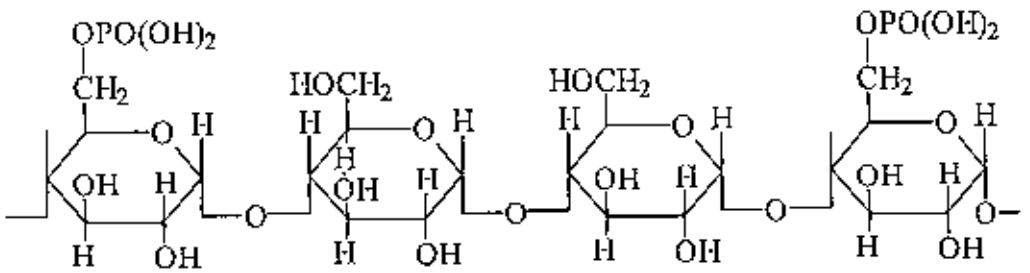
In sugar-phosphate chains[66], consisting of sugar rings alternating with phosphate groups can be obtained by entirely synthetic methods. Ring opening (Scheme - 4) has been shown to yield high molecular weight polymers.



(Scheme – 4)

Polymer chains consisting of alternating sugar rings and phosphate groups are found in nucleic acids and in some varieties of teichoic acids.

Reaction of cellulose with concentrated phosphoric acid or phosphoryl chloride, results in the replacement of a few of the -OH groups by $OP(O)(OH)_2$ groups (75). Phosphorylation at the C_6 atom is usually assumed, although other carbon atoms may also be involved in a more or less random manner.

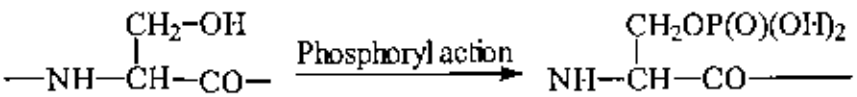


(75)

An increased flame-resistance can be obtained with phosphorylated cellulose but at the expense of partial degradation and loss of fiber strength and increased water solubility. Cellulose phosphate salts are useful as cation exchange resins in protein chromatography and for peptide separation. Amongst the biological polymers,

proteins[67-73] have the most diverse functions and are in fact the most complicated substances known to science, thousands of different varieties exist in every living organism.

Animals generally contain about ten times more protein than plants. All proteins are built from C, H, O, N and usually some S. The pure protein structures are devoid of phosphorus. Phosphoproteins only result when appropriate substitution is made. Proteins are usually of two types conjugated proteins and non-conjugated proteins. Proteins often occur naturally in close association with other biopolymers and such combinations are sometimes known as conjugated proteins. They include nucleoproteins, lipoproteins and glycoproteins. Either or both components of a conjugated protein may be phosphorylated. In the case of nucleoproteins, phosphorus is always present in the nucleic acid component. Some may prefer the prefix 'phospho' to be used to signify which component is phosphorylated e.g. phospholipoprotein or lipophosphoprotein. More than a hundred different phosphoproteins have now been recognized. The best known of these include milk casein, the egg proteins- phosvitin and ovalbumin and the iron-storage protein ferritin. Phosphorylation of proteins nearly always occurs on serine residues (76) but threonine, tyrosine, histidine and lysine can also be involved.



(76)

Many enzymes are phosphoproteins and enzyme action is frequently associated with phosphorylation dephosphorylation of the protein residues particularly in serine.

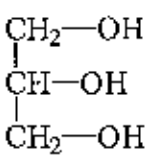
Phosphorylation replaces –OH with –OP $(O)(OH)_2$ and places a negative charge on the protein. Interference with the existing hydrogen bonding scheme and the introduction of a relatively large phosphate group can generally be expected to modify the secondary and tertiary structure of protein.

Protein phosphorylation is involved in numerous biochemical processes. These include the regulation of metabolic pathways, membrane transport, muscle

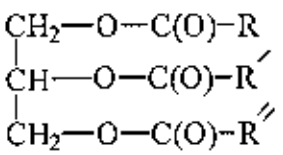
contraction, hormone response, photosynthesis, cell division, gene transcription and translation and brain processes such as learning and memory.[74-79]

Phosphoproteins can be extracted from bone and dentine with EDTA. The phosphoproteins in dentine form about 10% of the total protein present and have a very high serine and aspertine content with about half of the serine residues phosphorylated. Isolated phosphoprotein has been shown to catalyze the formation of apatite from amorphous tri-calcium phosphate and it may act in this way in teeth.[76] Casein is the most abundant protein in milk which consists of four phosphoproteins (α_{s1}, α_{s2}, β, κ) which occur in close association with calcium phosphate in the form of micelles.

Lipids are water-insoluble, oily or greasy substances that can be extracted from cells and tissues by non-polar solvents. The most abundant kinds are fats, which are triglycerides, and they act as major storage fuels in most organisms. Triglycerides are fatty acid esters of glycerol 76(a) with general formula 76(b), where R, R′, R″ are long hydrocarbon chains of composition - - $(CH_2)_n$. CH_3 derived from fatty acids HOOC $(CH_2)_n$ CH_3



76(a)

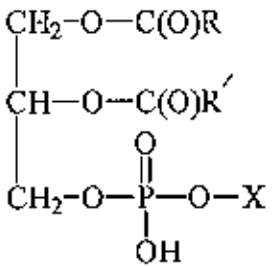


76(b)

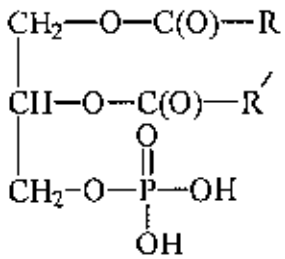
In addition to glycerolipids 76(b) if the lipid contains one or more polar phosphate group, it is called a phospholipid.

Phospholipids are major components of cell membranes and occurs widely in bacteria, animal and plant tissues. They are involved in enzyme action and transport of tri-glycerides through the liver and they have a role in electron transport and oxidative phosphorylation.

The most important commercial source of phospholipid is lecithin, which has numerous food and nonfood applications. The properties of starch and bread are modified by their small phospholipid content. The most abundant phospholipids are those with the general formula 77(a) where R is a long chain fatty-acid residue and X can be various groups. They are derivatives of glycerophosphoric acid and are sometimes called glycerophospholipids.



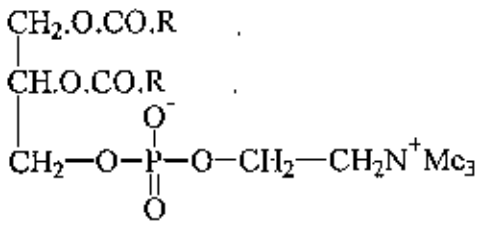
77(a)



77(b)

When X=H, these compounds are the parent phosphatidic acids 77(b)

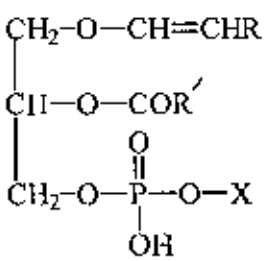
In naturally occuring phosphoglycerides 77(a), X is most frequently choline, ethanolamine, L-serine or inositol and R is a mixture, the principal components of which are palmitic and oleic together with smaller quantities of other long-chain residues. Lecithin (78) is found in egg yolk, brain tissue and in skin. It exists as zwitterions in its physiological environment



(78)

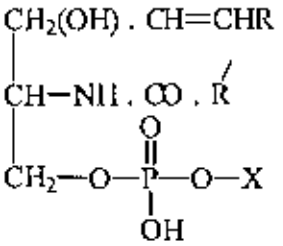
Most phospholipids are water soluble as well as fat soluble, because their molecule have hydrophobic as well as hydrophilic regions and are polar in character. So they are called amphiphatic lipids. In general, membrane lipids are amphiphatic phosphoesters, whereas storage lipids are not. Phospholipids are important for their emulsifying properties. In an oil water system the molecules concentrate at the interfaces and lower the surface tension thus enabling droplets to be formed, they act as a barrier at the interfaces and stabilise the emulsion.When heated with acids or

bases, most phosphoglycerides are split into their components i.e. fatty acids, glycerol, phosphoric acid and the base head group. Plasmalogens are phosphatidyl derivatives in which the fatty acid in the α-position has been replaced by an unsaturated ester (79a). There are found in brain and nervous tissue.



Plasmalogens

79(a)

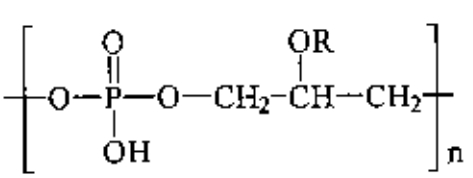


Sphingomyeclins

79(b)

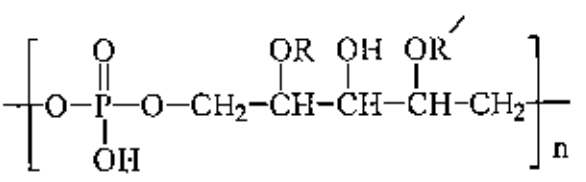
Sphingomyeclins are phosphorus containing members of the second large class of membrane lipids known as sphingolipids 79(b). The head group X is most commoly choline or ethanolamine, and these compounds resemble the corresponding phosphatidyl compounds in their general properties. They are found in most animal membranes, particularly in the 'myelin sheath' surrounding certain nerve cells.

Some lipids are conjugated with proteins to form lipoproteins. Lipovitellin and lipovitellenin are phospholipoproteins. Blood contains various types of plasma lipoproteins which consist of triglycerides, proteins, phospholipids and cholesterol. These closely associated units may be covalently linked to each other in some cases. Phosphate groups, glycerol, ribitol and saccharide units are the basic components, and the simpler derivatives can be represented by the formulae (80) :



R=H, sugar or D-alanyl

80(a)

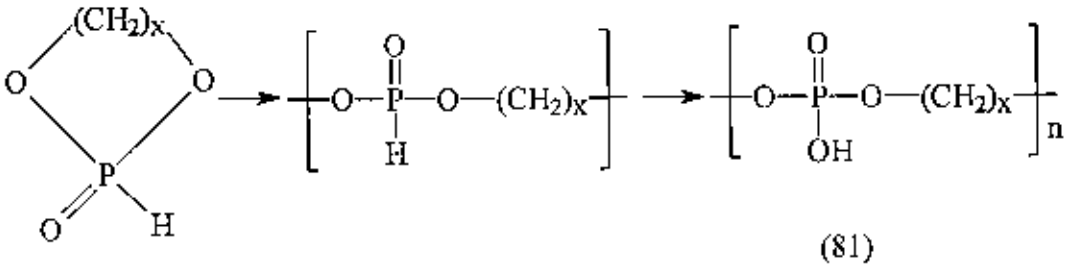


R= H or D-alanyl
R≤ H or sugar

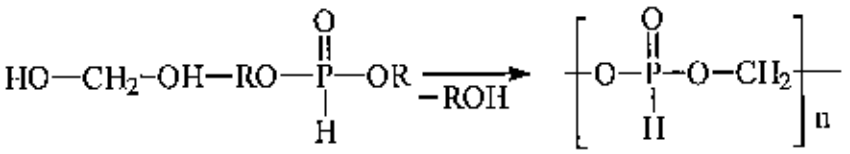
80(b)

The simplest parent compound poly (glycerol phosphate) R=H in 80(a) has been prepared by laboratory methods, poly (ribitol phosphate) R=R′=H in 80(b) has been prepared by phosphorylation of 80(a).

The polymer poly(alkylene phosphates) which can be made by ring opening polymerization (81) or by condensation of dialkyl phosphites (82). Molecular weights of over 10,000 have been achieved [69].



(81)

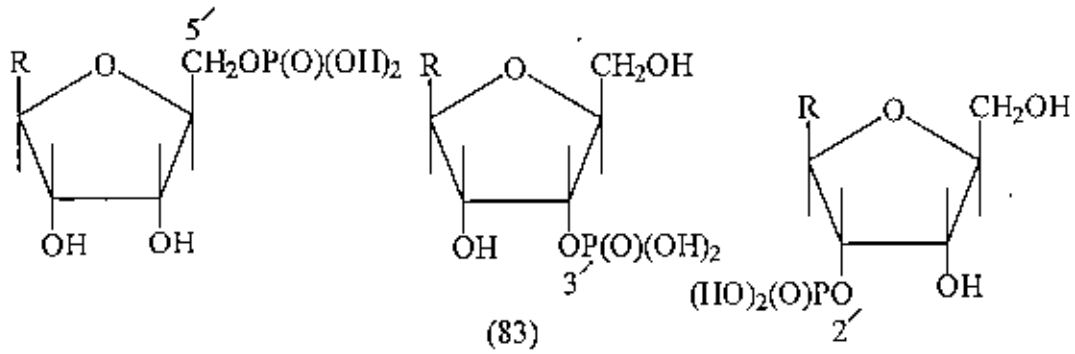


(82)

The nucleic acids are not only responsible for the storage and transmission between generations of genetic information[70], but they also pass on this information to direct the synthesis of the proteins characteristic of the cell. Nucleic acids frequently occur in close association with proteins as nucleoproteins. Nucleic acids are closely associated with mononucleotides, modified polynucleotides and nucleotide phosphates. They all contain phosphorous, mononucleotide units are built from three main components, a phosphate group, a sugar-ribose or deoxy-ribose, a nitrogen base, a purine or a pyrimidine.

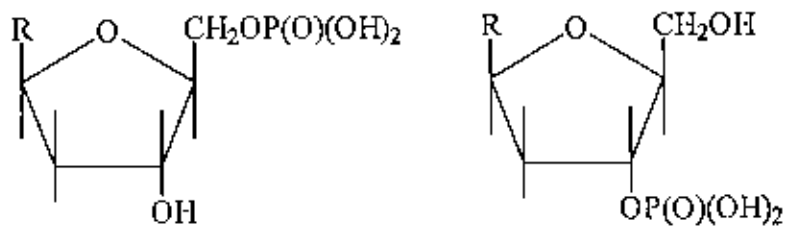
The mononucleotides (mononucleoside phosphates) are obtained by breaking down the polynucleotides or by phosphorylation of pre-formed nucleosides. Their main biochemical role is to function as sources of the nucleoside pyro and triphosphate.

Various isomers of mononucleotides are found. The ribonucleosides may be phosphorylated in the 2′, 3′ or 5′ positions (83).



(83)

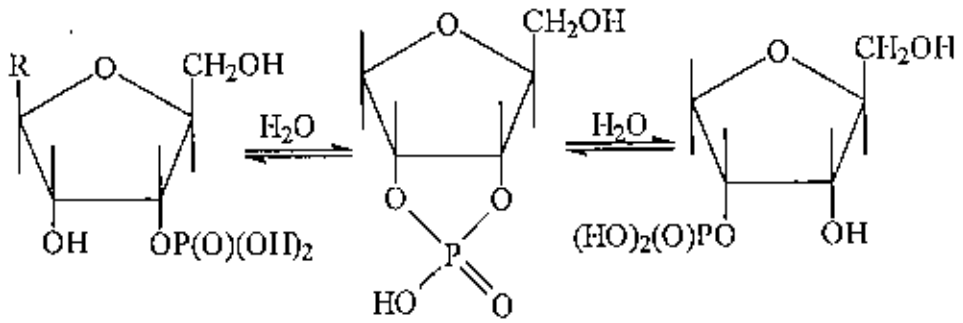
Whereas the deoxyribonucleosides my be phosphorylated only at 3′ or 5′ positions (84).



(84)

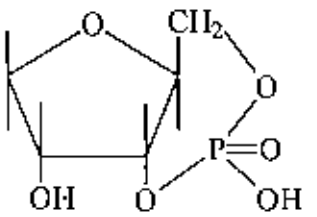
The 5′ ribonucleosides are strongly acidic. The RNA mononucleotide unit containing adenine is adenosine 5′- monophosphate (AMP). This compound is the hydrolyzed product of adenosine tri-phosphate (ATP).

The ribonucleoside 2′ and 3′ phosphates are readily interconvertible in acid solution and this inter-conversion proceeds through the cyclic 2′, 3′ phosphate (85).



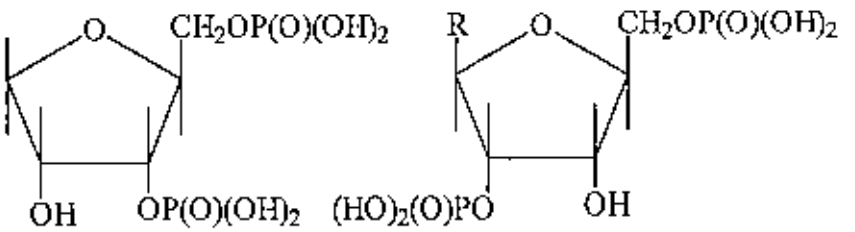
(85)

Adenosine 3′, 5′ mono-phosphate (Base = adenine) in 80(a) is of considerable importance in biochemistry.Hydrolysis of this compound with $Ba(OH)_2$ gives a mixture of adenosine 3′ phosphate and adenosine 5′ phosphate.



86(a)

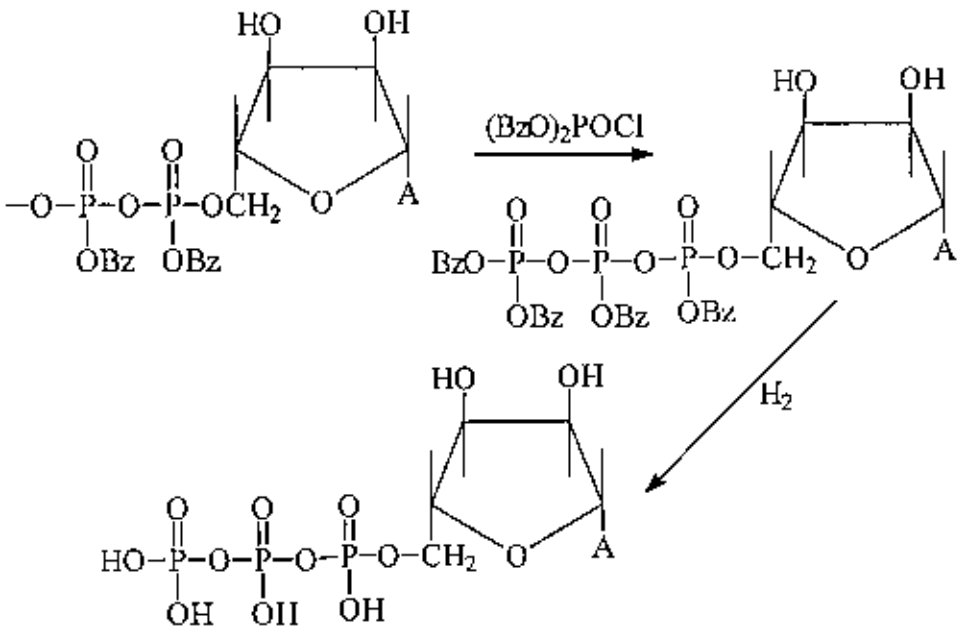
Nucleoside bis-phosphate 86(b) can be prepared and have considerable importance in biochemistry.



86 (b)

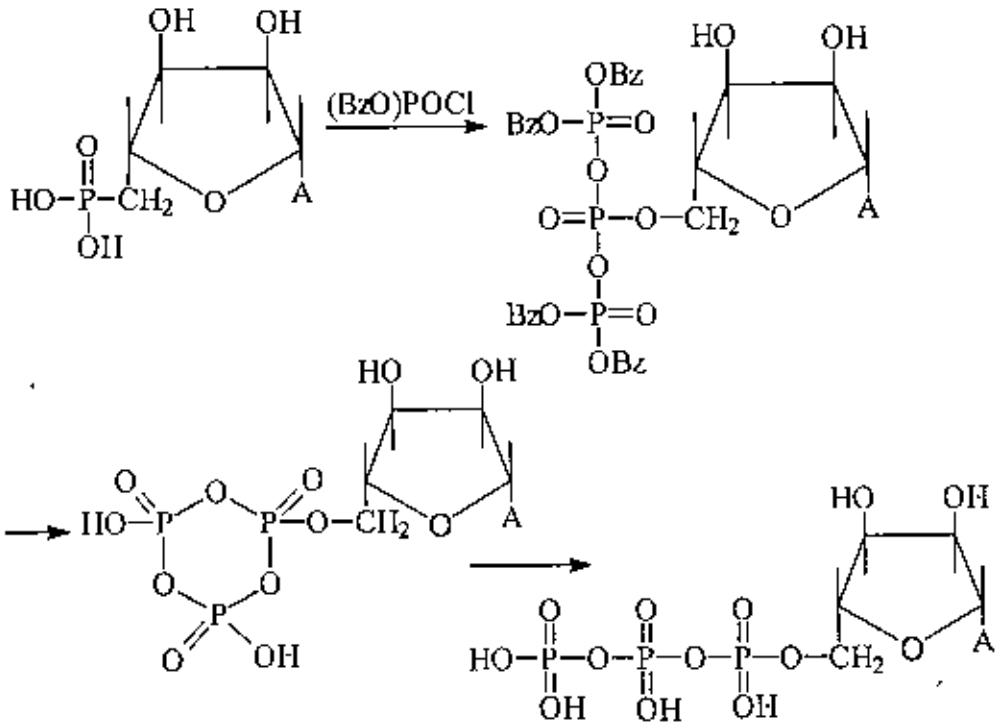
Although ATP was first discovered by Fiske and Subarrow in muscle in 1929[71], the first laboratory synthesis was achieved after 20 years by Todd as co-workers[72].

In their first method the silver salt of adenosine 5′- dibenzyl pyrophosphate was reacted with dibenzyl phosphorochloridate and this was followed by catalytic hydrogenolysis to remove the benzyl groups. The pyrophosphate salt had been prepared by a similar route using di-benzyl phosphorochloridate and adenosine-5′-monophosphate (Scheme- 5).



(Scheme – 5)

In another synthesis, the di-silver salt of adenosine-5′-phosphate was treated directly with an excess of dibenzyl phosphorochloridate and this was followed by hydrogenolysis and hydrolysis (Scheme - 6).



(Scheme – 6)

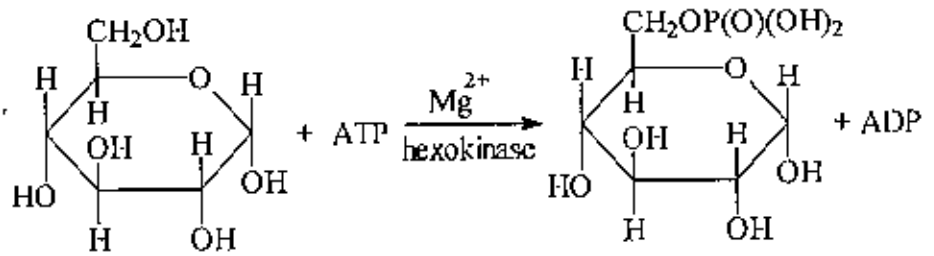
Almost all biochemical reactions are catalyzed by enzymes. Enzymes are a special kind of catalyst which are proteins and which are effective in extremely small concentrations. Enzymes are usually proteins, all enzymes contain nitrogen and most of the enzymes contain phosphorous, a very high proportions are involved with reactions of phosphate esters and phosphorus is often present in the cofactors.

Enzymes which catalyze hydrolysis are known as hydrolases and if the compounds acted upon (substrate) are esters they are known as esterases. If the action is specific to phosphate esters, these compounds are known as phosphoesterases or phosphatases.

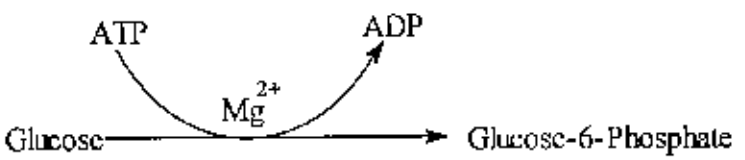
The enzymes which catalyze 'phosphate transfer' or phosphorylation is very important in biochemistry. These have been known variously as phosphotransferases, phosphorylases, phosphokinases, transphosphorylases etc.

There are two phosphorylation processes of fundamental importance of biochemistry. These are photophosphorylation, the process by which green plants convert light energy to chemical energy. And the oxidative phosphorylation, the process by which a large part of the energy in foods is conserved and made available to the cell.

Adenosine tri-phosphate, ATP phosphorylates glucose as it enters the living cell according to reaction 89(a) which can alternatively be written as 89(b). In this non-reversible reaction in which ATP act as the phosphorylating agent, the enzyme is given a special name hexokinase. Enzymes which catalyze transfers specially to and from ATP are sometimes called phosphokinases.

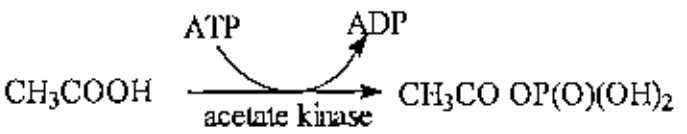


89(a)



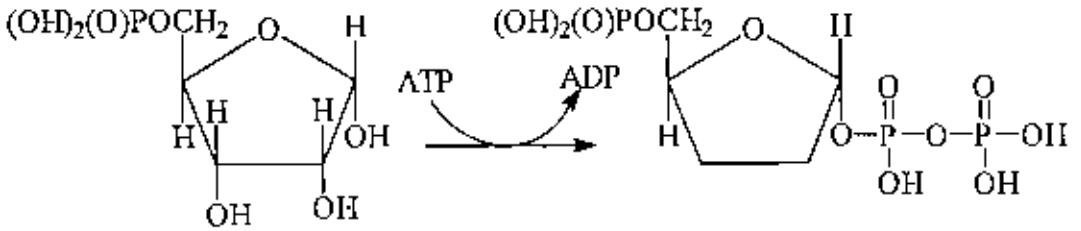
89(b)

Another example is provided by the phosphorylation of acetic acid (substrate) to form acetyl phosphate, which is catalyzed by the phosphokinase enzyme known as acetate kinase (84). This reaction can occur in reverse in which case the acetyl phosphate is said to phosphorylate the ADP to ATP. Both di-phosphate and tri-phosphate esters can act as phosphorylating agents.



(90)

Enzymes which catalyze the transfer of a pyrophosphate group are sometimes known as pyrophosphorylases, although ATP normally functions as a phosphorylating agent, it will sometimes act as a pyrophosphorylating agent, as in the conversion of ribose-5-phosphate to a α-5-phosphoribosyl-1-pyrophosphate (91).



