REACTIONS AND REACTIVITY
OF
NAPHTHYL AND BENZYL CARBAMATES

by

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A thesis submitted in partial fulfilment of the requirements for the degree of
MASTER OF SCIENCE, UNIVERSITY OF NATAL

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Pietermaritzburg
December 1996

DECLARATION

I hereby certify that this research is the result of my own investigation which has not been accepted in substance for any degree and is not being submitted in candidature for any other degree.

Signed : BLR Ramsingh
B.L.R. RAMSINGH

I hereby certify that this statement is correct.

Signed : ....
N.D. EMSLIE
SUPERVISOR

Signed : ....
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December 1996

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1.2.1. Pesticides

ACKNOWLEDGEMENTS

I would like to express my sincere thanks to Professor N.D. Emslie for his guidance and encouragement during the course of this project. His belief that anything is possible led to many character-building hours in the laboratory and for that I thank him. I would also like to thank Dr. B. Rahm and Professor S.E. Drewes for their help and ideas and for proofreading this document.

A special word of thanks goes to my colleagues for making my stay in the Warren Laboratory a very memorable one. My thanks especially to Debby Yoell, Frances van Staden and Paul Mason for their constant help and guidance.

I extend my thanks to the following people whose efforts were a necessary part of this work :

Mr. M. Watson and Mrs. Z. Hall for NMR and mass spectra;
Messrs. M. Somaru and W. Zondi for their willing assistance in the laboratory;
Mr. P. Forder for glassblowing;
Mr. G.D. Crawley and Mr. C. Morewood and their staff;
Ms. N. Ramesar for x-ray Crystallography.

To my parents and sisters, my deepest gratitude for the love and support they've given me all through my academic career. I have made it to this level only because of them.

I gratefully acknowledge the financial assistance of the Foundation for Research Development and the University of Natal.

And lastly, thank you to Villy for everything.

ABBREVIATIONS

am	:	amide
Ar	:	aryl
Bu	:	butyl
BuLi	:	butyl lithium
d	:	doublet
de	:	diastereomeric excess
DIBAL	:	diisobutylaluminium hydride
DMG	:	directed metalation group
D*o*M	:	directed *ortho* metalation
DMSO	:	dimethyl sulfoxide
E^+	:	electrophile
ee	:	enantiomeric excess
Et	:	ethyl
ether	:	diethyl ether
GC/MS	:	gas chromatography/mass spectrometry
h	:	hour
HMPA	:	hexamethylphosphoric triamide
^{i}Pr	:	isopropyl
LAH	:	lithium aluminium hydride
LDA	:	lithium diisopropylamide
M^+	:	molecular ion
MCPBA	:	meta-chloroperoxybenzoic acid
m	:	multiplet
Me	:	methyl
m.p.	:	melting point

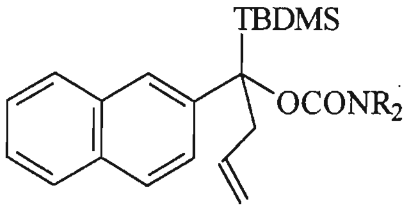
NMR	:	nuclear magnetic resonance
NOE	:	nuclear overhauser effect
Nu$^-$	:	nucleophile
PAH's	:	polycyclic aromatic hydrocarbons
Ph	:	phenyl
q	:	quartet
RT	:	room temperature
s	:	singlet
t	:	triplet
TBDMS	:	*tertiary* butyldimethylsilyl
TBDMSCl	:	*tertiary* butyldimethylsilyl chloride
THF	:	tetrahydrofuran
TMEDA	:	*N,N,N',N'*-tetramethylethylenediamine
TMS	:	trimethylsilyl, tetramethylsilane
TMSCl	:	trimethylsilyl chloride

SUMMARY

The exploitation of the synthetic utility of the carbamate functionality has largely been concerned with its effects in allylic and benzylic systems. A study was therefore undertaken to elucidate whether the functionality would display similar reactivity in naphthyl systems.

Hoppe[33] has successfully carried out electrophilic substitutions at the benzylic position of benzyl carbamates and the present work was to a certain extent concerned with extending his work to the naphthyl system. This was largely unsuccessful with a variety of electrophiles (alkyl halides, aldehydes and Michael acceptors), but electrophilic substitution of α-silyl substituted carbamates yielded interesting results.

The substitution of TBDMS-substituted *N,N*-dialkyl carbamates with allyl bromide yielded the expected disubstituted product **117**, while substitutions with piperonal yielded the Peterson olefination product **119** rather than the expected aldol alcohol **118**.



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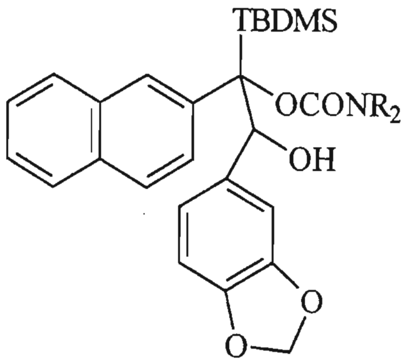
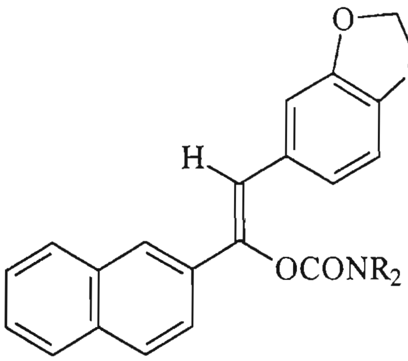


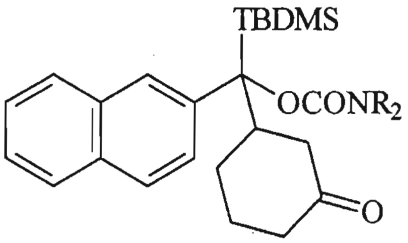
R = alkyl

(118)



(119)

The use of 2-cyclohexen-1-one as an electrophile yielded the expected product **125** as a mixture of diastereomers, while electrophilic substitution with methyl acrylate yielded the α,γ,γ-trisubstituted butanolide **129** *via* migration of the amide portion of the carbamate functionality.



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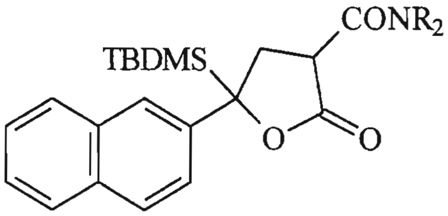
R = alkyl



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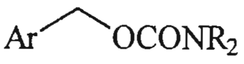
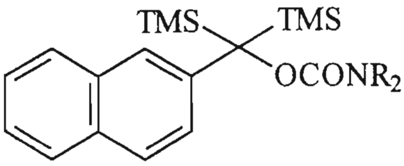
Attempts were also made to facilitate the unprecedented migration of the carbamate functionality in compounds of type **133**.



Ar = benzyl, naphthyl
R = alkyl

(133)

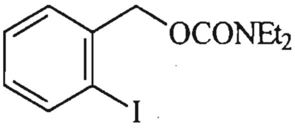
The benzylic positions which have the more acidic hydrogens were protected and migration reactions were carried out on substrates **108b** and **109b** using D*o*M techniques. However, these reactions met with no success.



R = Et **(108b)**

R = ^{i}Pr **(109b)**

The required migration reaction was successfully carried out by the use of a Li-halogen exchange reaction on 2-iodobenzyl carbamate **(142)** to yield **147**. This was cyclised to yield 1-phthalanone **148** which is found in a variety of natural products.



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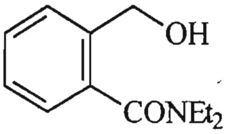

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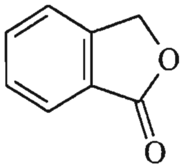

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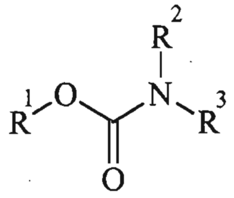
CHAPTER 1

INTRODUCTION

The aim of this project was to investigate the reactions and reactivity of the carbamate functionality **(1)**, with particular emphasis on its carbanion stabilising ability in systems where R^1 is naphthyl or benzyl.



(1)

R^1 = alkyl or aryl

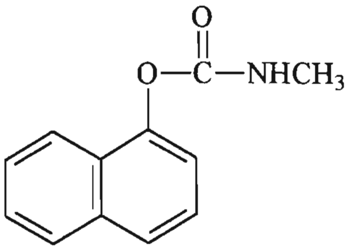
R^2, R^3 = alkyl, aryl or H

There is limited information on naphthyl carbamates in the literature and it was therefore our intention to investigate and exploit the chemistry of this system and seek areas where these carbamates might be synthetically useful.

1.1. NOMENCLATURE

1.1.1. THE CARBAMATE FUNCTIONALITY

Carbamates are esters of carbamic acid (NH_2COOH). The acid is an unstable compound which decomposes readily to carbon dioxide and ammonia.[1] Substituents attached to the nitrogen atom are termed *N*-alkyl or *N*-aryl while those attached to the oxygen are referred to by their alkyl or aryl IUPAC name. The insecticide Carbaryl **(2)** would be systematically named 1-naphthyl-*N*-methylcarbamate.



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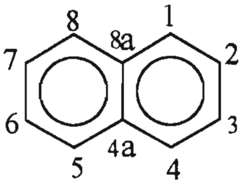
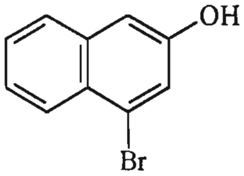
1.1.2. THE NAPHTHYL SYSTEM



(3)

In systematic nomenclature, carbon-1 of naphthalene **(3)** is the carbon adjacent to the bridgehead carbon. Substituents are given the lowest numbers consistent with this scheme and their relative priorities.[2] For example **(4)** is named 4-bromo-2-naphthol.



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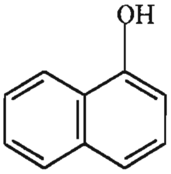

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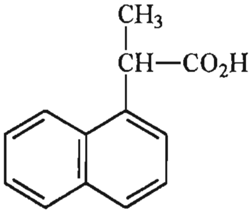


(6)

Naphthalene also has a common nomenclature that uses Greek letters. In this system, the 1-position is designated α and the 2- position as β. (5) is therefore α–naphthol or 1-naphthol.

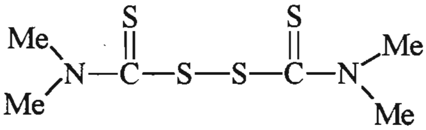
The naphthalene ring can also be named as a substituent group, the naphthyl group. The term naphthyl is analogous to the term phenyl for a benzene ring. Compound **(6)** is termed 2-(1-naphthyl)propanoic acid.

1.2. APPLICATIONS AND USES OF CARBAMATES

1.2.1. PESTICIDES

1.2.1.1. HISTORY

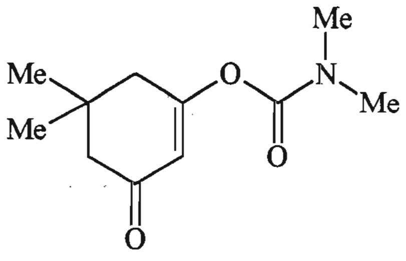
The use of chemicals to control insects dates back to classical Rome and Greece.[3] The 1800's saw the development of various pesticides like Paris green (impure copper arsenite used to control beetles). It was in 1934 that thiram **(7)**, the first of several dithiocarbamate fungicides, was patented in the USA.



$Me_2N-\overset{S}{\overset{\|}{C}}-S-S-\overset{S}{\overset{\|}{C}}-NMe_2$

(7)

In 1945, the first soil-acting carbamate herbicide was discovered by British workers and shortly afterwards the first carbamate insecticide was synthesised by Dr Hans Gysin at the Geigy Chemical company.[4] Dr Gysin's search for active insect repellents included the preparation of a series of cycloaliphatic carbamate esters, one of which was dimetan **(8)**.



(8)

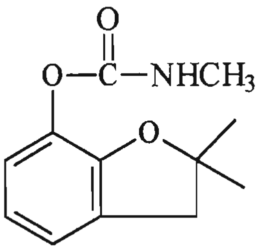
Biological testing of this compound revealed that it was remarkably toxic to houseflies, aphids and several other insects.

1.2.1.2. STRUCTURAL DIVERSITY OF CARBAMATE INSECTICIDES

There are three main structural subgroups and these are :

1. Aryl *N*-Methyl Carbamates *e.g.* Carbaryl **(2)**

2. Heterocyclic mono- or dimethylcarbamates e.g. Carbofuran (9)



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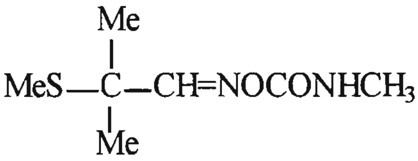
3. Oximes e.g. Aldicarb **(10)**



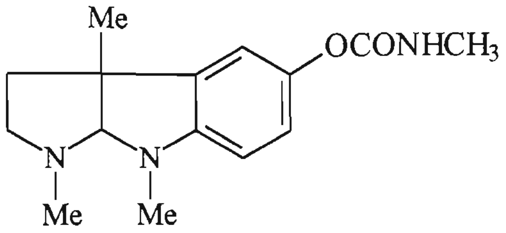
$$\mathrm{MeS{-}\overset{\displaystyle Me}{\underset{\displaystyle Me}{C}}{-}CH{=}NOCONHCH_3}$$

(10)

1.2.1.3. MODE OF ACTION

In the Calabar Province of Nigeria, during the 17th and 18th century, a person accused of witchcraft was forced to ingest a milky potion made from macerated Calabar bean seeds and a small quantity of water.[3] The condemned native was then ordered to walk around until justice was served in one of two ways. Either the prisoner was fortunate enough to regurgitate the 'milk', in which case he was declared innocent and allowed to go free, or he would develop the shakes, froth at the mouth and quickly die, thus establishing his guilt.

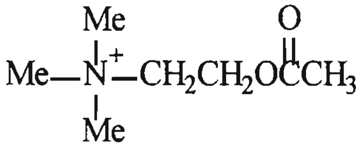
In the 1800's, the main alkaloid from these bean seeds was isolated, purified and named physostigmine (11).



(11)

Biochemically, physostigmine played a significant role in elucidating the mechanism of impulse transmission along the mammalian nervous system. It appeared that physostigmine was competing with the acetylcholine for the same sites on the enzyme that catalysed the deactivation of acetylcholine within the nervous system. This description of the mode of action of physostigmine, together with its chemical characterisation, prompted the synthesis and evaluation of numerous analogues for use in cholinergic drugs. Nearly all of these compounds possessed a carbamate moiety and, in addition, they contained either an ionisable or quaternary amine group.

Transmission of nerve impulses at the synapses depends on the successful and rapid equilibrium between acetylcholine and choline being maintained in the synapses. After the 'nerve message' has been transferred to the receptor in the post synapse membrane, the acetylcholine **(12)** is hydrolysed to choline by acetylcholinesterase and this maintains the equilibrium.



$$\mathrm{Me}-\overset{\mathrm{Me}}{\underset{\mathrm{Me}}{\overset{+}{\mathrm{N}}}}-\mathrm{CH_2CH_2O}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{CH_3}$$

(12)

If the action of acetylcholinesterase is inhibited by the carbamate, the nervous system is impeded by the slow hydrolysis of the carbamoylated intermediate, causing an undesirable accumulation of acetylcholine in the synapse and unless treated, results in the death of the affected organism.[5]

Compounds such as Aldicarb **(10)** are structurally similar to acetylcholine **(12)** by way of the trimethyl substitution and the ester type functionality, and this illustrates the way in which carbamates were specifically designed to resemble acetylcholine and yet remain sufficiently lipophilic to penetrate to their site of action in insects. This similarity of structure probably explains the very high toxicity of Aldicarb to both mammals and insects.[3]

In practice, ring systems confer on the carbamate compounds a balance of properties compatible with insecticidal action. These include sufficient penetration of lipid cuticle, transport in the haemolymph without rapid decomposition, sufficiently good attachment to acetycholinesterase to enable an enzyme-carbamate complex to be formed at low carbamate concentration and carbamoylation at an adequate rate.

The *N*-methyl carbamates inhibit acetylcholinesterase by *N*-methyl carbamoylation of the serine hydroxyl group of the enzyme in an exactly analogous way to dialkyl phosphorylation by organophosphate triesters.[6] The carbamate is destroyed in the process. Selectivity has been achieved by *N*-substitution with biodegradable groups, *e.g.* *N*-acetylation, *N*-alkyl or *N*-arylsulfenylation. Such substitution of the *N*- group of, for example, Carbofuran **(9)**, markedly reduces its toxicity to mammals whilst enhancing its insecticidal activity.

Carbamates are frequently used to control insects that, for some reason, do not readily respond to organophosphorous compounds.[3] The carbamate insecticides are particularly useful in eradicating aphids, whiteflies, ants, scale insects, cockroaches, earwigs and wasps. Some carbamates also posses special attributes that favour soil application either for the control of soil organisms or as a means of getting systemic action following uptake by the root system of the crop.

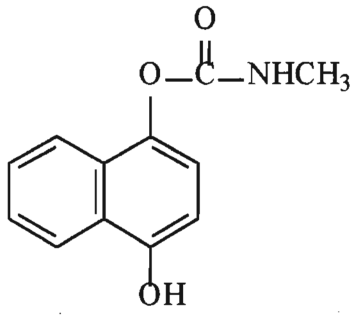
1.2.1.4. CARBARYL

Since the present work is concerned with naphthyl carbamates, some information on a well known and widely used naphthyl carbamate, Carbaryl **(2)**, is deemed necessary.

Carbaryl is a very potent contact and respiratory poison and its spectrum of action is different from that of most of the carbamic acid derivatives.[7] It is very effective against chewing insects and proved to be very effective in controlling insect pests in orchards. It is almost impossible to list all the uses of Carbaryl, but some of the most important include application to cotton, soybeans, various fruit, vegetables, cocoa, coffee, rice and sugar cane crops.[4]

Carbaryl's effectiveness against a wide range of insects and its low mammalian toxicity (rat acute oral LD_{50} is 500 mg/kg and dermal LD_{50} is >4000 mg/kg) make it an ideal compound for use around homes. With the exception of honey bees, Carbaryl presents minimal hazard to most non-target organisms including farm animals, birds, fish and other wildlife.

Owing to its widespread application, the metabolism of Carbaryl has been extensively investigated. In humans it is converted to 1-naphthol **(5)**, 4-hydroxycarbaryl **(13)** and 5,6-dihydro-5,6-dihydroxycarbaryl **(14)**.[7]



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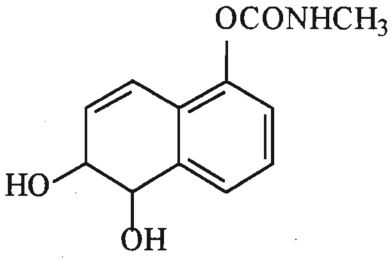
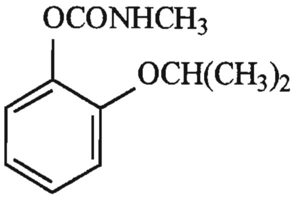


(14)

These metabolites are eliminated from the organism mainly as glucuronides or sulfates.

The success of Carbaryl encouraged the synthesis of *N*-methyl carbamates and other aromatic phenols. The most important representative of phenyl *N*-methylcarbamate containing alkoxysubstituents is 2-isopropoxyphenyl-*N*-methylcarbamate **(15)** known by the name Propoxur.



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1.2.1.5. BIOLOGICAL AND ENVIRONMENTAL STABILITY

The success of a compound as a commercial insecticide is largely dependent on its ability to resist chemical and biochemical transformations. Ideally the insecticide must be sufficiently stable to effect pest control and its degradation profile should be such that no toxic residues persist to create health and environmental hazards. This is impossible to balance completely and one can only attempt to establish the optimal ratio between efficiency and safety.

As a class, the carbamates are not long term contaminants and do not persist in the environment as long as many of the organochlorine insecticides do. Paradoxically, it is this apparent environmental instability that has restricted many of the carbamate insecticides to the laboratory and prohibited their commercial use.

From the standpoint of human exposure, commercial carbamates, when applied according to the instructions on the label, have a good safety record. They have not become a significant residue in the human diet, nor are they found in human body fat.[4] Research in countries such as Brazil, India and Venezuela where 40% of the pesticide poisoning-related deaths are caused by organophosphates and carbamates, indicates that carbamates are toxins nonetheless and there should therefore be concern about their use and the possible side effects which accompany their application.[8]

1.2.1.6. HYDROLYSIS OF CARBAMATES

Although the conditions required for destruction by air, light and heat are quite drastic, hydrolysis of carbamates in alkaline media occurs with relative ease and it is this degradative pathway that most seriously limits the chemical stability of carbamate insecticides.

Early studies demonstrated that susceptibility to hydrolysis is especially determined by the substituent attached either to the aromatic ring or to the carbamate nitrogen. Changing the *N*-substituents illustrated that resistance to attack followed the order, *N*-phenyl < *N*-ethyl < *N*-methyl, *i.e.* *N*-methyl carbamates were the most stable.[4]

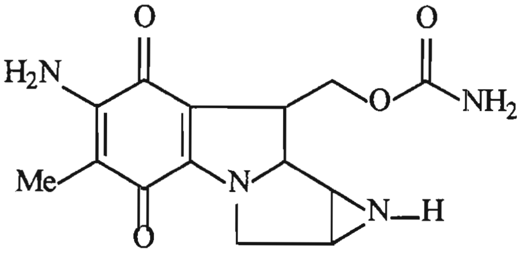
A later study with several different compounds confirmed the superiority of *N*-methyl derivatives by showing that the ability of *N*-alkyl groups to stabilise the carbamate ester bond was in the order *N*-isopropyl < *N*-diethyl < *N*-propyl < *N*-methyl. Furthermore, the corresponding N,N-disubstituted carbamates were even more resistant to hydrolysis than their mono-substituted counterparts. However, the relative ranking was different, particularly with respect to the dimethyl analogue as indicated by the following series - *N,N*-dimethyl < *N,N*-diethyl < *N,N*-dipropyl < *N,N*-dibutyl < *N,N*-diisopropyl.

Greater protection from hydrolysis by doubly substituting the carbamate nitrogen atom has also been demonstrated for various physostigmine derivatives. In addition it has been reported that a wide array of aromatic *N*-methylcarbamates hydrolyse 10^3 to 10^7 times faster than corresponding *N,N*-dimethylcarbamates.

1.2.2. MEDICINAL USES OF CARBAMATES

Carbamates are used as antiseptics,[9] local anaesthetics,[10] anti-convulsants,[11] anti-leukaemia agents[9] and muscle relaxants. [12] Physostigmine has recently been found to be useful in the treatment of Alzheimer's Disease.[13,14,15]

Mytomycin C **(16)** is a highly toxic antitumour antibiotic extracted from *Streptomyces caespitosis*. The molecule contains 3 recognised carcinostatic groups, *viz.* an aziridine, a carbamate and a quinone. It is clinically administered for the treatment of carcinomas of the breast, lung, colon and stomach.[16]



(16)

Ethyl carbamates inhibit mitosis, making it an effective agent for the treatment of leukaemia and multiple myeloma.[9]

1.2.3. INDUSTRIAL USES OF CARBAMATES

Carbamates have been used in hair conditioners,[17] as plasticisers for rubbers,[18] and as successful extractants of hydrocarbons from crude oil in the petroleum industry.[19] They have been found to be better insulators than most polystyrenes and therefore have an important use in the refrigeration industry.[20]

1.3. CARBAMATES IN ORGANIC SYNTHESIS

1.3.1. CARBAMATES AS PROTECTING GROUPS

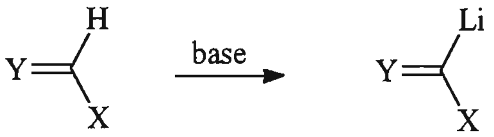
Many carbamates have been used as protecting groups in organic synthesis. Their use has been quite extensive in peptide synthesis,[21a,b,c] where they prevent racemization of activated amino acids, thereby preventing the formation of undesirable biologically inactive oligo- and cyclopeptides. As with any protecting group in organic synthesis, ease of removal is of great importance and here again carbamates demonstrate usefulness. Carbamates suit the criterion required for effective protecting groups in that individual carbamates have very specific conditions for their removal *e.g.* benzyl carbamates are cleaved by catalytic hydrogenation and hydrolysis while *tert*-butyl carbamates are cleaved only by β-elimination using a base.[22]

In addition to its use as a protecting group in organic synthesis, the carbamate moiety has been found to be an effective substituent on macrocyclic rings, where it improves the binding ability of macrocyclic receptors to alkali metal cations.[23] These macrocycles have found use in the development of host-guest chemistry.

1.3.2. ACTIVATING AND STABILISING ABILITY OF CARBAMATES

1.3.2.1. α-METALATION

Alpha-metalations are deprotonations of olefinic, aromatic or other π-systems at the sp^2 carbon alpha to a heteroatom[24] **(Scheme 1)**. The product of this deprotonation is usually a heteroatom-stabilised α-metalated complex which can in turn be reacted with electrophiles.



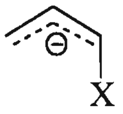
$X = NR_2, OR, SiR_3$

$Y = alkyl$

Scheme 1

The inductive effect of the α-activator greatly increases the acidity of the adjacent C-H bond and α-lithiations are therefore facile.

Heteroatom substituted allylic anions **(17)** serve as homoenolate anion equivalents.[25]

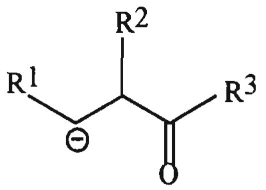


$X = NR_2, OR, SiR_3, SR$

(17)

Homoenolates have been found to be useful intermediates in the synthesis of γ-lactones.[26] Substitution can occur at both the α- or β-positions, creating problems with regioselectivity. The nature and size of the groups attached to the heteroatom, the counter ion, temperature and reaction time all influence the regioselectivity of the reaction.

Among the synthetic equivalents of the homoenolate anions[25,27] **(18)** are the *o*-substituted oxy-allyl anions **(19)**.



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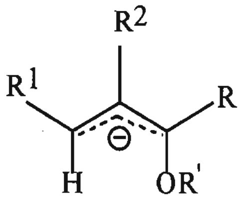
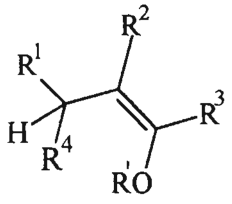


(19)

Oxy-allyl anions **(19)** are generally γ-alkylated to form enol ethers **(20)** using alkyl halides. However on addition of carbonyl compounds, the regioselectivity diminishes and the α-adduct **(21)** predominates.



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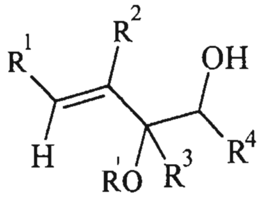
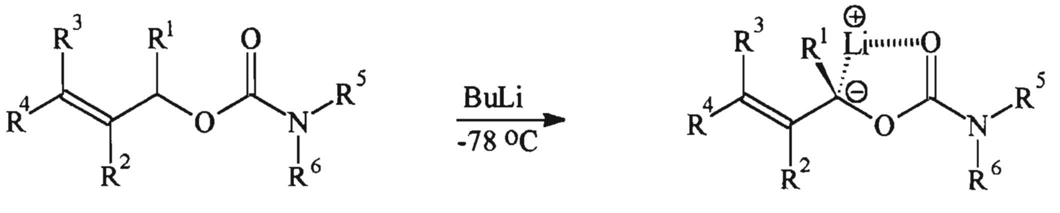


(21)

R^{1-4} = alkyl

In addition to the limitation associated with regioselectivity, it has been found that the stability of the anion **(19)** is drastically reduced by alkyl groups in the electron-rich α- and β-positions. Increasing the alkylation also makes it difficult to generate the allyl anions.

In 1980, Hoppe[28] reported a novel type of 1-oxy-allylanion which was found not to suffer the limitations discussed above. Hoppe found that in the presence of *N,N*-dialkycarbamoyloxy groups in the allylic ester **(22)**, highly stabilised carbamate lithium complexes **(23a)** resulted upon deprotonation **(Scheme 2)**.



(22)

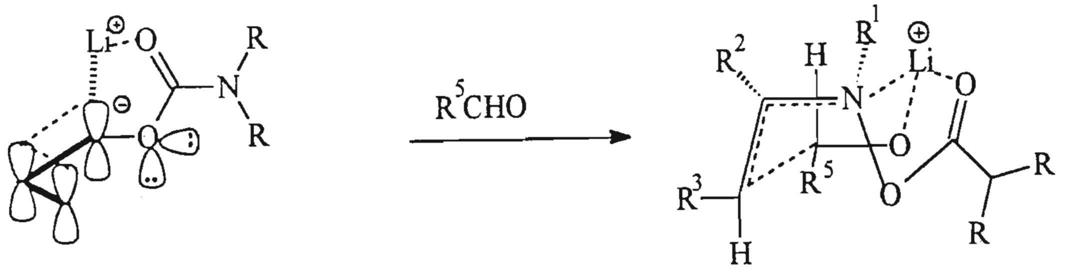
(23a)

R^{1-6} = alkyl

Scheme 2

It has been found that the presence of dialkylcarbamoyloxy groups in the ester increases the kinetic acidity of the α-protons, by chelation, to the extent that alkyl substituted allyl derivatives can also be deprotonated. Regioselectivity can be influenced by the steric interaction of the alkyl substituents attached to the nitrogen atom of the carbamate, as well as the position of the substituents, *i.e.* higher substitution of the α-position can be forced by the presence of substituents in the γ-position and *vice versa*.

A clearer illustration of the lithiated complex **(23a)** is given by **(23b)**, **Figure 1**. Species **(23b)** has been termed a "tight ion pair" in which the lithium counter ion is held at the α-position by complexing with the oxygen of the carbamoyl functionality, hence facilitating reaction of a carbonyl compound at the γ-position *via* a six-membered transition state **(24)**.



(23b) **(24)**

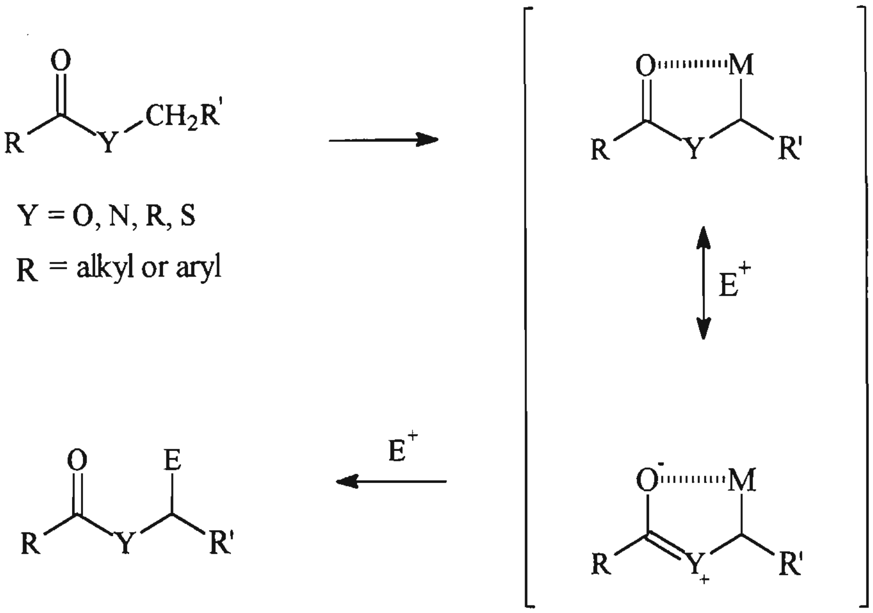
Figure 1

The advantages of having the carbamate group in the allylic system are:

a) The "tight ion pair" **(23a/23b)** is stable up to -50 ^{0}C, unlike allyl anions **(19)** which decompose rapidly at temperatures higher than -78 ^{0}C. The complexing ability of the carbamoyl oxygen[29] with the lithium cation is responsible for this high thermodynamic stability. The complexing power of the carbamate is also responsible for the enhanced kinetic acidity of the α-proton in **(22)**.

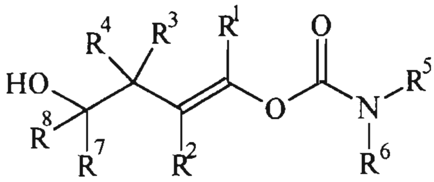
b) Reliable γ-regioselectivity is observed when **(23a/23b)** reacts with both alkyl halides and carbonyl compounds.[30]

Beak and co-workers[31a,b,c] have also presented evidence that metalations can occur adjacent to oxygen, nitrogen, and sulfur when the heteroatom is conjugated to a carbonyl group and they suggested that the resultant lithiated species be termed a dipole-stabilised carbanion. In addition they recognised the potential for synthetically useful electrophilic substitution at this position. In 1978, they presented evidence that stability of the carbanions was enhanced by the carbonyl group (**Scheme 3**).[32]

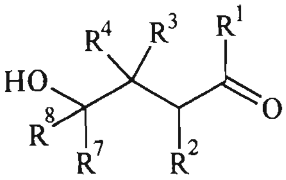


Scheme 3

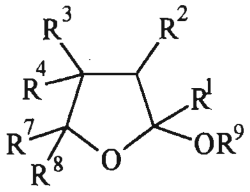
A particularly important use of **(23a/23b)** involves the formation of γ-hydroxyenolcarbamates **(25)** by reaction with aldehydes and ketones at the γ-position. These γ-hydroxyenolcarbamates are synthetically useful since they yield γ-hydroxycarbonyl compounds **(26)** (homoaldol products) and lactols **(27)** or lactol ethers **(28)** upon solvolysis with $TiCl_4/H_2O$ or MeOH.



(25)

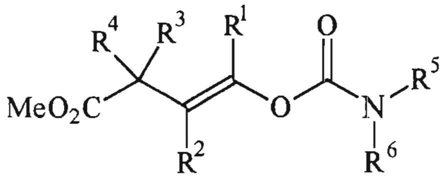


(26)

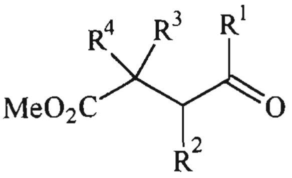


R^9= H **(27)**
R^9= CH_3 **(28)**

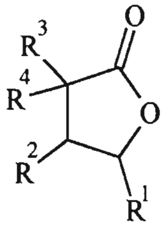
Reaction of **(23a/23b)** with dimethyl carbonate yields 4-carbamoyloxy-3-butenoate **(29)** which is a useful intermediate in the one-pot synthesis of 4-oxo-alkanoates **(30)** and butanolides **(31)**.[28]



(29)

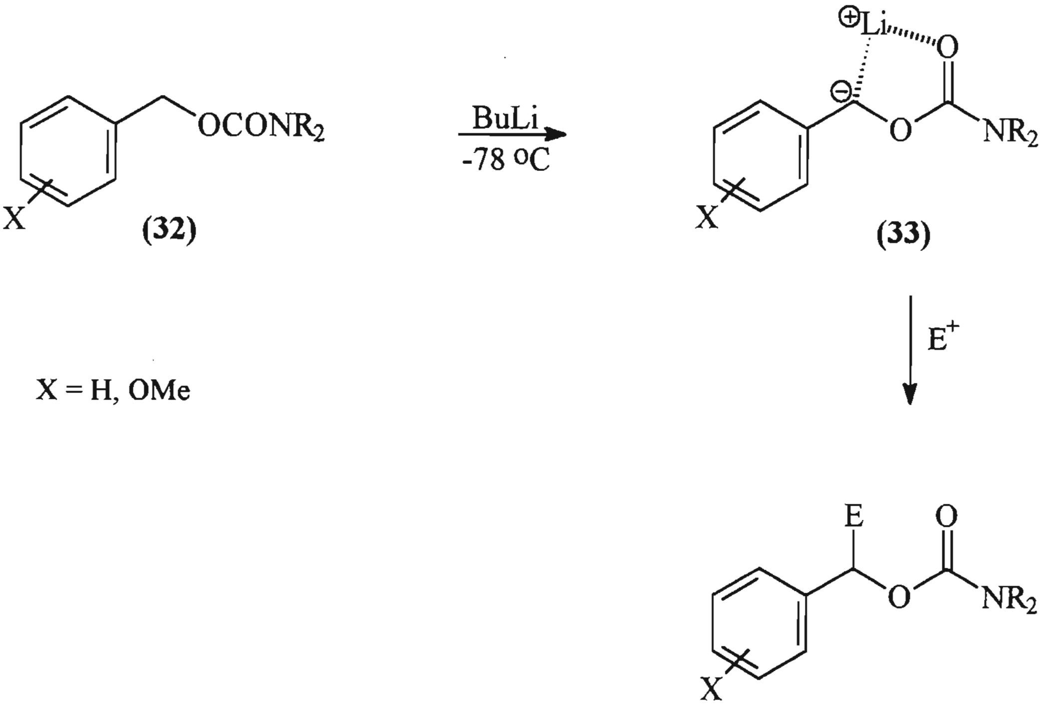


(30)



(31)

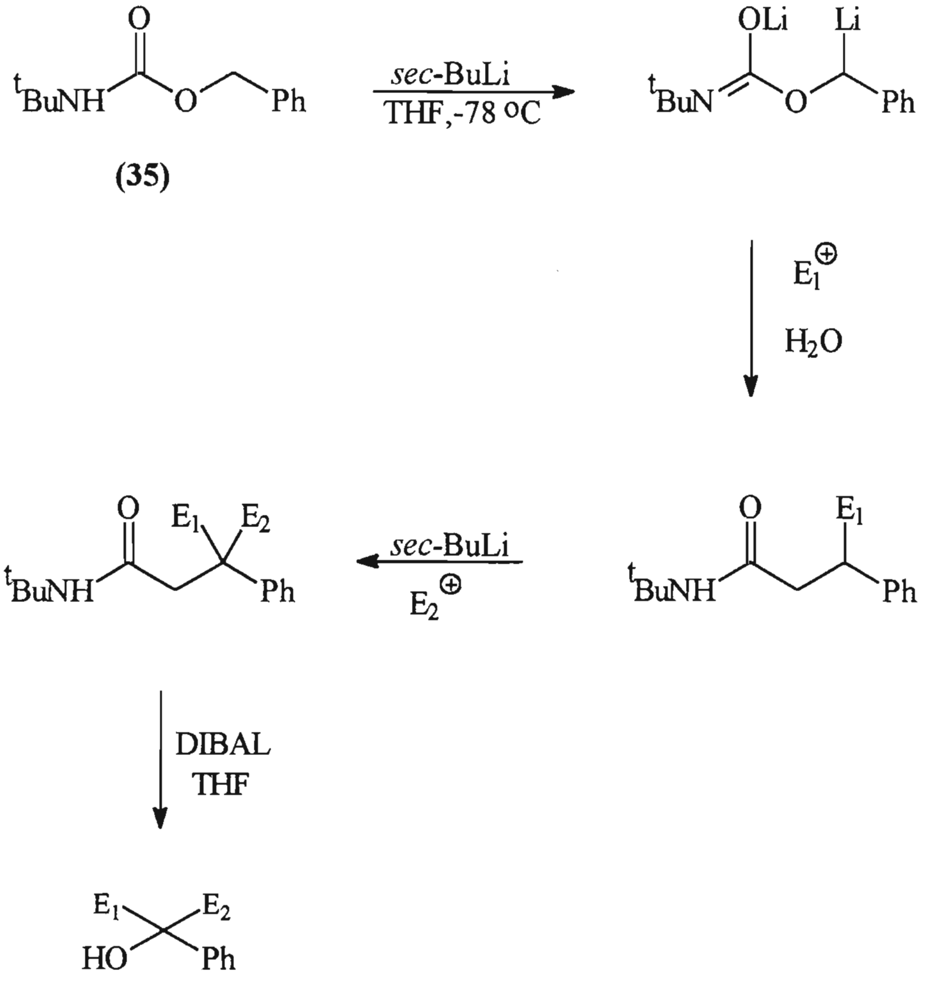
Benzylic type *N,N*-dialkylcarbamates **(32)** have been deprotonated and substituted with a variety of electrophiles (E^+) affording α-substituted benzyl carbamates **(34)** in generally high yields **(Scheme 4)**.[33,34]



Scheme 4

Here again, the carbamate system enhances C-H acidity and stabilises the lithium complex **(33)** to such an extent that benzyl carbamates with electron-donating substituents on the phenyl ring are smoothly deprotonated. In addition, there is no lithiation on the phenyl ring.

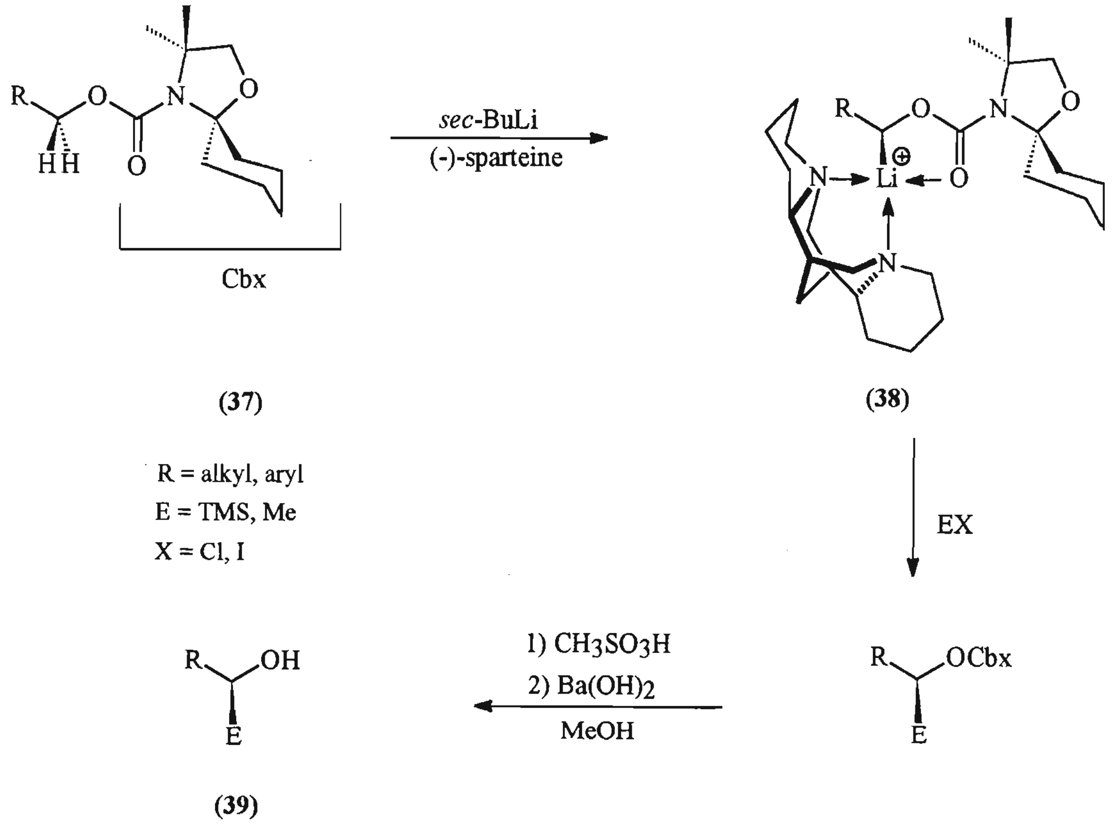
Tert-butyl benzyl carbamates **(35)** **(Scheme 5)** have provided building blocks for optically active secondary and tertiary benzyl alcohols.[35] Treatment of the carbamate with 2 equivalents of *sec*-BuLi prior to quenching with electrophiles yielded alkylated carbamates in over 80% yield. Treatment of the substituted carbamate with a further 2 equivalents of *sec*-BuLi and reaction with another electrophile led to disubstituted benzyl carbamates. Cleavage of the carbamate using DIBAL in THF, gave excellent yields of tertiary alcohols **(36)**.



(35)

(36) **Scheme 5**

Hoppe[34,36] has reported a method for the direct generation of highly enantiomerically pure α-oxycarbanions derived from 1-alkanols by simple asymmetric deprotonation. The reaction consists of the simultaneous protection of the hydroxy group and activation of the α-protons by a sterically demanding oxazolidine-derived carbamoyl residue **(37)** **(Scheme 6)**, followed by the application of the complex formed from *sec*-BuLi and the readily available alkaloid, (-)-sparteine. This chiral base system is capable of achieving a very efficient selection between enantiotopic protons. The lithium carbanion **(38)** is configurationally stable in ethereal solution below -30 °C and adds to electrophiles with good stereoretention. The oxazolidine carbamoyl residue is removed by sequential acid and base treatment to give the alcohols **(39)** usually with > 95% ee.



Scheme 6

The work has been extended to include 1,3- and 1,4-dioxy substituted carbanions[37] and the generation of configurationally stable enantioenriched α-oxy-α-methylbenzyllithium.[38] Enantioselective deprotonation is also useful in systems containing 2-hydroxyalkanoic acids, secondary alkanols[36] and alkanediols.

1.3.2.2. β-Metalation

Many modern synthetic targets, in particular those of interest for pharmacological and agrochemical preparations are either benzenoid or incorporate key aromatic or heteroaromatic components. Functional group introduction by classical electrophilic substitution to prepare contiguously substituted systems (1,2-,1,2,3- and 1,2,3,4-) can become a demanding challenge. These reactions often suffer from harsh conditions and formation of mixtures of positional isomers.

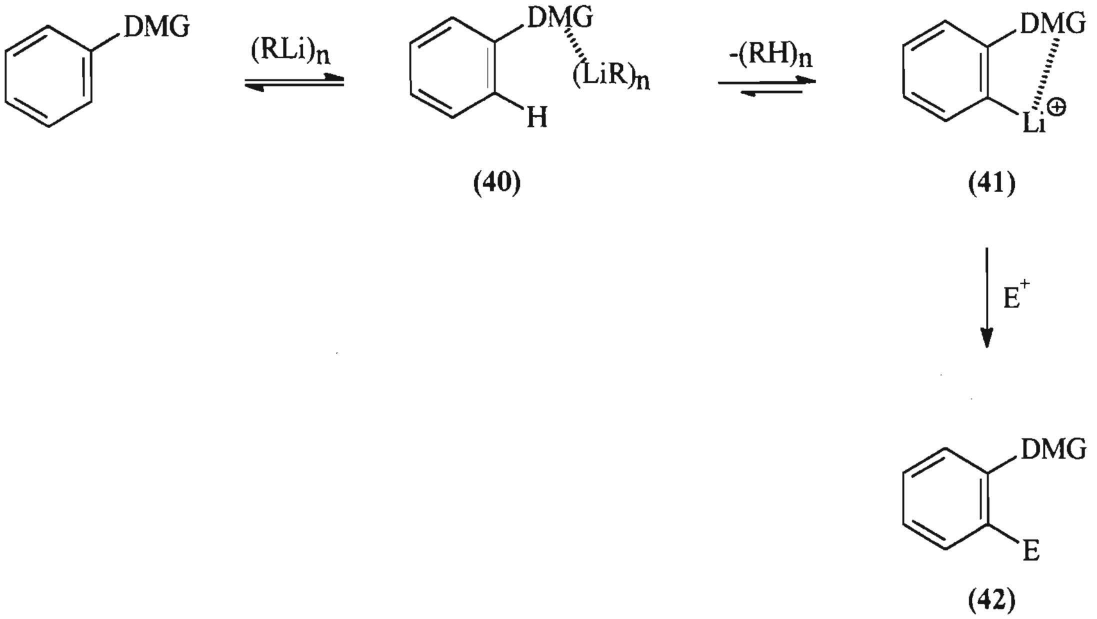
In 1939-1940, the independent discovery by Gilman and Bebb[39] and Wittig and Fuhrmann[40] of anisole *ortho*-deprotonation by *n*-BuLi constituted a new conceptual framework in synthetic organic chemistry. This Directed *ortho* Metalation (D*o*M) process initiated reactivity studies by Gilman[41] and Hauser[42] who expanded the scope of Directed Metalation Groups (DMG's). The complimentary technique of metal-halogen exchange also discovered by Gilman[43] and Wittig[44] provided further impetus into this area. Comprehensive reviews[24,45] of the D*o*M reaction have increased appreciation of this truly versatile reaction.

The D*o*M reaction **(Scheme 7)** comprises the deprotonation of a site *ortho* to a heteroatom-containing DMG by a strong base (usually an alkyllithium reagent). The reaction is believed to be a 3-step process[45]:

i) Co-ordination of $(RLi)_n$ to the heteroatom of the DMG **(40)**

ii) Deprotonation to give the co-ordinated lithiated species, *i.e.* the DMG stabilised ortho lithiated complex **(41)**

iii) Reaction with the electrophile to afford the product **(42)**



(40) (41) (42)

Scheme 7

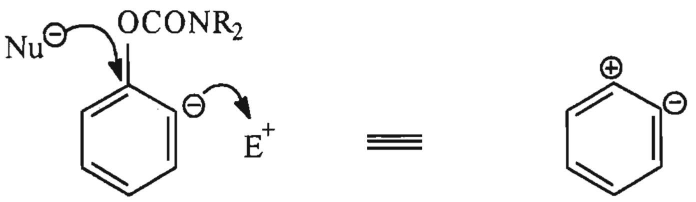
There are over forty different DMG's and one of the most powerful and successful of these is the carbamate. The carbamate moiety fulfills adequately the requirements of a DMG, *viz.* that it must behave as a good co-ordinating site for the alkyllithium and as a poor electrophilic site for attack by the base.

The stability of the lithiated species **(41)** is a result of the effective co-ordination of the lithium with the carbonyl oxygen of the carbamate group. This co-ordinating ability of the carbamate makes it a very powerful ortho-directing group resulting in products of high regioselectivity.

Subsequent hydrolysis of *o*-aryl carbamates results in *ortho*-substituted phenols. Hydrolysis can be achieved either by treatment with NaOH in MeOH or by refluxing with LAH in THF and protonating with a mild acid.

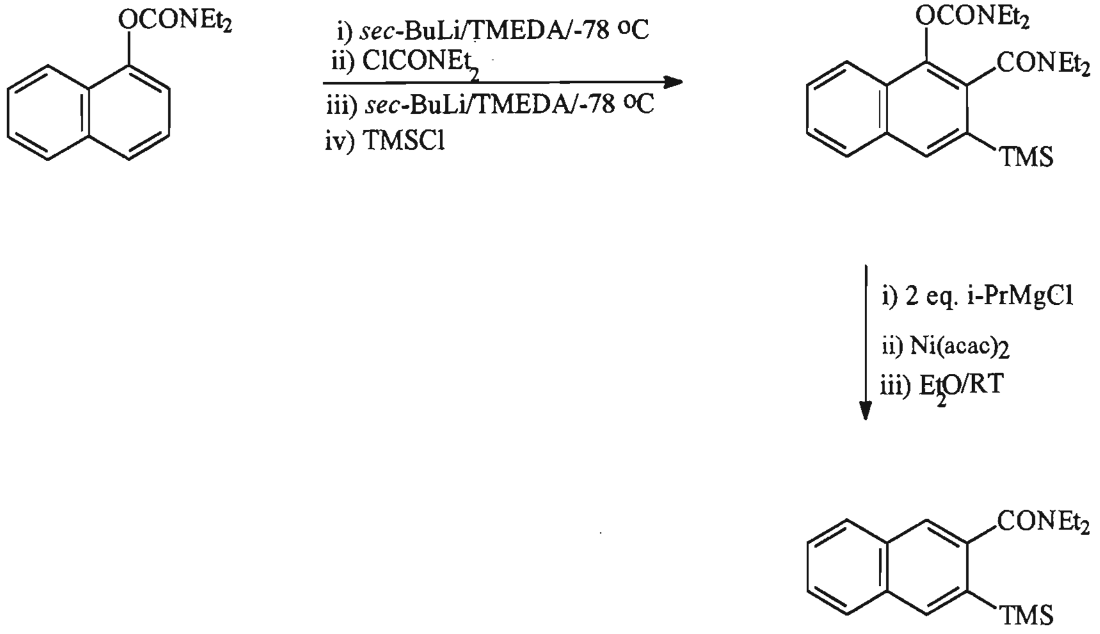
The only directing group with similar directing abilities to the carbamate is the amide DMG. Both these DMG's are not restricted to *o*-phenyl carbamates. Their synthetic utility has been exploited in both 1-naphthyl [46] and *o*-pyridyl[47] ring systems.

Carbamate protected phenols allow for ortho-substitution *via* combined D*o*M-nucleophilic substitutions and this introduces the concept of a 1,2-dipole equivalent **(43)**.



(43)

An example of the application of the 1,2, dipole equivalent is shown in **Scheme 8**.



Scheme 8

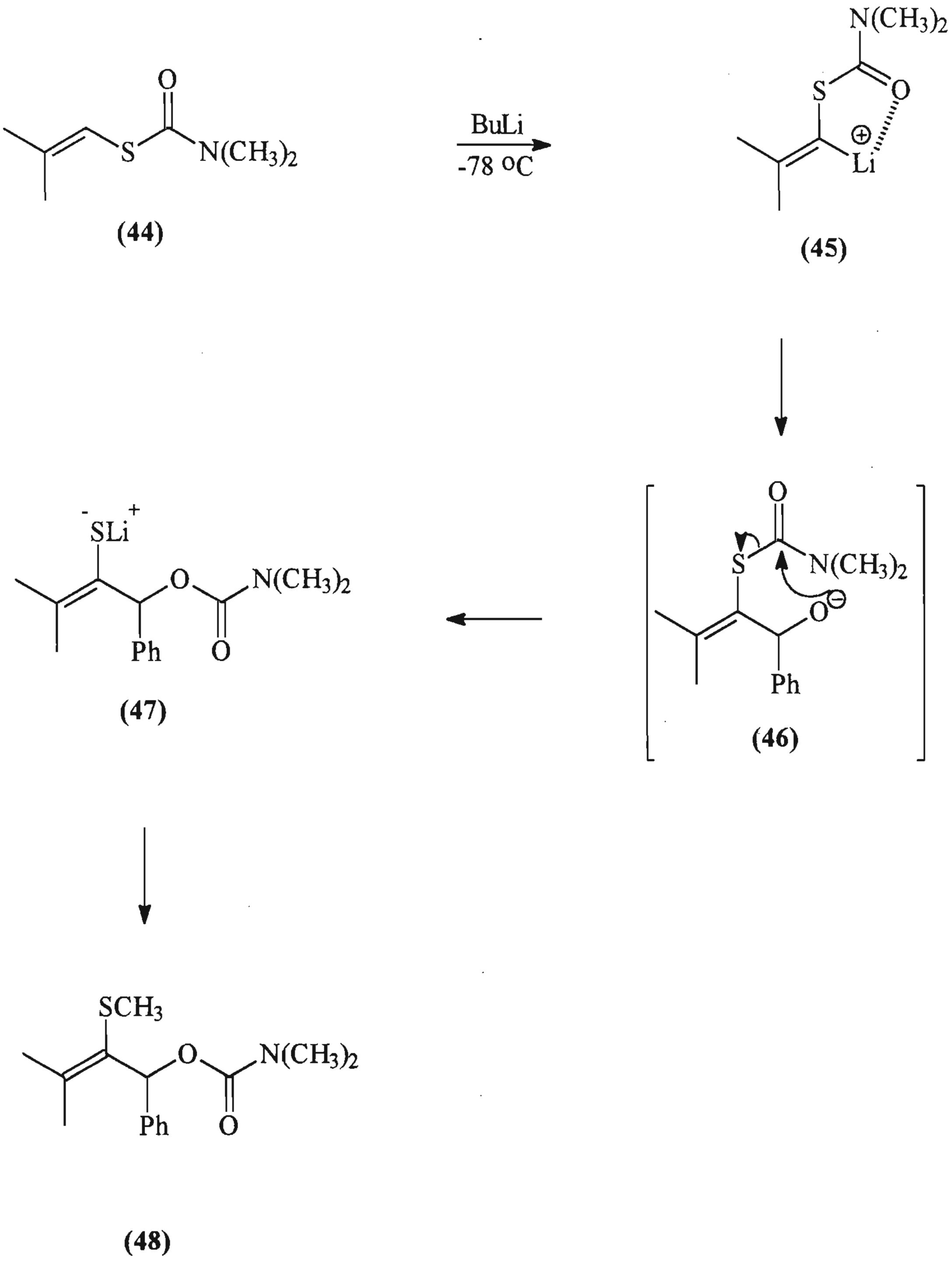
D*o*M applications have provided synthetic routes to polysubstituted aromatic compounds, polysubstituted pyridines,[47] naphthyls, phenanthryls, binaphthyls and quinolines.

1.3.3. MIGRATIONAL ABILITY OF CARBAMATES

The discovery of the migrational property of carbamates stimulated further use of this moiety in synthetic organic chemistry. The first reported migration of the carbamate was in 1980[49] and it involved the intramolecular transfer of the amide portion of the carbamate from a sulfur atom to an oxygen atom.

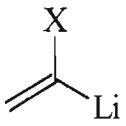
S-vinylthio-carbamate **(44)** was deprotonated at the α-position with BuLi at -78 °C yielding **(45)**, a carbamate stabilised lithium complex **(Scheme 9)**.

Reaction of **(45)** with benzaldehyde at -78 °C yielded the lithium enethiolate **(47)** which was trapped as the methyl vinyl thioether **(48)** with MeI without the initial adduct **(46)** being isolated.

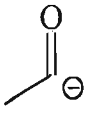


Scheme 9

The 'umpolung' (polarity reversal) principle first enunciated by Corey and Seebach[50] has become a powerful concept in synthetic design. The discovery of α-lithiation of allylvinyl ethers[51] and allylvinyl sulfides[52] has allowed the emergence of a distinct group of α-heteroaromatic substituted olefins **(49)** as valuable umpolung synthons. In their simplest form, these constitute readily available acyl anion equivalents **(50)**.



(49)

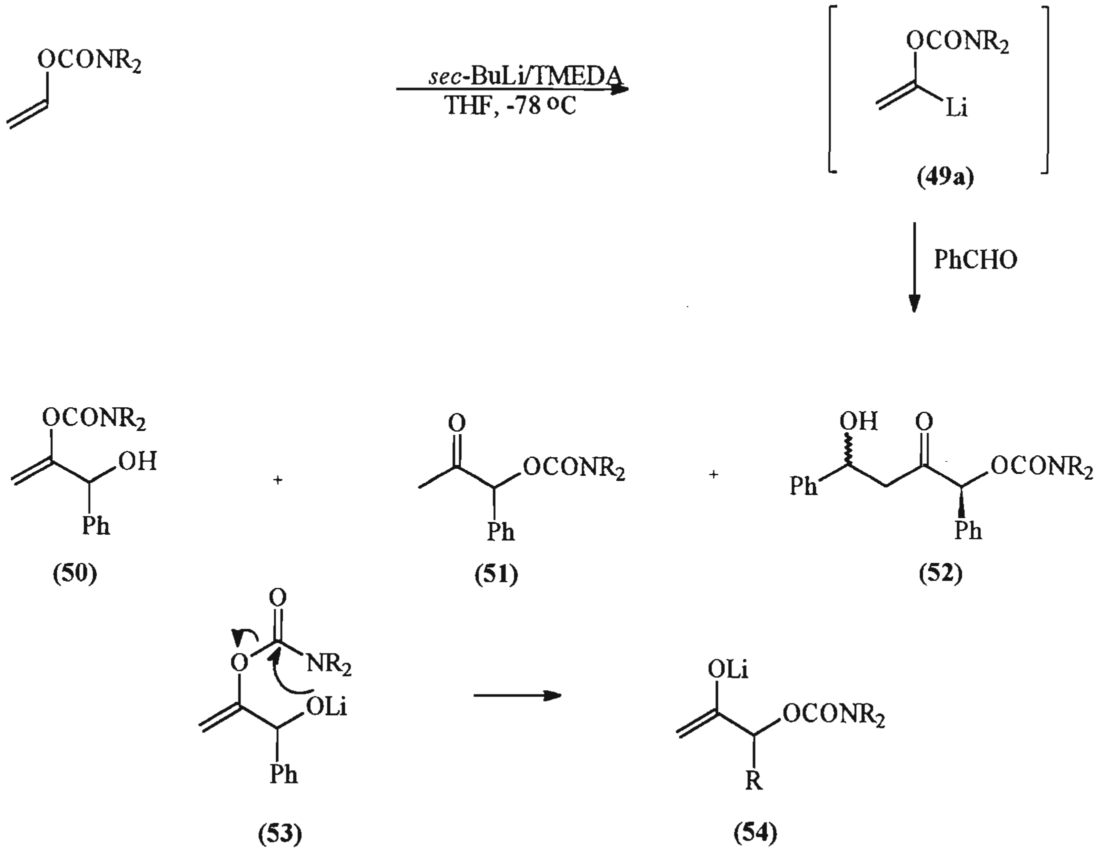


(50)

X = OR, SR, SO_2 R, SeR, NR_2,
Hal, $OCONR_2$

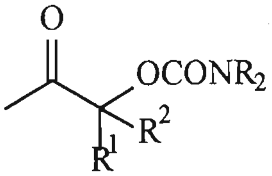
Work by Sengupta and Snieckus[53] involving the reaction of α-lithioenol carbamates (**49a**, X=$OCONR_2$) (**Scheme 10**) with aldehydes and ketones is markedly different from the reactions observed with other α-heteroatom vinylmetallics. Thus the reaction with benzaldehyde (-78 °C, 30 min) afforded **(51)** (53-60%) and **(52)** (20-30%) as major products with minor amounts of **(50)**.

The product distribution can be rationalised in terms of a facile carbamoyl transfer in the initial adduct **(53)** leading to the enolate **(54)** which upon further aldol condensation with benzaldehyde gives rise to **(52)**.



Scheme 10

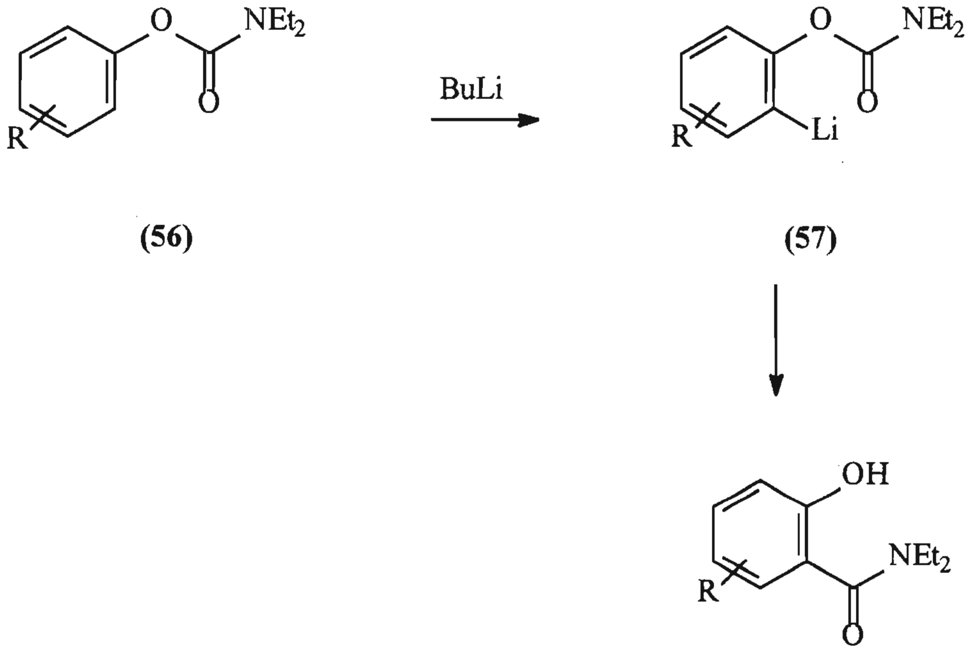
This intramolecular carbamoyl transfer is extremely rapid and remains unaffected by variations in temperature and solvents. Analogous carbamoyl transfer was observed in reactions of **(49a)** with ketones resulting in acyloin carbamates **(55)**.



