Heteroannulations mediated by titanium imido complexes : methods development and applications to the total syntheses of (½)-monomorine I and (+)-preussin
by Paul Leo McGrane

A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry
Montana State University

Abstract:
Highly reactive titanium imido complexes have been generated by the reaction of primary amines with monocyclopentadienyl titanium (IV) complexes. These transient imido complexes have been trapped via intramolecular [2 + 2] cycloadditions with tethered alkynyl moieties. This transformation has been used to prepare a variety of representative heterocycles via catalytic (CpTiCl3 mediated] and stoichiometric [CpTi(CH3)2Cl mediated] annulations of alkynylamines.

Additionally, the azatitanetines generated in stoichiometric [2+2] imido-alkyne cycloadditions have been shown to engage nucleophiles in subsequent bond-forming reactions.

The utility of these new methods in natural products synthesis was shown by their use in concise total syntheses of (±)-monomorine I and (+)-preussin.

HETEROANNULATIONS MEDIATED BY TITANIUM IMIDO COMPLEXES: METHODS DEVELOPMENT AND APPLICATIONS TO THE TOTAL SYNTHESES OF (±)-MONOMORINE I AND (+)-PREUSSIN

by

Paul Leo McGrane

A thesis submitted in partial fulfillment
of the requirements for the degree

of

Doctor of Philosophy

in

Chemistry

MONTANA STATE UNIVERSITY
Bozeman, Montana

January, 1993

APPROVAL

of a thesis submitted by

Paul Leo McGrane

This thesis has been read by each member of the thesis committee and has been found to be satisfactory regarding content, English usage, format, citations, bibliographic style, and consistency, and is ready for submission to the College of Graduate Studies.

12/20/92
Date

Tom Tylka
Chairperson, Graduate Committee

Approved for the Major Department

1/7/93
Date

John R Emard
Head, Major Department

Approved for the College of Graduate Studies

1/11/93
Date

R L Brown
Graduate Dean

STATEMENT OF PERMISSION TO USE

In presenting this thesis in partial fulfillment of the requirements for a doctoral degree at Montana State University, I agree that the Library shall make it available to borrowers under rules of the Library. I further agree that copying of this thesis is allowable only for scholarly purposes, consistent with "fair use" as prescribed in the U.S. Copyright Law. Requests for extensive copying or reproduction of this thesis should be referred to University Microfilms International, 300 North Zeeb Road, Ann Arbor, Michigan 48106, to whom I have granted "the exclusive right to reproduce and distribute copies of the dissertation in and from microfilm and the right to reproduce and distribute by abstract in any format."

Signature P. Lee McKeane

Date 1-10-93

Dedicated to the memory of my father and namesake, Leo Charles McGrane. May your Irish eyes always smile upon us.

ACKNOWLEDGEMENTS

As the successful compilation of a thesis is rarely an individual effort, there are a number of people who need to be acknowledged for their contributions.

Professor Tom Livinghouse has served most effectively as my research advisor and as a guide through the labyrinth of methods development and natural product synthesis. Professors A.C. Craig, P.W. Jennings and B.P. Mundy provided willing and capable guidance. The office staff, Mr. Lee David and Dr. Joe Sears furnished valuable services.

Dr. Mike Jensen was a valued coworker on the methods development portion of this work, and provided suggestions on the synthesis of monomorine I. Former group members Dr. Scott Harring and Klark Hanson, and current members Lydia McKinstry, Greg Luedtke and Derek Sheehan were available for discussion and lent their particular expertise as needed.

Mrs. Barb Hamblet deserves thanks for her word processing services. Her skill and patience are much appreciated.

Without the support and encouragement of my famiy and friends this work would not have been completed. My wife Michelle has been invaluable in this endeavor. Not only has she provided a loving home, she is also the chief architect behind the structures and spectra in this thesis.

Thank you all and God bless.

TABLE OF CONTENTS

TABLE OF CONTENTS--Continued

TABLE OF CONTENTS--Continued

TABLE OF CONTENTS--Continued

LIST OF TABLES

LIST OF FIGURES

LIST OF FIGURES--Continued

LIST OF FIGURES--Continued

LIST OF FIGURES--Continued

LIST OF FIGURES--Continued

LIST OF FIGURES--Continued

LIST OF FIGURES--Continued

LIST OF FIGURES--Continued

ABSTRACT

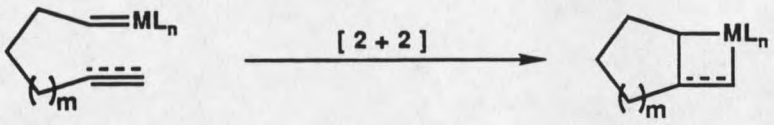
Highly reactive titanium imido complexes have been generated by the reaction of primary amines with monocyclopentadienyl titanium (IV) complexes. These transient imido complexes have been trapped *via* intramolecular [2 + 2] cycloadditions with tethered alkynyl moieties. This transformation has been used to prepare a variety of representative heterocycles *via* catalytic [$CpTiCl_3$ mediated] and stoichiometric [$CpTi(CH_3)_2Cl$ mediated] annulations of alkynylamines.

Additionally, the azatitanetines generated in stoichiometric [2 + 2] imido-alkyne cycloadditions have been shown to engage nucleophiles in subsequent bond-forming reactions.

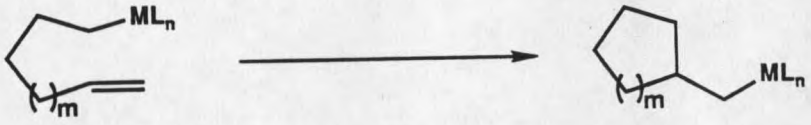
The utility of these new methods in natural products synthesis was shown by their use in concise total syntheses of (±)-monomorine I and (+)-preussin.

INTRODUCTION

The development of transition metal mediated carboannulation methods has greatly enhanced the chemist's ability to elaborate the cyclic skeletons of many biologically active carbogens. Two powerful examples of these methods are intramolecular carbene cycloaddition[1,2] and ligand cyclization reactions[3] (Eq. 1 and Eq. 2).



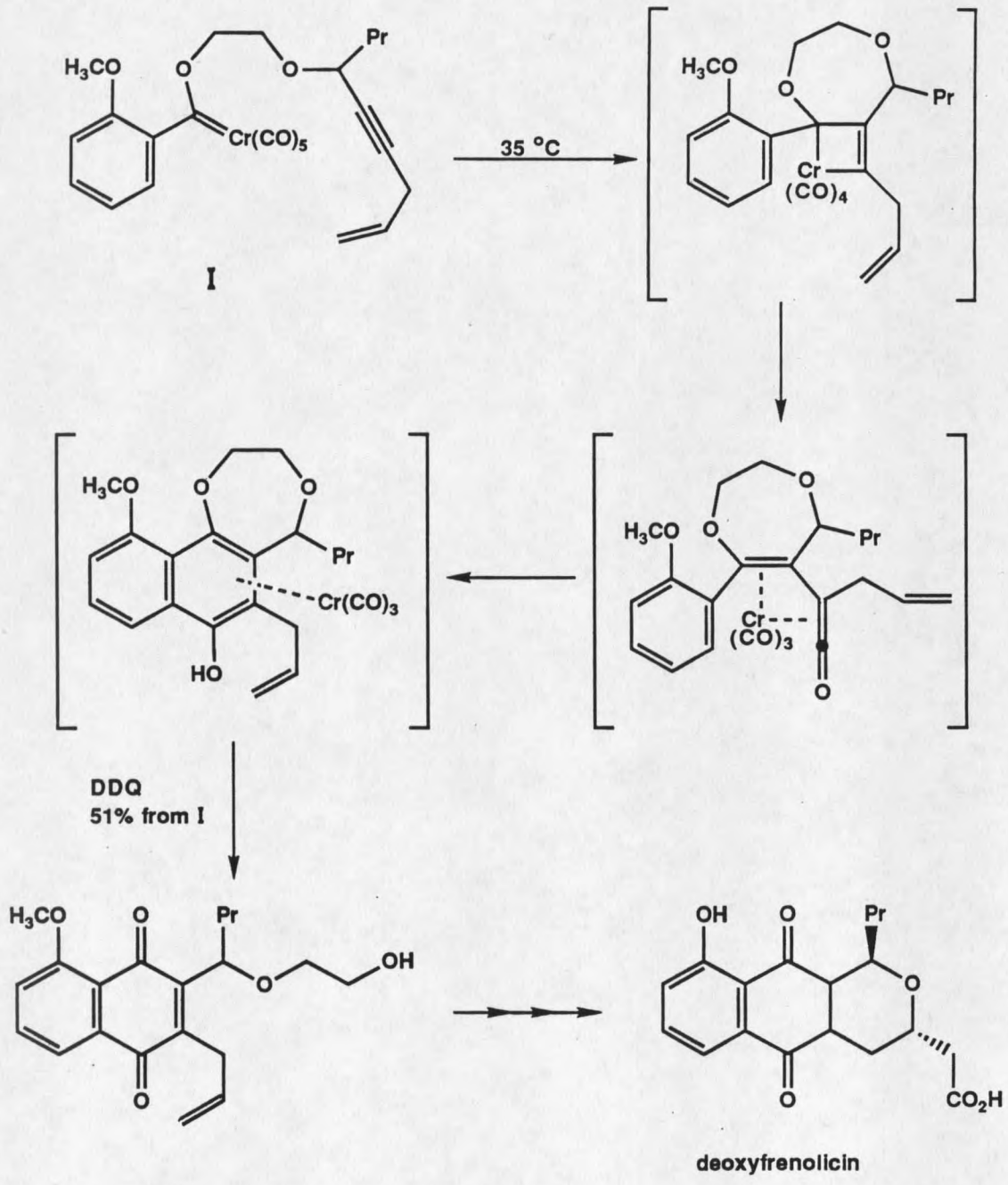
Eq. 1



Eq. 2

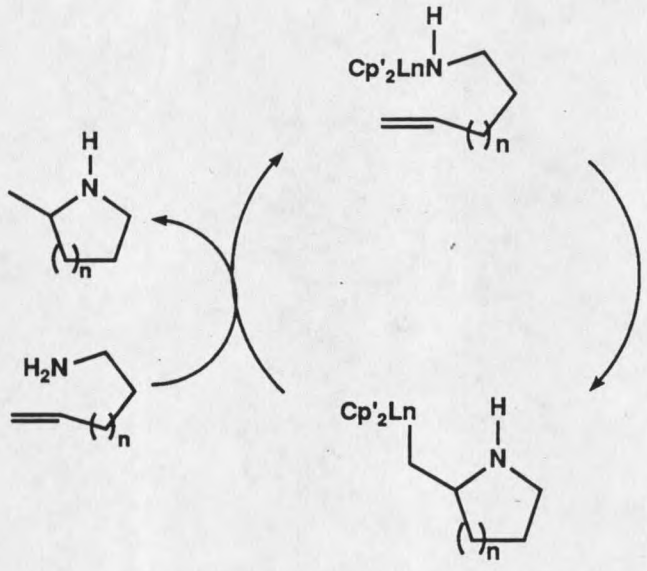
While the reactions in Eq. 1 and Eq. 2 both effect ring annulation, the [2 + 2] cycloaddition of Eq. 1 has the added advantage of generating a metallocyclobutane or metallocyclobutene which may serve as an intermediate for further elaboration. The utility of intramolecular carbene-alkyne cycloadditions in natural product synthesis was

exemplified by Semmelhack's synthesis of deoxyfrenolicin[4] (Scheme 1).



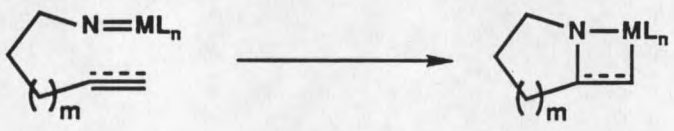
Scheme 1

The analogous transformations of amido and imido complexes that would lead to heterocyclic products have received little or no attention. Recently, Marks described the catalytic hydroamination of terminal alkenes proceeding *via* amidolanthanide complexes[5,6] (Scheme 2).



Scheme 2

Prior to the work reported in this thesis, there were no examples of the imido analog of the intramolecular carbene cycloaddition reaction. As with the carbene-olefin cycloaddition, imido complex-olefin cycloadditions could potentially provide exploitable metallocyclic intermediates (Eq. 3).



Eq. 3

BACKGROUND

Transition metal imido complexes[7,8] are defined as complexes bearing at least one imido ligand (N-R) on the metal. All monoimido complexes possess M-N-C bond angles greater than 155°, indicating extensive participation of the nitrogen lone pair in bonding interactions with the metal. With bisimido complexes it is possible to have smaller M-N-C bond angles due to saturation of the metal d-orbitals having π symmetry. However, there is only one clear example of a bent imido ligand. The molybdenum complex $Mo(NPh)_2(S_2CNEt_2)_2$ shown below has both a linear (169°) and a bent (139°) imido ligand[9] (Figure 1).

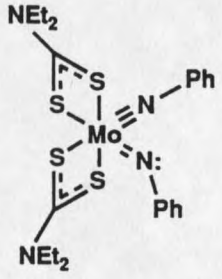
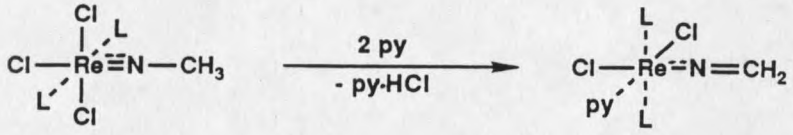


Figure 1. Linear and Bent Molybdenum Bisimido Complex.

The reaction chemistry of imido complexes, to the extent that it has been determined, is quite varied and depends largely on the metal and the other ligands present[7]. For example, methylimido rhenium complexes are readily deprotonated due to the increased acidity of the methyl (ß)

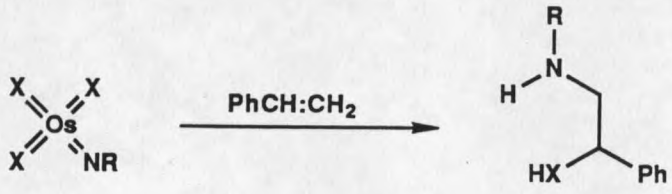
protons[10]. This is a direct reflection of the electronegativity of the metal (Eq. 4).



L=PPh_3, PCH_3Ph_2, $PEtPh_2$

Eq. 4

A more extreme case of the reactivity imparted on protons ß to the metal was seen with the related osmium complex OsO_3NCH_3[11]. Solutions of this methyl amido complex exploded when warmed to -40 °C. The inherent instability of osmium imido complexes bearing ß protons has been the major limitation in the otherwise useful oxyamination and diamination reactions mediated by imido osmium complexes[12] (Eq. 5).

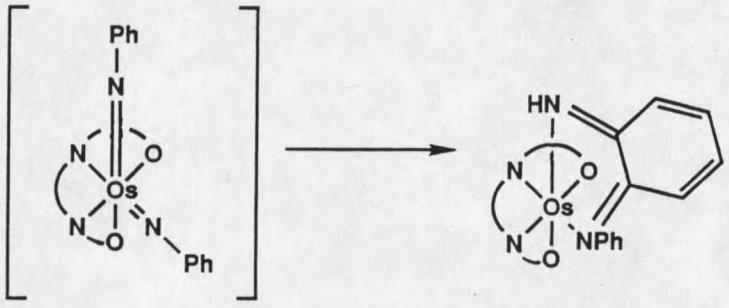


X=O, NR; R=tertiary alkyl

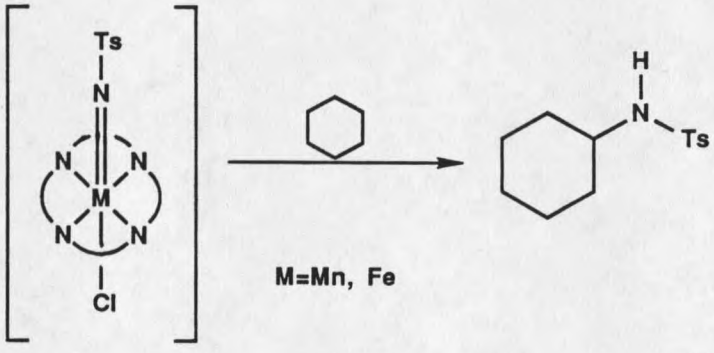
Eq. 5

Another mode of reactivity of imido complexes is C-H insertion. Two interesting examples are presented here

(Eq. 6[13] and Eq. 7[14]), and more recent examples with a direct bearing on the work in this thesis will be discussed later.



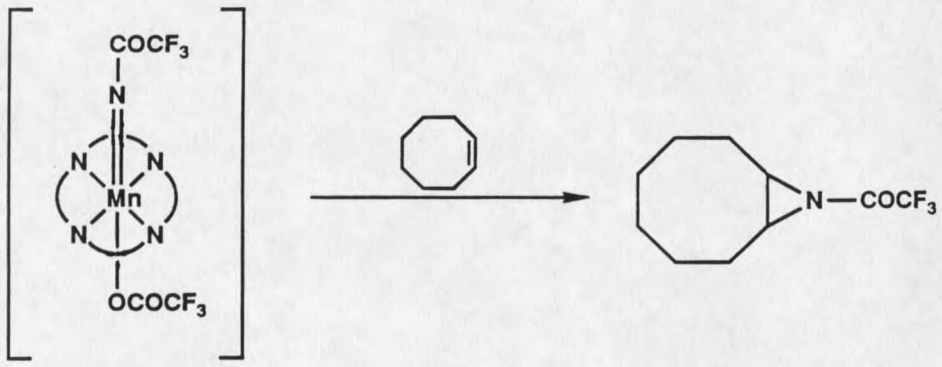
Eq. 6



Eq. 7

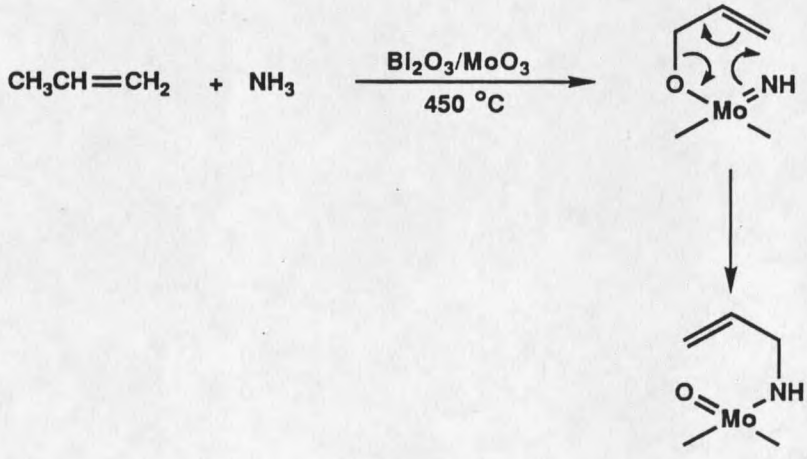
In contrast to the [3 + 2] addition mode of the imido osmium complexes observed in oxyamination and diaminations, a trifluoroacetimido manganese complex[15] effects aziridine formation when treated with cyclooctene (Eq. 8). This is currently the single example of the imido analog of the epoxidations mediated by oxo complexes[16].

Catalytic processes which have been suggested to proceed *via* imido complexes include the ammoxidation of



Eq. 8

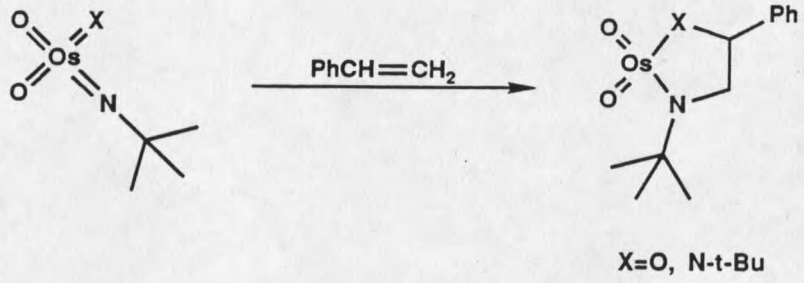
propylene and methylarenes[7]. A partial mechanism for the ammoxidation of propylene that includes a molybdenum imido complex has been advanced[17] (Scheme 3).



Scheme 3

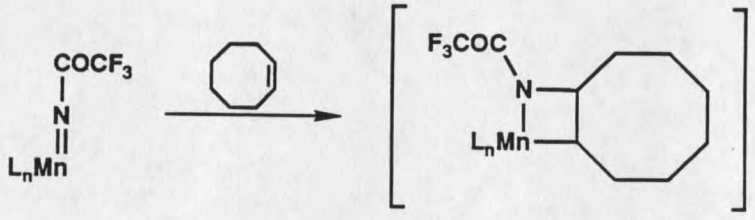
Although hundreds of transition metal-imido complexes are now known[7,18], only a few are known to engage olefins in cycloaddition reactions. Foremost among these are osmium

imido complexes which effect oxyamination or diamination of olefins *via* [3 + 2] cycloadditions[12] (Eq. 9).



Eq. 9

Additionally, aziridine formation with trifluoracetimido manganese complexes likely proceed *via* [2 + 2] cycloaddition onto the alkene[15] (Eq. 10).

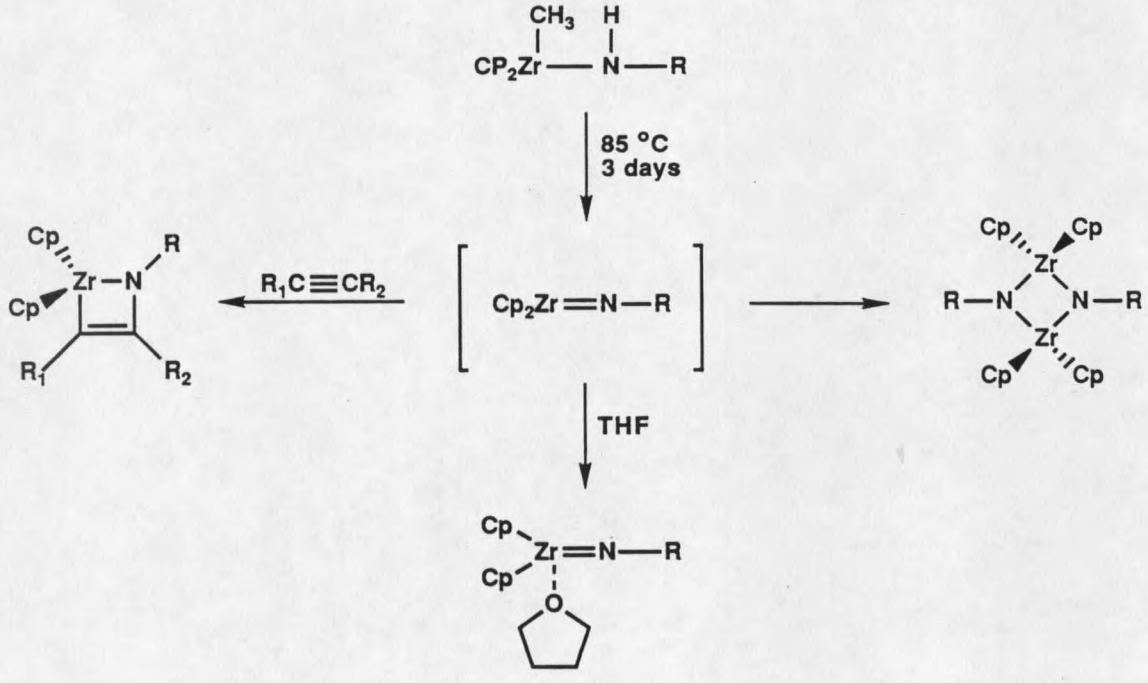


Eq. 10

Prior to 1988, [2 + 2] cycloaddition reactions of imido complexes onto alkynes were unknown. At this time, Bergman and Wolczanski, in concurrent publications, presented the first examples of monomeric zirconium imido complexes[19-21].

The imido zirconocene complexes described by Bergman were generated by thermolysis of the corresponding methyl amido complexes. When alkynes were present in the reaction

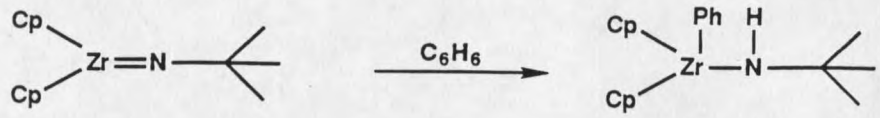
mixture, they were engaged in intermolecular [2 + 2] cycloadditions to give azazirconetines. In the absence of alkynes or stabilizing ligands, imido zirconocene complexes dimerized to bridging complexes[19] (Scheme 4).



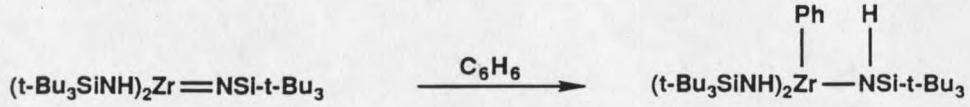
Scheme 4

An exception to this mode of reactivity was observed upon generation of the bulky t-butyl imido zirconocene complex. In this case the preferred pathway culminated in insertion into the C-H bonds of the solvent benzene. This was analogous to the reactivity observed by Wolczanski[21] wherein activation of benzene C-H bonds was achieved (Eq. 11 and Eq. 12).

Our entry into the arena of Group IV imido chemistry was precipitated by a combination of Bergman's report on

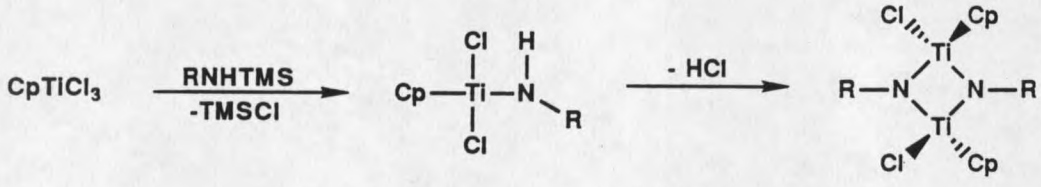


Eq. 11



Eq. 12

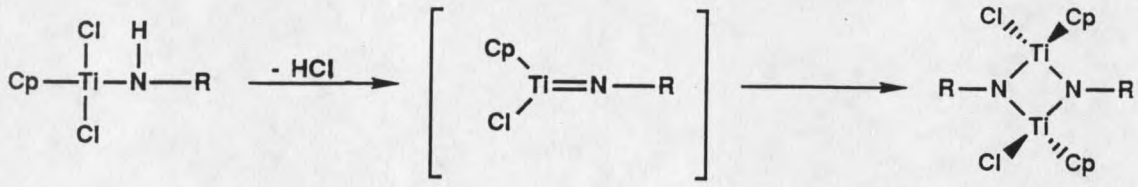
intermolecular couplings of imido zirconocene complexes with alkynes, and an earlier reaction observed by Teuben[22]. Specifically, it was noted by Teuben that monocyclopentadienyl titanium amido complexes spontaneously dimerized in solution with concomitant loss of HCl to give bridging imido dimers (Eq. 13).



Eq. 13

Though Teuben did not speculate that imido complexes were intermediates in this process, it seemed likely that the dimerization proceeded along a reaction pathway analogous to that later elucidated by Bergman for the formation of bridging imido zirconocene complexes. If true,

this would dictate imido complexes as intermediates (Eq. 14).

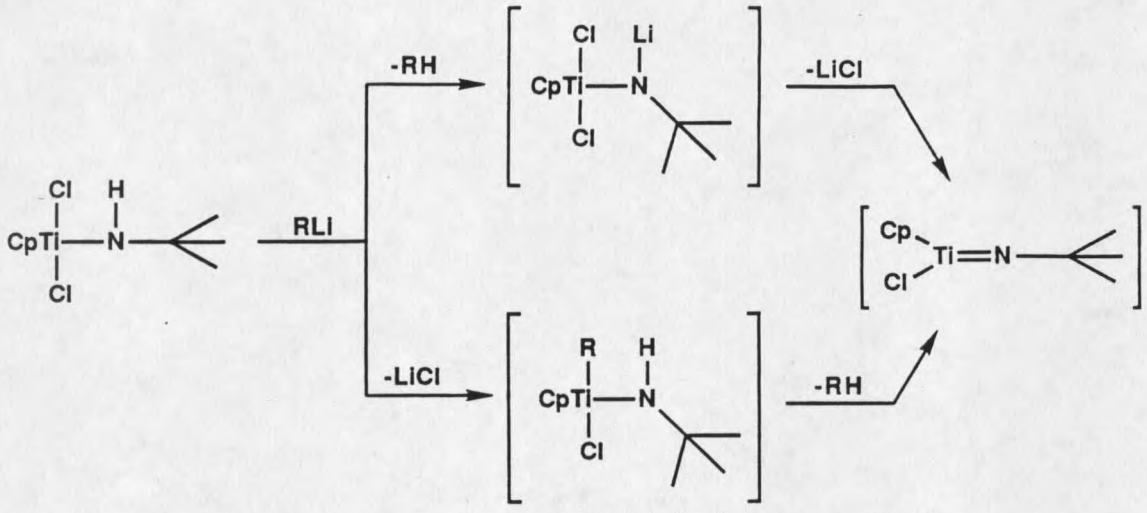


Eq. 14

Teuben also observed anomolous behavior with amido complexes derived from t-butylamine. In this case, dimerization (and thus imido complex formation) could only be effected by treatment of the amido complex with PhLi or CH_3Li. However, dimerization was still the preferred reaction pathway, not C-H activation as observed by Bergman[19].

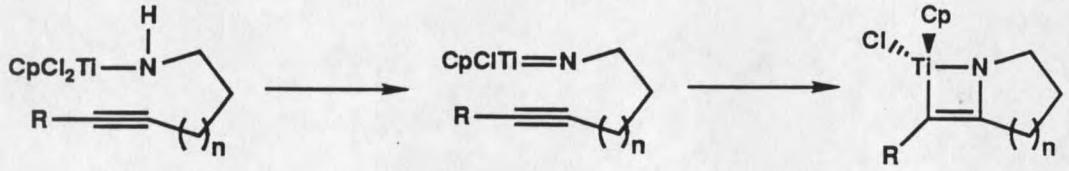
It has not been determined whether addition of the organolithium to the t-butylamido titanium complex results in displacement of a chloride on titanium, or in metallation of the amide nitrogen. However, either process would give an intermediate more prone to elimination than the parent amido complex itself (Scheme 5).

The ease of formation of the bridging imido dimers suggested that the putative monomeric imido complexes formed readily from the amido complexes. Additionally, these monocyclopentadienyl complexes would be expected to be more electron deficient than imido zirconocene complexes.



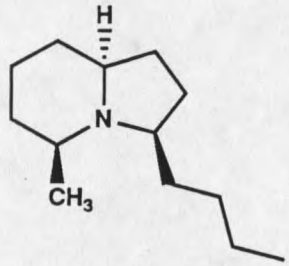
Scheme 5

Our goal at the outset of this research was to take advantage of this ease of imido complex formation and to exploit the reactivity of these transient species to effect *intramolecular* [2 + 2] cycloadditions (Eq. 15).

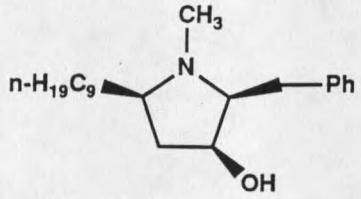


Eq. 15

Once the reactivity of these complexes had been ascertained, we hoped to utilize the [2 + 2] cycloaddition in total syntheses of (+)-monomorine (1)[23] and (+)-preussin (2)[24] (Figure 2).



1



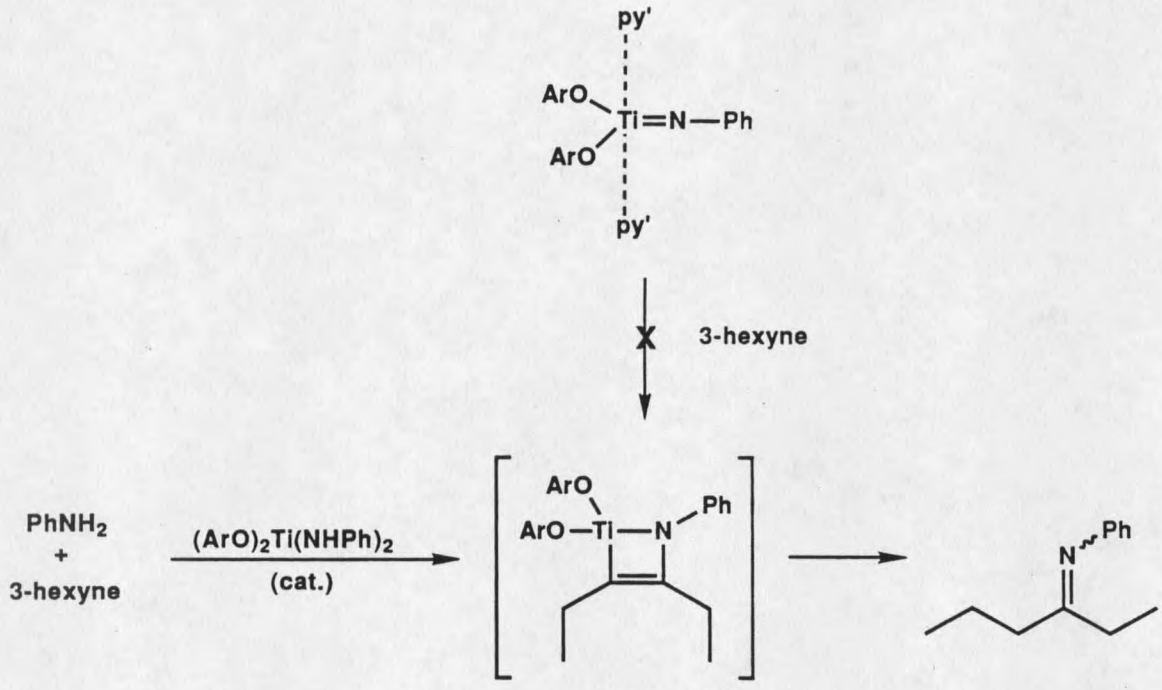
2

Figure 2. (+)-Monomorine I (1) and (+)-Preussin (2).

Since the inception of our research into Group IV imido complex [2 + 2] cycloaddition reactions, four publications dealing with monomeric, terminal titanium imido complexes have appeared. Inclusive in Rothwell's report[25] was some preliminary data on the reactivity of bis-(aryloxy)-phenylimido complexes. Although these solvated species did not induce benzene C-H activation or undergo cycloaddition reactions with 3-hexyne, the corresponding bisamido complex was effective in catalizing formation of the N-phenylimine of 3-hexanone from 3-hexyne and aniline (Scheme 6).

The authors suggested unsolvated imido complexes as the reactive intermediates in this process. If this was indeed the reactive intermediate, it would constitute the first probable example of a [2 + 2] cycloaddition of a titanium imido complex into an alkyne.

Roesky[26] has detailed the preparation and x-ray diffraction study of a dichlorotitanium imido complex (Figure 3). Although no studies on the reactivity of this



Scheme 6

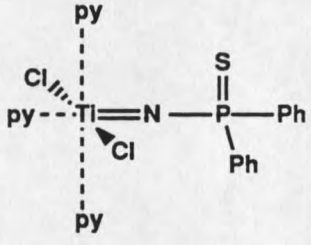
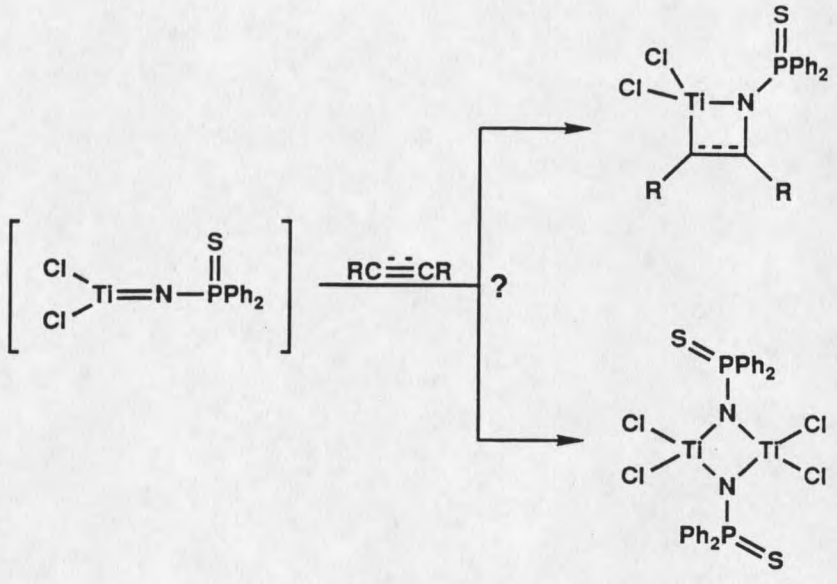


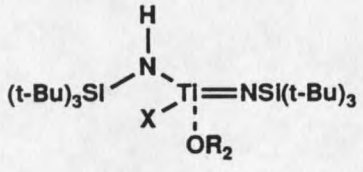
Figure 3. Dichlorotitanium Imido Complex.

complex have as yet been published, one might speculate that its unsolvated analog would exhibit either a marked reactivity towards olefins, or a propensity to dimerize (Scheme 7).



Scheme 7

More recently, Wolczanski[27] has reported a series of titanium imido complexes that are closely related to the zirconium imido complex, described earlier[21]. As with the analogous bisamido imido zirconium imido complex, bisamido imido titanium complexes (X=NH-t-Bu) promoted C-H activation of benzene (Figure 4).

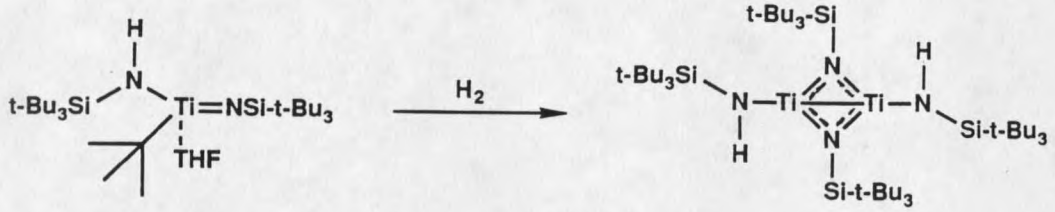


X	OR_2
t-Bu$_3$SiNH	OEt_2
t-Bu$_3$SiNH	THF
Cl	THF
Br	THF
CH_3	THF
t-Bu	THF

Figure 4. Silyl Substituted Titanium Imido Complexes.

When one of the complexes of this series (X=t-Bu) was exposed to hydrogen, an interesting dimerization occurred.

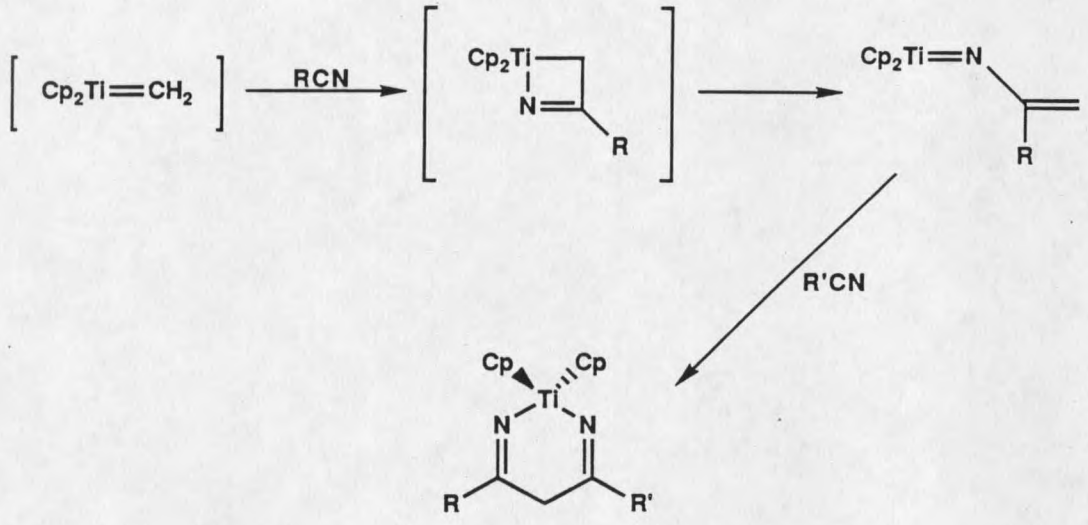
This dimer was found, by x-ray diffraction, to contain a metal-metal bond (Eq. 16).



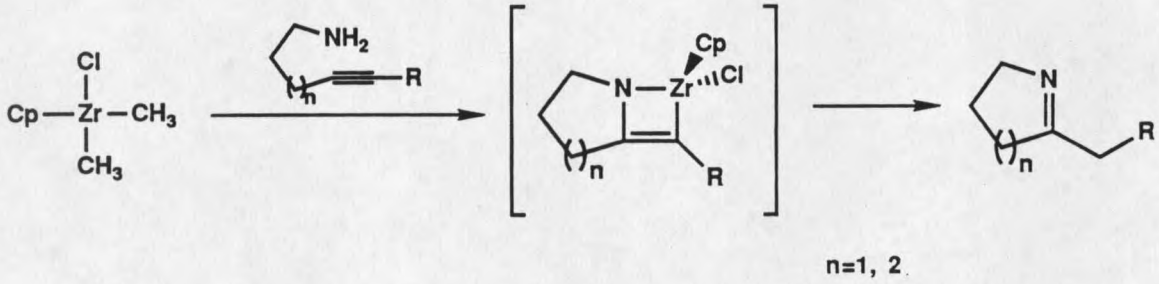
Eq. 16

Doxsee[28,29] reported the formation of vinylimidotitanocene complexes. The transient azatitanatines generated upon treatment of Tebbes' reagent with nitriles were isomeric to those obtained by Bergman[19]. A retro [2 + 2] reaction gave the isolable vinylimido complexes. Among the interesting chemistry associated with these vinylimido complexes was addition of a second nitrile, *via* a [4 + 2] cycloaddition, to form diazatitanacyclohexadienes (Scheme 8).

In work pursued concurrently with that presented in this thesis, Mike Jensen, formerly of these laboratories, developed annulation methods based on the intramolecular [2 + 2] cycloaddition of monocyclopentadienyl zirconium imido complexes onto tethered alkynes[30,31]. This method entailed treatment of $CpZrCl_3 \cdot DME$[32] with two equivalents of methyllithium to generate $CpZr(CH_3)_2Cl$. The resultant solution could then be treated with a variety of alkynylamines to give, after workup, the annulated products (Eq. 17).



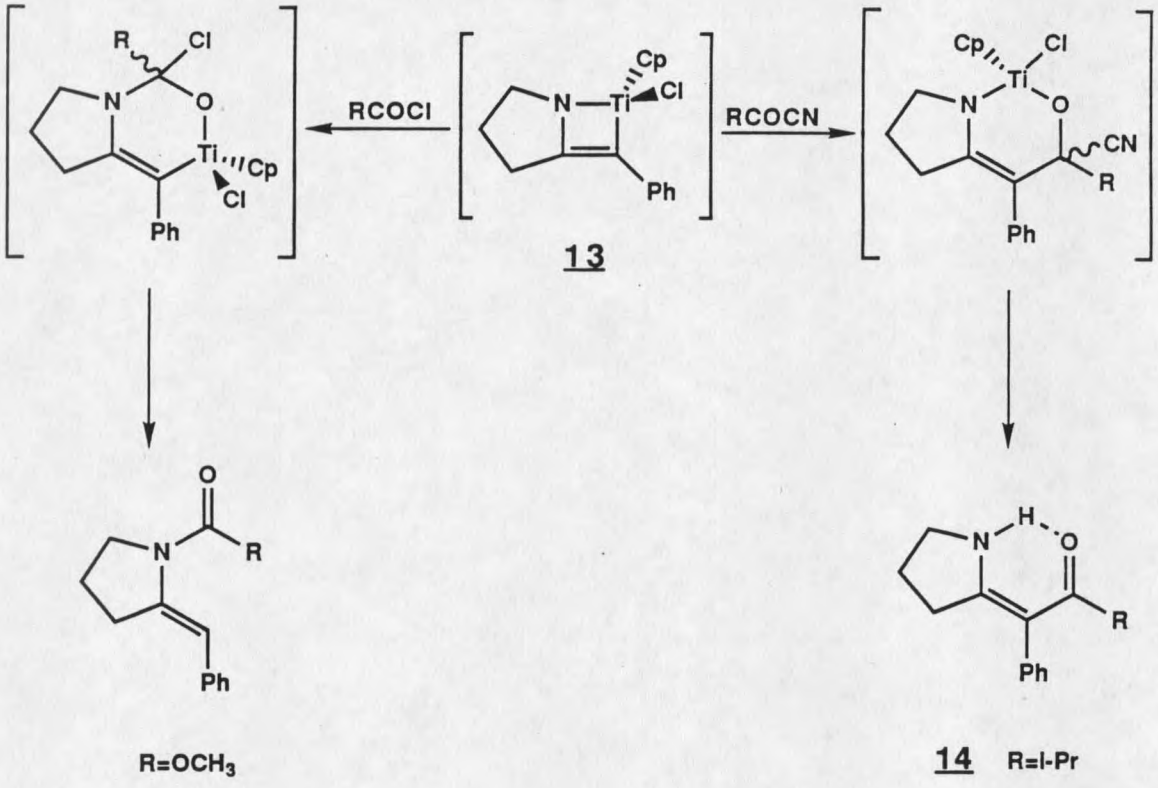
Scheme 8



Eq. 17

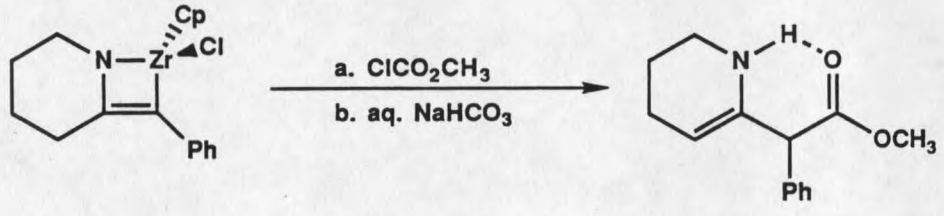
Another major focus of Jensen's work in this area was the selective functionalization of azametalletines. For example, azatitanetine 13 was selectively N-functionalized upon treatment with acyl chlorides, but C-functionalized upon exposure to acyl nitriles (Scheme 9).

Interestingly, this mode of functionalization was not observed when a similar azazirconetine was treated with



Scheme 9

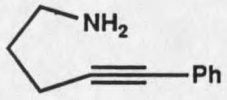
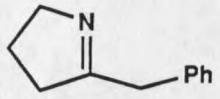
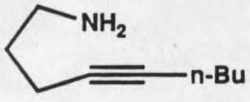
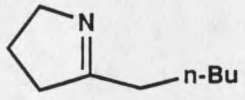
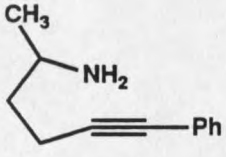
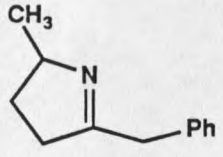
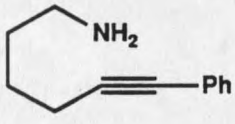
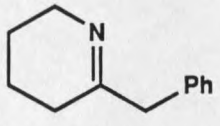
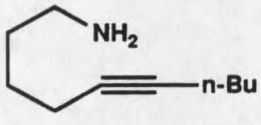
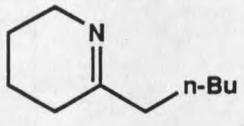
$ClCO_2CH_3$. In this case, C-C bond formation was observed (Eq. 18).



Eq. 18

Particularly noteworthy was the facile preparation of tetrahydropyridines **10** and **12** using this method. Table 1 contains the results of this study.

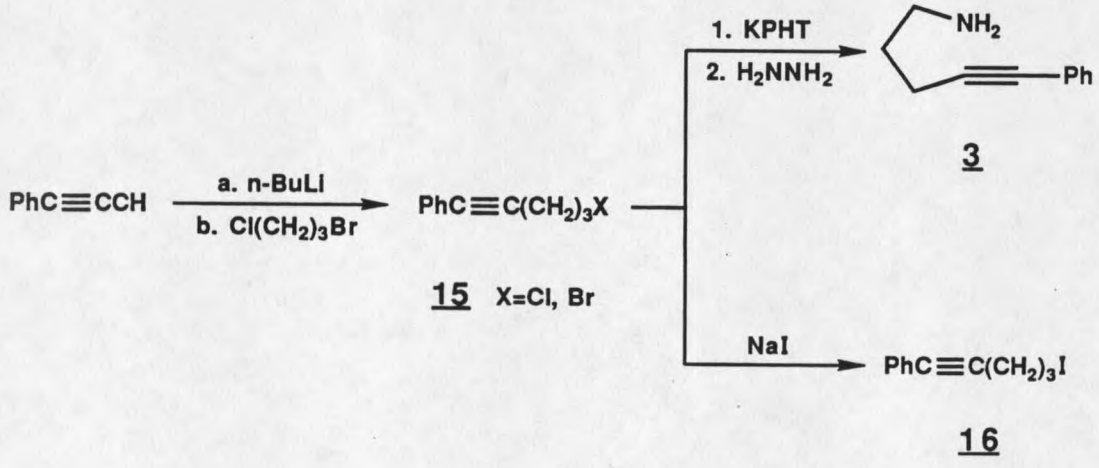
Table 1. Results of $CpZr(CH_3)_2Cl$ Annulation Study

Substrate	Yield, %	Product
3 	(83)	4 
5 	(82)	6 
7 	(77)	8 
9 	(69)	10 
11 	(74)	12 

RESULTS AND DISCUSSION

Methods Development

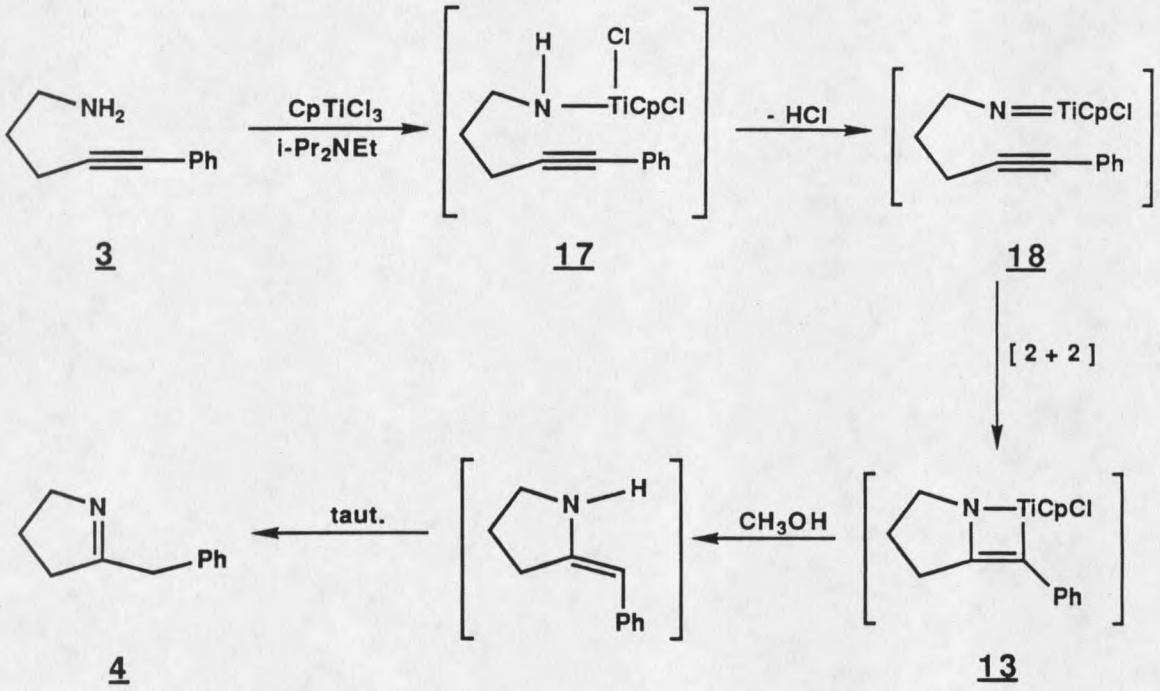
Our initial aim in this research was to establish the accuracy of our hypothesis that there existed a reactive monocyclopentadienyl titanium imido complex as an intermediate in the dimerization process observed by Teuben[22]. Towards this end, 5-phenylpent-4-yn-1-ylamine (3) was prepared (Scheme 10). It was reasoned that the alkynyl moiety of amine 3 could serve as an intramolecular trap of imido complexes if they were generated.



Scheme 10

We were quite pleased when an initial experiment in which amine 3 was added to $CpTiCl_3$[33,34] (1.0 eq.) and i-Pr_2NEt

(2.1 eq.) in THF at 25 °C yielded, after methanolysis, Δ^1-pyrroline **4** in 74 % yield (Scheme 11).



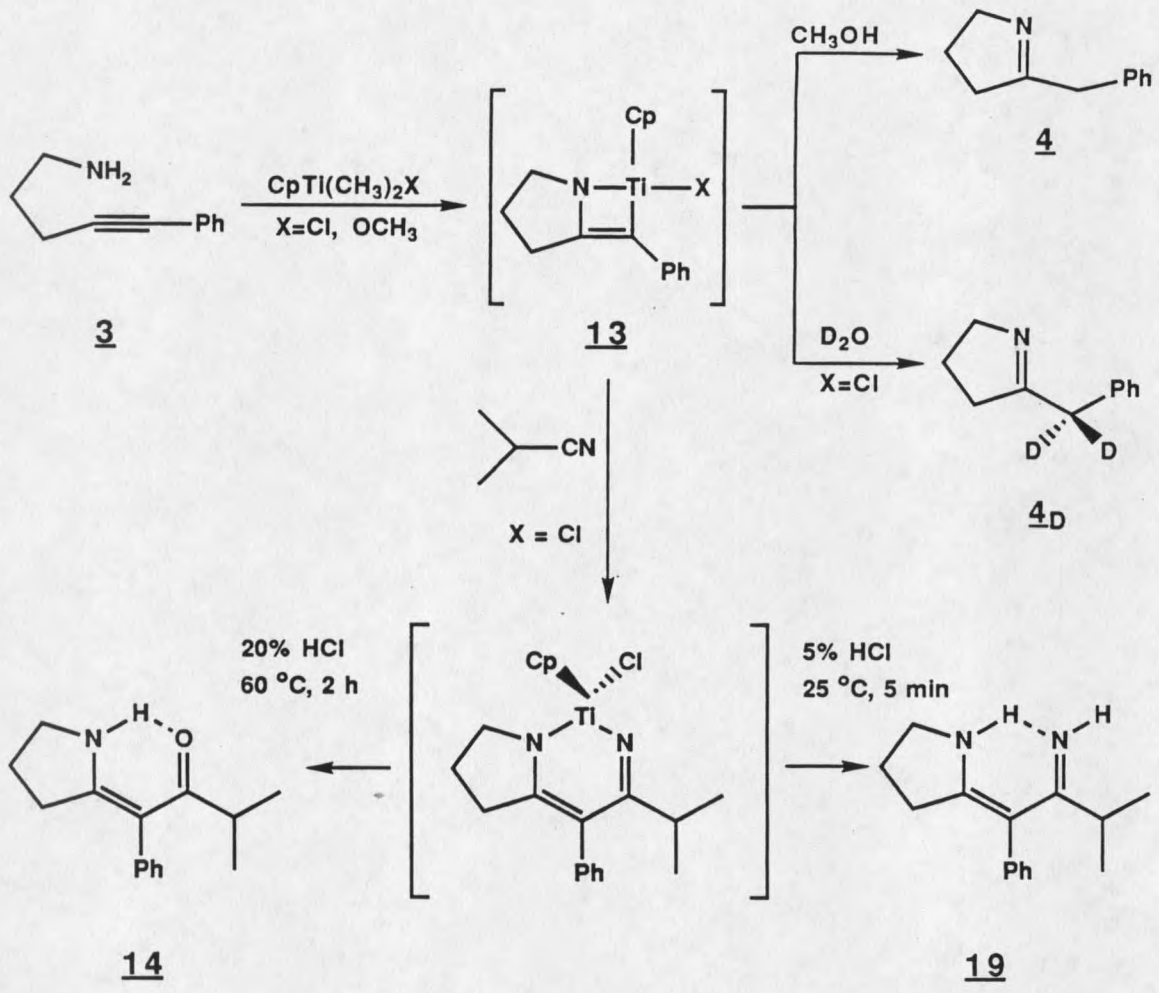
Scheme 11

The mechanism proposed in Scheme 11 was based, at this early stage, solely on the known chemistry of imido and amido complexes of the Group IV elements. Specifically, the amine **3** would be expected to react with $CpTiCl_3$ to form the amido complex **17**. This, along with a subsequent elimination of HCl to form the putative imido complex **18**, would be in accord with Teuben's observations[22]. An intramolecular [2 + 2] cycloaddition of **18** would then parallel the intermolecular cycloadditions of imidozirconocene complexes[19]. The fact that Δ^1-pyrroline **4** was the only

isolable product of this reaction was certainly consistent with the proposed mechanism.

Bergman[19] had noted that azazirconetines were intensely colored, presumably due to charge transfer from the azaallyl moiety to the empty orbital on the formally 16-electron zirconium center. As the titanium in azatitanetine 13 would be expected to be even more electron deficient, we were not surprised when amine addition in our pilot experiment induced formation of a deep burgundy color.

In a set of experiments designed to closely parallel those of Bergman[19], amine 3 was added to preformed solutions of $CpTi(CH_3)_2Cl$[36] and $CpTi(CH_3)_2OCH_3$[37] (Scheme 12). It was anticipated that azatitanetine 13 would be generated by elimination of two equivalents of methane and subsequent [2 + 2] cycloaddition. Indeed, both dimethyltitanium complexes were found to be suitable precursors to 13. Addition of amine 3 to the solution of $CpTi(CH_3)_2Cl$ was accompanied by immediate evolution of methane[39] and formation of a deep burgundy color. It is noteworthy that these transformations were complete in less than two hours at 25 °C. By way of comparison, reaction of amine 3 with $Cp_2Zr(CH_3)_2$ gives less than 10 % conversion to Δ^1-pyrroline 4 after 24 h at 80 °C. Although this rate differential was initially attributed to a more reactive imido complex being generated in our process, we have since determined that the reactivity difference in this case was due to a slow initial



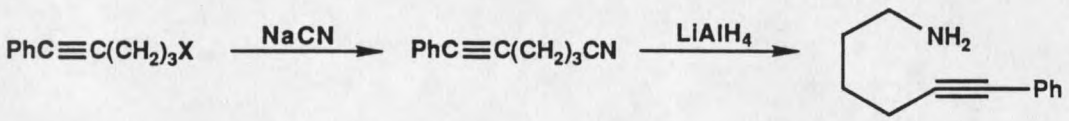
Scheme 12

reaction of the amine 3 with $Cp_2Zr(CH_3)_2$ to form an amido complex[40].

In an attempt to determine whether reactive nitrogen-titanium and carbon-titanium bonds were present, a solution of azatitanetine 13 was quenched with deuterium oxide. As anticipated, the dideuterated Δ^1-pyrroline 4_D was formed in 92 % yield. Indeed, azatitanetine 13 was also found to

react with nitriles as shown in Scheme 12, and with several other electrophiles, as demonstrated by Jensen[30].

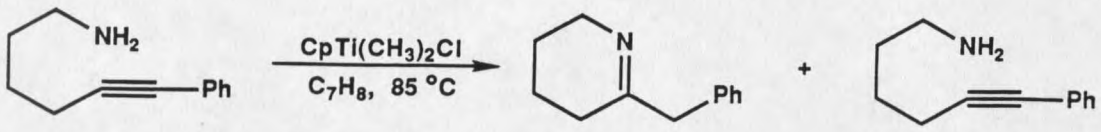
Because all attempts at isolation and characterization of 13 have failed, we cannot state for certain that 13 is an intermediate in this process. The subsequent reactions observed for the intermediate are, however, consistent with structure 13.



15 **20** **9**

Eq. 19

We next sought to extend this stoichiometric cycloaddition methodology to the formation of six-membered nitrogen heterocycles (e.g., tetrahydropyridines). For this purpose, 6-phenylhex-5-yn-1-ylamine 9 was prepared from the halide mixture 15 *via* nitrile displacement[41] and subsequent reduction with $LiAlH_4$[42] (Eq. 19). Unfortunately, only starting material was recovered when amine 9 was added to $CpTi(CH_3)_2Cl$ in THF at 25 °C. When more rigorous reaction conditions were employed (toluene, 85 °C, slow amine addition), we were able to obtain a mixture of tetrahydropyridine 10 and starting material (Eq. 20). As this conversion can be achieved at 25 °C with $CpZr(CH_3)_2Cl$[30], optimization with $CpTi(CH_3)_2Cl$ was not pursued.

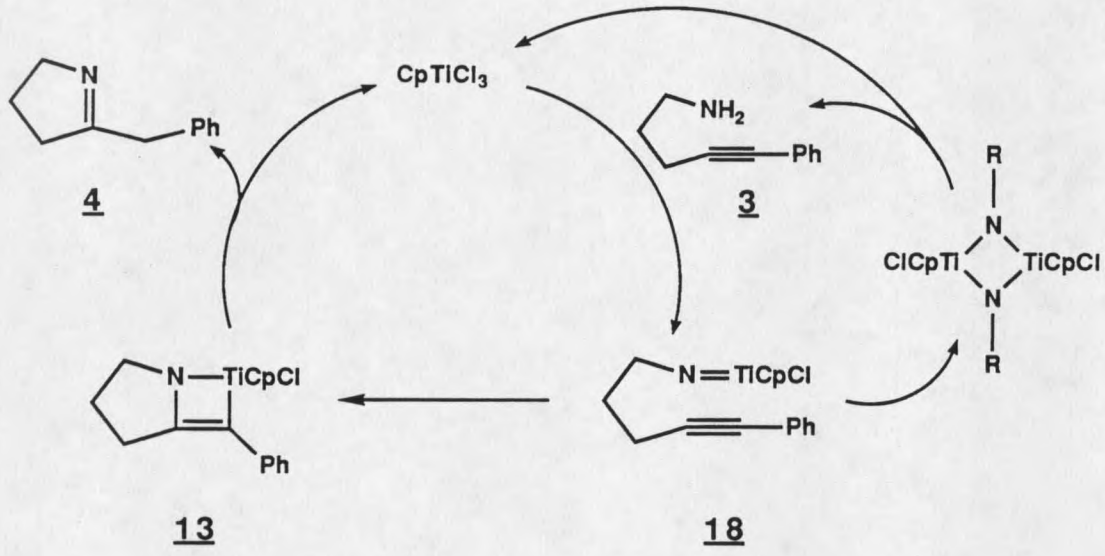


9 **10** **9**

Eq. 20

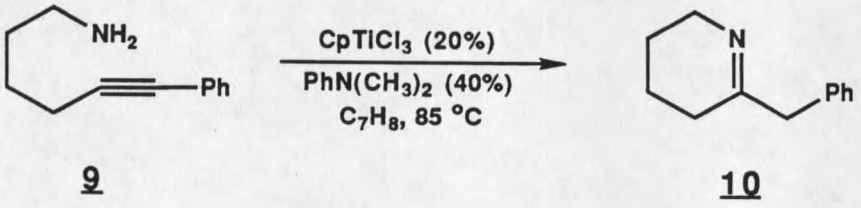
When a THF solution of $CpTiCl_3$ (1.0 eq.) and i-Pr_2NEt (2.1 eq.) was treated with amine 3 (*vide infra*, Scheme 11), but allowed to stir for a longer time, the initial dark burgundy color formed on amine addition begins to dissipate. Eventually (~2 h), the light red color of the $CpTiCl_3$/i-Pr_2NEt solution was restored. This suggested that the conversion of alkynylamine to Δ^1-pyrroline could be effected catalytically. Thus, addition of amine 3 to a solution of $CpTiCl_3$ (20 mole %) and i-Pr_2NEt (40 mole %) afforded Δ^1-pyrroline **4** in 94 % yield after two hours. A catalytic cycle that accounts for this transformation is proposed in Scheme 13. Note that dimer formation, if it did occur, would regenerate starting materials by a subsequent reaction with the amine hydrochloride present.

Although 6-phenylhex-5-yn-1-ylamine (**9**) was not cyclized under these conditions, the following modifications of the reaction conditions restored cyclization. For the generation of tetrahydropyridines, we found that addition of the amine to a preheated solution of $CpTiCl_3$ (20 mole %) and



Scheme 13

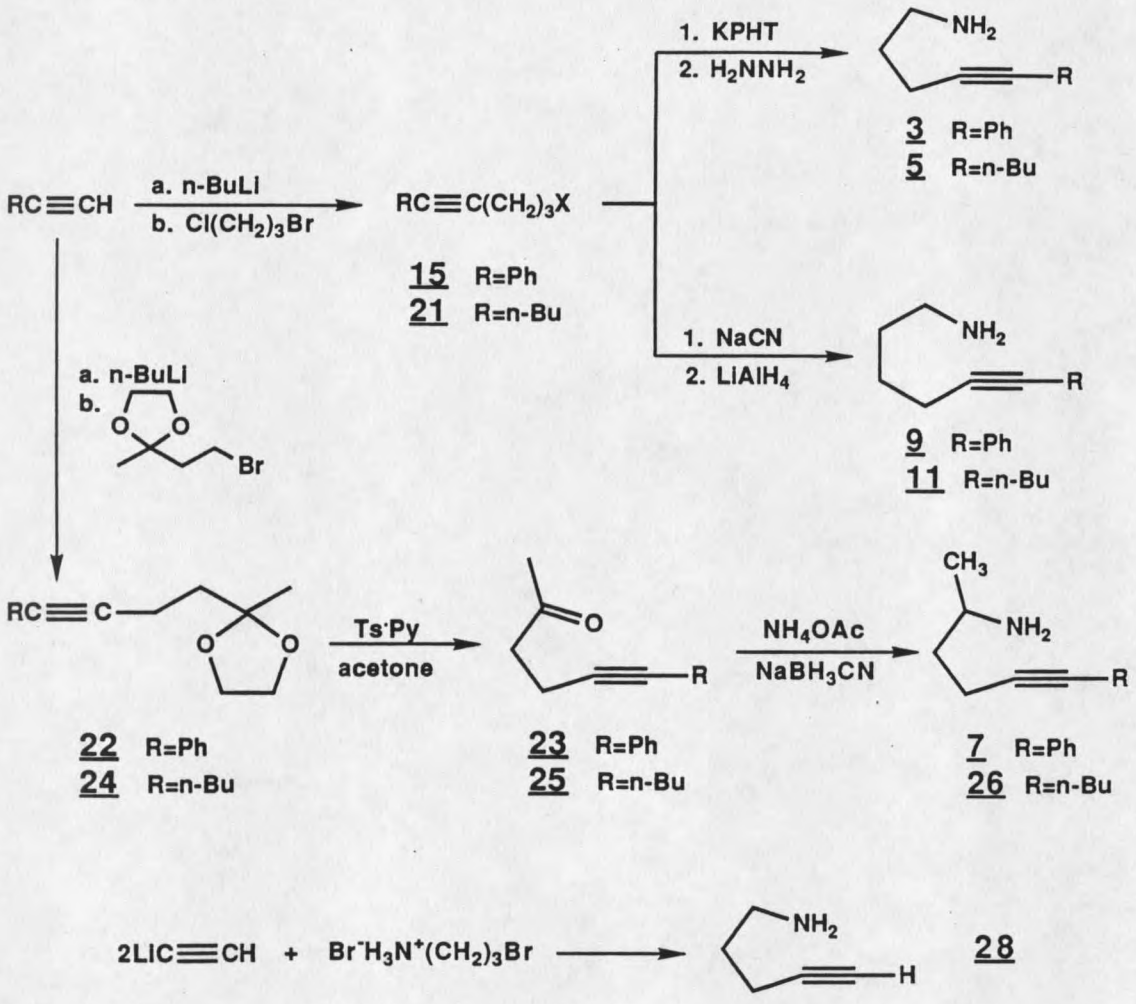
N,N-dimethylaniline (40 mole %) gave the expected product in high yield (Eq. 21).



Eq. 21

In an attempt to further probe the nature of the annulation, a series of experiments were run in which amine 3 was exposed to catalytic quantities of transition metal complexes possessing more ($TiCl_4$, $ZnCl_2$) or less (Cp_2TiCl_2, $CpTi(CH_3)_2Cl$) Lewis acidic character than $CpTiCl_3$. No other complex was found to effect Δ^1-pyrroline formation.

This observation, along with our results in the stoichiometric studies[30,31], strongly suggested that we were indeed dealing with a cycloaddition reaction and *not* a Lewis acid catalyzed hydroamination of alkynes.

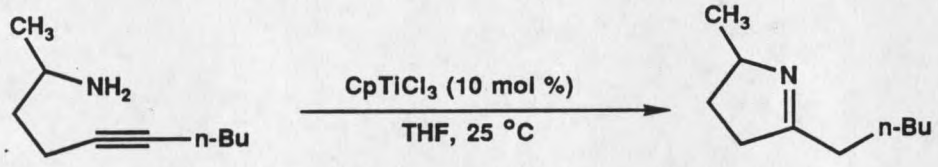


Scheme 14

With the two methods of cyclization fairly well developed, we sought to determine their generality. A variety of substrates were prepared for this reason (Scheme 14). In addition to the phenyl substituted

alkynylamines previously discussed, the substrates studied included dialkyl substituted alkynes, terminal alkynes, and substrates with the amine functionality on a secondary carbon. The results of this study on the facile preparation of Δ^1-pyrrolines and tetrahydropyridines are shown in Table 2.

In the hope that the substrate amine and/or the product (Δ^1-pyrroline or tetrahydropyridine) could function in place of the auxiliary amine, cyclization was attempted in the absence of added tertiary amine. Addition of amine 26 to a THF solution of $CpTiCl_3$ (10 mole %) gave complete conversion to Δ^1-pyrroline 27 in two hours (Eq. 22).



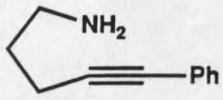
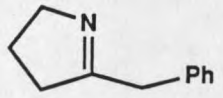
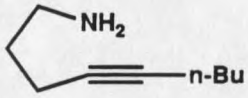
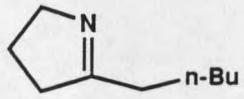
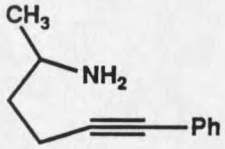
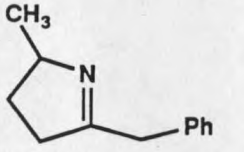
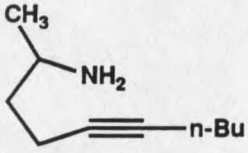
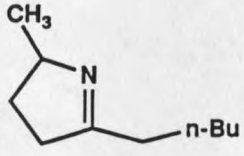
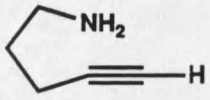
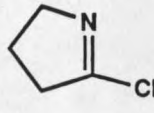
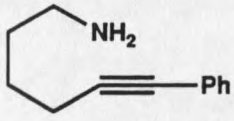
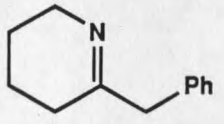
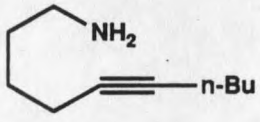
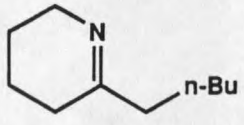
26 **27**

Eq. 22

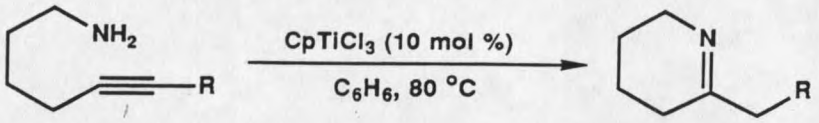
Amines 20 and 23 were converted to their respective tetrahydropyridines in high yield (>90 %) by heating for three hours with $CpTiCl_3$ (10 mole %) in benzene at 80 °C, This was quite gratifying in that we no longer had to deal with separating N,N-dimethylaniline from the products (Eq. 23).

The maximum turnover for $CpTiCl_3$ in the catalytic cycle was measured with amine 26. The amine was added to a THF solution of $CpTiCl_3$ in portions at intervals corresponding

Table 2. Results of $CpTiCl_3$ and $CpTi(CH_3)_2Cl$ Annulation Studies

Substrate		Method[a]	Yield, %[b]	Product	
3		A B	(94) (96)	4	
5		A B	(94) (94)	6	
7		B	(92)	8	
26		D	(94)	27	
28		D[c]	(100)[d]	29	
9		C E	(88) (91)	10	
11		C E	(89) (92)	12	

a. A: 20 mol % $CpTiCl_3$, 40 mol % i-Pr_2NEt, THF, 25 °C. B: $CpTi(CH_3)_2Cl$, THF, 25 °C. C: 20 mol % $CpTiCl_3$, 40 mol % $PhN(CH_3)_2$, C_7H_8, 80 °C. D: 10 mol % $CpTiCl_3$, THF, 25 °C. E: 10 mol % $CpTiCl_3$, C_6H_6, 80 °C. b. all yields are isolated yields unless specified otherwise. c. C_6D_6, 25 °C. d. ^1H NMR yield.



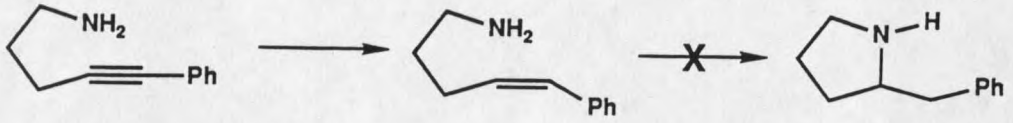
9 R=Ph
11 R=n-Bu

10 R=Ph
11 R=n-Bu

Eq. 23

to the dissipation of the color attributed to the metallocycle. The experiment was terminated when amine addition did not induce formation of the burgundy colored intermediate. The mass yield after workup was 96 % and was comprised of a 96:4 mixture of Δ^1-pyrroline **27** and amine **26**. By this method the turnover for $CpTiCl_3$ was between 50 and 55. Although this turnover is moderate, the ready availability of the catalyst should make the process extremely viable for many applications[34].

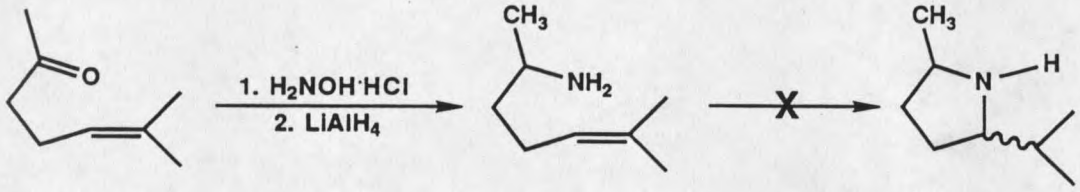
As carbenes were known to engage alkenes and dienes in cycloaddition reactions[2], we hoped to observe similar reactivity with imido complexes. We have made some preliminary attempts at inducing cycloaddition reactions between titanium imido complexes and other multiply bonded carbon-carbon systems. Specifically, alkenylamine **30** was subjected to all conditions found effective for the cycloaddition of alkynylamines (Eq. 24). Unfortunately, we were unable to obtain cyclized products. Even the more



3 **30**

Eq. 24

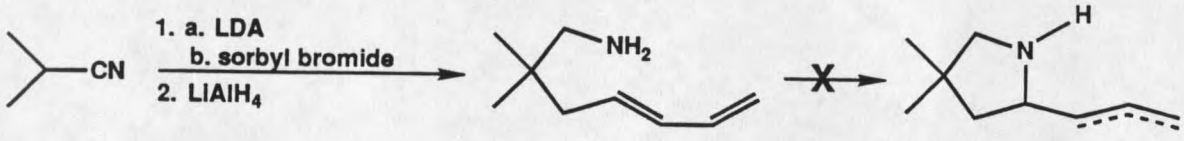
electron-rich alkenylamine 31 failed to undergo the desired transformation (Eq. 25).



31

Eq. 25

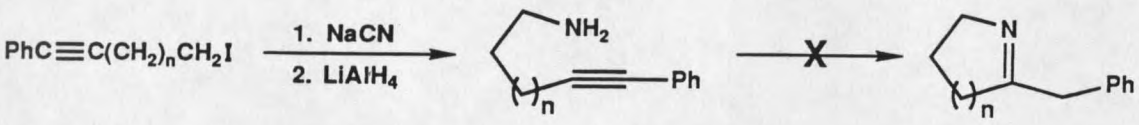
We also explored the possibility of inducing [4 + 2] or [2 + 2] cycloadditions of imido complexes onto diene functions. Dienylamine 32 was recovered unaltered from these attempted cycloadditions (Eq. 26).



32

Eq. 26

Finally, we have not yet been able to use these new annulation methods in the preparation of azepines or azocines (Eq. 27).



33 n=3
35 n=4

34 n=3
36 n=4

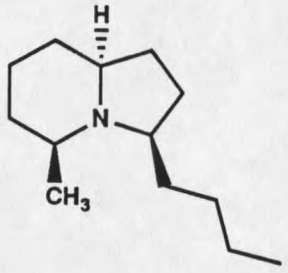
n=3, 4

Eq. 27

As alkynyl amines 34 and 36 would both be expected to readily form imido complexes with either $CpTiCl_3$ or $CpTi(CH_3)_2Cl$, competitive, nonproductive reaction pathways must be responsible for the lack of observable annulation. Competitive, irreversible dimerization, as observed by Bergman for imidozirconocene complexes[19], would account for the inefficiency of $CpTi(CH_3)_2Cl$. However, dimerization under catalytic conditions should not terminate formation of reactive imido complexes. In this case we speculate that the known propensity of cyclopentadiene to be displaced in the presence of an excess of amine[43] may give rise to an inactive amido complex of the general formula $Cl_nTi(NHR)_m$, $(n + m = 4)$. This observation was consistent with the inability of $TiCl_4$ to effect annulation of alkynyl amines. It also seems likely that displacement of cyclopentadiene accounts for the moderate turnover observed for $CpTiCl_3$ in the successful cyclizations discussed previously.

The Total Synthesis of (±)-Monomorine I (1).

The synthetic utility and functional group compatibility of $CpTiCl_3$ catalyzed cycloadditions of alkynylamines was demonstrated by a concise total synthesis of (±)-monomorine I (1)[44] (Figure 5).



1

Figure 5. (+)-Monomorine I (1).

This alkaloid is a trail pheromone of the Pharoah's Ant that also exhibits repellant activity toward other ant species[23,45]. Pharoah's Ants are common pests in the British Isles and are now becoming a problem in the United States. Infestations of these small ants are considered a serious problem because the ants have been shown to carry pathogenic bacteria and also possess the ability to penetrate sophisticated hospital isolation units[46].

Monomorine I was first described by Ritter in 1972[23]. The absolute stereochemistry was confirmed by synthesis in 1975[47]. Since then, 1 has been the subject of intense synthetic study. Although numerous syntheses have been

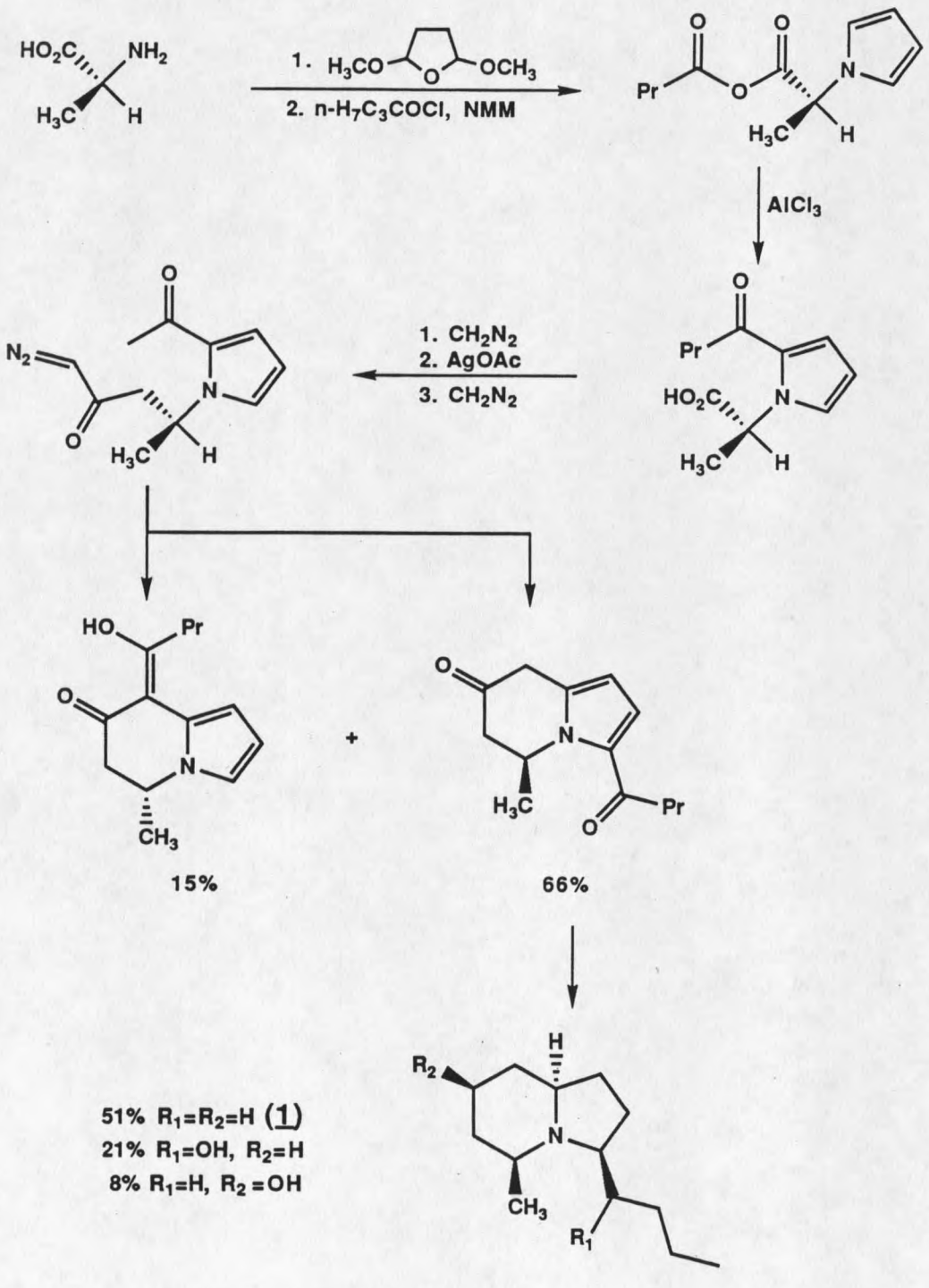
advanced, few are sufficiently high yielding to be of practical use in the preparation of 1 or similar indolizidine alkaloids. The most concise enantioselective synthesis of (+)-monomorine I utilized L-alanine as a chiral building block[48]. The synthesis was completed in seven steps in an overall yield of 7-11% (Scheme 15).

With some improvement this method may be conducive to the large scale preparation of (+)-1. At this time the alternatives are a 22-step[49] ($<<7\%$) procedure starting with L-tartrate, or a >20-step[50] ($<<4\%$) procedure commencing with diethyl L-tartrate[51].