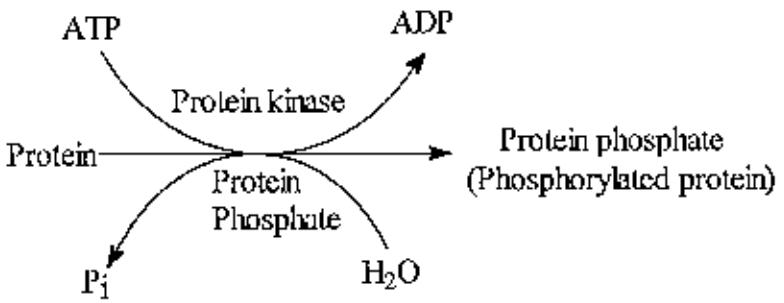
(91)

Oxidative phosphorylation occurs in the formation of ATP from ADP when it is coupled to the process of electron transfer from NADH or $FADH_2$ to oxygen (92). This occurs in the terminal oxidation of glucose. Electron transport and oxidative phosphorylation take place in nearly all types of aerobic cell.

$$NADH+H^+ + ½\ O_2 \longrightarrow NAD^+ + H_2O - 5.2 \text{ kcals.}$$

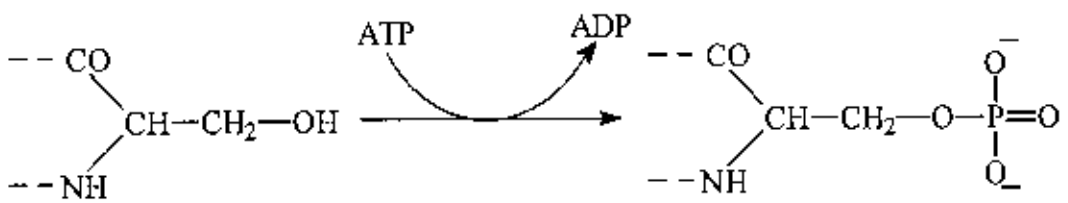
Photophosphorylation occurs when ADP is converted to ATP during the complex process of photosynthesis. Protein phosphorylation[73-84] is one of the important phenomenon of the living cells. Phosphorylation is one of the chief mechanisms whereby cells can rapidly activate or inactivate many of the enzymes which are present. These actions are believed to result from modification of the enzyme conformation, whereby its active sites are either exposed or masked.

The enzymatic phosphorylation and dephosphorylation of a protein can be summarized as in (Scheme - 7)



Scheme -7

Phosphorylation involves replacement of -OH groups along the protein chain most frequently on serine residues (Scheme – 8).



(Scheme – 8)

At least a hundred or out of the total of about 30,000 different proteins found in cells are known to be modified by phosphorylation. Even when a protein is phosphorylated, however, only a small proportion of the total -OH groups is generally involved. Whether or not a particular residue is phosphorylated in a given protein is determined by the specific amino-acid sequence around the site of potential phosphorylation.

AIM OF THE PROJECT

Organophosphorus compounds have tremendous importance in the field of food technology, animal foodstuffs, pesticides, medicinal compounds, synthetic polymers, fire retardants and natural products. These compounds can be used as flame retardants for fabrics and plastics, plasticizing and stabilizing agents in the plastic industries, additives in the petroleum products and corrosion inhibitors. The intimate involvement of organophosphate in living process is now well recognized and modern biochemistry is dominated by it such as ATP and DNA.

Phosphoryl transfer reaction is very important in some organophosphates because insecticidal action is increased and phosphorylating action can ensure the activity of that insecticides.

Nucleophilic substitutions at the carbon centre is very important topic in organic chemistry. In many aspects phosphorus rivals carbon in its structural versatility, the general variety of its compounds and its biochemical importance. The mechanism of nucleophilic substitutions at the carbon centre is very well known. Considerable amount of work have been carried out on nucleophilic substitutions at the carbon centre but much less is known about nucleophilic substitutions at the phosphorus centre. Nucleophilic substitutions at the phosphorus centre is very important topic in organophosphorus chemistry. The nucleophilic substitutions at the carbon centre is well established but the mechanism of nucleophilic substitution reactions at phosphorus is not well established. It has great interest to study nucleophilic substitutions reactions at phosphorus in solutions. The nucleophilic substitutions reactions at neutral phosphoryl species such as in phosphoryl chloride have been considered to proceed either stepwise through a pentacoordinate intermediate of trigonal bipyramidal shape or concertedly through a single transition state.

Therefore, the proposed research project is undertaken with the following objectives:

(a) To prepare the unavailable starting materials from available chemicals.

(b) To synthesize the organophosphorus compounds.

(c) To optimize the reaction condition.

(d) Characterization of the synthesized product by physical and chemical methods also by spectroscopic analysis.

Chapter 2

EXPERIMENTAL

2.0 Materials, Chemicals, Boiling point apparatus and Spectral Techniques

All the solvents for reaction, separation, extraction and recrystallization were purified and the tests were carried out as available in the laboratory and commercially. Analytical or laboratory grade reagents, solvents and chemicals were used in all my experiments and these were procured from E. Merck (Germany) and BDH(England). Reagent grade of n-hexane, ethylacetate, diethylether, acetone, phosphoryl chloride etc. were purified by distillation at the boiling point of the respective solvent. Ethylacetate and phosphoryl chloride from E. Merck (Germany) were used directly as these were bought commercially. The following methods were used for purification and drying of the solvents used for the syntheses.

a) Determination of melting points

Melting points of different synthesized compounds were determined on Gallenkamp (England) melting point apparatus and paraffin oil bath.

b) Infra-red (IR) spectra

The Infra-red spectra were recorded on KBr pellet for films with a Shimadzu FTIR spectrophotometer from the department of Chemistry, BUET, Dhaka, Bangladesh.

c) Nuclear Magnetic Resonance (NMR) spectra

The NMR spectroscopy is widely used for the detailed investigation of an unknown compound. With the help of this spectroscopy the structure or pattern of an unknown compound can be determined. ^{1}H NMR (400 MHz), 13C NMR and ^{31}P NMR (162 MHz) were recorded in deuteriochloroform ($CDCl_3$) with a Bruker DPX-400 spectrophotometer using tetramethylsilane (TMS) as internal standard at the Bangladesh Council of Scientific and Industrial Research laboratory (BCSIR), Dhaka, Bangladesh.

d) Drying

All organic extracts were dried over anhydrous sodium sulphate (Na_2SO_4) before concentration.

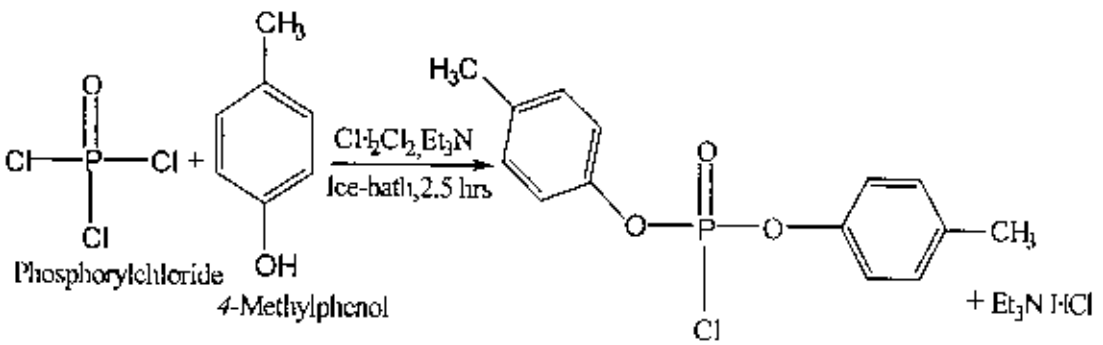
e) Evaporation

All evaporation were carried out under reduced pressure in Buchi rotatory evaporator (West Germany) with a bath temperature below 40^0 C.

f) Column chromatography

Column chromatography has been successfully applied to separate the individual components (having different R_f values) of mixture obtained from the reaction This technique was also employed for purification of the product.

2.1 Synthesis of Bis-(*4*-Methylphenyl) chlorophosphate



Bis-(*4*-Methylphenyl) chlorophosphate

1A

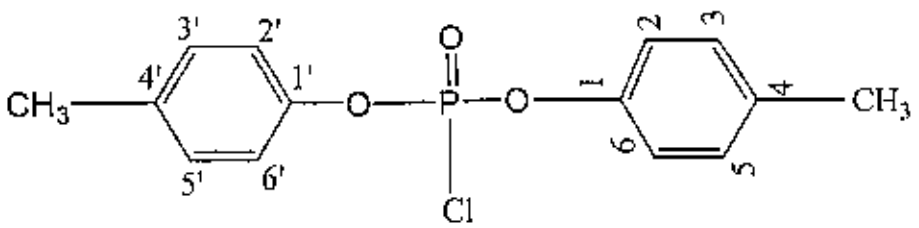
Procedure

A solution of phosphoryl chloride (330 mg, 2.152 mmol) in methylene chloride (5 mL) was taken in a round bottomed flask. The flask was then placed on an ice-bath with constant stirring for half an hour. A mixture of *4*-methylphenol (465.43 mg, 4.304 mmol) triethylamine (435.82 mg, 4.304 mmol) and methylene chloride (7 mL) was taken in another round bottomed flask and the flask was then placed on an ice bath with constant stirring for half an hour. The phenolic triethylamine mixture was then added drop-wise to the phosphoryl chloride solution and was stirred for two and half hours at the same temperature. The progress of the reaction was monitored by TLC. The reaction mixture was then filtered and the solvent was evaporated by a rotary evaporator. The resultant solid mass was then dissolved in diethyl ether and treated with 5% $NaHCO_3$ solution to remove excess *4*-methylphenol. The reaction mixture was then washed with water three times and dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvent, a yellowish crude product was obtained. The crude product was then purified by column chromatography. A yellow crystalline product 1A having a yield of 62 % with m.p. 62^0 C was obtained. The product was found to be homogeneous on TLC plate, R_f = 0.65 (Ethyl acetate: n-Hexane = 1: 9)

The product 1A was characterized by spectral evidences.

Physical and spectral evidences of the compound —1A

The synthesized compound **1A** was a yellow solid having a yield of 62% with m. p.62^{0}C. The compound **1A** was found to be homogeneous on TLC plate, R_f = 0.65 (Ethyl acetate: n-Hexane = 1: 9).The product **1A** was characterized by its IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectral data.



Bis-(*4*-Methylphenyl) chlorophosphate

1A

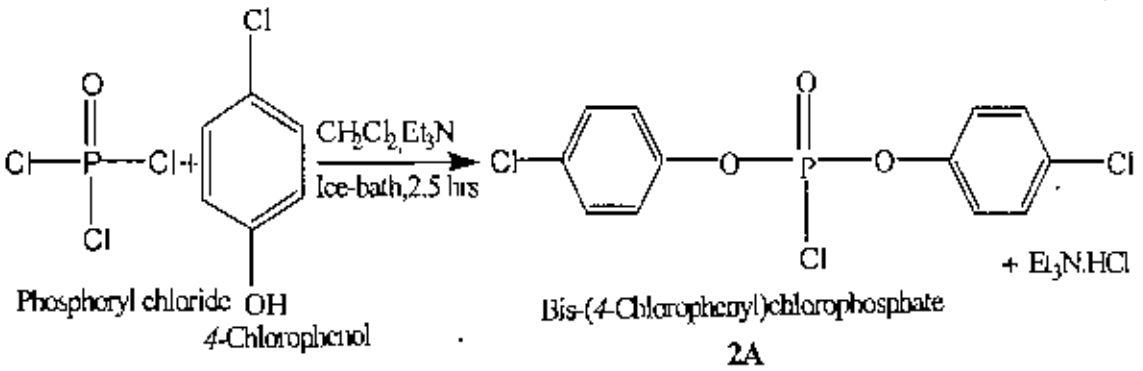
IR (KBr) : υ_{max} cm^{-1} 3050 (C-H, aromatic), 2922 (C-H, CH_3), 1732 (P=O), 1589 (C = C, aromatic), 1485 (C = C, aromatic), 1450 (C = C, aromatic),1269. 1236 (P-O-C_6H_4) , 1139 (P-Cl).

^{1}H NMR (400 MHz, $CDCl_3$) : δH 8.05 (s, C_6H_4-H, 4H), 7.24 (s, C_6H_4-H, 4H), 2.28 (s, *p*-CH_3, 6H)

^{13}C NMR (100 MHz,$CDCl_3$) : δC 23.8 (1C, -CH_3), 29.6 (1C, -CH_3), 116.3 (4C, C-3, C-5, C-3',C-5' aromatic), 129.8 (4C, C-2, C-2',C-6,C- 6', aromatic), 135.1 (2C, C-4, C-4', aromatic), 148.6 (2C, C-1, C-1', aromatic)

^{31}P NMR (162 MHz,$CDCl_3$) : δP 2.5 (P=O, 1P, s).

2.2 Synthesis of Bis-(*4*-Chlorophenyl) chlorophosphate.



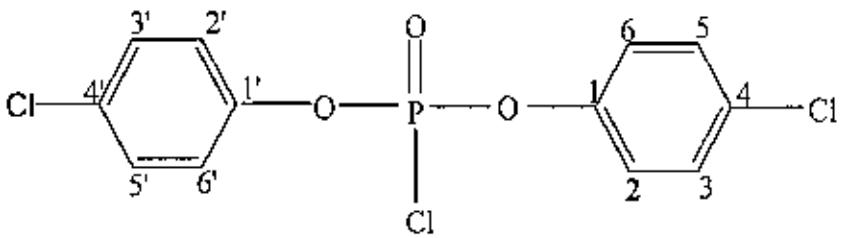
Procedure

A solution of phosphoryl chloride (900 mg, 5.869 mmol) in methylene chloride (5 mL) was taken in a round bottomed flask. The flask was then placed on an ice-bath with constant stirring for half an hour. A mixture of *4*-Chlorophenol (1.509 g, 11.739 mmol), triethylamine (1.187 g, 11.739 mmol) and methylene chloride (7 mL) was taken in another round bottomed flask and the flask was then placed on an ice bath with constant stirring for half an hour.The phenolic triethylamine mixture was then added drop-wise to the phosphoryl chloride solution and was stirred for two and half hours at the same temperature.The progress of the reaction was monitored by TLC. The reaction mixture was then filtered and the solvent was evaporated by a rotary evaporator. The resultant solid mass was then dissolved in diethyl ether and treated with 5% $NaHCO_3$ solution to remove excess *4*-chlorophenol. The reaction mixture was then washed with water three times and dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvent, a yellowish crude product was obtained. The crude product was then purified by column chromatography. A yellow solid product **2A** having a yield of 59% with m.p.103^0 C was obtained. The product was found to be homogeneous on TLC plate, R_f= 0.52 (Ethyl acetate: n-Hexane = 1: 9)

The product **2A** was characterized by spectral evidences.

Physical and spectral evidences of the compound —2A

The synthesized compound **2A** was a yellow solid having a yield of 59% with m. p.103^{0}C. The compound **2A** was found to be homogeneous on TLC plate, R_f = 0.52 (Ethyl acetate: n-Hexane = 1: 9).The product **2A** was characterized by its IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectral data.



Bis-(*4*-Chlorophenyl) chlorophosphate

2A

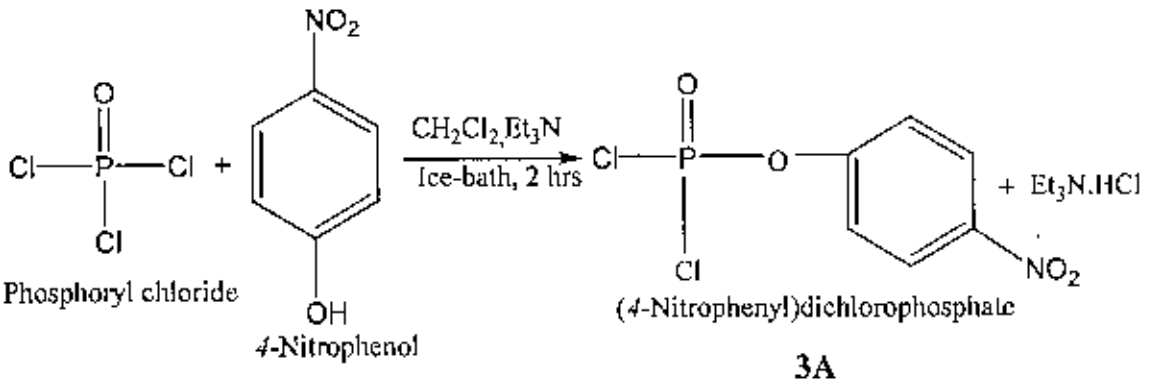
IR (KBr) : υ_{max} cm^{-1} 3095 (C-H, aromatic), 1718 (P=O), 1590 (C = C, aromatic), 1485 (C = C, aromatic), 1410 (C = C, aromatic),1299, 1230 (P-O-C_6H_4) , 1161 (P-Cl), 1091 (C-Cl), 1014 (C-Cl).

^{1}H NMR (400 MHz, $CDCl_3$) : δH 7.13 (d, 4H, J= 8 Hz), 7.29 (d, 4H, J=8 Hz).

^{13}C NMR (100 MHz,$CDCl_3$) : δC 121.3 (C-3, C-5, C-3', C-5'), 128.8 (C-2, C-6, C-2',C-6'), 131.3 (C-4, C-4'), 148.5 (C-1, C-1').

^{31}P NMR (162 MHz,$CDCl_3$) : δP -16.4 (P=O, 1P, s).

2.3 Synthesis of *4*-Nitrophenyldichlorophosphate.



Phosphoryl chloride

4-Nitrophenol

(*4*-Nitrophenyl)dichlorophosphate

3A

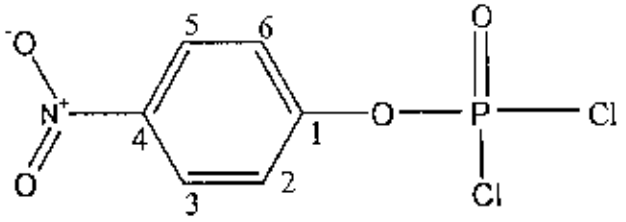
Procedure

A solution of phosphoryl chloride (1.0 g, 0.0065 mol) in methylene chloride (5 mL) was taken in a round bottomed flask. The flask was then placed on an ice-bath with constant stirring for half an hour. A mixture of *4*-Nitrophenol (0.9072 g, 0.0065 mol) triethylamine (0.6599 g, 0.0065 mol) and methylene chloride (8 mL) was taken in another round bottomed flask and the flask was then placed on an ice bath with constant stirring for half an hour.The phenolic triethylamine mixture was then added drop-wise to the phosphoryl chloride solution and was stirred for two hours at the same temperature.The progress of the reaction was monitored by TLC. The reaction mixture was then filtered and the solvent was evaporated by a rotary evaporator. The resultant solid mass was then dissolved in diethyl ether and treated with 5% $NaHCO_3$ solution to remove excess *4*-nitro phenol. The reaction mixture was then washed with water three times and dried over anhydrous Na_2SO_4 . After filtration and evaporation of the solvent, a yellowish crude product was obtained. The crude product was then purified by column chromatography. A yellow solid product **3A** having a yield of 53 % with m.p.132^0 C was obtained. The product was found to be homogeneous on TLC plate, R_f = 0.65 (Ethyl acetate: n-Hexane = 1 : 19)

The product **3A** was characterized by spectral evidences.

Physical and spectral evidences of the compound —3A

The synthesized compound **3A** was a yellow solid having a yield of 53% with m. p.132^{0}C. The compound **3A** was found to be homogeneous on TLC plate, R_f = 0.65 (Ethyl acetate: n-Hexane = 1 : 19).The product **3A** was characterized by its IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectral data.



4-Nitrophenyldichlorophosphate

3A

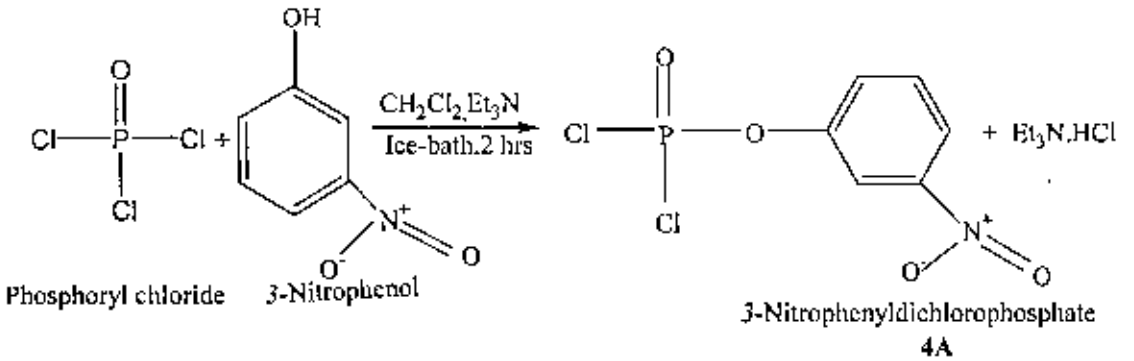
IR (KBr) : υ_{max} cm^{-1} 3087 (C-H, aromatic), 1727 (P=O), 1560 (C = C, aromatic), 1485 (C = C, aromatic),1450 (C = C, aromatic), 1282, 1265 (P-O-C_6H_4) , 1215 (N-O), 1197 (N-O), 1161 (P-Cl),1085 (P-Cl).

^{1}H NMR (400 MHz, $CDCl_3$) : δH 8.32 (d, 2H, J= 7.52 Hz), 7.42 (d, 2H, J=7.48 Hz),

^{13}C NMR (100 MHz,$CDCl_3$) : δC 115 (C-4), 116 (C-3, C-5), 150 (C-2, C-6), 163 (C-1).

^{31}P NMR (162 MHz,$CDCl_3$) : δP 8.6 (P=O, 1P, s).

2.4 Synthesis of *3*-Nitrophenyldichlorophosphate



Phosphoryl chloride *3*-Nitrophenol

3-Nitrophenyldichlorophosphate
4A

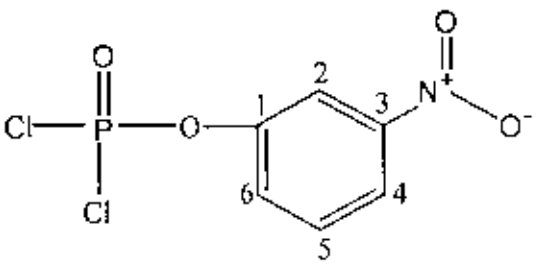
Procedure

A solution of phosphoryl chloride (1.0 g, 0.0065 mol) in methylene chloride (5 mL) was taken in a round bottomed flask. The flask was then placed on an ice-bath with constant stirring for half an hour. A mixture of *3*-Nitrophenol (0.9072 g, 0.0065 mol) triethylamine (0.6599 g, 0.0065 mol) and methylene chloride (8 mL) was taken in another round bottomed flask and the flask was then placed on an ice bath with constant stirring for half an hour.The phenolic triethylamine mixture was then added drop-wise to the phosphoryl chloride solution and was stirred for two hours at the same temperature. The progress of the reaction was monitored by TLC. The reaction mixture was then filtered and the solvent was evaporated by a rotary evaporator. The resultant solid mass was then dissolved in diethyl ether and treated with 5% $NaHCO_3$ solution to remove excess *3*-nitrophenol. The reaction mixture was then washed with water three times and dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvent, a yellowish crude product was obtained. The crude product was then purified by column chromatography. A white solid product **4A** having a yield of 58% with m.p. 90^0 C was obtained. The product was found to be homogeneous on TLC plate, R_f = 0.71 (Ethyl acetate: n-Hexane = 1 : 19)

The product **4A** was characterized by spectral evidences.

Physical and spectral evidences of the compound —4A

The synthesized compound **4A** was a white solid having a yield of 58% with m. p. 90^0C. The compound **4A** was found to be homogeneous on TLC plate, R_f= 0.71(Ethyl acetate: n-Hexane = 1 : 19).The product **4A** was characterized by its IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectral data.



(3-Nitrophenyl)dichlorophosphate

4A

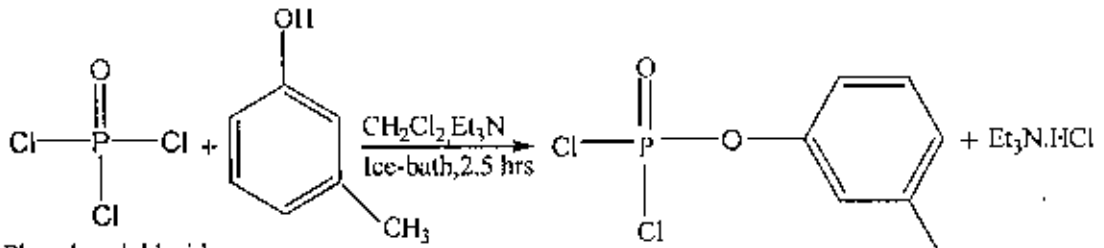
IR (KBr) : υ_{max} cm^{-1} 3103 (C-H, aromatic), 1735(P=O), 1533 (C = C, aromatic), 1487 (C = C, aromatic),1477 (C = C, aromatic), 1263, 1209 (P-O-C_6H_4) , 1178 (P-Cl). 1011 (P-Cl).

^{1}H NMR (400 MHz, $CDCl_3$) : δH 8.2 (d, 1H, C-6, J= 7.52 Hz), 7.6 (bs, 1H, C-2), 7.5 (bs, 2H, C-5, C-4).

^{13}C NMR (100 MHz,$CDCl_3$) : δC 110 (C-5), 116 (C-4), 122 (C-2), 130 (C-6), 149 (C-3), 159 (C-1).

^{31}P NMR (162 MHz,$CDCl_3$) : δP 6.8 (P=O, 1P, s).

2.5 Synthesis of *3*-Methylphenyldichlorophosphate



Phosphorylchloride *3*-Methylphenol *(3*-Methylphenyl)dichlorophosphate

5A

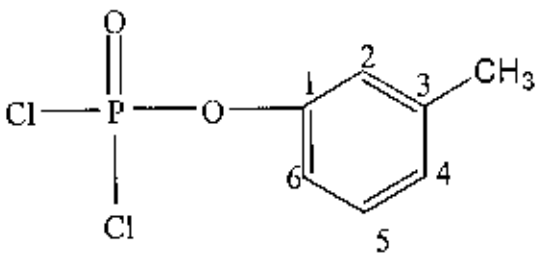
Procedure

A solution of phosphoryl chloride (2.0 g, 0.0130 mol) in methylene chloride (8 mL) was taken in a round bottomed flask. The flask was then placed on an ice-bath with constant stirring for half an hour. A mixture of *3*-Methylphenol (1.4101 g, 0.0130 mol) triethylamine (1.3195g, 0.0130 mol) and methylene chloride (8 mL) was taken in another round bottomed flask and the flask was then placed on an ice bath with constant stirring for half an hour.The phenolic triethylamine mixture was then added drop-wise to the phosphoryl chloride solution and was stirred for two and half hours at the same temperature.The progress of the reaction was monitored by TLC. The reaction mixture was then filtered and the solvent was evaporated by a rotary evaporator. The resultant solid mass was then dissolved in diethyl ether and treated with 5% $NaHCO_3$ solution to remove excess *3*-methylphenol. The reaction mixture was then washed with water three times and dried over anhydrous Na_2SO_4 . After filtration and evaporation of the solvent, a yellow solid crude product was obtained. The crude product was then purified by column chromatography. A yellow solid product **5A** having a yield of 68% with m.p. 41^0 C was obtained. The product was found to be homogeneous on TLC plate, R_f = 0.52 (Ethyl acetate: n-Hexane = 1 : 19)

The product **5A** was characterized by spectral evidences.

Physical and spectral evidences of the compound —5A

The synthesized compound **5A** was a yellow solid having a yield of 68% with m. p.41^{0}C. The compound **5A** was found to be homogeneous on TLC plate, R_f = 0.52 (Ethyl acetate: n-Hexane = 1: 19).The product **5A** was characterized by its IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectrum data.