(55)

Similar reactivity between lithium enolates of difluoroketones and non-enolisable aldehydes has been noted.[54] The reactions result in difluoroaldol products in 55-70% yield.

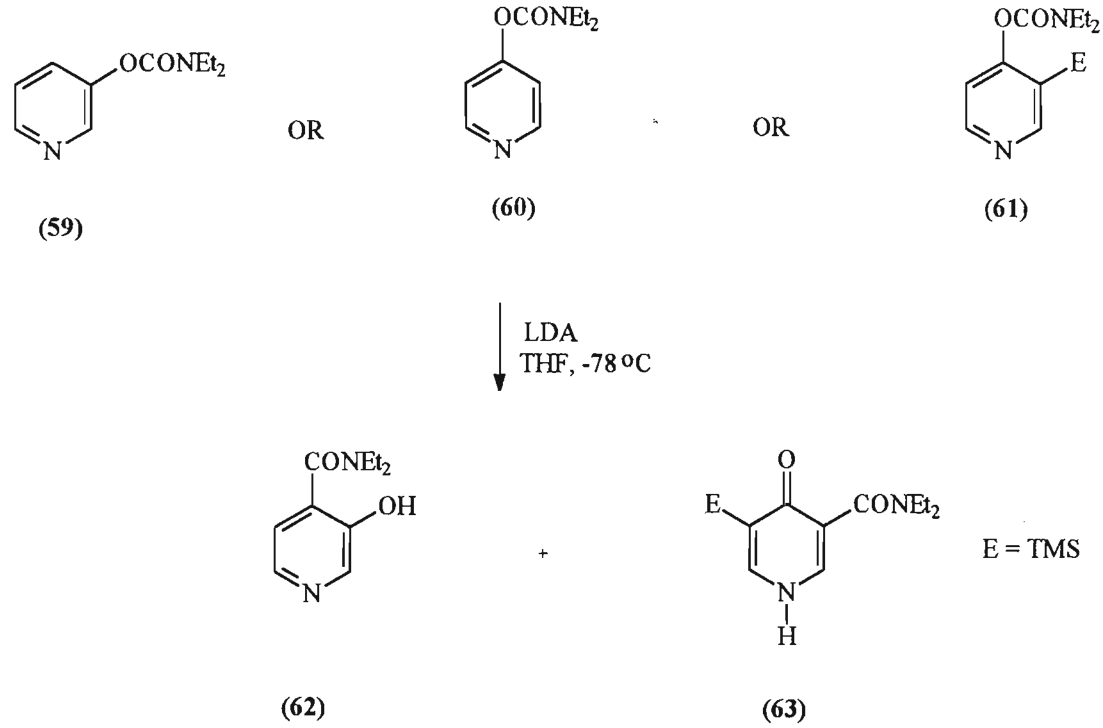
In 1983 Snieckus[46] reported the directed metalation reaction of *o*-aryl carbamate **(56→57)** and described the unprecedented O→C 1,3-carbamoyl migration of the ortho-lithiated species **(57)** to give salicylamides **(58)** **(Scheme 11)**.



Scheme 11

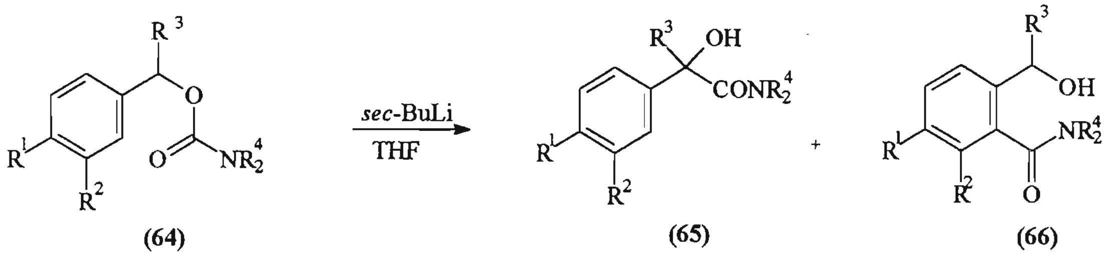
The migration occurred when **(57)** was allowed to warm up to room temperature in the absence of electrophiles. This oxygen to carbon migration is the anionic equivalent of the Fries rearrangement[55a-c] and is synthetically useful since it transfers an amide which is a powerful DMG to an ortho site from which it may promote further metalation reactions.

By analogy to the *o*-aryl carbamates, the metalated pyridyl carbamates **(59, 60, 61)** undergo the anionic Fries rearrangement to give isonicotinamide **(62)** and nicotinamide **(63)** **(Scheme 12)**.[47] These diversely functionalised pyridines are useful in heterocyclic and natural product synthesis.



Scheme 12

Gawley[56] reported an interesting combination of the work of Snieckus[46] **(Scheme 11)** and Hoppe[29]**(Scheme 4)**. He reported that lithiated benzylic carbamates derived by treatment with LDA/*sec*-BuLi in THF undergo two different carbamoyl migration reactions *viz.* 1,4 transfer to the *ortho* position **(66)** or 1,2- transfer to the benzylic position **(65)** **(Scheme 13)**.

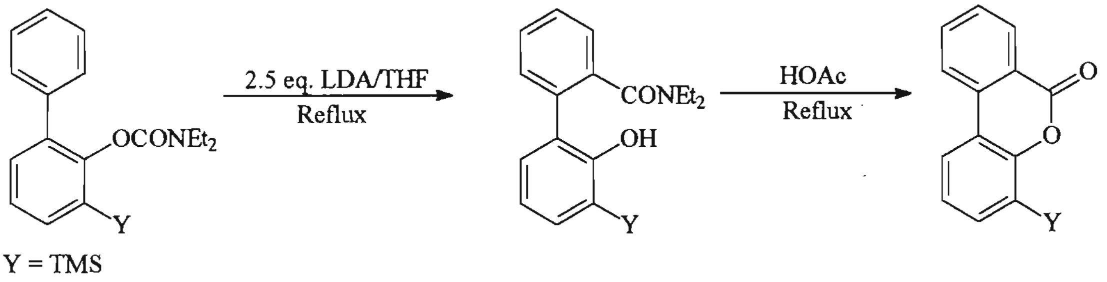


Scheme 13

Similar transfers were previously noted as side reactions,[57] but the process is useful in its own right.

Under Gawley's conditions,[56] when $R^1 = R^2 = R^3 = H$, $R^4 = Et$, only the 1,2 migration product was observed. They found that only if $R^1 = R^2$ = methylene dioxy, did they get metalation on the ring and hence formation of the 1,4- migration product.

Wang and Snieckus[58] further exploited the carbamoyl migrational ability and reported a carbanion induced ring to ring carbamoyl transfer reaction **(67→68) (Scheme 14)**, formally a remote anionic Fries rearrangement. The reaction provides general regiospecific entries into sterically encumbered benzyls and substituted dibenzo[b,d]pyranones and fluorenones including the natural product dengibsin **(72)**.

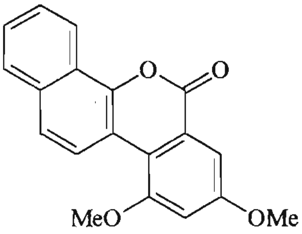


(67) **(68)** **(69)**

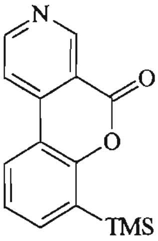
Scheme 14

The discovery of the reaction was based on the logic that by prior protection of the normal site of metalation, alternate ring remote deprotonation is thermodynamically favoured by a complex induced proximity effect (CIPE),[59,60] a useful mechanistic concept which postulates that acid-base co-ordination may identify weakly acidic remote C-H sites for potential deprotonation. Acid catalysed cyclisations led to the dibenzopyranone **(69)**.

The synthesis of benzo[d]naphtho[1,2-b]pyranone **(70)** represents the ring system of Ravidomycin and related classes of antitumour antibiotics, while the azadibenzopyranone (71) constitutes part of the skeleton of the chromone alkaloids.



(70)



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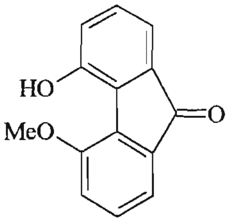
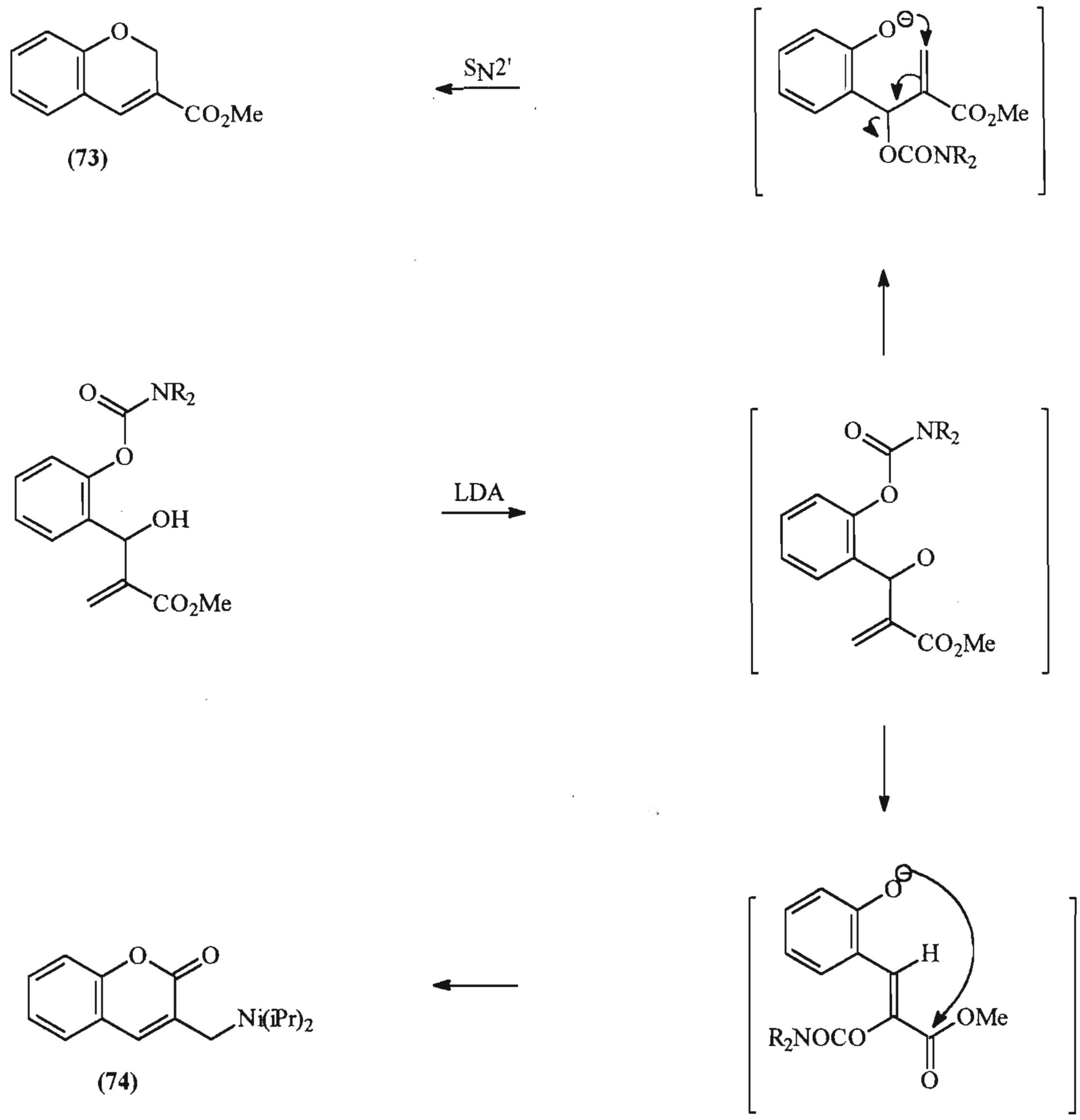


(72)

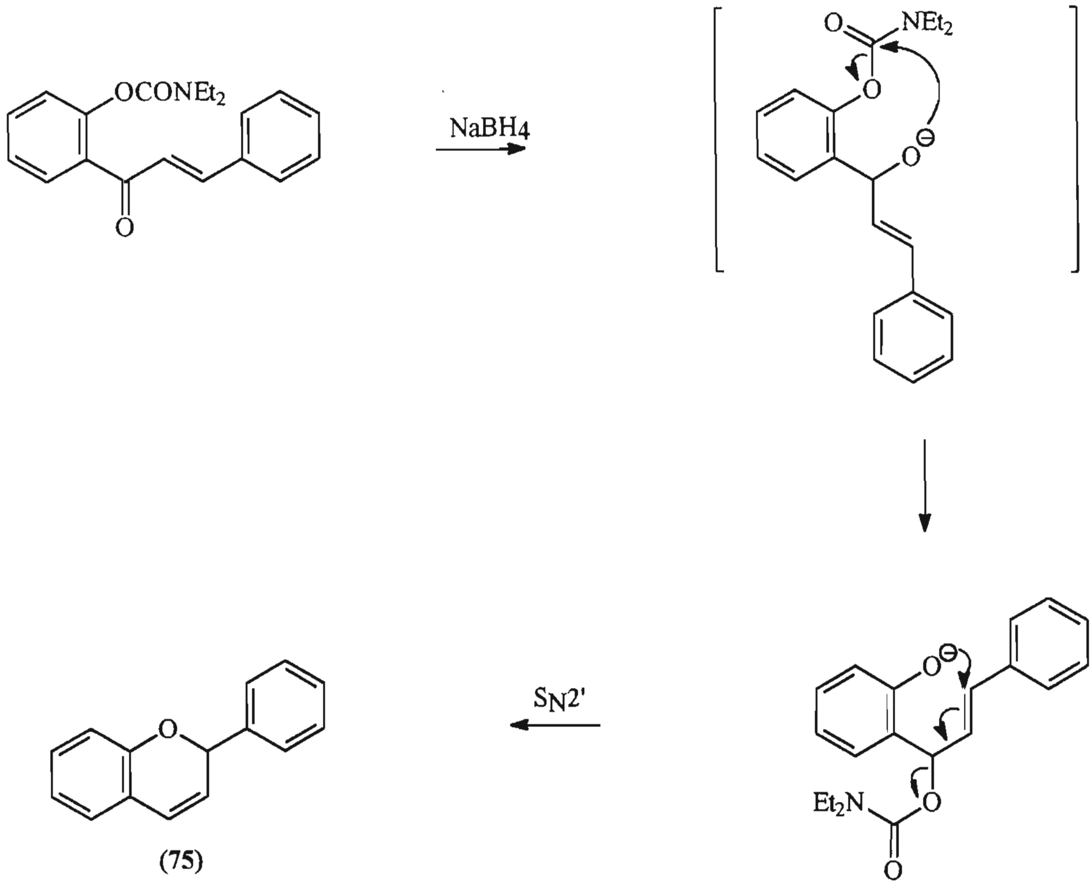
The migrational ability and leaving group capability of the carbamate group has been exploited in the synthesis of substituted chromenes **(73)**, coumarins **(74)**, substituted cyclohexenes and β-amino esters.[61] Substituted chromenes and coumarins were synthesised from the DABCO catalysed Baylis-Hillman reaction product of the *N,N*-dialkylcarbamate of salicylaldehyde and methyl acrylate **(Scheme 14)**.



Scheme 14

The intramolecular migration of the carbamate is promoted by the deliberate abstraction of the acidic alcohol proton and cyclisation occurs with the S_N2' elimination of the carbamate group.

Working in our laboratories, Mahabir[62] used the migratory and leaving group capability of the carbamate for the synthesis of flav-3-ene **(75)** **(Scheme 15)**.



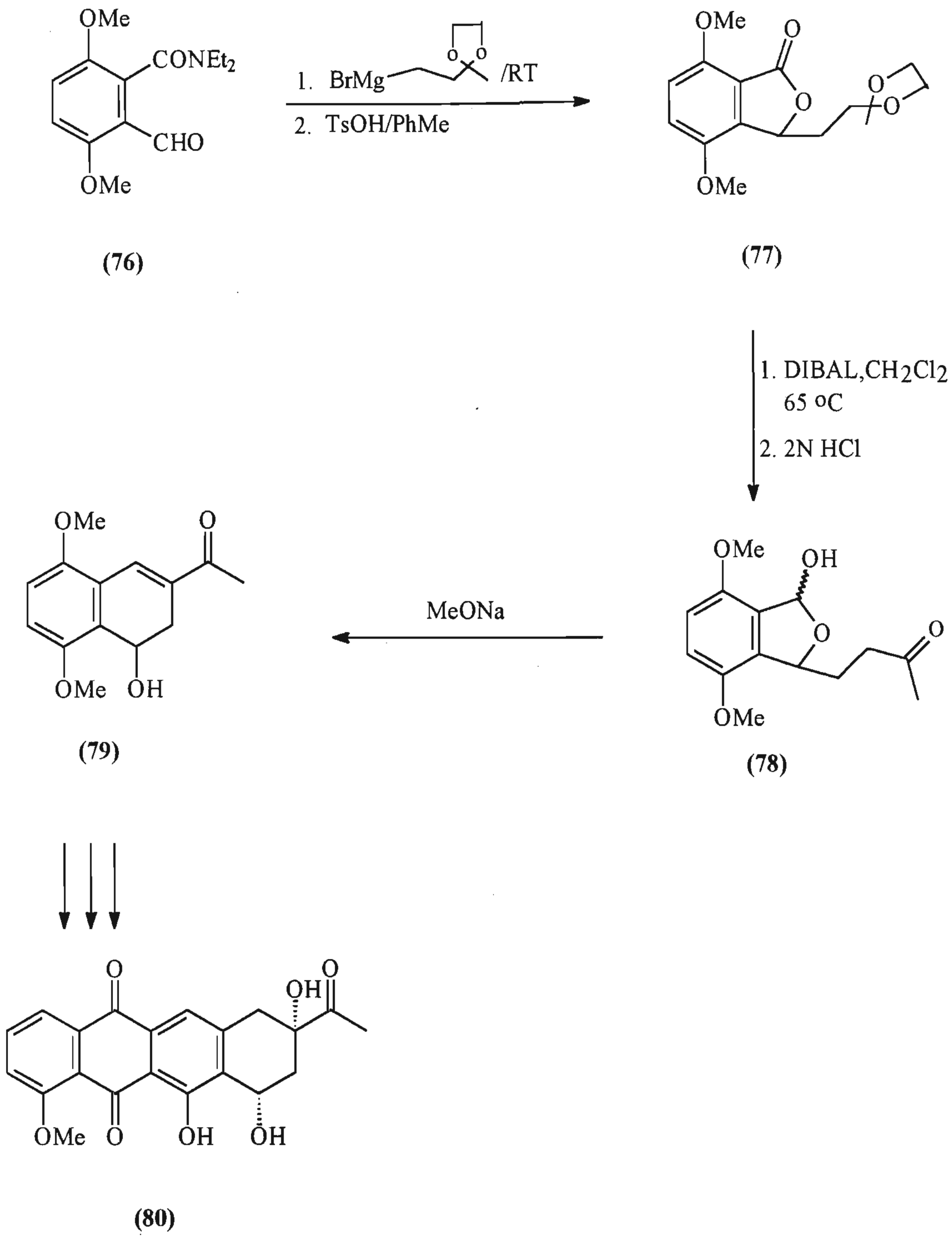
(75)

Scheme 15

1.4. PHTHALIDES AND COUMARINS

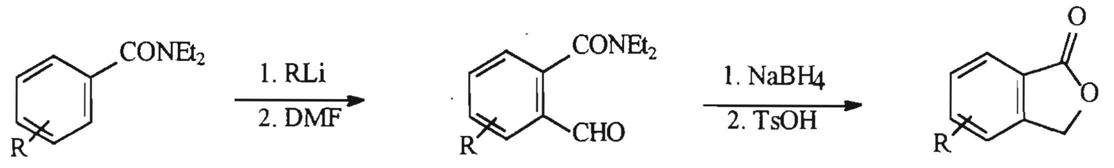
Much work has been done on phthalide and coumarin type compounds. The following examples illustrate methods of synthesis and the various uses of these compounds.

Phthalides are useful synthons for natural products especially in the synthesis of antitumour compounds.[45] An example of this is the antitumour antibiotic daunomycinone **(80)** **(Scheme 16)**. The construction of the synthon **(79)** of this antibiotic was initiated by the incorporation of a 4-carbon Grignard into the *o*-formyl benzamide **(76)**. The phthalide **(77)** resulting from subsequent acid catalysed cyclisation was partially reduced and carefully hydrolysed to give the hemi-acetal **(78)** which upon intramolecular aldol condensation furnished **(79)** in 38 % overall yield[63].



Scheme 16

The preparation of C-3 unsubstituted phthalides[64] has been pursued *via* a 3-step process **(81→82→83) (Scheme 17)**. The method incorporates the powerful tertiary amide DMG.

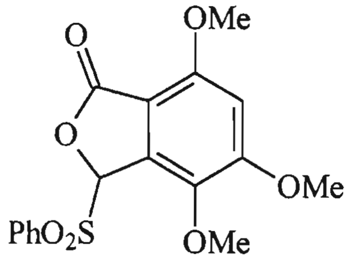


(81) **(82)** **(83)**

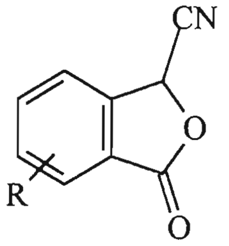
Scheme 17

C-3 substituted phthalides[65] are obtained by hydroxyalkylation of ortho-lithiated benzamides followed by acid catalysed cyclisations.

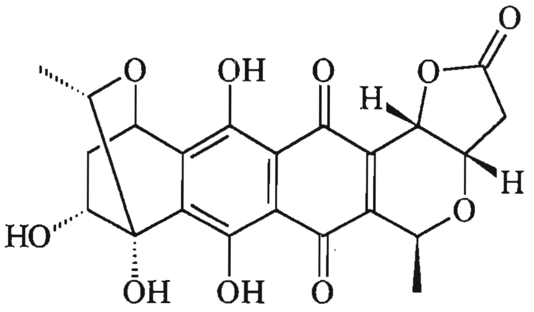
Oxygenated phthalide sulfones **(84)** are coupled with chromones in synthetic routes to antiprotozoal pigments.[66] Cyanophthalides **(85)** have been used in the rapid construction of anthraquinones[67] and granaticin **(86)**,[68]an antibiotic with powerful and diverse biological activity.



(84)

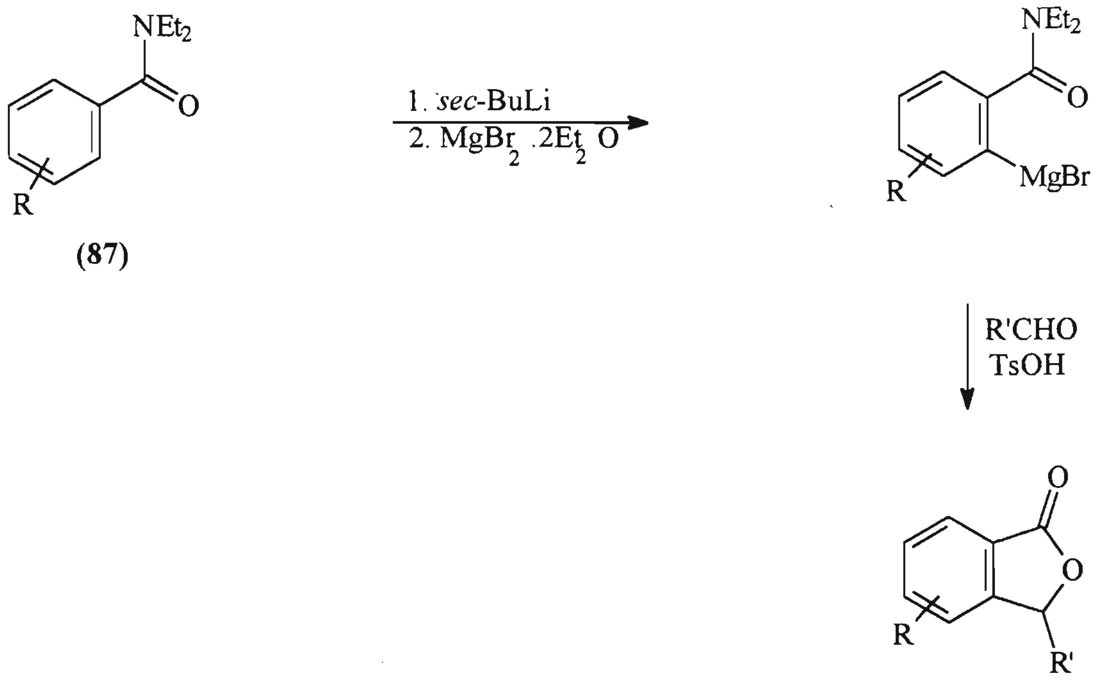


(85)



(86)

The efficient tertiary amide[69] D*o*M is useful in the construction of polysubstituted aromatics, phthalides, heterocyclic benzoquinones and polycyclic aromatic hydrocarbons (PAH's). Li-Mg transmetalation of these tertiary benzamides **(87)** has also been explored in the synthesis of phthalides **(Scheme 19)**.[70]



(87)

Scheme 19

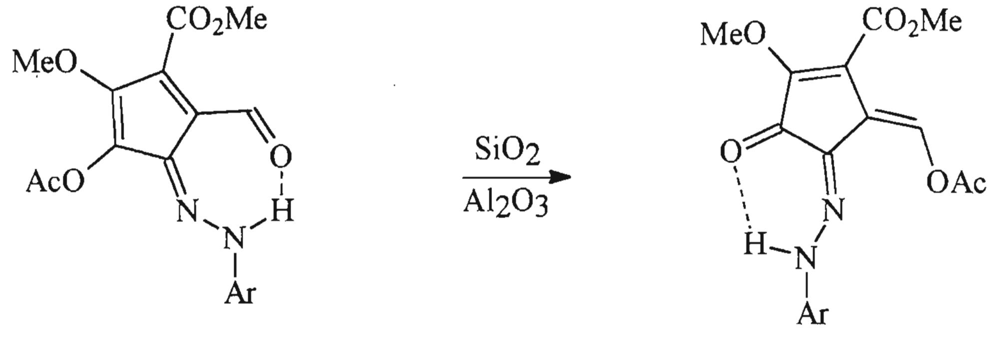
PAH's are carcinogenic substances present in the environment. These may be prepared *via* phthalide intermediates[71] and this rapid and efficient preparation is of value in analytical, metabolic and carcinogenicity studies.

1.5. MIGRATIONS OF ACYL AND SULFUR-CONTAINING GROUPS

1.5.1. ACYL MIGRATIONS

Lewis-catalysed acyl migrations have proved useful in the methodology used for the elaboration of quaternary carbon centres. [73a,b] Their use has been extended to include the generation of spiro carbon centres.

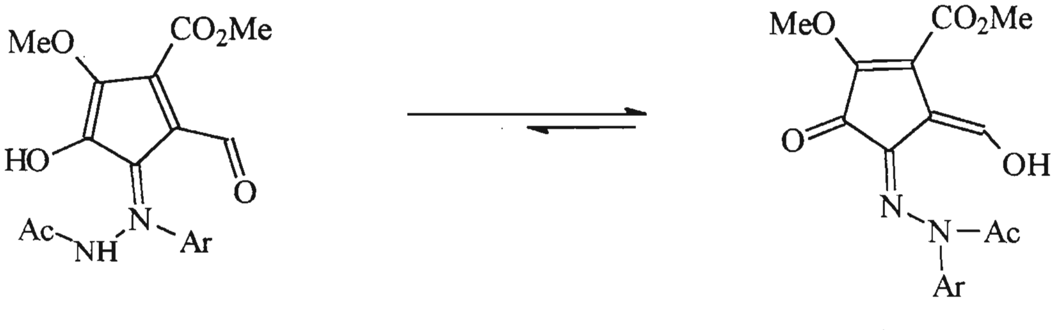
More recently, intramolecular 1,2-*O,O'*-acyl migration[74] has been observed during flash chromatography of diazonium coupling products **(Scheme 20)**.



(88) **(89)**

Scheme 20

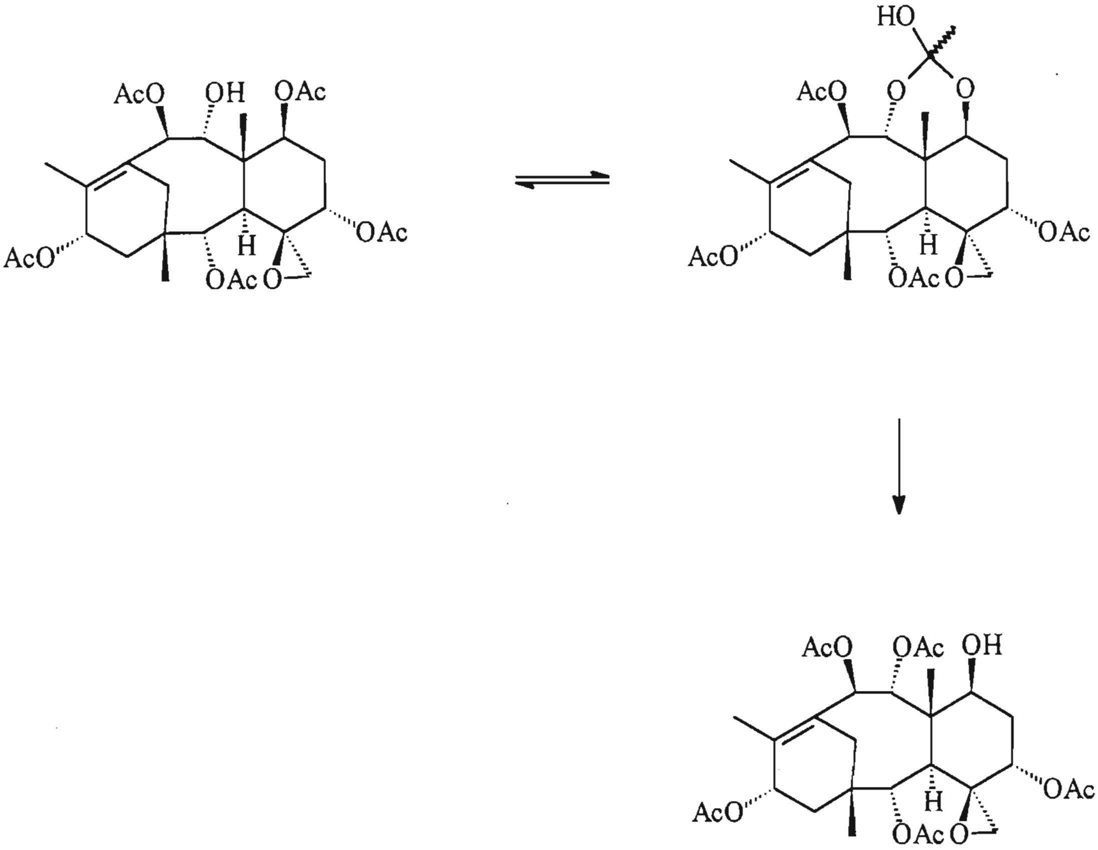
The nature of the migration was determined by isotopic labelling studies and mass spectrometry. A co-operative transportation by the hydrazono group is proposed to explain the phenomenon. The authors postulate that the nitrogen atom linked to the aryl group may trap the acetyl group and through isomerisation of the hydrazono group bring it to the other side of the molecule. A simultaneous π-system re-organisation and the subsequent transfer of the acyl group to the formyl group oxygen lead to the migratory products. Therefore, the 1,7-intramolecular acyl migration is the result of two consecutive intramolecular rearrangements. The greater stability of the migratory product compared to the starting material is considered to be the driving force in the reaction. Also, the postulated intermediate **(91)** is more stable than **(90)**.



(90) **(91)**

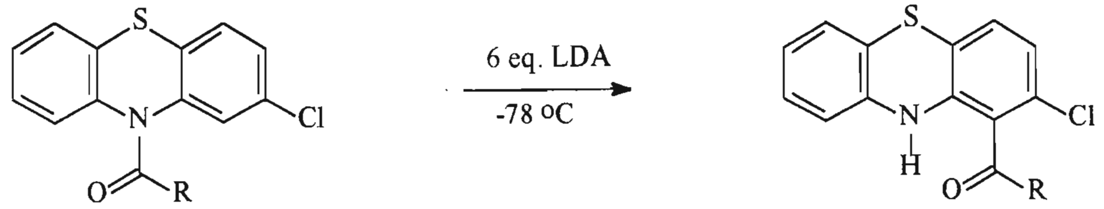
Intramolecular acyl migrations have also been noted in the taxanes, which are anti-tumour agents isolated from *Taxus brevifolia*.[75] The taxane epoxides that were isolated from this Pacific Yew tree were found to readily isomerise *via* acyl migration upon standing in $CDCl_3$

solution **(Scheme 21)**.[76] This represents the first example of intramolecular transesterification in the large family of Taxane metabolites.



Scheme 21

An intramolecular anionic Fries rearrangement of *N*-acylphenothiazines[77] was observed upon treatment of **(92)** **(Scheme 22)** with six equivalents of LDA at -78 °C for 30 minutes. The nicotinoyl derivative **(93)** was obtained. This is an example of the anionic N→C migration which is rarely observed although the analogous anionic N→C migration of the aryl sulfonamides has been reported.[78]



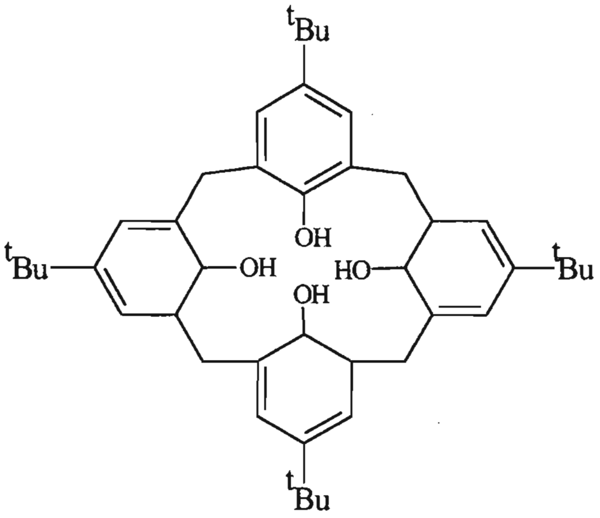
(92) **(93)**

Scheme 22

This rearrangement differs from the anionic O→C 1,3- migration of *o*-aryl carbamates (Snieckus Rearrangement)[46] in that the Snieckus rearrangement requires only one equivalent of the metalating agent and migration is sufficiently slow to permit trapping of the *ortho* metalated intermediate with electrophiles.

1.5.2. MIGRATION OF SULFUR-CONTAINING GROUPS

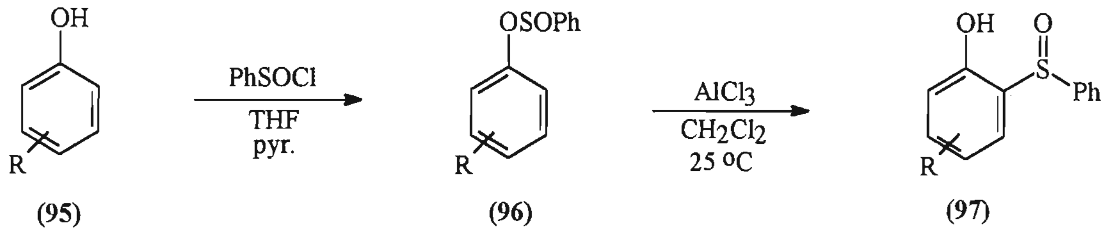
Calixarenes **(94)** are compounds that are used as building blocks for the construction of more elaborate structures used for the complexation of cations and neutral substrates.[79]



(94)

Sulfonates have found widespread use as activating[80a-c] or protecting[22] groups of phenols. They now also find use as activating groups in the calixarenes. Gonzalez and co-workers[81] have reported the unprecedented intermolecular migration of sulfonyl groups, providing new mono- and trisulfonyl calixarene derivatives. Previously exchange of sulfonyl groups had only been observed intermolecularly in the reaction of aryl triflates with the potassium salts of phenols in liquid ammonia.[82]

The Fries rearrangement[55a-c] is useful for the preparation of acyl phenols *via* Lewis catalysed rearrangement of phenyl esters. This rearrangement has been extended by Jung[83] to facilitate the successful preparation of *o*-and *p*-(phenylsulfinyl)phenols from phenylsulfinates *via* a 'thia-Fries rearrangement'. Treatment of the phenol **(95)** **(Scheme 23)** with phenylsulfinyl chloride in THF with an equivalent of pyridine afforded the desired phenylsulfinate **(96)** in good yield (87-92%). The best rearrangement conditions were found to be the addition of 2 equivalents of $AlCl_3$ in one batch to the phenylsulfinate in CH_2Cl_2 with stirring for one hour at 25 °C. Aqueous workup and recrystallisation yielded the (phenylsulfinyl)phenol **(97)** in 72-87% yield.



Scheme 23

The closest analogy of this rearrangement is the rearrangement of aryl sulfonates to give aryl sulfones[84] but this requires drastic conditions ($AlCl_3$, neat at 120 °C or in refluxing nitrobenzene) and the process is low-yielding. The thia-Fries rearrangement on the other hand requires mild conditions and proceeds in very good yields.

CHAPTER 2

DISCUSSION

In our laboratories, the exploitation of the synthetic utility of the carbamate functionality has largely been concerned with the effects of this functionality in allylic and benzylic systems. It was therefore the aim of this project to extend the usefulness of the carbamate functionality to naphthyl systems and elucidate whether the functionality demonstrated similar reactivity to that observed in allylic and benzylic systems.

Hoppe[33] has shown that electrophilic substitutions can be readily carried out at the benzylic position of benzyl carbamates **(Scheme 4)** thus illustrating the stability of such anions.

By analogy with the work of Hoppe, two areas of investigation were undertaken :

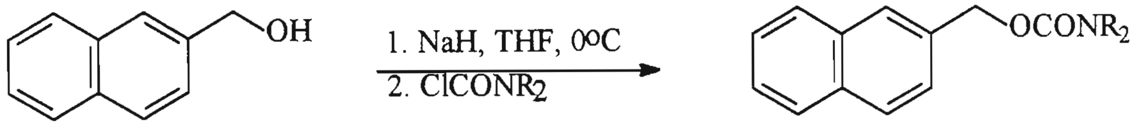
1. The electrophilic substitution of the benzylic protons of the naphthyl carbamate system, and
2. investigation of the migrational ability of the amide portion of the carbamate onto the naphthalene ring.

To broaden the synthetic utility of the naphthyl carbamates, investigations were carried out using α-silyl substituted carbamates as a means of further stabilising the anion at the benzylic position, thereby improving its reactivity with various electrophiles.

Attempts to migrate the amide portion of the carbamate in the naphthyl system were unsuccessful, but the use of a Li-halogen exchange reaction on 2-iodobenzyl carbamate proved successful in this regard.

2.1 SYNTHESIS OF CARBAMATES

A search of the literature indicated that there is a wide array of available synthetic routes to carbamates.[85a-f] A suitable laboratory preparation is the reaction of an alcohol with the commercially available *N,N*-dialkyl carbamoyl chlorides to afford the corresponding carbamates. Thus all naphthyl carbamates were prepared by the facile reaction of *N,N*-dialkyl carbamoyl chloride with naphthalene-2-methanol **(98)** in THF **(Scheme 24)**. The alcohol proton was abstracted using sodium hydride and subsequent addition of the carbamoyl chloride followed by acidification, afforded the desired carbamates after purification by flash chromatography on silica gel. The yields of the naphthyl carbamates synthesised are shown in **Table 1**.



(98)

R = Et (99a)
R = ^{i}Pr (99b)

Scheme 24

Table 1

CARBAMATE	% YIELD[a]
99a	56
99b	60

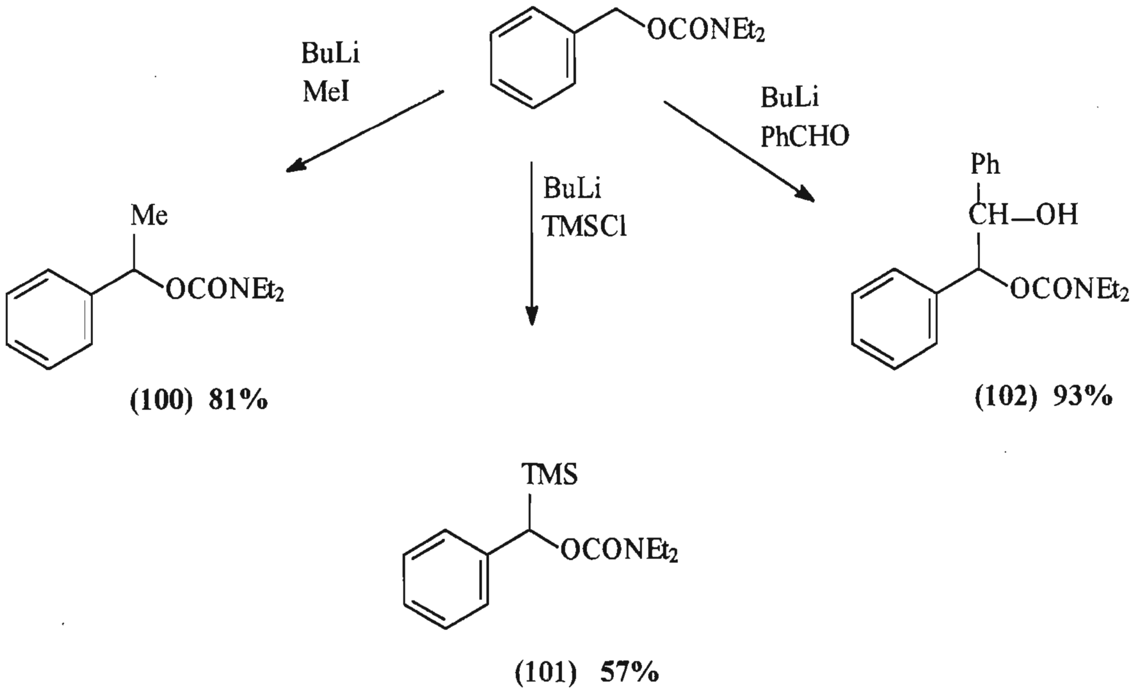
a = isolated yields

Longley,[86] in his work on allylic carbamates, found that increasing the bulk of the substituents on the nitrogen atom reduced the yield of the corresponding carbamate. One would therefore expect compound **99a** to be produced in higher yield than compound **99b**. The slightly lower yield of **99a** is possibly due to the difficulty experienced in separating this compound from other impurities in the reaction mixture.

2.2 ELECTROPHILIC SUBSTITUTION OF NAPHTHYL CARBAMATES

2.2.1. Reactions of *N,N*-dialkylnaphthyl carbamates with Electrophiles

As mentioned previously, Hoppe[33] has successfully substituted benzyl carbamates with various electrophiles. The products **(100-102)** and yields obtained in some of the reactions are depicted in **Scheme 25**.



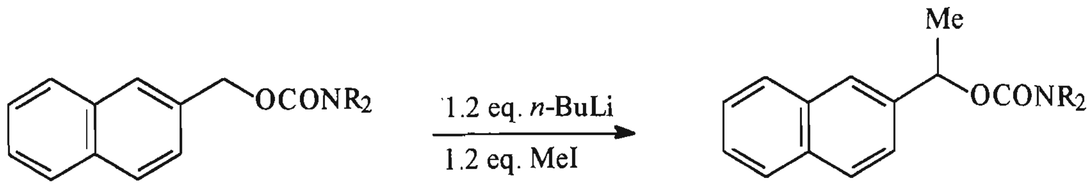
Scheme 25

These reactions proceeded in good to excellent yield and we therefore expected that the treatment of carbamates **99a** and **99b** successively with 1.2 equivalents of *n*-BuLi and 1.2 equivalents of each of the electrophiles listed in **Figure 2** would yield similar products to those obtained by Hoppe.

1. MeI
2. EtI
3. Allyl bromide
4. Methoxymethyl chloride
5. Piperonal
6. Benzaldehyde
7. Pivaldehyde
8. 4-Quinoline carboxaldehyde
9. 4-Pyridine carboxaldehyde
10. Methyl acrylate
11. 2-Cyclohexen-1-one

Figure 2

Of the substitutions attempted, only the use of MeI afforded the desired products **103a** and **103b (Scheme 26)** in 55% and 49% yield respectively.



R = Et (99a)
R = ^{i}Pr (99b)

R = Et (103a)
R = ^{i}Pr (103b)

Scheme 26

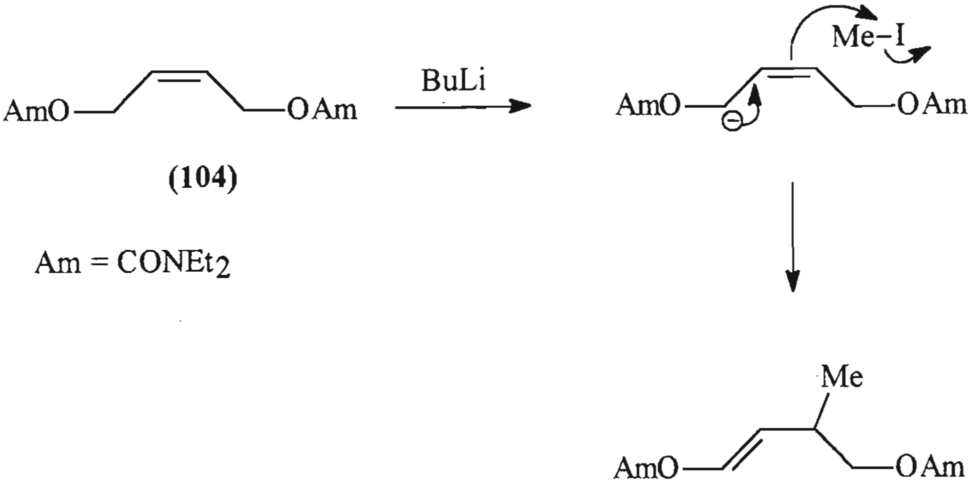
The products **103a** and **103b** were detected by GC/MS. NMR of the purified product indicated that a mixture of the starting material and the substituted product was present. Substitution with the small methyl group does not make the products **103a** and **103b** significantly different from the starting material and repeated attempts to obtain the substituted products as pure compounds by gradient elution were unsuccessful.

Interestingly, the generation of the anion in the benzylic position was facile (evident from the emerald green solution produced on addition of the *n*-BuLi). The problem with the electrophilic substitution therefore did not lie here. It is postulated that the low reactivity of the electrophiles hindered substitution. In addition to methods to improve the reactivity of the electrophiles, methods to further stabilise the anions were sought.

2.3. STABILISATION OF BENZYL CARBANIONS

The use of the *N,N*-dialkylcarbamate group to stabilise an anion has been extensively discussed in **Chapter 1, Sections 1.3.2.1** and **1.3.2.2**. One would therefore expect that the use of a dicarbamate might afford better stabilisation. This has been investigated by Mason and Emslie[87] and yielded some surprising results.

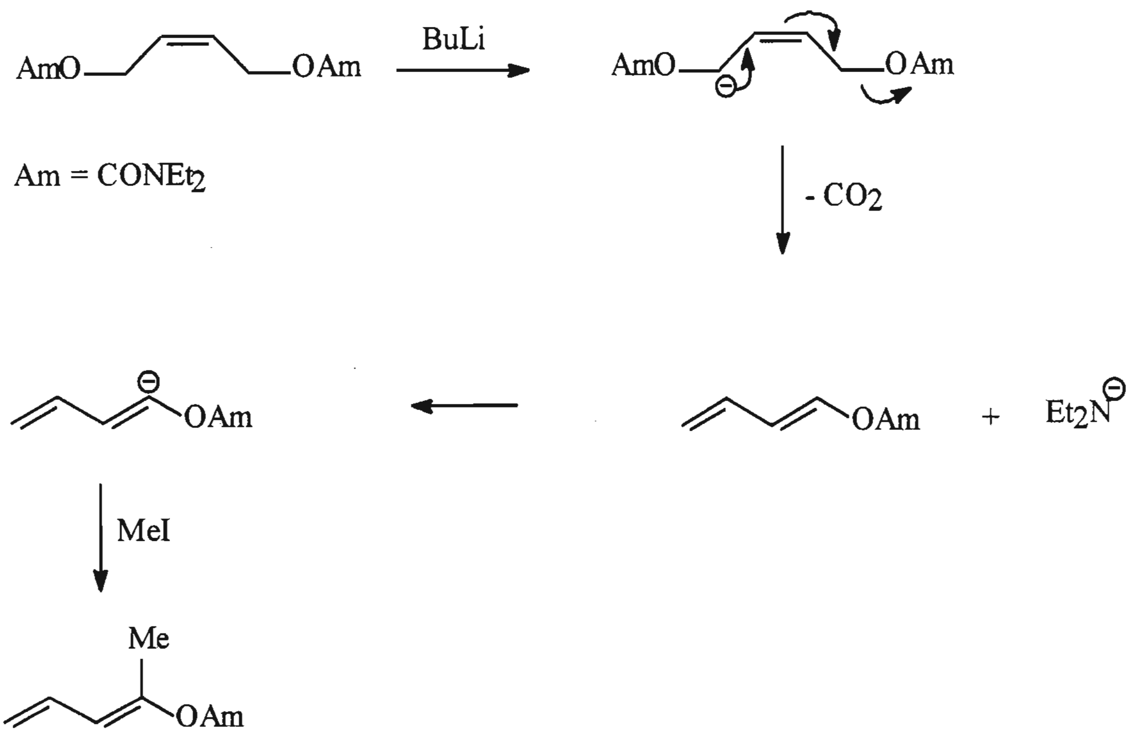
The reaction of *cis*-1,4-di-(*N,N*-diethylcarbamoyloxy)but-2-ene **(104)** **(Scheme 27)** with MeI yielded the 1-methyl-1,3-butadiene derivative **(106)** **(Scheme 28)**, instead of the expected product **(105)** **(Scheme 27)**. The mechanism for the formation of **106** is outlined in **Scheme 28**.



(104)

(105)

Scheme 27



(106)

Scheme 28

The formation of the product **(106)** is accounted for by the initial elimination of one of the carbamate groups and this further emphasises the leaving ability of the carbamate functionality.

Selenium[86] and sulfur[89] have also found wide applicability as carbanion-stabilising reagents, but it is silicon that demonstrated usefulness in the present work.

2.3.1. STABILISATION OF ANIONS BY SILICON

2.3.1.1 Mechanism of Stabilisation by Silicon

Silicon-stabilised carbanions have attracted considerable interest because of their multiple synthetic utility.[26,90] This wide applicability of organosilicon reagents in stereoselective bond-forming reactions can be attributed to the large number of functional groups and the variety of reaction conditions that can be accommodated by silicon and its ability to function as an electron acceptor. The silicon reagents can also be subsequently transformed to other electrophilic equivalents,[91] and this enhances their usefulness in organic synthesis.

There are various factors that contribute to silicon's versatility in organic synthesis, but the *p-d* π-bonding effect[92,93] **(Figure 3)** is most applicable here.

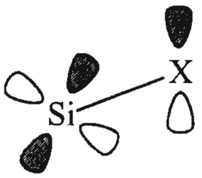


Figure 3

From the illustration it can be seen that the electron density from the *p*-orbital on X can be delocalised onto the silicon through a donor-acceptor interaction with the vacant silicon 3*d*-orbitals. An example of such a system is the stabilisation of an anion by silicon in the carbamate compounds that is to be discussed in the following section.

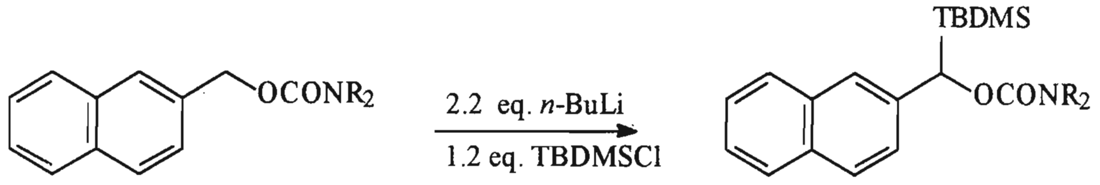
Once the silicon has served its purpose in promoting electrophilic substitution, one might choose to remove the silicon moiety. The facile desilylation by the use of a fluoride ion **(Scheme 29)** is another reason for the extensive use of trialkylsilanes as protecting groups in synthesis.[98]

$$RO{-}SiMe_3 \xrightarrow{F^{\ominus}} FSiMe_3 + RO^{\ominus}$$

Scheme 29

2.3.1.2. Silylation of Carbamates

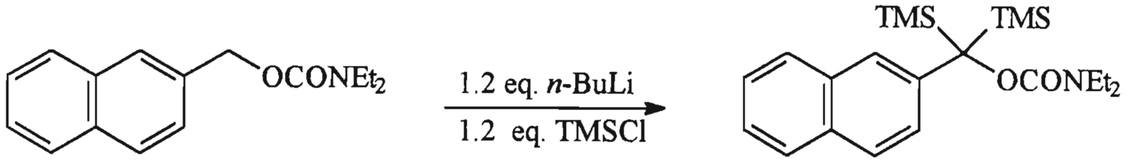
Silylation of carbamates **99a** and **99b** was carried out using *n*-BuLi and either *tert*-butyldimethylsilyl chloride (TBDMSCl) or trimethylsilyl chloride (TMSCl). The reactions are depicted in **Schemes 30 and 31**.



R = Et (99a)
R = ⁱPr (99b)

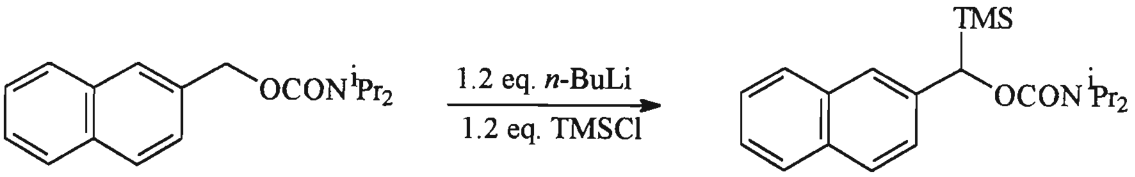
R = Et (107a)
R = ⁱPr (107b)

Scheme 30



(99a)

(108b)



(99b)

(109a)

Scheme 31

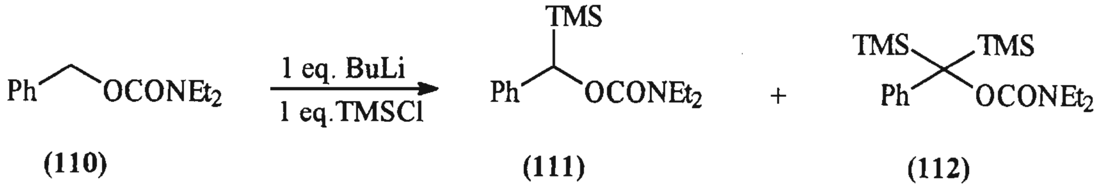
The yields of the α-silylation reactions are shown in **Table 2**.

Table 2

PRODUCT	% YIELD
107a	60
107b	50
108b	29
109a	30

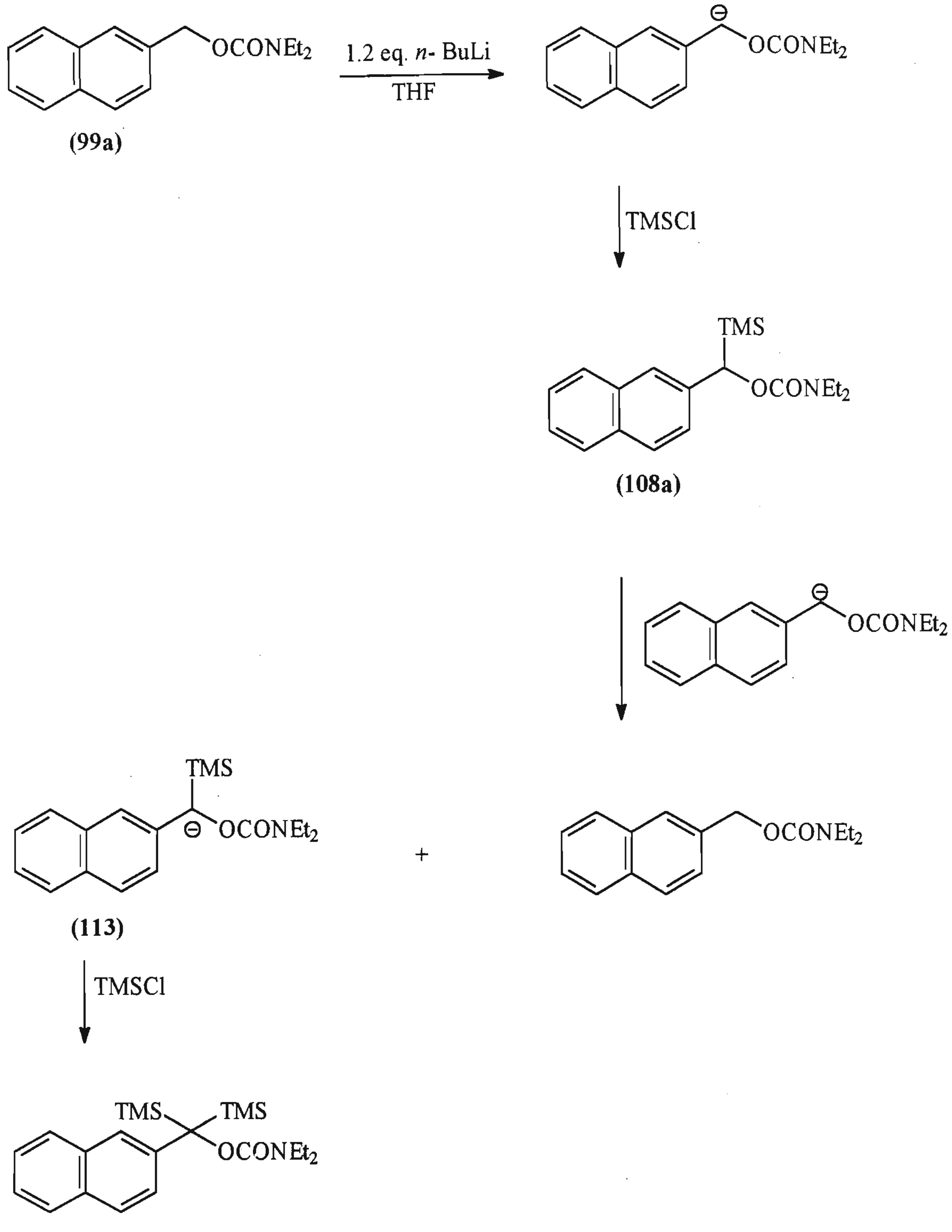
The 10% lower yield of **107b** compared to **107a (Scheme 30)** can be attributed to the steric hindrance caused by the bulky diisopropyl groups in **99b**. In addition, the bulk of the TBDMS group prevents the formation of the bis-TBDMS derivative. Also, 2.2 equivalents of *n*-BuLi were required for the reaction to go to completion. These results are similar to those reported by Mason and Emslie[94] in their work on cinnamyl carbamates.

It is interesting to note that the addition of 1.2 equivalents of *n*-BuLi and 1.2 equivalents of TMSCl to compound **99a (Scheme 31)** did not yield any of the mono-TMS derivative. This is in contrast to the results obtained by Mason and co-workers[96] in their work on cinnamyl and benzyl carbamates. They found that under similar conditions **(Scheme 32)**, equimolar amounts of the mono-**(111)** and bis-**(112)** silylated derivatives of the *N,N*-diethylbenzyl carbamate **(110)** were isolated.



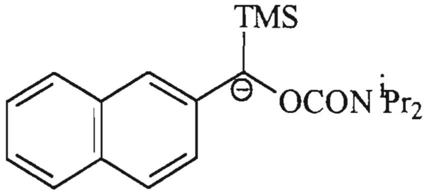
Scheme 32

The mechanism for the formation of the bis-TMS derivative of the *N,N*-diethylnaphthyl carbamate **(108b) (Scheme 31)** is shown in **Scheme 33**.



Scheme 33

The carbamate **99a** is rapidly deprotonated and the slower substitution with TMSCl yields the mono-silylated intermediate **108a**. The α-proton on **108a** is however, more acidic than the proton on **99a**, so proton exchange occurs to give the anion of the mono-silylated intermediate **113** which reacts with a further molecule of TMSCl to yield the bis-silylated compound **108b**. The bis-silylated derivative of **99b** does not form under similar conditions, possibly due to the difficulty experienced in introducing another TMS group to an already sterically hindered substrate **(114)**.

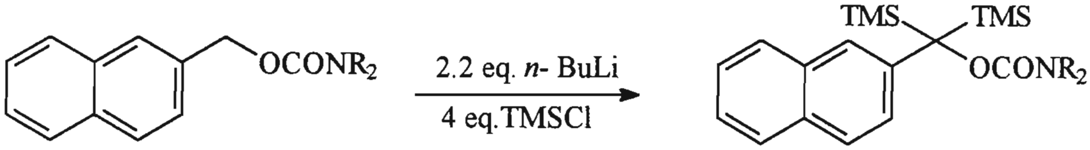


(114)

The mono-TMS derivative of **99a,** *i.e.* **108a (Scheme 33)**, can be formed exclusively if *n*-BuLi is substituted by the more hindered base LDA, and if the TMSCl is added rapidly 15 minutes after addition of the BuLi.

Hoppe[33] did not report the presence of the bis-TMS compound **(112) (Scheme 32)** in his electrophilic substitutions. Emslie and co-workers[95] found that the reaction of cinnamyl and benzyl carbamates with 2 equivalents of *n*-BuLi and 2 equivalents of TMSCl gave the bis-silylated compounds in 72% and 60% yields, respectively. Reaction of **99a** and **99b** with 2 equivalents each of *n*-BuLi and TMSCl still resulted in the mono-(30%) and bis-(50%) TMS derivatives being formed.

It was found that the bis-TMS derivatives of the naphthyl carbamates could be formed exclusively and in good yield if the substrates **99a** and **99b** were treated with 2.2 equivalents of *n*-BuLi and 4 equivalents of TMSCl **(Scheme 34)**. The yields of these optimised reactions are recorded in **Table 3**.



R = Et (99a)

R = ^{i}Pr (99b)

R = Et (108b)

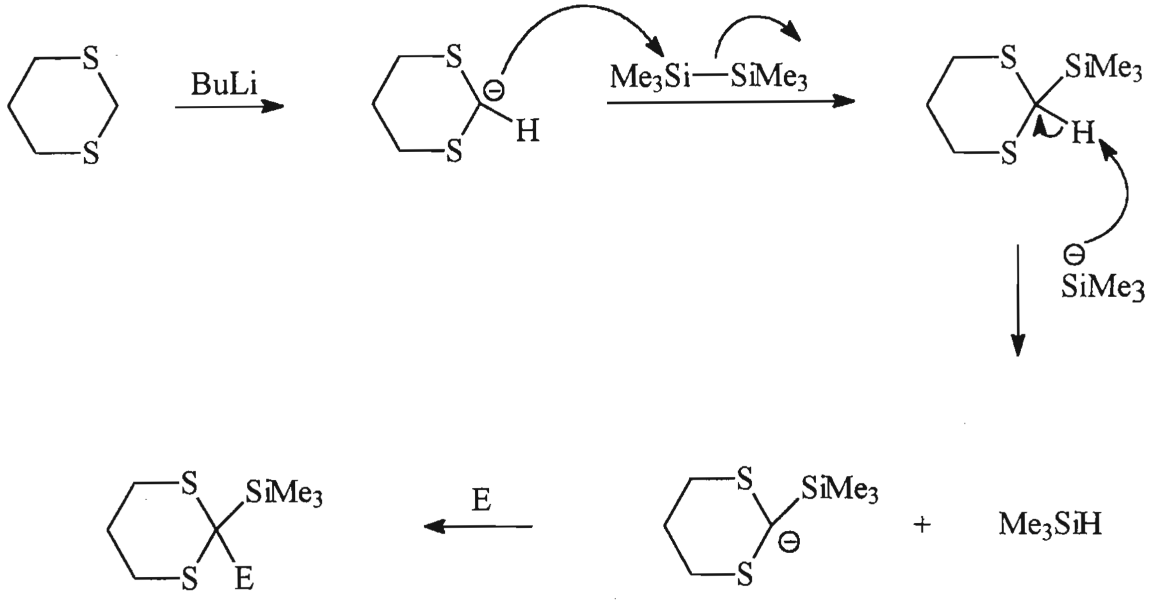
R = ^{i}Pr (109b)

Scheme 34

Table 3

PRODUCT	% YIELD
108b	54
109b	58

The mechanism shown in **Scheme 33** can be likened to that of a counterattack agent.[96] This methodology was used in the successful synthesis of ketene dithioacetals from 1,3-dithianes[97] **(Scheme 35)** by the use of hexamethyldisilane as a counterattack agent.