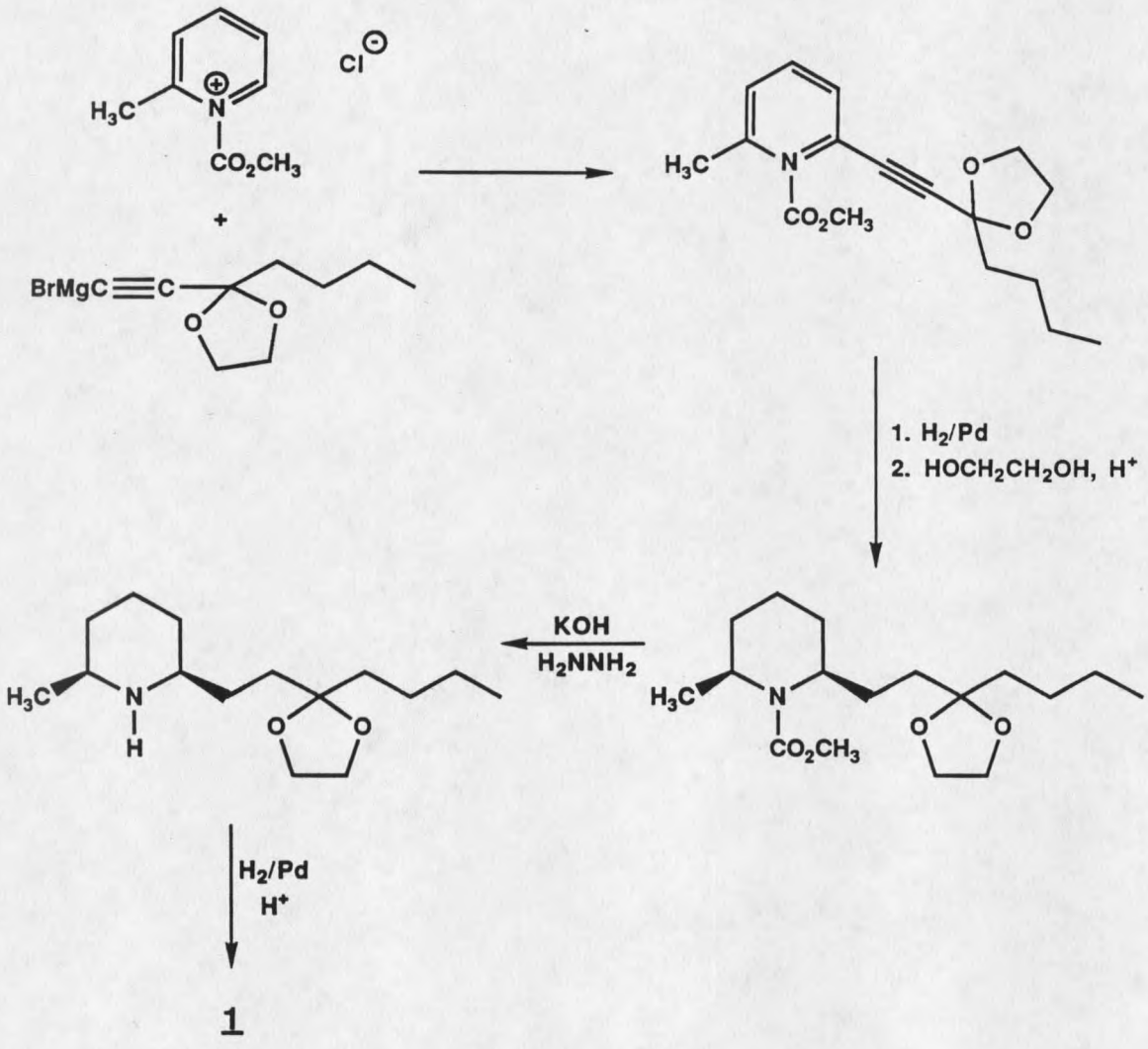
The most promising racemic synthesis of monomorine I was advanced by Yamaguchi in 1987[52]. This synthesis employed the nucleophilic addition of an alkynyl Grignard to a pyridinium chloride as a key bond forming step (Scheme 16).

The overall yield for this synthesis, based on the Grignard, was 28 %. The addition of the Grignard to the pyridinium chloride was not, and likely could not be induced to be, enantioselective. Because the stereochemical outcome of the synthesis was set at this stage, it is doubtful that this approach could be parlayed into an enantioselective synthesis of (+)-monomorine I.

Our interest in 1 was based primarily on its use to probe the synthetic utility and functional group compatibility of the catalytic $CpTiCl_3$ mediated annulation


1. H3CO OCH3
2. n-H7C3COCl, NMM
AlCl3
1. CH2N2
2. AgOAc
3. CH2N2
15%
66%
51% R1=R2=H (1)
21% R1=OH, R2=H
8% R1=H, R2=OH

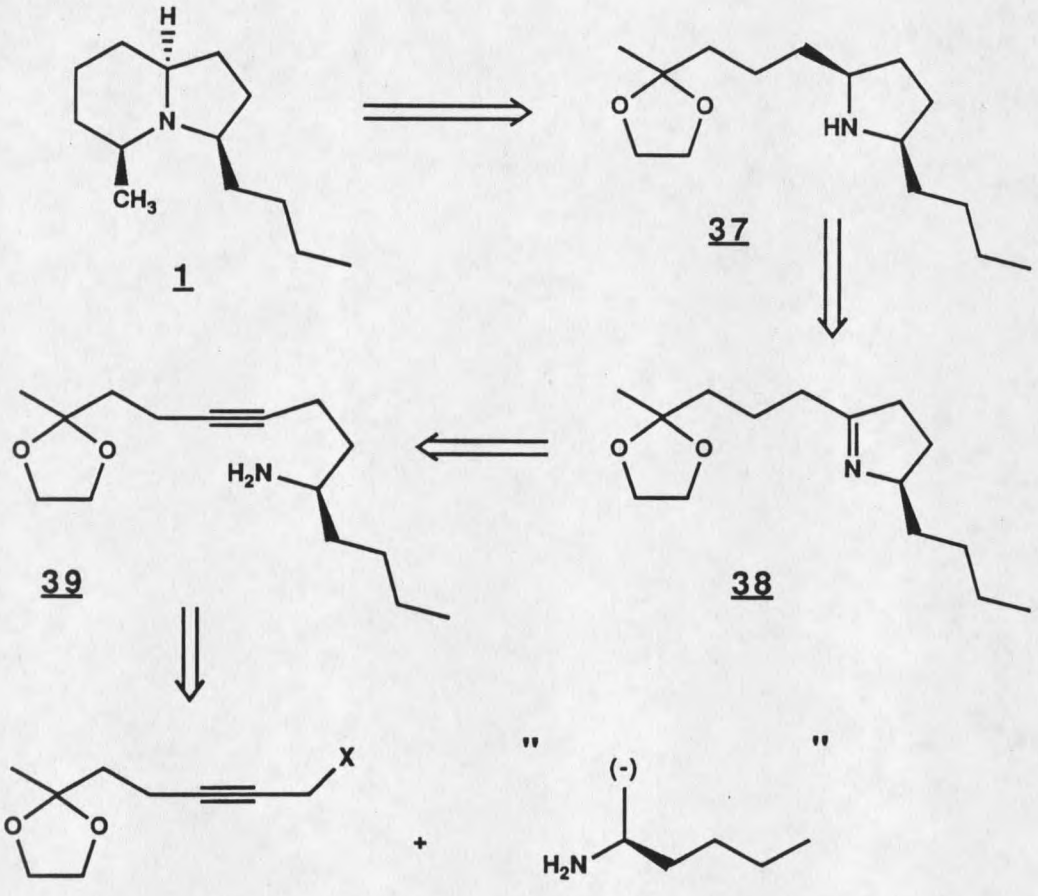
Scheme 15



Scheme 16

of alkynylamines. A secondary goal was to facilitate a future enantioselective synthesis of 1 by developing a racemic synthesis that either 1) employed, at an early stage in the synthesis, an intermediate that could be derived in an enantiopure form from a readily available ("chiral pool") source, or 2) proceeded *via* an intermediate that was

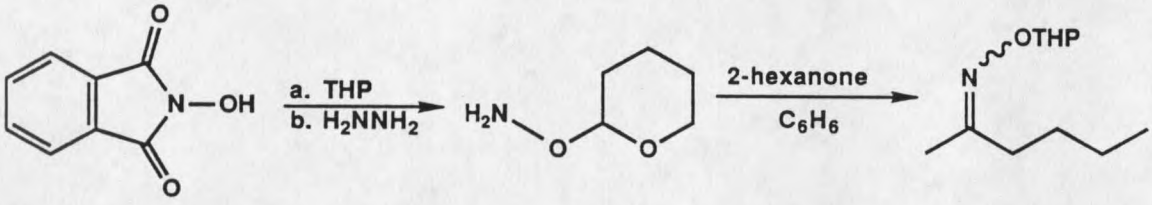
stereogenic and, possibly, amenable to an asymmetric transformation (e.g., reduction, alkylation).



Scheme 17

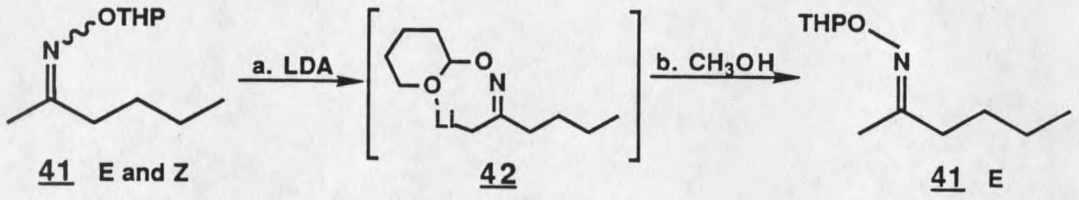
Retrosynthetic analysis of **1** revealed an intramolecular reductive amination that had been exploited previously by Stevens[56]. We envisioned intermediate **37** to arise *via* a $CpTiCl_3$ mediated cycloaddition followed by selective reduction of the anticipated Δ^1-pyrroline **38**. The precyclic alkynylamine **39** required as the key intermediate could likely be prepared *via* alkylation of an δ-amino anion

equivalent with an appropriate propargylic halide (Scheme 17). The successful application of this general strategy to the total synthesis of monomorine I is described below.



40 **41** E and Z

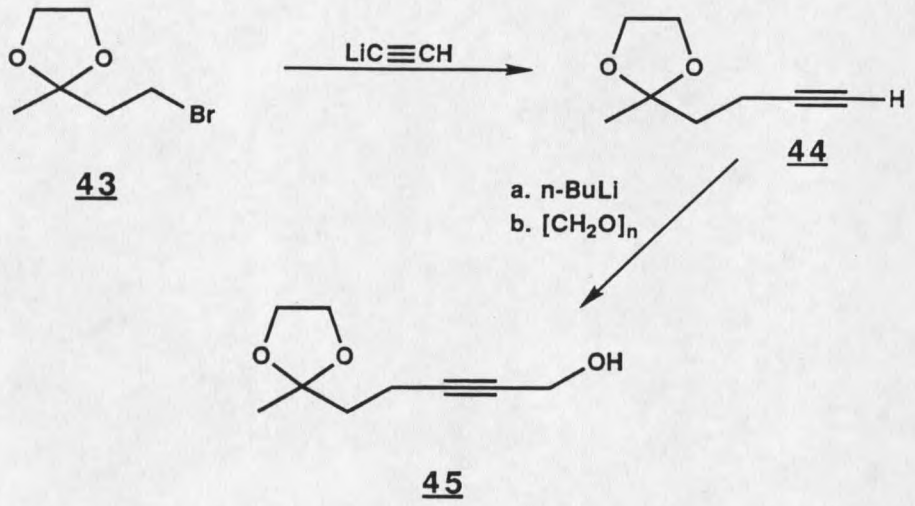
Eq. 28



41 E and Z **42** **41** E

Eq. 29

Hydroxylamine **40** was prepared using a modification of the literature procedure[59]. Condensation of **40** with 2-hexanone under Dean-Stark conditions gave oximes **41** in excellent yield (Eq. 28). THP-oximes of this type were known to react with LDA under equilibrating conditions to give anions corresponding to deprotonation of the methyl group selectively[60]. This method was applicable to oximes **41** as shown by the deprotonation-quenching experiment depicted in Eq. 29. Although lithiated oximes similar to **42** had previously been alkylated with acetone[60], we needed to extend the field of alkylating agents to include halides in order to elaborate the carbon backbone of alkynylamine **39**.

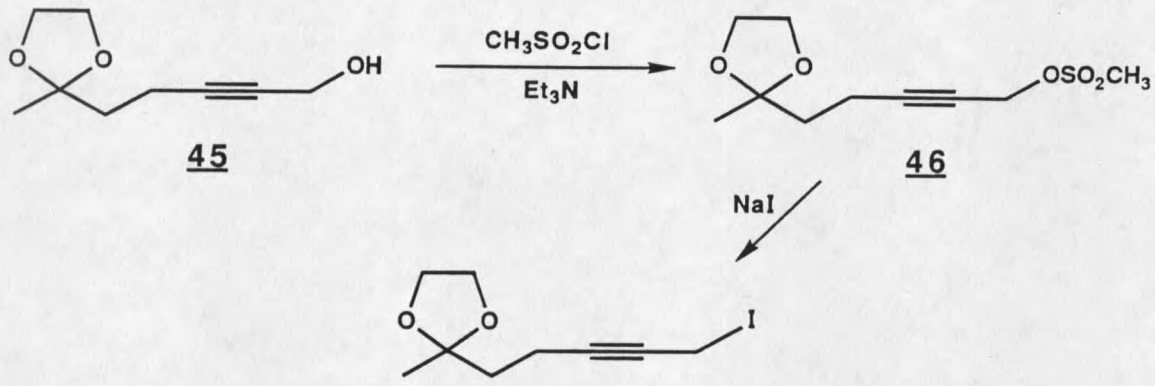


43 44 45

Scheme 18

The halide required as the alkylating agent for lithiated oxime **42** was prepared as follows. 2-(2-bromoethyl)-2-methyl-1,3-dioxolane (**43**)[61,62] was converted to the terminal alkyne **44** by displacement with lithium acetylide[63,64]. Lithiation of alkyne **44** with n-BuLi followed by treatment with paraformaldehyde afforded the alcohol **45** (Scheme 18)[65]. The crude alcohol **45** was mesylated[66] using standard conditions, and the product was purified by recrystallization from Et_2O to give the mesylate **46** as a white solid. Iodide mediated displacement[67] of **46** gave the requisite propargylic iodide **47** (Scheme 19).

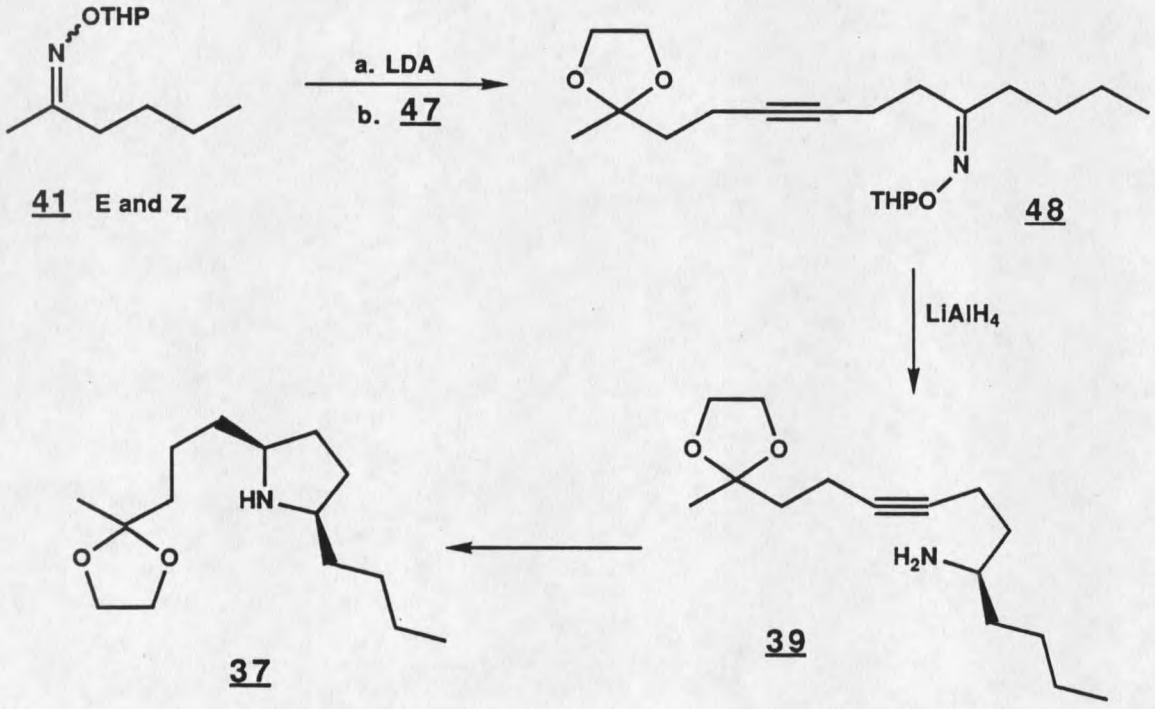
With the iodide **47** and the oximes **41** in hand, we were in a position to attempt the alkylation experiment. We were pleased to find that treatment of the oximes **41** first with LDA, and then with the iodide **47**, gave oxime **48** in good



45 46 47

Scheme 19

yield. Oxime **48** was converted directly to the key precyclic alkynylamine **39** by reduction with $LiAlH_4$[68] (Scheme 20).

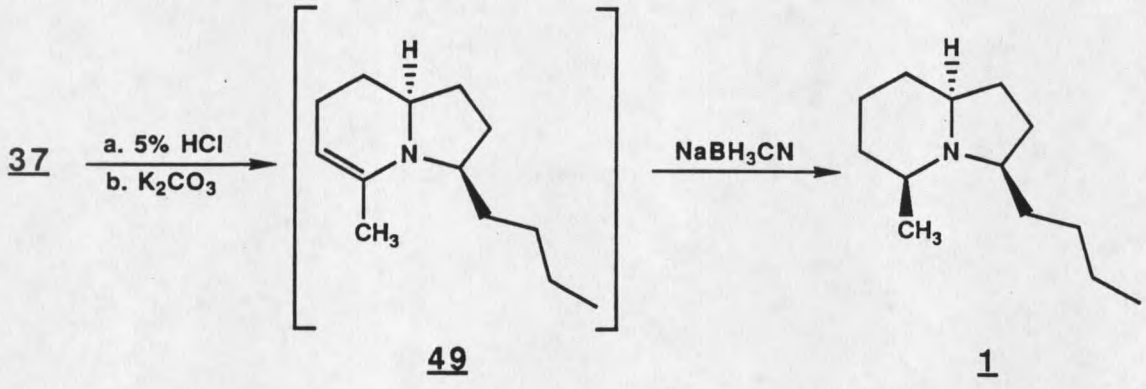


41 E and Z **48** **39** **37**

Scheme 20

Alkynylamine **39** was smoothly converted to the Δ^1-pyrroline **38** in 93 % yield using the *catalytic* $CpTiCl_3$

cycloaddition protocol described earlier. To this end, **39** was added to a solution of $CpTiCl_3$ and NEt_3 in THF at 25 °C. After the usual workup, **38** was recovered as the sole reaction product. Selective reduction of **38** to the cis-pyrrolidine **37** was accomplished with DiBAL-H[69] (Scheme 20).

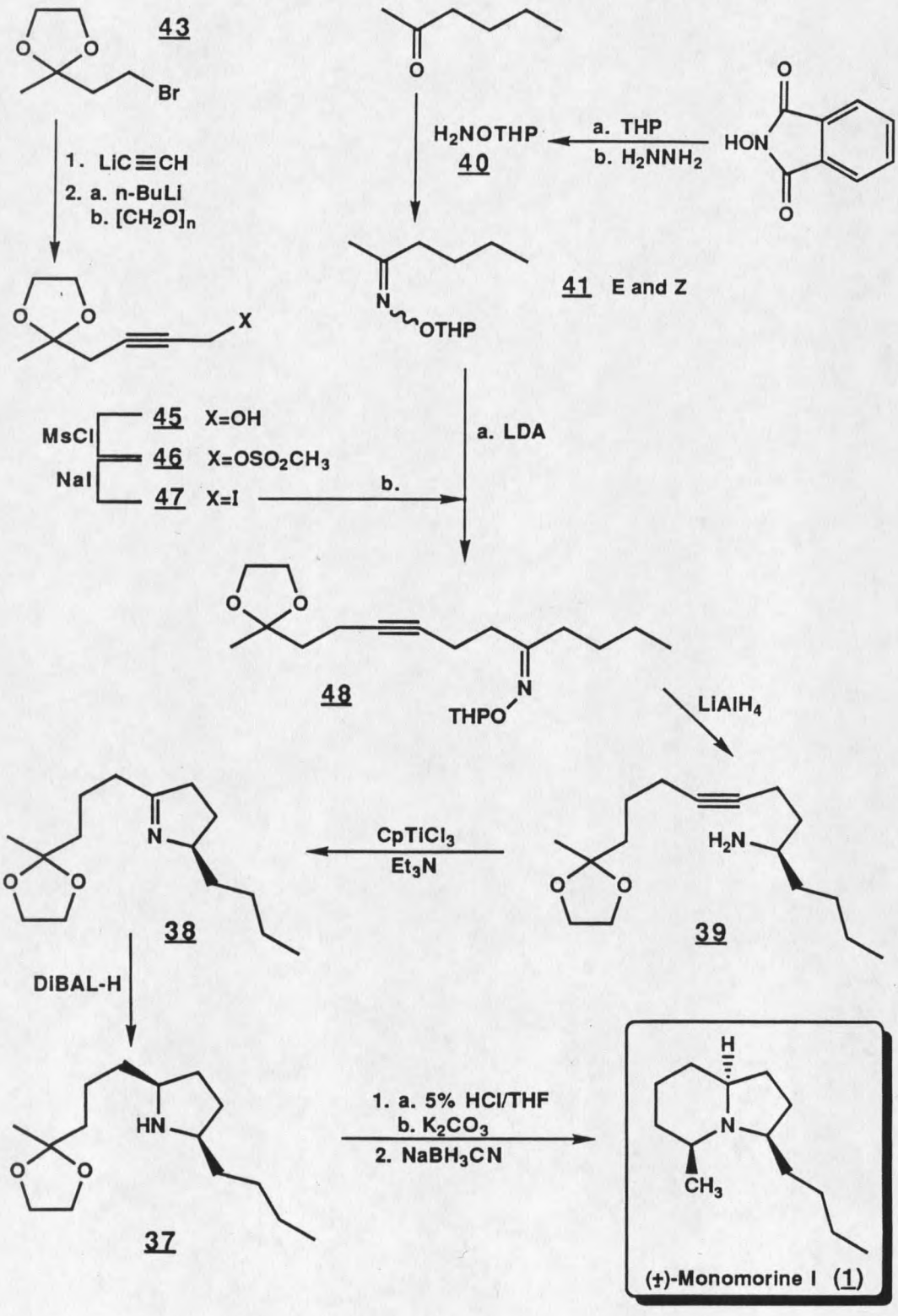


49 **1**

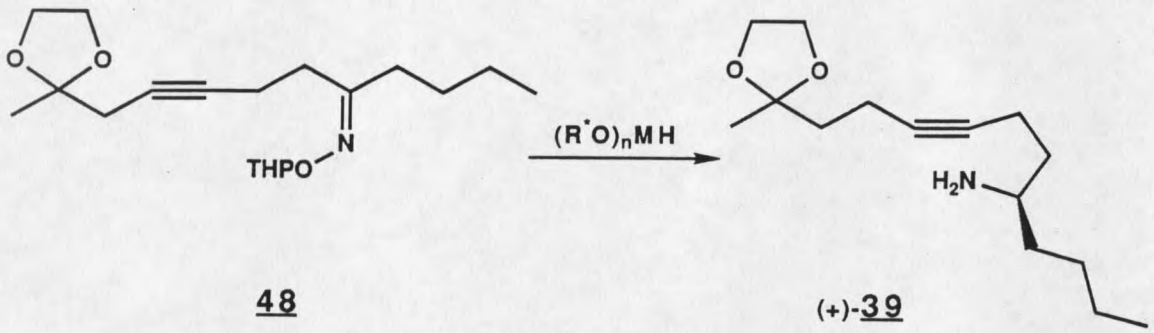
Eq. 30

The synthesis was then completed using the general procedure of Stevens[56]. Accordingly, **37** was treated with 5 % HCl followed by a basic workup. The unstable enamine **49** was immediately reduced with $NaBH_3CN$ to furnish (±)-monomorine I in 72 % chromatographed[70] yield (Eq. 30). The spectroscopic characteristics of synthetic (±)-**1** as prepared above were identical in all respects with those reported[48] for other synthetic samples of the alkaloid. The overall synthesis is illustrated in Scheme 21.

Some key points of merit for this synthesis are the high yield (53 % from the point of convergence), the functional group compatibility of the catalytic cyclization,


43
Br
1. LiC≡CH
2. a. n-BuLi
b. [CH2O]n
X
H2NOTHP
40
a. THP
b. H2NNH2
HON
O
O
N
OTHP
41 E and Z
MsCl
NaI
45 X=OH
46 X=OSO2CH3
47 X=I
b.
a. LDA
48
THPO
N
LiAlH4
N
38
CpTiCl3
Et3N
H2N
39
DiBAL-H
HN
37
1. a. 5% HCl/THF
b. K2CO3
2. NaBH3CN
H
N
CH3
(±)-Monomorine I (1)

Scheme 21



48 (+)-**39**

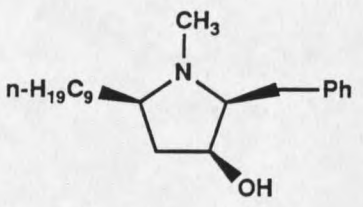
Eq. 31

and the novel use of oximes **41** as an δ-amino anion equivalent. Because it was beyond the scope of this thesis, we have not attempted to utilize this general approach to indolizidines in the asymmetric synthesis of these alkaloids. However, it may be possible to apply the known methods[71-73] for the asymmetric reductions of oximes to oxime **48**. If successful, this would generate (+)-**39**, leading eventually to (+)-monomorine (**1**) (Eq. 31).

The Enantioselective Total Synthesis of (+)-Preussin (**2**).

The synthetic utility of titanium imido-alkyne cycloaddition reactions was further demonstrated in a short, highly convergent and enantioselective synthesis of (+)-preussin (**2**) (Figure 6).

Preussin, first described by Schwartz in 1988, has been shown to be a broad spectrum antifungal agent possessing activity against both fungi and yeast[24]. The relative and absolute stereochemistry of **2** were assigned in 1989[74], and



2

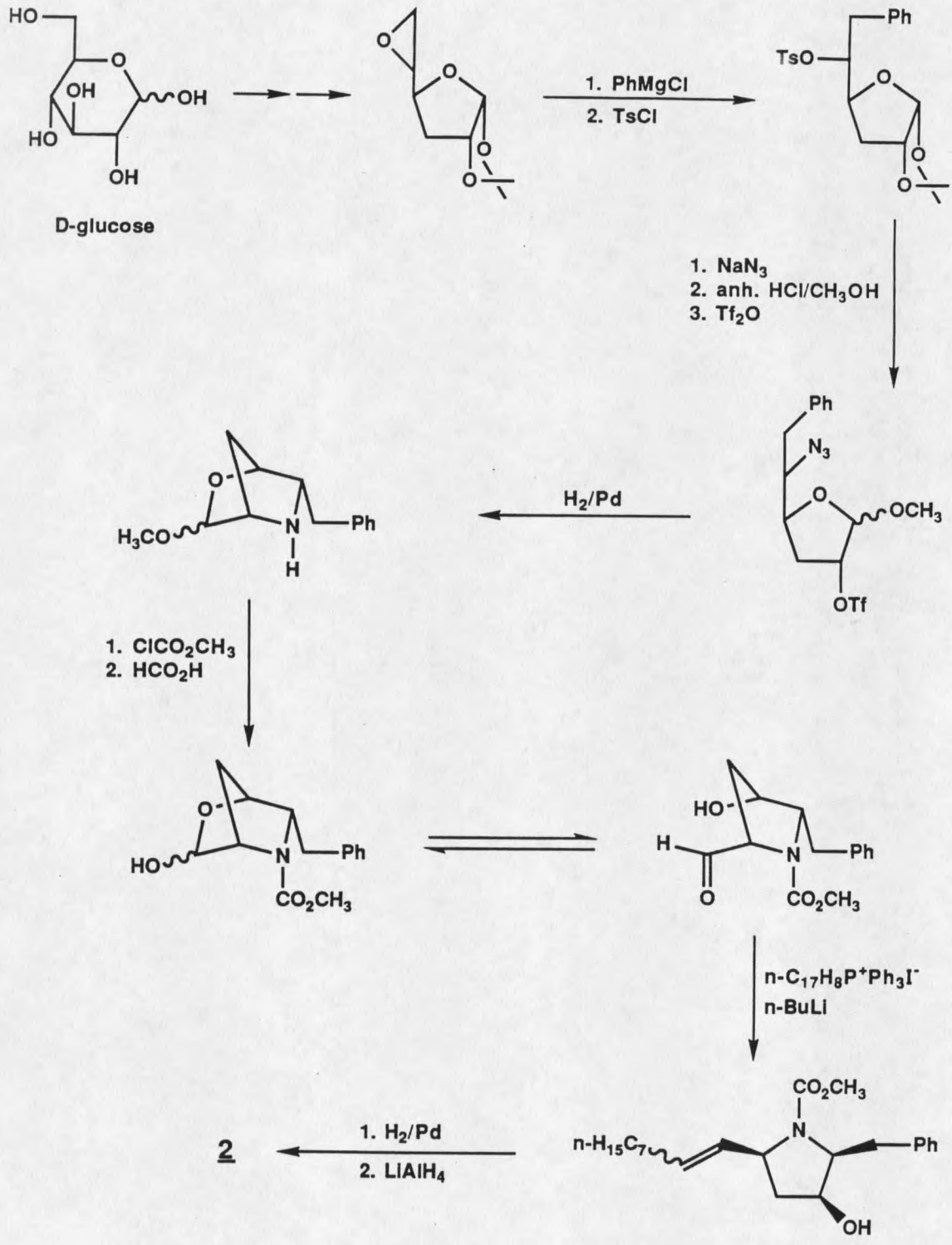
Figure 6. (+)-Preussin (2).

it has since been the subject of one synthesis[75]. This interesting approach to (+)-preussin employed D-glucose as the starting material (Scheme 22).

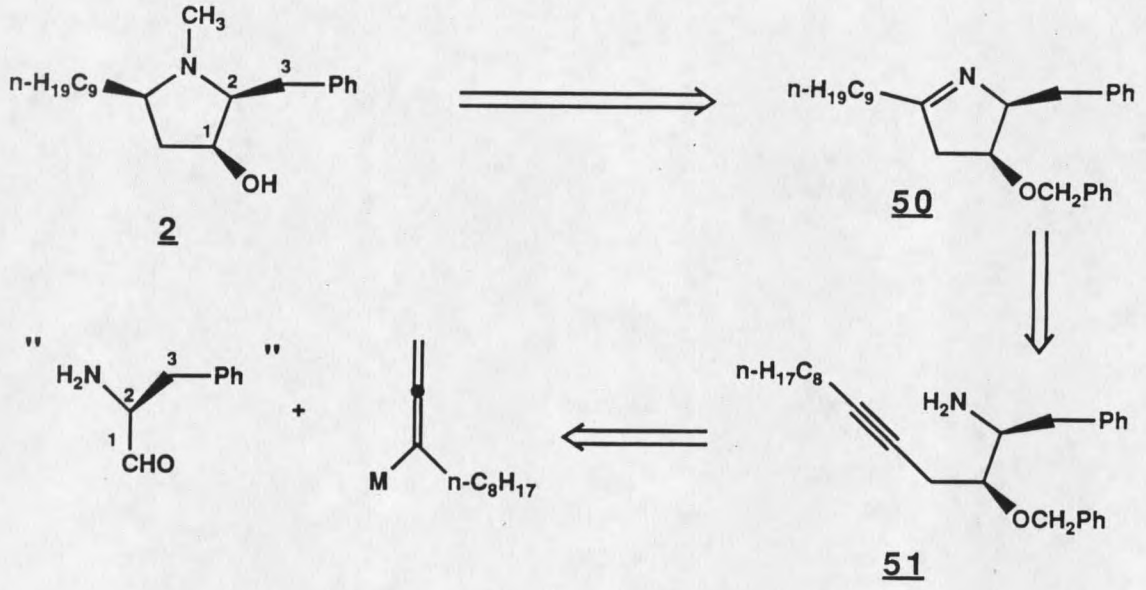
In contrast to this previous synthesis, we envisioned an approach that exploited the L-phenylalanine backbone inherent in **2**. Our initial retrosynthetic analysis of **2** implicated Δ^1-pyrroline **50** as a likely target. One-pot cis-reduction, N-methylation and hydrogenolysis of the benzyl protecting group would be expected to yield **2**. The Δ^1-pyrroline **50** was anticipated to arise *via* a $CpTiCl_3$ mediated cycloaddition of the alkynylamine **51**.

As alkynylamine **51** was a protected threo aminoalcohol, it seemed likely that it could be prepared by chelation-controlled addition of an organometallic to a phenylalaninal equivalent (Scheme 23). The application of this general strategy to the preparation of alkynylamine **51** is described below.

In recent publications[76,77], Polt has described the use of diphenylmethylidene protected aminoesters as equivalents

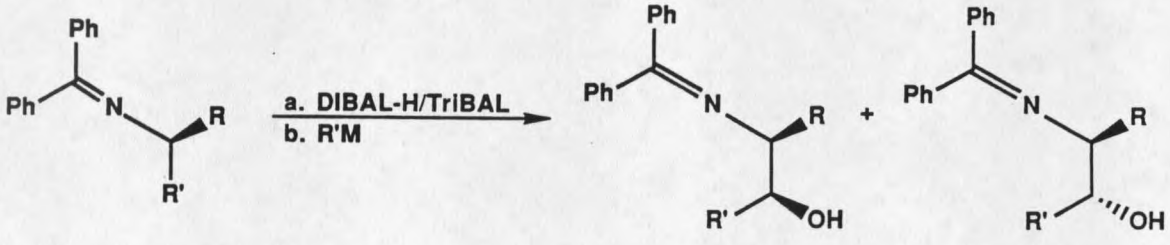

HO
OH
HO
OH
OH
D-glucose
1. PhMgCl
2. TsCl
Ph
TsO
1. NaN3
2. anh. HCl/CH3OH
3. Tf2O
Ph
N3
OCH3
OTf
H2/Pd
H3CO
Ph
1. ClCO2CH3
2. HCO2H
HO
Ph
CO2CH3
HO
H
Ph
CO2CH3
n-C17H8P+Ph3I-
n-BuLi
CO2CH3
n-H15C7
Ph
OH
2
1. H2/Pd
2. LiAlH4

Scheme 22

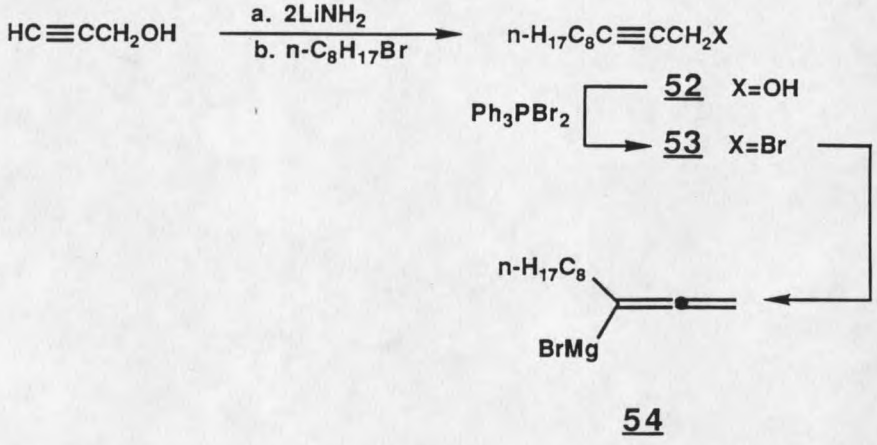


Scheme 23

for threo aminoalcohols (Eq. 32). Although this work employed either aryl magnesium halides or vinyl lithiums as the organometallic, it seemed likely that allenyl Grignards could also function in this capacity. For this purpose, the propargylic bromide 53 was prepared and converted to the allenyl Grignard 54 (Scheme 24).

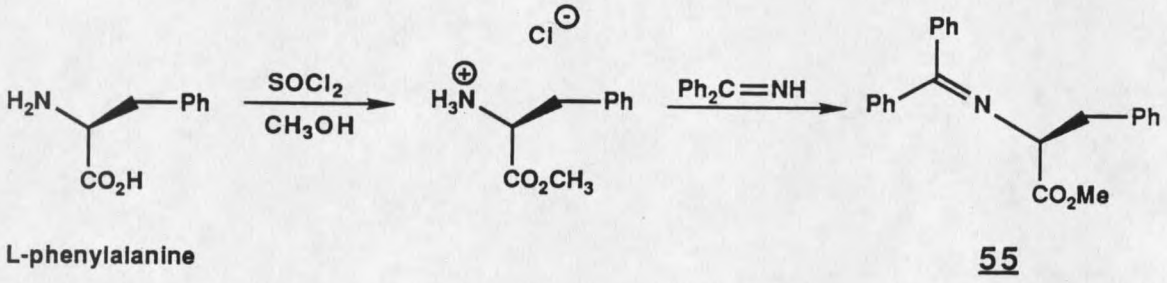


Eq. 32



54

Scheme 24



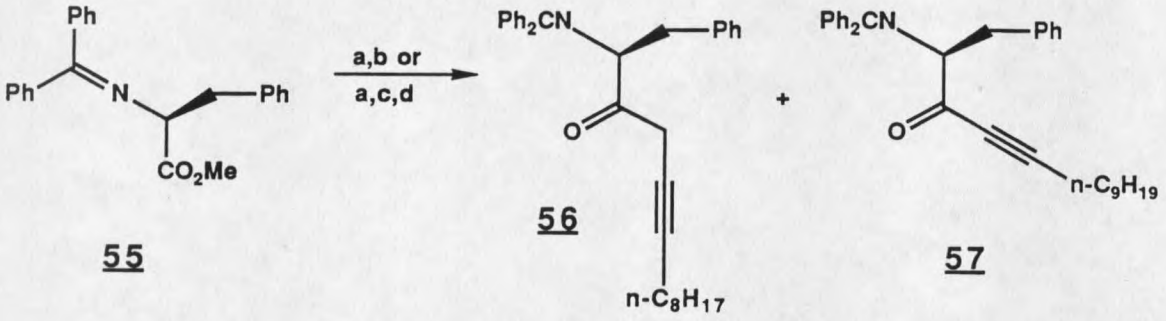
L-phenylalanine

55

Eq. 33

The protected aminoester 55 required in this sequence was prepared according to Eq. 33[78,79]. Much to our dismay, treatment of 55 with DiBAL-H/TriBAL, followed by three equivalents of the allenyl Grignard 54, did not lead to the expected alcohol. The product mixture was comprised of a mixture of ketones, most likely 56 and 57 based on their ^{1}H and ^{13}C NMR spectra. Interestingly, the same product mixture was obtained when first two equivalents of PhMgBr

and then one equivalent of the allenyl Grignard 54 were employed (Eq. 34).

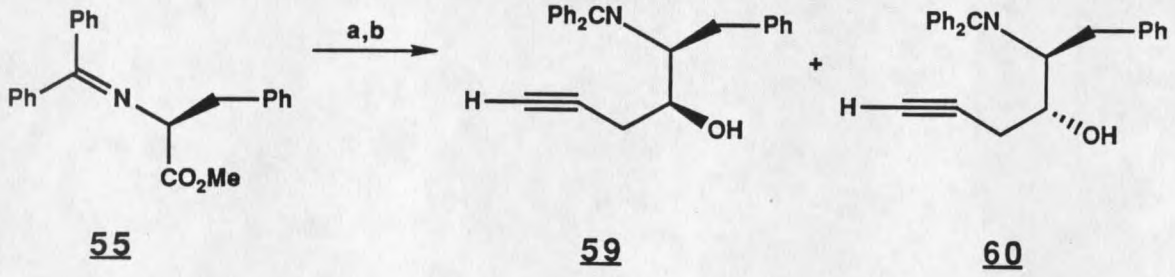


55 56 57

a. DiBAL-H/TriBAL (1 eq) b. 54 (3 eq)
c. PhMgBr (2 eq) d. 54 (1 eq)

Eq. 34

This obstacle was removed by substitution of the parent allenyl Grignard 58 for 54. Accordingly, we were able to obtain iminoalcohols 59 and 60 (Eq. 35). Chromatographic separation[70] of the diastereomeric mixture gave 59 and 60 in a 3.2:1 ratio and 74 % combined yield.

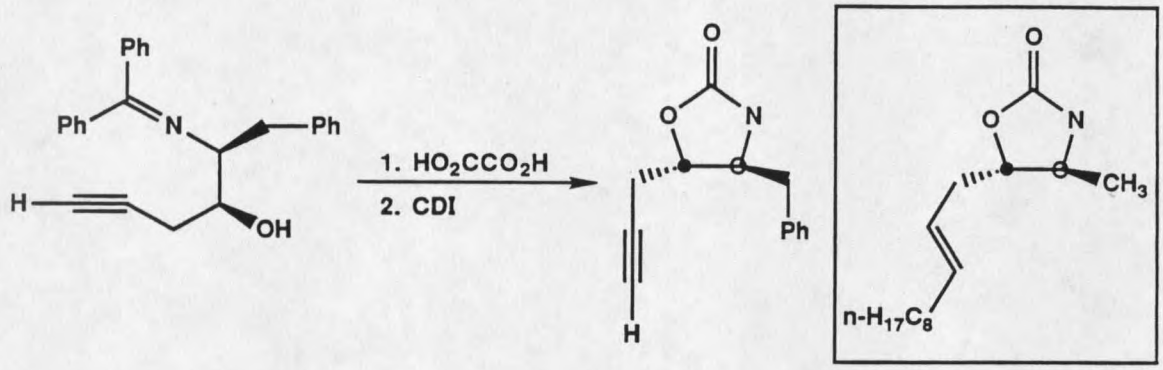


55 59 60

a. DIBAL-H/TriBAL (1 eq)
b. $H_2C{:}C{:}C(H)MgBr$ (58) (3 eq)

Eq. 35

Support for our initially intuitive assignment of the diastereomers was derived by hydrolysis of **59** and conversion of the resulting amine to the oxazolidinone **61**[80] (Eq. 36). The vicinal coupling constant of 6.6 Hz for the -OCH-HCN- resonances was consistent with that reported for the similar oxazolidinone **62** (7.6 Hz)[77].

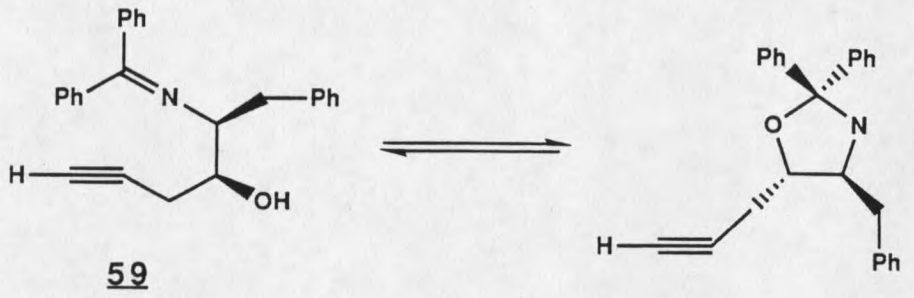


59 **61** **62**

Eq. 36

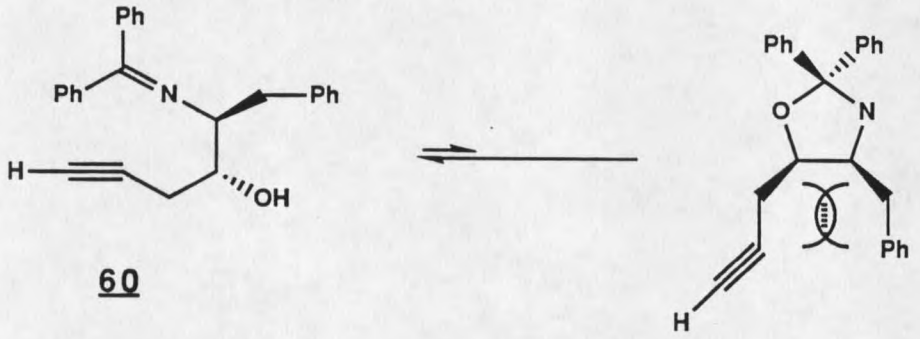
Additional support for this assignment was garnered from the observation that gelatinous **59** existed in equilibrium with its oxazolidine tautomer (Eq. 37), whereas crystalline **60** exhibited no tautomeric equilibrium as observed by ^{1}H or ^{13}C NMR. This observation was consistent with the nonbonding interaction expected upon tautomerization of **60** (Eq. 38).

Iminoalcohol **59** was selectively O-alkylated to give **63** by deprotonation with KH followed by treatment with benzyl bromide[81]. The efficacy of C-lithiation was demonstrated



59

Eq. 37

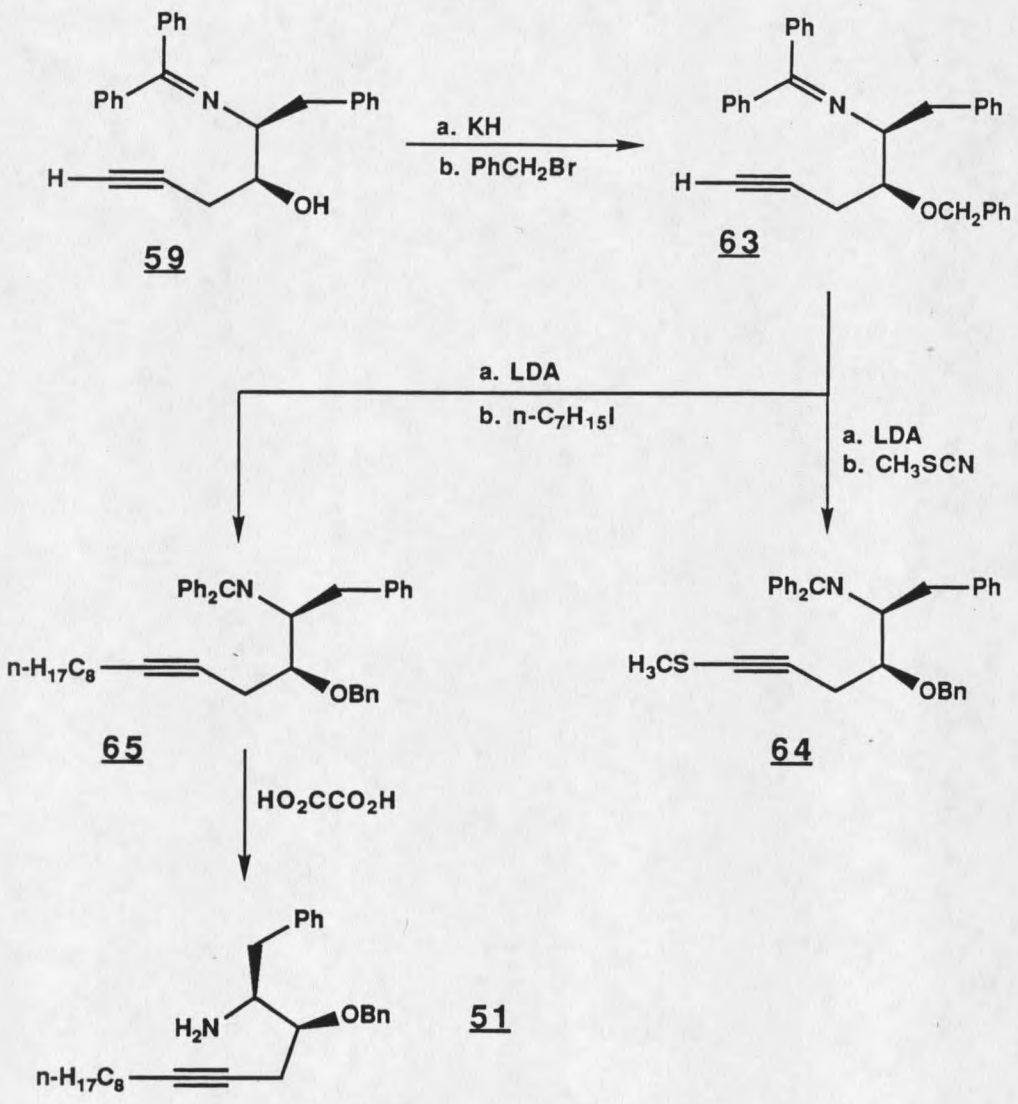


60

Eq. 38

using CH_3SCN to yield **64** before n-octyl iodide was employed. Hydrolysis of the diphenylmethylidene protecting group of **65** afforded the desired alkynylamine **51** (Scheme 25).

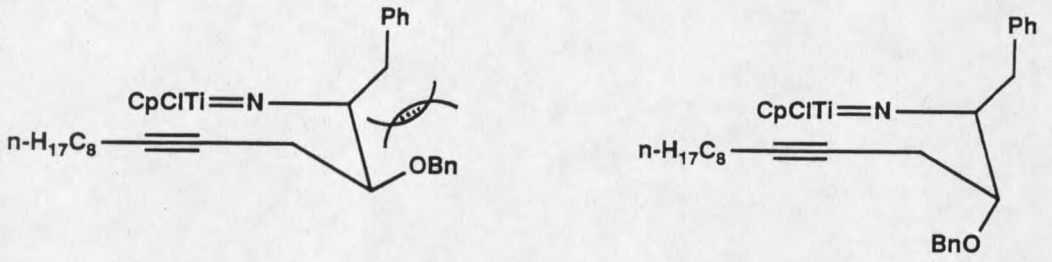
Much to our dismay, alkynylamine **51** was not amenable to $CpTiCl_3$ mediated cyclization. Even the forcing conditions implemented to effect tetrahydropyridine formation (80 °C, C_6H_6) failed with **51**. A likely cause of this failure was thought to be the unfavorable eclipsing interactions that would develop with syn coplaner approach[82] of the alkynyl moiety and the imido linkage. However, attempted cyclization of **51**'s (2S,3R) diastereomer, **66**, in which the



Scheme 25

developing eclipsing interactions during cyclization would be greatly diminished, also failed (Figure 7).

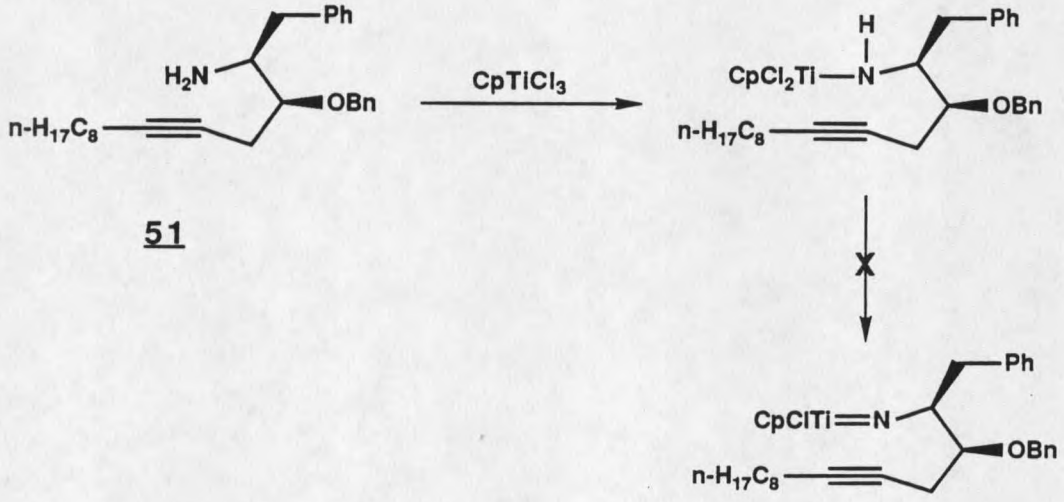
Although not conclusive, this result suggested that an unfavorable transition state was not the causative agent of annulation failure. In fact, it was determined by ^{1}H NMR of an equimolar solution of 51 and $CpTiCl_3$ that the elimination



51 (2S,3S) **66** (2S,3R)

Figure 7. Proposed Transition States For Cycloaddition.

of the second HCl equivalent did not occur. Thus, a reactive imido complex 67 was not being generated (Scheme 26).

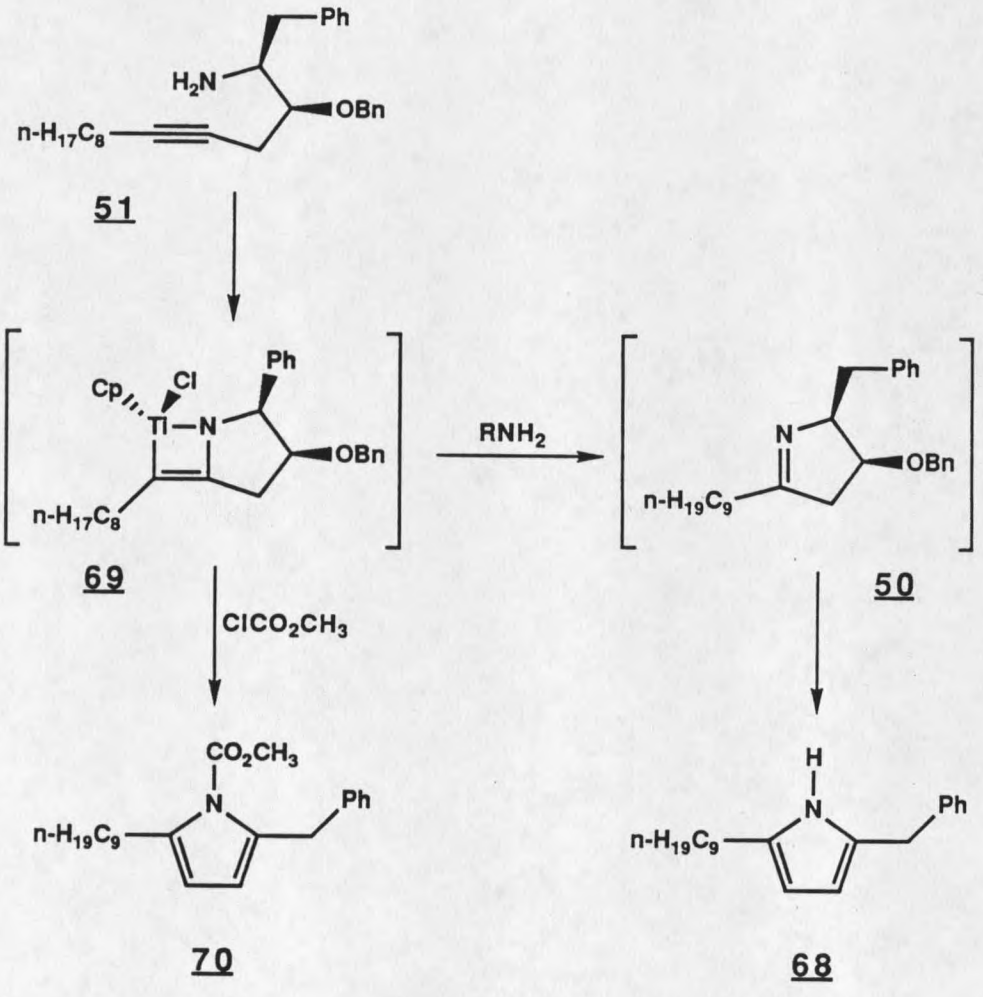


51 **67**

Scheme 26

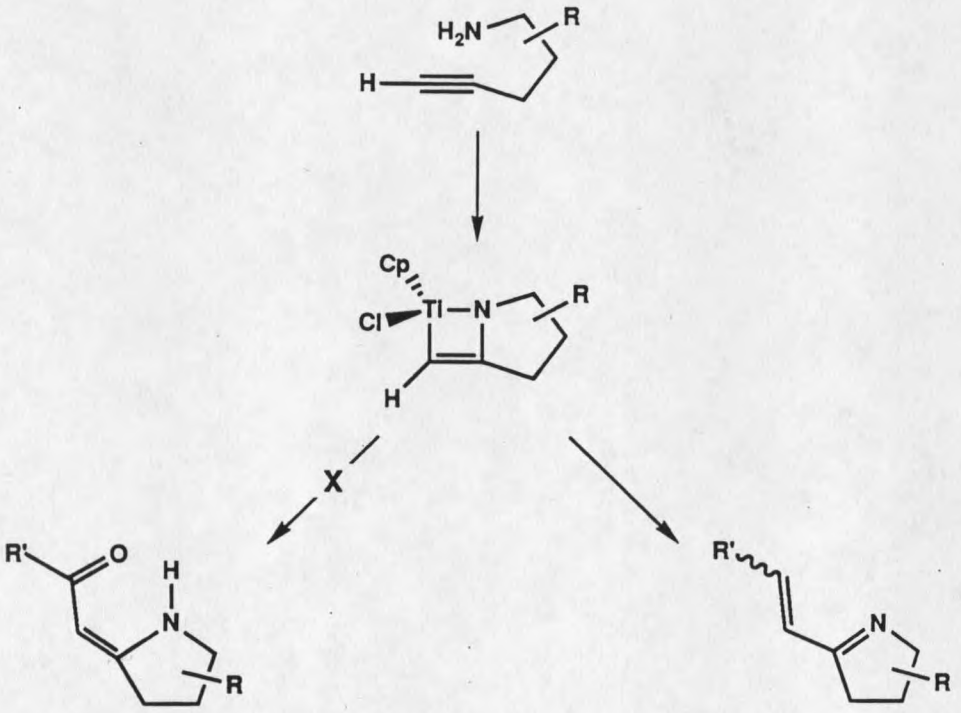
In anticipation of a more facile elimination of methane from a methyl amido complex, refluxing solutions of $CpTi(CH_3)_2Cl$ in THF, DME and benzene were treated with

alkynylamine **51**. The reaction conducted in THF afforded only starting material, whereas both the reaction in DME and that in benzene yielded the pyrrole **68**. Although it was encouraging that cyclization had occurred, we had lost the two key stereocenters *via* elimination of benzyl alcohol. We sought to circumvent this elimination by treating the putative metallocycle **69** with methyl chloroformate. In this case we recovered the N-carbomethoxy pyrrole **70** (Scheme 27).



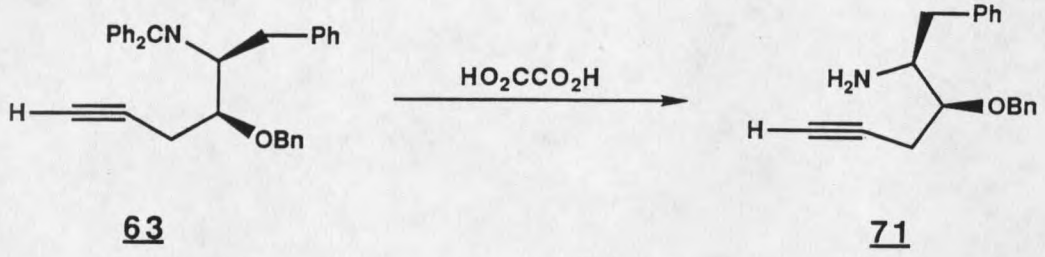
Scheme 27

Rather than attempt to elucidate a specialized set of conditions that would allow cyclization of **51** to **50** with retention of the two stereocenters, we sought a more general solution. We had noted earlier that terminal alkynes were markedly more reactive toward imido complexes. We planned to combine this reactivity difference with a nucleophilic addition of the metallocycle[30] to generate a stabilized vinylogous amide or conjugated Δ^1-pyrroline (Scheme 28).



Scheme 28

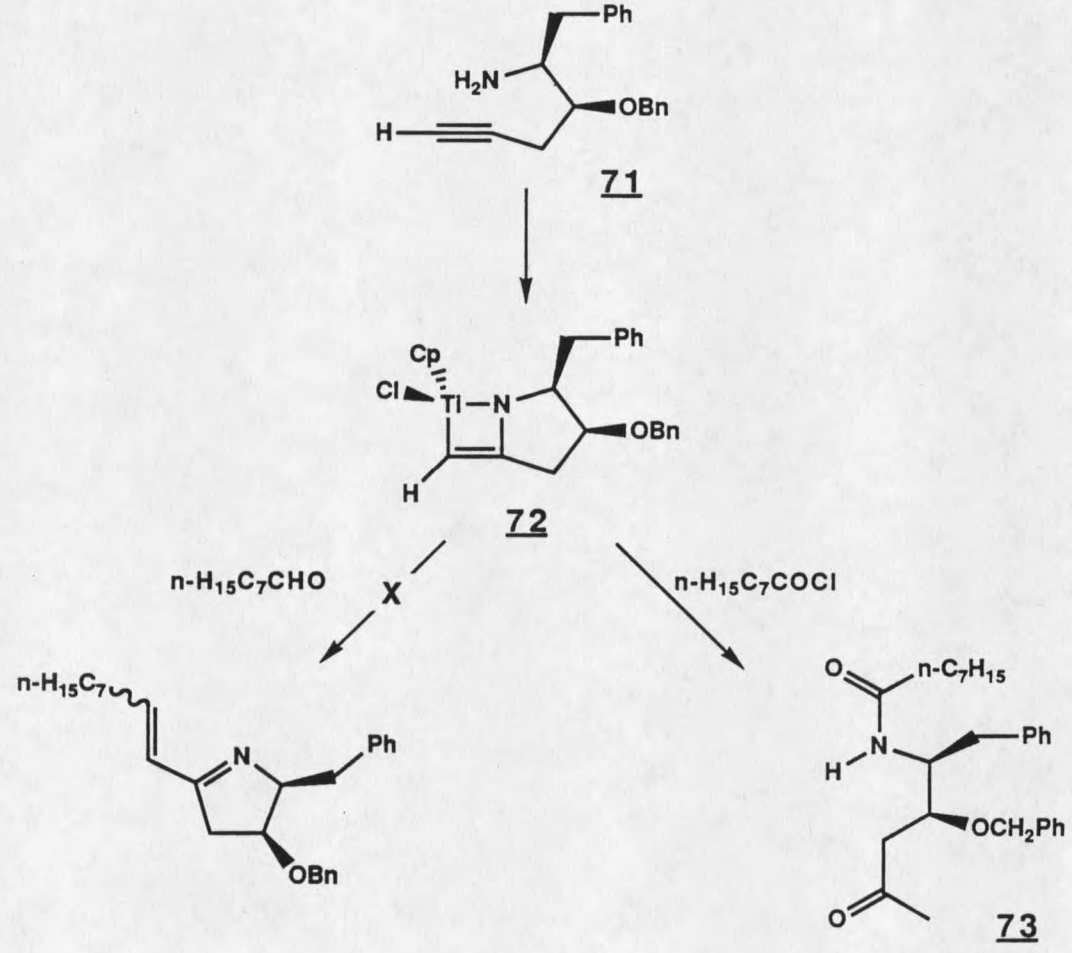
The terminal alkynylamine **71** was readily available *via* N-deprotection of the Schiff base **63** we had prepared previously (Eq. 39). This substrate was found to undergo



63 71

Eq. 39

facile cycloaddition when added to $CpTi(CH_3)_2Cl$ at 0 °C, followed by warming to 25 °C (Scheme 29).



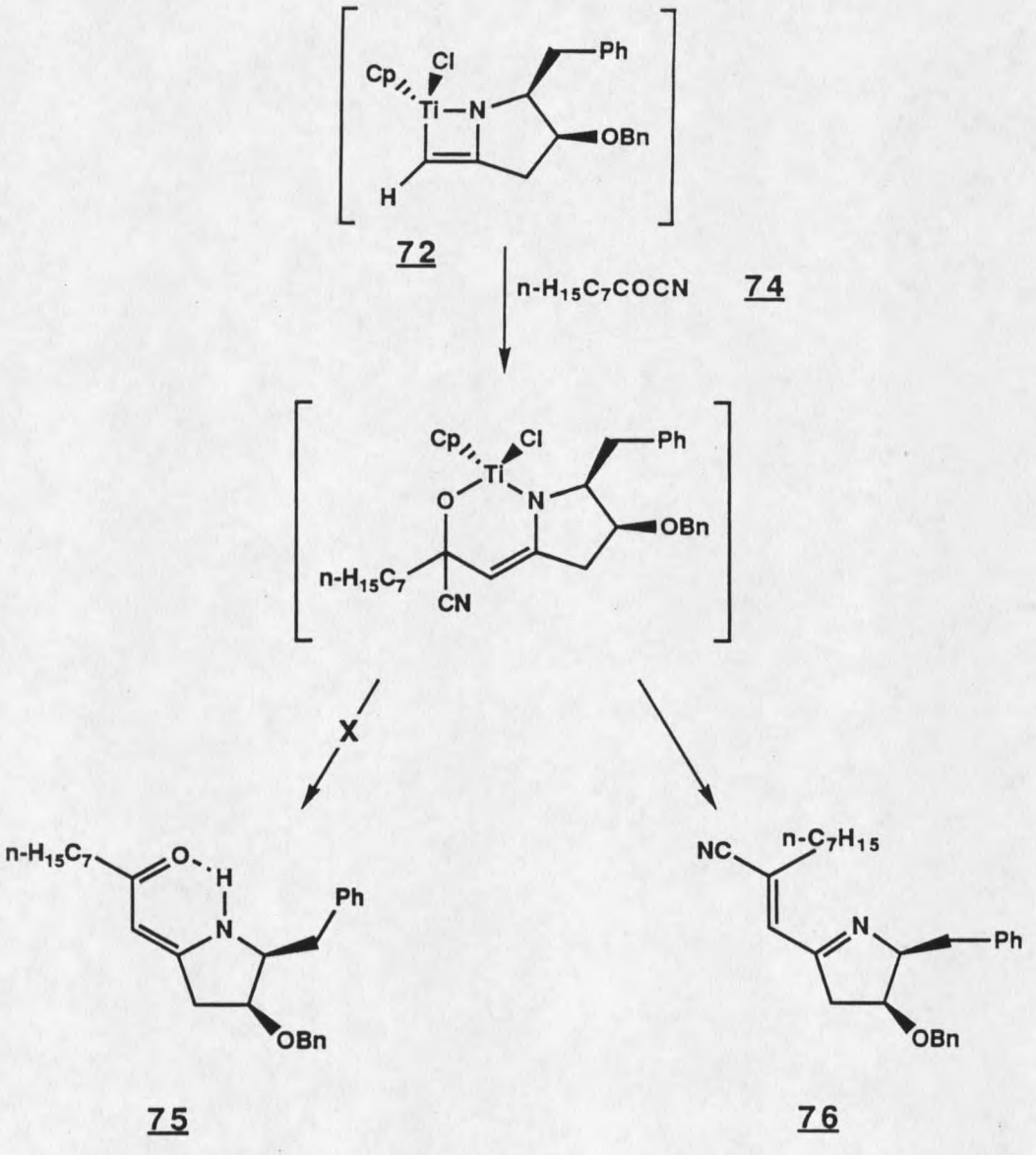
Scheme 29

Although Jensen[30] had noted that acyl chlorides reacted with the Ti-N bond of azatitanetines, we had hoped that the

relatively unhindered Ti-C bond of azatitanetine **72** would allow for reaction at that site in preference to the Ti-N bond. Despite this, ketoamide **73** was obtained exclusively in accord with Jensen's observations.

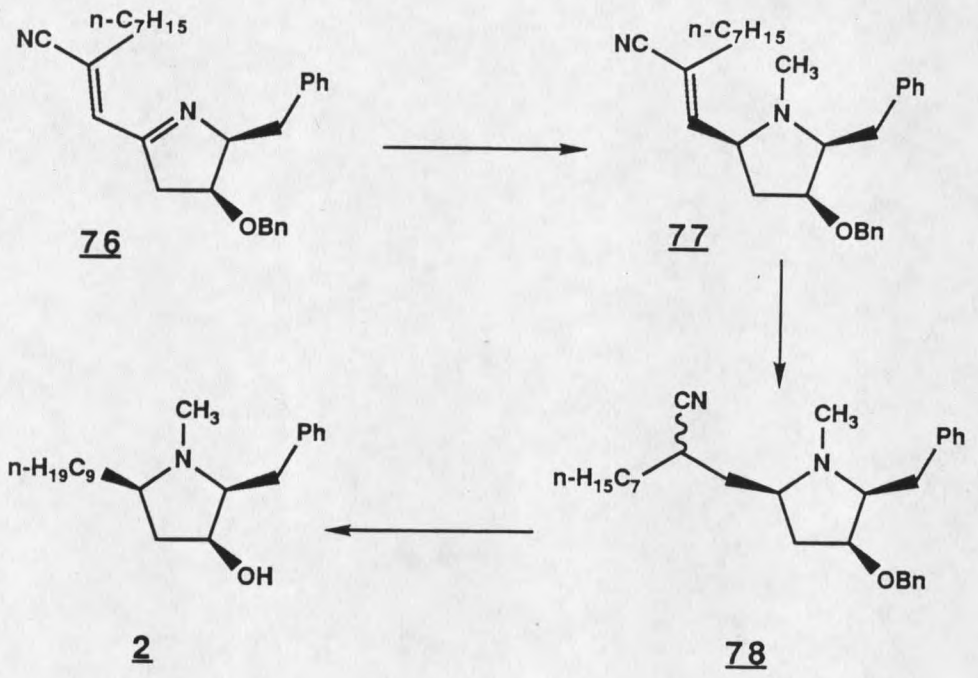
The reaction of n-octanal with **72**, to the extent that it did occur, did not yield an isolable, stabilized product. Fortuitously, Jensen had determined that acyl nitriles[83] reacted exclusively with the Ti-C bond of azatitanetines. Accordingly, azatitanetine **72** was treated with n-octanoylnitrile (**74**). Formation of vinylogous amide **75** would have been in accord with Jensen's findings. Interestingly, the unhindered azatitanetine **72** gave the unsaturated nitrile **76** as the primary product (Scheme 30).

While nitrile **76** was unstable in pure form at 25 °C, it was stable in solution at 25 °C or neat at -20 °C. This stability, and the lack of a suitable alternative, motivated us to pursue the conversion of **76** to (+)-preussin. This was accomplished in a straightforward manner as described below. Treatment of the nitrile **76** with CH_3OTF, followed by $NaBH_3CN$ afforded the N-methylated pyrrolidine **77**. Conjugate reduction[84] of **77** was accomplished with Mg/CH_3OH to afford the diastereomeric nitriles **78**. Reductive decyanation[85] and cleavage of the benzyl protecting group were then effected with K/HMPA in Et_2O/C_7H_8. It should be noted that the literature procedure does not employ toluene as a cosolvent, in which case reduction of aromatic rings was also observed.



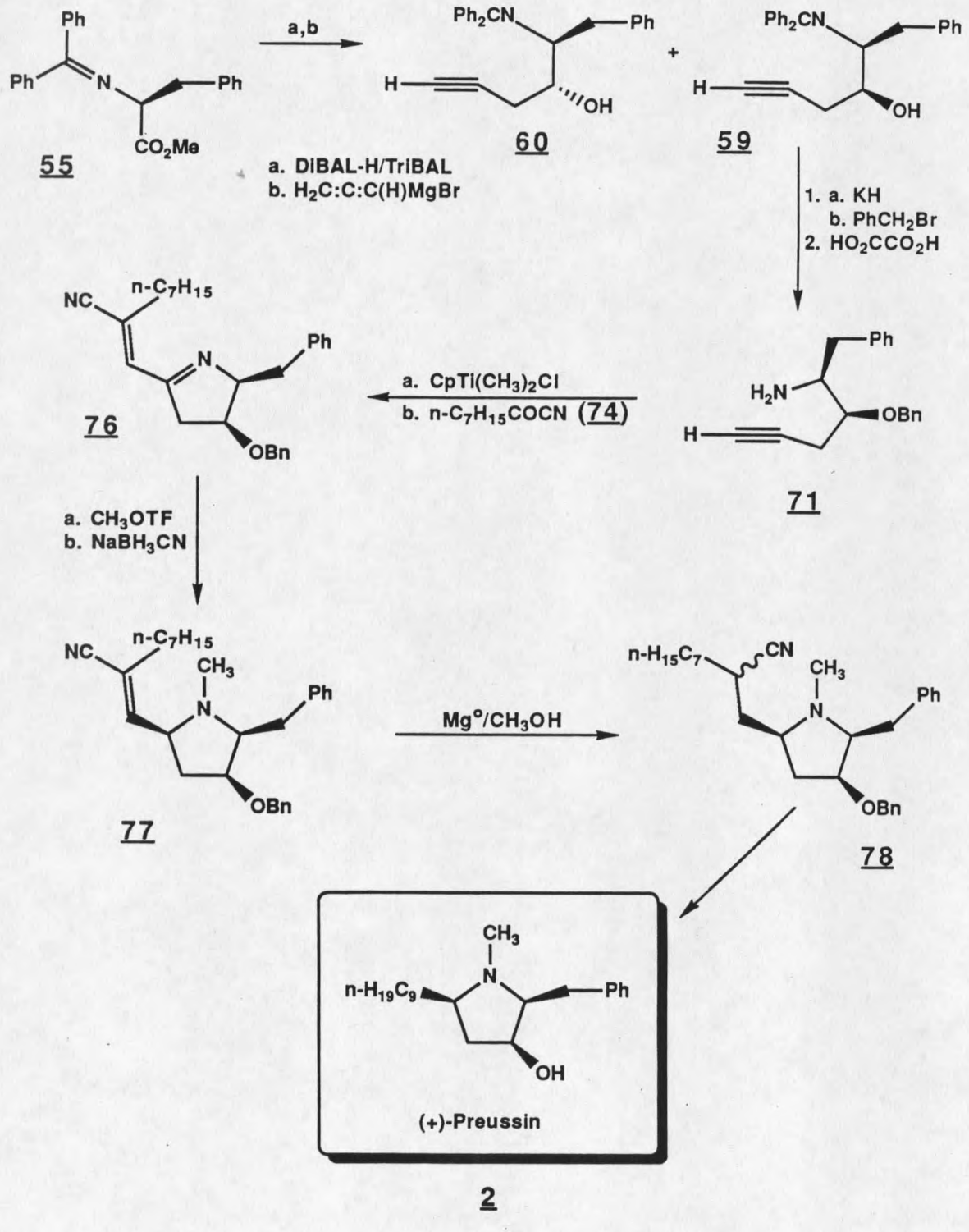
Scheme 30

The utilization of toluene as cosolvent eliminates this limitation. Also in accord with literature precedent, this procedure gave rise to some reductive elimination products. However, simple exposure of the crude reaction mixture to Pd-C/H_2 reduced these products to 2 (Scheme 31).



Scheme 31

The spectroscopic properties of synthetic (+)-preussin 2 were in excellent agreement with those of authentic[24] and synthetic[75] preussin. The overall synthesis of (+)-preussin is presented in Scheme 32. The short length, high convergence and enantioselectivity of the synthesis are particularly noteworthy. Additionally, as can be seen from Scheme 32, this approach should be quite amenable to the preparation of analogs *via* substitution of alternative acyl nitriles or amino esters for those we employed in the synthesis of (+)-preussin (2).


Ph
Ph
N
Ph
CO2Me
55
a,b
a. DIBAL-H/TriBAL
b. H2C:C:C(H)MgBr
Ph2CN
Ph
H
OH
60
59
1. a. KH
b. PhCH2Br
2. HO2CCO2H
H2N
OBn
71
a. CpTi(CH3)2Cl
b. n-C7H15COCN (74)
NC
n-C7H15
76
a. CH3OTF
b. NaBH3CN
CH3
77
Mg°/CH3OH
n-H15C7
CN
78
n-H19C9
(+)-Preussin
2

Scheme 32

CONCLUSION

New methods for effecting formation of Δ^1-pyrrolines or tetrahydropyridines that rely on catalytic *or* stoichiometric [2 + 2] cycloadditions of transient monocyclopentadienyl titanium imido complexes onto tethered alkynes have been developed. The $CpTiCl_3$ required for either method is a stable, readily accessible complex. More importantly, the azatitanetines generated *via* treatment of $CpTi(CH_3)_2Cl$ with 1,3-disposed alkynylamines have been shown to engage in subsequent bond forming reactions. This combination of stoichiometric annulation and subsequent nucleophilic addition of the metallocycle has already shown itself to be a valuable synthetic tool by its application in the total synthesis of (+)-preussin. This stoichiometric cycloaddition methodology is a good complement to the intermolecular cycloadditions of zirconocene imido complexes.

Additionally, the facile $CpTiCl_3$ mediated catalytic annulation of alkynylamines has been employed in a concise total synthesis of (±)-monomorine. The catalytic formation of Δ^1-pyrrolines and tetrahydropyridines by $CpTiCl_3$ complements the amidolanthanide catalized formation of pyrollidines and piperidines from alkenylamines, as well as the $[(ArO)_2Ti{=}NR]$ mediated preparation of arylimines from alkynes.

EXPERIMENTAL

Physical Data: ^{1}H NMR and ^{13}C NMR were measured at 300 and 75 MHz respectively, with a Bruker AL-300 spectrometer. ^{1}H NMR chemical shifts are reported as δ values in ppm relative to the residual protons of $CDCl_3$ (7.24) or C_6H_6 (7.15). ^{13}C chemical shifts are reported in ppm relative to $CDCl_3$ (δ77.0) or C_6D_6 (δ128) ^{1}H NMR coupling constants are reported in Hz and refer to real or apparent multiplicities which are indicated as follows: s (singlet), d (doublet), t (triplet, q (quartet), p (pentet), sex (sextet), br (broad), m (multiplet) and app (apparent). Combinations of these descriptors were also used when appropriate. For example, a signal which appears as a triplet (t) but is truly an unresolved doublet of doublets (dd) would be reported as an apparent triplet (app t).

Infrared spectra were recorded with either a Perkin Elmer 1800 FTIR or 237B grating IR. High resolution mass spectra were measured on a VG Analytical 7070E spectrometer by Dr. L.J. Sears. Melting points were determined with a Fisher-Johns melting point aparatus and are uncorrected. Optical rotations were measured with a Perkins-Elmer 241 MC Polarimeter. Elemental analysis was performed by Desert Analytics, Tucson, AZ.

Chromatography: Gas chromatography was performed on a Varian Model 3700 Gas Chromatograph equipped with a flame ionization detector, a Hewlett-Packard 3390A Reporting Integrator and a 15m x 0.53mm ID column with a DB5 (or equivalent) bonded phase.

Thin layer chromatography was performed on plates supplied by Alltech Associates (K42-G). Visualization of plates was effected by one or more of the following: a) UV illumination; b) exposure to I_2 vapor; c) $KMnO_4$ oxidation; or d) anisaldehyde derivitization. All column chromatography[70] was conducted on E. Merck silica gel 60. Solvent systems used for elution are reported in %volume/volume.

Materials: A listing of the common solvents and reagents purified by distillation is shown in Table 3. Atmospheric pressure distillations were conducted in an inert atmosphere of argon or nitrogen.

Commercially available 10M n-BuLi was diluted with heptane and then titrated against a standard solution of 2-butanol in xylene using 1,10-phenanthroline as indicator. Grignard reagents were titrated in the same manner as n-BuLi. These reagents were also checked periodically for total base content. This was accomplished by adding an aliquat to ice and titration of the resulting mixture with a standard solution of potassium biphthalate using phenolphthalein as the indicator.

Table 3. Solvent and Reagent Purification.

Et_2O[a]	Na-Ph_2CO
THF	K
CH_3CN	CaH_2
toluene	CaH_2
DME	K
CH_2Cl_2	CaH^2
benzene	K
heptane	K
DMSO[b]	CaH_2
DMF[b]	CaH_2
HMPA[c]	CaH_2
CH_3OH	$Mg(OCH_3)_2$
2-butanol	CaH_2
TMS-Cl	CaH_2
xylene[b]	CaH_2
pentane	Na-K
hexane	K
amines[e]	CaH_2

a. Et_2O used in the preparation of CH_3Li was distilled from Na-K[d]. b. reduced pressure. c. vacuum pressure. d. 1:3 Na:K. e. Et_2NH, i-Pr_2NEt, i-Pr_2NH and $PhN(CH_3)_2$.

Unless indicated otherwise, reactions were performed in oven or flame dried vessels under an atmosphere of nitrogen or argon. Temperatures reported are bath temperatures unless noted otherwise. Concentrations were performed under reduced pressure with a Büchi rotary evaporator and "drying" of an organic solution was accomplished with anhydrous Na_2SO_4.

2,4-Cyclopentadien-1-yltrimethylsilane. Three moles of freshly cracked cyclopentadiene were generated by heating a mixture of the dimer and silicone oil at 230-245 °C under an air cooled spiral condensor. The monomer (B.P. 36 °C) was

collected in a dry ice cooled receiver. The cyclopentadiene was then added slowly to NaH (72 g, 3 moles) suspended in THF (3L) at 0 °C. After stirring 1 h at 0 °C, the solution of sodium cyclopentadienide was added *via* cannula to a -78 °C solution of TMSCl (326 g, 3 moles) in THF (1L) over 40 min. After stirring an additional 20 min, H_2O (500 mL) was added. The resultant layers separated after 20-30 min, allowing the organics to be decanted. The organic layer was concentrated and the crude product distilled under reduced pressure to yield 187 g (45 %) of the title compound as a colorless oil. Dimerization can be minimized by storage at -20 °C[35].

Cyclopentadienyltitanium trichloride. To a solution of $TiCl_4$ (12.5 g, 66 mmol) in toluene (30 mL) cooled to -78 °C was added dropwise over 20 min a solution of TMSCp (9.17 g, 66 mmol) in toluene (10 mL). Yellow solids precipitate during the addition of the TMSCp. After stirring an additional 45 min at -78 °C, the mixture was transferred quickly *via* cannula to a Schlenk filter. The solids were washed with cold toluene (10 mL), cold 1:1 toluene-heptane (10 mL) and cold 1:2 toluene-heptane (15 mL). Residual solvent was removed under high vacuum to yield bright yellow crystals (8.7 g, 60 %)[33].

Mixture of 1-chloro-5-phenylpent-4-yne and 1-bromo-5-phenylpent-4-yne(15)[86] n-Butyllithium (3 M in heptane,

13.33 mL, 40.0 mmol) was added over 5 min to a brine-ice cooled solution of phenylacetylene (4.09 g, 40.0 mmol) in THF (60 mL) and HMPA (6.5 mL)[87]. After 15 min, 1-bromo-3-chloropropane (6.30 g, 40 mmol) was added rapidly *via* syringe. After 2 h at 25 °C the reaction mixture was poured into sat. aqueous NH_4Cl (50 mL) and Et_2O (50 mL). The layers were separated, the organic phase was washed twice with sat. aqueous NH_4Cl (50 mL), and subsequently was concentrated to a yellow oil. Distillation of the crude product (75-85 °C and 0.025 torr) affords the product mixture as a colorless oil which was characterized as the iodide **16**.