(3-Methylphenyl)dichlorophosphate

5A

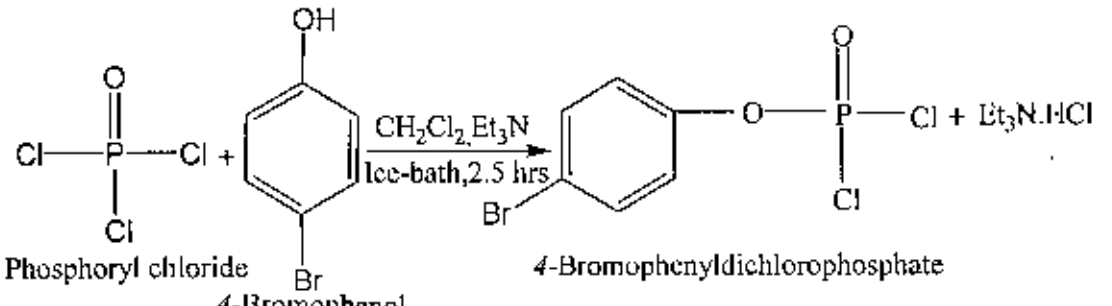
IR (KBr) : υ_{max} cm^{-1} 3103 (C-H, aromatic), 2928 (C-H, CH_3), 1732 (P=O), 1595 (C=C, aromatic), 1495 (C=C, aromatic), 1450 (C=C, aromatic), 1269,1236 (P-O-C_6H_4) , 1139 (P-Cl),1080(P-Cl),

^{1}H NMR (400 MHz, $CDCl_3$) : δH 8.18 (d, 1H, C-6, J = 8.0 Hz), 7.59 (d, 1H, C-2, J = 8.0 Hz), 7.47 (t,1H, C-5, J = 8.0 Hz), 7.26 (d, 1H, C-4, J=8.0 Hz), 2.28 (s, 3H, -CH_3)

^{13}C NMR (100 MHz,$CDCl_3$) : δC 28 (*m*-CH_3), 122 (2C, C-3, C-6), 133 (2C, C-4, C-5), 135 (C-2), 149 (C-1).

^{31}P NMR (162 MHz,$CDCl_3$) : δP 12.47 (P=O, 1P, s).

2.6 Synthesis of *4*-Bromophenyldichlorophosphate.



Phosphoryl chloride

4-Bromophenol

4-Bromophenyldichlorophosphate

6A

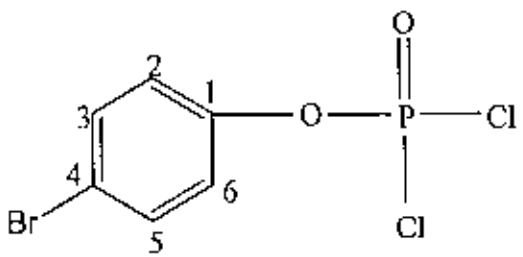
Procedure

A solution of phosphoryl chloride (4.0 g, 0.0260 mol) in methylene chloride (8 mL) was taken in a round bottomed flask. The flask was then placed on an ice-bath with constant stirring for half an hour. A mixture of *4*-Bromophenol (4.513 g, 0.0260 mol) triethylamine (2.6397g, 0.0260 mol) and methylene chloride (10 mL) was taken in another round bottomed flask and the flask was then placed on an ice bath with constant stirring for half an hour.The phenolic triethylamine mixture was then added drop-wise to the phosphoryl chloride solution and was stirred for two and half hours at the same temperature.The progress of the reaction was monitored by TLC. The reaction mixture was then filtered and the solvent was evaporated by a rotary evaporator. The resultant solid mass was then dissolved in diethyl ether and treated with 5% $NaHCO_3$ solution to remove excess *4*-bromophenol. The reaction mixture was then washed with water three times and dried over anhydrous Na_2SO_4 . After filtration and evaporation of the solvent, a white solid crude product was obtained. The crude product was then purified by column chromatography. A white solid product **6A** having a yield of 61% with m.p. 104^0 C was obtained. The product was found to be homogeneous on TLC plate, R_f = 0.54 (Ethyl acetate: n-Hexane = 1 : 19)

The product **6A** was characterized by spectral evidences.

Physical and spectral evidences of the compound --6A

The synthesized compound **6A** was a white solid having a yield of 61% with m. p.104^{0}C. The compound **6A** was found to be homogeneous on TLC plate, R_f = 0.54 (Ethyl acetate: n-Hexane = 1: 19).The product **6A** was characterized by its IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectral data.



4-Bromophenyldichlorophosphate

6A

IR (KBr) : υ_{max} cm^{-1} 3087 (C-H, aromatic), 1732(P=O), 1560 (C=C, aromatic), 1485 (C=C, aromatic), 1450 (C=C, aromatic), 1285 (P-O-C_6H_4) , 1255 (C- O), 1215 (P- Cl),1197(P- Cl), 1161 (C-Br).

^{1}H NMR (400 MHz, $CDCl_3$) : δH 8.17 (d, 2H, J = 7.83 Hz, C-2, C-6), 7.62 (d, 2H,J = 7.41 Hz. C-3, C-5).

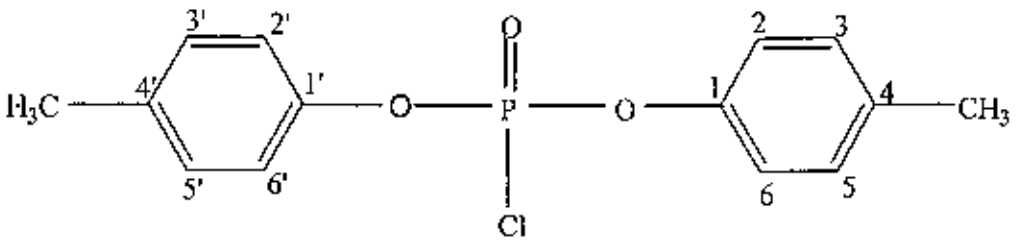
^{13}C NMR (100 MHz,$CDCl_3$) : δC 114 (C-3, C-5), 115 (C-4), 119 (C-2, C-6), 156 (C-1)

^{31}P NMR (162 MHz,$CDCl_3$) : δP -14.29 (P = O, 1P, s)

Chapter 3

RESULTS AND DISCUSSION

3.1 Characterization of Bis- (4-Methylphenyl)chlorophosphate



Bis-(*4*-Methylphenyl) chlorophosphate

1A

The structure of the yellow crystalline compound **1A** was established from the spectral evidences such as IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectral data.

The IR spectrum (**Fig.1a**) showed absorption band at 3050 cm^{-1} was due to the aromatic C-H stretching. The band at 2922 cm^{-1} was assigned for the stretching vibration of C-H bond of methyl group. The sharp and intensified peak at 1732 cm^{-1} was indicated for P = O group. It showed absorption at comparatively higher frequency due to the attachment of three electron withdrawing groups.The bands at 1589, 1485, 1450 cm^{-1} were assigned for aromatic carbon-carbon double bond vibration. The characteristic bands at 1269 cm^{-1} and 1236 cm^{-1} were indicated for two P-O groups. The sharp peak at 1139 cm^{-1} was due to the P-Cl bond.

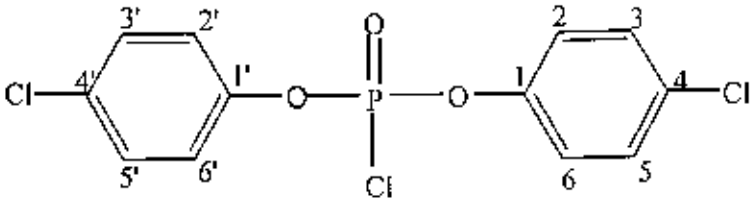
The $^{1}_{H}$ NMR spectrum (**Fig.1b**) of the compound showed the singlet at $^{\delta}H$ 8.05 was due to the similar four aromatic protons at C-3, C-5 and C-3′, C-5′ of both the aromatic ring. The chemical shift value at $^{\delta}H$ 7.24 was due to the similar four aromatic protons at C-2, C-6 and C-2′, C-6′ of the two aromatic rings.The sharp and intensified peak at $^{\delta}H$ 2.28 was indicated as six aliphatic protons of methyl group at para positions of the two rings.

The ^{13}C NMR spectrum (**Fig. 1c**) of the compound showed the peaks at $^{\delta}C$ 23.8 and 29.6 were designated for methyl carbon at para positions of the rings. The peaks at $^{\delta}C$ 116.3, 129.8, 135.1 and 148.6 were for the carbons (C-3, C-5, C-3′, C-5′), (C-2, C-2′, C-6 C-6′), (C-4, C-4′) and (C-1, C-1′) respectively.

The ^{31}P NMR spectrum (**Fig.1d**) showed the peak at $^{\delta}P$ 2.5 was assigned for the single phosphorus of the compound.

The spectral evidences support harmony in favour of the given structure of the compound **1A.**

3.2 Characterization of Bis-(4-Chlorophenyl) chlorophosphate



Bis-(4-Chlorophenyl)chlorophosphate

2A

The structure of the above compound **2A** was established from the evidences of IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectral data.

The IR spectrum (**Fig.2a**) of the compound showed the weak absorption band at 3095 cm^{-1} was due to the aromatic C-H stretching. The sharp peak at 1718 cm^{-1} was assigned for P = O group. The P = O group showed absorption at higher frequency due to the attachment of electron withdrawing groups. The peaks at 1590, 1485 and 1410 cm^{-1} were identified as aromatic carbon-carbon double bonds vibration. The sharp band at 1299 and 1230 cm^{-1} were assigned for P-O groups attached with electron withdrawing groups. The characteristic absorption band at 1161 cm^{-1} was designated for P- Cl bond vibration. The peaks at 1091 and 1014 cm^{-1} were indicated for C- Cl bonds with aromatic ring carbon.

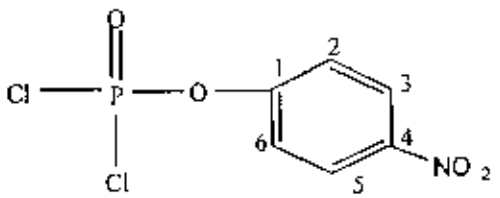
The ^{1}H NMR spectrum (**Fig. 2b**) of the compound showed doublets at δH 7.13 containing four protons with coupling constant J = 8 Hz were due to the similar aromatic protons at C-2, C-6 and C-2′,C-6′ of both the aromatic ring. The chemical shift value at δH 7.29 were assigned for four protons at C-3, C-5 and C-3′, C-5′ of both the aromatic ring having doublet with coupling constant 8 Hz.

The ^{13}C NMR spectrum (**Fig. 2c**) of the compound showed the peaks at δC 121.3 were designated aromatic similar carbon for C-3, C-5 and C-3′, C-5′.The peak at δC 128.8 was identified for C-2, C-6 and C-2′, C-6′. The peak at 131.3 was assigned for C-4 and C-4′. The peak at 148.5 was designated for C-1 and C-1′.

The ^{31}P NMR spectrum (**Fig.2d**) showed only single peak at δP -16.4 for phosphorus of P = O group of the compound.

The above spectral evidences completely satisfies the above given structure for the compound **2A**.

3.3 Characterization of 4-Nitrophenyldichlorophosphate



(4-Nitrophenyl)dichlorophosphate

3A

The structure of the compound **3A** was established from the study of IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectral data.

The IR spectrum **(Fig. 3a)** of the pale yellow solid compound **3A** showed the absorption band at 3087 cm^{-1} was due to the aromatic C-H stretching. The sharp band at 1727 cm^{-1} was assigned for P=O group. The characteristic absorption band at 1560, 1485 and 1450 cm^{-1} were designated for aromatic C = C stretching .The bands at 1282 and 1265 cm^{-1} were due to P-O bond attached with aromatic ring. The stretching frequency at 1215 and 1197 cm^{-1} were due to the N-O bond of nitro group. The bands at 1161 and 1085 cm^{-1} were ascribed for P-Cl bond of phosphoryl group.

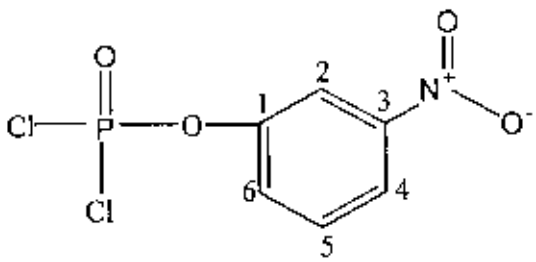
The ^{1}H NMR spectrum **(Fig. 3b)** of the compound showed the doublets for 2H with coupling constant J = 7.52 Hz at δH 8.32 was assigned for C-2 and C-6 protons. The another doublet at δH 7.42 was designated for two similar aromatic protons at C-3 and C-5 positions in the aromatic ring.

The ^{13}C NMR spectrum **(Fig. 3c)** of the compound showed the peaks at δC 115 was indicated for C-4 position of the ring. The intensified peak at δC 116 was assigned for similar carbon at C-3 and C-5 position .The other two similar carbons C-2 and C-6 showed the peaks at δC 150. The peak at δC 163 was ascribed for deshielded carbon C-1.

The ^{31}P NMR spectrum **(Fig. 3d)** showed the peak at δP 8.6 was assigned for the single phosphorus of phosphoryl group.

The above spectral evidences completely satisfied the above given structure for the compound **3A.**

3.4 Characterization of *3*-Nitrophenyldichlorophosphate



(3-Nitrophenyl)dichlorophosphate

4A

The compound **4A** was a white crystalline solid and was characterized by its IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectral data.

The IR spectrum **(Fig. 4a)** of the compound **4A** showed the absorption band at 3103 cm^{-1} was due to the aromatic C-H stretching. The absorption band at 1735 cm^{-1} was assigned for P = O of the phosphoryl group. The band at 1533, 1487, and 1477 were ascribed for aromatic carbon-carbon double bond stretching. The absorption band at 1263 and 1209 cm^{-1} were designated for P-O of phosphoryl group.The bands at 1178 and 1101 cm^{-1} were designated for P-Cl bonds.

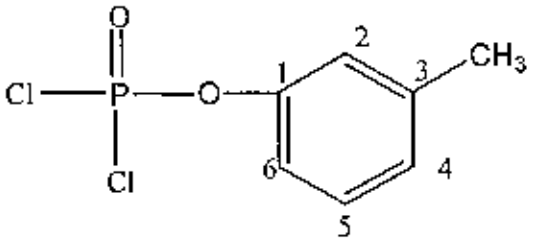
The ^{1}H NMR spectrum **(Fig. 4b)** of the compound showed the peaks at δH 8.2 (d, 1H, J = 7.68 Hz) was indicated the C-4 aromatic proton whereas the peak at δH 7.6 (bs,1H) was assigned for the C-2 aromatic proton in the ring. The chemical shift value δH 7.5 (bs, 2H) was designated for two aromatic protons at C-5 and C-4 position.

The ^{13}C NMR spectrum **(Fig. 4c)** of the compound showed the peaks at δC 110 for C-5 122 for C-2, 130 for C-6, 149 for C-3 and 159 for C-1 for the aromatic ring carbons.

The ^{31}P NMR spectrum **(Fig. 4d)** showed the peak at δP 6.8 was designated for the single phosphorus of **4A** compound.

The above spectral evidences completely supported the co-relation in favour of the given structure of the compound **4A**.

3.5 Characterization of *3*-Methylphenyldichlorophosphate



(*3*-Methylphenyl)dichlorophosphate

5A

The structure of the compound **5A** was established from the IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectral evidences.

The IR spectrum **(Fig. 5a)** of the compound **5A** showed the absorption band at 3103 cm^{-1} was due to the aromatic C-H stretching. The band at 2928 cm^{-1} was assigned for the stretching vibration of C-H bond of methyl group. The sharp absorption band at 1732 cm^{-1} was indicative for P = O of phosphoryl group. The characteristic absorption band at 1595, 1495 and 1450 cm^{-1} were assigned for aromatic C = C bond vibration. The absorption band at 1269 and 1236 cm^{-1} were ascribed for P-O bond of phosphoryl group attached to the aromatic ring. The bands at 1139 and 1080 cm^{-1} were indicative for C - Cl bonds attached to the P = O group.

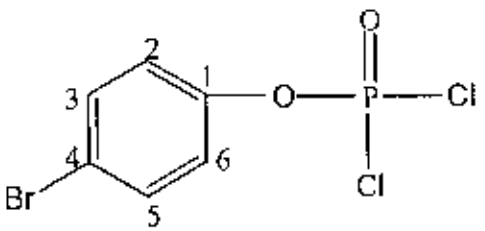
The ^{1}H NMR spectrum **(Fig. 5b)** of the compound showed the peaks at δ_H 8.18 (d, 1H, J = 8.0 Hz) was found for aromatic proton at C-6.The chemical shift value at δ_H 7.59 (d, 1H,J = 8.0 Hz) was represented to aromatic one proton at C-2. The triplet at δ_H 7.47 was indicative for one proton at C-5 position.The other peak at δ_H 7.26 (d, 1H, J = 8.0 Hz) was assigned for one proton of C-4. The chemical shift value at δ_H 2.28 was designated for three protons of methyl group attached to aromatic ring.

The ^{13}C NMR spectrum **(Fig. 5c)** of the compound showed the peaks at δ_C 122 for two carbons at C-3 and C-4, δ_C 133 for two carbons at C-4 and C-5, 135 for one carbon at C-2, 149 for C-1 position and δ_C 28 for one carbon of methyl group.

The ^{31}P NMR spectrum **(Fig.5d)** showed the peak at δ_P 12.47 was assigned for the single phosphorus of the compound.

The above spectral evidences expresses the harmony in favour of the given structure of the compound **5A.**

3.6 Characterization of *4*-Bromophenyldichlorophosphate



4-Bromophenyldichlorophosphate

6A

The structure of the above compound **6A** was established from the study of IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectral data.

The IR spectrum **(Fig. 6a)** of the compound showed the absorption band at 3087 cm^{-1} was due to the aromatic C-H stretching. The band at 1732 cm^{-1} was ascribed for P = O group of phosphoryl moiety. The characteristic absorption band at 1560, 1485 and 1450 cm^{-1} were designated for aromatic C = C bond vibration. The band at 1285 and 1255 cm^{-1} were assigned for P-O group attached to the aromatic ring. The weak band at 1215 and 1197 cm^{-1} were ascribed for P-Cl bonds and the band at 1161 cm^{-1} was due to the C-Br stretching vibration.

The ^{1}H NMR spectrum **(Fig. 6b)** of the compound showed the doublets at δH 8.17 (d, 1H, J= 7.83 Hz) was assigned for two protons at C-2 and C-6 position. The chemical shift value at δH 7.62 (d, 2H, J = 7.41 Hz) was designated for two aromatic protons at C-3 and C-5 position of the aromatic ring.

The ^{13}C NMR spectrum **(Fig. 6c)** of the compound showed the peaks at δC 114 for C-2 and C-3 carbons, 115 for C-4 carbon, 119 for C-2 and C-6 carbons and 156 for C-1 aromatic carbon.

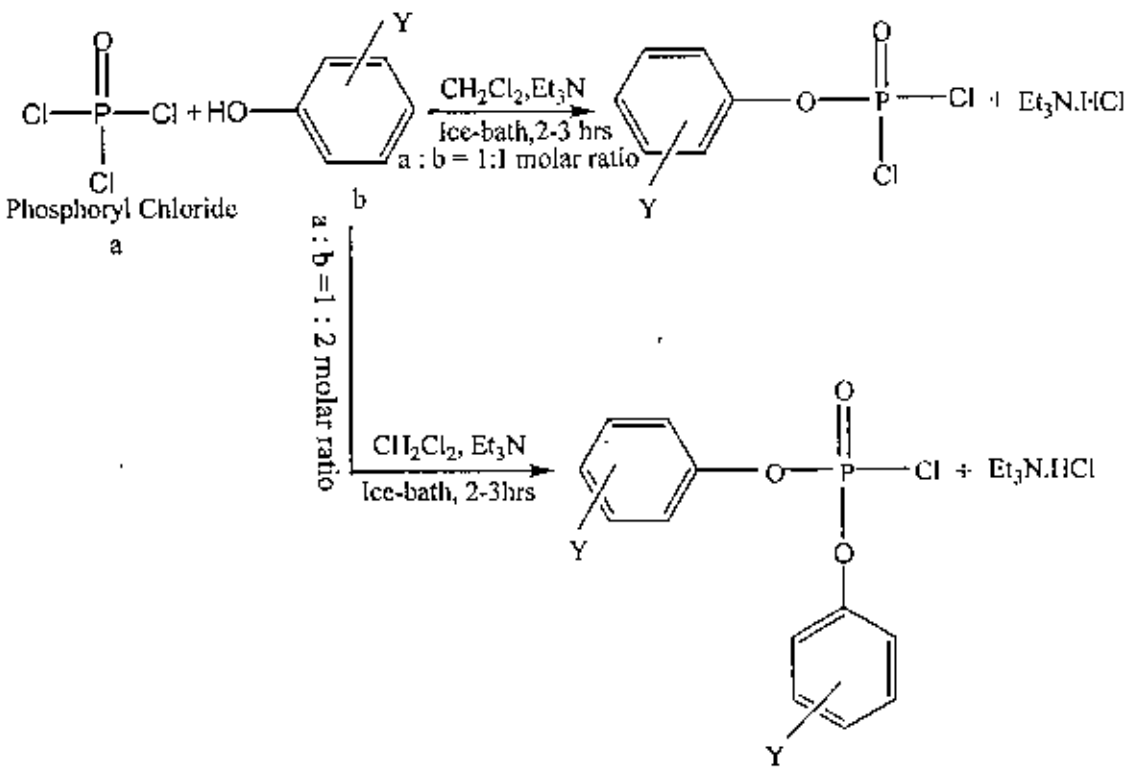
The ^{31}P NMR spectrum **(Fig.6d)** showed the peak at δP -14.7 was assigned for the single phosphorus of phosphoryl group.

The above spectral evidences completely supported the co-relation in favour of the given structure of the compound **6A.**

3.7 MECHANISM OF THE SYNTHESIS

Synthesis of Phenyl substituted Chlorophosphates

Synthetic scheme :



Here, Y= *p*-CH_3, *m*-CH_3, *p*-Cl, *p*-Br, *m*-NO_2 and *p*-NO_2

Probable mechanism :

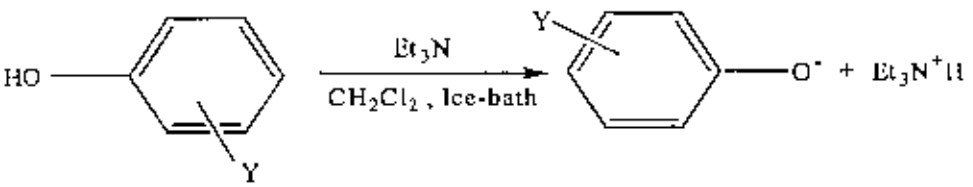
The above nucleophilic substitution reaction at phosphorus centre may proceed through two mechanistic pathways:

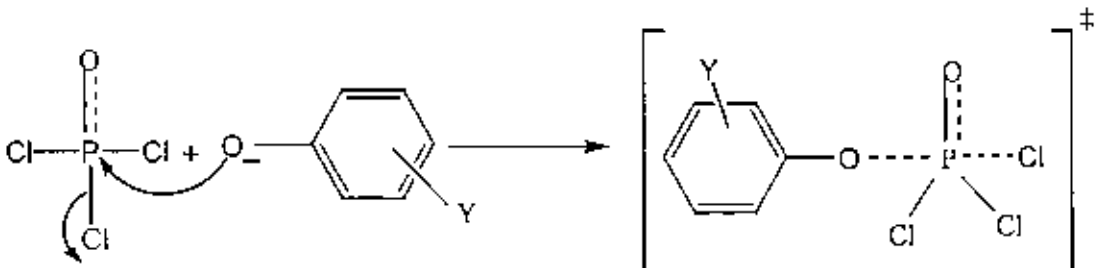
a) Concerted mechanism

b) Stepwise mechanism

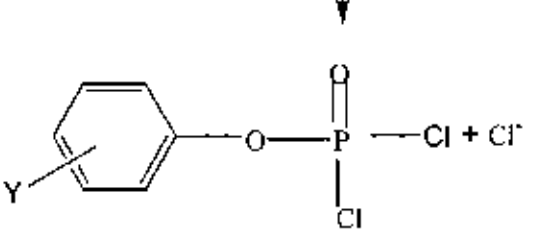
a) Concerted mechanism :

The reaction of Phosphoryl chloride and substituted phenoxide nucleophiles proceed through concerted mechanism for nucleophilic attack at the phosphorus center of P = O substrate.The reaction have been considered to proceed through a single transition state in which bond formation and bond breaking occur simultaneously in the transition state. Substituted phenoxide anion act as nucleophile and Cl^- ion act as a leaving group in the reaction system.





Phosphoryl Chloride

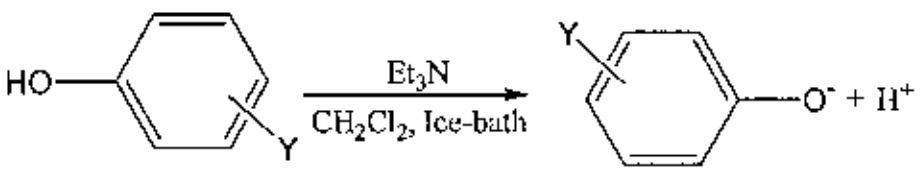


$$Et_3N + H^+ + Cl^- \longrightarrow Et_3N.HCl$$

b) Step-wise mechanism :

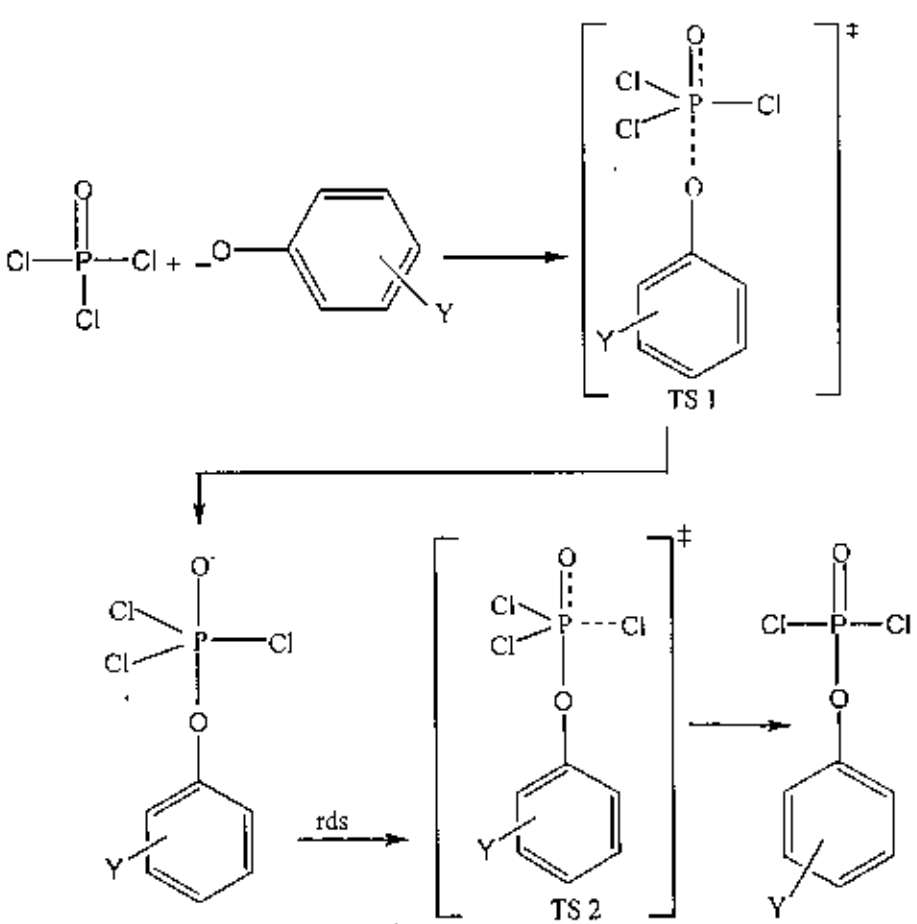
Step -1 :

In this step nucleophile is produced from substituted phenol.