(115)

E = aldehydes, ketones and alkyl halides

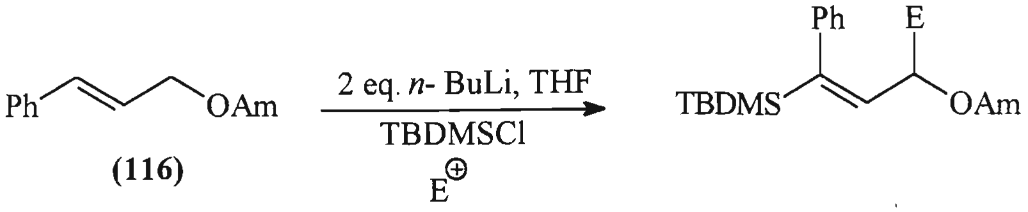
Scheme 35

In addition to its similarity with **Scheme 33**, the formation of the Si-stabilised anion **(115)** and subsequent reaction with electrophiles finds analogy with work to be discussed in the following section.

2.4. ELECTROPHILIC SUBSTITUTIONS OF TBDMS-SUBSTITUTED CARBAMATES

The facile generation of compounds **107a** and **107b (Scheme 30)** paved the way for the introduction of a second electrophile onto the naphthyl carbamate system. This type of disubstitution has been carried out on cinnamyl carbamates **116 (Scheme 36)** by Mason and

Emslie,[94] where introduction of a TBDMS group at the γ-position facilitated introduction of a second electrophile (E) at the α-position.



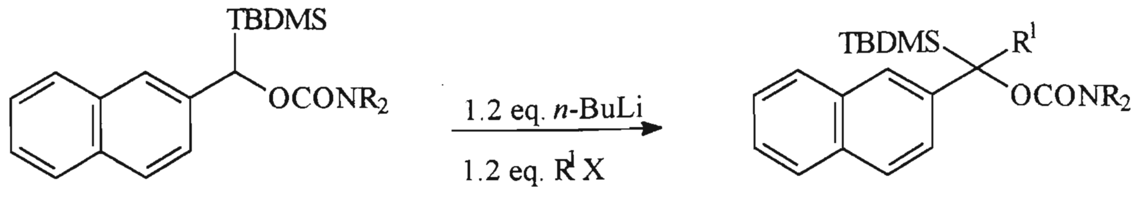
Scheme 36

Hoppe[98] has reported similar work on allylic carbamates, but the introduction of the first electrophile is carried out before formation of the carbamate. Barner and Mani[35] have reported similar disubstitutions of *N-tert*-butylbenzyl carbamates **(Scheme 5)**.

Electrophilic substitutions of **107a** and **107b (Scheme 30)** were carried out using the electrophiles listed in **Figure 2**. Discussion of the results will be done according to the various categories of electrophile, *i.e.* alkyl halides, aldehydes and Michael acceptors. All substitutions were carried out as two-pot procedures since these have been found to yield better results.[94]

2.4.1. Electrophilic Substitution of TBDMS-Substituted Carbamates with Alkyl Halides

Alkyl halides such as MeI, EtI and allyl bromide are popular electrophiles due to their relative ease of substitution. **Scheme 37** shows the reaction of **107a** and **107b** with these alkyl halides.



R = Et (107a)

R = ^{i}Pr (107b)

(117)

Scheme 37

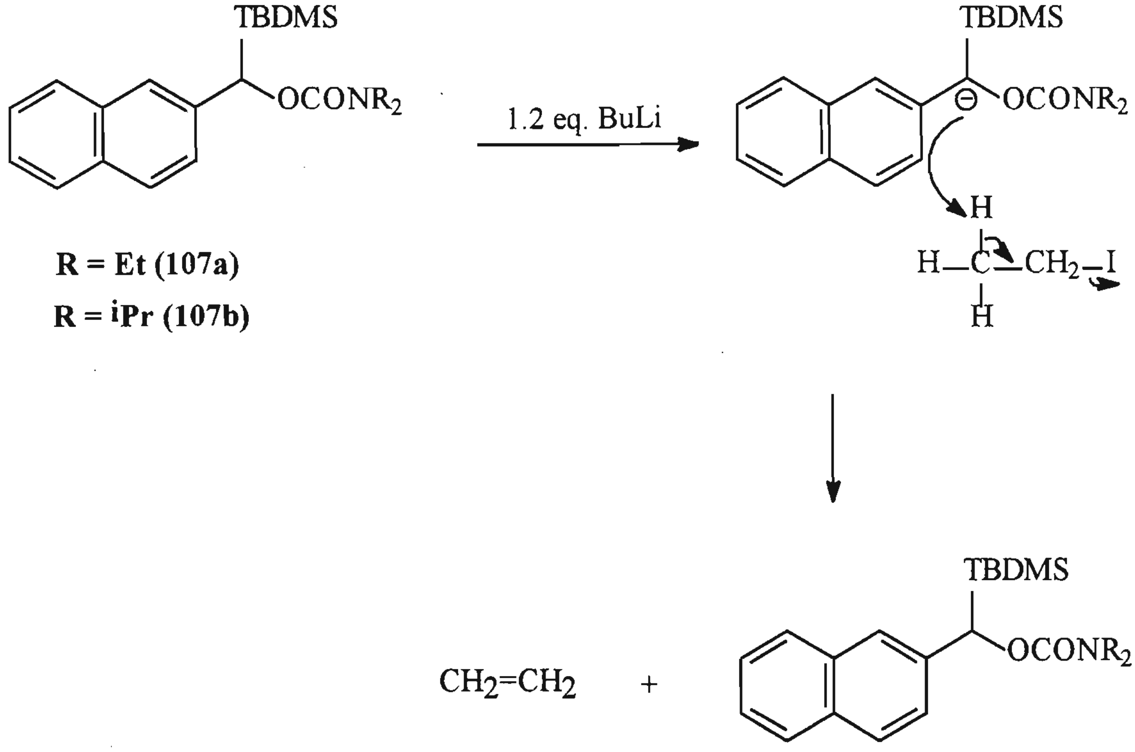
The results are summarised in **Table 4**.

Table 4

ENTRY	SUBSTRATE	R^1	X	PRODUCT	% YIELD
1	**107a**	Me	I	SM[a]	0
2	**107b**	Me	I	SM[a]	0
3	**107a**	Et	I	SM[a]	0
4	**107b**	Et	I	SM[a]	0
5	**107a**	allyl	Br	**117a**	47
6	**107b**	allyl	Br	**117b**	34

a (SM = starting material)

The recovery of starting material (entries **1** and **2**) **(Table 4)** is surprising since the methyl group is one of the smallest electrophiles and readily reacts with nucleophiles.[28] The ethyl group also generally adds on successfully, but the recovery of the starting material in entries **3** and **4** may be explained by the formation of ethene as shown in **Scheme 38**.



R = Et (107a)
R = ^{i}Pr (107b)

Scheme 38

Attempts to improve the reactivity of MeI and EtI towards the nucleophiles included carrying out the reactions as one-pot procedures and increasing the quantity of electrophile to 4 equivalents. We also investigated the activation of these electrophiles by the use of the Lewis acid, $AlCl_3$, with subsequent addition of this 'activated' species to the nucleophile. These reactions were unsuccessful and only starting material was isolated.

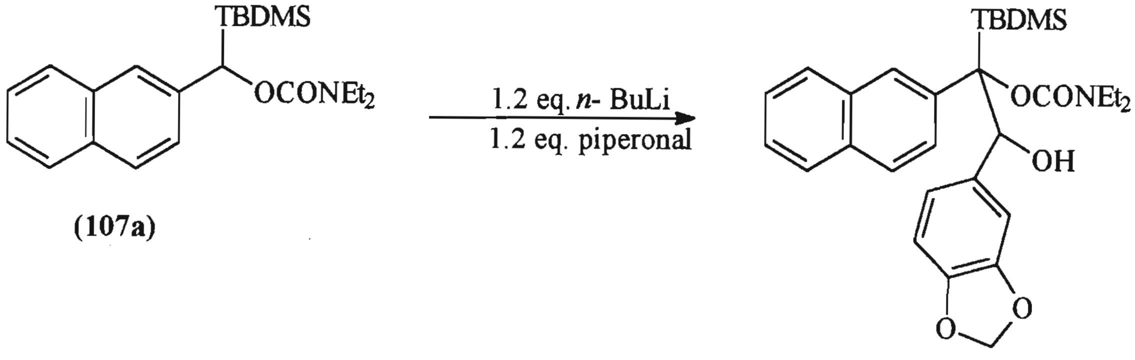
Ando and co-workers,[99] in their work on asymmetric Michael reactions of chiral lithioenamines, found that the addition of TMSCl (5 equivalents) helped to improve the reactivity of Michael acceptors, and Lipshutz and co-workers[100] have examined the role of TMSCl as an additive in Gilman cuprate 1,4-addition reactions and have found it to have a stereochemical impact. The use of excess TMSCl to activate the alkyl halides looked promising, but met with no success.

The reactions of **107a** and **107b** with allyl bromide (entries **5** and **6**, **Table 4**) were successful, yielding **117a** and **117b** in 47% and 34% yield, respectively. Here again the lower yield in the diisopropyl system is accounted for by the steric hindrance of the bulky diisopropyl groups. This steric bulk is now increased by the presence of the TBDMS group, making entry of electrophiles even more difficult.

2.4.2 Electrophilic Substitution of TBDMS-Substituted Carbamates with Aldehydes

Aldehydes have found extensive use in organic synthesis having proved useful in carbon-carbon bond-forming reactions in aldol-type syntheses.[89, 101-103]

In initial experiments of **107a** with piperonal, we expected products of type **118 (Scheme 39)** to be formed.

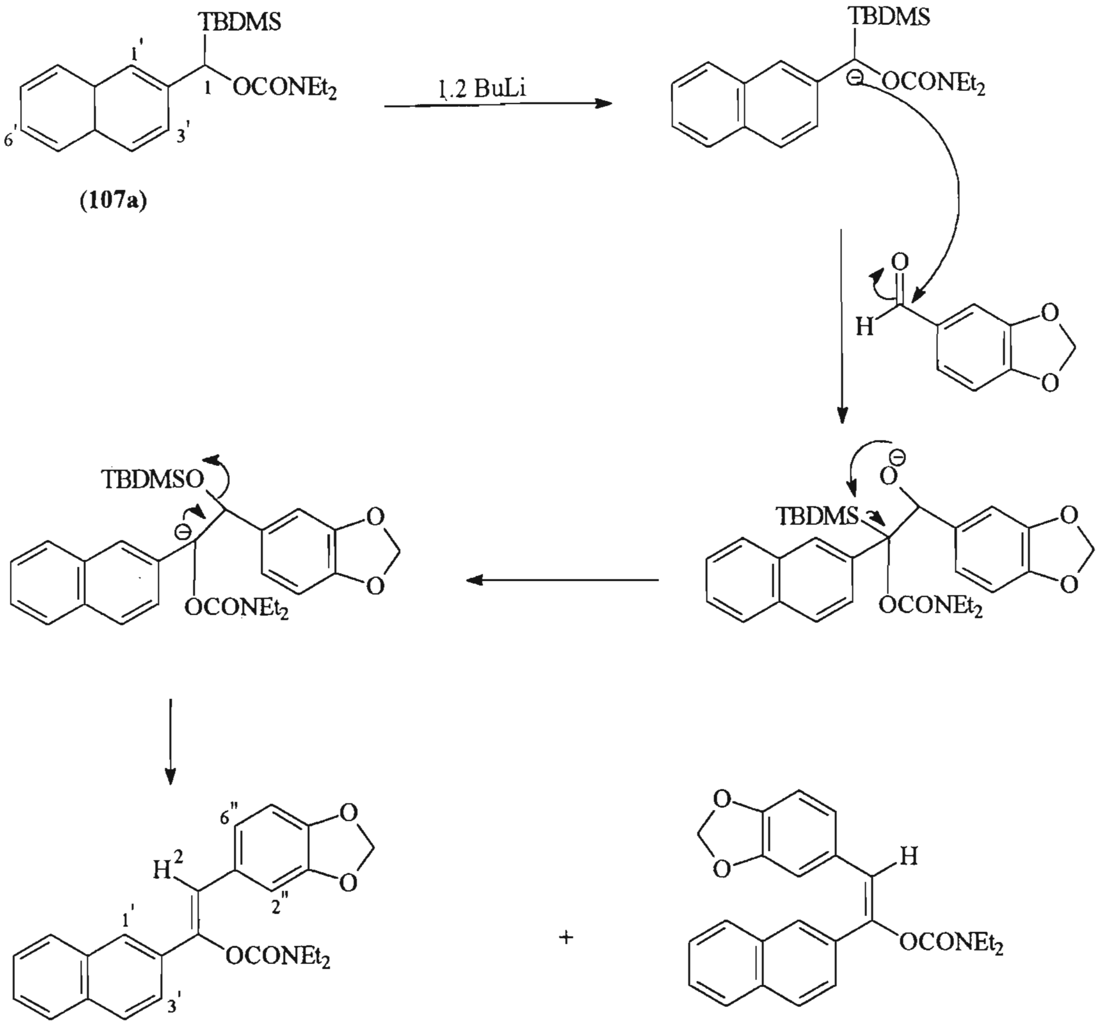


(107a)

(118)

Scheme 39

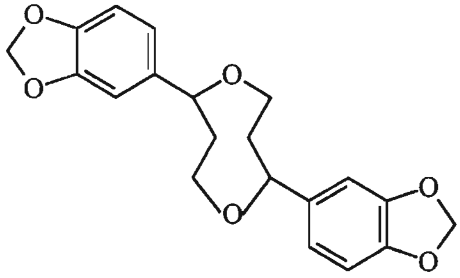
GC/MS of the crude mixture indicated that no product of the expected molecular mass, *i.e.* 521, was present, but there were two products with a molecular mass of 389 in the mixture. Purification and isolation of the compounds indicated that the two products were the *E* and *Z* isomers **(119a)** and **(119b) (Scheme 40)** from a Peterson olefination reaction. This olefination reaction has been extensively reviewed.[104] The mechanism for the formation of the isomers is shown in **Scheme 40**.



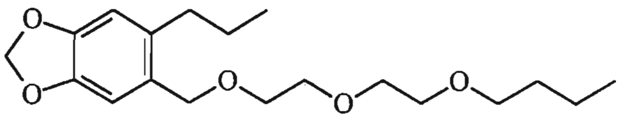
Z isomer (119a) **E isomer (119b)**

Scheme 40

Compounds that contain a methylenedioxy benzene derivative such as sesamin **(120)** and piperonylbutoxide **(121)**, have proved to be effective synergists, *i.e.* they increase the insecticidal activity of various insecticides.[7] It is therefore postulated that the presence of both the carbamate moiety and the methylenedioxy group in the same molecule as in compounds **119a** and **119b** could lead to these being extremely effective pesticides.



(120)

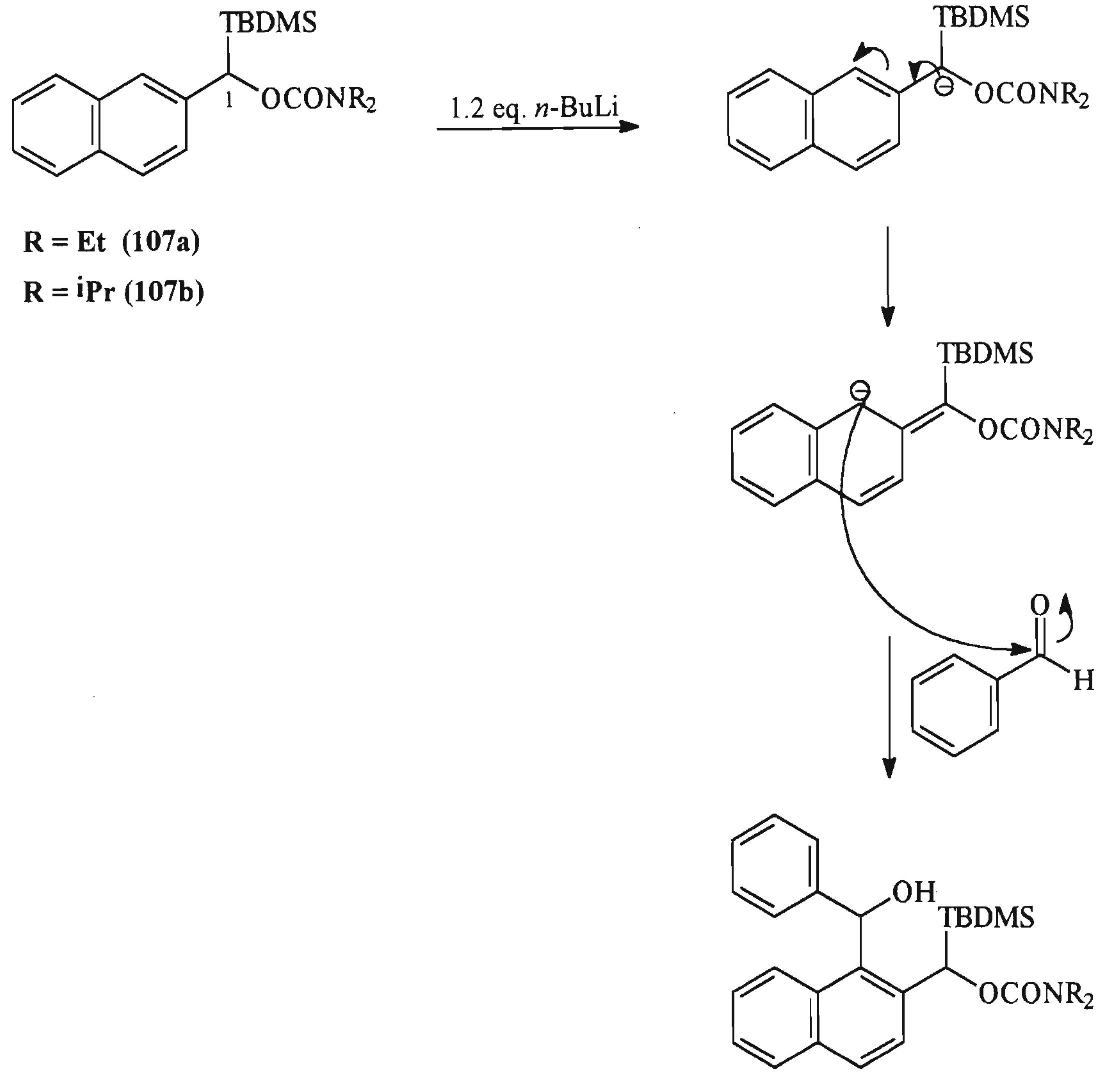


(121)

The isomers **119a** and **119b** were isolated in 67% overall yield and the *E*:*Z* ratio was determined to be 47:53. Only the fluorescent *Z* isomer could be isolated and this has been fully characterised. The proton NMR of the Z isomer **(119a)** (page 148) shows well defined splitting patterns for the ethyl protons in the carbamate moiety. These come up as two distinct sets of quartets and triplets. This compares favourably with the splitting pattern observed for the *Z* isomer of the benzyl derivative of this alkene, which has been synthesised in our laboratories.[105] The ethyl protons of the *E* isomer of the benzyl derivative come up as the broad signals normally associated with carbamates, and this indicates the similar environment that the protons are found in. NOE experiments on the *Z* isomer of the naphthyl derivative **(119a)**, where the signal of the alkene proton (H^2) was irradiated, showed interaction with protons 1' and 3' as well as with protons 2" and 6"**(119a)** **(Scheme 40)**. This served to confirm the structure of the isomer.

Although elimination of β-silylalkoxides was noted in 1947,[106] it was not until 1968 when Peterson[107] described the preparation of functionalised alkenes from α-silyl carbanions that the full potential of the reaction became apparent. It has been found that the bulk of the silyl group influences the diastereomeric ratio of the alkenes formed[108] so future work could include the reaction of the mono-TMS carbamate **108a** **(Scheme 32)** with piperonal and other aldehydes.

Experiments with **107a** and **107b** and benzaldehyde in THF which was dried by refluxing over $LiAlH_4$, resulted in poor yields of the *E* and *Z* Peterson olefination reaction isomers as detected by GC/MS. When the reaction was repeated in THF that was refluxed over a Na/K amalgam, the yields of the isomers increased significantly. Purification of the reaction mixture yielded a mixture of three compounds, *viz.* the two isomers and a third component that was initially thought to be starting material since it presented the same fragmentation pattern as the starting material **107a** as detected by GC/MS. Repeated attempts to separate this third component from the isomers proved unsuccessful. NMR of the mixture seemed to indicate that the third component was not starting material but a compound possibly of type **122** **(Scheme 41)**, where the benzaldehyde had added onto the naphthalene ring by rearrangement of the anion **(Scheme 41)**. Evidence in support of this is that the proton at the 1-position of compound **107a** normally comes up as a singlet at 5.87 ppm downfield from tetramethylsilane. The NMR of the mixture showed no signal at this particular shift, but a proton at 4.98 ppm could be the benzylic proton adjacent to the silyl group in compound **122**. The ^{13}C spectrum of the mixture showed an extremely complex aromatic region. Since the starting material has a higher R_f than the products and is therefore readily separated from these, this increased complexity cannot be due to the starting material.



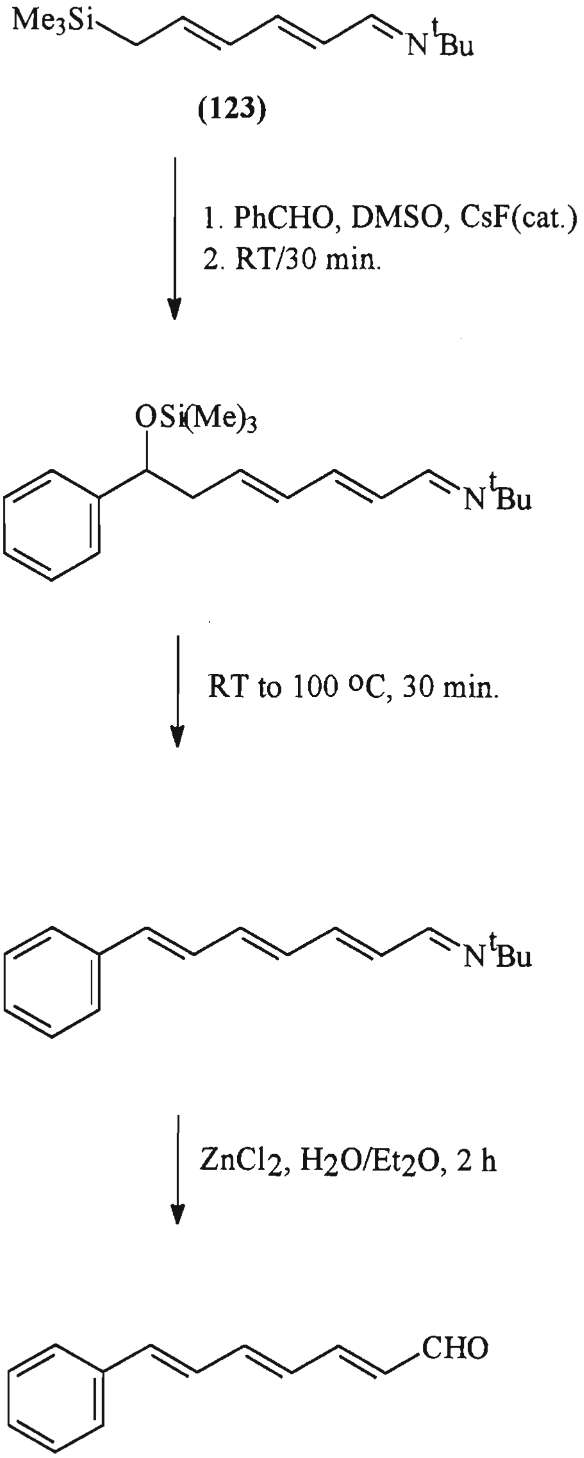
R = Et (107a)
R = ⁱPr (107b)

(122)

Scheme 41

The benzaldehyde could have added onto the 3-position of the naphthalene ring just as easily as it might have added onto the 1-position. Further structural elucidation of **122** is necessary to confirm this structure.

The structures of several natural products with various fungicidal and anti-tumour properties contain long polyenic chains with *E* configuration. Bellassoued and co-workers[109] have recently reported the preparation of such a chain by doing a one-pot conversion of an aldehyde to a trienal by the use of an organosilicon reagent. The reaction is shown in **Scheme 42**.



(123)

(124)

Scheme 42

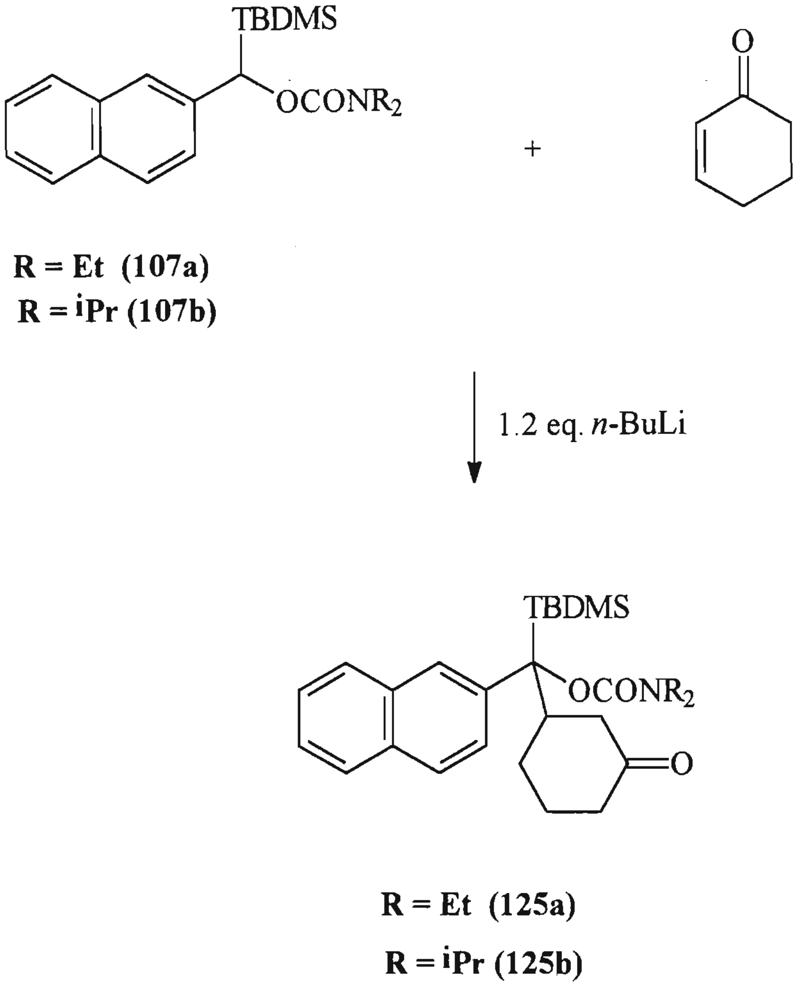
This reaction finds analogy with the present work in that the addition of an aldehyde to an organosilicon reagent results in the formation of an alkene species.

The organosilicon reagent is 6-trimethylsilyl-*N-tert*-butyl sorbaldimine **(123)** which is readily prepared in 74% yield by deprotonation of *N-tert*-butyl sorbaldimine with LDA and subsequent quenching of the lithium intermediate with TMSCl.

Nucleophilic addition of **123** to benzaldehyde in the presence of a catalytic amount of CsF (10%) in anhydrous DMSO, followed by a very mild hydrolysis of the *tert*-butylimine affords the 2*E*, 4*E*, 6*E*-7-phenyl heptatrienal **(124)** in 70% yield.

2.4.3. Electrophilic Substitution of TBDMS-Substituted Carbamates with Michael Acceptors

The reactions of two Michael acceptors, *viz.* 2-cyclohexen-1-one and methyl acrylate, with 1-silylnaphthyl carbamates **107a** and **107b** were investigated. 2-Cyclohexen-1-one was found to undergo a 1,4-addition to afford compounds **125a** and **125b** **(Scheme 43)** as a mixture of diastereomers.



R = Et (107a)
R = ^{i}Pr (107b)

R = Et (125a)
R = ^{i}Pr (125b)

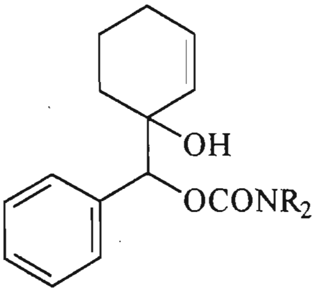
Scheme 43

The diastereomers were separated by centrifugal chromatography and the de's were determined by mass. The yields and de's are shown in **Table 5**.

Table 5

SUBSTRATE	PRODUCT	% YIELD	% de
107a	**125a**	14	59
107b	**125b**	17	20

Yoell[110] observed that in the absence of a silicon group at the α-position, 1,2-addition products of type **126a** and **126b** are preferred.



R = Et (126a)
R = ^{i}Pr (126b)

It is therefore proposed that the silicon moiety may be acting us a Lewis acid, co-ordinating to the carbonyl oxygen of the 2-cyclohexen-1-one (**Figure 4**) thus enhancing the electrophilicity of the Michael acceptor and facilitating the reaction of the benzylic anion with the Michael acceptor.

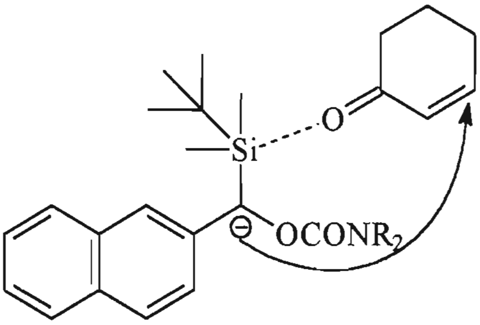


Figure 4

The reactions of **107a** and **107b** with methyl acrylate yielded interesting products. Instead of isolating the expected 1,4-addition products **127a** and **127b** (**Scheme 44**), the diastereomerically pure lactones (**129a** and **129b**) (**Scheme 45**) were isolated. The yields of the lactones are quoted in **Table 6**. The stucture of (**129a**) was confirmed by X-ray crystallography (**Figure 5**).

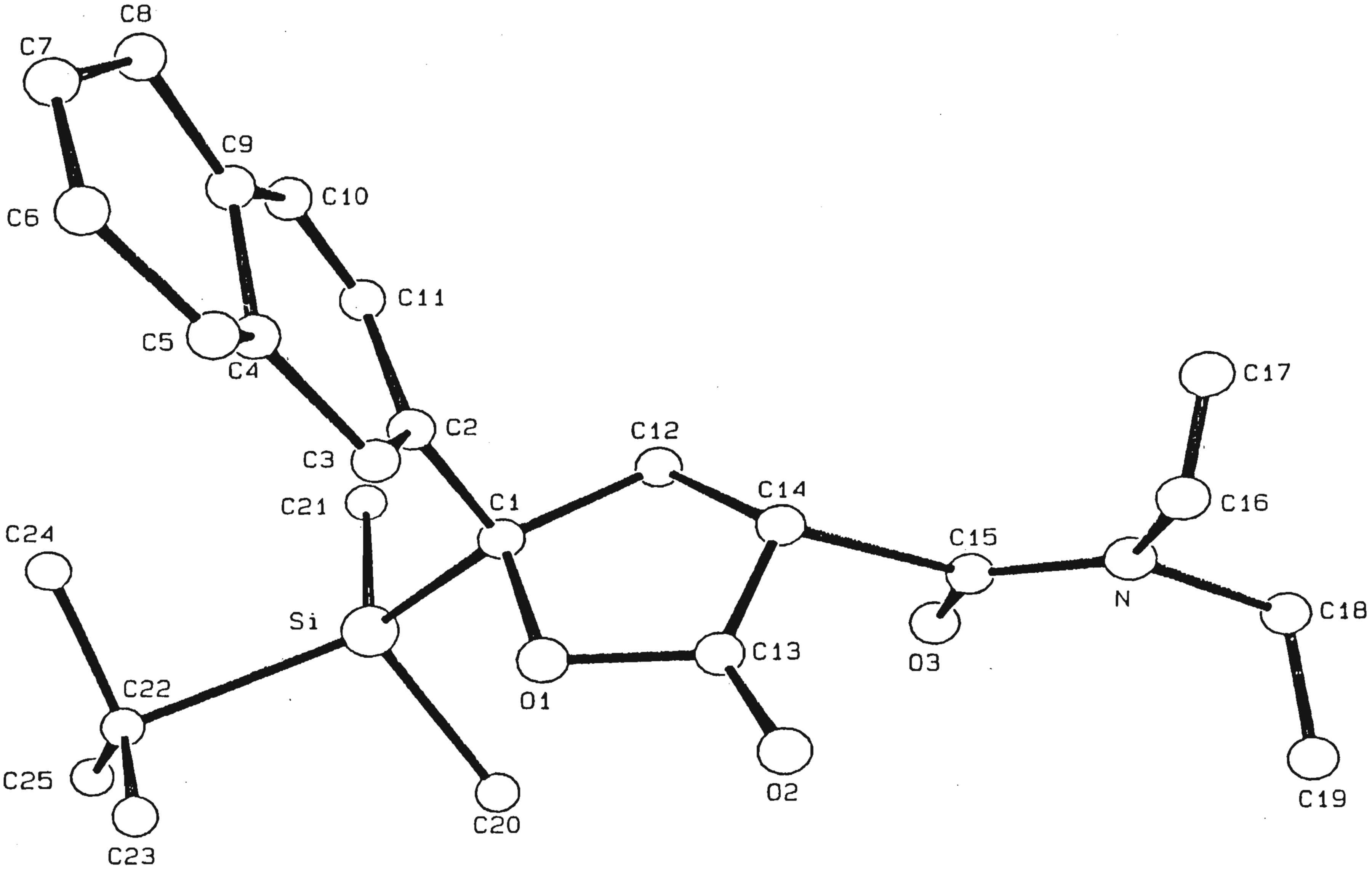
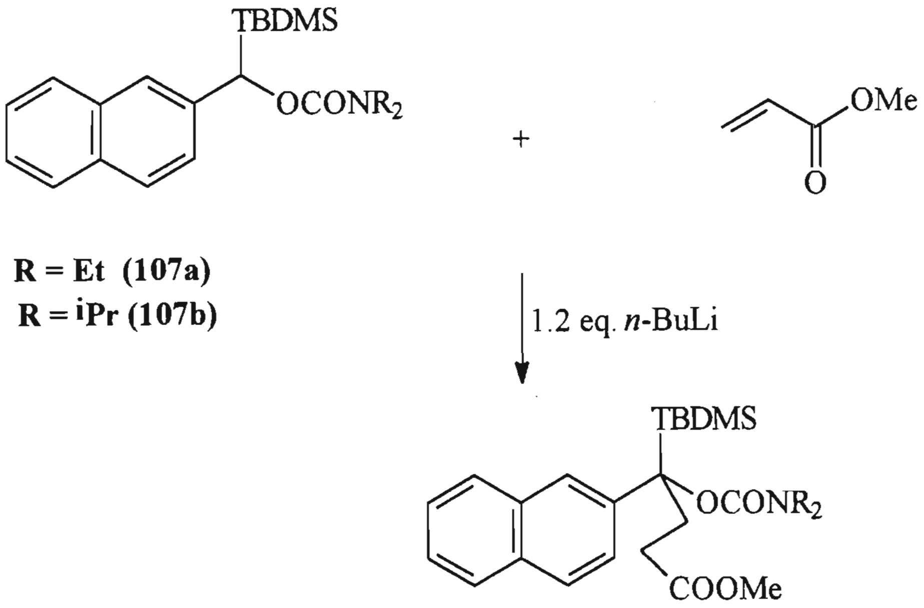


Figure 5. 4-*tert*-Butyldimethylsilyl-2-*N,N*-diethylaminocarbonyl-4-(2'-naphthyl)-γ-butyrolactone (129a)



R = Et (107a)
R = ⁱPr (107b)

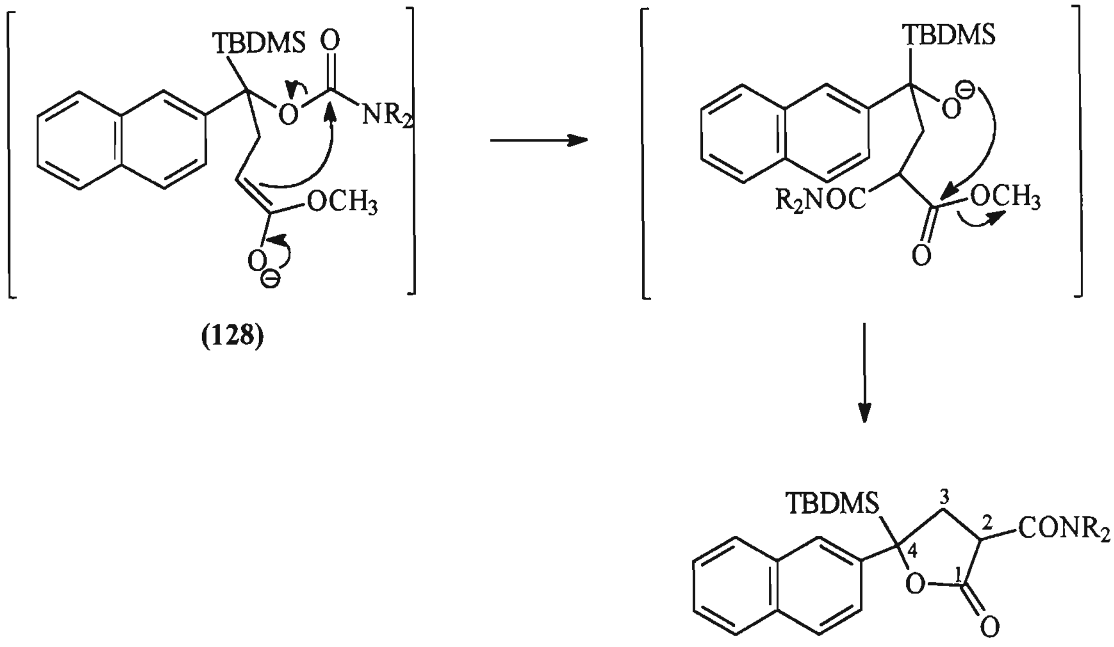
R = Et (127a)
R = ⁱPr (127b)

Scheme 44

Table 6

SUBSTRATE	**% YIELD**
129a	35
129b	7

The mechanism for the formation of these α,γ,γ-trisubstituted butyrolactones (**129a** and **129b**) is illustrated in (**Scheme 45**). The expected Michael reaction had occurred, but, in addition, the amide portion of the carbamate migrated on attack of the enolate anion on the carbamate carbonyl. Once migration had occurred, the oxyanion attacked the ester functionality to form the diastereomerically pure α,γ,γ-trisubstituted butanolides.



(128)

R = Et (129a)
R = ^{i}Pr (129b)

Scheme 45

This one-pot reaction illustrates the potential of the naphthyl alcohol system to act as a tri-ionic species **(Figure 6)** with the initial masking of the oxyanion as the carbamate.

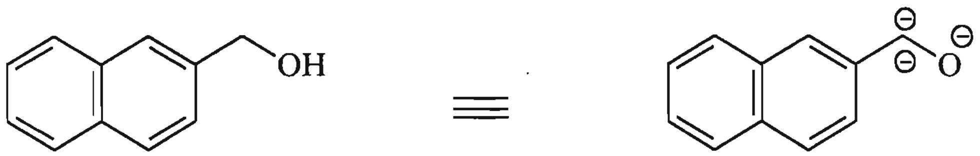
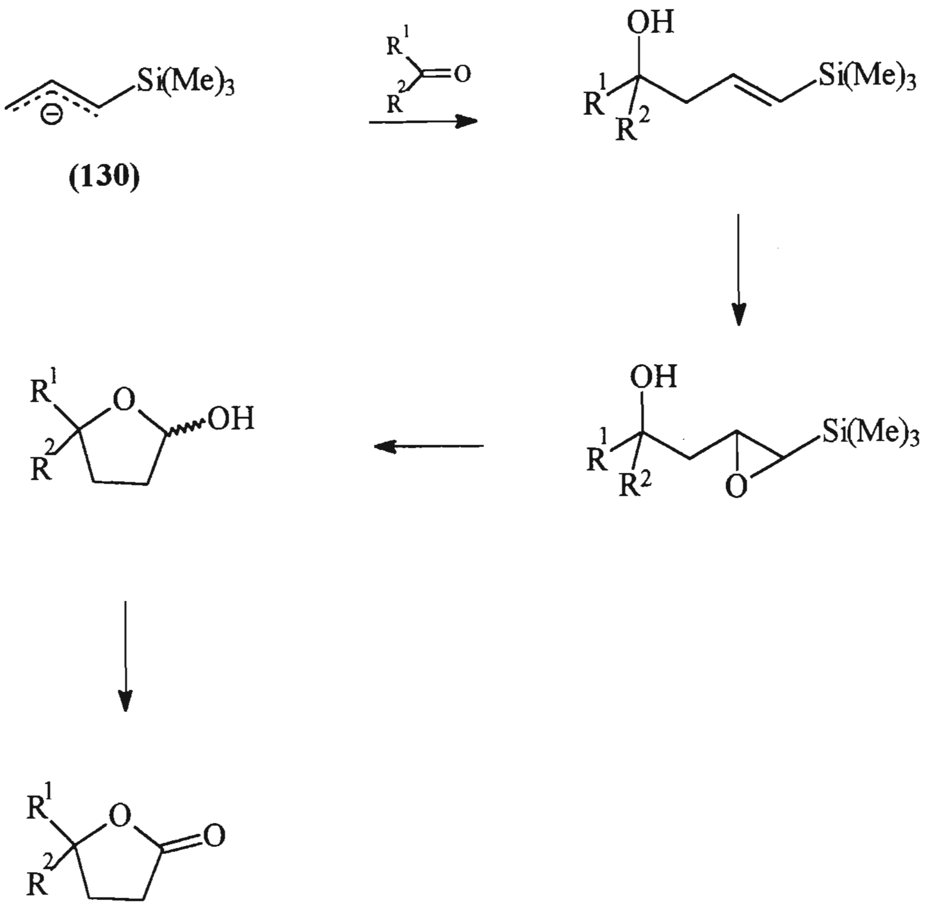


Figure 6

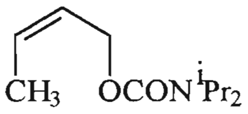
The lactones are easily recognised by the doublet of doublets splitting pattern observed for the proton at the 2-position in compounds **(129a)** and **(129b) (Scheme 45)**. Also, the methyl protons no longer appear as broad signals as they do in the carbamate functionality. They are now observed as two distinct triplets which is indicative of amide type connectivity.

Chan[26] has reported another method to synthesise these butyrolactones, *viz* the reaction of α-silyl anions **(130)** with carbonyl compounds **(Scheme 46)**.

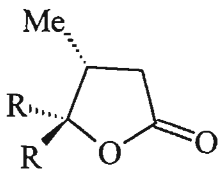


Scheme 46

Hoppe[111] has successfully prepared β-γ-*cis*-di- and tri-substituted γ-lactones **(132)** from homoaldol reactions between *(Z)*-2-butenyl carbamates **(131)** and aldehydes and ketones.



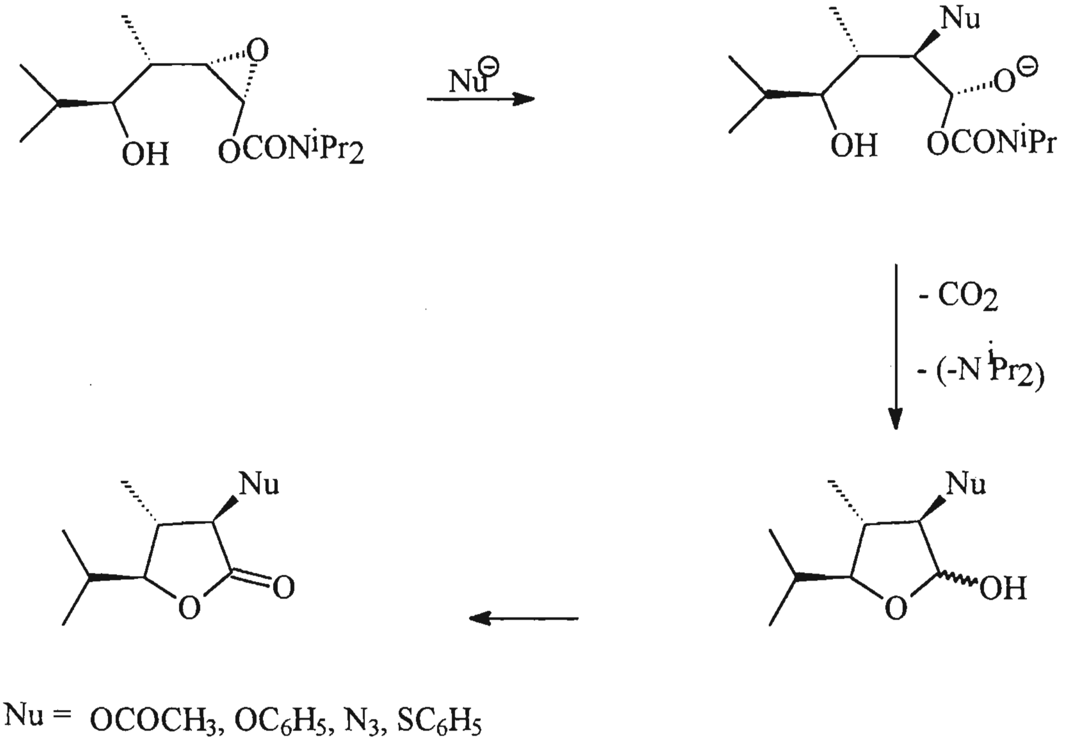
(131)



R = alkyl

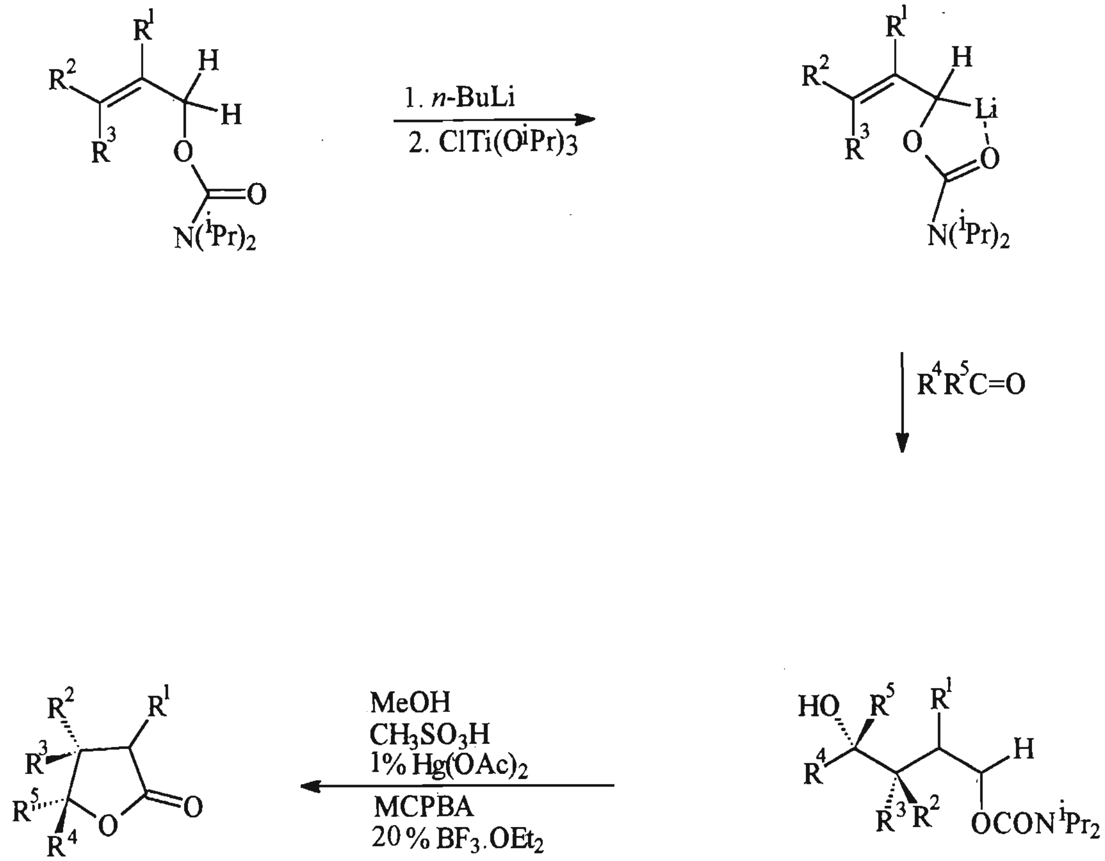
(132)

Hoppe[112] has also achieved impressive diastereoselectivity (>98:2) in the synthesis of γ-lactones *via* the regio- and stereocontrolled opening of 1,2-epoxy-4-hydroxyallyl carbamates with heteronucleophiles **(Scheme 47)** and *via* the addition of aldehydes and ketones to allylic homoenolate reagents[113] **(Scheme 48)**.



Nu = $OCOCH_3$, OC_6H_5, N_3, SC_6H_5

Scheme 47

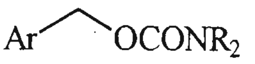


Scheme 48

2.5. ATTEMPTED REARRANGEMENT OF THE CARBAMATE MOIETY

As discussed at length in **Chapter 1, Section 1.3.3**, the migration of the carbamate moiety occurs with relative ease under favourable conditions.

The Snieckus rearrangement[46] of *o*-phenyl carbamates resulted in salicylamides **(Scheme 11)**. This type of rearrangement of *o*-benzyl carbamates of type **133** is unprecedented.

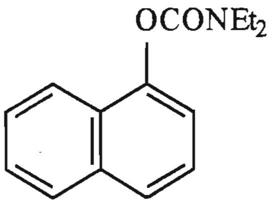


Ar = benzyl, naphthyl
R = alkyl

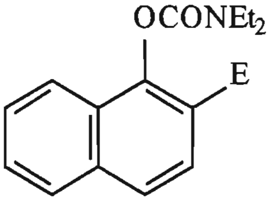
(133)

Although Gawley[56] attempted this type of rearrangement on compounds of type **(133)**, he found that only the 1,2-migration products were observed **(Scheme 13)**.

It is interesting to note that while Snieckus[46] carried out *ortho*-substitutions on 1-naphthyl carbamates **(134)** to afford the 2-substituted products **(135)**, he does not report any attempt at migrating the amide onto the naphthalene ring.



(134)

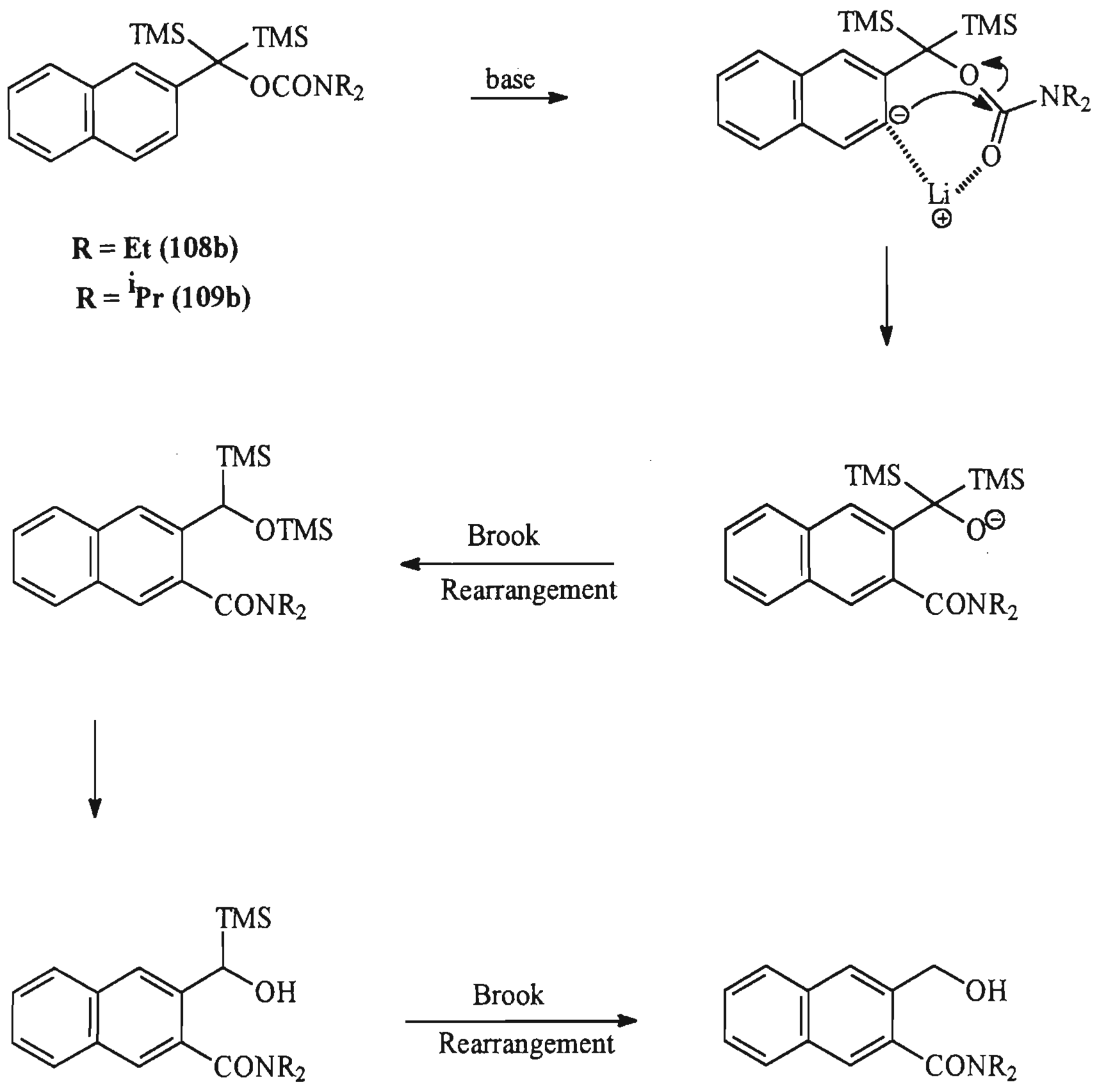


(135) E = Me

If one were to attempt the migration of the amide portion of the carbamate onto the aromatic ring, protection of the normal sites of deprotonation, *i.e.* the benzyl protons is necessary. This type of protection of the preferred D*o*M sites by the use of silyl groups has been reported previously.[113]

The synthesis of the bis-silylated compounds **108b** and **109b** **(Scheme 34)** in good yield **(Table 3)** provided ready substrates for migration reactions.

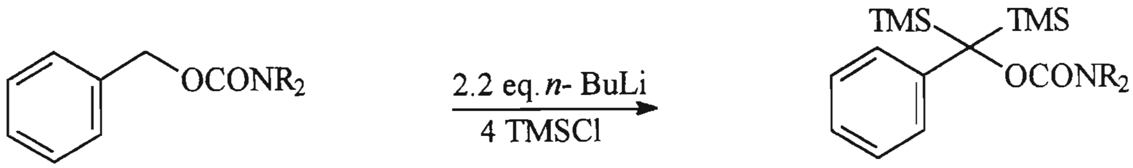
We envisaged the reaction shown in **Scheme 49** taking place on deprotonation of compounds **108b** and **109b**.



R = Et (108b)
R = ^{i}Pr (109b)

Scheme 49

In addition to the attempts made to rearrange compounds **108b** and **109b**, attempts to rearrange the benzyl derivatives **112** and **137 (Scheme 50)** of these compounds were also made. The latter were synthesised as shown in **(Scheme 50)**.



R = Et (110)

R = ^{i}Pr (136)

R = Et (112)

R = ^{i}Pr (137)

Scheme 50

The yields from the reaction are shown in **Table 7**.

Table 7

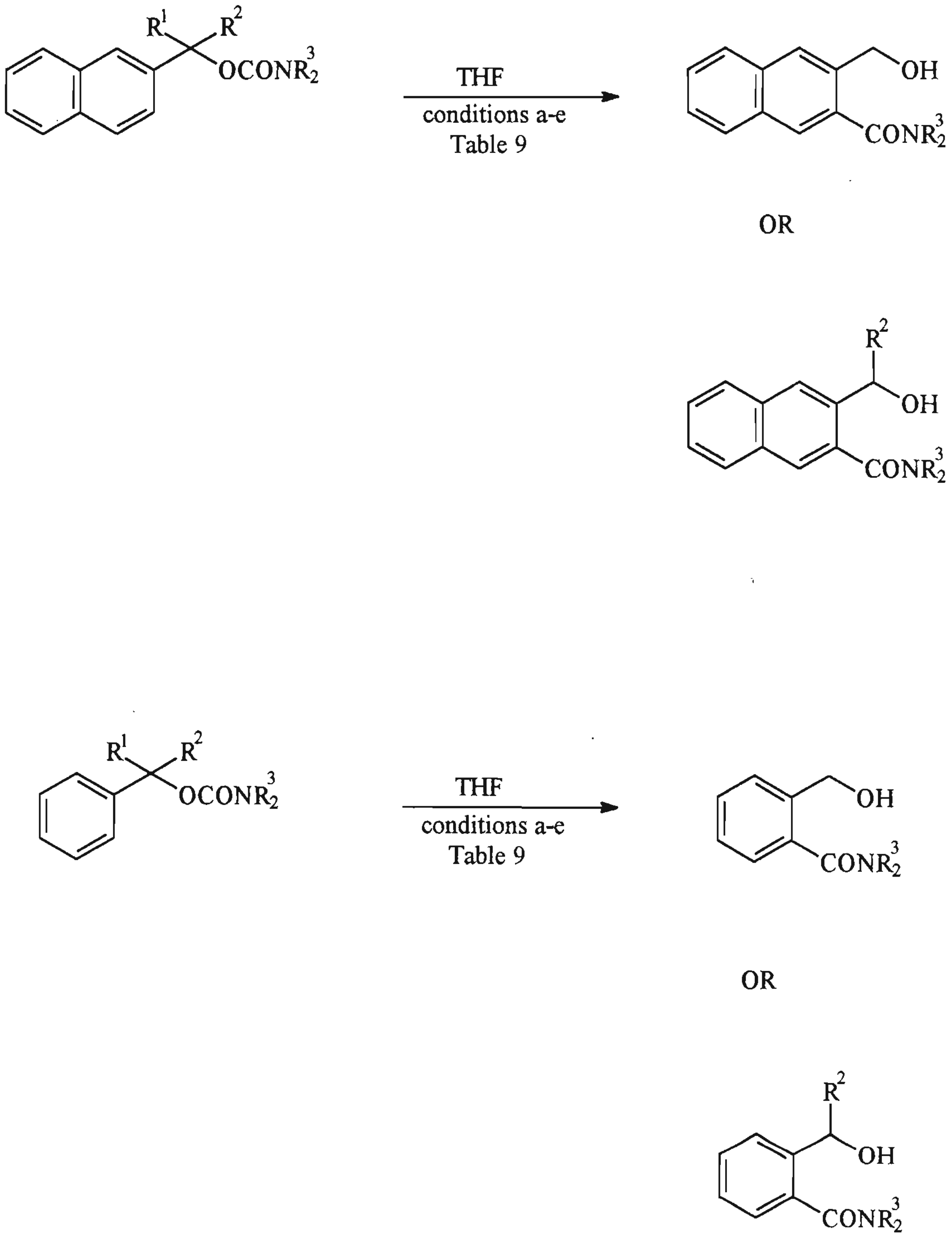
PRODUCT	% YIELD
112	60
137	55

The conditions used by various authors to facilitate amide migrations are summarised in **Table 8**.

Table 8

AUTHORS	CONDITIONS
1. Sibi and Snieckus[46]	sec-BuLi, -78 °C→RT, 10-12 h
2. Zhang and Gawley[56]	sec-BuLi, -78 °C, 2-6 h
3. Wang and Snieckus[58]	2.5/5 eq. LDA, 0 °C→RT→reflux
4. Miah and Snieckus[47]	sec-BuLi/TMEDA, -78 °C, 2-6 h
5. Fu and co-workers[60]	2 eq. LDA/tert-BuLi, 0 °C→RT
6. Beaulieu and Snieckus[114]	3 eq. LDA, -78 °C→0 °C

We attempted the conditions listed in **Table 8** and adaptations thereof on various silylated carbamates in order to achieve migration of the carbamate moiety. A general scheme for the rearrangement is shown in **Scheme 51** and the results are summarised in **Table 9**.


R^1
R^2
OCONR$^3_2$
THF
conditions a-e
Table 9
OH
CONR$^3_2$
OR
R^2
OH
CONR$^3_2$
R^1
R^2
OCONR$^3_2$
THF
conditions a-e
Table 9
OH
CONR$^3_2$
OR
R^2
OH
CONR$^3_2$

Scheme 51

Table 9

ENTRY	Ar	R^1	R^2	R^3	CONDITIONS
1	naphthyl	TMS	TMS	$^{i}\mathrm{Pr}_2$	a
2	naphthyl	TMS	TMS	$^{i}\mathrm{Pr}_2$	b
3	naphthyl	TMS	TMS	$^{i}\mathrm{Pr}_2$	c
4	naphthyl	TMS	TMS	$^{i}\mathrm{Pr}_2$	d
5	naphthyl	TMS	TMS	$^{i}\mathrm{Pr}_2$	e
6	naphthyl	TMS	TMS	Et	a
7	naphthyl	TMS	TMS	Et	b
8	naphthyl	TMS	TMS	Et	c
9	naphthyl	TMS	TMS	Et	e
10	benzyl	TMS	TMS	$^{i}\mathrm{Pr}_2$	b
11	benzyl	TMS	TMS	Et	b
12	naphthyl	H	TBDMS	Et	c

a) 3 eq. LDA, -78 °C→0 °C→RT→reflux

b) 5 eq. LDA, -78 °C→0 °C→RT→reflux

c) 3 eq. *tert*-BuLi, 1 eq. TMEDA, -78 °C→0 °C→RT→reflux

d) 3 eq. *n*-BuLi, 2 eq. TMEDA, -78 °C→0 °C→RT→reflux

e) 3 eq. *n*-BuLi, 2 eq. HMPA, -78 °C→0 °C→RT→reflux

Although *sec*-BuLi-TMEDA is reported to be a very efficient deprotonating agent,[56] this base was unavailable and reactions were therefore carried out using *n*-BuLi, *tert*-BuLi or LDA to generate the required anion.