1-Iodo-5-phenylpent-4-yne(16). The halide mixture **15** (obtained from 100 mmol of phenylacetylene) was added to a solution of NaI (18.7 g, 125 mmol) in CH_3CN (250 mL). The resulting mixture was maintained at reflux overnight. The reaction mixture was then partitioned between H_2O (500 mL) and hexane (100 mL). The organic phase was separated and combined with three hexane extractions (100 mL) of the aqueous phase for drying. Filtration and concentration affords **16** (16.74 g, 62 % from phenylacetylene) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.45-7.2 (m, 5H, Ph); 3.35 (t, J = 6.7 Hz, 2H, CH_2I); 2.55 (t, J = 6.7 Hz, 2H, C:CCH_2); 2.08 (app p, J = 6.7 Hz 2H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.30, 127,98, 127.50, 123.33, 87.66,

81.50, 31.94, 20.27, 5.33; IR (film) 3050-2800, 2210, 1600, 1490, 1440, 1420, 1215, 1165, 760, 680 cm^{-1}

Mixture of **1-Chlorononon-4-yne** and **1-bromononon-4-yne(21).** This mixture was prepared in a fashion analogous to that used to prepare **15**, but employing 1-hexyne (3.29 g, 40 mmol) in place of phenylacetylene. After distillation (65-75 °C and 0.025 torr) the product mixture was obtained as a colorless oil that was characterized upon conversion to the iodide.

1-Iodonon-4-yne. The halide mixture **21** (obtained from 100 mmol of 1-hexyne) was added to CH_3CN (250 mL) containing NaI (18.7 g, 125 mmol). After refluxing overnight, the reaction was worked up as for **16** to afford the title compound (15.0 g, 60 % from 1-hexyne) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 3.28 (t, J = 6.9 Hz, 2H, CH_2I); 2.27 (tt, J = 6.6 and 2.4 Hz, 2H, $C{:}CCH_2$); 2.12 (tt, J = 6.9 and 2.4 Hz, 2H, $C{:}CCH_2$); 1.94 (app p, J = 6.8 Hz, 2H, ICH_2CH_2); 1.55-1.25 (m, 4H, $2CH_2$); 0.88 (t, J = 7.1 Hz, 3H, CH_3) ^{13}C NMR (75 MHz, $CDCl_3$) δ 81.46, 77.61, 32.56, 31.06, 21.86, 19.77, 18.34, 13.53, 5.46; IR (film) 2950-2850, 1470, 1410, 1340, 1255, 1210, 1160 cm^{-1}.

7-Iodo-1-phenylhept-1-yne(35). A solution of phenylacetylene (8.78 mL, 80 mmol) in THF (120 mL) and HMPA (13.0 mL) at 0 °C was treated with n-BuLi (3.0 M in heptane, 26.7 mL, 80 mmol). After 15 min, $Cl(CH_2)_5Cl$ (10.2 mL,

80 mmol) was added. The resultant mixture was allowed to warm to 25 °C and maintained overnight. Workup as for **15** and vacuum distillation provides 6.9 g of a colorless oil. Conversion to the iodide was accomplished as for **16**, giving after vacuum distillation 9.5 g (40 % from phenylacetylene) of **35** as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 - 7.2 (m, 5H, Ph), 3.20 (t, J = 6.8 Hz, 2H, CH_2I), 2.41 (t, J = 6.6 Hz, 2H, $C{\equiv}CCH_2$), 1.87 (app pent, J = 7.1 Hz, 2H, CH_2), 1.59 (m, 4H, $2CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.48, 128.13, 127.50, 123.86, 89.69, 80.91, 32.98, 29.69, 27.57, 19.20, 6.65; IR (film) 2920, 2850, 2215, 1590, 1480, 1430, 1200, 755, 690 cm^{-1}.

2-(2-Bromoethyl)-2-methyl-1,3-dioxolane(43). HBr (108 g, 1.34 mole) was dissolved in ethylene glycol (161 g, 2.6 mole) cooled in an ice bath. Freshly distilled methyl vinyl ketone (63 g, 0.9 mole) was then added slowly so that the internal temperature did not exceed 10 °C. The mixture was stirred 1 h at 25 °C and then extracted with pentane (3 x 100 mL). The combined extractions were washed with sat. aqueous $NaHCO_3$ (2 x 100 mL), dried and concentrated. Short path distillation under aspirator pressure afforded **43** (108 g, 65 %) as a colorless oil[61,62].

2,2-Ethylenedioxydec-5-yne(24). n-BuLi (10.0 M, 10 mL, 100 mmol) was added dropwise to a -72 °C solution of 1-hexyne (11.5 mL, 100 mmol) and HMPA (15 mL) in THF (150 mL).

The resultant mixture was stirred 1 h at 0 °C and then recooled to -72 °C. 2-(2-bromoethyl)-2-methyl-1,3-dioxolane(**24**) (17.55 g, 90 mmol) in THF (50 mL) was added, followed by NaI (0.5 g). The mixture was allowed to slowly warm to 25 °C and, after 16 h, was extracted with sat. aqueous NH_4Cl (1 x 150 mL, 2 x 75 mL) and brine (1 x 100 mL). The organics were dried and concentrated. Distillation (60 °C and 0.025 torr) afforded 14.62 g (83 %) of **24** as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 4.0-3.8 (m, 4H, $2CH_2O$), 2.10 (tt, J = 6.8 and 2.3 Hz, 2H, $C{\equiv}CCH_2$), 2.10 (tt, J = 6.6 and 2.3 Hz, 2H, $C{\equiv}CCH_2$), 1.84 (t, J = 6.8 Hz, 2H, CH_2CO_2), 1.5-1.3 (m, 4H, $2CH_2$), 1.29 (s, 3H, CH_3), 0.87 (t, J = 6.7 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.08, 79.82, 79.56, 64.57, 38.58, 31.08, 23.63, 21.78, 18.29, 13,56, 13,46; IR (film) 2950-2850, 1370, 1210, 1130, 1055, 860 cm^{-1}.

Dec-5-yn-2-one(25). A solution of **24** (14.5 g, 74 mmol) in acetone (400 mL) and H_2O (40 mL) was treated with pyridinium tosylate (12.6 g, 50 mmol)[88]. The mixture was maintained at reflux for 16 h and then concentrated to 100 mL. The concentrate was partitioned between H_2O (250 mL) and hexane (100 mL). The organic layer was separated and combined with two hexane extractions (50 mL) of the aqueous phase. The organics were washed with brine (100 mL), filtered, and concentrated to yield **25** as a colorless oil (10.8 g, 96 %). ^1H NMR (300 MHz, $CDCl_3$)

δ 2.59 (t, J = 7.6 Hz, 2H, CH_2CO), 2.36 (tt, J = 6.6 and 2.3 Hz, 2H, $C{:}CCH_2$), 2.13 (s, 3H, CH_3), 2.08 (tt, J = 6.9 and 2.3 Hz, 2H, $C{:}CCH_2$), 1.48-1.25 (m, 4H, $2CH_2$), 0.86 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.58, 80.52, 78.18, 42.76, 30.86, 29.55, 21.65, 18.11, 13.32, 13.25; IR (film) 2950-2850, 1710, 1420, 1370, 1160 cm^{-1}.

Dec-5-yn-2-ylamine(26). A mixture of alkynone 25 (7.6 g, 50 mmol), NH_4OAc (38.5 g, 500 mmol) and $NaBH_3CN$ (2.2 g, 35 mmol) in absolute CH_3OH (150 mL) was stirred 48 h at 25 °C[89]. The mixture was concentrated *via* rotovap and the resultant slurry diluted with H_2O (200 mL). Concentrated HCl was then added until a pH ~3 was obtained. The aqueous layer was extracted with hexane (2 x 50 mL) which was discarded. The aqueous phase was made basic by addition of NaOH and then saturated with NaCl. Three 1:1 Et_2O-hexane extractions (100 mL ea.) of the aqueous phase were then taken. The combined organics were concentrated. The resultant material was dried as a solution in 1:1 CH_2Cl_2-pentane and reconcentrated. Distillation (vacuum) afforded 5.74 g (75 %) of **26** as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 2.99 (app sex, J = 6.3 Hz, 1H, NCH), 2.19 (tt, J = 7.1 and 2.3 Hz, 2H, $C{:}CCH_2$), 2.11 (tt, J = 6.8 and 2.3 Hz, 2H, $C{:}CCH_2$), 1.6-1.25 (m, 6H, $3CH_2$), 1.09 (br s, 2H, NH_2), 1.04 (d, J = 6.3 Hz, 3H, CH_3), 0.87 (t, J = 7.0 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 80.19, 79.19, 45.81,

38.87, 30.94, 23.57, 21.64, 18.13, 15.63, 13.29; IR (film) 3300, 2950-2850, 1590, 1460, 1370, 825 cm^{-1}.

6-Phenylhex-5-yn-2-ylamine(7). The title compound was prepared in a fashion similar to that used to prepare 26, but employing phenylacetylene in the place of 1-hexyne. Filtration of the crude dioxolane 22 through silica gel yielded 6.05 g (70 %) as a slightly yellow oil exhibiting the following ^1H NMR (300 MHz, $CDCl_3$): δ 7.45-7.25 (m, 5H, Ph), 3.95 (m, 4H, $2CH_2O$), 2.49 (t, 2H, CH_2), 1.98 (t, 2H, CH_2), 1.35 (s, 3H, CH_3). The crude 6-phenylhex-5-yn-2-one obtained *via* dioxolane exchange was used in the reductive amination. Distillation of the crude alkynylamine (80 °C and 0.01 torr) afforded 3.53 g (51 % based on phenylacetylene) of 7 as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.34 (m, 2H, Ph), 7.24 (m, 3H, Ph), 3.07 (m, 1H, NCH), 2.45 (t, J = 7.2 Hz, 2H, $CH_2C{:}C$), 1.59 (m, 2H, CH_2), 1.15 (br s, 2H, NH_2), 1.09 (d, J = 6.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.56, 128.14, 127.50, 124.01, 89.76, 80.88, 46.19, 38.79, 23,94, 16.54, IR (film) 3300, 3656, 2962, 2926, 2870, 2234, 1576, 1560, 1490, 1442, 788, 756 cm^{-1}; high resolution mass spectrum calcd. for $C_{12}H_{15}N(M^+)$ 173.1204. Found 173.1202.

5-Phenylpent-4-yn-1-ylamine(3)[90]. The halide mixture 15 (obtained from 40 mmol of phenylacetylene) was diluted with DMF (50 mL). To this solution was added potassium

phthalimide (9.26 g, 50 mmol), and the reaction mixture was brought to reflux for 10 h[91]. The DMF was removed under reduced pressure (65 °C) and the resultant solids were triturated with 10 % KOH (2 x 30 mL) to yield pale yellow crystals. These were suspended in 95 % EtOH (50 mL), treated with hydrazine monohydrate (2.43 mL, 50 mmol) and brought to reflux for 4 h. The reaction mixture was then cooled to 0 °C, brought to pH 2 by addition of conc. HCl, and filtered. The solids were washed thoroughly with ethanol and the organic phase was concentrated to a solid mass. The solids were triturated with 1:1 Et_2O-hexane until white, and then taken into H_2O (50 mL), cooled to 0 °C and carefully saturated with K_2CO_3. The aqueous phase was then extracted with Et_2O (4 x 30 mL). The combined organics were dried and concentrated. Distillation (67 °C and 0.025 torr) afforded 3 (3.94 g, 62 %) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.35 (m, 2H, Ph), 7.24 (m, 3H, Ph), 2.83 (t, J = 6.8 Hz, 2H, NCH_2), 2.45 (t, J = 7 Hz, 2H, $CH_2C{:}C$), 1.71 (m, 2H, $CH_2CH_2CH_2$), 1.16 (br s, 2H, NH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.55, 128.17, 127.53, 124.00, 89.61, 80.97, 41.36, 32.60, 16.88; IR (film) 3298, 3056, 2938, 2866, 2228, 1598, 1570, 1560, 1490, 1442, 756, 692 cm^{-1}; high resolution mass spectrum calcd. for $C_{11}H_{13}N(M^+)$ 159.1048. Found 159.1043.

Non-4-yn-1-ylamine(5). This compound was prepared in analogous fashion to 3, but employing 21 (obtained from

40 mmol of 1-hexyne). After distillation, 3.11 g (56 %) of 5 was obtained as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.74 (t, J = 6.8 Hz, 2H, NCH_2), 2.16 (m, 2H, $CH_2C{:}C$), 2.09 (m, 2H, $CH_2C{:}C$), 1.56 (m, 2H, NCH_2CH_2), 1.45-1.2 (m, 6H, $2CH_2$, NH_2), 0.85 (t, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 80.60, 79.37, 41.29, 32.90, 31.20, 21.87, 18.37, 16.18, 13.49; IR (film) 3342, 2958, 2932, 2872, 2862, 2154, 1484, 1468, 1434, 1320 cm^{-1}; high resolution mass spectrum calcd. for $C_9H_{17}N(M^+)$ 139.1361. Found 139.1357.

6-Phenylhex-5-yn-1-ylamine(9). The halide mixture 15 (obtained from 40 mmol of phenylacetylene) was slowly added to a solution of NaCN (2.11 g, 43 mmol) and NaI (0.6 g, 4 mmol) in DMSO (10 mL) at 25 °C. The reaction mixture was allowed to stir overnight at 25 °C and was then poured into a separatory funnel containing ice water (100 mL). The aqueous phase was extracted with hexane (5 x 100 mL) and the combined extractions were dried and concentrated. The nitrile obtained exhibits the following ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.2 (m, 5H, Ph), 2.56 (app pent, 4H, $2CH_2$), 1.95 (m, 2H, CH_2). The crude nitrile was diluted with Et_2O (40 mL) and added slowly to a suspension of $LiAlH_4$ (0.42 g, 11 mmol) in Et_2O (40 mL) cooled to 0 °C. After 2 h the reaction mixture was carefully quenched *via* sequential addition of H_2O (1 mL), 15 % NaOH (1 mL) and H_2O (2 mL). The organic phase was decanted, combined with two Et_2O washings of the solids, dried, and concentrated. Distilla-

tion (80-85 °C and 0.005 torr) afforded 5.40 g (78 %) of **9** as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (m, 2H, Ph), 7.25 (m, 3H, Ph), 2.73 (t, J = 6.5 Hz, 2H, NCH_2), 2.41 (t, J = 6.6 Hz, 2H, $CH_2C{:}C$), 1.62 (m, 4H, $2CH_2$), 1.04 (s, 2H, NH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.53, 128.14, 127.46, 124.08, 90.00, 80.56, 41.83, 33.14, 26.15, 19.30; IR (film) 3346, 3056, 2936, 2864, 2232, 1560, 1542, 1522, 1490, 756, 692 cm^{-1}; high resolution mass spectrum calcd. for $C_{12}H_{15}N(M^+)$ 173.1204. Found 173.1207.

Dec-5-yn-1-ylamine(11)[92]. This amine was prepared in analogous fashion to **9**, but utilizing the halide mixture **21** (obtained from 40 mmol of 1-hexyne). Distillation (66-72 °C and 0.75 torr) afforded 4.16 g (68 %) of **11** as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.68 (t, J = 6.6 Hz, 2H, NCH_2), 2.15 (t, J = 6.9 Hz, 2H, $CH_2C{:}C$), 2.12 (t, J = 7.2 Hz, 2H, $CH_2C{:}C$), 1.5-1.4 (m, 10H, $4CH_2$, NH_2), 0.88 (t, J = 7 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 79.95, 79.32, 41.40, 32.60, 30.85, 26.09, 21.51, 18.22, 18.00, 13.17; IR (film) 3338, 2958, 2934, 2862, 2158, 1570, 1488, 1466, 1434, 1382, 1328 cm^{-1}; high resolution mass spectrum calcd. for $C_{10}H_{19}N(M^+)$ 153.1517. Found 153.1516.

Pent-4-yn-1-ylamine(28)[93]. A solution of 3-bromopropylamine hydrobromide (9.0 g, 41.1 mmol) in DMSO (20 mL) was added over 30 min to a 10 °C suspension of $LiC{:}CH{\cdot}H_2N(CH_2)_2NH_2$ (9.2 g, 100 mmol) in DMSO (50 mL). The

resultant mixture was stirred 12 h at 25 °C and then quenched by cautious addition of ice. The fraction of the hydrolized reaction mixture that distilled under 130 °C was diluted with H_2O (10 mL), which was then made basic by addition of NaOH. The aqueous phase was extracted with Et_2O (3 x 15 mL) and the combined organics were dried and concentrated (rotovap, 0-5 °C). The concentrate was diluted with abs. EtOH (20 mL) and was then added to a suspension of $AgNO_3$ (7.14 g, 42 mmol) in abs. EtOH (100 mL). The silver acetylide so produced was collected on a frit and was washed with abs. EtOH (3 x 15 mL). The solids were treated with 3 % HCl (3 x 20 mL) while still on the frit. The aqueous filtrate collected was refiltered through celite and then made basic by addition of NaOH. After saturating with NaCl, the aqueous phase was extracted with 1:1 CH_2Cl_2-pentane (4 x 15). Drying and concentration of the combined organics afforded crude product which was subsequently distilled from CaH_2 (122-125 °C). ^1H NMR (300 MHz, $CDCl_3$) δ 2.79 (t, J = 6.9 Hz, 2H, NCH_2), 2.34 (dt, J = 7.0 and 2.6 Hz, 2H, $C{:}CCH_2$), 1.93 (t, J = 2.6 Hz, 1H, $C{:}CH$), 1.64 (app pent, J = 7.0 and 6.9 Hz, 2H, CH_2), 1.09 (br s, 2H, NH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 83.83, 68.36, 40.92, 32.01, 15.68; IR (film) 3250, 2920, 2840, 2110, 1580, 1420, 1080, 1050, 850, 750 cm^{-1}.

3,4-Dihydro-5-(phenylmethyl)-2H-pyrrole(4). Method A: To $CpTiCl_3$ (44 mg, 0.2 mmol) in THF (3 mL) was added

i-Pr_2NEt (70 μL, 0.4 mmol) followed by dropwise addition of a solution of 3 (159 mg, 1 mmol) in THF (2 mL). After 30 min a few drops of 5 % methanolic NaOH were added, and the reaction mixture was taken to dryness. The solids were triturated with hexane, the organic phases were filtered through powdered K_2CO_3 and concentrated to afford 149 mg (94 %) of 4 as the sole reaction product. **Method B:** To $CpTiCl_3$ (219 mg, 1 mmol) in THF (3 mL) at 0 °C was added CH_3Li (1.4 M in Et_2O, 1.43 mL, 2 mmol). The reaction mixture was warmed to 25 °C over 15 min and 3 (159 mg, 1 mmol) in THF (2 mL) was added dropwise over 5 min. After 1 h, 5 % methanolic NaOH (0.5 mL) was carefully added, and the reaction mixture was taken to dryness. Trituration with hexane, followed by filtration through powdered K_2CO_3 and concentration afforded 4 in 96 % yield. In cases where filtration through K_2CO_3 was not sufficient, the product was filtered through a small plug of silica (1:1 Et_2O-hexane). ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (m, 5H, Ph), 3.83 (m, 2H, NCH_2), 3.68 (s, 2H, $PhCH_2$), 2.39 (m, 2H, $N{=}CCH_2$), 1.83 (m, 2H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.56, 137.12, 129.02, 128.57, 126.57, 61.05, 40.75, 36.53, 22.29; IR (film) 3100-2850, 1604, 1496 cm^{-1}; high resolution mass spectrum calcd. for $C_{11}H_{13}N(M^+)$ 159.1048. Found 159.1046.

2-(Phenylmethyl)-3,4,5,6-tetrahydropyridine(10)[94]. **Method C:** To a solution of $CpTiCl_3$ (44 mg, 0.2 mmol) and $PhN(CH_3)_2$ (51 μL, 0.4 mmol) in C_7H_8 (3 mL) at 80 °C was added

a solution of **9** (173 mg, 1 mmol) in C_7H_8 (2 mL). After 2 h at 80 °C, the reaction mixture was cooled to 25 °C and quenched by the addition of sat. aqueous K_2CO_3 (0.5 mL). The solvent was removed and the solids were triturated with hexane while under a blanket of argon. The organic phase was filtered through powdered K_2CO_3 and then concentrated. The crude oil was subjected to high vacuum evaporation (<0.05 torr) to remove $PhN(CH_3)_2$ and yielded **10** (152 mg, 88 %) as an unstable oil. **Method E:** To a solution of $CpTiCl_3$ (11 mg, 0.05 mmol) in C_6H_6 (1.5 mL) at 25 °C was added **9** (87 mg, 0.5 mmol). The mixture was heated to 80 °C for 3 h and then cooled to 25 °C and worked up as in Method C to give **10** (79 mg, 91 %). ^1H NMR (300 MHz, $CDCl_3$) δ 7.18 (m, 5H, Ph), 3.53 (m, 2H, NCH_2), 3.40 (s, 2H, $PhCH_2$), 1.97 (t, J = 7 Hz, 2H, $N{=}CCH_2$), 1.50 (m, 4H, $2CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.65, 137.91, 128.99, 128.43, 126.38, 49.45, 48.28, 28.20, 21.79, 19.54; IR (film) 3100-2850, 1673 cm^{-1}; high resolution mass spectrum calcd. for $C_{12}H_{15}N(M^+)$ 173.1204. Found 173.1200.

3,4-Dihydro-5-pentyl-2H-pyrrole(6). Submission of **5** to **Method A** gave **6** in 94 % yield. **Method B** also effected the desired transformation (94 %) to give **6** as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 3.63 (m, 2H, NCH_2), 2.29 (m, J = 7.9 and 1.5 Hz, 2H, $N{=}CCH_2$), 2.16 (t, J = 7.5 Hz, 2H, $N{=}CCH_2$), 1.68 (m, 2H, NCH_2CH_2), 1.44 (m, 2H, CH_2), 1.16 (m, 4H, $2CH_2$), 0.73 (t, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (75 MHz,

$CDCl_3$) δ 177.87, 60.53, 36.85, 33.48, 31.45, 25.82, 22.32, 22.14, 13.58; IR (film) 2958-2856, 1478 cm^{-1}; high resolution mass spectrum calcd. for $C_9H_{17}N(M^+)$ 139.1361. Found 139.1358.

3,4-Dihydro-2-methyl-5-(phenylmethyl)-2H-pyrrole(8). Submission of 7 to **Method B** afforded **8** (92 %) as a clear oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.27 (m, 5H, Ph), 4.04 (m, 1H, NCH), 3.65 (s, 2H, $PhCH_2$), 2.34 (m, 2H, $N=CCH_2$), 2.00 (m, 1H), 1.4-1.25 (m, 1H), 1.22 (d, J = 6.7 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.02, 137.06, 128.88, 128.50, 126.48, 67.79, 40.75, 36.56, 30.71, 21.93; IR (film) 3100-2855, 1493 cm^{-1}; high resolution mass spectrum calcd. for $C_{12}H_{15}N(M^+)$ 173.1204. Found 173.1207.

3,4-Dihydro-2-methyl-5-pentyl-2H-pyrrole(27). **Method D:** A solution of $CpTiCl_3$ (11 mg, 0.05 mmol) in THF (2 mL) was treated with **26** (76 mg, 0.5 mmol). The mixture was stirred 2 h at 25 °C before working up as in Method A to give **27** (72 mg, 94 %). ^1H NMR (300 MHz, $CDCl_3$) δ 3.96 (m, 1H, NCH), 2.55-2.41 (m, 1H), 2.41-2.29 (m, 1H), 2.25 (app dt, J = 7.7 and 0.8 Hz, 2H), 2.08-1.94 (m, 1H), 1.6-1.45 (m, 2H), 1.38-1.22 (m, 5H), 1.18 (d, J = 6.9 Hz, 3H, CH_3), 2.51 (t, J = 7.0 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.47, 67.21, 36.88, 33.47, 31.33, 30.30, 25.85, 22.03, 21.69, 13.54; IR (film) 2950, 2920, 2860, 1620, 1425, 1410, 1360 cm^{-1}.

2-Pentyl-3,4,5,6-tetrahydropyridine(12). Submission of **11** to **Method C** or **E** afforded **12** (89 and 92 %, respectively) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.52 (m, 2H, NCH_2), 2.08 (m, 4H, $N{=}C(CH_2)_2$), 1.63 (m, 2H, CH_2), 1.51 (m, 4H, $2CH_2$), 1.28 (m, 4H, $2CH_2$), 0.86 (t, J = 7 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.07, 49.20, 41.13, 31.75, 29.01, 26.19, 22.50, 21.98, 19.68, 13.94; IR (film) 2958, 2934, 2860, 1660 cm^{-1}; high resolution mass spectrum calcd. for $C_{10}H_{19}N(M^+)$ 153.1517. Found 153.1519.

3,4-Dihydro-5-methyl-2H-pyrrole(29)[95,96]. A solution of $CpTiCl_3$ (6 mg, 0.027 mmol) in C_6D_6 (0.4 mL) was treated with **28** (22 mg, 0.26 mmol). There ensued a mild exotherm accompanied by formation of a dark red color. A ^{1}H NMR spectrum collected within 10 min of amine addition shows only resonances attributed to Δ^1-pyrroline **29** and none of the signals exhibited by amine **28**. This sample, though frozen, showed significant (5-10 %) degradation after 12 h. ^{1}H NMR (300 MHz, C_6D_6) δ 3.98 (m, 2H, NCH_2), 2.17 (app t, J = 8.1 Hz, $N{:}CCH_2$) 2.03 (s, 3H, CH_3), 1.69 (app pent, 2H, CH_2); ^{13}C NMR (75 MHz, C_6D_6) δ 172.22, 61.26, 38.25, 22.93, 19.12.

Reaction of 13 with Isobutyronitrile. To **13** (0.5 mmol, prepared by **Method B**) was added isobutyronitrile (114 μL, 1.25 mmol). The septum was replaced with a screw cap and the reaction mixture was heated to 65 °C for 19 h. The reaction mixture was then heated with 20 % HCl (5 mL) for an

additional 2 h. After saturating the resultant solution with K_2CO_3, the product was extracted with 1:1 Et_2O-hexane. Filtration of the organic phases through silica gel and subsequent concentration gave the vinylogous amide **14** (77 mg, 67 %). An alternative workup procedure yields **19**. In this case the reaction mixture was added to 5 % HCl and the aqueous phase quickly extracted twice with Et_2O (which was found to contain small amounts of **14**). The aqueous phase was then saturated with K_2CO_3 and extracted with hexane. Filtration of the organic phases through K_2CO_3 followed by concentration and distillation afforded **19** (72 mg, 63 %) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.3-7.1 (m, 5H, Ph), 3.96 (t, J = 7.5 Hz, 2H, CH_2), 2.42 (app p, J = 6.9 Hz, H, CH), 2.17 (t, J = 8 Hz, 2H, CH_2), 1.65 (app p, J = 7.5 and 8 Hz, 2H, CH_2), 1.01 (d, J = 6.9 Hz, 6H, $2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.39, 158.64, 141.44, 131.81, 128.01, 126.07, 102.06, 60.26, 38.39, 30.28, 22.01, 20.89; IR (film) 3451, 3054, 2964, 2853, 1614, 1514, 1488, 1336, 1298, 748, 704 cm^{-1}.

(E,E)-2,2-Dimethyl-4,6-octadiene-1-ylamine(32). ^1H NMR (300 MHz, $CDCl_3$) δ 5.99 (m, 2H, 2C:CH), 5.54 (m, 2H, 2C:CH), 2.41 (s, 2H, NCH_2), 1.93 (d, J = 7.6 Hz, 2H, $C:CCH_2$), 1.70 (d, J = 6.6 Hz, 3H, $C:CCH_3$), 0.95 (br s, 2H, NH_2), 0.81 (s, 6H, $2CH_3$); ^{13}C NMR (57 MHz, $CDCl_3$) δ 132.73, 131.64, 128.11, 127.07, 52.77, 42.76, 35.46, 24.68, 17.91; IR (film) 3350, 3000, 2920-2820, 1470, 1355, 985 cm^{-1}.

(Z)-5-Phenyl-4-penten-1-ylamine(30). A solution of $Ni(OAc)_2 \cdot 4H_2O$ (187 mg, 0.75 mmol) in abs. EtOH (6 mL) under an atmosphere of H_2 was treated with ethanolic $NaBH_4$ (1 M, 0.75 mL, 0.75 mmol)[97]. To the resulting black solution was added $H_2N(CH_2)_2NH_2$ (99 μL, 1.25 mmol) and a solution of **3** (0.64 g, 4 mmol) in EtOH (1 mL). After stirring vigorously for 12 h under H_2, the reaction mixture was concentrated. The resultant solids were triturated with CH_2Cl_2. The organics were filtered through florisil and concentrated. Vacuum distillation affords **30** (0.55 g, 85 %) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4-7.1 (m, 5H, Ph), 6.43 (d, J = 11.6 Hz, 1H, C:CHPh), 5.65 (dt, J = 11.6 and 7.3 Hz, 1H, C:C**H**CH_2), 2.69 (t, J = 7.1 Hz, 2H, NCH_2), 2.36 (app dq, J = 7.4 and 7.3 Hz, 2H, C:CCH_2), 1.57 (app p, J = 7.4 and 7.1 Hz, 2H, CH_2), 1.09 (s, 2H, NH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.52, 132.18, 129.12, 128.55, 127.96, 126.35, 41.66, 33.85, 25.76.

6-Methyl-5-hepten-2-ylamine(31). A refluxing solution of $HONH_2 \cdot HCl$ (16.6 g, 240 mmol) and NaOAc (19.7 g, 240 mmol) in H_2O (80 mL) and EtOH (3.2 mL) was treated with 6-methylhept-5-en-2-one (11.8 mL, 80 mmol). The mixture was maintained at reflux 40 h and then cooled to 25 °C. The layers were separated and the aqueous layer was extracted with 1:1 Et_2O-hexane (2 x 30 mL)[98]. The combined organics were concentrated and then rediluted with Et_2O (100 mL).

This solution was added over 2 h to a brine-ice cooled suspension of $LiAlH_4$ (10.4 g, 274 mmol) in Et_2O (250 mL)[66]. After refluxing 23 h, the reaction mixture was cooled in a brine-ice bath and quenched *via* sequential addition of H_2O (10 mL), 15 % NaOH (10 mL) and H_2O (30 mL). The mixture was stirred 1 h, saturated with K_2CO_3, and then allowed to settle. The organics were decanted and combined with two Et_2O washes of the solids. The combined organics were dried and concentrated. Distillation affords 6.35 g (62 % from ketone) of **31** as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 5.09 (app tt, J = 6.2 and 1.1 Hz, 1H, C:CH), 2.85 (app sex, J = 6.2, 1H, NCH), 1.99 (app q, J = 7.1 Hz, 2H, CH_2), 1.66 (s, 3H, CH_3), 1.59 (s, 3H, CH_3), 1.33 (m, 2H, CH_2), 1.17 (br s, 2H, NH_2), 1.03 (d, J = 6.2 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.39, 124.21, 46.53, 40.18, 25.59, 24.94, 23.90, 17.54; IR (film) 3300, 2895, 2830, 1600, 1450, 1390, 820 cm^{-1}.

5,5-Ethylenedioxyhex-2-yne(44). To a slurry of $LiC{:}CH{\cdot}H_2N(CH_2)_2NH_2$ (22 g, 222 mmol) in DMSO (75 mL) at 5 °C was slowly added 2-(2-bromoethyl)-2-methyl-1,3-dioxolane **43** (27.3 g, 148 mmol). After 2 h at 25 °C the reaction mixture was carefully poured into ice water (500 mL) and the aqueous layer was extracted with hexane (6 x 100 mL). The combined organic phases were then back extracted sequentially with H_2O (2 x 200 mL), sat. aqueous NH_4Cl (2 x 200 mL) and brine

(200 mL). Drying, concentration and distillation (< 60 °C and 0.1 torr) gave 44 (13.9 g, 67 %) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.91 (m, 4H, $2CH_2O$), 2.23 (m, 2H, $C{:}CCH_2$), 1.90 (m, 3H, CH_2, C:CH), 1.30 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 108.97, 84.31, 67.88, 64.72, 37.92, 23.81, 13.24; IR (film) 3294, 2984, 2962, 2936, 2884, 2118, 1718, 1448, 1378, 1256, 1220, 1144, 1102, 1056, 948, 862, 642 cm^{-1}; high resolution mass spectrum calcd. for $C_8H_{13}O_2(MH^+)$ 141.0916. Found 141.0920.

2,2-Ethylenedioxyhept-5-yn-7-ol (45)[99]. To **44** (7.46g, 53.3 mmol) in THF (90 mL) at 0 °C was added *n*-BuLi (1.7 M in hexane, 34.5 mL, 58.65 mmol). After 15 min, dry paraformaldehyde (2.23g, 74.5 mmol) was added in one portion. The reaction mixture was stirred 2 h at 25 °C and was then poured into sat. aqueous NH_4Cl (75 mL). The organic layer was separated, combined with three Et_2O extractions of the aqueous layer and dried. Concentration and distillation of the residue afforded **45** (8.61 g, 95 %) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.15 (t, J = 2 Hz, 2H, CH_2O), 3.88 (m, 4H, $2CH_2O$), 2.57 (br s, 1H, OH), 2.45 (m, J = 8 and 2 Hz, 2H, $C{:}CCH_2$), 1.84 (t, J = 8 Hz, 2H, CH_2), 1.26 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.02, 85.67, 78.23, 64.60, 50.99, 37,84, 23.69, 13.46; IR (film) 3418, 2982, 2958, 2934, 2888, 1448, 1378, 1256, 1222, 1146, 1132, 1102, 1054, 1024, 860, 788 cm^{-1}; high

resolution mass spectrum calcd. for $C_8H_{15}O_3(M^+)$ 171.1021. Found 171.1024.

2,2-Ethylenedioxy-7-iodohept-5-yne(47). CH_3SO_2Cl (3.4 mL, 44 mmol) was added dropwise to a solution of **45** (6.8 g, 40 mmol) and Et_3N (8.36 mL, 60 mmol) in CH_2Cl_2 (200 mL) at 0 °C. The reaction mixture was stirred 1 h at 25 °C and then transferred to a separatory funnel containing ice water (200 mL). The organic phase was separated and washed sequentially with sat. aqueous solutions of NH_4Cl, $NaHCO_3$ and NaCl. Concentration gave the crude mesylate **46** which was recrystallized from Et_2O (-70 °C) to give white crystals (9.0 g, 91 %, m.p. 34 °C). Although this mesylate was not extremely stable, we were able to obtain satisfactory ^1H and ^{13}C spectra (Appendix). The mesylate was dissolved in CH_3CN (200 mL) containing NaI (11.6 g, 77.5 mmol). The reaction mixture was protected from light and, after 4 h, concentrated to a sludge which was diluted with 1:1 Et_2O-hexane and filtered through basic alumina. Concentration and distillation of the residue (0.05 torr) gave **47** (10.2 g, 94 %) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 3.85 (m, 4H, $2CH_2O$), 3.61 (t, J = 2.5 Hz, 2H, CH_2I), 2.21 (tt, J = 8 Hz and 2.5, 2H, $C{\equiv}CCH_2$), 1.78 (t, J = 8 Hz, 2H, CH_2), 1.23 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 108.76, 96.90, 86.11, 64.66, 37.43, 23.68, 13.80, -16.87; IR (film) 2982, 2958, 2934, 2882, 2230, 2204, 1446, 1378, 1254, 1220, 1176, 1144, 1100, 1054,

862 cm^{-1}; high resolution mass spectrum calcd. for $C_8H_{13}IO_2(M^+)$ 279.9960. Found 279.9966.

O-2,3,5,6-Tetrahydropyran-2-ylhydroxylamine(40). N-hydroxyphthalimide (36.63 g, 0.2 mol) suspended in C_6H_6 (400 mL) was treated with dihydropyran (20.1 mL, 0.22 mol) and a few drops of $POCl_3$. The reaction mixture was brought to reflux for 16 h, at which time the heating bath was removed. The reaction mixture was subsequently maintained at reflux by the slow addition of hydrazine monohydrate (12.01 g, 0.24 mol). After an additional 4 h at reflux, the reaction mixture was cooled to 25 °C and filtered. The solids were washed with C_6H_6 and the combined organic phases were dried. Concentration gave a red oil which upon distillation yielded **40** (20.1 g, 85 %) as a white solid (m.p. 38 °c): ^1H NMR (300 MHz, $CDCl_3$) δ 5.44 (br s, 2H, NH_2), 4.59 (t, J = 3.4 Hz, 1H, HCO_2), 3.79 (m, 1H, OCH_2), 3.46 (m, 1H, OCH_2), 1.8-1.3 (m, 6H, $3CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 102.09, 62.06, 28.52, 24.96, 19.34.

(E) and (Z)-O-(2,3,5,6-Tetrahydropyran-2-yl)-hexan-2-one oxime(41). A solution of 2-hexanone (5.0 g, 50 mmol) and **40** (5.9 g, 50 mmol) in C_6H_6 (100 mL) was refluxed under Dean-Stark conditions for 1 h. Concentration of the reaction mixture followed by distillation (74-76 °C and 16 mm) gave **41** (9.77 g, 98 %) as a clear oil composed of a mixture of the E and Z isomers. For characterization, the

isomer mixture (0.2 g, 1 mmol) in THF (0.5 mL) was added to LDA (1.1 mmol) in THF (1.5 mL) at -48 °C. After 5 h at -48 °C the reaction mixture was quenched by slow addition of absolute CH_3OH. Filtration and concentration afforded the E isomer of **41** (0.192 g, 96 %) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 5.14 (m, 1H, O_2CH), 3.95-3.45 (m, 2H, OCH_2), 2.15 (m, 2H, $N{:}CCH_2$), 1.83 (s, 3H, CH_3), 1.8-1.0 (m, 10H, $5CH_2$), 0.84 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.62, 100.27, 63.11, 35.49, 29.04, 28.60, 25.17, 22.28, 20.14, 13.86, 13.68; IR (film) 2954, 2872, 1466, 1456, 1368, 1202, 1112, 1080, 1042, 982, 936 cm^{-1}; high resolution mass spectrum calcd. for $C_{11}H_{21}NO_2(M^+)$ 199.1572. Found 199.1573.

O-(2,3,5,6-Tetrahydropyran-2-yl)-2,2-ethylene-dioxytridec-5-yn-7-one oxime(48). To i-Pr_2NH (1.62 mL, 11.55 mmol) in THF (8 mL) at 0 °C was added n-BuLi (3M in heptane, 3.85 mL, 11.55 mmol). After 15 min the reaction mixture was cooled to -48 °C and **41** (2M in THF, 5.25 mL, 10.5 mmol) was added. After 5h at -45 to -48 °C, **47** (2.80 g, 10 mmol) in THF (6 mL) was added dropwise, and the reaction mixture was maintained for 1 h at -48 °C. CH_3OH (1 mL) was then added and the reaction mixture was concentrated. Dilution with 1:1 Et_2O-hexane (20 mL) followed by filtration through neutral alumina and concentration afforded **48** (3.44 g, 98 %) as a light yellow oil which could not be distilled: ^1H NMR (300 MHz, $CDCl_3$)

δ 5.17 (m, 1H, HCO_2), 3.90 (m, 5H, OCH_2CH_2O, OCH_2), 3.60 (m, 1H, OCH_2), 255-2.15 (m, 8H, $4CH_2$), 1.9-1.2 (m, 12H, $6CH_2$), 1.29 (s, 3H, CH_3), 0.88 (t, J = 7.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.6, 109.00, 100.15, 80.35, 78.73, 64.61, 62.80, 38.36, 34.26, 28.95, 28.56, 28.00, 25.19, 23.68, 22.45, 19.88, 15.49, 13.73, 13.51; IR (film) 2956, 2930, 2874, 2852, 1456, 1376, 1204, 1134, 1112, 1078, 1058, 1042, 946, 788, 764 cm^{-1}; high resolution mass spectrum calcd. for $C_{20}H_{34}NO_4(MH^+)$ 352.2488. Found 352.2448.

(±) 7-amino-2,2-ethylenedioxytridec-5-yne(39). A solution of **48** (19.7 g, 56 mmol) in Et_2O (100 mL) was slowly added to $LiAlH_4$ (4.25 g, 112 mmol) in Et_2O (100 mL) which was cooled to -78 °C. The reaction mixture was brought to reflux for 2 h, cooled to -78 °C and was subsequently quenched with 10 % KOH. The organic phase was decanted, concentrated, dried as a solution in 1:1 CH_2Cl_2-pentane and reconcentrated. Distillation (100 °C and 0.1 torr) gave **39** (12.04 g, 85 %) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 3.80 (m, 4H, OCH_2CH_2O), 2.69 (m, 1H, NCH), 2.11 (m, 4H, $CH_2C{:}CCH_2$), 1.74 (m, 2H), 1.55-1.4 (m, 1H), 1.35-1.1 (m, 10H), 1.03 (br s, 2H, NH_2), 0.79 (t, J = 7.6 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 108.93, 79.84, 79.34, 64.48, 50.15, 38.41, 37.57, 36.91, 28.09, 23.56, 22.62, 15.52, 13.87, 13.45; IR (film) 3374, 3306, 2980, 2956, 2930, 2874, 2860, 1582, 1448, 1378, 1254, 1220, 1132, 1102, 1056, 860 cm^{-1};

high resolution mass spectrum calcd. for $C_{15}H_{27}NO_2(M^+)$ 253.2042. Found 253.2046.

(±) 2-Butyl-3,4-dihydro-5-(4,4-ethylenedioxypentyl)-2H-pyrrole(38). To Et_3N (260 μl, 1.9 mmol) and $CpTiCl_3$ (208mg, 0.95 mmol) in THF (10 mL) at 25 °C was added **39** (1.20 g, 4.74 mmol) in THF (10 mL). After 1 h, 5 % methanolic NaOH (4 mL) was added, and the reaction mixture brought to dryness. The resultant mass was triturated with hexane (3 x 10 mL) which was then filtered through powdered K_2CO_3. Concentration yielded **38** (1.12 g, 93 %) as a slightly colored oil: ^1H NMR (300 MHz, $CDCl_3$) δ 3.88 (m, 4H, OCH_2CH_2O), 2.55-2.2 (m, 5H, $N=C(CH_2)_2$, NCH), 2.1-1.7 (m, 1H), 1.7-1.55 (m, 5H), 1.45-1.1 (m, 9H), 0.86 (m, J = 7, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.70, 109.83, 72.48, 64.56, 38.71, 36.81, 36.36, 33.90, 28.82, 28.55, 23.69, 22.80, 21.14, 14.02; IR (film) 2956, 2928, 2872, 1644, 1458, 1376, 1256, 1218, 1132, 1060; high resolution mass spectrum calcd. for $C_{15}H_{27}NO_2(M^+)$ 253.2042. Found 253.2034.

(±) 2-Butyl-5-(4,4-ethylenedioxypentyl)-2β,3,4,5β-tetrahydro-1H-pyrrole(37). Δ^1-pyrroline **38** (1.265 g, 5 mmol) was added over 10 min to a solution of DiBAL-H (1M in C_7H_8, 20 mL, 20 mmol) in THF (15 mL) at -78 °C. After 30 min the reaction mixture was warmed to -50 °C, and then to 0 °C over 3 h. The reaction mixture was quenched by careful addition of 10 % aqueous KOH (6 mL) and then

saturated with K_2CO_3. The organic phase was separated and combined with two Et_2O extractions of the aqueous phase. Concentration gave **37** (1.21 g, 95 %) as an unstable red oil which was used without purification: ^1H NMR (300 MHz, $CDCl_3$) δ 3.81 (m, 4H, OCH_2CH_2O), 2.8 (m, 2H, 2NCH), 1.72(m, 2H, CH_2), 1.53 (m, 2H, CH_2), 1.45-1.0 (m, 15H, $6CH_2$, CH_3), 0.96 (app d, J = 6.6 Hz, 1H), 0.77 (t, J = 7 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.84, 64.40, 59.19, 59.10. 39.19, 36.84, 36.32, 31.12, 29.51, 23.53, 22.71, 21.86, 20.40, 13.86; IR (film) 3854, 2954, 2872, 1652, 1462, 1376, 1252, 1220, 1142, 1060, 948 cm^{-1}; high resolution mass spectrum calcd. for $C_{15}H_{29}NO_2(M^+)$ 255.2198. Found 255.2191.

(±)-Monomorine(1). A solution of **37** (1.275 g, 5 mmol) in THF (15 mL) was stirred overnight with 5 % HCl (5 mL). The reaction mixture was saturated with K_2CO_3, the organic phase was separated and combined with two Et_2O extractions of the aqueous phase. The solvent was removed and the resultant oil was diluted with THF (10 mL) to which $NaBH_3CN$ (0.314 g, 5 mmol) in CH_3OH (3 mL) and 5 % HCl (1 mL) were added. After 2 h the reaction mixture was saturated with K_2CO_3, the organic phase was separated and combined with two Et_2O extractions of the aqueous phase. Concentration and flash chromatography of the residue (silica gel, 10 % Et_2O/hexane) gave **1** (0.70 g, 72 %) as colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 2.44 (tt, J = 10 and 2.5 Hz, 1H, NCH), 2.18 (m, 1H, NCH), 2.03 (m, 1H, NCH), 1.87-1.15 (m, 16H,

8CH_2), 1.10 (d, J = 6.4 Hz, 3H, CH_3), 0.86 (t, J = 7 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 67.07, 62.77, 60.14, 39.68, 35.85, 30.91, 30.30, 29.70, 29.26, 24.87, 22.85, 22.79, 14.07; IR (film) 3402, 2956, 2930, 2872, 2860, 1456, 1378, 1320, 1302, 1206, 1130, 788 cm^{-1}; high resolution mass spectrum calcd. for $C_{13}H_{25}N(M^+)$ 195.1987. Found 195.1982.

Undec-2-yn-1-ol(52). Lithium metal (3.82 g, 0.55 mole) was added in small portions to a dry ice condensor equipped flask containing liquid NH_3 (350 mL) and a crystal of ferric nitrate. After the blue color was discharged, propargyl alcohol (14.5 mL, 0.25 mole) was added dropwise over 15 min. After an additional 15 min, octyl bromide (34.5 mL, 0.2 mole) was added, followed by DMSO (175 mL). The reaction mixture was allowed to warm to 25 °C overnight and was then diluted to 750 mL with ice water. The aqueous layer was extracted with Et_2O (4 x 150 mL). The combined extractions were washed with brine, dried and filtered. Following concentration, the crude product was distilled through an 8" vigeroux column (72 °C and 0.025 torr) to afford 27 g (80 %) of 52 as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 4.22 (dt, J = 6.0 and 2.2 Hz, 2H, CH_2O), 2.33 (s, 1H, OH), 2.18 (tt, J = 7.0 and 2.2 Hz, 2H, C≡CH_2), 1.48 (app pent, J = 7.2 Hz, 2H, CH_2), 1.4-1.15 (m, 10H, 5CH_2), 0.86 (t, J = 6.7 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 86.27, 78.28, 51.07, 31.74, 29.08, 29.01, 28.80, 28.55,

22.54, 18.64, 13.94; IR (film) 3300, 2900, 2820, 2200, 1460, 1130, 1010 cm^{-1}.

1-Bromoundec-2-yne(53). A solution of Br_2 (6.3 g, 39.5 mmol) in CCl_4 (25 mL) was added dropwise to a 0 °C solution of Ph_3P (10.3 g, 39.5 mmol) in CCl_4 (100 mL). After 15 min a solution of **52** (6.72 g, 40 mmol) in CCl_4 (25 mL) was added. The reaction mixture was brought to reflux for 1 h and was then cooled to 0 °C and filtered. The solids were washed with CCl_4 (2 x 20 mL) and the combined organics were concentrated to a white mass. The solids were triturated with hexane (2 x 50 mL) which was subsequently concentrated to an oil. Vacuum distillation affords 7.56 g (81 %) of **53** as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 3.90 (t, J = 2.4 Hz, 2H, CH_2Br), 2.21 (tt, J = 7.0 and 2.4 Hz, 2H, $C{:}CCH_2$), 1.48 (app pent, J = 7.2 Hz, 2H, CH_2), 1.55-1.15 (m, 10H, $5CH_2$), 0.86 (t, J = 6.7 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 88.32, 75.24, 31.80, 29.12, 29.02, 28.81, 28.36, 22.62, 18.93, 15.69, 14.05; IR (film) 2890, 2820, 2210, 1450, 1200 cm^{-1}.

L-Phenylalanine methyl ester hydrochloride. A -5 °C suspension of phenylalanine (20 g, 121 mmol) in CH_3OH (120 mL) was treated with $SOCl_2$ (15.7 mL, 1.78 eq) at such a rate that the internal temperature did not exceed 0 °C. The mixture was allowed to stir 4 h at 25 °C and was then concentrated. The resultant solids were diluted with and

stripped of CH_3OH (60 mL) four times. The solids were then slurried with Et_2O (150 mL) and filtered. After washing the solids with Et_2O (2 x 50 mL) the residual solvent was removed under vacuum. Grinding in a mortar with a pestle yields 25.5 g (98 %) of the title compound as a white powder. Due to the limited solubility of this salt, it was converted to the free amine for characterization. ^1H NMR (300 MHz, $CDCl_3$) δ 7.25-7.05 (m, 5H, Ph), 3.63 (dd, J = 7.8 and 5.2 Hz, 1H, NCH), 3.61 (s, 3H, CH_3), 2.99 (dd, J = 13.5 and 5.2 Hz, PhCH), 2.77 (dd, J = 13.5 and 7.8 Hz, PhCH), 1.42 (s, 2H, NH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.99, 136.96, 128.90, 128.14, 126.40, 55.47, 51.48, 40.76.

Methyl N-(diphenylmethylene)-L-phenylalaninate(55). The preparation of this compound has been described by Polt. ^1H NMR (300 MHz, $CDCl_3$) δ 7.7-6.6 (m, 15H, Ph), 4.29 (dd, J = 9.3 and 4.3 Hz, 1H, NCH), 3.74 (s, 3H, CH_3), 3.31 (dd, J = 13.3 and 4.3 Hz, 1H, PhCH), 3.21 (dd, J = 13.3 and 9.3 Hz, 1H, PhCH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.17, 170.74, 139.29, 137.82, 135.97, 130.17, 129.76, 128.68, 128.24, 128.06, 127.90, 127.53, 126.22, 67.13, 52.06, 39.70.

(2S, 3S) and (2S, 3R)-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yn-3-ol(59) and (60). A 1 L flask charged with methyl N-(diphenylmethylene)-L-phenylalaninate (19.5 g, 57 mmol) and CH_2Cl_2 (440 mL) was cooled to -73 °C. A mixture of TriBAL (1 M in C_7H_8, 57 mL, 1 eq) and DiBAL-H

(1 M in C_7H_8, 57 mL, 1 eq) was then added slowly *via* addition funnel so that the temperature did not exceed -68 °C. Upon completion of the addition, the yellow solution was treated with $H_2C{:}C{:}C(H)MgBr$ (1.8 M in Et_2O, 95 mL, 3 eq), again at a rate such that the temperature did not exceed -68 °C. The resulting green reaction mixture was stirred 10 h at -73 °C before slowly warming to 15 °C for 4 h. After cooling to 0 °C, aqueous NaOH (5 M, 63 mL) was added slowly over 1 h. The red organic layer was then decanted and combined with 3 x 100 CH_2Cl_2 washes of the green solids for drying. The concentrated organics were rediluted with CCl_4 and filtered through a pad of basic alumina. Concentration gave 19.15 g (55.8 mmol, 95 %) of the diastereomeric mixture as a viscous red oil. When 10 g of this mixture was chromatographed on 600 mL of silica gel (10 % EtOAc/Hexane) there was obtained 5.755 g (16.8 mmol, 55 %) of the 2S,3S diastereomer (**59**) as a yellow-green, gelatinous solid and 1.761 g (4.99 mmol, 16.8 %) of the 2S,3R diastereomer **(60)** as a white solid:

(2S,3S)-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yn-3-ol(59). ^1H NMR (300 MHz, $CDCl_3$) δ 7.8-6.7 (m, 15H, Ph), 3.93 (app q, J = 6.7 and 6.0 Hz, 0.6H, NCH), 3.83 (app t, J = 6.4 Hz, 0.4H), 3.75 (app dt, J = 7.0, 6.2 and 1.7 Hz, 0.4H), 3.47 (app q, J = 7.4 and 5.7 Hz, 0.6H), 3.06, 2.95, 2.88 and 2.86 (all dd, J = 13.2 and 6.8 Hz, 14.1 and 5.7 Hz, 13.2 and 4.5 Hz, and 14.1 and 8.0 Hz, respectively, 2H,

$PhCH_2$), 2.46 and 2.40 (m, 1H, C:CCH), 2.32-2.18 (m, 1H, C:CCH), 1.97 (app t, J = 2.7 and 2.4, 0.6H, C:CH), 1.92 (app t, J = 2.7 and 2.4, 0.4H, C:CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.92, 144.94, 144.78, 139.10, 138.42, 138.32, 136.09, 130.33, 129.77, 129.02, 128.41, 128.19, 128.10, 128.04, 127.98, 127.62, 127.49, 127.28, 126.40, 126.19, 126.09, 126.05, 99.45, 80.89, 80.62, 79.91, 71.00, 70.14, 65.50, 64.77, 39.54, 39.37, 25.52, 24.00; (note: oxazolidine-imine tautomerism); IR (film) 3460, 3250, 3050, 3030, 2990, 2890, 2100, 1655, 1615, 1595, 1485, 1445, 1310, 1275, 1240, 1065, 1030, 950, 780, 755, 710 cm^{-1}.

(2S,3R)-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yn-3-ol(60). ^1H NMR (300 MHz, $CDCl_3$) δ 7.7-6.3 (m, 15H, Ph), 3.94 (app q, J = 5.4 Hz, 1H, OCH), 3.64 (ddd, J = 9.5, 5.4 and 3.1 Hz, 1H, NCH), 3.05 (dd, J = 13.0 and 3.1 Hz, 1H, PhCH), 2.90 (dd, J = 13.0 and 9.5 Hz, 1H, PhCH), 2.68 (br s, 1H, OH), 2.57 (ddd, J = 16.7, 5.6 and 2.7 Hz, 1H, C:CCH), 2.48 (ddd, J = 16.7, 7.5 and 2.5 Hz, 1H, C:CCH), 1.98 (app t, J = 2.7 and 2.5 Hz, 1H, C:CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.79, 139.56, 138.94, 136.30, 130.18, 130.00, 128.46, 128.11, 127.97, 127.85, 127.65, 125.94, 80.88, 73.01, 70.75, 67.03, 37.83, 23.73; IR (KBr) 3230, 3090, 3010, 2990, 2905, 2850, 2100, 1605, 1480, 1440, 1325, 1280, 1105, 1045, 1015, 775, 690 cm^{-1}.

(4S,5S)-5-(Phenylmethyl)-4-(prop-2′-yn-1′-yl)-2-oxazolidinone (61). A solution of (2S,3S)-3-hydroxy-1-phenylhex-5-yn-2-ylamine (140 mg, 0.74 mmol), prepared by hydrolysis of 59) and carbonyldiimidazole (156 mg, 0.96 mmol) in THF (3 mL) was stirred at 25 °C for 2 h. The mixture was concentrated and the resultant solids dissolved in Et_2O. The organic phase was washed with 1 M HCl (2 x 5 mL) and sat. aqueous $NaHCO_3$ (5 mL). Filtration of the organics through powdered K_2CO_3 and concentration provided a viscuous oil. Chromatography (50 % EtOAc/Hex) affords 100 mg (47 %) of **61** as a white solid: ^1H NMR (300 MHz, $CDCl_3$) δ 7.4-7.1 (m, 5H, Ph), 6.21 (s, 1H, NH), 4.36 (app q, J = 6.6 and 5.1 Hz, 1H), 3.90 (app q, J = 6.6 and 5.1 Hz, 1H), 2.88 (d, J = 7.0 Hz, 2H, $PhCH_2$), 2.46 (m, 2H, $C{:}CCH_2$), 1.97 (app t, J = 2.7 Hz, C:CH); ^{13}C NMR (7.5 MHz, $CDCl_3$) δ 158.18, 135.65, 129.12, 128.85, 127.16, 78.36, 77.42, 71.56, 58.04, 41.62, 24.19; IR (CCl_4) 3300, 2900, 1750, 1390, 1240, 790, 760, 710 cm^{-1}.

(2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yne(63). A solution of 59 (5.4 g, 15.3 mmol) in THF (30 mL) was added over 15 min to a suspension of KH (1.2 g, 30 mmol) in THF (50 mL) at 25 °C. After 2 h at 25 °C, the dark red solution was cooled to 0 °C and $PhCH_2Br$ (3.57 mL, 30 mmol) was added. After 10 min at 0°C, the mixture was warmed to 25 °C for 1 h. The mixture was then poured into ice water (100 mL) and Et_2O (100 mL). The

organics were separated, dried and concentrated. After redrying as a solution in 1:1 CH_2Cl_2-pentane, the organics were again concentrated to yield 6.916 g (102 %) of crude 63. An analytical sample was prepared by chromatography on silica gel (5 % EtOAc/Hexane): ^1H NMR (300 MHz, $CDCl_3$) δ 7.6-6.4 (m, 20 H, Ph), 4.76 (d, J = 11.8 Hz, 1H, PhCHO), 4.62 (d, J = 11.8 Hz, 1H, PhCHO), 3.89 (ddd, J = 9.8, 5.35 and 3.0 Hz, 1H, NCH), 3.75 (ddd, J = 7.6, 5.35 and 3.7 Hz, 1H, OCH), 3.09 (dd, J = 12.8 and 3.0 Hz, 1H, PhCH), 2.96 and 2.94 (overlapping dd, J = 12.8 and 9.8 Hz, 1H, PhCH and ddd, J = 17, 3.7 and 2.4 Hz, 1H, C:CCH), 2.69 (ddd, J = 17, 7.6 and 2.7 Hz, 1H, C:CCH), 1.34 (app t, J = 2.7 and 2.4 Hz, 1H, C:CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.52, 139.67, 139.30, 138.49, 136.50, 129.80, 129.73, 128.36, 128.12, 127.97, 127.88, 127.82, 127.75, 127.65, 127.58, 127.37, 125.74, 82.14, 80.47, 72.51, 69.53, 66.36, 37.31, 20.94; IR (film) 3270, 3050, 3000, 2900, 2115, 1740, 1650, 1625, 1490, 1455, 1445, 1910, 1275, 1240, 1060, 1025, 745, 695 cm^{-1}; high resolution mass spectrum calcd. for $C_{32}H_{28}NO(M-H^+)$ 442.2211. Found 442.2216.

(2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenyl-6-(thiomethyl)hex-5-yne(64). A solution of i-Pr_2NEt (73 μl, 0.522 mmol, 1.05 eq) in THF (3 mL) at 0 °C was treated with n-BuLi (2.53 M in heptane, 206 μl, 0.522 mmol, 1.05 eq). After 30 min the mixture was cooled to -35 °C and 63 (0.25 M in THF, 2 mL, 0.497 mmol) was added dropwise.

HMPA (86 μl, 0.497 mmol) was added after 1 h and the mixture was then warmed to 0 °C for 1 h. CH_3SCN (40 μl, 0.577 mmol) was then added dropwise. After 30 min at 25 °C the reaction mixture was partitioned between Et_2O and sat. aqueous NH_4Cl. The layers were separated and the organic phase was washed with sat. aqueous NH_4Cl. Concentration of the organics gave a red oil which was filtered through neutral alumina (20 % EtOAc/Hexane). Concentration affords 0.234 g (96 %) of **64** as a red oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.8-6.5 (m, 20H, Ph), 4.78 (d, J = 11.9 Hz, 1H, PhCHO), 4.67 (d, J = 11.9 Hz, 1H, PhCHO), 3.94 (m, 1H), 3.79 (m, 1H), 3.17 (dd, J = 12.7 and 3.0 Hz, 1H), 3.08 (dd, J = 17.2 and 4.0 Hz, 1H), 3.02 (dd, J = 12.7 and 9.8 Hz, 1H), 2.85 (dd, J = 17.2 and 7.3 Hz, 1H), 2.36 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.33, 139.57, 139.23, 138.41, 136.43, 129.70, 129.62, 128.25, 128.02, 127.86, 127.74, 127.66, 127.53, 127.50, 127.26, 125.64, 90.52, 80.37, 72.24, 71.37, 68.35, 37.35, 22.44, 18.75; IR (film) 3050, 3020, 2940, 1970, 1670, 1620, 1600, 1500, 1455, 1450, 1320, 1280, 1080, 1030, 780, 690 cm^{-1}.

(2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenyltetradec-5-yne(65). A solution of **63** (3.46 g of crude product, ~7.65 mmol) in THF (25 mL) was added to a solution of LDA (9.56 mmol, 1.25 eq) in THF (50 mL) maintained at -35 °C. After 10 min, HMPA (1.33 mL, 1.0 eq) was added and the mixture was warmed to 0 °C for 45 min. The blue-green

solution was then treated with n-$C_8H_{17}I$ (2.76 mL, 2 eq) and allowed to stir 11 h at 25 °C. The reaction mixture was then partitioned between Et_2O (100 mL) and sat. aqueous NH_4Cl (100 mL). The organics were separated and washed twice with sat. aqueous NH_4Cl (50 mL) and were then dried and concentrated. The crude material was chromatographed on silica gel (5 % EtOAc/Hexane) to afford 2.22 g (52 % from 59) of 65 as a light orange, viscous oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.7-6.4 (m, 20H, Ph), 4.73 (d, J = 11.8 Hz, 1H, PhCHO), 4.59 (d, J = 11.8 Hz, 1H, PhCHO), 3.87 (ddd, J = 9.6, 5.6 and 3.0 Hz, 1H, NCH), 3.68 (ddd, J = 7.1, 5.6 and 4.0 Hz, 1H, OCH), 3.06 (dd, J = 12.8 and 3.0 Hz, 1H, PhCHC), 2.92 (dd, J = 12.8 and 9.6 Hz, 1H, PhCHC), 2.84 (app d pent, J = 16.9, 4.0 and 2.3 Hz, 1H, C:CCHCO), 2.63 (ddt, J = 16.9, 7.1 and 2.3 Hz, 1H, C:CCHCO), 2.19 (m, J = 6.9 and 2.3 Hz, 2H, $C:CCH_2$), 1.50 (p, J = 6.9, 2H, $C:CCH_2CH_2$), 1.43-1.28 (br s, 10H, $5CH_2$), 0.96 (t, J = 6.6, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.30, 139.88, 139.52, 138.80, 136.67, 129.86, 129.62, 128.34, 128.08, 127.94, 127.85, 127.81, 127.74, 127.67, 127.55, 127.27, 125.69, 81.59, 80.98, 77.42, 72.41, 66.62, 37.66, 31.83, 29.17, 29.14, 28.98, 28.95, 22.61, 21.30, 18.84, 14.06.

(2S,3S)-3-benzyloxy-1-phenyltetradec-5-yn-2-ylamine(51). To 65 (0.812 g, 1.48 mmol) in THF (14 mL) was added oxalic acid (0.317 M, 5 mL, 1.585 mmol, 1.07 eq). After 7 h at 25 °C, the reaction mixture was stirred

vigorously with KOH (0.5 M, 15 mL) and Et_2O (10 mL) for 10 min. The organics were separated and combined with three additional Et_2O extractions (8 mL) of the aqueous phase. Chromatography of the concentrated organics (10 % EtOAC/Hex - 10 % CH_3OH/CH_2Cl_2) affords 51 (0.376 g, 65 %) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.4-7.1 (m, 10H, Ph), 4.75 (d, J = 11.6 Hz, 1H, PhCHO), 4.51 (d, J = 11.6 Hz, 1H, PhCHO), 3.44 (app q, J = 10, 5.8 and 4.1 Hz, 1H, NCH), 3.27 (app p, J = 8.8, 4.5 and 4.1 Hz, 1H, OCH), 2.89 (dd, J = 13.3 and 5.1 Hz, 1H, PhCHC), 2.62 (dd, J = 13.3 and 9.0 Hz, 1H, PhCHC), 2.58 (m, J = 8.8 and 2.7 Hz, 2H, $OCCH_2$), 2.16 (app t, J = 6.9 Hz, 2H, $C{:}CCH_2$), 1.55-1.20 (m cont br s, 14H, $6CH_2$, NH_2), 0.90 (t, J = 6.5, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.45, 138.45, 129.15, 128.36, 128.28, 127.73, 127.56, 126.10, 82.32, 80.27, 76.35, 72.04, 55.09, 41.06, 31.79, 29.14, 29.08, 28.92, 28.86, 22.58, 20.96, 18.75, 14.02.

(2S,3S)-3-benzyloxy-1-phenylhex-5-yn-2-ylamine(71). A solution of 63 (7.24 g, 16.35 mmol) and oxalic acid monohydrate (2.6 g, 20 mmol) in THF (30 mL), H_2O (1 mL) and CH_3OH (6 mL) was allowed to stir 3 h at 25 °C. A solution of KOH (1.2 g) in H_2O (25 mL) was added. The mixture was transferred to a separatory funnel and extracted with hexane (1 x 20 mL) and 1:1 Et_2O-hexane (2 x 50 mL). The combined organics were dried and concentrated. Chromatography of the crude product (10 % EtOAc/Hexane-5 % CH_3OH/CH_2Cl_2) afforded

3.42 g (75 %) of 71 as a viscuous light yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45-7.1 (m, 10H, Ph), 4.74 (d, J = 11.5 Hz, 1H, PhCHO), 4.51 (d, J = 11.5 Hz, 1H, PhCHO), 3.48 (m, 1H), 3.24 (app pent, J = 4.6 Hz, 1H), 2.87 (dd, J = 13.3 and 5.0 Hz, 1H, PhCH), 2.7-2.5 (m, 3H, C:CCH), 2.01 (app t, J = 2.7 Hz, 1H, C:CH), 1.41 (s, 2H, NH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.29, 138.25, 129.20, 128.47, 128.40, 127.84, 127.73, 126.24, 81.12, 79.92, 72.31, 70.23, 55.09, 41.18, 20.76; IR (film) 3290, 3010, 2900, 2110, 1590, 1490, 1450, 1340, 1060, 1020, 770, 690 cm^{-1}; high resolution mass spectrum calcd. for $C_{19}H_{22}NO(MH^+)$ 280.1702. Found 280.1703. Anal. Calcd. for $C_{19}H_{21}NO$: C, 81.68; H, 7.58. Found: C, 81.13; H, 7.51.

5-Nonyl-2-(phenylmethyl)pyrrole(68). A solution of $HNEt_2$ (62 μl, 0.6 mmol) in DME (2 mL) was treated with n-BuLi (2.58 M in heptane, 233 μl, 0.6 mmol). The resultant mixture was added to a solution of $CpTiCl_3$ (66 mg, 0.3 mmol) in DME (1 mL). The mixture was brought to reflux and amine **51** (98 mg, 0.25 mmol) in DME (1 mL) was added dropwise over 1 h. After an additional 1 h the mixture was cooled to 25 °C and quenched with sat. aqueous $NaHCO_3$. The aqueous phase was extracted with Et_2O (3 x 5 mL) and the combined extractions were concentrated. Chromatography (10 % ETOAc/Hexane) provides a 53 % unoptimized yield of pyrrole **68** as an unstable oil. The same product was obtained upon treatment of DME or C_6H_6 solutions of $CpTi(CH_3)_2Cl$ with 51:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (br m, 1H, NH), 7.45-7.15 (m, 5H, Ph), 5.89 (app t, J = 2.8 Hz, 1H, NC:CH), 5.83 (app t, J = 2.8 Hz, 1H, NC:CH), 3.96 (s, 2H, $PhCH_2$), 2.53 (t, J = 7.7 Hz, 2H, $NCCH_2$), 1.60 (app pent, J = 7.5 Hz, 2H, CH_2), 1.30 (br s, 12H, $6CH_2$), 0.92 (t, J = 7.0 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.87, 132.30, 128.82, 128.60, 128.49, 126.25, 106.39, 104.68, 34.17, 31.86, 29.63, 29.50, 29.41, 29.36, 29.37, 27.78, 22.64, 14.06; IR (film) 3350, 2900, 2840, 1450, 1255, 1225, 770, 700 cm^{-1}.

N-Carbomethoxy-5-nonyl-2-(phenylmethyl)pyrrole(70). A solution of $CpTiCl_3$ (96 mg, 0.44 mmol) in C_6H_6 (2 mL) at 25 °C was treated with CH_3Li (0.644 M, 1.37 mL, 0.88 mmol). The mixture was brought to reflux and amine **51** (0.4 M in C_6H_6, 1 mL, 0.4 mmol) was added over 0.5 h. After 15 min the mixture was cooled to 25 °C and $ClCO_2CH_3$ (78 μl, 1 mmol) was added. After 2 h the reaction mixture was quenched with CH_3OH and concentrated. Trituration of the resultant solids with 30 % EtOAc/Hexane followed by filtration of the organics through a silica plug and concentration provided crude product. Chromatography (5 % EtOAc/Hexane) afforded **70** (61 mg, 45 %) as an unstable oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.1 (m, 5H, Ph), 5.89 (d, J = 3.4 Hz, 1H, NC:CH), 5.78 (d, J = 3.4 Hz, 1H, NC:CH), 4.15 (s, 2H, $PhCH_2$), 3.77 (s, 3H, CH_3O), 2.80 (t, J = 7.6 Hz, 2H, $NCCH_2$), 1.60 (app pent, 2H, CH_2), 1.45-1.15 (m, 12H, $6CH_2$), 0.91 (t, J = 6.8, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.19, 140.02,

137.37, 133.80, 128.39, 128.20, 128.16, 125.93, 112.34, 109.54, 53.13, 35.91, 31.87, 29.55, 29.48, 29.41, 29.28, 29.02, 22.64, 14.06; IR (film) 2900, 2820, 1745, 1445, 1325, 1110, 1025, 780, 700 cm^{-1}.

Octanoyl Nitrile(74). Octanoyl chloride (4.27 mL, 25 mmol) was added to a suspension of CuCN (2.69 g, 30 mmol) in CH_3CN (30 mL). The resultant mixture was brought to reflux for 30 min, at which time the CH_3CN was allowed to distill from the reaction mixture. The residue was then distilled from the copper salts under aspirator pressure. Redistillation at aspirator pressure (98-102 °C) afforded 2.5 g (65 %) of **74** as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 2.71 (t, J = 7.3 Hz, 2H, CH_2CO), 1.71 (app pent, J = 7.3 Hz, 2H, CH_2CH_2CO), 1.4-1.2 (m, 8H, $4CH_2$), 0.87 (t, J = 6.7 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.06, 113.24, 44.98, 31.38, 28.68, 28.48, 22.72, 22.43, 13.89; IR (film) 2910, 2845, 2205, 1725, 1460, 1380, 1370, 1120, 1070, 1015, 740 cm^{-1}.

(4S,5S)-4-benzyoxy-2-[2'-cyano-1'-nonen-1'-yl]-5-(phenylmethyl)-2H-pyrrole(76). A solution of $CpTiCl_3$ (230 mg, 1.05 mmol) in THF (3 mL) at 25 °C was treated with CH_3Li (1.8 M in Et_2O, 1.17 mL, 2.10 mmol). After 15 min the mixture was cooled to 0 °C and **71** (270 mg, 0.97 mmol) in THF (1 mL) was added. The mixture was stirred 2 h in the dark at 25 °C. The dark burgundy solution was then cooled to

0 °C and **74** (168 mg, 1.1 mmol) was added. After 2 h at 25 °C florisil (~0.5 g) and hexane (5 mL) were added. The resultant slurry was filtered through florisil (2") with the aid of 1:1 Et_2O-hexane (50 mL). Concentration of the organics yields crude **76** (307 mg, 76 %) as a yellow oil. The major product can be isolated by column chromatography (10 % EtOAc/Hexane) in 40-60 % yield. However, better overall yields were obtained when crude **76** was employed in the preparation of **77**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.5-7.15 (m, 10H, Ph), 6.92 (s, 1H, C:CH), 4.56 (d, J = 11.7 1H, PhCHO), 4.33 (d, J = 11.7 1H, PhCHO), 4.25-4.12 (m, 2H, NCH, OCH), 3.41 (d, J = 17.7 Hz, 1H, PhCH), 3.33 (dd, J = 13.8 and 6.5 Hz, 1H, N:CCH), 3.23 (dd, J = 13.8 and 8.2 Hz, 1H, N:CCH), 2.97 (ddd, J = 17.7, 5.0 and 1.3 Hz, 1H, PhCH), 2.39 (t, J = 7.46 Hz, 2H, C:CCH_2), 1.64 (m, 2H, CH_2), 1.45-1.25 (m, 10H, 5CH_2), 0.93 (t, J = 6.7 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.63, 139.83, 139.80. 137.74, 129.02, 128.20, 128.13, 127.45, 125.86, 120.29, 117.51, 78.20, 76.81, 71.20, 41.82, 35.98, 34.84, 31.43, 28.68, 28.43, 27.66, 22.40, 13.85; IR (film) 3020, 3000, 2930, 2900, 2850, 2195, 1700, 1495, 1455, 1345, 1100, 1060, 1030, 730, 690 cm^{-1}; MS (ESI^+) chemical mass calcd for $C_{28}H_{35}N_2O(MH^+)$ 415.6. Found 415.6. Anal. Calcd for $C_{28}H_{34}N_2O$: C, 81.12; H, 8.27. Found: C, 80.30; H, 8.54.

(2S,3S,5R)-4-benzyloxy-2-[2'-cyano-1'-nonen-1'-yl]-1-methyl-5-(phenylmethyl)-pyrrolidine(77). To a solution of

crude **76** (307 mg, 0.741 mmol) in CH_2Cl_2 (3 mL) at 0 °C was added CH_3OTF (100 μL, 0.888 mmol). After 2 h at 25 °C the mixture was cooled to -72 °C and a solution of $NaBH_3CN$ (56 mg, 0.888 mmol) in CH_3OH (1 mL) was added *via* syringe. The cooling bath was removed and the mixture was stirred vigorously for 2 h at 25 °C. After quenching with 1 M NaOH (3 mL), the mixture was diluted with pentane (4 mL). The organic phase was separated and combined with two 1:1 CH_2Cl_2-pentane extractions (3 mL) of the aqueous phase. The organics were dried and concentrated to afford **77** (258 mg, 81 %) as an orange oil. An analytical sample was prepared by column chromatography (5 % EtOAc/Hexane): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4-7.1 (m, 10H, Ph), 6.17 (d, J = 9.3 Hz, 1H, C:CH), 4.43 (d, J = 11.6 Hz, 1H, PhCHO), 4.22 (d, J = 11.6 Hz, 1H, PhCHO), 3.72 (m, J = 2.3 Hz, 1H, OCH), 3.25 (app q, J = 8.6 Hz, 1H, NCHC:C), 3.04 (dd, J = 13.2 and 10.1 Hz, 1H, PhCH), 2.83 (dd, J = 13.2 and 4.3 Hz, 1H, PhCH), 2.56 (app p, J = 5.0 and 4.5 Hz, 1H, NCHBn), 2.31 (s, 3H, NCH_3), 2.28-2.17 (m, 3H, C:CCH_2, β-H), 1.64 (ddd, J = 13.9, 7.4 and 2.3 Hz, 1H, α-H), 1.53 (m, 2H, CH_2), 1.26 (m, 8H, $4CH_2$), 0.87 (t, J = 6.6 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.32, 139.69, 139.25, 129.26, 128.23, 128.17, 127.97, 127.52, 125.89, 117.37, 115.94, 77.55, 72.64, 71.02, 66.00, 39.30, 36.45, 34.16, 33.87, 31.62, 28.81, 28.52, 27.84, 22.52, 13.95; IR (film) 3050, 3000, 2900, 2850, 2190, 1470, 1440, 1330, 1140, 1085, 1055, 1020, 755, 690 cm^{-1}.

high resolution mass spectrum calcd. for $C_{29}H_{38}N_2O(M^+)$ 430.2985. Found 430.2988.

Diastereomeric Nitriles 78. To crude **77** (250 mg, 0.58 mmol) in abs. CH_3OH (5 mL) was added magnesium turnings (0.56 g, 23 mmol). The flask was then placed in a water bath at 25 °C and stirred 5 h. The mixture was concentrated and then subjected to vacuum. The resultant mass was triturated with hexane (3 X 4 mL). After filtering through a plug of florisil the organics were concentrated to afford **78** (230 mg, 90 %) as a reddish oil. Chromatographic purification (5 % EtOAc/Hexane) provided 147 mg (35 % from **71**) of the diastereomeric mixture **78**. The ^1H NMR spectrum of the mixture (Appendix) exhibits two NCH_3 resonances in a ratio of 0.76:1. IR (film) 3040, 3000, 2900, 2830, 2215, 1470, 1450, 1430, 1330, 1110, 1080, 1050, 1015, 755, 690 cm^{-1}; high resolution mass spectrum calcd. for $C_{29}H_{40}N_2O(M^+)$ 432.3140. Found 432.3147.

(2S,3S,5R)-1-methyl-5-nonyl-2-(phenylmethyl)-3-pyrrolidinol(2). To potassium (100 mg, 2.6 mmol) in Et_2O (2 mL) at 0 °C was added first HMPA (0.5 mL), followed by a solution of the nitriles **78** (43.3 mg, 0.1 mmol) and t-BuOH (100 mg, 1.35 mmol) in Et_2O (0.8 mL) and toluene (0.8 mL). In the absence of toluene as cosolvent, reduction of the phenylmethyl substituent was also observed. The resultant mixture was stirred 4 h at 25 °C and then diluted with

hexane (4 mL). The organics were decanted and extracted with sat. aqueous NH_4Cl (6 x 3 mL). Drying and concentration afforded crude product which exhibited olefinic resonances in its ^1H NMR spectrum. The crude material was diluted with abs. EtOH (5 mL) and 10 % Pd-C (3 mg) was added. The flask was flushed with H_2 and the mixture then stirred 4 h under H_2 (40 psi). After filtering through celite with the aid of EtOAc/Hexanes, the organics were concentrated to a red oil. Chromatography on silica gel (5 % CH_3OH/CH_2Cl_2) afforded **2** (27 mg, 85 %) as a waxy solid: $[\alpha]^{25}_D$ +30.0° (c 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.35-7.1 (m, 5H, Ph), 3.86 (m, 1H, OCH), 2.90 (dd, J = 13.3 and 10.4 Hz, 1H, NCH), 2.87 (dd, J = 13.3 and 4.3 Hz, 1H, NCH), 2.40 (s, 3H, NCH_3), 2.35-2.1 (m, 3H), 1.8-1.15 (m, 17H), 0.85 (t, J = 6.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$ δ 138.96, 129.36, 128.45, 126.24, 74.10, 70.19, 66.45, 39.29, 38.34, 34.03, 33.19, 31.87, 29.76, 29.56, 29.52, 29.26, 26.31, 22.64, 14.03; IR (film) 3360, 3015, 3000, 2920, 2900, 2830, 2760, 1480, 1455, 1130, 1025, 780, 695 cm^{-1}; high resolution mass spectrum calcd. for $C_{21}H_{34}NO(M^+-H)$ 316.2641. Found 316.2644.

REFERENCES

REFERENCES

1. Dötz, K.H. *Angew. Chem. Int. Ed. Engl.* **1984**, 23, 587.
2. Sayatkovskii, A.I.; Babitskii, B.D. *Russ. Chem. Rev.* **1985**, 53, 672.
3. Young, J.R.; Stille, J.R. *J. Am. Chem. Soc.* **1992**, 114, 4937.
4. Semmelhack, M.F.; Bozell, J.J.; Sato, T.; Wulff, W.; Spiess, E.; Zask, A. *J. Am. Chem. Soc.* **1982**, 104, 5850.
5. Gagné, M.R.; Marks, T.J. *J. Am. Chem. Soc.* **1989**, 111, 4108.
6. Gagné, M.R.; Stern, C.L.; Marks, T.J. *J. Am. Chem. Soc.* **1992**, 114, 275.
7. Nugent, W.A.; Mayer, J.M. Metal-Ligand Multiple Bonds, Wiley-Interscience, New York, 1988.
8. Chrisholm, M.H.; Rothwell, I.P. *Comprehensive Coordination Chemistry*, Pergamon Press, New York, 1987.
9. Haymore, B.L.; Maatta, E.A.; Wentworth, R.A.D. *J. Am. Chem. Soc.* **1979**, *101*, 2063.
10. Chatt, J.; Dosser, R.J.; King, F.; Leigh, G.J. *J. Chem. Soc., Dalton Trans.* **1976**, 2435.
11. Clifford, A.F.; Kobayashi, C.S. *Abstracts, 130th Nat. Meeting of the Am. Chem. Soc.*, **1956**, p. 50R.
12. Patrick, D.W.; Truesdale, L.K.; Biller, S.A.; Sharpless, K.B. *J. Org. Chem.* **1978**, 43, 2628.
13. Barner, C.J.; Collins, T.J.; Mapes, B.E.; Santarsiero, B.D. *Inorg. Chem.* **1986**, *25*, 4322.
14. Breslow, R.; Gellman, S.H. *J. Chem. Soc., Chem. Comm.* **1982**, 1400.
15. Groves, J.T.; Takahashi, T. *J. Am. Chem. Soc.* **1983**, *105*, 2073.
16. See ref. 7, pp. 248-251.

17. Burrington, J.D.; Kartisek, C.T.; Grasselli, R.K. *J. Catal.* **1984**, *87*, 363.

18. For a review of terminal and briding imido complexes for the years through 1978, see Nugent, W.A.; Haymore, B.L. *Coord. Chem. Rev.* **1980**, *31*, 123.

19. Walsh, P.J.; Hollander, F.J.; Bergman, R.G. *J. Am. Chem. Soc.* **1988**, *110*, 8729.

20. Carney, M.J.; Walsh, P.J.; Hollander, F.J.; Bergman, R.G. *J. Am. Chem. Soc.* **1989**, *111*, 8751.

21. Cummins, C.C.; Baxter, S.M.; Wolczanski, P.T. *J. Am. Chem. Soc.* **1988**, *110*, 8731.

22. Jekel-Vroegop, C.T.; Teuben, J.H. *J. Organomet. Chem.* **1985**, *286*, 309.

23. Ritter, F.J.; Rotgans, I.E.M.; Talman, E.; Verwiel, P.E.J.; Stein, F. *Experientia* **1973**, *29*, 530.

24. Schwartz, R.E.; Liesch, J.; Hensens, O.; Zitano, L.; Honeycutt, S.; Garrity, G.; Fromtling, R.A. Onishi, J.; Monaghan, R. *J. Antibiot.* **1988**, *41*, 1774. We thank Dr. Schwartz for graciously supplying an authentic sample of (+)-preussin for direct spectral comparison.

25. Hill, J.E.; Profilet, R.D.; Fanwick, P.E.; Rothwell, I.P. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 664.

26. Roesky, H.W.; Voelker, H.; Witt, M.; Noltemeyer, M. *Angew. Chem. Int. Ed. Engl.* **1990** *29*, 669.

27. Cummins, C.C.; Schaller, C.P.; VanDuyne, G.D.; Wolczanski, P.T.; Chan, A.W.E.; Hoffman, R. *J. Am. Chem. Soc.* **1991**, *113*, 2985.