Step- 2 :

In this step produced nucleophile readily attacks the positive center of phosphorus of the phosphoryl chloride forming a transition state-1. As this state had very short life period it readily rearranged and formed a trigonal bipyramidal pentacoordinate (TBP-5C) intermediate. This intermediate stage instantly converted to transition state-2 and then it decomposed rapidly to produce the phenyl substituted chlorophosphate.



Trigonal bipyramidal pentacoordinate (TBP-5C) intermediate

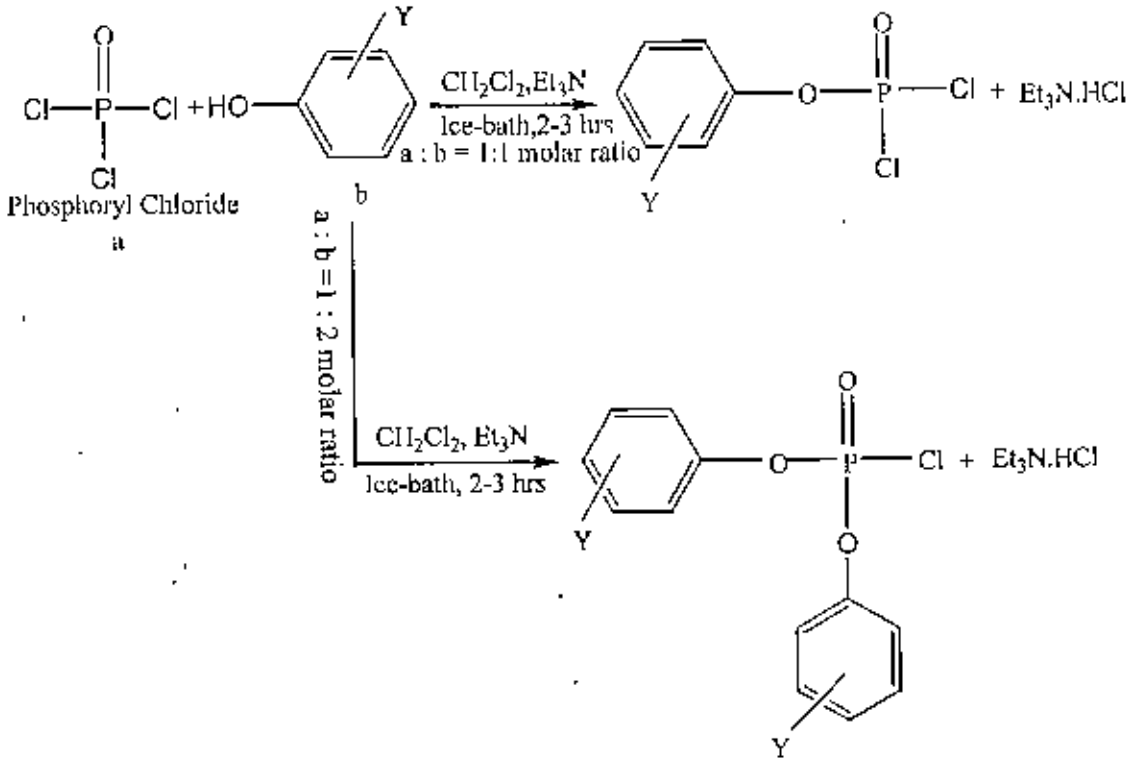
$$Et_3N + H^+ + Cl^- \longrightarrow Et_3N.HCl$$

Chapter 4

SUMMARY

SUMMARY

Organophosphorus compounds have tremendous importance in the field of food technology, animal foodstuffs, pesticides, medicinal compounds, synthetic polymers, fire retardants and natural products. Nucleophilic substitutions at the carbon centre is very important topic in organic chemistry.Considerable amount of work have been carried out on nucleophilic substitutions at the carbon centre but much less is known about nucleophilic substitutions at the phosphorus centre. Nucleophilic substitutions at the phosphorus centre is very important topic in organophosphorus chemistry. The nucleophilic substitutions at the carbon centre is well established but the mechanism of nucleophilic substitution reactions at phosphorus is not well established. It has great interest to study nucleophilic substitutions reactions at phosphorus in solutions. In view of the extensive use of the chlorophosphates we synthesize phenyl substituted chlorophosphates from substituted phenols through the following synthetic scheme.



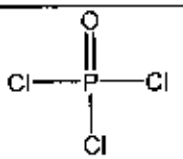
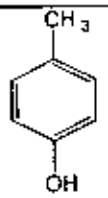
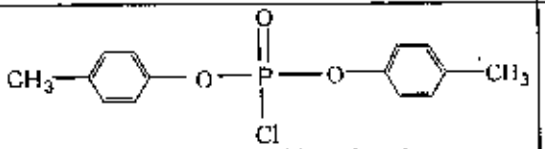
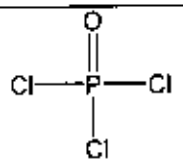
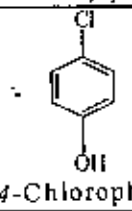
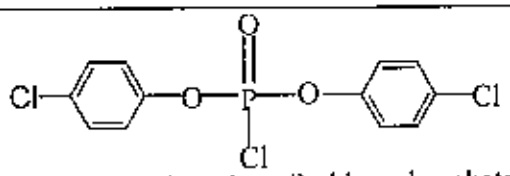
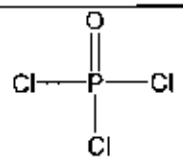
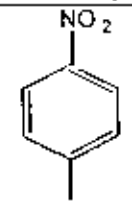
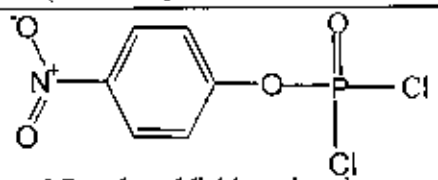
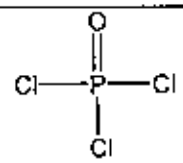
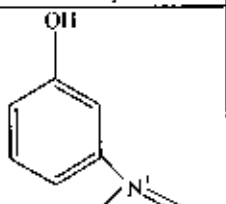
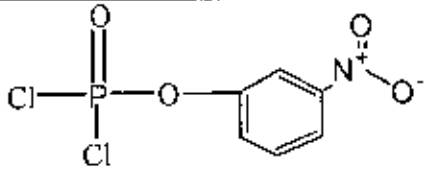
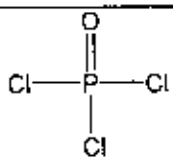
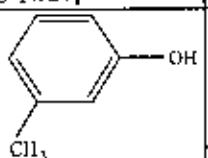
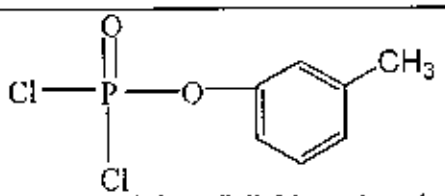
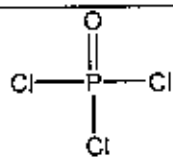
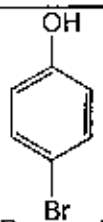
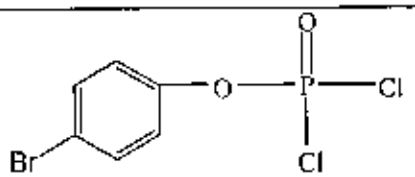
Here, Y= *p*-CH_3, *m*-CH_3, *p*-Cl, *p*-Br, *m*-NO_2 and *p*-NO_2

All the synthesized compounds were characterized by using analytical data obtained from m. p., IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR.

The mechanism of the synthesis of organophosphorus compounds in this project follows nucleophilic substitution reaction at phosphorus centre of phosphoryl chloride

with substituted phenol in presence of triethylamine and methylene chloride. The synthetic scheme are given in this chapter. The following table shows the synthesized compound in brief.

Table 1 : Synthesis of Organophosphorus Compounds.

Sl No.	Starting materials		Product	% Yield
1.	 Phosphorylchloride	 *4*-Methylphenol	 Bis-(*4*-Methylphenyl)chlorophosphate	62
2.	 Phosphorylchloride	 *4*-Chlorophenol	 Bis-(*4*-Chlorophenyl) chlorophosphate	59
3.	 Phosphorylchloride	 *4*-Nitrophenol	 *4*-Nitrophenyldichlorophosphate	53
4.	 Phosphorylchloride	 3-Nitrophenol	 (*3*-Nitrophenyl)dichlorophosphate	58
5.	 Phosphorylchloride	 *3*-Methylphenol	 (*3*-Methylphenyl)dichlorophosphate	68
6.	 Phosphorylchloride	 *4*-Bromophenol	 *4*-Bromophenyldichlorophosphate	61

All the synthesized organophosphorus compounds were characterized by using analytical data obtained from m.p., IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR.

Compound Spectra

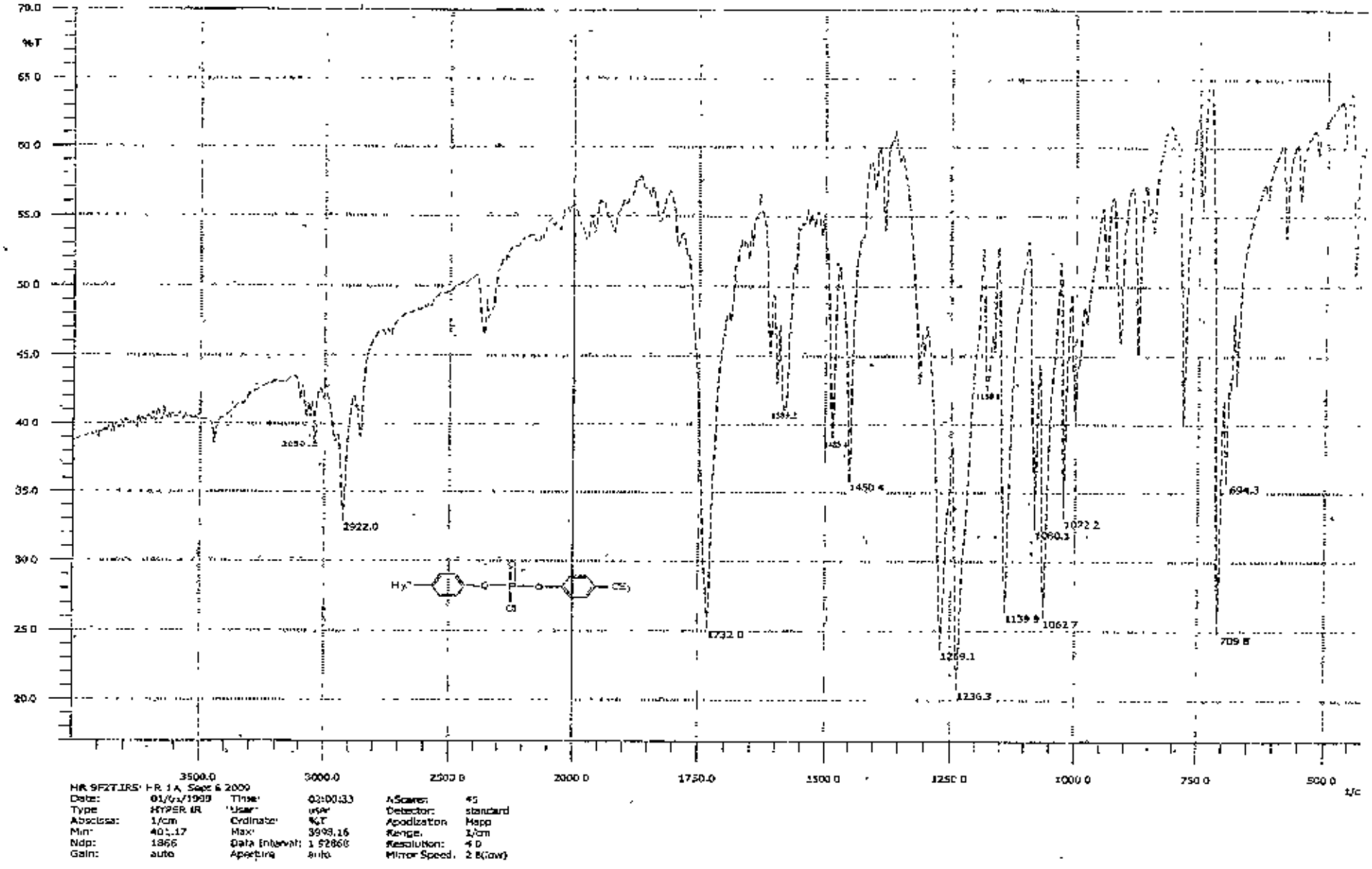
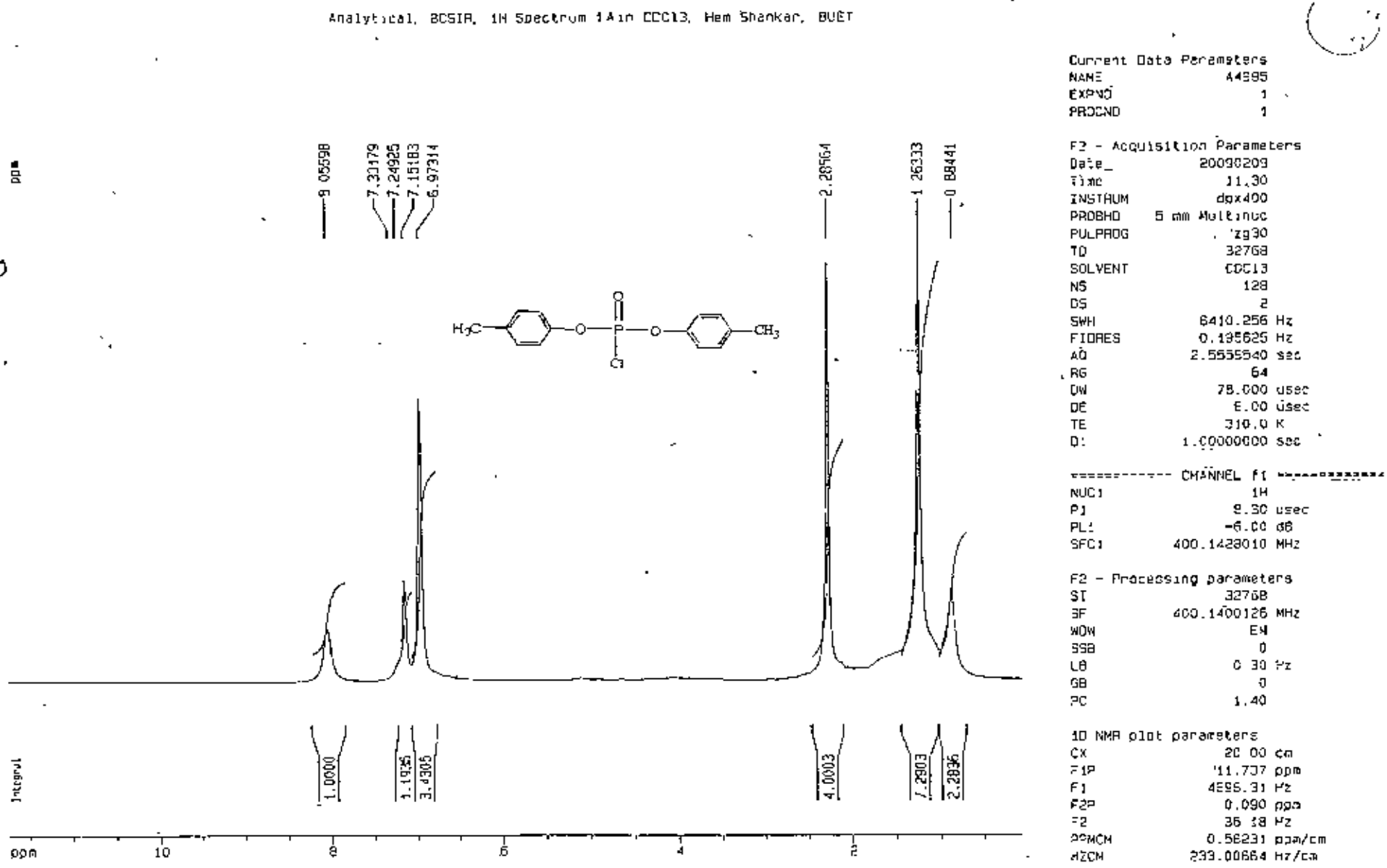


Fig. 1a IR Spectrum of Compound 1A



Current Data Parameters

NAME	44895
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

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PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	128
DS	2
SWH	6410.256 Hz
FIDRES	0.195625 Hz
AQ	2.5555540 sec
RG	64
DW	78.000 usec
DE	6.00 usec
TE	310.0 K
D1	1.00000000 sec

CHANNEL f1

NUC1	1H
P1	9.30 usec
PL1	-6.00 dB
SFO1	400.1428010 MHz

F2 - Processing parameters

SI	32768
SF	400.1400126 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
F1P	11.737 ppm
F1	4695.31 Hz
F2P	0.090 ppm
F2	36.18 Hz
PPMCM	0.58231 ppm/cm
HZCM	233.00664 Hz/cm