The generation of an anion in solution by the abstraction of a proton using an alkyllithium base is readily distinguished by the highly coloured solution that ensues. In spite of the numerous colour changes that took place during the course of these reactions **(Entries 1-12)**, no products indicative of a migration reaction were isolated. The reactions yielded only starting material or the mono-TMS derivative **(Entries 1-11)**. **Entry 12** gave rise to a complex mixture. Inspection of molecular models indicated that bulky bases such as *tert*-BuLi and LDA might not be able to effect deprotonation on the ring due to steric hindrance and the use of *n*-BuLi was then advocated (conditions **d** and **e**). It was hoped that the use of

TMEDA (conditions **c** and **d**) would further stabilise the anion that formed by coordination **(Figure7)**.[56]

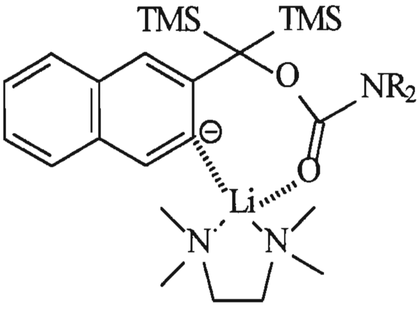
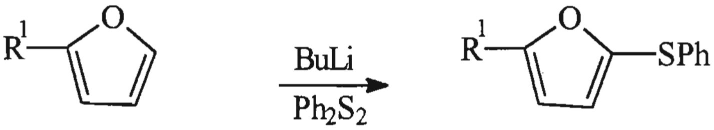


Figure 7

It has been shown that in the 4-substitution of 2-alkylfurans[115] **(138)**, when $R^1 = CH(OC_2H_5)_2$ **(Scheme 52)**, the required anion would only form if hexamethylphosphoric triamide (HMPA) was added to the reaction solvent. We hoped that the HMPA would display similar reactivity if incorporated into the migration reactions **(Table 9**, condition **e)**.



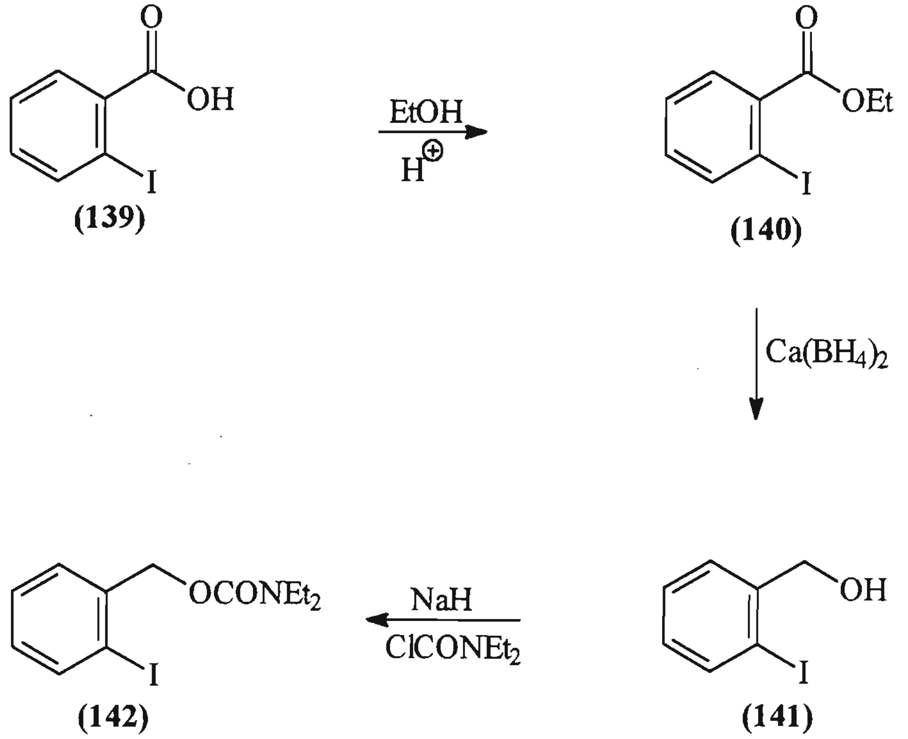
(138)

Scheme 52

In spite of the various additives and conditions employed, no products indicative of a migration reaction were detected, thus the conditions of the 'thia-Fries Rearrangement' **(Scheme 23)** were employed. Treatment of the compounds from **entries 1, 6, 10** and **11 (Table 9)** with 4 equivalents of $AlCl_3$ in CH_2Cl_2 at 25 °C for 3 hours and subsequent reflux also resulted in the recovery of starting material only.

2.6. Li-HALOGEN EXCHANGE TO FACILITATE CARBAMOYL MIGRATION

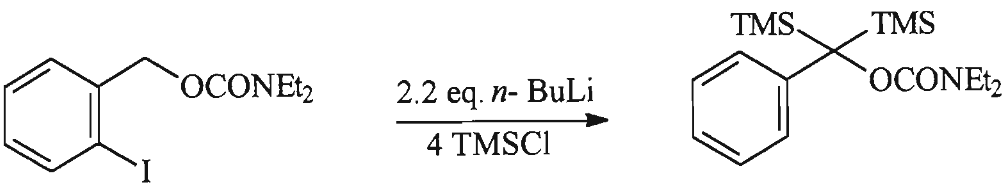
The final approach to facilitate migration of the amide portion of the carbamate was based on the work of Lamas and co-workers[116] who achieved carbamoyl transfer *via* Li-halogen exchange in alkaloids. The approach was to prepare 1-*N,N*-diethylcarbamoyloxy-1-(2'-iodophenyl)methane **(142) (Scheme 53)**. This was accomplished by starting with the readily available 2-iodobenzoic acid **(139)**. The acid was converted to the ester **(140)** in 59% yield by refluxing in EtOH with a catalytic amount of H_2SO_4. A mild reduction procedure was required to reduce the ester to the alcohol while retaining the iodine. $Ca(BH_4)_2$ reduction[117] presented a viable solution and produced the alcohol **(141)** in 88% yield. The alcohol was then converted to the carbamate **(142)** in 75% yield.



Scheme 53

Since we still envisaged that successful migration would take place only if the preferred sites of deprotonation were protected, we attempted the synthesis of the bis-silylated derivative of compound **142**.

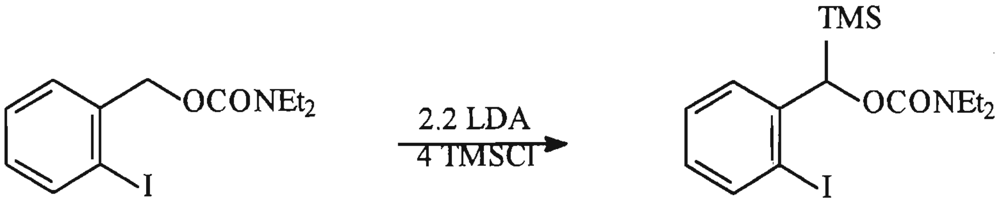
We employed the use of a previously high yielding method, *i.e.* 2.2 equivalents of *n*-BuLi and 4 equivalents of TMSCl **(Scheme 54)**, but were only able to isolate compound **(112)** in 30% yield.



(142) **(112)**

Scheme 54

This indicated the affinity that *n*-BuLi has for a halogen even when a proton source is available. When 2.2 equivalents of LDA and 4 equivalents of TMSCl were used, only the mono-TMS derivative **(143)** **(Scheme 55)** was isolated, even after prolonged reaction times and warming the reaction mixture up from -78 °C to 0 °C. A small amount (3%) of compound **(112)** was isolated in addition to compound **(143)** (61%).

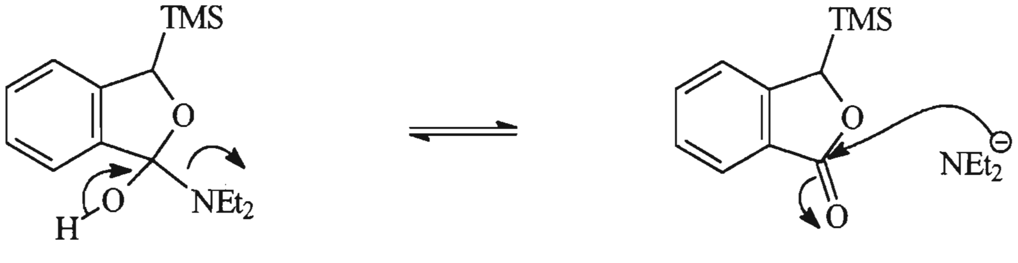


(142) **(143)**

Scheme 55

Attempted abstraction of the second benzylic proton with LDA and substitution with a methyl group was unsuccessful. It was then evident that the addition of *n*-BuLi to compound **(143)** might facilitate the required migration since deprotonation would now occur on the aromatic ring.

n-BuLi (2.2 equivalents) was added to a solution of **(143)** in THF at -78 °C. A dark purple solution ensued indicating the generation of an anion. After work up and isolation of the most abundant product from a complex mixture, GC/MS indicated the presence of two products - one with a mass of 279 and the other with a mass of 206. Separation of the two compounds was impossible and mass spectra of the same sample run at hourly intervals indicated that there was an equilibrium between the two products. IR spectra showed that both a carbonyl and a hydroxyl group were present. We were fortunate to obtain a proton NMR of one of the compounds when the other seemed to be present in a low amount. This spectrum (page 174) indicated that the benzylic proton at 4.49 ppm was still present together with 2 ethyl groups (1.05 and 1.24 ppm, 2 x CH_2CH_3 and 3.15 and 3.53 ppm, 2 x CH_2CH_3), a TMS group (0.08 ppm) and a hydroxyl group (2.51 ppm). We therefore proposed that this compound was the hemiaminal **(144)** **(Scheme 56)** and the equilibrium was as shown.

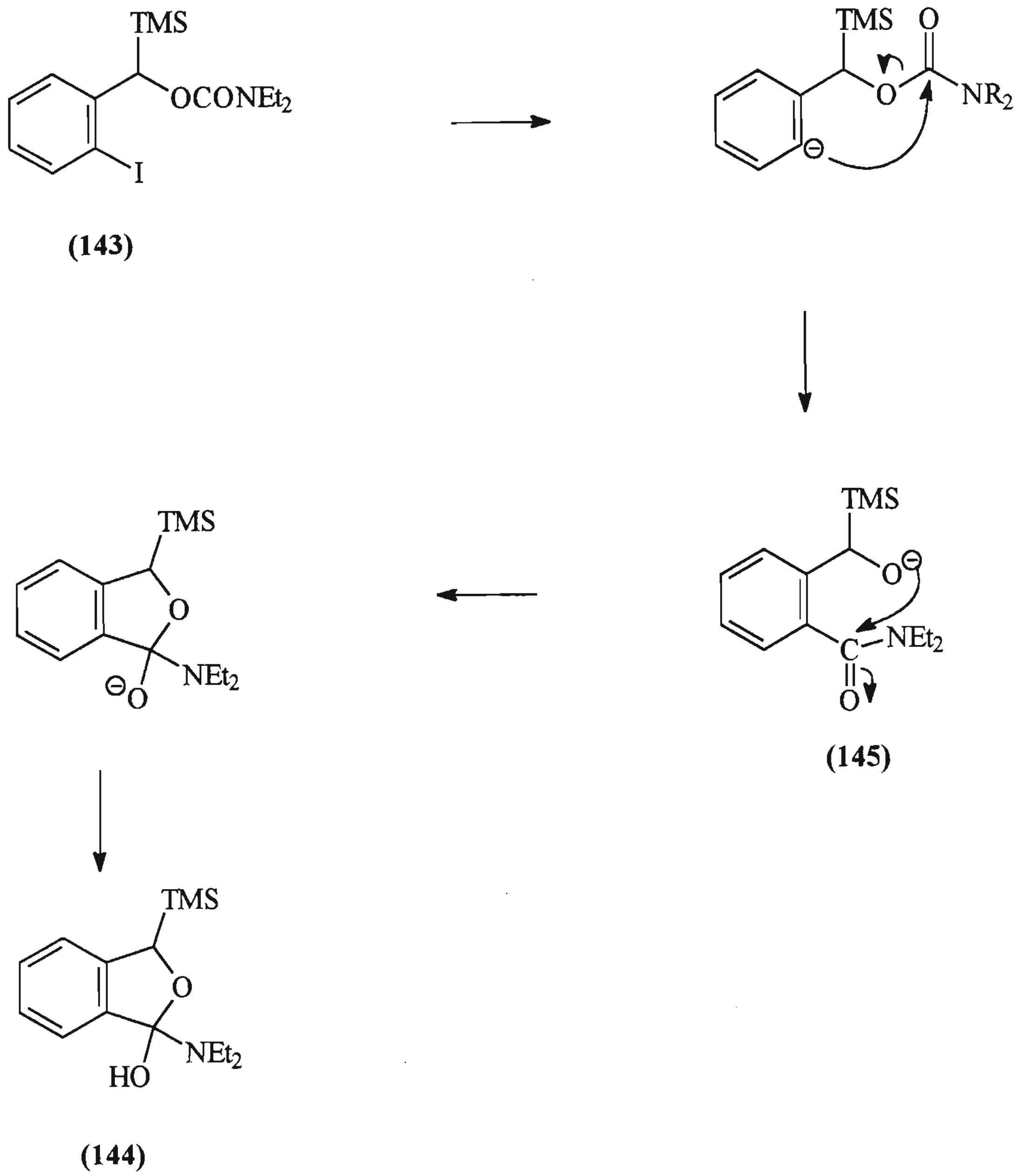


(144) MW = 279

(145) MW = 206

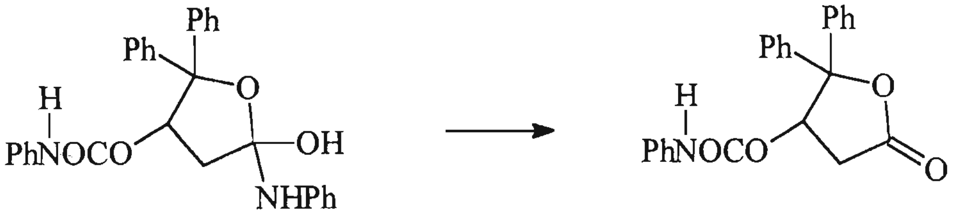
Scheme 56

It is proposed that the hemiaminal **(144)** forms by the mechanism shown in **Scheme 57**.



Scheme 57

It is interesting that formation of the lactol by attack of the oxyanion on the carbonyl in the intermediate **145** occurs before the expected migration of the silyl group onto the oxyanion (Brook Rearrangement). A search of the literature revealed some evidence in support of compound **144**. Hauser and Adams[118] in their study on the mechanism of lactone formation, proposed the intermediate **146 (Scheme 58)** which is similar to compound **144**.



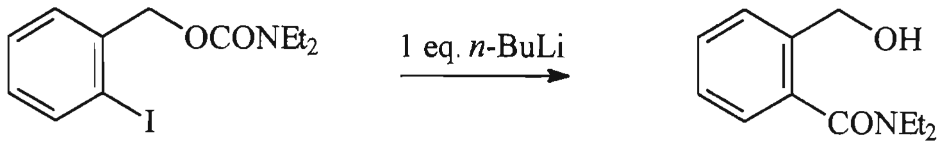
(146)

Scheme 58

Workers^{110} in our laboratories have found that reactions requiring 2 equivalents of base proceed in higher yield and with greater success if these equivalents are added one at a time, with a period of stirring between the additions.

We therefore added one equivalent of *n*-BuLi to a solution of **143** in THF at -78 °C, but we still obtained the equilibrium shown in **Scheme 56**. The addition of one equivalent of *n*-BuLi to a solution of **142** in THF at -78 °C proved interesting.

Although no colour change was observed after addition of the base, GC/MS of the crude mixture after 3 hours showed three peaks with the required mass of 207. The reaction was quenched with saturated NH_4Cl and a polar product was isolated which was identified to be the product **147** resulting from a 1,4-migration **(Scheme 59)**.



(142) **(147)**

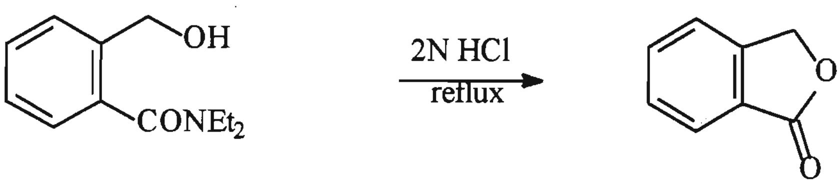
Scheme 59

Compound **147** was isolated in 27% yield together with 3% of the benzyl carbamate **(110)** **(Scheme 50)**.

Increasing the reaction time to 7 hours increased the yield of **(147)** to 35%. Bailey and Punzalan,^{119} in their study on Li-halogen exchange, found that diethyl ether was a better solvent for the reactions than THF. When we replaced the THF with diethyl ether in the reaction shown in **Scheme 59**, we found a 10% increase in the yield of **147** to 45%.

To confirm the structure of **147** and to obtain the 1-phthalanone **148**, a structure that is found in a variety of natural products, cyclisation of the migrated product was carried out.

The conditions of Alo and co-workers[120] **(Scheme 60)** were employed and compound **(148)** was isolated in 68% yield.

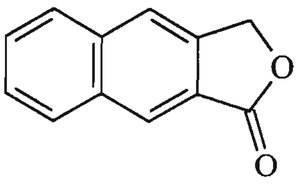


(147) **(148)**

Scheme 60

The use of base catalysed cyclisation conditions (1 equivalent NaOH, EtOH) similar to the conditions used by Superchi and co-workers[121] also yielded the phthalanone in 65% yield.

This successful Li-halogen exchange was to be extended to the naphthyl system to form products of type **150**.

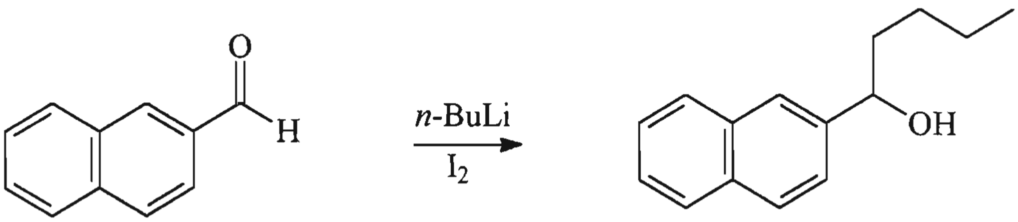


(150)

For this we required a halogenated naphthalene ring.

2.7. ATTEMPTS TO HALOGENATE THE NAPHTHALENE RING

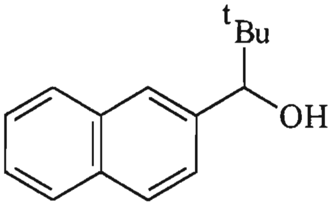
We first attempted a D*o*M reaction of 2-naphthalene carboxaldehyde **(151)** **(Scheme 61)**.



(151) **(152)**

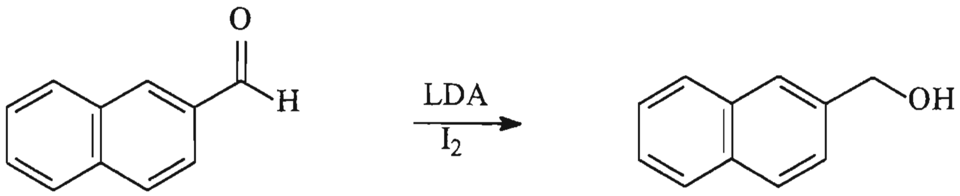
Scheme 61

This yielded the alcohol **(152)** (47% yield) as a result of nucleophilic attack of the BuLi on the aldehyde. Use of the bulkier base, *tert*-BuLi, yielded the tertiary butyl alcohol **(153)** (38% yield).



(153)

The use of the non-nucleophilic base, LDA, yielded naphthalene-2-methanol **(98)** (30% yield) **(Scheme 62)**.



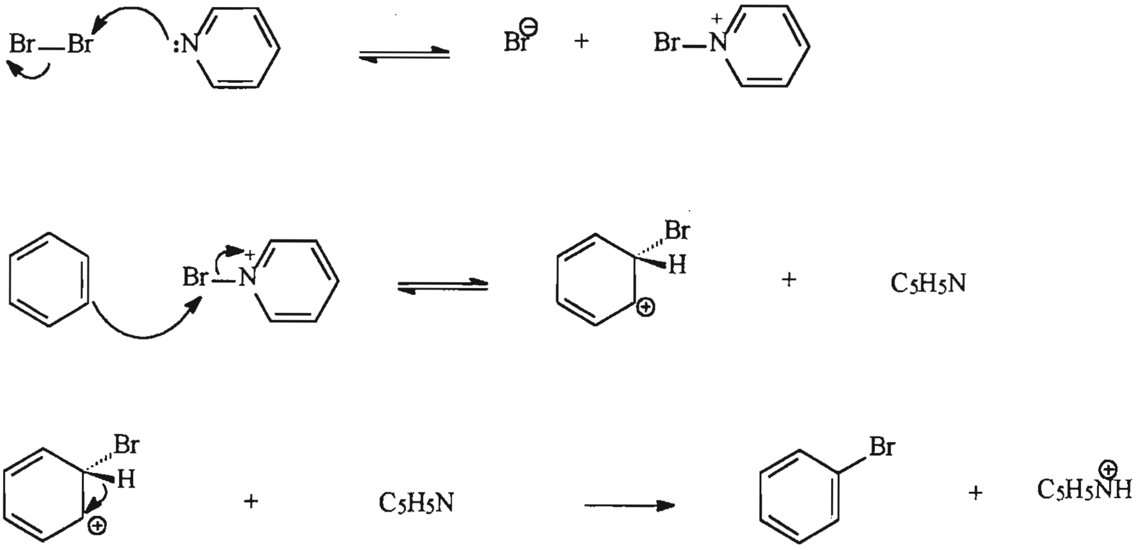
(151) **(98)**

Scheme 62

This is unusual in that LDA does not usually act as a reducing agent. The mechanism of formation of the alcohol is not known at this time.

We then proceeded to use the method of Lamas and co-workers[116] which involved refluxing the carbamate **99a** **(Scheme 24)** in a mixture of sodium acetate, glacial acetic acid and iodine, but this yielded only starting material.

A method described in Vogel[122] for bromination of a benzene ring invokes the use of pyridine and bromine **(Scheme 63)**.



Scheme 63

We employed similar methodology to effect halogenation of the naphthalene ring. The carbamate **99a** **(Scheme 24)** was refluxed in pyridine and bromine for 5 hours. GC/MS of the crude mixture at this point indicated that a minute amount of brominated product was present. Optimisation of this reaction and elucidation of the product is necessary to determine whether bromination has occurred on the aromatic ring or at the benzylic position. Due to time constraints, this reaction was not pursued any further.

2.8 Future Work

The work described herein indicates that the naphthyl system demonstrates similar reactivity to allylic and benzylic systems in certain instances, but a few interesting reactions require further elucidation.

1. As mentioned in Section 2.4.2., it has been found that the bulk of the silyl group influences the diastereomeric ratio of the alkenes formed in the Peterson olefination reaction. It is therefore necessary to carry out electrophilic substitutions on the mono-TMS derivatives of the carbamates, *i.e.* **108a (Scheme 33)** and **109a (Scheme 31)**. The reduced steric bulk in these substrates might also facilitate reaction with the electrophiles listed in **Figure 2** that were previously found to be unsuccessful.

2. It was also found during the course of this investigation that the use of THF dried over a Na/K amalgam improved the yields of the Peterson olefination products. Reactions of the TBDMS-substituted carbamates **(107a and 107b, Scheme 30)** with the pyridine and quinoline aldehydes listed in **Figure 2** resulted in complex mixtures when carried out in THF that was dried over $LiAlH_4$. The use of the former THF might yield the desired olefination products.

3. Further structural elucidation of **122 (Scheme 41)** is necessary to determine whether rearrangement of the anion has in fact occurred.

4. Elucidation of the mechanism for the formation of the alcohol in **Scheme 62** is required.

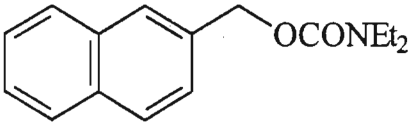
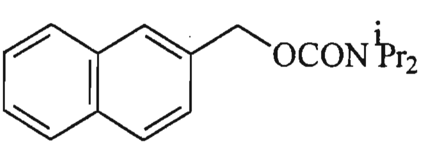
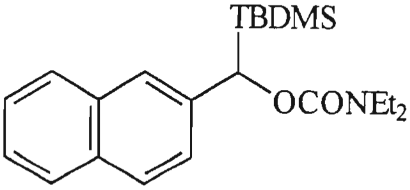
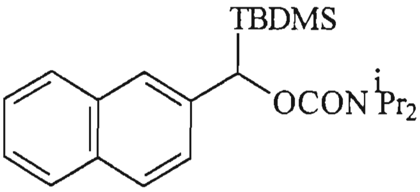
5. In order to obtain the phthalanone **(150)**, a successful route to a halogenated naphthalene ring has to be found. Optimisation of the reaction outlined in **Scheme 63** could prove rewarding in this regard.

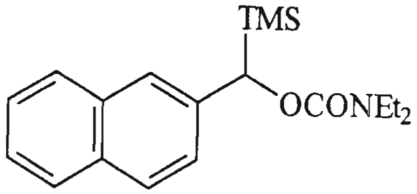
6. Once the Li-halogen exchange reaction has been successfully carried out on the naphthyl system, this methodology may be extended to the anthracene system. Carbamoylation of the anthracyl alcohols was found to be facile during the course of this investigation.

CHAPTER 3

EXPERIMENTAL

3.1. INDEX OF COMPOUNDS PREPARED

Compound Number and Structure	Page Numbers of Characterisation ^{1}H Spectrum ^{13}C Spectrum
 **(99a)**	89 124 125
 **(99b)**	90 126 127
 **(107a)**	91 128 129
 **(107b)**	92 130 131

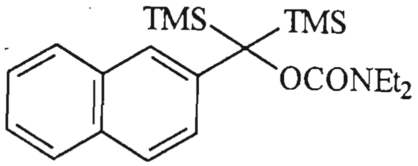


(108a)

93

132

133

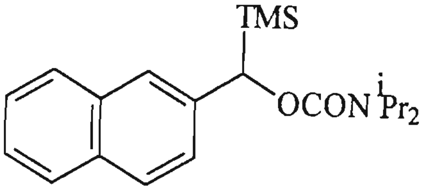


(108b)

94

134

135



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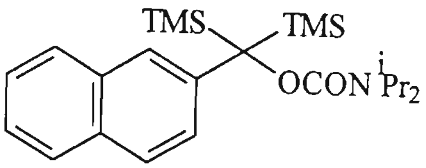
(109a)

136

137



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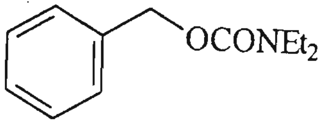
(109b)

138

139



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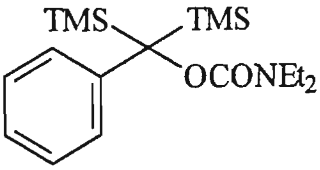
(110)

140

141

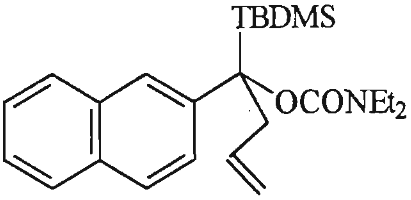


(112)

98

142

143

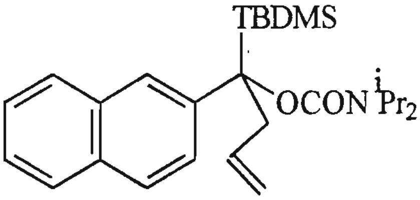


(117a)

99

144

145



(117b)

100

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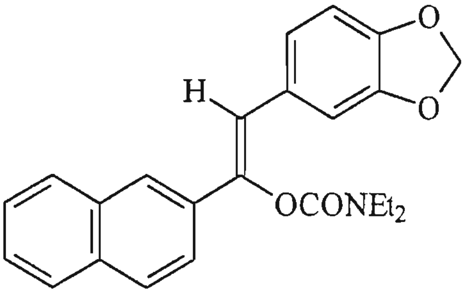
147

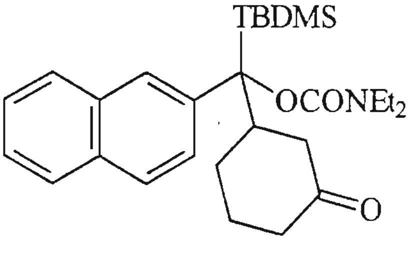


(119a)

101

148

149

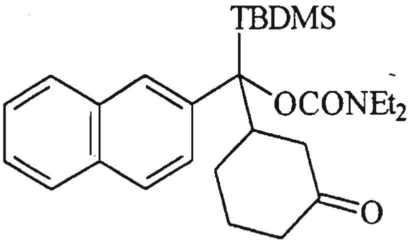


(125a1)

102

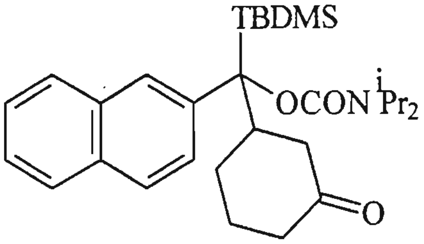
150

151



(125a2)

103
152
153



(125b1)

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154
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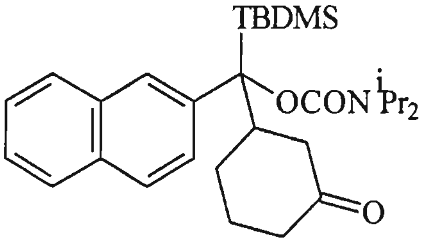

(125b2)

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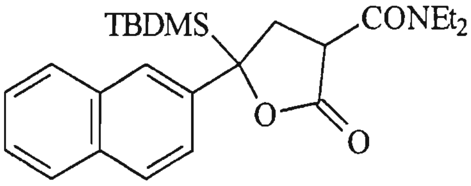

(129a)

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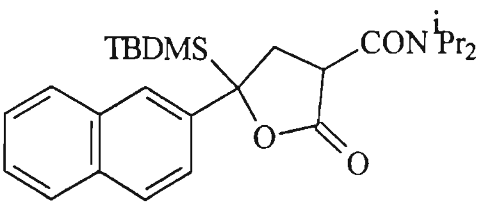

(129b)

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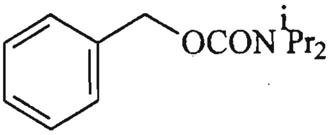
160
161



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162
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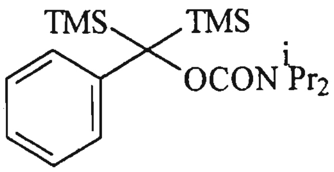

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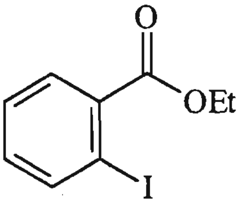

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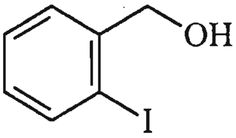
167



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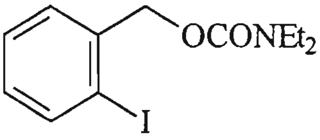
168
169



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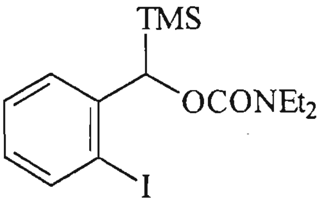

(143)

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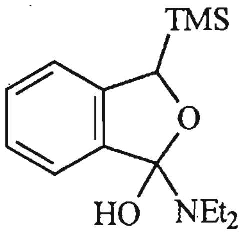
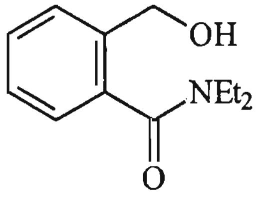


(144)

174 (^{1}H)

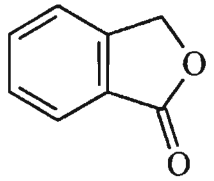


(147)

114

175

176

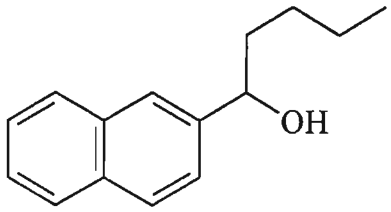


(148)

115

177

178

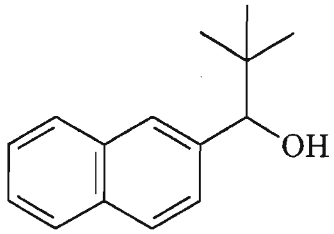


(152)

116

179

180



(153)

117

181

182

3.2. CHEMICALS AND INSTRUMENTATION

All solvents were distilled according to standard procedures before use.[123] Flash chromatography was performed using Merck silica gel (200-400 mesh) by the technique of Still *et al.*[124] Pre-coated Kieselgel $60F_{254}$ Merck plastic sheets were used for thin layer chromatography. Centrifugal chromatography was carried out using a Harrison Research chromatotron Model 7924T on 1 mm, 2 mm or 4 mm Merck silica gel (200-400 mesh) coated glass plates. Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. NMR spectra (^{1}H 200 MHz and ^{13}C 50 MHz) were recorded on a Varian Gemini 200 instrument. All chemical shifts are reported in ppm downfield from tetramethylsilane as internal standard, using $CDCl_3$ as solvent unless otherwise stated. J-values are quoted in Hertz. Mass spectra were recorded on a Hewlett-Packard mass spectrometer (HP5988A). *E:Z* ratios were determined on a Varian 3300 Gas Chromatograph using a DB-1 (15m x 32 mm) column. Low temperatures were maintained using dry-ice solvent baths according to the procedure of Phipps and Hume.[125]

3.3. PREPARATIONS

GENERAL PROCEDURE 1

Preparation of *N,N*-Dialkyl carbamates

To a suspension of NaH (1.5 equivalents) in THF (50 ml) was added the alcohol slowly with cooling in an ice-bath. The mixture was warmed to room temperature and stirred for 30 minutes. After cooling again to 0 °C, the carbamoyl chloride (1.2 equivalents) dissolved in THF (10 ml) was added dropwise and the mixture was stirred at room temperature for 2 h. The reaction was quenched with saturated NH_4Cl. The THF was then removed under reduced pressure and the residue was extracted with ether (3 x 20 ml). The combined ether extracts were washed with water (3 x 20 ml), dried over $MgSO_4$ and the ether was removed under reduced pressure. The product was purified by flash chromatography (hexane/ether) on silica gel.

GENERAL PROCEDURE 2

Silylation of *N,N*-Dialkyl Carbamates

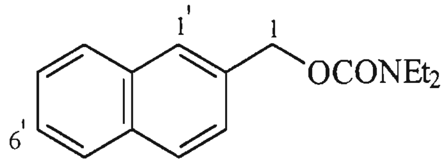
To a solution of carbamate in THF (10 ml) at -78 °C was added *n*-BuLi under a N_2 atmosphere. The solution was stirred for 30 minutes at this temperature. The silyl chloride, dissolved in THF, was then added and the reaction mixture was stirred at -78 °C for 7 h and then quenched with saturated NH_4Cl. After warming the solution to room temperature, the THF was removed under reduced pressure and the residue was extracted with ether (3 x 20 ml). The ether extracts were washed with water (3 x 20 ml), dried over $MgSO_4$ and the ether was removed under reduced pressure. The product was purified by centrifugal chromatography (hexane/ether) on silica gel.

GENERAL PROCEDURE 3

Electrophilic Substitution of Silylated Carbamates

To a solution of silylated carbamate in THF (10 ml) at -78 °C was added *n*-BuLi (1.2 equivalents) under a N_2 atmosphere. The solution was stirred for 30 minutes at this temperature. The electrophile (1.2 equivalents) was then added dropwise and the reaction mixture was stirred for 7 h at -78 °C. The reaction was quenched with saturated NH_4Cl. After warming the solution to room temperature, the THF was removed under reduced pressure and the residue was extracted with ether (3 x 20 ml). The combined ether extracts were washed with water (3 x 20 ml), dried over $MgSO_4$ and the ether was removed under reduced pressure. The product was purified by centrifugal chromatography (hexane/ether) on silica gel.

1-*N,N*-Diethylcarbamoyloxy-1-(2'-naphthyl)methane (99a)



(99a)

$C_{16}H_{19}NO_2$
MW = 257

Compound **(99a)** was prepared according to general procedure 1 using naphthalene-2-methanol (5.00 g, 31.61 mmol) and *N,N*-diethylcarbamoyl chloride (5.14 g, 37.92 mmol). The product was purified by flash chromatography (5:1 hexane/ether) to yield **(99a)** as a pale yellow oil (4.55 g, 56%).

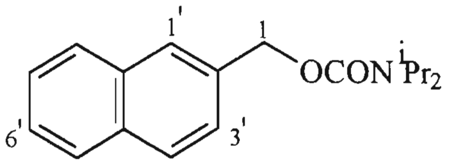
δ_H (200 MHz) : 1.11 (6H, broad t, 2 x CH_2CH_3); 3.29 (4H, broad d, 2 x $\mathbf{CH_2}CH_3$); 5.28 (2H, s, $\mathbf{CH_2}$**-O**); 7.42-7.49 (3H, m, Ar-H); 7.79-7.83 (4H, m, Ar-**H**)

δ_C (50 MHz) : 13.52-14.08 (2 x q, 2 x CH_2CH_3), 41.29-41.88 (2 x t, 2 x CH_2CH_3); 66.87 (t, C_1); 125.75, 126.01, 126.13, 126.77, 127.65, 127.93, 128.18 (7 x d, 7 x Ar-CH); 132.95 and 133.18 (2 x s, $\mathbf{C_{4a'}}$ and $\mathbf{C_{8a'}}$); 134.51 (s, $C_{2'}$); 157.77 (s, C=O)

m/z : (EI) 257 (M^+, 7%), 198 (2), 141 (100), 115 (15), 100 (33), 72 (6)

HRMS. Calcd. for $C_{16}H_{19}NO_2$: 257.1416 Found : 257.1410

1-*N,N*-Diisopropylcarbamoyloxy-1-(2'-naphthyl)methane (99b)



$C_{18}H_{23}NO_2$
MW = 285

(99b)

Compound **(99b)** was prepared according to general procedure 1 using naphthalene-2-methanol (5.00 g, 31.61 mmol) and *N,N*-diisopropylcarbamoyl chloride (6.21 g, 37.92 mmol). The reaction mixture was purified by flash chromatography (5:1 hexane/ether) to afford compound **(99b)** as a white crystalline solid. The crystals were recrystallised from hexane to yield white needles (5.45 g, 60%). m. p. 50 °C.

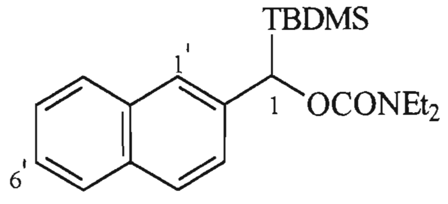
δ_H (200 MHz) : 1.20 (12H, d, 2 x $CH(CH_3)_2$); 3.90 (2H, broad s, 2 x $CH(CH_3)_2$); 5.25 (2H, s, CH_2-O); 7.21-7.50 (3H, m, Ar-H); 7.56-7.83 (4H, m, Ar-H)

δ_C (50 MHz) : 20.92 (4 x q, 2 x $CH(CH_3)_2$); 45.71 (2 x d, 2 x $CH(CH_3)_3$); 66.51 (t, CH_2-O); 125.83, 125.87, 125.99, 126.80, 127.53, 127.81, 128.04 (7 x d, 7 x Ar-CH); 132.82 and 133.08 (2 x s, **$C_{4a'}$** and **$C_{8a'}$**); 134.41 (s, **$C_{2'}$**); 155.35 (s, C=O)

m/z : (EI) 285 (M^+, 6%), 226 (3), 141 (100), 86 (4), 57 (3)

HRMS. Calcd for $C_{18}H_{23}NO_2$: 285.1729 Found : 285.1730

1-*tert*-Butyldimethylsilyl-1-*N,N*-diethylcarbamoyloxy-1-(2'-naphthyl)methane (107a)



$C_{22}H_{33}NO_2Si$
MW = 371

(107a)

Compound **(107a)** was prepared according to general procedure 2 using 1-*N,N*-diethylcarbamoyloxy-1-(2'-naphthyl)methane **(99a)** (1.50 g, 5.83 mmol), *n*-BuLi (2.2 equivalents) and *tert*-butyldimethylsilyl chloride (1.05 g, 7.00 mmol). The product was purified by centrifugal chromatography (5:1 hexane/ether) to yield **(107a)** as a white crystalline solid. The product was recrystallised from MeOH to yield white plates (1.29 g, 60%). m. p. 80 °C.

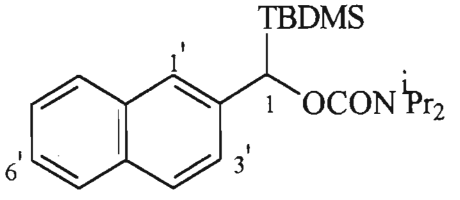
δ_H (200 MHz) : -0.15 and 0.12 (6H, 2 x s, Si(CH_3)$_2$); 0.92 (9H, s, C(CH_3)$_3$); 1.14 (6H, broad t, 2 x CH_2CH_3); 3.38 (4H, broad q, 2 x $\mathbf{CH_2}CH_3$); 5.87 (1H, s, **CH**-O); 7.29-7.44 (3H, m, **H$_{1'}$**, **H$_{4'}$**, **H$_{8'}$**); 7.59 (1H, m, **H$_{3'}$**); 7.74-7.80 (3H, m, **H$_{5'}$**, **H$_{6'}$**, **H$_{7'}$**)

δ_C (50 MHz) : -8.42 and -7.02 (2 x q, Si(CH_3)$_2$); 13.43-14.32 (2 x q, 2 x CH_2CH_3); 17.04 (s, C(CH_3)$_3$); 26.83 (3 x q, C(CH_3)$_3$); 41.09-41.93 (2 x t, 2 x $\mathbf{CH_2}CH_3$); 70.14 (d, **C$_1$**); 123.72, 124.61, 125.11, 125.84, 127.59, 127.68, 127.74 (7 x d, 7 x Ar-CH); 132.15 and 133.39 (2 x s, **C$_{4a'}$** and **C$_{8a'}$**); 139.24 (s, **C$_{2'}$**); 155.79 (s, **C=O**)

m/z : (EI) 371 (M^+, 2%), 314 (10), 271 (5), 230 (59), 186 (69), 159 (34), 115 (38), 100 (26), 73 (100)

HRMS. Calcd for $C_{22}H_{33}NO_2Si$: 371.2281 Found : 371.2276

1-*tert*-Butyldimethylsilyl-1-*N,N*-diisopropylcarbamoyloxy-1-(2'-naphthyl)methane (107b)



$C_{24}H_{37}NO_2Si$
MW = 399

(107b)

Compound **(107b)** was prepared according to general procedure 2 using 1-*N,N*-diisopropylcarbamoyloxy-1-(2'-naphthyl)methane **(99b)** (1.50 g, 5.26 mmol), *n*-BuLi (2.2 equivalents) and *tert*-butyldimethylsilyl chloride (0.95 g, 6.31 mmol). The reaction mixture was purified by centrifugal chromatography (5:1 hexane/ether) to yield **(107b)** as a white crystalline solid. The crystals were recrystallised from hexane to afford white needles (1.03 g, 50%). m. p. 112 °C.

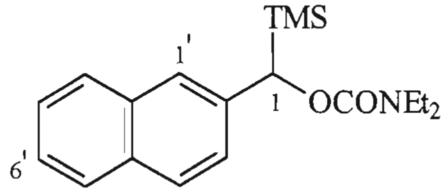
δ_H (200 MHz) : -0.14 and 0.13 (6H, 2 x s, $Si(CH_3)_2$); 0.93 (9H, s, $Si(CH_3)_3$); 1.24 (12H, broad d, 2 x $CH(CH_3)_2$); 3.72 and 4.22 (2H, 2 x broad s, 2 x $\mathbf{CH}(CH_3)_2$); 5.94 (1H, s, Si-CH); 7.61-7.78 (3H, m, $\mathbf{H_{1'}}$, $\mathbf{H_{4'}}$, $\mathbf{H_{8'}}$); 7.61 (1H, d, $\mathbf{H_{3'}}$); 7.22-7.47 (3H, m, $\mathbf{H_{5'}}$, $\mathbf{H_{6'}}$, $\mathbf{H_{7'}}$)

δ_C (50 MHz) : -8.07 and -6.88 (2 x q, $Si(CH_3)_2$); 17.03 (s, $\mathbf{C}(CH_3)_3$); 21.00 (4 x q, 2 x $CH(CH_3)_2$); 26.83 (3 x q, $C(\mathbf{CH_3})_3$); 45.94 (2 x d, 2 x $\mathbf{CH}(CH_3)_2$); 69.52 (d, $\mathbf{C_1}$); 123.96, 124.87, 125.10, 125.83, 127.58, 127.69 (6 x d, 7 x Ar-CH); 132.11 and 133.40 (2 x s, $\mathbf{C_{4a'}}$ and $\mathbf{C_{8a'}}$); 139.36 (s, $\mathbf{C_{2'}}$); 155.66 (s, C=O)

m/z : (EI) 342 (M^+-57, 4%), 258 (39), 214 (20), 185 (11), 141 (10), 115 (34), 73 (100)

HRMS. Calcd for $C_{24}H_{37}NO_2Si$: 399.2594 Found : 399.2592

1-*N,N*-diethylcarbamoyloxy-1-(2'-naphthyl)-1-trimethylsilylmethane (108a)



(108a)

$C_{19}H_{27}NO_2Si$
MW = 329

To a solution of DIPA (2.2 equivalents, 0.26 g, 2.57 mmol) in THF (10 ml) at 0 °C under a N_2 atmosphere was added dropwise *n*-BuLi (2.2 equivalents). The solution was stirred at this temperature for 30 minutes. The solution was then cooled to -78 °C and 1-*N,N*-diethylcarbamoyloxy-1-(2'-naphthyl)methane **(99a)** (0.3 g, 1.17 mmol) was added dropwise. TMSCl (1.2 equivalents, 0.15 g, 1.40 mmol) was then added rapidly and the reaction mixture was stirred at -78 °C for 7 h. The reaction was quenched with saturated NH_4Cl. After warming the reaction mixture to room temperature, the THF was removed under reduced pressure and the residue was extracted with ether (3 x 20 ml). The combined ether extracts were washed with water (3 x 20ml), dried over $MgSO_4$ and the ether was removed under reduced pressure. The product was purified by centrifugal chromatography (20:1 hexane/ether) to yield **(108a)** as a pale yellow oil (0.14 g, 36%).

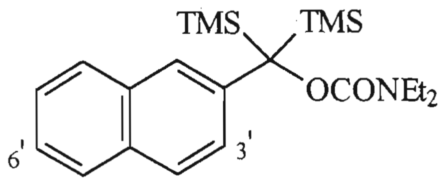
δ_H (200 MHz) : 0.06 (9H, s, $Si(CH_3)_3$); 1.17 (6H, broad d, 2 x CH_2CH_3); 3.30 (4H, broad s, 2 x CH_2CH_3); 5.72 (1H, s, CH-Si); 7.21-7.46 (3H, m, $\mathbf{H_{1'}}$, $\mathbf{H_{4'}}$, $\mathbf{H_{8'}}$); 7.56 (1H, s, $\mathbf{H_{3'}}$); 7.74-7.79 (3H, m, $\mathbf{H_{5'}}$, $\mathbf{H_{6'}}$, $\mathbf{H_{7'}}$)

δ_C (50 MHz) : -3.68 (3 x $Si(CH_3)_3$); 13.53-14.28 (2 x q, 2 x CH_2CH_3); 41.47-41.97 (2 x t, 2 x CH_2CH_3); 72.12 (d, C_1); 122.98, 124.07, 125.06, 125.87, 127.60, 127.64, 127.75 (7 x d, 7 x Ar-CH); 132.11 and 133.43 (2 x s, $\mathbf{C_{4a'}}$ and $\mathbf{C_{8a'}}$); 155.96 (s, C=O)

m/z : (EI) 329 (M^+, 1%), 314 (2), 229 (4), 199 (4), 188 (29), 144 (59), 100 (29), 73 (100)

HRMS. Calcd for $C_{19}H_{27}NO_2Si$: 329.1811 Found : 329.1802

1,1-Bis(trimethylsilyl)-1-*N,N*-diethylcarbamoyloxy-1-(2'-naphthyl)methane (108b)



$C_{22}H_{35}NO_2Si_2$
MW = 401

(108b)

Compound **(108b)** was prepared according to general procedure 2 using 1-*N,N*-diethylcarbamoyloxy-1-(2'-naphthyl)methane **(99a)** (0.25 g, 0.97 mmol), *n*-BuLi (2.2 equivalents) and excess trimethylsilyl chloride (4 equivalents, 0.42 g, 3.88 mmol). The reaction mixture was purified by centrifugal chromatography (10:1 hexane/ether) to yield compound **(108b)** as a white crystalline solid. The product was recrystallised from MeOH to yield white needles (0.21 g, 54%). m.p. 107 °C.

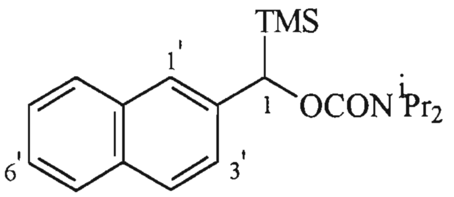
δ_H (200 MHz) : 0.16 (9H, s, $Si(CH_3)_2$); 1.17 and 1.32 (6H, 2 x t, 2 x CH_2CH_3, J = 7.08, J = 7.14); 3.34 and 3.50 (4H, 2 x q, 2 x $\mathbf{CH_2}CH_3$, J = 7.07, J = 7.16); 7.06-7.11 (1H, m, $H_{3'}$); 7.24 (1H, dd, $H_{1'}$); 7.33-7.44 (2H, m, $H_{4'}$ and $H_{8'}$); 7.68-7.78 (3H, m, $H_{5'}$, $H_{6'}$, $H_{7'}$)

δ_C (50 MHz) : -0.15 (2 x q, $Si(CH_3)_2$); 13.71 and 14.58 (2 x q, 2 x CH_2CH_3); 41.60 and 42.09 (2 x t, 2 x $\mathbf{CH_2}CH_3$); 77.27 (s, C_1); 120.59, 123.04, 124.35, 125.60, 126.63, 127.37, 127.49 (7 x d, 7 x Ar-CH); 130.89 and 133.16 (2 x s, $C_{4a'}$ and $C_{8a'}$); 141.31 (s, $C_{2'}$); 155.97 (s, C=O)

m/z : (EI) 386 (M^+ -15,< 1%), 185 (2), 174 (100), 100 (8), 72 (10)

HRMS. Calcd for $C_{22}H_{35}NO_2Si_2$: 401.2206 Found : 401.2218

1-*N,N*-diisopropylcarbamoyloxy-1-trimethylsilyl-1-(2'-naphthyl)methane (109a)



$C_{21}H_{31}NO_2Si$
MW = 357

(109a)

Compound **(109a)** was prepared according to general procedure 2 using 1-*N,N*-diisopropylcarbamoyloxy-1-(2'-naphthyl)methane **(99b)** (0.3 g, 1.05 mmol), *n*-BuLi (1.2 equivalents) and TMSCl (1.2 equivalents, 0.14 g, 1.26 mmol). The product was purified by centrifugal chromatography (15:1 hexane/ether) to yield **(109a)** as a pale yellow oil (0.11 g, 30%).

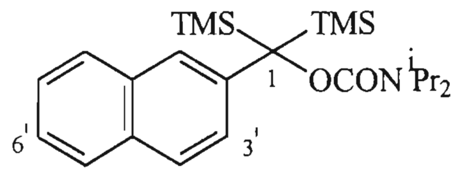
δ_H (200 MHz) : 0.04 (9H, s Si(CH$_3$)$_3$); 1.27 (12H, broad s, 2 x CH(CH$_3$)$_2$); 3.99 (2H, m, 2 x CH(CH$_3$)$_2$); 5.75 (1H, s, CH-O); 7.25-7.44 (3H, m, **H$_{1'}$**, **H$_{4'}$**, **H$_{8'}$**); 7.58 (1H, s, **H$_{3'}$**); 7.51-7.74 (3H, m, **H$_{5'}$**, **H$_{6'}$**, **H$_{7'}$**)

δ_C (50 MHz) : -3.44 (3 x q, Si(CH$_3$)$_3$); 21.37 (4 x q, 2 x CH(CH$_3$)$_2$); 46.05 (2 x d, 2 x CH(CH$_3$)$_2$); 72.22 (d, **C$_1$**); 123.28, 124.37, 125.04, 125.83, 127.59, 127.67, 127.71 (7 x d, Ar-CH); 132.06 and 133.43 (2 x s, **C$_{4a'}$** and **C$_{8a'}$**); 138.81 (s, **C$_{2'}$**); 155.60 (s, C=O)

m/z : (EI) 342 (M$^+$-15, 3%), 216 (46), 172 (42), 141 (16), 130 (16), 73 (100)

HRMS. Calcd for $C_{21}H_{31}NO_2Si$: 357.2124 Found 357.2136

1,1-Bis(trimethylsilyl)-1-*N,N*-diisopropylcarbamoyloxy-1-(2'-naphthyl)methane (109b)



$C_{24}H_{39}NO_2Si_2$
MW = 429

(109b)

Compound **(109b)** was prepared according to general procedure 2 using 1-*N,N*-diisopropylcarbamoyloxy-1-(2'-naphthyl)methane **(99b)** (1.30 g, 4.56 mmol), *n*-BuLi (2.2 equivalents and excess TMSCl (4 equivalents, 1.98 g, 18.24 mmol). The product was purified by centrifugal chromatography (10:1 hexane/ether) to yield **(109b)** as a white crystalline solid. The product was recrystallised from MeOH to yield white needles (1.14 g, 58%). m. p. 94 °C.

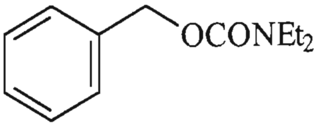
δ_H (200 MHz) : 0.16 (18H, s, 2 x $Si(CH_3)_3$); 1.32 (12H, m, 2 x $CH(CH_3)_2$); 3.77 and 4.32 (2H, 2 x m, 2 x $CH(CH_3)_2$); 7.09 (1H, dd, **$H_{3'}$**, J = 1.94, J = 8.71); 7.24 (1H, d, **$H_{1'}$**); 7.30-7.43 (2H, m, **$H_{8'}$**, **$H_{4'}$**); 7.66-7.77 (3H, m, **$H_{5'}$**, **$H_{6'}$**, **$H_{7'}$**)

δ_C (50 MHz) : 0.00 (6 x q, 2 x $Si(CH_3)_3$); 20.72 and 21.27 (4 x q, 2 x $CH(CH_3)_2$); 45.63 and 46.54 (2 x d, 2 x $CH(CH_3)_2$); 76.30 (s, C_1); 120.71, 123.10, 124.22, 125.49, 126.46, 127.30, 127.39 (7 x d, 7 x Ar-CH); 130.38 and 132 75 (2 x s, **$C_{4a'}$** and **$C_{8a'}$**); 141.88 (s, **$C_{2'}$**); 155.45 (s, C=O)

m/z : (EI) 414 (M^+-15,< 1%), 202 (100), 160 (7), 118 (5), 72 (25)

HRMS. Calcd for $C_{24}H_{29}NO_2Si_2$: 429.2519 Found : 429.2525

1-*N*,*N*-Diethylcarbamoyloxy-1-phenylmethane (110)



$C_{12}H_{17}NO_2$
MW = 207

(110)

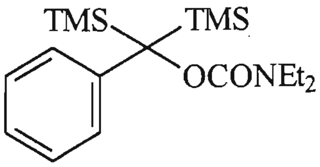
Compound **(110)** was prepared according to general procedure 1 using benzyl alcohol (5.00 g, 46.24 mmol) and *N,N*-diethylcarbamoyl chloride (7.52 g, 55.49 mmol). The product was purified by flash chromatography (5:1 hexane/ether) to yield **(110)** as a colourless oil (6.12 g, 64%).

δ_H (200 MHz) : 1.09 (6H, t, 2 x CH_2CH_3); 3.26 (4H, broad d, 2 x $\mathbf{CH_2}CH_3$); 5.11 (2H, s, CH_2-O); 7.28 (5H, m, Ar-**H**)

δ_C (50 MHz) : 13.91 (2 x q, 2 x CH_2CH_3); 41.46 (2 x t, 2 x CH_2CH_3); 66.68 (t, CH_2-O), 127.73, 127.80, 128.42 (3 x d, Ar-CH); 137.18 (s, $\mathbf{C_{1'}}$); 155.68 (s, **C**=O)

m/z : (EI) 207 (M^+, 12%), 148 (6), 116 (13), 100 (8), 91 (100), 65 (11)

1,1-Bis(trimethylsilyl)-1-*N,N*-diethylcarbamoyloxy-1-phenylmethane (112)



$C_{18}H_{33}NO_2Si_2$
MW = 351

(112)

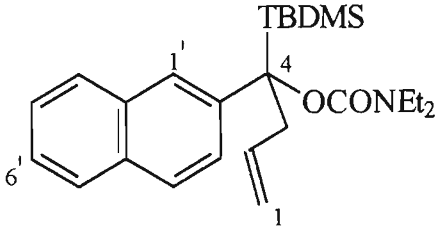
Compound **(112)** was prepared according to general procedure 2 using 1-*N,N*-diethylcarbamoyloxy-1-phenylmethane **(110)** (1.00 g, 4.83 mmol), *n*-BuLi (2.2 equivalents and excess TMSCl (4 equivalents, 2.10 g, 19.32 mmol). The product was purified by centrifugal chromatography (10:1 hexane/ether) to yield **(112)** as a white crystalline solid. The crystals were recrystallised from MeOH to afford white needles (1.01 g, 60%). m. p. 73 °C.

δ_H (200 MHz) : 1.14 and 1.26 (18H, 2 x t, 2 x CH_2CH_3); 3.37 (4H, m, 2 x CH_2CH_3); 6.83-6.88 (2H, m, H_2, H_6); 7.03-7.06 (1H, m, H_4); 7.19-7.26 (2H, m, H_3, H_5)

δ_C (50 MHz) : 0.00 (6 x q, 2 x $Si(CH_3)_3$); 13.98 and 14.80 (2 x q, 2 x CH_2CH_3); 41.78 and 42.30 (2 x t, 2 x CH_2CH_3); 77.19 (s, C_1); 123.34, 123.93, 127.58 (3 x d, Ar-CH); 143.54 (s, $C_{1'}$); 156.20 (s, C=O)

m/z : (EI) 336 (M^+-15, 6%), 188 (93), 144 (100), 100(48), 73 (71)

4-*tert*-Butyldimethylsilyl-4-*N,N*-diethylcarbamoyloxy-4-(2'-naphthyl)but-1-ene (117a)



$C_{25}H_{37}NO_2Si$
MW = 411

(117a)

Compound **(117a)** was prepared according to general procedure 3 using 1-*tert*-butyldimethylsilyl-1-*N,N*-diethylcarbamoyloxy-1-(2'-naphthyl)methane **(107a)** (0.25, 0.67 mmol) and allyl bromide (0.097 g, 0.80 mmol). The reaction mixture was purified by centrifugal chromatography (20:1 hexane/ether) to yield **(117a)** as a pale yellow oil (0.13 g, 47%).

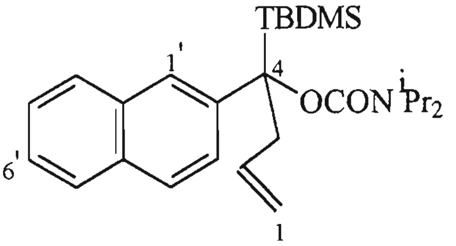
δ_H (200 MHz) : 0.16 and 0.22 (6H, 2 x s, $Si(CH_3)_2$); 0.67 (9H, s, $C(CH_3)_3$); 1.10 and 1.23 (6H, 2 x t, 2 x CH_2CH_3, J = 7.07, J = 7.05); 3.21-3.49 (6H, complex m, 2 x CH_2CH_3, J = 7.05, and CH_2=CH-CH_2, J = 6.98); 4.99-5.22 (2H, dddd, CH=CH_2, J = 2.2, J = 10.5, J = 17.12); 5.77-5.86 (1H, m, -CH=CH_2, J = 6.96, J = 10.09, J = 17.01); 7.37-7.43 (3H, m, $H_{1'}$, $H_{4'}$, $H_{8'}$); 7.64(1H, d, $H_{3'}$); 7.74-7.78 (3H, m, $H_{5'}$, $H_{6'}$, $H_{7'}$)

δ_C (50 MHz) : -4.80 and -4.96 (2 x q, $Si(CH_3)_2$); 13.44 and 14.54 (2 x q, 2 x CH_2CH_3); 18.89 (s, C-$(CH_3)_3$); 27.60 (3 x q, C-$(CH_3)_3$); 40.42 (t, CH_2-C=C); 41.45 and 41.63 (2 x d, 2 x $CH(CH_3)_2$); 82.08 (s, C_1); 117.67 (CH_2=CH); 123.48, 124.45, 125.16, 125.74, 126.95, 127.36, 127.89 (7 x d, 7 x Ar-CH); 131.60 and 133.09 (2 x s, $C_{4a'}$ and $C_{8a'}$); 134.40 (d, CH=CH_2); 142.14 (s, $C_{2'}$); 154.58 (s, C=O)

m/z : (EI) 296 (M^+-115, 2%), 294 (36), 237 (100), 209 (27), 178 (57), 165 (12), 109 (15), 73 (46), 59 (63)

HRMS. Calcd for $C_{25}H_{37}NO_2Si$: 411.2594 Found : 411.2583

4-tert-Butyldimethylsilyl-4-*N,N*-diisopropylcarbamoyloxy-4-(2'-naphthyl)but-1-ene (117b)



$C_{27}H_{41}NO_2Si$
MW = 439

(117b)

Compound **(117b)** was prepared according to general procedure 3 using 1-*tert*-butyldimethylsilyl-1-*N,N*-diisopropylcarbamoyloxy-1-(2'-naphthyl)methane **(107b)** (0.25 g, 0.63 mmol) and allyl bromide (0.091 g, 0.76 mmol). The product was purified by centrifugal chromatography (15:1 hexane/ether) to yield **(117b)** as a pale yellow oil (0.094, 34%).