28. Doxsee, K.D.; Farahi, J.B. *J. Am. Chem. Soc.* **1988**, *110*, 7239.

29. Doxsee, K.D.; Farahi, J.B.; Hope, H. *J. Am. Chem. Soc.* **1992**, submitted for publication.

30. Jensen, M. Ph.D. Thesis "Carbocycle and Heterocycle Annulations Mediated by Group IV Transition Metal Complexes."

31. McGrane, P.L.; Jensen, M.; Livinghouse, T. *J. Am. Chem. Soc.* **1992** 114, 5459.

32. Lund, E.C.; Livinghouse, T.S. *Organometallics* **1990**, *9*, 2426.

33. Cardoso, A.M.; Clark, R.J.H.; Moorhouse, S. *J. Chem. Soc., Dalt. Trans.* **1980**, 1156.

34. Though $CpTiCl_3$ is commercially available, both it and the TMSCp[35] used in the preparation of $CpTiCl_3$ are quite expensive. For this reason, these compounds were prepared in-house by modifications of the literature procedures[33,35].

35. Frisch, K.C. *J. Am. Chem. Soc.* **1953**, 75, 6050.

36. Prepared *in situ*. This is, however, a known complex. Erskine, G.J.; Hunter, B.K.; McCowan, J.D. *Tetrahedron Lett.* **1985**, *26*, 1371.

37. Prepared *in situ via* treatment of $CpTiCl_2OCH_3$[38] with two equivalents of CH_3Li.

38. Gorsich, R.D. *J. Am. Chem. Soc.* **1960**, *82*, 4211.

39. Effluent from the reaction was submitted to Dr. L.J. Sears and was analyzed by GLC on a 6 ft x 2 mm i.d. glass column packed with 100-120 mesh alumina. Methane was confirmed by comparison to an authentic sample.

40. Subsequent elimination and cycloaddition are quite rapid. Treatment of an equimolar solution of Cp_2ZrCl_2 and 5-phenylpent-4-yn-1-ylamine with 2 eq. of CH_3Li gives the expected pyrrole in reasonable yield in less than two hours.

41. Friedman, L.; Schechter, H. *J. Org. Chem.* **1960**, *25*, 877.

42. Nystrom, R.F.; Brown, W.G. *J. Am. Chem. Soc.* **1948**, *70*, 3738.

43. Anagnostopoulos, A., Nicholls, D. *J. Inorg. Nuclear Chem.* **1966**, *28*, 3045.

44. McGrane, P.L.; Livinghouse, T. *J. Org. Chem.* **1992**, *57*, 1323.

45. Ritter, F.J.; Brüggèman-Rotgans, I.E.M.; Verwiel, P.E.J.; Talman, E.; Stein, F.; LaBrun, J.; Persoons, C.J. *Proc. VIII Int. Congr. IUSSI*, Wageningen, Netherlands, pp. 41-43.

46. Beatson, S.H. *Lancet* **1972**, *2*, 425.

47. Oliver, J.E., Sonnet, P.E. *J. Org. Chem.* **1974**, *39*, 2662.

48. Jefford, C.W.; Tang, Q.; Zaslona, A. *J. Am. Chem. Soc.* **1991**, *113*, 3513.

49. Yamazaki, N.; Kibayashi, C. *Tetrahedron Lett.* **1988**, *29*, 5767.

50. Ito, M.; Kiboyashi, C. *Tetrahedron Lett.* **1990**, *31*, 5065.

51. One additional synthesis of (+)-monomorine has been advanced. Momose, T.; Toyooka, N.; Seki, S.; Hirai, Y. *Chem. Pharm. Bull.* **1990**, *38*, 2072.

52. Yamaguchi, R.; Hata, E.I.; Matsuki, T.; Kawanishi, M. *J. Org. Chem.* **1987**, *52*, 2094. For other syntheses of (±) Monomorine, see refs. 47 and 53-58.

53. Macdonald, T.L. *J. Org. Chem.* **1980**, *45*, 193.

54. Sonnet, P.E.; Netzel, D.A.; Mendoza, R. *J. Heterocycl. Chem.* **1979**, *16*, 1041.

55. Sonnet, P.E.; Oliver, J.E. *J. Heterocycl. Chem.* **1975**, *12*, 289.

56. Stevens, R.V.; Lee, A.W.N. *J. Chem. Soc. Chem. Commun.* **1982**, *23*, 102.

57. Watanabe, Y.; Iida, H.; Kibayashi, C. *J. Org. Chem.* **1989**, *54*, 4088.

58. Iida, H.; Watanabe, Y.; Kibayashi, C. *Tetrahedron Lett.* **1986**, *27*, 5513.

59. Warrener, R.N.; Cain, E.N. *Angew. Chem. Int. Edit. Engl.* **1966**, *5*, 511.

60. Ensley, H.E.; Lohr, R. *Tetrahedron Lett.* **1978**, *19*, 1415.

61. Sato, T.; Kawara, T.; Sakata, K.; Fujisawa, T. *Bull. Chem. Soc. Jpn.* **1981**, 54, 505.

62. Büchi, G.; Wuest, H. *J. Org. Chem.* **1969**, *34*, 1122.

63. Smith, W.N.; Beumel, O.F. *Synthesis*, **1974**, 441.

64. An alternative preparation of this alkyne has been published. Heather, J.B.; Sood, R.; Price, P.; Peruzzotti, G.P.; Lee, S.S.; Lee, L.H.; Sih, C.J. *Tetrahedron Lett.* **1973**, *14*, 2313.

65. Brandsma, L. *Preparative Acetylenic Chemistry*, 2nd Ed., Elsevier Science Publishers, Amsterdam, The Netherlands, 1988, p. 81.

66. Crossland, R.K.; Servis, K.L. *J. Org. Chem.* **1970**, *35*, 3195.

67. Holton, R.A.; Zoeller, J.R. *J. Am. Chem. Soc.* **1985**, *107*, 2124.

68. Harding, K.E.; Burks, S.R. *J. Org. Chem.* **1981**, 46, 3921.

69. Matsumura, Y.; Maruoka, K.; Yamamoto, H. *Tetrahedron Lett.* **1982**, *23*, 1929.

70. Still, W.C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

71. Itsuno, S.; Nakano, M.; Miyazaki, K.; Masuda, H.; Ito, K.; Hirao, A.; Nakahama, S. *J. Chem. Soc., Perkin I* **1985**, *2039*.

72. Itsuno, S.; Nakano, M.; Ito, K.; Hirao, A.; Owa, M.; Kanda, N.; Nakahama, S. *J. Chem. Soc., Perkin I* **1985**, *2615*.

73. Olah, G.A.; Rochin, C. *J. Org. Chem.* **1987**, *52*, 702.

74. Johnson, J.H.; Phillipson, D.W.; Kahle, A.D. *J. Antibiot.* **1989**, *42*, 1185.

75. Pak, C.S.; Lee, G.H. *J. Org. Chem.* **1991**, *56*, 1128.

76. Polt, R.L.; Peterson, M.A. *Tetrahedron Lett.* **1990**, *31*, 4985.

77. Polt, R.L.; Peterson, M.A.; DeYoung, L. *J. Org. Chem.* **1992**, 57, 5469. We thank Professor Polt for providing us a copy of this manuscript prior to publication.

78. O'Donnell, M.J.; Polt, R.L. *J. Org. Chem.* **1982**, *47*, 2663.

79. Aminoester hydrochlorides are readily available from the amino acids. *Helv. Chim. Acta.* **1961**, 721.

80. Wright, W.B. *J. Heterocyclic Chem.* **1965**, 2, 41.

81. Greene, T.W.; Wuts, P.G.M. *Protective Groups in Organic Synthesis*, John Wiley & Sons, Inc., New York, 1991, p. 47.

82. This mode of approach has been demonstrated for ligand cyclization reactions (ref. 3 and ref. therein) and may be applicable to this system.

83. Acyl nitriles are readily prepared by reaction of the corresponding acyl chloride with CuCN in CH_3CN. Hünig, S.; Schaller, R. *Angew, Chem. Int. Ed., Engl.* **1982**, 21, 36.

84. Profitt, J.A.; Watt, D.S. *J. Org Chem.* **1975**, 40, 127.

85. Cuvigny, Thérèsa; Larcheveque, Marc; Normant, Henri, *Bull. Soc. Chim. France*, **1973**, 1174.

86. Although it was initially thought that 1-chloro-3-iodopropane would provide the best selectivity for monosubstitution, it was found that 1-bromo-3-chloropropane is superior in this respect. This is due to the relative propensities of iodide and bromide ion to displace chloride ion.

87. Brandsma, L. *ibid.*, p. 24.

88. Sterzycki, R. *Synthesis* **1979**, 724.

89. Borch, R.F.; Bernstein, M.D.; Durst, H.D. *J. Am. Chem. Soc.* **1971**, *93*, 2897.

90. The published protocol for workup of phthalimide forming (Gabriel) reactions is less than optimal. Specifically, extraction of the phthalimide from aqueous DMF is cumbersome, complicated by formation of emulsions, and accompanied by coextraction of DMF. We found it efficacious simply to remove the DMF at 60-65 °C on a rotoevaporator and then rid the product of inorganic salts by trituration with water. Alternative workup procedures for the initial step of the Gabriel amine synthesis have since been published[5,6].

91. An alternative to the Gabriel amine synthesis that uses $NaN(TMS)_2$ is also known. Bestmann, H.J.; Wöfel, G. *Chem. Ber.* **1984**, *117*, 1250.

92. Miesel, J.L. U.S. Pat. #3927020 (Cl. 260-309.2; C07D), 1975, CA #85:94361y.

93. Dumont, J.L.; Chodkiewicz, W.; Cadiot, P. *Bull. Chim. Soc. Fr.* **1967**, 588.

94. For a general reference on tetrahydropyridines, see Klingsberg, E. (ed.), "The Chemistry of Heterocyclic Compounds," Vol. 14, Part I, pp. 83-91, Interscience Pub. Inc., New York **1960**.

95. Etienne, A.; Correia, Y. *Bull. Soc. Chim. France* **1969**, 3704.

96. Bielawski, J.; Brandänge, S.; Lindblom, L. *J. Heterocyclic Chem.* **1978**, 15, 97.

97. Brown, H.C.; Brown, C.A. *J. Am. Chem. Soc.* **1963**, 85, 1005.

98. House, H.O.; Lee, L.F. *J. Org. Chem.* **1976**, 41, 863.

99. A potentially more direct approach to alkynols of this type involves alkylation of dimetallated propargyl alcohol. Unfortunately, neither 2-(2-bromoethyl)-1,3-dioxolane nor the corresponding iodide functioned adequately as an alkylating agent.

APPENDIX

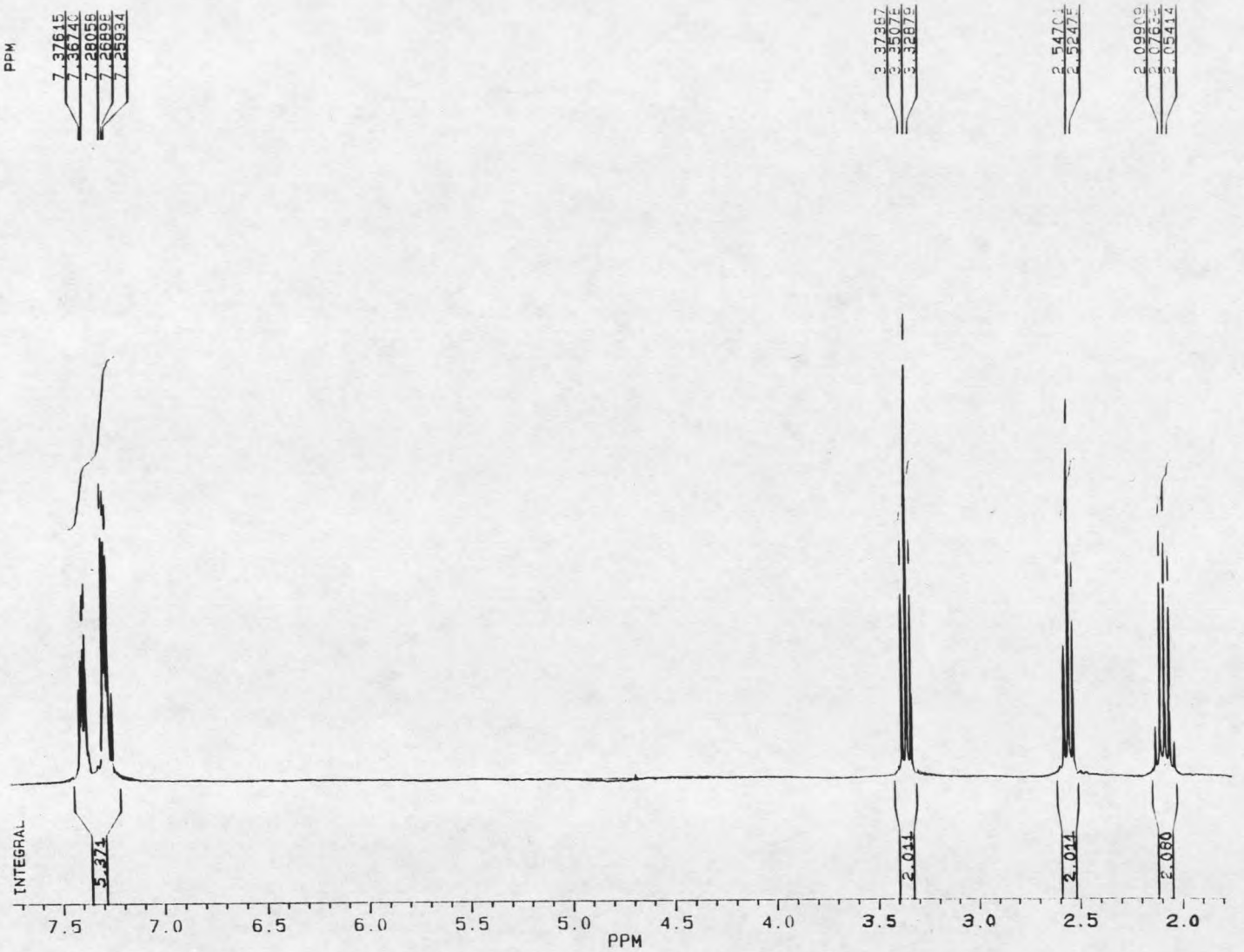


Figure 8. ^{1}H NMR Spectrum of 1-Iodo-5-phenylpent-4-yne(16).

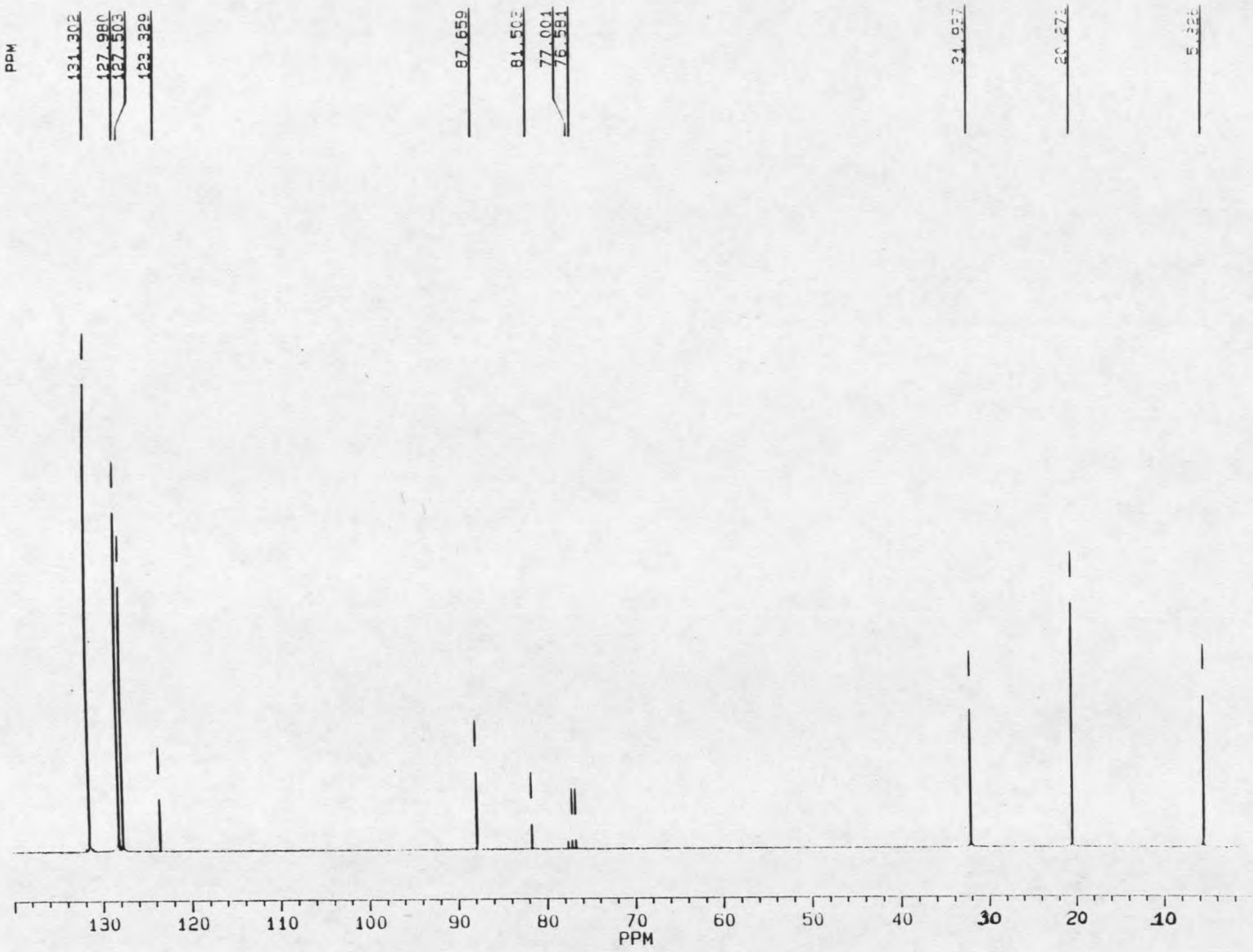


Figure 9. ^{13}C NMR Spectrum of 1-Iodo-5-phenylpent-4-yne(16).

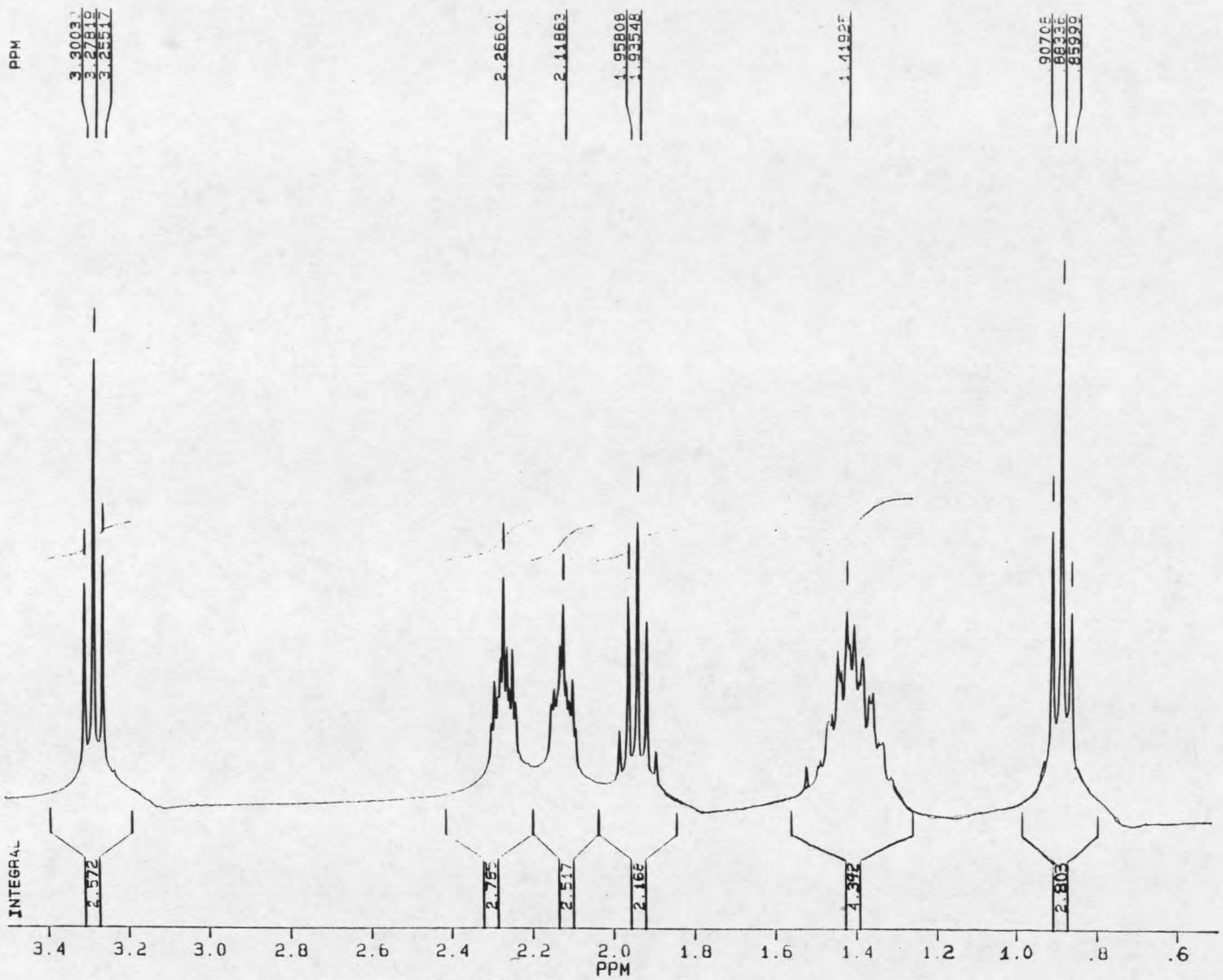


Figure 10. ^{1}H NMR Spectrum of 1-Iodonon-4-yne.

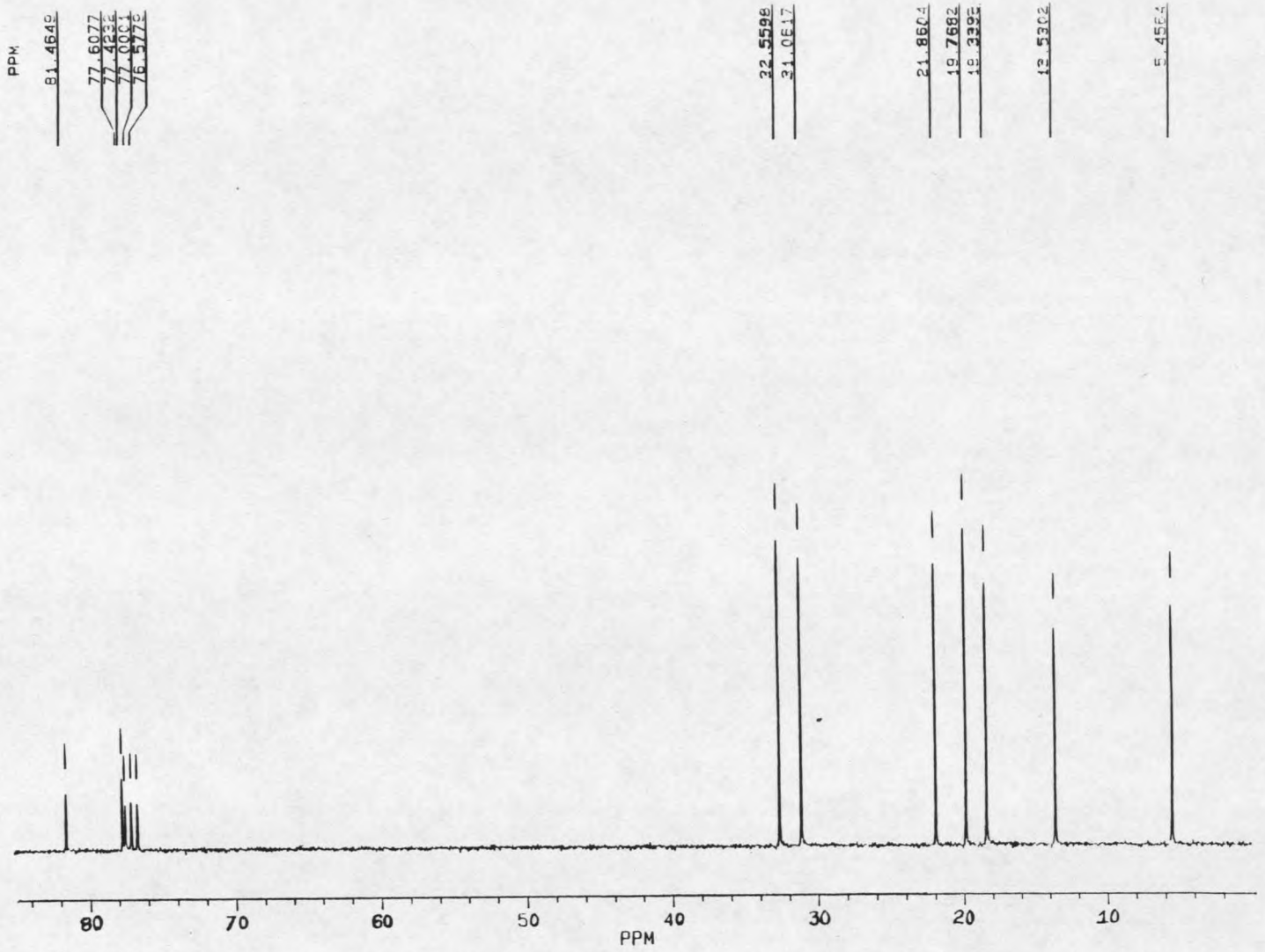


Figure 11. ^{13}C NMR Spectrum of 1-Iodonon-4-yne.

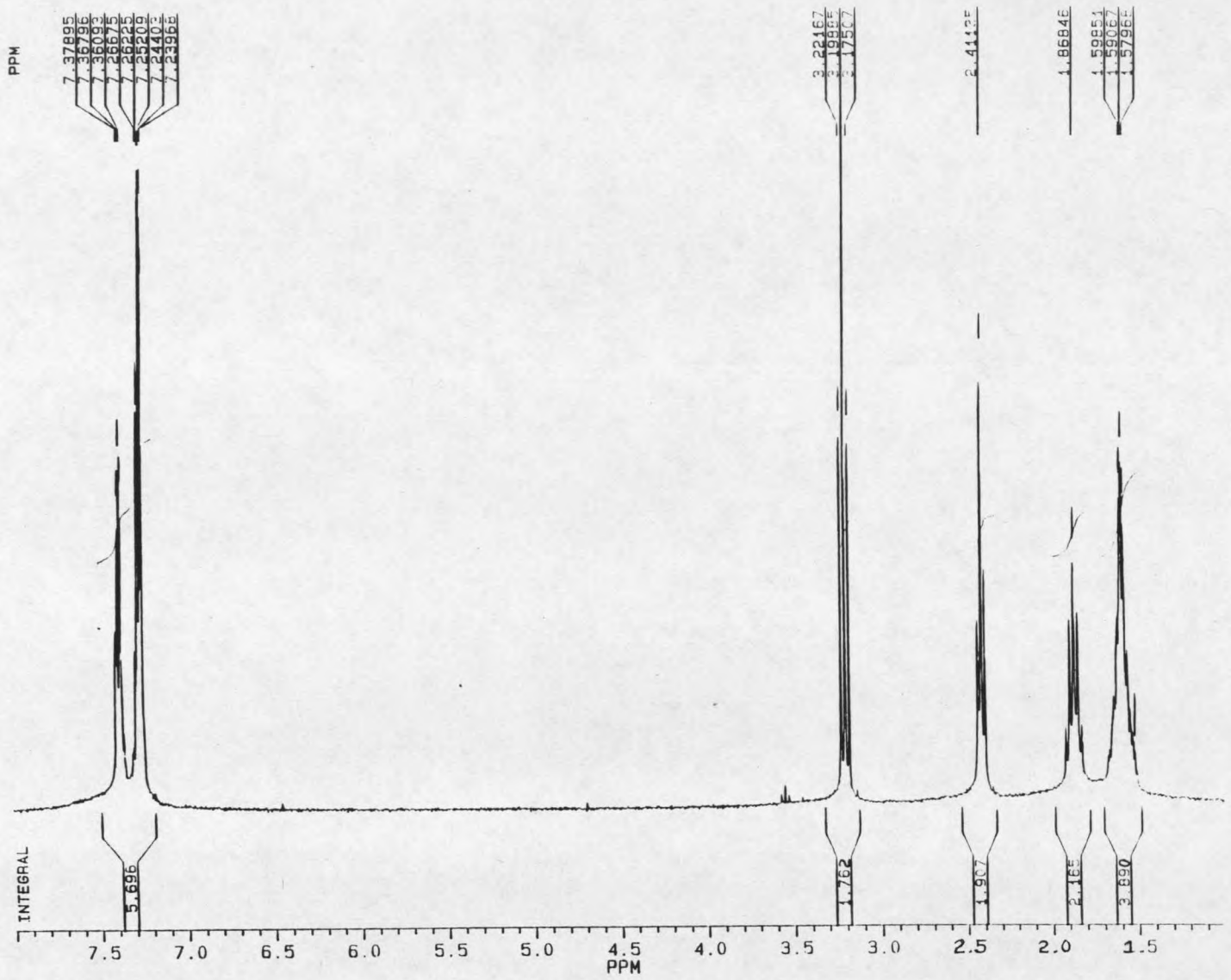


Figure 12. ^{1}H NMR Spectrum of 7-Iodo-1-phenylhept-1-yne(35).

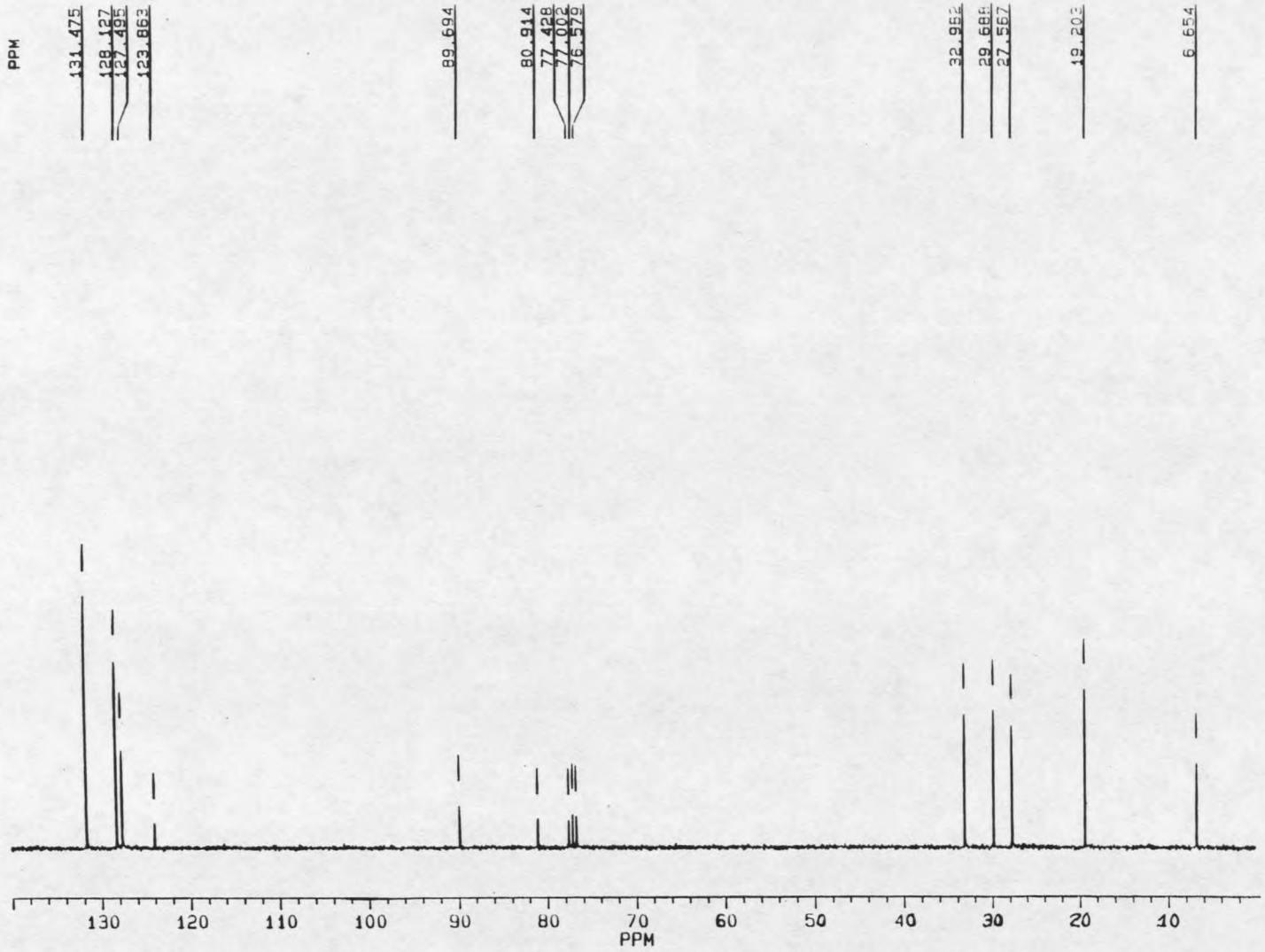


Figure 13. ^{13}C NMR Spectrum of 7-Iodo-1-phenylhept-1-yne(35).

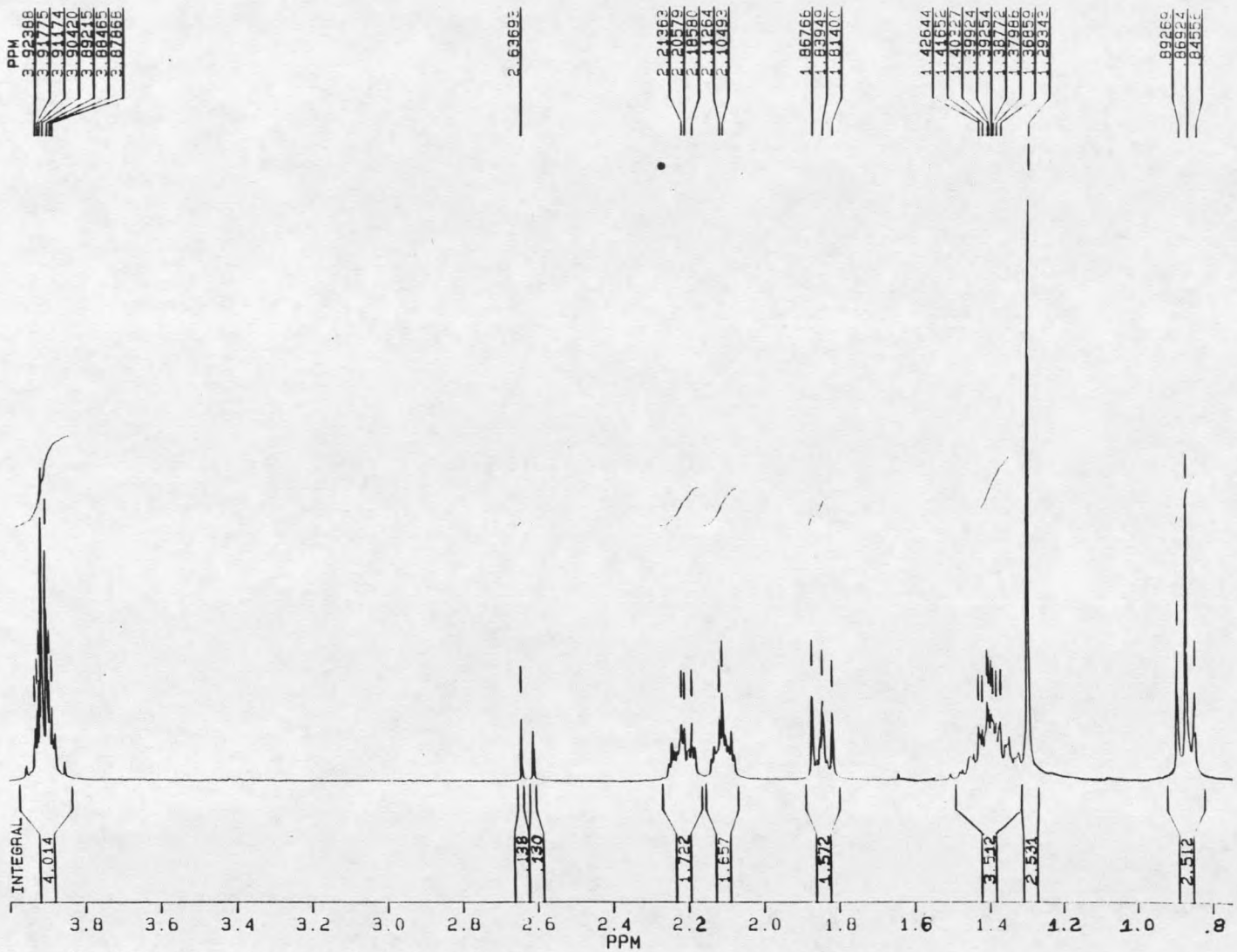


Figure 14. ^{1}H NMR Spectrum of 2,2-Ethylene-dioxydec-5-yne(24).

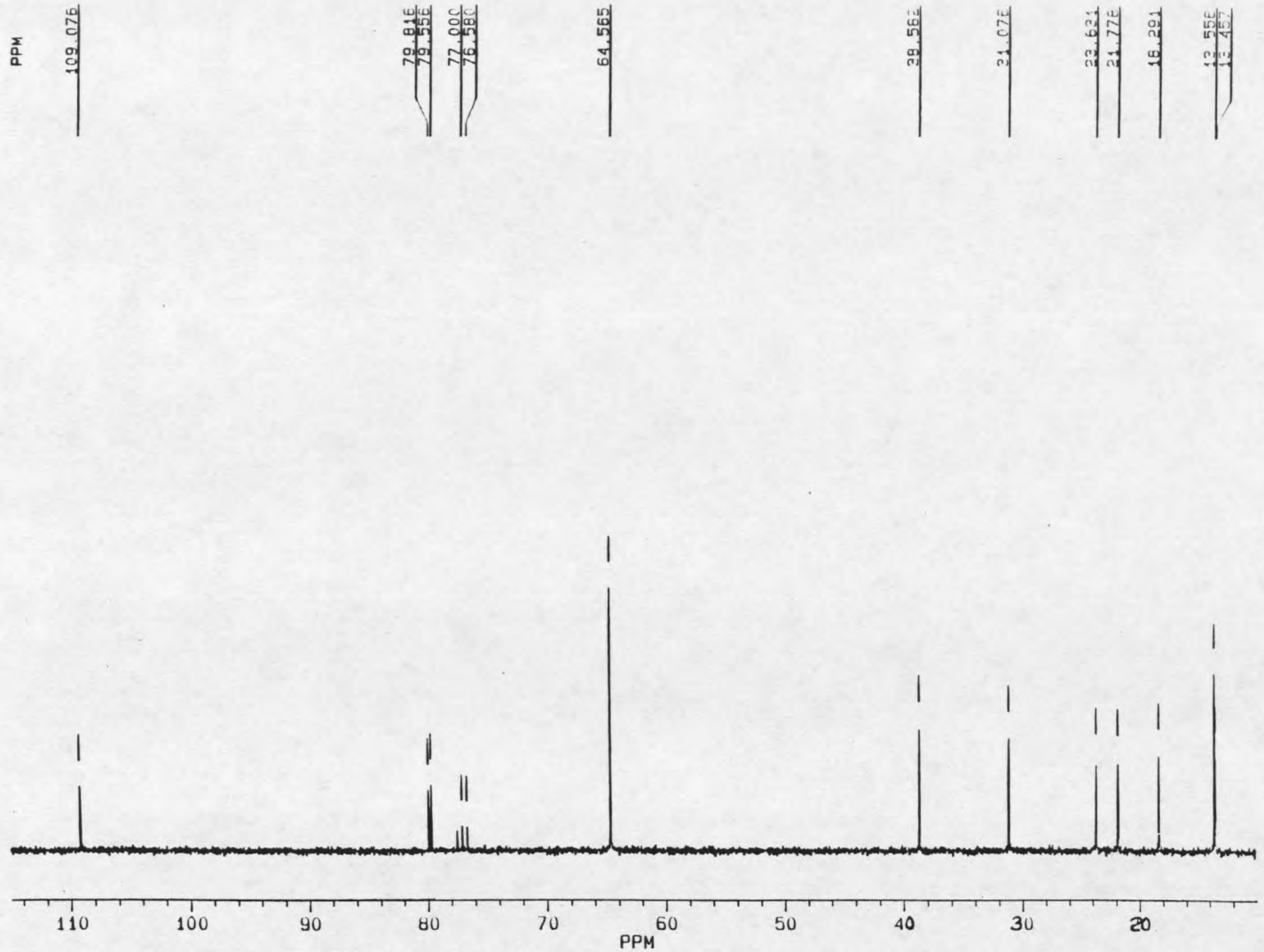


Figure 15. ^{13}C NMR Spectrum of 2,2-Ethylene-dioxydec-5-yne(24).

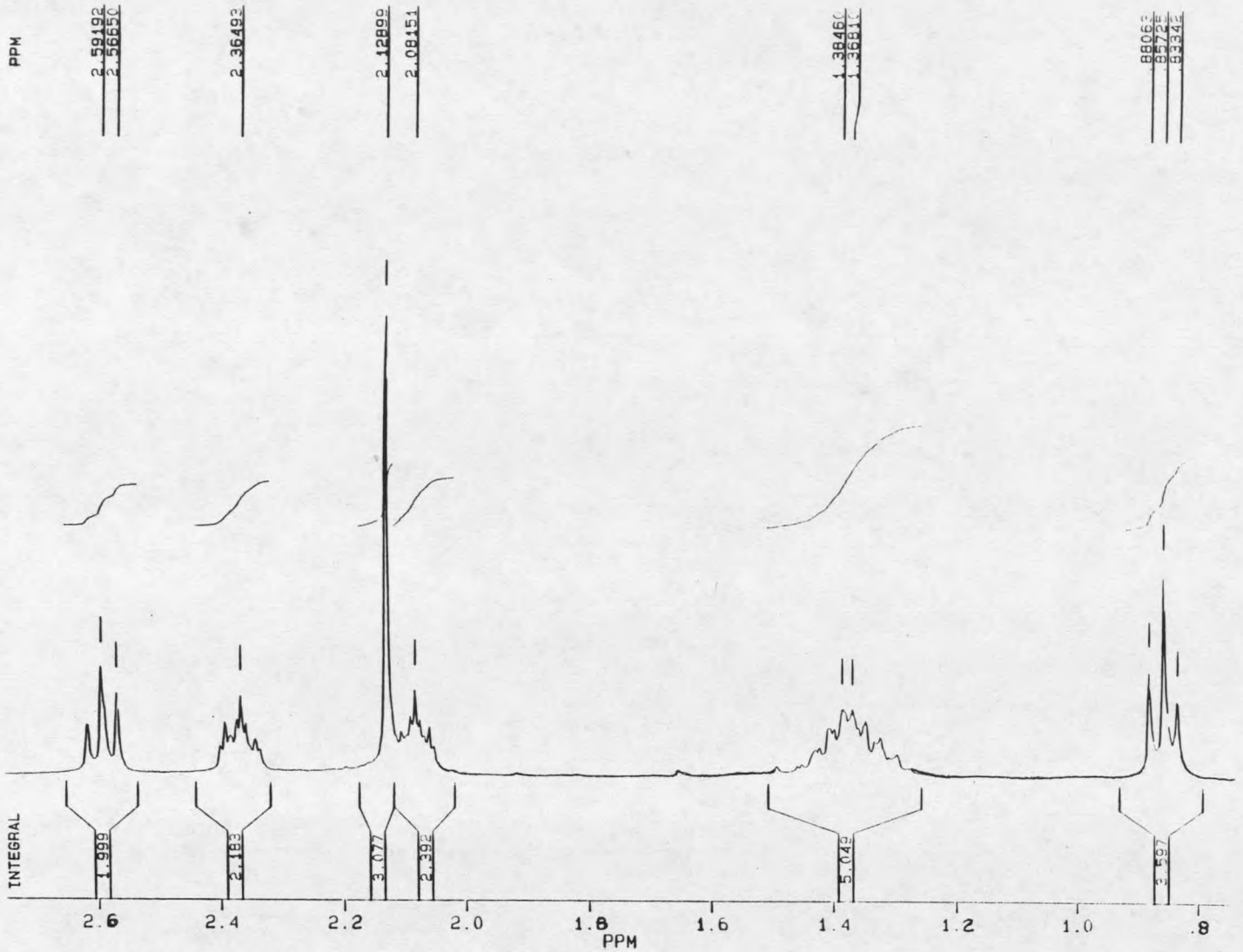


Figure 16. ^{1}H NMR Spectrum of Dec-5-yn-2-one(25).

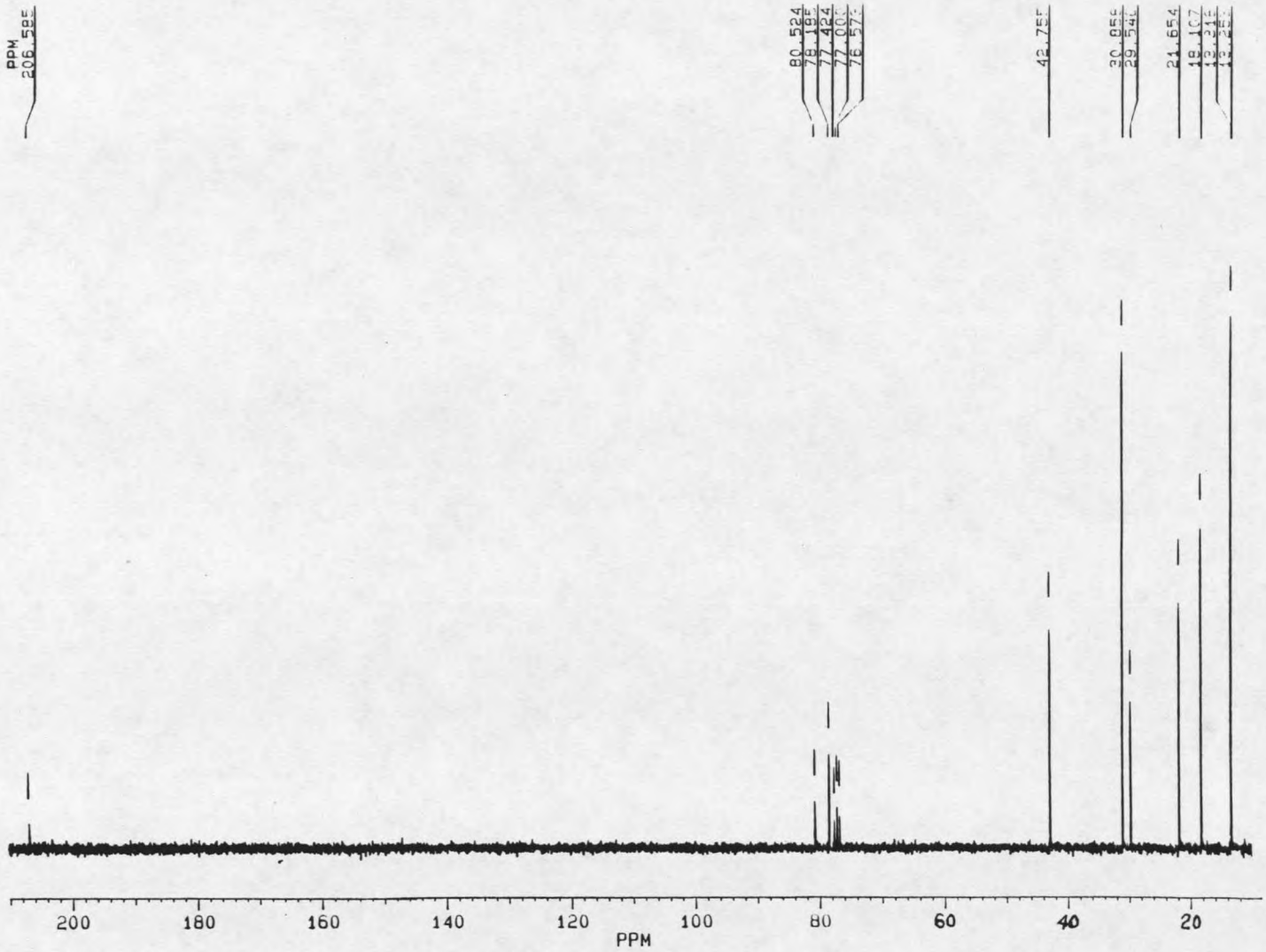


Figure 17. ^{13}C NMR Spectrum of Dec-5-yn-2-one(25).

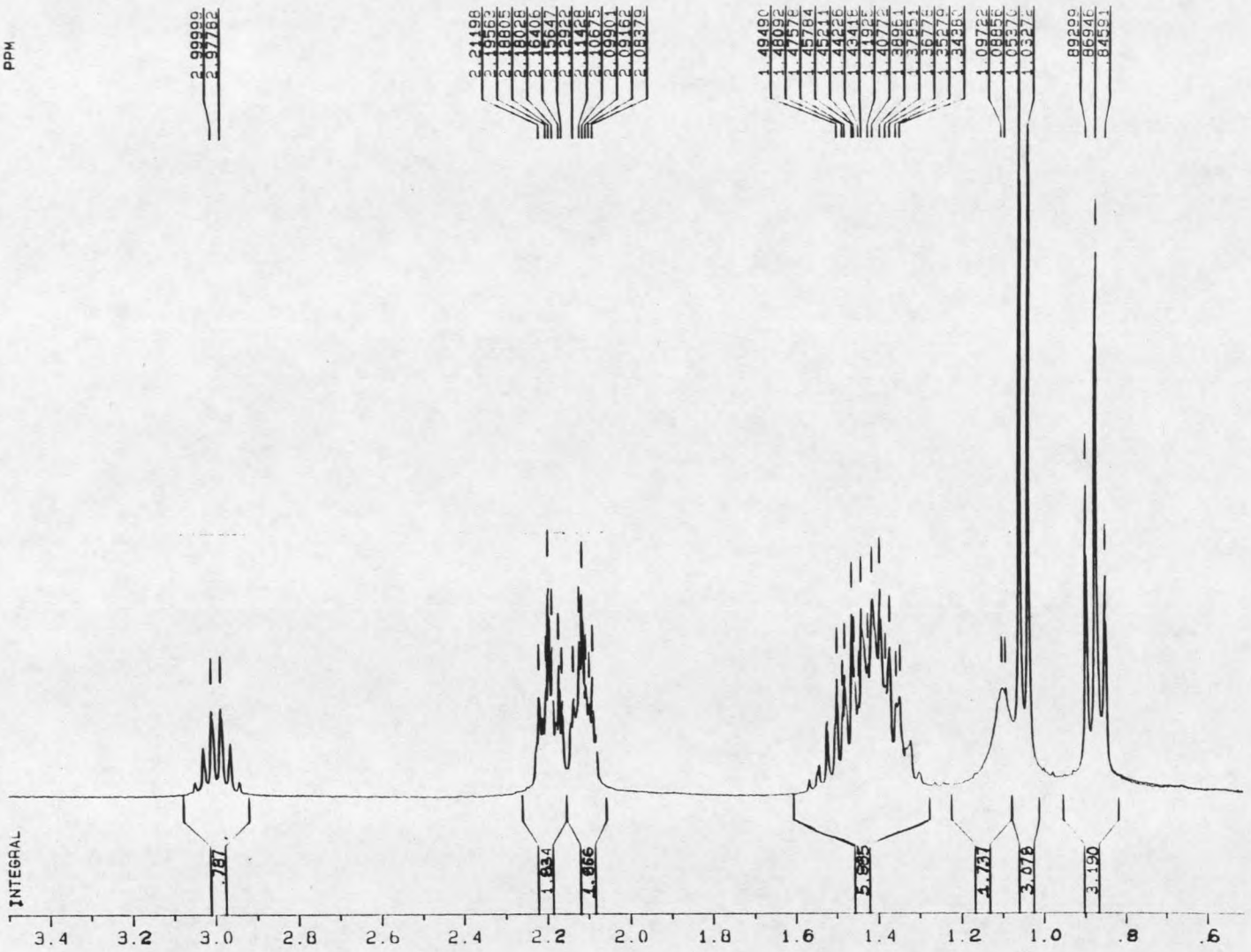


Figure 18. ^{1}H NMR Spectrum of Dec-5-yn-2-ylamine(26).

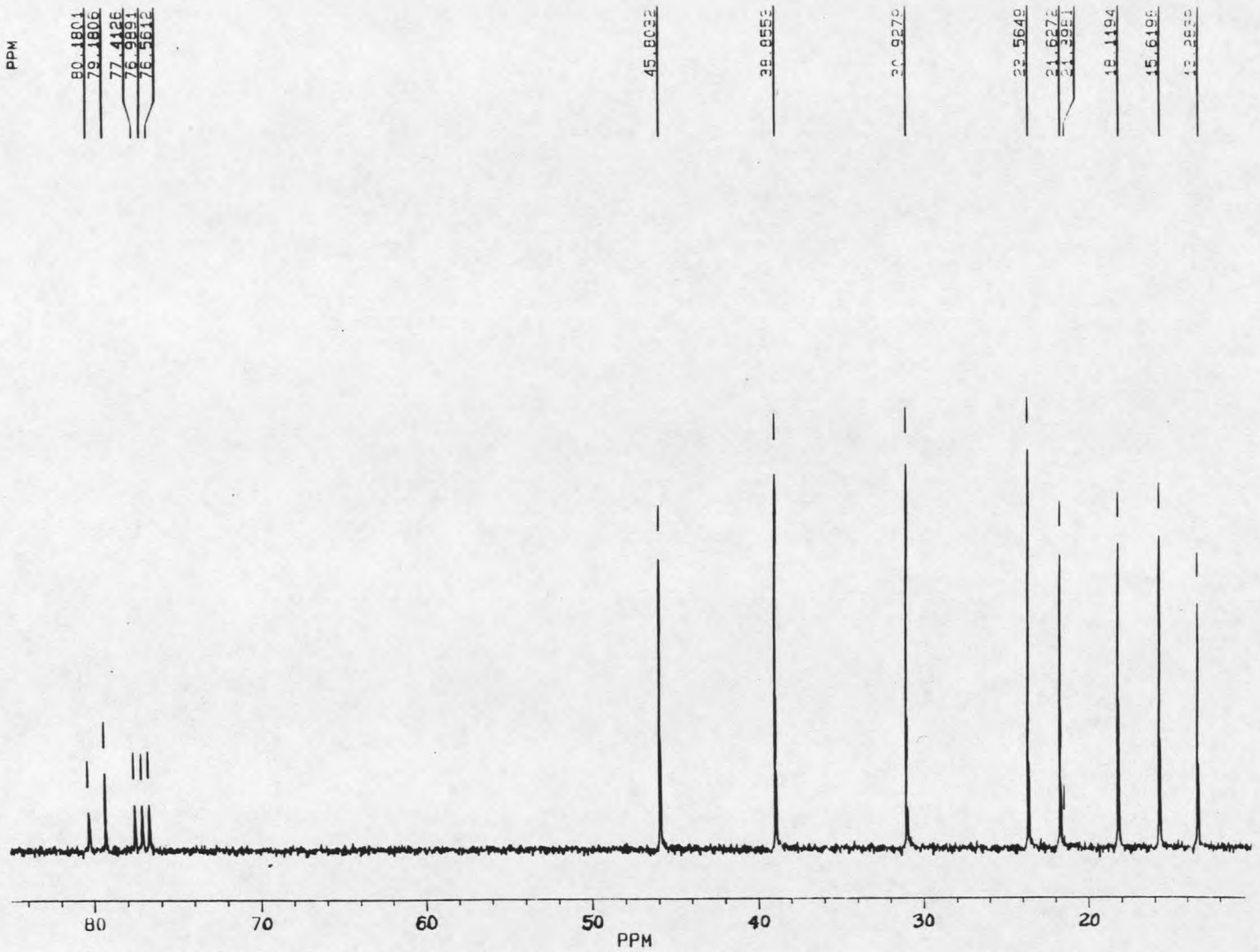


Figure 19. ^{13}C NMR Spectrum of Dec-5-yn-2-ylamine(26).

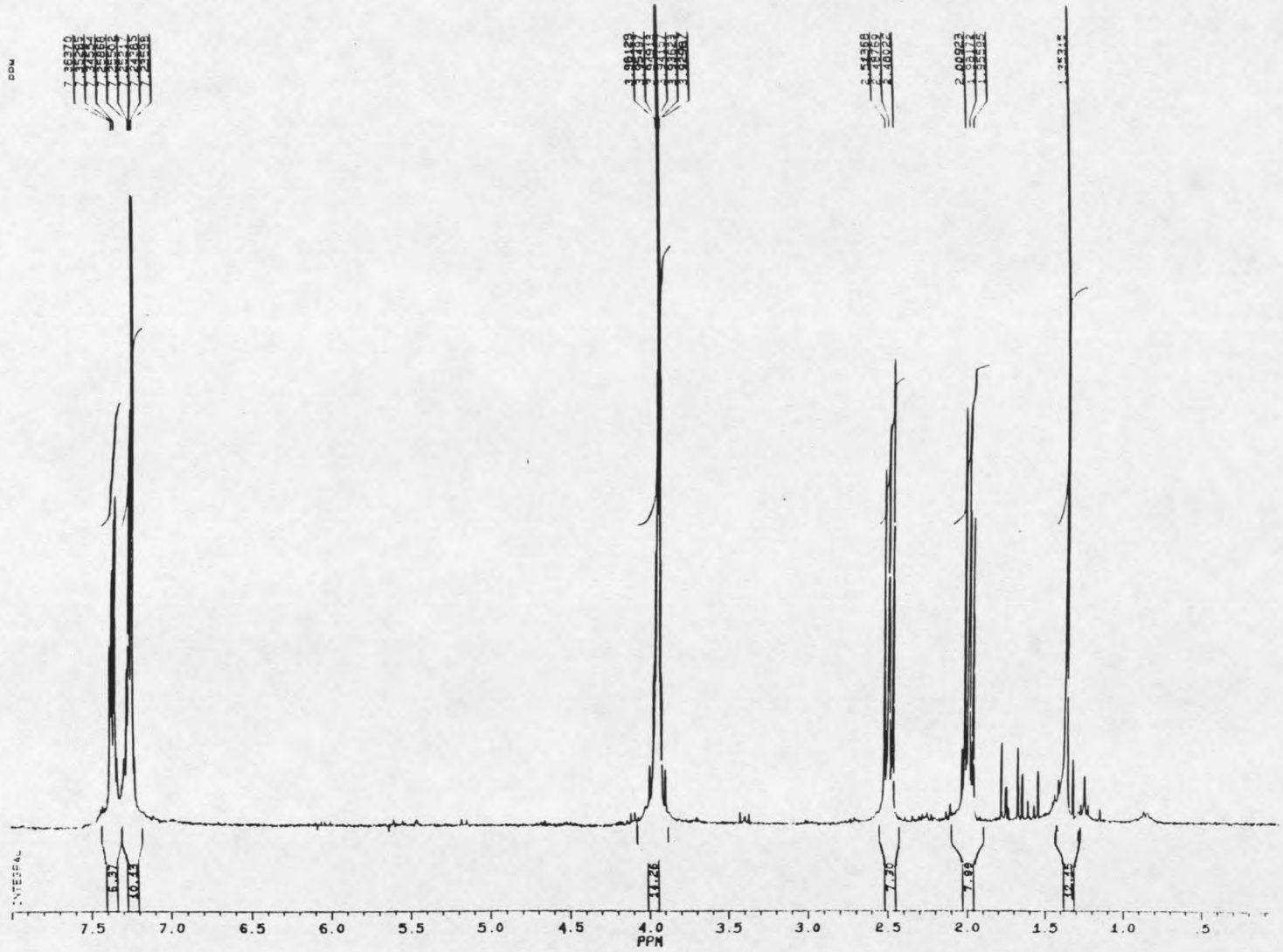


Figure 20. ^{1}H NMR Spectrum of 2,2-ethylenedioxy-5-phenylhex-5-yne(23).

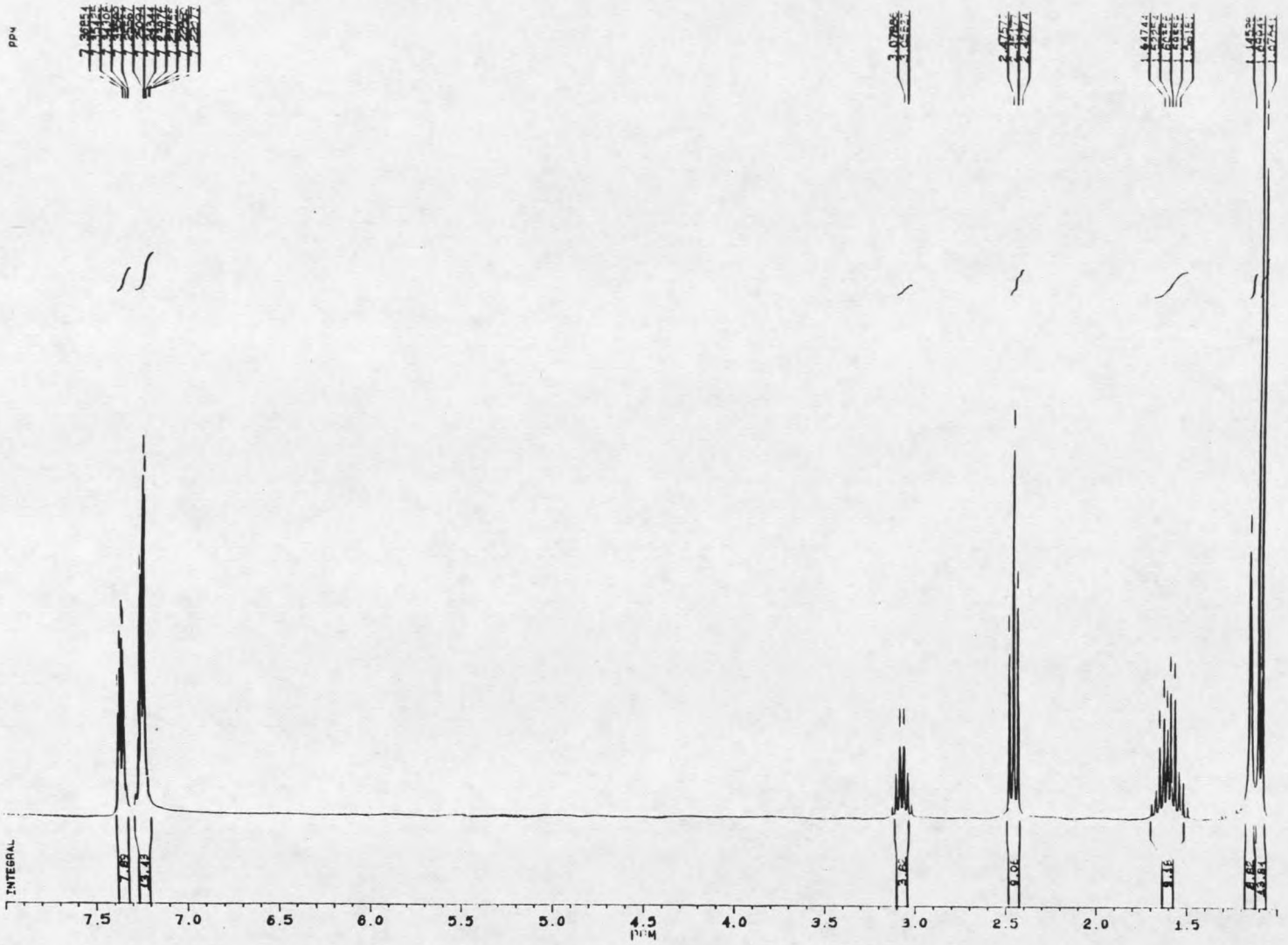


Figure 21. ^{1}H NMR Spectrum of 6-Phenylhex-5-yn-2-ylamine(7).

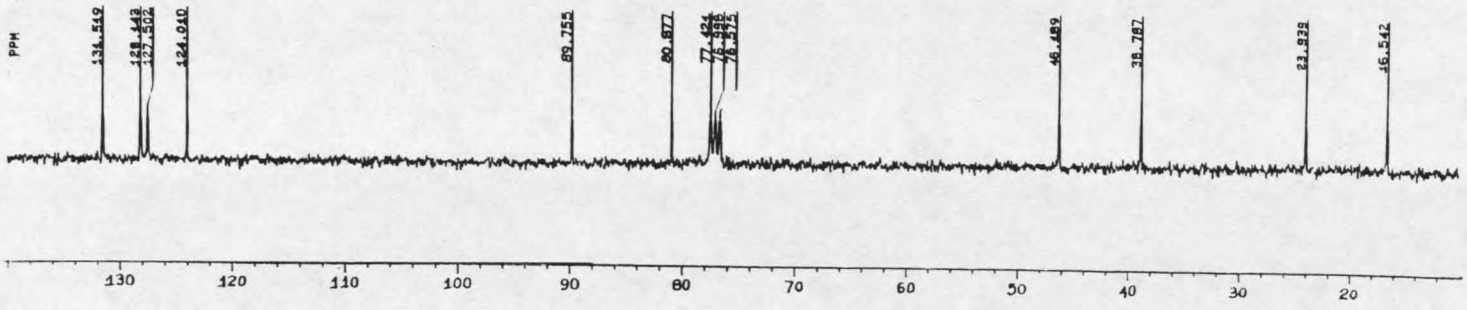


Figure 22. ^{13}C NMR Spectrum of 6-Phenylhex-5-yn-2-ylamine(7).

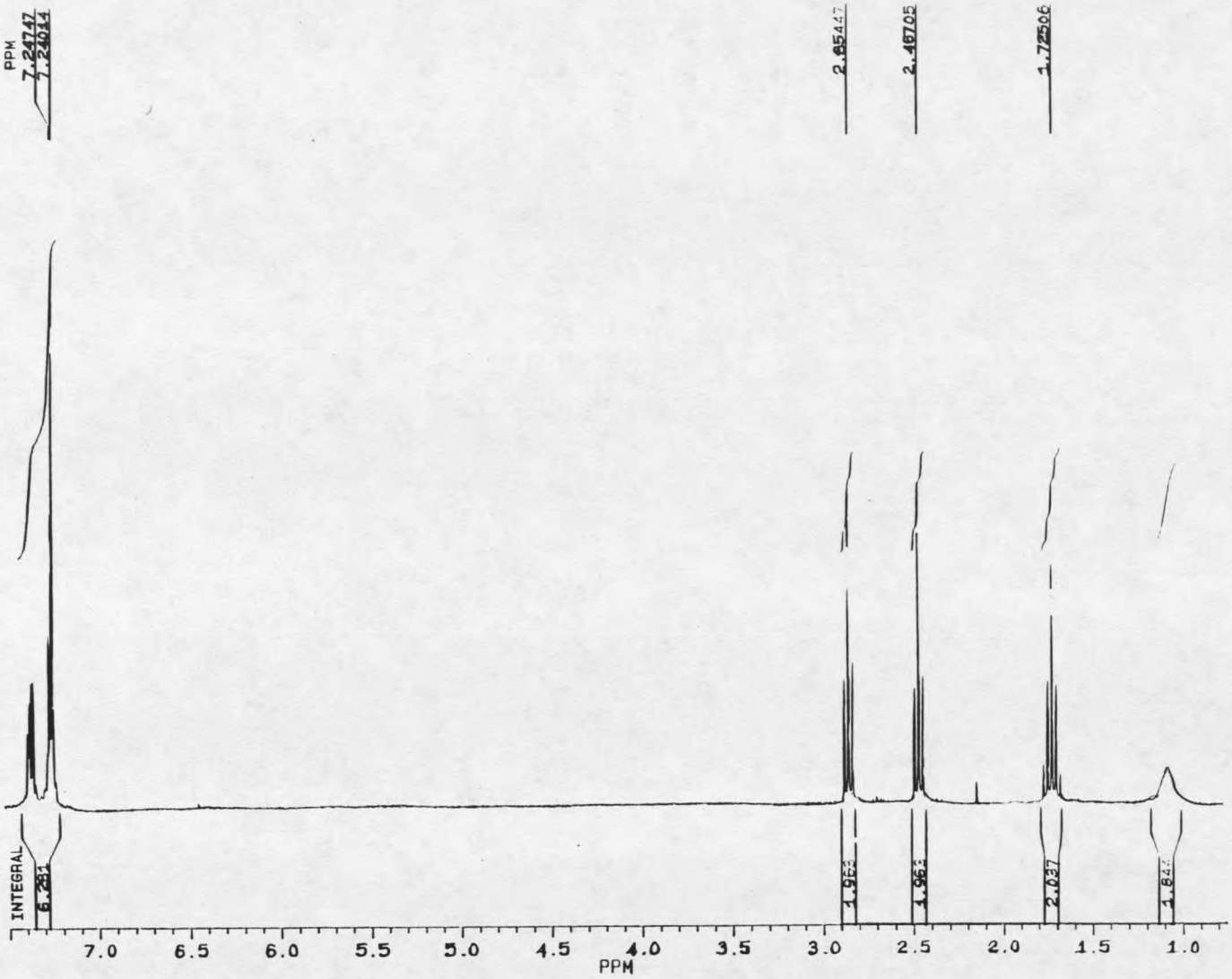


Figure 23. ^{1}H NMR Spectrum of 5-Phenylpent-4-yn-1-ylamine(3).

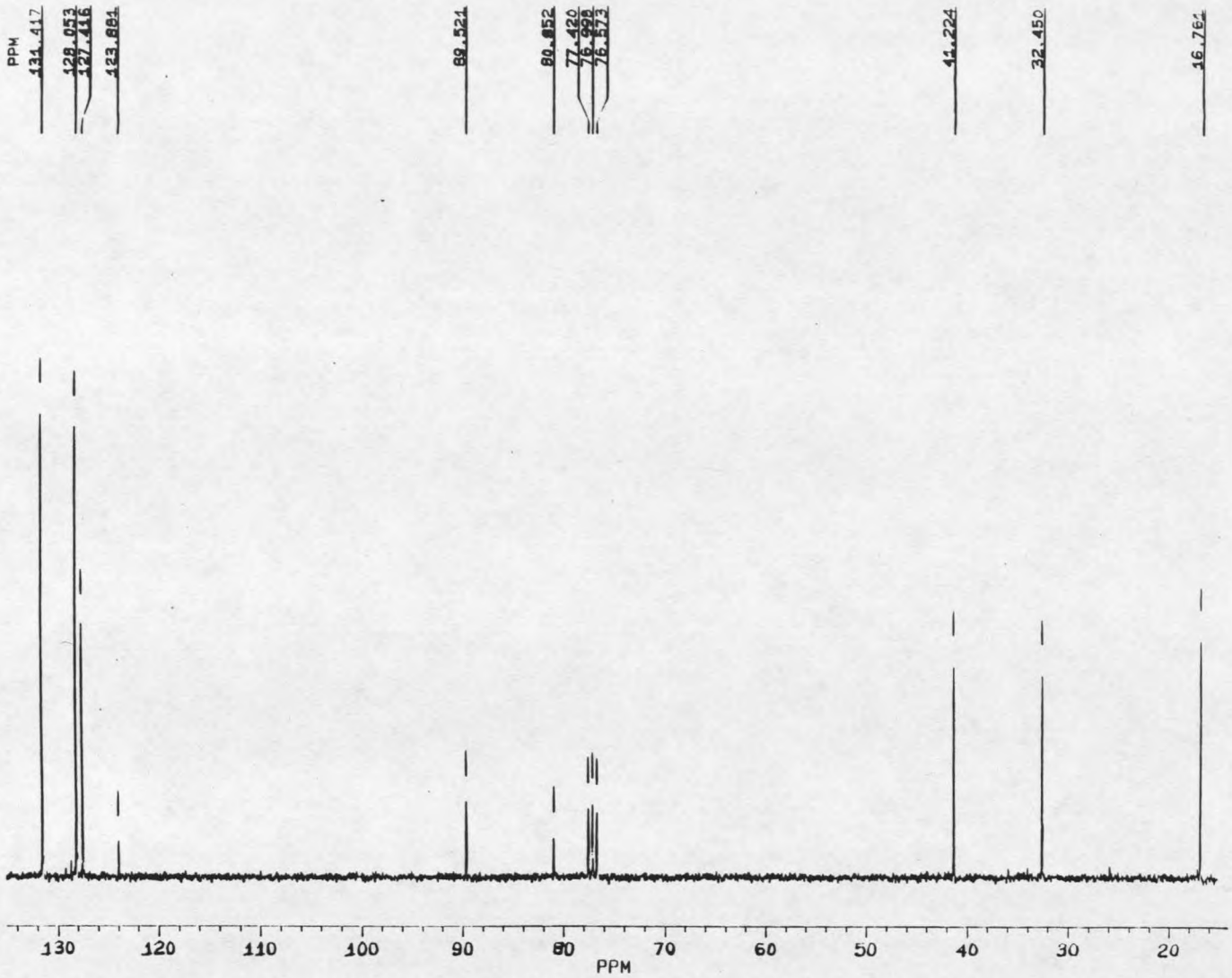


Figure 24. ^{13}C NMR Spectrum of 5-Phenylpent-4-yn-1-ylamine(3).

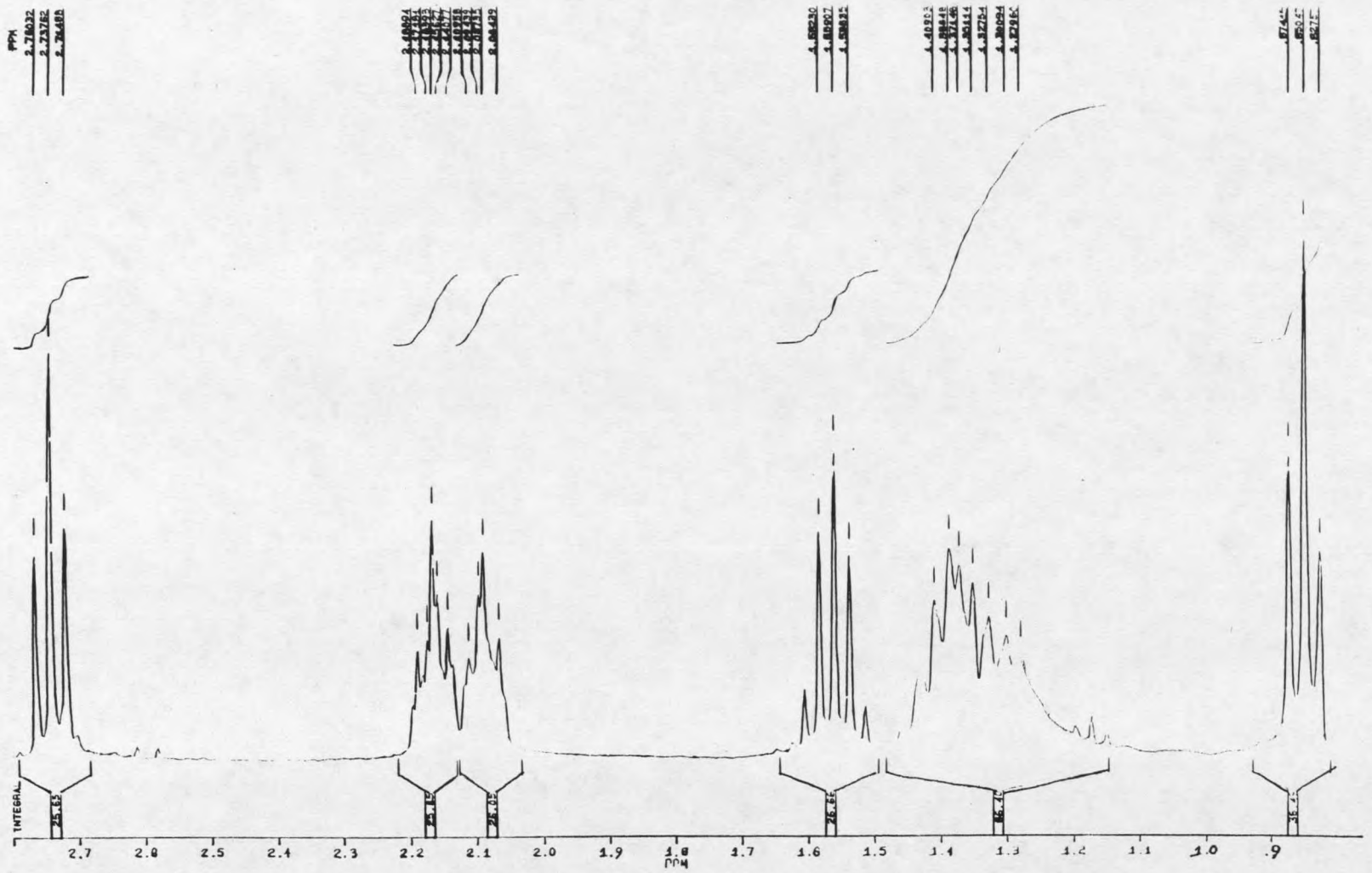


Figure 25. ^{1}H NMR Spectrum of Non-4-yn-1-ylamine(5).

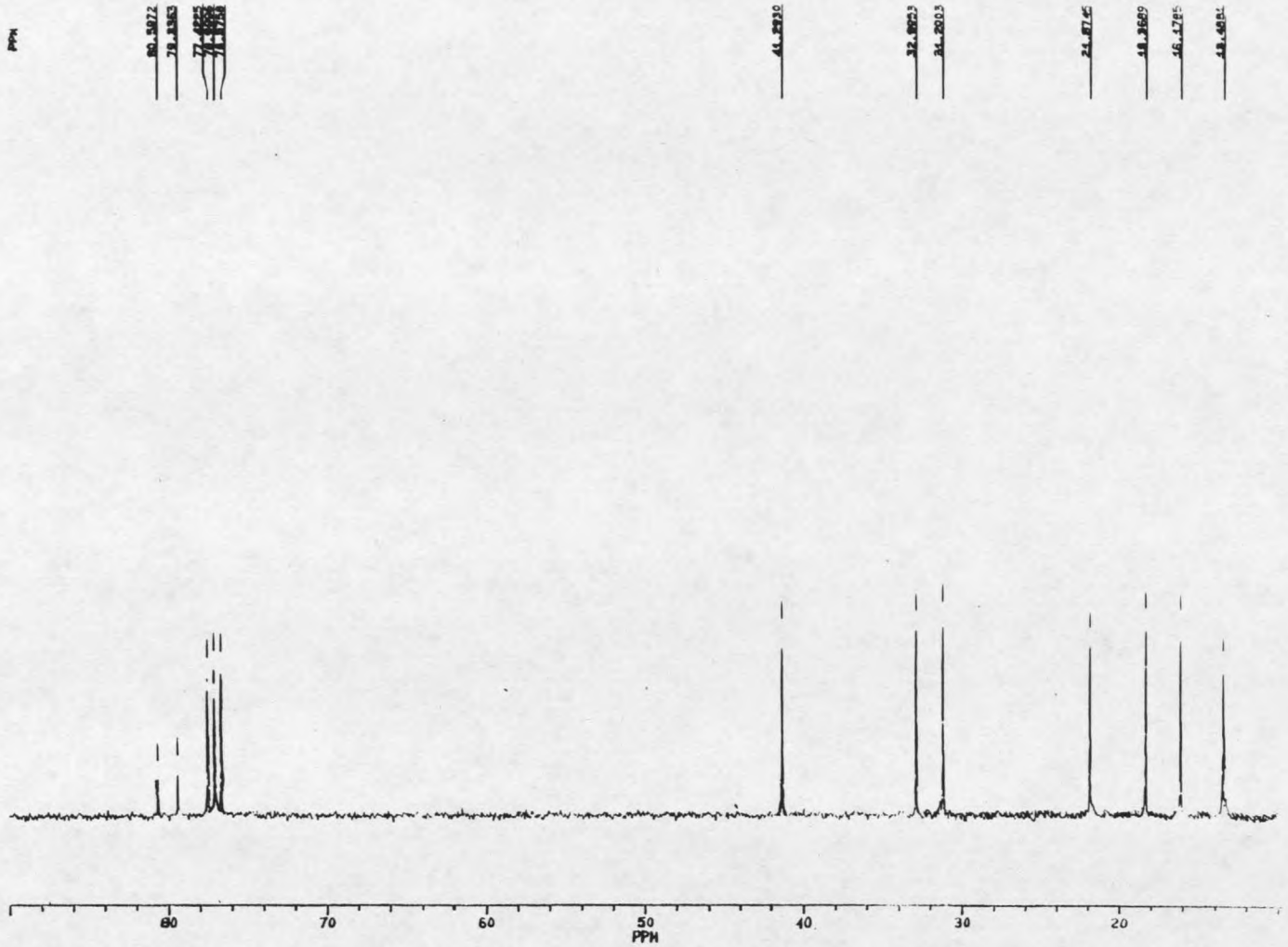


Figure 26. ^{13}C NMR Spectrum of Non-4-yn-1-ylamine(5).

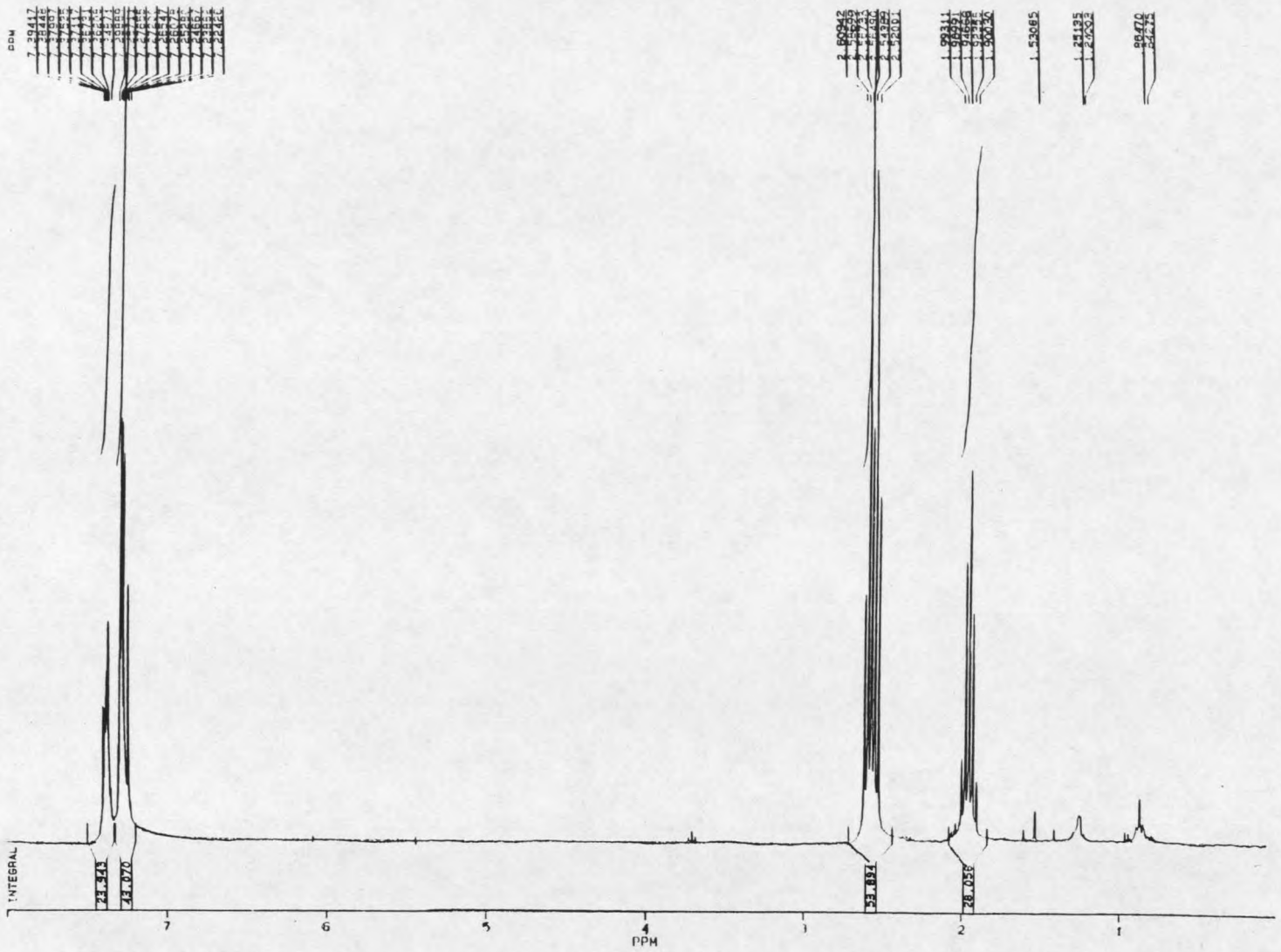


Figure 27. ^{1}H NMR Spectrum of 6-Phenylhexanenitrile.