Fig. 1b ^{1}H NMR Spectrum of Compound 1A

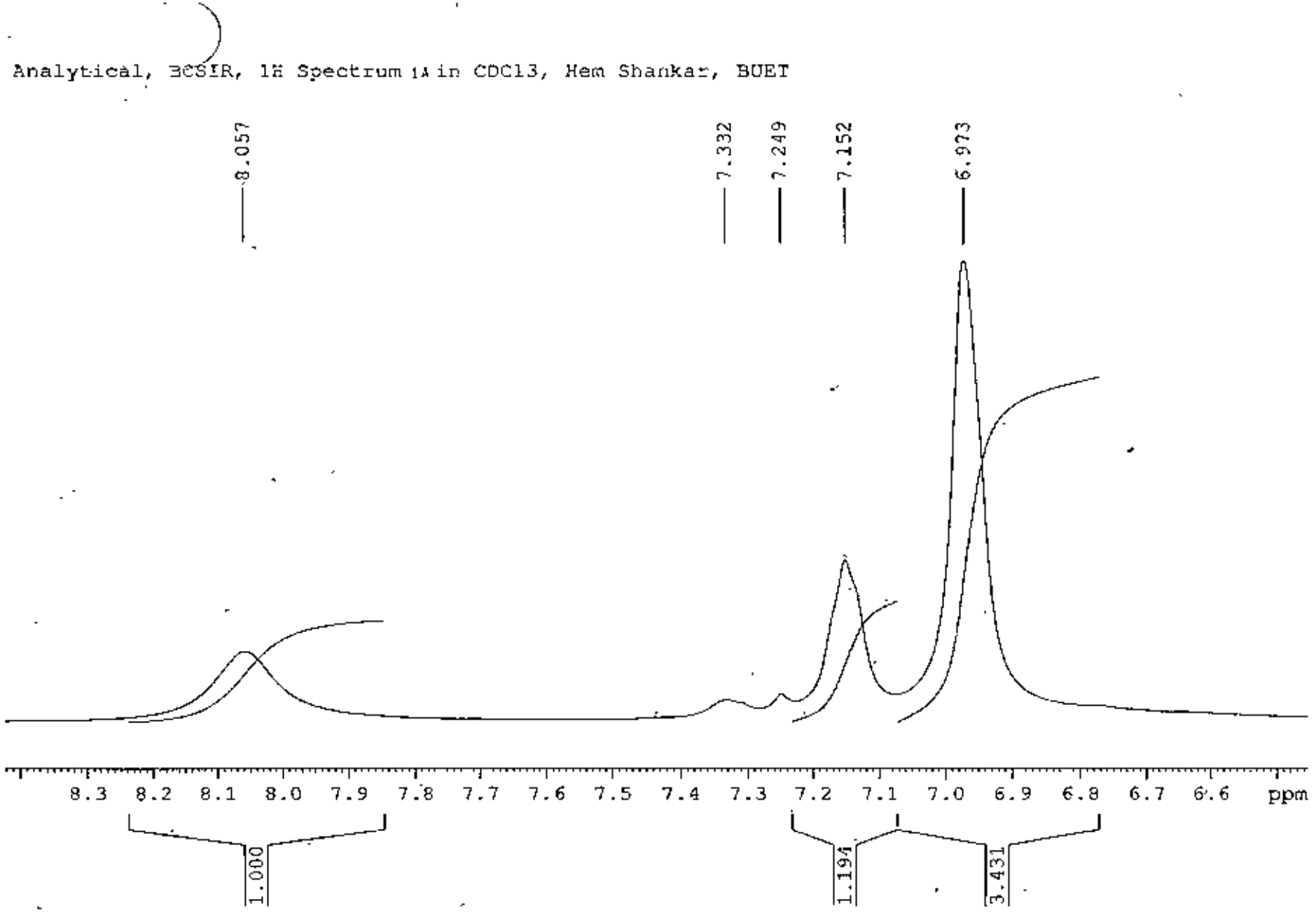


Fig. 1b ^{1}H NMR Spectrum of Compound 1A

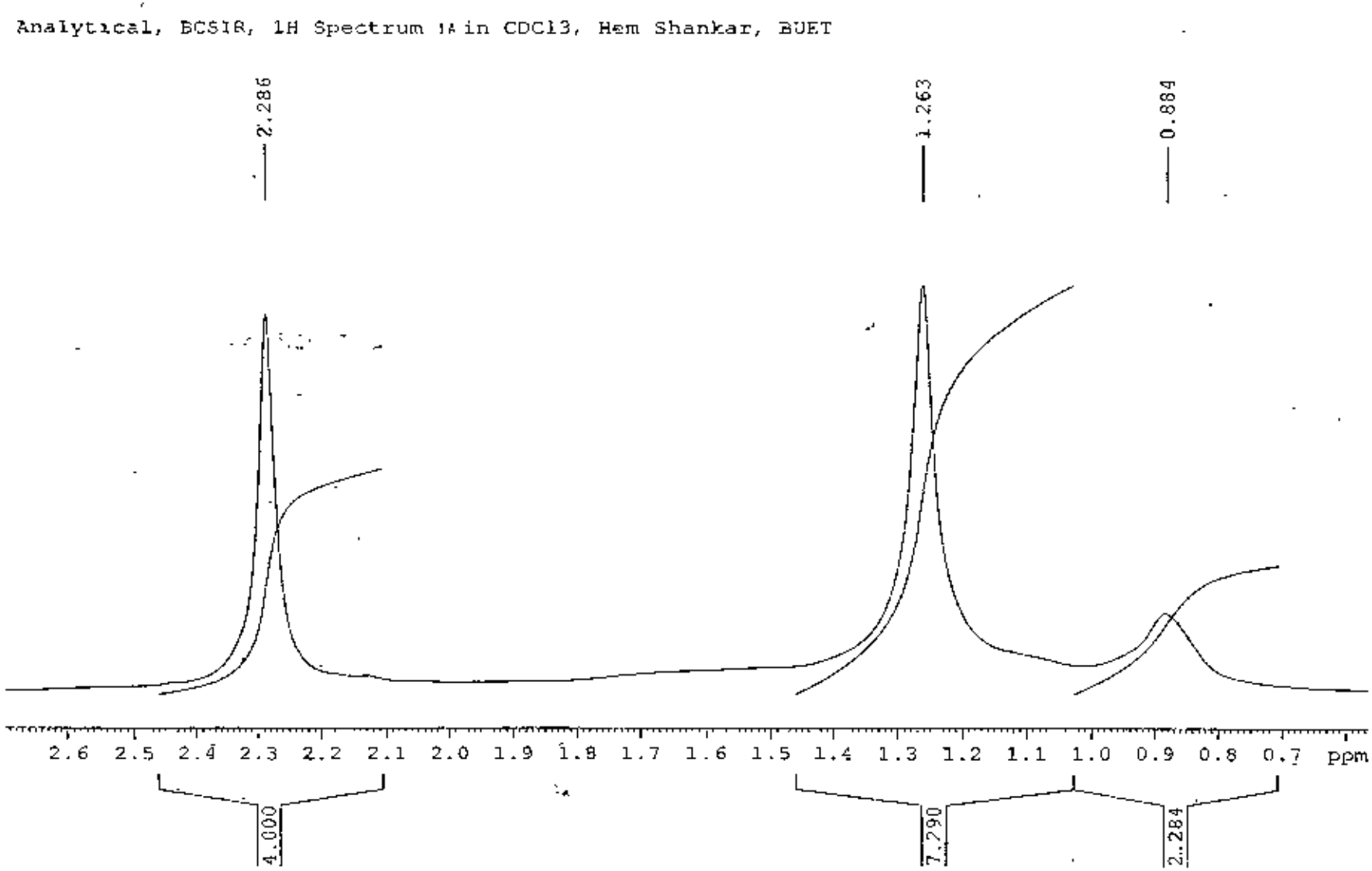


Fig. 1b ^{1}H NMR Spectrum of Compound 1A

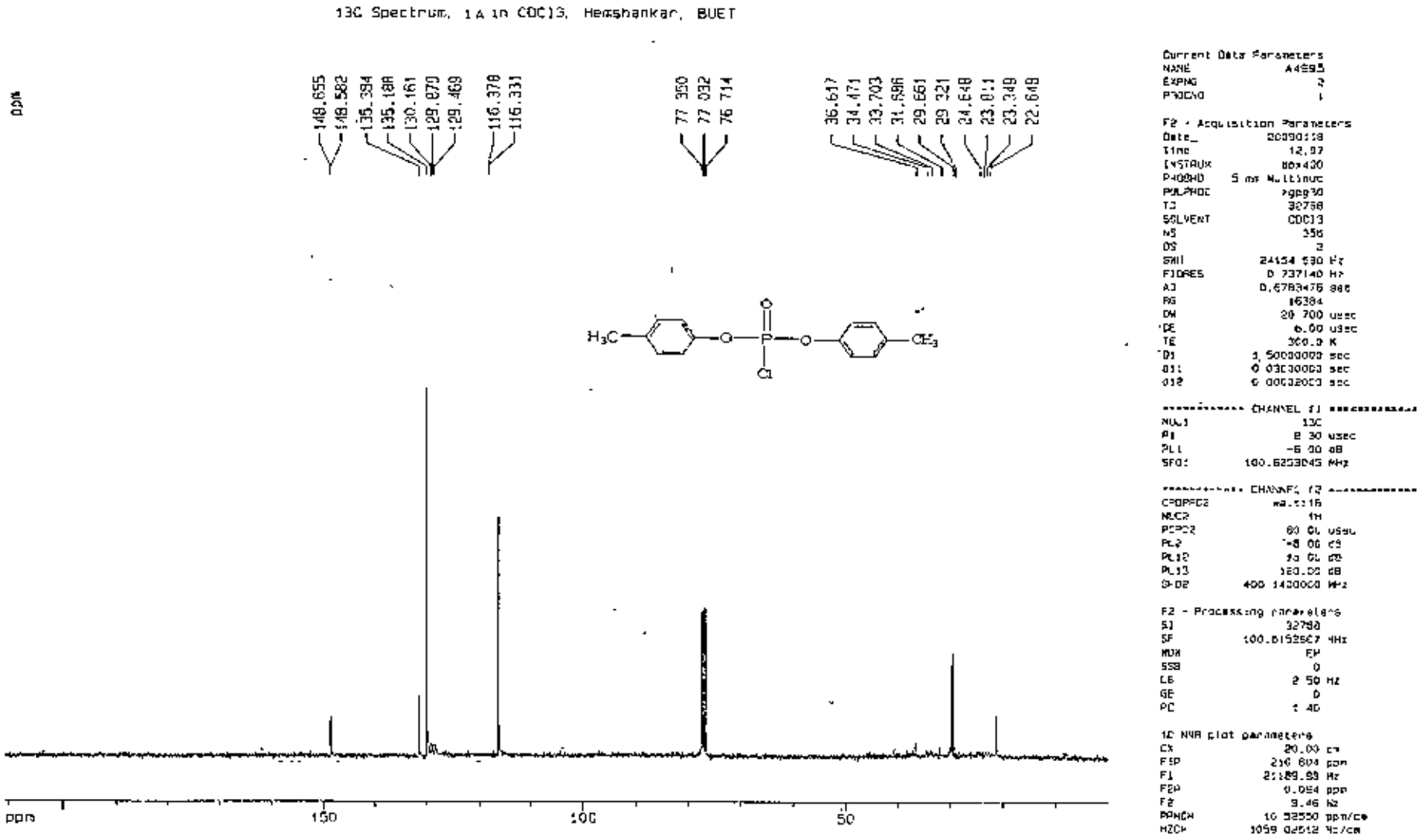


Fig. 1c ^{13}C NMR Spectrum of Compound 1A

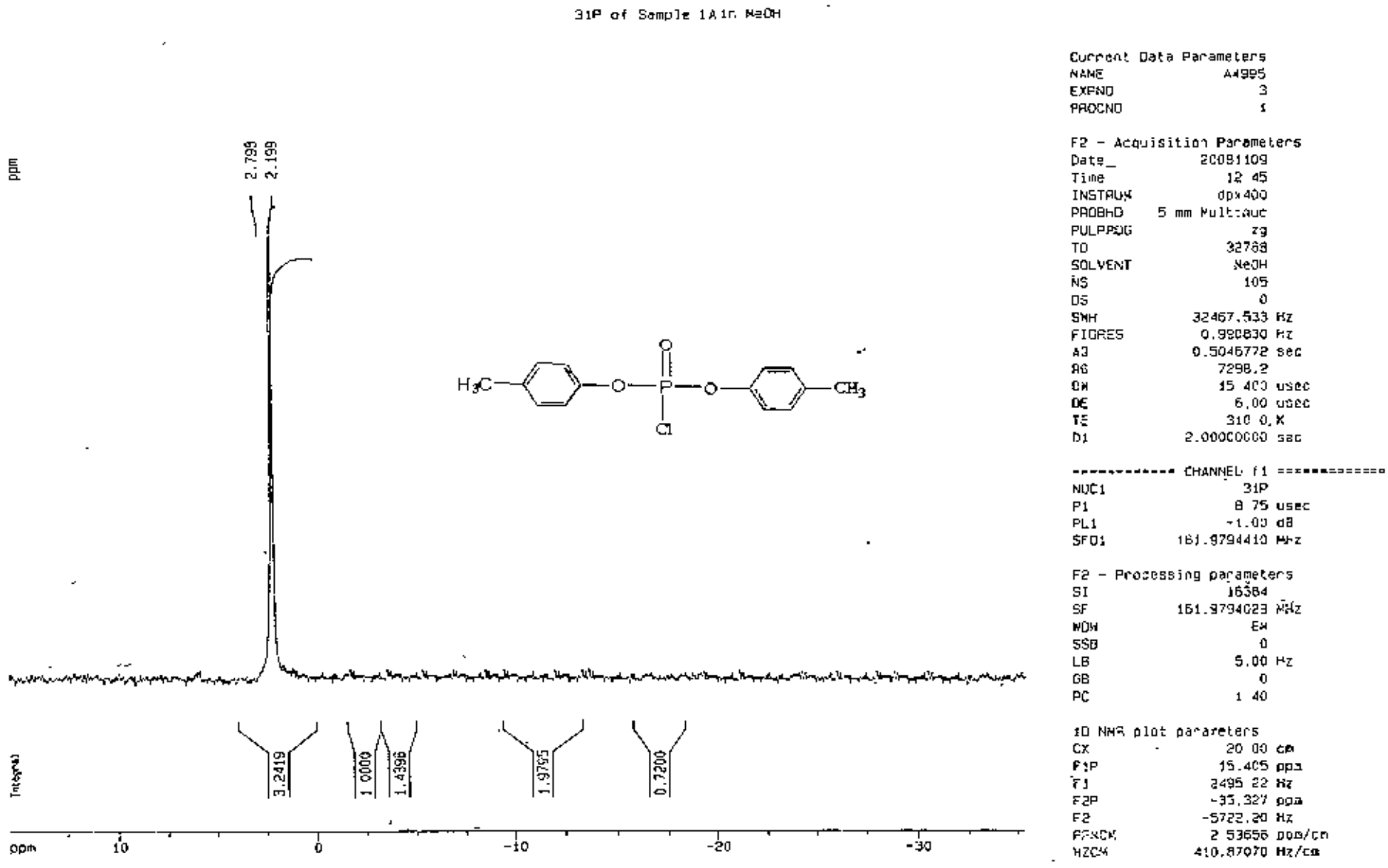


Fig. 1d ^{31}P NMR Spectrum of Compound 1A

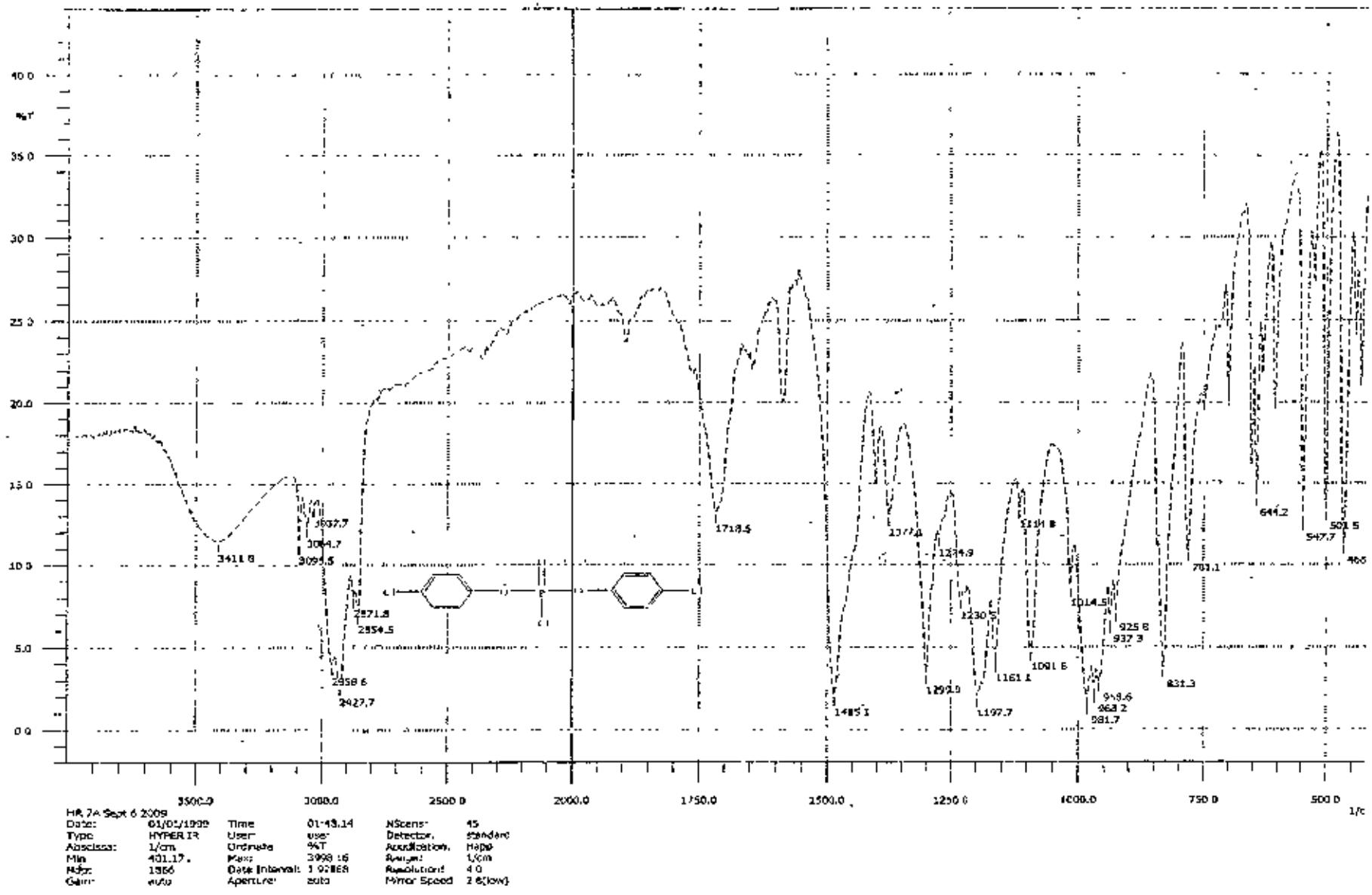


Fig. 2a IR Spectrum of Compound 2A

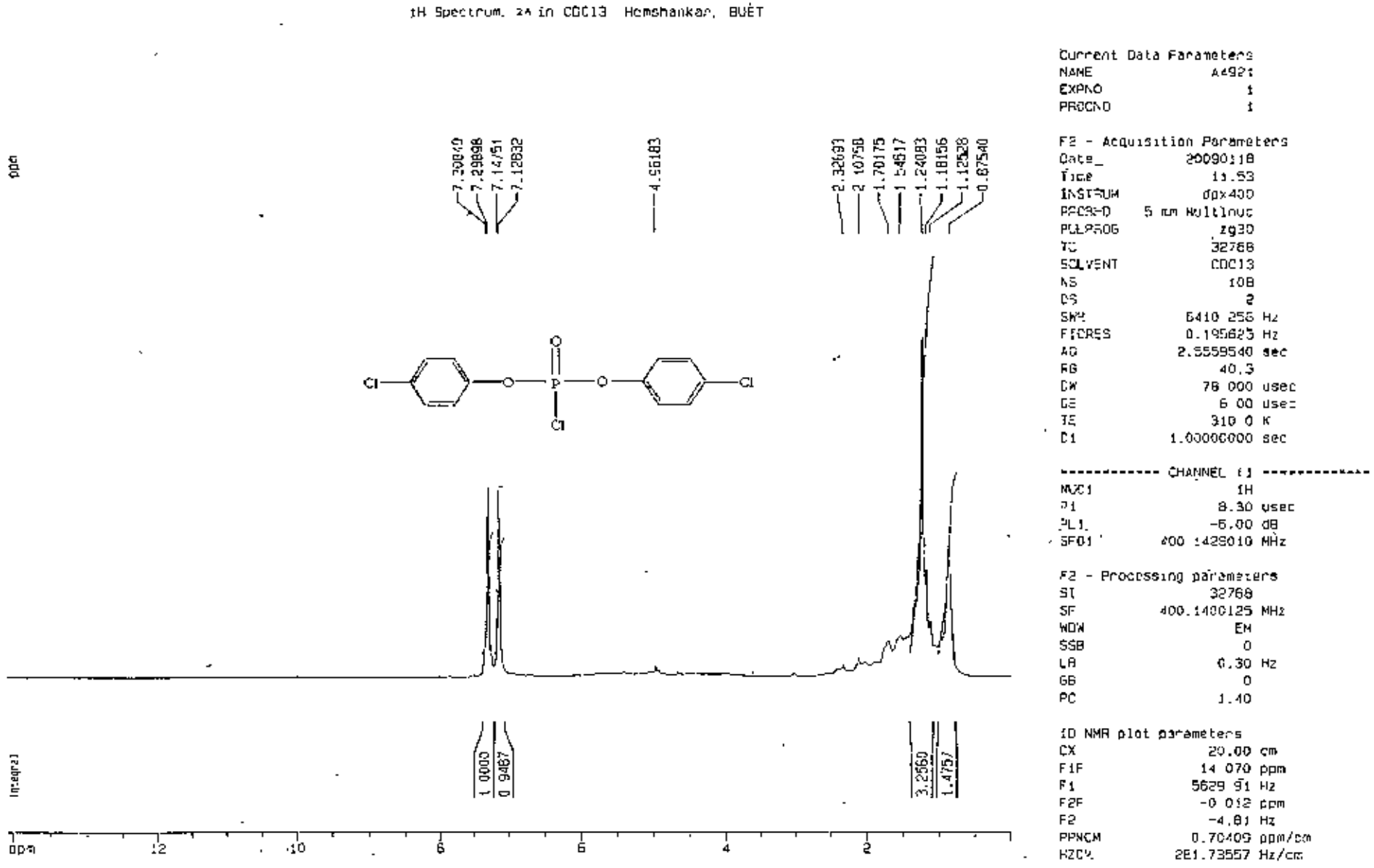


Fig. 2b ^{1}H NMR Spectrum of Compound 2A

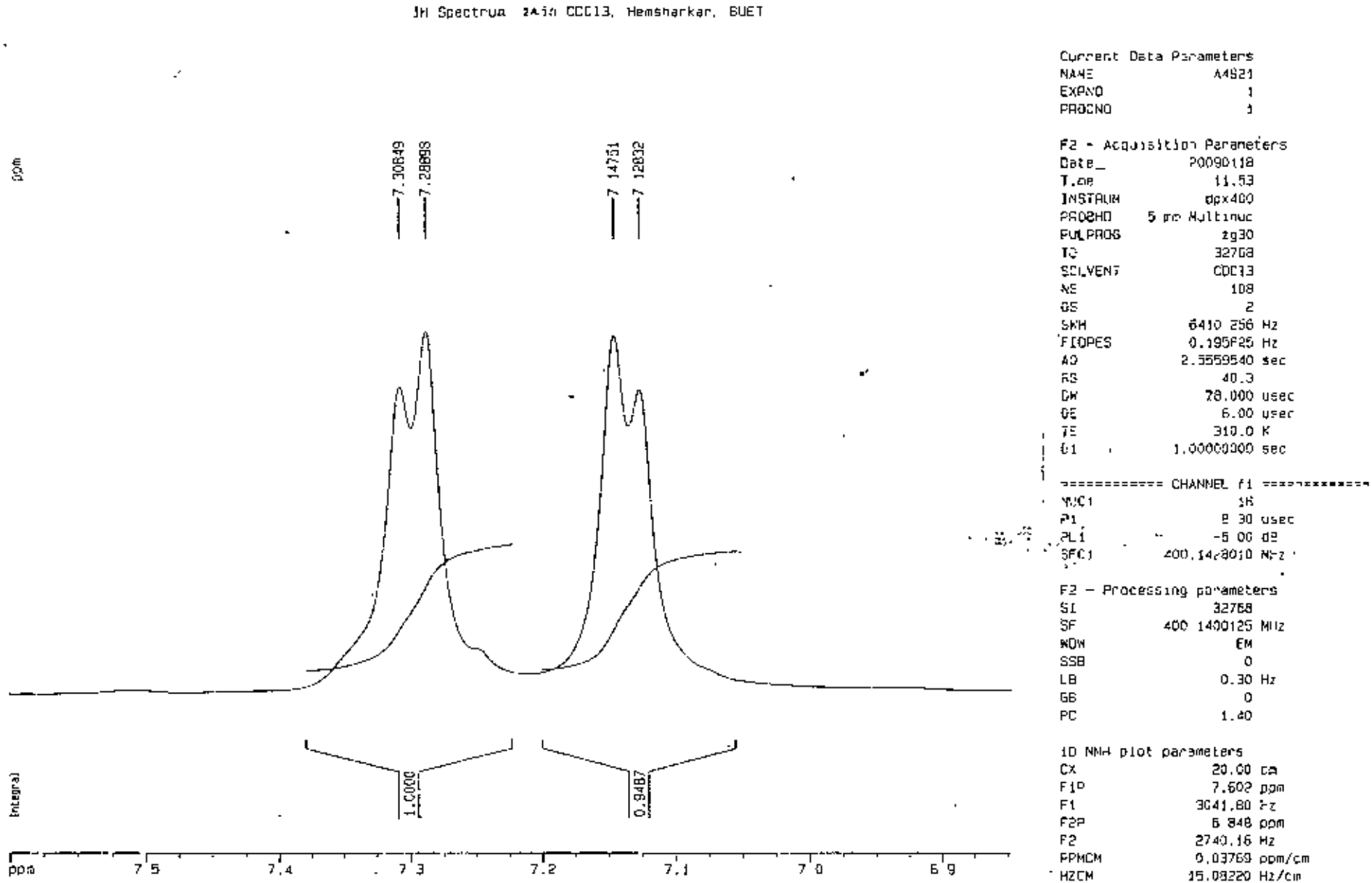


Fig. 2b ^{1}H NMR Spectrum of Compound 2A

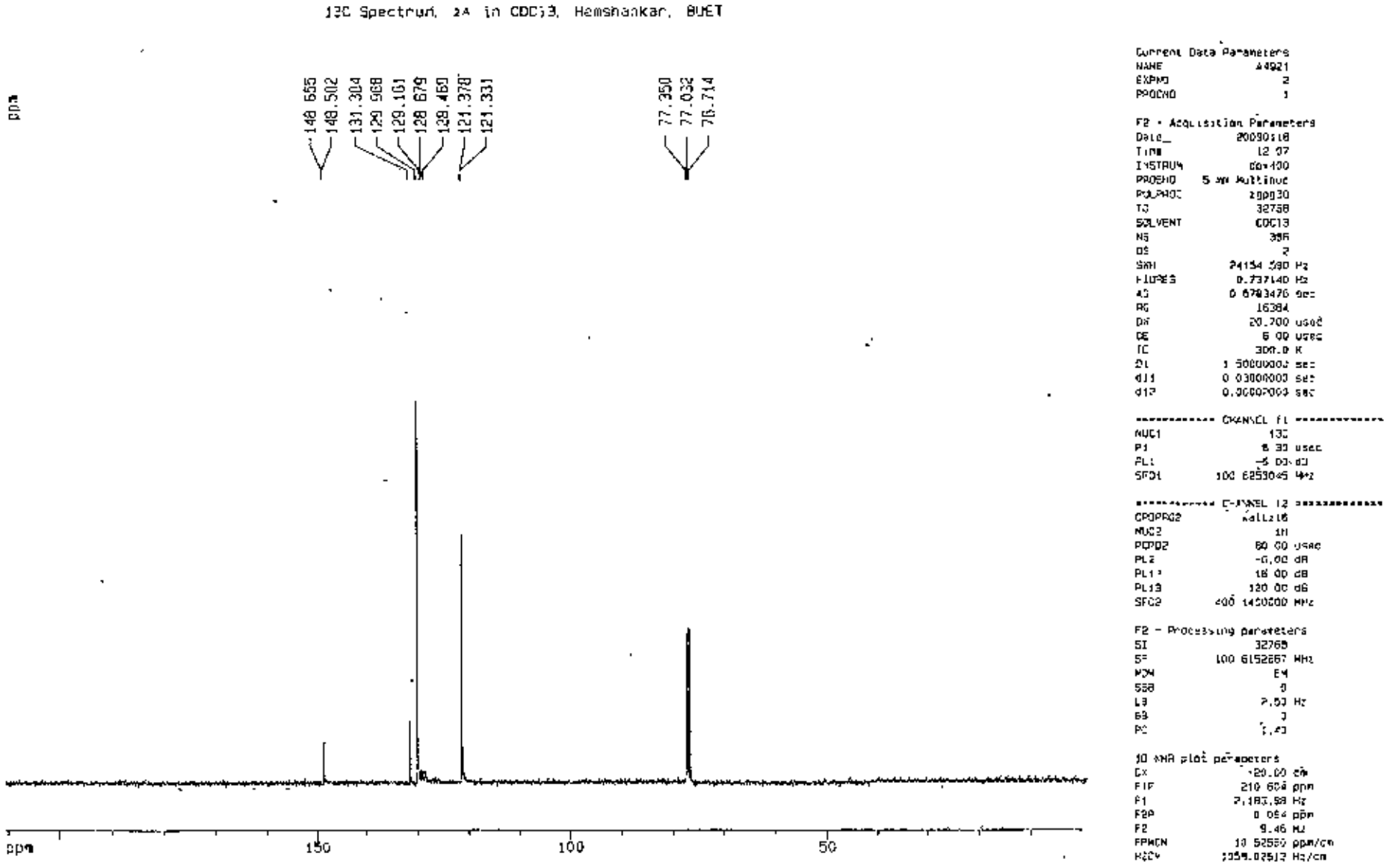


Fig. 2c ^{13}C NMR Spectrum of Compound 2A

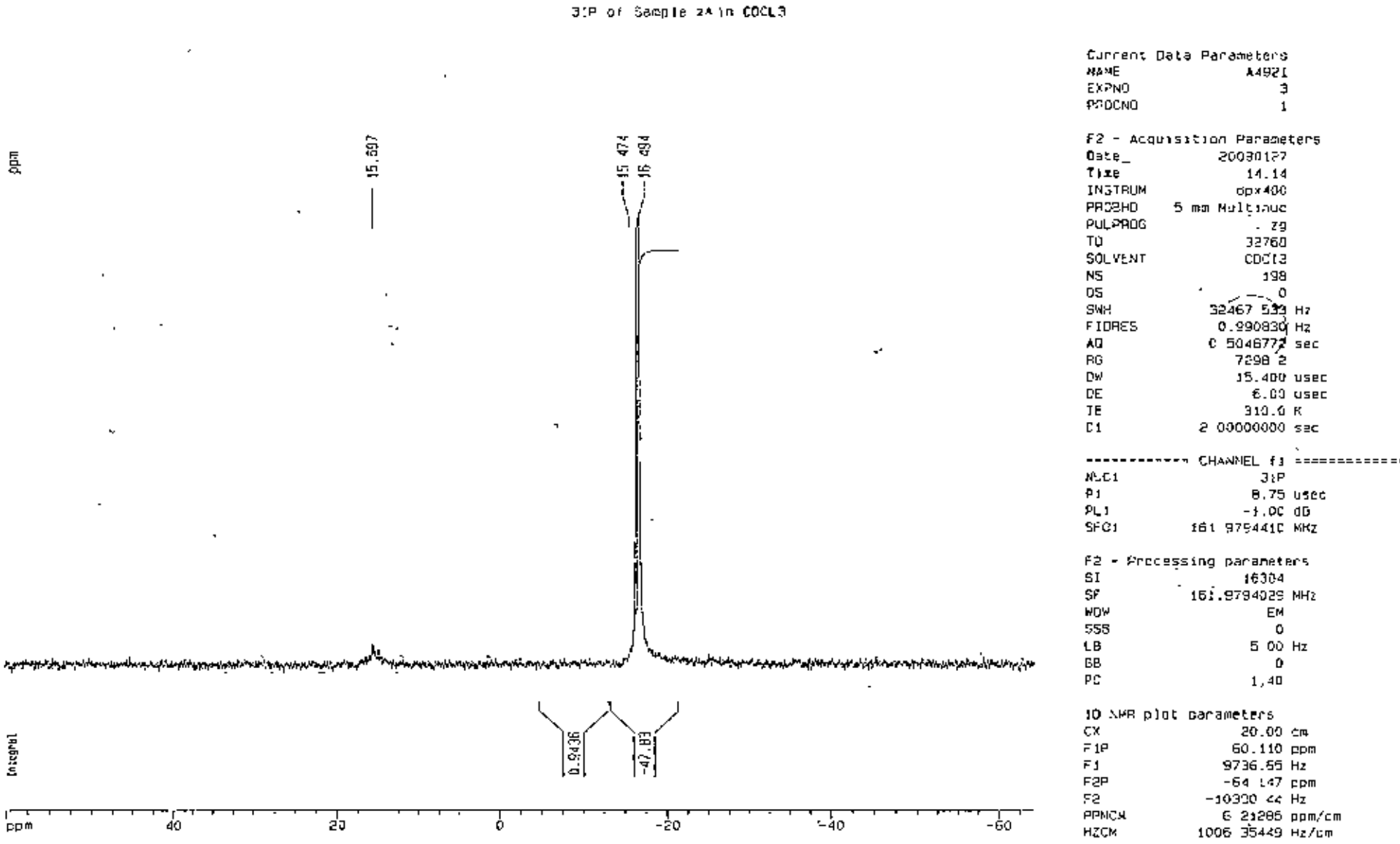


Fig. 2d ^{31}P NMR Spectrum of Compound 2A

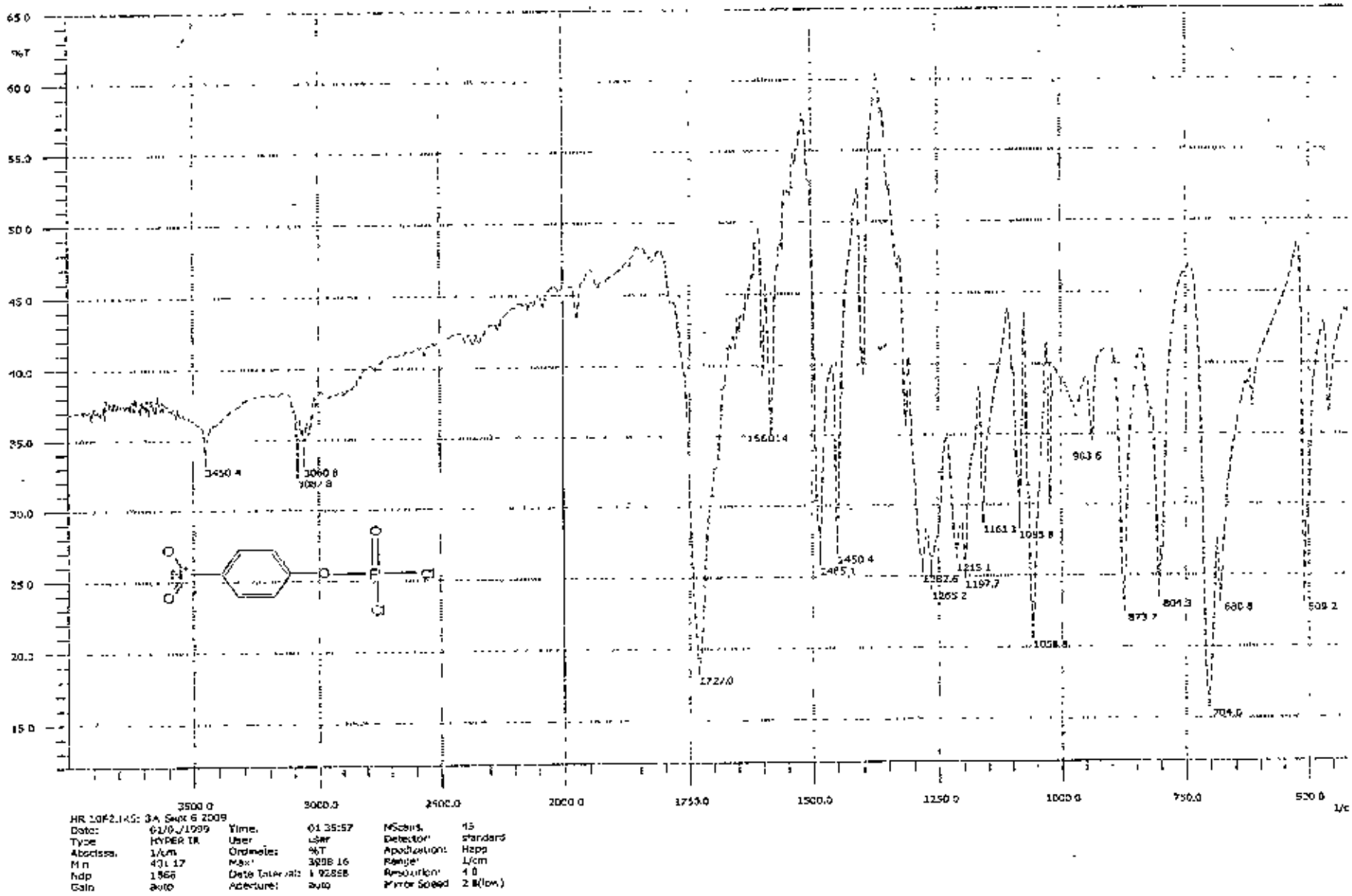


Fig. 3a IR Spectrum of Compound 3A

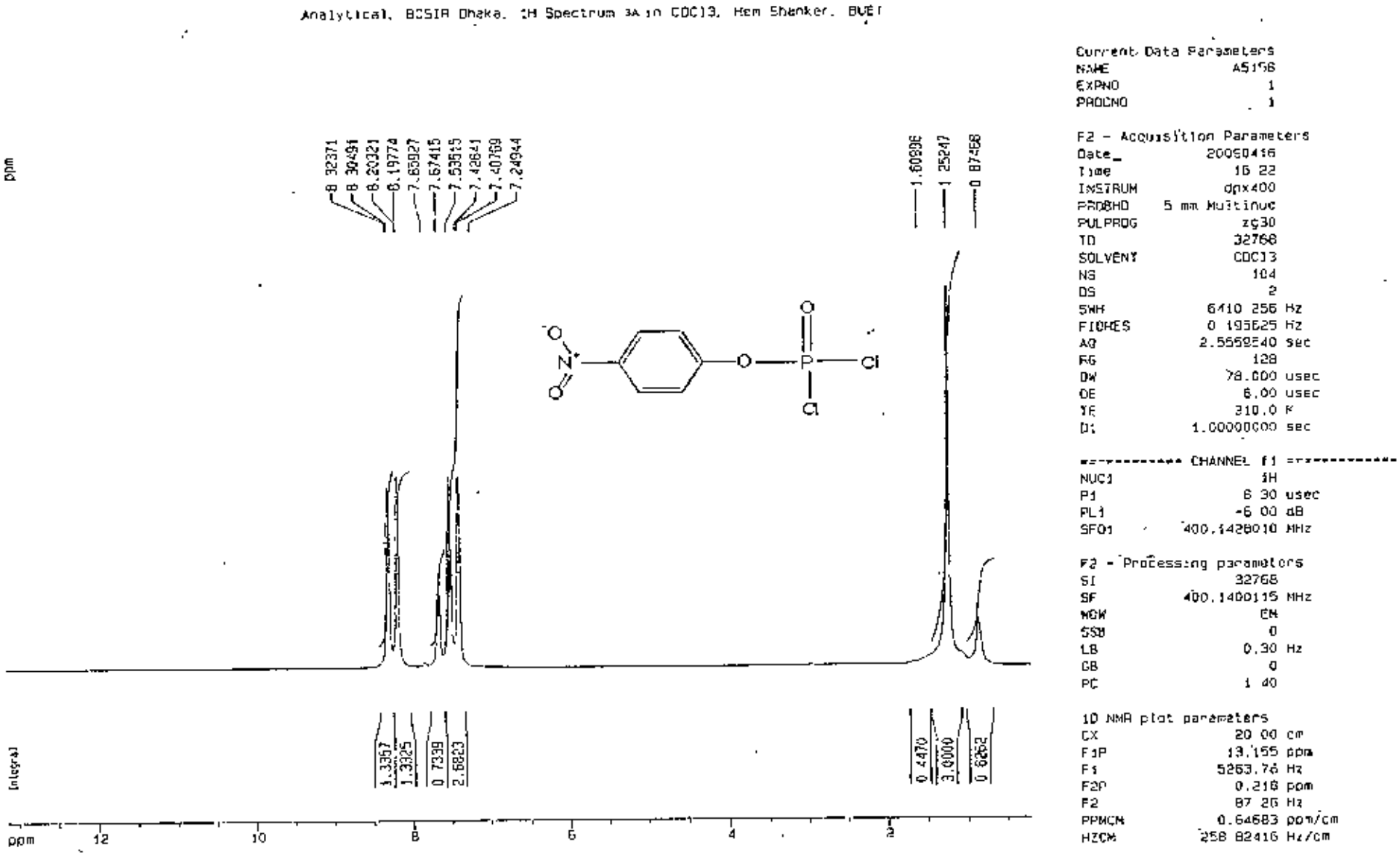


Fig. 3b ^{1}H NMR Spectrum of Compound 3A

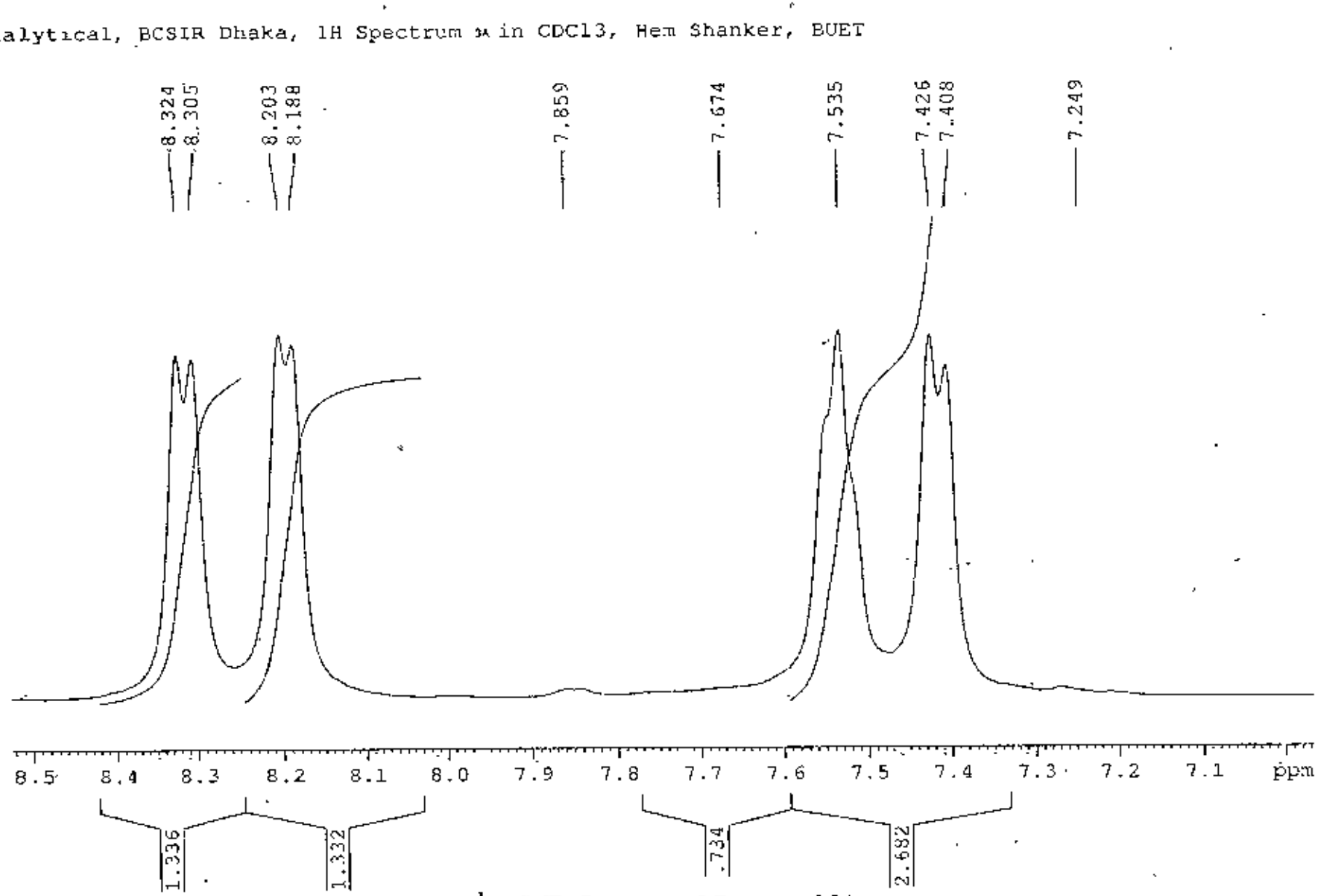


Fig. 3b ^{1}H NMR Spectrum of Compound 3A

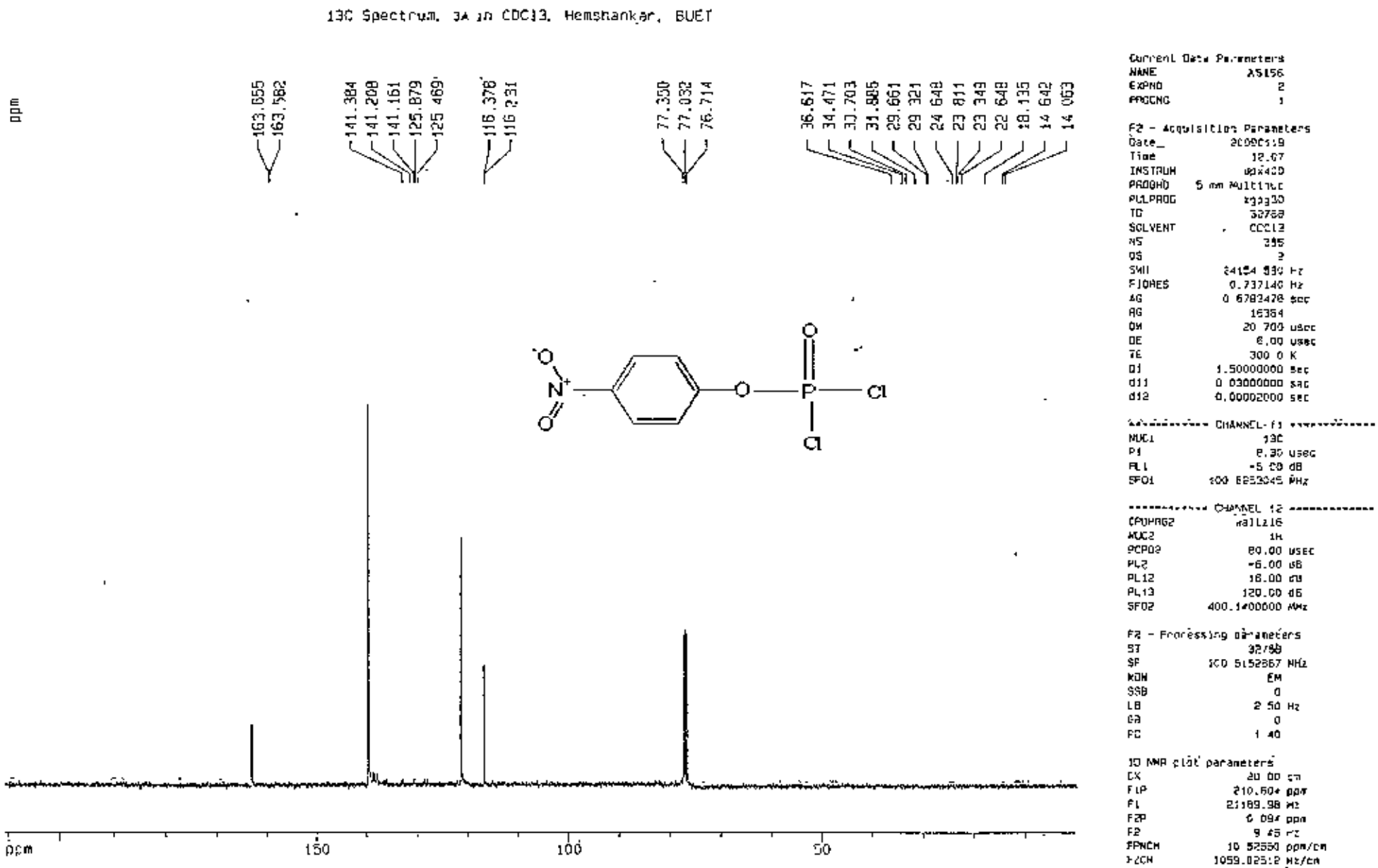
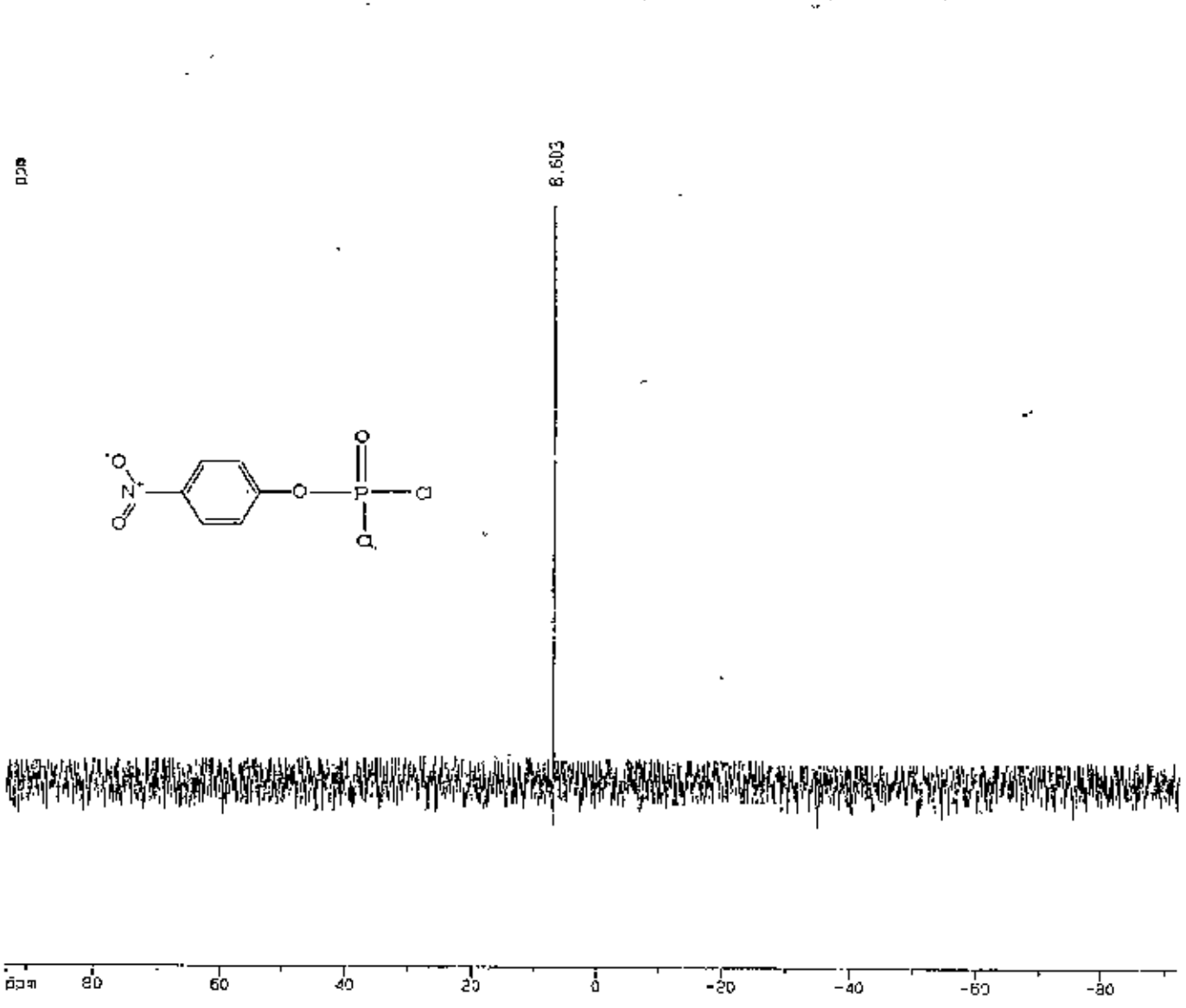


Fig. 3c ^{13}C NMR Spectrum of Compound 3A



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EXPNO 2
PROCNO 1

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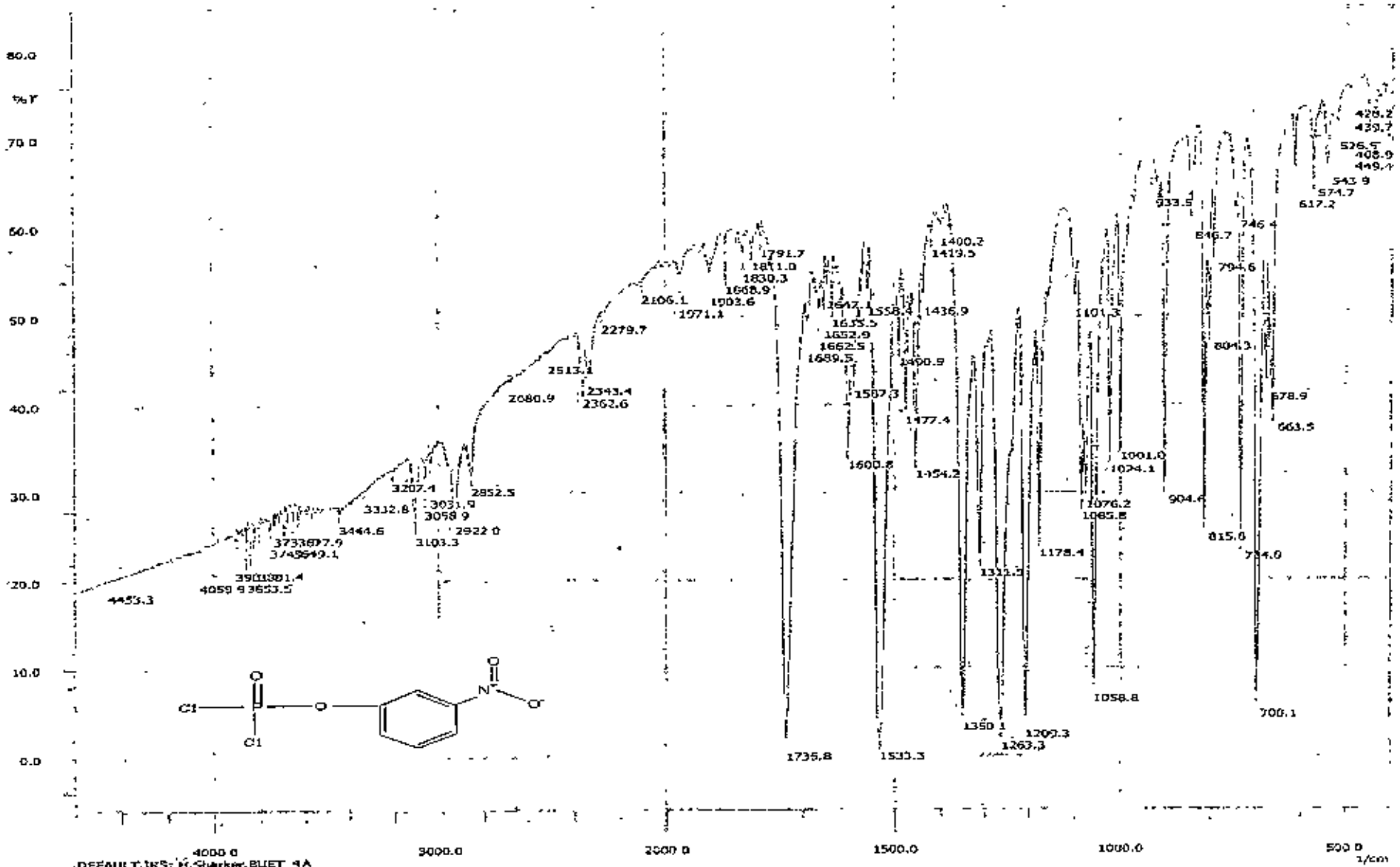
PROBHD 5 mm Multinuc
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 512
DS 0
SWH 32467.533 Hz