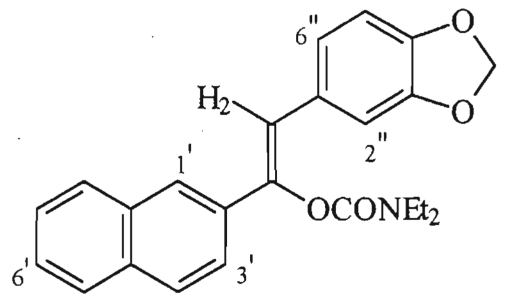
δ_H (200 MHz) : 0.15 and 0.22 (6H, 2 x s, Si($CH_3)_2$); 0.68 (9H, s, C-(CH3)$_3$); 1.25 (12H, t, 2 x CH($CH_3)_2$); 3.44 (2H, d, CH_2-CH=CH_2, J = 7.05); 3.61 and 4.35 (2H, 2 x m, 2 x CH($CH_3)_2$); 5.10 (2H, dddd, CH=CH_2, J = 2.29, J = 10.07, J = 17.12); 5.74-5.91 (1H, m, CH=CH_2, J = 7.05, J = 10.07, J = 17.12); 7.34-7.45 (3H, m, $H_{1'}$, $H_{4'}$, $H_{8'}$); 7.63 (1H, d, $H_{3'}$); 7.73-7.78 (3H, $H_{5'}$, $H_{6'}$, $H_{7'}$)

δ_C (50 MHz) : -4.73 and -4.68 (2 x q, Si(CH$_3$)2); 18.99 (s, C-($CH_3)_3$; 20.73 and 21.21 (2 x q, 2 x CH(CH_3); 27.71 (3 x q, C($CH_3)_3$); 40.71 (t, CH2-CH=CH_2); 45.12 and 46.76 (2 x d, 2 x CH($CH_3)_2$); 81.77 (s, C_1); 117.76 (t, CH_2=CH); 123.56, 124.63, 125.11, 125.71, 126.85, 127.36, 127.90 (7 x d, 7 x Ar-CH); 131.61 and 133.11 (2 x s, $C_{4a'}$, $C_{8a'}$); 143.55 (d, CH=CH_2); 142.32 (s, $C_{2'}$); 153.33 (s, C=O)

m/z : (EI) 294 (M^+-145, 18%), 237 (99), 209 (36), 178 (87), 165 (16), 141 (5), 109 (21), 73 (65), 59 (100)

HRMS. Calcd for $C_{27}H_{42}NO_2Si$: 439.2907 Found : 439.2914

Z-1-*N,N*-diethylcarbamoyloxy-1-(2'-naphthyl)-2-piperonylethene (119a)



(119a)

$C_{24}H_{23}NO_4$
MW = 389

Compound **(119a)** was prepared according to general procedure 3 using 1-*tert*-butyldimethylsilyl-1-*N,N*-diethylcarbamoyloxy-1-(2'-naphthyl)methane **(107a)** (0.50 g, 1.35 mmol) and piperonal (0.24 g, 1.62 mmol). The reaction mixture was purified by centrifugal chromatography (50:1 hexane/ether) to yield a mixture of *E* and *Z* isomers (0.35 g, 67%). *E* : *Z* = 47 : 53. The *Z*- isomer **(119a)** was isolated as a white crystalline solid (0.065 g, 12%). m.p. 110 °C.

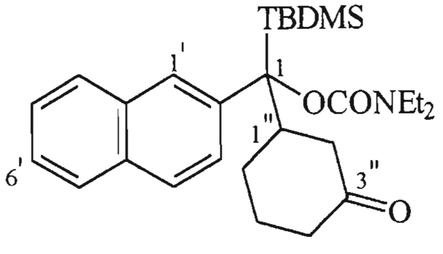
δ_H : (200 MHz) 1.16 (3H, t, CH_2CH_3, J = 7.09); 1.37 (3H, t, CH_2CH_3, J = 7.14); 3.37 (2H, q, $\mathbf{CH_2}CH_3$, J = 7.09); 3.63 (2H, q, CH_2CH_3, J = 7.15); 5.95 (2H, s, O-$\mathbf{CH_2}$-O); 6.72 (1H, s, $\mathbf{H_2}$); 6.79 (1H, d, $\mathbf{H_{5''}}$, J = 8.06); 6.99 (1H, ddd, $\mathbf{H_{6''}}$, J = 8.06, J = 1.72, J = 0.53); 7.13 (1H, d, $\mathbf{H_{2''}}$, J = 1.72); 7.45 (2H, m, $\mathbf{H_{6'}}$, $\mathbf{H_{7'}}$); 7.65 (1H, dd, $\mathbf{H_{3'}}$, J = 1.80, J = 8.74); 7.80 (3H, m, $\mathbf{H_{4'}}$, $\mathbf{H_{5'}}$, $\mathbf{H_{8'}}$); 7.89 (1H, d, $\mathbf{H_{1'}}$, J = 1.37)

δC : (50 MHz) 13.28 and 14.55 (2 x q, 2 x CH2CH3); 41.72 and 41.98 (2 x t, 2 x CH2CH3); 101.07 (t, O-CH2-O); 108.30 (d, $C_{5''}$); 108.39 (d, $C_{2''}$); 117.02 (d, C_2); 122.63 (d, $C_{6'}$); 123.46 (d, $C_{6''}$); 123.59 (d, $C_{3'}$); 126.16 (d, $C_{1'}$); 126.31 (d, $C_{8'}$); 127.59 (d, $C_{7'}$); 128.29 (d, $C_{5'}$); 128.33 (d, $C_{4'}$); 128.90 (s, $C_{1''}$); 133.12 and 133.30 (2 x s, $C_{4a'}$ and $C_{8a'}$); 134.02 (s, $C_{2'}$); 145.73 (s, C_1); 146.89 (s, $C_{4''}$); 147.75 (s, $C_{3''}$); 153.02 (s, C=O)

m/z : (EI) 389 (M^+, 6%), 202 (5), 155 (3), 100 (100), 72 (40)

HRMS. Calcd for $C_{24}H_{23}NO_4$: 389.1627 Found : 389.1620

1-*tert*-Butyldimethylsilyl-1-*N,N*-diethylcarbamoyloxy-1-(2'-naphthyl)-1-(3"-oxocyclohexyl)methane (125a)



$C_{28}H_{41}NO_3Si$
MW = 467

(125a)

Compound **(125a)** was prepared according to general procedure 3 using 1-*tert*-butyldimethylsilyl-1-*N,N*-diethylcarbamoyloxy-1-(2'-naphthyl)methane **(107a)** (0.25 g, 0.67 mmol) and 2-cyclohexen-1-one (0.077 g, 0.80 mmol). The product was purified by centrifugal chromatography (20:1 hexane/ether) to yield **(125a)** as a pale yellow oil containing a mixture of diastereomers (de = 59%) (0.044 mg, 14%). The ^{1}H and ^{13}C NMR were run in a mixture of CCl_4 and $CDCl_3$.

125a1

δ_H (200 MHz) : 0.19 and 0.23 (6H, 2 x s, $Si(CH_3)_2$); 0.79 (9H, s, $C(CH_3)_3$); 1.21-1.35 (6H, m, 2 x CH_2**CH_3**); 1.69-2.73 (9H, m, cyclohexyl); 3.35-3.51 (4H, m, 2 x **CH_2**CH_3); 7.13-7.18 (1H, dd, **$H_{3'}$**, J = 2.01, J = 8.79); 7.31-7.41 (3H, m, **$H_{1'}$**, **$H_{4'}$**, **$H_{8'}$**); 7.64-7.75 (3H, m, **$H_{5'}$**, **$H_{6'}$**, **$H_{7'}$**)

δ_C (50 MHz) : -0.58 and-0.04 (2 x q, $Si(CH_3)_2$); 13.96 and 14.93 (2 x q, 2 x CH_2CH_3); 21.03 (s **$C(CH_3)_3$**); 25.08 and 29.15 (2 x CH_2, cyclohexyl); 30.04 (3 x q, $C(CH_3)_3$; 41.38 and 41.76 (2 x t, 2 x CH_2CH_3); 42.25 and 43.83 (2 x t, 2 x CH_2-C=O); 46.82 (d, CH_2-CH-CH_2, cyclohexyl); 85.87 (s **C_1**); 123.50, 123.58, 125.56, 126.15, 127.56, 127.61, 128.08 (7 x d, 7 x Ar-CH); 131.76 and 133.12 (2 x s, **$C_{4a'}$** and **$C_{8a'}$**); 140.18 (s, O=C-N); 209.69 (s, C=O)

No satisfactory GC/MS results could be obtained.

HRMS. Calcd for $C_{28}H_{41}NO_3Si$: 467.2856 Found : 467.2851

125a2

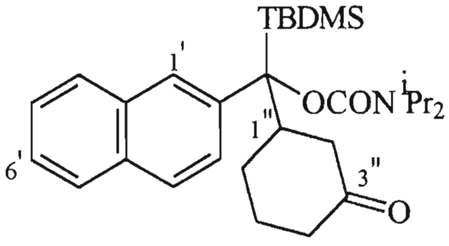
δ_H (200 MHz) : 0.16 and 0.26 (6H, 2 x s, $Si(CH_3)_2$); 0.78 (9H, s, $C(CH_3)_3$); 1.19-1.37 (6H, m, 2 x CH_2CH_3); 1.44-2.73 (9H, m, cyclohexyl); 3.37-3.52 (4H, m, 2 x CH_2CH_3); 7.19-7.25 (1H, m, $H_{3'}$, J = 2.01, J = 8.74); 7.36-7.41 (3H, m, $H_{1'}$, $H_{4'}$ $H_{8'}$); 7.65-7.78 (3H, m, $H_{5'}$, $H_{6'}$, $H_{7'}$)

δ_C (50 MHz) : -0.37 and -0.10 (2 x q, $Si(CH_3)_2$); 13.93 and 14.90 (2 x q, 2 x CH_2CH_3); 20.95 (s, C-$(CH_3)_3$); 25.16 and 27.25 (2 x t, 2 x CH_2, cyclohexyl); 29.97 (3 x q, C-$(CH_3)_3$); 41.28 and 41.76 (2 x t, 2 x CH_2CH_3); 42.22 and 45.64 (2 x t, 2 x CH_2-C=O); 47.11 (d, CH_2-CH-CH_2); 85.95 (s, C_1); 123.62, 123.86, 125.54, 126.15, 127.29, 127.51, 128.06 (7 x d, 7 x Ar-CH); 131.70 and 133.09 (2 x s, $C_{4a'}$ and $C_{8a'}$); 141.02 (s, $C_{2'}$); 155.05 (s, O=C-N); 209.48 (s, C=O)

No satisfactory GC/MS results could be obtained.

HRMS. Calcd for $C_{28}H_{41}NO_3Si$: 467.2856 Found 467.2853

1-*tert*-butyldimethylsilyl-1-*N,N*-diisopropylcarbamoyloxy-1-(2'-naphthyl)-1-(3"-oxocyclohexyl)methane (125b)



$C_{30}H_{45}NO_3Si$
MW = 495

(125b)

Compound **(125b)** was prepared according to general procedure 3 using 1-*tert*-butyldimethylsilyl-1-*N,N*-diisopropylcarbamoyloxy-1-(2'-naphthyl)methane **(107b)** (0.3 g, 0.75 mmol) and 2-cyclohexen-1-one (0.087 g, 0.90 mmol). The product was purified by centrifugal chromatography (20:1 hexane/ether) to yield a pale yellow oil containing a mixture of diastereomers (de = 20%) (0.062 g, 17%).

125b1

δ_H (200 MHz) : 0.19 and 0.25 (6H, 2 x s, $Si(CH_3)_2$); 0.96 (9H, s $C(CH_3)_2$); 1.24-1.34 (12H, m, 2 x $CH(CH_3)_2$); 1.49-2.35 (8H, m, cyclohexyl); 3.62-3.71 (2H, m, 2 x $CH(CH_3)_2$); 4.22-4.28 (1H, m, $H_{1''}$); 6.39-6.46 (1H, 2 x d, $H_{1'}$); 6.93 (1H, dd, $H_{3'}$); 7.05-7.27 (5H, m, $H_{4'}$, $H_{5'}$, $H_{6'}$, $H_{7'}$, $H_{8'}$)

δ_C (50 MHz) : -5.10 and -3.92 (2 x q, $Si(CH_3)_2$); 18.41 (s, $C(CH_3)_3$); 20.50 and 20.58 (2 x q, 2 x $CH(CH_3)$; 21.13 and 21.43 (2 x q, 2 x $CH(CH_3)$; 25.32 and 26.71 (2 x t, 2 x CH_2 (cyclohexyl); 27.07 (3 x q, $C(CH_3)_3$); 41.11 (t, CH_2 (cyclohexyl)); 45.10 and 45.54 (2 x d, 2 x $CH(CH_3)_2$); 47.08 (t, CH_2 (cyclohexyl)); 47.18 (d, CH (cyclohexyl)); 125.73, 126.37, 126.56, 126.63, 126.98, 127.95, 129.16 (7 x d, Ar-CH); 133.91 and 135.12 (2 x s, $C_{4a'}$ and $C_{8a'}$); 142.51 (s, $C_{2'}$); 153.94 (s, N-C=O); 211.62 (s, C=O)

No satisfactory GC/MS results could be obtained

HRMS. Calcd for $C_{30}H_{45}NO_3Si$: 495.3169 Found : 495.3158

125b2

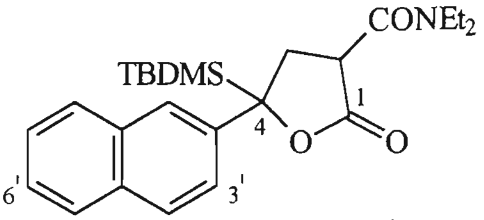
δH : (200 Mhz) 0.09 and 0.26 (2 x s, $Si(CH_3)_2$); 0.84 (9H, s, $C(CH_3)_3$); 1.33-1.39 (12H, m, 2 x $CH(CH_3)_2$); 1.52-2.64 (9H, m, cyclohexyl); 3.85 and 4.31 (2H, 2 x m, 2 x $CH(CH_3)_2$); 7.19 (1H, m, $H_{3'}$); 7.35-7.44 (3H, m, $H_{1'}$, $H_{4'}$, $H_{8'}$); 7.65-7.79 (3H, m, $H_{5'}$, $H_{6'}$, $H_{7'}$)

δC : (50 MHz) (-1.63 and -5.61 (2 x q, $Si(CH_3)_2$); 18.18 (s, $C(CH_3)_3$); 20.75 and 20.89 (2 x q, 2 x $CH(CH_3)_2$); 21.53 and 21.79 (2 x q, $CH(CH_3)_2$); 25.62 (t, CH_2(cyclohexyl)); 27.06 (3 x q, $C(CH_3)_3$); 27.64 (t, CH_2(cyclohexyl)); 41.34 (t, CH_2(cyclohexyl)); 46.28 and 46.37 (2 x d, 2 x $CH(CH_3)_2$); 47.41 (t, CH_2(cyclohexyl)); 47.61 (d, CH(cyclohexyl)); 123.94, 126.71, 127.09, 127.28, 128.29, 129.06 (6 x d, 6 x Ar-CH); 134.05 and 135.83 (2 x s, $C_{4a'}$ and $C_{8a'}$); 141.94 (s, $C_{2'}$); 153.66 (s, N-C=O); 212.16 (s, C=O)

No satisfactory GC/MS results could be obtained.

HRMS. Calcd for $C_{30}H_{45}NO_3Si$: 495.3169 Found : 495.3162.

4- *tert*- Butyldimethylsilyl-2-*N,N*-diethylaminocarbonyl- 4-(2'-naphthyl)-γ-butyrolactone (129a)



(129a)

$C_{25}H_{35}NO_3Si$
MW = 425

Compound **(129a)** was prepared according to general procedure 3 using 1-*tert*-butyldimethylsilyl-1-*N,N*-diethylcarbamoyloxy-1-(2'-naphthyl)methane **(107a)** (0.25 g, 0.67 mmol) and methyl acrylate (0.070 g, 0.80 mmol). The reaction mixture was purified using centrifugal chromatography (20:1 hexane/ether) to yield compound **(129a)** as a white crystalline solid. The crystals were recrystallised from MeOH to yield white needles (0.20 g, 35%) m. p. 125 °C.

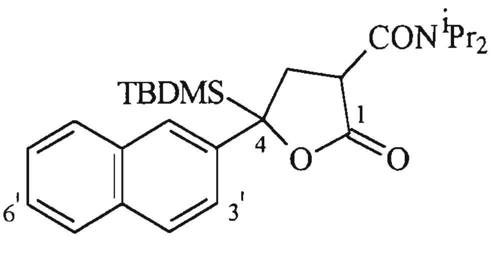
δ_H (200 MHz) : 0.15 and 0.24 (6H, 2 x s, $Si(CH_3)_2$); 0.75 (9H, s, $C(CH_3)_3$); 1.06 and 1.15 (6H (2 x t, 2 x CH_2CH_3, J = 7.14); 2.72 (1H, dd, CH-CH_2, J = 4.42); 3.17-3.57 (6H, complex m, 2 x $\mathbf{CH_2}CH_3$, J = 7.14 and Si-C-$\mathbf{CH_2}$); 7.37-7.53 (3H, m, $\mathbf{H_{1'}}$, $\mathbf{H_{3'}}$, $\mathbf{H_{4'}}$); 7.79-7.88 (4H, m, $\mathbf{H_{5'}}$, $\mathbf{H_{6'}}$, $\mathbf{H_{7'}}$, $\mathbf{H_{8'}}$)

δ_C (50 MHz) : -7.66 and -7.23 (2 x q, $Si(CH_3)_2$); 12.94 and 14.56 (2 x q, 2 x CH_2CH_3); 18.16 (s, $\mathbf{C}$-$(CH_3)_3$); 27.04 (3 x q, $C(CH_3)_3$); 37.19 and 41.04 (2 x t, 2 x $\mathbf{CH_2}CH_3$); 41.36 (d, $\mathbf{C_2}$); 42.24 (t, $\mathbf{C_3}$); 83.74 (s, $\mathbf{C_4}$); 122.59, 122.79, 125.97, 126.59, 127.58, 127.99, 128.34 (7 x d, 7 x Ar-CH); 132.06 and 133.07 (2 x s, $\mathbf{C_{4a'}}$ and $\mathbf{C_{8a'}}$); 141.42 (s, $\mathbf{C_{2'}}$) 165.85 (s, O=C-N); 174.57 (s O-C=O)

m/z : (EI) 425 (M^+, 2%), 396 (3), 324 (4), 256 (30), 242 (43), 165 (10), 155 (11), 100 (19), 73 (100)

HRMS. Calcd for $C_{25}H_{35}NO_3Si$: 425.2386 Found : 425.2399

4-*tert*-butyldimethylsilyl-2-*N,N*-diisopropylaminocarbonyl-4-(2'-naphthyl)-γ-butyrolactone (129b)



(129b)

$C_{27}H_{39}NO_3Si$
MW = 453

Compound **(129b)** was prepared according to general procedure 3 using 1-*tert*-butyldimethylsilyl-1-*N,N*-diisopropylcarbamoyloxy-1-(2'-naphthyl)methane **(107b)** (0.3 g, 0.75 mmol) and methyl acrylate (0.077 g, 0.90 mmol). The product was purified by centrifugal chromatography (10:1 hexane/ether) to yield **(109b)** as a white crystalline solid. The solid was recrystallised from MeOH to yield white needles (0.023 g, 7%) m. p. 129 °C.

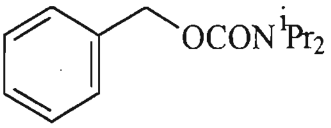
δ_H (200 MHz) : 0.16 and 0.23 (6H, 2 x s, $Si(CH_3)_2$); 0.73 (9H, s, $C(CH_3)_3$); 1.24-1.43 (12H, m, 2 x $CH(CH_3)_2$, J = 6.57); 2.66 (1H, dd, CH-CH$_2$, J = 4.62, J = 9.29); 3.44-3.57 (3H, complex m, **Si-C-CH$_2$** and **CH-CH$_3$**); 3.91-3.97 (1H, m, **CH**(CH$_3$), J = 6.59); 7.36-7.42 (1H, dd, **H$_{1'}$**, J = 1.90, J = 8.67); 7.47-7.53 (2H, m, **H$_{4'}$**, **H$_{8'}$**); 7.78-7.88 (4H, m, **H$_{3'}$**, **H$_{5'}$**, **H$_{6'}$**, **H$_{7'}$**)

δ_C (50 MHz) : -7.65 and 7.25 (6 x q, $Si(CH_3)_2$); 18.13 (s, **C**(CH$_3$)$_3$); 20.22-21.28 (4 x q, 2 x CH(CH$_3$)$_2$); 36.72 (t, C$_3$); 42.63 and 46.41 (2 x d, 2 x **CH**(CH$_3$)$_2$); 49.00 (d, **C2**); 83.43 (s, **C$_4$**); 122.58, 122.88, 125.94, 126.57, 127.59, 128.02, 128.32 (7 x d, 7 x Ar-CH); 132,03 and 133.07 (2 x s, **C$_{4a'}$** and **C$_{8a'}$**); 141.24 (s, **C$_{2'}$**); 164.47 (s, N-C=O); 174.67 (s, C=O)

m/z : (EI) 410 (M$^+$-47, 2%), 284 (11), 270 (11), 228 (6), 155 (12), 127 (8), 73 (100)

HRMS. Calcd for $C_{27}H_{39}NO_3Si$: 453.2699 Found : 453.2711

1-*N*,*N*-Diisopropylcarbamoyloxy-1-phenylmethane (136)



$C_{14}H_{21}NO_2$
MW = 235

(136)

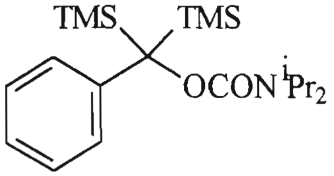
Compound **(136)** was prepared according to general procedure 1 using benzyl alcohol (5.00 g, 46.24 mmol) and *N,N*-diisopropylcarbamoyl chloride (9.08 g, 55.49 mmol). The product was purified by flash chromatography (5:1 hexane/ether) to yield **(136)** as a colourless oil (7.87 g, 72%).

δ_H (200 MHz) : 1.21 (12H, m, 2 x CH(CH_3)$_2$); 3.90 (2H, broad s, 2 x **CH**(CH_3)$_2$); 5.13 (2H, s, **CH$_2$-O**); 7.33 (5H, m, **Ar-H**)

δ_C (50 MHz) : 20.96 (4 x q, 2 x CH(CH_3)$_2$); 45.79 (2 x t, 2 x **CH**(CH_3)$_2$); 66.46 (t, CH$_2$-O); 127.75, 127.86, 128.40 (3 x d, Ar-CH); 137.12 (s, C$_{1'}$); 155.39 (s, **C**=O)

m/z : (EI) 235 (M^+, 3%), 220 (4), 176 (10), 144 (10), 91 (100), 65 (8)

1,1-Bis(trimethylsilyl)-1-*N,N*-diisopropylcarbamoyloxy-1-phenylmethane (137)



$C_{20}H_{37}NO_2Si_2$
MW = 379

(137)

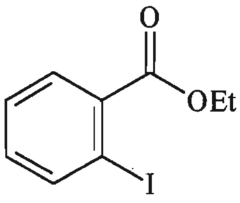
Compound **(137)** was prepared according to general procedure 2 using 1-*N,N*-diisopropylcarbamoyloxy-1-phenylmethane **(136)** (1.00 g, 4.26 mmol), *n*-BuLi (2.2 equivalents) and excess TMSCl (4 equivalents, 1.85 g, 17.04 mmol). The product was purified by centrifugal chromatography (20:1 hexane/ether) to yield **(137)** as a white crystalline solid. The crystals were recrystallised from MeOH to afford white needles (0.50 g, 31%).
m. p. 84 °C.

δ_H (200 MHz) : -0.13 (18H, 2 x $Si(CH_3)_3$); 1.29 (12H, t, 2 x $CH(CH_3)_2$); 375 and 4.25 (2H, 2 x m, 2 x **$CH(CH_3)_2$**); 6.84-6.89 (2H, m, **H_2, H_6**); 6.98-7.07 (1H, m, **H_4**); 7.17-7.27 (2H, m, **H_3,H_5**)

δ_C (50 MHz) : 0.00 (6 x q, 2 x $Si(CH_3)_3$); 20.84 and 21.35 (4 x q, 2 x $CH(CH_3)_2$); 45.71 and 46.55 (2 x d, 2 x **$CH(CH_3)_2$**); 76.50 (s, **C1**); 143.56 (s, **$C_{1'}$**); 155.50 (s, **C=O**)

m/z : (EI) 364 (M^+-15, 2%), 216 (6), 202 (20), 172 (60), 100 (7), 73 (100)

Ethyl-2-iodobenzoate (140)



(140)

$C_9H_9O_2I$
MW =276

To 2-iodobenzoic acid (5.00 g, 20.16 mmol) in EtOH (150 ml) was added concentrated H_2SO_4 (5 ml). The mixture was refluxed overnight. The EtOH was then removed under reduced pressure and the residue was extracted with ether (3 x 20 ml). The combined ether extracts were washed with 10% $NaHCO_3$ solution (2 x 20 ml) and then with water (4 x 20 ml). The ether extracts were then dried over $MgSO_4$ and the ether was removed under reduced pressure. The product was purified by flash chromatography (15:1 hexane/ether) to afford **(140)** as a pale yellow oil (3.26 g, 59%).

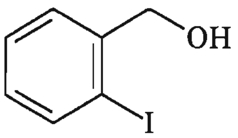
δ_H (200 MHz) : 1.38 (3H, t, CH_2CH_3); 4.37 (2H, q, $\mathbf{CH_2}CH_3$); 7.09 (1H, ddd, $\mathbf{H_4}$, $J_{4\text{-}5}$ = 7.40, $J_{4\text{-}3}$ = 7.9, $J_{4\text{-}6}$ = 1.8); 7.35 (1H, ddd, $\mathbf{H_5}$, $J_{5\text{-}4}$ = 7.40, $J_{5\text{-}6}$ = 7.8, $J_{5\text{-}3}$ = 1.2); 7.76 (1H, ddd, $\mathbf{H_6}$, $J_{6\text{-}5}$ = 7.80, $J_{6\text{-}4}$ = 1.80, $J_{6\text{-}3}$ = 0.36); 7.94 (1H, ddd, $\mathbf{H_3}$, $J_{3\text{-}4}$ = 7.90, $J_{3\text{-}5}$ = 1.2, $J_{3\text{-}6}$ = 0.37)

δ_C (50 MHz) : 14.18 (q, CH_2CH_3); 61.51 (t, CH_2CH_3); 93.93 (s, $\mathbf{C_2}$); 127.78(d, C_5); 130.67 (d, **C6**); 132.40(d, $\mathbf{C_4}$); 135.25 (d, $\mathbf{C_3}$); 141.02 (s, $\mathbf{C_1}$); 166.27 (s, **C=O**)

m/z : (EI) 276 (M^+, 49%), 248 (27), 231 (100), 203 (35), 127 (10), 104 (15), 76 (64)

HRMS.Calcd for $C_9H_9O_2I$: 275.9647 Found : 275.9634

2-iodobenzyl alcohol (141)



(141)

C_7H_7OI

MW =234

To a solution of ethyl-2-iodobenzoate **(140)** (3.00 g, 10.87 mmol) and $NaBH_4$ (4 equivalents, 1.64 g, 43.48 mmol) in a THF:EtOH mixture (1:2) was added $CaCl_2$ (2 equivalents, 2.41 g, 21.74 mmol) with cooling on an ice-bath. The mixture was warmed up to room temperature and stirred overnight. The reaction was quenched with citric acid (1 M). After the THF/EtOH mixture was removed under reduced pressure, the residue was extracted with ether (4 x 20 ml). The combined ether extracts were washed with 10% $NaHCO_3$ solution (3 x 20 ml) and water (4 x 20 ml) and then dried over $MgSO_4$. The ether was then removed under reduced pressure to yield **(141)** as an off-white crystalline solid. The crystals were recrystallised from hexane to afford off-white needles (2.24 g, 88%). m.p. 80 °C. (literature m.p. 89.5 ^{0}C).[126]

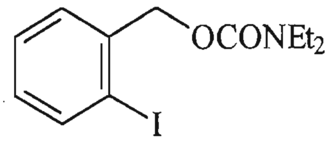
δ_H (200 MHz) : 2.32 (1H, broad s, CH_2-**OH**); 4.65 (2H, s, CH_2-OH); 6.98 (1H, ddd, H_4, J = 7.50, J = 7.49, J = 1.90); 7.38 (2H, m, H_5, J = 7.56, J = 7.49, J = 1.10 and H_6, J = 7.60, J = 7.80, J = 1.10)

δ_C (50 MHz) : 69.22 (t, CH_2); 97.43 (s, C_2); 128.38 and 128.45 (2 x d, C_5, C_6); 129.13 (d, C_4); 139.13 (d, C_3); 142.51 (s, C_1)

m/z : (EI) 234 (M^+, 100%), 127 (18), 105 (48), 89 (13), 77 (95)

HRMS. Calcd for C_7H_7OI : 233.9542 Found : 233.9550

1-*N,N*-Diethylcarbamoyloxy-1-(2'-iodophenyl)methane (142)



$C_{12}H_{16}NO_2I$

MW = 333

(142)

Compound **(142)** was prepared according to general procedure 1 using 2-iodobenzyl alcohol **(141)** (2.00 g, 8.55 mmol) and *N,N*-diethylcarbamoyl chloride (1.39 g, 10.26 mmol). The product was purified by flash chromatography (20:1 hexane/ether) to yield **(142)** as a pale yellow oil (2.12 g, 75%).

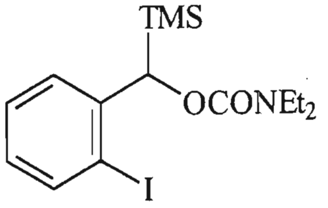
δ_H (200 MHz) : 1.10 (6H, t, 2 x CH_2CH_3); 3.28 (4H, q, 2 x $\mathbf{CH_2}CH_3$); 5.09 (2H, s, $\mathbf{CH_2}$**-O**); 6.90-6.99 (1H, m, $\mathbf{H_4}$); 7.25-7.37 (2H, m, $\mathbf{H_{5'}}$, $\mathbf{H_{6'}}$); 7.78 (1H, dd, $\mathbf{H_{3'}}$)

δ_C (50 MHz) : 13.62 (2 x q, 2 x CH_2CH_3); 41.36 (2 x t, 2 x CH_2CH_3); 70.21 (t, $\mathbf{C_1}$); 97.84 (s, $\mathbf{C_{2'}}$); 127.97 (d, $\mathbf{C_{6'}}$); 128.88 (d, $\mathbf{C_{5'}}$); 129.24 (d, $\mathbf{C_{4'}}$); 139.07 (s and d, $\mathbf{C_{1'}}$, $\mathbf{C_{3'}}$); 155.05 (s, **C=O**)

m/z : (EI) 333 (M^+, 1%), 274 (2), 217 (100), 206 (57), 127 (3), 100 (57), 90 (54)

HRMS. Calcd for $C_{12}H_{16}NO_2I$: 333.0225 Found : 333.0237

1-*N,N*-Diethylcarbamoyloxy-1-phenyl-1-trimethylsilylmethane (143)



$C_{15}H_{24}NO_2SiI$
MW = 405

(143)

To a solution of DIPA (2.2 equivalents, 0.67 g, 6.60 mmol), in THF (15 ml) at 0 °C under a N_2 atmosphere was added dropwise *n*-BuLi (2.2 equivalents). The solution was stirred at this temperature for 30 minutes. The solution was then cooled to -78 °C and 1-*N,N*-diethylcarbamoyloxy-1-(2'-iodophenyl)methane **(142)** (1.00 g, 3.00 mmol) was added dropwise. TMSCl (4 equivalents, 1.30 g, 12.00 mmol) was added dropwise and the reaction mixture was then warmed to 0 °C and stirred at this temperature overnight. The reaction was quenched with saturated NH_4Cl and the reaction mixture was then warmed to room temperature. The THF was removed under reduced pressure and the residue was extracted with ether (3 x 20 ml). The combined ether extracts were washed with water (3 x 20 ml), dried over $MgSO_4$ and the ether was removed under reduced pressure. The product was purified by centrifugal chromatography (15:1 hexane/ether) to yield **(143)** as a viscous yellow oil (0.74 g, 61%).

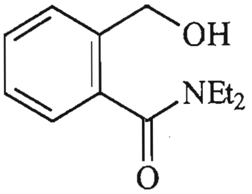
δ_H (200 MHz) : 0.00 (9H, $Si(CH_3)_3$); 1.02 (6H, broad t, 2 x CH_2CH_3); 3.16 (4H, broad s, 2 x $\mathbf{CH_2}CH_3$); 5.69 (1H, s, **CH**-Si); 6.66-6.74 (1H, m, $\mathbf{H_{4'}}$); 7.00-7.22 (2H, m, $\mathbf{H_{5'}}$, $\mathbf{H_{6'}}$); 7.61-7.66 (1H, dd, $\mathbf{H_{3'}}$, J = 1.19, J = 7.96)

δ_C (50 MHz) : 0.00 (3 x q, $Si(CH_3)_3$); 15.49-17.29 (2 x q, 2 x CH_2CH_3); 44.37-44.96 (2 x t, 2 x CH_2CH_3); 78.14 (d, $\mathbf{C_1}$); 100.09 (s, $\mathbf{C_{2'}}$); 129.25(d, $\mathbf{C_{6'}}$); 130.54 (d, $\mathbf{C_{5'}}$); 131.02 (d, $\mathbf{C_{4'}}$); 142.23 (d, $\mathbf{C_{3'}}$); 146.71 (s, $\mathbf{C_{1'}}$); 158.48(, s, **C=O**)

m/z : (EI) 390 (M^+-15, <1%), 346 (0.5), 275 (1), 231 (0.7), 188 (51), 144 (63), 100 (44), 73 (100)

HRMS. Calcd for $C_{15}H_{24}NO_2Si$: 405.0620 Found : 405.0624

N,N-**Diethyl-2-hydroxymethyl benzamide (147)**



$C_{12}H_{17}NO_2$
MW = 207

(147)

To a solution of 1-*N,N*-diethylcarbamoyloxy-1-(2'-iodophenyl)methane **(142)** (0.50 g, 1.50 mmol) in ether (10 ml) at -78 °C under a N_2 atmosphere was added dropwise *n*-BuLi (1.1 equivalents). The reaction mixture was stirred at this temperature for 7 h and then quenched with saturated NH_4Cl. After warming the reaction mixture to room temperature, it was washed with water (3 x 20 ml). The organic phase was then dried over $MgSO_4$ and the ether was removed under reduced pressure. The product was purified by centrifugal chromatography (15:1 hexane/ether) to yield **(147)** as a pale yellow liquid (0.14 g, 45%).

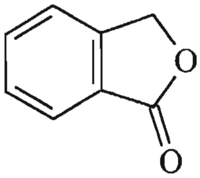
δ_H : (200 MHz) 1.08 and 1.27 (6H, 2 x t, 2 x CH_2CH_3); 3.23 and 3.59 (4H, 2 x q, 2 x CH_2CH_3); 3.87 (1H, broad s, CH_2-OH); 4.51 (2H, broad s, CH_2-OH); 7.23-7.44 (4H, complex m, Ar-CH)

δ_C (50 MHz) 12.76 and 14.04 (2 x q, 2 x CH_2CH_3); 39.28 and 43.37 (2 x t, 2 x CH_2CH_3); 63.56 (t, CH_2-OH); 125.70 (d, $C_{3'}$); 127.40 (d, $C_{4'}$); 129.47 (d, $C_{5'}$); 129.60 (d, $C_{6'}$); 135.94 (s, $C_{1'}$); 138.51 (s, $C_{2'}$); 171.30 (s, C=O)

m/z : (EI) 207 (M^+, 13%), 178 (4), 135 (69), 118 (13), 105 (39), 77 (68), 74 (100)

HRMS. Calcd for $C_{12}H_{17}NO_2$: 207.1259 Found : 207.1268

1-Phthalanone (148)



(148) $C_8H_6O_2$

MW =134

Method A

N,N-Diethyl-2-hydroxymethyl benzamide **(147)** (0.05g, 0.24 mmol) was refluxed in HCl (2N, 50 ml) overnight. After cooling to room temperature, the product was extracted with ether (3 x 20 ml). The ether extracts were washed with 10% $NaHCO_3$ (3 x 20 ml) and with water (3 x 20 ml) and then dried over $MgSO_4$. The ether was removed under reduced pressure and the residue was purified by centrifugal chromatography (100% ether) to afford **(148)** as a white crystalline solid. The crystals were recrystallised from $CHCl_3$ to afford white plates (0.022 g, 68%) m. p. 65 °C.

Method B

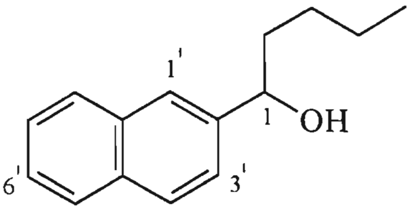
N,N-Diethyl-2-hydroxymethyl benzamide **(147)** (0.071 g, 0.34 mmol) and NaOH (1 equivalent, 0.01 g, 0.34 mmol)) were refluxed in EtOH (50 ml) overnight. After removing the EtOH under reduced pressure, the residue was extracted with ether. The ether extracts were washed with dilute HCl (10 ml) and water(3 x 20 ml). The extracts were then dried over $MgSO_4$ and the ether was removed under reduced pressure. The product was purified by centrifugal chromatography (100% ether) to afford **(148)** as a white crystalline solid. The crystals were recrystallised from $CHCl_3$ to afford **(148)** as white plates (0.03 g 65%).

δ_H (200 MHz) : 5.34 (2H, s, **CH_2-O**); 7.51-7.58 (2H, m, **$H_{3'}$, $H_{6'}$**); 7.67-7.75 (1H, m, **$H_{5'}$**); 7.89-7.93 (1H, m, **$H_{4'}$**)

δ_C (50 MHz) : 69.73 (t, CH_2-O); 122.20 (d, $C_{6'}$); 125.63 (d, $C_{4'}$); 129.02 (d, $C_{5'}$); 134.07 (d, $C_{3'}$); 146.57 (2 x s, $C_{1'}$, $C_{2'}$); 171.17 (s, C=O)

m/z : (EI) 134 (M^+, 52%), 105 (100), 89 (4), 77 (55)

1-(2'-naphthyl)pentan-1-ol (152)



$C_{15}H_{18}O$
MW = 214

(152)

To a solution of 2-naphthalene carboxaldehyde (0.5 g, 3.21 mmol) in THF (20 ml) at -78 °C was added *n*-BuLi (1.2 equivalents) under a N_2 atmosphere. The mixture was stirred at this temperature for 30 minutes. A solution of I_2 (0.98 g, 3.86 mmol) in THF (10 ml) was added dropwise and the mixture was stirred for 5 h. The reaction was quenched with saturated NH_4Cl. The THF was removed under reduced pressure and the residue was extracted with ether (3 x 20 ml). The combined ether extracts were then washed with water (3 x 20 ml), dried over $MgSO_4$ and the ether was removed under reduced pressure. The product was purified by centrifugal chromatography (10:1 hexane/ether) to yield **(152)** as a white crystalline solid (0.32 g, 47%) m.p. 65 °C.

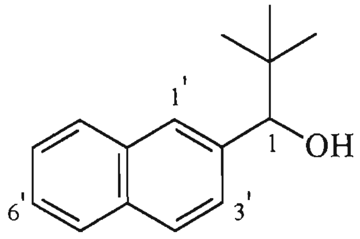
δH : (200 MHz) 0.86 (3H, t, CH_2CH_3); 1.22-1.35 (4H, m, $\mathbf{CH_2}CH_2CH_3$); 1.75-1.83 (2H, m, CH-$\mathbf{CH_2}$); 2.27 (1H, broad s, CH-**OH**); 4.74 (1H, t, **CH**-OH); 7.39-7.46 (3H, m, Ar-**H**); 7.70-7.82 (4H, m, Ar-**H**)

δC : (50 MHz) 14.01 (q, $\mathbf{CH_3}$); 22.60 and 27.95 (2 x t, $CH_2CH_2CH_3$); 38.63 (t, CH-CH_2); 74.71 (d, **CH**-CH_2); 124.11, 124.57, 125.70, 126.04, 127.64, 127.89, 128.18 (7 x d, 7 x Ar-CH); 132.91 and 135.23 92 (2 x s, $\mathbf{C_{4a'}}$ and $\mathbf{C_{8a'}}$); 142.26 ($\mathbf{C_{2'}}$)

m/z : (EI) 214 (M^+, 13%), 157 (100), 129 (83), 102 (3), 77 (6), 57 (3)

HRMS. Calc'd for $C_{15}H_{18}O$: 214.1358 Found ; 214.1345.

2,2-Dimethyl-1-hydroxy-1-(2'-naphthyl)propane (153)



$C_{15}H_{18}O$
MW = 214

(153)

To a solution of 2- naphthalene carboxaldehyde (0.5 g, 3.21 mmol) in THF (20 ml) at -78 °C was added *tert*-BuLi (1.2 equivalents) under a N_2 atmosphere. The mixture was stirred at this temperature for 30 minutes. A solution of I_2 (0.98 g, 3.86 mmol) in THF (10 ml) was added dropwise and the mixture was stirred for 5 h. The reaction was quenched with saturated NH_4Cl. The THF was removed under reduced pressure and the residue was extracted with ether (3 x 20 ml). The combined ether extracts were then washed with water (3 x 20 ml), dried over $MgSO_4$ and the ether was removed under reduced pressure. The product was purified by centrifugal chromatography (10:1 hexane/ether) to yield **(153)** as a white crystalline solid (0.26 g, 38%) m.p. 68 °C.

δH : (200 MHz) 0.95 (9H, s, $C(CH_3)_3$); 2.12 (1H, broad s, CH-OH); 4.51 (1H, s, CH-OH); 7.40-7.49 (3H, m, Ar-H); 7.71-7.84 (4H, m, Ar-H)

δC : (50 MHz) 25.99 (3 x q, $C(CH_3)_3$); 28.13 (s, $C(CH_3)_3$); 82.39 (d, CH-OH); 125.64, 125.88, 125.98, 126.26, 126.90, 127.53, 127.94 (7 x d, 7 x Ar-CH); 132.77 (s, $C_{4a'}$ and $C_{8a'}$); 139.76 (s, $C_{2'}$)

m/z (EI) 214 (M^+, 12%), 157 (100), 129 (67), 102 (2), 77 (4), 57 (6)

HRMS. Calcd for $C_{15}H_{18}O$: 214.1358 Found : 214.1352.

CHAPTER 4

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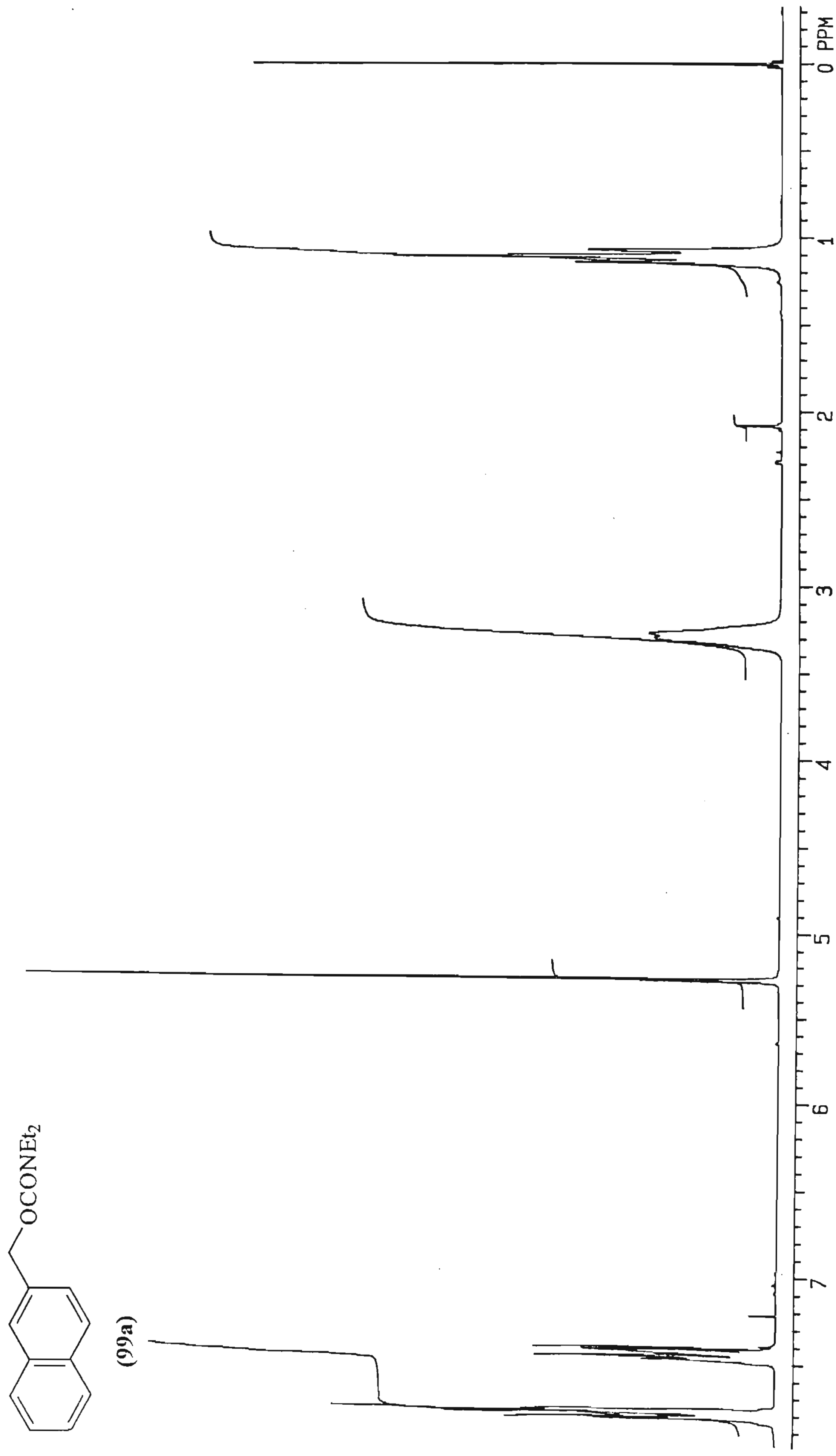
CHAPTER 5

APPENDIX

^{1}H and ^{13}C spectra



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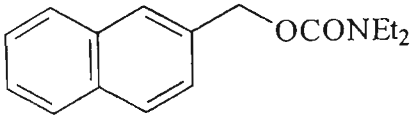

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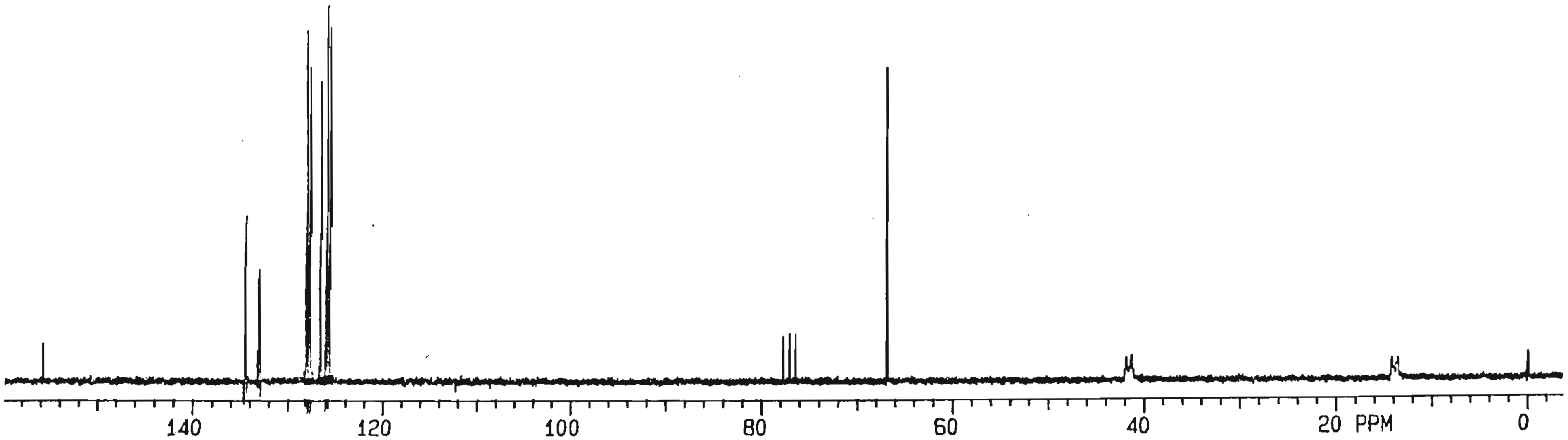

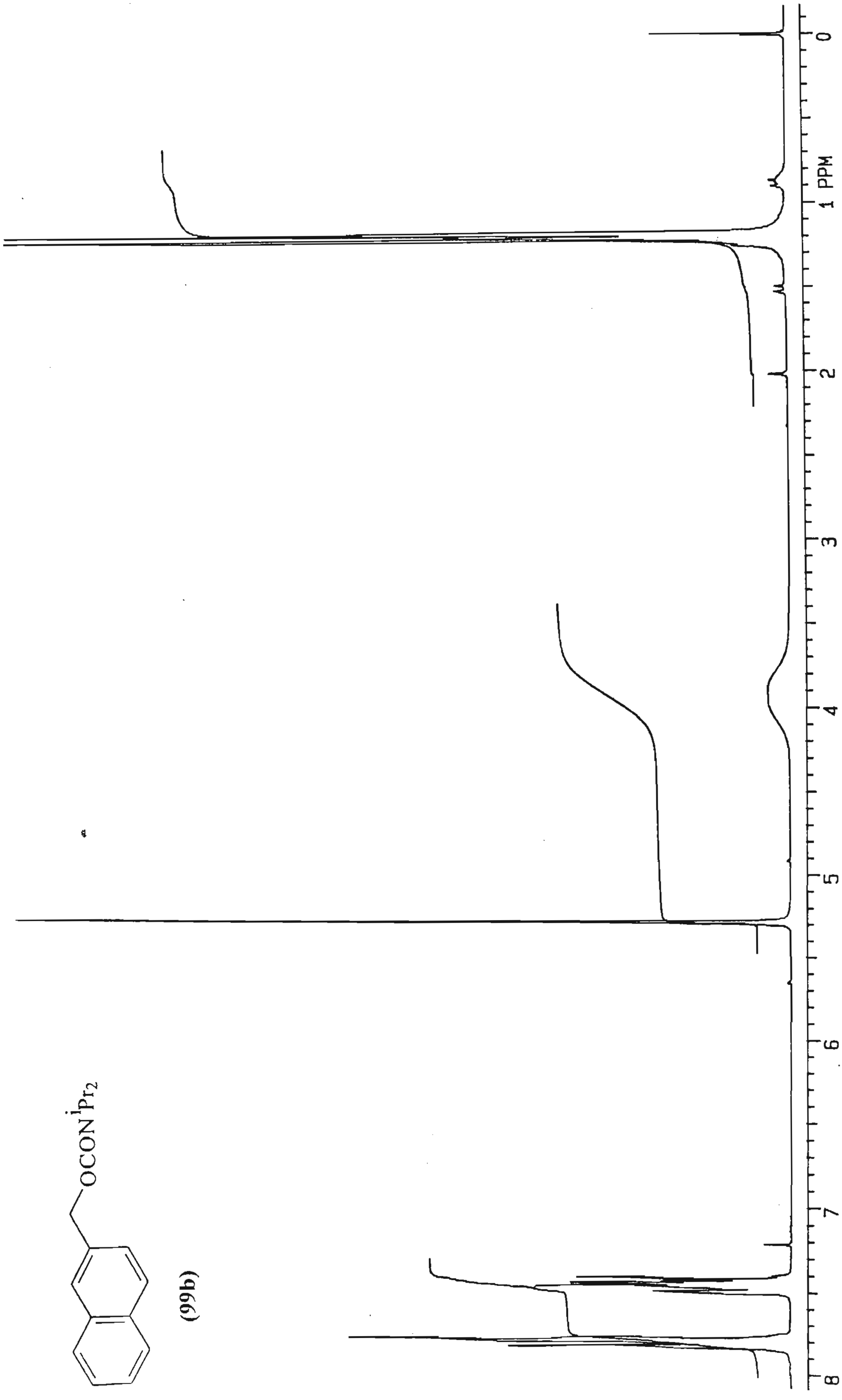

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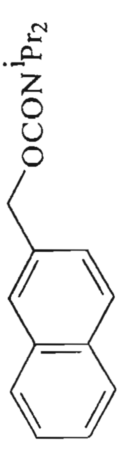

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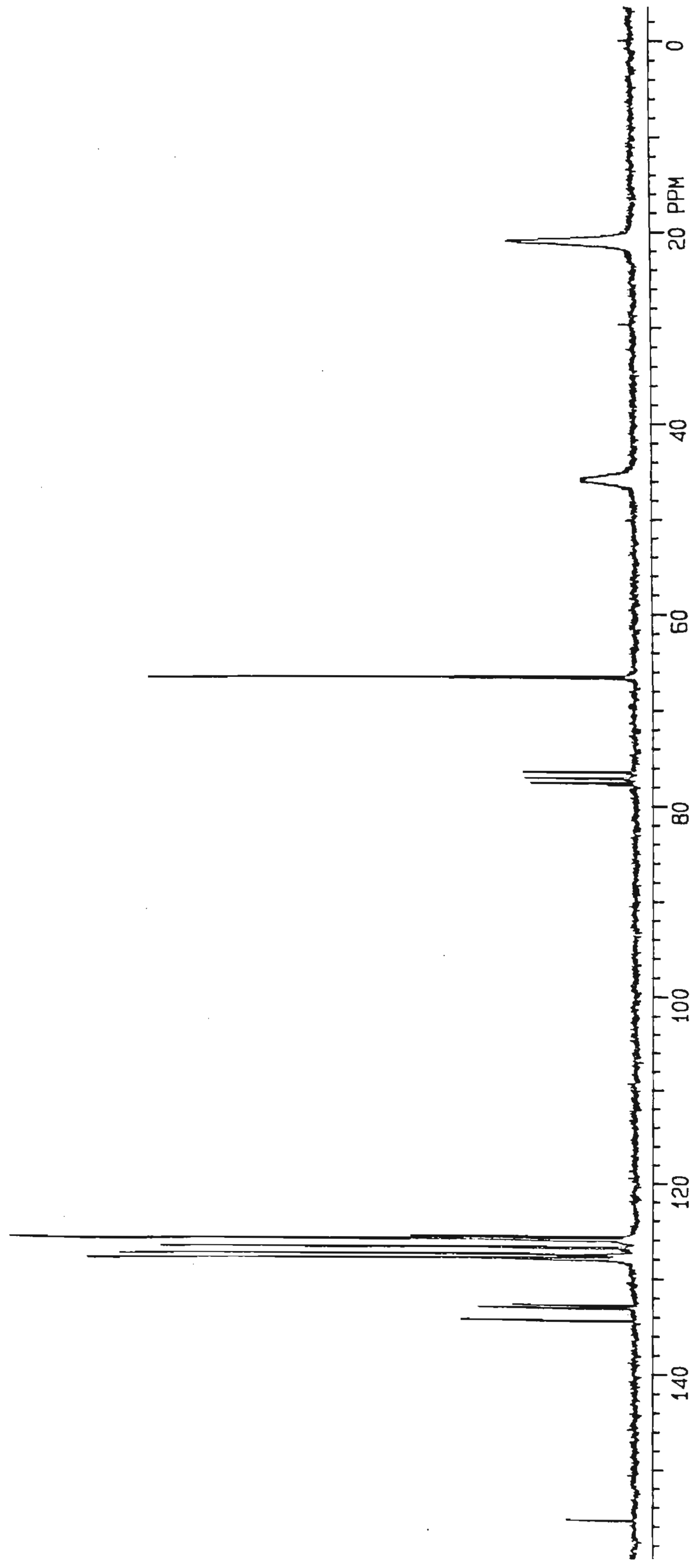

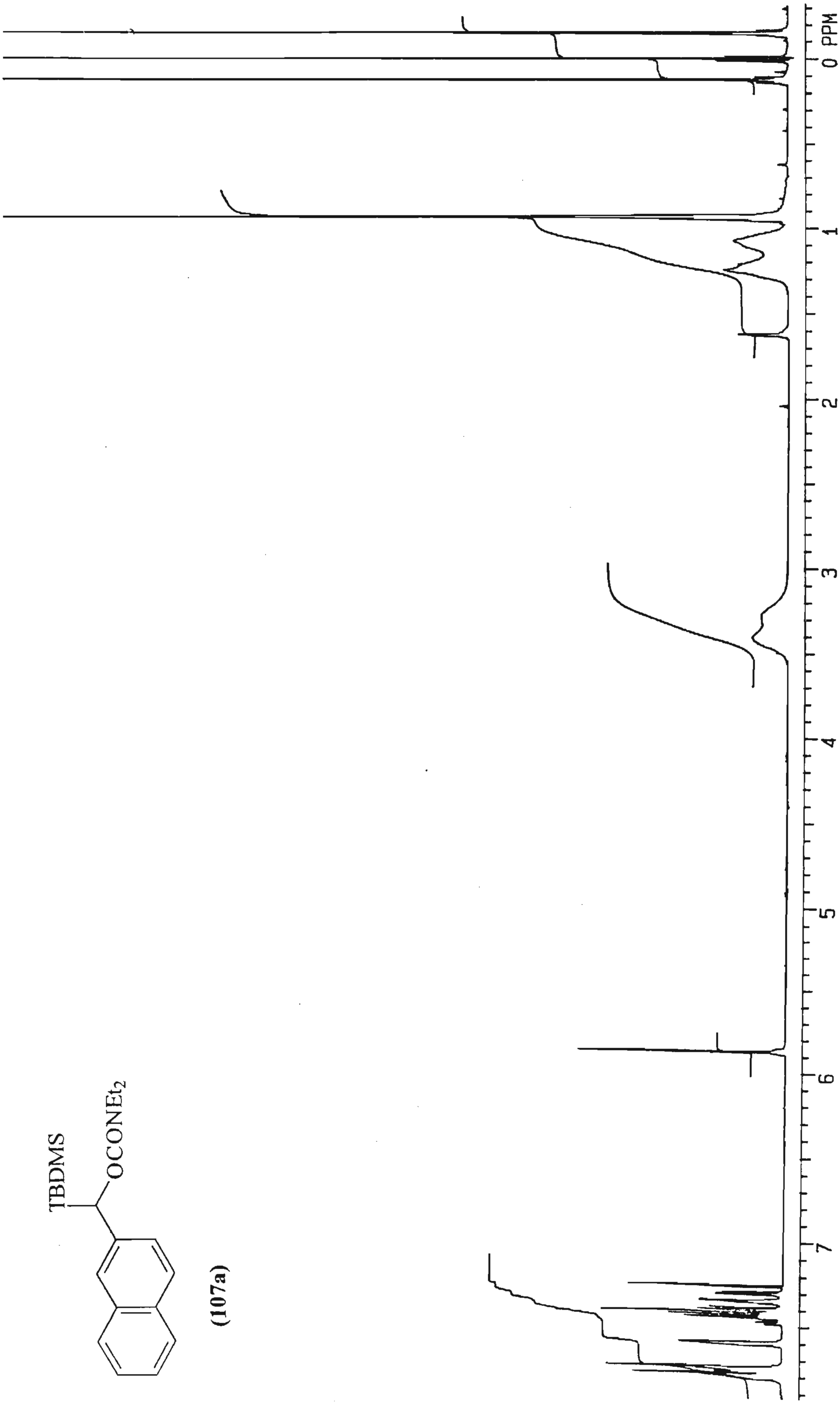

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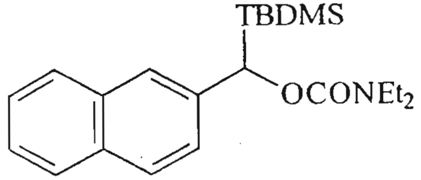

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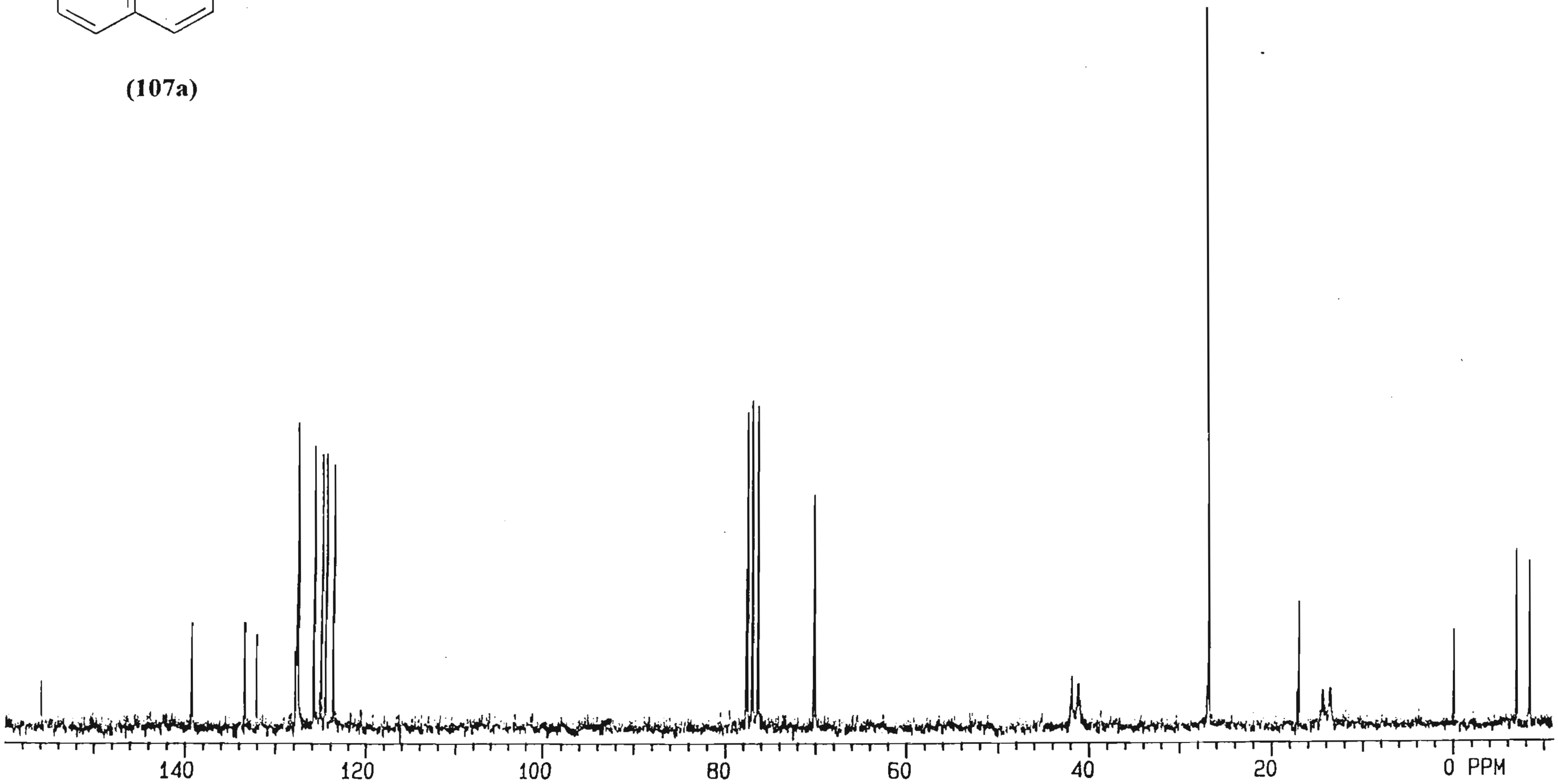