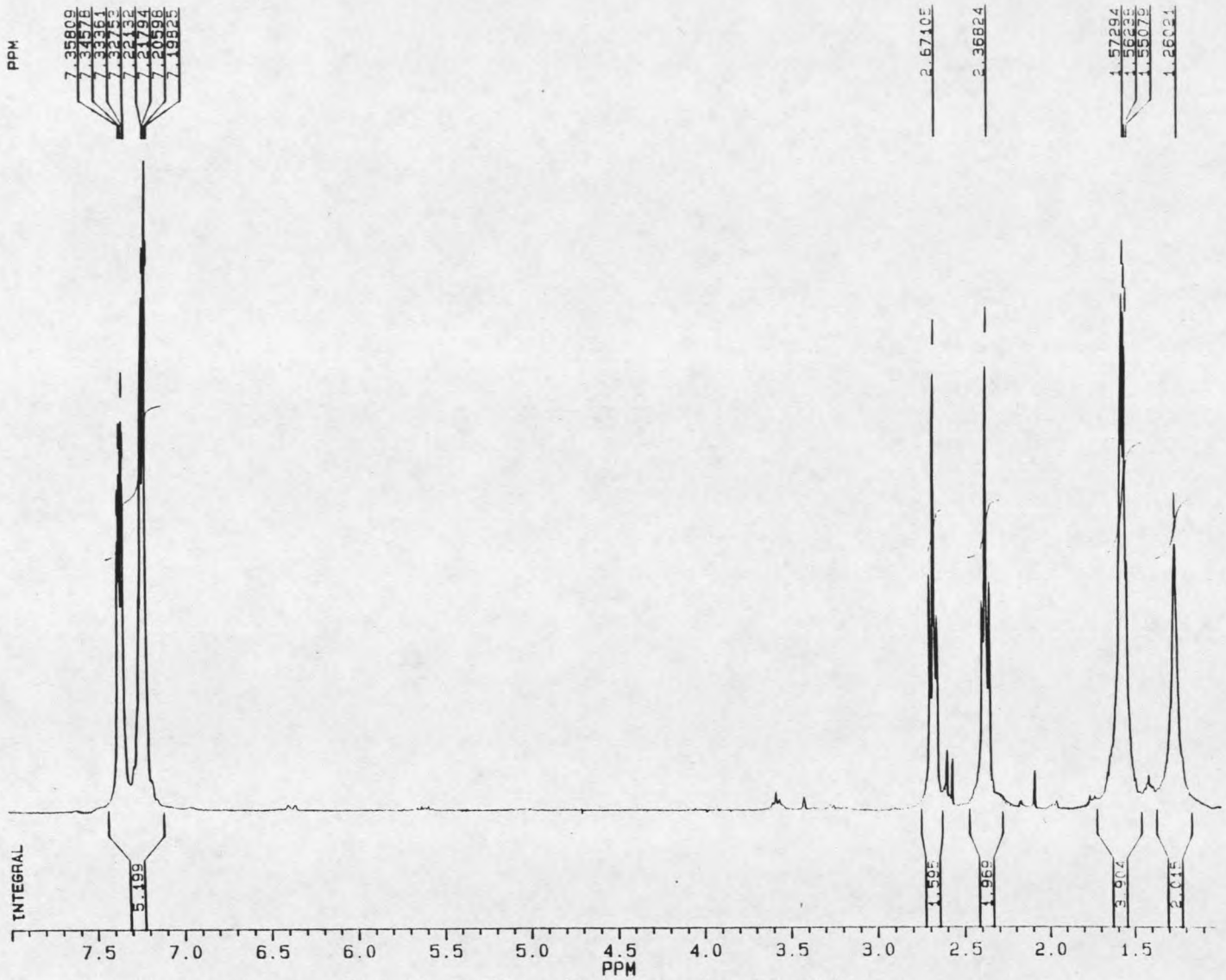


Figure 28. ^{1}H NMR Spectrum of 6-Phenylhex-5-yn-1-ylamine(9).

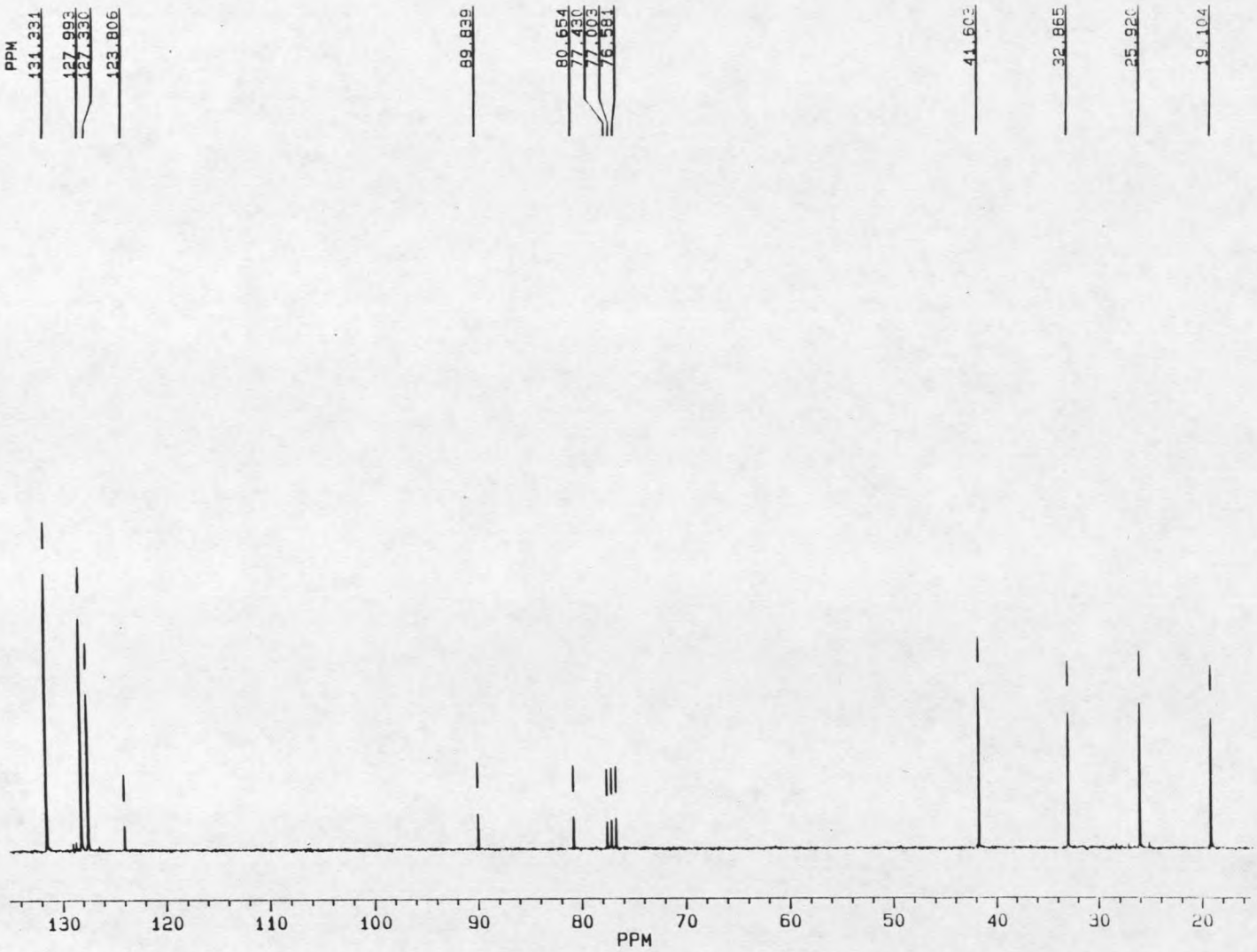


Figure 29. ^{13}C NMR Spectrum of 6-Phenylhex-5-yn-1-ylamine(9).

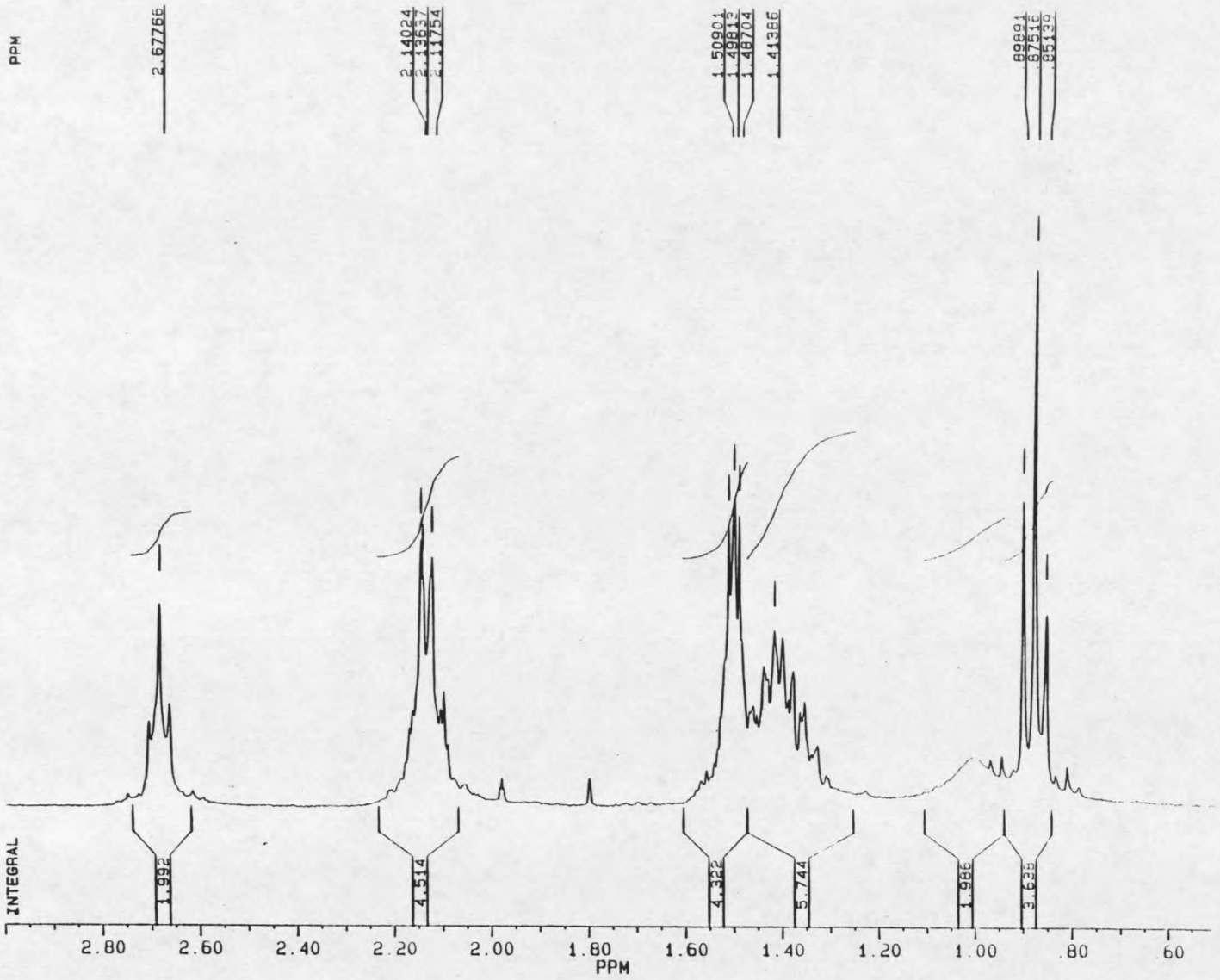


Figure 30. ^{1}H NMR Spectrum of Dec-5-yn-1-ylamine(11).

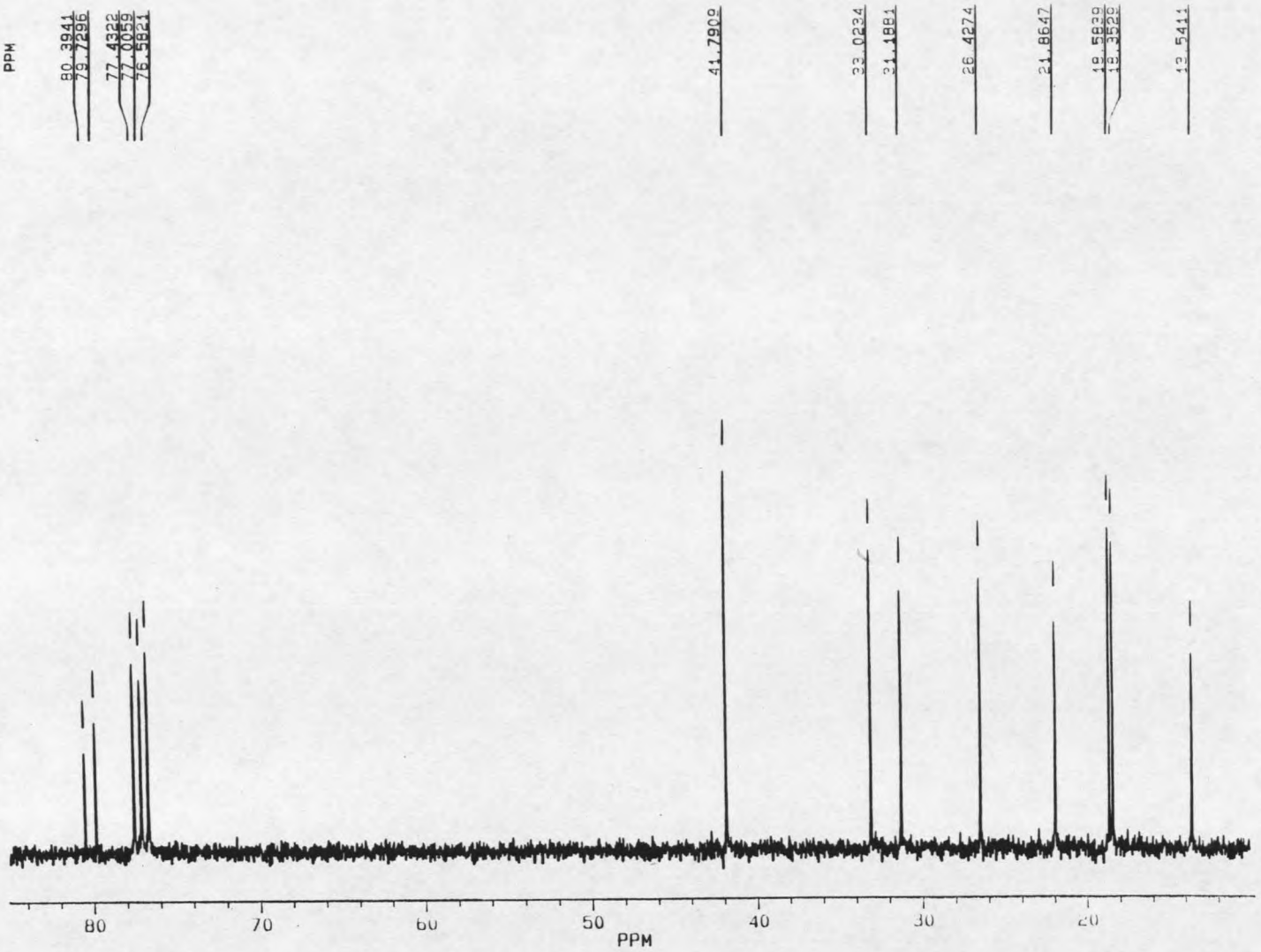


Figure 31. ^{13}C NMR Spectrum of Dec-5-yn-1-ylamine(11).

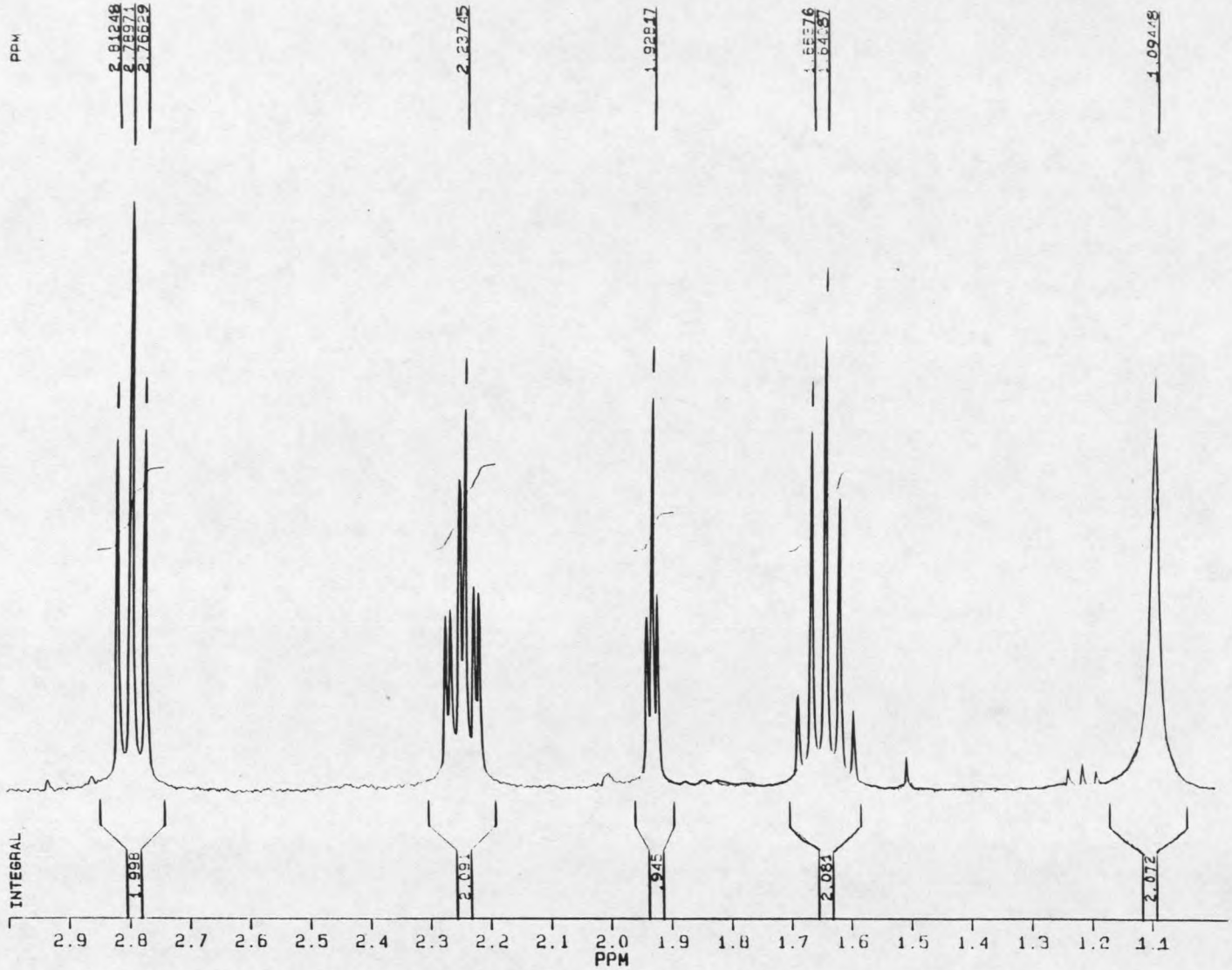


Figure 32. ^{1}H NMR Spectrum of Pent-4-yn-1-ylamine(28).

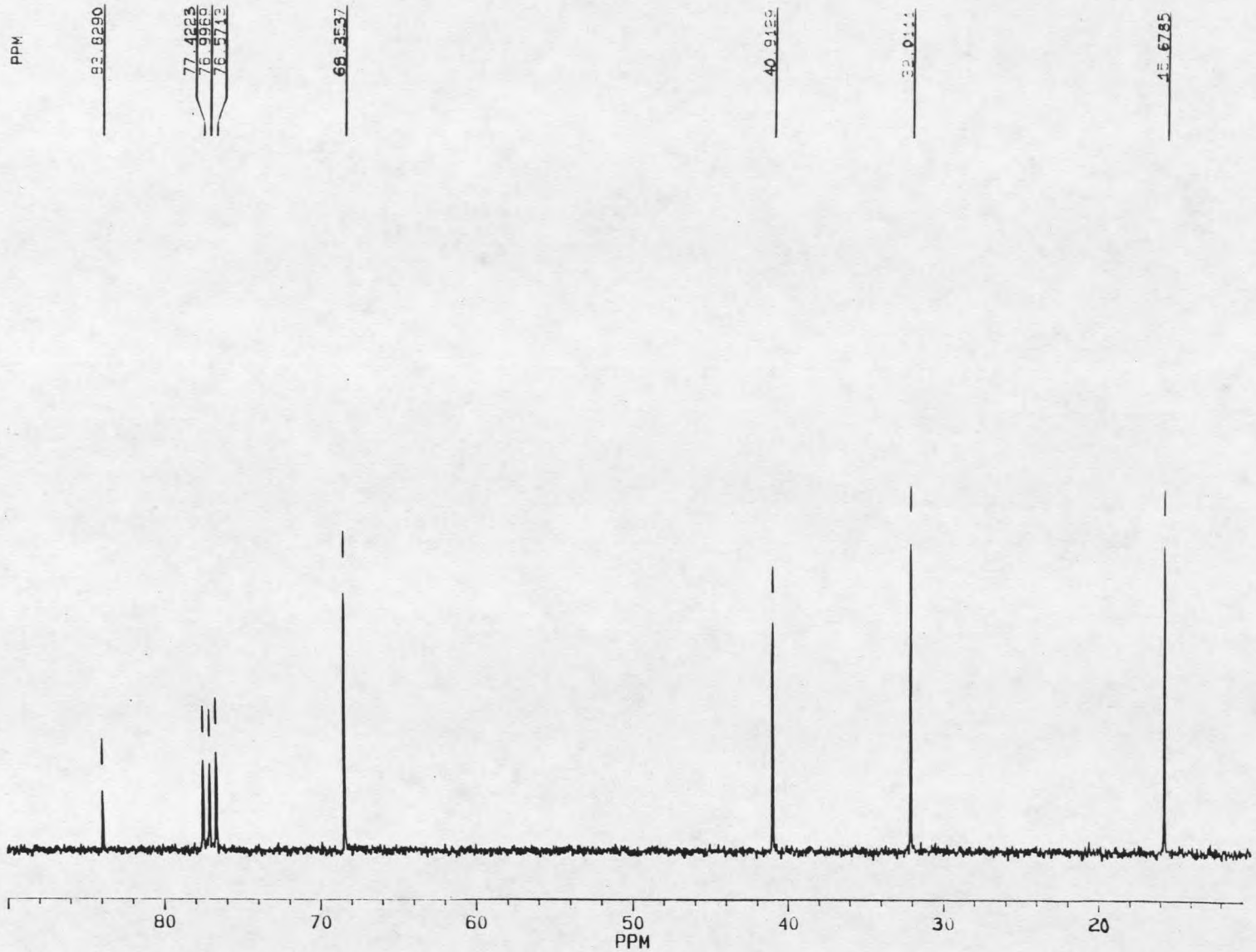


Figure 33. ^{13}C NMR Spectrum of Pent-4-yn-1-ylamine(28).

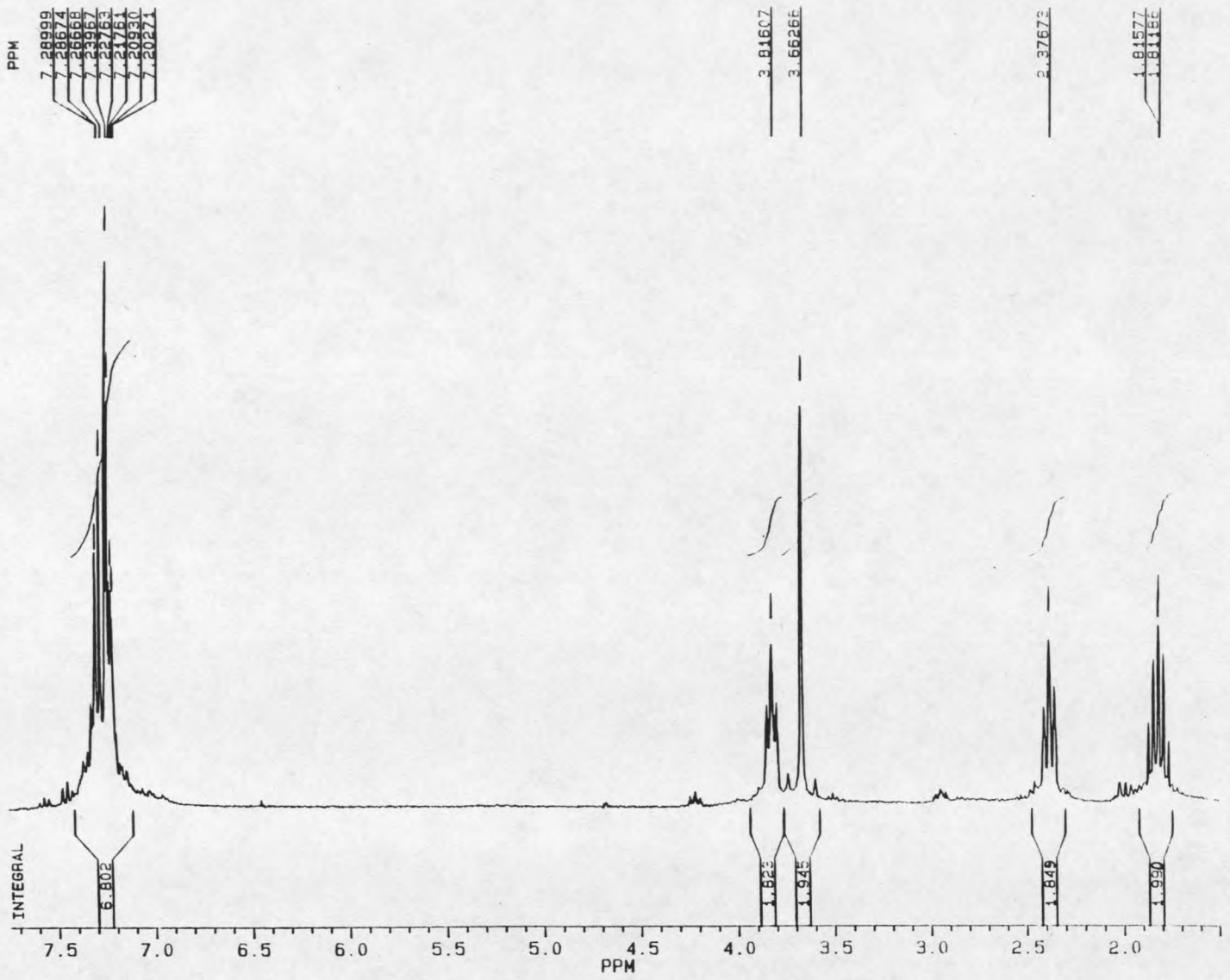


Figure 34. ^{1}H NMR Spectrum of 3,4-Dihydro-5-(phenylmethyl)-2H-pyrrole(4).

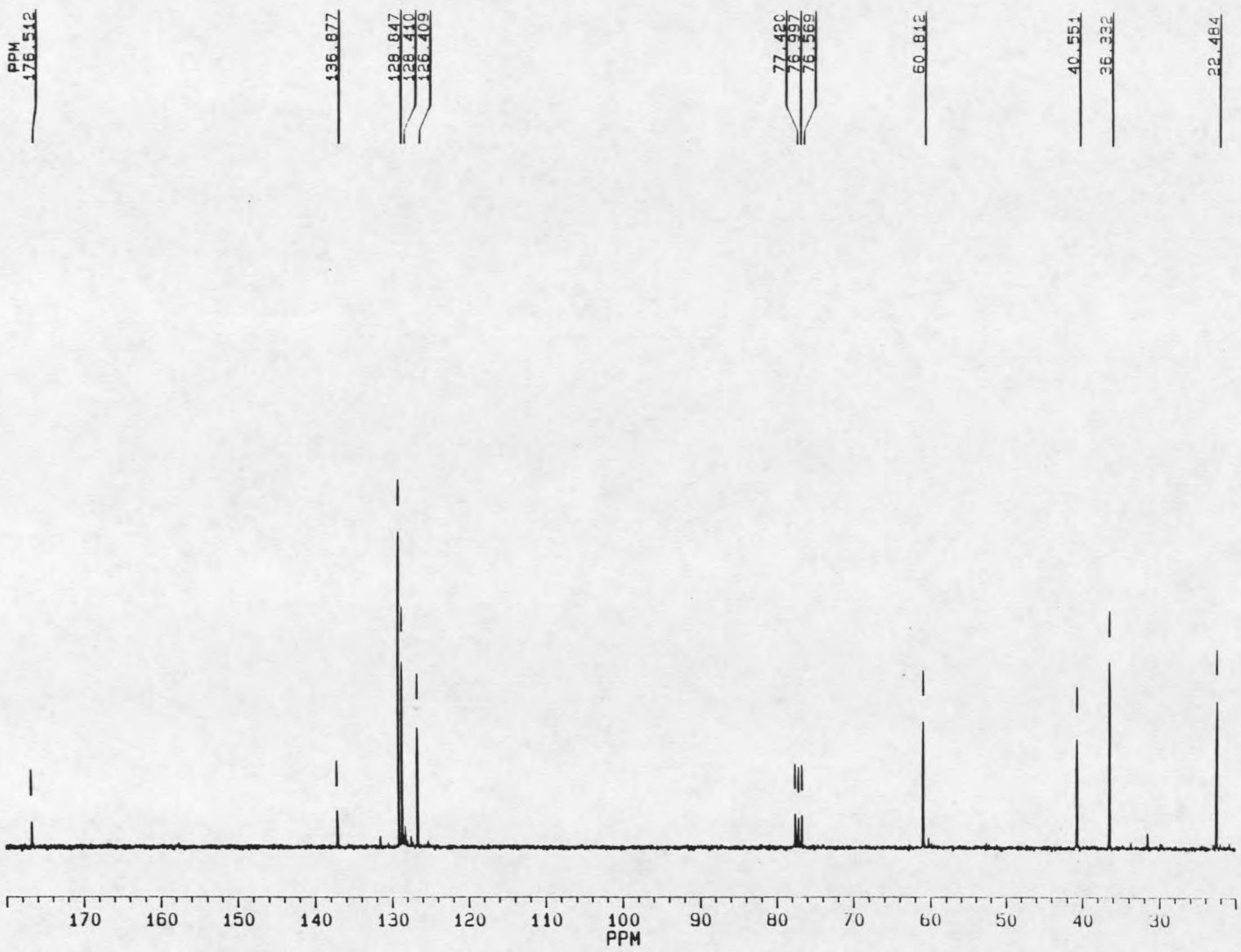


Figure 35. ^{13}C NMR Spectrum of 3,4-Dihydro-5-(phenylmethyl)-2H-pyrrole(4).

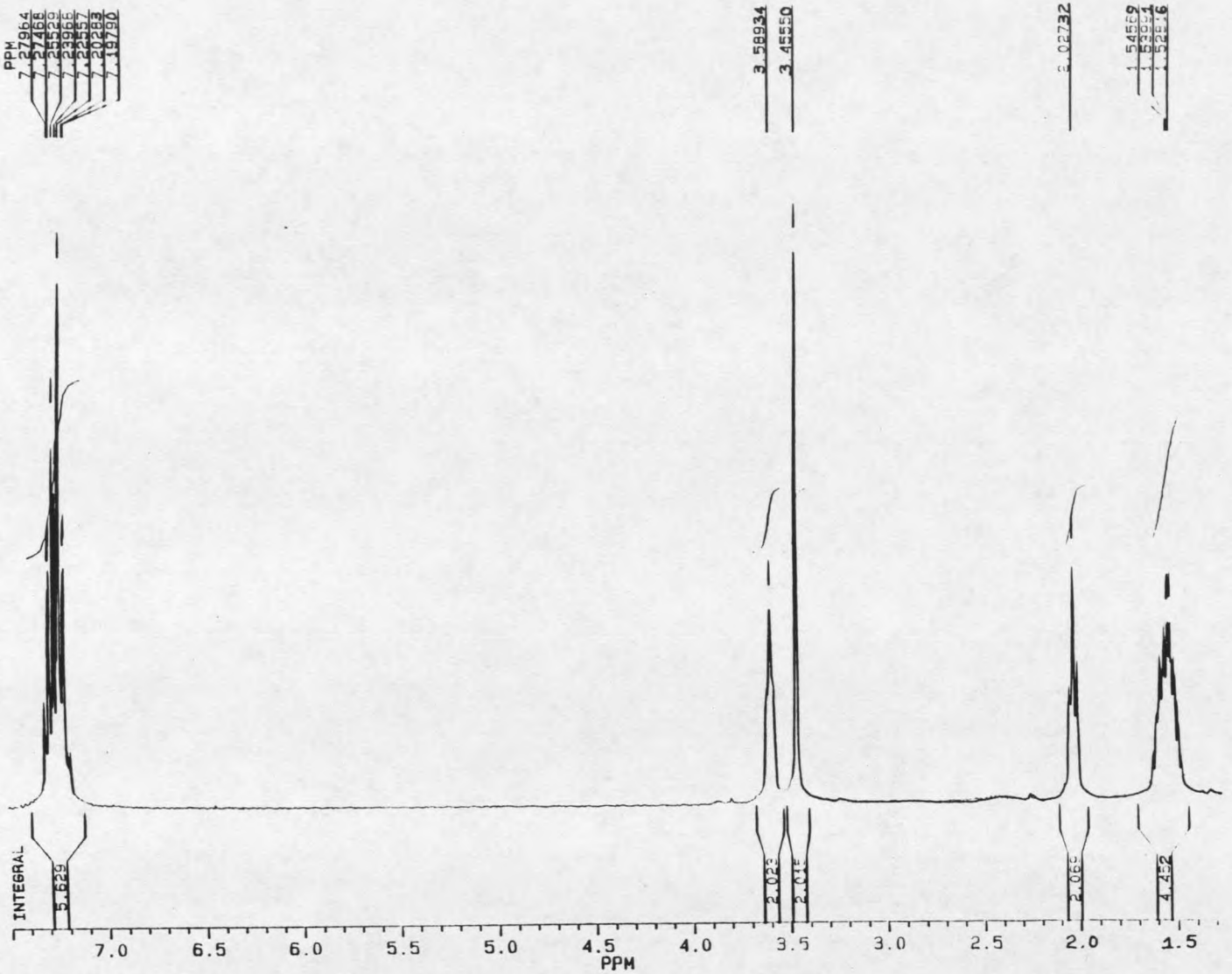


Figure 36. ^{1}H NMR Spectrum of 2-(Phenylmethyl)-3,4,5,6-tetrahydro-pyridine(10).

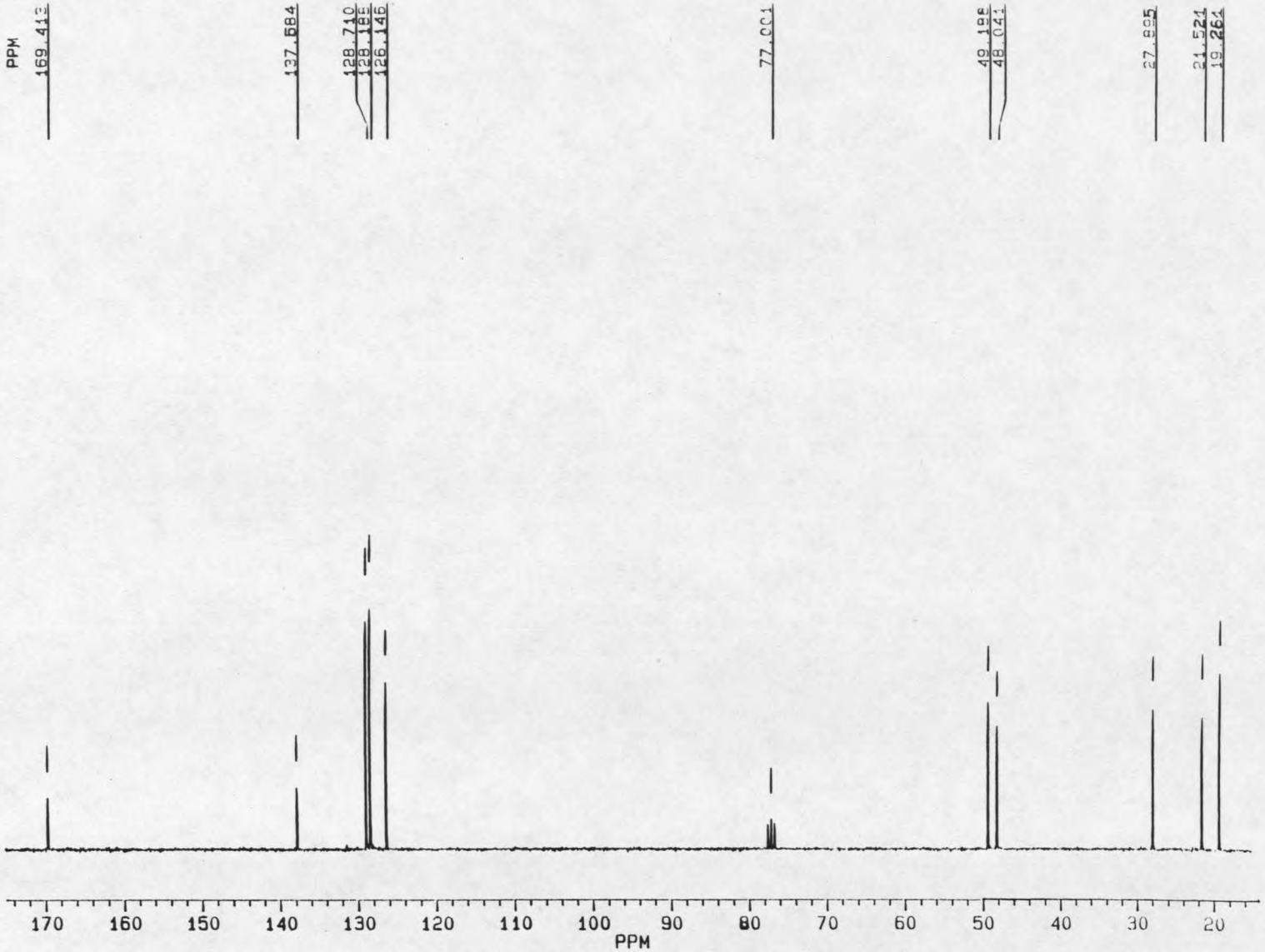


Figure 37. ^{13}C NMR Spectrum of 2-(Phenylmethyl)-3,4,5,6-tetrahydro-pyridine(10).

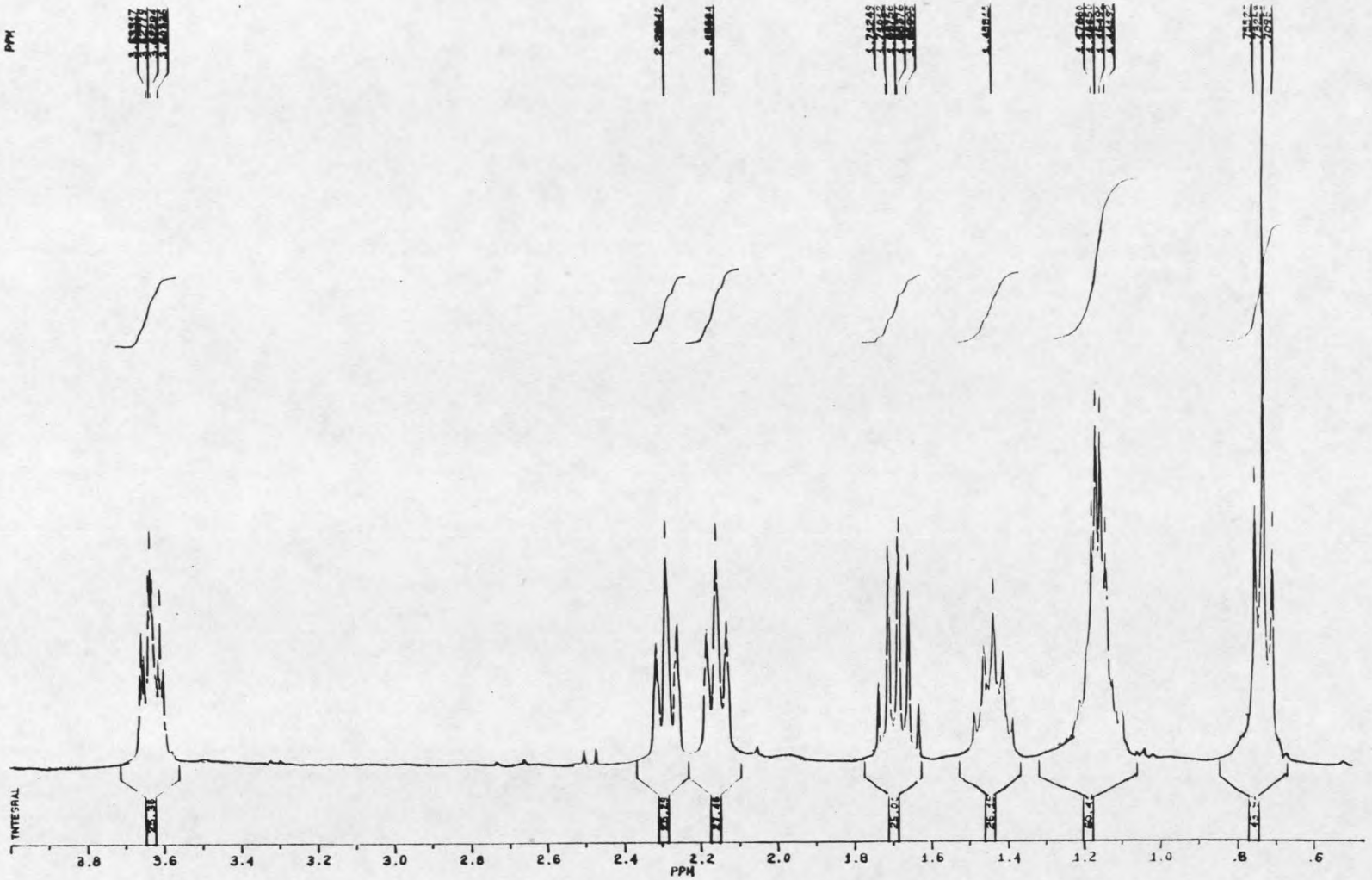


Figure 38. ^{1}H NMR Spectrum of 3,4-Dihydro-5-pentyl-2H-pyrrole(6).

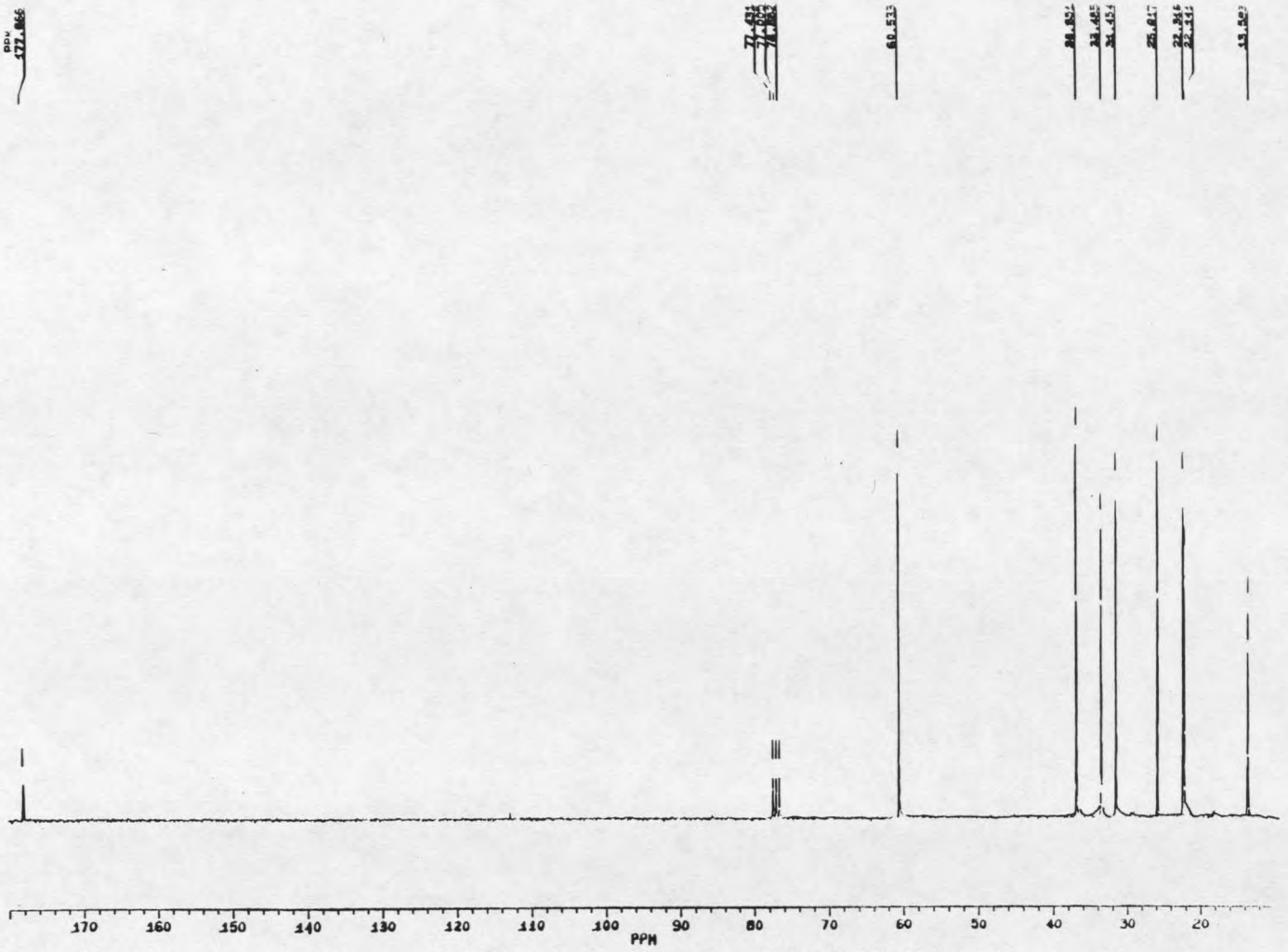


Figure 39. ^{13}C NMR Spectrum of 3,4-Dihydro-5-pentyl-2H-pyrrole(6).

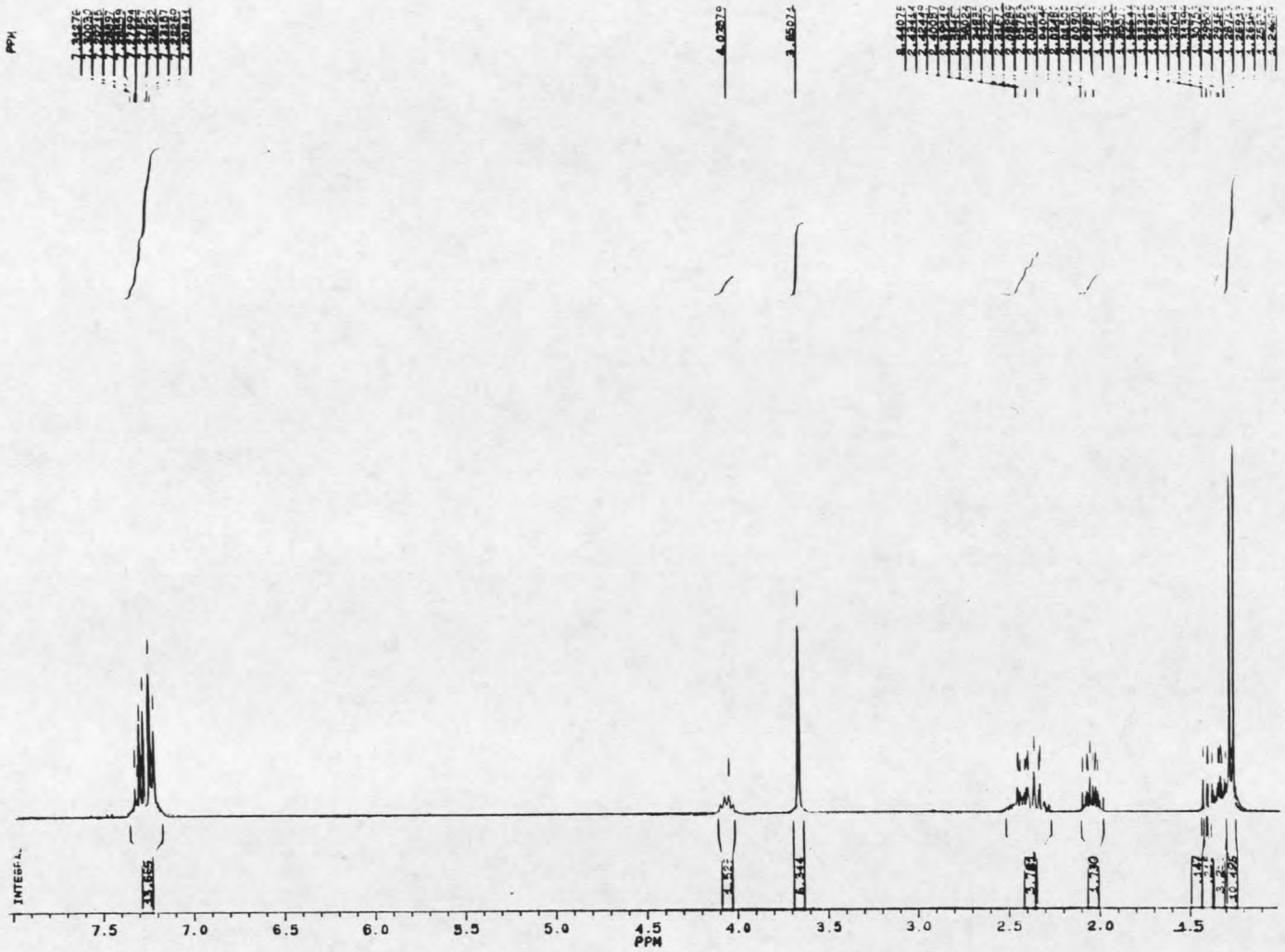


Figure 40. ^{1}H NMR Spectrum of 3,4-Dihydro-2-methyl-5-(phenylmethyl)-2H-pyrrole(8).

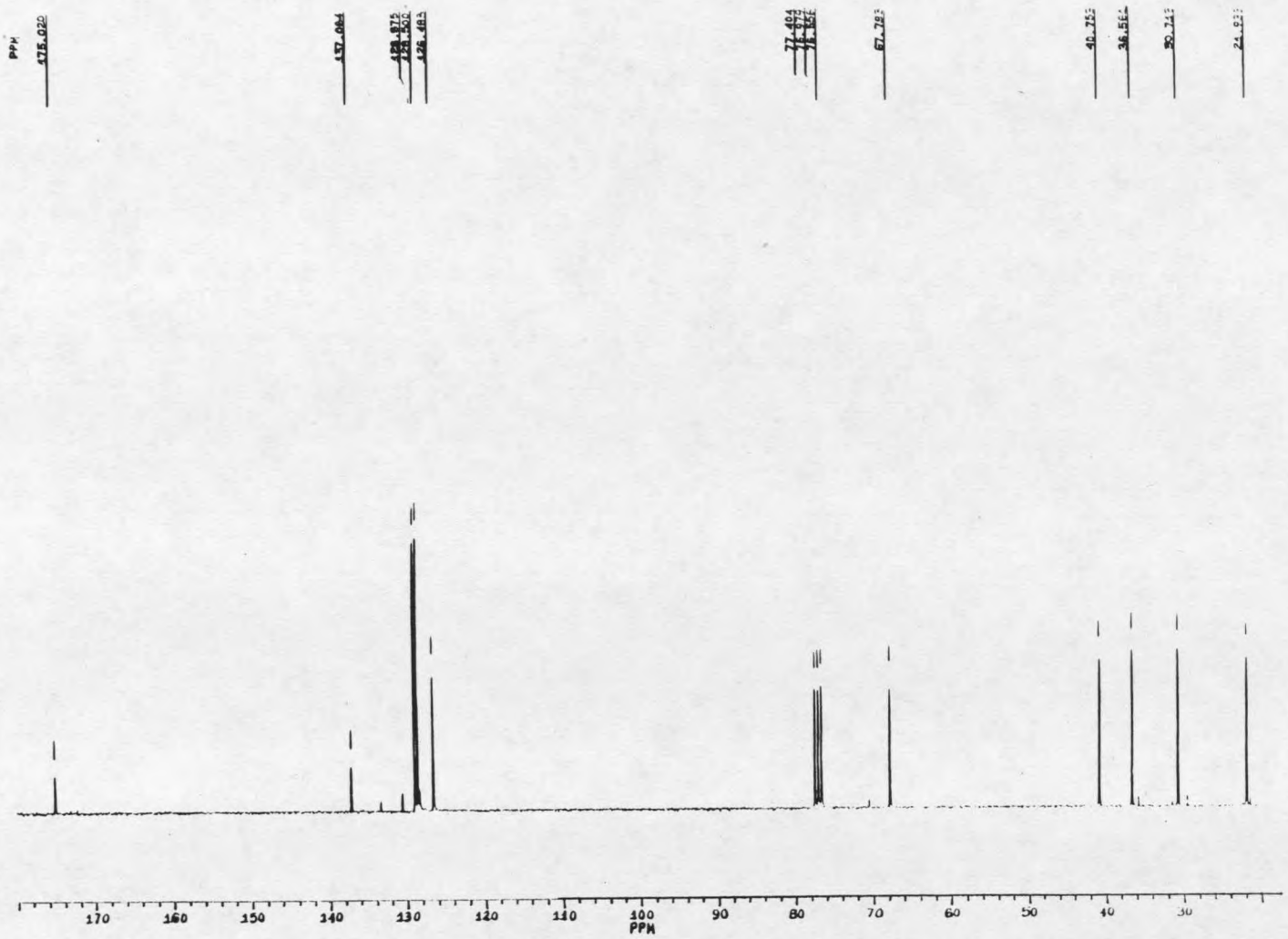


Figure 41. ^{13}C NMR Spectrum of 3,4-Dihydro-2-methyl-5-(phenylmethyl)-2H-pyrrole(8).

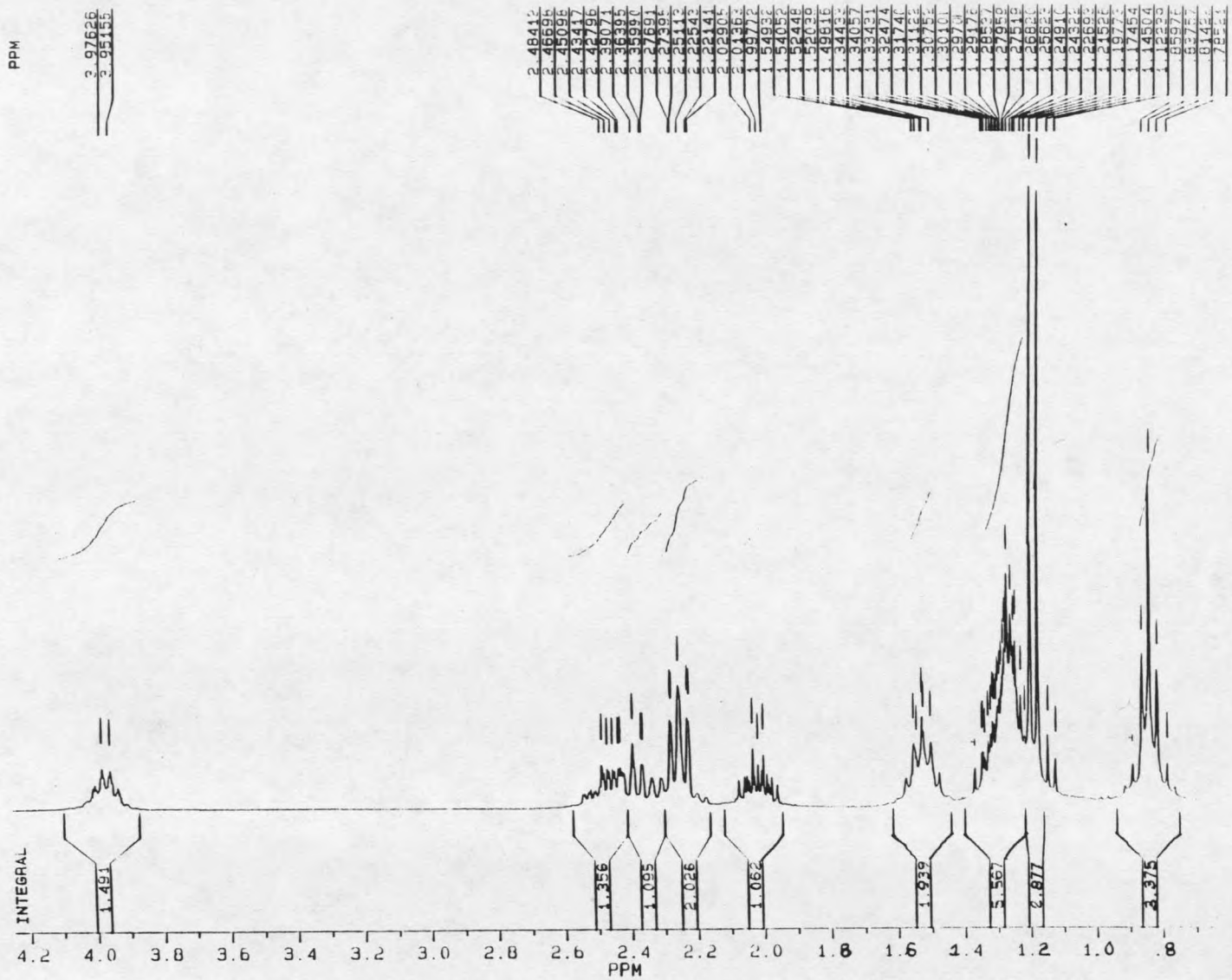


Figure 42. ^{1}H NMR Spectrum of 3,4-Dihydro-2-methyl-5-pentyl-2H-pyrrole(27).

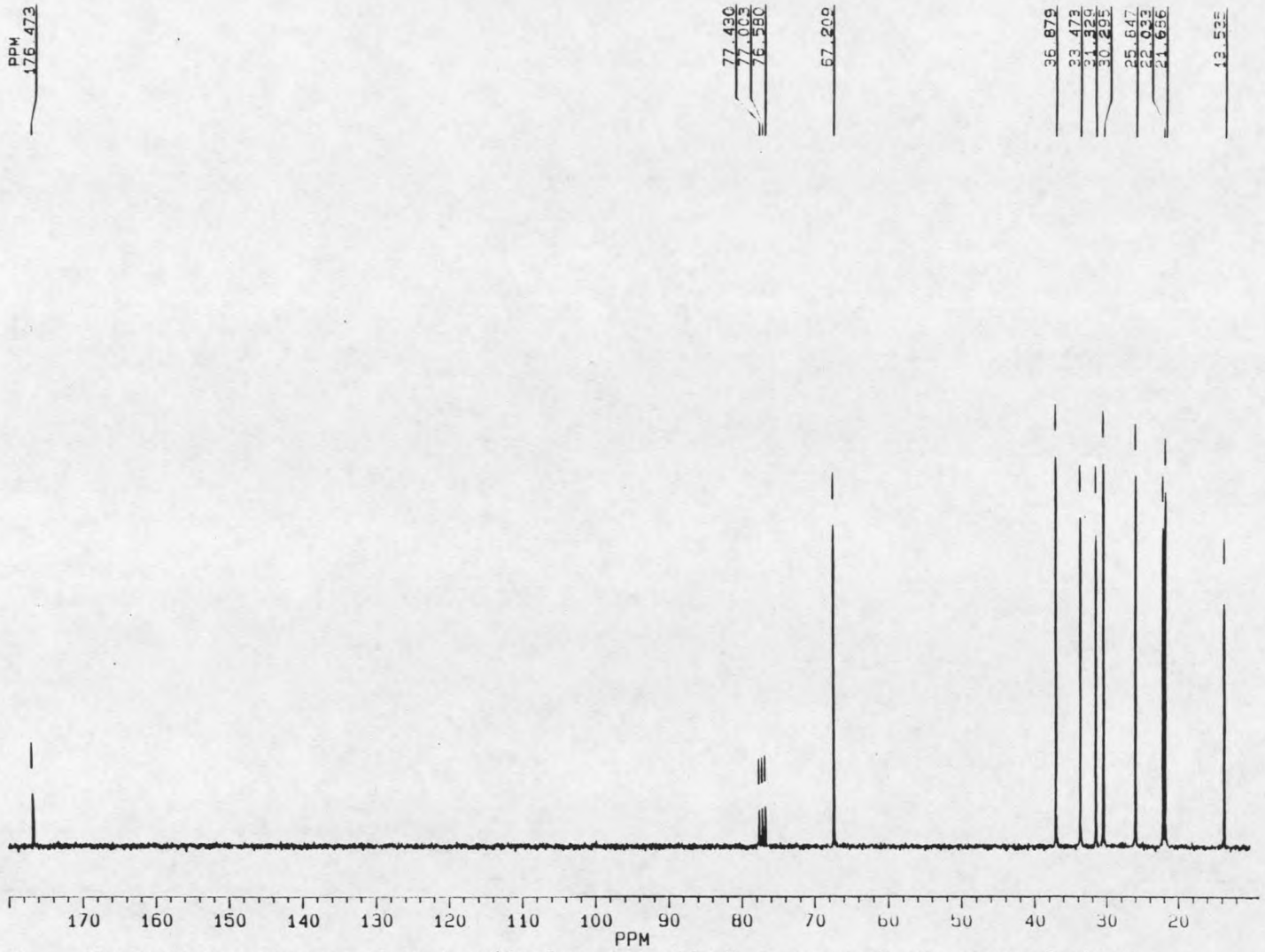


Figure 43. ^{13}C NMR Spectrum of 3,4-Dihydro-2-methyl-5-pentyl-2H-pyrrole(27).

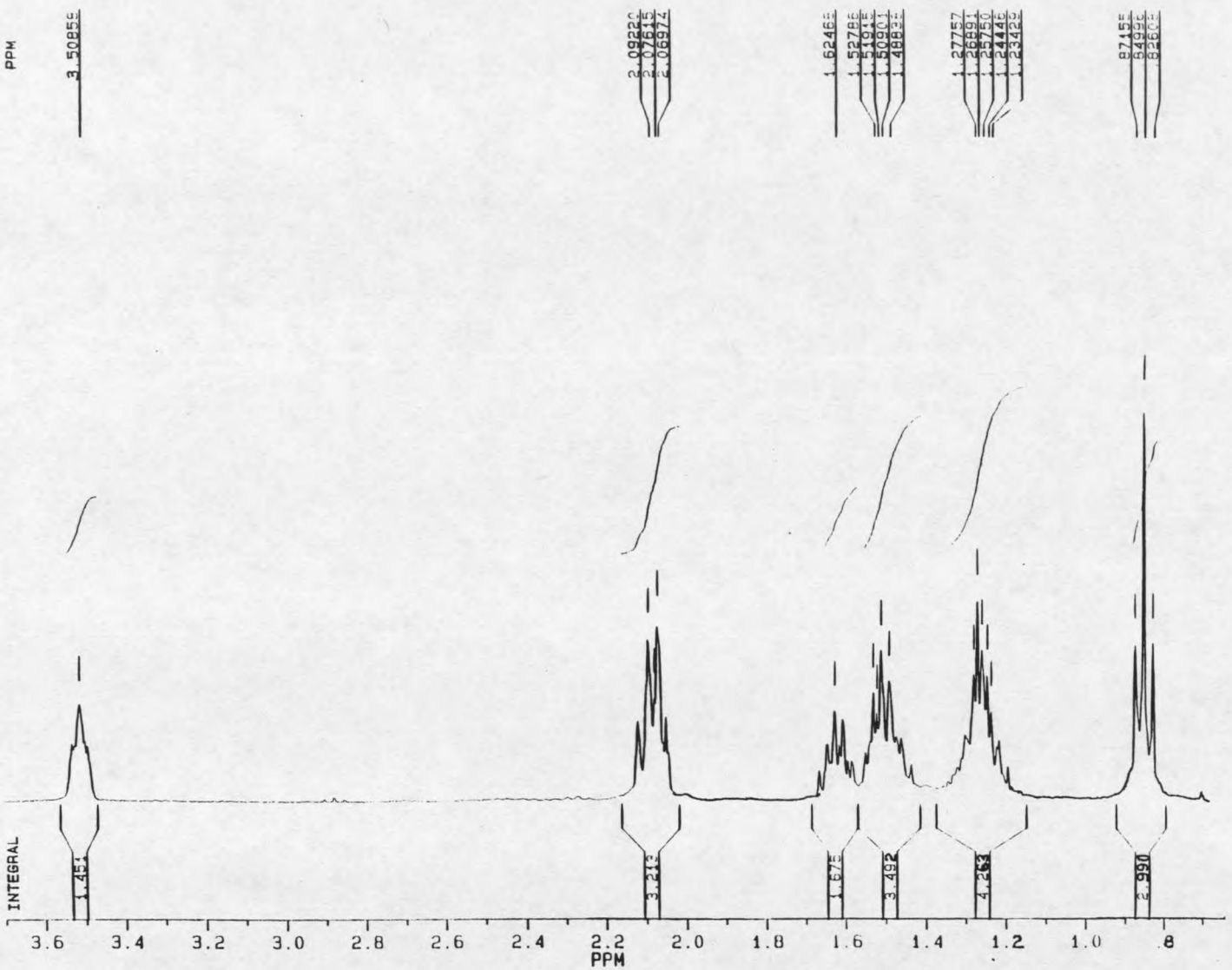


Figure 44. ^{1}H NMR Spectrum of 2-Pentyl-3,4,5,6-tetrahydropyridine(12).

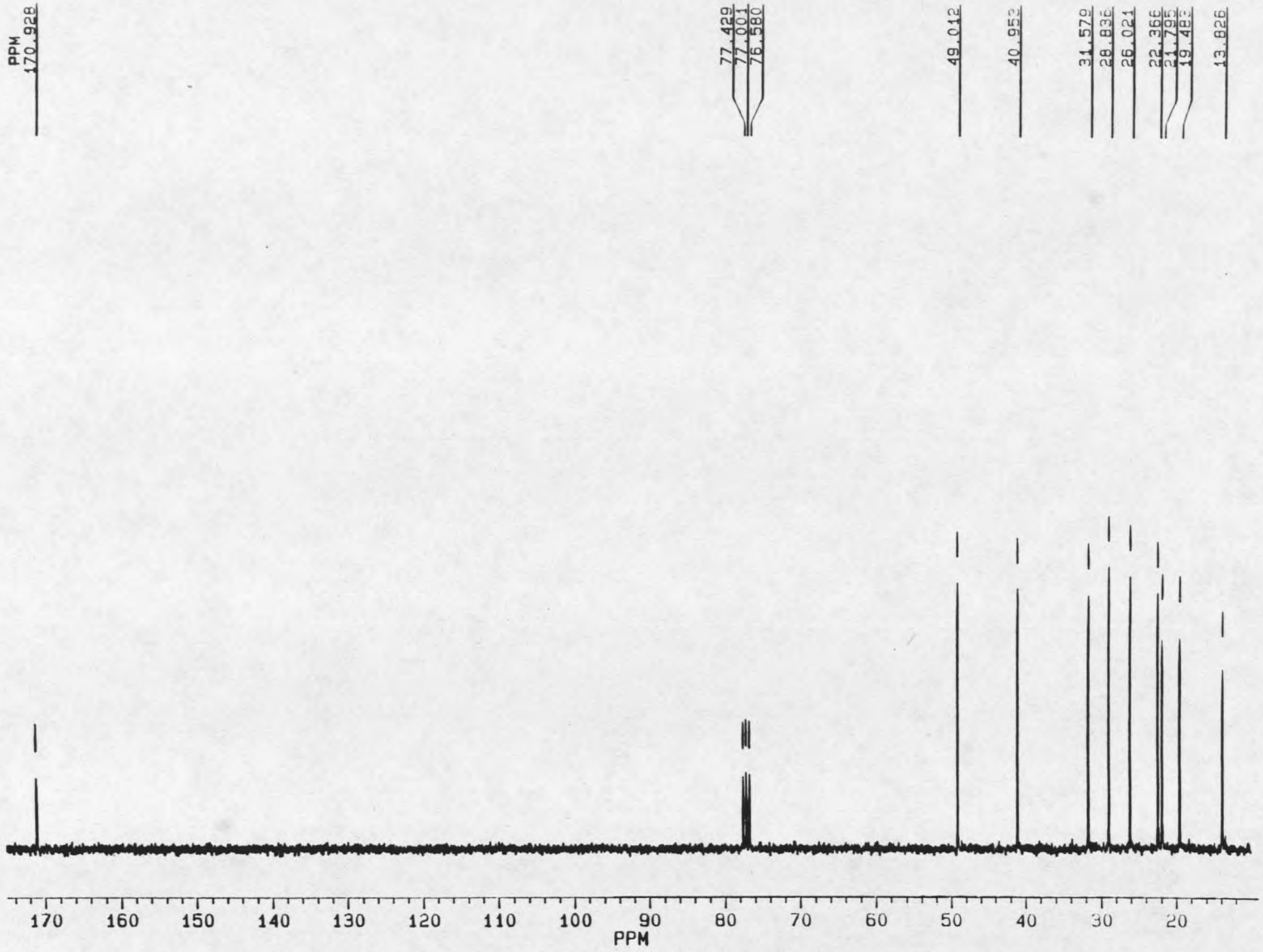


Figure 45. ^{13}C NMR Spectrum of 2-Pentyl-3,4,5,6-tetrahydropyridine(12).

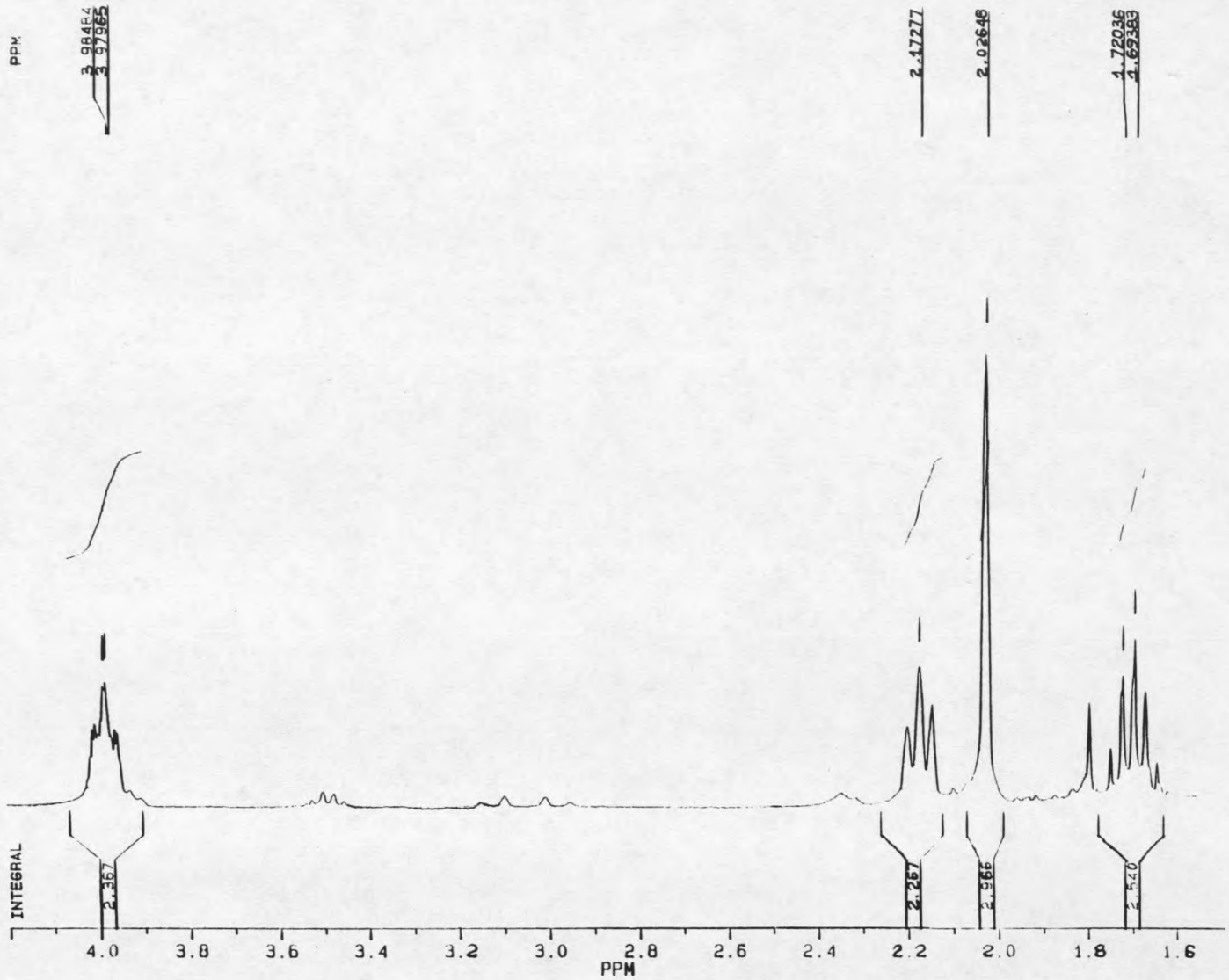


Figure 46. ^{1}H NMR Spectrum of 3,4-Dihydro-5-methyl-2H-pyrrole(29).

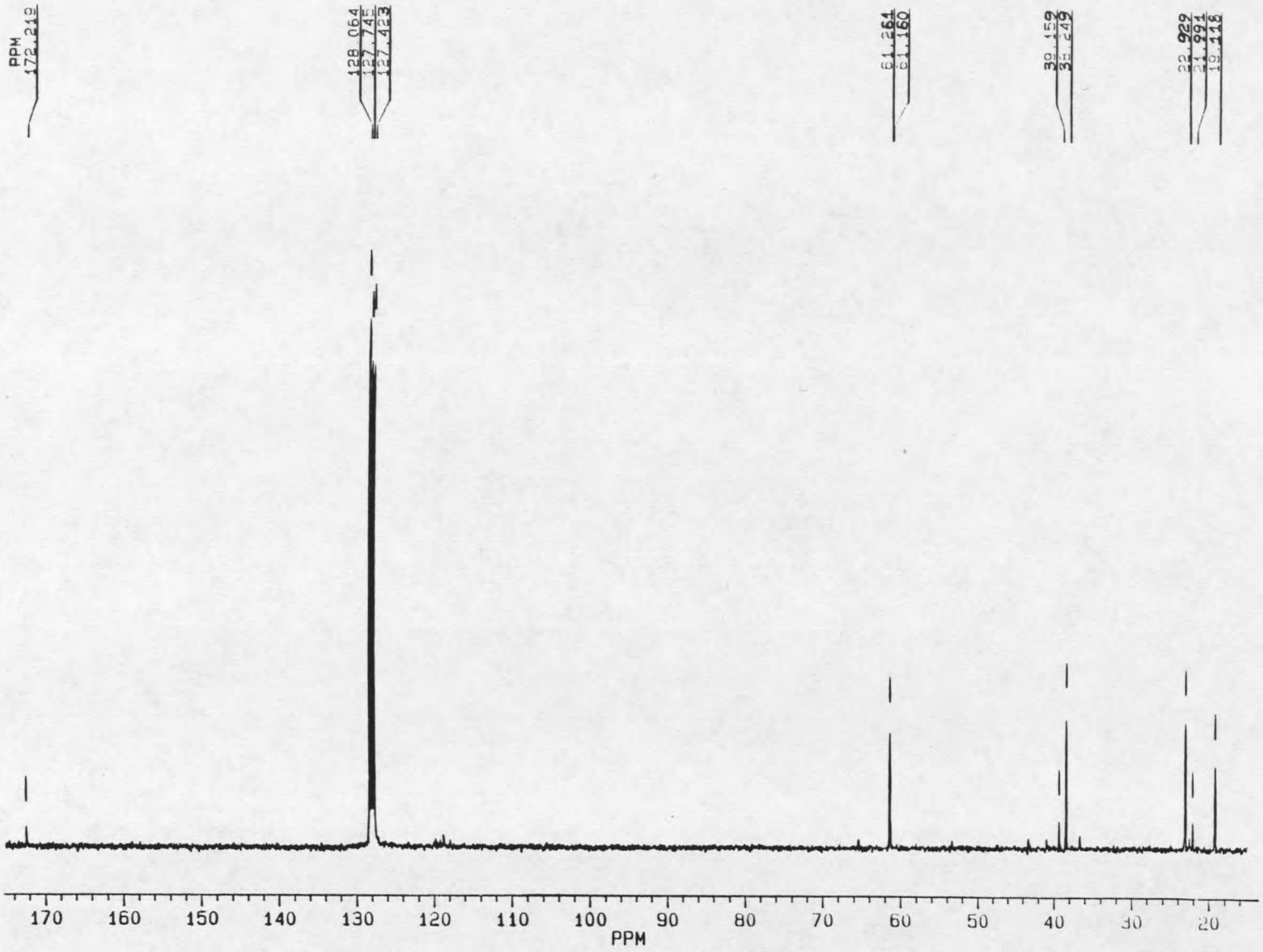


Figure 47. ^{13}C NMR Spectrum of 3,4-Dihydro-5-methyl-2H-pyrrole(29).

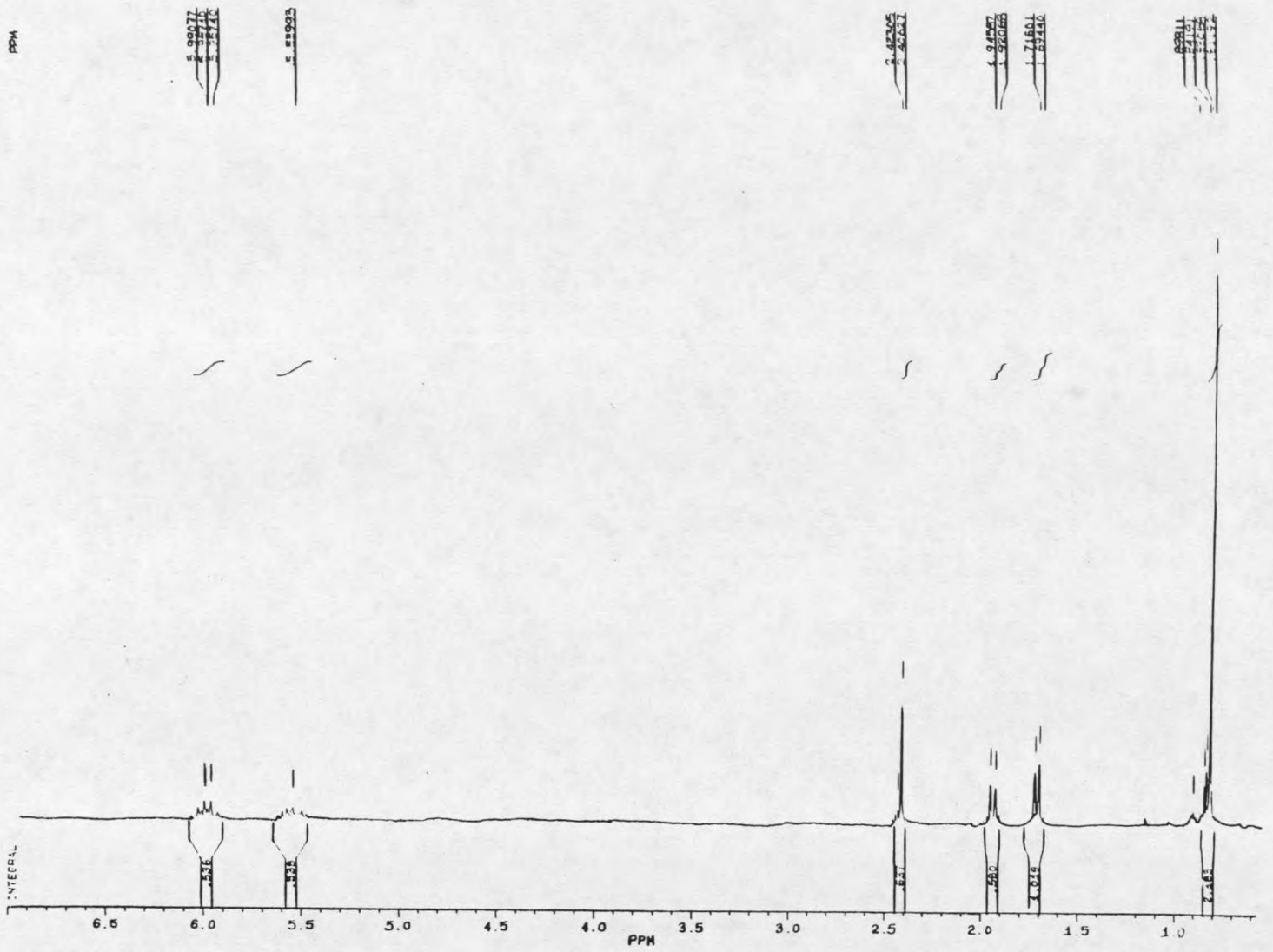


Figure 48. ^{1}H NMR Spectrum of (E,E)-2,2-Dimethyl-4,6-octadiene-1-ylamine(32).