FIDRES 0.990830 Hz
AQ 0.5040772 sec
RG 2560.3
DW 15.400 usec
DE 6.00 usec
TE 310.0 K
D1 2.00000000 sec

======== CHANNEL f1 ========
NUC1 31P
P1 8.75 usec
PL1 -1.00 dB
SFO1 161.9794410 MHz

F2 - Processing parameters
SI 16384
SF 161.9794029 MHz
WDW EM
SSB 0
LB 5.00 Hz
GB 0
PC 1.40

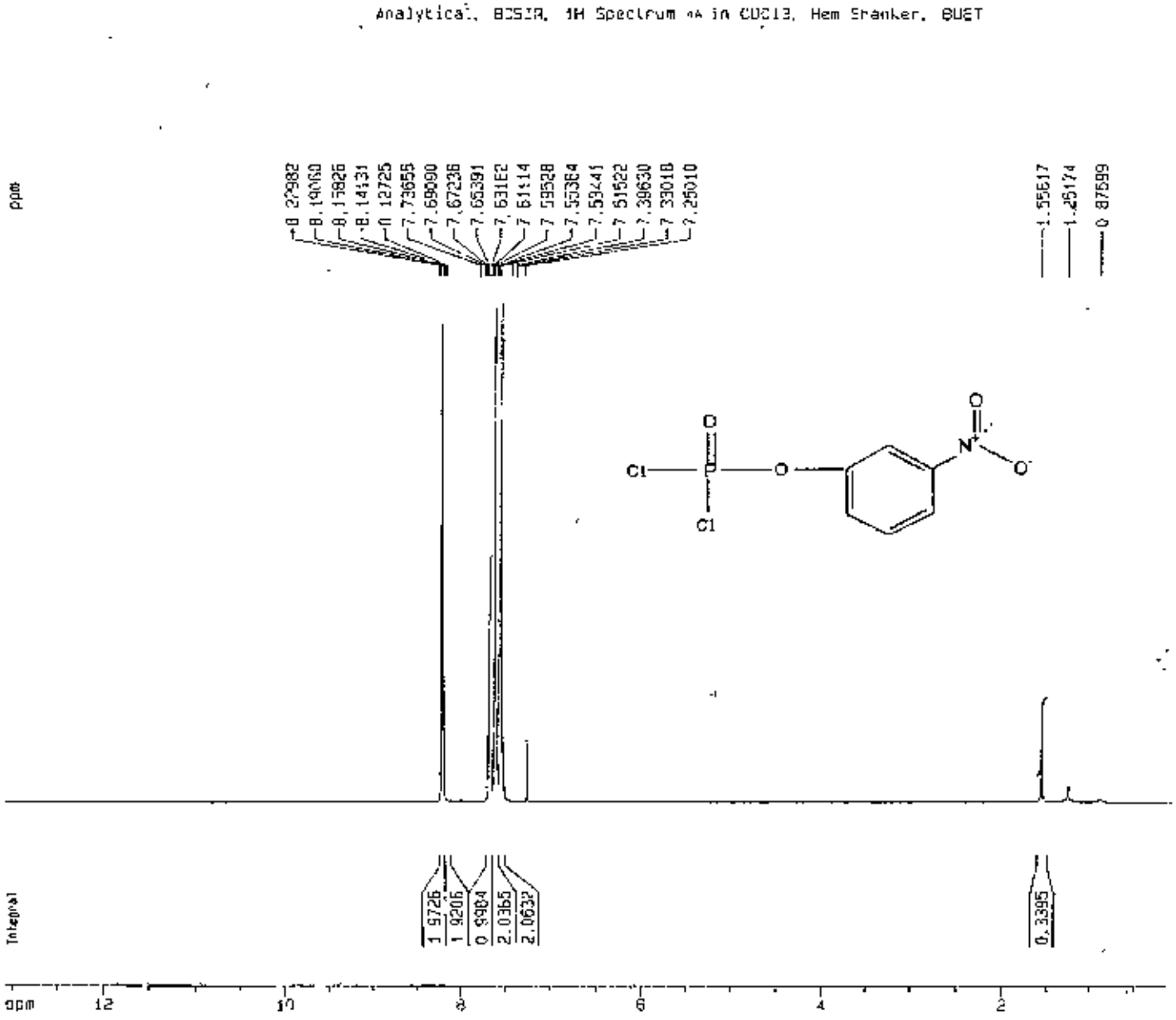
1D NMR plot parameters
CX 20.00 cm
F1P 93.118 ppm
F1 15083.20 Hz
F2P -92.019 ppm
F2 -14905.12 Hz
PPMCM 9.25683 ppm/cm
HZCM 1499.41684 Hz/cm

Fig. 3d ^{31}P NMR Spectrum of Compound 3A



DEFAULT.IRS:	H.Shankar.BUET 4A				
Date:	08/23/2009	Time:	13:21:09	NScans:	25
Type:	MYPER IR	User:	CRD	Detector:	standard
Abscissa:	1/cm	Ordinate:	%T	Apodization:	Happ
Min:	401.17	Max:	4599.91	Range:	1/cm
Ndp:	2178	Data Interval:	1.92068	Resolution:	4.0
Gain:	auto	Aperture:	auto	Mirror Speed:	2.8(low)

Fig. 4a IR Spectrum of Compound 4A



Current Data Parameters
NAME A5157
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20090416
Time 16 31
INSTRUM cpx400
PROBHD 5 mm Multinuc
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 78
DS 2
SWH 5410.256 Hz
FIDRES 0.165625 Hz
AQ 2.5559540 sec
RG 181
DW 70.000 usec
DE 6.00 usec
TE 310.0 K
D1 1.00000000 sec

========== CHANNEL f1 ==========
NUC1 1H
P1 6.30 usec
PL1 -6.00 dB
SFO1 400.1428010 MHz

F2 - Processing parameters
SI 32768
SF 400.1400123 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
F1P 13.066 ppm
F1 5236.16 Hz
F2P 0.132 ppm
F2 52.97 Hz
PPMCM 0.64757 ppm/cm
HZCM 259.15345 Hz/cm