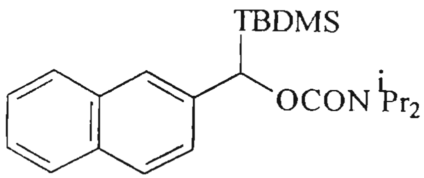

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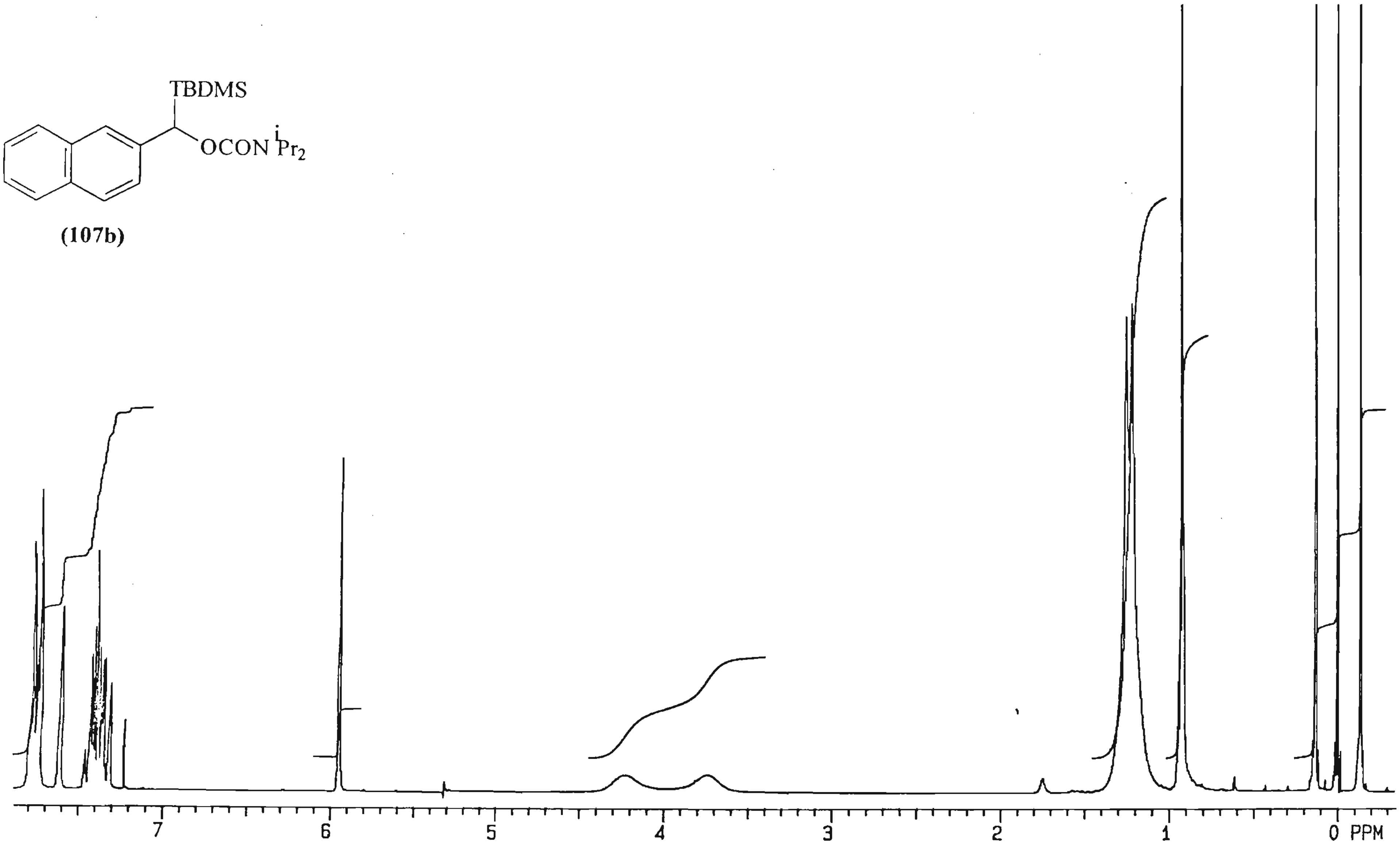

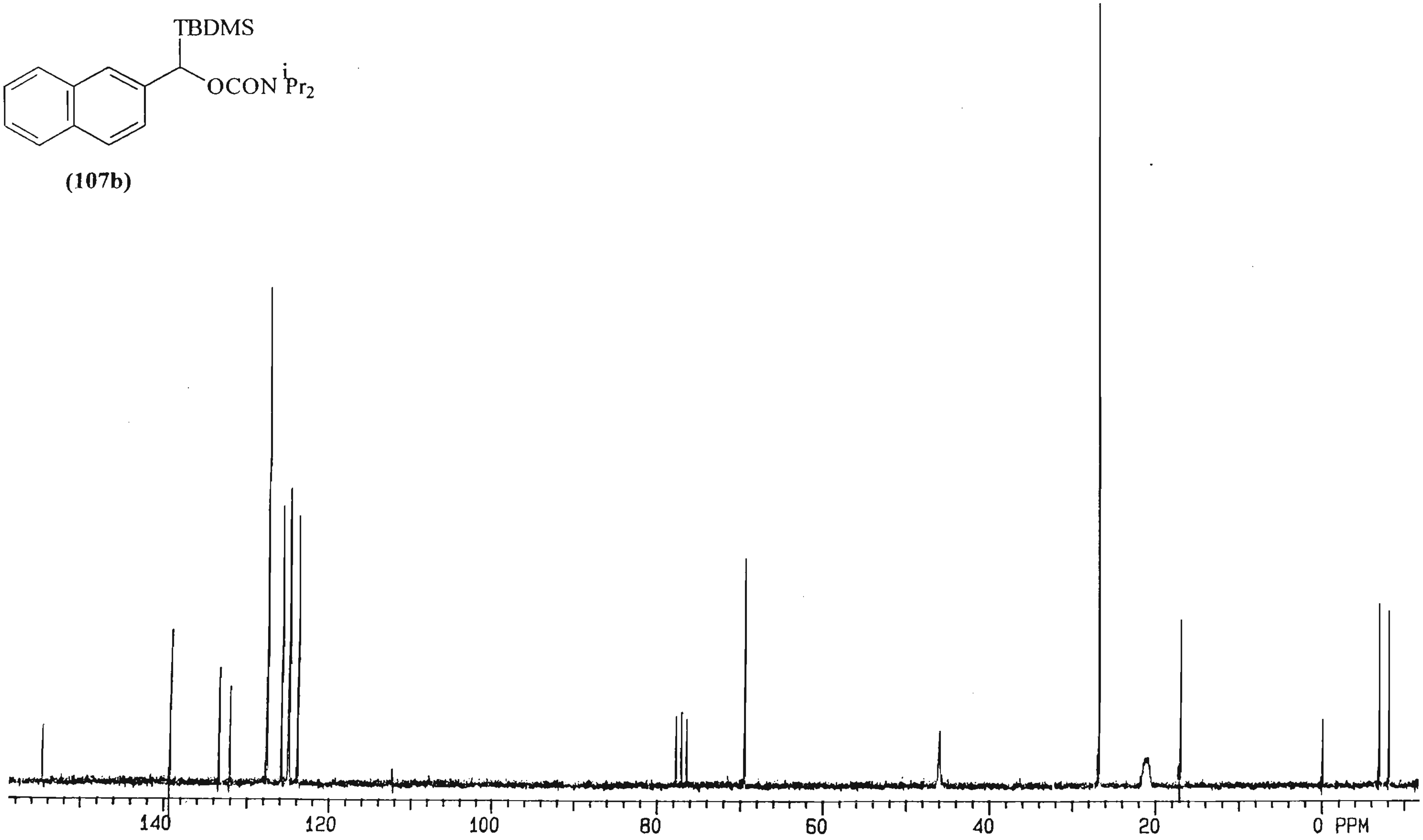

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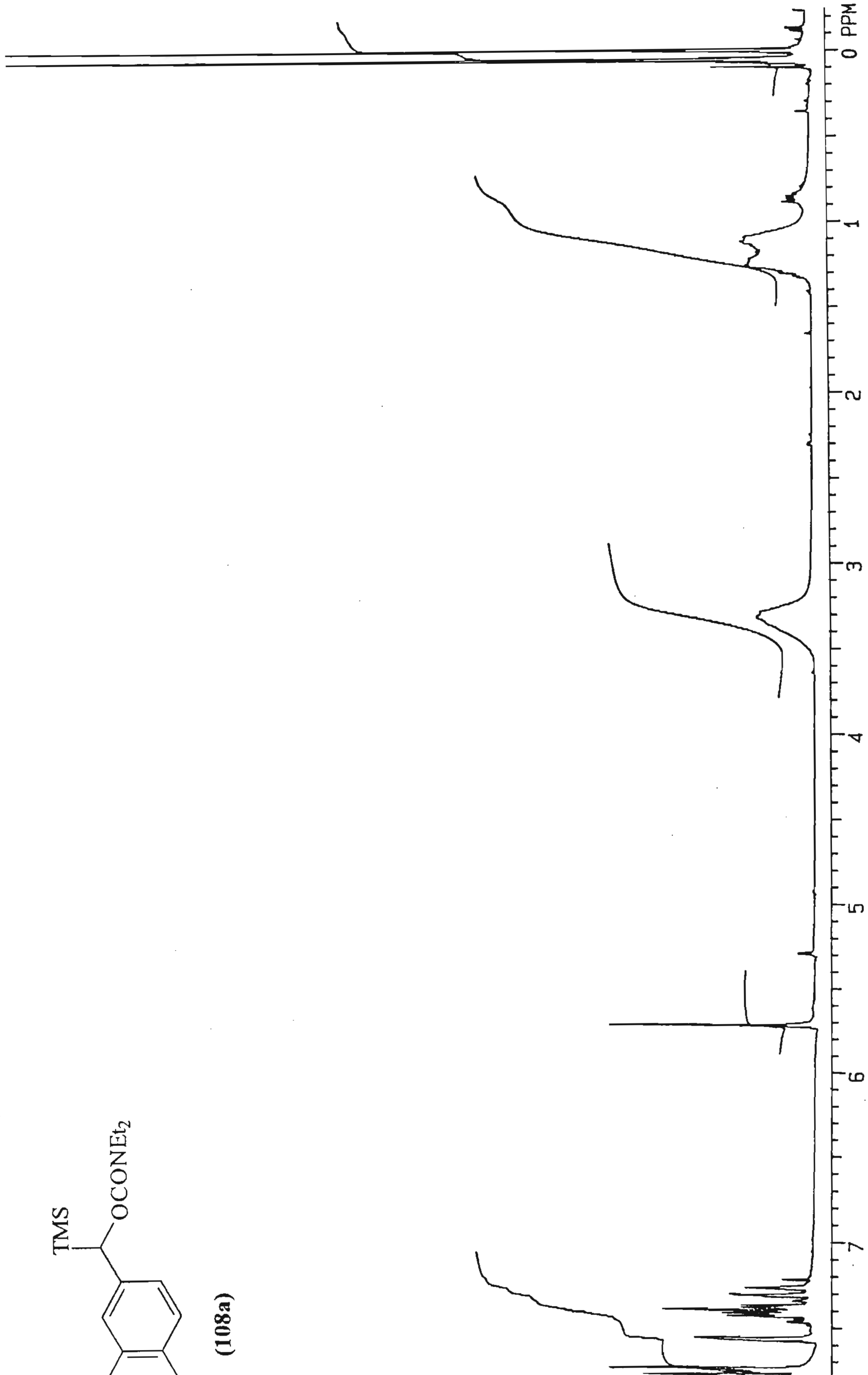

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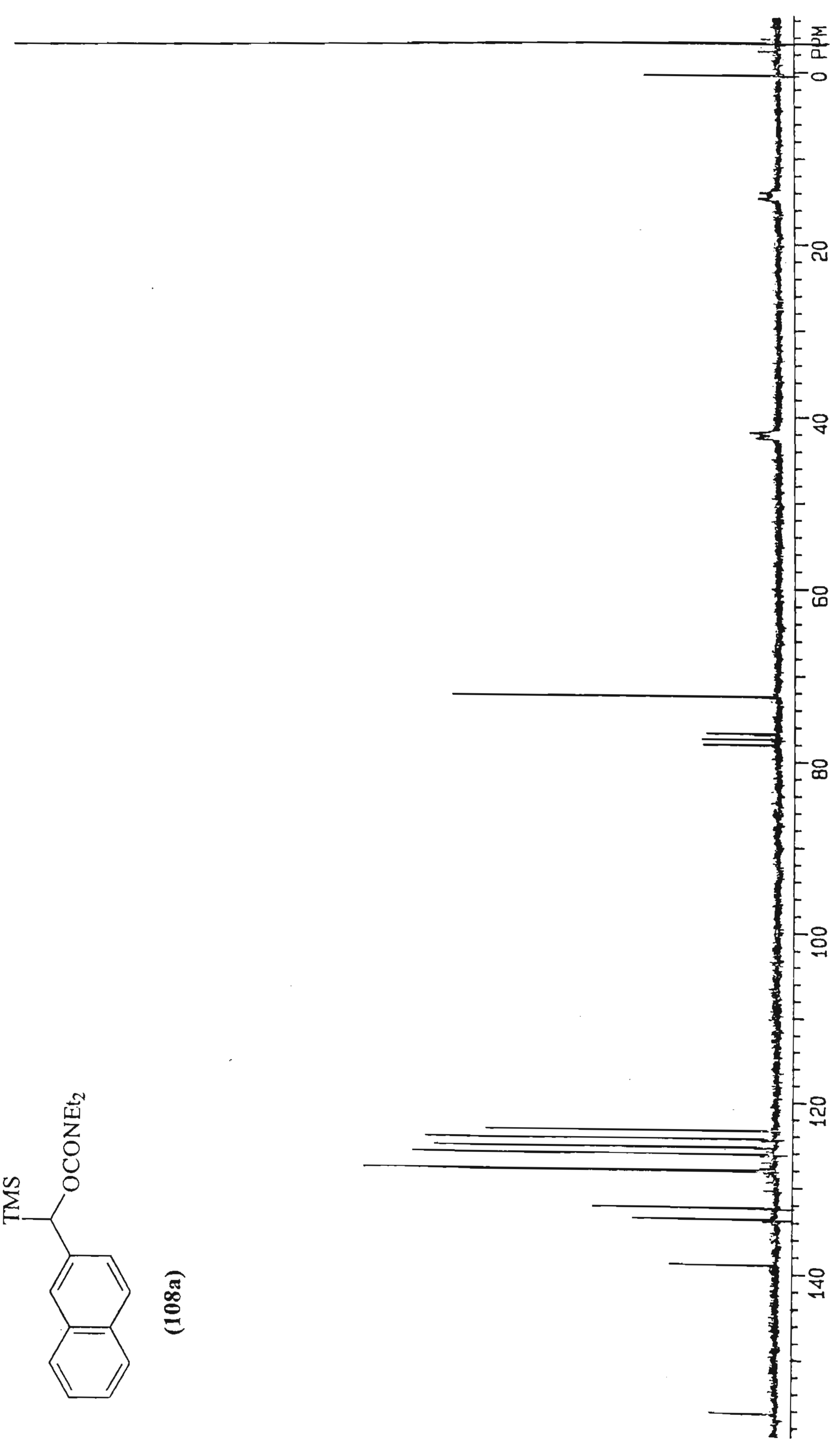

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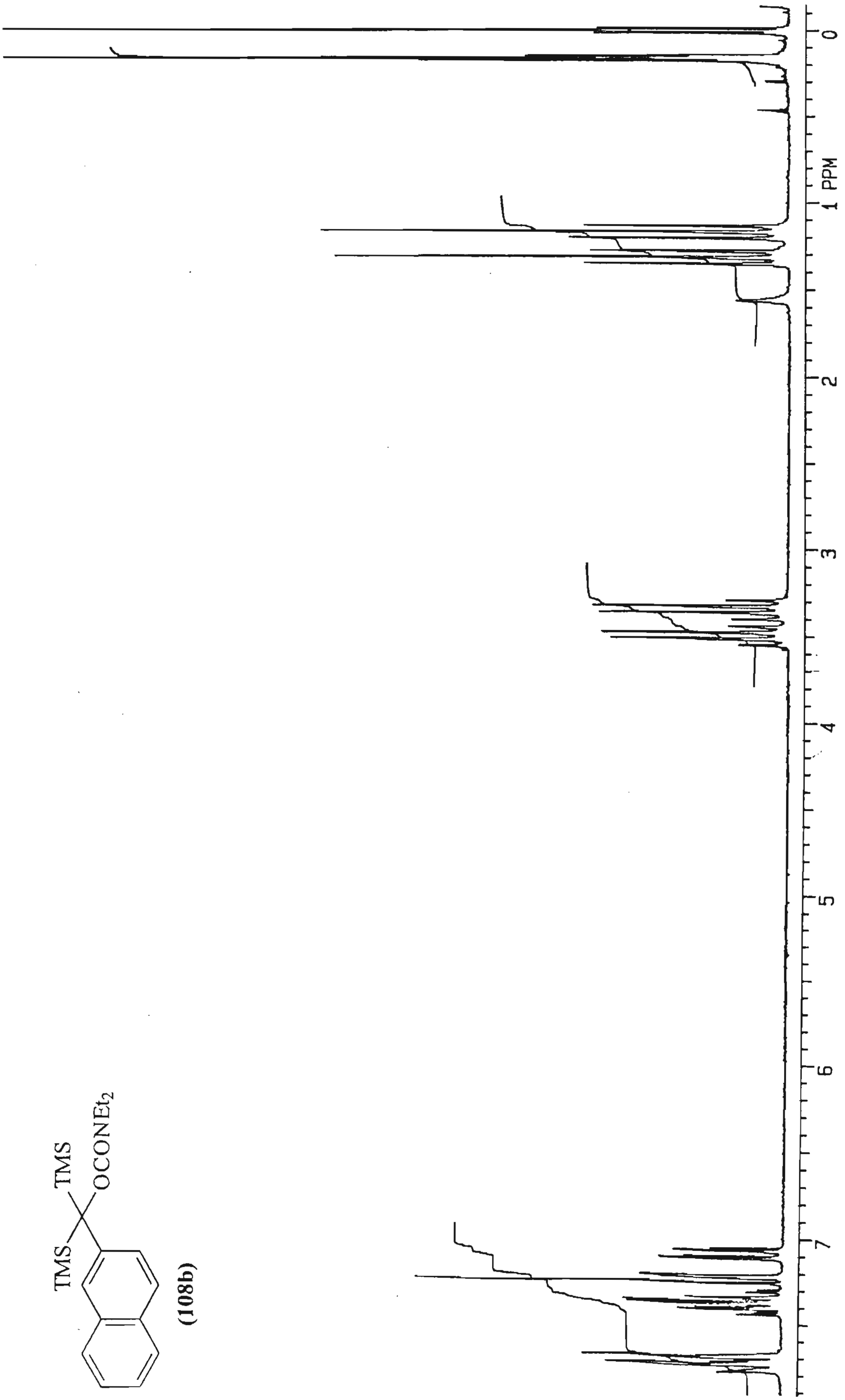

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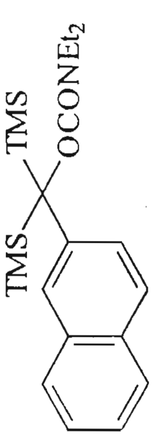

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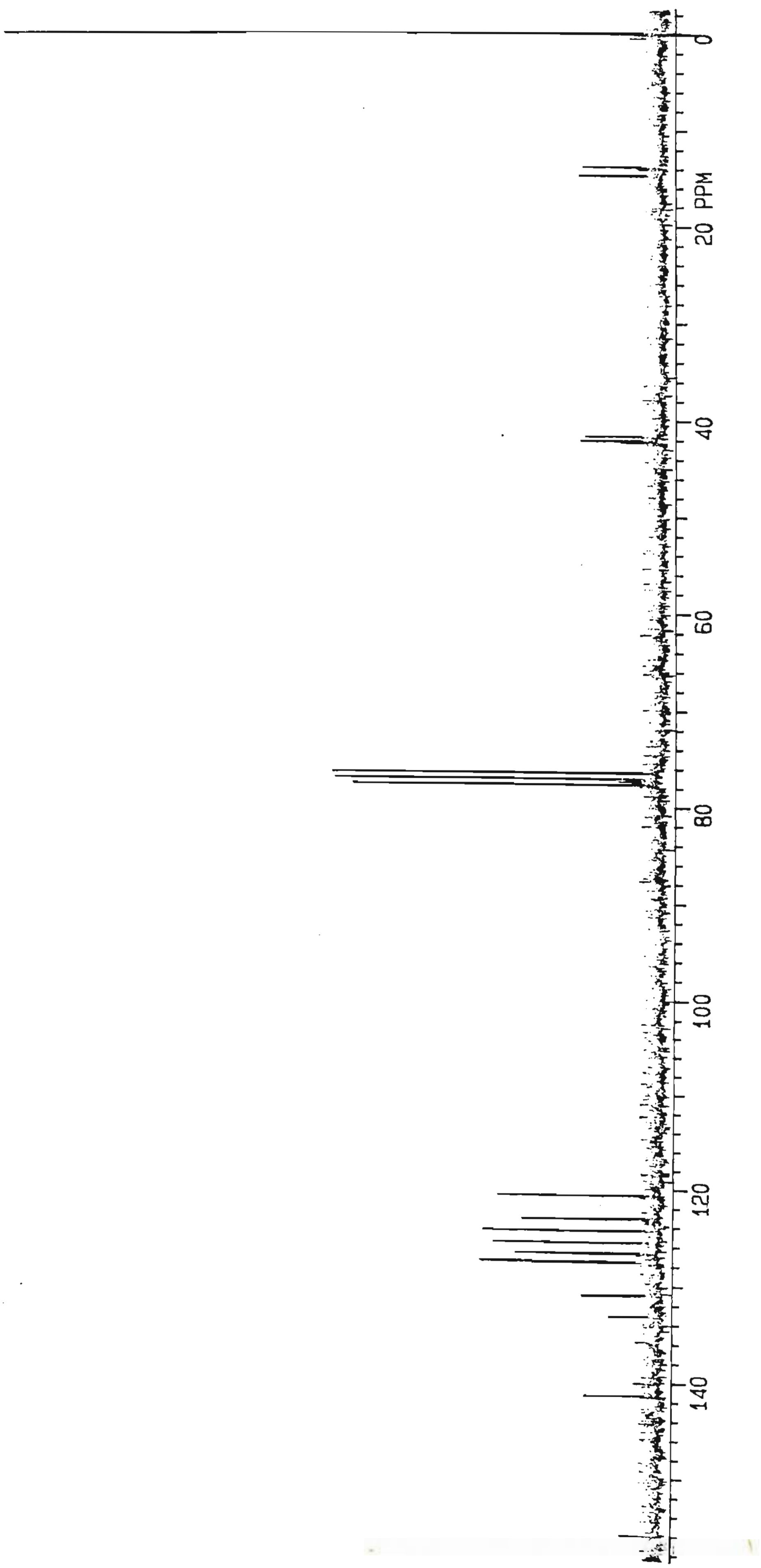

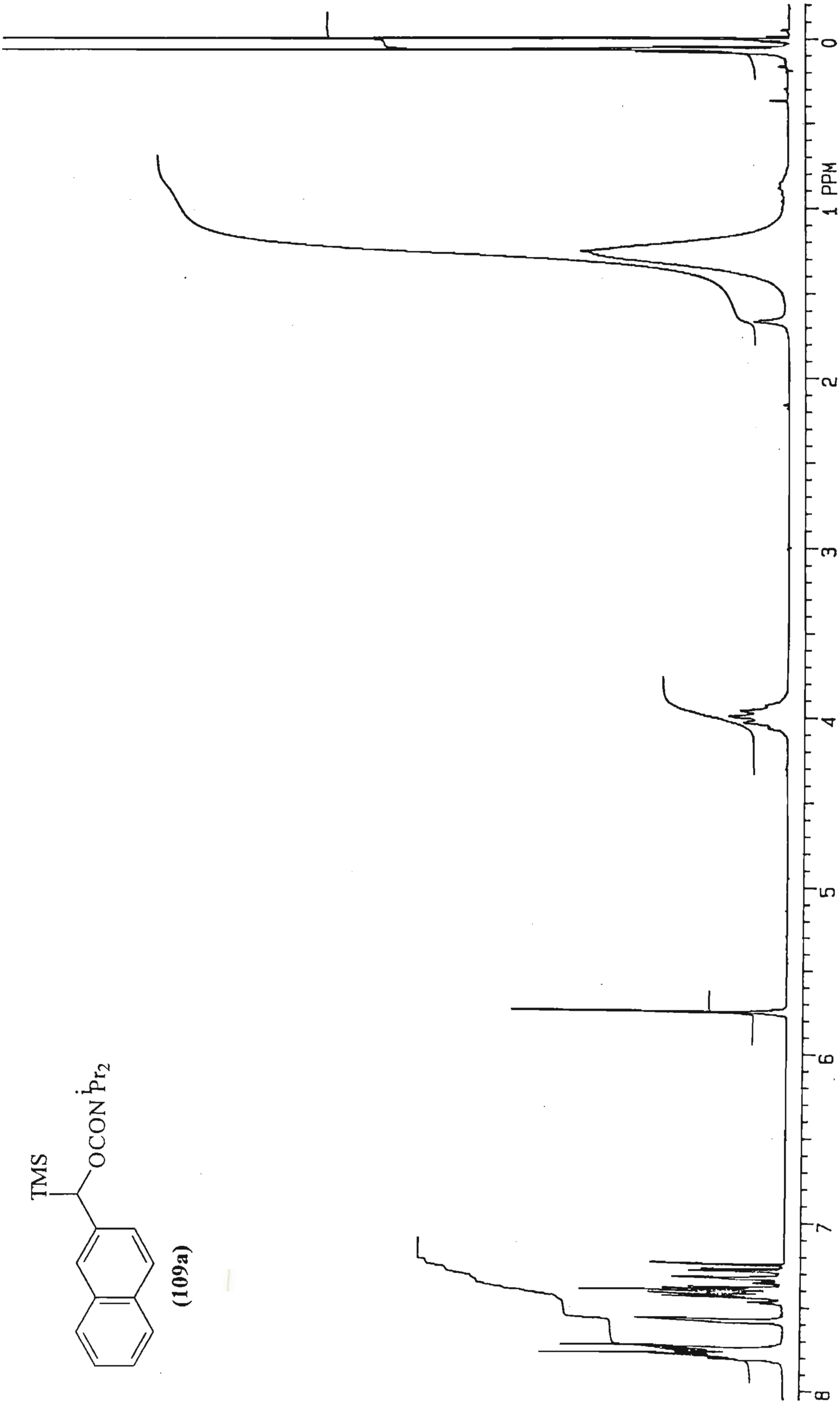

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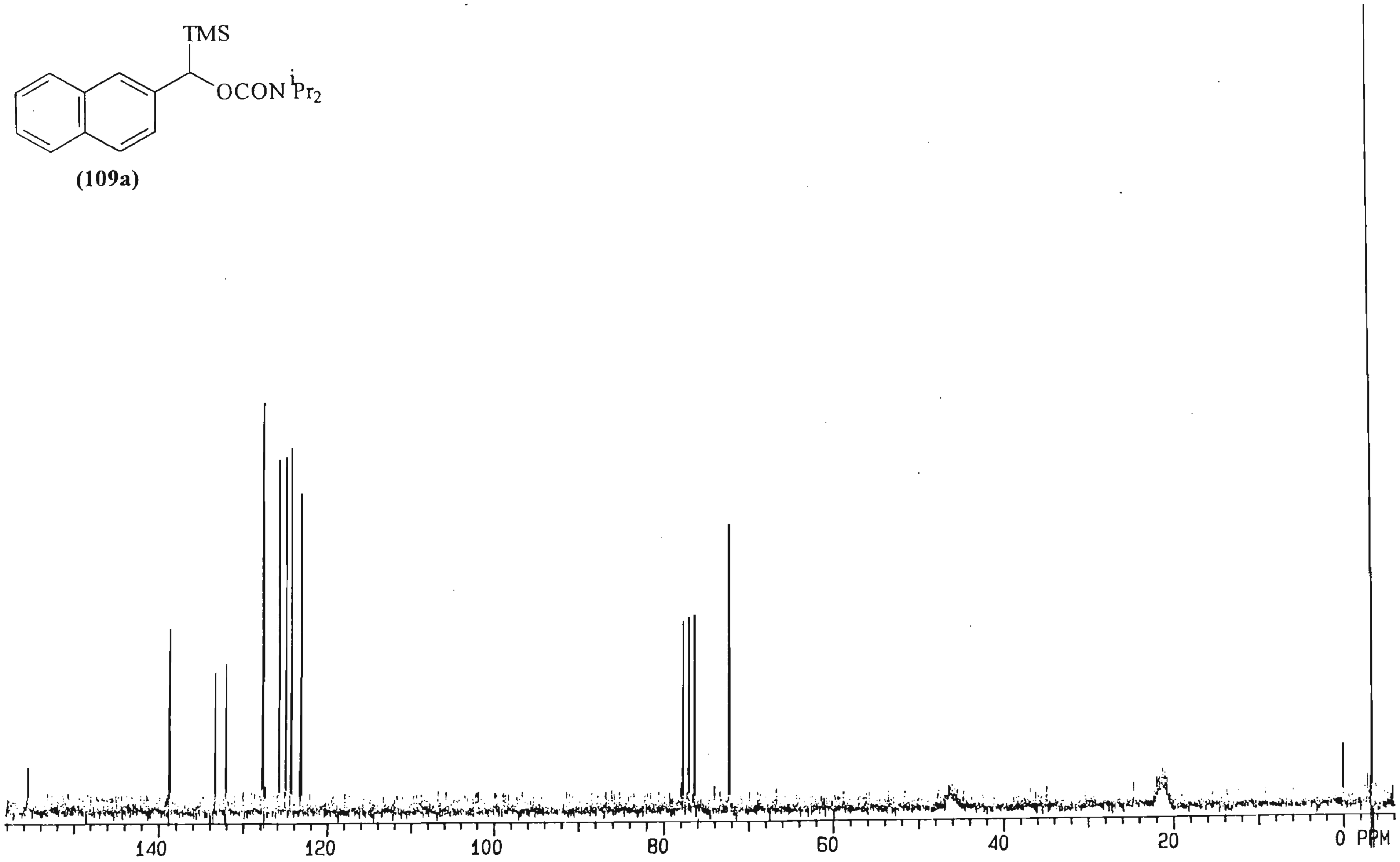

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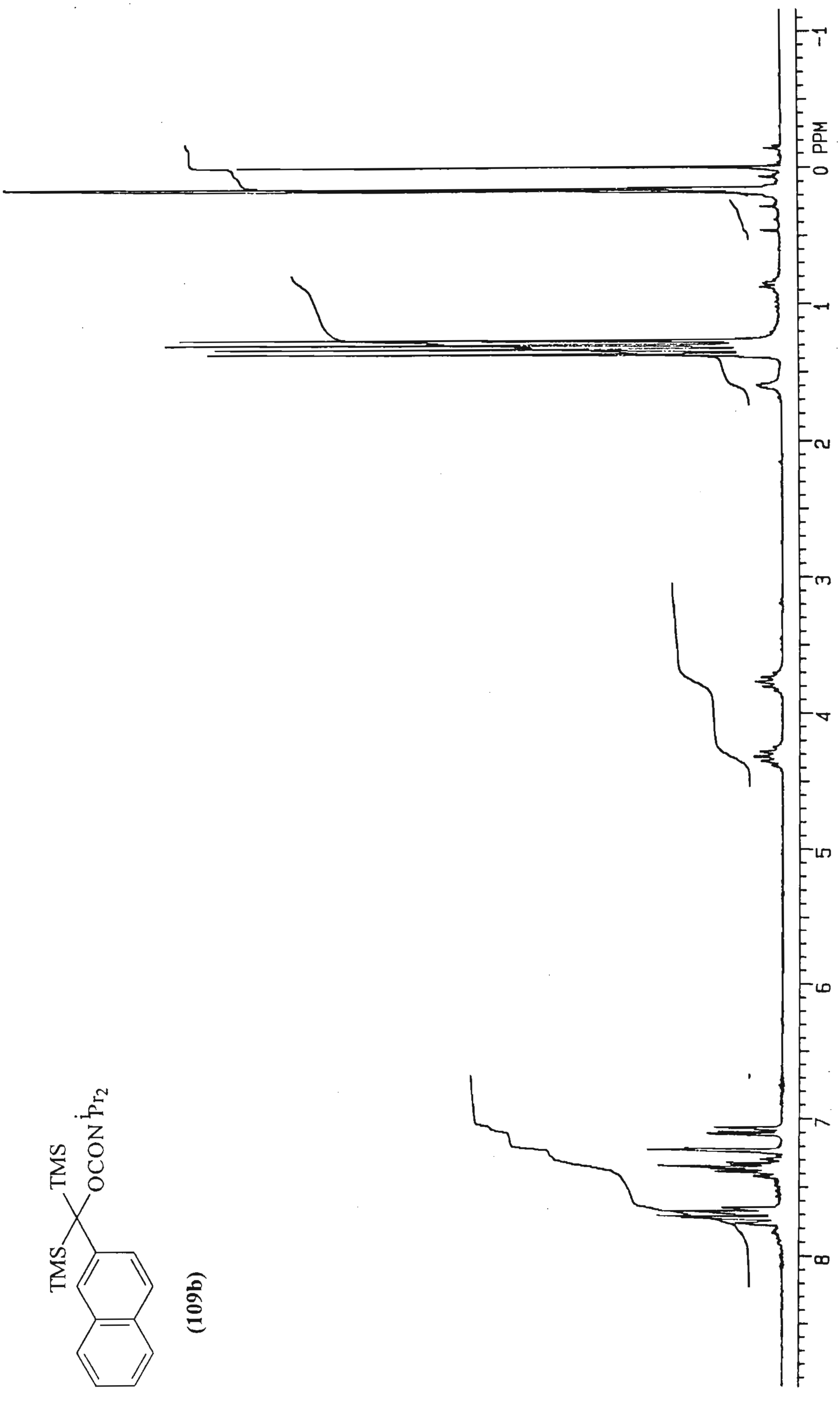

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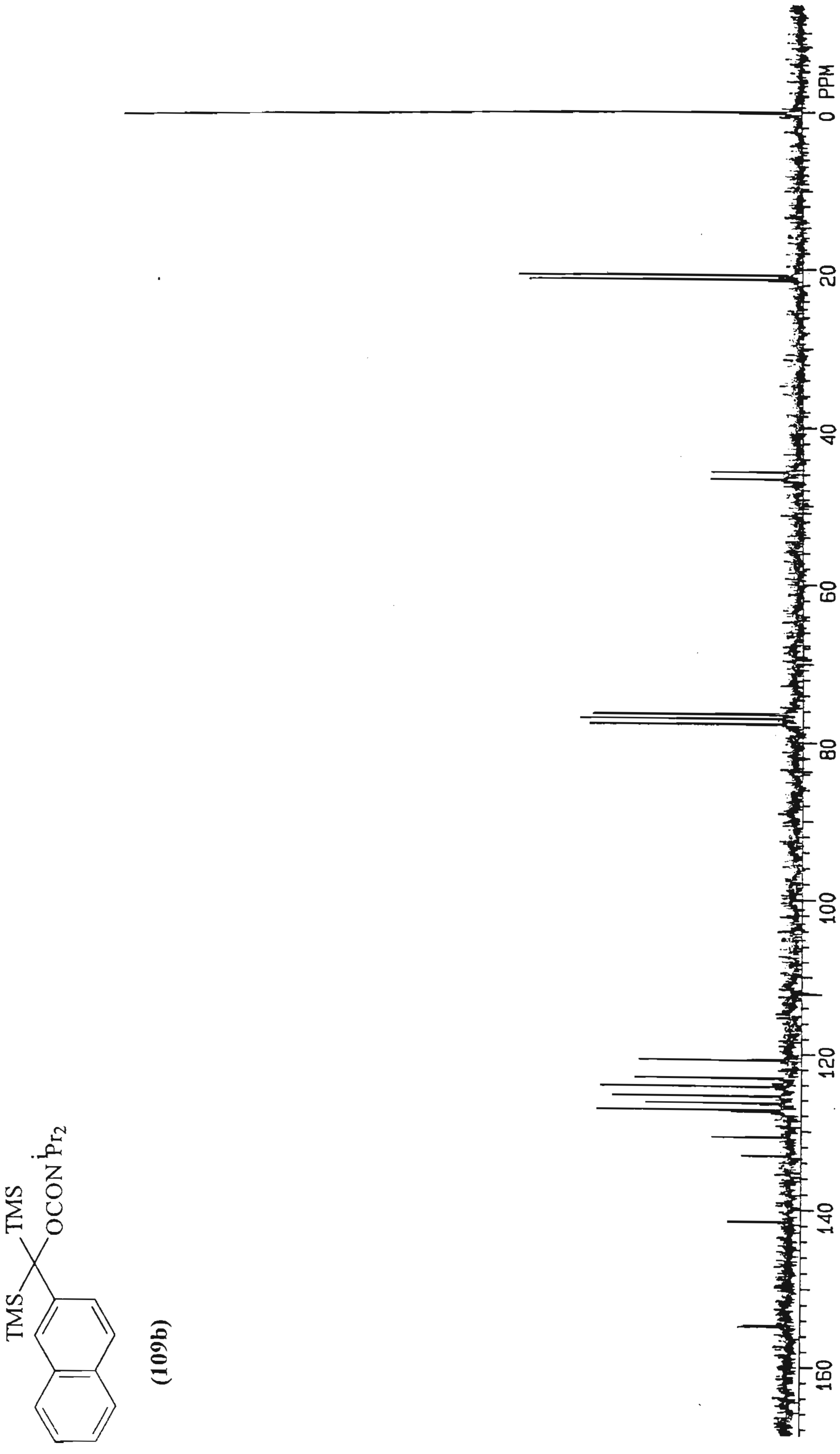

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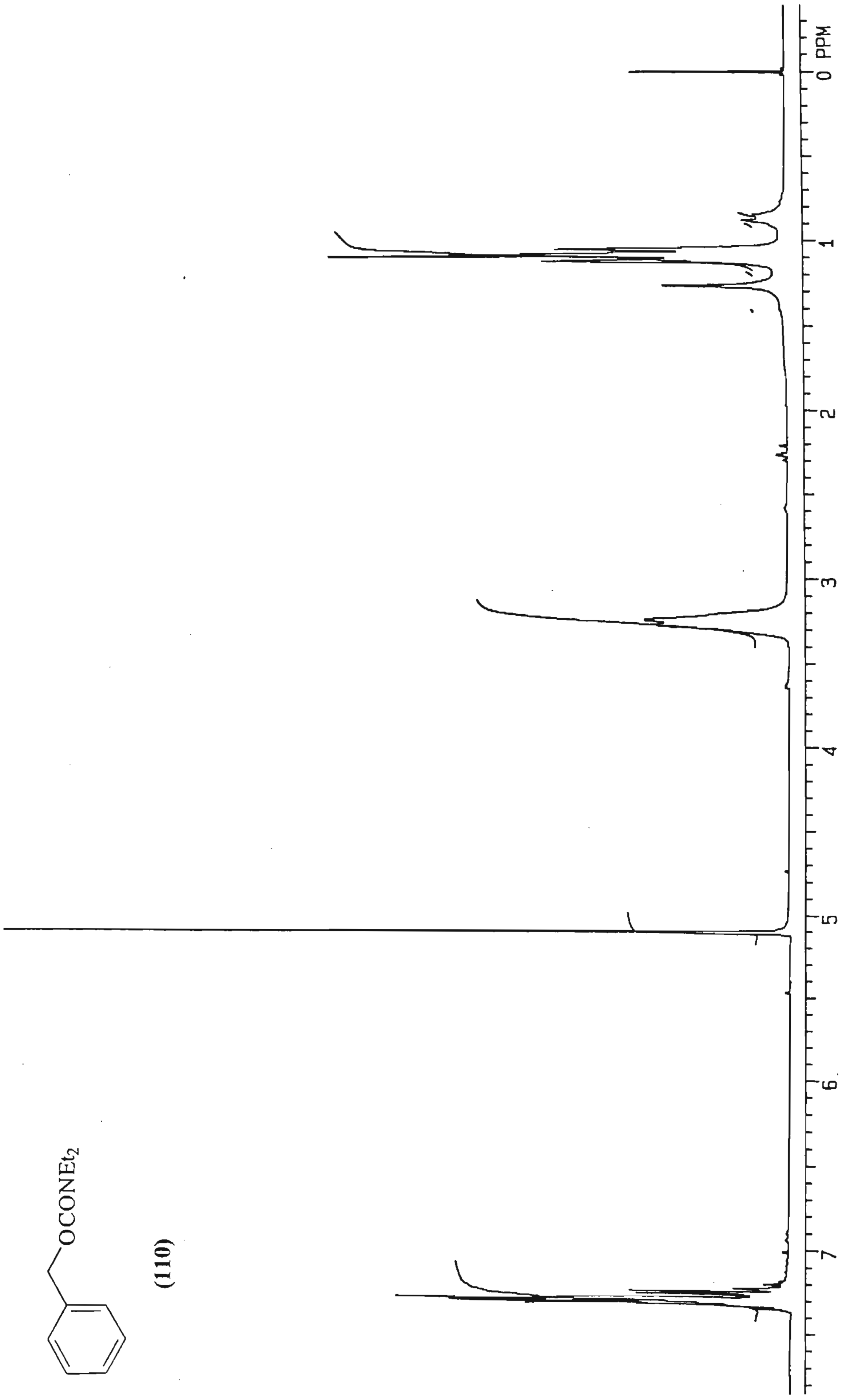

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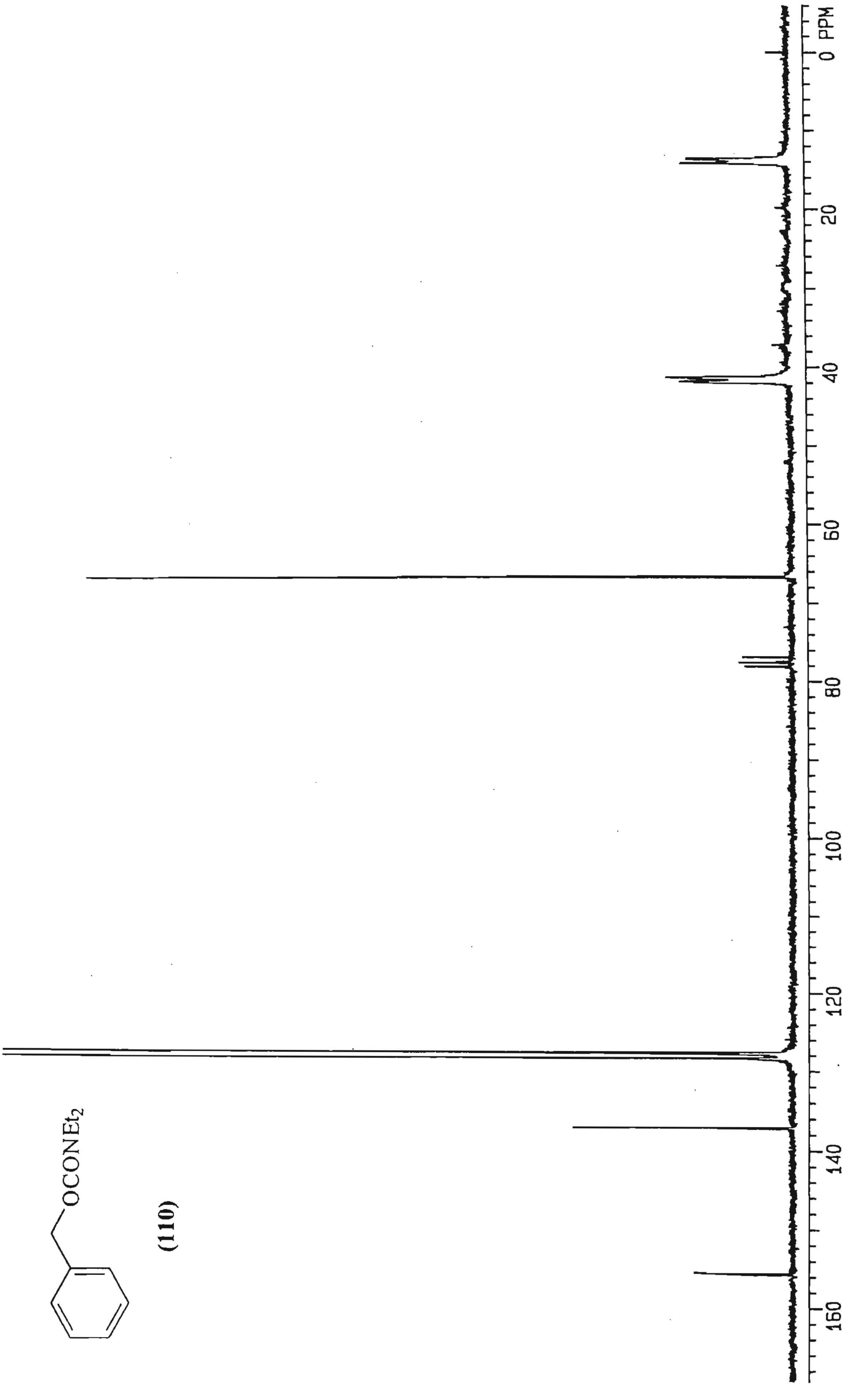

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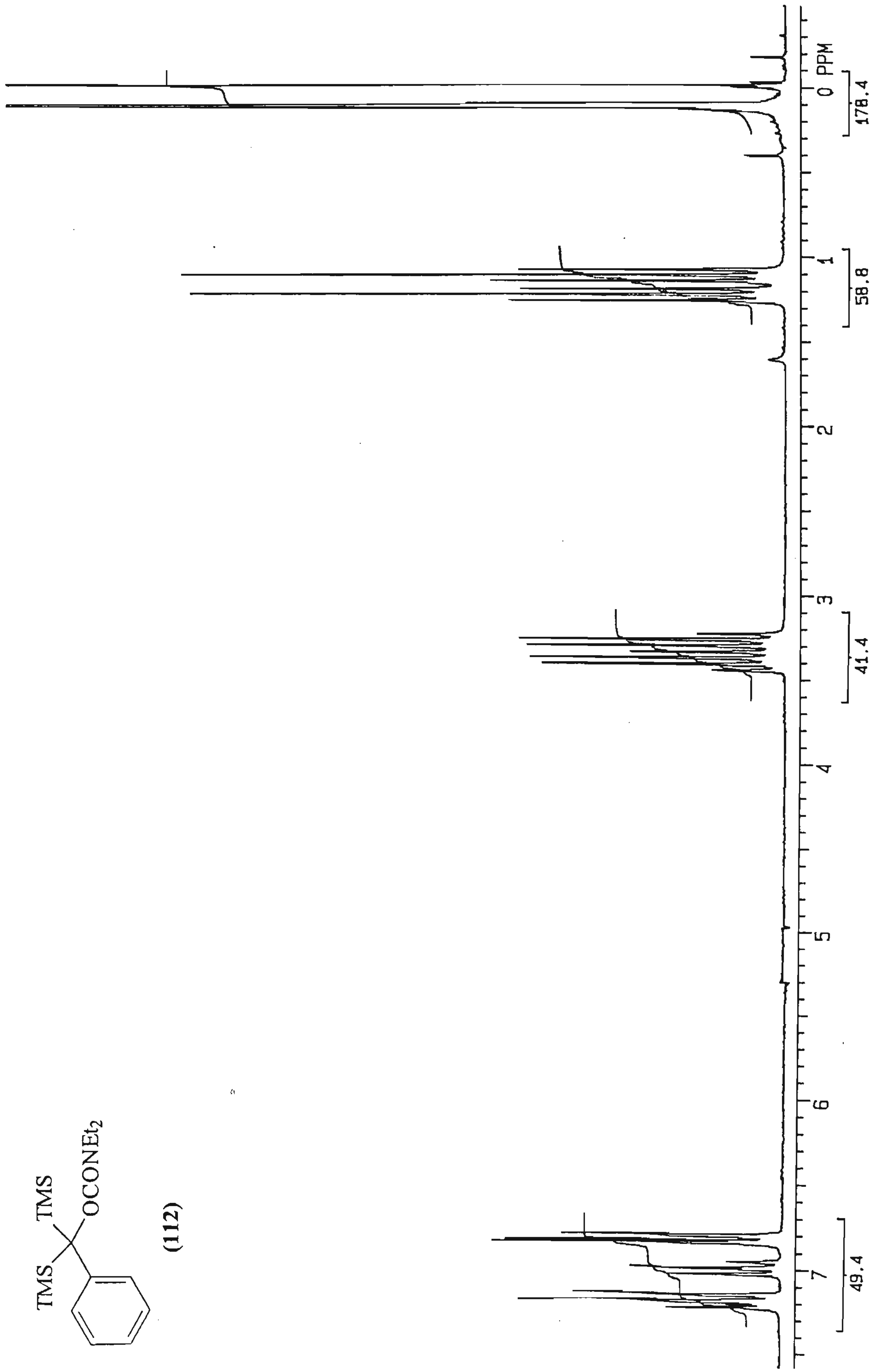

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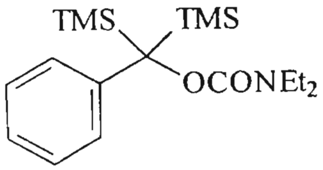

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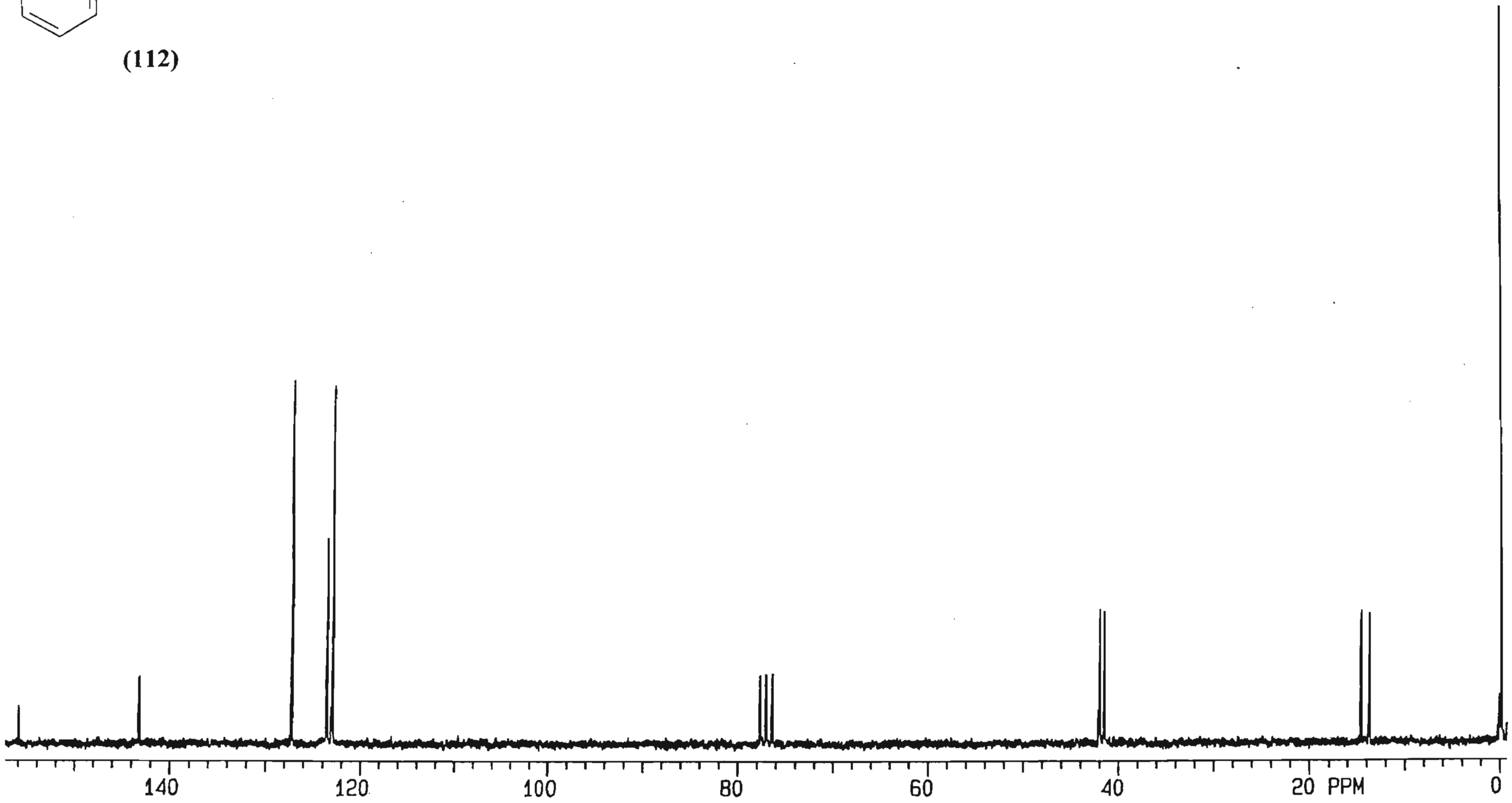

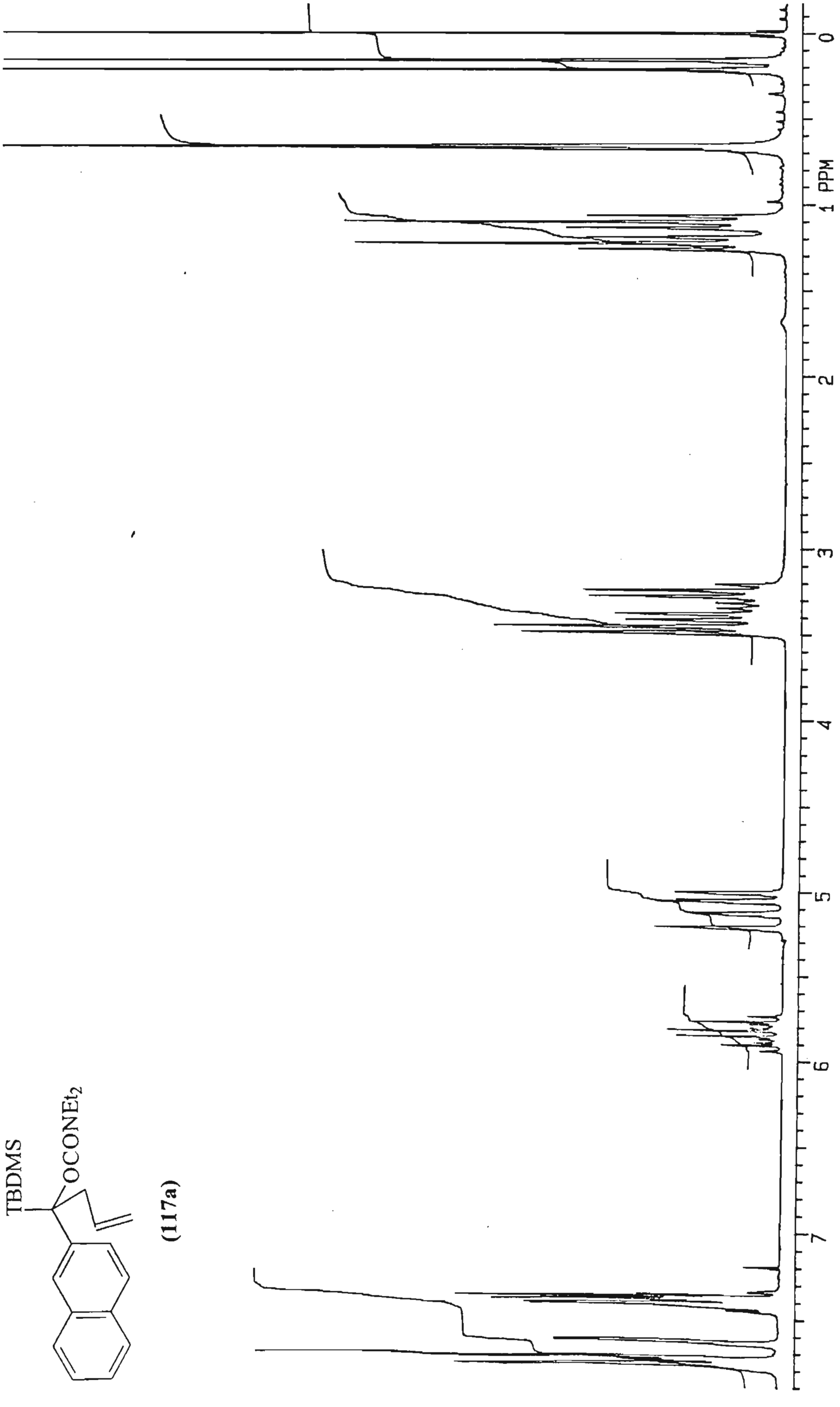

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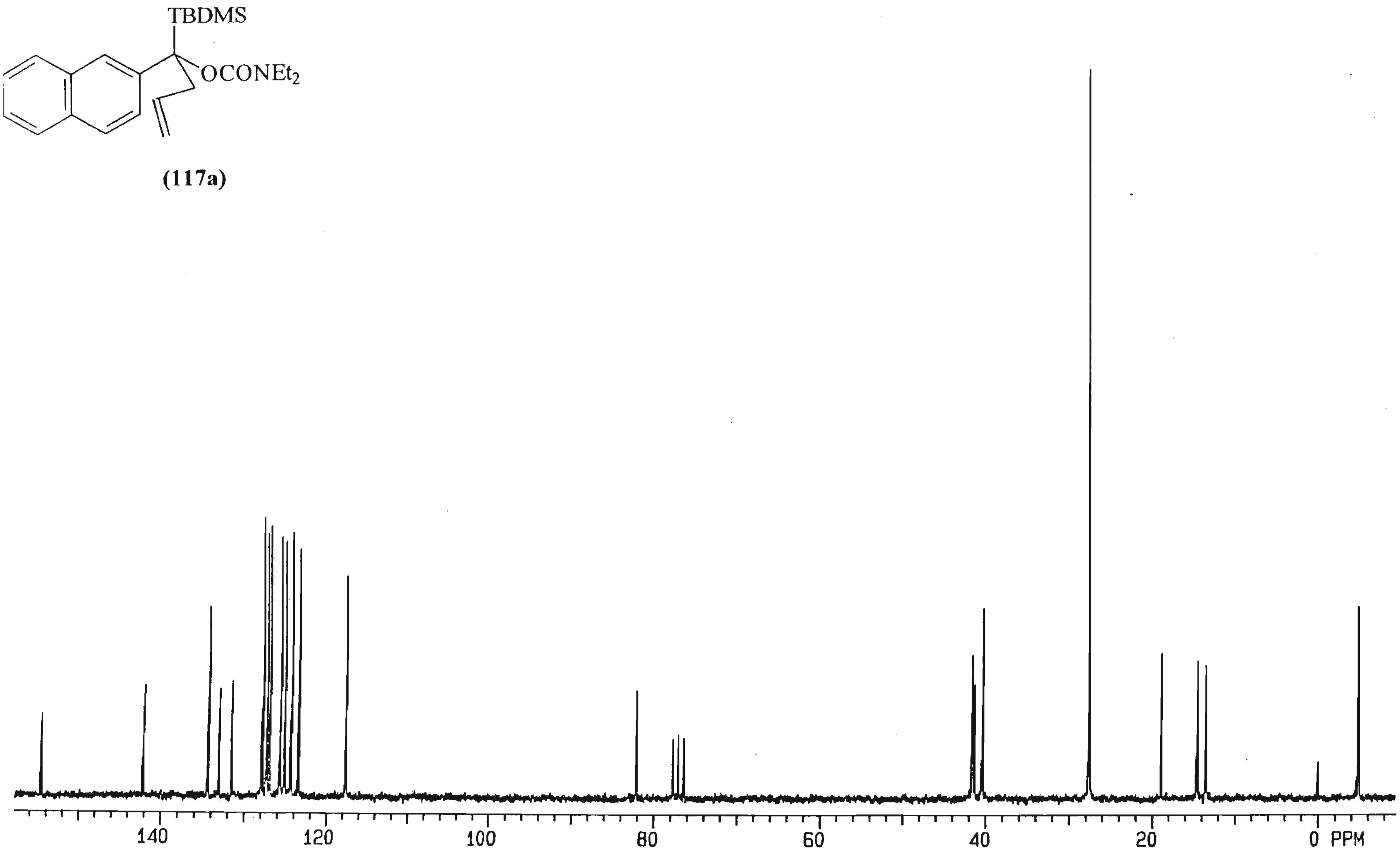

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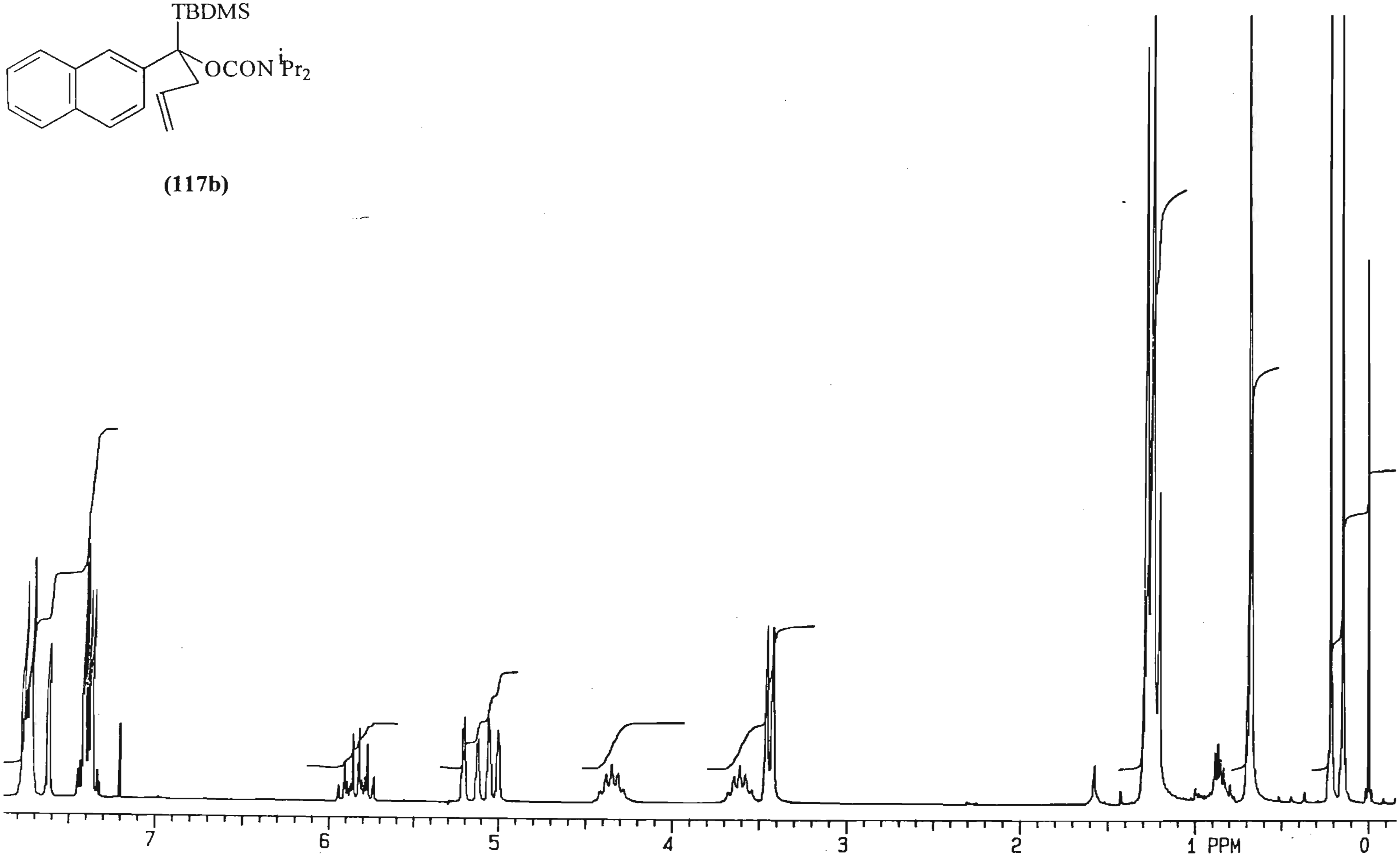

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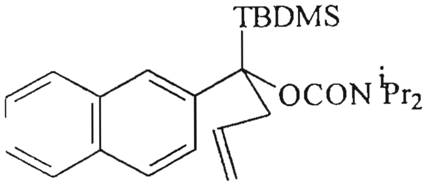