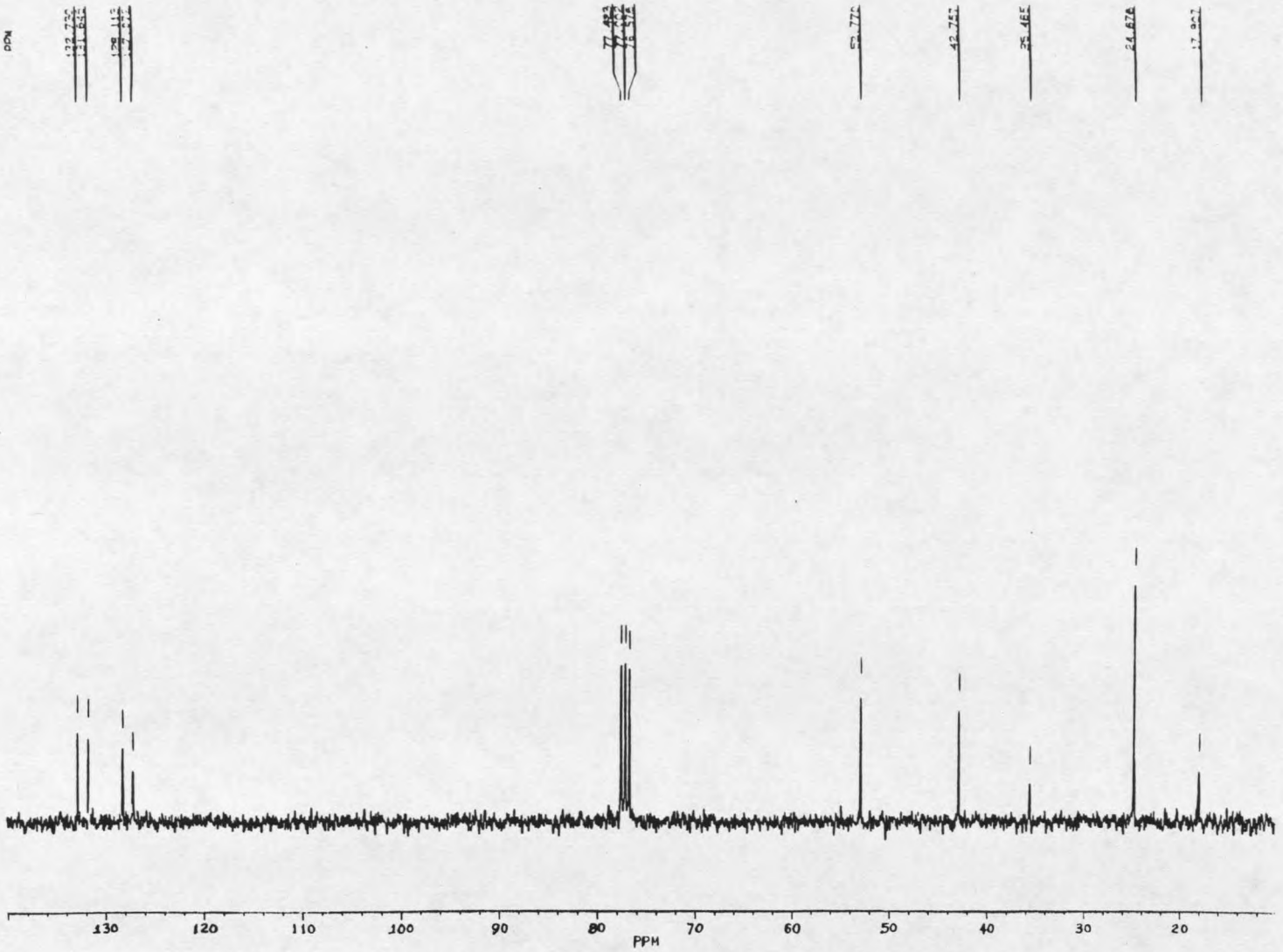


Figure 49. ^{13}C NMR Spectrum of (E,E)-2,2-Dimethyl-4,6-octadiene-1-ylamine(32).

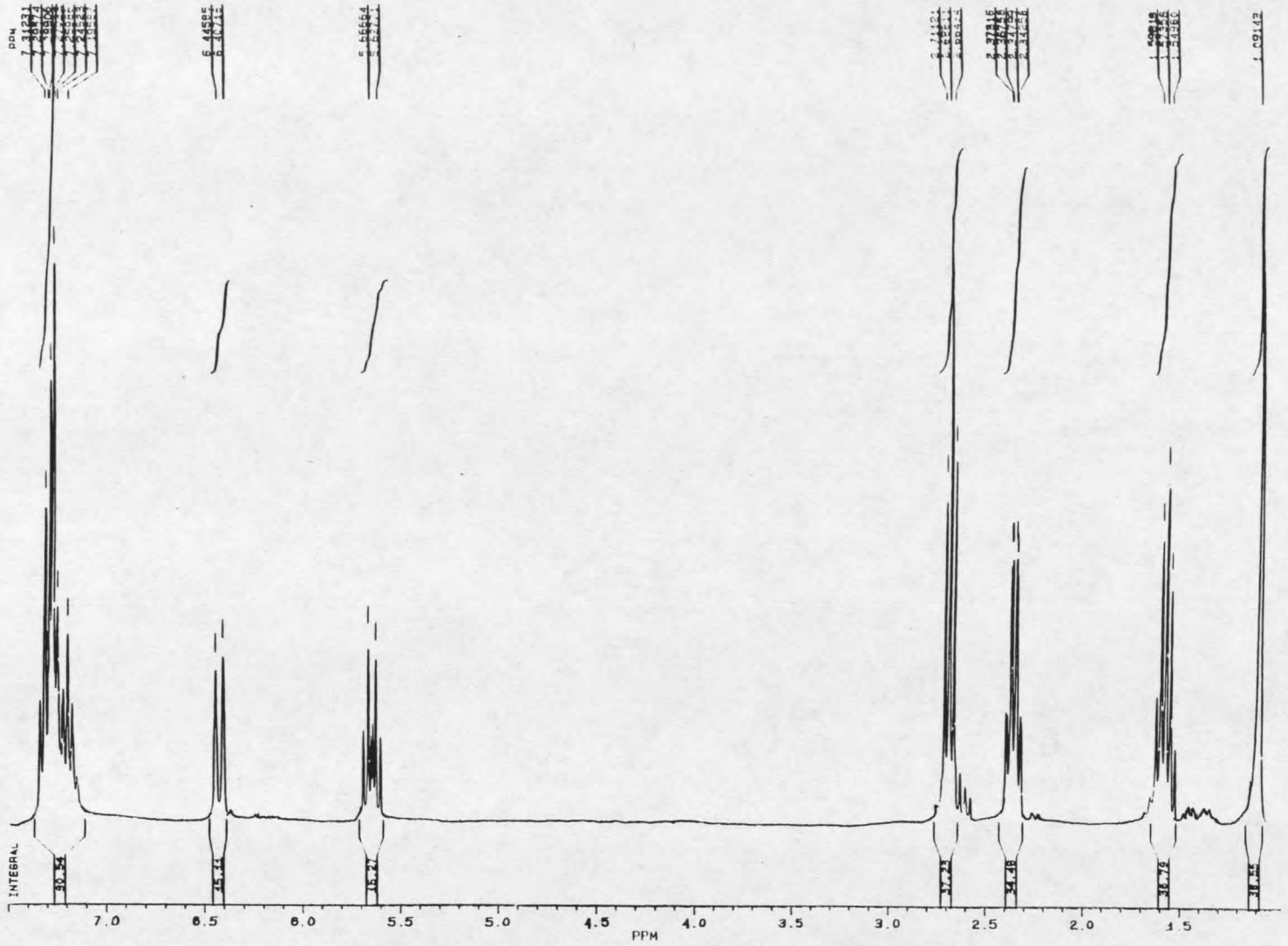


Figure 50. ^{1}H NMR Spectrum of (Z)-5-Phenyl-4-penten-1-ylamine(30).

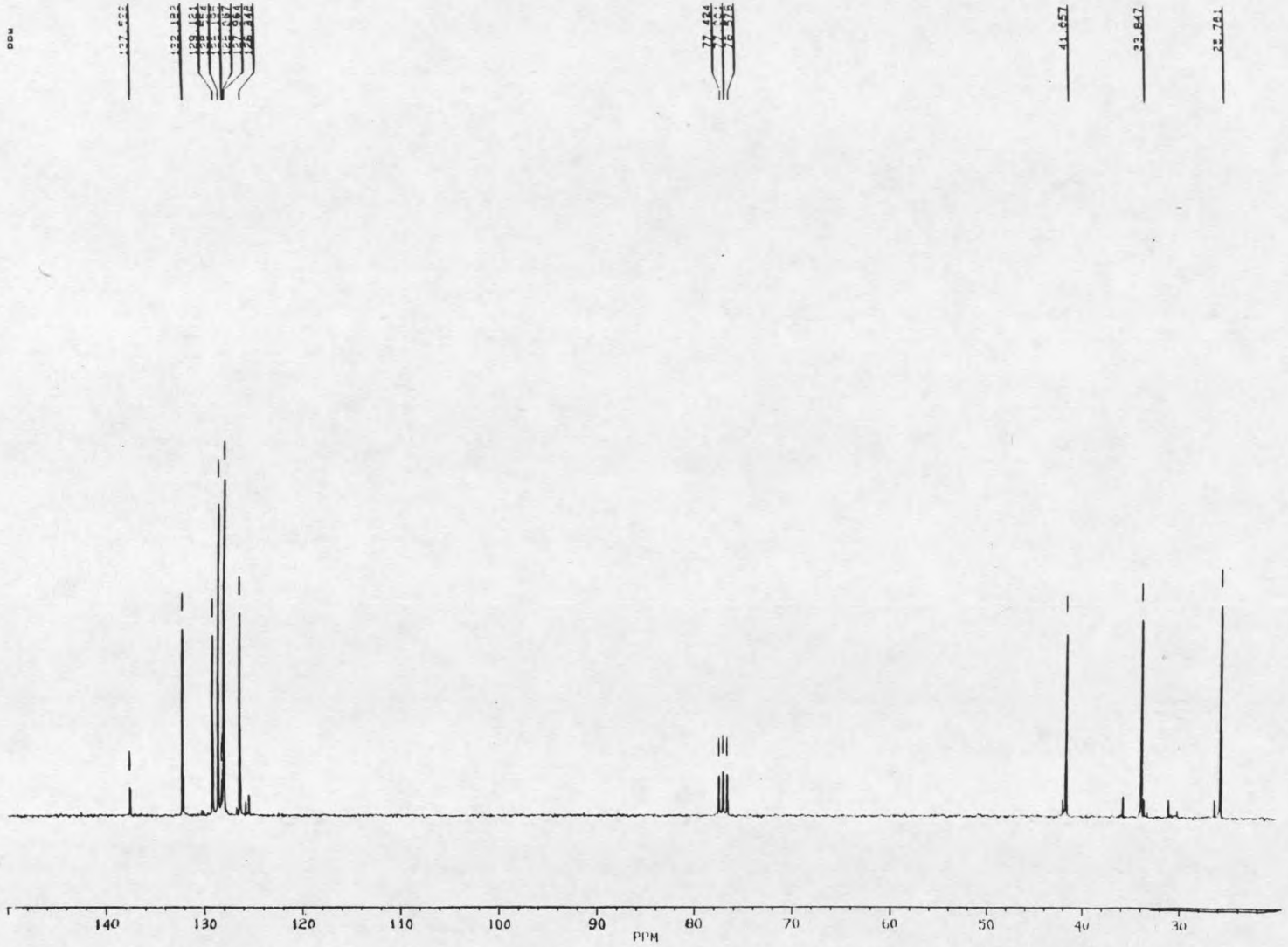


Figure 51. ^{13}C NMR Spectrum of (Z)-5-Phenyl-4-penten-1-ylamine(30).

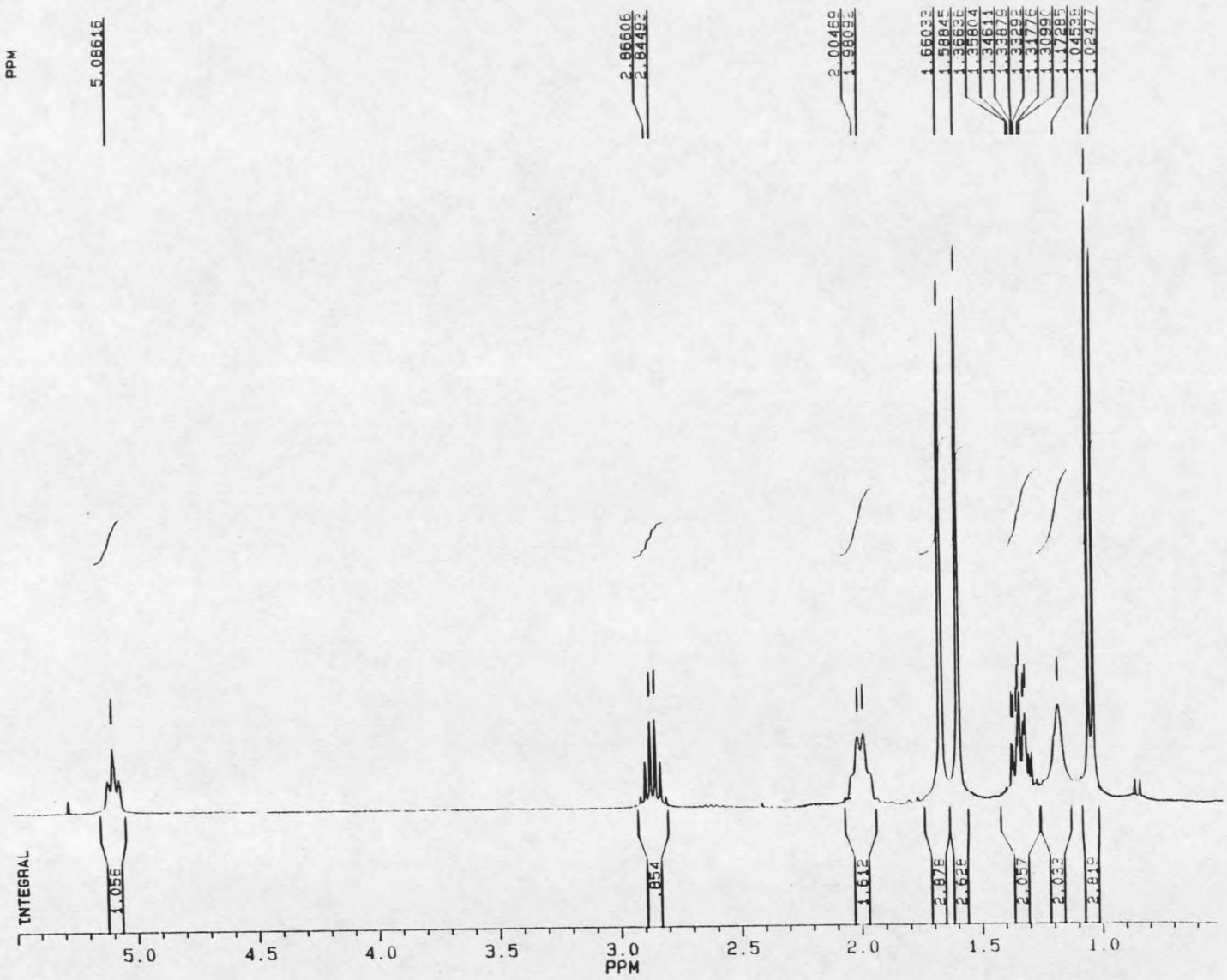


Figure 52. ^{1}H NMR Spectrum of 6-Methyl-5-hepten-2-ylamine(31).

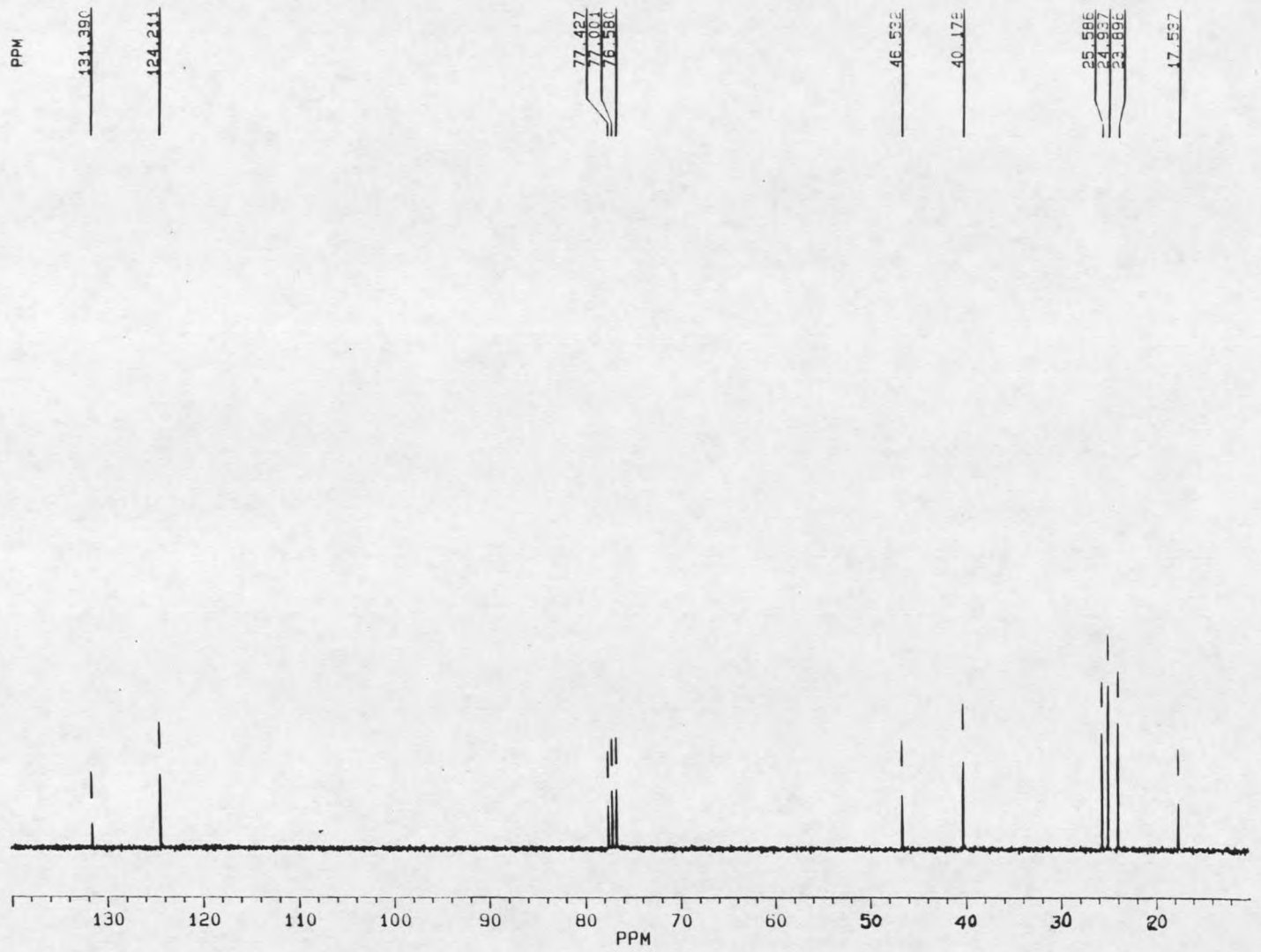


Figure 53. ^{13}C NMR Spectrum of 6-Methyl-5-hepten-2-ylamine(31).

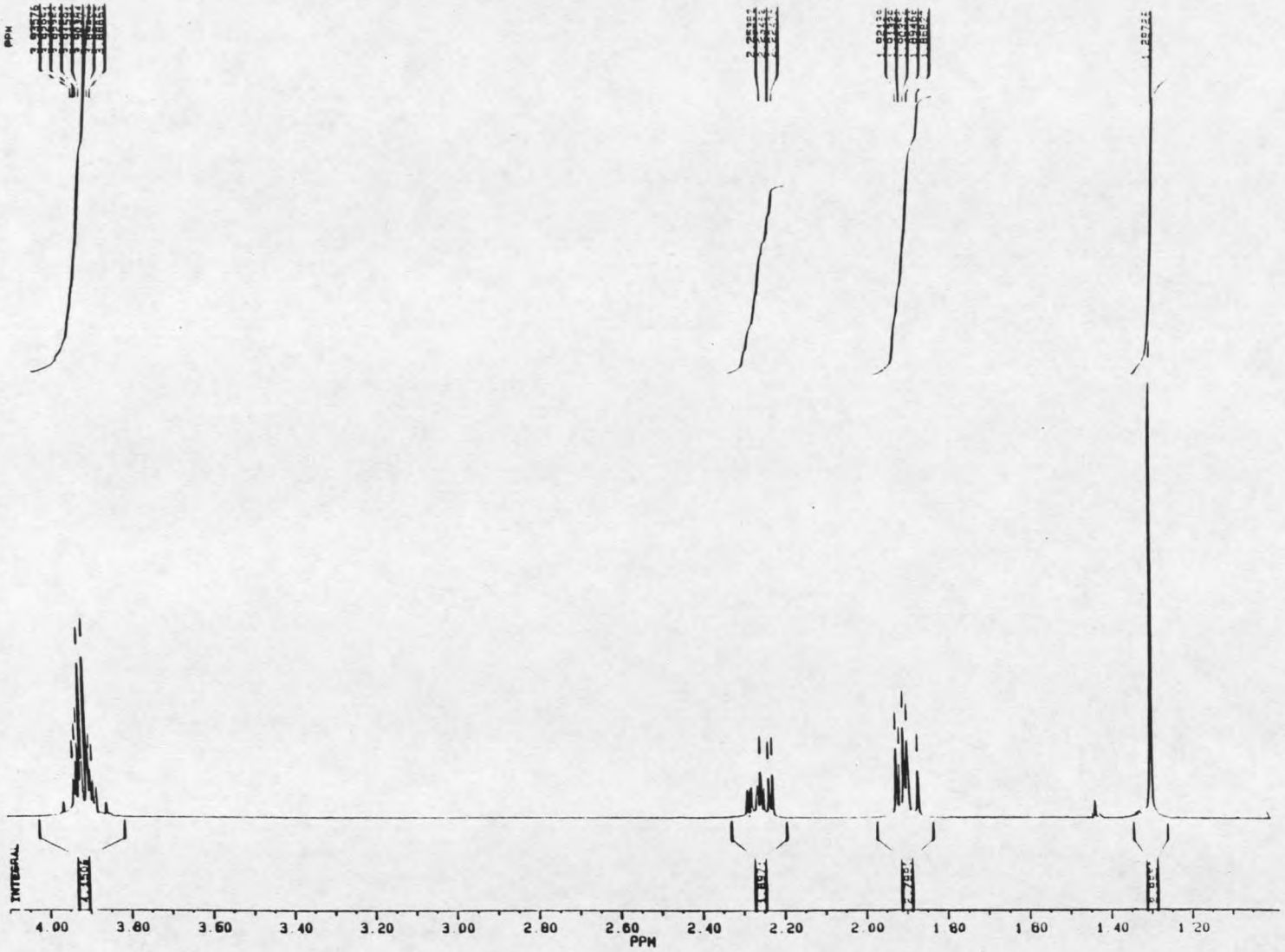


Figure 54. ^{1}H NMR Spectrum of 5,5-Ethylenedioxyhex-2-yne(44).

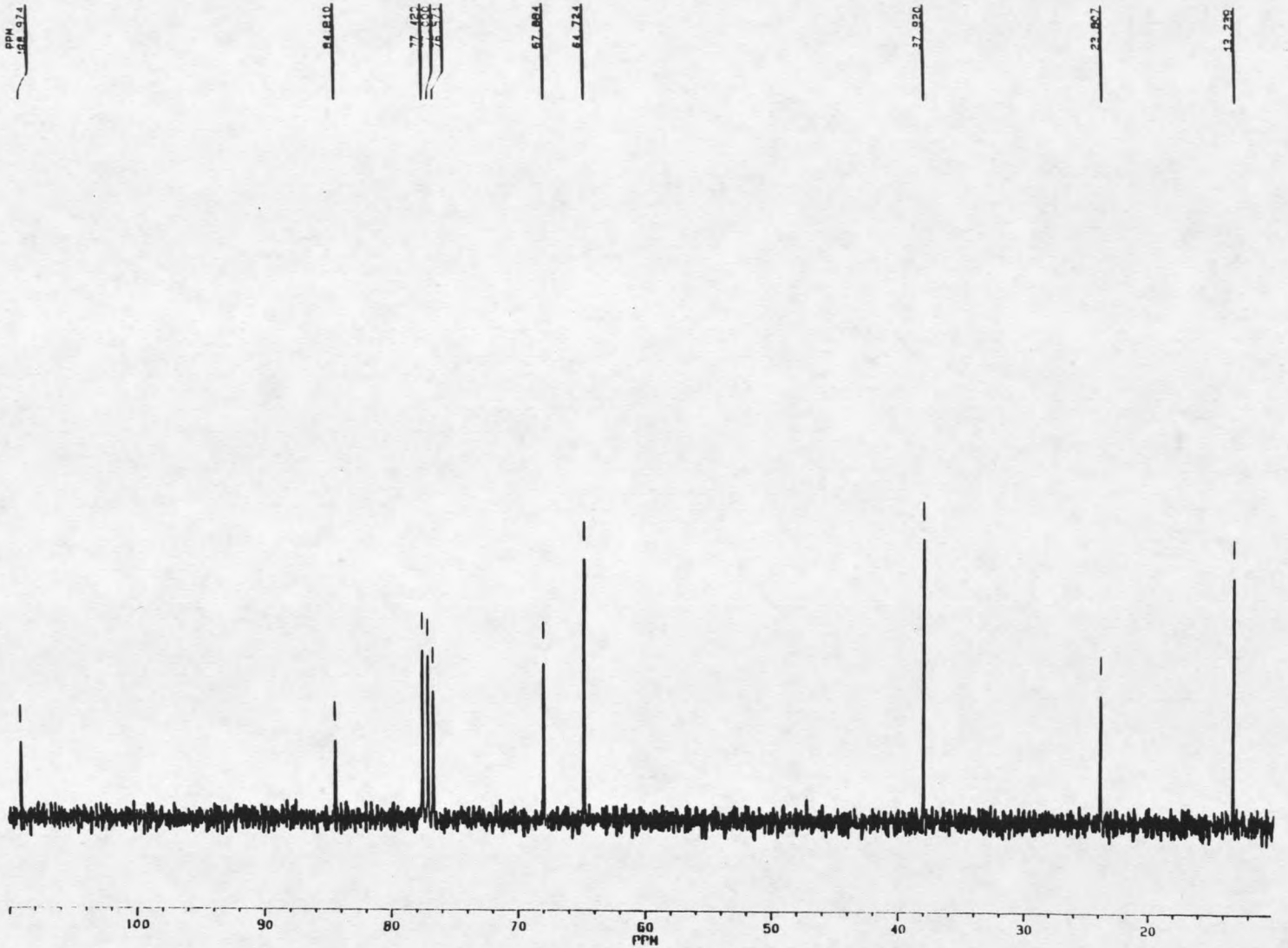


Figure 55. ^{13}C NMR Spectrum of 5,5-Ethylenedioxyhex-2-yne(44).

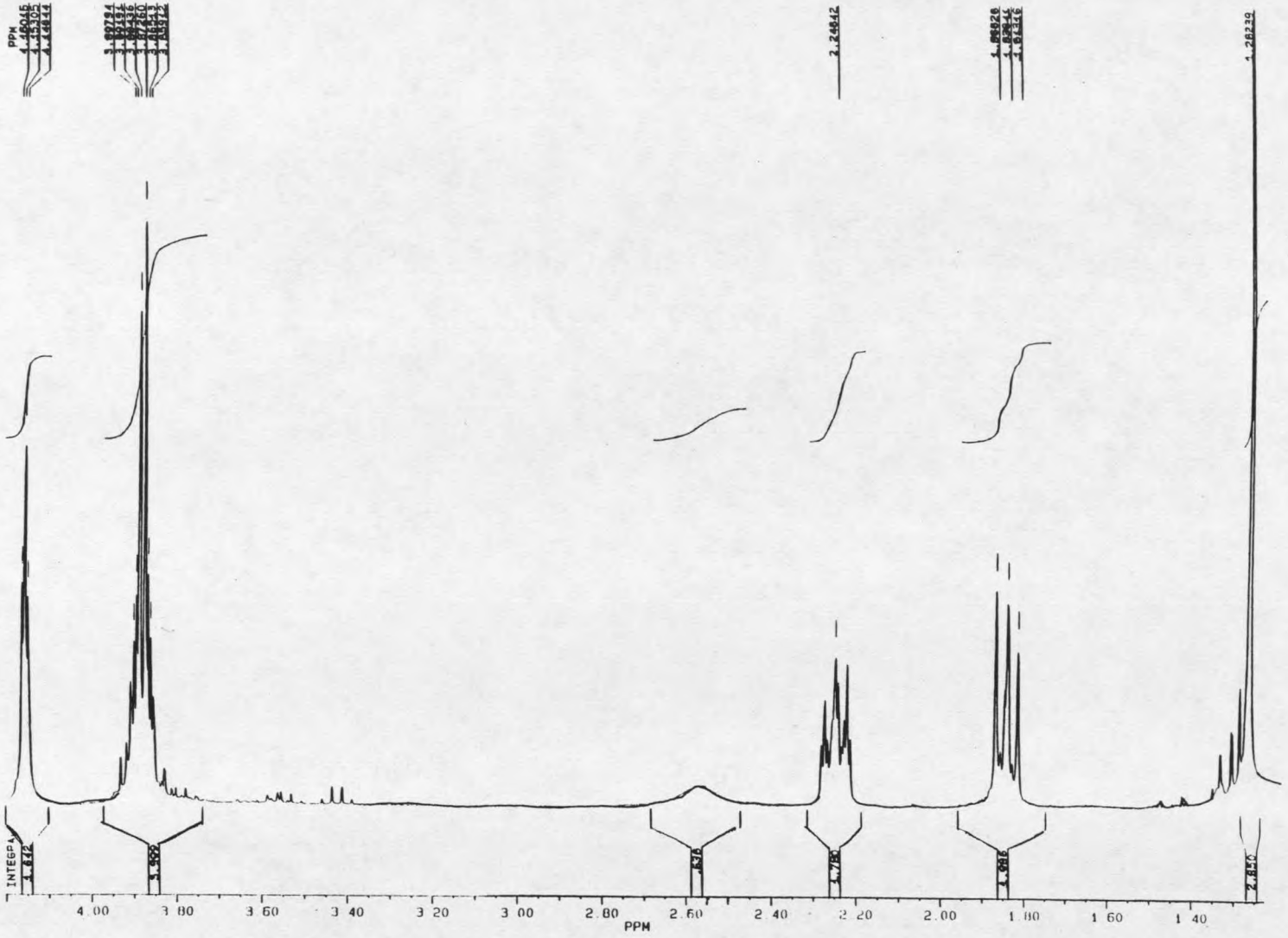


Figure 56. ^{1}H NMR Spectrum of 2,2-Ethylenedioxyhept-5-yn-7-ol(45).

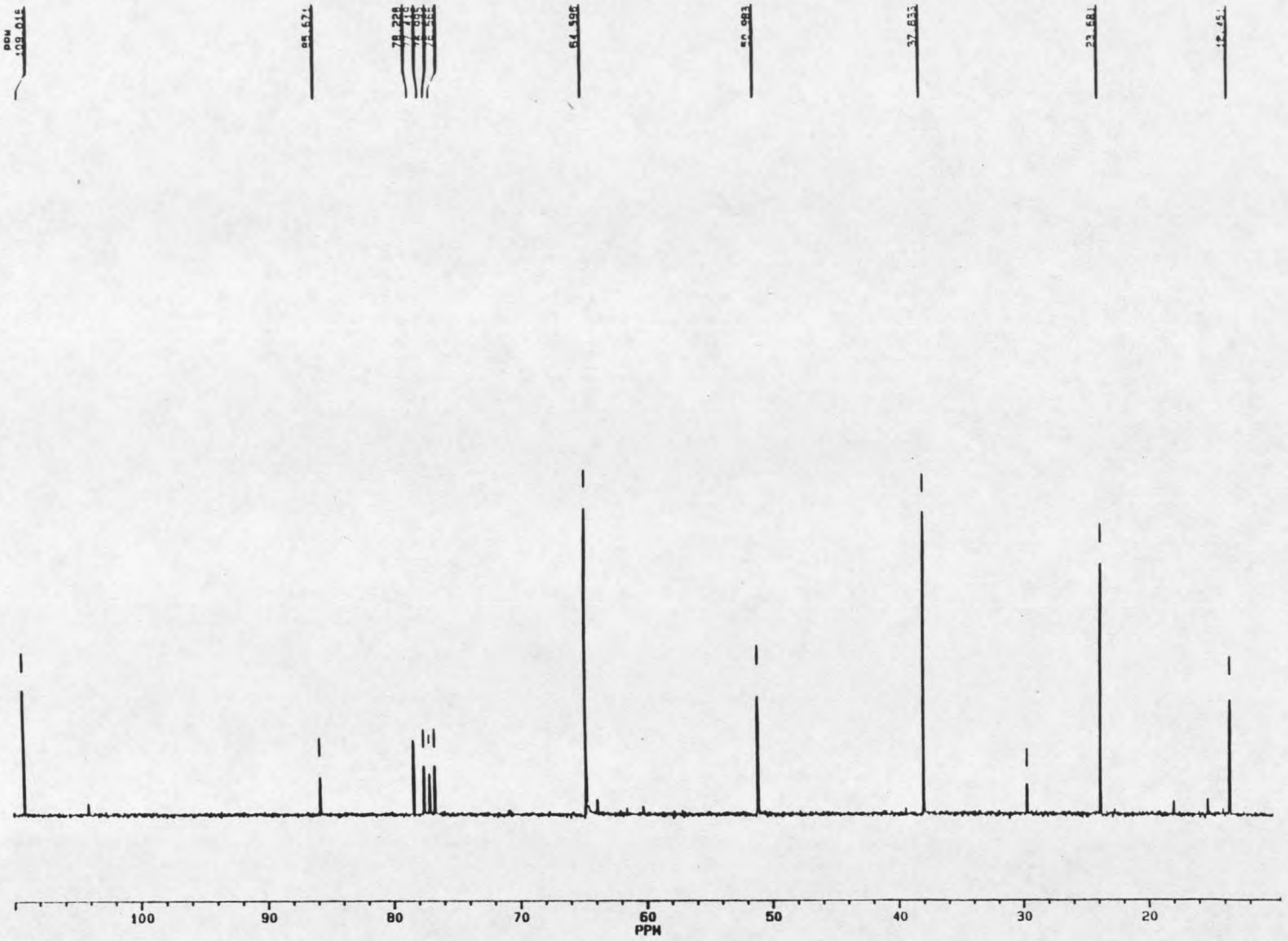


Figure 57. ^{13}C NMR Spectrum of 2,2-Ethylenedioxyhept-5-yn-7-ol(45).

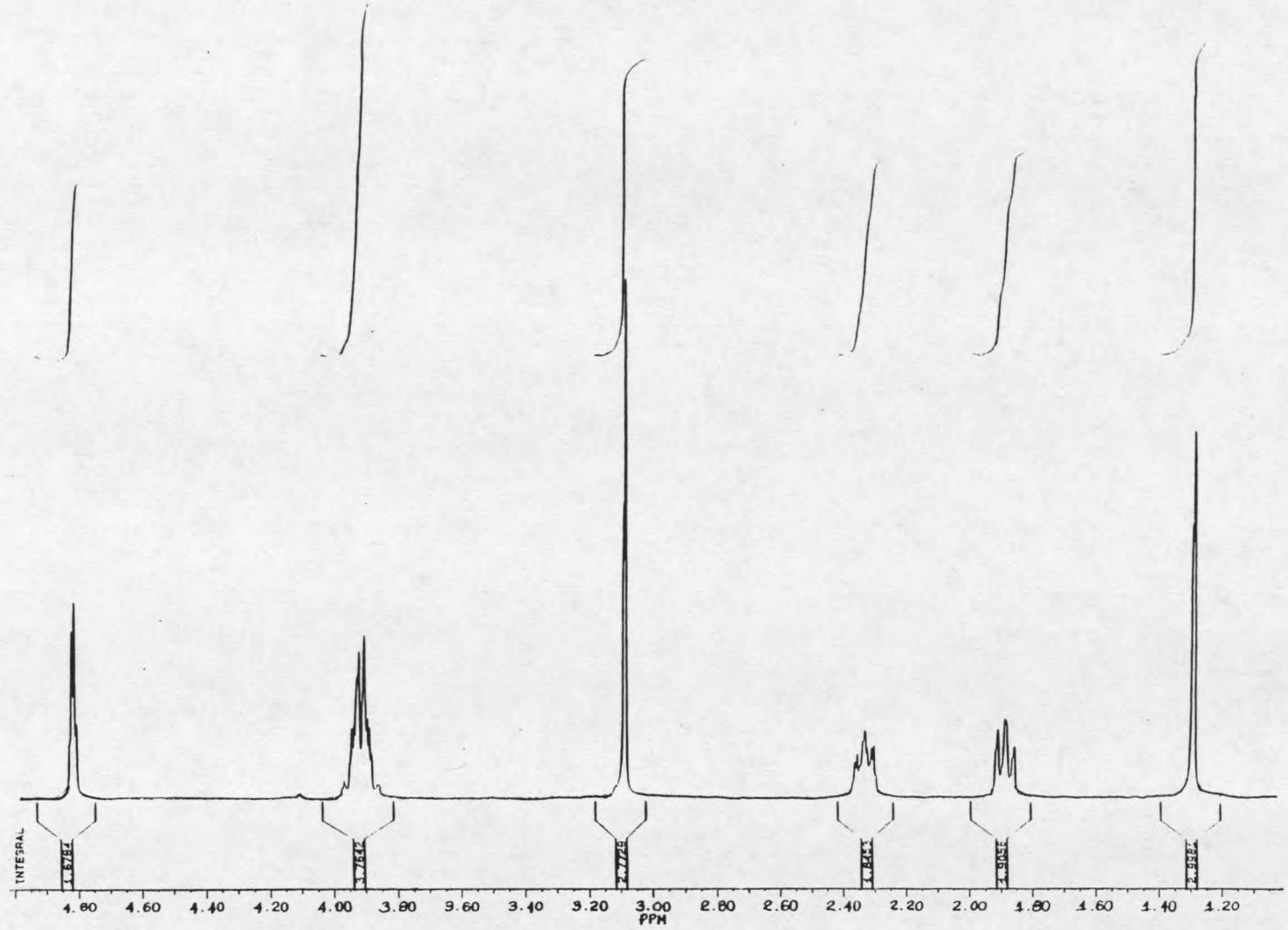


Figure 58. ^{1}H NMR Spectrum of 2,2-Ethylenedioxyhept-5-yn-7-ol methane sulfonate ester(46).

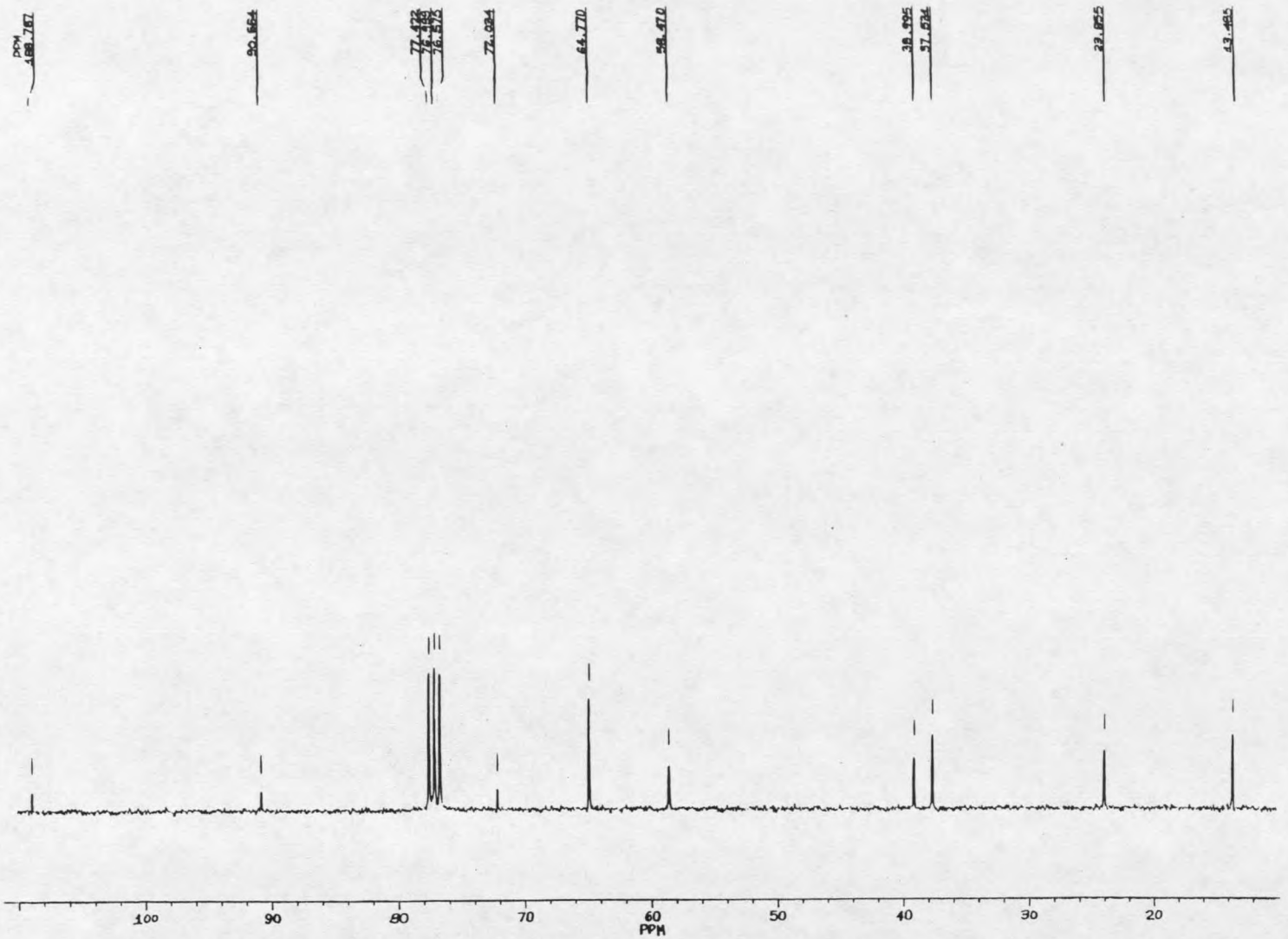


Figure 59. ^{13}C NMR Spectrum of 2,2-Ethylenedioxyhept-5-yn-7-ol methane sulfonate ester(46).

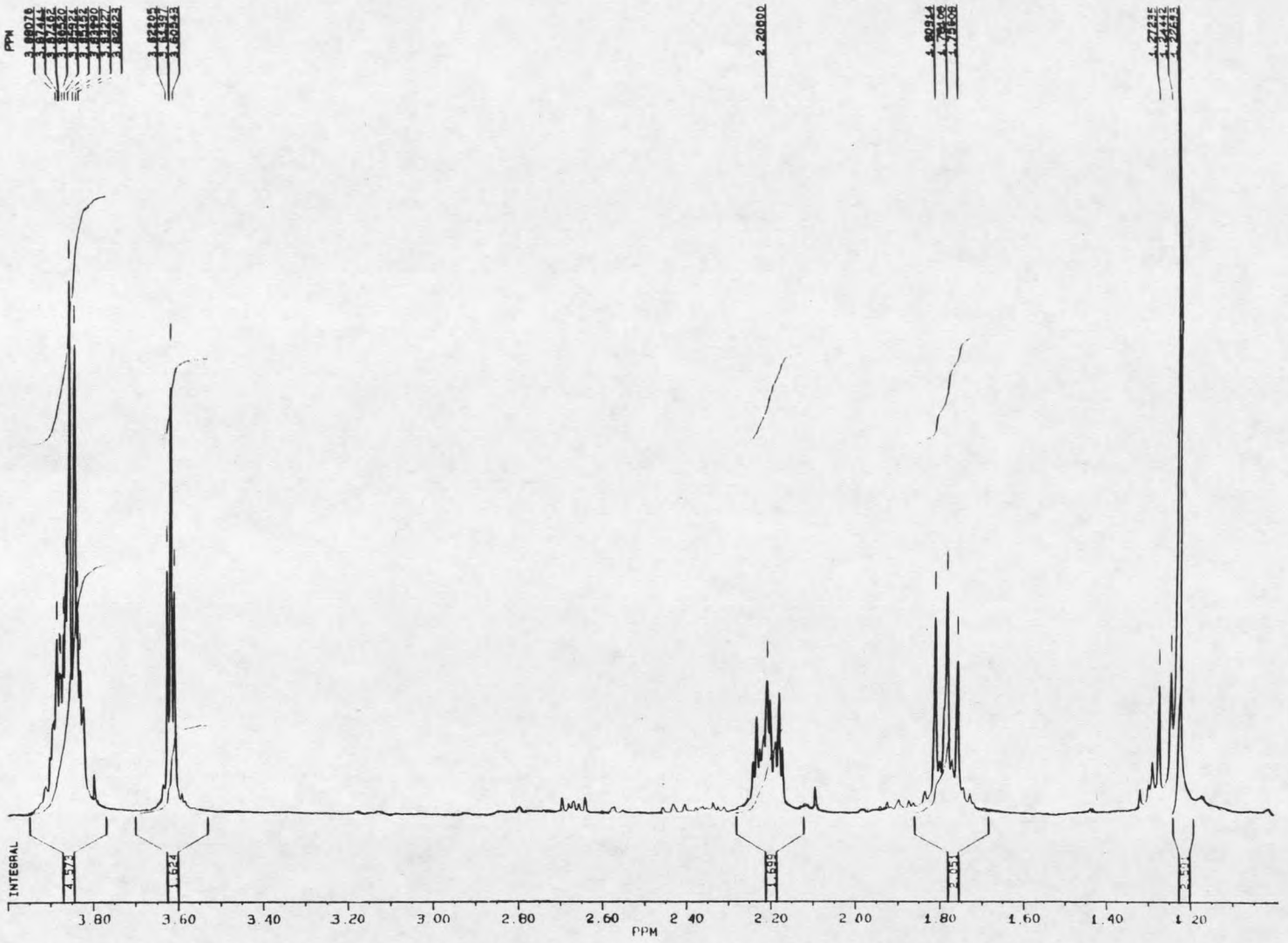


Figure 60. ^{1}H NMR Spectrum of 2,2-Ethylenedioxy-7-iodohept-5-yne(47).

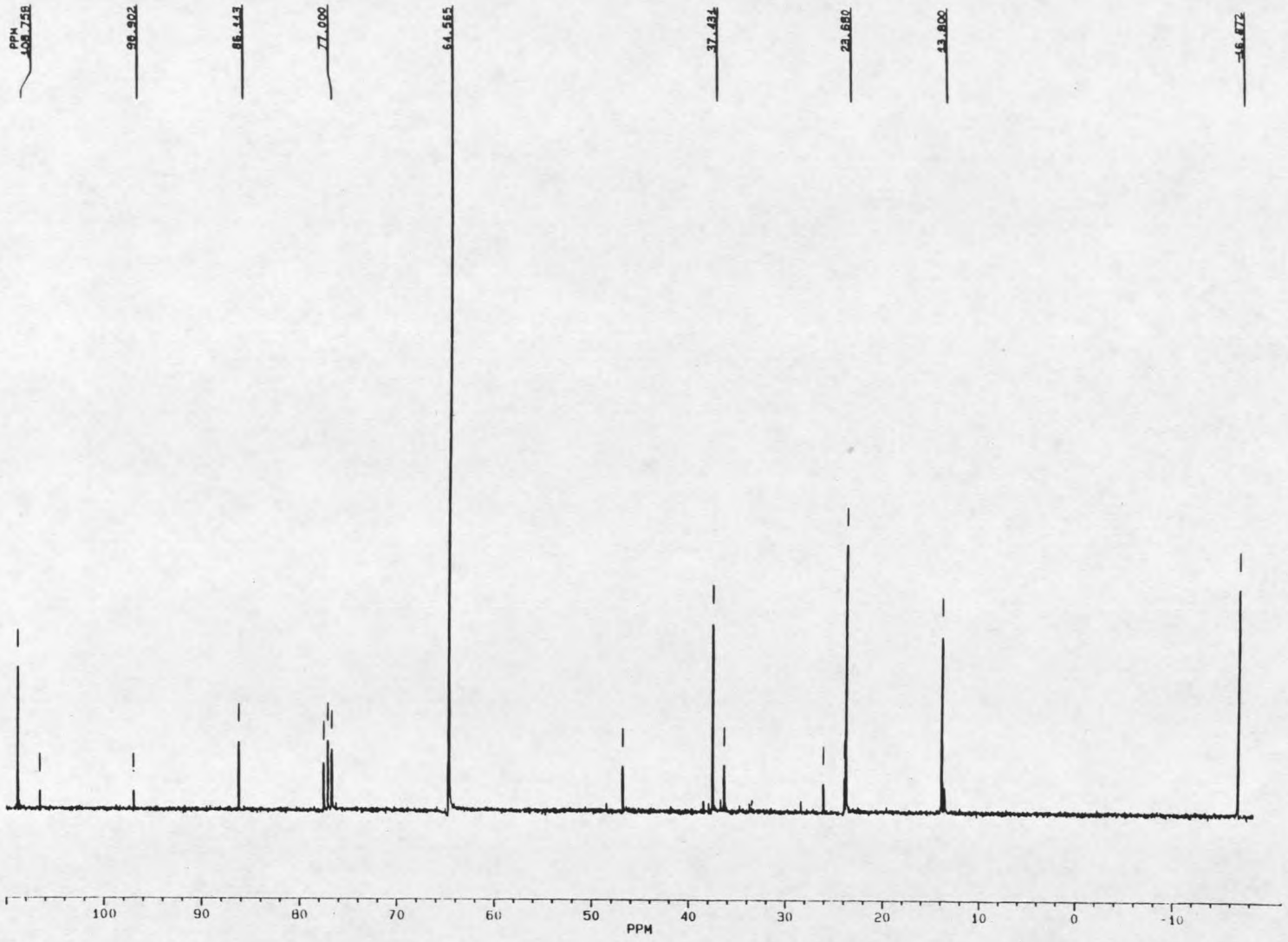


Figure 61. ^{13}C NMR Spectrum of 2,2-Ethylenedioxy-7-iodohept-5-yne(47).

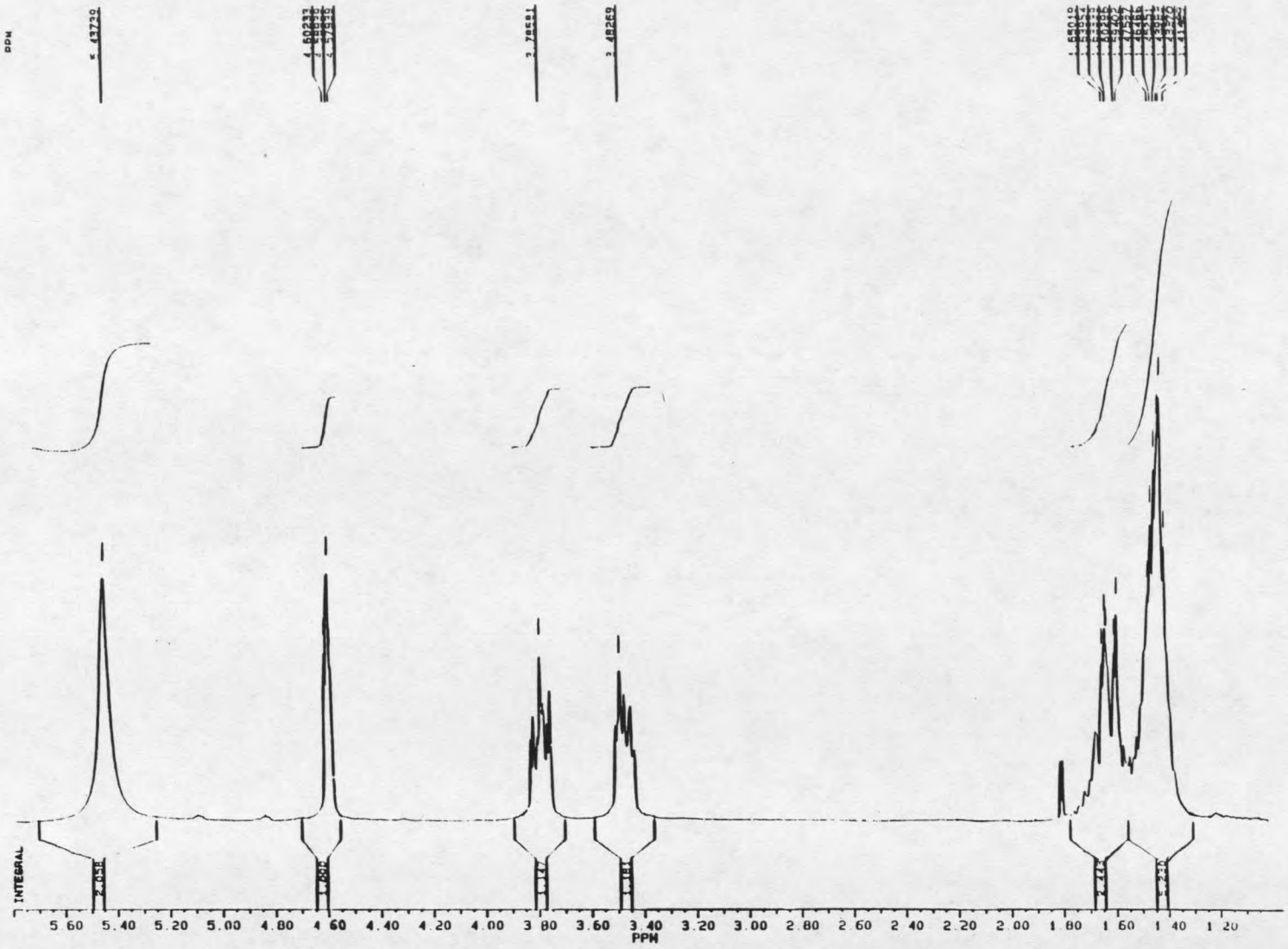


Figure 62. ^{1}H NMR Spectrum of O-2,3,5,6-Tetrahydropyran-2-ylhydroxyl-amine(40).

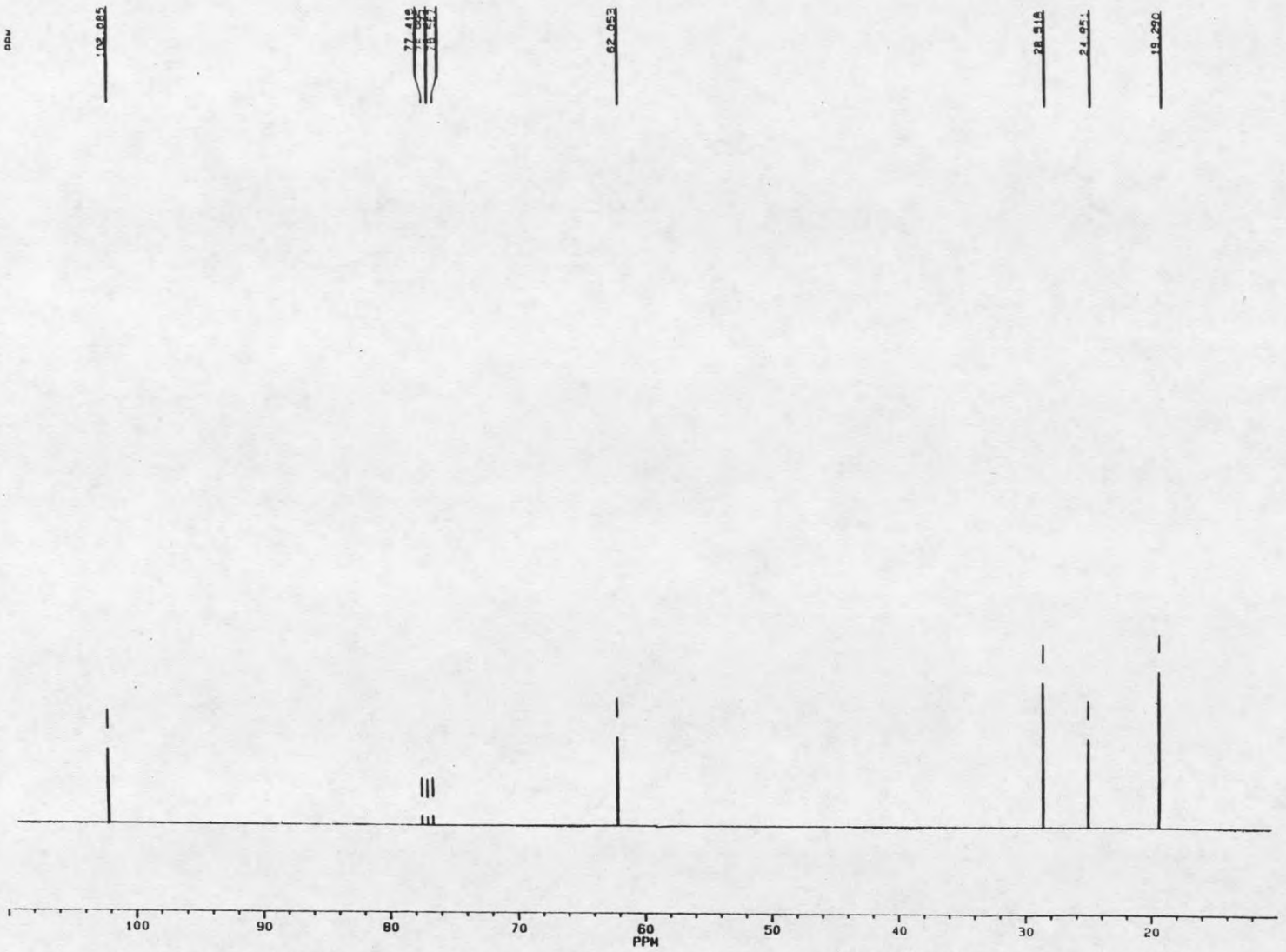


Figure 63. ^{13}C NMR Spectrum of O-2,3,5,6-Tetrahydropyran-2-ylhydroxyl-amine(40).

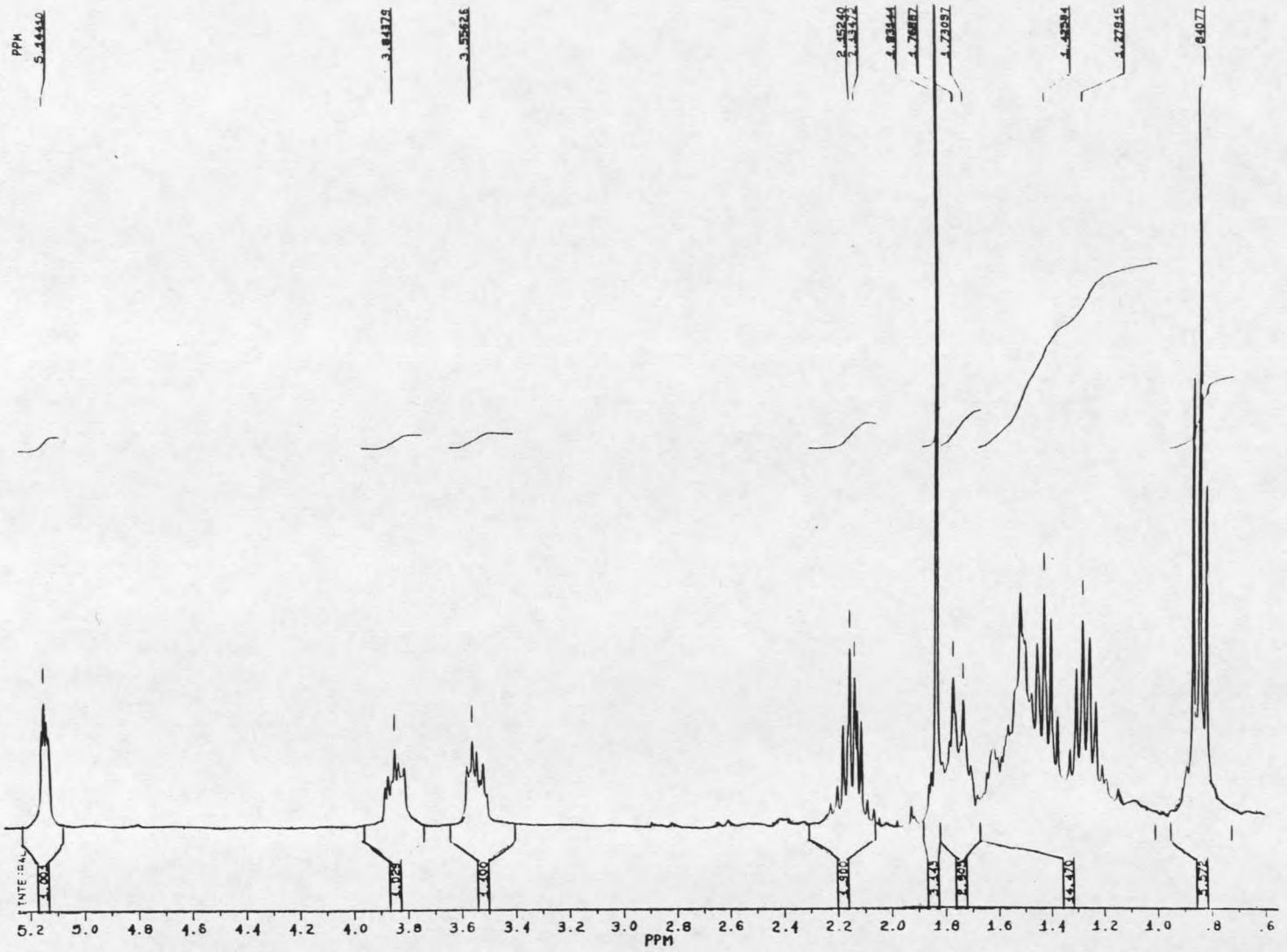


Figure 64. ^{1}H NMR Spectrum of (E) and (Z)-O-(2,3,5,6-Tetrahydropyran-2-yl)-hexan-2-one oxime(41).

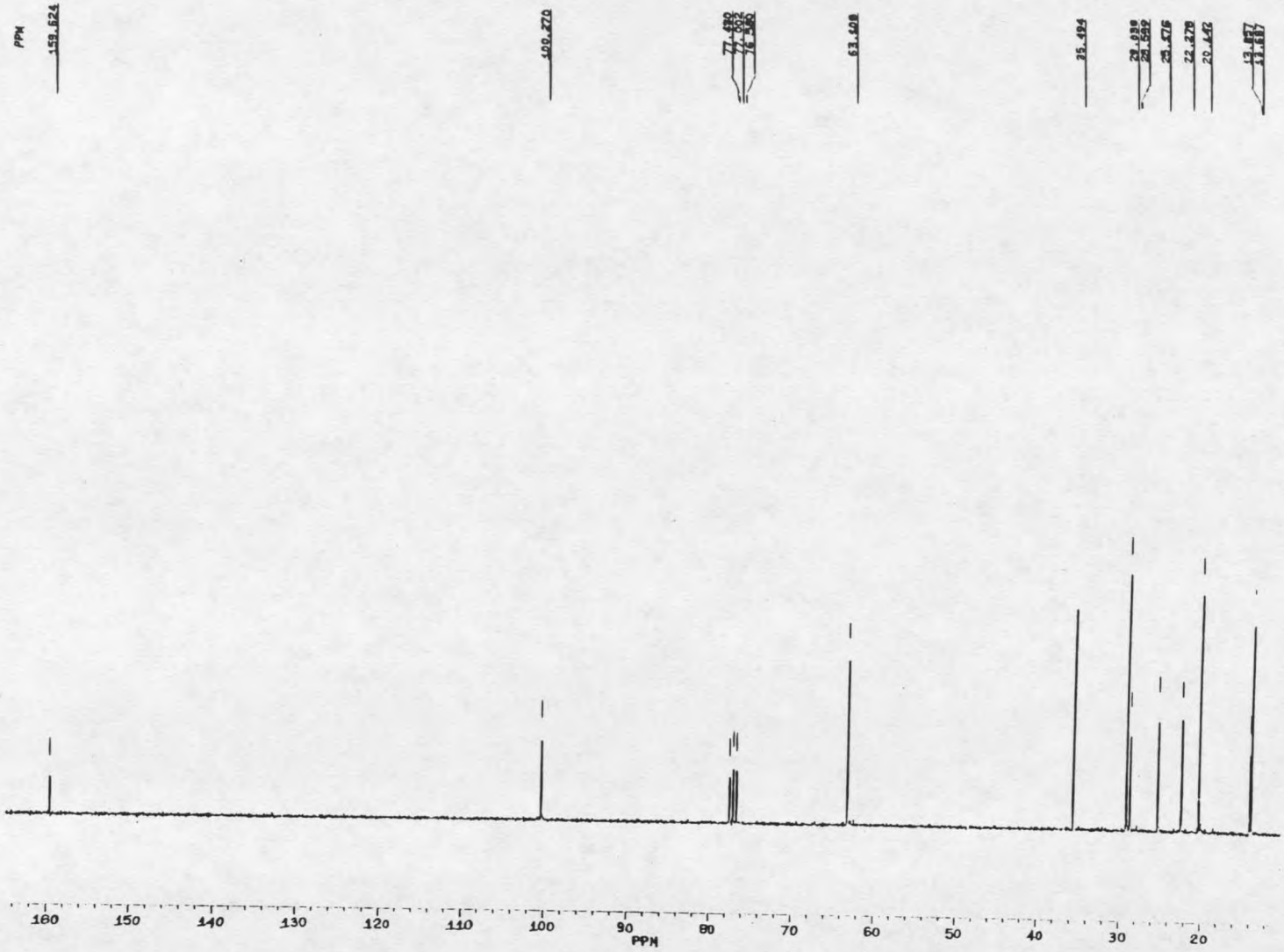


Figure 65. ^{13}C NMR Spectrum of (E) and (Z)-O-(2,3,5,6-Tetrahydropyran-2-yl)-hexan-2-one oxime(41).

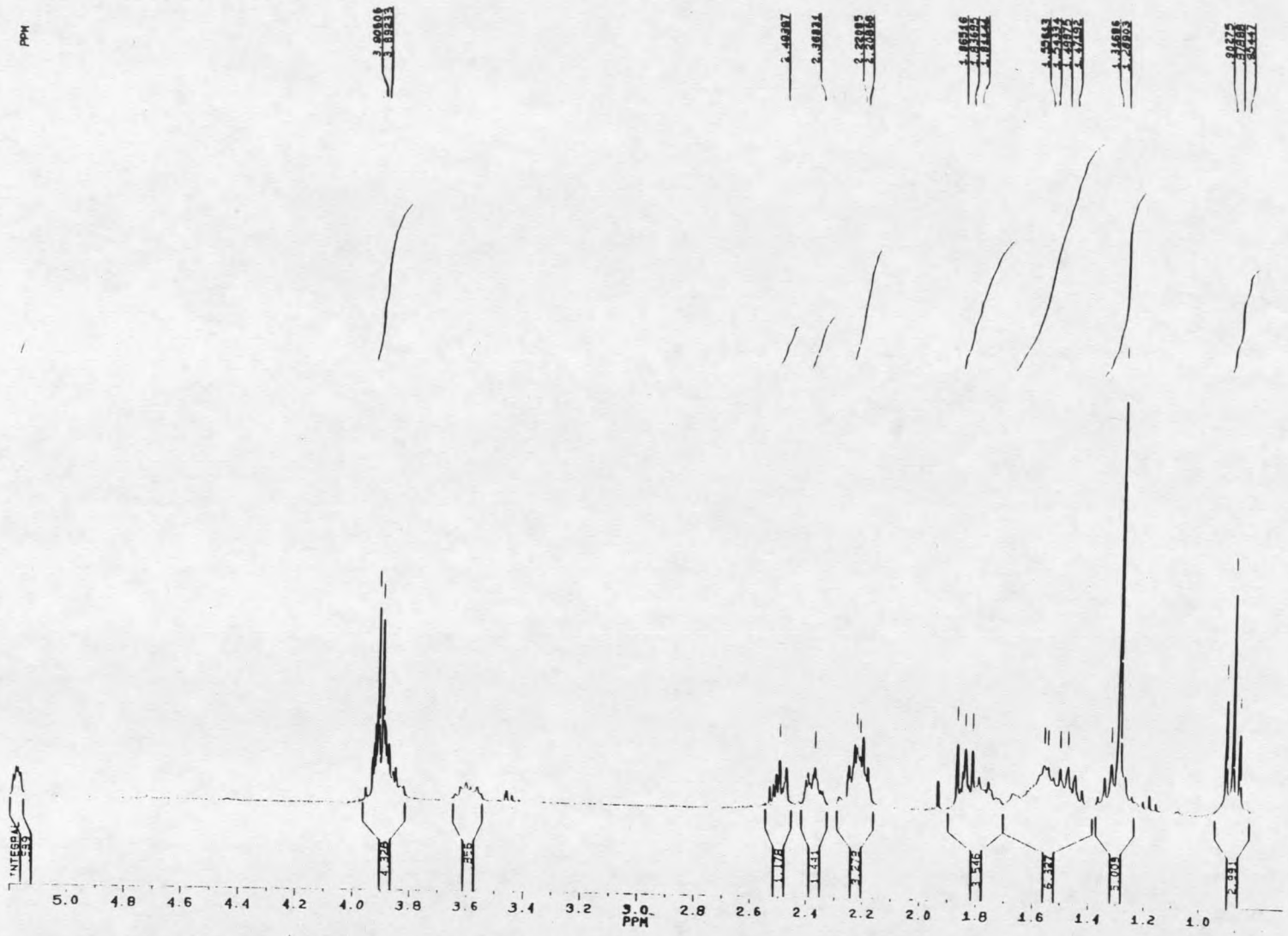


Figure 66. ^{1}H NMR Spectrum of O-(2,3,5,6-Tetrahydro-pyran-2-yl)-2,2-ethylene-dioxytridec-5-yn-7-one oxime(48).

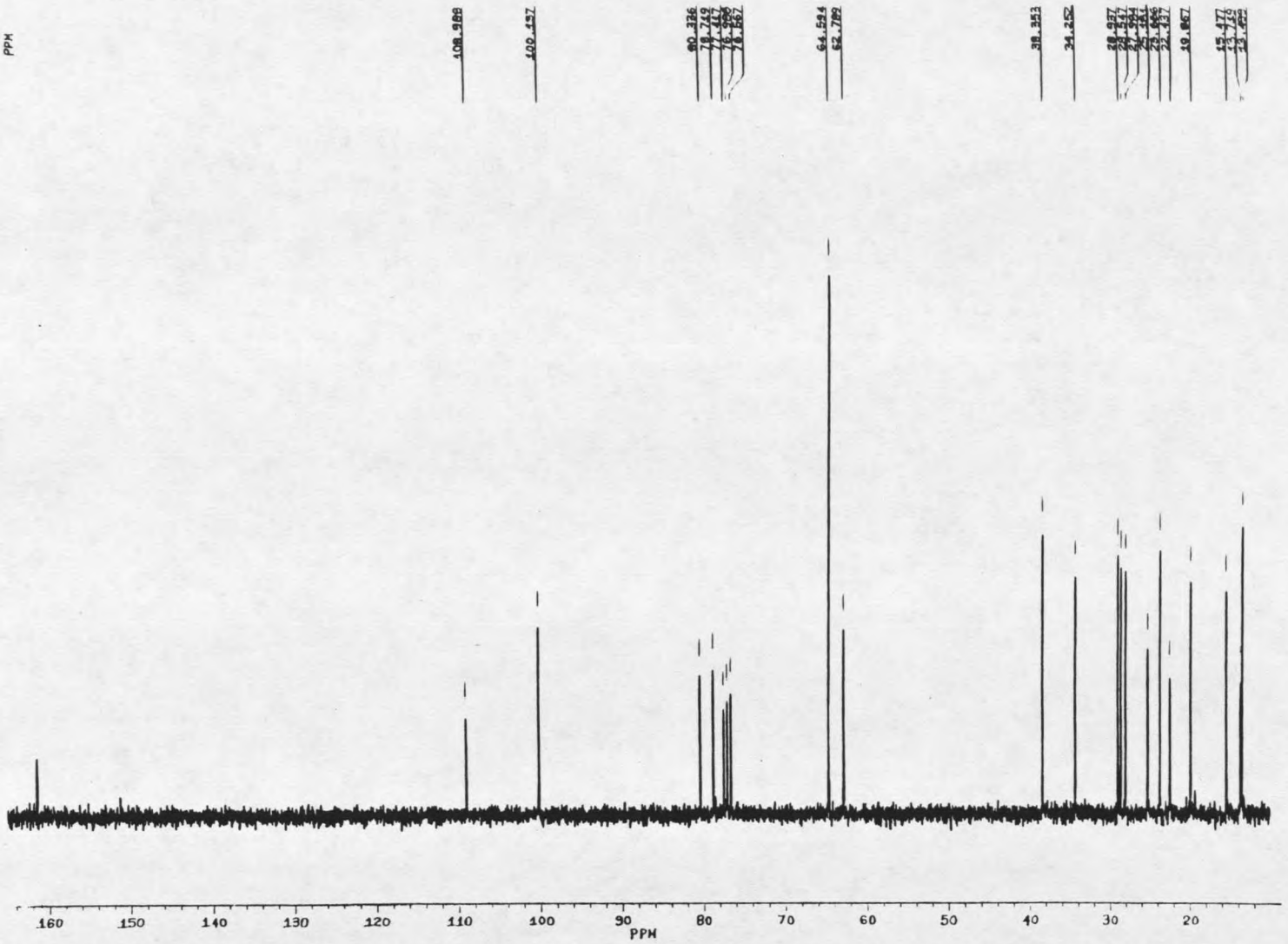


Figure 67. ^{13}C NMR Spectrum of O-(2,3,5,6-Tetrahydro-pyran-2-yl)-2,2-ethylene-dioxytridec-5-yn-7-one oxime(48).

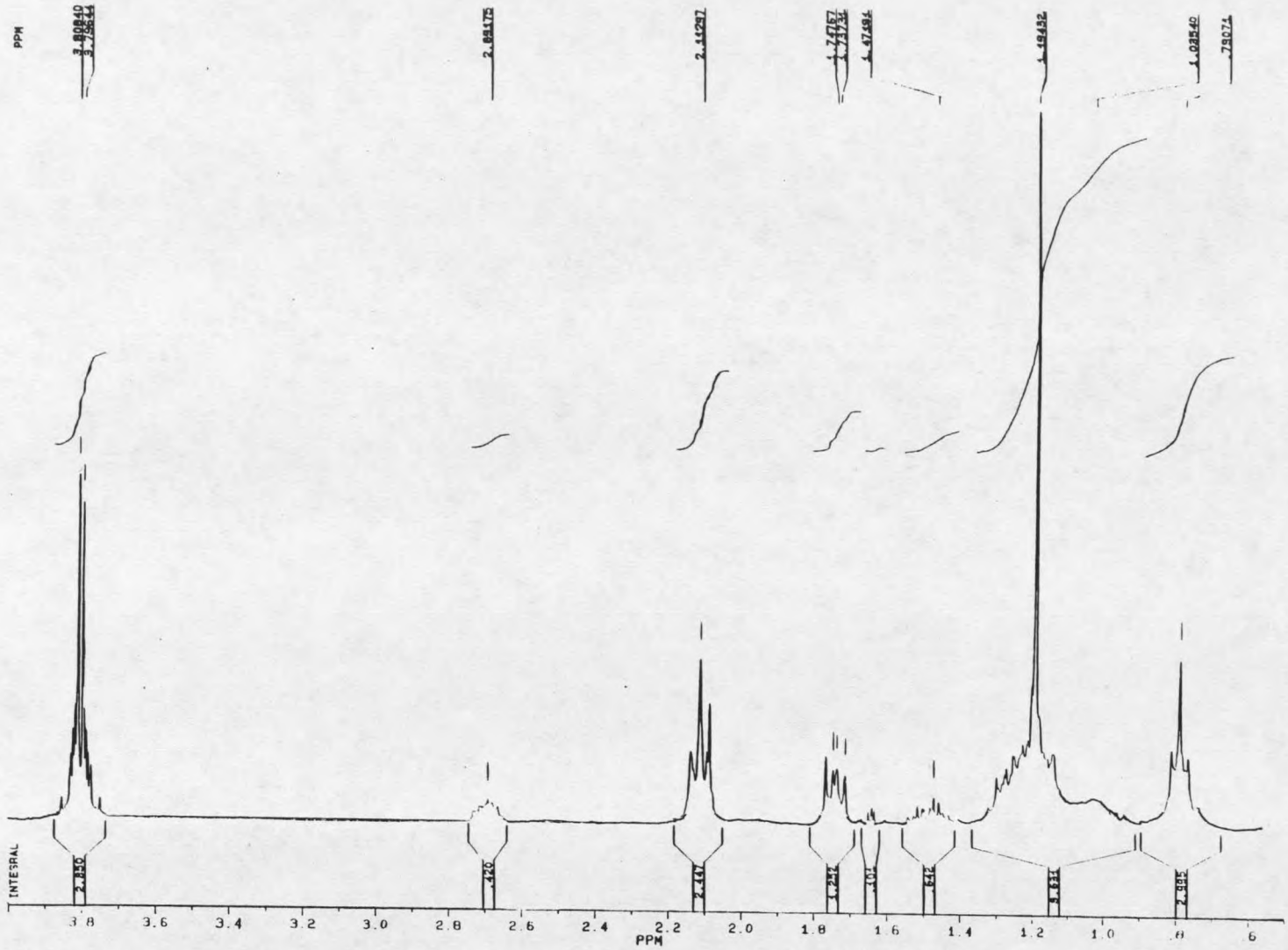


Figure 68. ^{1}H NMR Spectrum of (±) 7-amino-2,2-ethylene-dioxytridec-5-yne(39).

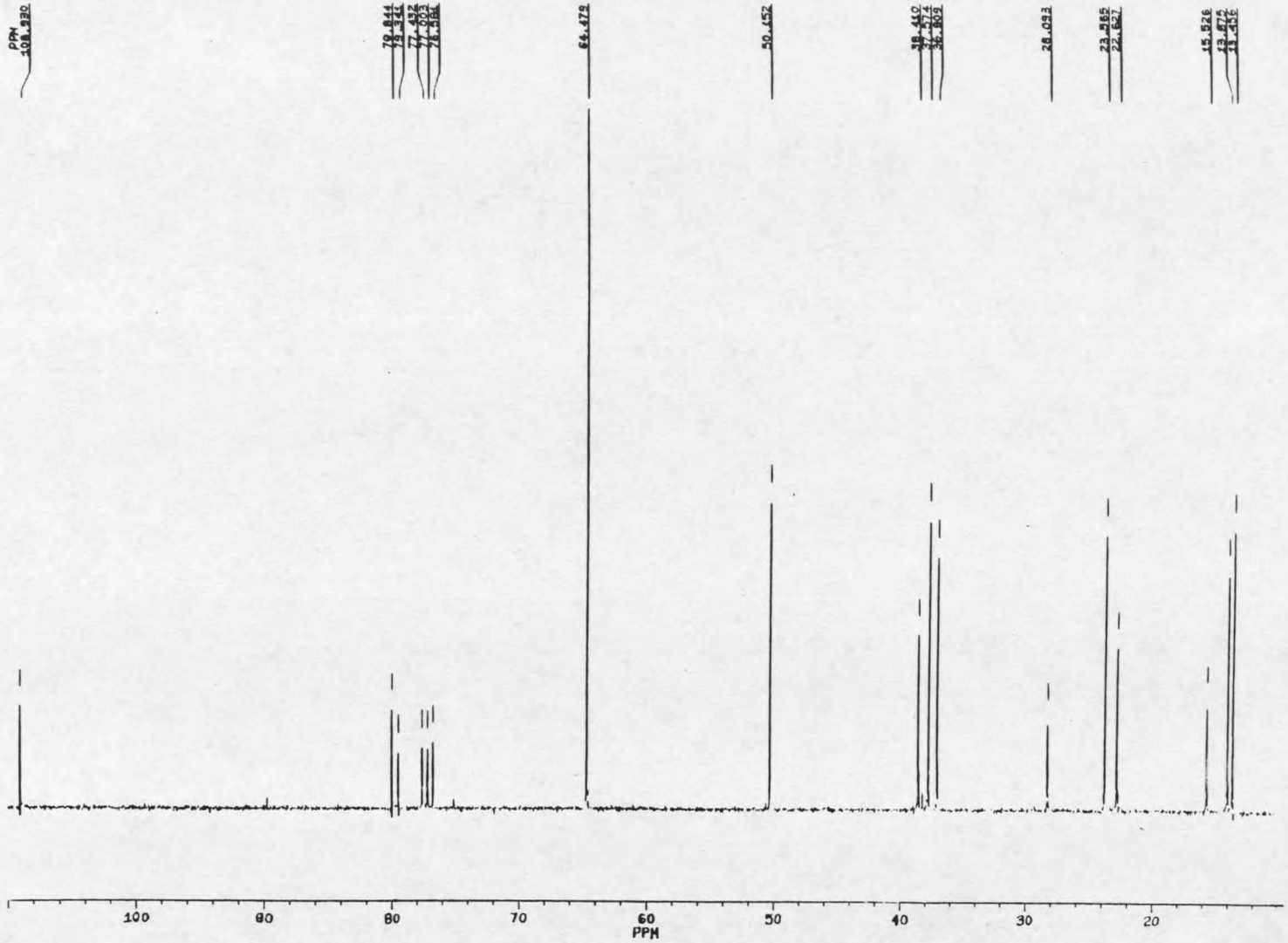


Figure 69. ^{13}C NMR Spectrum of (±) 7-amino-2,2-ethylene-dioxytridec-5-yne(39).

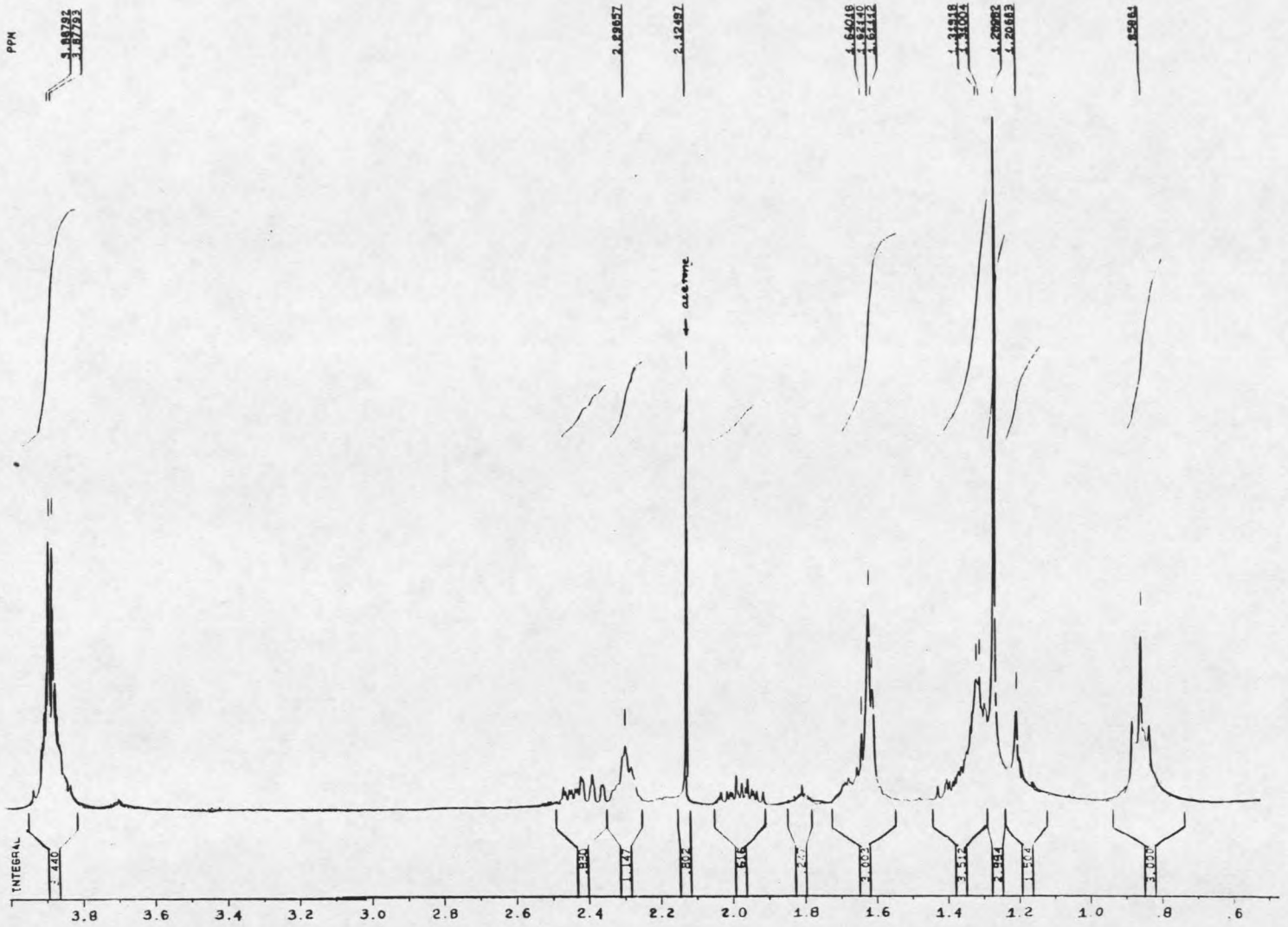


Figure 70. ^{1}H NMR Spectrum of (±) 2-Butyl-3,4-dihydro-5-(4,4-ethylene-dioxypentyl)-2H-pyrrole(38).