Fig. 4b ^{1}H NMR Spectrum of Compound 4A

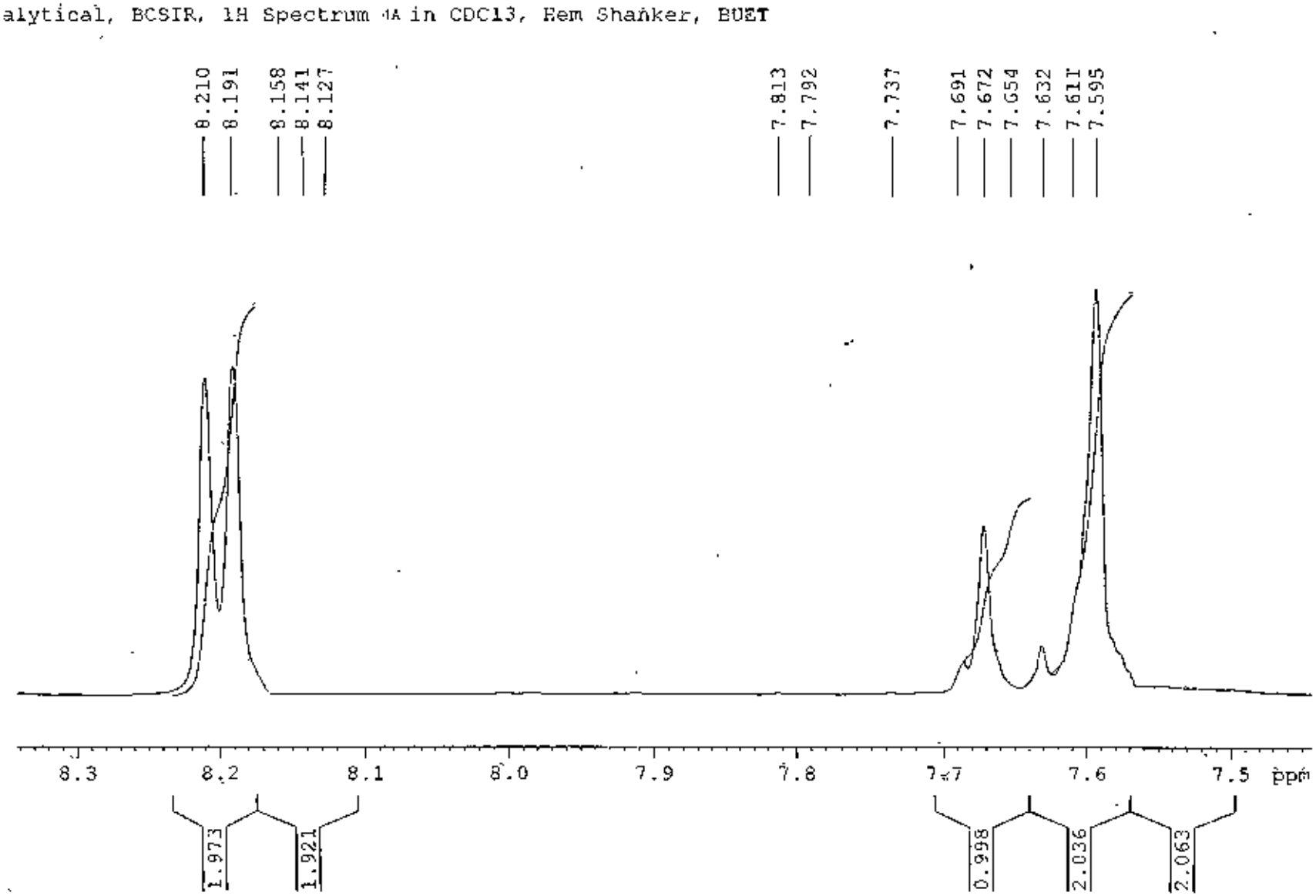
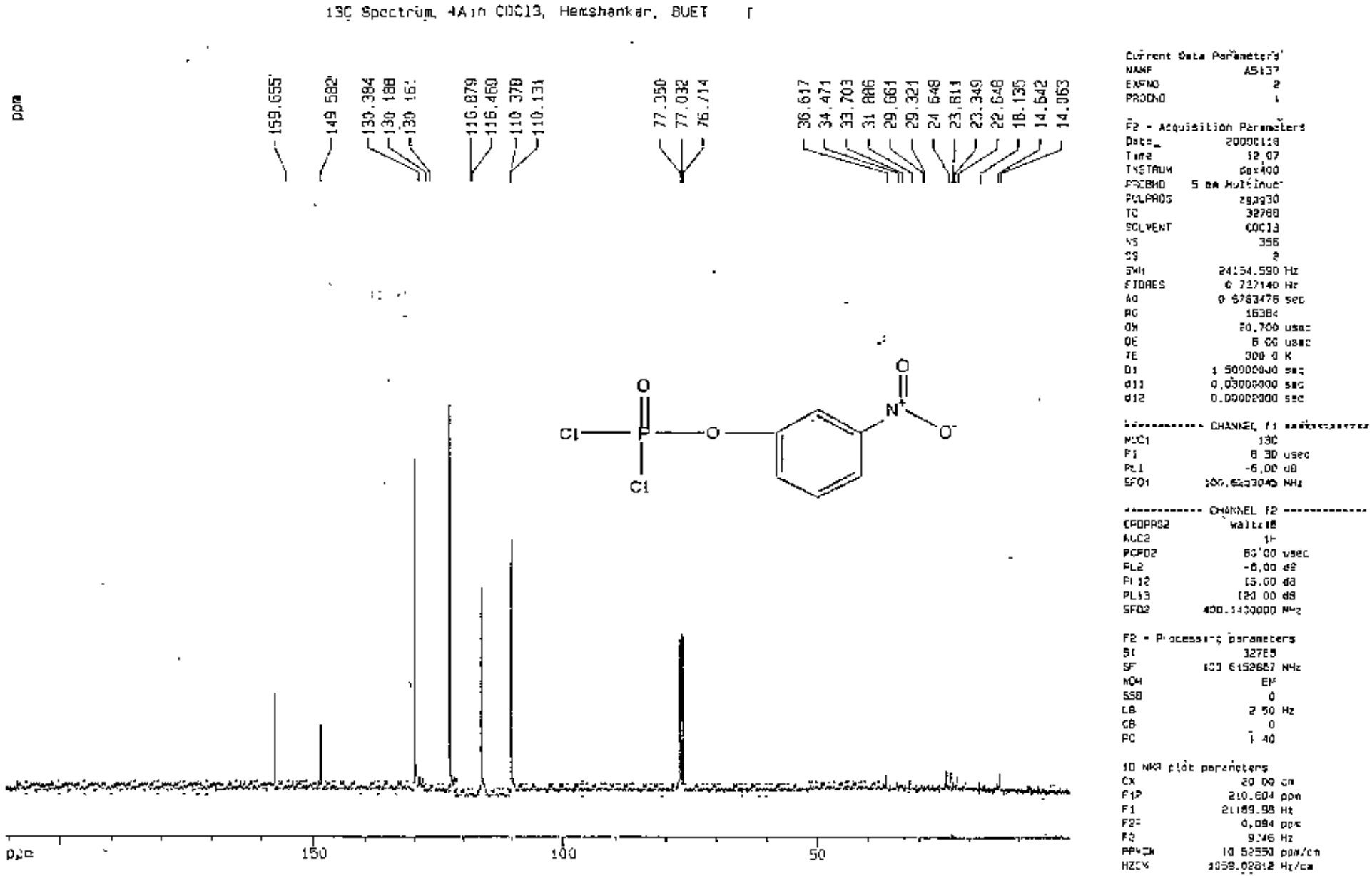


Fig. 4b ^{1}H NMR Spectrum of Compound 4A



Current Data Parameters
NAME A5137
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20000118
Time 12.07
INSTRUM qnx400
PROBHD 5 mm Multinuc
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 356
DS 2
SWH 24154.590 Hz
FIDRES 0.737140 Hz
AQ 0.6783476 sec
RG 16384
DW 20.700 usec
DE 6.00 usec
TE 300.0 K
D1 1.50000000 sec
d11 0.03000000 sec
d12 0.00002000 sec

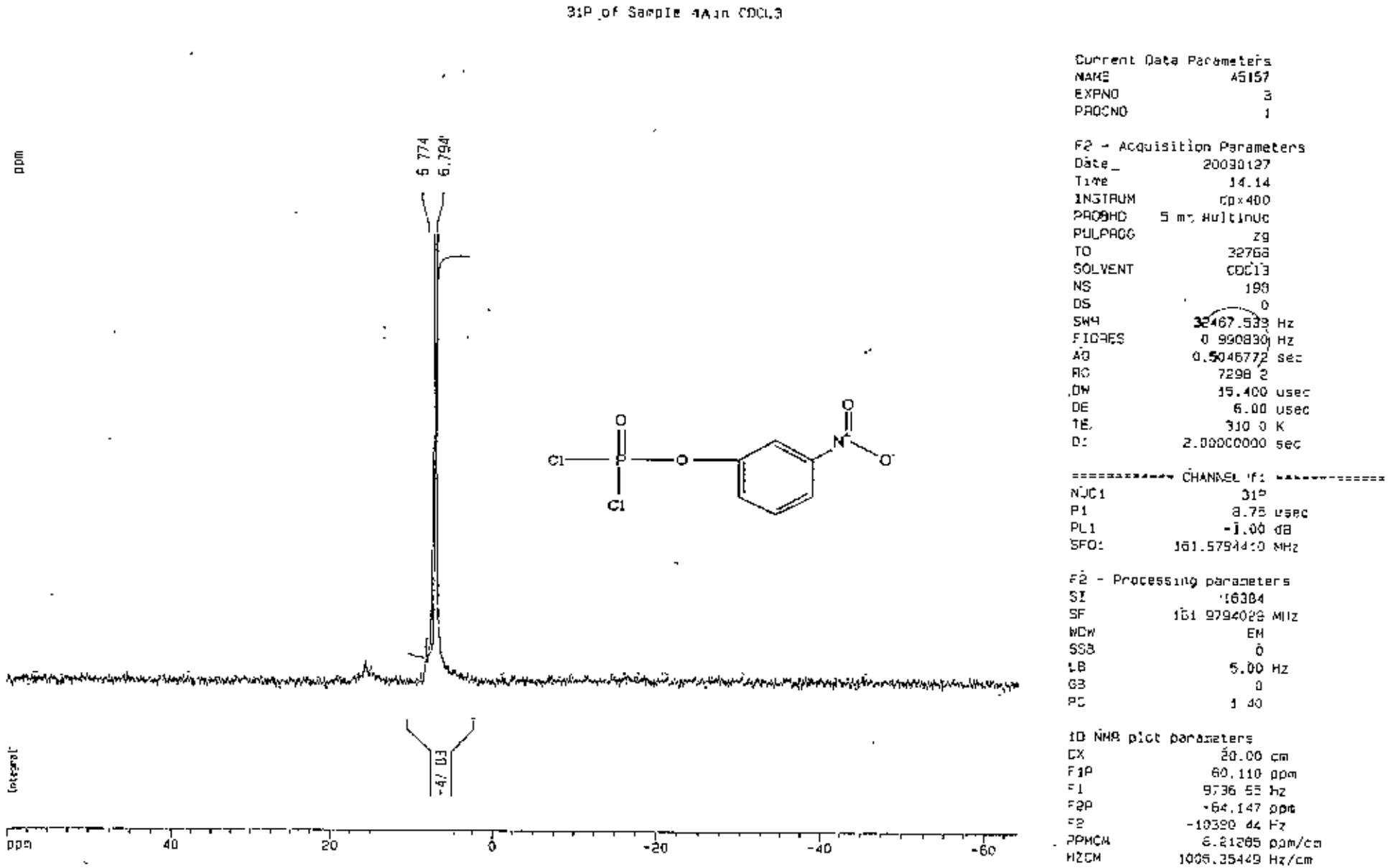
---------- CHANNEL f1 ----------
NUC1 13C
P1 8.30 usec
PL1 -6.00 dB
SFO1 100.6229045 MHz

---------- CHANNEL f2 ----------
CPDPRG2 waltz16
NUC2 1H
PCPD2 63.00 usec
PL2 -6.00 dB
PL12 15.00 dB
PL13 120.00 dB
SFO2 400.1400000 MHz

F2 - Processing parameters
SI 32768
SF 100.6152827 MHz
WDW EM
SSB 0
LB 2.50 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
F1P 210.604 ppm
F1 21189.98 Hz
F2P 0.094 ppm
F2 9.46 Hz
PPMCM 10.52550 ppm/cm
HZCM 1059.02812 Hz/cm

Fig. 4c ^{13}C NMR Spectrum of Compound 4A



Current Data Parameters
NAME A5157
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20030127
Time 14.14
INSTRUM cpx400
PROBHD 5 mm Multinuc
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 100
DS 0
SWH 32467.533 Hz
FIDRES 0.990830 Hz
AQ 0.5046772 sec
RG 7298.2
DW 15.400 usec
DE 6.00 usec
TE 310.0 K
D1 2.00000000 sec

CHANNEL f1
NUC1 31P
P1 8.75 usec
PL1 -1.00 dB
SFO1 161.5794410 MHz

F2 - Processing parameters
SI 16384
SF 161.9794029 MHz
WDW EM
SSB 0
LB 5.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
F1P 60.110 ppm
F1 9736.55 Hz
F2P -64.147 ppm
F2 -10390.44 Hz
PPMCM 6.81285 ppm/cm
HZCM 1085.35449 Hz/cm