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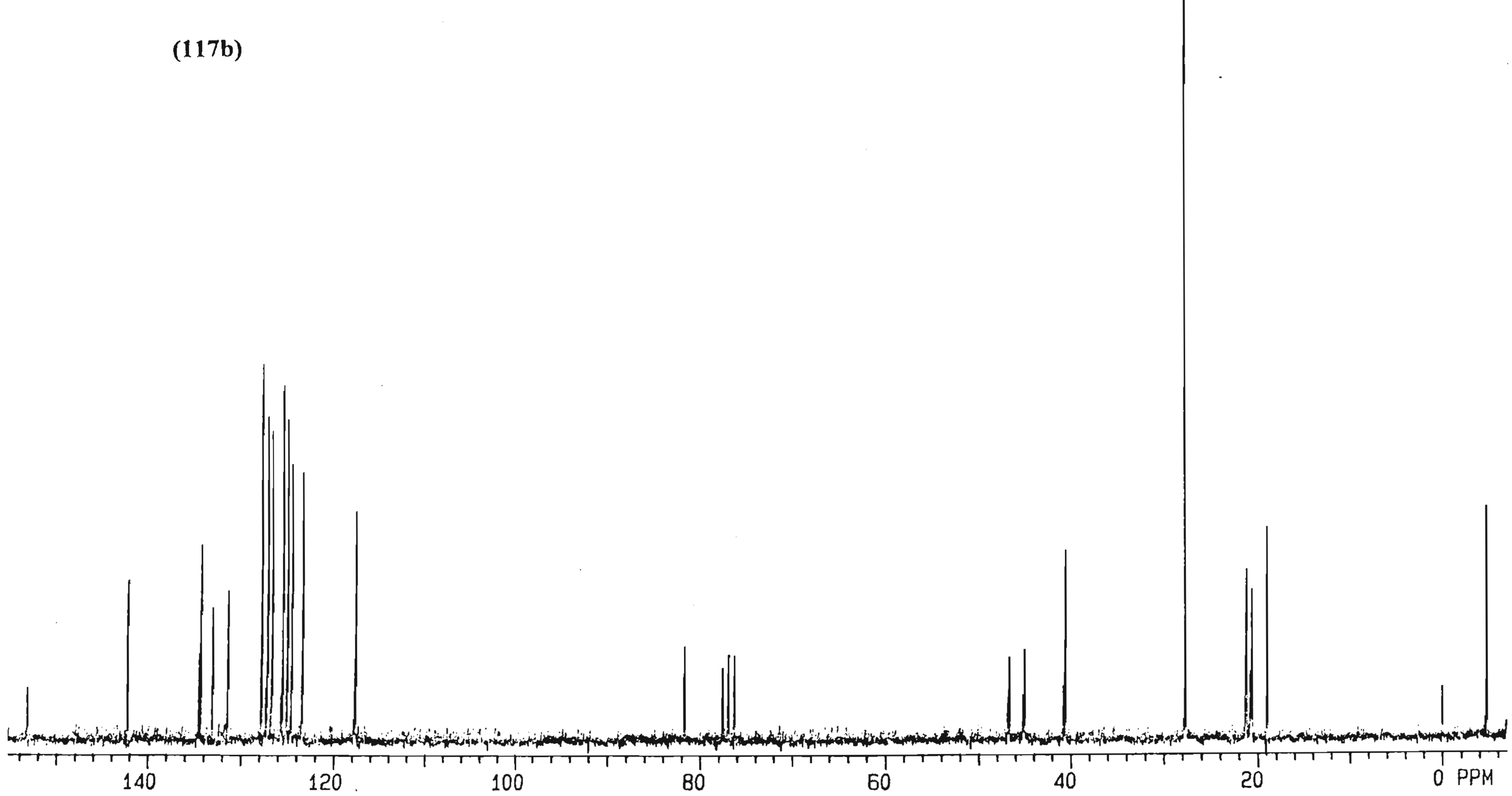

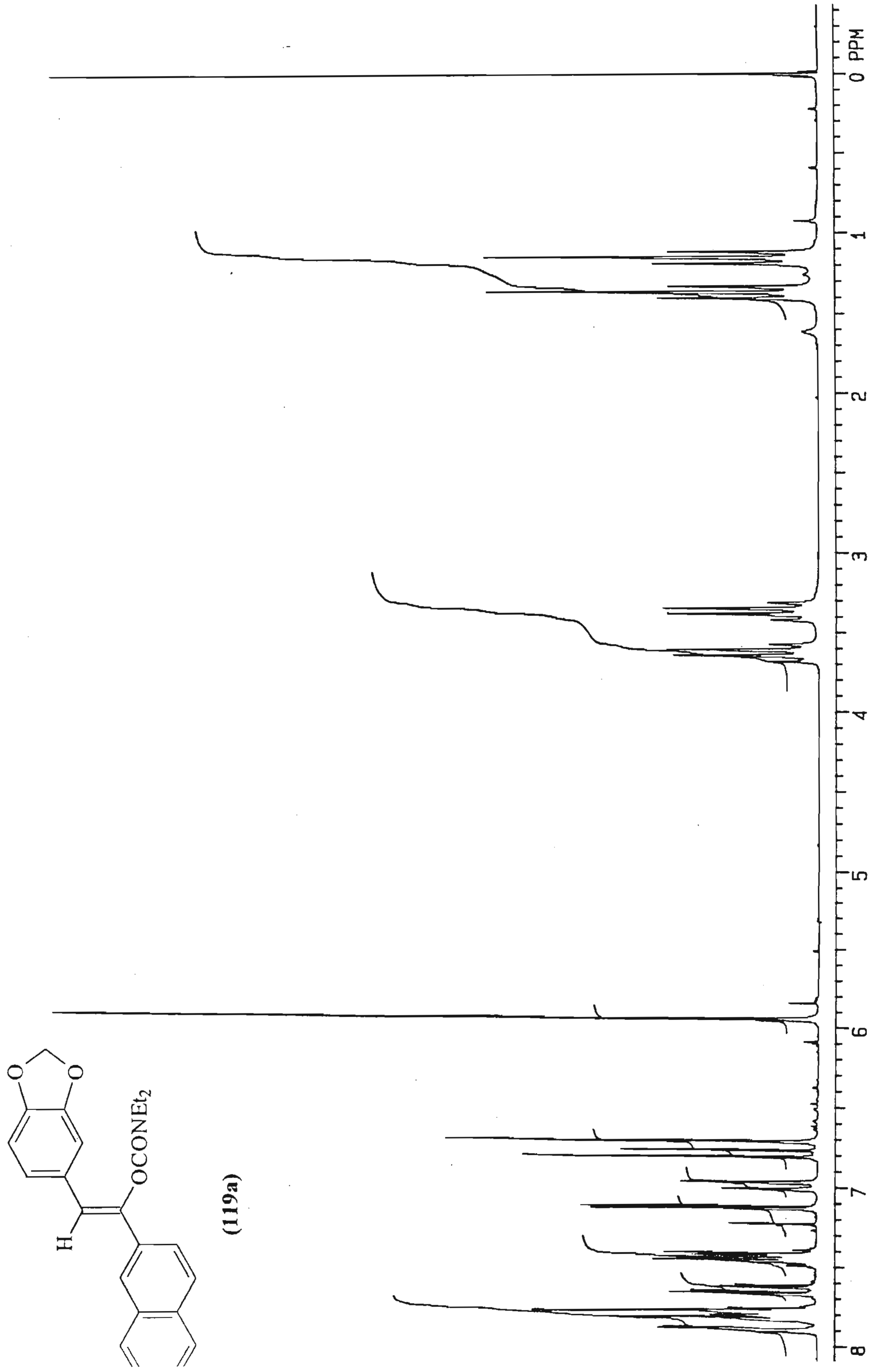

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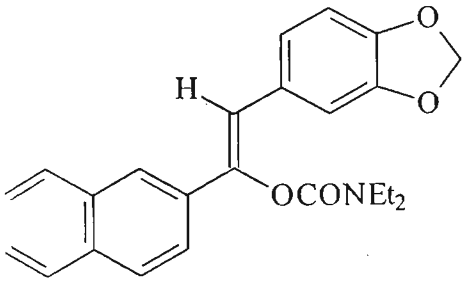

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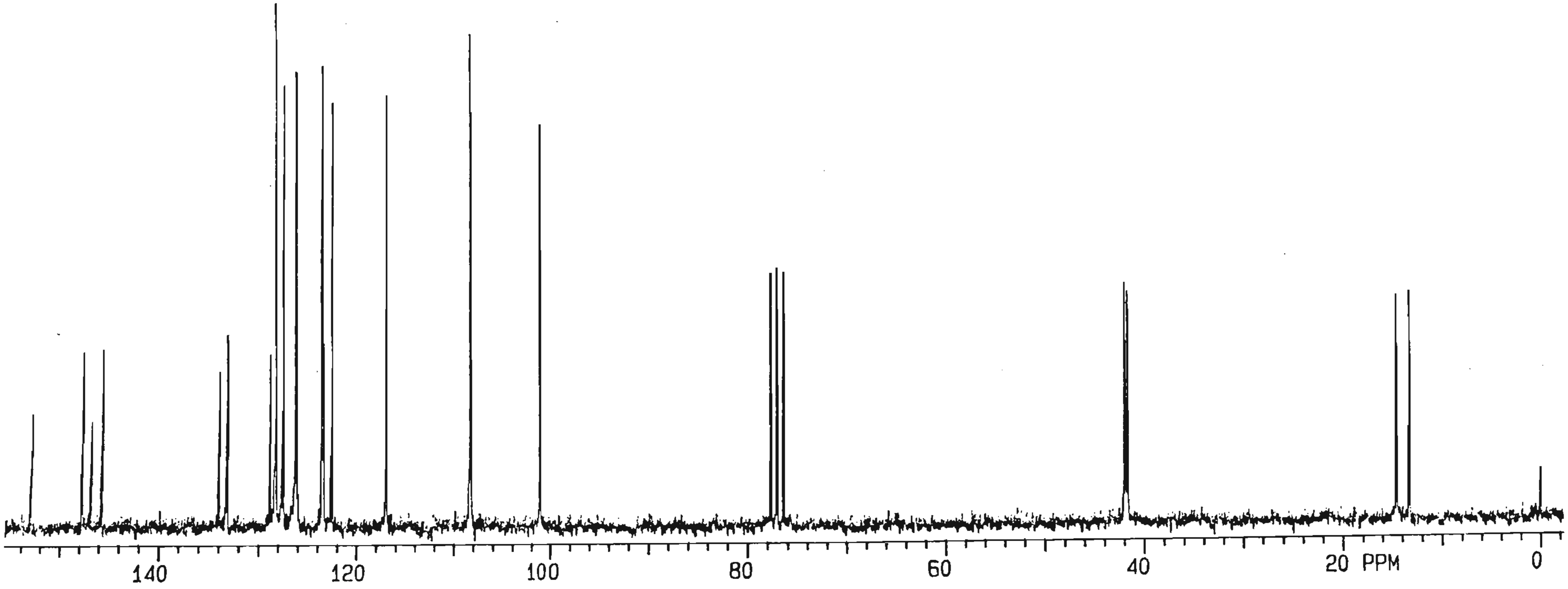

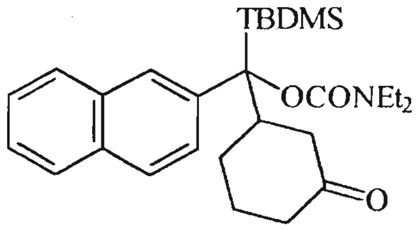

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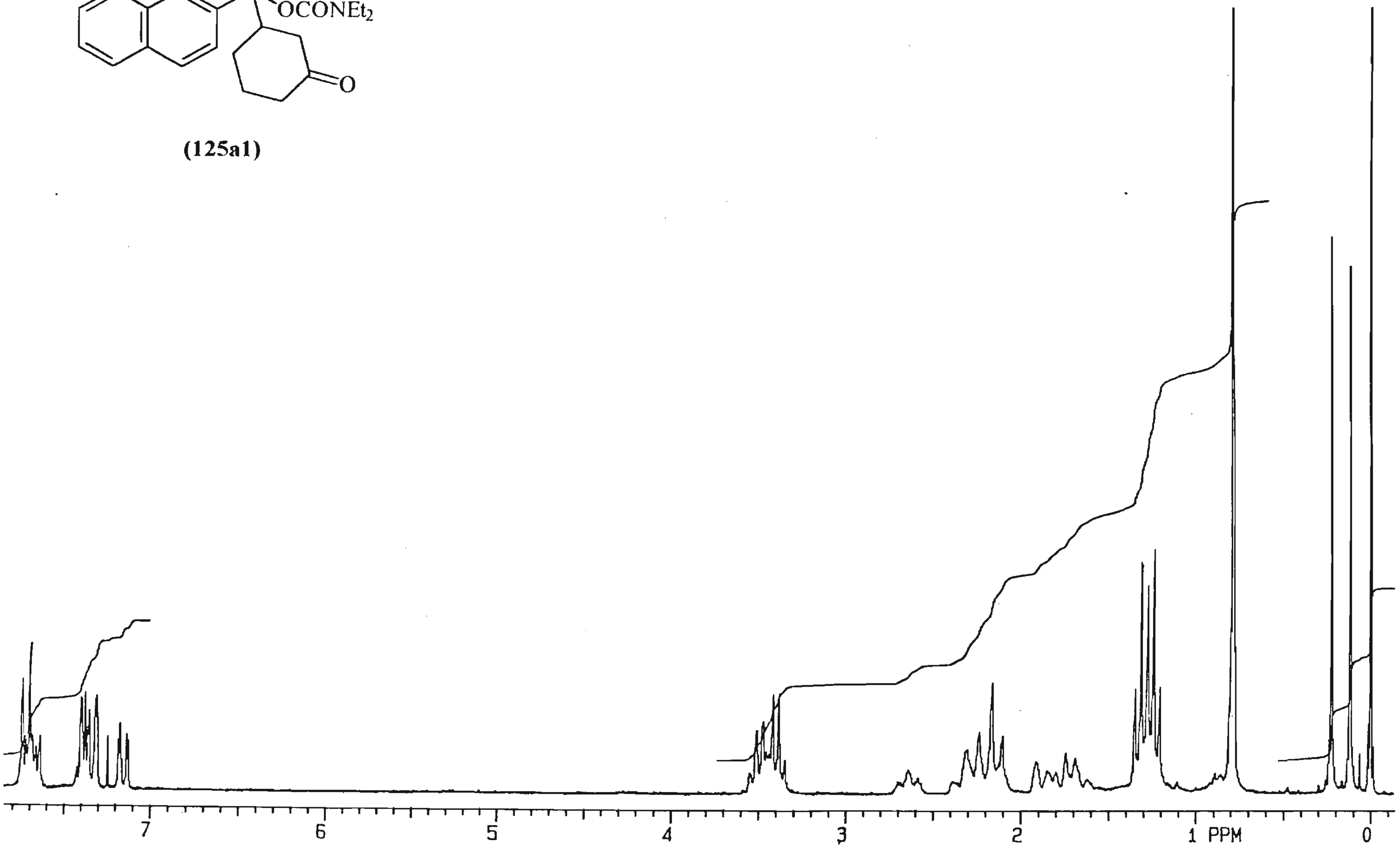

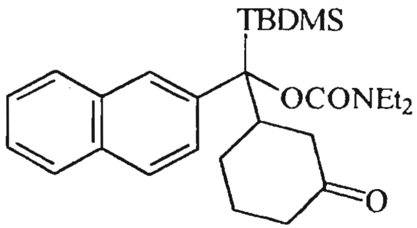

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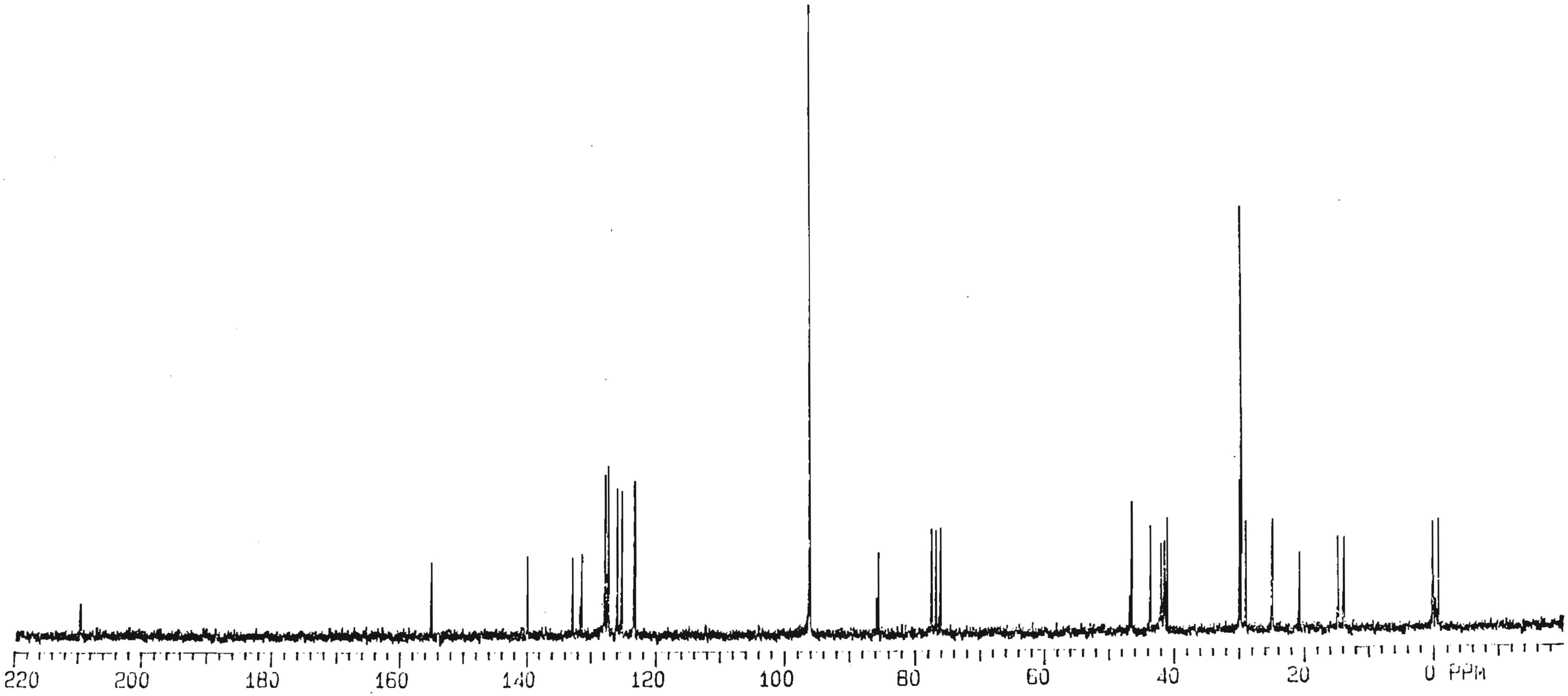

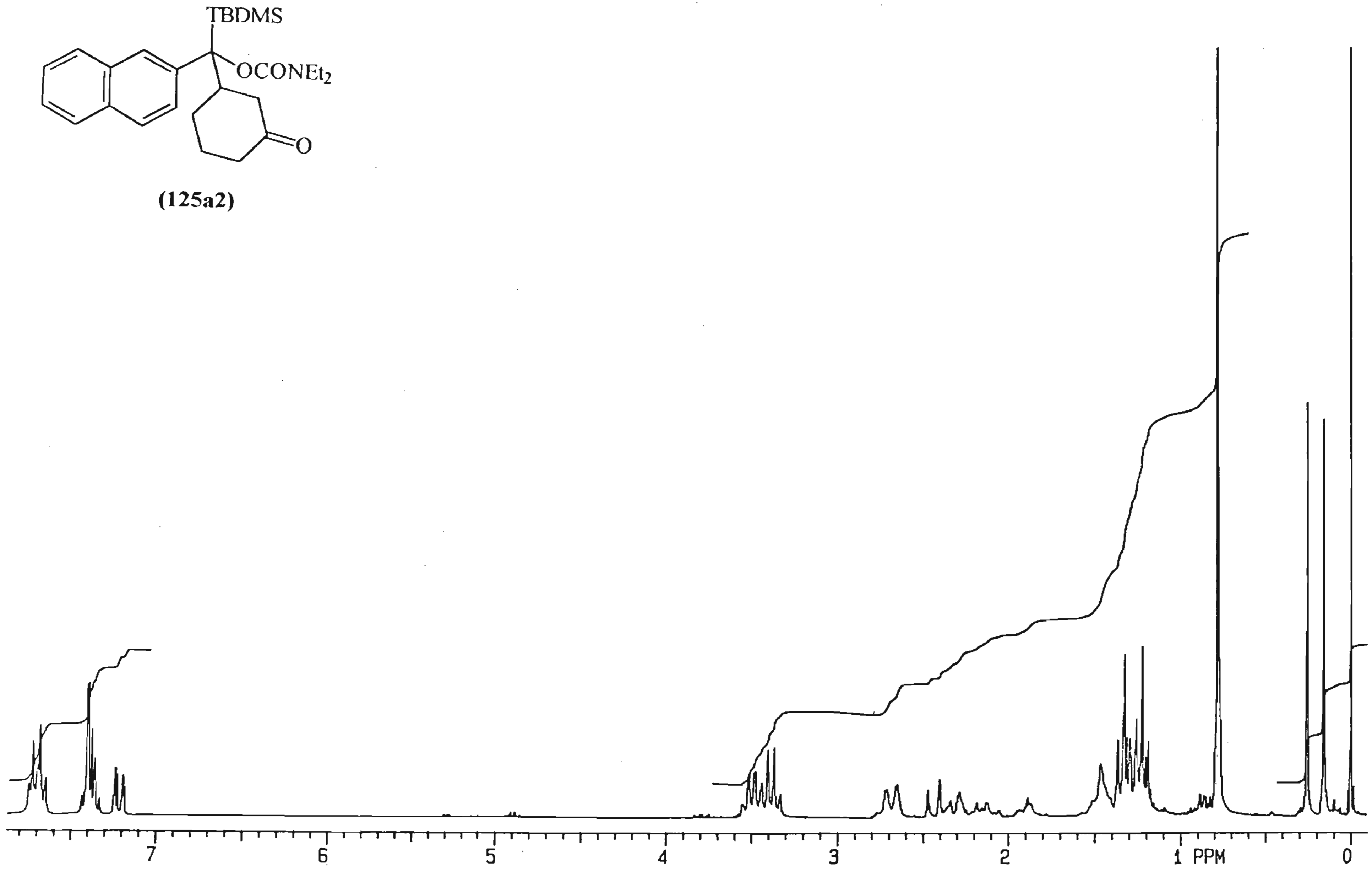

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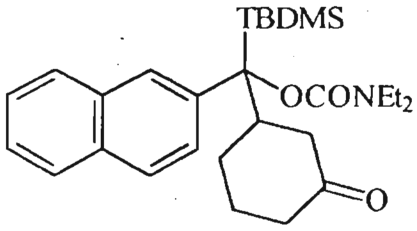

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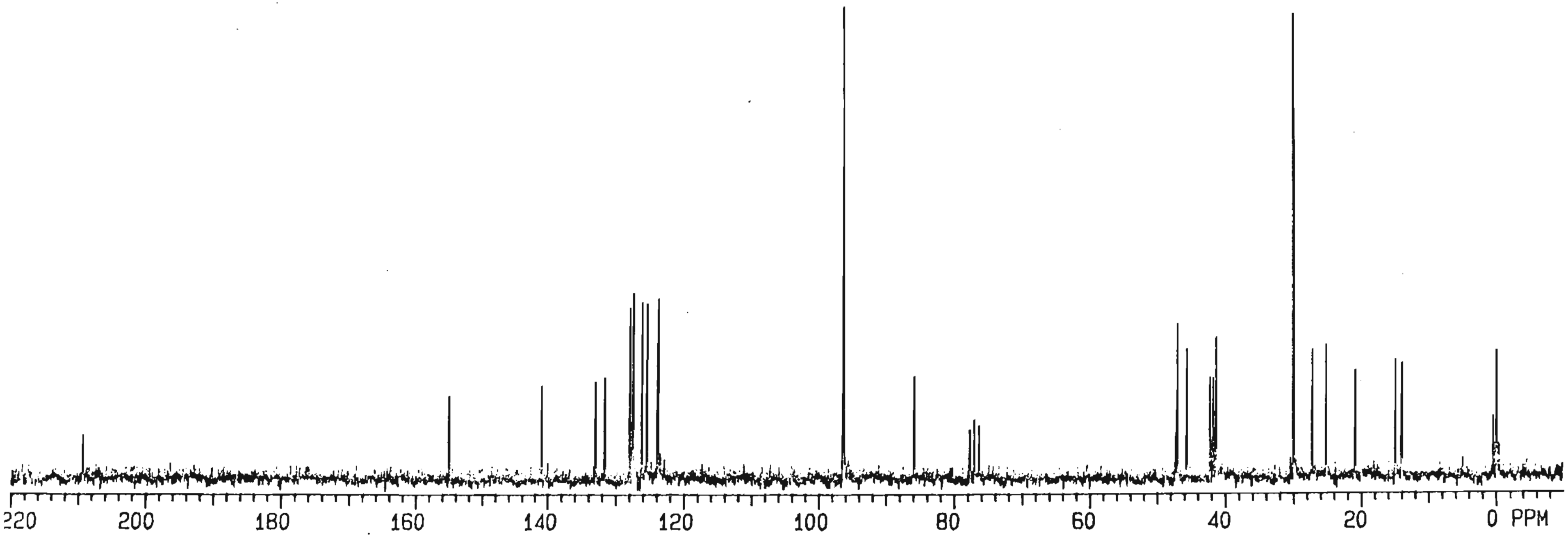

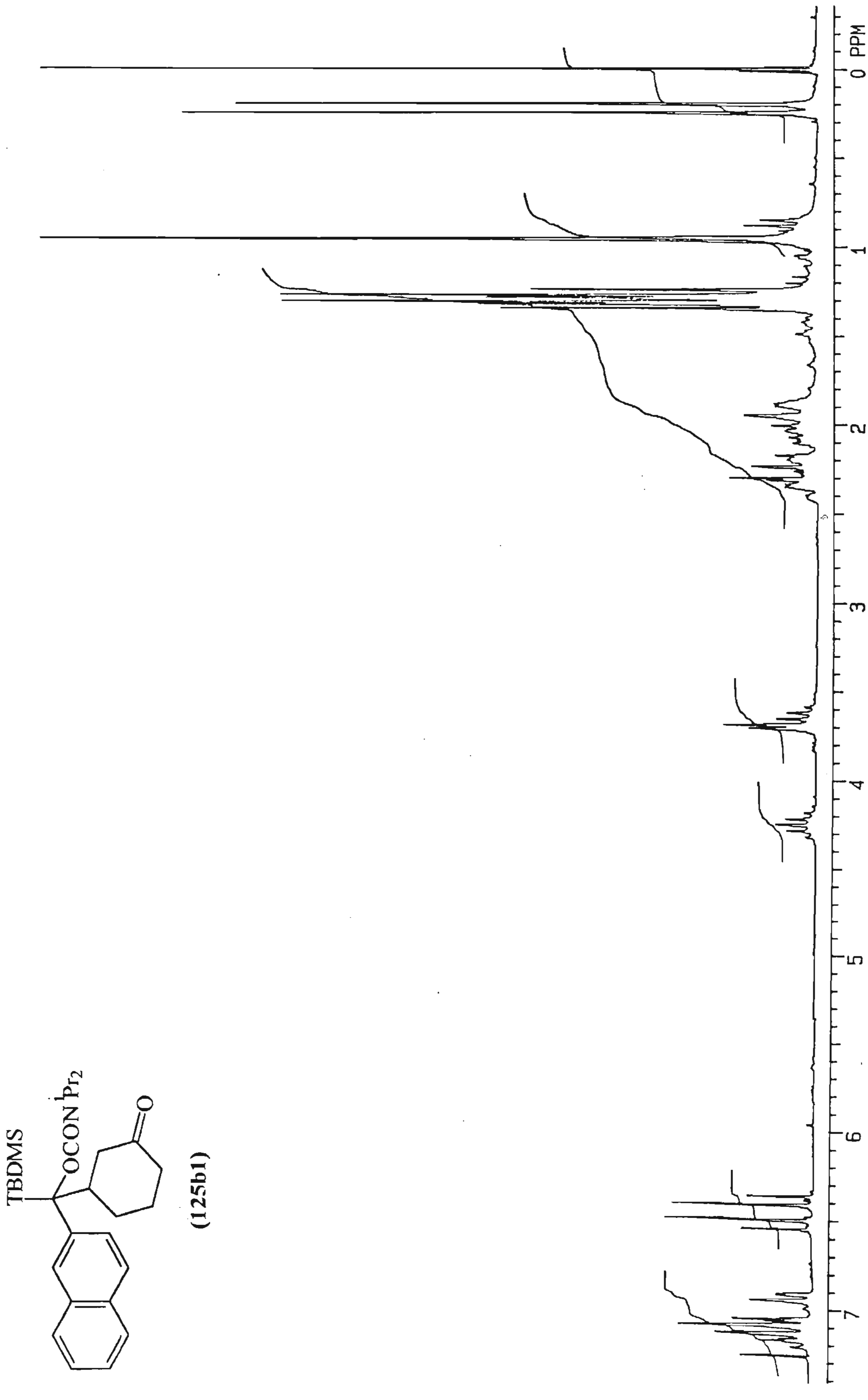

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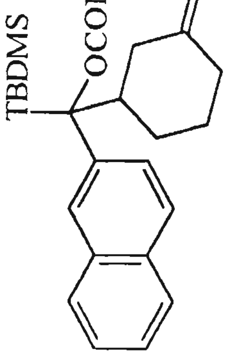

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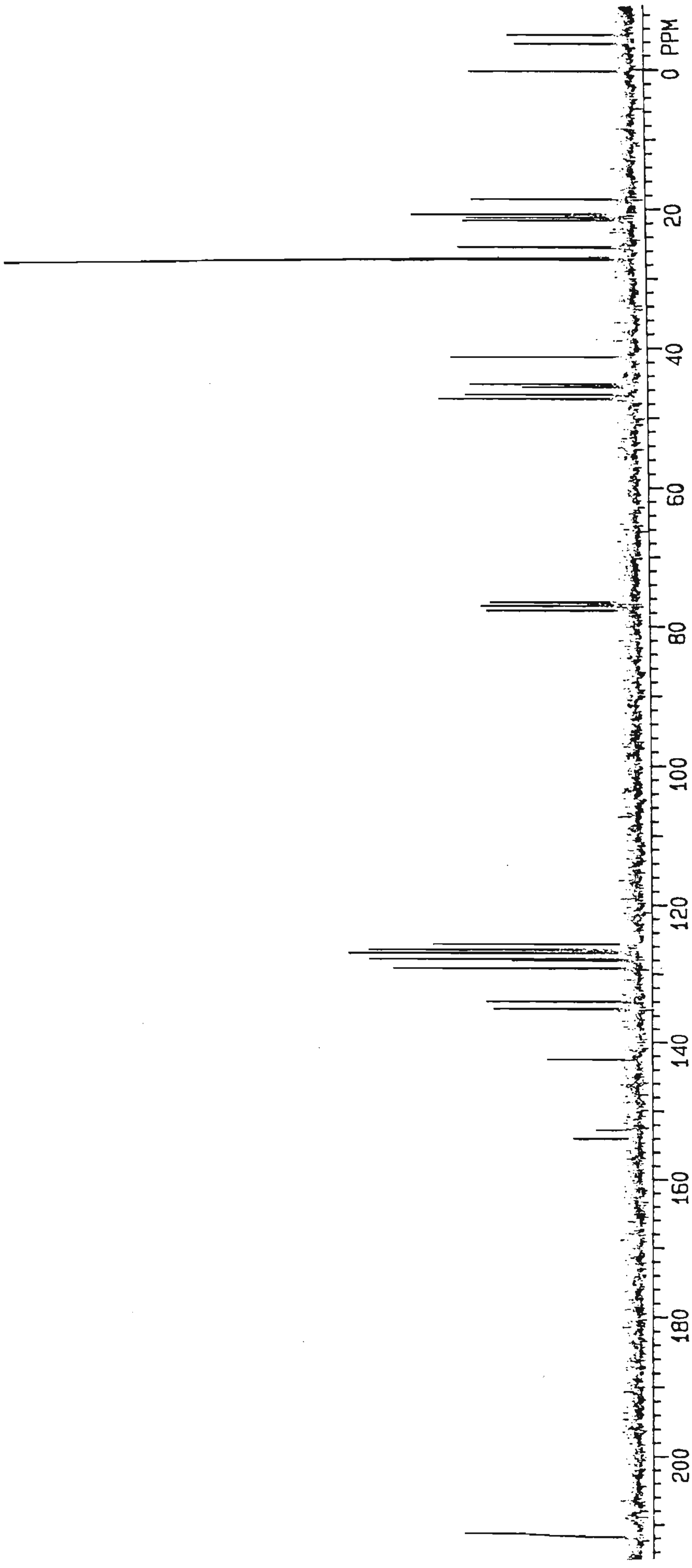

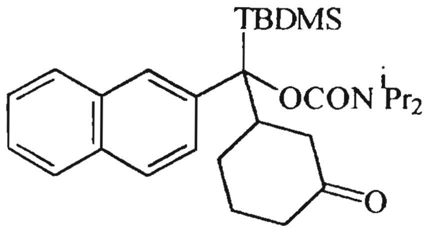

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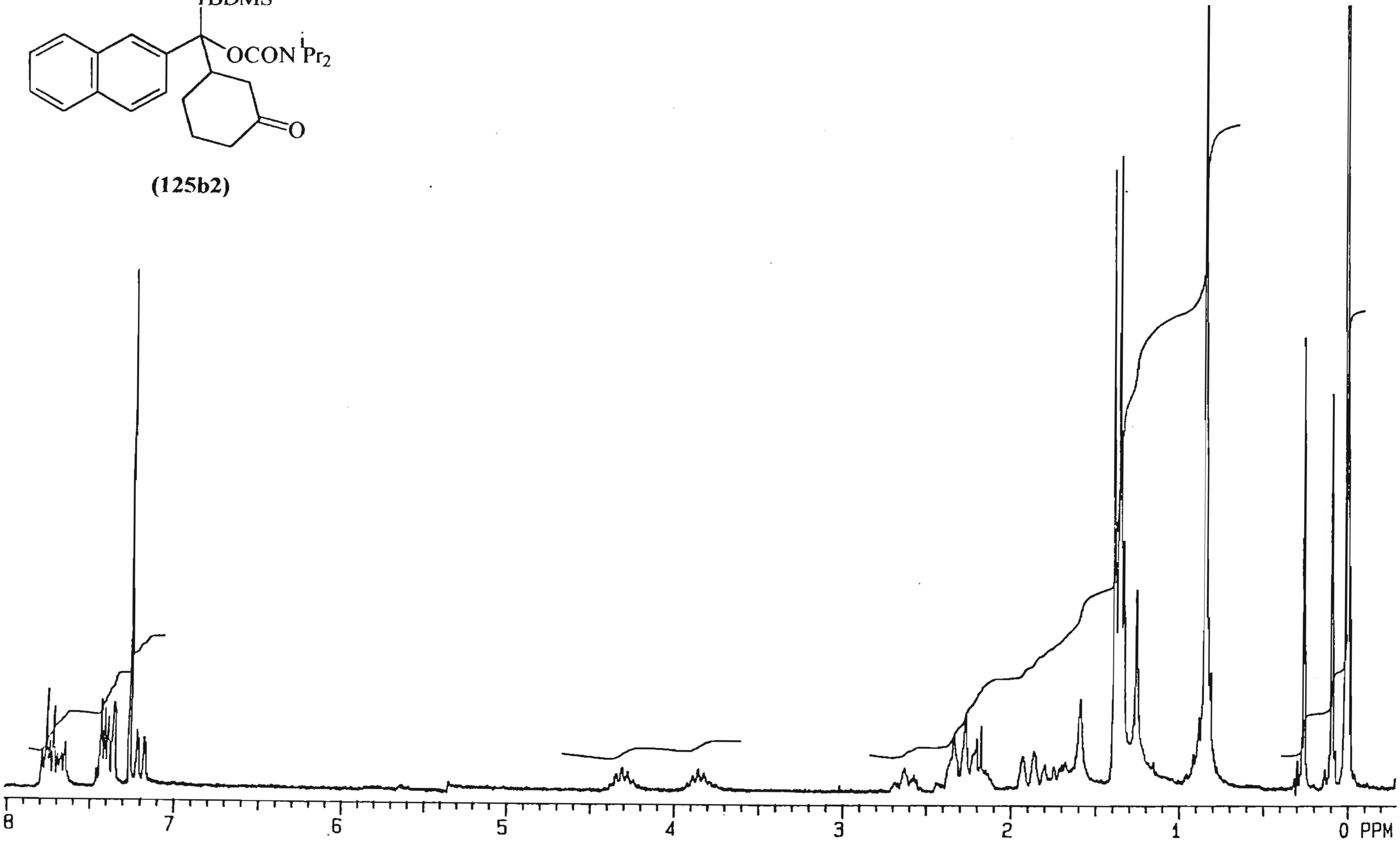

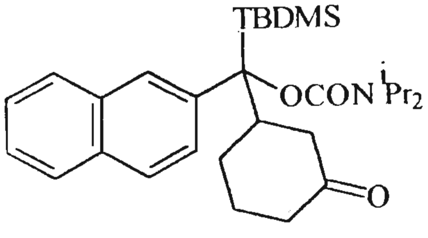

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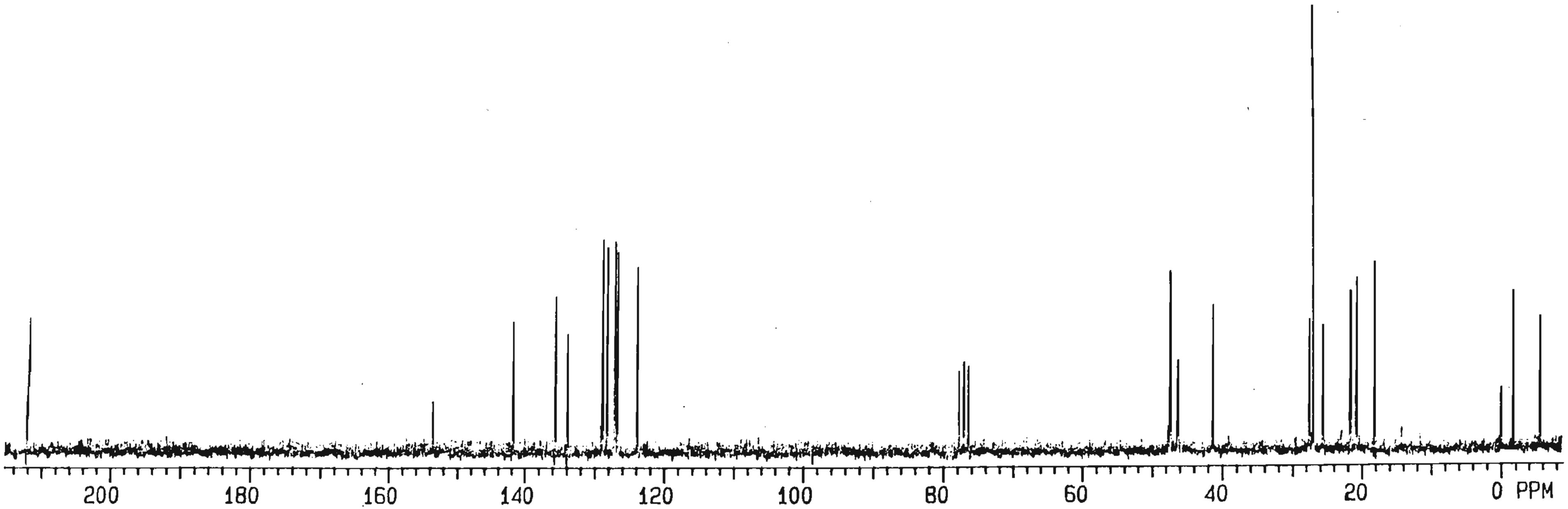

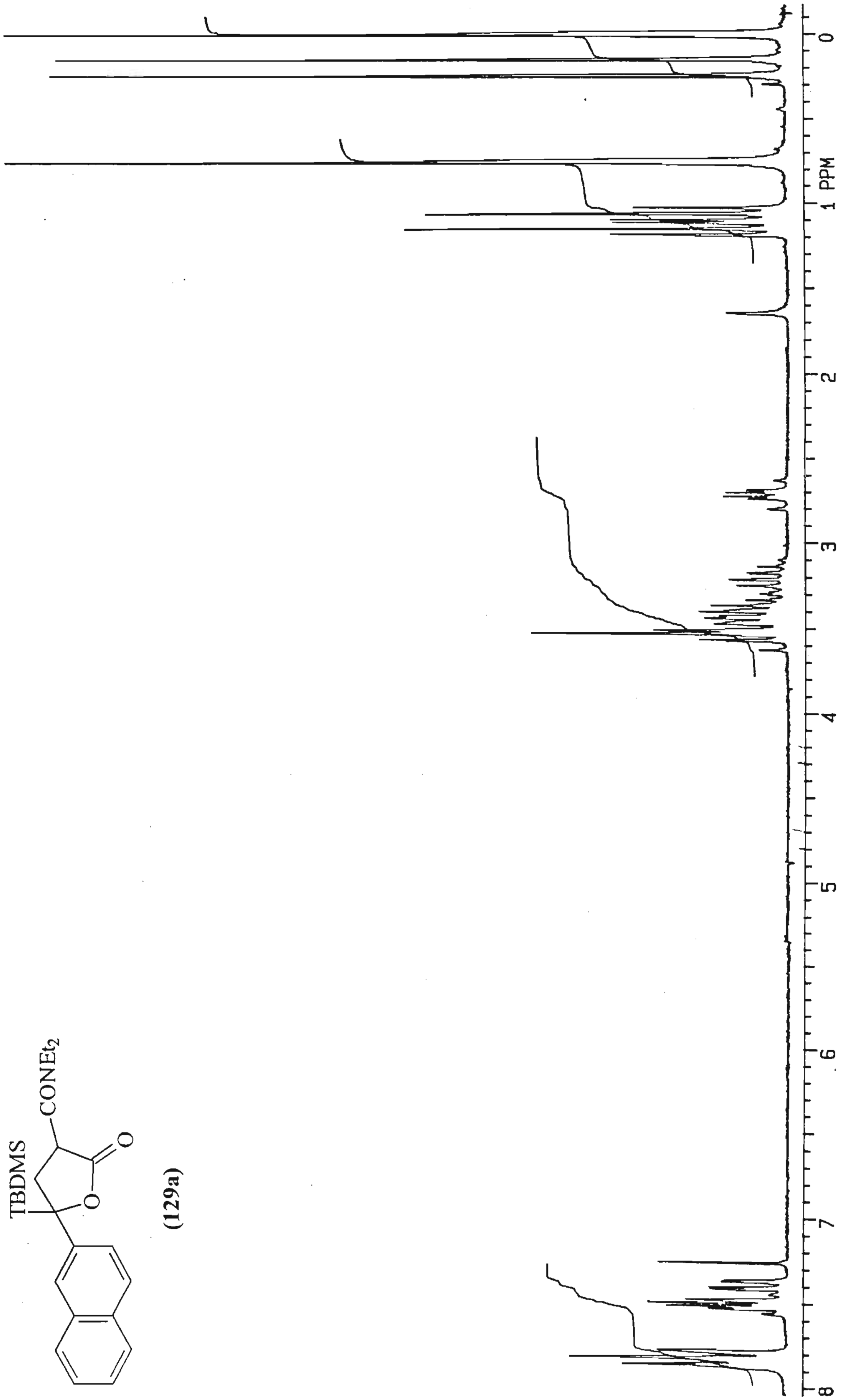

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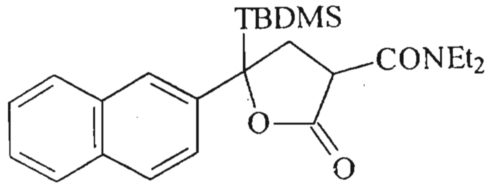

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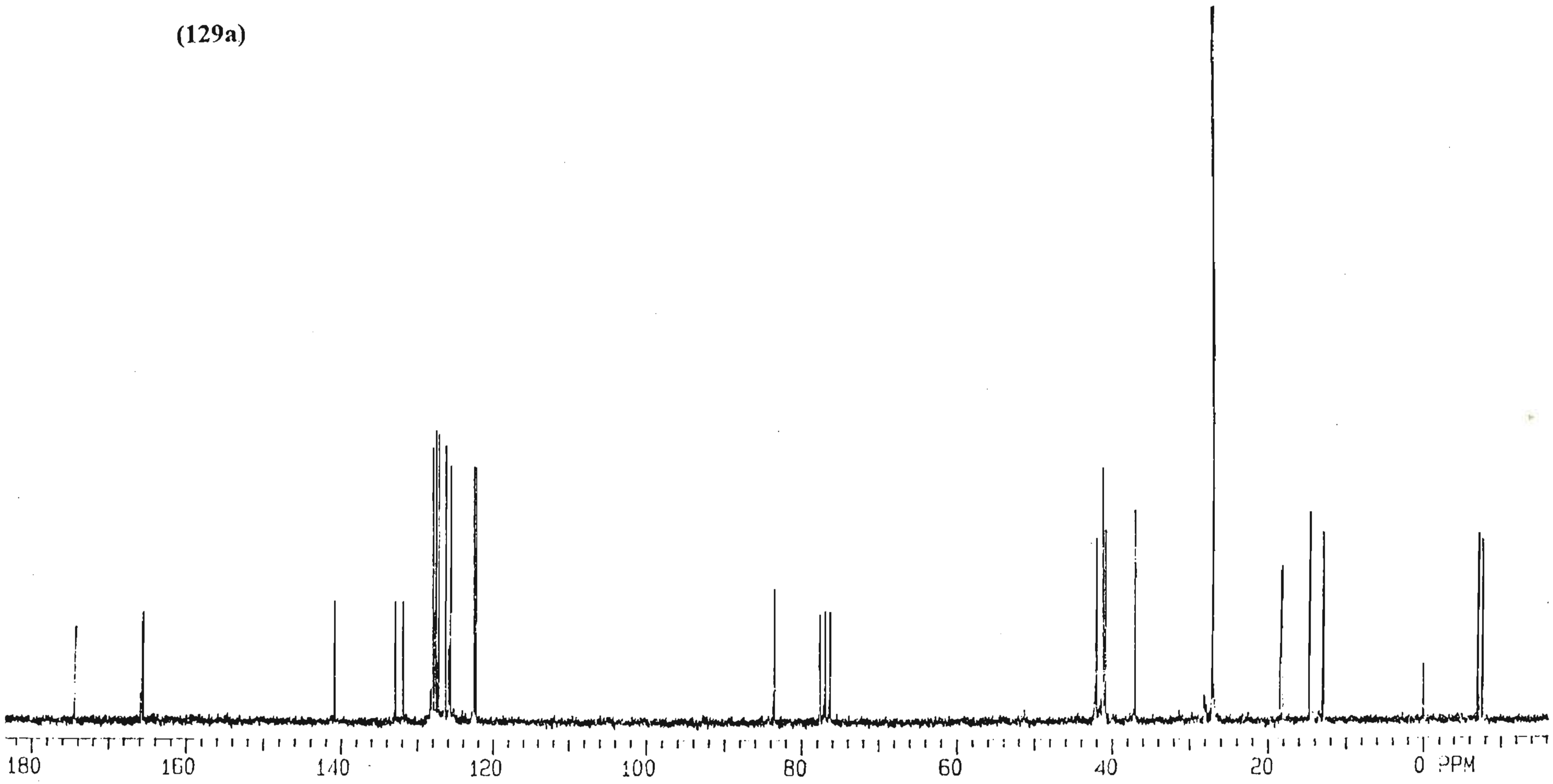

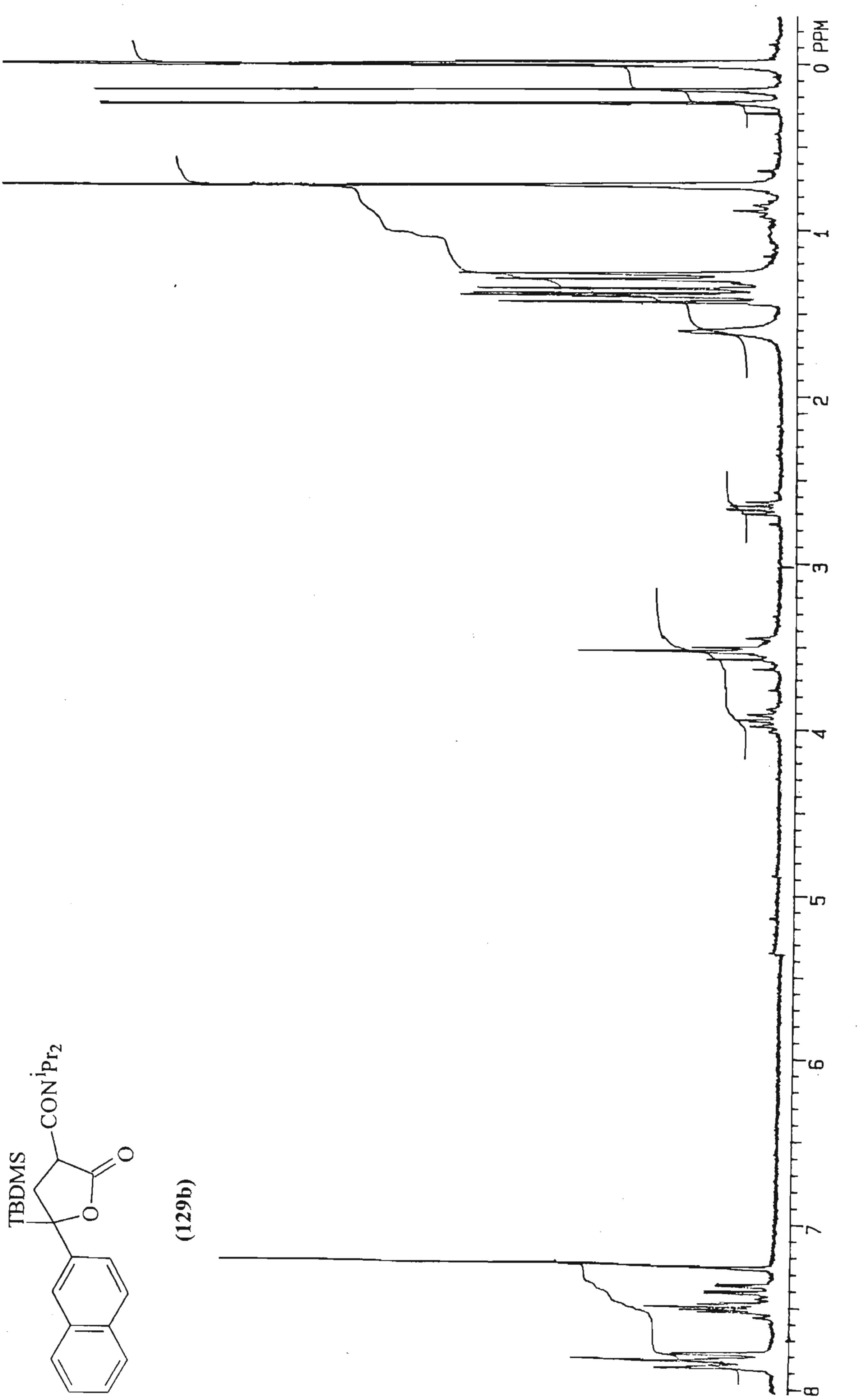

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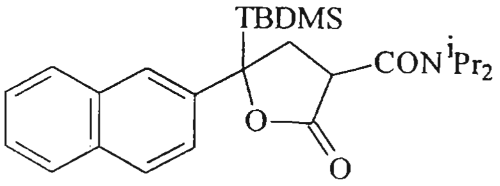

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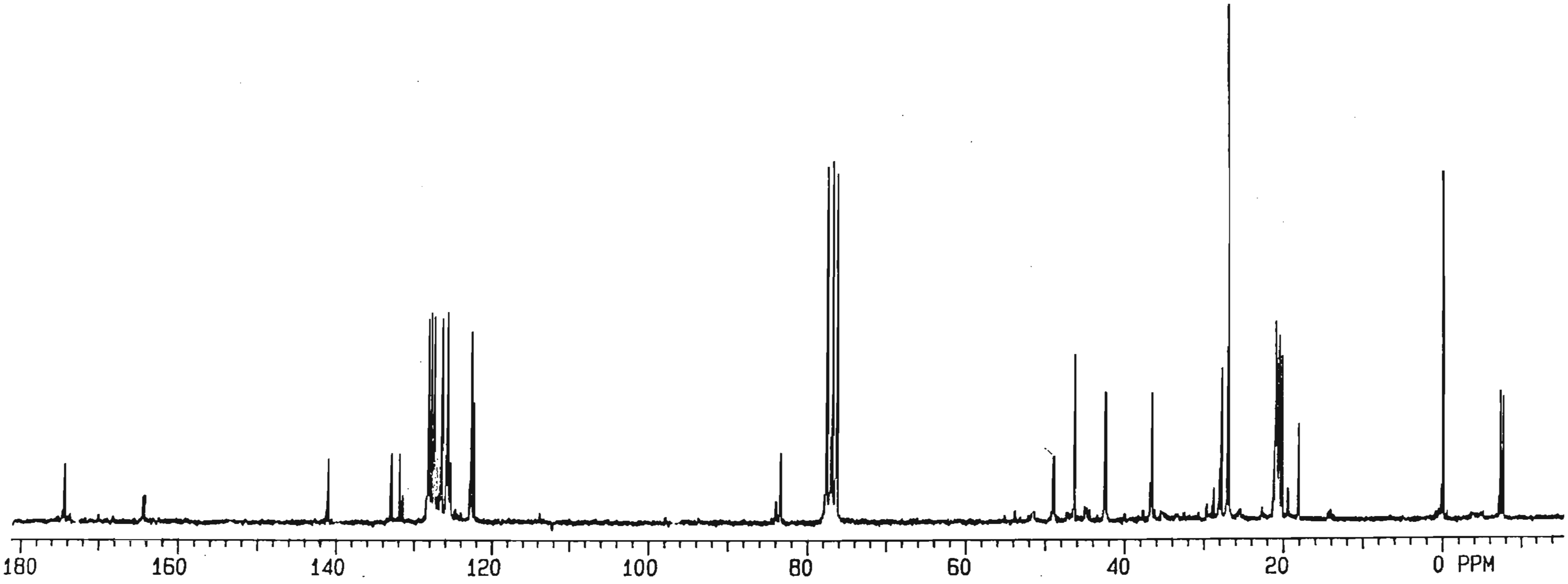

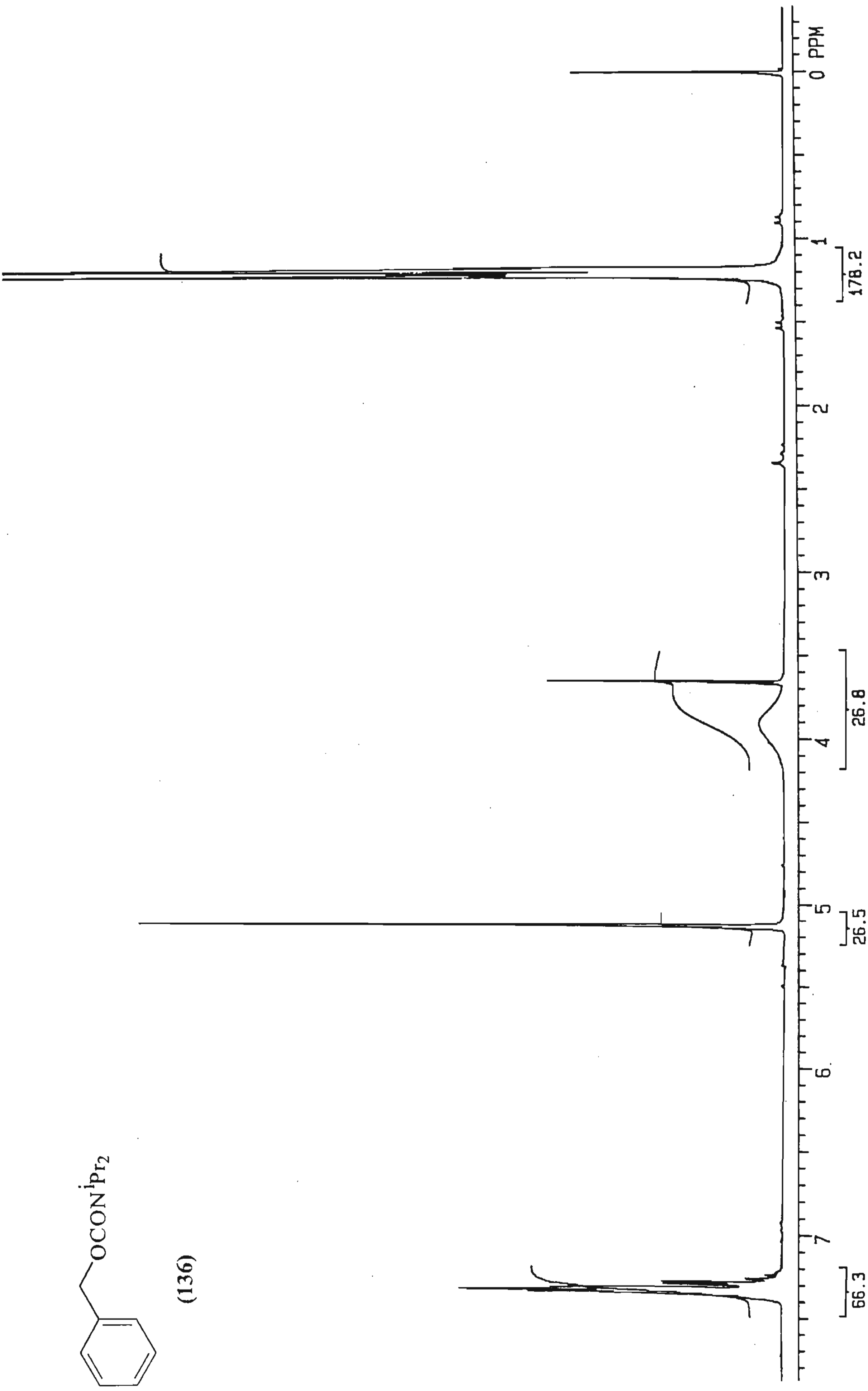

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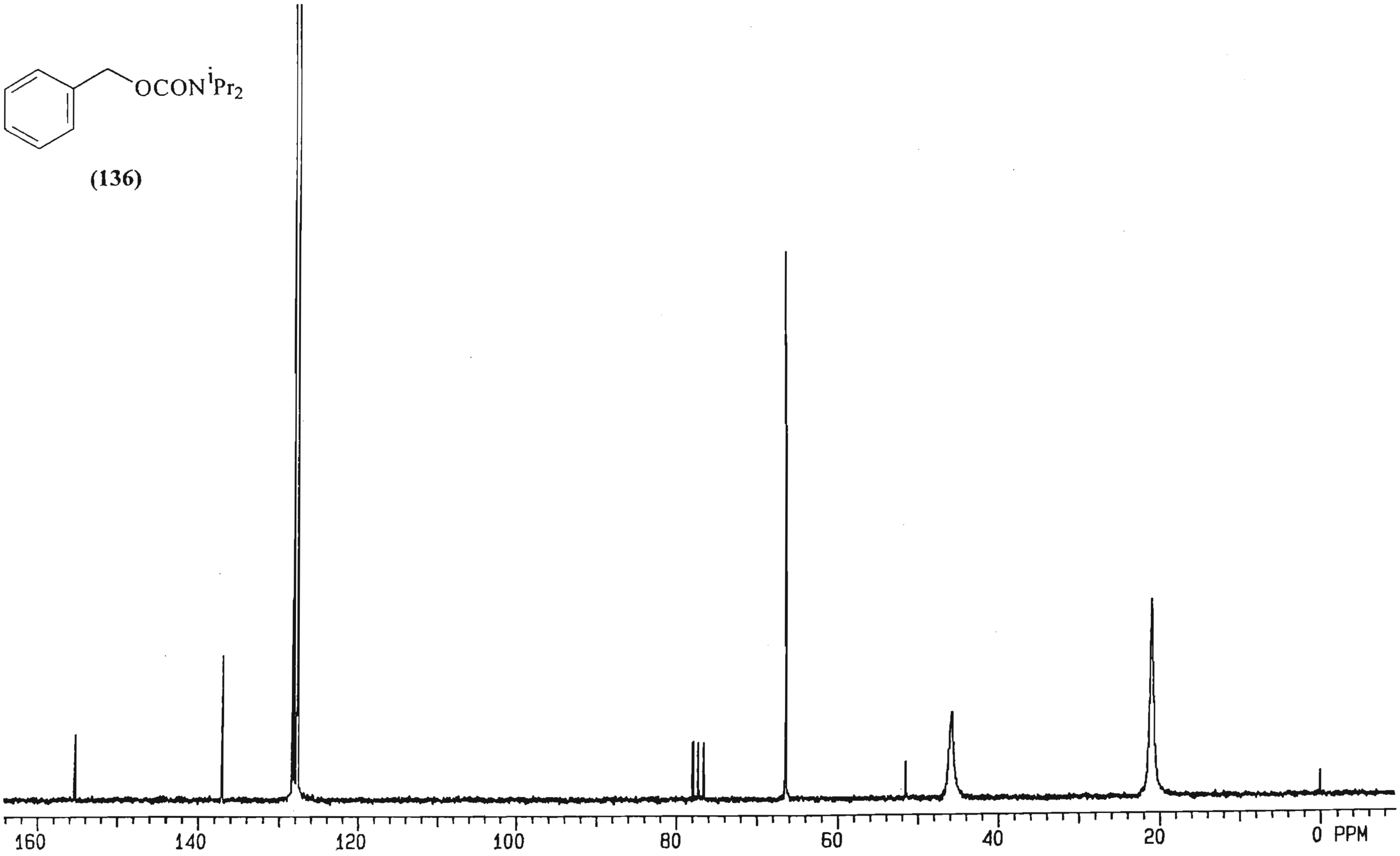

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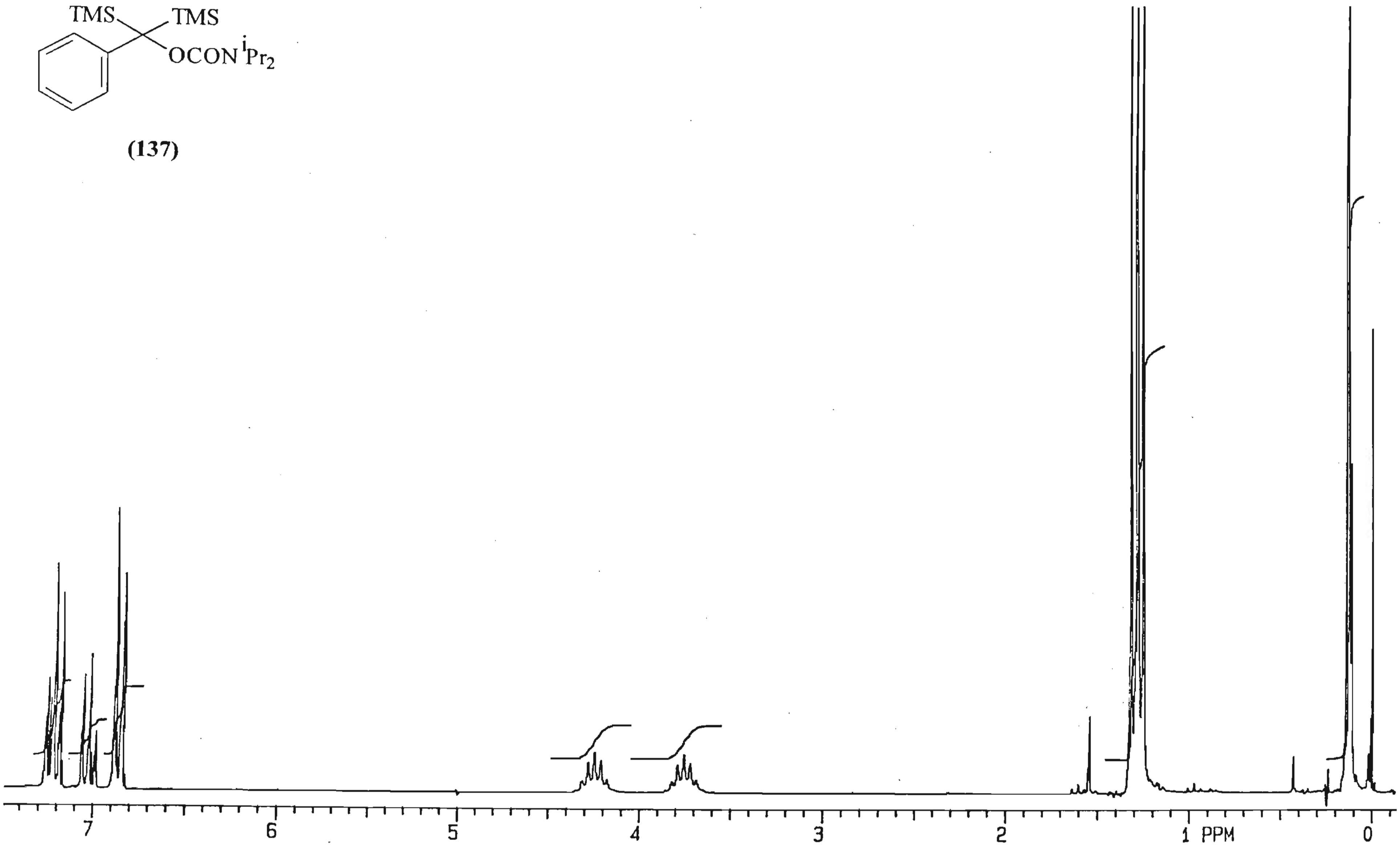