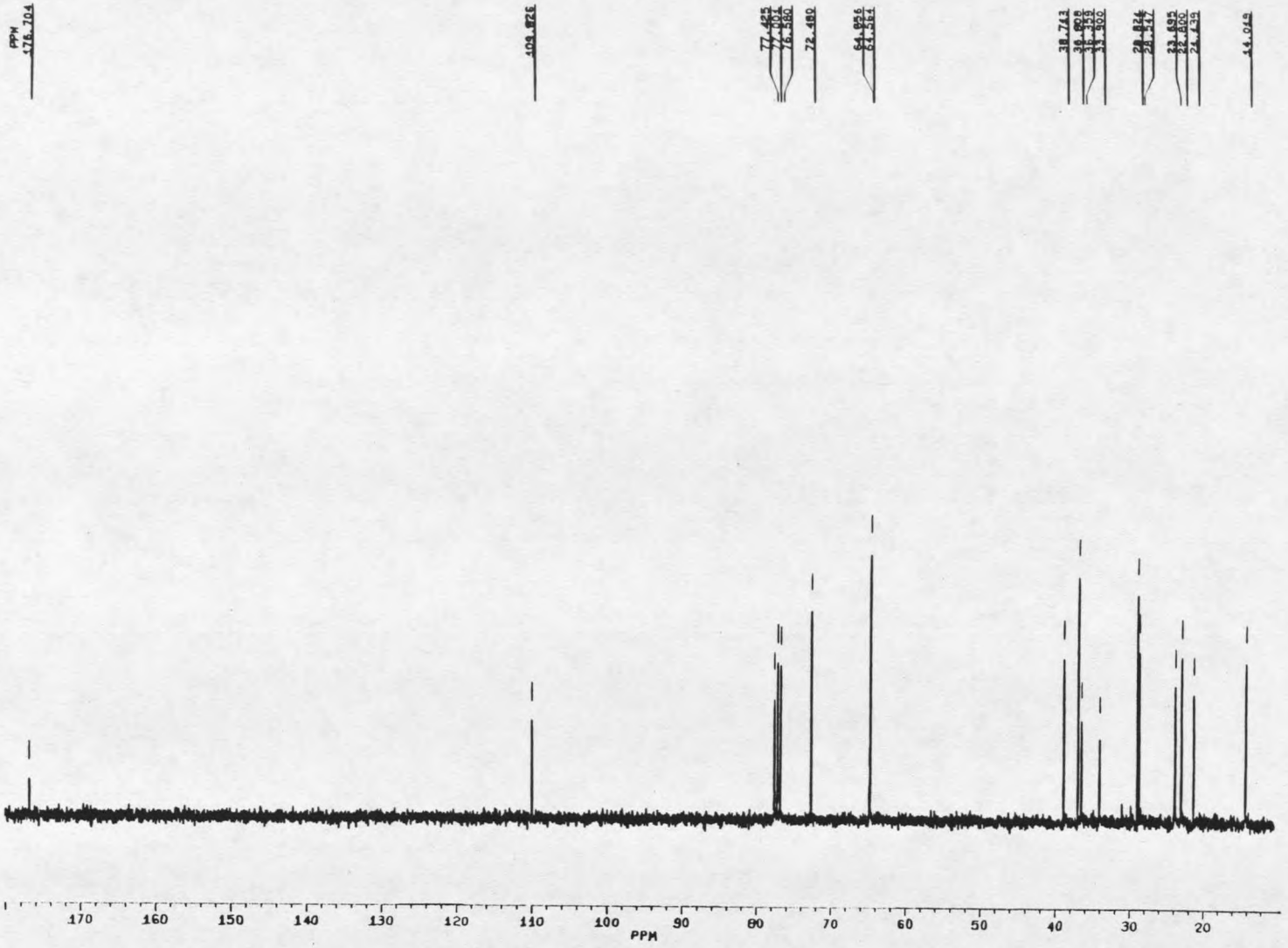


Figure 71. ^{13}C NMR Spectrum of (±) 2-Butyl-3,4-dihydro-5-(4,4-ethylene-dioxypentyl)-2H-pyrrole(38).

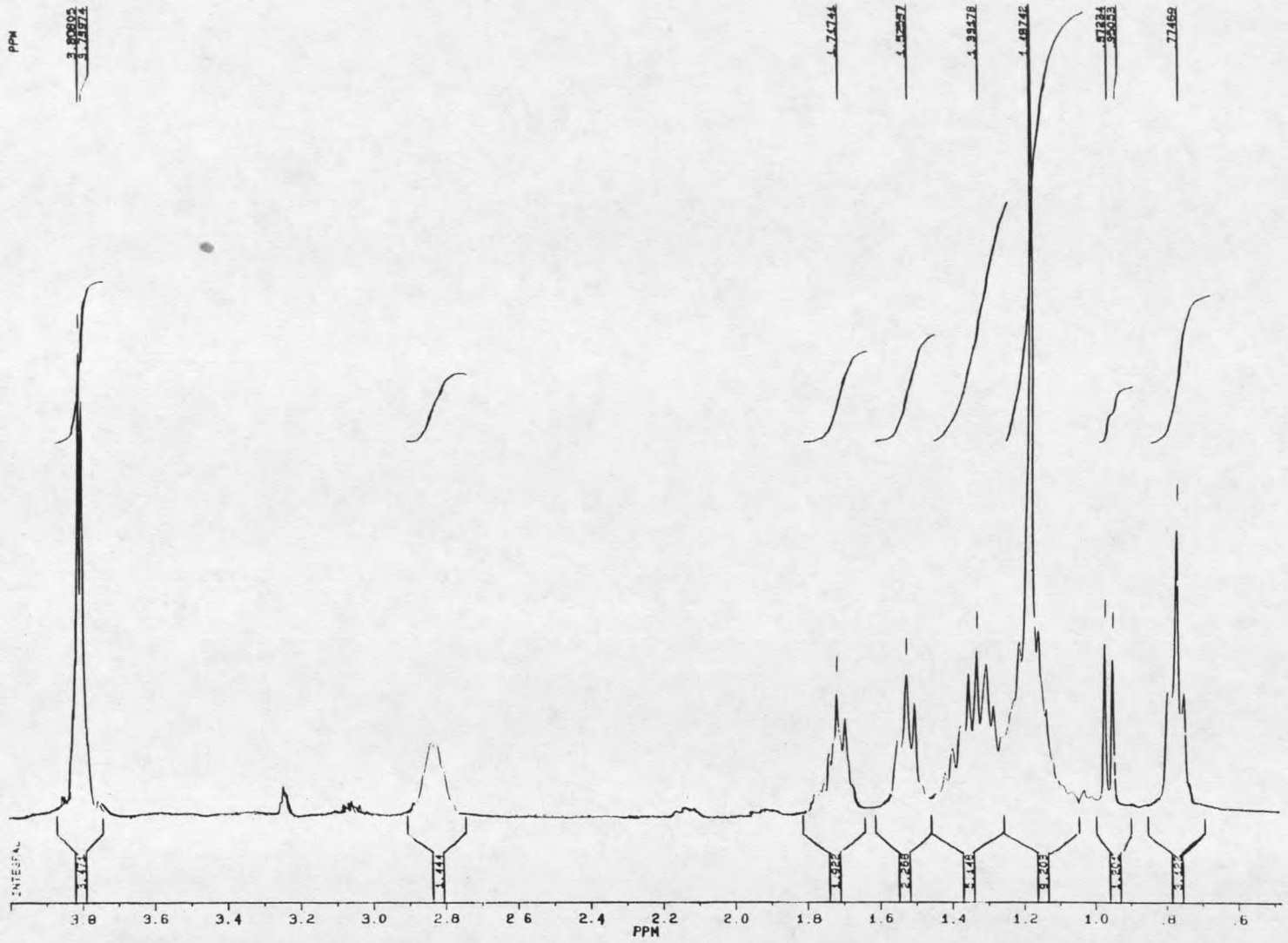


Figure 72. ^{1}H NMR Spectrum of (±) 2-Butyl-5-(4,4-ethylenedioxypentyl)-2ß,3,4,5ß-tetrahydro-1H-pyrrole(37).

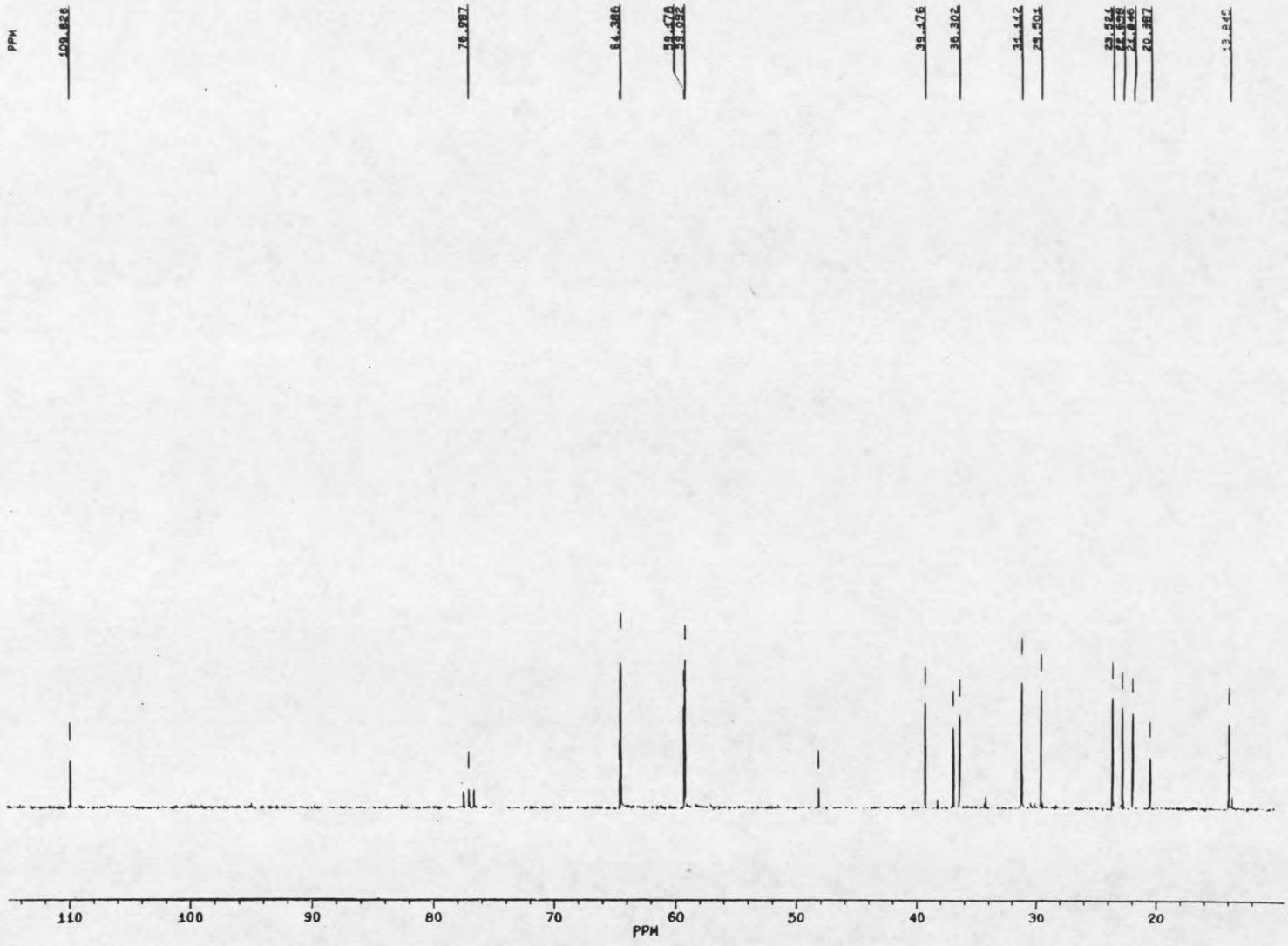


Figure 73. ^{13}C NMR Spectrum of (±) 2-Butyl-5-(4,4-thylenedioxypentyl)-2ß,3,4,5ß-tetrahydro-1H-pyrrole(37).

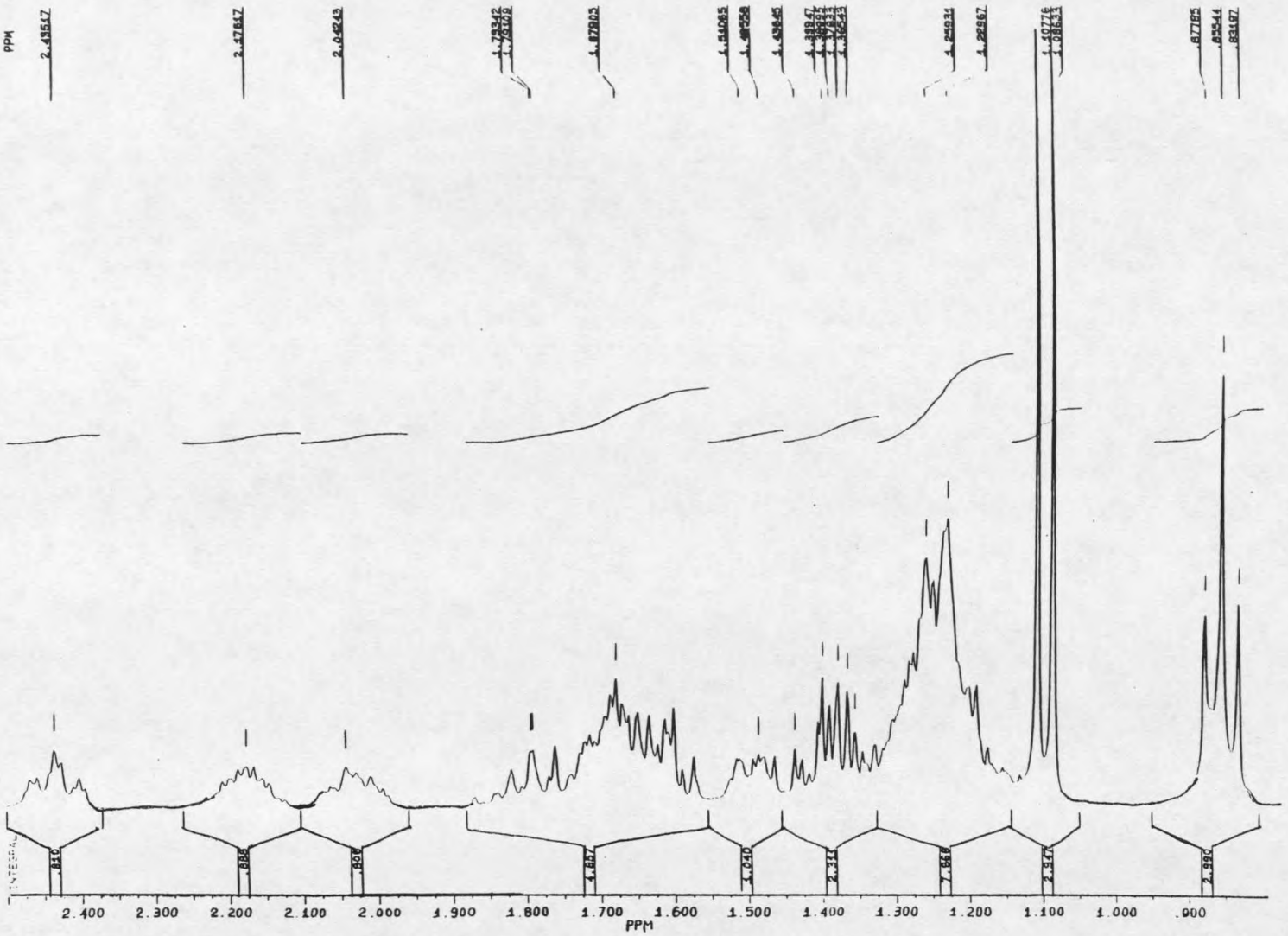


Figure 74. ^{1}H NMR Spectrum of (±)-Monomorine(1).

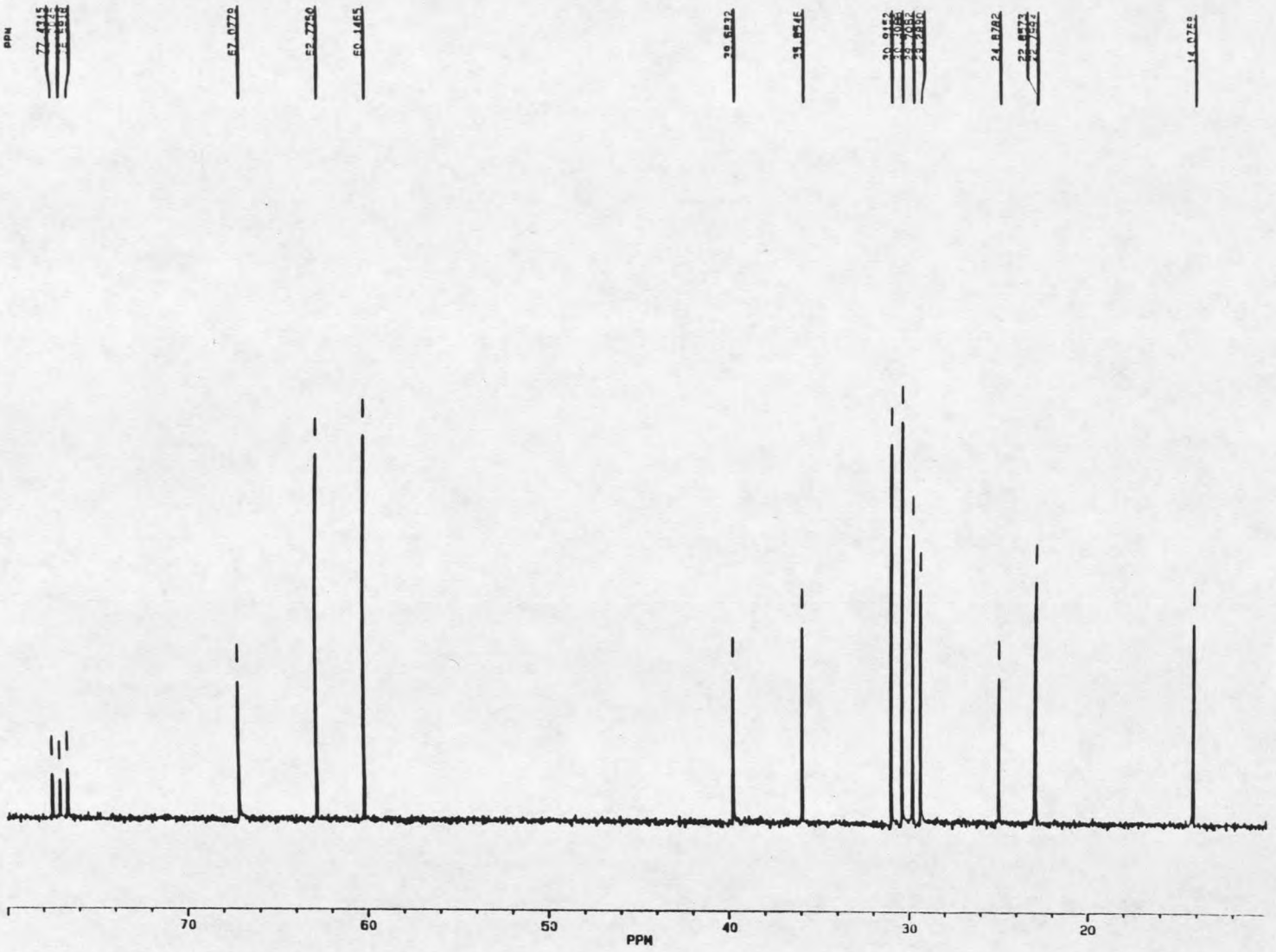


Figure 75. ^{13}C NMR Spectrum of (±)-Monomorine(1).

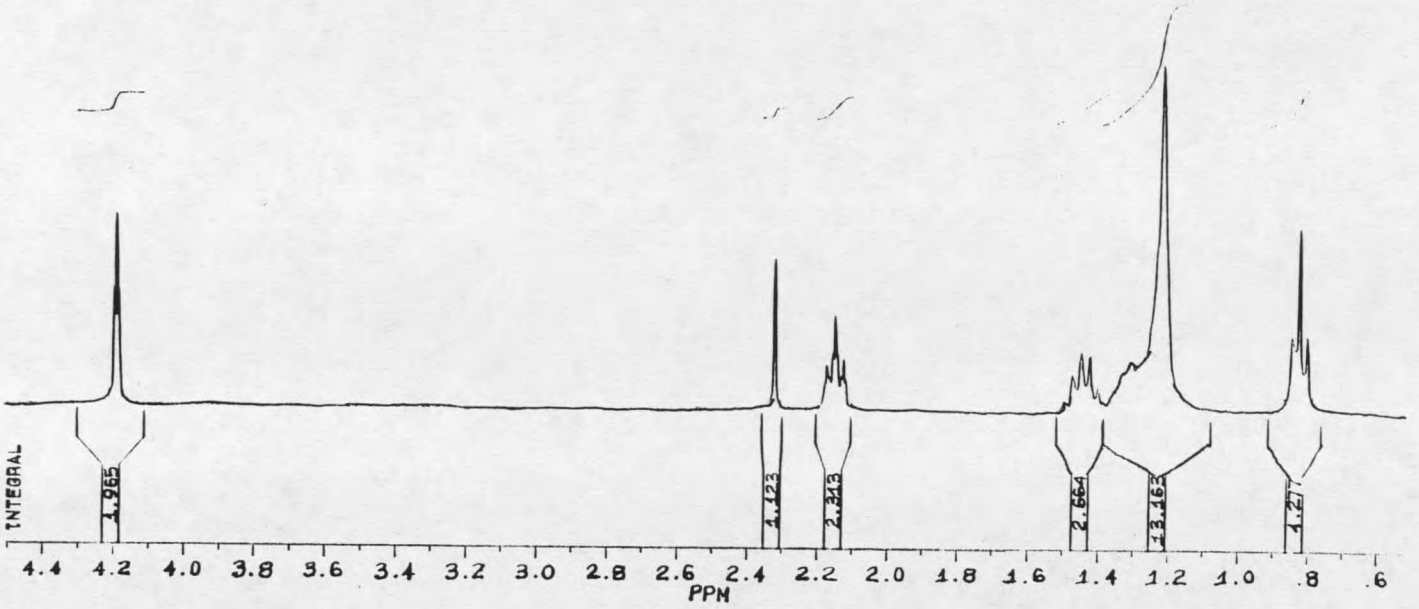


Figure 76. ^{1}H NMR Spectrum of Undec-2-yn-1-ol(52).

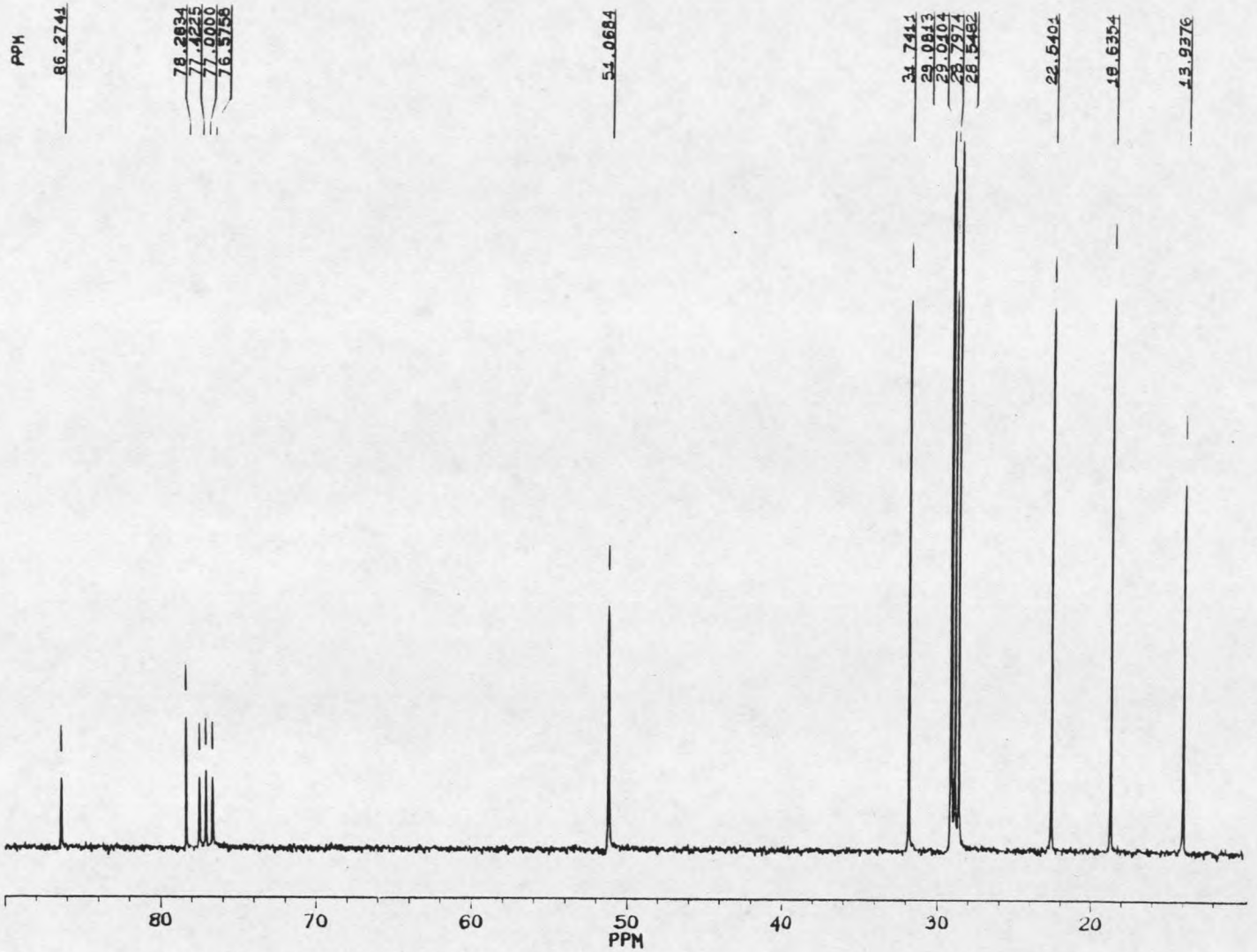


Figure 77. ^{13}C NMR Spectrum of Undec-2-yn-1-ol(52).

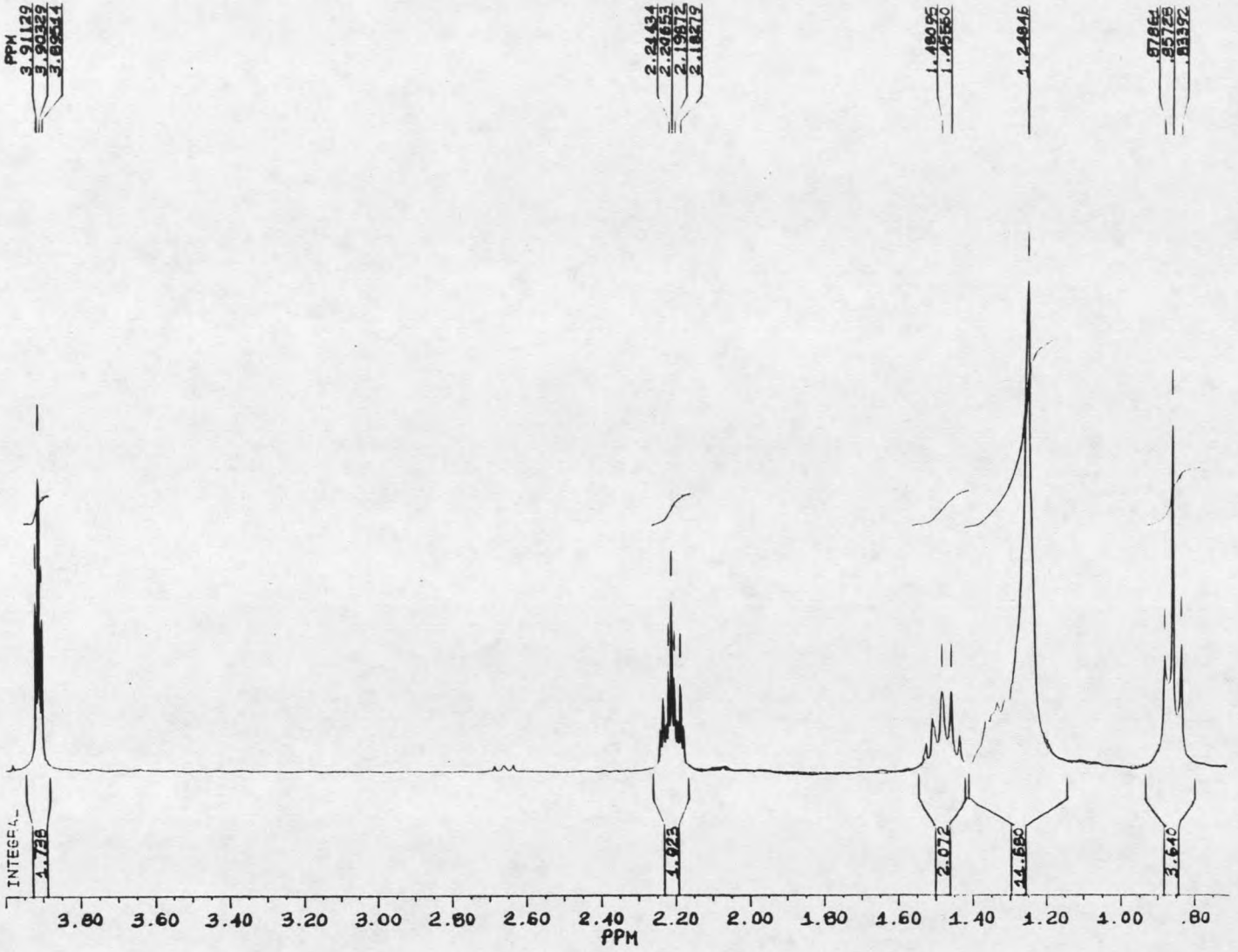


Figure 78. ^{1}H NMR Spectrum of 1-Bromoundec-2-yne(53).

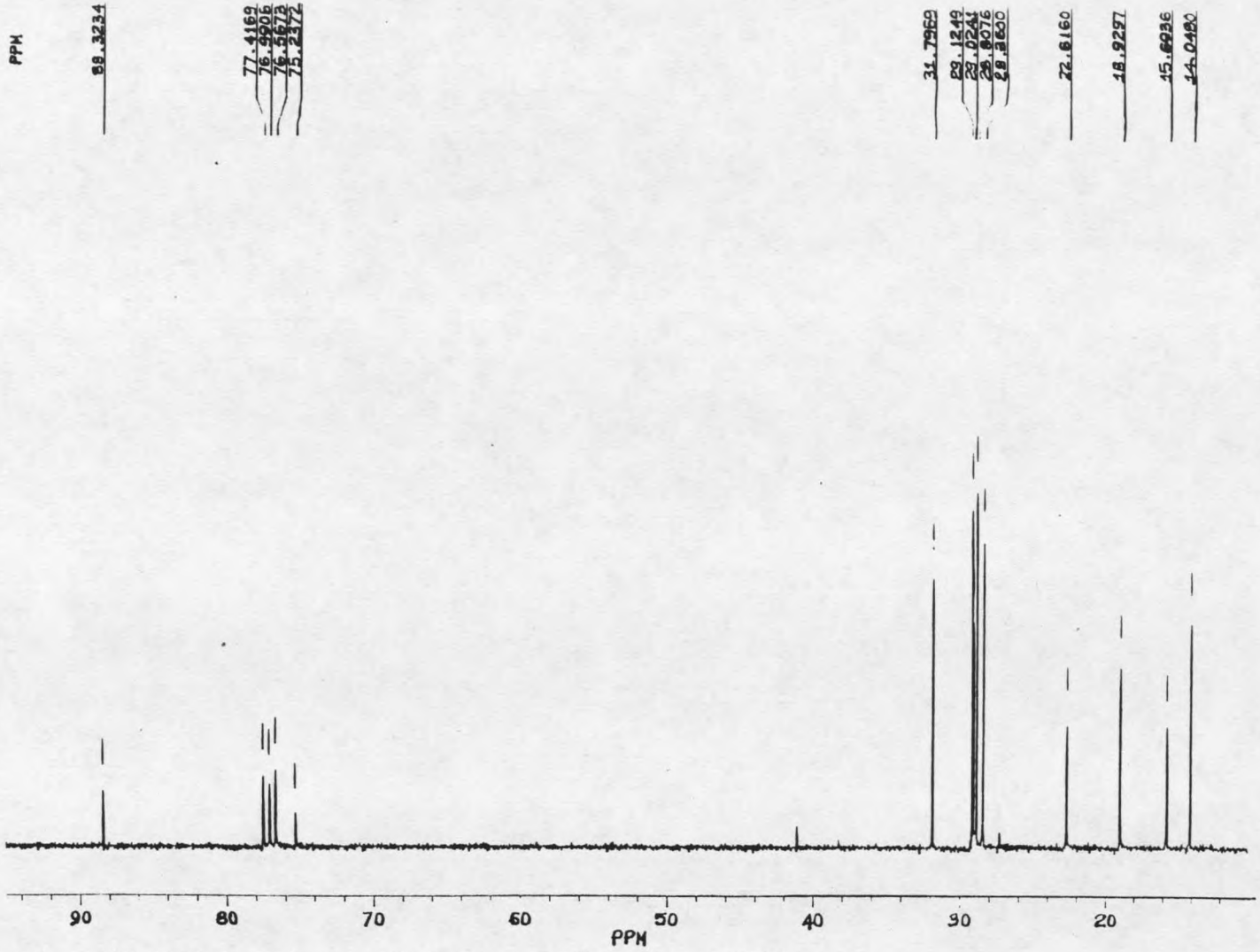


Figure 79. ^{13}C NMR Spectrum of 1-Bromoundec-2-yne(53).

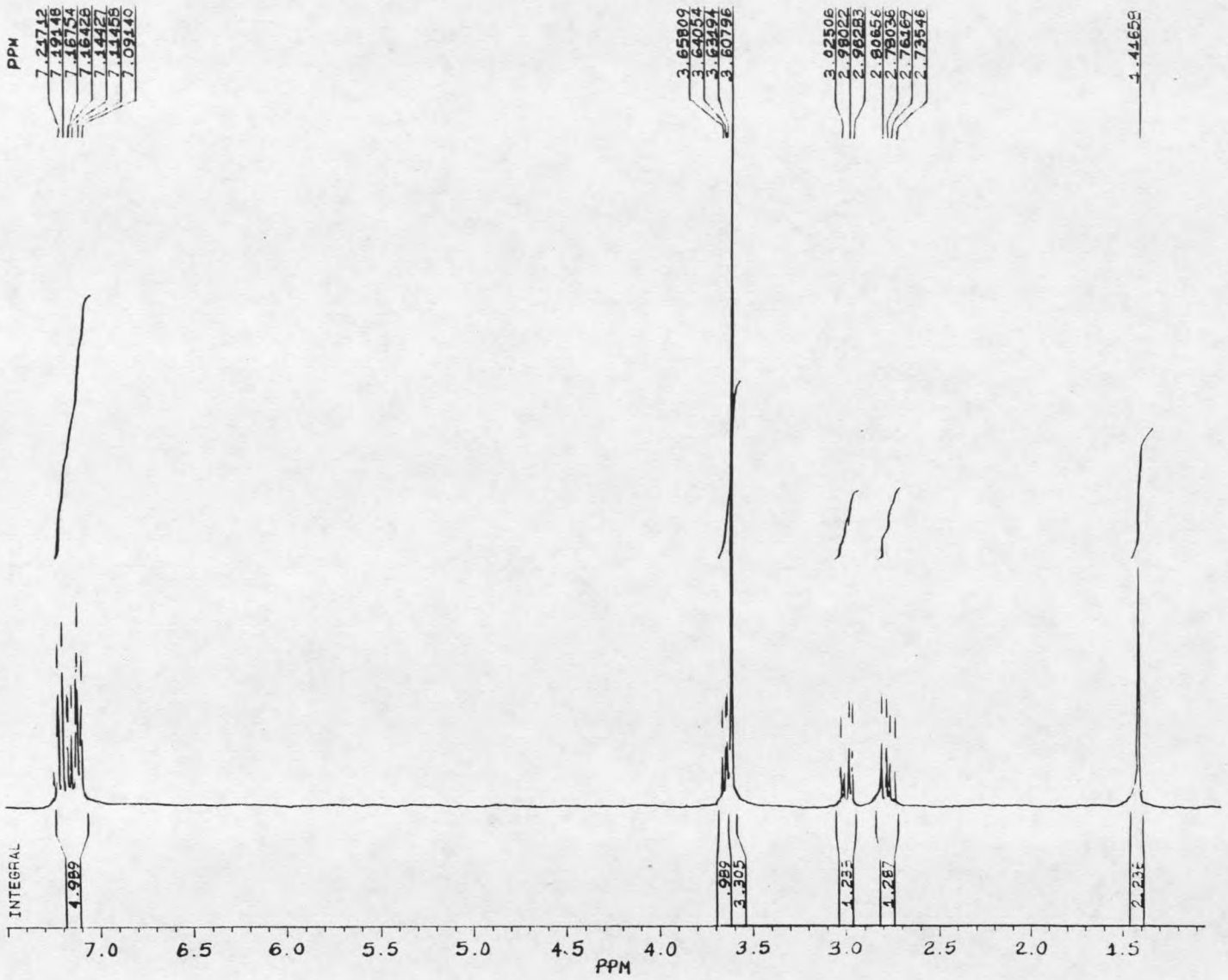


Figure 80. ^{1}H NMR Spectrum of Methyl L-Phenylalaninate.

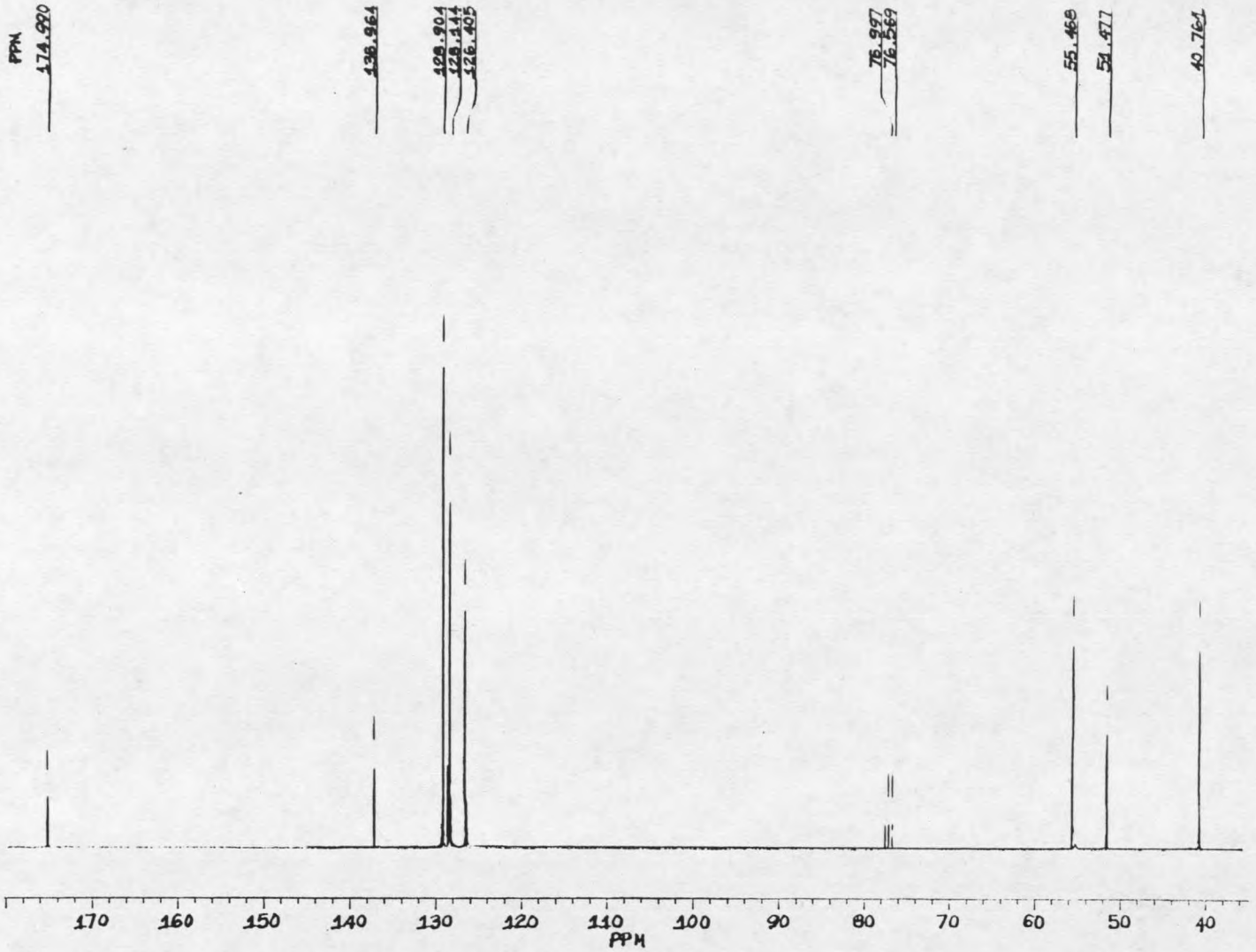


Figure 81. ^{13}C NMR Spectrum of Methyl L-Phenylalaninate.

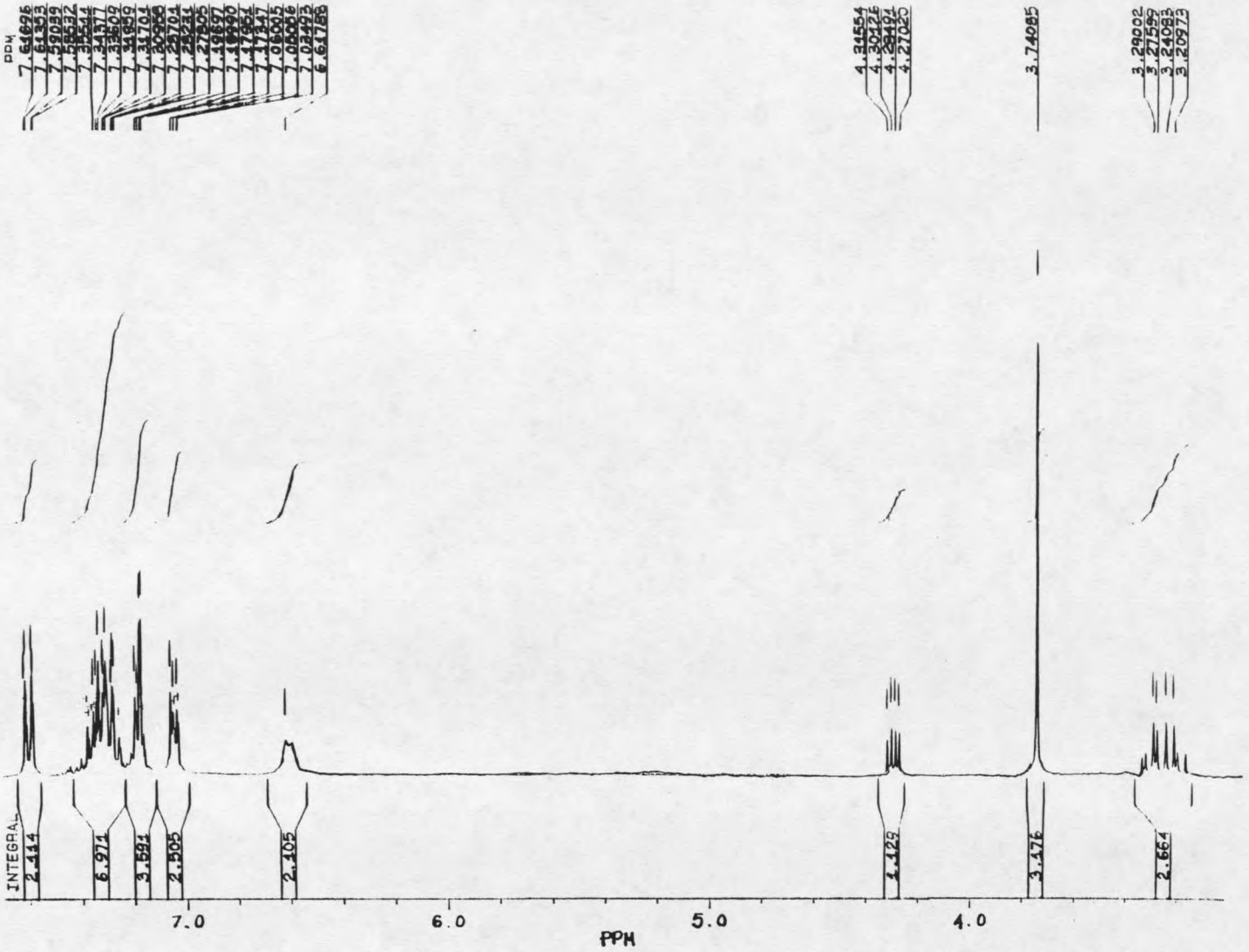


Figure 82. ^{1}H NMR Spectrum of Methyl N-(diphenylmethylene)-L-phenylalaninate(55).

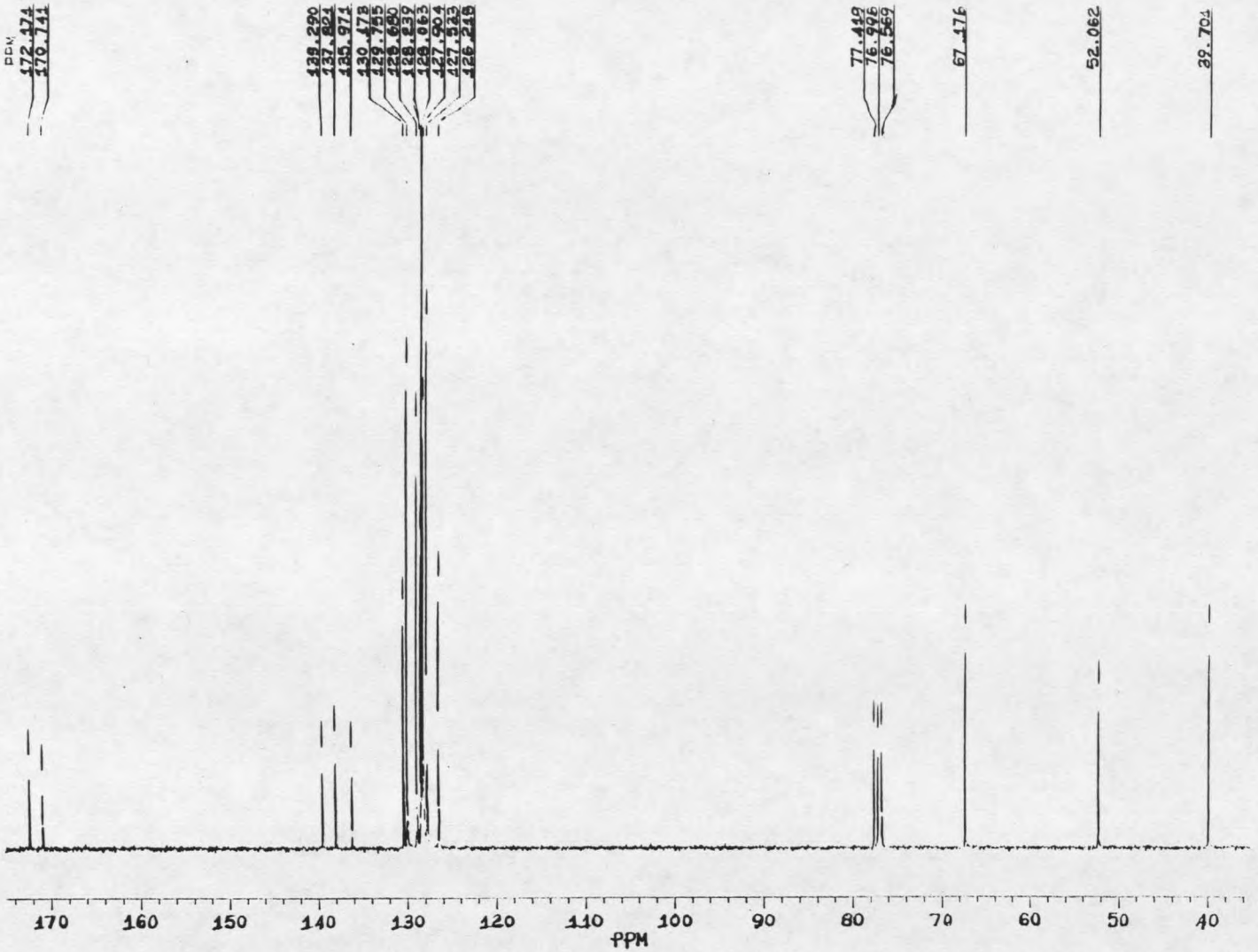


Figure 83. ^{13}C NMR Spectrum of Methyl N-(diphenylmethylene)-L-phenylalaninate(55).

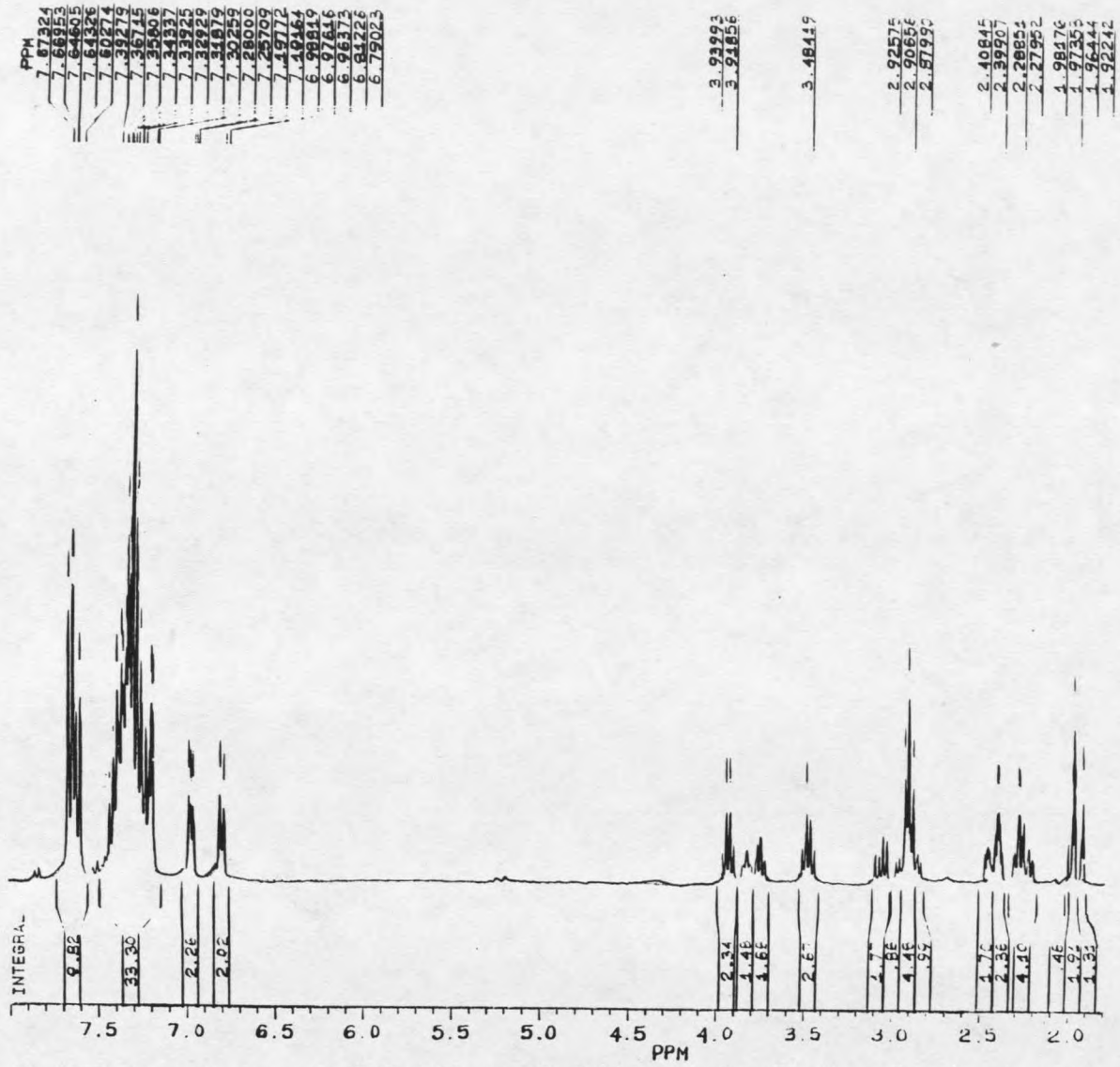


Figure 84. ^{1}H NMR Spectrum of (2S,3S)-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yn-3-ol(59).

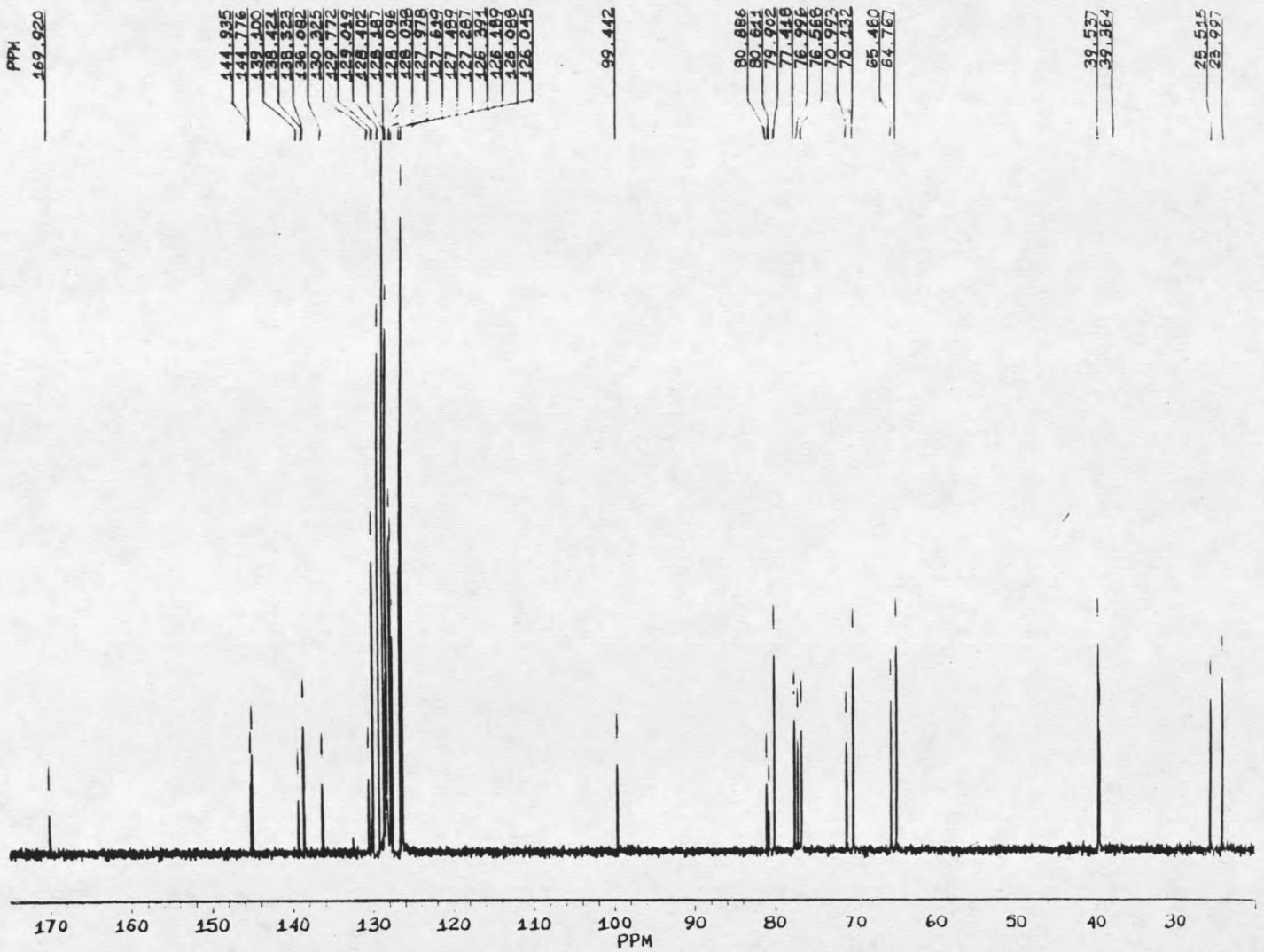


Figure 85. ^{13}C NMR Spectrum of (2S,3S)-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yn-3-ol(59).

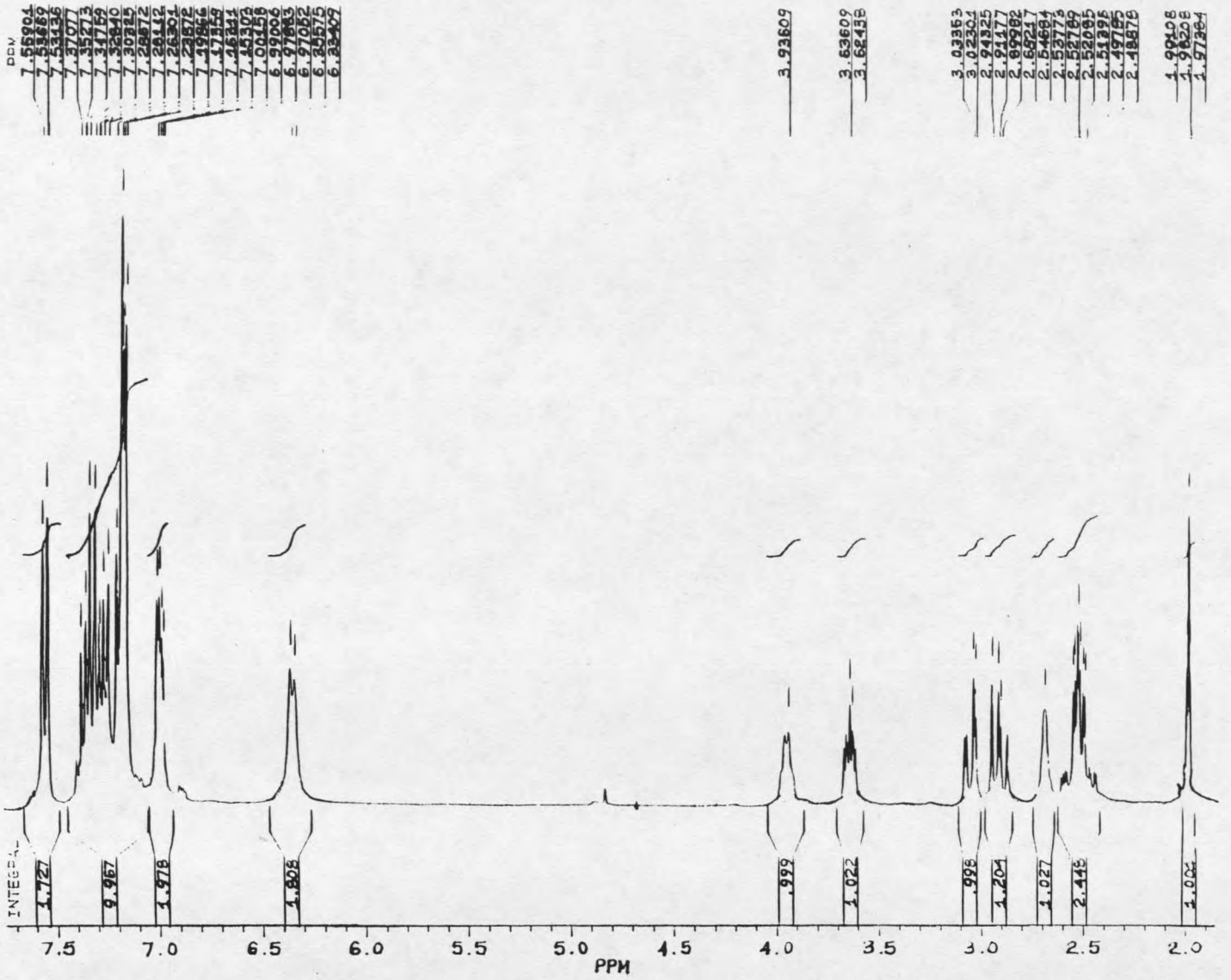


Figure 86. ^{1}H NMR Spectrum of (2S,3R)-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yn-3-ol(60).

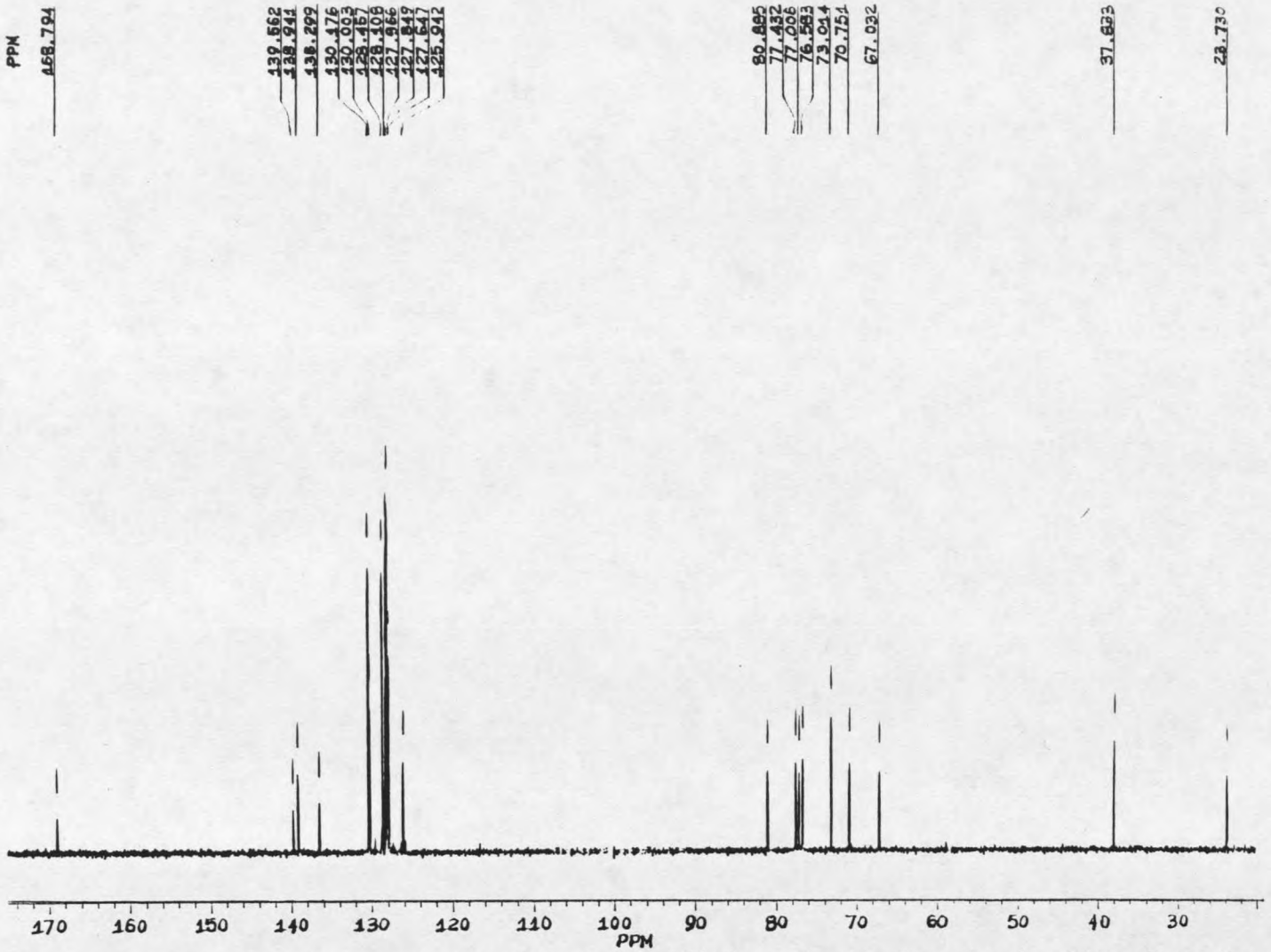


Figure 87. ^{13}C NMR Spectrum of (2S,3R)-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yn-3-ol(60).

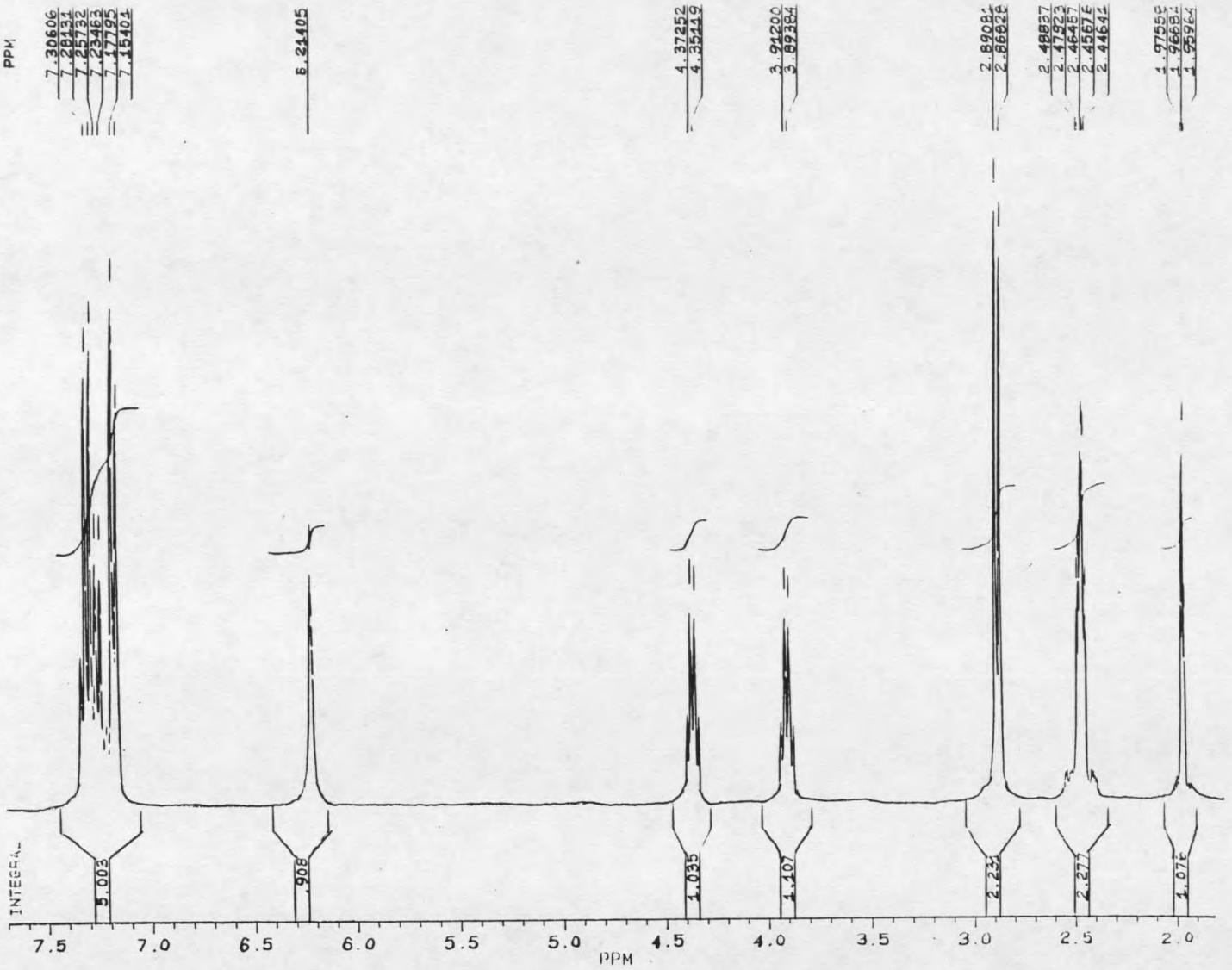


Figure 88. ^{1}H NMR Spectrum of (4S,5S)-5-(Phenylmethyl)-4-(prop-2′-yn-1′-yl)-2-oxazolidinone(61).

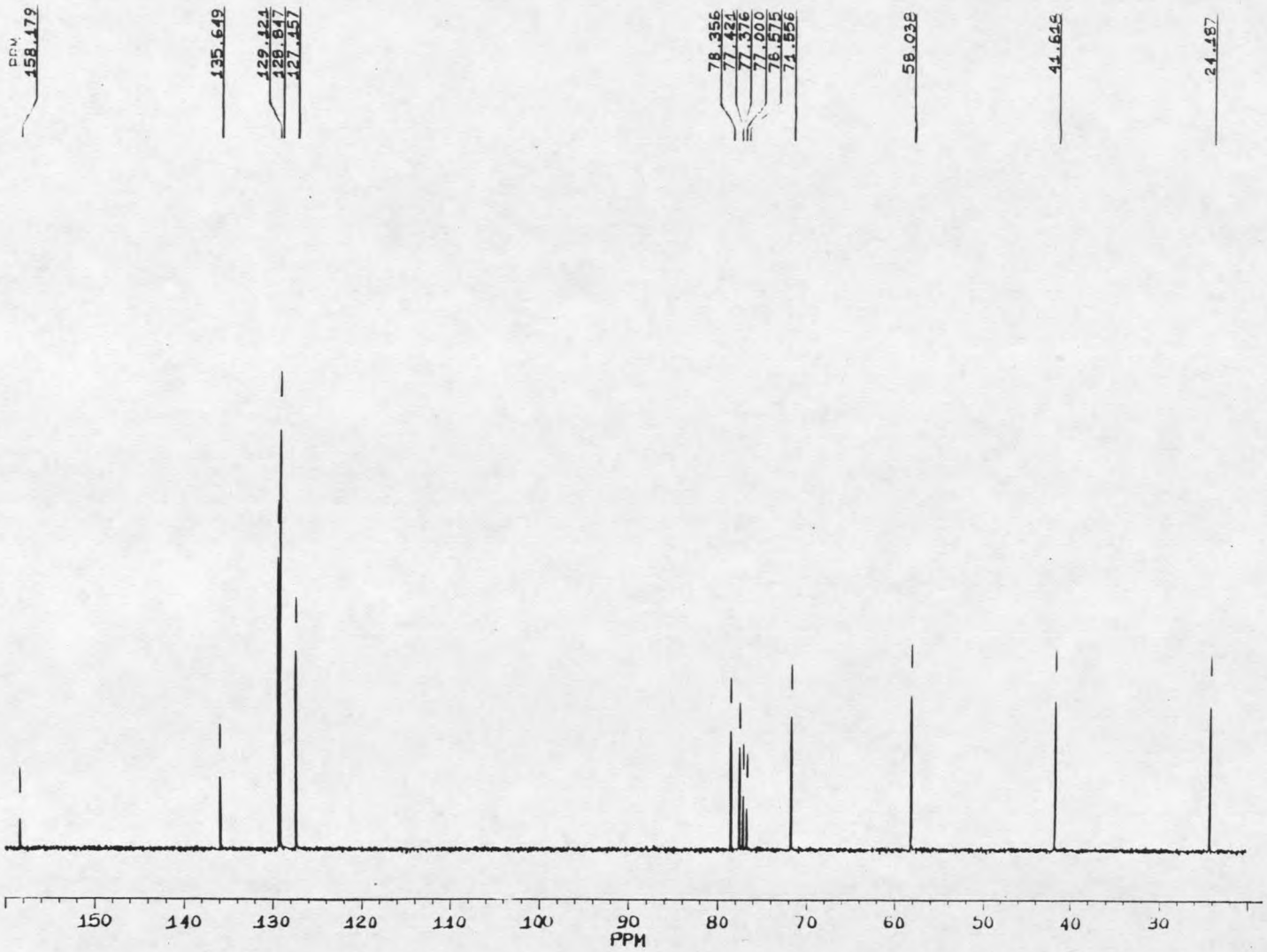


Figure 89. ^{13}C NMR Spectrum of (4S,5S)-5-(Phenylmethyl)-4-(prop-2′-yn-1′-yl)-2-oxazolidinone(61).

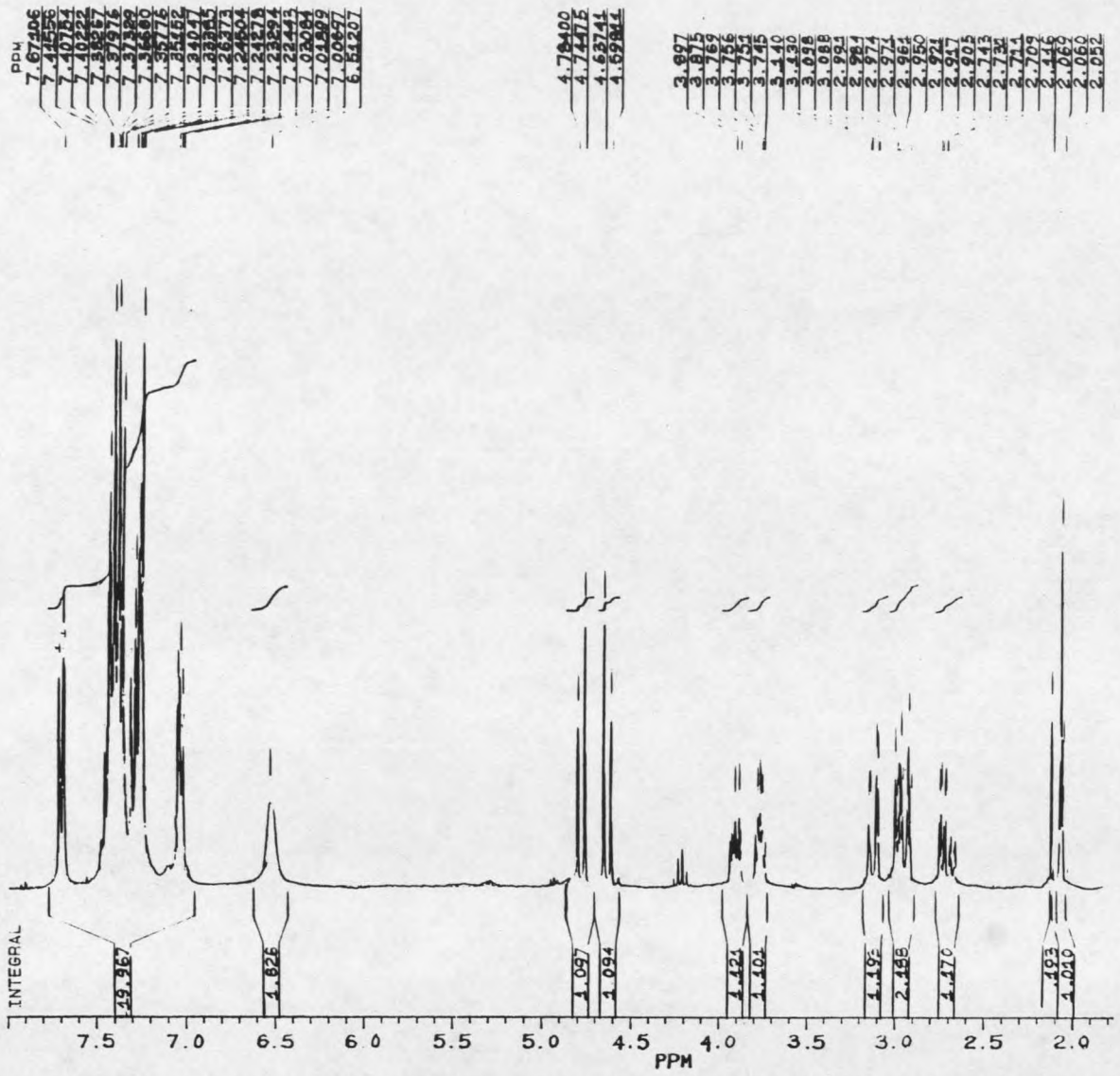


Figure 90. ^{1}H NMR Spectrum of (2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yne(63).

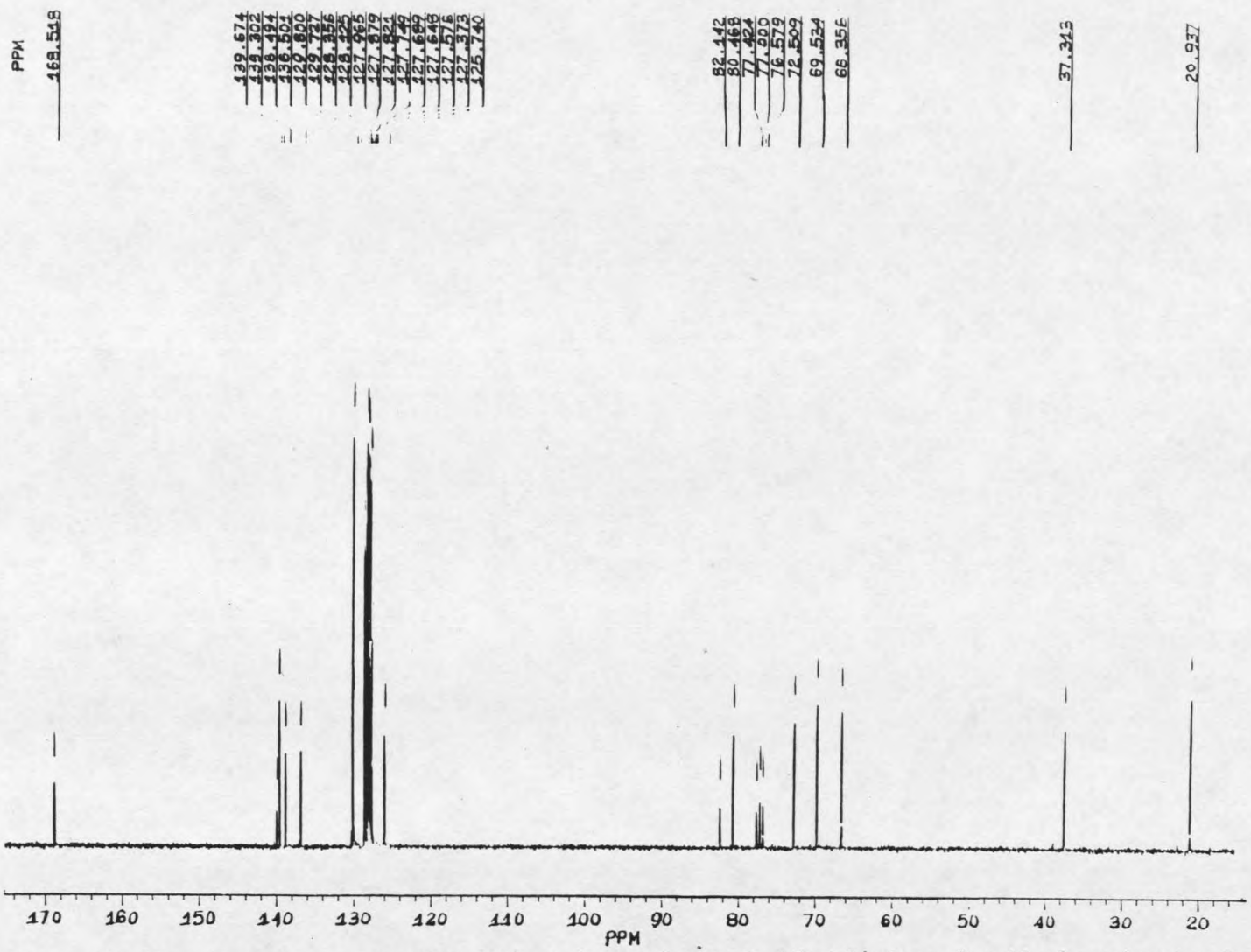


Figure 91. ^{13}C NMR Spectrum of (2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yne(63).