Fig. 4d ^{31}P NMR Spectrum of Compound 4A

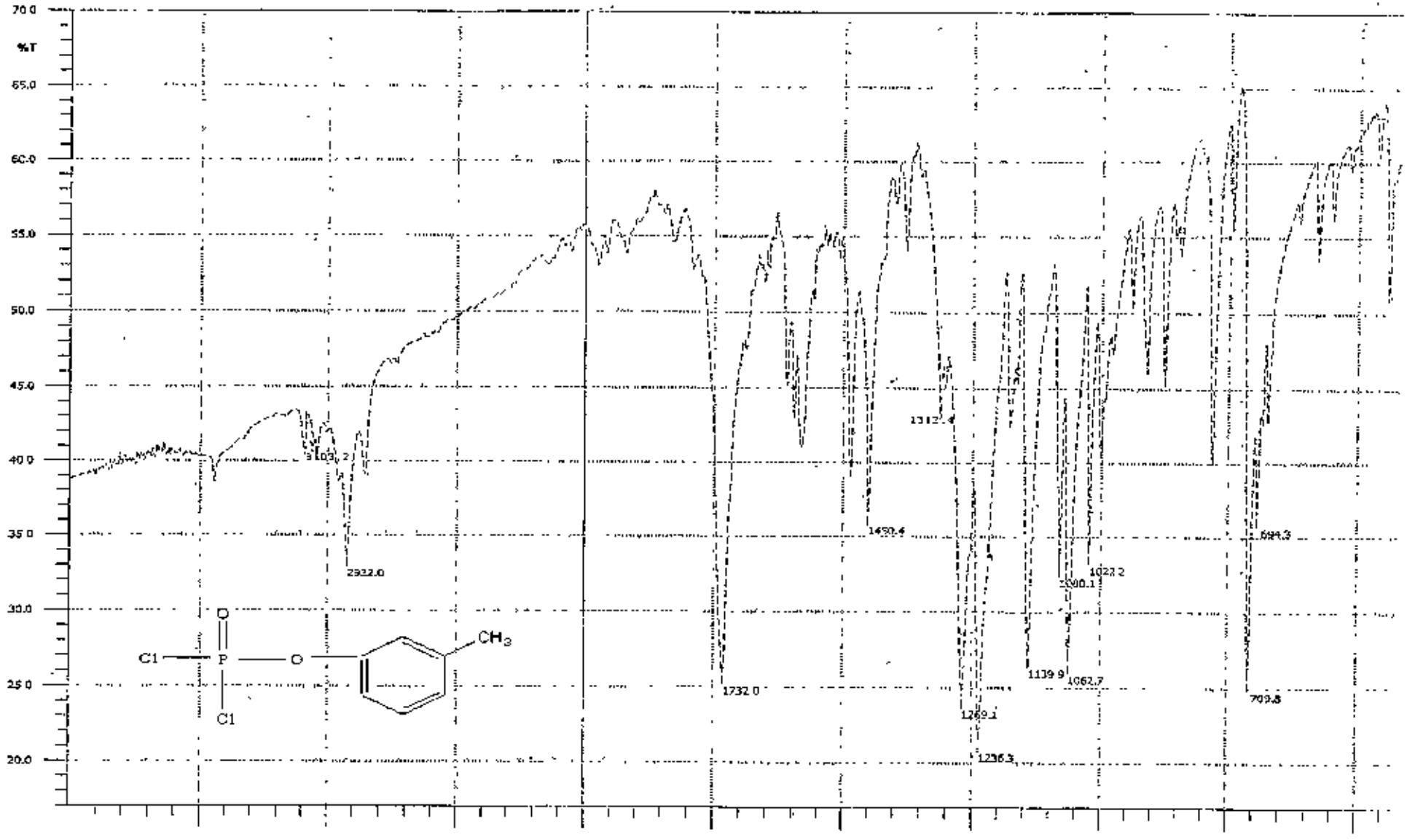


Fig. 5a IR Spectrum of Compound 5A

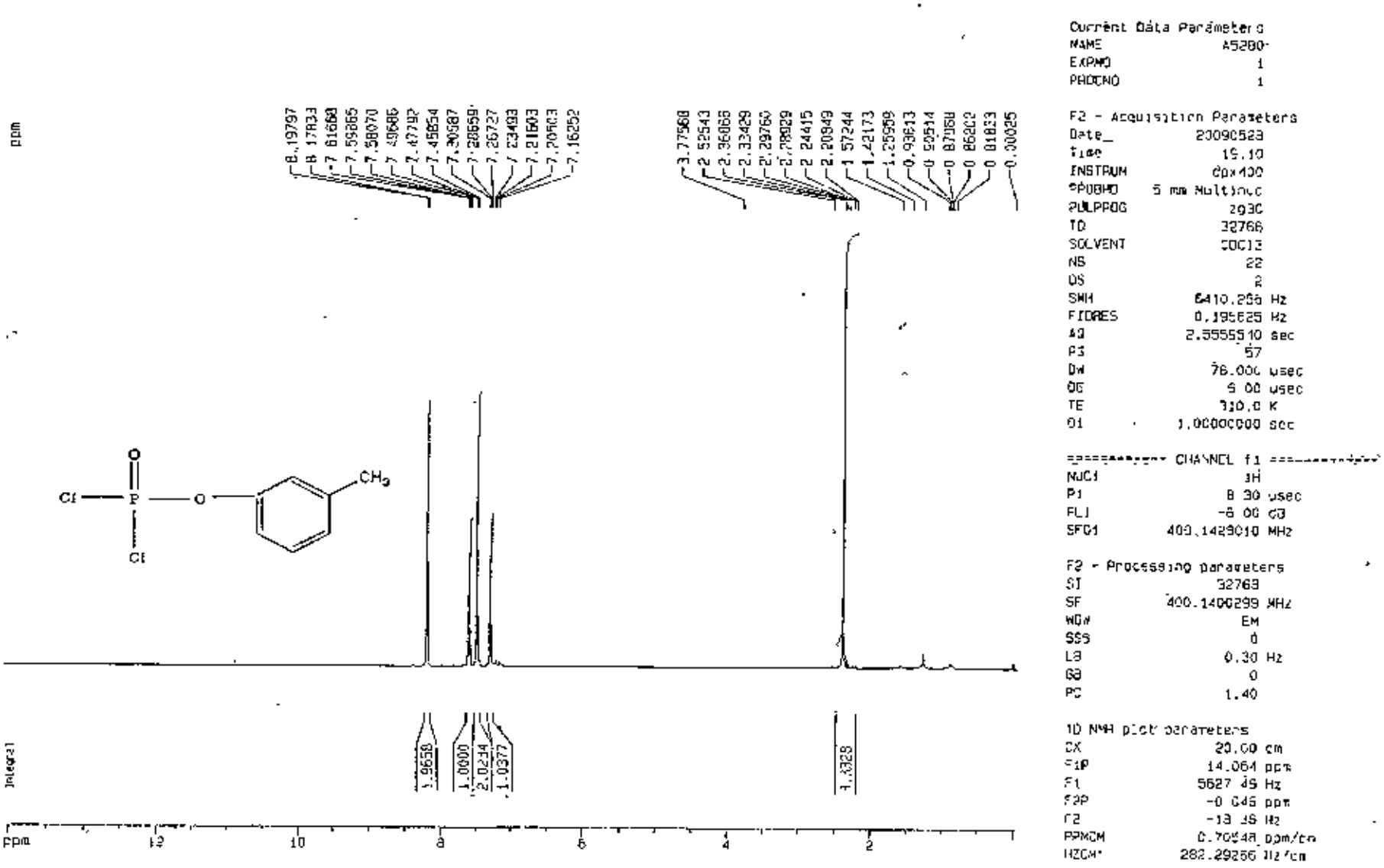


Fig. 5b ^{1}H NMR Spectrum of Compound 5A

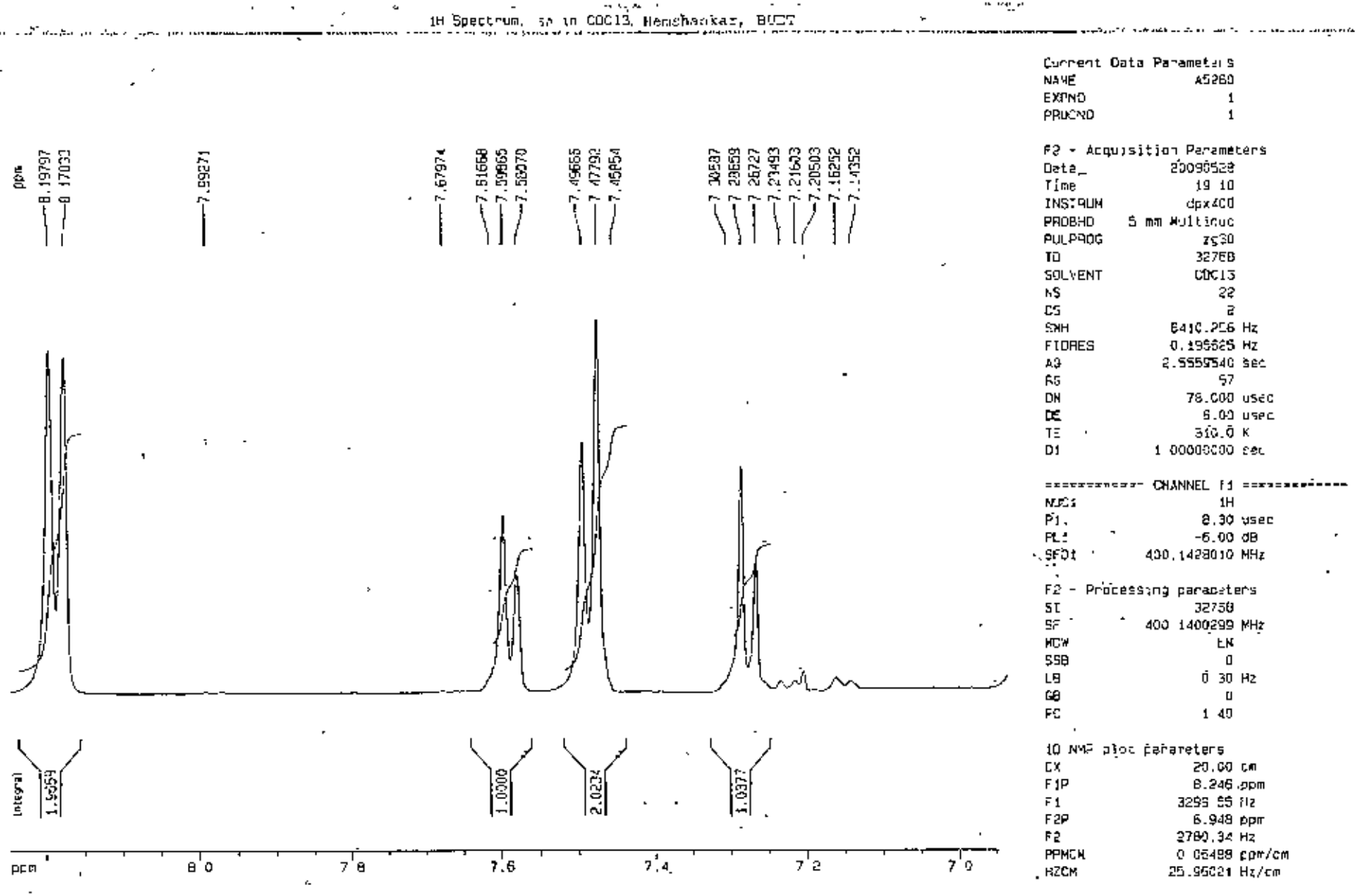


Fig. 5b ^{1}H NMR Spectrum of Compound 5A

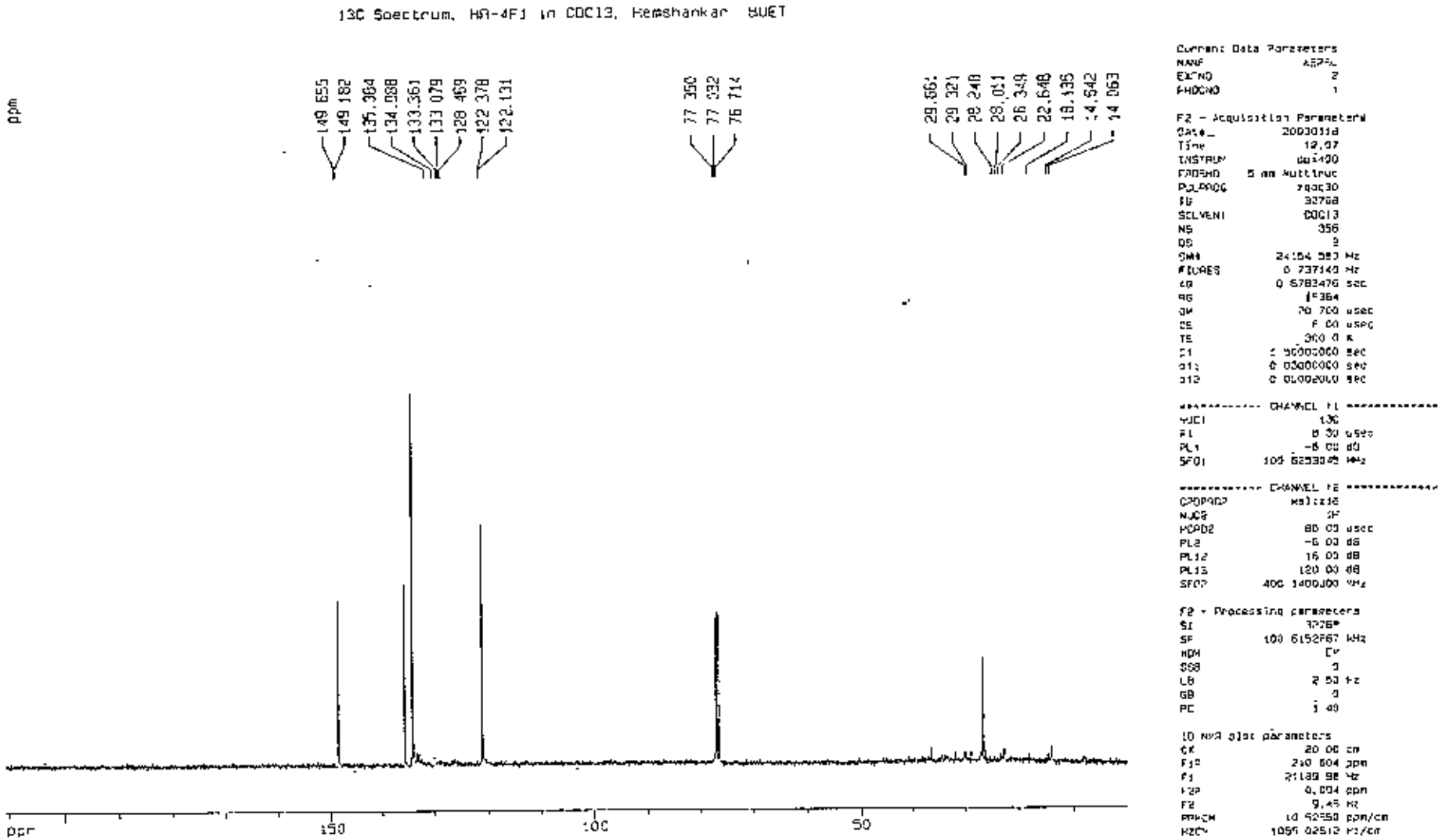
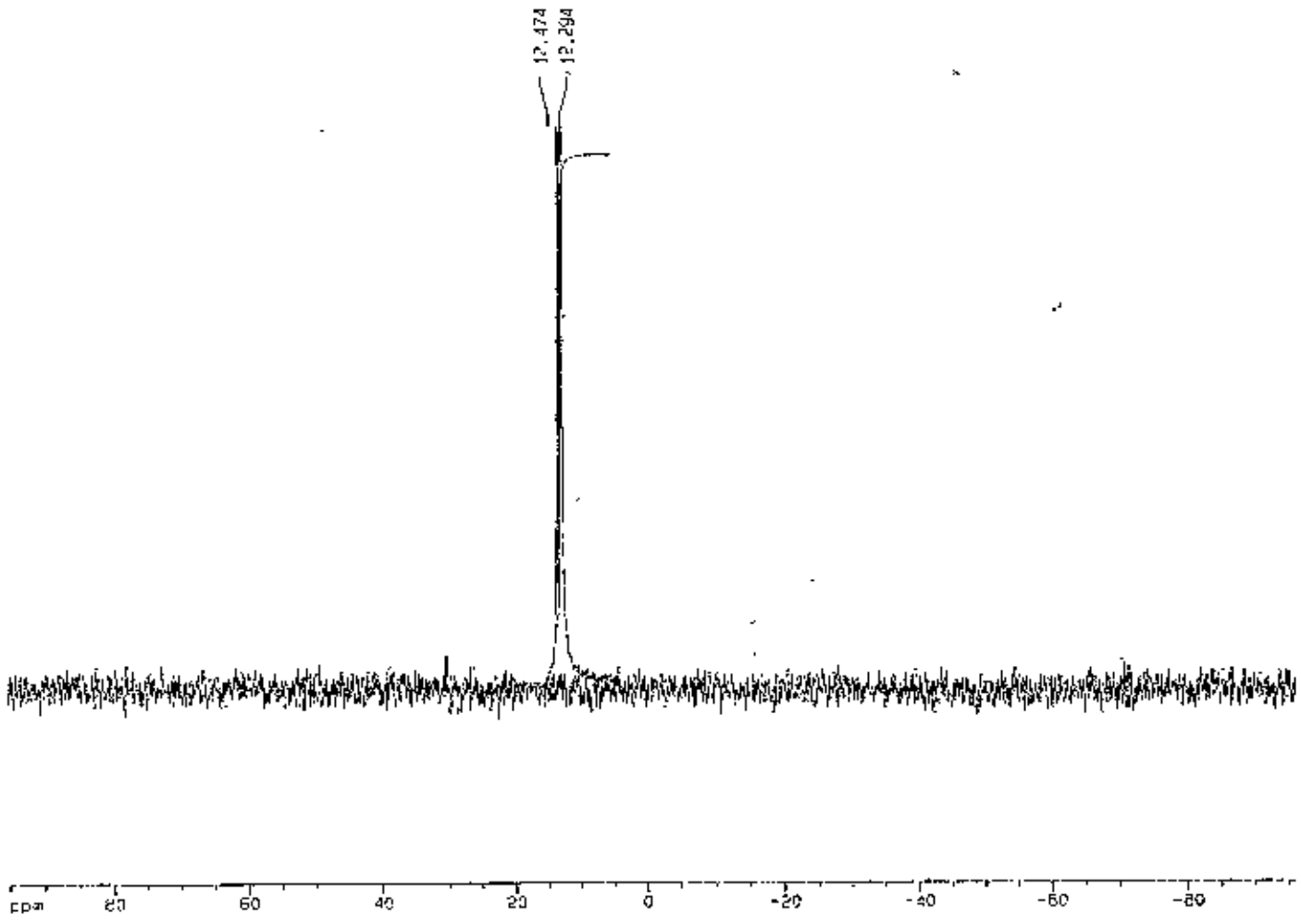


Fig. 5c ^{13}C NMR Spectrum of Compound 5A



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EXPNO 2
PROCNO 1

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PROBHD 5 mm Multinuc
PULPROG zg
TD - 32768
SOLVENT CDCl3
NS 148
DS 0
SWH 32467.533 Hz
FIDRES 0.990830 Hz
AQ 0.5045772 sec
RG 7298.2
DW 15.400 usec
DE 6.00 usec
TE 310.0 K
D1 2.00000000 sec

CHANNEL f1
NUC1 31P
P1 8.75 usec
PL1 -1.00 dB
SFO1 161.9794410 MHz

F2 - Processing parameters
SI 16384
SF 161.9794029 MHz
WDW EM
SSB 0
LB 5.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
F1P -95.215 ppm
F1 15422.82 Hz
F2P -96.002 ppm
F2 -15550.36 Hz
PPMCM 9.58085 ppm/cm
HZCM 1548.86077 Hz/cm

Fig. 5d ^{31}P NMR Spectrum of Compound 5A

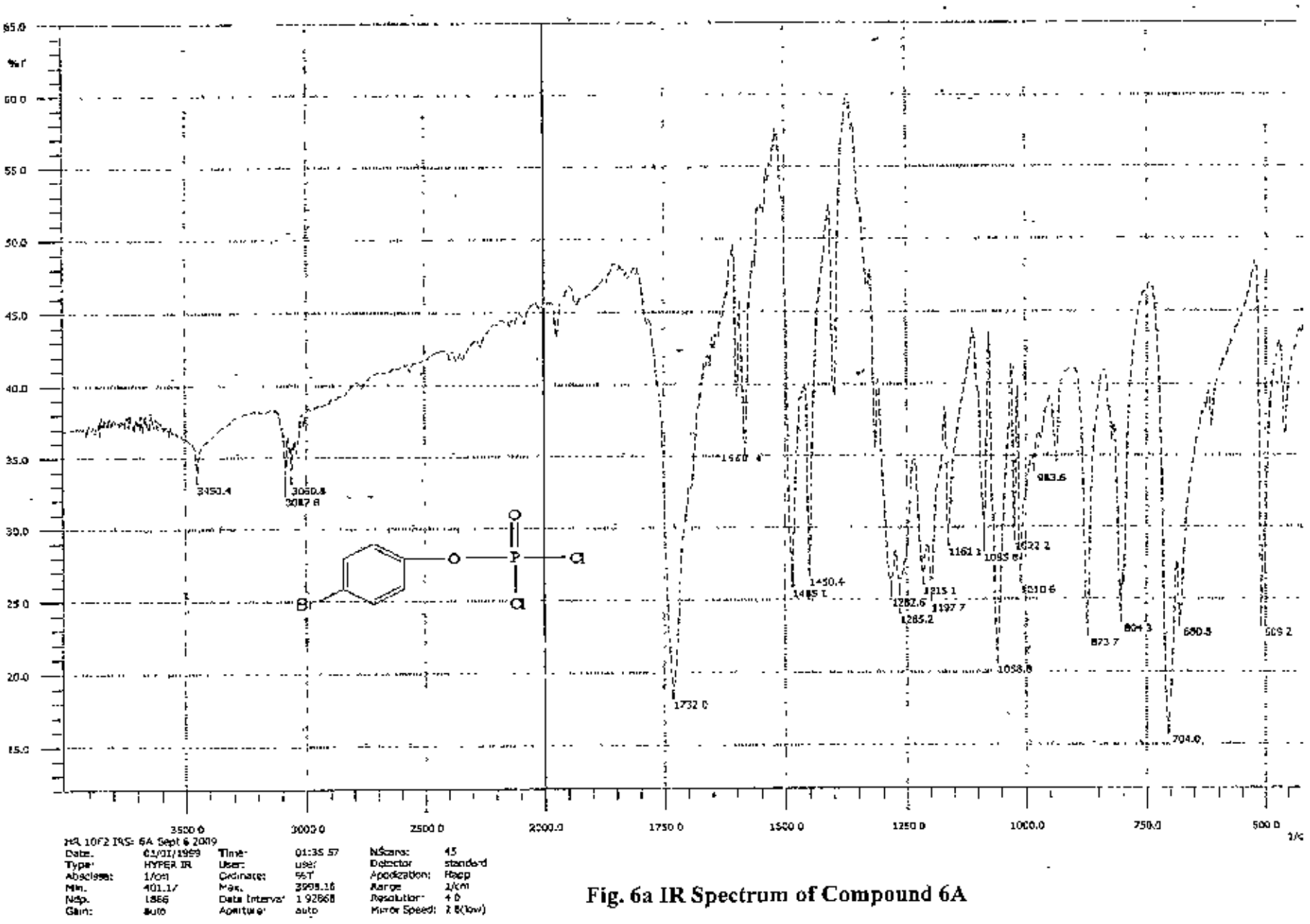
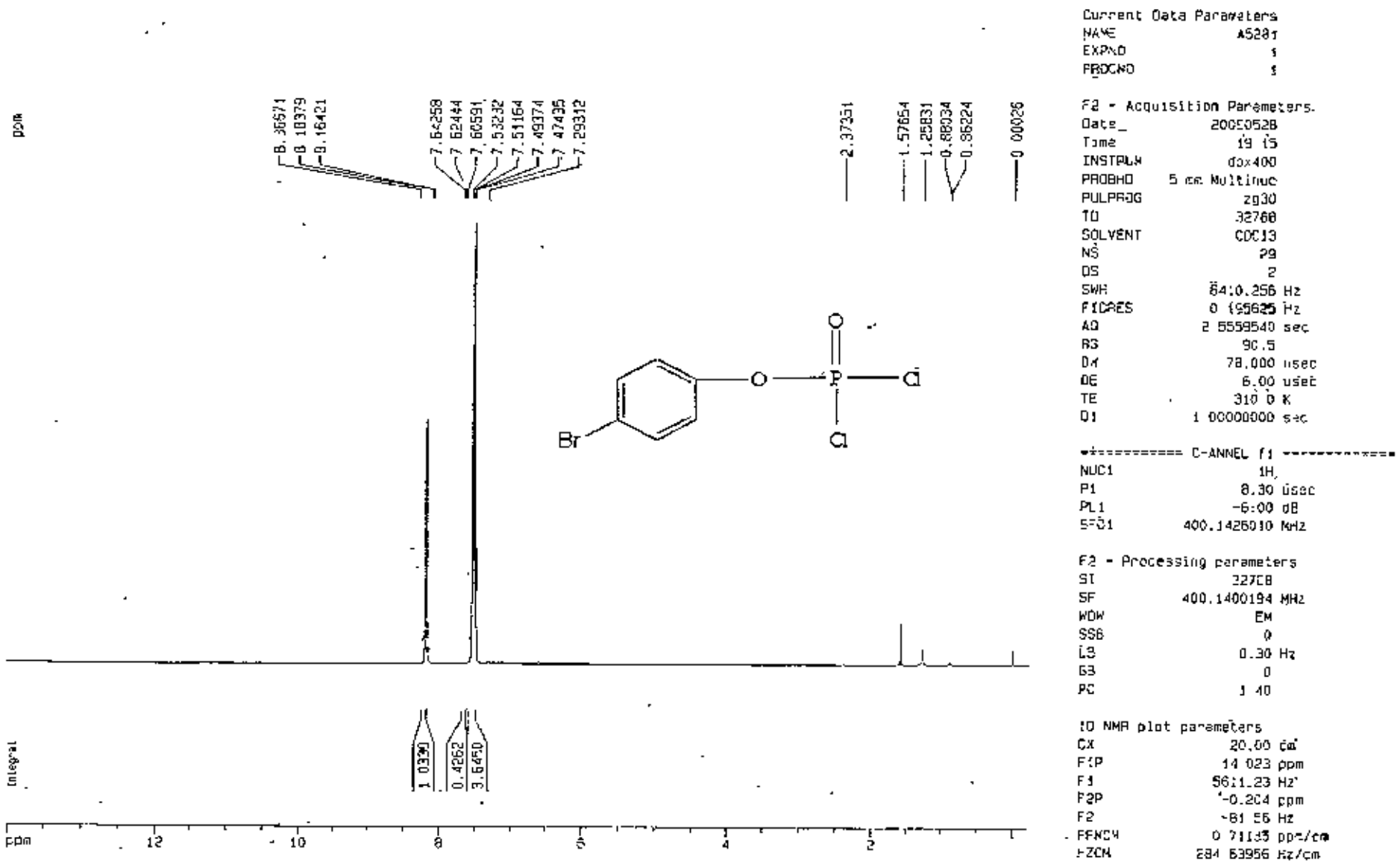


Fig. 6a IR Spectrum of Compound 6A

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Current Data Parameters
NAME                  A5281
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
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Time                   19 15
INSTRUM              dpx400
PROBHD     5 mm Multinuc
PULPROG               zg30
TD                   32768
SOLVENT              CDCl3
NS                      29
DS                       2
SWH              6410.256 Hz
FIDRES           0.195625 Hz
AQ               2.5559540 sec
RG                    90.5
DW                78.000 usec
DE                 6.00 usec
TE                 310.0 K
D1               1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 8.30 usec
PL1                -6.00 dB
SFO1         400.1426010 MHz

F2 - Processing parameters
SI                   32768
SF           400.1400194 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.40

1D NMR plot parameters
CX                  20.00 cm
F1P                14.023 ppm
F1                 5611.23 Hz
F2P                -0.204 ppm
F2                 -81.56 Hz
PPMCM           0.71183 ppm/cm
HZCM          284.83956 Hz/cm
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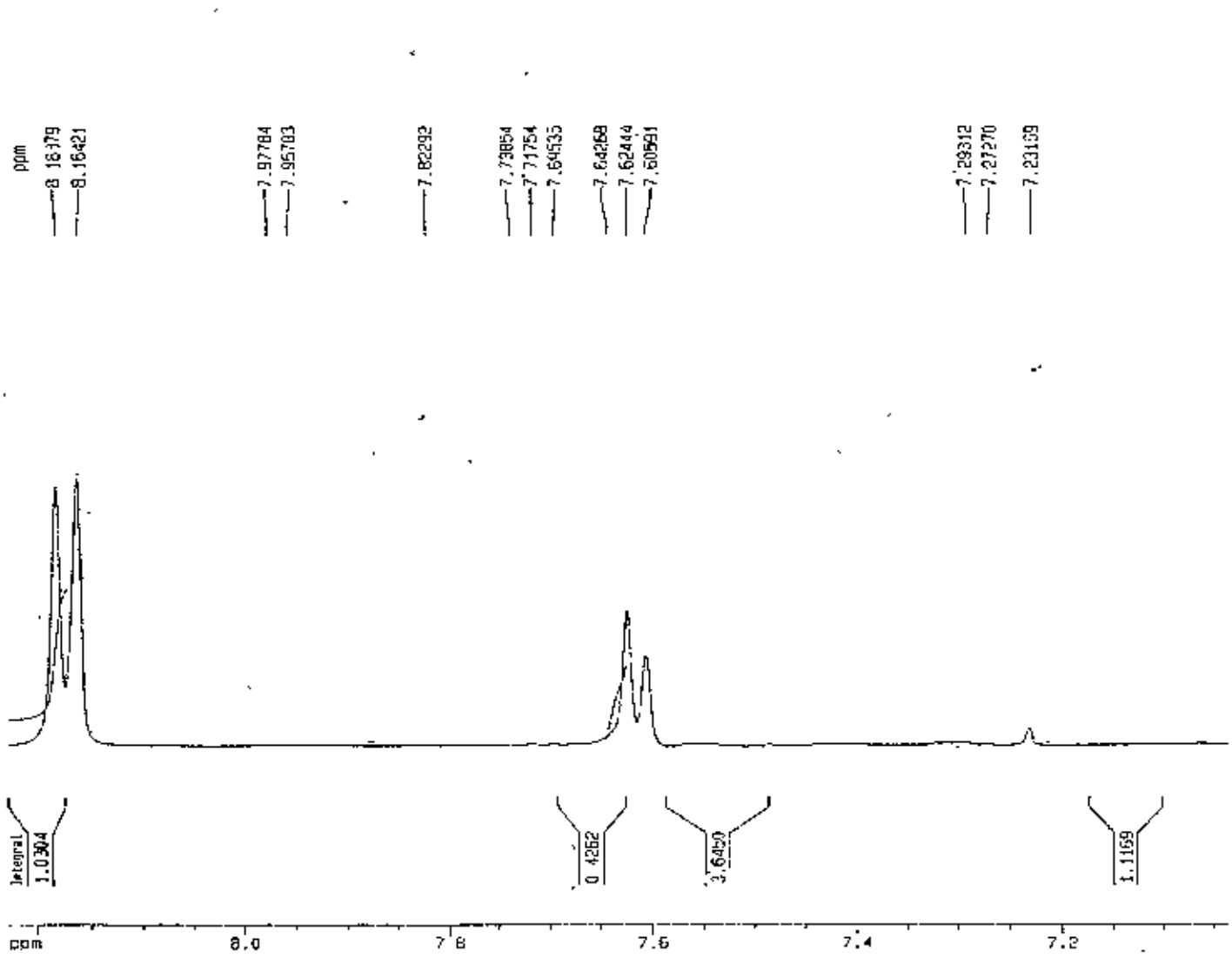
Fig. 6b ^{1}H NMR Spectrum of Compound 6A

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EXPNO                     1
PROCNO                    1

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PULPROG              zg30
TD                  32768
SOLVENT              CDCl3
NS                      29
DS                       2
SWH              6410.256 Hz
FIDRES           0.195625 Hz
AQ               2.5559540 sec
RG                    90.5
DW                78.000 usec
DE                 6.00 usec
TE                 310.0 K
D1            1.00000000 sec

========== CHANNEL f1 ==========
NUC1                  1H
P1                 8.30 usec
PL1                -6.00 dB
SFO1         400.1428010 MHz

F2 - Processing parameters
SI                   32768
SF          400.1400194 MHz
WDW                     EM
SSB                      0
LB                  0.30 Hz
GB                       0
PC                    1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                  8.227 ppm
F1                 3292.10 Hz
F2P                  7.037 ppm
F2                 2815.59 Hz
PPMCM            0.05954 ppm/cm
HZCM            23.82544 Hz/cm
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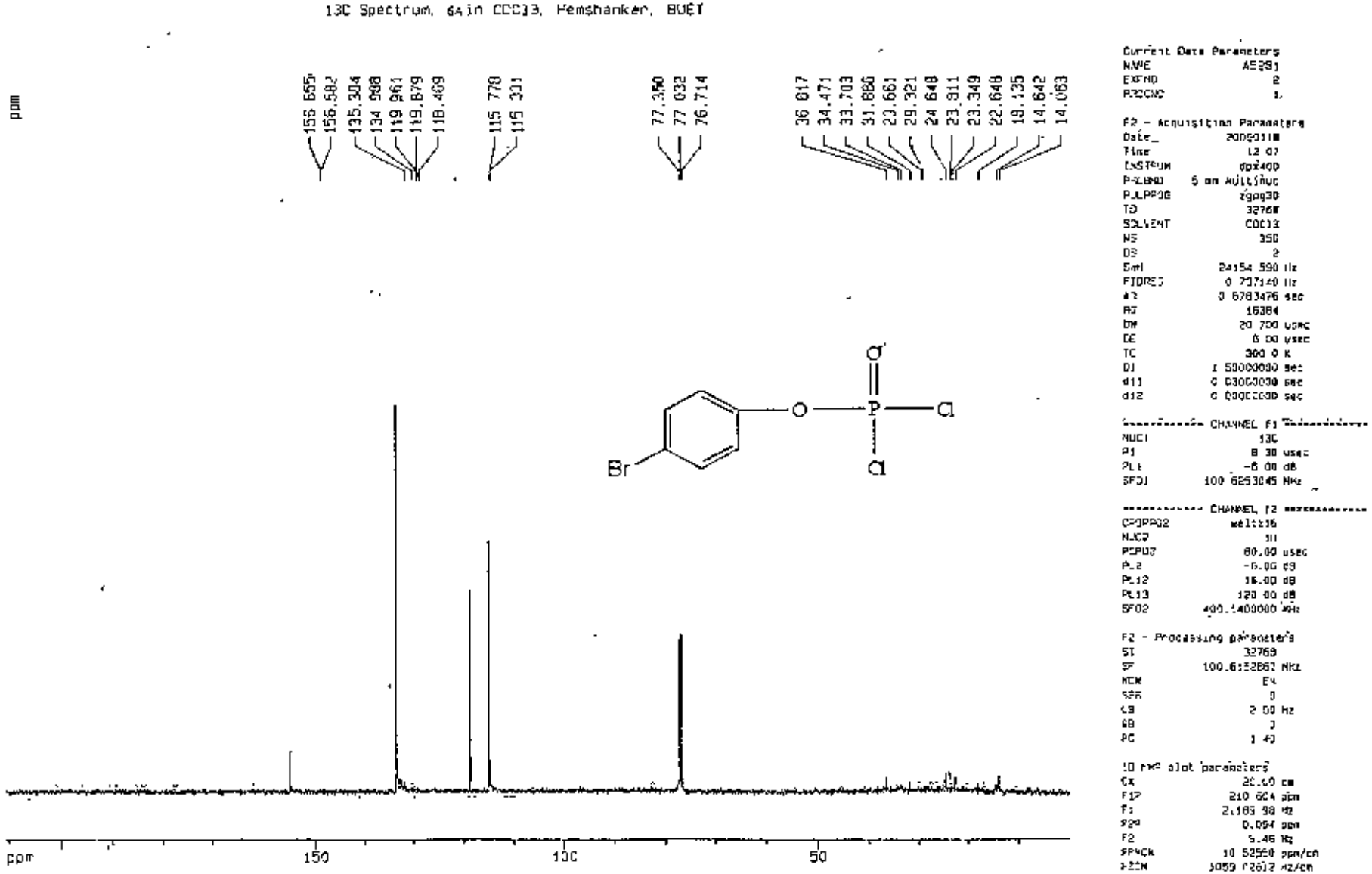
Fig. 6b ^{1}H NMR Spectrum of Compound 6A



Current Data Parameters
NAME AE281
EXPNO 2
PROCNO 1

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Date_ 20050118
Time 12 07
INSTRUM dpx400
PROBHD 5 mm Multinuc
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 350
DS 2
SWH 24154.590 Hz
FIDRES 0.737140 Hz
AQ 0.6783476 sec
RG 16384
DW 20.700 usec
DE 6.00 usec
TE 300.0 K
D1 1.50000000 sec
d11 0.03000000 sec
d12 0.00001000 sec

CHANNEL f1
NUC1 13C
P1 8.30 usec
PL1 -6.00 dB
SFO1 100.6253045 MHz

CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -6.00 dB
PL12 16.00 dB
PL13 120.00 dB
SFO2 400.1400000 MHz

F2 - Processing parameters
SI 32768
SF 100.6152867 MHz
WDW EM
SSB 0
LB 2.50 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
F1P 210.604 ppm
F1 21189.98 Hz
F2P 0.054 ppm
F2 5.46 Hz
PPMCM 10.52550 ppm/cm
HZCM 1059.72612 Hz/cm

Fig. 6c ^{13}C NMR Spectrum of Compound 6A

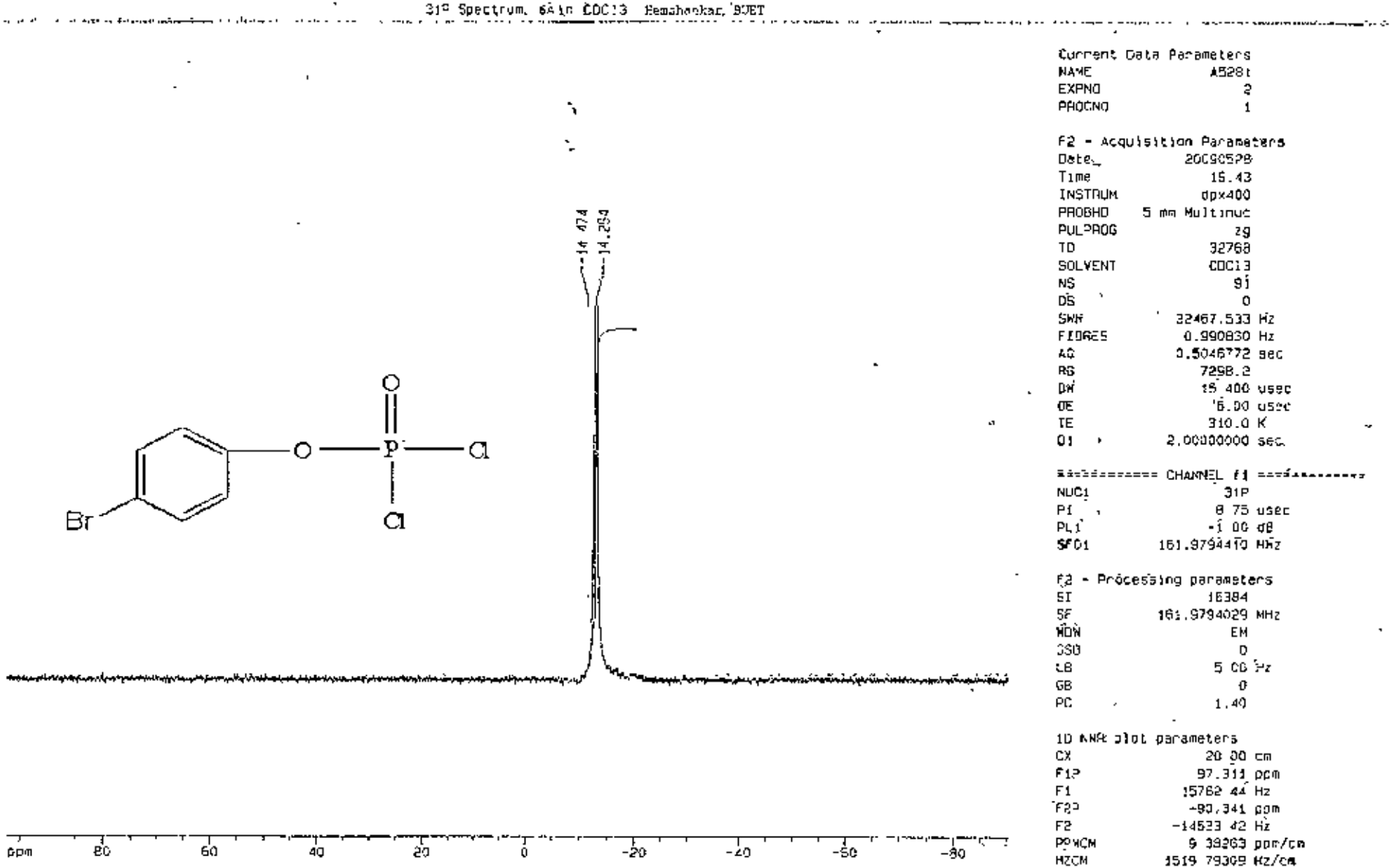

Fig. 6d ^{31}P NMR Spectrum of Compound 6A

References

REFERENCES

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