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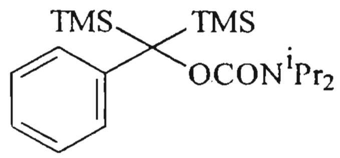

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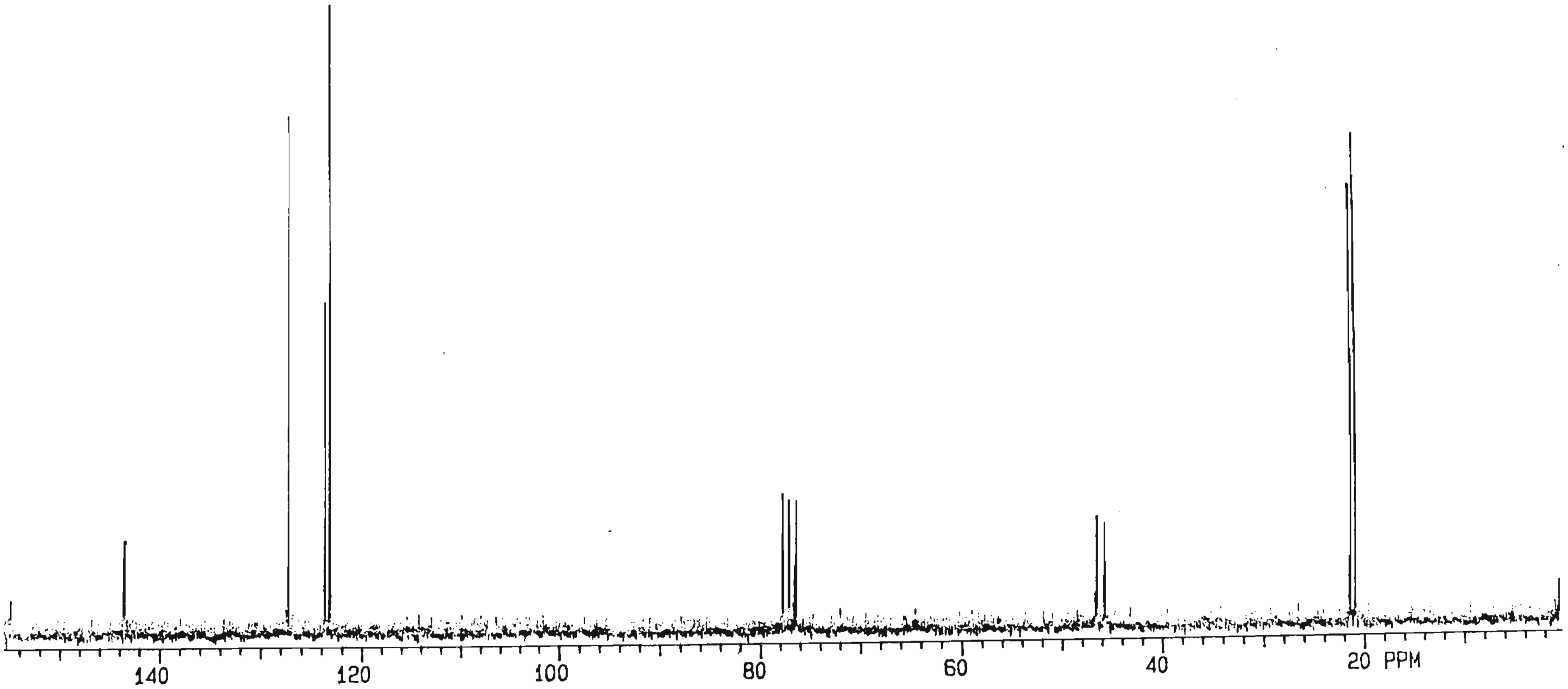

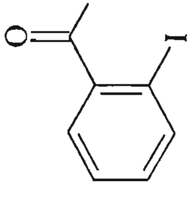

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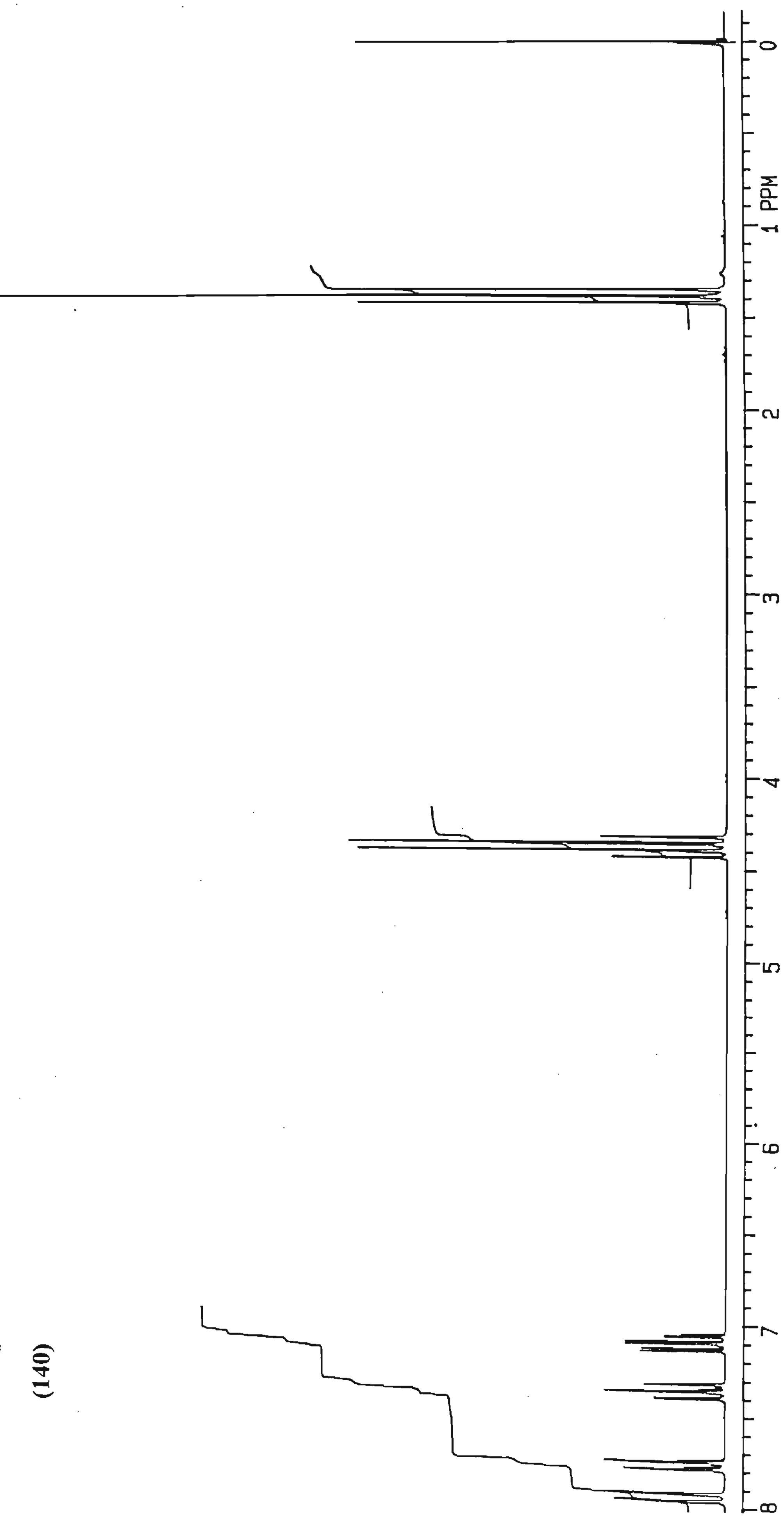

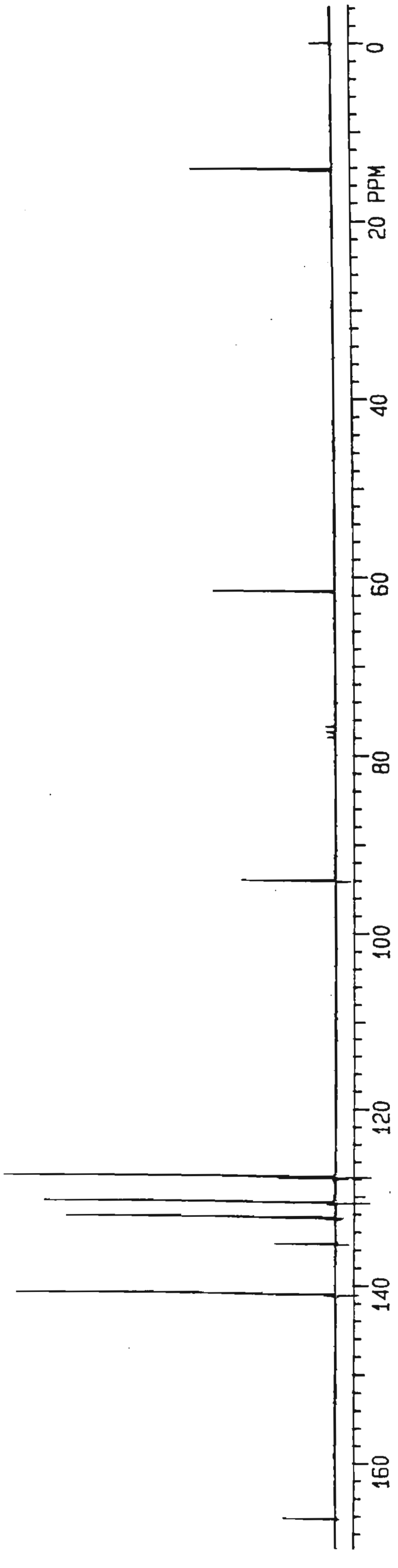

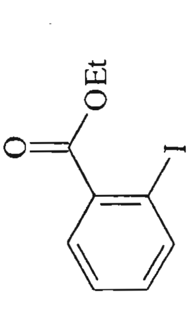

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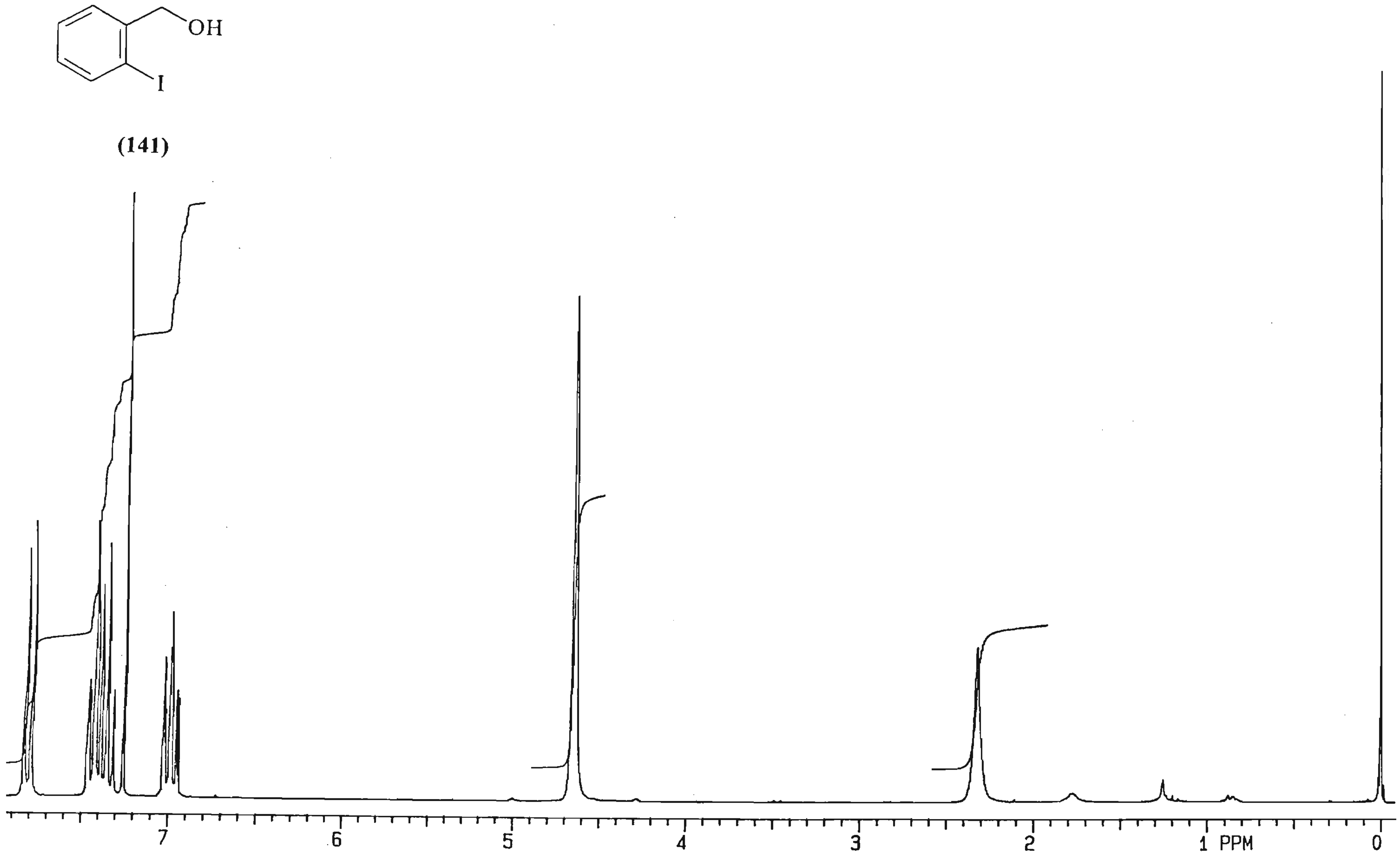

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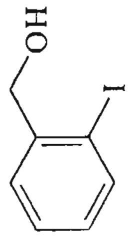

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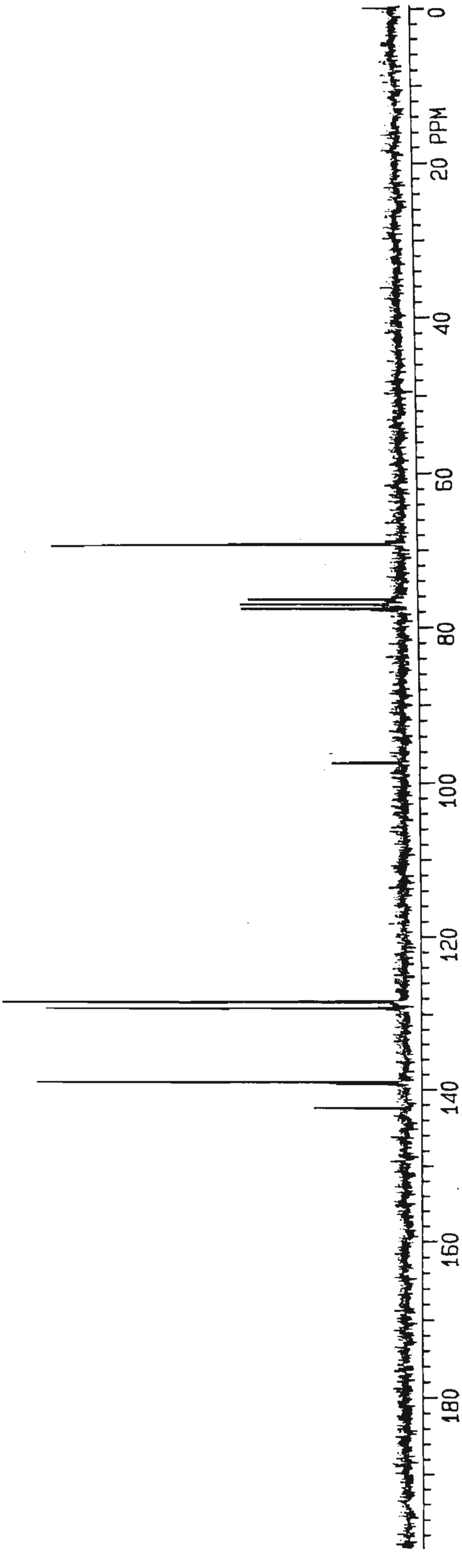

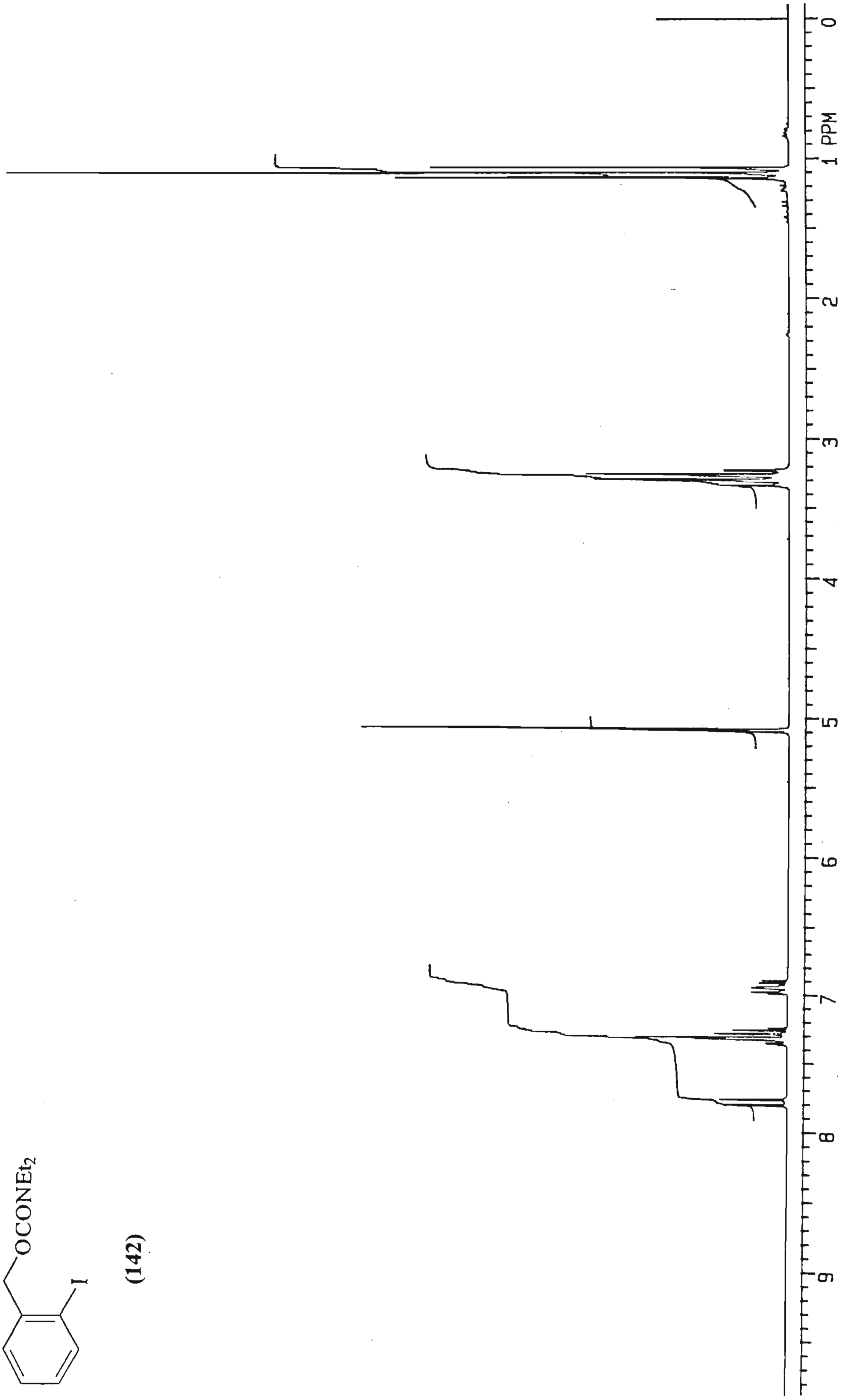

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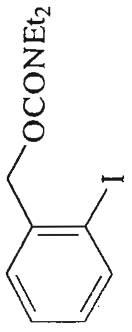

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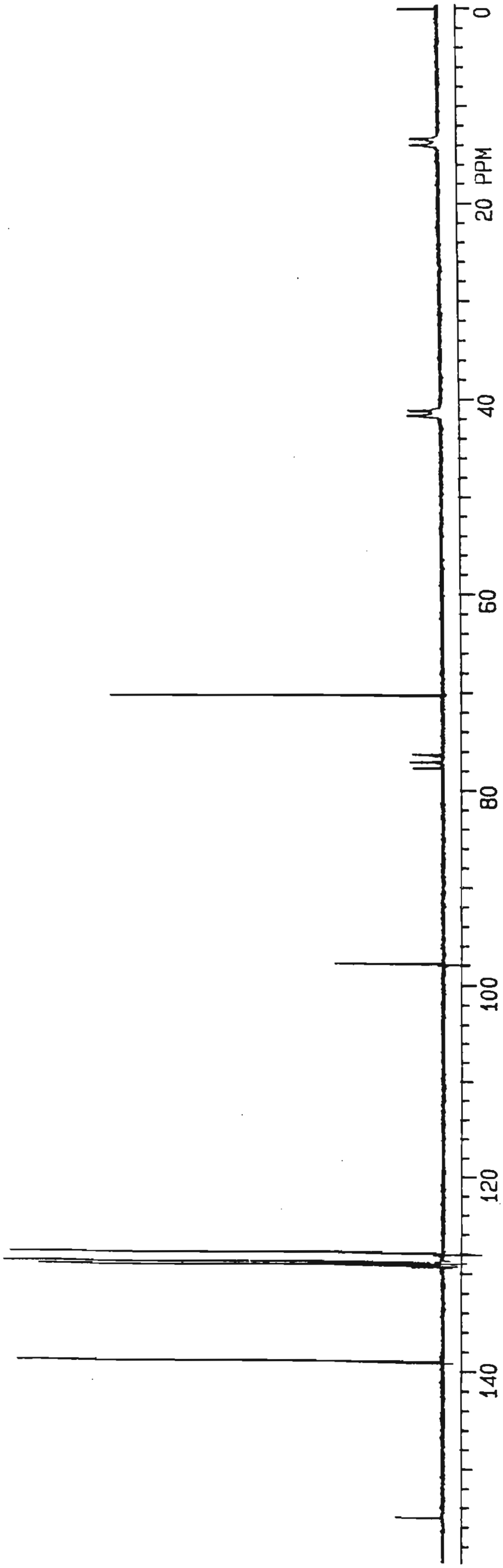

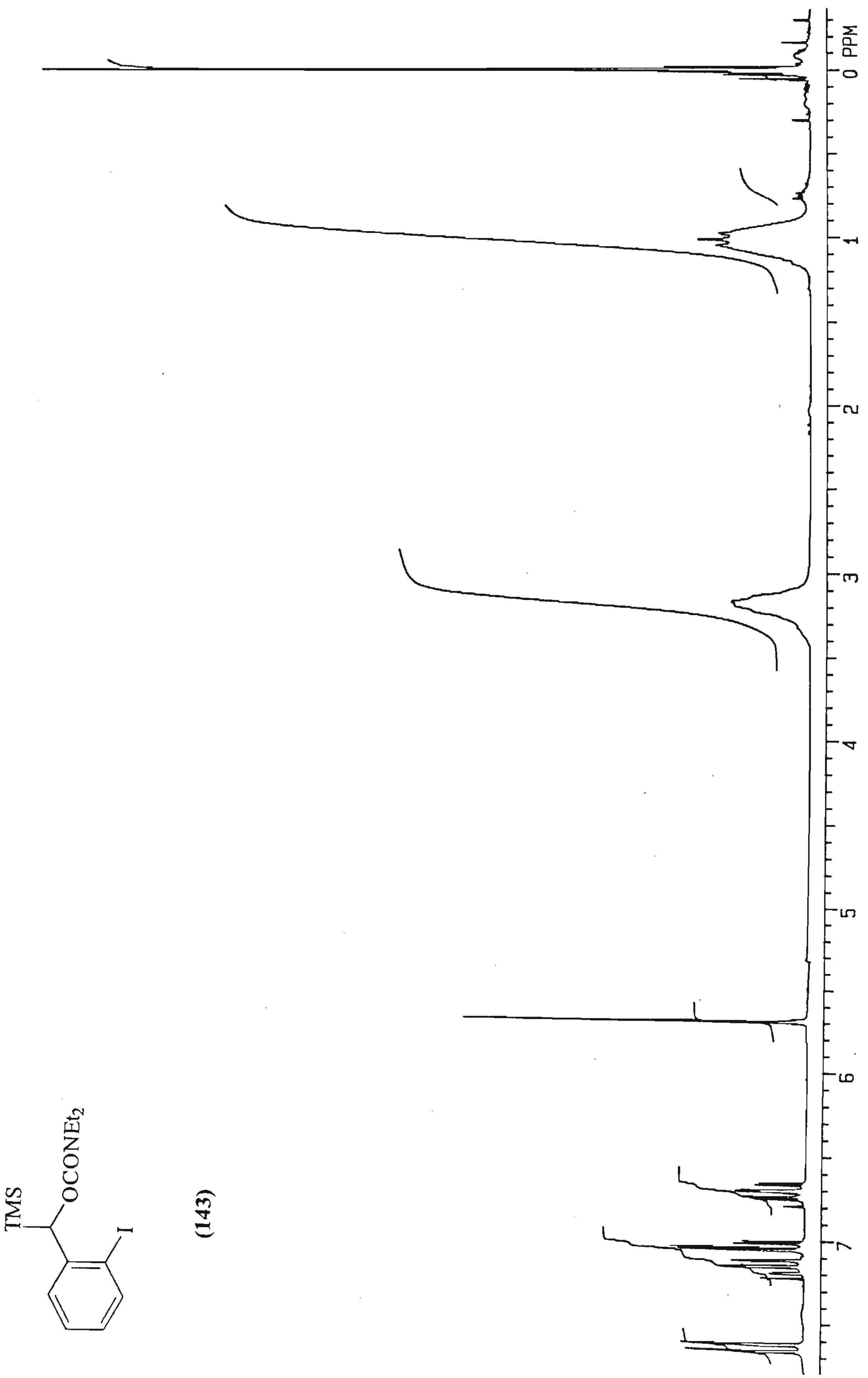

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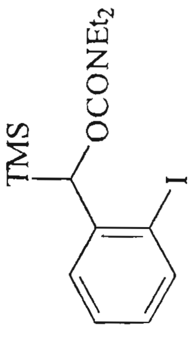

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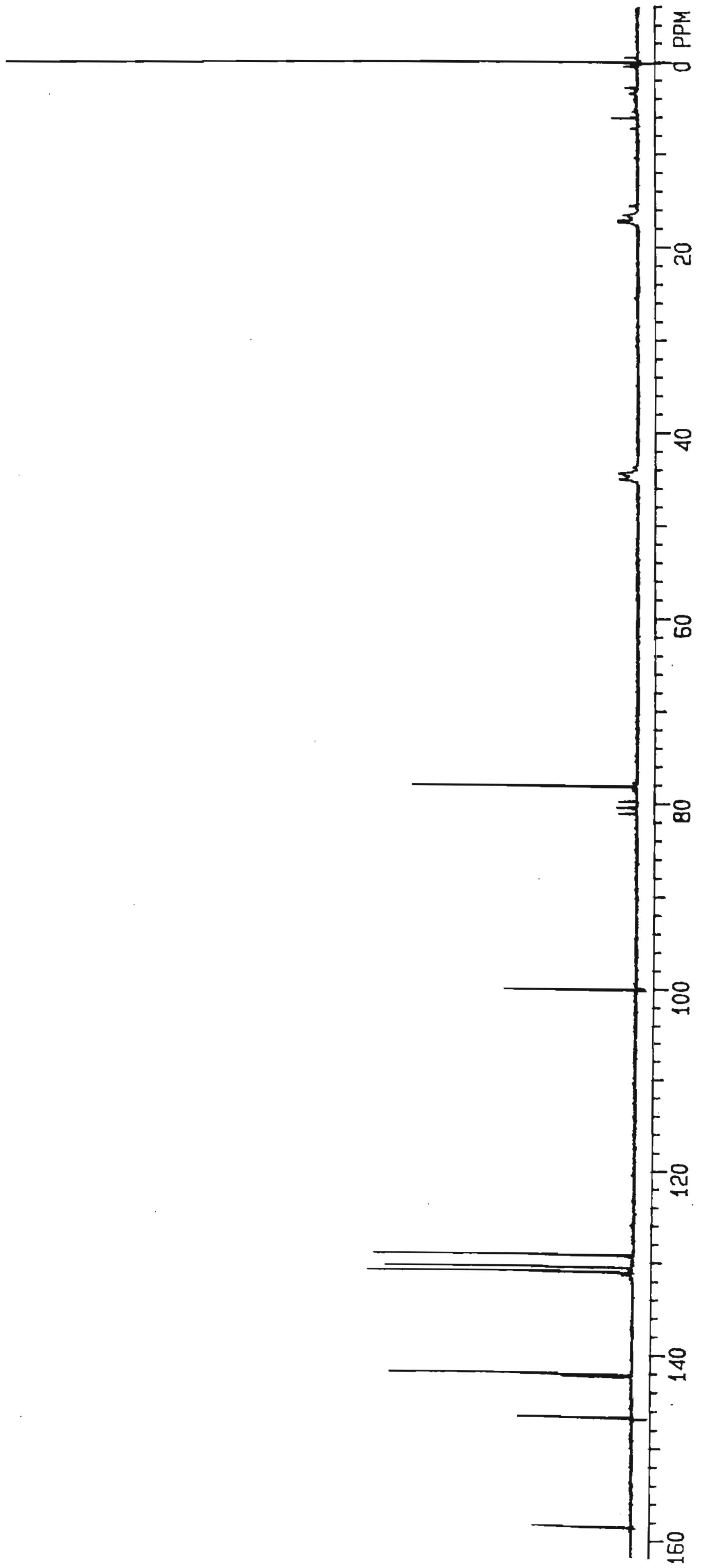

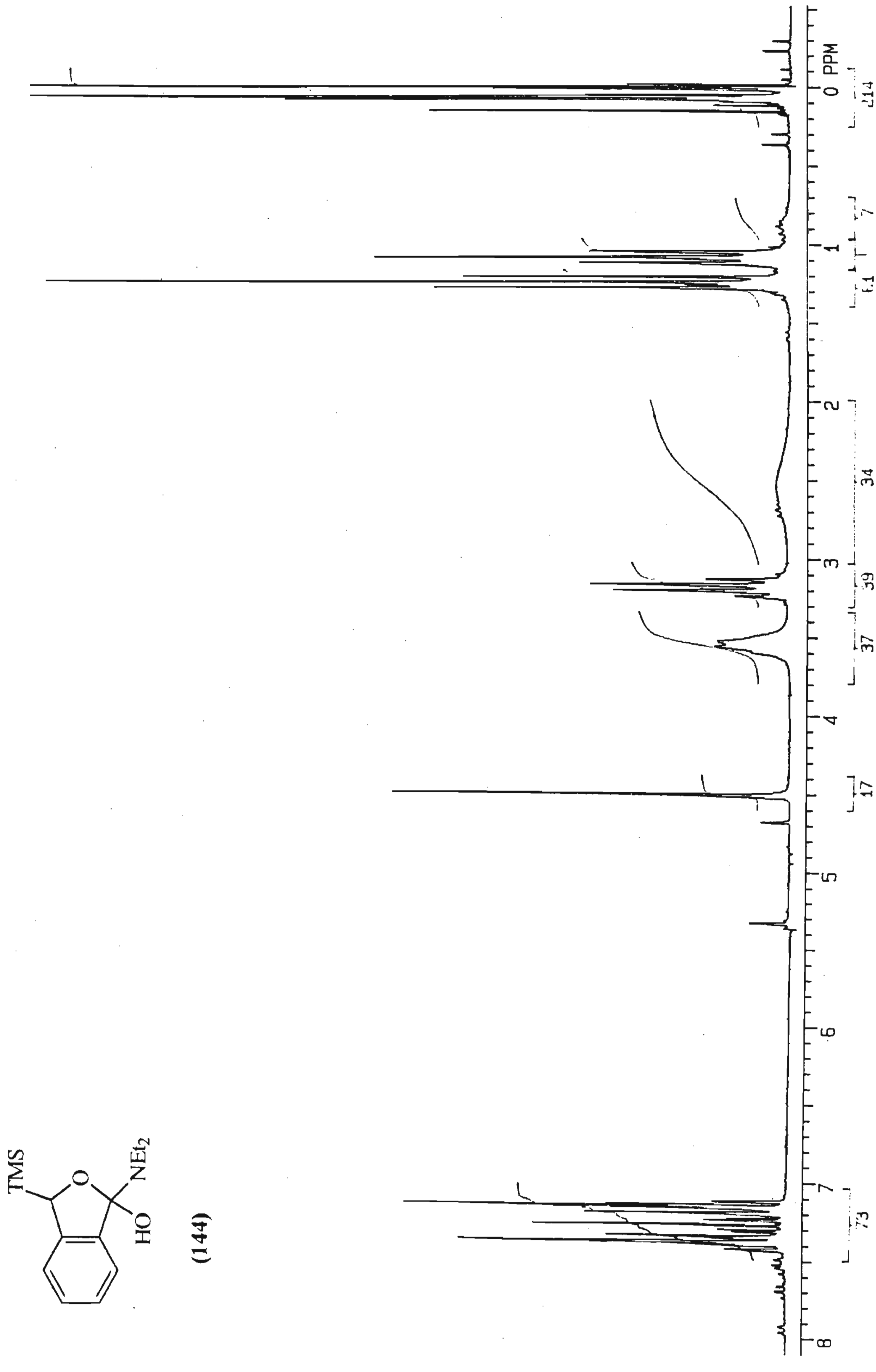

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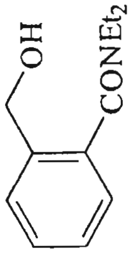

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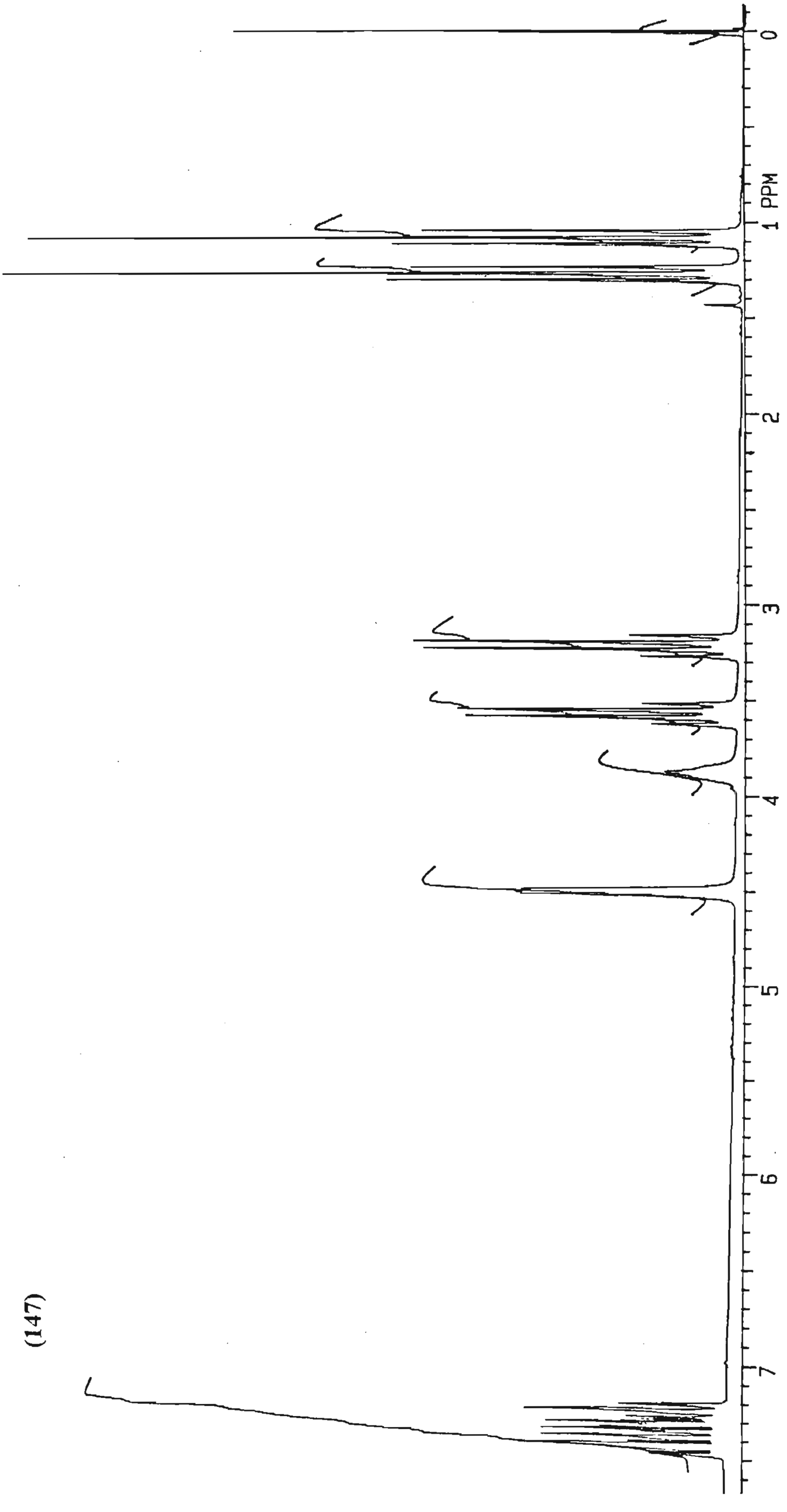

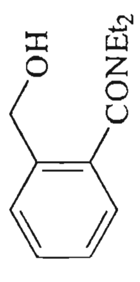

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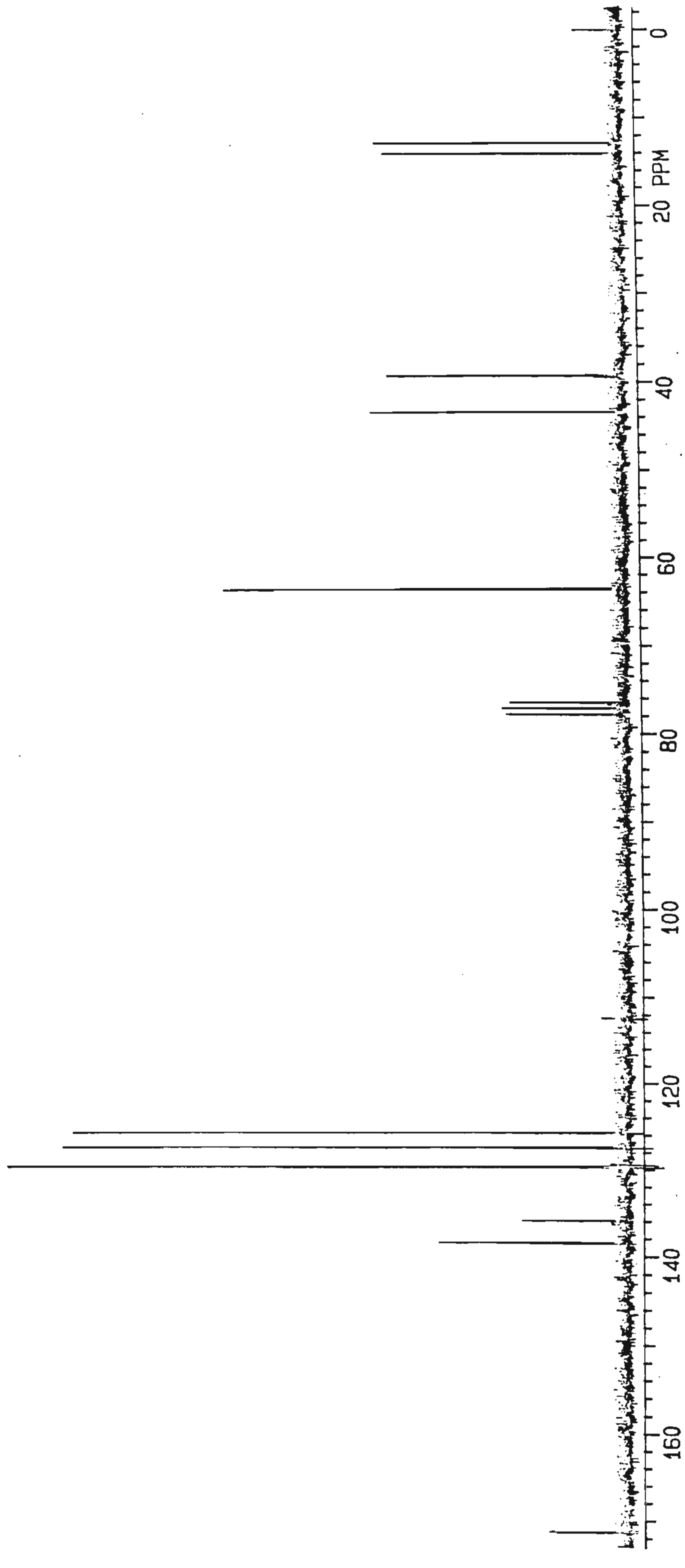

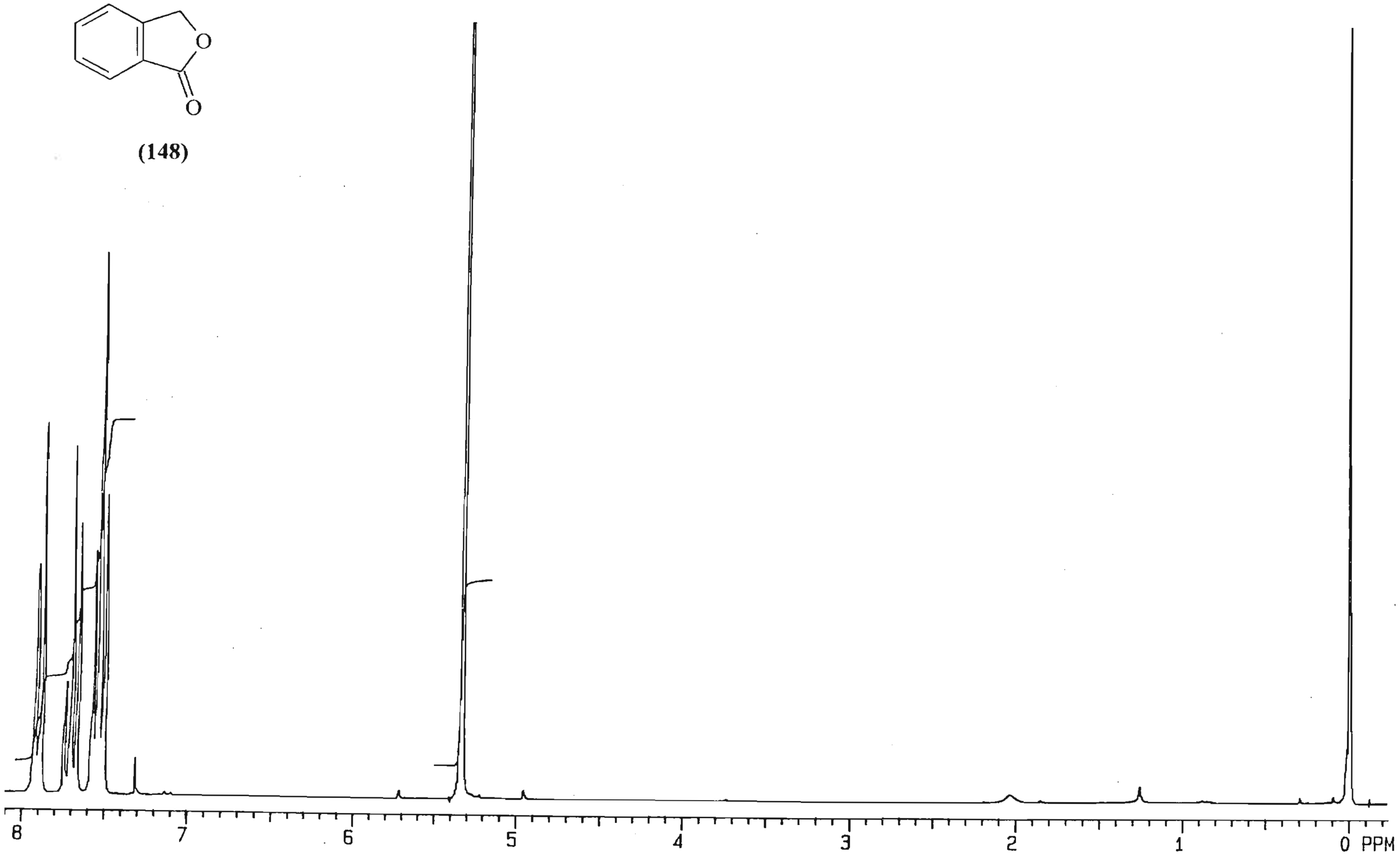
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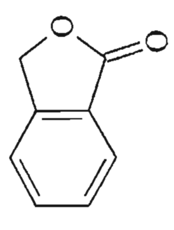

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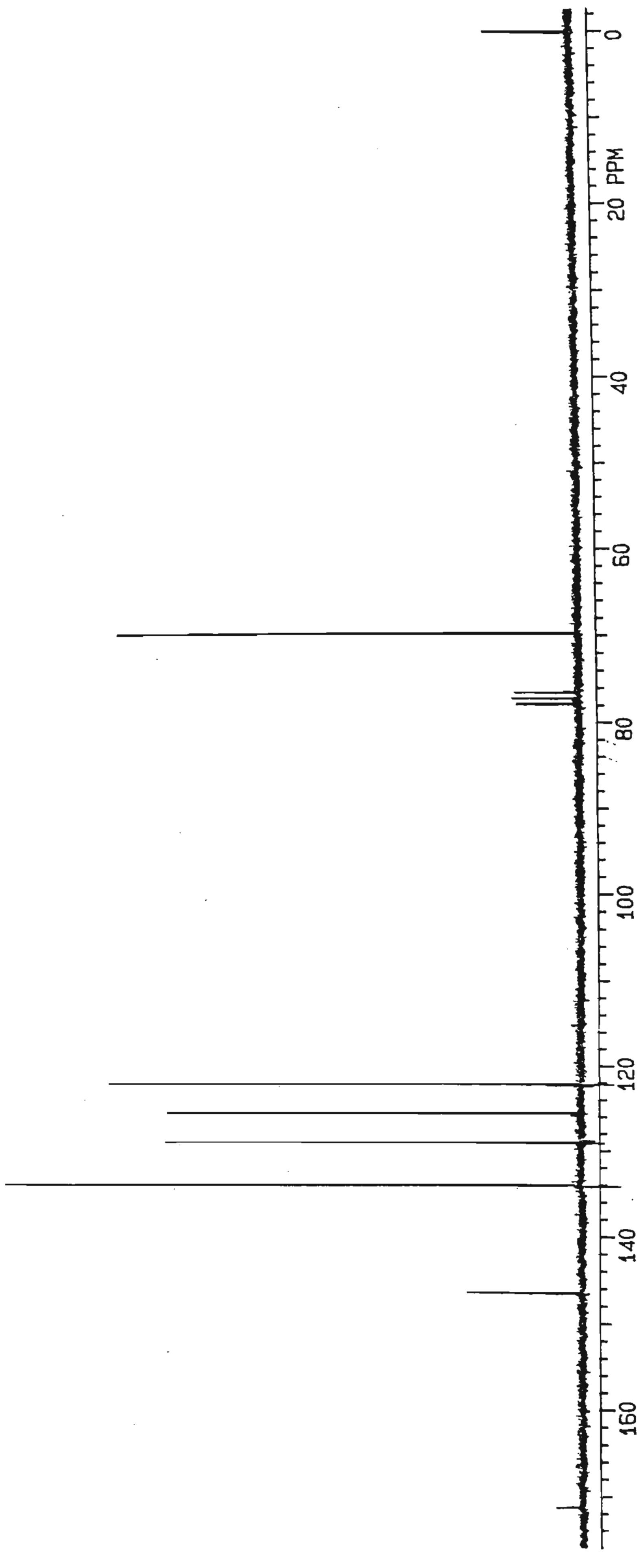

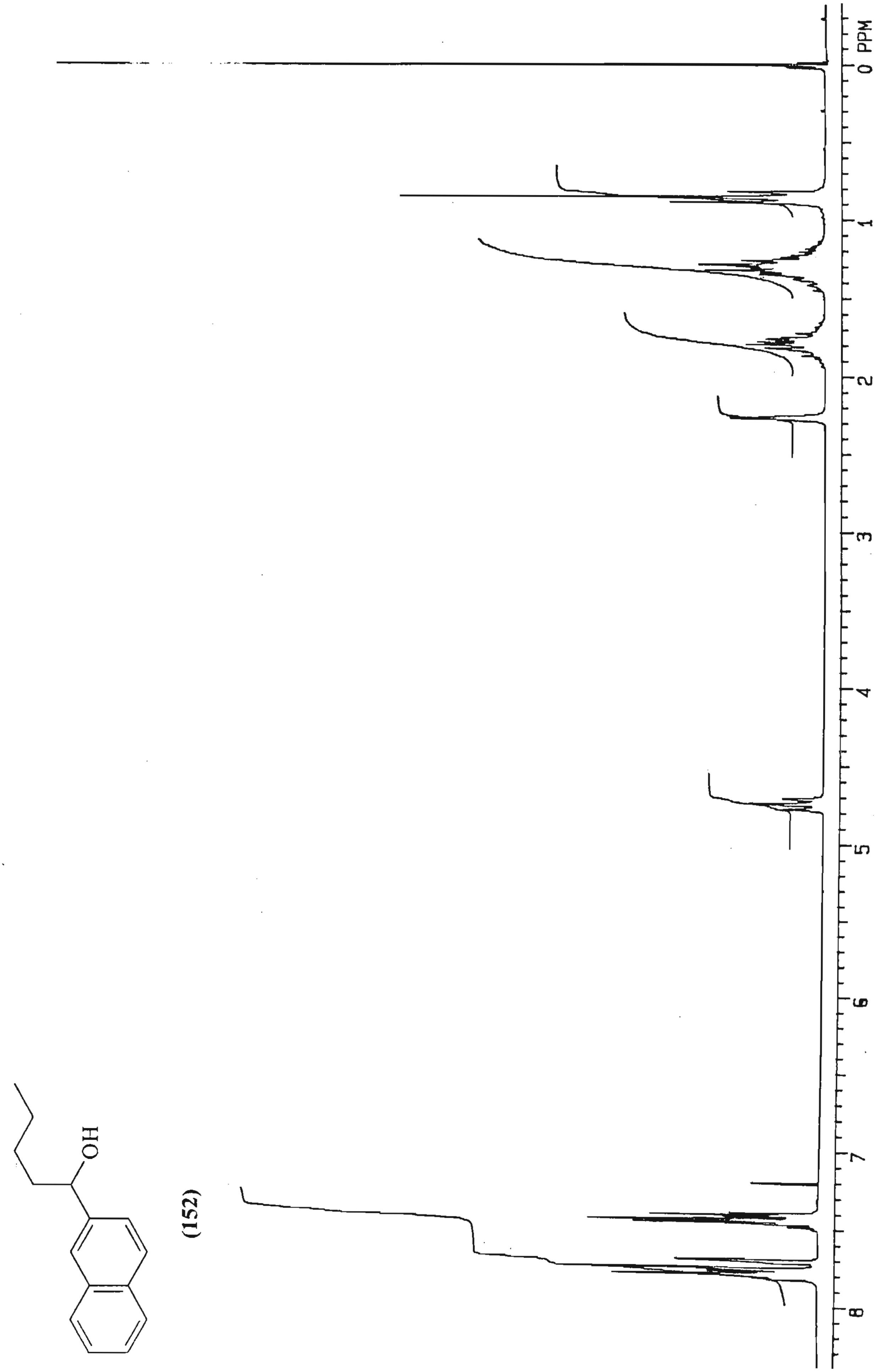

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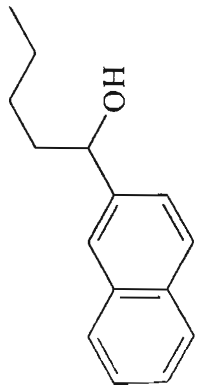

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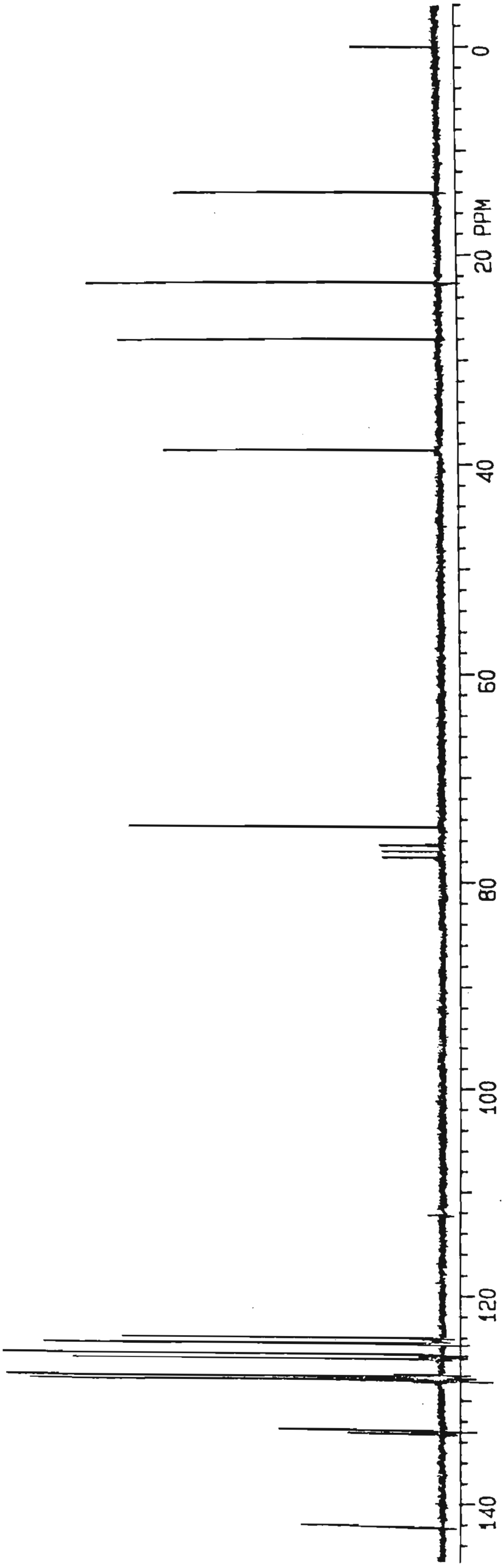

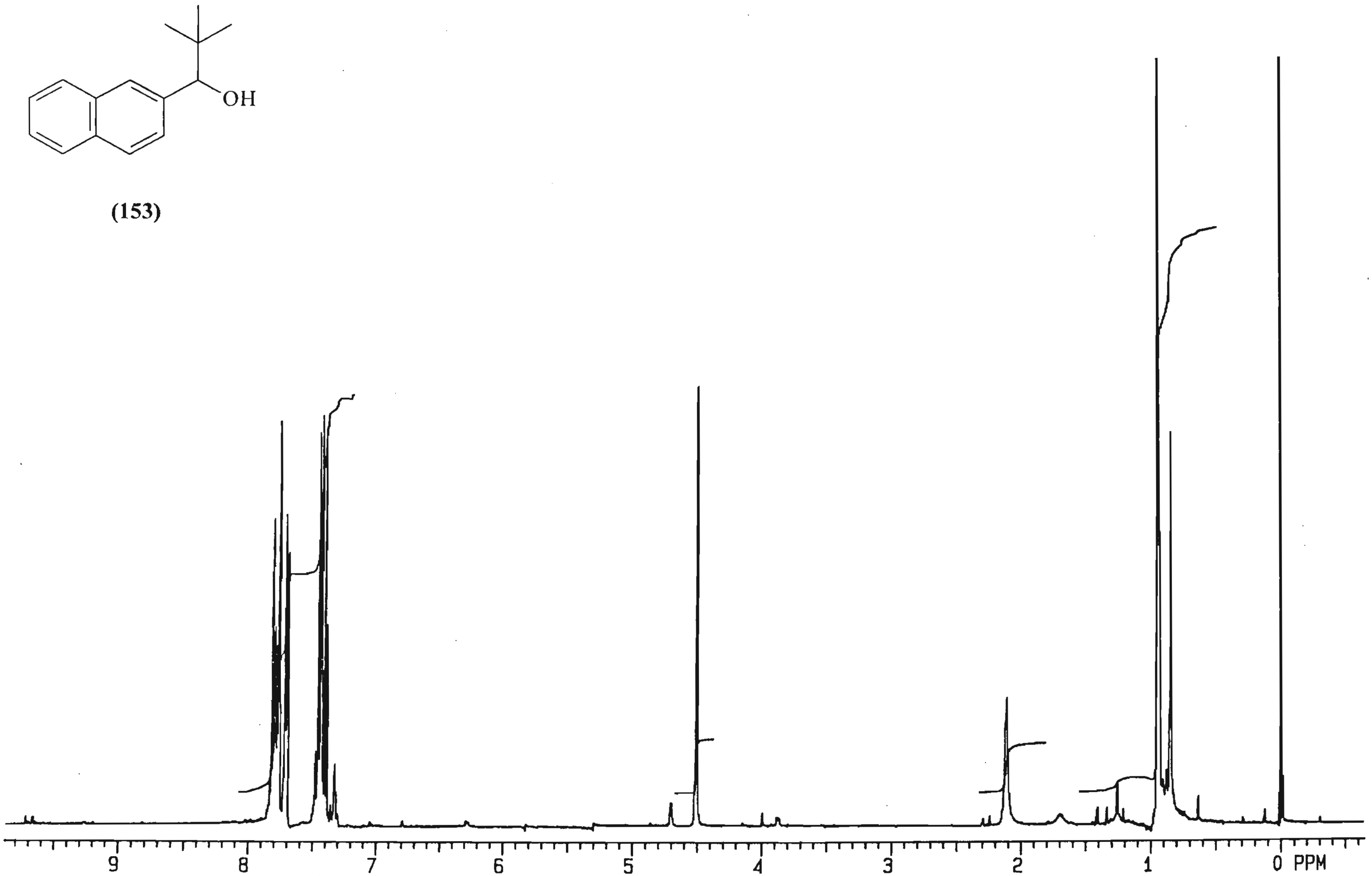

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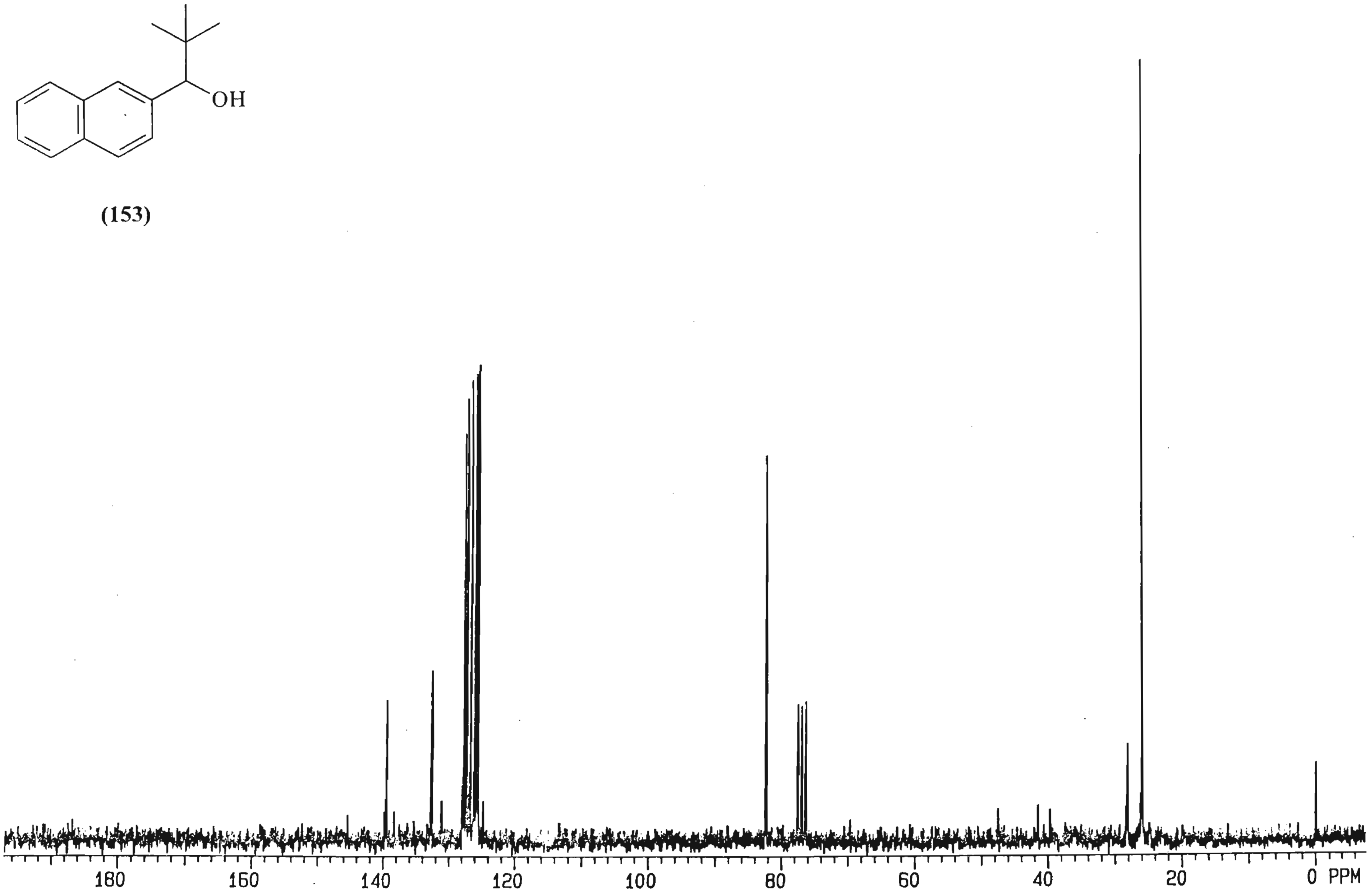

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