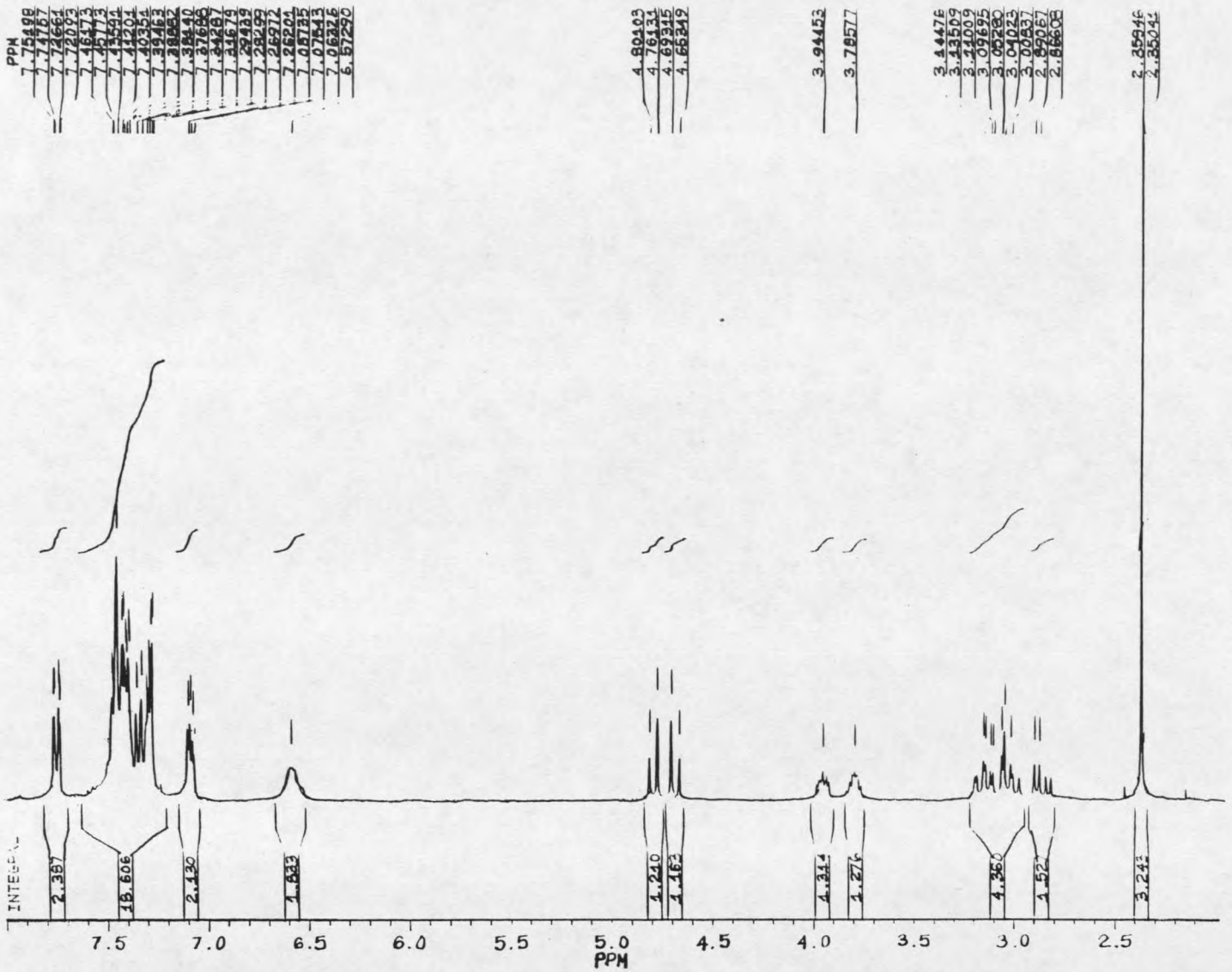


Figure 92. ^{1}H NMR Spectrum of (2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenyl-6-(thiomethyl)hex-5-yne(64).

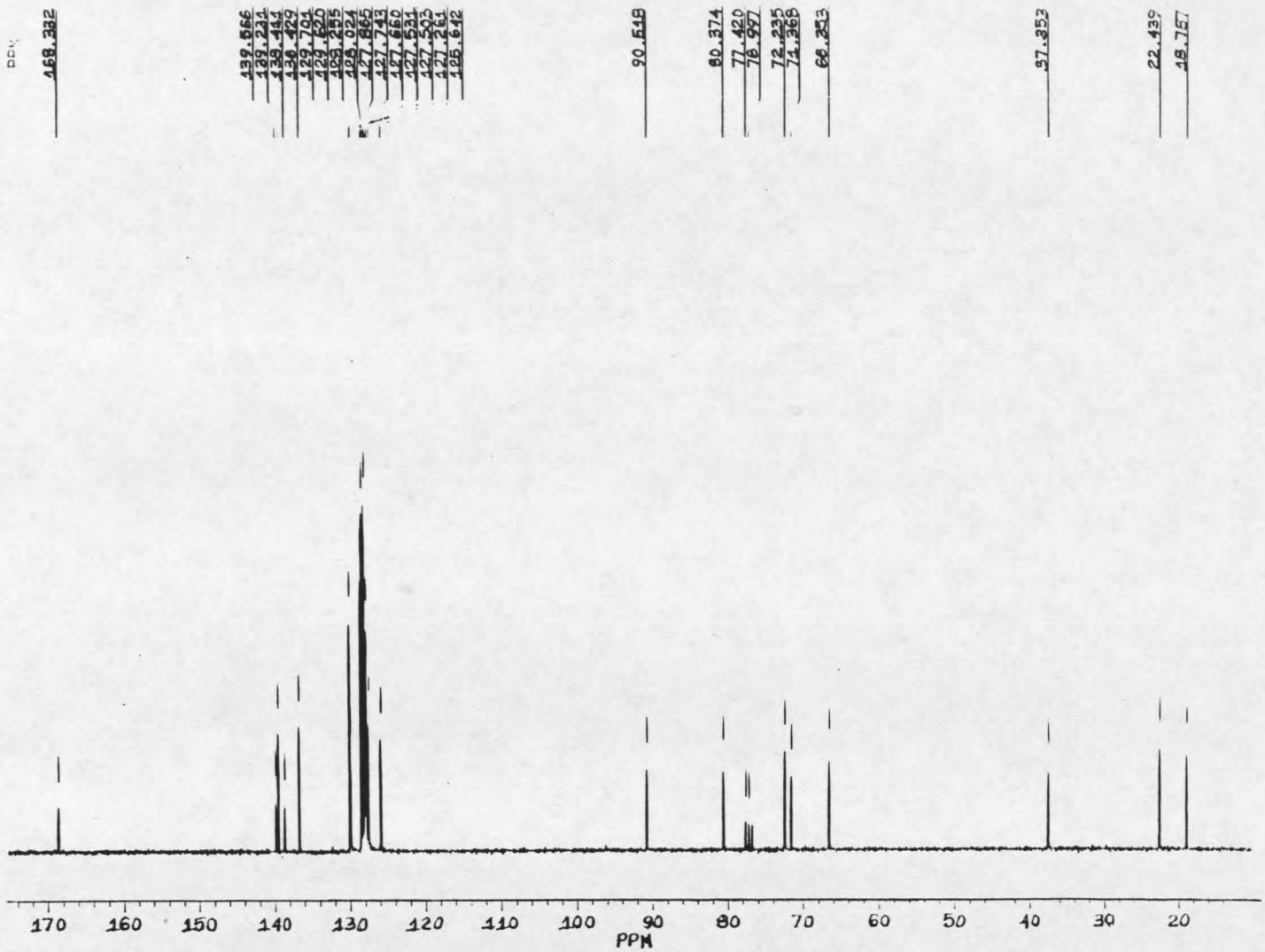


Figure 93. ^{13}C NMR Spectrum of (2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenyl-6-(thiomethyl)hex-5-yne(64).

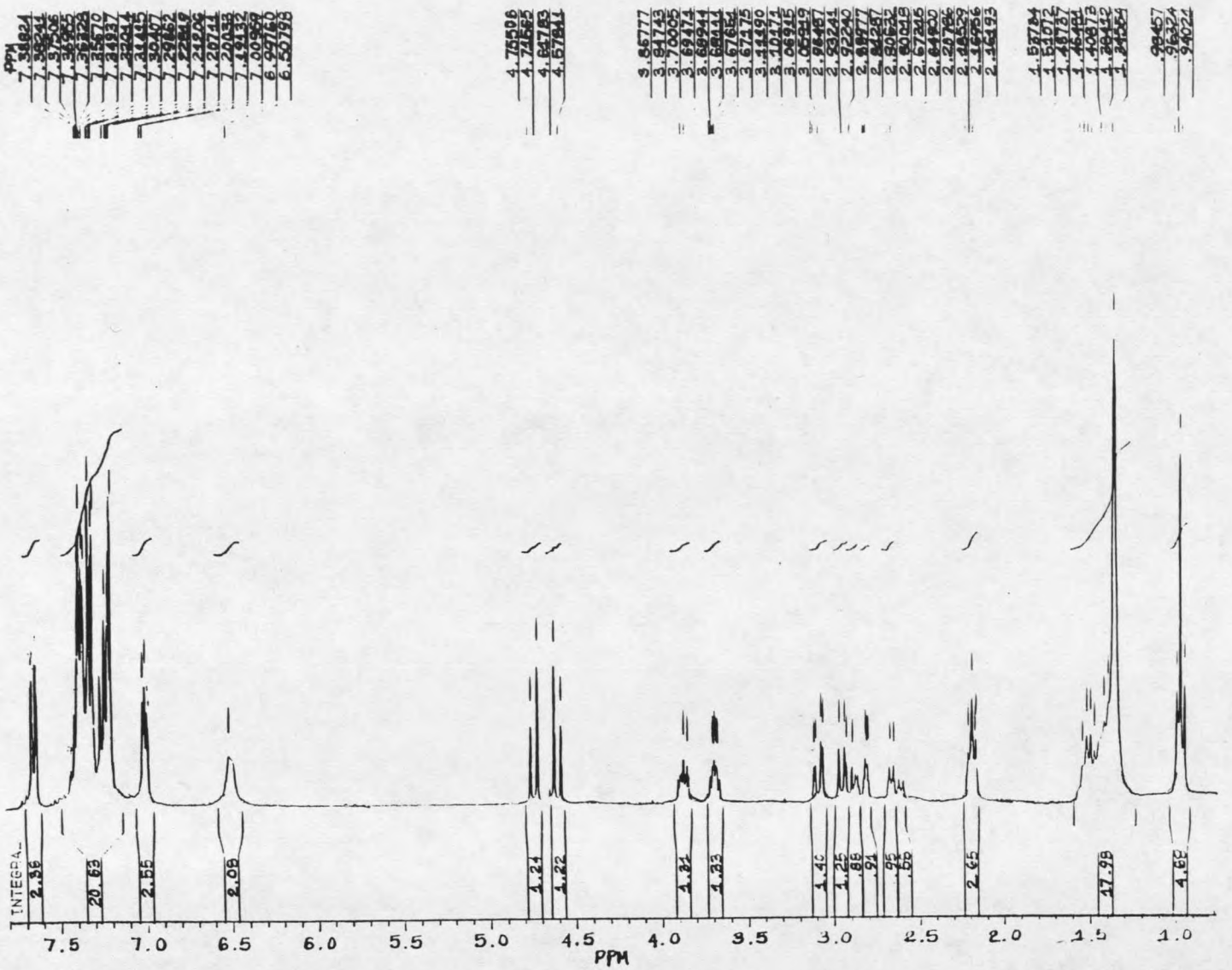


Figure 94. ^{1}H NMR Spectrum of (2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenyltetradec-5-yne(65).

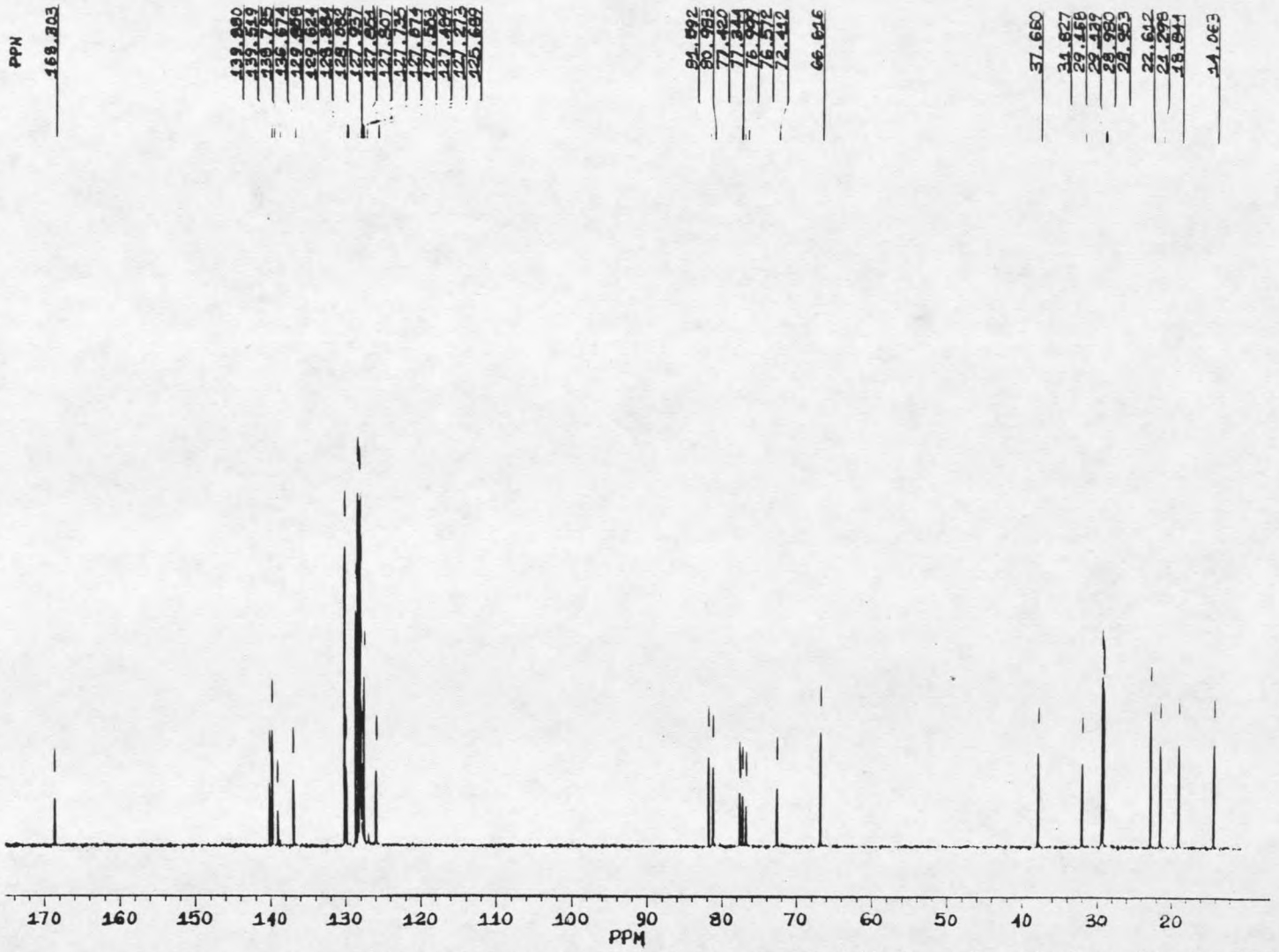


Figure 95. ^{13}C NMR Spectrum of (2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenyltetradec-5-yne(65).

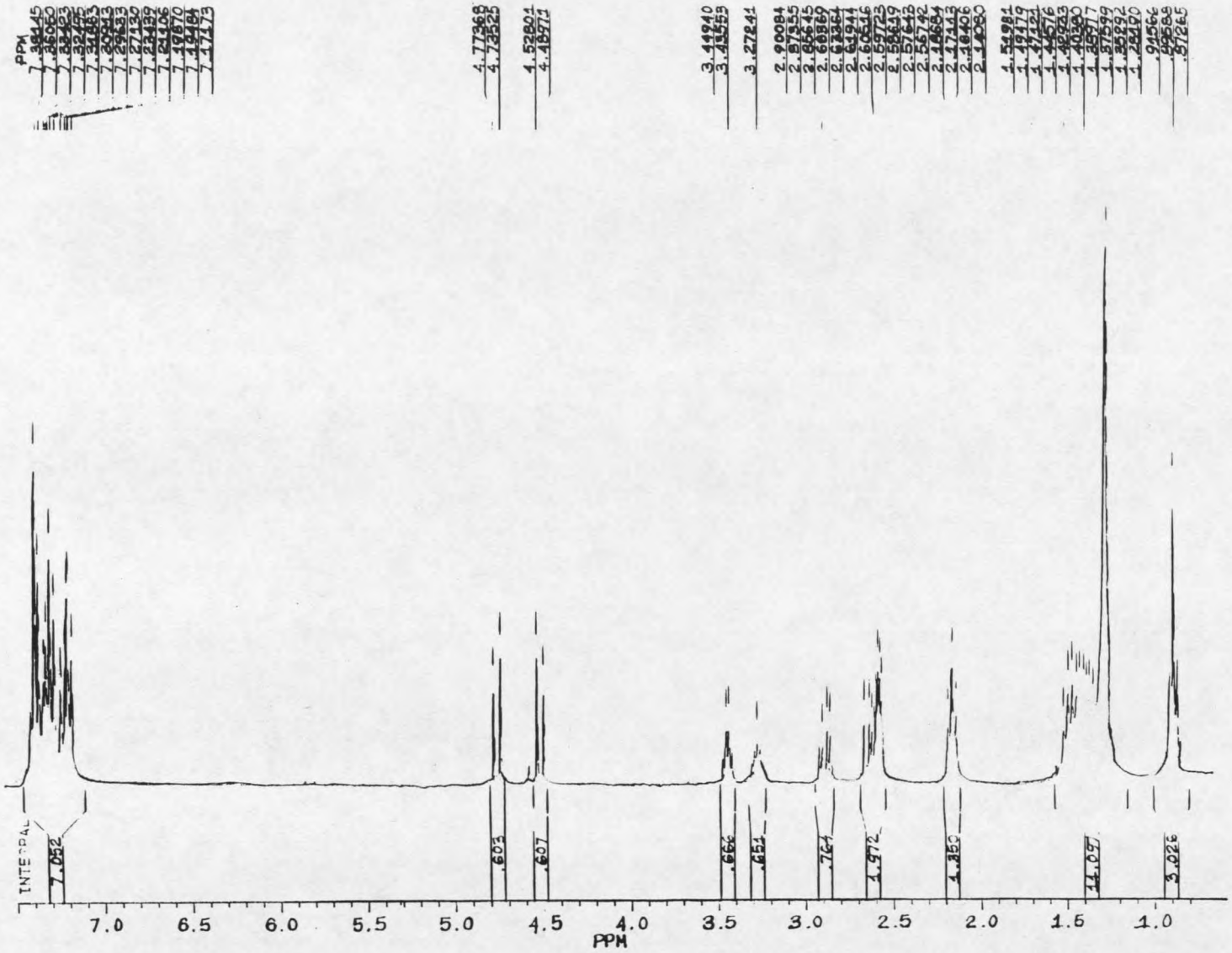


Figure 96. ^{1}H NMR Spectrum of (2S,3S)-3-benzyloxy-1-phenyltetradec-5-yn-2-ylamine(51).

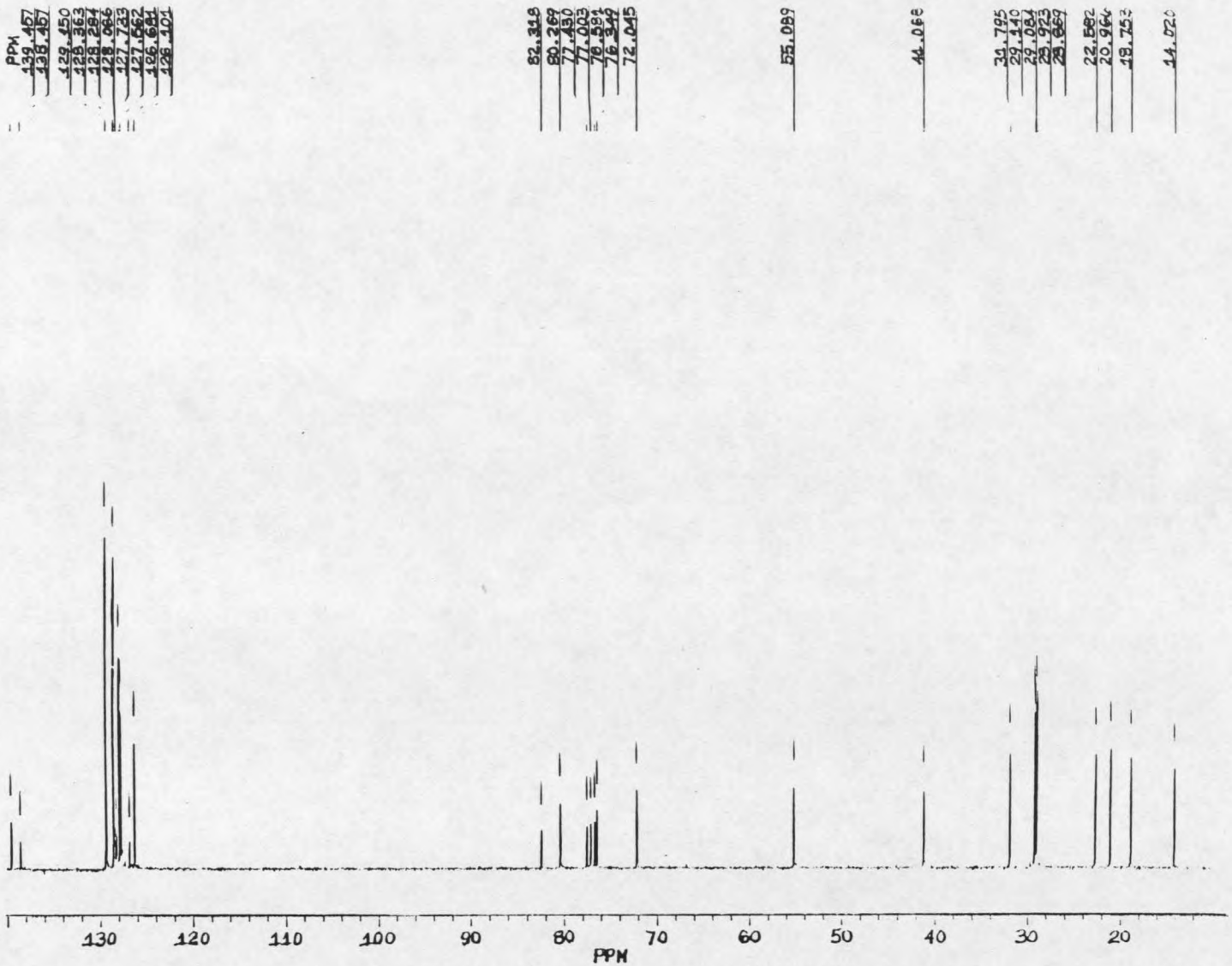


Figure 97. ^{13}C NMR Spectrum of (2S,3S)-3-benzyloxy-1-phenyltetradec-5-yn-2-ylamine(51).

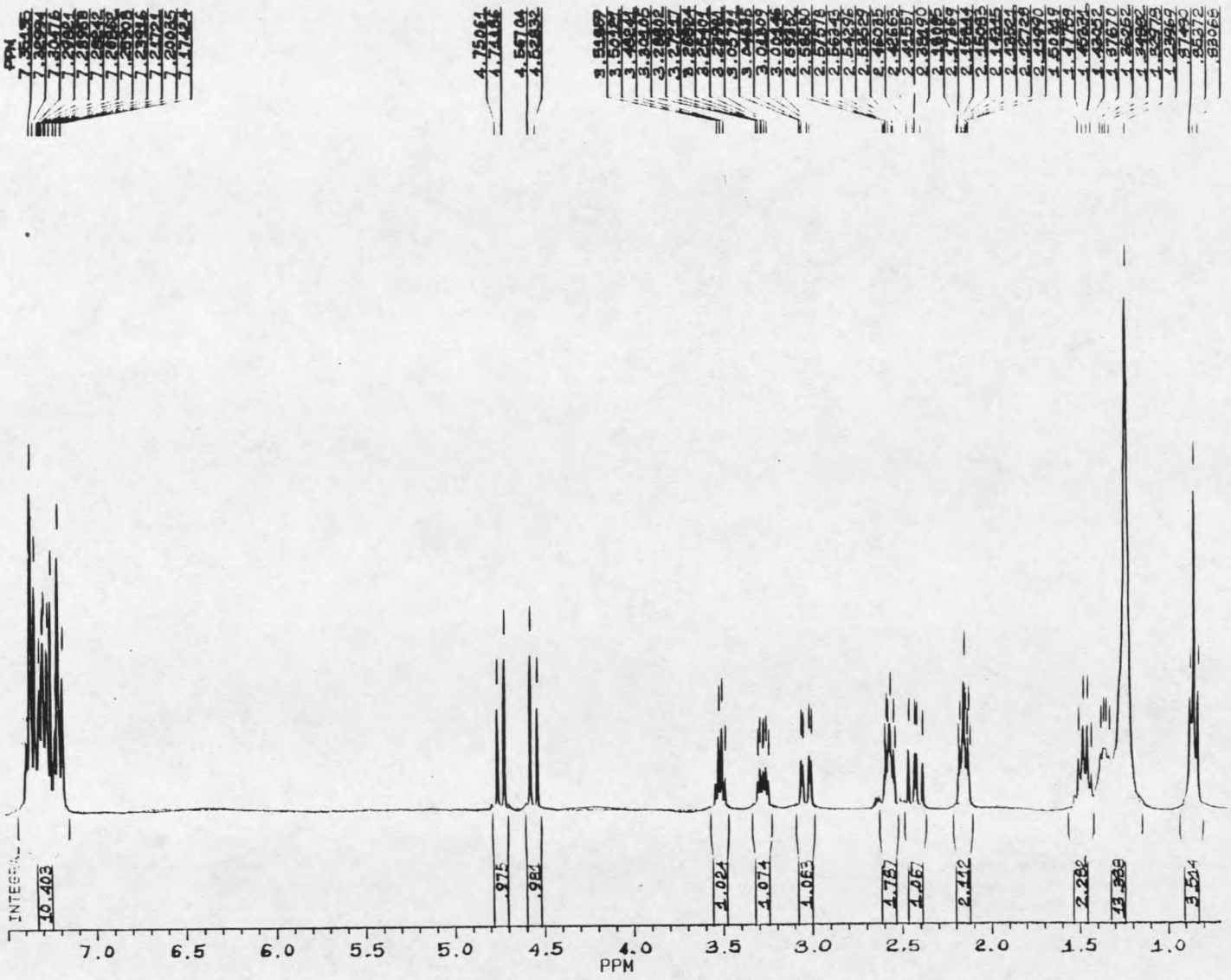


Figure 98. ^{1}H NMR Spectrum of (2S,3R)-3-benzyloxy-1-phenyltetradec-5-yn-2-ylamine(66).

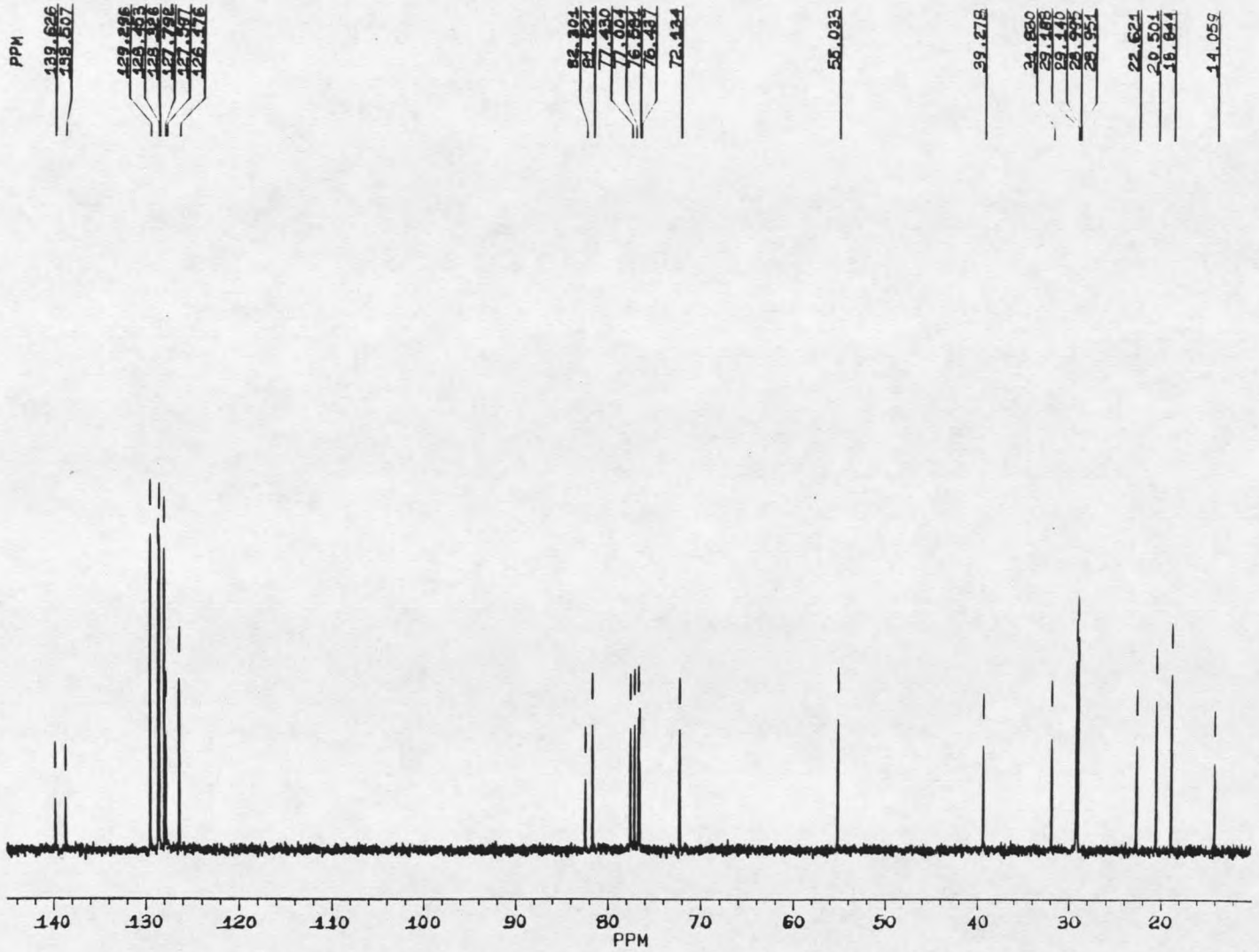


Figure 99. ^{13}C NMR Spectrum of (2S,3R)-3-benzyloxy-1-phenyltetradec-5-yn-2-ylamine(66).

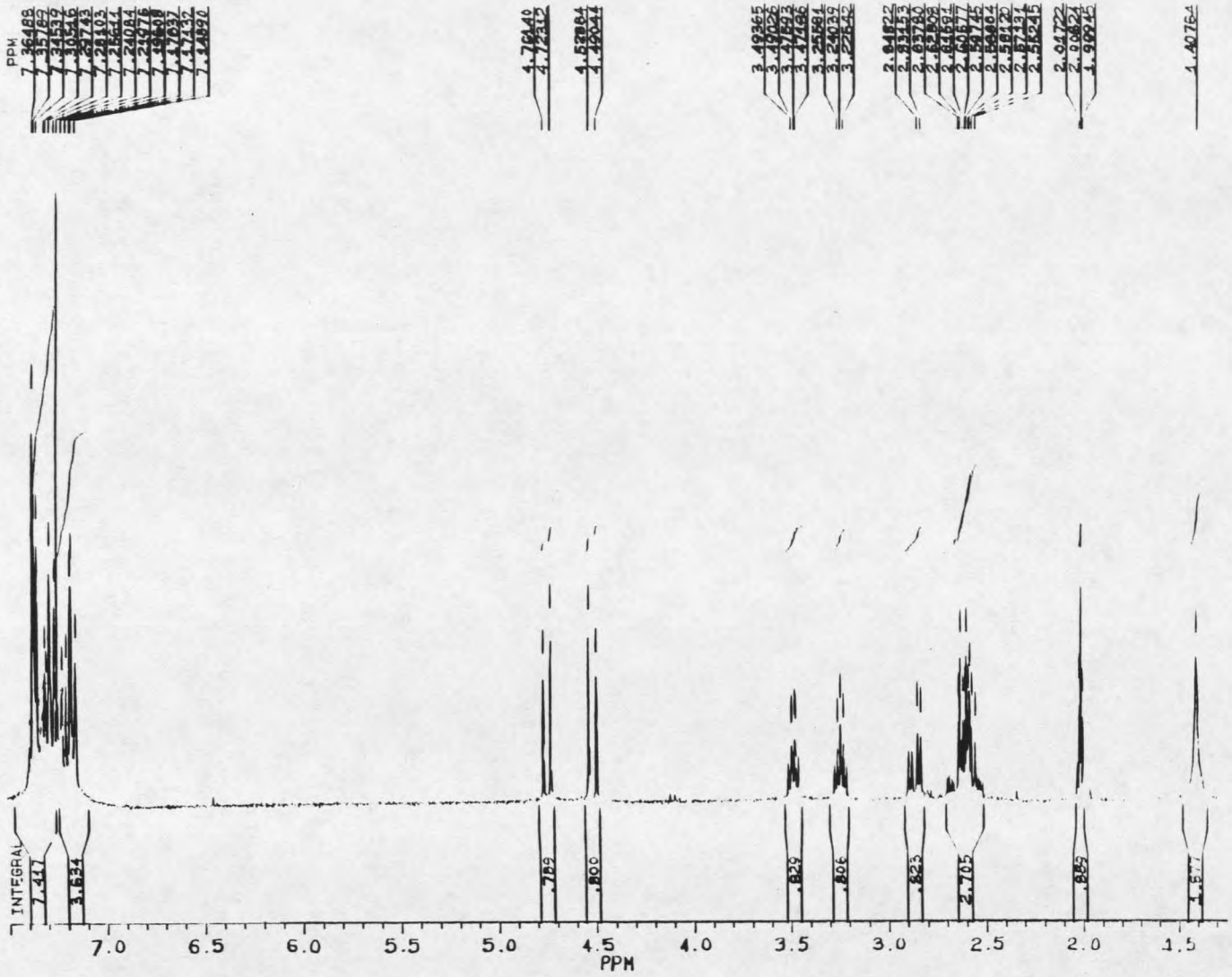


Figure 100. ^{1}H NMR Spectrum of (2S,3S)-3-benzyloxy-1-phenylhex-5-yn-2-ylamine(71).

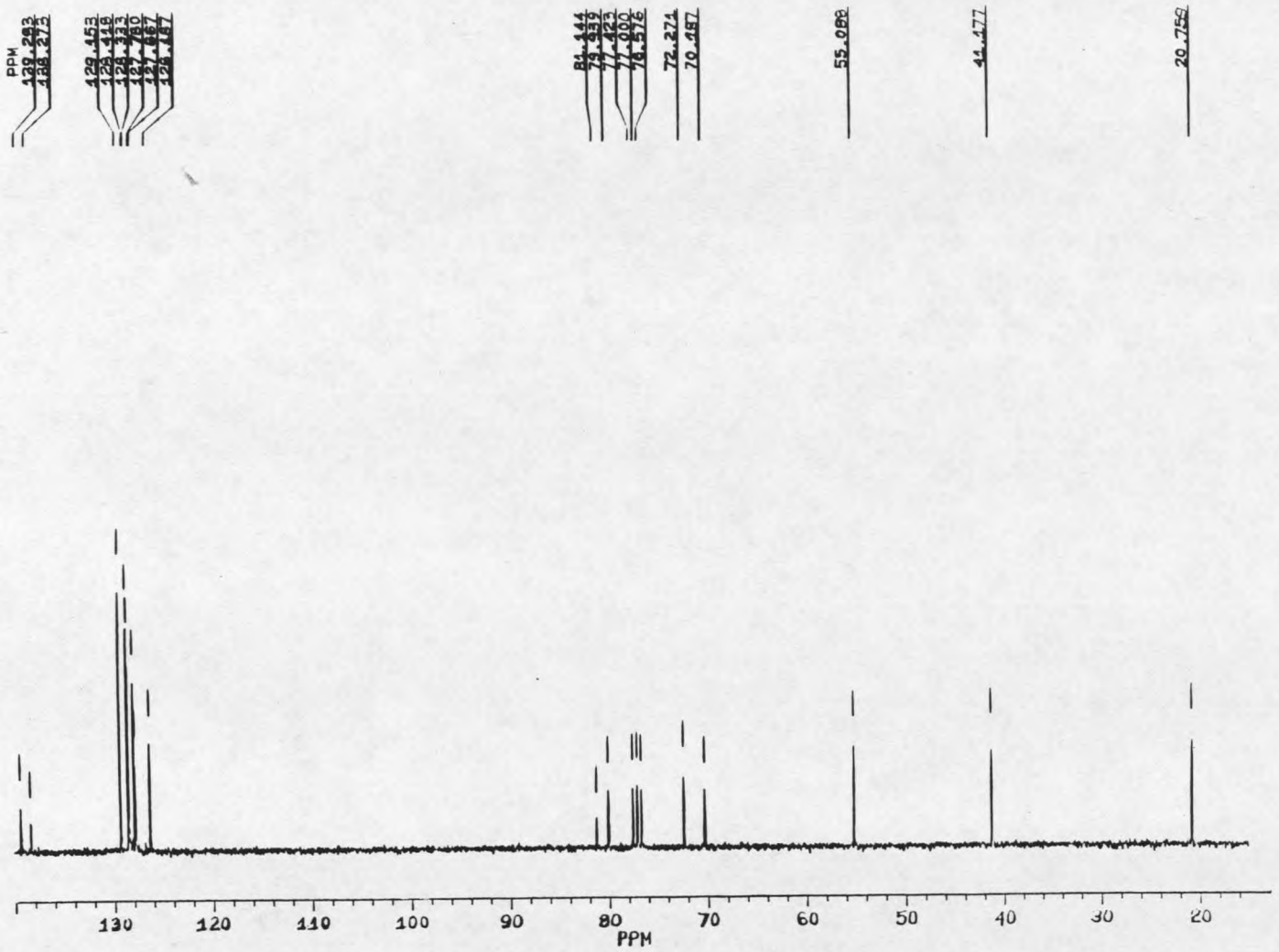


Figure 101. ^{13}C NMR Spectrum of (2S,3S)-3-benzyloxy-1-phenylhex-5-yn-2-ylamine(71).

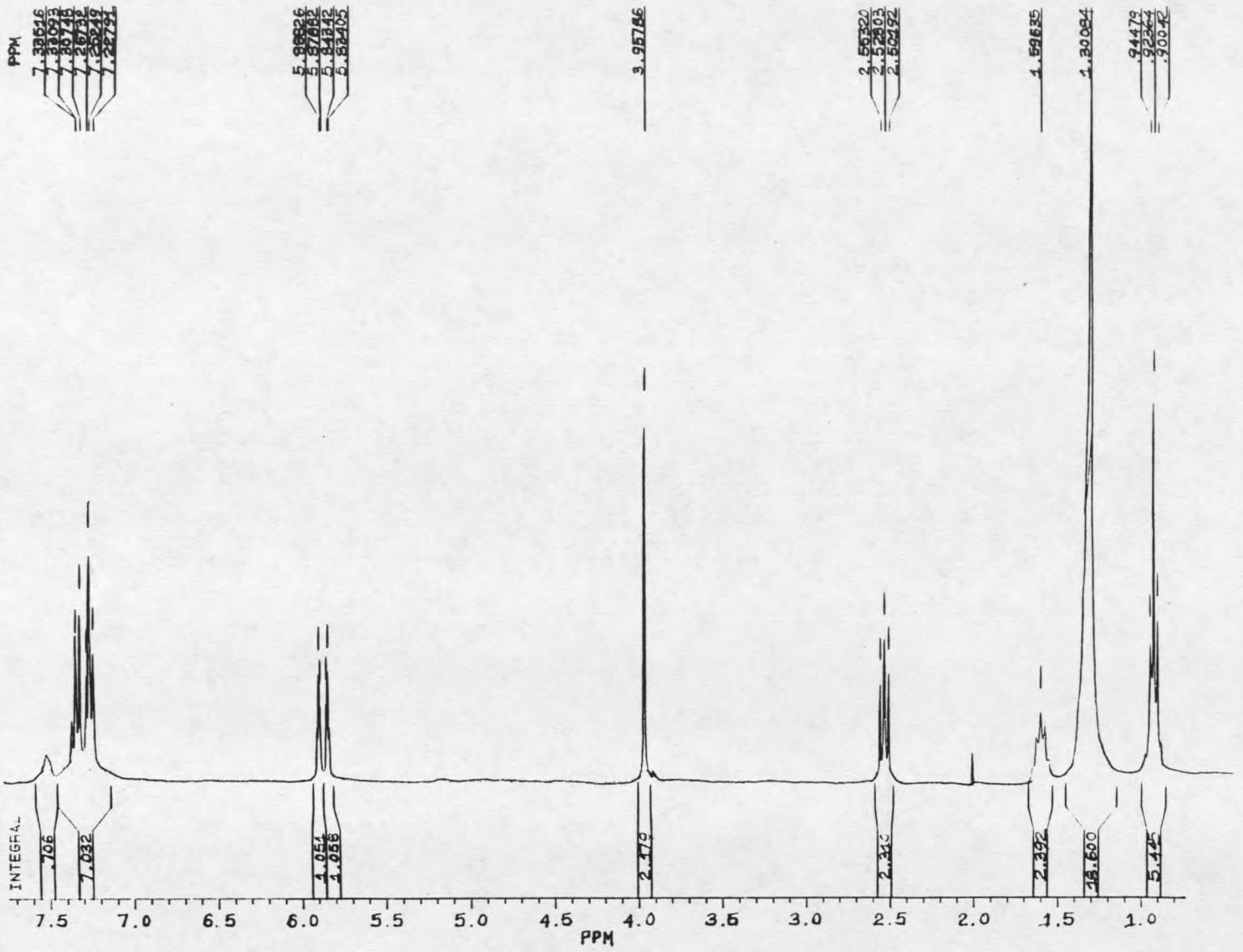


Figure 102. ^{1}H NMR Spectrum of 5-Nonyl-2-(phenyl-methyl)pyrrole(68).

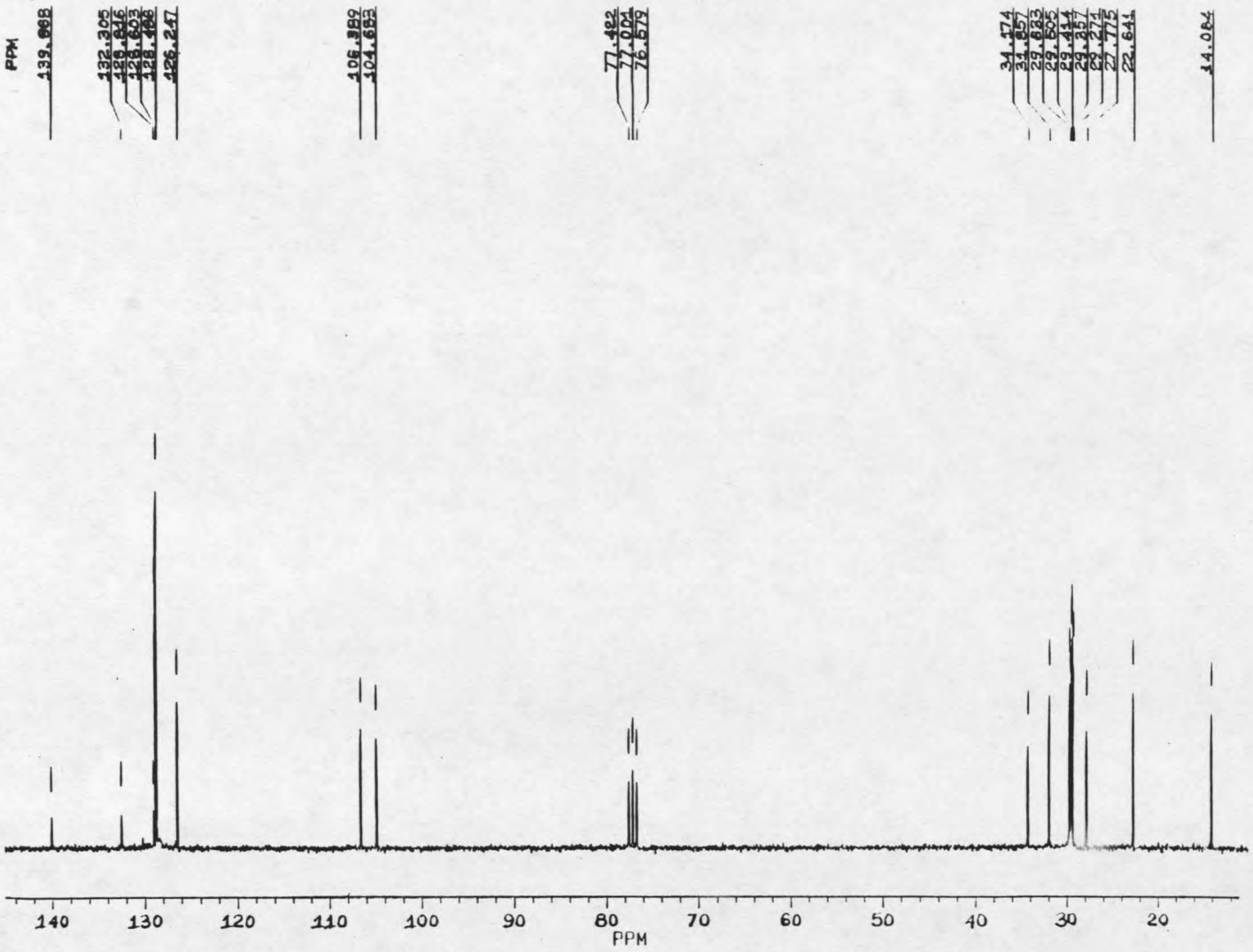


Figure 103. ^{13}C NMR Spectrum of 5-Nonyl-2-(phenyl-methyl)pyrrole(68).

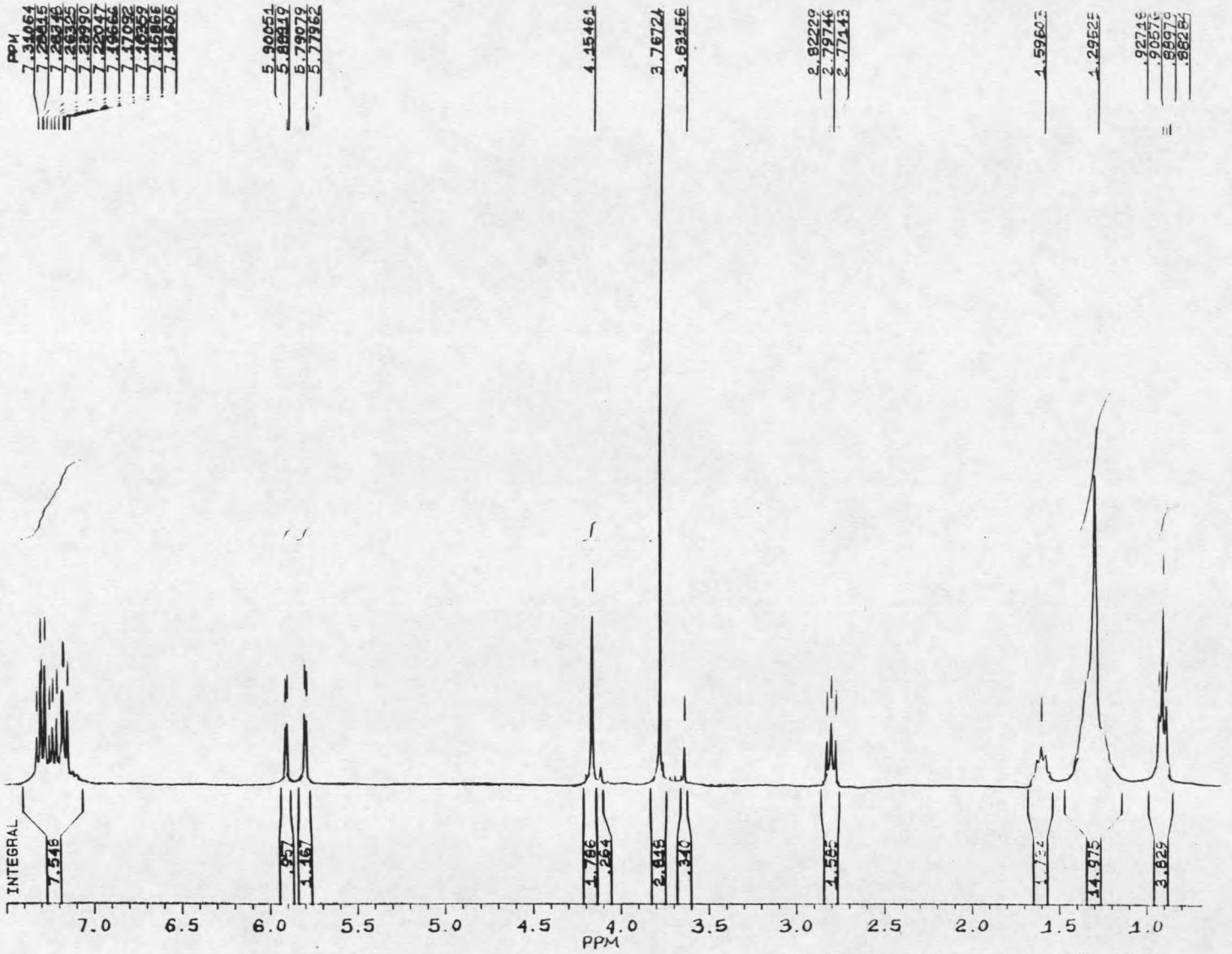


Figure 104. ^{1}H NMR Spectrum of N-Carbomethoxy-5-nonyl-2-(phenylmethyl)pyrrole(70).

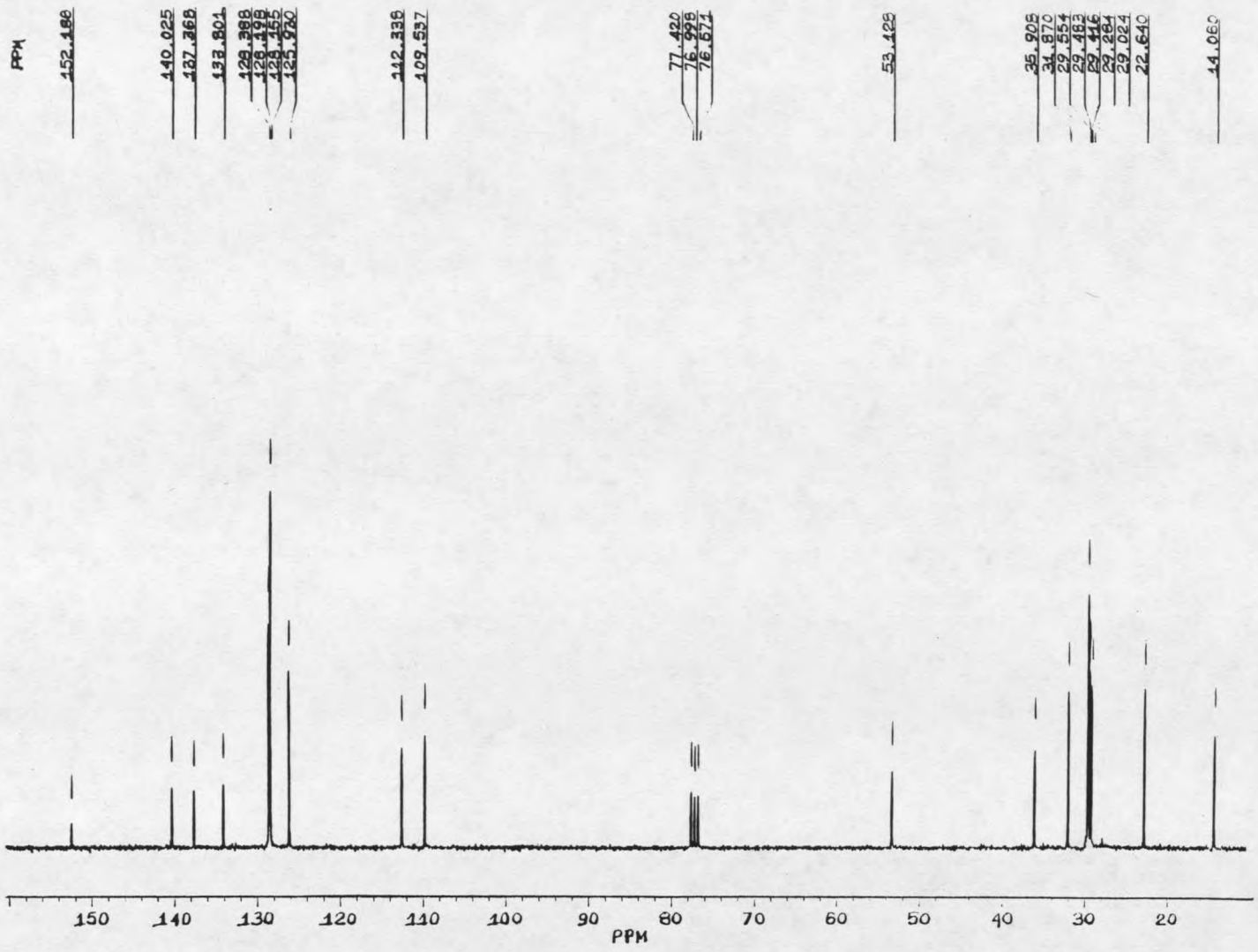


Figure 105. ^{13}C NMR Spectrum of N-Carbomethoxy-5-nonyl-2-(phenylmethyl)pyrrole(70).

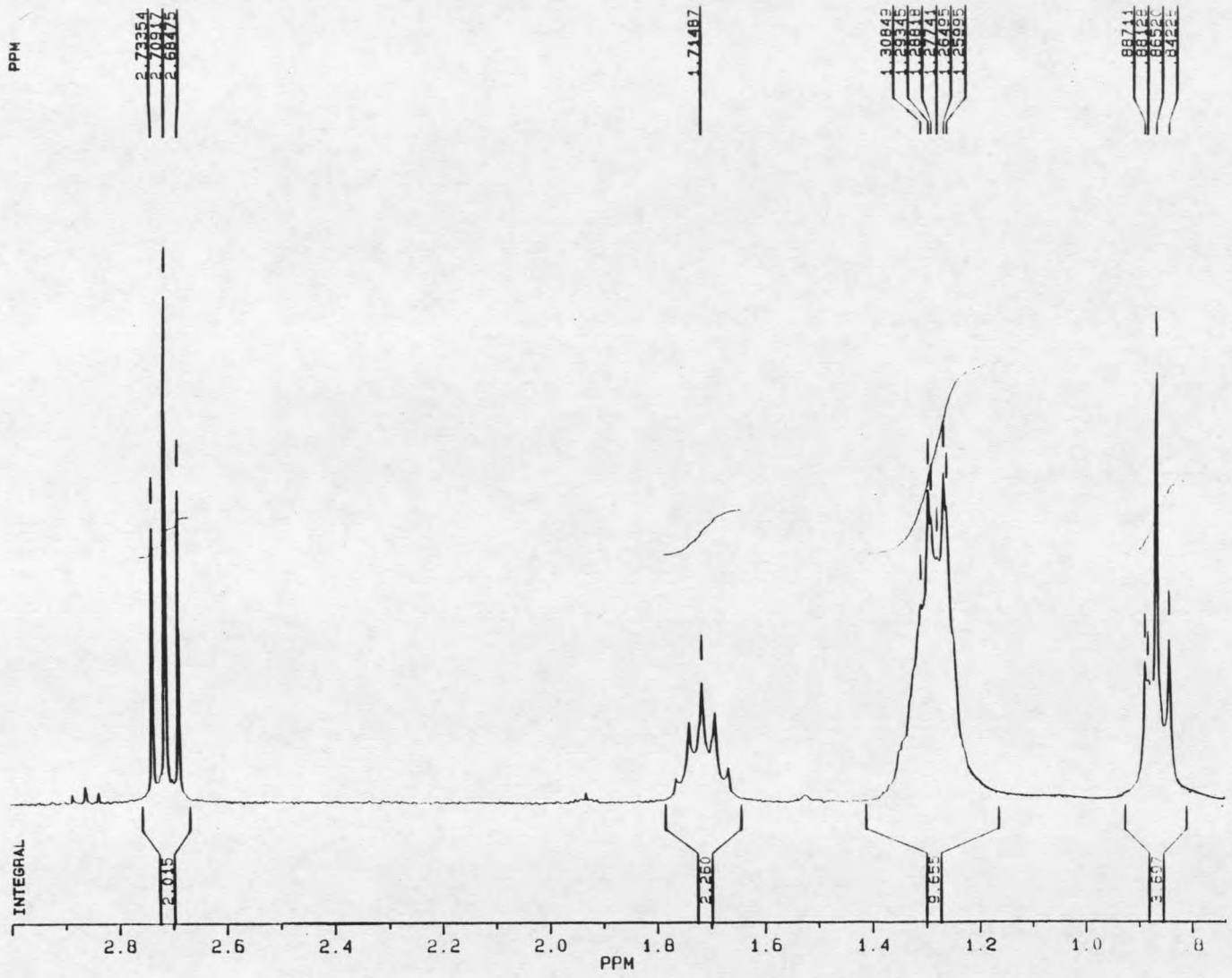


Figure 106. ^{1}H NMR Spectrum of Octanoyl Nitrile(74).

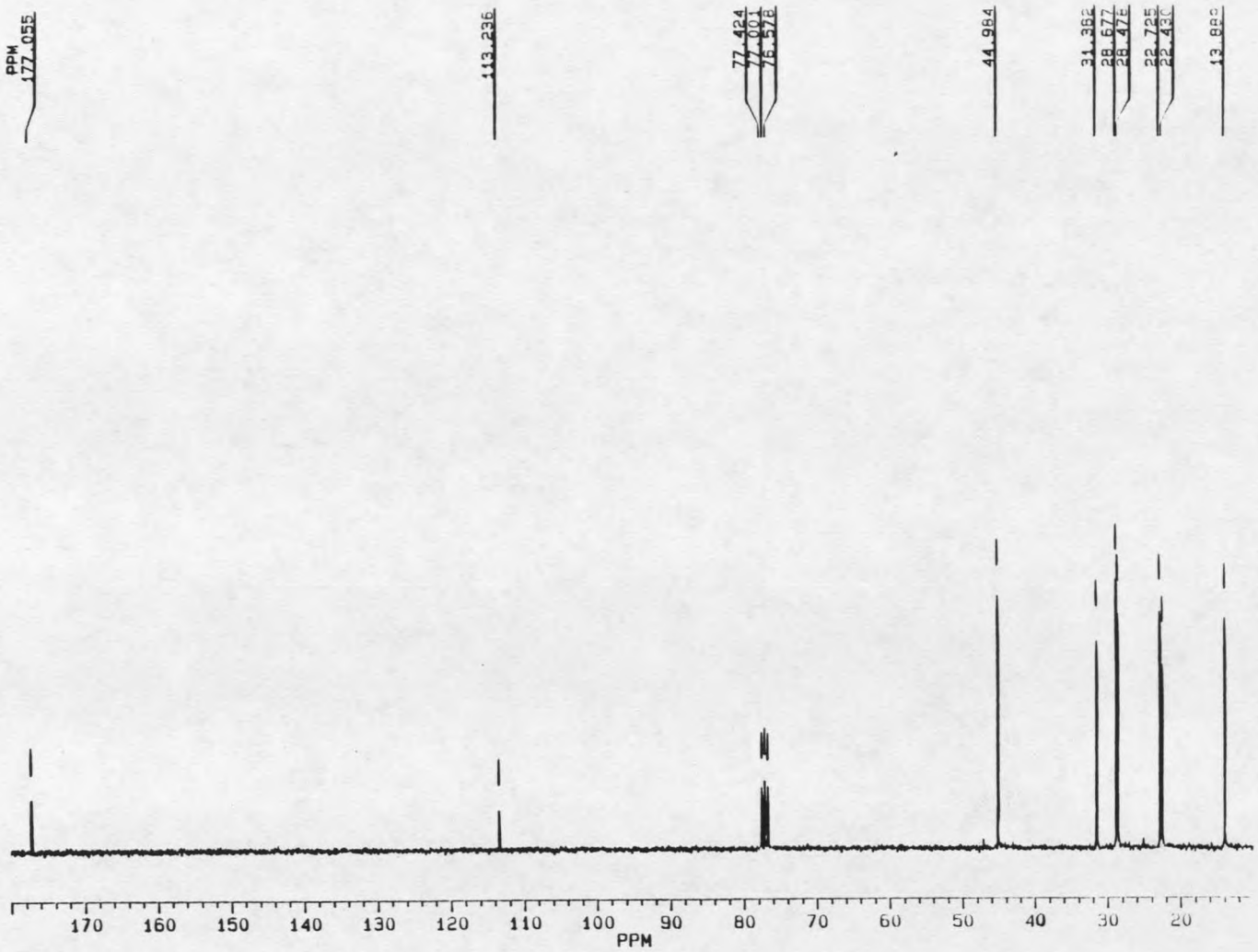


Figure 107. ^{13}C NMR Spectrum of Octanoyl Nitrile(74).

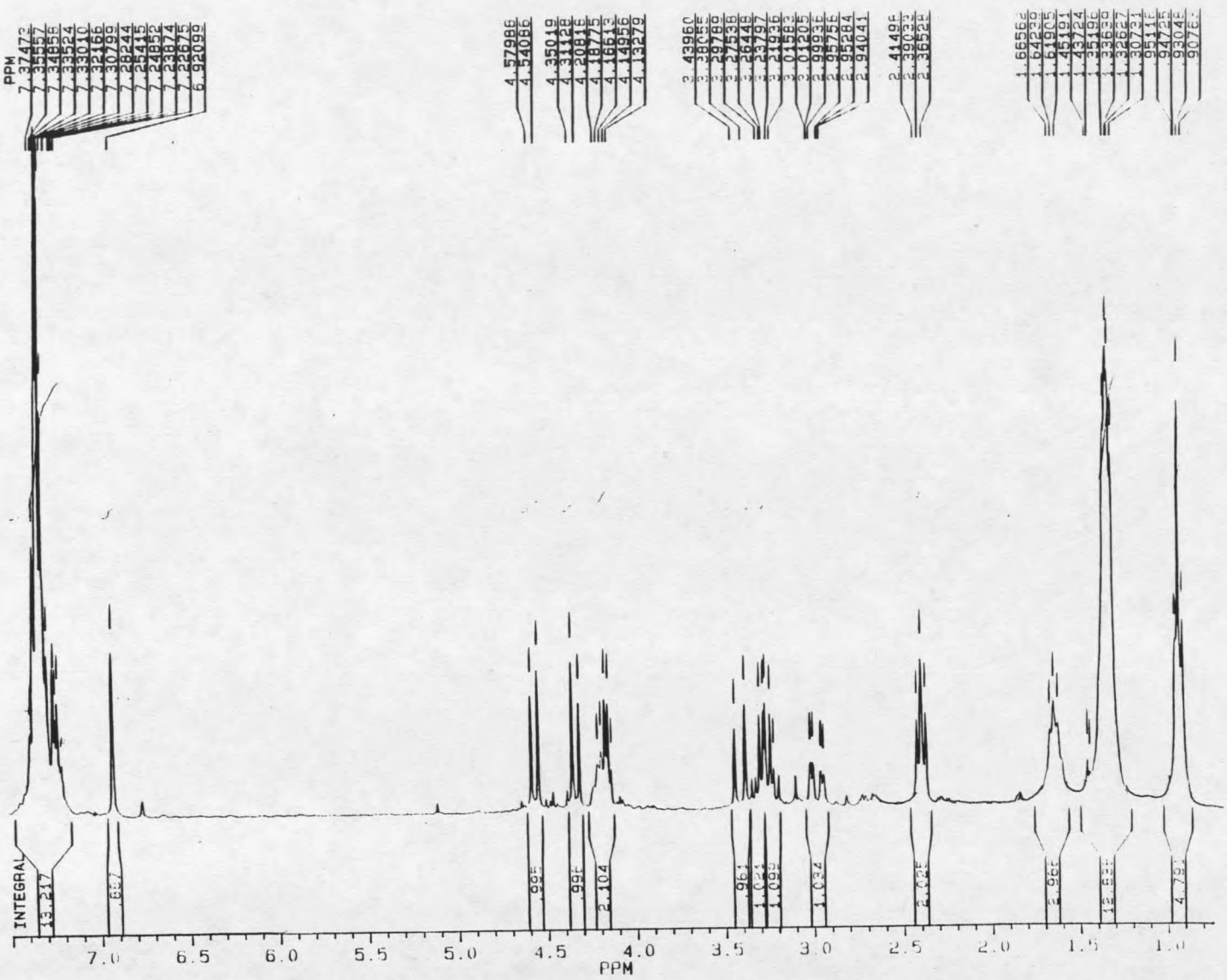


Figure 108. ^{1}H NMR Spectrum of (4S,5S)-4-benzyoxy-2-[2′-cyano-1′-nonen-1′-yl]-5-(phenyl-methyl)-2H-pyrrole(76).

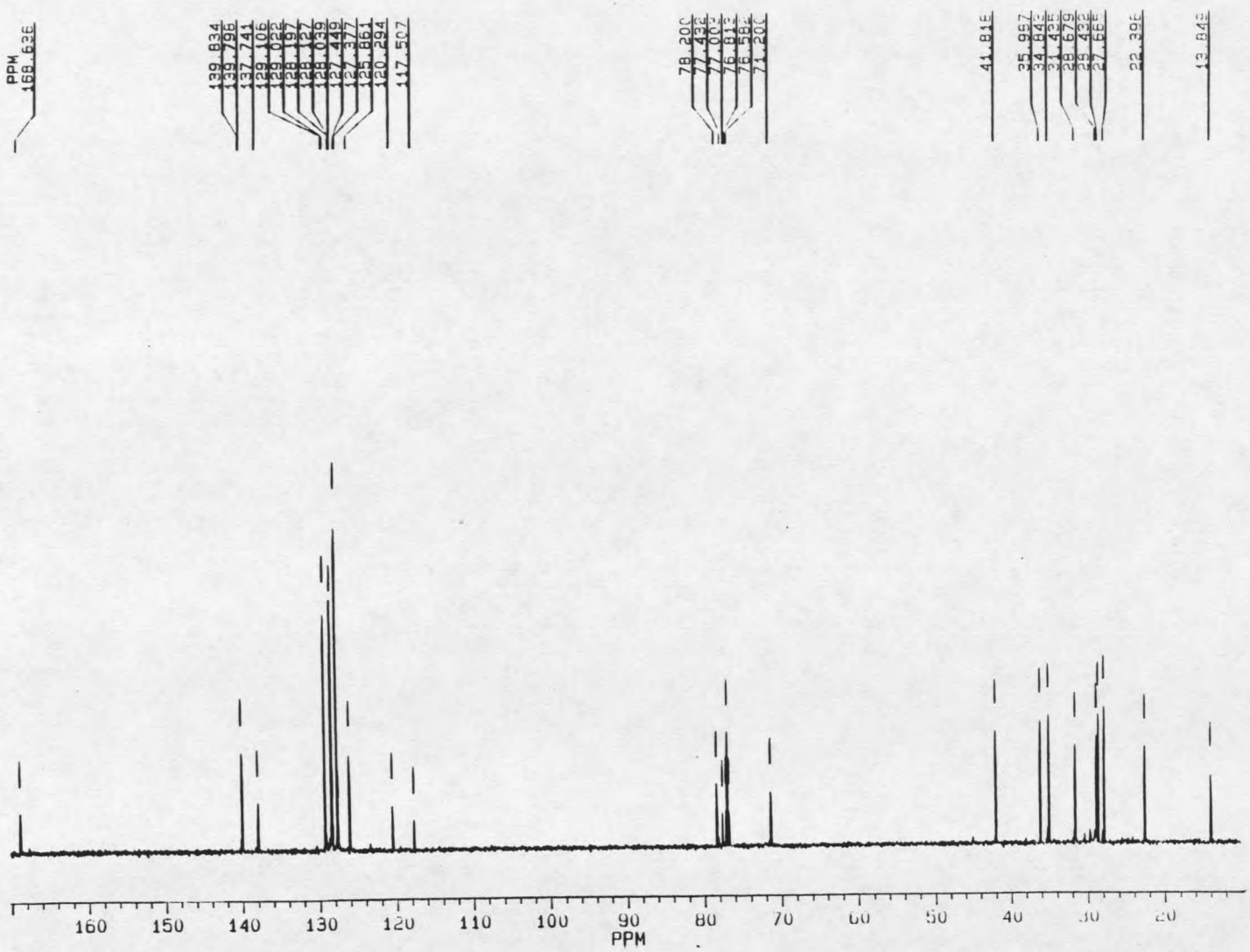


Figure 109. ^{13}C NMR Spectrum of (4S,5S)-4-benzyoxy-2-[2′-cyano-1′-nonen-1′-yl]-5-(phenyl-methyl)-2H-pyrrole(76).

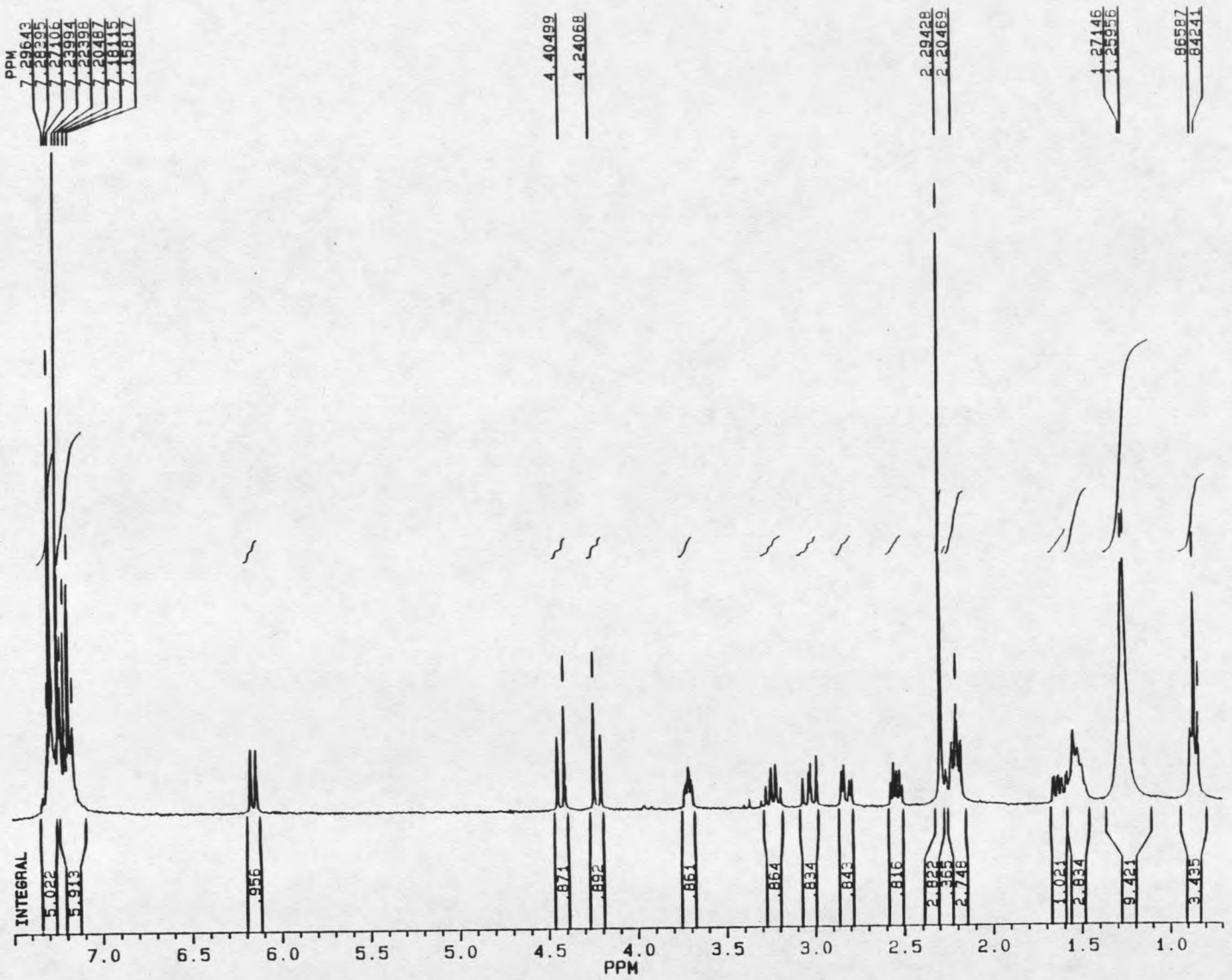


Figure 110. ^{1}H NMR Spectrum of (2S,3S,5R)-4-benzyloxy-2-[2′-cyano-1′-nonen-1′-yl]-1-methyl-5-(phenylmethyl)-pyrrolidine(77)

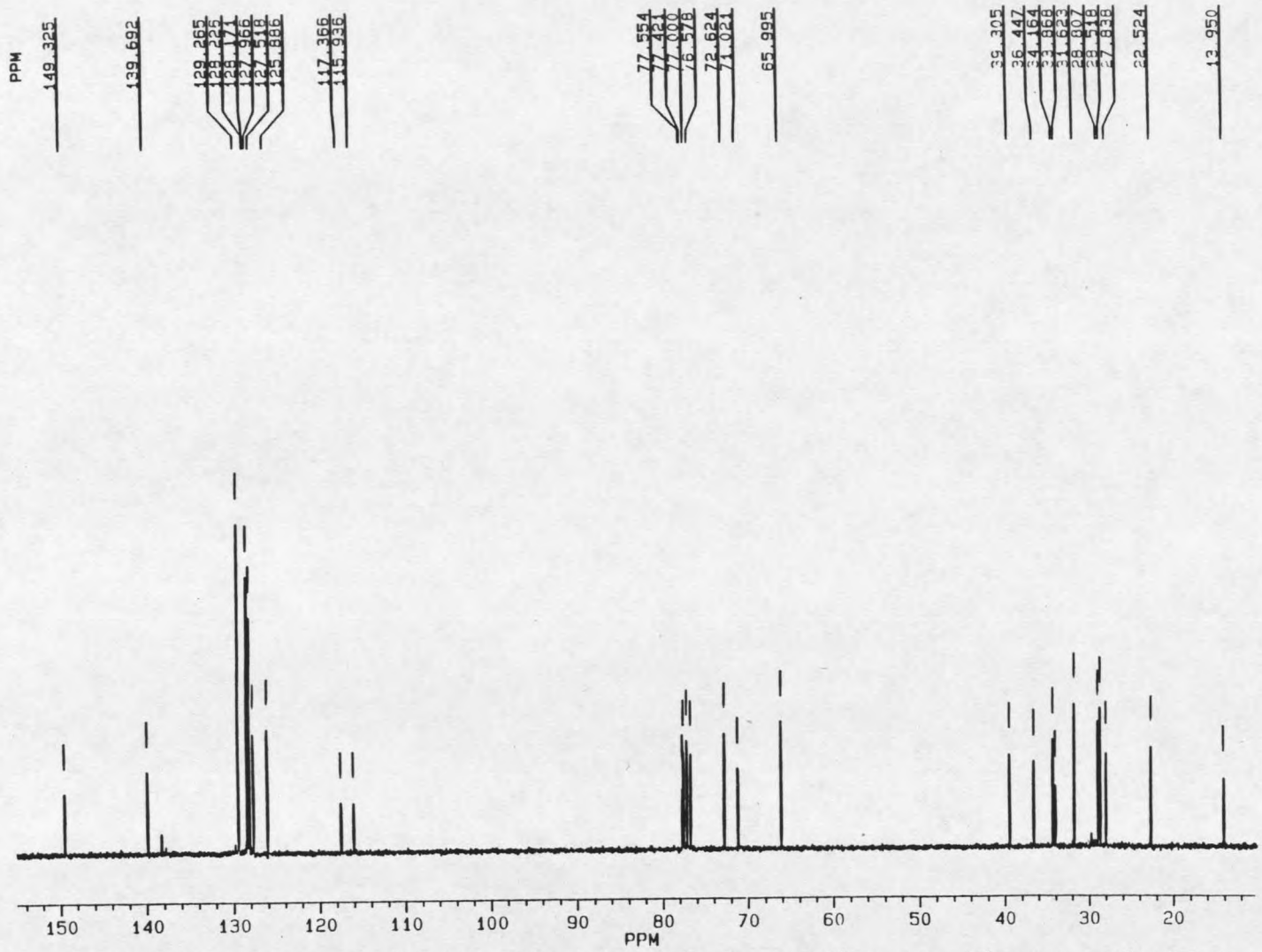


Figure 111. ^{13}C NMR Spectrum of (2S,3S,5R)-4-benzyloxy-2-[2′-cyano-1′-nonen-1′-yl]-1-methyl-5-(phenylmethyl)-pyrrolidine(77)

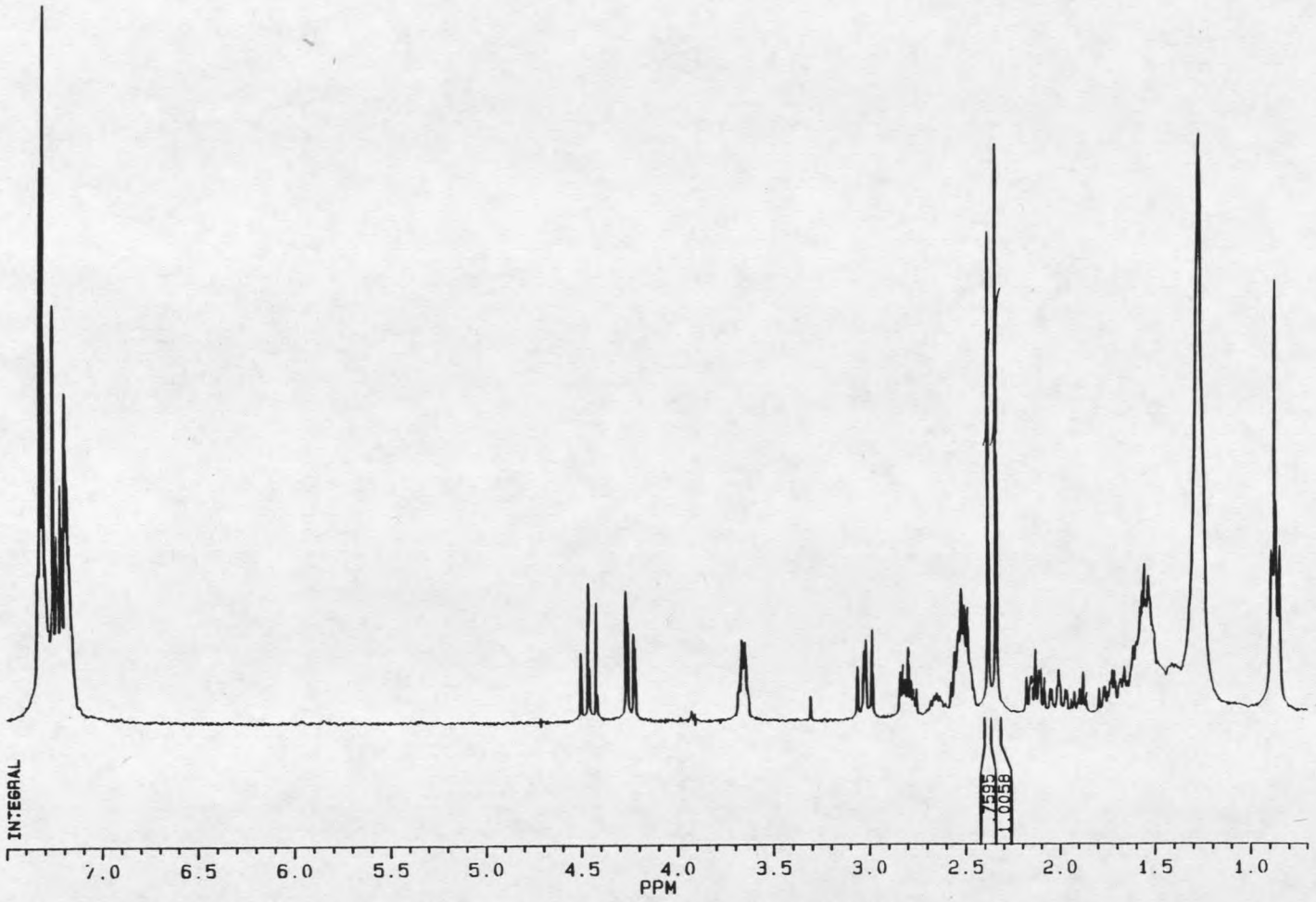


Figure 112. ^{1}H NMR Spectrum of Diastereomeric Nitriles(78)

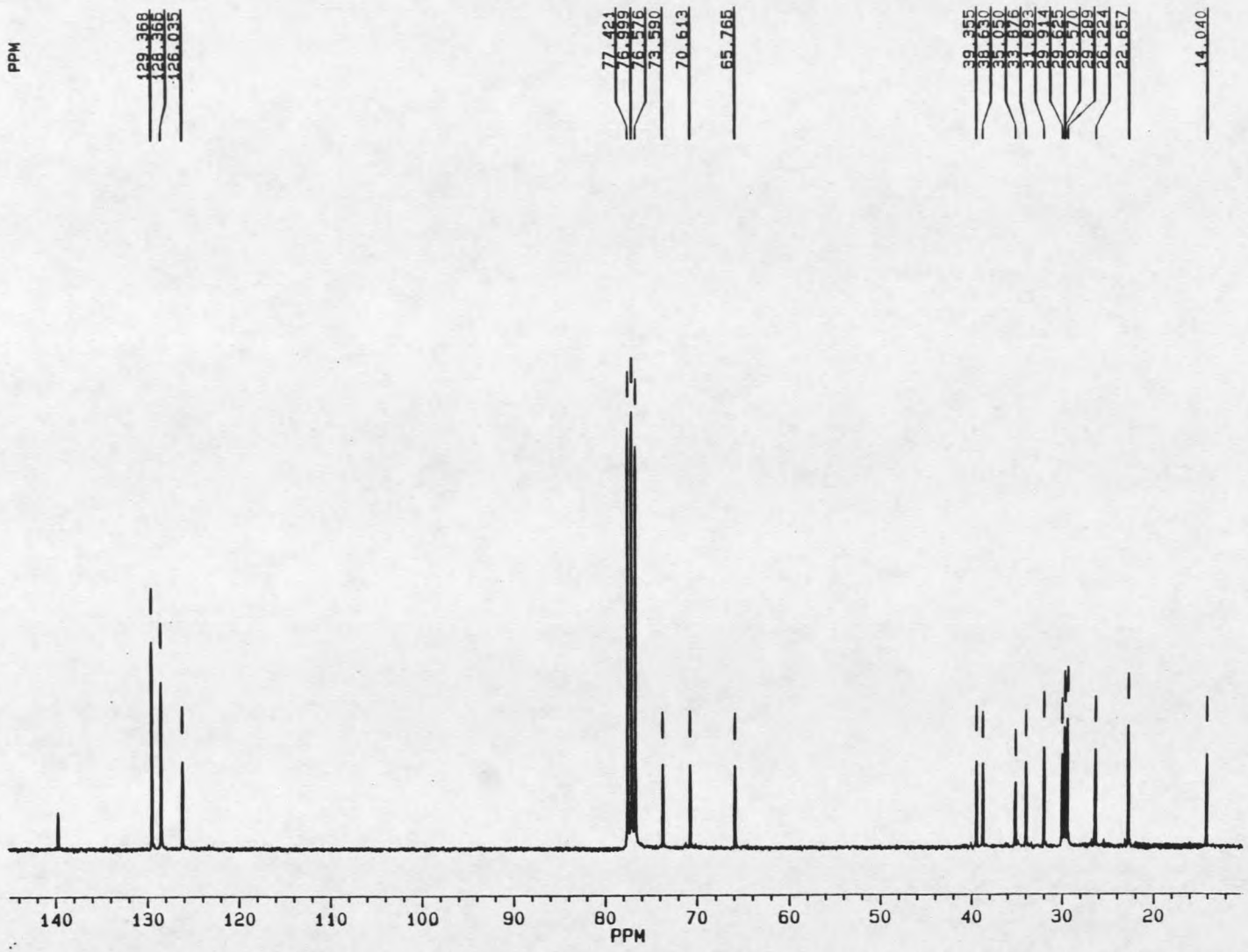


Figure 113. ^{13}C NMR Spectrum of (2S,3S,5R)-1-methyl-5-nonyl-2-(phenylmethyl)-3-pyrrolidinol(2)